# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**WASHINGTON, D.C. 20549**

# FORM 8-K

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

**Date of Report (Date of earliest event reported): January 8, 2024**

# WEREWOLF THERAPEUTICS, INC.
**(Exact name of registrant as specified in its charter)**

| **Delaware** | **001-40366** | **82-3523180** |
|---|---|---|
| **(State or Other Jurisdiction of Incorporation)** | **(Commission File Number)** | **(IRS Employer Identification No.)** |

| | |
|---|---|
| **200 Talcott Ave, 2nd Floor**<br>**Watertown, Massachusetts**<br>**(Address of Principal Executive Offices)** | **02472**<br>**(Zip Code)** |

**Registrant's telephone number, including area code: (617) 952-0555**

**(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, $0.0001 par value per share | HOWL | The Nasdaq Global Select Market |

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

Emerging growth company ☒

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

**Item 7.01. Regulation FD Disclosure**

On January 8, 2024, Werewolf Therapeutics, Inc. (the "Company") issued a press release to provide a business update and highlight the Company's 2024 strategy outlook. A copy of the press release is furnished as Exhibit 99.1 hereto and is incorporated herein by reference. Also on January 8, 2024, the Company made publicly available on its website an updated corporate presentation. A copy of the presentation is furnished as Exhibit 99.2 hereto and is incorporated herein by reference.

The information furnished under this Item 7.01, including Exhibits 99.1 and 99.2, 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 a filing.

**Item 9.01. Financial Statements and Exhibits.**

(d) Exhibits

| Exhibit No. | Description |
|---|---|
| 99.1 | Press Release, dated January 8, 2024 |
| 99.2 | Investor Presentation, dated January 2024 |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document) |

**SIGNATURES**

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

**WEREWOLF THERAPEUTICS, INC.**

Date: January 8, 2024

By: /s/ Timothy W. Trost
Timothy W. Trost
Chief Financial Officer and Treasurer

**Exhibit 99.1**

**Werewolf Therapeutics Provides Business Update and Highlights 2024 Strategic Outlook**

*- Prioritizing development of wholly owned clinical assets, WTX-124 and WTX-330; key updates from both INDUKINE™ programs anticipated in 2024 -*

*- WTX-124: updated interim monotherapy dose-escalation data and initial combination dose escalation data from Phase 1/1b clinical trial expected in 1H 2024 -*

*- WTX-330: preliminary dose-escalation data from Phase 1 clinical trial expected in 2Q 2024 -*

*- Updated cash guidance provides runway through at least the first quarter of 2025 -*

**Watertown, Mass., January 8, 2024** – Werewolf Therapeutics, Inc. (the "Company" or "Werewolf") (Nasdaq: HOWL), an innovative biopharmaceutical company pioneering the development of conditionally activated therapeutics engineered to stimulate the body's immune system for the treatment of cancer, today provided a business update and outlined its strategic outlook and expected milestones for 2024.

Werewolf outlined the following objectives as the Company's strategic priorities for 2024:

1. **Prioritize development of wholly owned clinical-stage programs –** present data updates from WTX-124 and WTX-330 while advancing their clinical development.
2. **Progress preclinical programs through IND-enabling work –** demonstrate the breadth of Werewolf's platform and portfolio opportunities.
3. **Apply PREDATOR™ platform for non-core opportunities and external innovation –** leverage Werewolf's validated technical capabilities, preclinical programs and opportunities in inflammatory diseases.
4. **Maintain disciplined spend –** prudently allocate resources according to these priorities to optimize cash runway with continued focus on clinical development of lead programs.

"2023 was an important year for Werewolf, highlighted by preliminary monotherapy data from our IL-2 program that offered proof of concept for WTX-124 and for our INDUKINE design more broadly," said Daniel J. Hicklin, Ph.D., President and Chief Executive Officer of Werewolf. "In 2024, we expect to share progress from our wholly owned clinical programs, with updated monotherapy data and initial combination data from WTX-124 as well as our first look at WTX-330. In particular, for WTX-124, we hope to build upon the promising signals of antitumor activity and improved therapeutic index that we observed in the highest dose cohort presented at SITC."

Dr. Hicklin continued, "In parallel, we expect to continue to progress our preclinical candidates through IND-enabling work to provide additional validation of the INDUKINE approach for novel targets, namely IL-21 and IL-18. Alongside this prioritization, we intend to seek partners who understand our unique conditional-activation expertise and protein engineering approach in areas beyond Werewolf's core focus of oncology, such as inflammatory diseases, where we believe our approach is viable."

Based on these strategic priorities, Werewolf has provided the following guidance for 2024:

**WTX-124:** *a systemically delivered, conditionally activated Interleukin-2 (IL-2) INDUKINE molecule being developed as monotherapy or in combination with checkpoint inhibitors in multiple solid tumor types.*

In November 2023, Werewolf presented first-in-human monotherapy data from the Phase 1/1b clinical trial of WTX-124 at the Society for Immunotherapy of Cancer's (SITC) 38th annual meeting. The preliminary data established proof of concept for WTX-124 and for Werewolf's INDUKINE design hypothesis. In the first half of 2024, Werewolf plans to:

- Report updated interim data from the monotherapy dose-escalation arm of the Phase 1/1b study;
- Select a recommended dose for expansion (RDE) and initiate monotherapy dose expansion arms; and
- Report initial data from the combination dose escalation cohorts of the Phase 1/1b study.

**WTX-330:** *a systemically delivered, conditionally activated Interleukin-12 (IL-12) INDUKINE molecule being developed in refractory and/or immunologically unresponsive tumors.*

Werewolf continues to progress the Phase 1 clinical trial evaluating WTX-330 as a monotherapy in patients with immunotherapy insensitive or resistant advanced or metastatic solid tumors or non-Hodgkin lymphoma. In 2024, Werewolf plans to report initial data from the Phase 1 clinical trial in the second quarter of 2024.

**Preclinical Portfolio:** *includes development candidates WTX-712 and WTX-518, INDUKINE molecules respectively targeting IL-21 and IL-18 for treatment of cancer, as well as numerous leads in discovery.*

Werewolf intends to progress these programs through IND-enabling work. In 2024, Werewolf plans to:

- Present preclinical data from WTX-712 in the first half of 2024.
- Present preclinical data from WTX-518 in the first half of 2024.
- Present preclinical data demonstrating the potential of INDUKINE molecules for inflammatory diseases by the fourth quarter of 2024.

**Cash Position and Financial Guidance:**

Based on updated forecasting reflecting the Company's streamlined development plans and careful cash management to date, Werewolf now expects that its cash and equivalents will be sufficient to fund its operational expenses and capital expenditure requirements through at least the first quarter of 2025.

**About Werewolf Therapeutics:**

Werewolf Therapeutics, Inc. is an innovative clinical-stage biopharmaceutical company pioneering the development of therapeutics engineered to stimulate the body's immune system for the treatment of cancer. We are leveraging our proprietary PREDATOR™ platform to design conditionally activated molecules that stimulate both adaptive and innate immunity with the goal of addressing the limitations of conventional proinflammatory immune therapies. Our INDUKINE™ molecules are intended to remain inactive in peripheral tissue yet activate selectively in the tumor microenvironment. Our most advanced product candidates, WTX-124 and WTX-330, are systemically delivered, conditionally activated Interleukin-2 (IL-2), and Interleukin-12 (IL-12) INDUKINE molecules for the treatment of solid tumors. WTX-124 is in development as a monotherapy and in combination with KEYTRUDA® (pembrolizumab) in multiple solid tumor types. WTX-330 is in development as a single agent in refractory and/or immunotherapy unresponsive or resistant advanced or metastatic solid tumors and non-Hodgkin lymphoma. To learn more visit www.werewolftx.com.

**Cautionary Note Regarding Forward-Looking Statements**

This press release contains forward-looking statements that involve substantial risk and uncertainties. All statements, other than statements of historical facts, contained in this press release, including statements regarding Werewolf's strategy, future operations, prospects, plans, and objectives of management; the projection of the cash runway; the expected timeline for the preclinical and clinical development of product candidates and the availability of data from such preclinical and clinical development; the potential activity and efficacy of product candidates in preclinical studies and clinical trials; and the anticipated safety profile of product candidates; constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. The words "aim," "anticipate," "approach," "believe," "contemplate," "continue," "could," "design," "designed to," "engineered," "estimate," "expect," "goal," "intend," "may," "might," "objective," "ongoing," "plan," "potential," "predict," "project," "promise," "should," "target," "will," or "would," or the negative of these terms, or other comparable terminology are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The Company may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various important factors, including: uncertainties inherent in the development of product candidates, including the conduct of research activities and the initiation and completion of preclinical studies and clinical trials; uncertainties as to the availability and timing of results from preclinical studies and clinical trials; the timing of and the Company's ability to submit and obtain regulatory approval for investigational new drug applications; whether results from preclinical studies will be predictive of the results of later preclinical studies and clinical trials; whether preliminary data from a clinical trial will be predictive of the results of the trial and future clinical trials; the Company's ability to manage cash resources and obtain additional cash resources to fund the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements; as well as the risks and uncertainties identified in the "Risk Factors" section of the Company's most recent Form 10-Q filed with the Securities and Exchange Commission ("SEC"), and in subsequent filings the Company may make with the SEC. In addition, the forward-looking statements included in this press release represent the Company's views as of the date of this press release. The Company anticipates that subsequent events and developments will cause its views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this press release.

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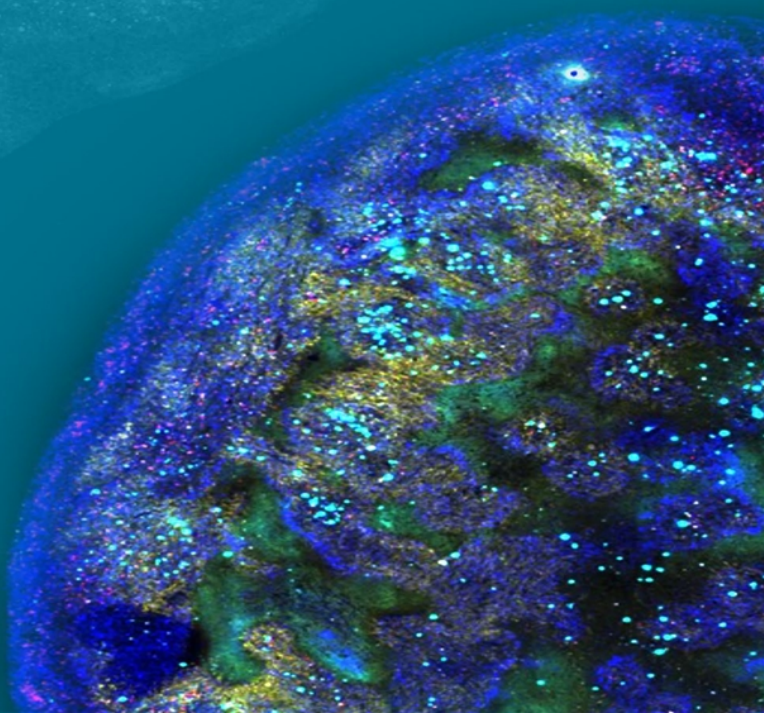
Exhibit 99.2

Werewolf THERAPEUTICS

# Shifting the Balance in Cytokine Therapeutics



Corporate Overview | January 2024

# Cautionary Statements

This presentation contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this presentation, including statements regarding Werewolf Therapeutics, Inc.'s (the "Company") strategy, future operations, prospects, plans, objectives of management, the projection of the cash runway, the expected timeline for the preclinical and clinical development of product candidates and the availability of data from such preclinical and clinical development, the potential activity and efficacy of product candidates in future preclinical studies and clinical trials, and the anticipated safety profile of product candidates, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. The words "aim," "anticipate," "approach," "believe," "contemplate," "continue," "could," "design," "designed to," "engineered," "estimate," "expect," "goal," "intend," "may," "might," "objective," "ongoing," "plan," "potential," "predict," "project," "promise," "should," "target," "will," or "would," or the negative of these terms, or other comparable terminology are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. The Company may not actually achieve the plans, intentions or expectations disclosed in these forward-looking statements, and you should not place undue reliance on these forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in these forward-looking statements as a result of various important factors, including: uncertainties inherent in the development of product candidates, including the conduct of research activities, the initiation and completion of preclinical studies and clinical trials; uncertainties as to the availability and timing of results from preclinical studies and clinical trials; the timing of and the Company's ability to submit and obtain regulatory approval for investigational new drug applications; whether results from preclinical studies will be predictive of the results of later preclinical studies and clinical trials; whether preliminary data from a clinical trial will be predictive of the results of the trial and future clinical trials; the Company's ability to manage cash resources and obtain additional cash resources to fund the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements, as well as the risks and uncertainties identified in the "Risk Factors" section of the Company's most recent Form 10-Q filed with the Securities and Exchange Commission ("SEC") and in subsequent filings the Company may make with the SEC. In addition, the forward-looking statements included in this presentation represent the Company's views as of the date of this presentation. The Company anticipates that subsequent events and developments will cause its views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this presentation.

## Who we are

# Our mission is to unlock the promise of cytokines as more effective immunotherapies

We are a clinical-stage biopharmaceutical company developing next generation, conditionally activated cytokine therapies for the treatment of cancer and other serious diseases

We have two investigational drugs in Phase 1 clinical trials

Our headquarters and research facilities are located in Watertown, Massachusetts

# Clinical-Stage Company with Compelling Portfolio of Innovative Cytokine Therapeutics

*Designed on a platform capable of addressing broad therapeutic applications in oncology and beyond*

## Clinical Programs

**WTX-124**
Ongoing enrollment in the dose escalation stage of a Phase 1/1b study as a monotherapy and in combination with pembrolizumab

**WTX-330**
Ongoing enrollment in the dose escalation stage of a Phase 1 study as a monotherapy

## Key Catalysts

**WTX-124**
Initial clinical data demonstrated WTX-124 monotherapy clinical activity and PoC for INDUKINE™ design

Anticipating additional monotherapy dose escalation data to inform RDE and opening of expansion arms in 1H24

## Robust Pipeline

**JZP898**
IFNα INDUKINE licensed to Jazz Pharmaceuticals; Enrolling in Phase 1 trial

**WTX-712**
IL-21 INDUKINE development candidate

**WTX-518**
IL-18 INDUKINE development candidate

## Scalable Platform

**PREDATOR™ Platform**
Capability for pipeline expansion for a broad range of mechanisms and indications

**Business Development**
Broad portfolio of clinical and preclinical stage assets available for partnering

## Financial Stability

Cash and cash equivalents of $130.1M (*as of 9/30/2023*) provides runway through at least 1Q 2025



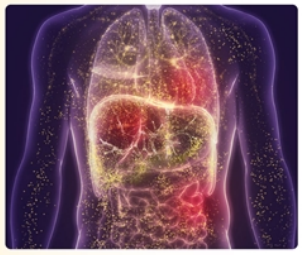


Werewolf THERAPEUTICS

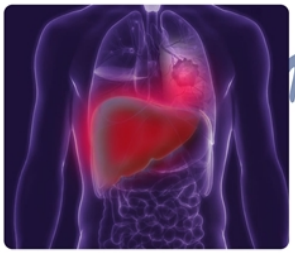
# Overcoming Off-Target Toxicity has been a Key Challenge for Cytokine Therapy

## The Challenge:
## Off-Tumor Cytokine Toxicity Limits Therapeutic Index

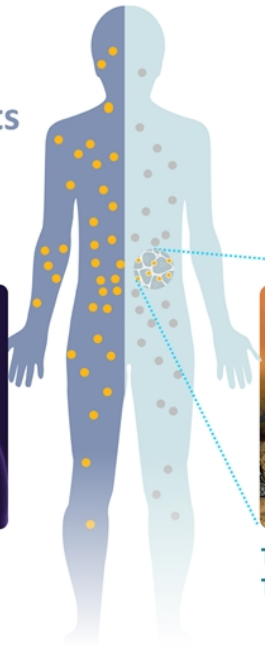
### Suboptimal Pharmaceutical Properties



Toxicity

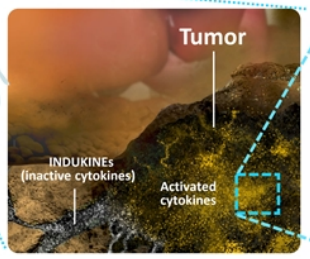


Poor Clinical Outcomes



## Our Solution:
## Conditionally Activated Immunotherapy

### With Optimized Therapeutic Index




Targeted Delivery to the Tumor Microenvironment


On-Target Immune Activation



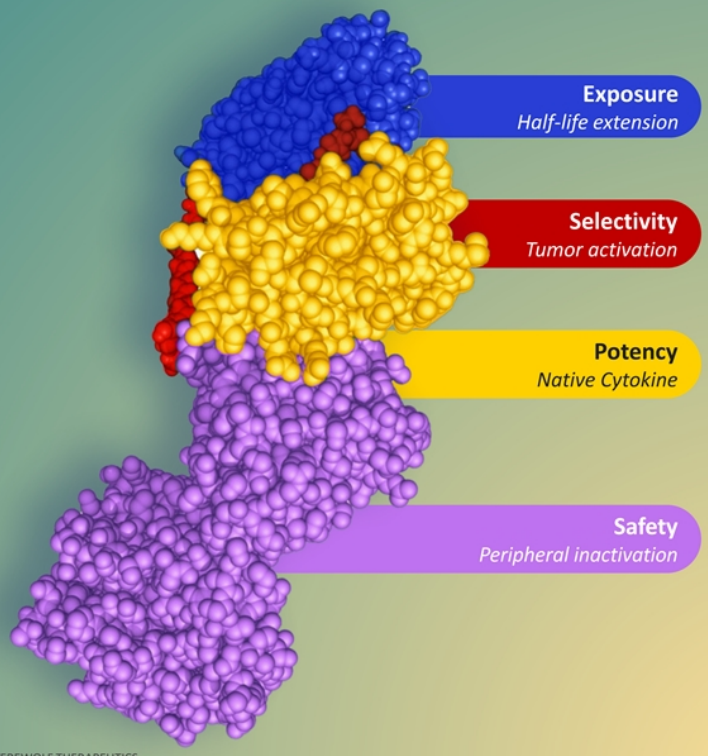


Werewolf THERAPEUTICS

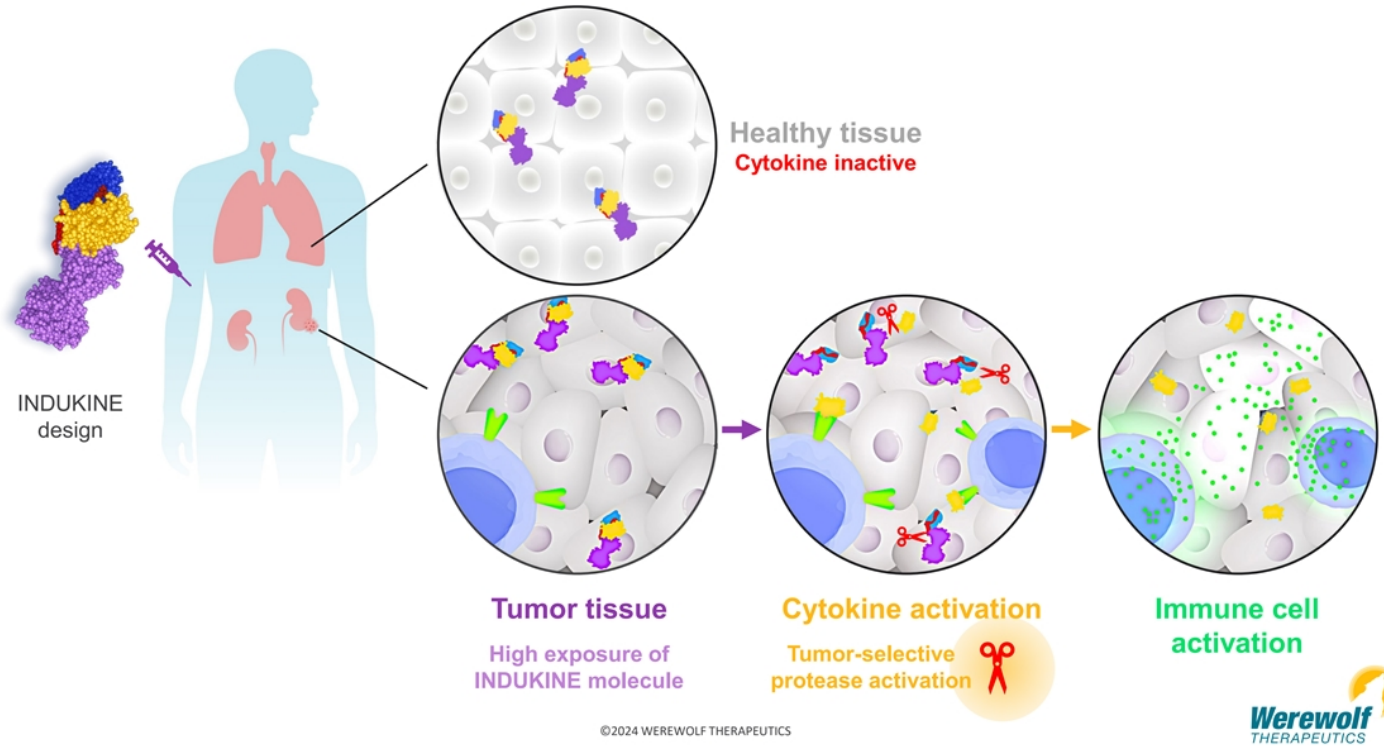
**PREDATOR**
Platform

# Tunable, Tissue-targeted Therapeutics for Cancer and other Diseases

INDUKINE molecules contain multiple domains, each with a unique function that can be 'tuned' for specific mechanisms and pharmaceutical properties necessary to treat disease

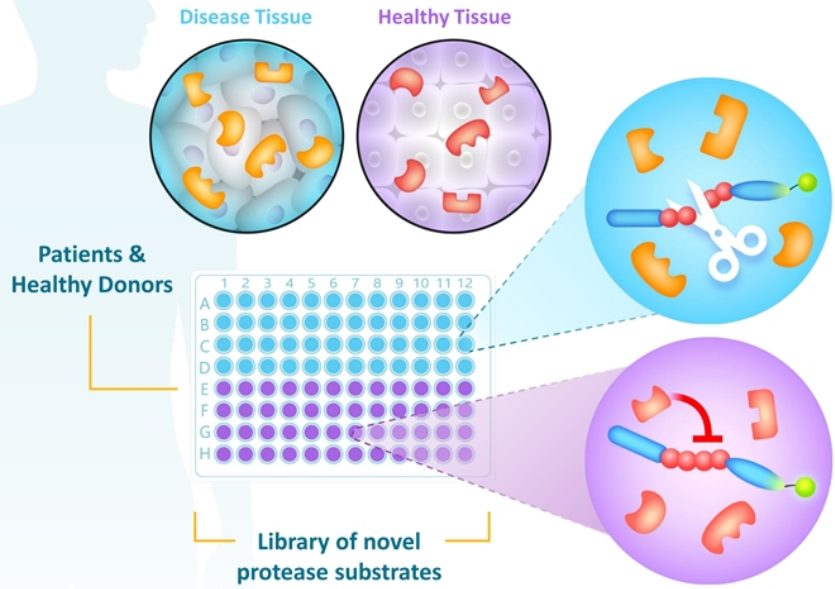


# INDUKINE Molecules: Targeting Cytokine Activity to Diseased Tissue



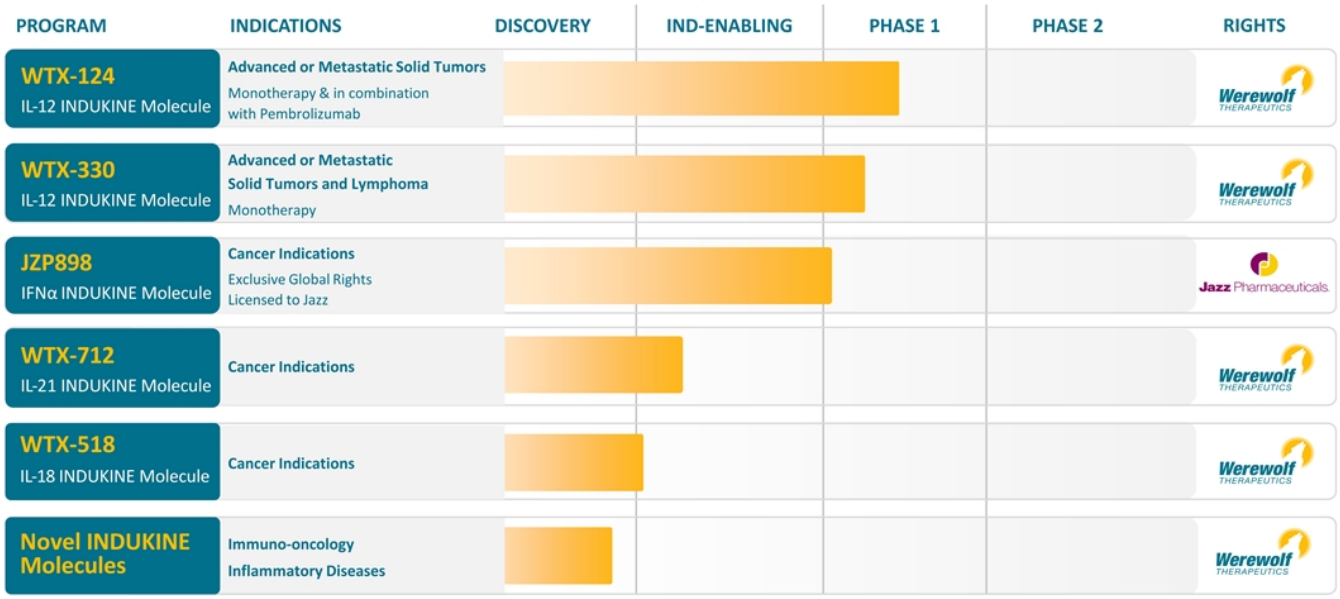
# PREDATOR Platform: Disease Selective Protease (DSP) Substrate Screen

*Innovative Linker Discovery Approach to Address Protease Heterogeneity Across Diseases and Patients*




- Highly diverse substrate library
- Unique protease specificities
- Innovative screening approach
- Substrates selected in the context of a globular protein
- Screens possible with a variety of diseased tissues

# A Balanced Portfolio of Clinical and Preclinical Drug Candidates



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# WTX-124: Expanding the Utility of IL-2 Therapy

*Delivering IL-2 to the Tumor Microenvironment with Improved Safety and Therapeutic Index*

## The Challenge

Deliver the benefits of IL-2 therapy with less toxicity to a broader range of patients

## Potential WTX-124 Advantages and Opportunity

- Delivery of IL-2 selectively to the TME to improve the therapeutic index
- Potential for activity beyond approved indications for rhIL2
- IL-2 therapy with an improved therapeutic index could address an immediate unmet medical need for patients who have progressed on checkpoint therapy
- Strong rationale for combination with checkpoint inhibitors in earlier lines of therapy

## Status

- Enrolling patients in Phase 1 clinical trial both as a single agent and in combination with Pembrolizumab
- Released preliminary clinical data at 2023 Society for Immunotherapy of Cancer Annual Meeting
- Additional monotherapy dose escalation data, RDE declaration and opening of expansion arms anticipated 1H 2024

Abbreviations: TME-tumor microenvironment; RDE-recommended dose for expansion





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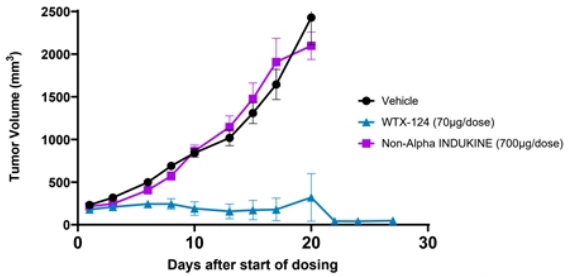
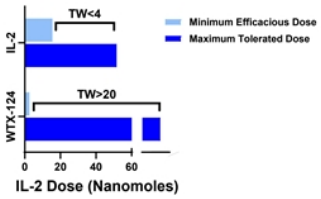
# WTX-124 has an Improved Therapeutic Index Compared to Native IL-2

*Full potency IL-2 is required for complete tumor regression in preclinical models; WTX-124 generates immune memory*

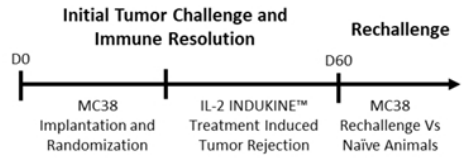
## WTX-124 antitumor activity is substantially more potent than non-alpha IL-2 INDUKINE in MC38 tumor model

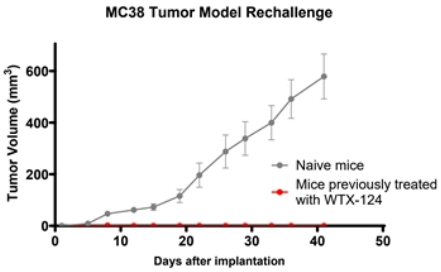


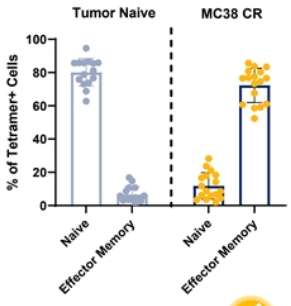

## Improved therapeutic window compared to IL-2 cytokine




## WTX-124 activates long-term antitumor immune memory




Nirschl CJ et al., SITC 2023 Poster: Optimal Antitumor Immunity is Triggered by WTX-124, a Clinical Stage Conditionally Activated INDUKINE™ Molecule

Abbreviations: TW-therapeutic window; CR-complete regression





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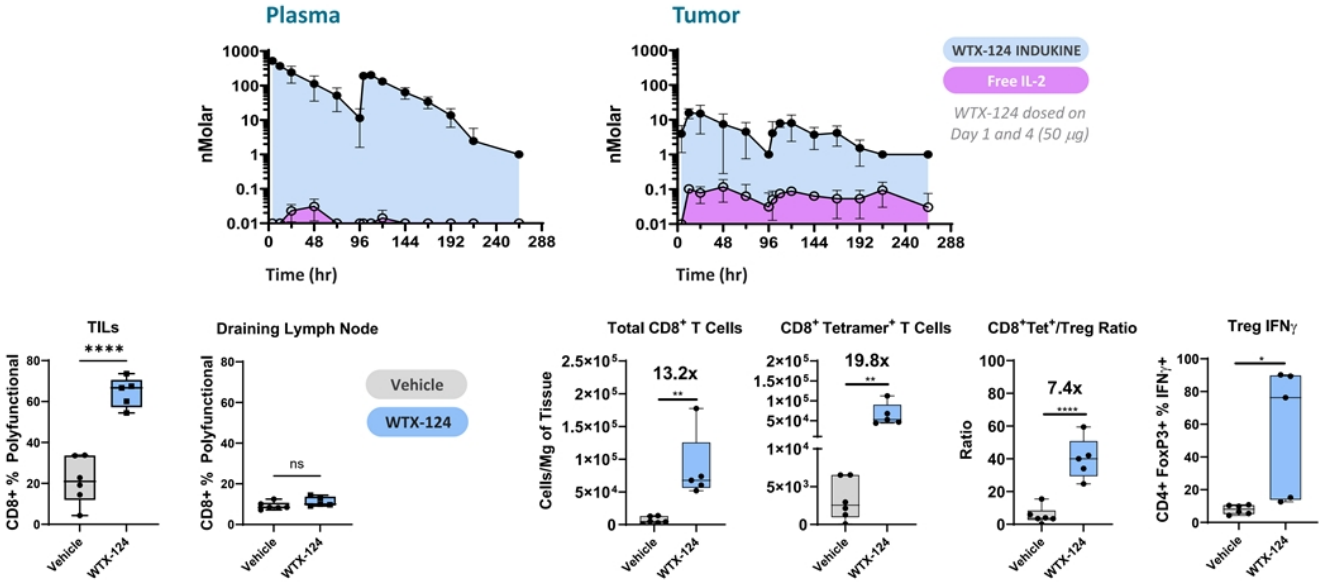
# WTX-124 Delivers IL-2 Selectively to Tumor Tissue in Preclinical Models

*Robust expansion and activation of antitumor CD8+ T effector cells in the TME*




Nirschl CJ et al., Cancer Immunology Research 2022 10(5):581-596

Abbreviations: TIL-tumor infiltrating lymphocytes; TME-tumor microenvironment

# First-In-Human Study of WTX-124 Monotherapy and in Combination with Pembrolizumab

Patients with IO sensitive tumor types who have exhausted all SOC options or for whom SOC is not indicated

## Monotherapy Dose Escalation

1 mg n = 5 | 3 mg n = 5 | 6mg n = 5 | 12 mg n = 5 | 18 mg *enrolling* | TBD

Determination of monotherapy MTD/RDE

## Combination Dose Escalation

WTX-124 in Combination with Pembrolizumab (*enrollment ongoing*)

Determination of *combination therapy* MTD/RDE

## Monotherapy/Combination Dose Expansion

- Advanced or metastatic renal cell carcinoma
- Advanced or metastatic cutaneous malignant melanoma
- Other advanced or metastatic IO sensitive tumor types TBD

**Trial Details**

| | | | |
|---|---|---|---|
| Monotherapy and combination therapy dose escalations enrolled in parallel with staggered start for combination | mTPI (Modified Toxicity Probability Interval) design<br><br>Enrolling ~ 150 patients total | Assessment of safety, pharmacokinetics, MTD/RDE, biomarkers, ADA and efficacy | Concurrent biomarker analysis to evaluate proof of mechanism and tumor-selective conditional activation |

**1H 2024**: Additional monotherapy dose escalation data, RDE declaration and opening of expansion arms anticipated

Abbreviations: MTD-maximum tolerated dose; RDE-recommended dose for expansion; ADA-anti drug antibody; IO-immuno-oncology; SOC-standard of care





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# Patient Demographics from Early Monotherapy Dose Escalation Cohorts (n=16)

## Demographics

| | | |
|---|---|---|
| AGE (years) | Mean (SD) | **66.9** (10.62) |
| | Median | **66.0** |
| SEX, n (%) | Female | **8** (50.0%) |
| | Male | 8 (50.0%) |
| RACE, n (%) | Black/African-American | **1** ( 6.2%) |
| | White | **13** (81.2%) |
| | Unknown | **2** (12.5%) |

## Prior lines of systemic therapy, (including immunotherapy)

| | n (%) |
|---|---|
| 1 | **2** (12.5%) |
| 2 | **4** (25.0%) |
| 3 | **5** (31.2%) |
| ≥4 | **5** (31.2%) |

## Tumor type

| | n (%) |
|---|---|
| Melanoma* | **8** (50.0%) |
| NSCLC | **5** (31.3%) |
| Renal Cell Carcinoma | **2** (12.5%) |
| Cutaneous SCC | **1** (6.3%) |

- ***Enrollment of heavily pretreated patients with tumor types for which immunotherapy, including Proleukin, is indicated***
- ***All patients received prior immunotherapy and progressed***
- ***Nine patients (56.3%) developed immune-related adverse events while receiving prior immunotherapy***

*Includes patients with cutaneous, uveal and mucosal melanoma; all patients enrolled in Cohorts 1-4 previously progressed on standard-of-care immunotherapy regimens

Note: Preliminary clinical data as of October 18, 2023, from 16 patients in an ongoing Phase 1/1b clinical trial.





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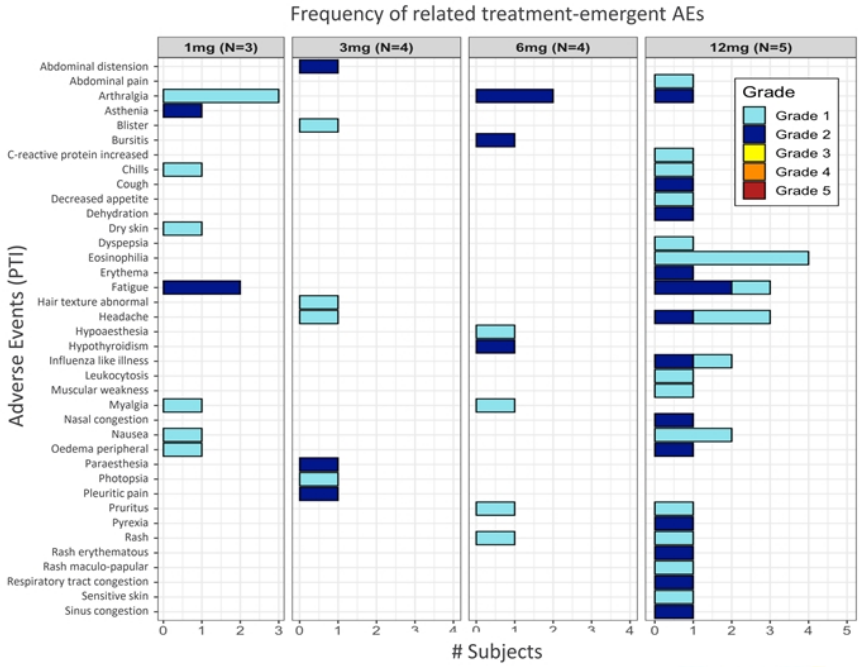
# WTX-124 was Generally Well-Tolerated in the Outpatient Setting at Relevant Doses

*Sixteen patients in four dose escalation cohorts (1-12 mg IV Q2W) were evaluable for safety*

## Key safety findings to date:

- Drug related TEAEs: no Grade 3 or higher
- Arthralgias and fatigue were the most common related TEAEs
- No vascular leak syndrome of any grade (adverse event common to HD IL-2)
- No evidence of cytokine release syndrome
- No patient developed dose-limiting toxicity or treatment-related serious AE
- No patient discontinued study drug due to treatment-related AE




Abbreviations: TEAEs-treatment-emergent adverse events; HD-high dose; Q2W-once every two weeks

Note: Preliminary clinical data as of October 18, 2023, from 16 patients in an ongoing, open label Phase 1/1b clinical trial.





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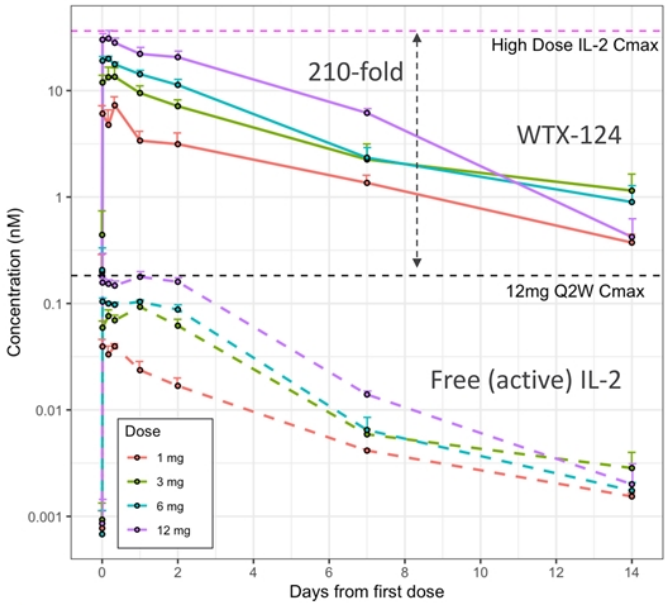
# Plasma PK Data Show an Extended WTX-124 Half-Life with Low Free (Active) IL-2 Exposure

*Preliminary PK data validate INDUKINE design and support improved therapeutic index and safety profile of WTX-124*

Cycle 1 PK profiles for WTX-124 and free (active) IL-2 compared to high-dose IL-2 Cmax (mean ± SEM)




## Key safety findings to date:

- Dose-dependent increase in WTX-124 plasma exposure
- Low free (active) IL-2 levels (<1.6% of prodrug) during dosing
- WTX-124 prodrug Cmax at 12 mg IV Q2W comparable to HD IL-2
- Free (active) IL-2 at 12 mg IV Q2W: ~210-fold lower than HD IL-2
- Preliminary WTX-124 half-life range: 1.86-5.79 days
- Preliminary ADA data: 5/15 patients exhibited non-dose dependent, treatment-emergent ADA (4/5 are low titer) w/ no impact on repeat dose exposure
- Data suggest wide therapeutic index consistent with INDUKINE hypothesis, continued dose escalation supported

Abbreviations: HD-high dose; Q2W-once every two weeks





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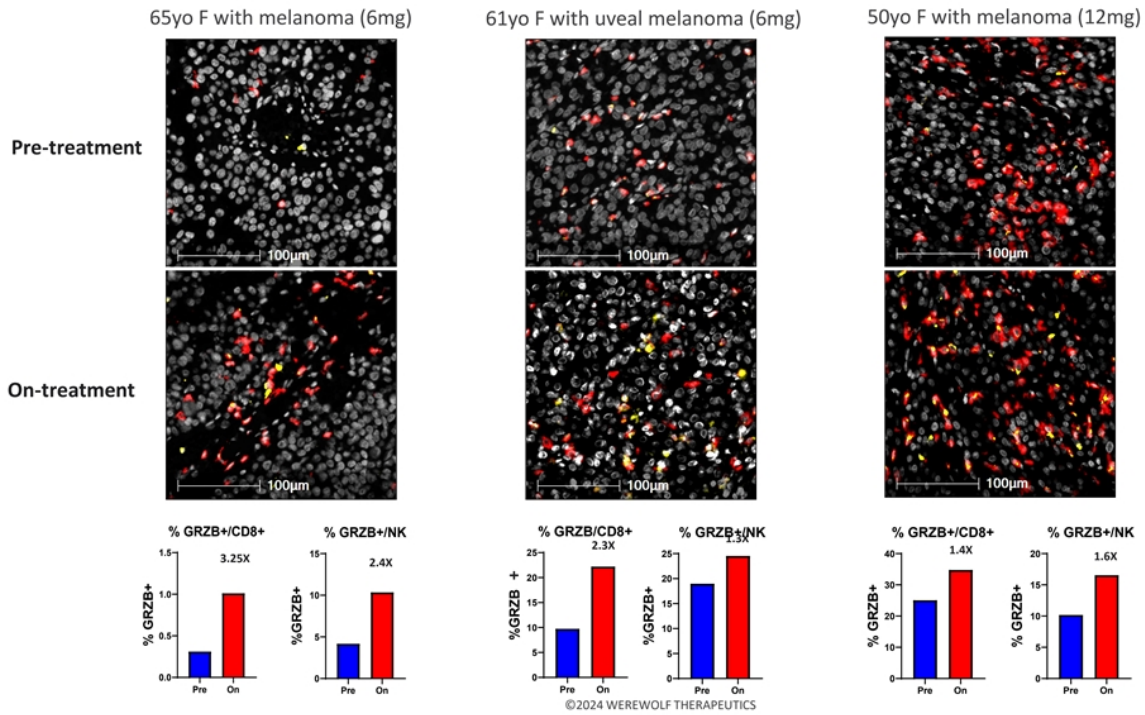
# Immunofluorescence Staining of Tumor Biopsies from Patients Treated with WTX-124

*Tumor-specific expansion and activation of CD8 T cells and NK cells differentiate WTX-124 among next-gen IL-2 molecules*




DAPI

CD8

GRZB

*Granzyme B (GRZB) is one of the primary markers of activated T cells*





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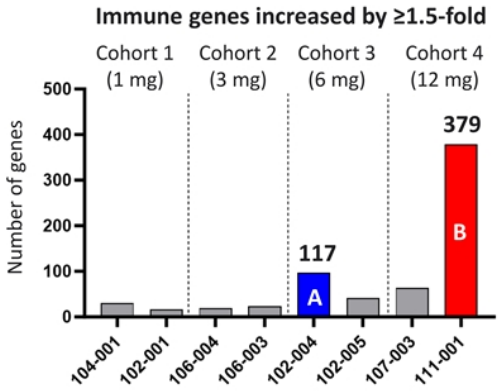
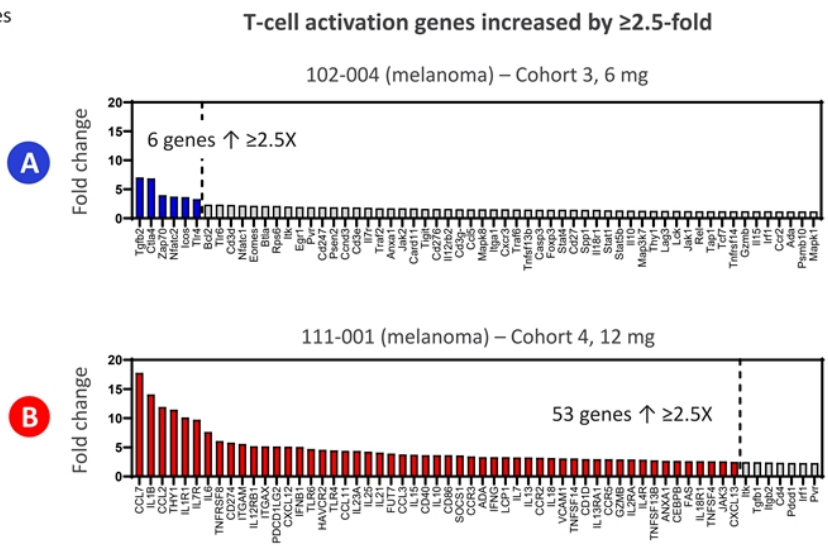
# WTX-124 Induced Dose-Dependent Changes in Immune Gene Expression Consistent with IL-2 Activity in the Tumor Microenvironment


Note: Data presented for eight patients for whom on-treatment biopsies were available as of October 11, 2023





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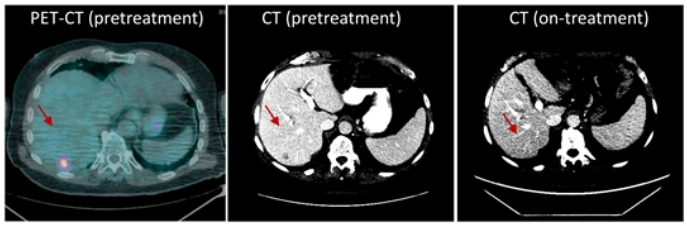
# WTX-124 Demonstrated Monotherapy Antitumor Activity in Patients Refractory to ICI Therapy

*At 12 mg dose level, WTX-124 shrank treatment-refractory tumor metastatic deposits (3/5 patients)*

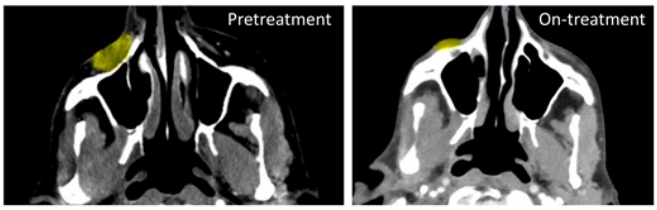
**1. Patient 107-002: unconfirmed PR (RECIST 1.1)**

- 78-year-old man with melanoma who progressed on nivolumab/relatlimab (Opdualag™)
- Achieved a RECIST 1.1 partial response (PR; unconfirmed) at the first restaging scan (8 weeks) after two cycles of WTX-124
- Imaging studies (*below*) show complete resolution of a 1.4 cm target lesion in the liver
- Stable non-target bone lesion in the T11 vertebral body




**2. Patient 102-006: unconfirmed PR (RECIST 1.1)**

- 72-year-old man with cutaneous SCC who progressed on cemiplimab (Libtayo®); initial 8-week restaging CT scan showed uPR (>60% reduction in premaxillary target lesion)




**3. Patient 106-006**

- 76-year-old man with refractory NSCLC with rapid necrosis of a large, visible scalp lesion after the first dose of study drug; mixed response, remained on study drug for 14 wks

Abbreviation: ICI-immune checkpoint inhibitors; PR-partial response; SCC-squamous cell carcinoma; NSCLC-Non-small cell lung cancer

Note: Preliminary clinical data as of November 1, 2023, from 16 patients in an ongoing, open label Phase 1/1b clinical trial.





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# Proof of Mechanism for WTX-124 and Proof of Concept for INDUKINE Design Established

## Monotherapy WTX-124 administered in an outpatient setting has been well tolerated and has reached exposures associated with clinical responses in dose escalation

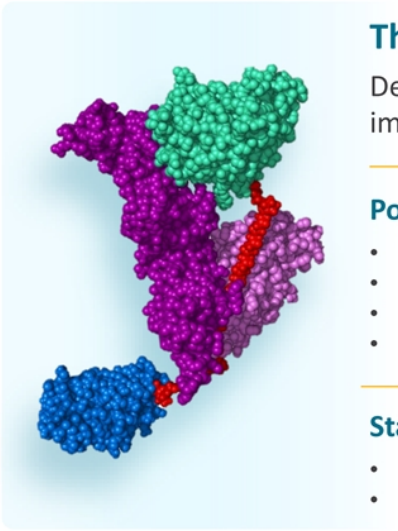
- Majority of patients treated would not have been eligible to receive HD IL-2 due to age, indication, or underlying organ function
- Among 16 patients treated with WTX-124 at doses up to 12 mg IV Q2W, there were no cases of vascular leak syndrome and no DLTs
- PK data showed extended prodrug exposure and low levels of free (active) IL-2 resulting in improved therapeutic index and opportunity for continued dose escalation
- WTX-124 administered at doses of 6-12 mg IV Q2W demonstrated CD8+ T cell and NK cell activation and antitumor activity (including 2 uPR at 12 mg) in multiple tumor types

## Additional interim data from monotherapy dose escalation and data informing RDE declaration expected to be reported in 1H 2024

Abbreviations: AE-adverse event; SAE-serious adverse event; DLT-dose limiting toxicity; HD-high dose; TME-tumor microenvironment; RDE-recommended dose for expansion; uPR-unconfirmed partial response; Q2W-once every two weeks

Note: Based on preliminary clinical data as of November 1, 2023, from 16 patients in an ongoing, open label Phase 1/1b clinical trial.

# WTX-330: Leveraging the Potential of IL-12 Therapy



## The Challenge

Develop a tolerable IL-12 therapy to stimulate innate and adaptive antitumor immune responses

## Potential WTX-330 Advantages and Opportunity

- Delivery of IL-12 mechanism selectively to the TME with an improved therapeutic index
- Potent preclinical antitumor activity in poorly immunogenic, anti-PD-1 therapy refractory tumors
- Leverage IL-12 biology in the clinic to address mechanisms of checkpoint inhibitor resistance
- Potential for multiple combination strategies to enhance anti-tumor activity

## Status

- Phase 1 clinical trial actively enrolling
- Release of initial data from Phase 1 clinical trial anticipated in 2Q 2024

Abbreviation: TME-tumor microenvironment





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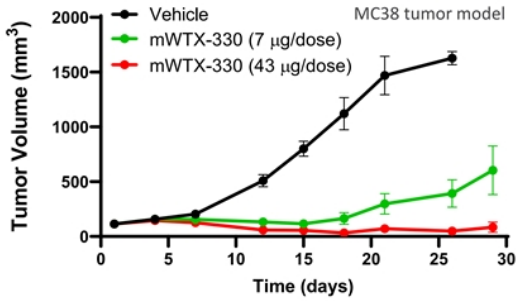
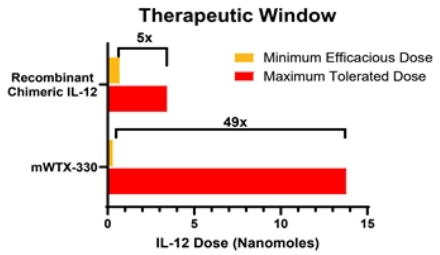
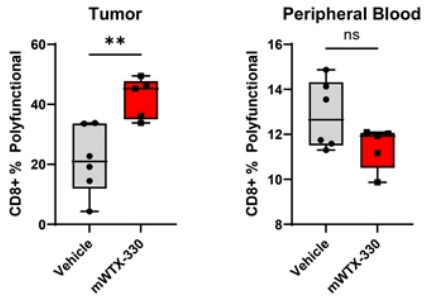
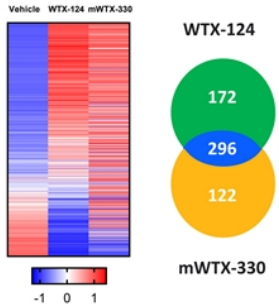
# IL-12 INDUKINE Delivers IL-12 Selectively to Tumor Tissue with an Improved Therapeutic Index

*Robust activation of antitumor CD8+ T effector cells and pleiotropic immune activation in the TME in preclinical models*







**Differential Gene Signatures**

- ✓ Intratumoral IL-12 pathway activation
- ✓ Activation of multiple antigen presentation mechanisms
- ✓ Th1 lineage skewing
- ✓ Treg instability
- ✓ Increased chemokine expression

Nirschl CJ et al., Cancer Immunology Research, 1 July 2023; 11 (7): 962–977

Abbreviation: TME-tumor microenvironment





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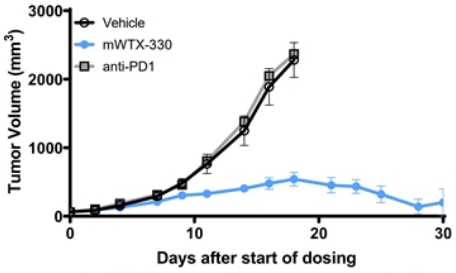
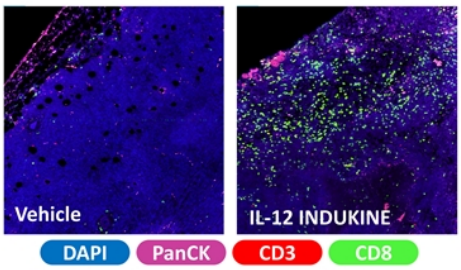
# IL-12 INDUKINE Inhibits Growth of Poorly Immunogenic EMT-6 Mouse Tumors

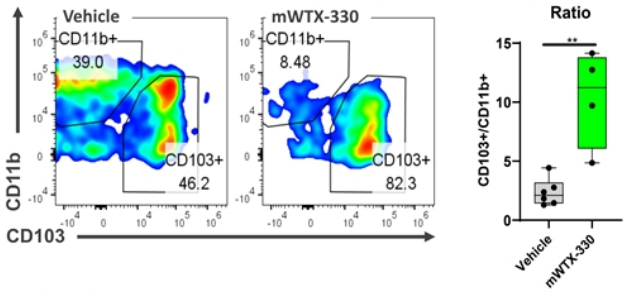
*Increased Clonality of Tumor Infiltrating CD8+ T Cells in preclinical models*

## Efficacy in anti-PD-1 refractory EMT-6 tumors

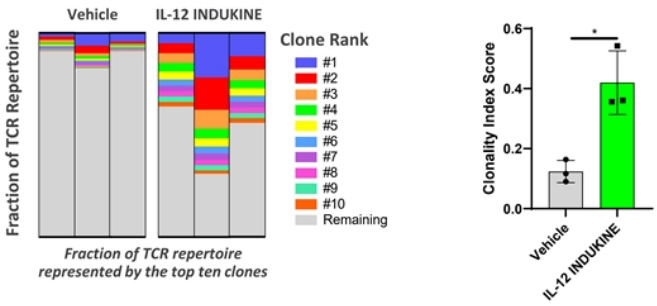



## Increase of cross-presenting DCs in tumors




## Increased TCR clonality of tumor infiltrating T cells




Nirschl CJ et al., Cancer Immunology Research, 1 July 2023; 11 (7): 962–977





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# First-In-Human Study of WTX-330 Evaluating Safety, Tolerability and Clinical Activity

## Monotherapy Dose Escalation

Relapsed/refractory advanced or metastatic solid tumors failing SOC, including immune checkpoint inhibitors

Monotherapy expansion arms to open after determination of MTD/RDE

## Monotherapy Dose Expansion

CPI-naïve relapsed or refractory advanced tumor indications (tumor types for which CPIs are not approved, including NHL and mCRPC)

CPI primary or secondary resistant relapsed or refractory advanced tumor indications

**Trial Details**

CPI-unapproved and CPI-resistant indications supported by IL-12 biology and preclinical data

Bayesian study design, n~75

Assessment of safety, MTD/RDE, pharmacokinetics, biomarkers, ADA and efficacy

Concurrent biomarker analysis on blood and tumor tissue to evaluate proof of mechanism and confirm differential activity based on conditional activation

**STATUS: Actively enrolling patients – preliminary data anticipated in 2Q 2024**

Abbreviations: MTD-maximum tolerated dose; RDE-recommended dose for expansion; ADA-anti drug antibody; NHL-Non-Hodgkin lymphoma; mCRPC-metastatic castration-resistant prostate cancer; CPI-checkpoint inhibitor





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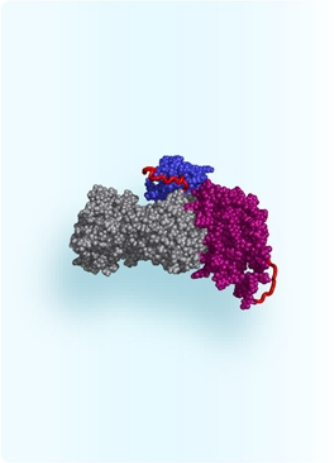
# WTX-712: Expanding the Utility of IL-21 Therapy



## Potential WTX-712 Advantages and Opportunity

- IL-21 distinctively leads to an effective anti-tumor response driven by activation and differentiation of multiple anti-tumor cell types including Tfh cells, B cells, and cytotoxic effector cells (CD8+ T cells, NK, and NKT cells) as well as inhibiting Tregs and promoting M1 macrophage function
- IL-21 supports the generation and maintenance of lymphoid structures including TLS, which are increasingly recognized as critical for antitumor immunity
- IL-21 cytokine therapy showed signs of clinical activity but has been limited by toxicity, suggesting an opportunity for approaches with an improved therapeutic index
- Our preclinical data demonstrate a positive combination effect of WTX-712 with CPI
- WTX-712 provides a differentiated anti-tumor immunity approach to common gamma-chain-cytokines, complementing our IL-2 INDUKINE WTX-124

## Status

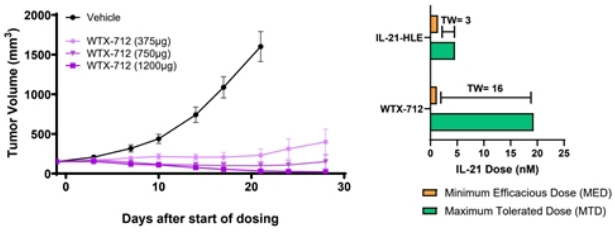
- IND-enabling studies

Abbreviations: TLS-tertiary lymphoid structure; CPI-checkpoint inhibitor

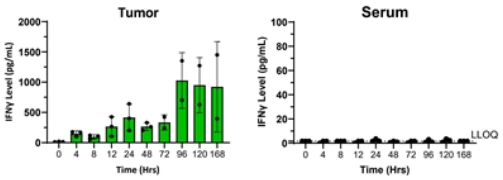
# WTX-712 has an Improved Therapeutic Index Compared to Native IL-21

*Tumor selective activity results in robust anti-tumor immune activation in preclinical studies*

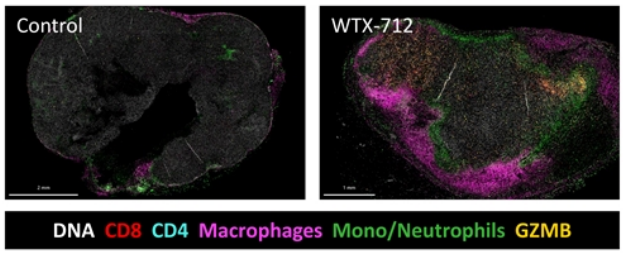
## WTX-712 antitumor activity in MC38 tumor model with an improved therapeutic window compared to IL-21 cytokine



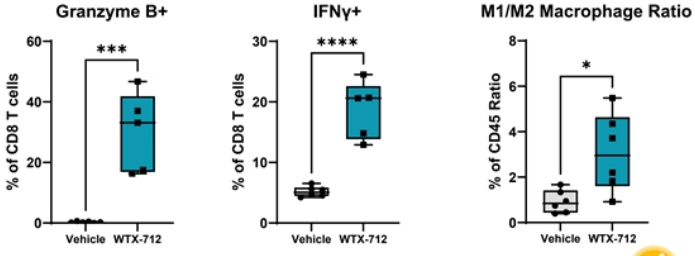

## WTX-712 specifically induces IFNγ in the tumor




## WTX-712 treatment transforms the tumor microenvironment




## CD8 T Cells Expressing Effector Molecules





Sullivan JM et al., AACR 2023 Poster: Generation of IL-21 INDUKINE™ Molecules for the Treatment of Cancer

Sullivan JM et al., SITC 2023 Poster: Development of WTX-712, a Conditionally Active IL-21 INDUKINE™ Molecule for the Treatment of Cancer



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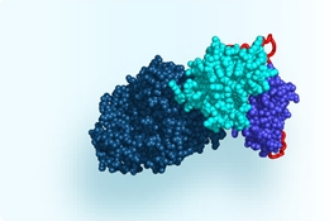
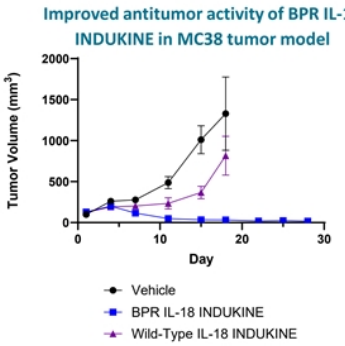
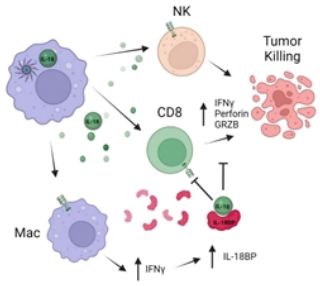
# WTX-518: Overcoming the Limitations of IL-18 Therapy






## Potential WTX-518 Advantages and Opportunity




- IL-18 activates innate (strong NK activator) and adaptive immune cells promoting production of IFN-γ from antigen experienced T cells and favoring Th1 differentiation of naïve T cells
- IL-18 activity is heavily regulated by the decoy protein IL-18BP, which when overcome, can promote effective antitumor immunity but with an increased risk of IL-18 mediated toxicity
- The design of WTX-518 uniquely eliminates the ability of IL-18BP to inhibit IL-18 and systemically delivers IL-18 prodrug for conditional activation within the TME, providing optimal antitumor immunity with an improved therapeutic window
- IL-18 and IL-12 synergize to drive T cell activation and release of IFN-γ. WTX-518 complements our current portfolio already containing WTX-330 (IL-12 INDUKINE).

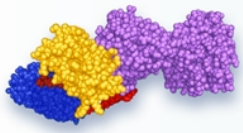
## Status

- IND-enabling studies

Abbreviations: TME-tumor microenvironment; BPR-binding protein resistant

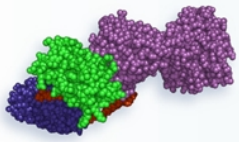
# PREDATOR Platform

**Werewolf's innovative PREDATOR Platform offers value creation through pipeline expansion and partnering opportunities**



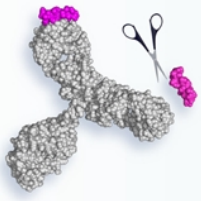
### Oncology-focused INDUKINE Therapeutics

- Additional proinflammatory mechanisms
- Cell-based therapies
- mRNA therapies



### Non-Oncology INDUKINE Therapeutics

- Inflammation
- Other diseases



### Expanding Conditional-Activation Technology to New Modalities

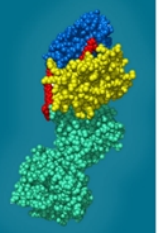
- Targeted antibodies, T cell engagers, ADCs
- Cell-based therapies
- Disease-specific linkers

# Shifting the Balance in Cytokine Therapeutics

- Two lead programs in Phase 1 development are wholly owned by Werewolf
- Collaboration is central to our growth strategy with Jazz global partnership on JZP898

## WTX-124

**Phase 1/1b Clinical Trial** in Advanced and Metastatic Solid Tumors



## WTX-330

**Phase 1 Clinical Trial** in Advanced and Metastatic Solid Tumors and Lymphoma

### PREDATOR Platform: Value Creation Engine

Our protein engineering technology optimizes the design of conditionally activated cytokine therapeutics (INDUKINE molecules) to diseased tissues.

Opportunity to pursue non-cancer indications such as inflammatory diseases.

### Deep Pipeline

**JZP898, an IFNα INDUKINE molecule,** in clinical development by Jazz Pharmaceuticals

**WTX-712, an IL-21 INDUKINE molecule**, in preclinical development for the treatment of cancer

**WTX-518, an IL-18 INDUKINE molecule,** in preclinical development for the treatment of cancer

### Strong Cash Position

Approximately $130.1M in cash and cash equivalents (as of September 30, 2023)

Financial runway through at least 1Q 2025 with opportunity for multiple value-enhancing catalysts in the near term

Approximately 36.19M shares outstanding (as of November 10, 2023)





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# Experienced Leadership

**Daniel J. Hicklin, PhD**
President and CEO

**Randi E. Isaacs, MD**
Chief Medical Officer

**Chulani Karunatilake, PhD**
Chief Technology Officer

**Ellen Lubman, MBA**
Chief Business Officer

**Cynthia Seidel-Dugan, PhD**
Chief Scientific Officer

**Tim Trost, CPA**
Chief Financial Officer


# Thank You!