Werewolf THERAPEUTICS

Delivering the Power of Immunotherapy

CORPORATE PRESENTATION | November 2024

Cautionary Statements

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Note: Certain graphics contained in this presentation are created with BioRender.com.

Werewolf THERAPEUTICS

Who we are

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

Werewolf is developing next generation cytokine therapies designed to harness their innate immunological potential to transform the lives of patients with cancer and other serious diseases.

Werewolf
THERAPEUTICS

Clinical-Stage Biopharma Company – Next Generation Conditionally Activated Therapies

PREDATOR® Platform
Validated & Differentiated

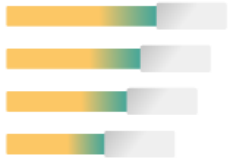
Tunable, tissue-targeted INDUKINE design delivers highly potent payloads with improved therapeutic index over recombinant counterpart molecules

Validation of conditional activation platform demonstrated through clinical and preclinical testing of multiple INDUKINE molecules

Clinical Focus
High-Value Opportunities

WTX-124, an IL-2 prodrug, is potentially a best-in-class pipeline-in-a-product for immunotherapy-sensitive tumors

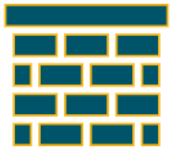
WTX-330, an IL-12 prodrug, has the potential to be a first-in-class molecule to address poorly immunogenic cancers as a monotherapy or in combination with standard of care



Robust Discovery Engine
Novel INDUKINE™ molecules

Deep preclinical pipeline with WTX-712 (IL-21), WTX-518 (IL-18), WTX-910 (IL-10), and IFNα INDUKINE (licensed to Jazz)

Modular platform extends pipeline expansion and collaboration potential to additional targets, tumor types, opportunities beyond oncology, additional modalities



Strong Foundation
Disciplined & Experienced

$122.8M in cash and equivalents as of September 30, 2024

Runway through at least 2Q26 with multiple near-term catalysts

Experienced leadership with expertise advancing immunotherapy R&D

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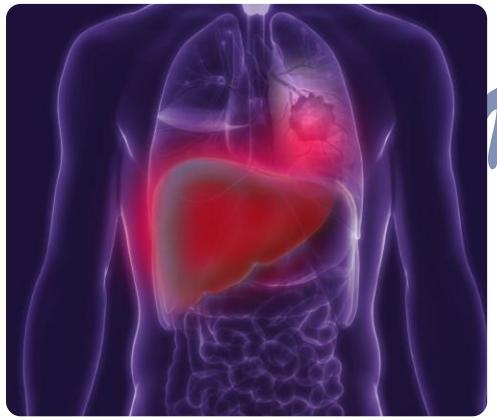
Overcoming Off-Target Toxicity has been a Key Challenge for Cytokine Therapy

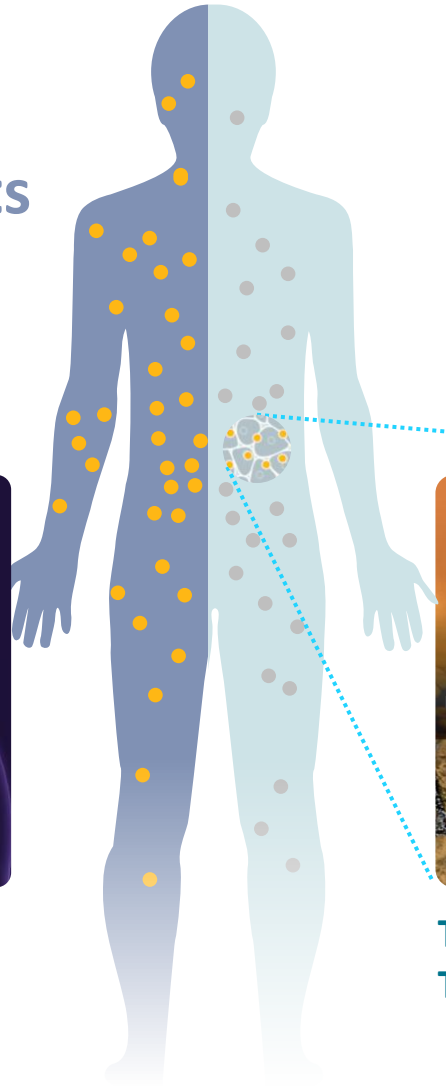
The Challenge:
Off-Tumor Cytokine Toxicity Limits Therapeutic Index

Suboptimal Pharmaceutical Properties

Toxicity

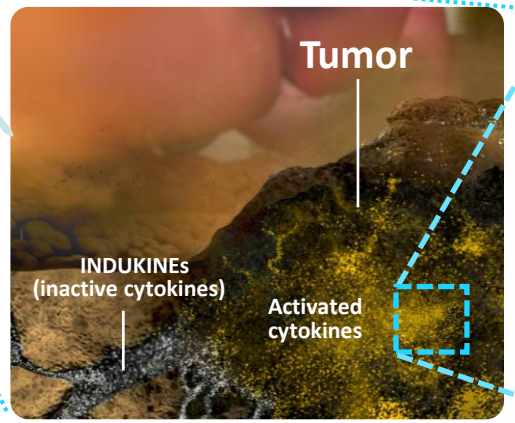


Poor Clinical Outcomes

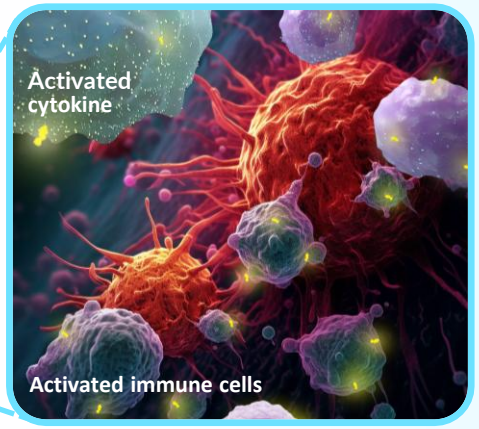


Our Solution:
Conditionally Activated Immunotherapy

With Optimized Therapeutic Index



Targeted Delivery to the Tumor Microenvironment



On-Target Immune Activation

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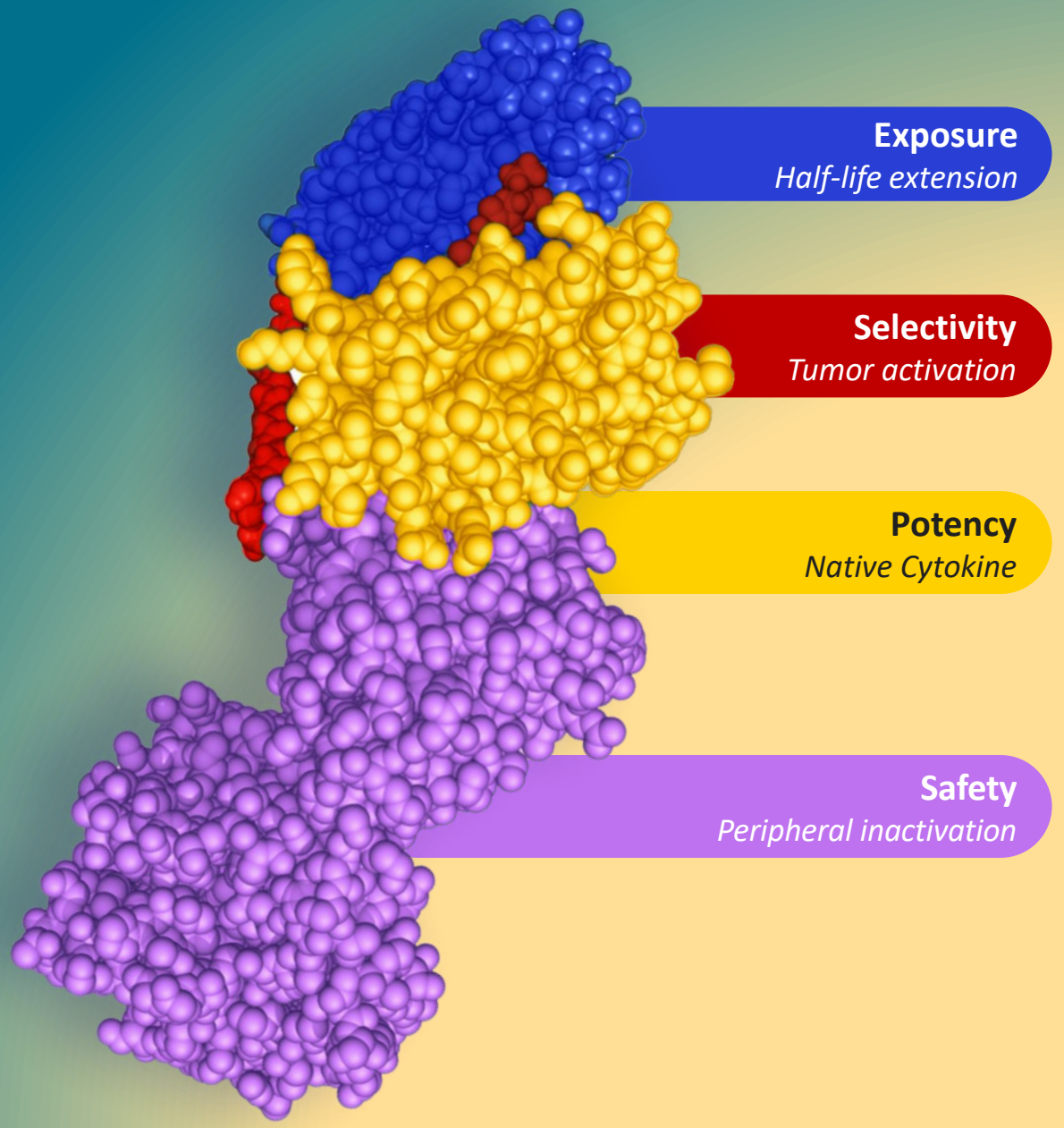
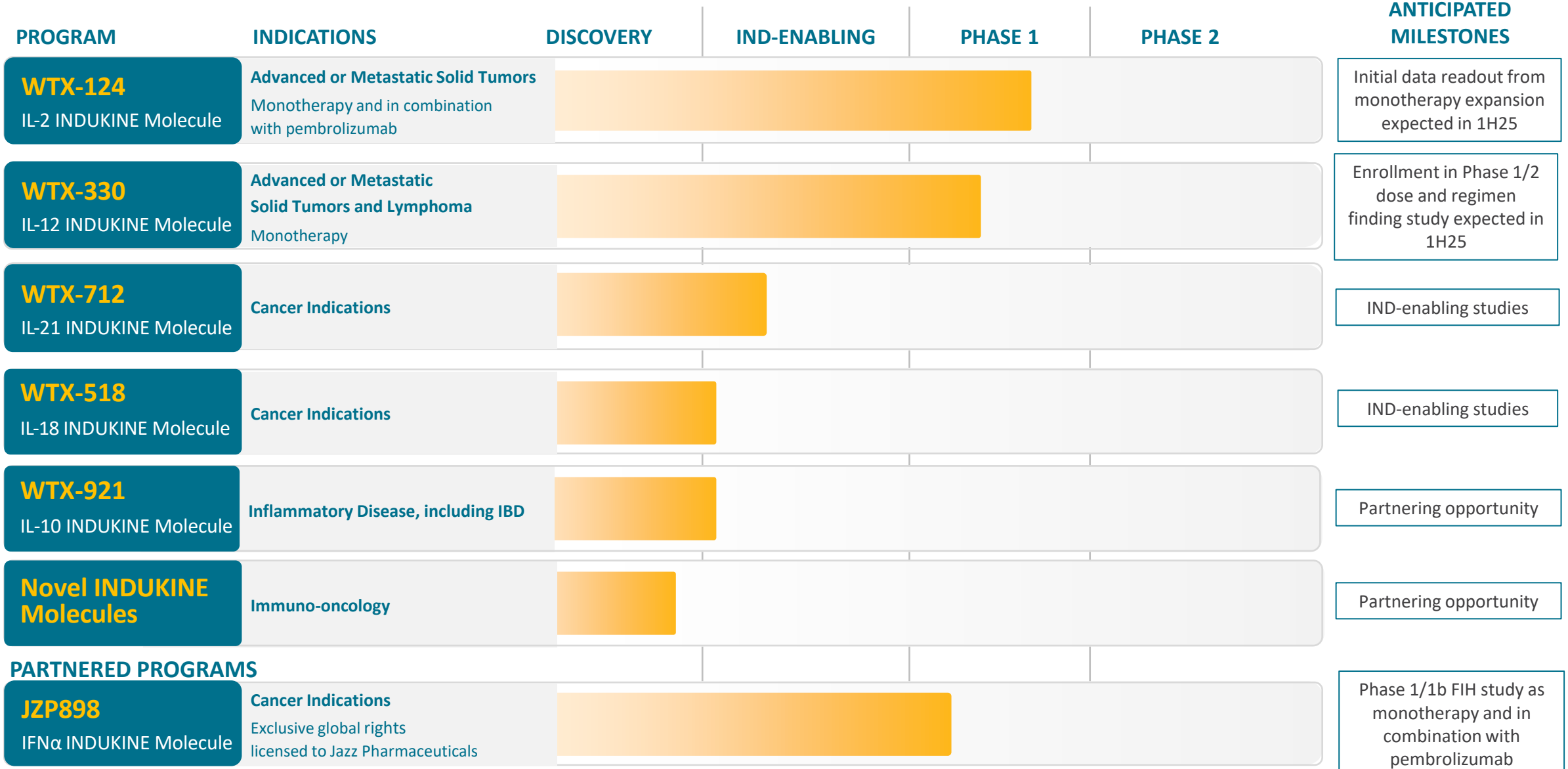
PREDATOR
Platform

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



A Portfolio of Novel Clinical and Preclinical Drug Candidates



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WTX-124

WTX-124: Improving the Efficacy and Tolerability of IL-2

THE CHALLENGE

Approved high-dose IL-2 therapy (HD IL-2) with aldesleukin (Proleukin®) produces durable responses in patients with cutaneous melanoma and renal cell carcinoma, but its use is limited by severe toxicity

Unique Advantages of WTX-124, an IL-2 INDUKINE Molecule

Novel prodrug engineered with enhanced pharmaceutical properties to selectively release a fully potent IL-2 in the tumor microenvironment to stimulate antitumor immunity with reduced toxicity

Key Opportunities

- Provide IL-2 therapy broadly to patients with advanced or metastatic cutaneous melanoma and renal cell carcinoma who are ineligible for HD IL-2
- IL-2 therapy may have potential benefit in any of the ICI-sensitive solid tumor indications
- Address an unmet medical need for ICI-relapsed/refractory patients
- Safely combine IL-2 therapy with SOC agents including ICIs in earlier lines of therapy

Abbreviations: SOC-standard of care; ICI-immune checkpoint inhibitor

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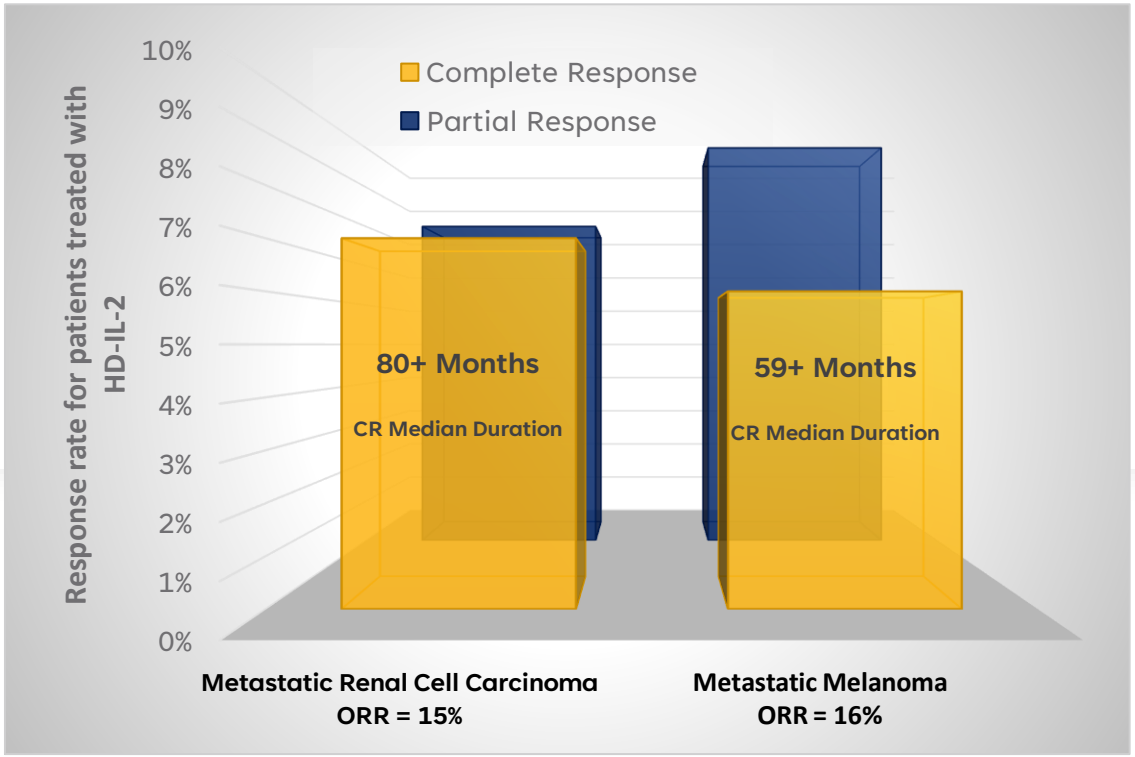
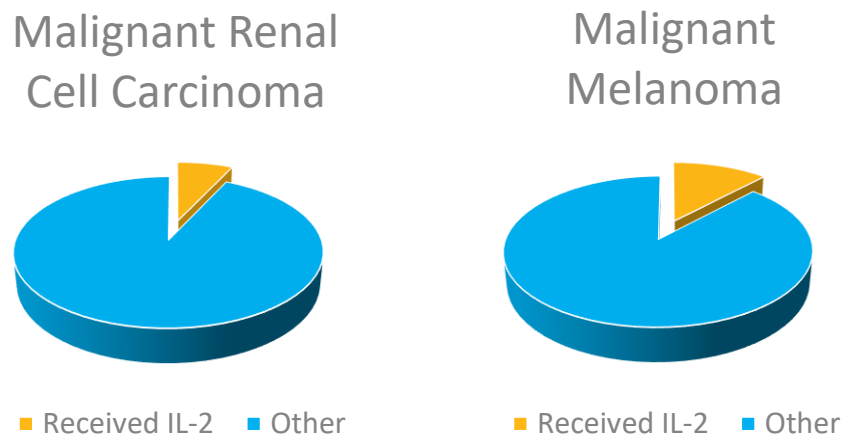
Goal to Significantly Expand Patient Populations Who Might Benefit from IL-2

HD IL-2 has potential for profound patient benefit



But most patients don't receive HD IL-2 due to toxicity



Large % of patients across multiple tumor types currently unable to receive HD IL-2 could be treated with a more tolerable IL-2 therapy that retains the profound clinical benefit

Abbreviations: HD-high dose; CR-complete response; ORR-objective response rate

Proleukin (aldesleukin) injection label, Reference ID: 3165255; Proleukin (aldesleukin) injection label (fda.gov), accessed Sept. 2, 2024

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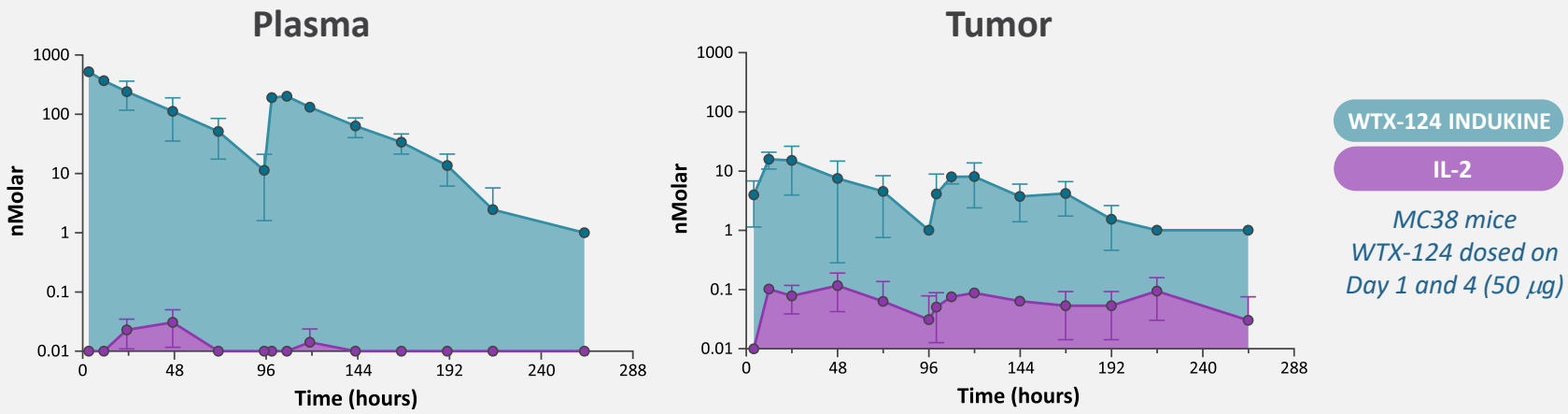
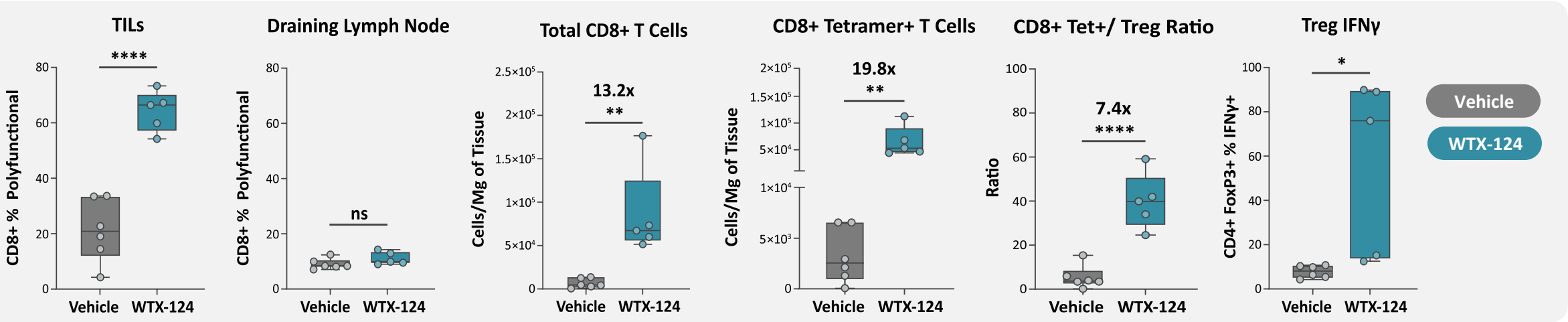
WTX-124 Delivers IL-2 Selectively to Tumors in Preclinical Models

Released IL-2 expands and activates antitumor CD8+ T effector cells preferentially over Tregs





Abbreviation: TIL-tumor infiltrating lymphocytes

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

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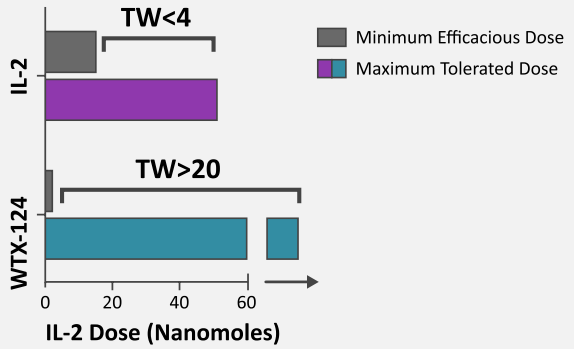
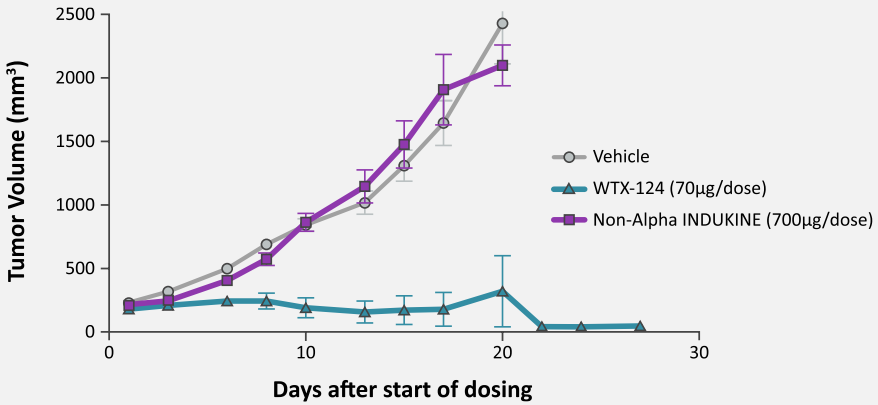
INDUKINE Molecule Strategy Markedly Improves the Therapeutic Window for IL-2

Incorporation of wild type IL-2 in WTX-124 is required for complete tumor regressions and immune memory formation

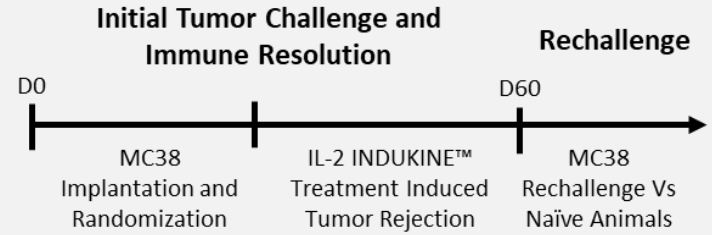
Improved therapeutic window compared to recombinant IL-2

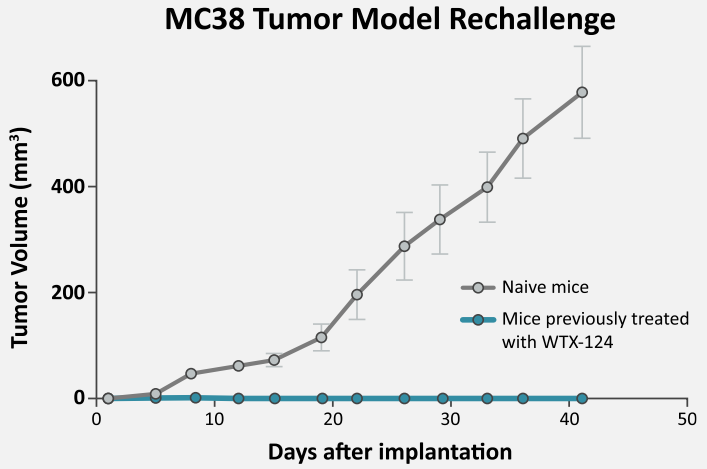


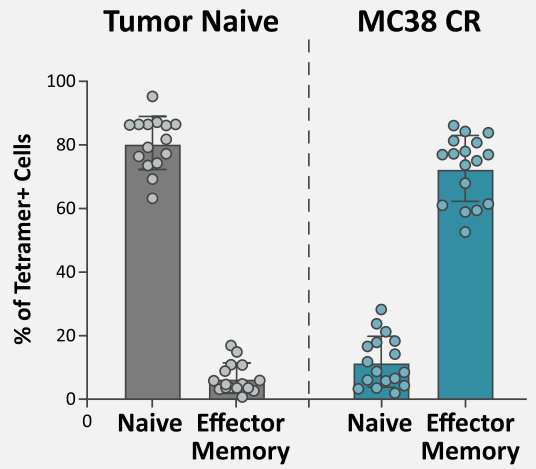
WTX-124 antitumor activity is substantially more potent than a "non-alpha" IL-2 INDUKINE in MC38 tumor model



WTX-124 activates long-term antitumor immune memory







Abbreviations: TW-therapeutic window; CR-complete regression

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

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Data from Ongoing WTX-124 Phase 1/1b Study in ICI-treated Patient Population

Safety

- Generally well tolerated in the outpatient setting
- No evidence of vascular leak syndrome, cytokine release syndrome (≥Grade 2) or infusion reactions
- Majority of related TEAEs were Grade 1-2 (all were reversible)
- No related Grade 4 or 5 TEAEs
- No new safety signals when combined with pembrolizumab

Clinical Activity

- Confirmed, durable responses and anti-tumor activity noted at WTX-124 doses ≥12 mg in multiple solid tumors with both monotherapy WTX-124 and in combination with pembrolizumab
- Durable regression of target lesions in patients who responded to therapy
- Dose-dependent expansion and activation of effector T cells in the tumor microenvironment, further enhanced with combination therapy

WTX-124 has monotherapy antitumor activity in patients refractory to SOC ICI regimens

Abbreviations: TEAE-treatment-emergent adverse events; CR-complete response; CSCC-cutaneous squamous cell carcinoma; PR-partial response; SOC-standard of care; ICI-immune checkpoint inhibitor

Note: Preliminary clinical data as of October 25, 2024, for an ongoing, open label Phase 1/1b clinical trial.

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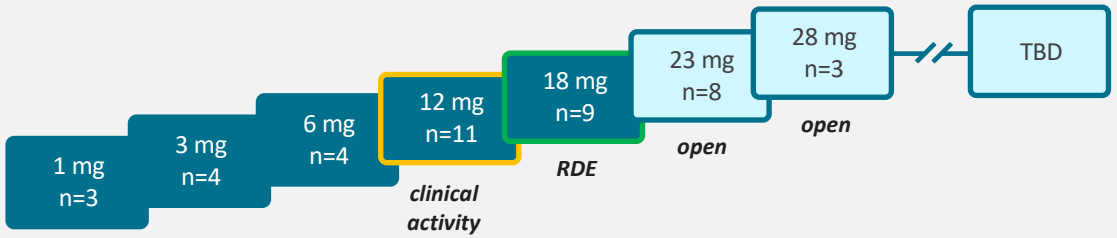
WTX-124 Monotherapy and Combination Expansion Arms are Open and Enrolling

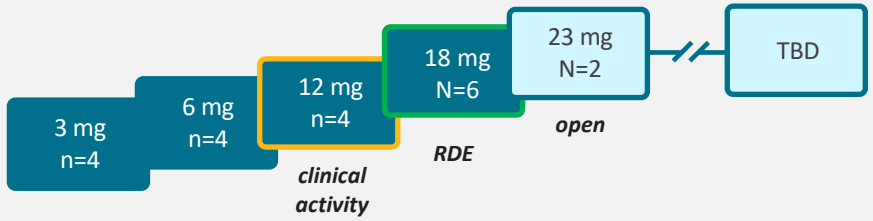
*67 patients have received at least one dose of WTX-124 (n=47 monotherapy, n=20 combination therapy)**

MONOTHERAPY DOSE ESCALATION



Determination of **WTX-124 IV Q2W** RDE/ MTD as a monotherapy

COMBINATION THERAPY DOSE ESCALATION



Determination of **WTX-124 IV Q2W** RDE/MTD in combination with pembrolizumab IV Q6W

Monotherapy/Combination Dose Expansion

Advanced or metastatic (to be enrolled):

- Renal cell carcinoma (*monotherapy and combination*; n=20 each)
- Cutaneous melanoma (*monotherapy and combination*; n=20 each)
- Cutaneous squamous cell carcinoma (*monotherapy only*; n=10)
- Non-small cell lung cancer (*combination only*; n=20)

Trial Details

mTPI-2 (Modified Toxicity Probability Interval 2) study design; enrolling ~160 patients with IO-sensitive tumors

Monotherapy and combination therapy dose escalations enrolled in parallel with staggered start for combination

Assessment of safety, efficacy, pharmacokinetics, biomarkers, and ADA

Tumor biopsies obtained on treatment to evaluate PD biomarkers supporting proof of mechanism

Abbreviations: RDE-recommended dose for expansion; IV-intravenous; Q2W-once every two weeks; Q6W-once every six weeks MTD-maximum tolerated dose; ADA-antidrug antibody; IO-immunotherapy; SOC-standard of care; PD-pharmacodynamic

*Enrollment as of November 5, 2024

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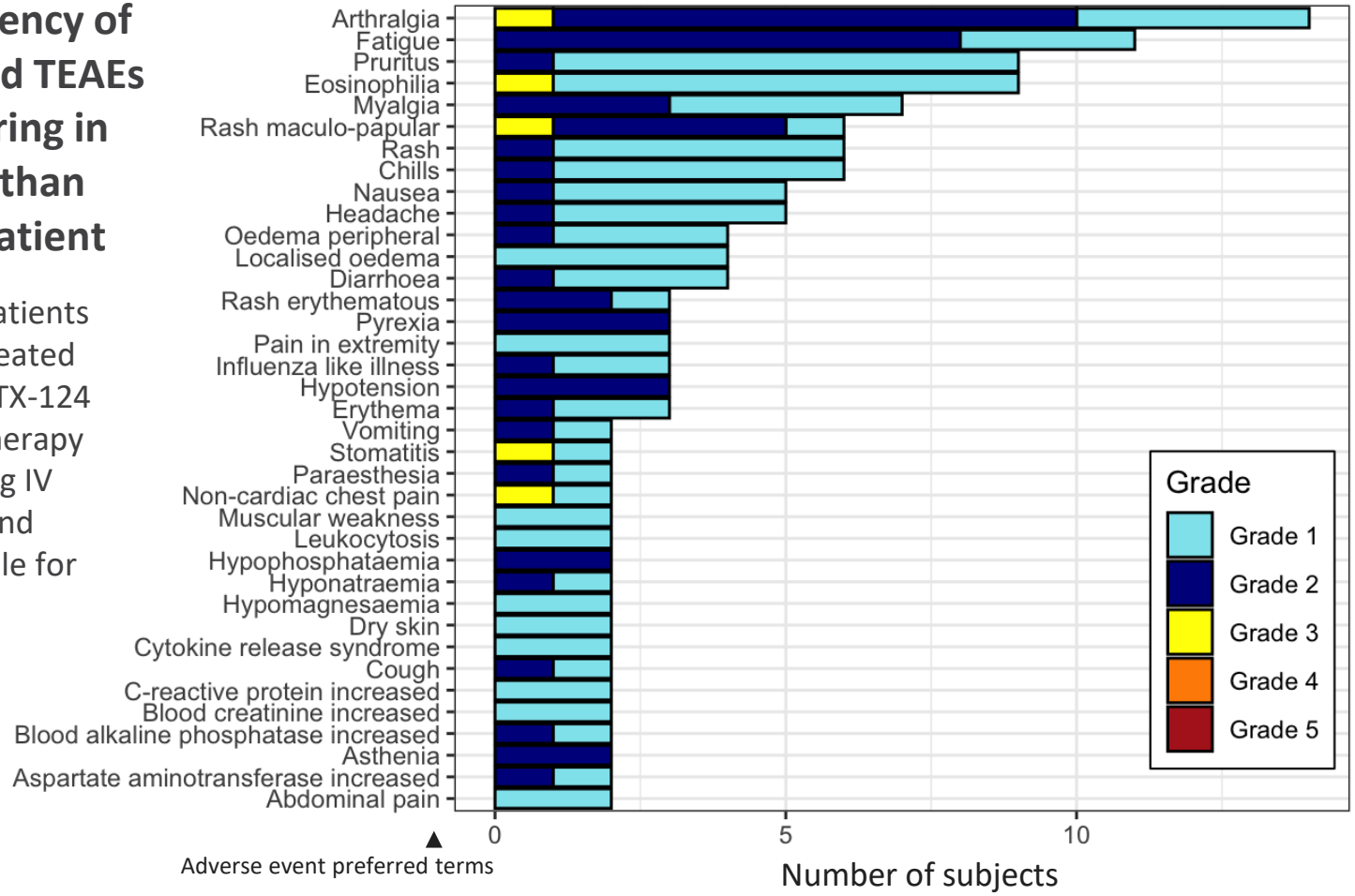
WTX-124 was Generally Well Tolerated as a Monotherapy in the Outpatient Setting

Key Safety Findings:

- Most frequent related TEAEs were arthralgia, fatigue, pruritis and eosinophilia
- Majority of related TEAEs were Grade 1 and 2, Grade 3 TEAEs at ≥18mg were manageable, reversible
- No evidence of VLS, ≥ Grade 2 CRS, or infusion reactions
- No recurrence to date of irAEs that had previously occurred on ICI therapy
- No new safety signals seen in combination with pembrolizumab

Frequency of related TEAEs occurring in more than one patient

N=35 patients were treated with WTX-124 monotherapy (1-28 mg IV Q2W) and evaluable for safety



Abbreviations: TEAEs-treatment-emergent adverse events; Q2W-once every two weeks; irAEs-immune related adverse events; ICI-immune checkpoint inhibitor; CRS-cytokine release syndrome; VLS-vascular leak syndrome

Note: Preliminary clinical data as of May 1, 2024, for an ongoing, open label Phase 1/1b clinical trial.

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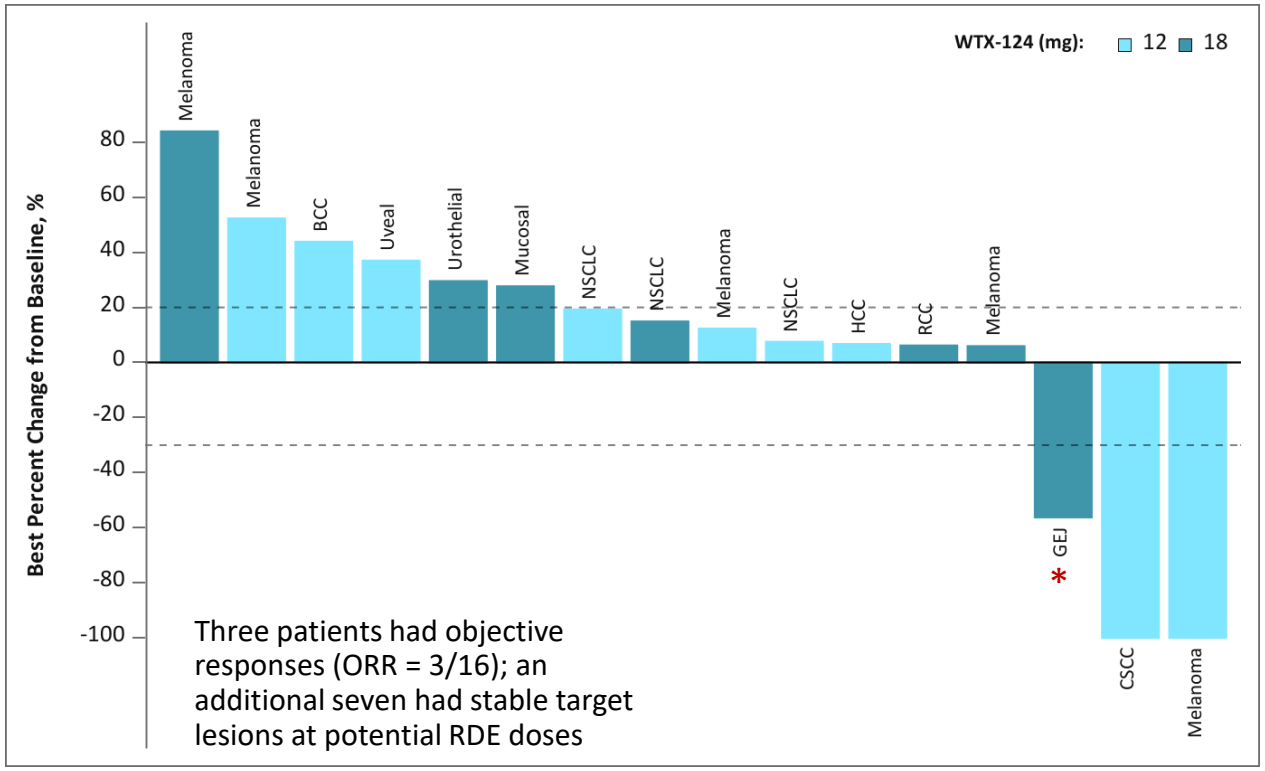
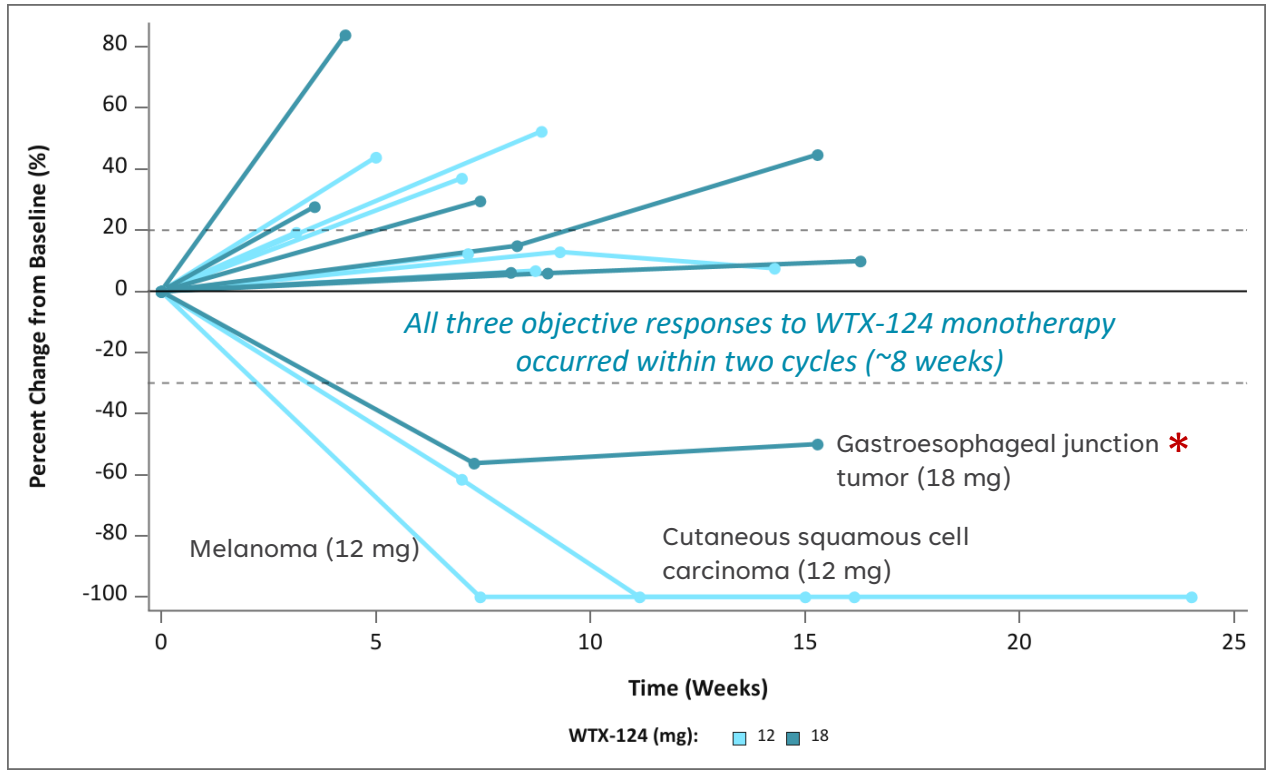
WTX-124 Monotherapy Induced Rapid, Durable Regressions of Target Lesions





*Metastatic lymph node target lesion normalized in size (<1 cm)

Abbreviations: RDE-recommended dose for expansion; BCC-basal cell carcinoma; NSCLC-non-small cell lung cancer; HCC-hepatocellular carcinoma; RCC-renal cell carcinoma; GEJ-gastroesophageal junction tumor; CSCC-cutaneous squamous cell cancer; ORR-objective response rate

Note: Preliminary clinical data as of May 1, 2024, for an ongoing, open label Phase 1/1b clinical trial.

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Complete Response (CR) Ongoing at 12+ Months in a Patient with ICI-Refractory Cutaneous SCC

72-year-old man with metastatic cutaneous SCC who progressed on RT/cetuximab and had no response to four doses (12 weeks) of cemiplimab (Libtayo®; anti-PD-1) – *panel a*

Initiated treatment with **12 mg WTX-124 IV Q2W** three months after discontinuing cemiplimab

Baseline CT showed a 2.6 cm premaxillary target lesion (T) and a non-target lesion (NT) extending into the pterygopalatine fossa – *panel b*

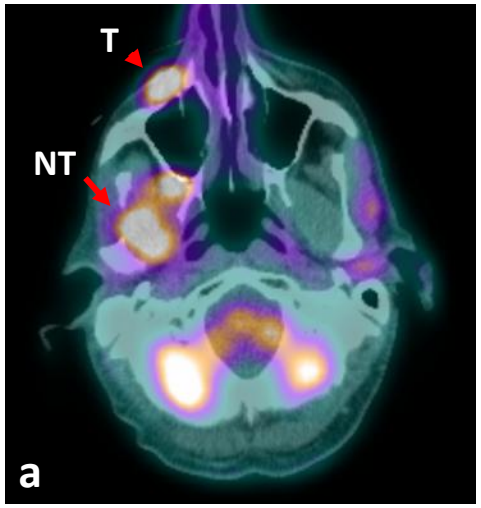
WTX-124 TREATMENT RESPONSE

- **3 weeks**: On-treatment biopsy of target lesion showed no tumor
- **8 weeks**: restaging CT showed a partial response (PR) with a 62% decrease of target lesion, no increase of non-target lesion – *panel c*
- **12 weeks**: confirmatory PET-CT showed a complete metabolic response of target/non-target lesions, consistent with a CR – *panel d*

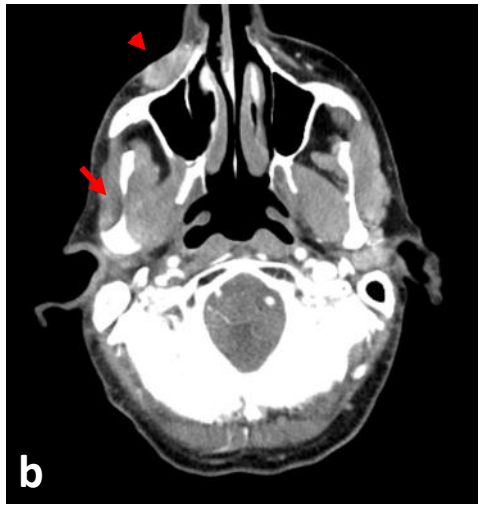
Patient tolerated therapy well with only Grade 2 arthralgias, Grade 2 rash

WTX-124 treatment stopped at 21 weeks in the setting of confirmed CR (ongoing at 12+ months)

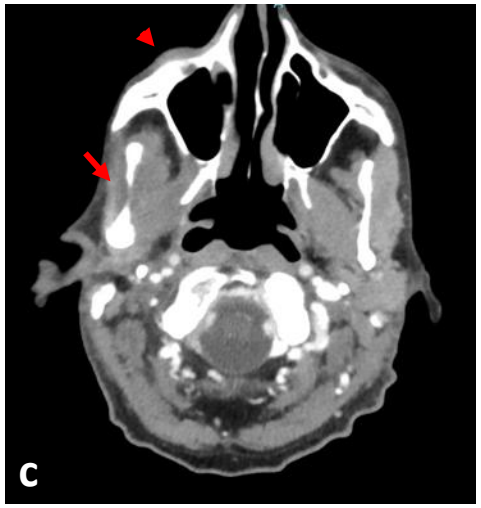
June 2023: PET-CT at time of progression on cemiplimab



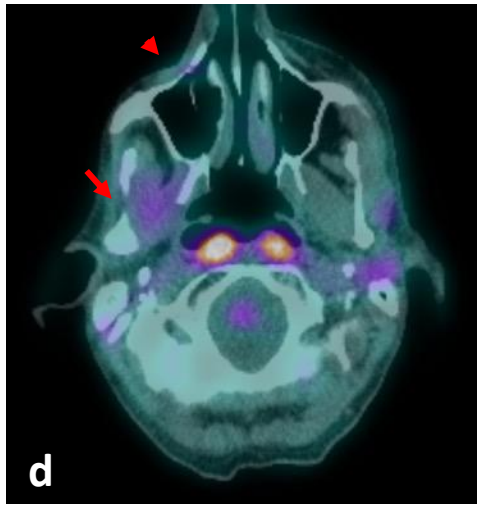
September 2023: Baseline CT performed at study entry



November 1, 2023: First restaging CT at 8 weeks



November 30, 2023: Confirmatory PET-CT at 12 weeks



Abbreviations: SCC-squamous cell carcinoma; CT-computed tomography scan; IV-intravenous; Q2W-every two weeks; PET-positron emission tomography; ICI-immune checkpoint inhibitor
Note: Preliminary clinical data as of October 25, 2024, for an ongoing, open label Phase 1/1b clinical trial.

WTX-124 in Combination with Pembrolizumab Demonstrated Durable Responses in ICI-treated Patients

Dose	Tumor Type	Prior Therapies	Response	Duration
12mg	Melanoma	1. Pembrolizumab/propranolol 2. TVEC	• 3w: Increased T cell activation (biopsy) • 8w: 28.7% ↓ of both TLs • 16w: 39.4% ↓ of both TLs **(RECIST uPR)** • 24w: 39.4% ↓ of both TLs **(confirmed PR)**	• Treatment ongoing >7m • Progression-free
12mg	Melanoma	1. Pembrolizumab 2. Ipilimumab/nivolumab 3. Nivolumab	• 8w: 41.3% ↓ of both TLs **(RECIST uPR)** • 16w: 46% ↓ of both TLs **(confirmed PR)**	• Treatment ongoing >7m • Progression-free

- Combination dose escalation and expansion enrollment are ongoing
- Early evidence of combination anti-tumor activity at clinically active WTX-124 dose

Abbreviations: ICI-immune checkpoint inhibitor; TL-target lesion; uPR-unconfirmed partial response; PR-partial response
Note: Preliminary clinical data as of October 25, 2024, for an ongoing, open label Phase 1/1b clinical trial.

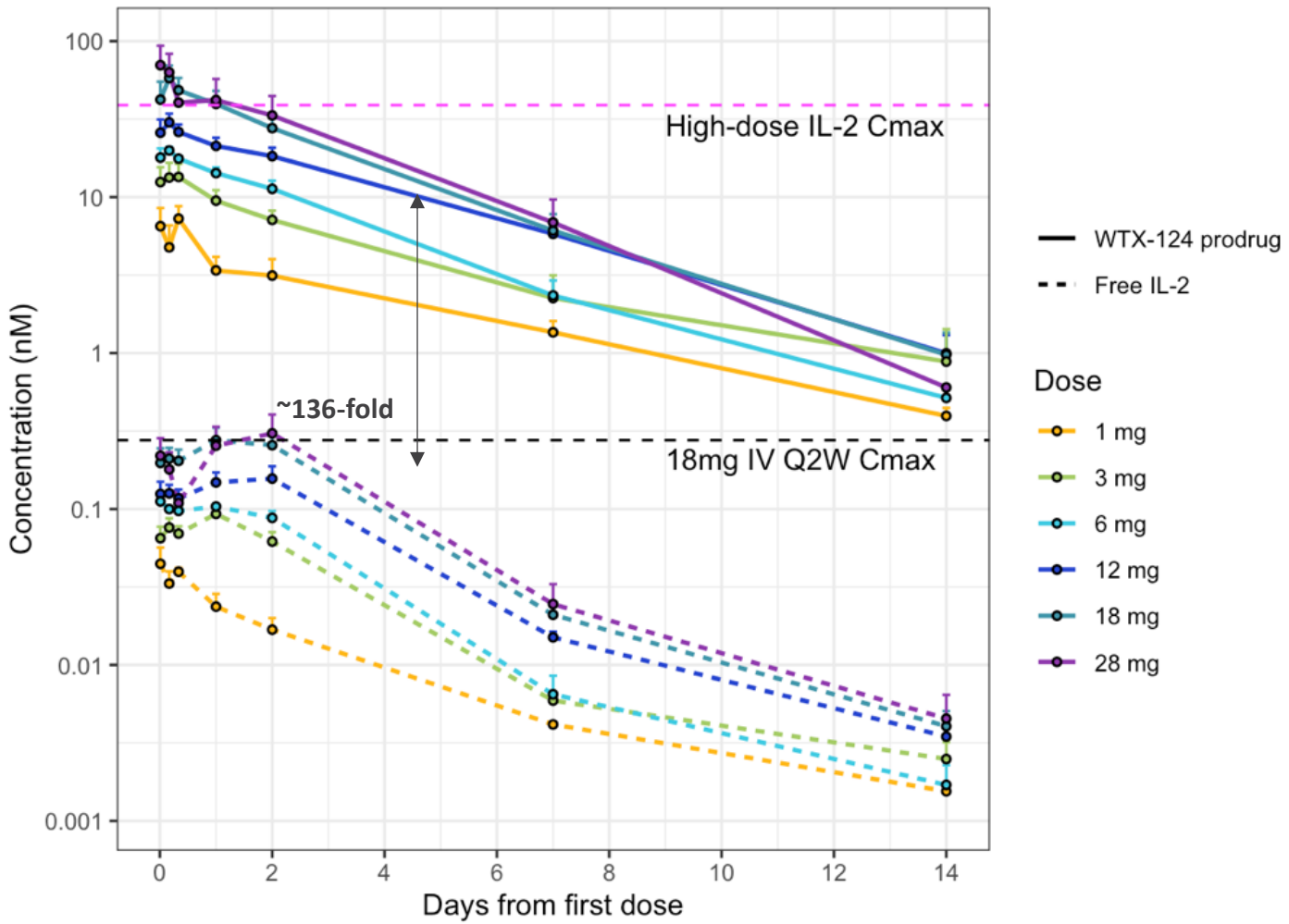
INDUKINE Strategy Successfully Delivered IL-2 to the TME with Low Plasma Exposures

Data support the improved therapeutic index and safety profile of WTX-124 compared to HD IL-2

Preliminary PK findings:

- WTX-124 dosed at 18 mg IV Q2W has a ~1.5-fold higher Cmax than HD IL-2
- Peak free IL-2 exposure after WTX-124 18 mg is ~136-fold lower than HD IL-2
- Across all dose levels, free IL-2 levels are very low (<1.6% of prodrug exposure)
- Accounts for improved tolerability profile compared to HD IL-2

Cycle 1 PK profiles for WTX-124 and free IL-2



Abbreviations: PK-pharmacokinetics; HD-high dose; IV-intravenous; Q2W-once every two weeks

Note: Preliminary clinical data as of May 1, 2024, for an ongoing, open label Phase 1/1b clinical trial.

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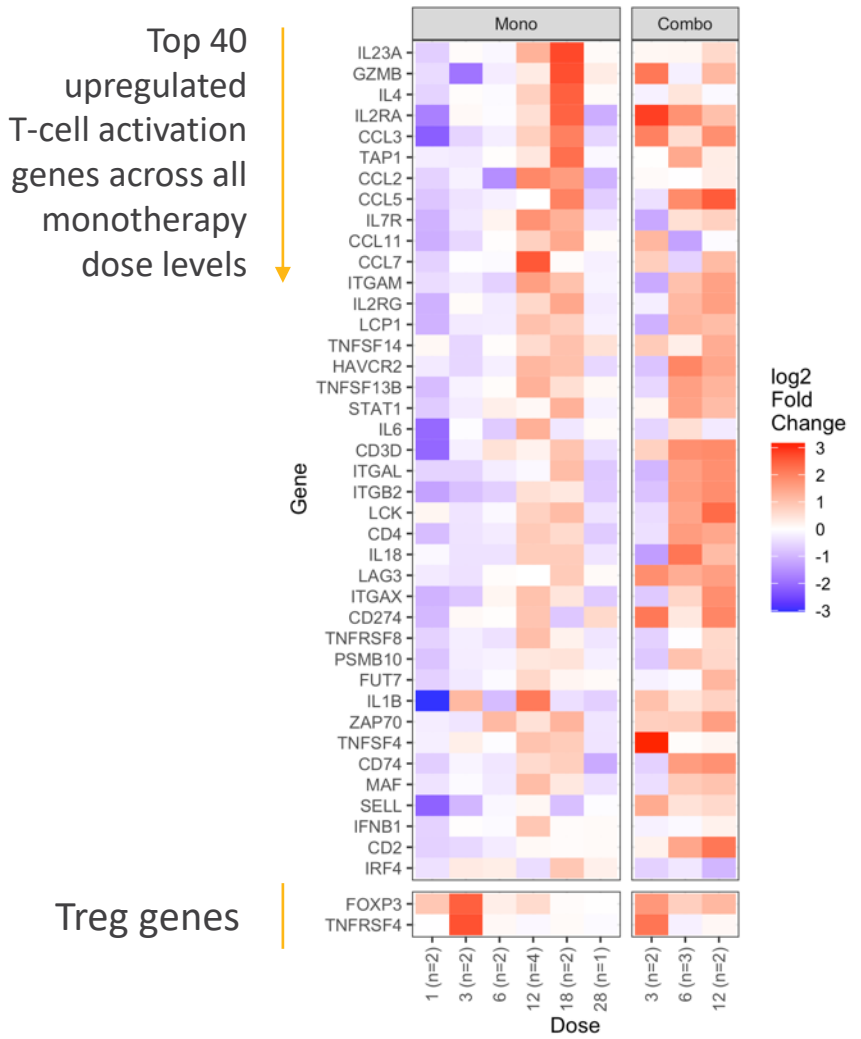
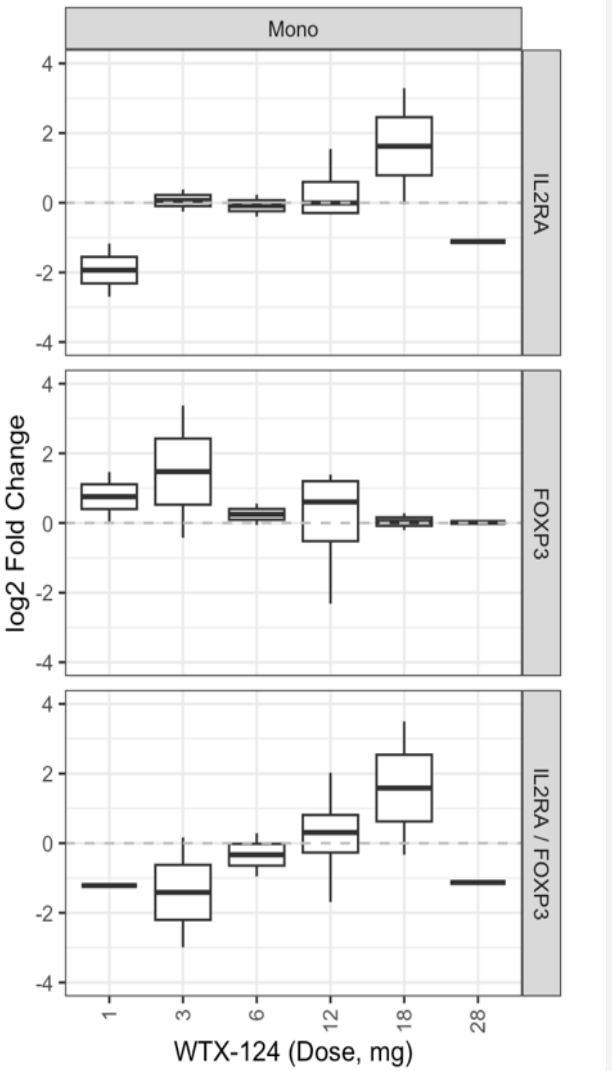
WTX-124 Caused Dose Dependent Increases in Intratumoral T-cell Activation by NanoString

Key insights from tumor biomarkers:

- Largest changes seen at 18 mg (monotherapy) and 12 mg (combination)
- Upregulation of *GRZB* and *IL2RA* signify enhanced effector T cell function
- Treg genes including *FOXP3* and *TNFRSF4* did not increase with dose
- Data indicated preferential expansion of effector T cells over Tregs
- No observed carry-over effect from prior checkpoint inhibitors based on distinct NanoString signature for monotherapy vs. combination at 3 and 6 mg





Note: Data presented for patients for whom on-treatment biopsies were available as of May 1, 2024.

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Preliminary WTX-124 Clinical Data Demonstrate Potential for Best-in-Class IL-2 Therapy

Key Takeaways

- ✓ Monotherapy activity and an improved tolerability profile demonstrated in heavily pretreated patients refractory to all SOC therapies, including immune checkpoint inhibitors
- ✓ Combinations with ICIs and other SOC, including in earlier lines of therapy, supported by tolerable safety profile
- ✓ Patient with primary ICI-resistant CSCC remains in complete response for > 12 months
- ✓ Durable, confirmed partial responses (> 7 months) noted in 2 melanoma patients treated with combination WTX-124 and pembrolizumab
- ✓ WTX-124 18 mg was selected as both the monotherapy and combination RDE based on clinical activity and outpatient safety profile, all expansion arms now open for enrollment

Next Steps

- ✓ Preliminary monotherapy expansion data anticipated in 1H25
- ✓ Engage regulators to discuss potential registrational pathways, including accelerated approval for monotherapy
- ✓ Initiated planning for registrational clinical trial in selected tumor types based on regulatory feedback

Abbreviations: SOC-standard of care; ICI-immune checkpoint inhibitor; CSCC-cutaneous squamous cell carcinoma; RDE-recommended dose for expansion

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Development Strategy Designed to Realize WTX-124 Commercial Opportunity

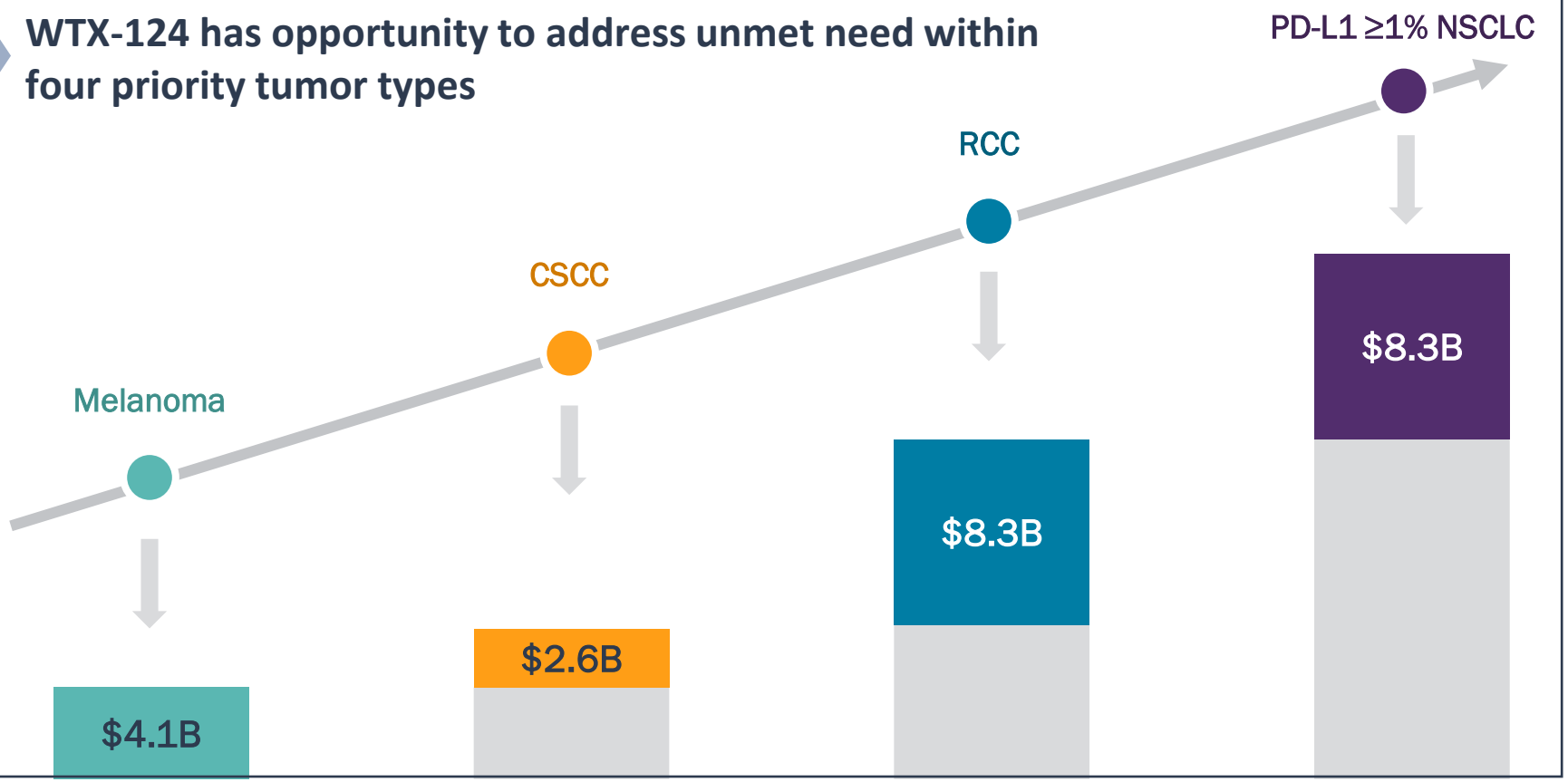
Fast to Market	**Priority Indications:** Engaging with FDA on potential registrational path for monotherapy expansion indications in 2L+ melanoma, RCC, CSCC
Indication Expansion	**Other IO-Sensitive Tumors:** Development in additional indications in expansion based on evolving data
Move Upstream	**Combine with SOC in Earlier Lines:** Safety profile supports combinations in earlier lines of therapy across multiple indications where PD-(L)1 therapy is approved

Abbreviations: RCC-renal cell carcinoma; ICI-immune checkpoint inhibitor; CSCC-cutaneous squamous cell carcinoma; IO-immunotherapy; SOC-standard of care

~$23B Total Market for Four Tumor Types in WTX-124 Development Strategy

Market Size for Melanoma, CSCC, RCC, and PD-L1 ≥1% NSCLC

WTX-124 has opportunity to address unmet need within four priority tumor types



Future WTX-124 Development Plan

WTX-124 has the potential to expand into additional tumor types where PD-(L)1 is approved

A total of ~20 additional tumor types with US revenue of **~$27B**[1] (in 2023)

Source: Bluestar analysis

[1] Based on disclosed 2023 revenue for PD-(L)1

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Market Potential in the US in Advanced/Metastatic Melanoma ~$4.1B Spanning 1L-3L

	US
Incident Cases	14,500

1L Treatment (12,800 pts)

~12,800 patients			
PD-1 monotherapy (KEYNOTE-006)	Nivolumab + Ipilimumab (CheckMate-067)	Nivolumab + LAG3 (RELATIVITY-047)	BRAF + MEK (40-60% pts BRAFmut) Less often 1L Sequenced after IO

$2.5B

2L/3L Treatment (7,700)

~7,700 patients					
PD-1 monotherapy (KEYNOTE-001)	BRAF +/- MEK (Sequencing based on 1L)	PD-1 + CTLA-4 (Sequencing based on 1L)	PD-1 + LAG-3 (Sequencing based on 1L)	TILs (C-144-01)	Chemotherapy

$1.6B

Source: SEER; Melanoma CancerMPact Treatment Architecture 2022

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WTX-330

WTX-330: Leveraging the Potential of IL-12 Therapy to Address IO Resistance

THE CHALLENGE

IL-12 is a potent, pleiotropic cytokine that could address a substantial unmet medical need for patients who are resistant to SOC immunotherapies. Unfortunately, systemic administration of recombinant human IL-12 therapy is associated with severe, unmanageable toxicities that have precluded its clinical development

Unique Advantages of WTX-330, an IL-12 INDUKINE Molecule

Novel prodrug engineered to release a fully potent, wild type IL-12 cytokine selectively in the tumor microenvironment to improve the therapeutic index

Key Opportunities

- Enable patients to benefit from IL-12 therapy for the first time through improved tolerability
- Leverage IL-12 biology to address a significant unmet medical need for patients with poorly immunogenic tumors or tumors resistant to SOC immunotherapies
- Investigate complementary combination strategies to further enhance antitumor activity

Abbreviations: IO-immunotherapy; SOC-standard of care

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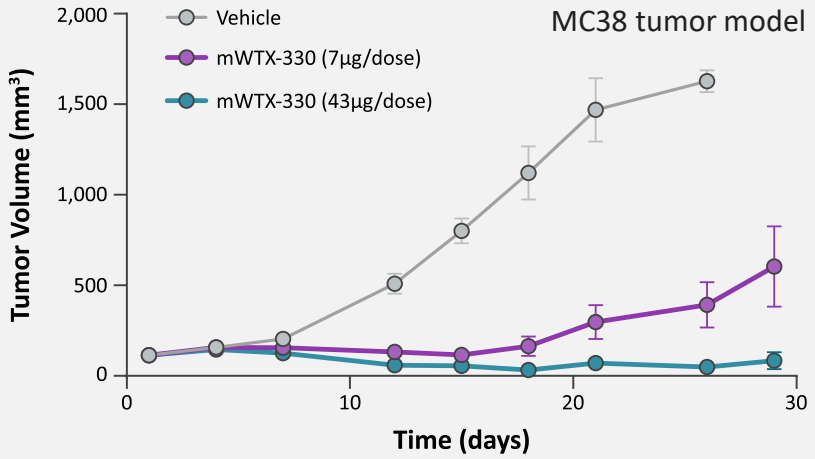
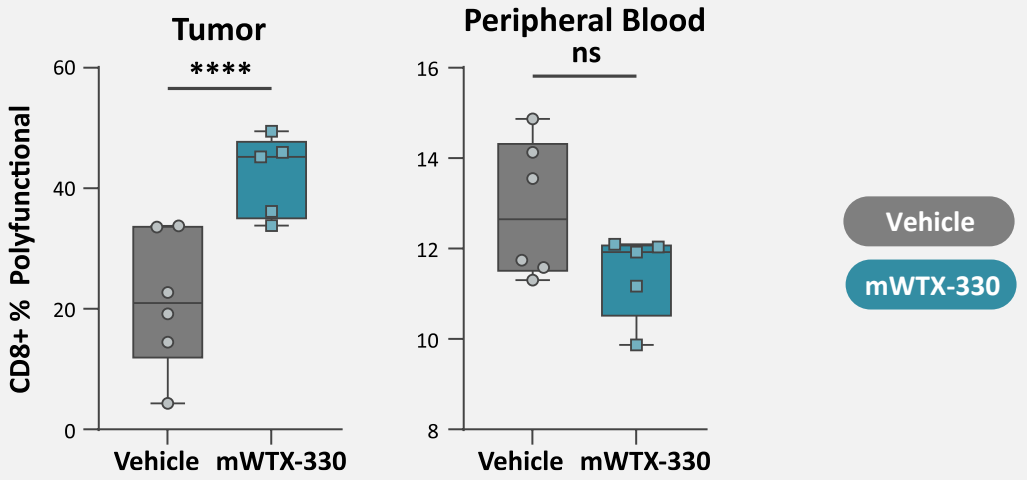
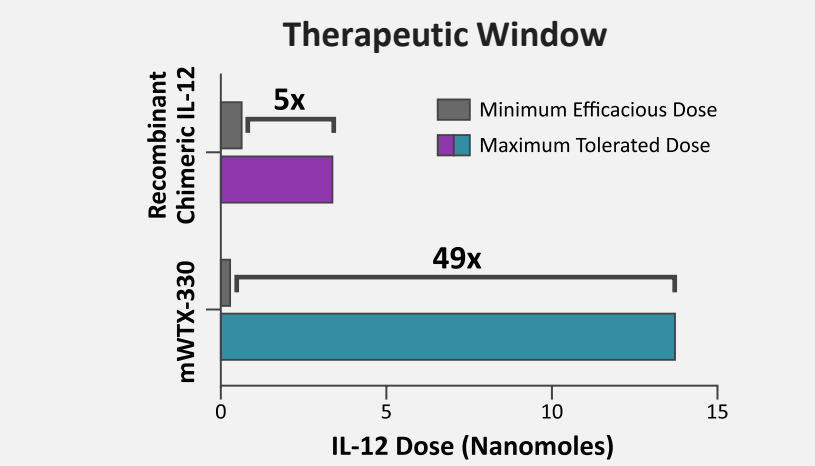
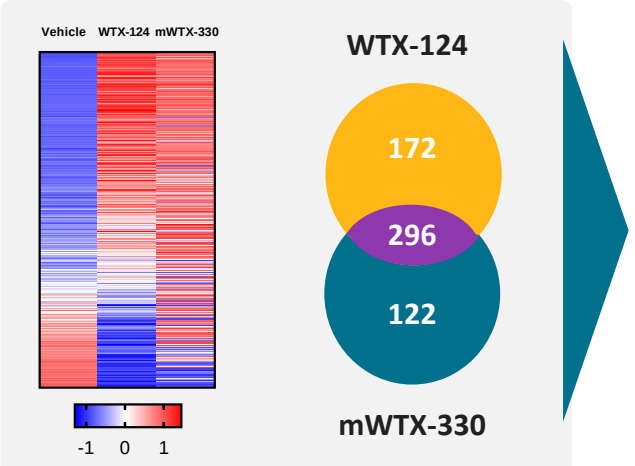
INDUKINE Delivers IL-12 Selectively to Tumor Tissue with an Improved Therapeutic Index

Activation of antitumor CD8+ T effector cells & 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 fragility
- ✓ 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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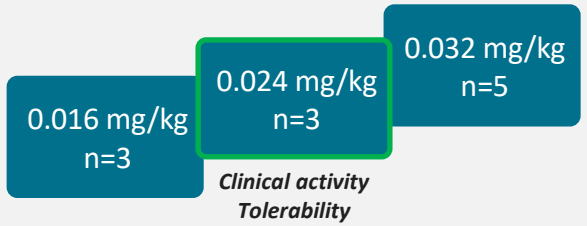
WTX-330 FIH study: Study design and status update

Twenty-five patients have received at least one dose of WTX-330 to date (n=11 in escalation, n=14 in expansion)

Monotherapy Dose Escalation

Patients with solid tumors relapsed/refractory to all SOC



0.024 mg/kg IV Q2W selected for dose expansion arms

Dose Expansion

ARM A (N=5): Patients with IO-sensitive solid tumors who have been treated with a SOC ICI regimen and who have 1° or 2° resistance

ARM B (N=9): Patients with tumors for which ICI therapy is not indicated/approved (IO-naïve)

Trial Details

Bayesian logistic regression model study design

Monotherapy escalation followed by two basket expansion arms

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

Assessment of safety, efficacy, PK, biomarkers, and ADA

On-treatment biomarker analysis (tumor, blood) evaluating proof of mechanism including conditional activation

Abbreviations: FIH-first in human; ICI-immune checkpoint inhibitor; IO-immunotherapy; IV-intravenous; SOC-standard of care; PK-pharmacokinetics; ADA-antidrug antibody; Q2W-once every two weeks
Note: Status of an ongoing, open label Phase 1 clinical trial as of October 7, 2024

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WTX-330 FIH Patient Population was Heterogeneous and Heavily Pretreated

Demographics

AGE (years)	**Mean** (SD)	**64.4** (9.4)
	Median	**64.0**
SEX, n (%)	**Female**	**12** (48.0%)
	Male	**13** (52.0%)
RACE, n (%)	**Black/African-American**	**2** (8.0%)
	White	**21** (84.0%)
	Other/ Unknown	**2** (8.0%)

Tumor Types

Eligible patients had relapsed solid tumors refractory to all SOC

	n (%)
CRC (MSS)	**9** (36.0%)
Melanoma	**4** (16.0%)
PDAC	**3** (12.0%)
NSCLC	**2** (8.0%)
Cholangiocarcinoma	**1** (4.0%)
Endometrial (MSS)	**1** (4.0%)
Urothelial (bladder)	**1** (4.0%)
Soft tissue sarcoma	**1** (4.0%)
Other	**3** (12.0%)

Prior Therapies

Prior lines for metastatic disease[1]

	n (%)
0	**3** (12.0%)
1	**3** (12.0%)
2	**3** (12.0%)
3	**5** (20.0%)
≥4	**11** (44.0%)

Prior lines of immunotherapy

	n (%)
0	**11** (44.0%)
1	**9** (36.0%)
2	**3** (12.0%)
3	**0** (0.0%)
≥4	**2** (8.0%)

Abbreviations: FIH-first-in-human; CRC-colorectal cancer; MSS-microsatellite stable; PDAC-pancreatic ductal adenocarcinoma; NSCLC-non-small cell lung cancer
Note: Preliminary clinical data as of October 7, 2024, in an ongoing Phase 1 clinical trial
[1]Adjuvant treatment regimens were not included

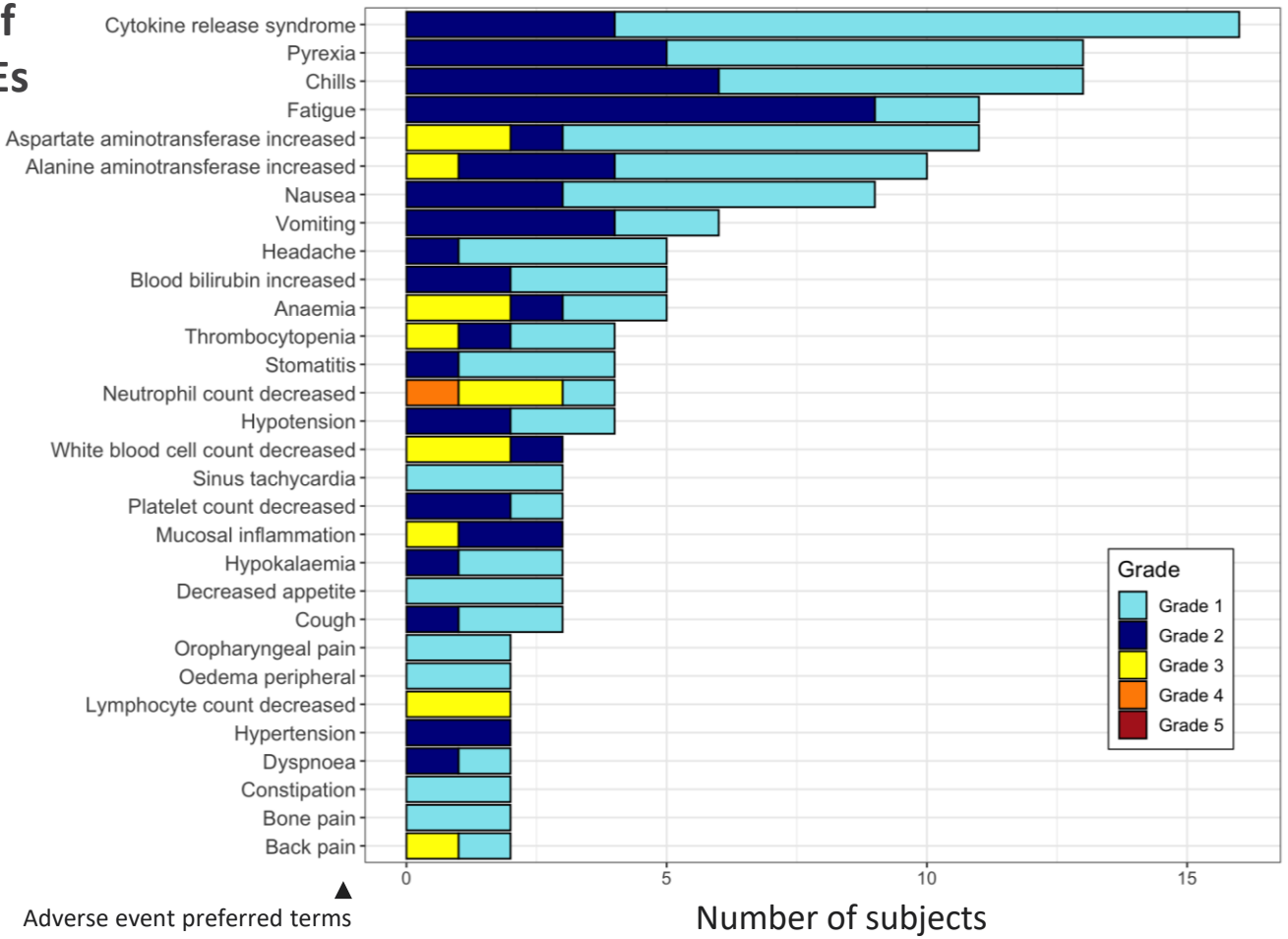
WTX-330 was Generally Well Tolerated as a Monotherapy in the Outpatient Setting

Key safety findings:

- Most frequent related TEAEs were CRS[1], pyrexia, chills, fatigue, and elevated liver function test abnormalities
- Gr3 and Gr4 related TEAEs were manageable, reversible
- Toxicities were typical for systemic IL-12 therapy, less severe compared to rhIL-12, and improved with continued dosing
- Expansions opened at 0.024 mg/kg - two DLTs observed at 0.032 mg/kg (Gr3 mucositis, Gr3 AST increase); no MTD reached

Frequency of related TEAEs occurring in more than one patient

N=25 patients treated with at least one dose of WTX-330 across three dose levels (0.016-0.032 mg/kg IV Q2W)



Abbreviations: TEAEs-treatment-emergent adverse events; CRS-cytokine release syndrome; Gr-grade; DLTs-dose limiting toxicities; AST-aspartate aminotransferase; MTD-maximum tolerated dose
Note: Preliminary clinical data as of October 7, 2024, for an ongoing, open label Phase 1 clinical trial
[1]CRS graded by ASTCT grading scale (see: Lee DW, et al. *Biol Blood Marrow Transplant* 2019;25(4):625–38)

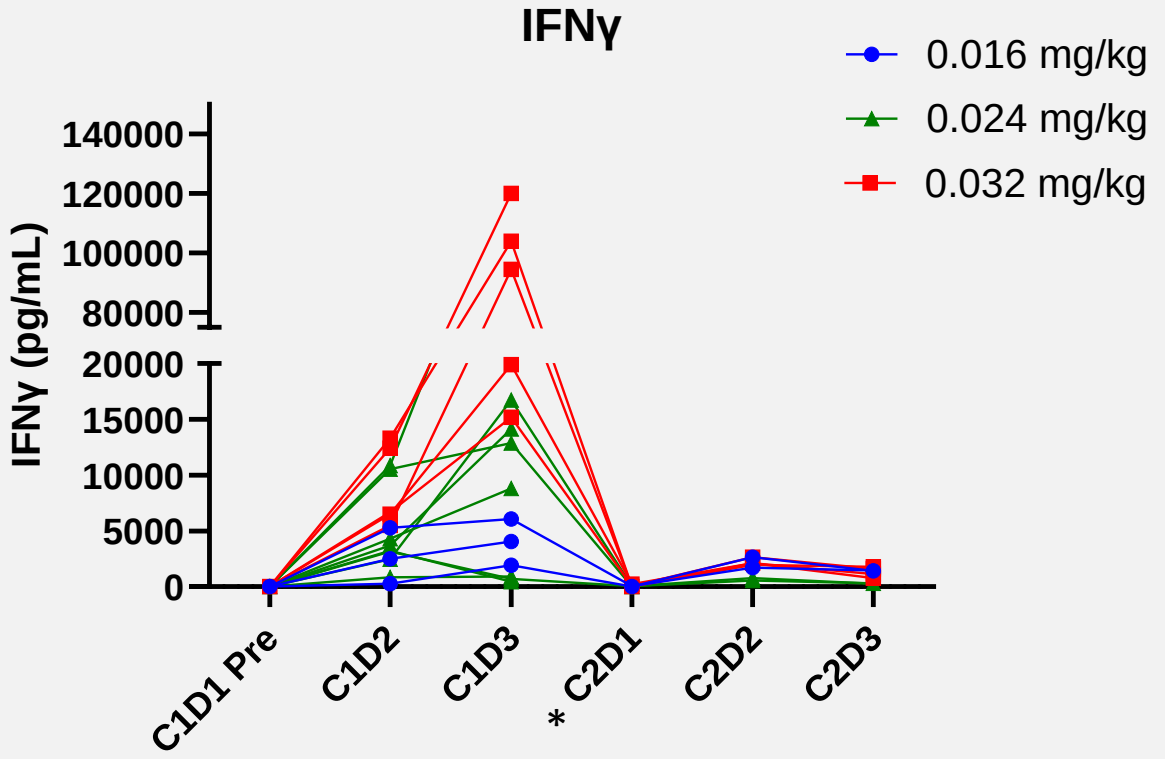
Decreasing Peripheral IFNγ Levels with WTX-330 Dosing Correlate with Improved Tolerability

Analysis of plasma IFNγ levels after WTX-330 dosing showed:

- Dose-related IL-12 induction of IFNγ after the first dose
- IFNγ "tachyphylaxis" beyond the first dose (levels were not measured after 2nd dose)

Implications:

- Elevated IFNγ levels likely account for early WTX-330 adverse events, like CRS
- Decreased IFNγ levels with peripheral IL-12 exposure could potentially be *leveraged* to improve WTX-330 tolerability and maximize tumor IL-12 exposure



*Note that peripheral IFNγ levels were not measured after C1D15 dose

Abbreviations: IFN-interferon; CRS-cytokine release syndrome
Note: Preliminary clinical data as of October 7, 2024, from an ongoing, open label Phase 1 clinical trial

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Early Signs of Clinical Antitumor Activity Across Solid Tumor Indications

Metastatic cutaneous melanoma

- 76-year-old woman with diffuse melanoma in-transit metastases who had progressed on adjuvant pembrolizumab achieved a confirmed PR (RECIST 1.1) for 16 weeks
- 77-year-old woman with melanoma who had discontinued ipilimumab and nivolumab due to toxicity had a 24% target lesion decrease (*ongoing at 12 weeks*)

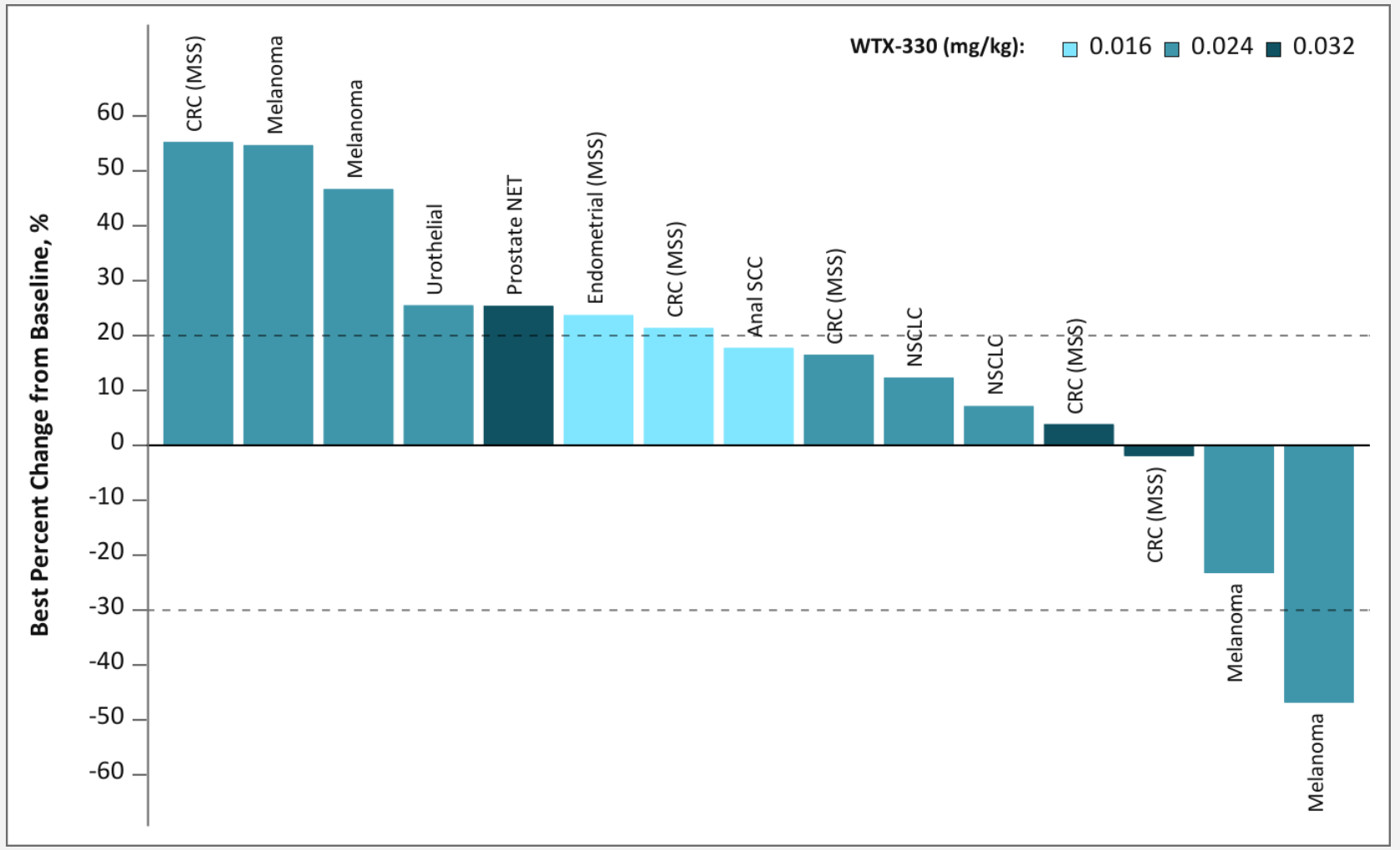
Microsatellite-stable colorectal cancer (MSS CRC) and other GI malignancies

- 50-year-old man who had progressed on seven prior lines of therapy including investigational immunotherapies had stable disease for 24 weeks
- 61-year-old woman who had progressed on SOC chemotherapy combined with bevacizumab had stable disease for 16 weeks
- 74-year-old man with pancreatic ductal adenocarcinoma who had progressed on SOC chemotherapy and radiation therapy demonstrated no growth of the target lesion and no increase in the non-target lesion on the first restaging scan at 8 weeks (*patient ongoing*)

Abbreviation: PR-partial response; MSS-microsatellite stable; CRC-colorectal cancer; GI-gastrointestinal; SOC-standard of care

WTX-330 Demonstrated Monotherapy Clinical Activity Across Diverse Tumor Types

One patient with a confirmed PR (RECIST 1.1) and an additional seven patients with stable target lesions (n=15)[1]



Abbreviations: MSS-microsatellite stable; CRC-colorectal cancer; NET-neuroendocrine tumor; SCC-squamous cell cancer; NSCLC-non-small cell lung cancer; PR-partial response

Note: Preliminary clinical data as of October 7, 2024, for an ongoing, open label Phase 1 clinical trial

[1]An additional patient with pancreatic ductal adenocarcinoma was evaluable and had an overall response of RECIST SD, but the data were not entered at the time of the database snapshot

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Treatment Response in Melanoma Patient with a Confirmed RECIST PR

76-year-old woman with a *BRAF* wild type metastatic in-transit melanoma who progressed while receiving adjuvant pembrolizumab

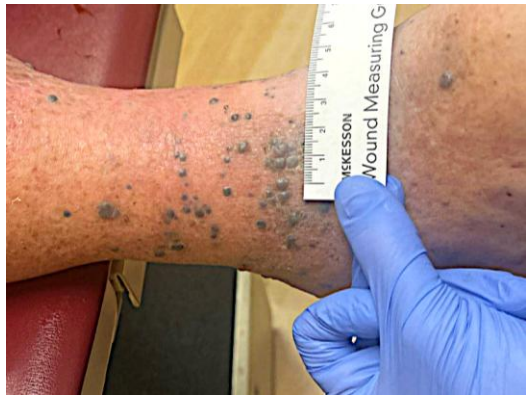
Patient had diffuse RLE cutaneous metastases, a non-healing melanomatous ulcer and an enlarged right inguinal lymph node

Initiated treatment with **0.024 mg/kg WTX-330 IV Q2W** more than two months after discontinuing pembrolizumab

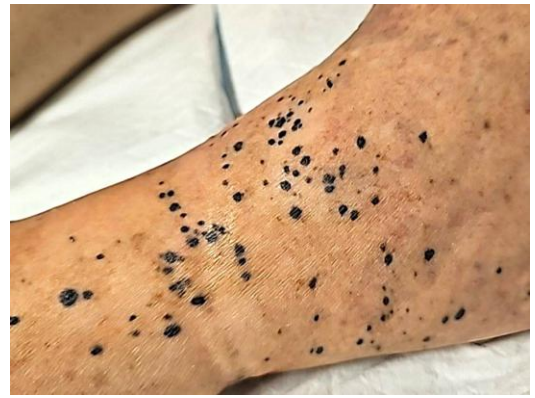
Timeline of response to WTX-330:

- **3 weeks:** On-treatment excisional biopsy of RLE skin nodules showed no tumor
- **7-8 weeks:** 47% decrease of TL (cluster of RLE skin nodules); no increase in NTLs (=unconfirmed PR). Punch biopsies of two pigmented lesions showed no active melanoma
- **10 weeks:** PET-CT showed reduced tumor metabolic activity
- **16 weeks:** RECIST PR confirmed with ongoing TL response, complete resolution of one NTL and no increase in second NTL. Patient discontinued therapy due to a related anemia

March 2024 (pretreatment): Patient progressing at melanoma in-transit metastases of RLE

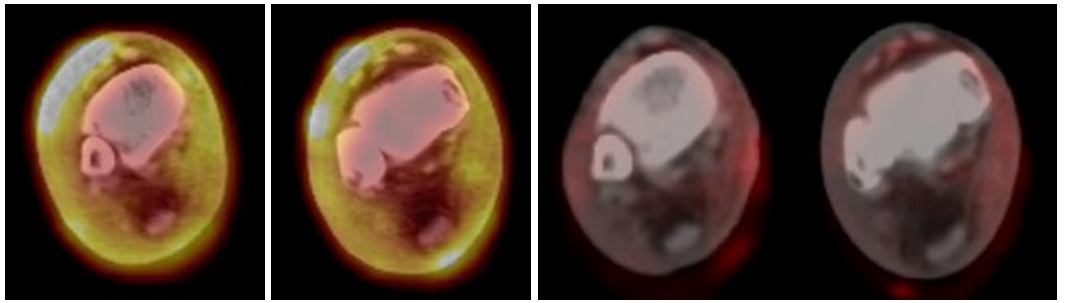


May 2024: After three doses of WTX-330, many nodules have flattened and/or regressed



January 2024 (pretreatment): PET-CT shows progression of melanoma in-transit metastases during adjuvant pembrolizumab

May 2024: After three doses of WTX-330, repeat PET-CT shows markedly decreased tumor metabolic activity in RLE



Shown are two different transverse sections of RLE at each timepoint

Abbreviations: PR-partial response; IV-intravenous; Q2W-once every two weeks; EOT-end of treatment; RLE-right lower extremity; TL-target lesion; NTL-non-target lesion

Note: Preliminary clinical data as of October 7, 2024, for an ongoing, open label Phase 1 clinical trial

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Evidence of Durable Treatment Effect in Melanoma Patient with Confirmed PR

At **28 weeks**, approximately 12 weeks after discontinuing WTX-330, the patient was noted to have an ongoing response at a subset of lesions (off all therapy)

- **Pretreatment (March 2024)**: Prior to initiating treatment with WTX-330, the patient was progressing at a melanomatous ulcer (medial RLE) and at numerous in-transit metastases (medial, lateral RLE)
- **Post-treatment (September 2024)**: After a total of four doses of WTX-330, the ulcer had healed and a subset of nodules showed durable regression despite the overall mixed response

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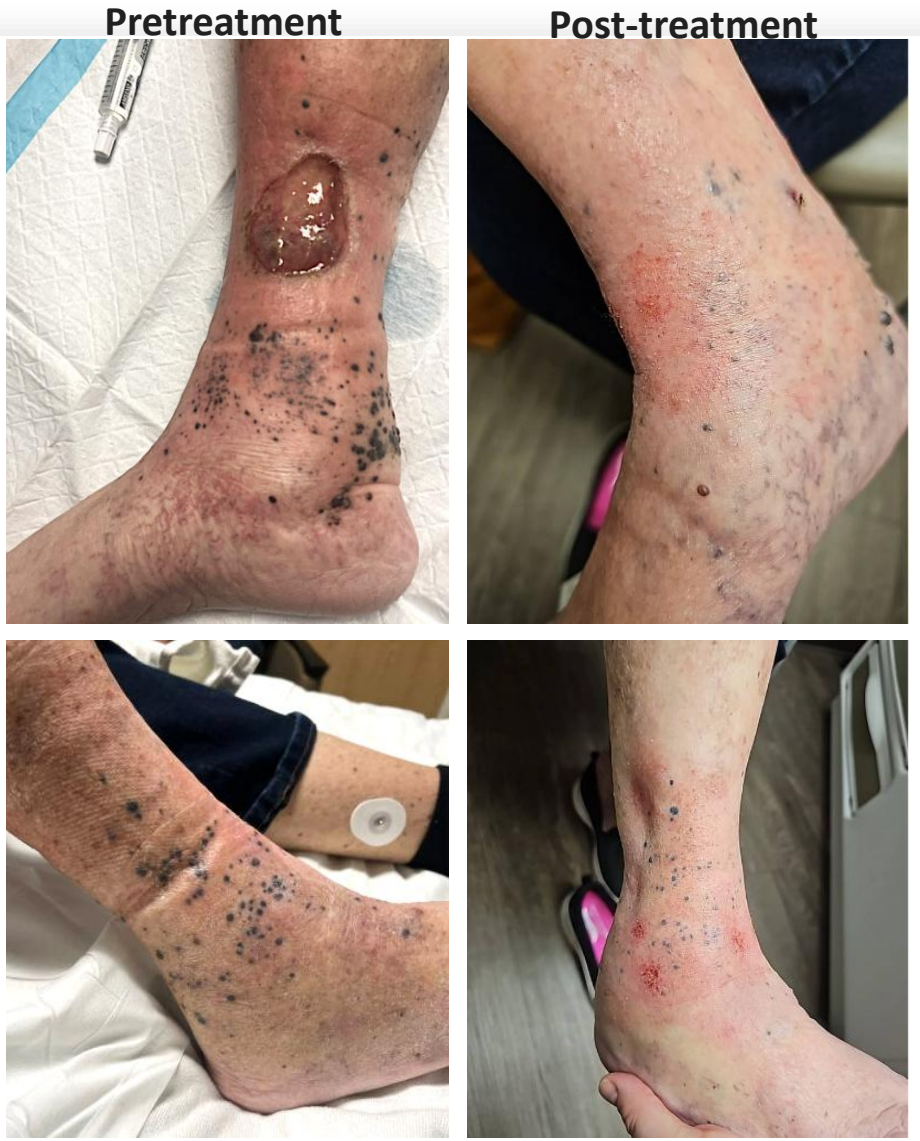

Abbreviations: PR-partial response; RLE-right lower extremity

Note: Preliminary clinical data as of October 7, 2024, for an ongoing, open label Phase 1 clinical trial

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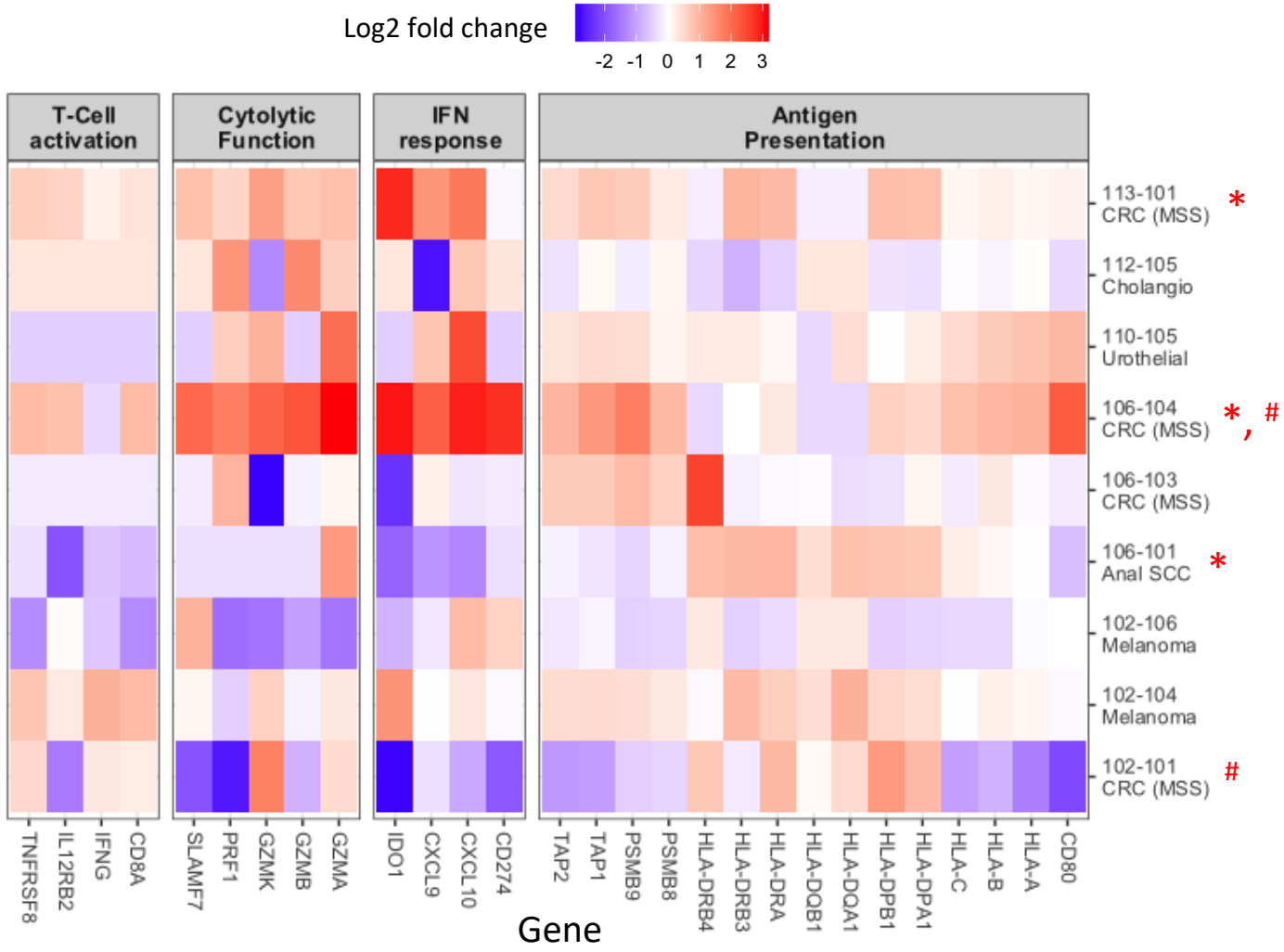
WTX-330 Increased Expression of T/NK Cell Activation & Antigen Presentation Genes

NanoString data show evidence of pleotropic IL-12 activities in the tumor microenvironment, including in MSS CRC

Changes in gene expression caused by WTX-330 demonstrating IL-12 activity:

- Increased expression of *IFNG, IL12RB2, CD8A, GRZMB and PRF1* associated with T cell activation and/or cytolytic function
- Increased expression of *CD274*, *CXCL10* and *CXCL9* consistent with an IFN response
- Upregulation of genes involved with antigen processing and presentation



Abbreviations: IFN-interferon; MSS-microsatellite stable; CRC-colorectal cancer; Cholangio-cholangiocarcinoma; SCC-squamous cell cancer; PD-pharmacodynamic

* Indicates that biopsied lesion was a liver metastasis; # representative multiplexed immunofluorescence analyses shown on next slide for these patients

Note: Preliminary clinical data as of October 7, 2024, from an ongoing, open label Phase 1 clinical trial; figure does not include data from responding melanoma patients as biopsies showed no tumor

N=9 patients contributing paired tumor biopsies

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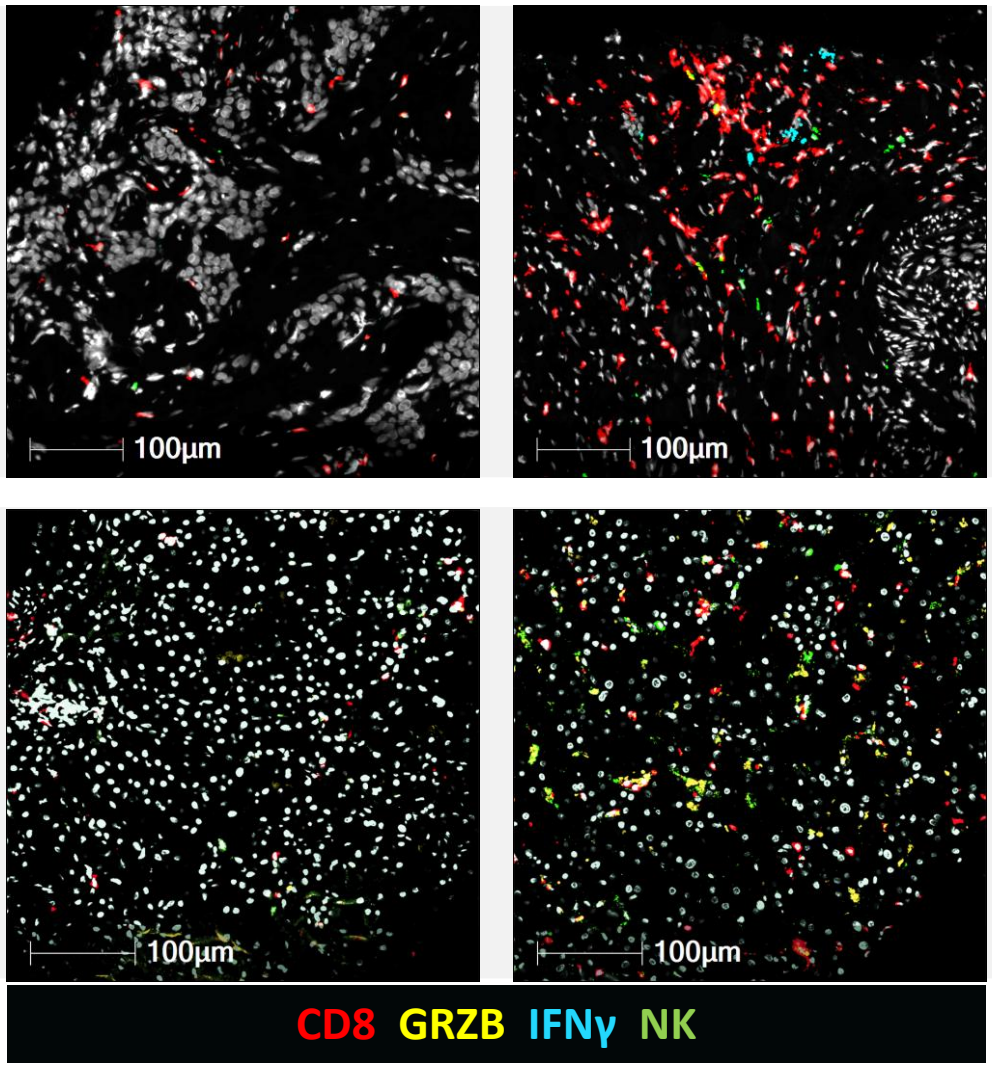
Additional Evidence of Increased T/NK cell Expansion and Activation in MSS CRC

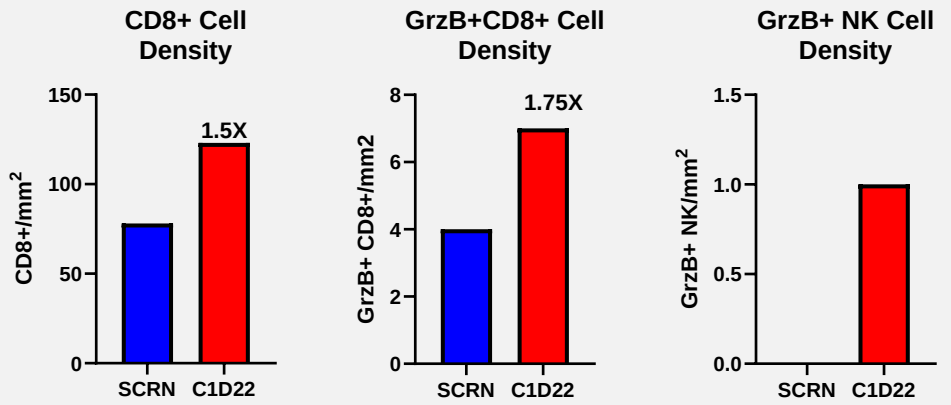
102-101
MSS CRC
Retroperitoneal lymph node

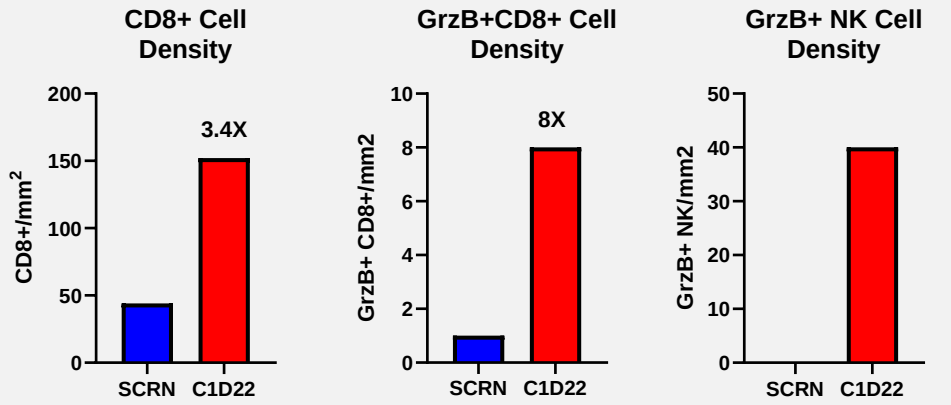
Overall response:
SD x 24wks

106-104
MSS CRC
Liver metastasis

Overall response:
PD







Abbreviations: NK-natural killer; MSS-microsatellite stable; CRC-colorectal cancer; SD-stable disease; PD-progressive disease; wks-weeks, GrzB-granzyme B; scrn-screening (i.e., baseline/pretreatment)
Note: Preliminary clinical data as of October 7, 2024, from an ongoing, open label Phase 1 clinical trial

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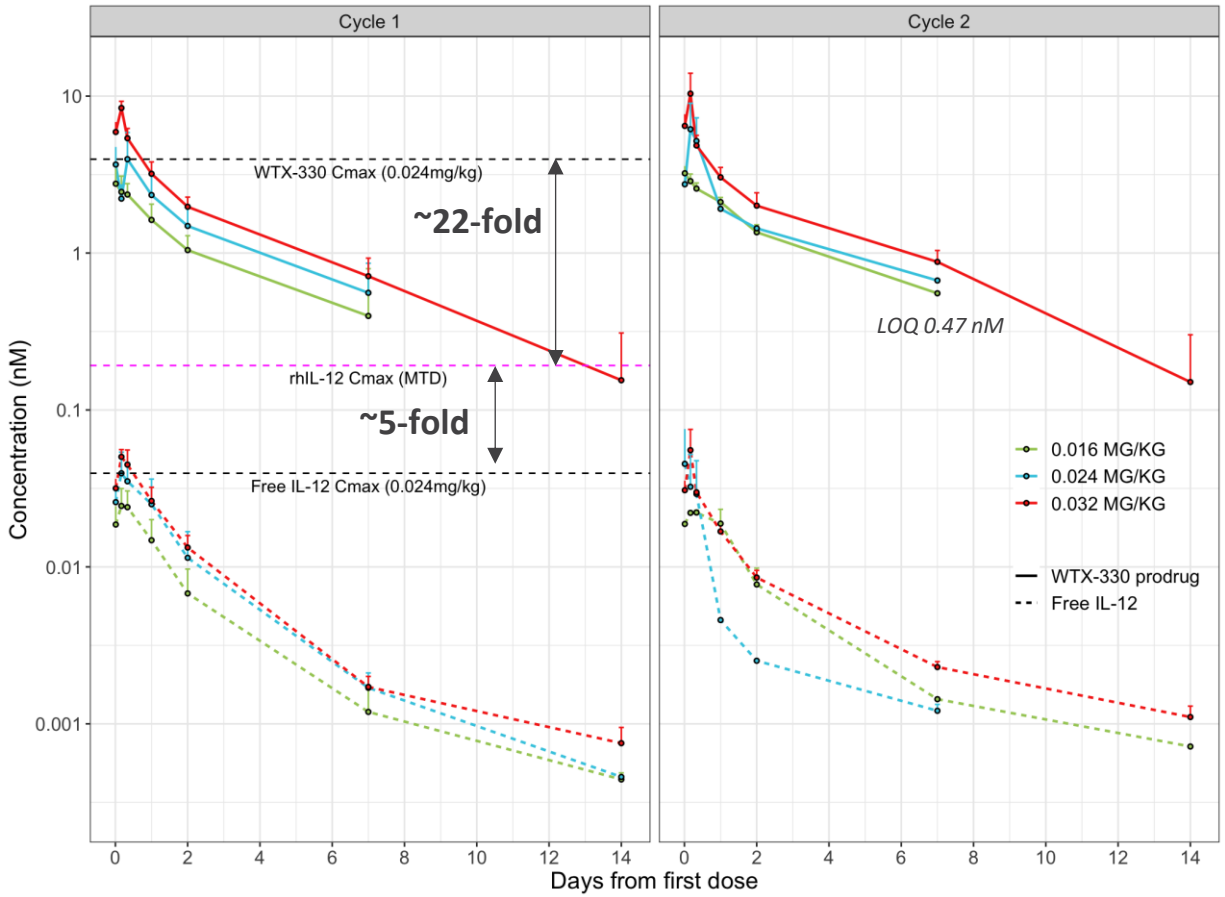
WTX-330 Delivered 22-fold > IL-12 Compared to Recombinant Human IL-12 Therapy at its MTD

PK data account for the improved therapeutic index of WTX-330 compared to rhIL-12

Preliminary PK findings:

- WTX-330 dosed at 0.024 mg/kg IV Q2W has a ~22-fold higher Cmax than rhIL-12 at its MTD (500 ng/kg; Atkins MB et al. 1997)
- Peak free IL-12 exposure after 0.024 mg/kg WTX-330 is ~5-fold lower than rhIL-12 at its MTD
- Across all dose levels, free IL-12 levels are very low (<1.6% of prodrug exposure)
- WTX-330 PK is approximately dose-proportional from 0.016 to 0.032 mg/kg
- PK exposure generally preserved upon repeat dosing

PK profiles for WTX-330 and free IL-12 compared to rhIL-12 Cmax at its MTD (mean ± SEM)



Abbreviations: MTD-maximum tolerated dose; PK-pharmacokinetic; IV-intravenous; Q2W-once every two weeks

Note: Preliminary PK data as of June 21, 2024, from an ongoing, open label Phase 1 clinical trial

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WTX-330 is a Potentially First-in-Class Systemically Administered IL-12 Therapy

Key Takeaways

- ✓ **First systemically administered IL-12 therapy with monotherapy clinical activity and a generally tolerable safety profile**
- ✓ **Increased therapeutic window:** WTX-330 delivered 22-fold more IL-12 on a molar basis than rhIL-12 therapy at its MTD
- ✓ **INDUKINE design proof-of-concept:** Second clinical program validating the INDUKINE design for delivery of toxic immune payloads with improved tolerability and clinical benefit
- ✓ **Safety and tolerability profile:** Related TEAEs were primarily mild to moderate in severity and consistent with known IL-12 safety profile; severe AEs were manageable and reversible
- ✓ **Antitumor Activity:** Demonstrated by a confirmed RECIST PR and target lesion shrinkage in two melanoma patients and stable disease for 16 and 24 weeks in two MSS CRC patients
  - NanoString data showed evidence of pleotropic IL-12 activity in the TME
  - Tumor biopsies from four patients with MSS CRC showed immune activation, including in liver metastases

Next Steps

- ✓ Planning underway for Phase 1/2 dose- and regimen-finding study to optimize WTX-330 exposure in TME –expected to begin enrolling 1H25
- ✓ Exploring antitumor activity in selected tumor types

Abbreviations: MTD-maximum tolerated dose; TEAE-treatment-emergent adverse events; AE-adverse event; MSS-microsatellite stable; CRC-colorectal cancer; PR-partial response; TME-tumor microenvironment

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WTX-712

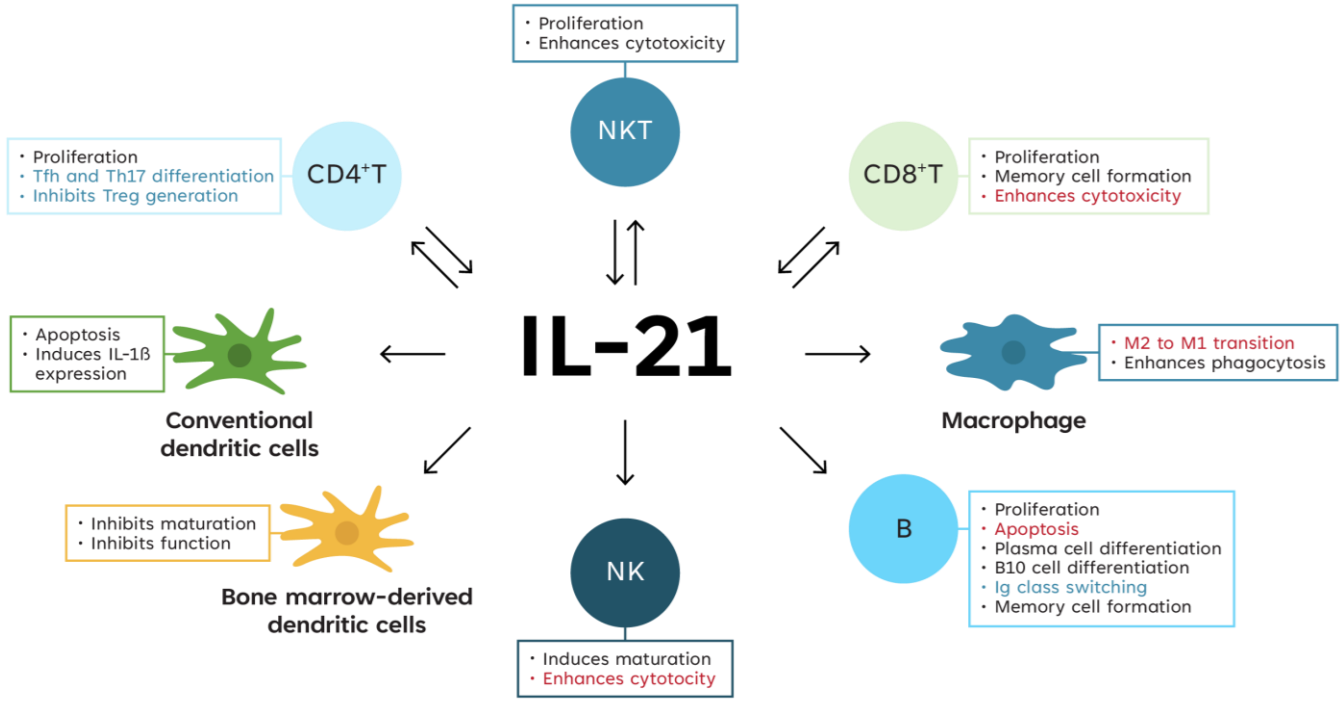
WTX-712: Expanding the Utility of IL-21 Therapy

Potential WTX-712 Advantages

- IL-21 is a differentiated, pleiotropic cytokine that drives effective antitumor response by activating multiple immune cell types
- Recombinant IL-21 has shown clinical antitumor activity but has not been developed due to dose-limiting toxicities
- Preclinical data demonstrated that IL-21 is active in ICI-resistant models
- WTX-712 is designed to deliver IL-21 to the TME and improve the therapeutic index

Status

- IND-enabling studies



From IL-21 Signaling in Immunity | F1000Research

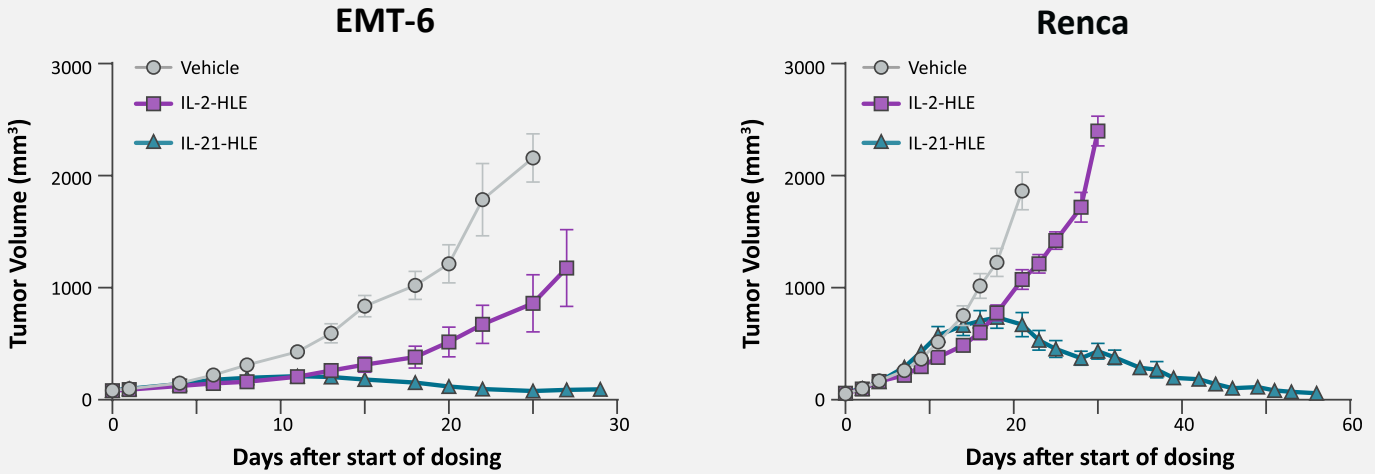
IL-21 activates multiple immune cell types, inhibiting Tregs and promoting M1 macrophage function. By driving a less terminally differentiated stage of CD8+ T cells, IL-21 results in sustained CTL expansion and activity in tumors.

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
Sullivan JM et al., AACR 2024 Poster: WTX-712, a Conditionally Active IL-21 INDUKINE™ Molecule, Induces a Strong Anti-tumor Phenotype Through a Differentiated Mechanism

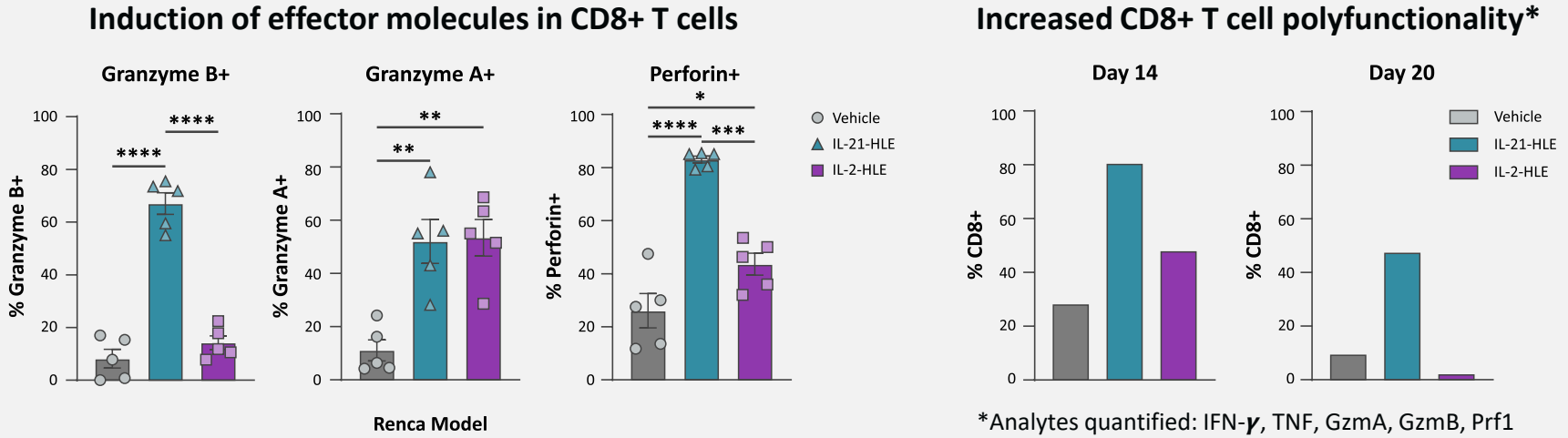
Abbreviations: ICI-immune checkpoint inhibitor; CTL-cytotoxic T lymphocyte

IL-21 Elicits a Highly Effective CD8+ T Cell Response in ICI-Refractory Preclinical Models

IL-21 is active in several ICI refractory models and can provide greater antitumor activity than IL-2



IL-21 treatment results in a sustained intratumoral polyfunctional CD8+ T cell response optimally suited to cell killing



*Analytes quantified: IFN-γ, TNF, GzmA, GzmB, Prf1

Sullivan JM et al., AACR 2024 Poster: WTX-712, a Conditionally Active IL-21 INDUKINE™ Molecule, Induces a Strong Anti-tumor Phenotype Through a Differentiated Mechanism

Abbreviations: ICI-immune checkpoint inhibitor

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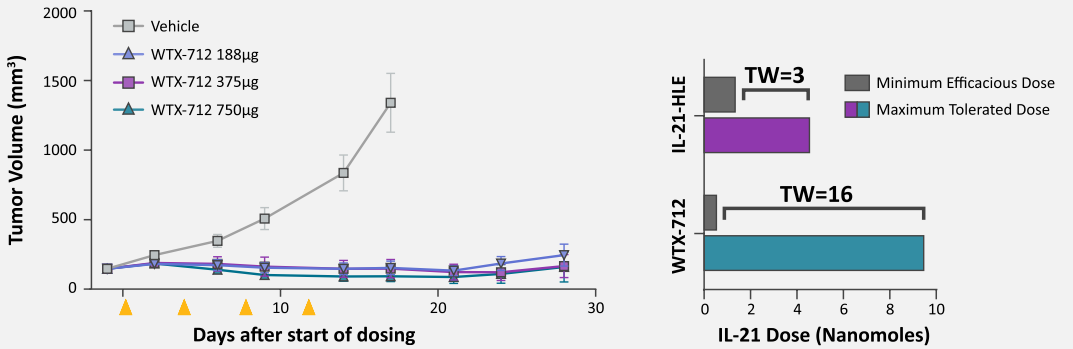
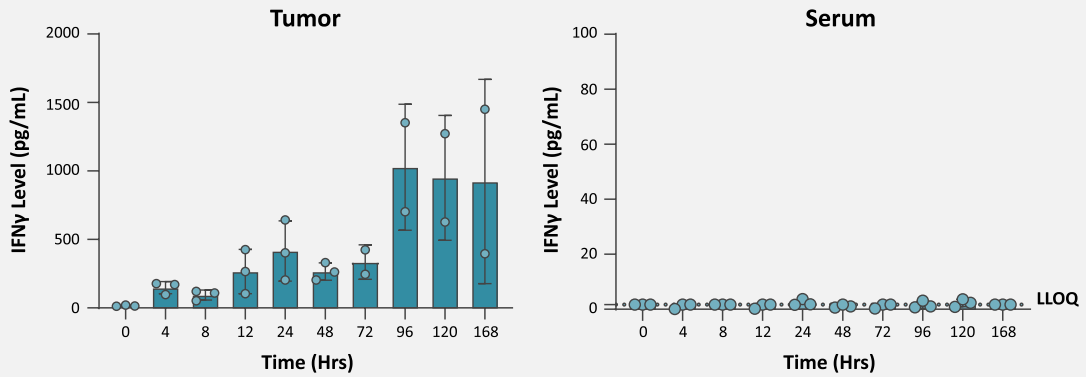
WTX-712 Tumor Selective Activity Results in Robust Antitumor Immune Activation in Preclinical Models

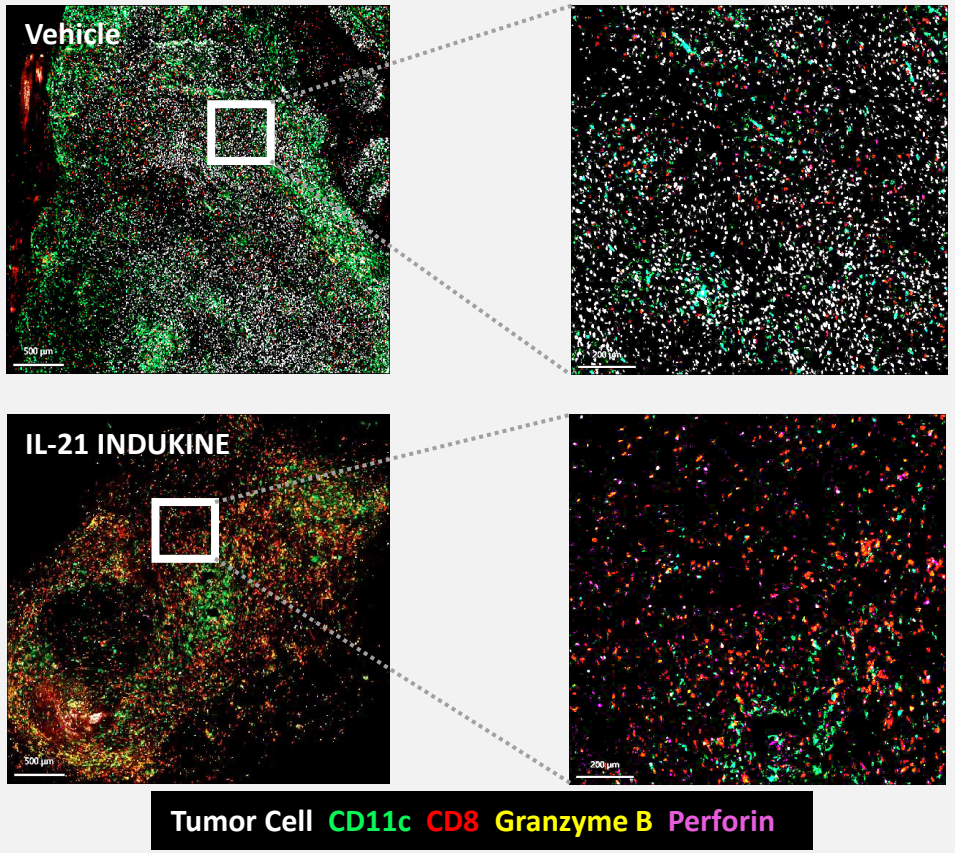
WTX-712 antitumor activity in MC38 tumor model with an improved therapeutic window compared to IL-21 cytokine



WTX-712 specifically induces IFNγ in the tumor



IL-21 INDUKINE treatment transforms the tumor microenvironment with robust and rapid effector CD8+ T cell response to drive tumor regressions



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
Sullivan JM et al., AACR 2024 Poster: WTX-712, a Conditionally Active IL-21 INDUKINE™ Molecule, Induces a Strong Anti-tumor Phenotype Through a Differentiated Mechanism

Abbreviation: TW-therapeutic window

Werewolf THERAPEUTICS

WTX-518

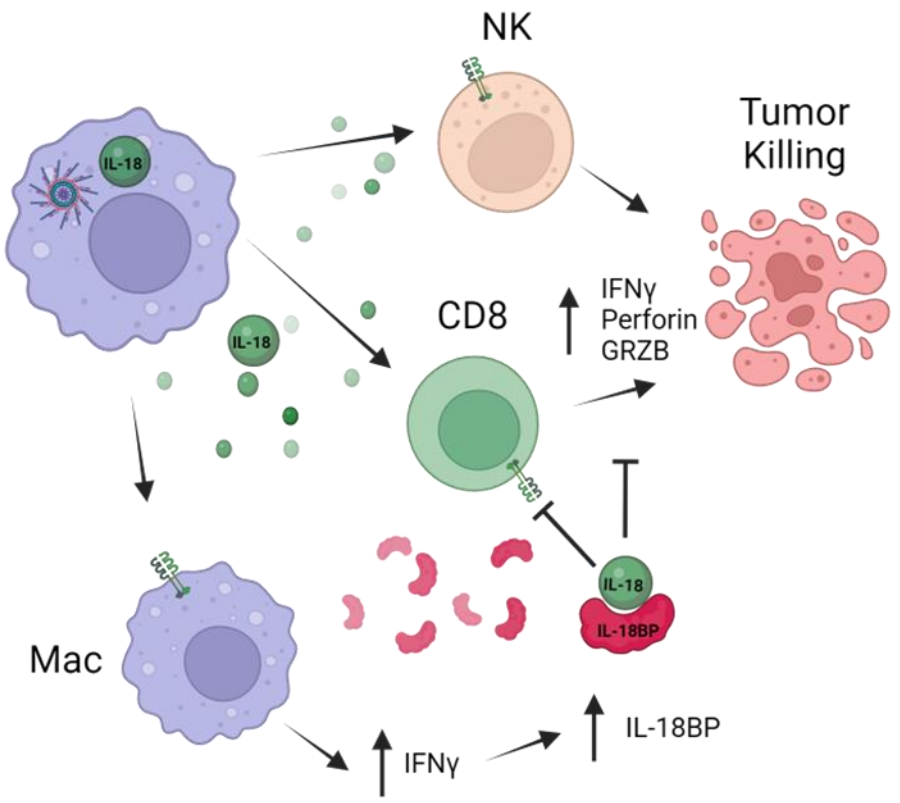
WTX-518: Regulating Multiple Immune Cell Types to Drive Antitumor Immunity

Potential WTX-518 Advantages

- IL-18 elicits an antitumor immune response by promoting the collaboration of multiple immune cell types and increasing stem-like CD8+ T cells
- WTX-518 is designed to uniquely eliminate the ability of IL-18BP to inhibit IL-18 and systemically deliver IL-18 within the TME
- Potential to complement WTX-330 based on the known synergy of IL-18 and IL-12 to drive T cell activation

Status

- IND-enabling studies



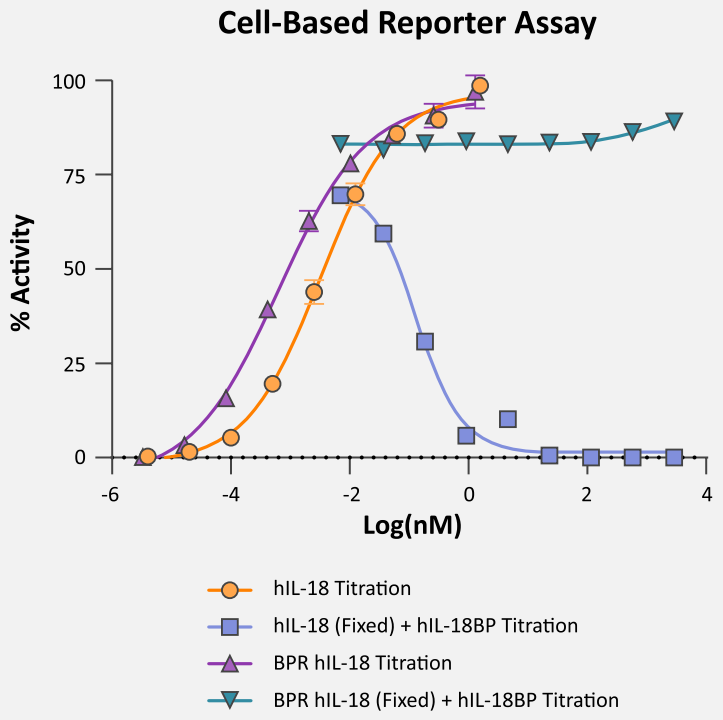
IL-18 activates innate and adaptive immune cells promoting IFN-γ production by antigen-experienced T cells and favoring Th1 differentiation of naïve T cells

Morris KR et al., AACR 2024 Poster: Discovery of WTX-518, an IL-18 pro-drug that is conditionally activated within the tumor microenvironment and induces regressions in mouse tumor models
Abbreviations: TME-tumor microenvironment; BP-binding protein

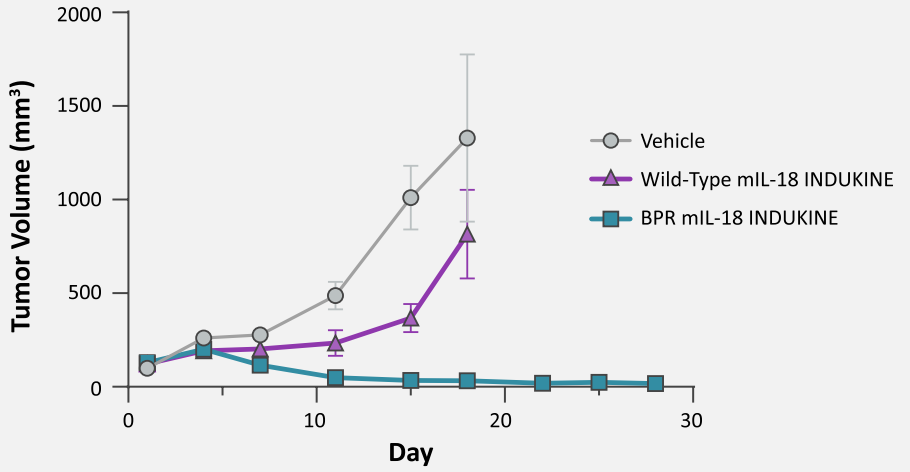
WTX-518 is Resistant to IL-18 Binding Protein with Improved Antitumor Activity

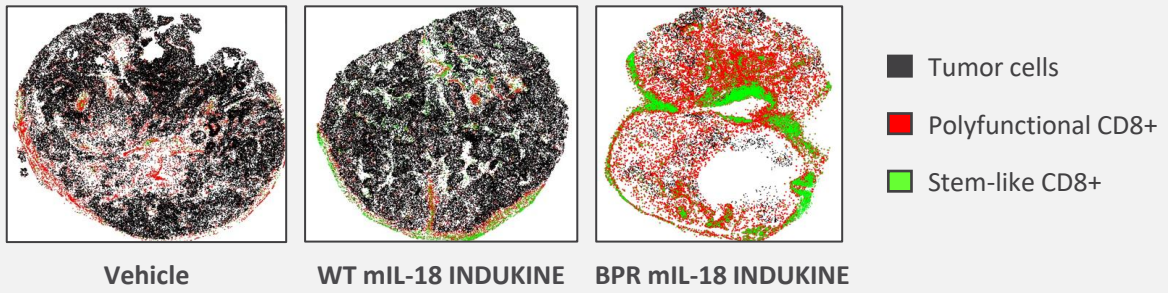
BPR mIL-18 INDUKINE triggers tumor cytotoxicity and transforms the TME

WTX-518 retains potency while preventing binding to IL-18BP



BPR mIL-18 INDUKINE provides greater efficacy than wild-type IL-18 INDUKINE in the MC38 tumor model and increased density of polyfunctional and stem-like CD8+ T cells





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

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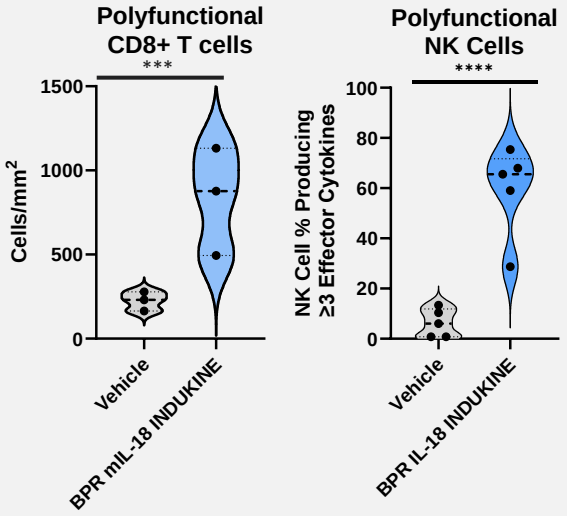
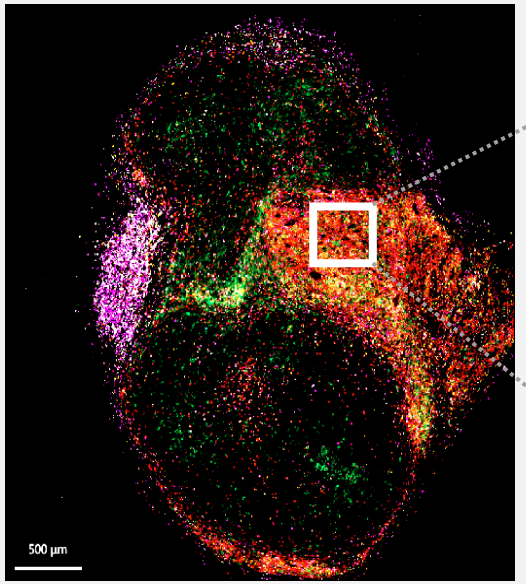
BPR mIL-18 INDUKINE Treatment Promotes Robust Effector Activation and Immune Cell Interactions

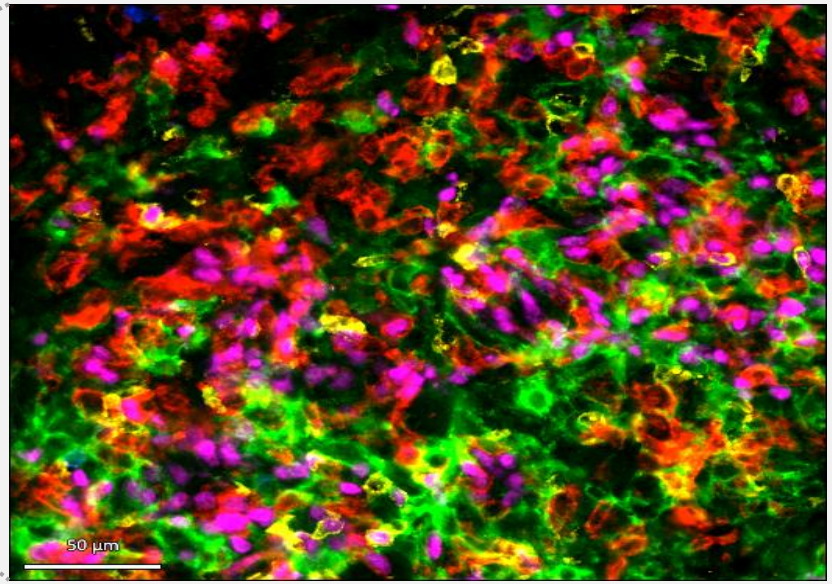
BPR mIL-18 INDUKINE increases density of polyfunctional effector cells



BPR mIL-18 INDUKINE triggers the formation of immune cell hubs, including stem-like CD8+ T cells, driving the regression of established tumors



Tumor Cell CD11c CD8
Granzyme B Perforin



CD11c CD8 TCF1 CD4 Nkp46

Abbreviation: BPR-binding protein resistant

Werewolf THERAPEUTICS

WTX-921

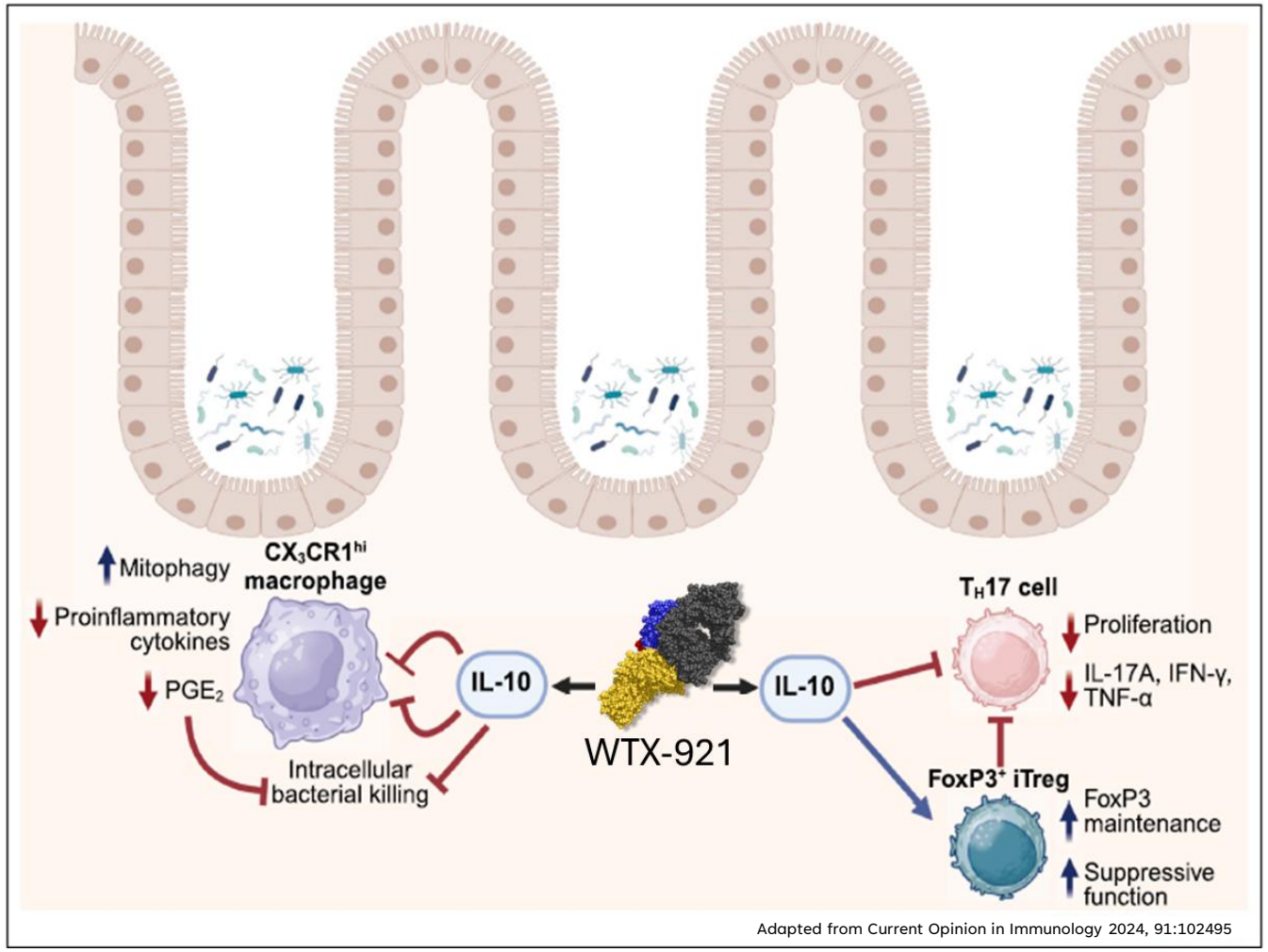
WTX-921: IL-10 INDUKINE Therapy for Inflammatory Bowel Disease

Potential WTX-921 Advantages

- Selective delivery of IL-10 to inflamed tissues to minimize systemic toxicity
- Multipronged effect by inhibiting disease driving innate and adaptive immune cell populations
- Targeted delivery of IL-10 can potentially block several disease driving effector molecules and cytokines

Status

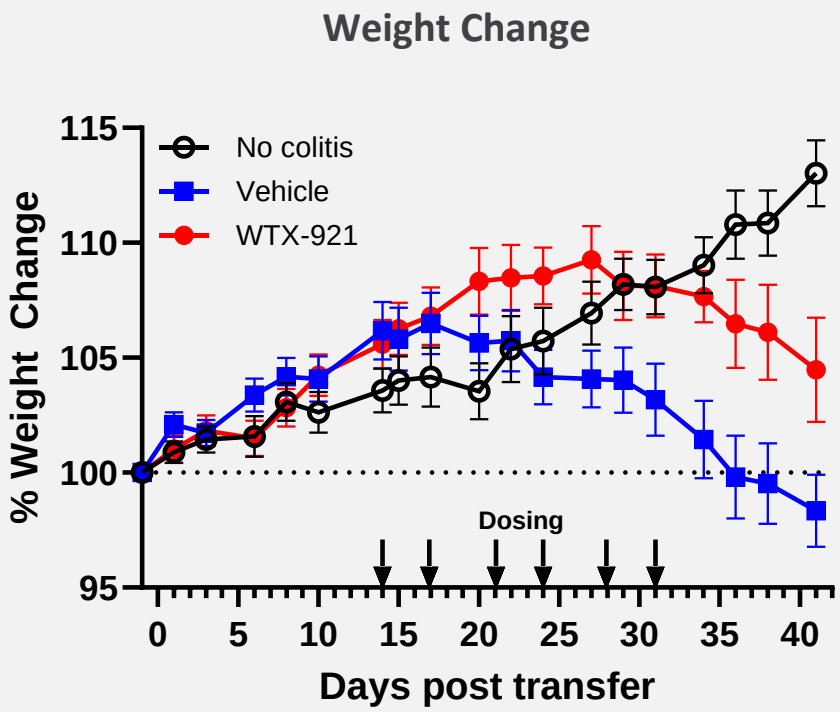
- Available for partnership

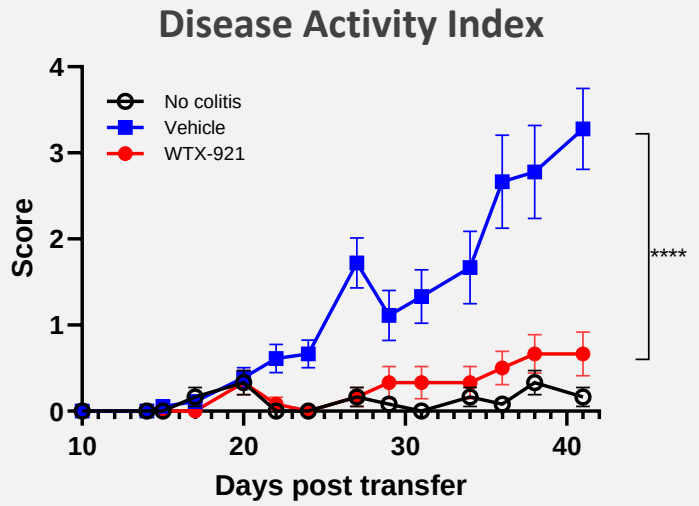


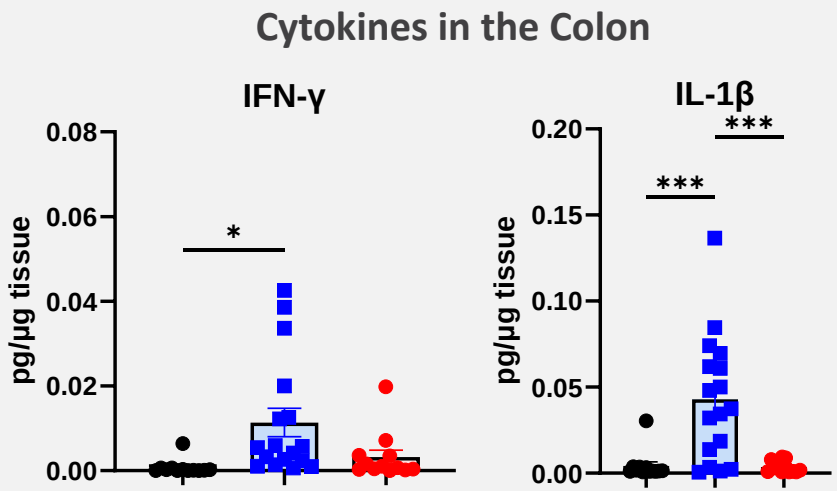
Sullivan J et al., AAI 2024 Poster: Development of Conditionally Active IL-10 INDUKINE™ Molecules for the Treatment of Inflammatory Bowel Disease

WTX-921 Treatment Inhibits Disease in Mouse ACT Model of IBD

IL-10 INDUKINE treatment blocks disease as measured by multiple metrics







Abbreviations: ACT-adoptive cell transfer; IBD-inflammatory bowel disease

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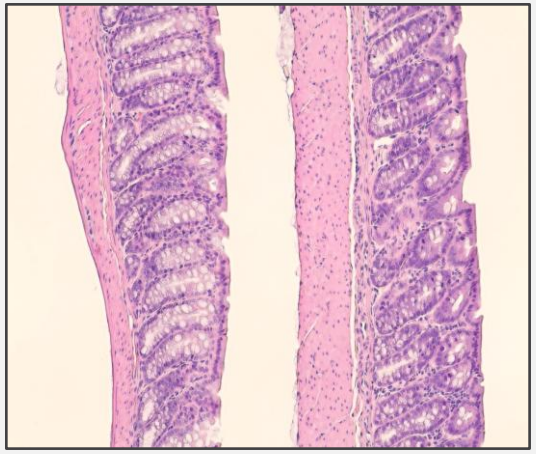
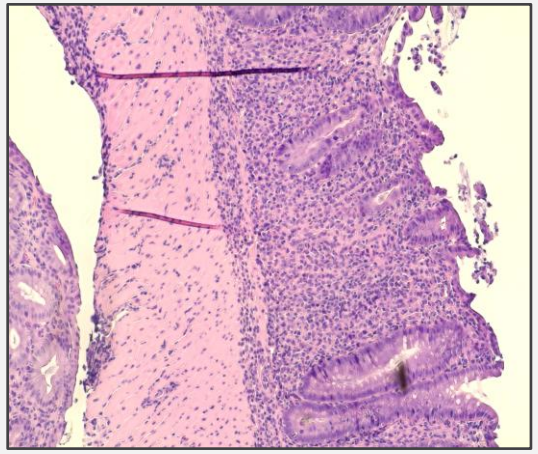
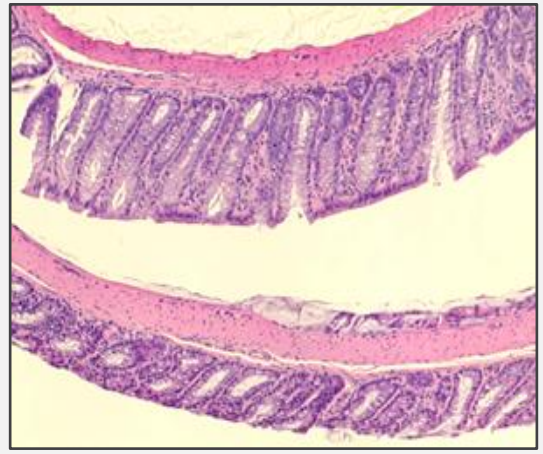
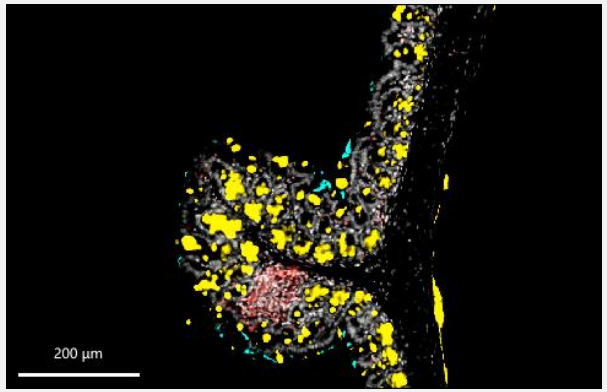
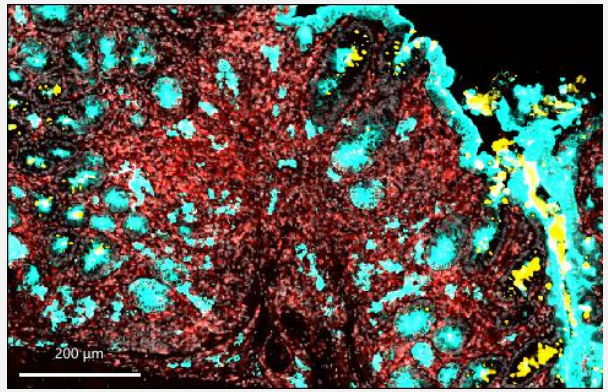
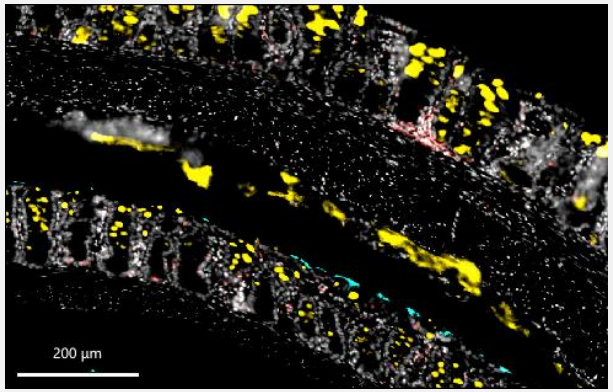
WTX-921 Treatment Inhibited Disease in Mouse ACT Model of IBD

IL-10 INDUKINE treatment prevents immune cell expansion/activation and tissue destruction

	Control-No Colitis	Disease Induced-Vehicle Treated	Disease Induced-INDUKINE Treated
H&E			
IF		 DAPI CD45 iNOS MUC2	

Abbreviations: ACT-adoptive cell transfer; IBD-inflammatory bowel disease; H&E-hematoxylin and eosin; IF-immunofluorescence

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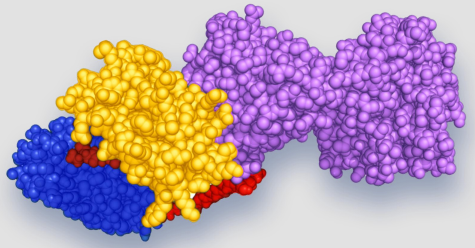
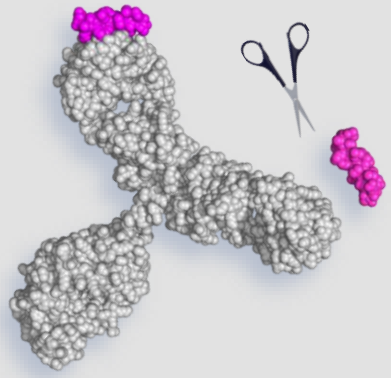
PREDATOR Platform Offers Value Creation through Pipeline Expansion and Partnering



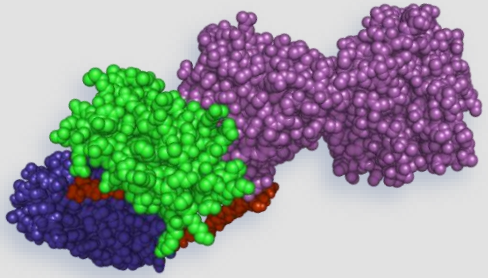
Oncology-focused INDUKINE Therapeutics

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



Expanding Conditional-Activation Technology to New Modalities

- T cell engagers
- Antibody drug conjugates
- Cell-based therapies



Non-Oncology INDUKINE Therapeutics

- Inflammation
- Other diseases

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Shifting the Balance in Cytokine Therapeutics

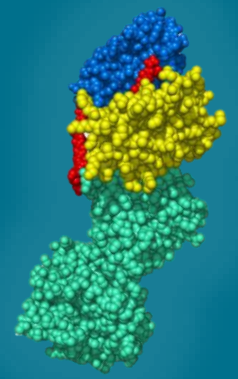
PREDATOR Platform: Value Creation Engine

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

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

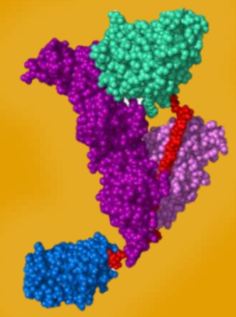
WTX-124

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



Strategic Clinical Development

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*

Deep Pipeline

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

WTX-921, an IL-10 INDUKINE molecule with selective delivery of IL-10 to inflamed tissues for inflammatory/autoimmune diseases

Strong Cash Position

Approximately $122.8M in cash and cash equivalents (as of September 30, 2024)

Runway through at least 2Q26 with multiple value-enhancing catalysts expected in the near term

Approximately 44.6M shares outstanding (as of November 1, 2024)

*JZP898, an IFNα INDUKINE molecule, in a Phase 1 clinical trial with Jazz Pharmaceuticals

Werewolf THERAPEUTICS

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

Tim Trost, CPA
Chief Financial Officer

William Winston, PhD
Senior Vice President, Research

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Thank you!