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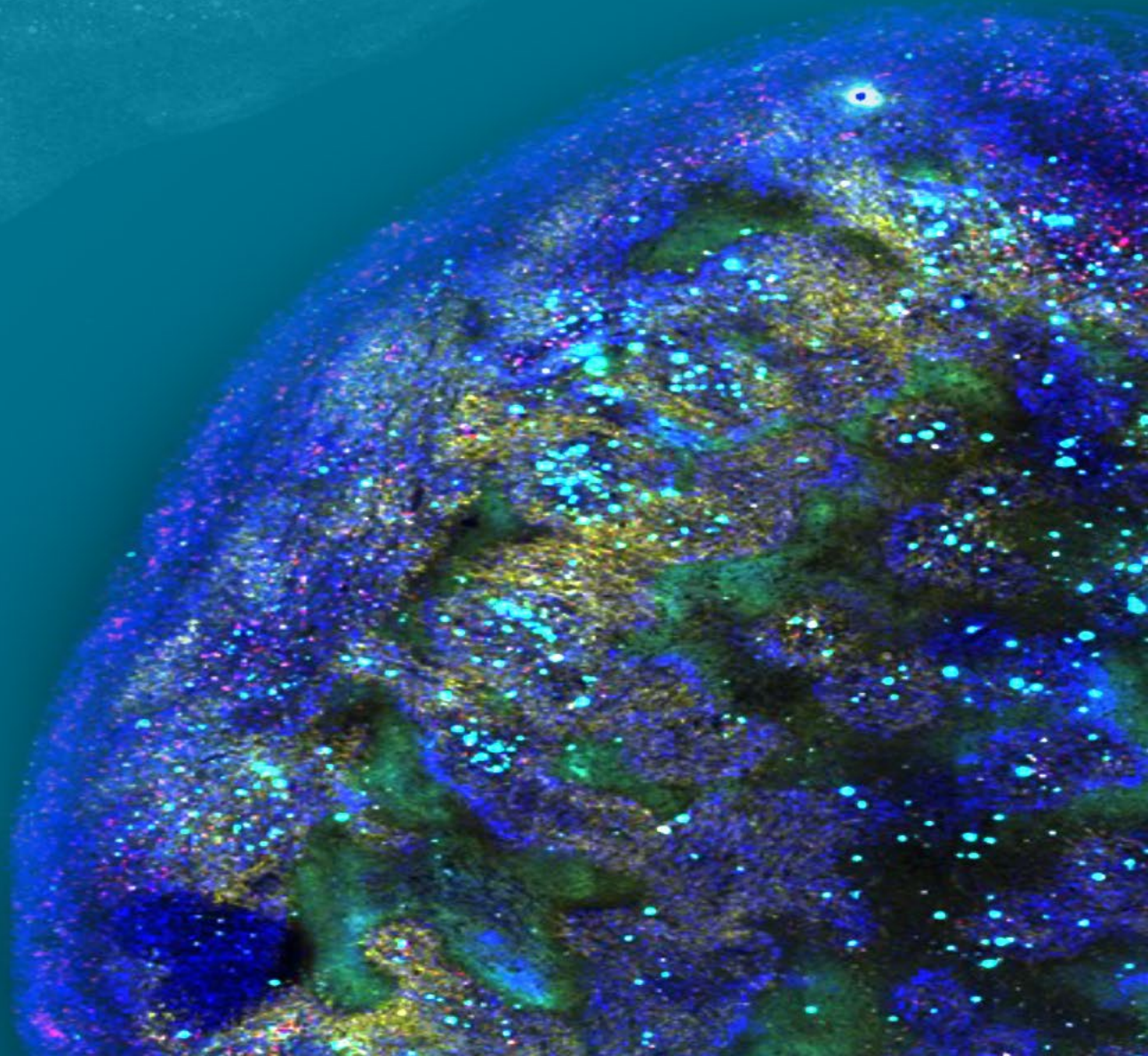
Shifting the Balance in Cytokine Therapeutics



SITC 2023

WTX-124 Phase 1/1b Clinical Trial
Preliminary Data Overview

Investor Webcast

November 3, 2023

Cautionary Note Regarding Forward-Looking 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 expected timeline regarding preclinical and clinical development for product candidates, including the announcement of data, the potential activity and efficacy of product candidates in future preclinical studies and clinical trials, and the Company's expected cash runway, 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 obtain sufficient 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.

Key Value-drivers

WTX-124

Preliminary clinical data*
establish proof of mechanism for WTX-124 and proof of concept for INDUKINE™ design

Dose-escalation ongoing
in both monotherapy and pembrolizumab combination

Recommended dose for expansion (RDE) and opening of expansion arms
expected in 1H 2024

WTX-330

Ongoing enrollment
in monotherapy dose escalation

JZP898

IND application clearance received
for Phase 1 clinical development

WTX-712

Selection of IL-21
development candidate

On-going Value Creation

PREDATOR™ Platform

Capability to expand the pipeline with new INDUKINE molecules
for a broad range of mechanisms and indications

Business Development

Broad portfolio of clinical and preclinical stage assets for potential partnering

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

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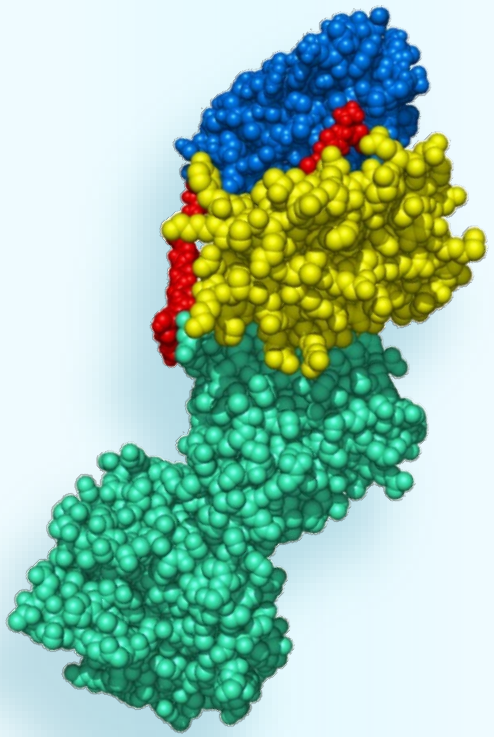
WTX-124 Phase 1/1b
Preliminary Data

Preliminary clinical data collected as of October 18, 2023,
from an ongoing Phase I/1b study

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



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 rhIL-2
- IL-2 therapy with an improved therapeutic index could address an immediate unmet medical need for patients whose disease has progressed despite treatment with checkpoint therapy
- Strong rationale for combination with checkpoint inhibitors in earlier lines of therapy

Status

- Enrolling patients in Phase 1/1b clinical trial both as a single agent and in combination with pembrolizumab
- Wholly owned

Abbreviation: TME-tumor microenvironment

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

Phase 1/1b clinical trial (WTX-124x2101)

Monotherapy Dose Escalation

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

Determination of *monotherapy* MTD/RDE

Combination Dose Escalation with Pembrolizumab

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

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 to enroll in parallel with staggered start for combination
- mTPI (Modified Toxicity Probability Interval) design
- Enrolling ~150 patients total
- Assessment of safety, pharmacokinetics, MTD/RDE, biomarkers, ADA and efficacy
- Concurrent biomarker analysis on blood and tumor tissue to evaluate POM and confirm differential activity based on conditional activation

SITC November 3, 2023: Announced initial safety, tolerability, pharmacokinetics and biomarker data

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

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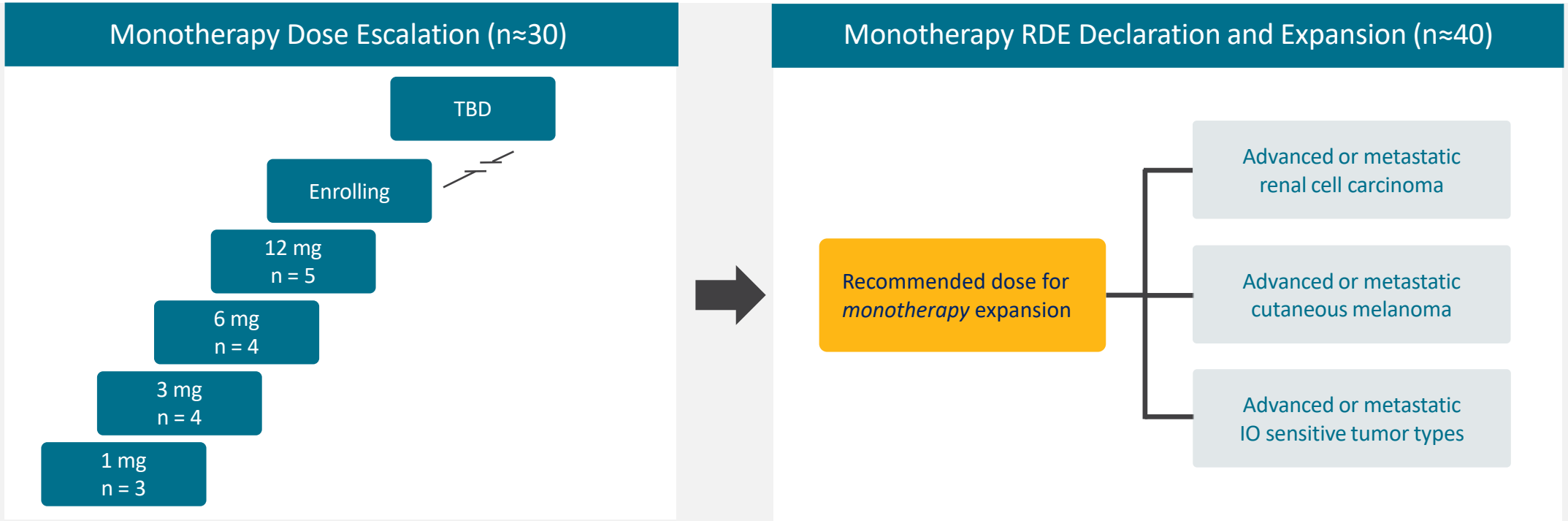
Study Schema for Monotherapy Dose Escalation Portion of WTX-124x2101



- Patients with IO sensitive tumor types who have exhausted all SOC options or for whom SOC is not indicated
- mTPI (Modified Toxicity Probability Interval) design, ability to add enrichment cohorts at meaningful dose levels
- Assessment of safety, pharmacokinetics, MTD/RDE, biomarkers, ADA and efficacy
- Concurrent biomarker analysis on blood and tumor tissue to evaluate POM and confirm differential activity based on conditional activation

1H 2024: Anticipated additional monotherapy dose escalation data, RDE declaration and opening of expansion arms

Abbreviations: RDE-recommended dose for expansion; POM-proof of mechanism; SOC-standard of care; MTD-maximum tolerated dose; ADA-antidrug antibody

Patient Demographics from Early Monotherapy Dose Escalation Cohorts

Enrollment of heavily pretreated patients with tumor types for which immunotherapy, including Proleukin, is indicated

Characteristic		1 mg (N=3)	3 mg (N=4)	6 mg (N=4)	12 mg (N=5)	Total (N=16)
Age (years)	Mean (SD)	70.7 (12.42)	69.5 (7.33)	57.8 (9.36)	69.8 (11.32)	66.9 (10.62)
	Median	64.0	67.5	61.0	73.0	66.0
Sex, n (%)	Female	2 (66.7%)	2 (50.0%)	3 (75.0%)	1 (20.0%)	8 (50.0%)
	Male	1 (33.3%)	2 (50.0%)	1 (25.0%)	4 (80.0%)	8 (50.0%)
Race, n (%)	Black/African-American	0 (0.0%)	0 (0.0%)	1 (25.0%)	0 (0.0%)	1 (6.2%)
	White	2 (66.7%)	3 (75.0%)	3 (75.0%)	5 (100.0%)	13 (81.2%)
	Unknown	1 (33.3%)	1 (25.0%)	0 (0.0%)	0 (0.0%)	2 (12.5%)
	Melanoma*	1 (33.3%)	2 (50.0%)	2 (50.0%)	3 (60.0%)	8 (50.0%)
Tumor type, n (%)	NSCLC	1 (33.3%)	2 (50.0%)	1 (25.0%)	1 (20.0%)	5 (31.3%)
	Renal Cell Carcinoma	1 (33.3%)	0 (0.0%)	1 (25.0%)	0 (0.0%)	2 (12.5%)
	Cutaneous SCC	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (20.0%)	1 (6.3%)
Prior lines of systemic therapy (including immunotherapy), n (%)	1	0 (0.0%)	0 (0.0%)	1 (25.0%)	1 (20.0%)	2 (12.5%)
	2	0 (0.0%)	2 (50.0%)	0 (0.0%)	2 (40.0%)	4 (25.0%)
	3	2 (66.7%)	1 (25.0%)	2 (50.0%)	0 (0.0%)	5 (31.2%)
	≥4	1 (33.3%)	1 (25.0%)	1 (25.0%)	2 (40.0%)	5 (31.2%)

*Includes patients with cutaneous, uveal and mucosal melanoma; all patients enrolled in Cohorts 1-4 previously progressed on standard-of-care immunotherapy regimens; 9/16 (56.3%) previously developed immune-related adverse events while receiving immunotherapy

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

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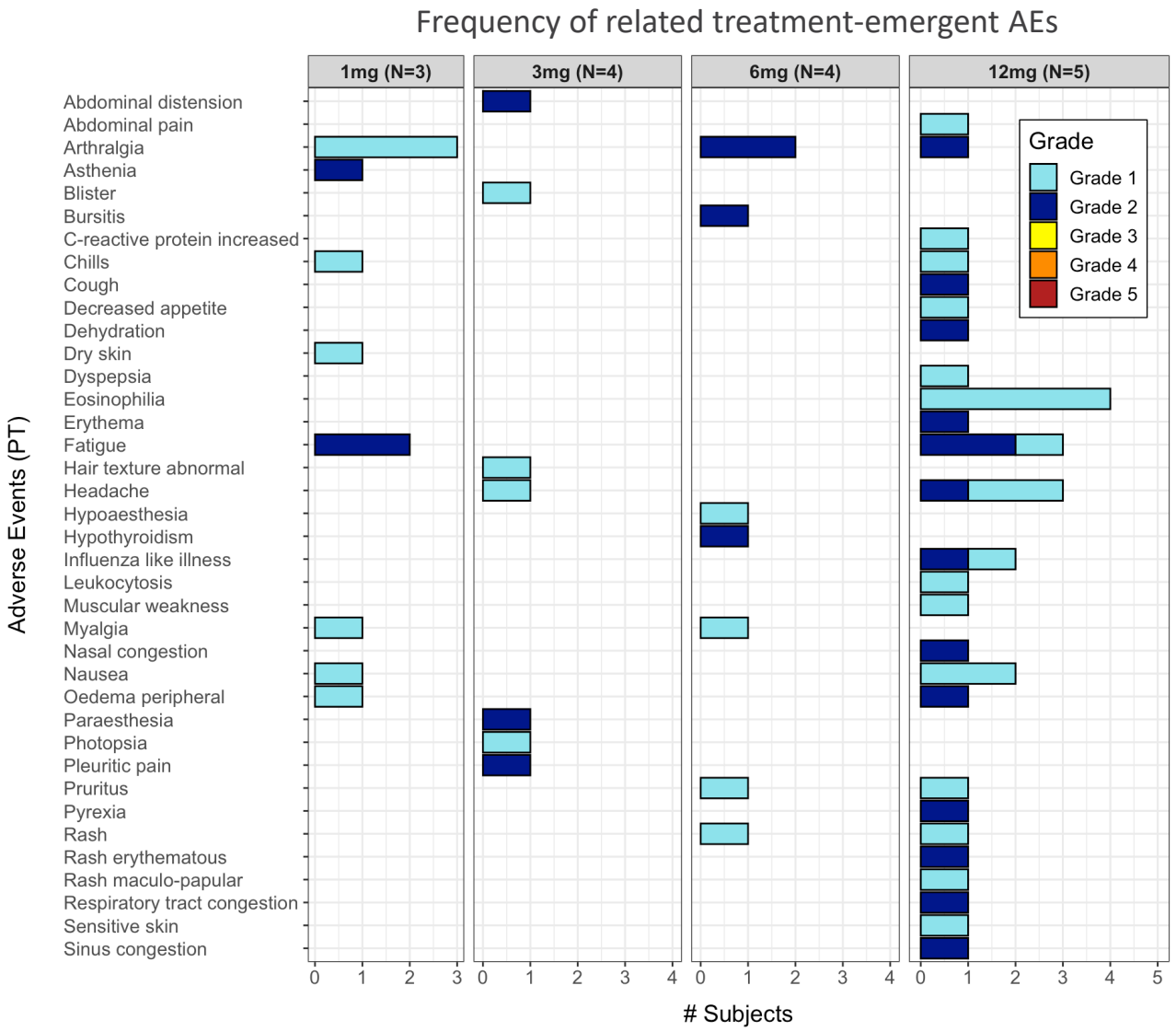
WTX-124 was Generally Well-Tolerated in the Outpatient Setting at Relevant Doses

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

Key safety findings to date:

- All study drug related treatment-emergent adverse events (TEAEs) were mild to moderate in severity
- Arthralgias and fatigue were the most common related TEAEs
- No patient developed vascular leak syndrome of any grade (adverse event common to HD IL-2)
- No evidence of cytokine release syndrome
- No patient developed a dose-limiting toxicity or a treatment-related serious AE
- No patient discontinued study drug due to a treatment-related AE

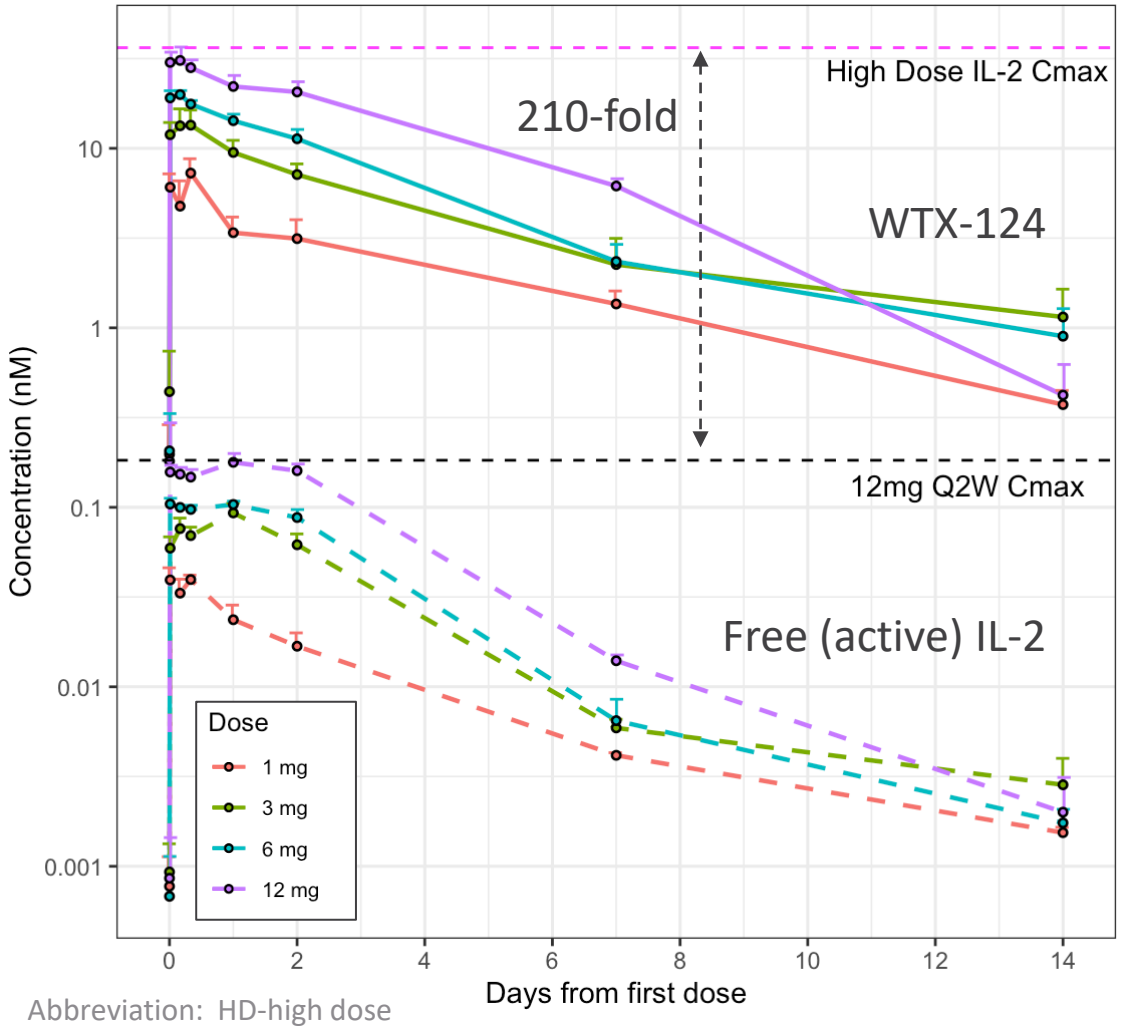
Abbreviation: HD-high dose



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)



Abbreviation: HD-high dose

Key findings include:

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

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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

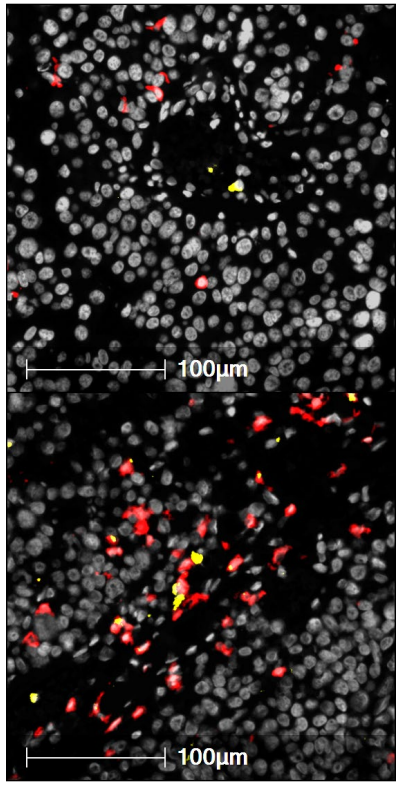
65yo F with melanoma (6mg)

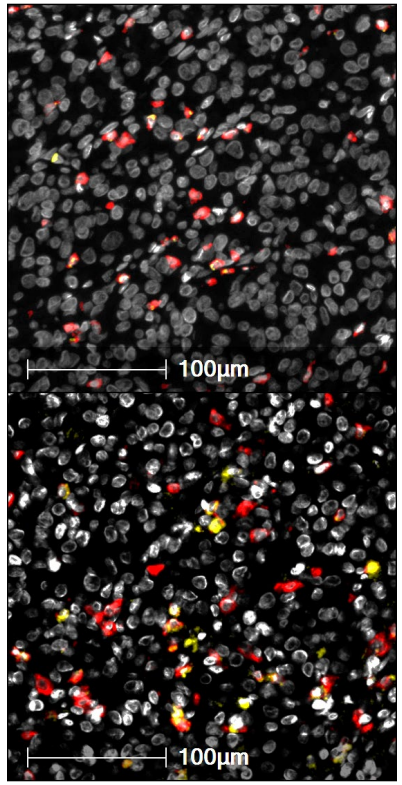
61yo F with uveal melanoma (6mg)

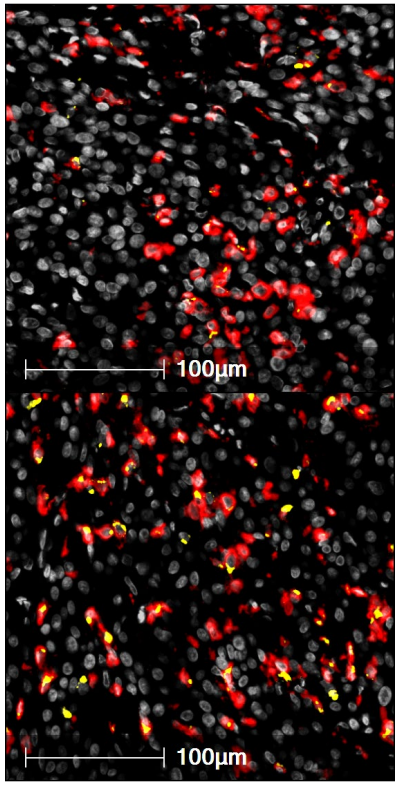
50yo F with melanoma (12mg)

Pre-treatment

On-treatment





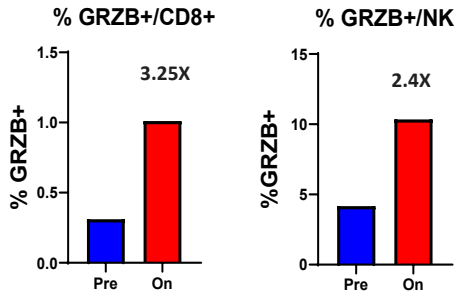


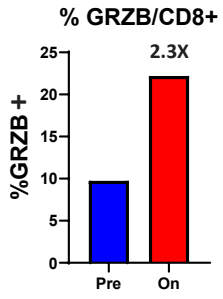
DAPI

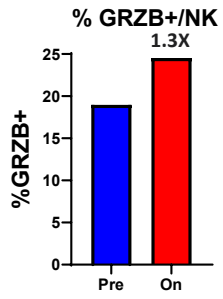
CD8

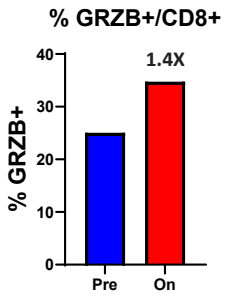
GRZB

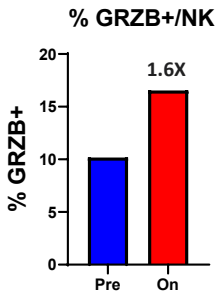
Granzyme B (GRZB) is one of the primary markers of activated T cells











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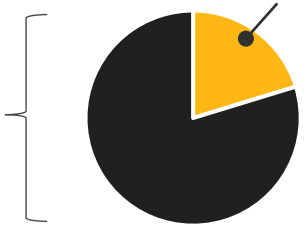
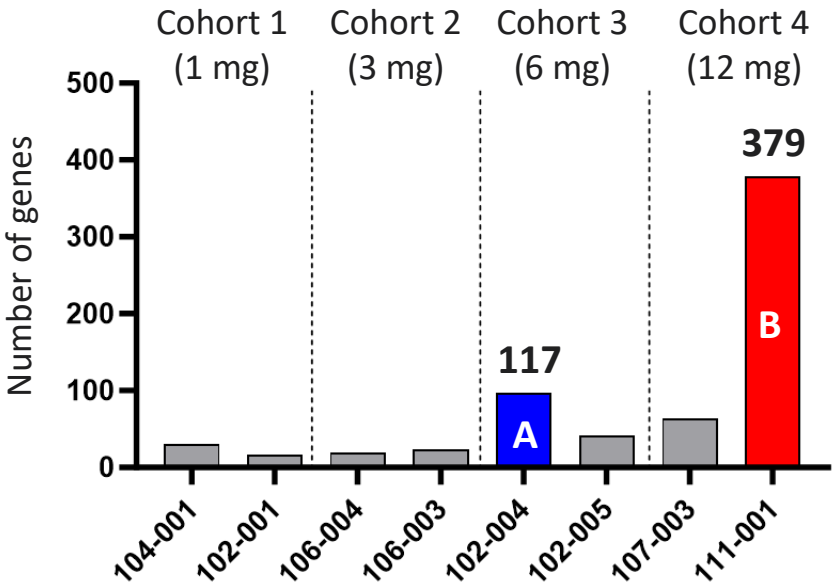
WTX-124 Induced Dose-Dependent Changes in Immune Gene Expression Consistent with IL-2 Activity in the Tumor Microenvironment

NanoString nCounter®
PanCancer immune panel
(770 genes)

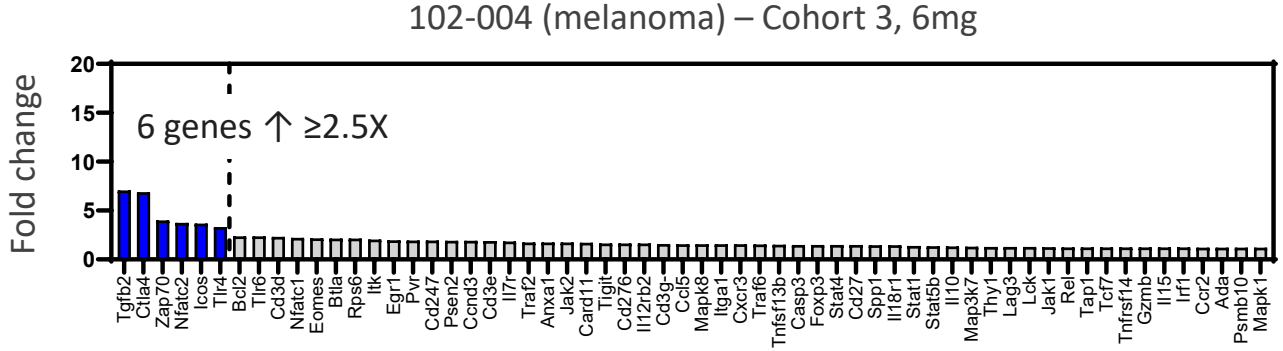


Immune genes increased by ≥1.5-fold



T-cell activation genes increased by ≥2.5-fold

A



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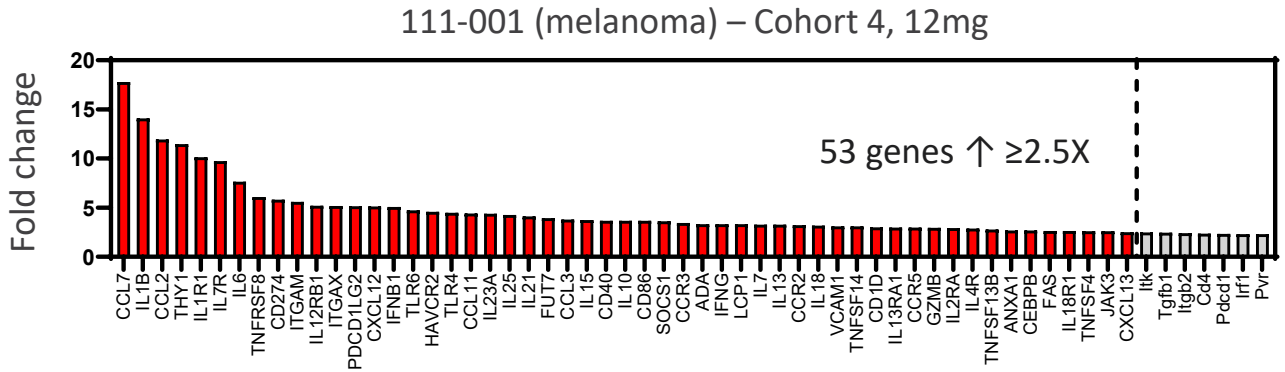

*Data presented for eight patients for whom on-treatment biopsies were available as of October 18, 2023

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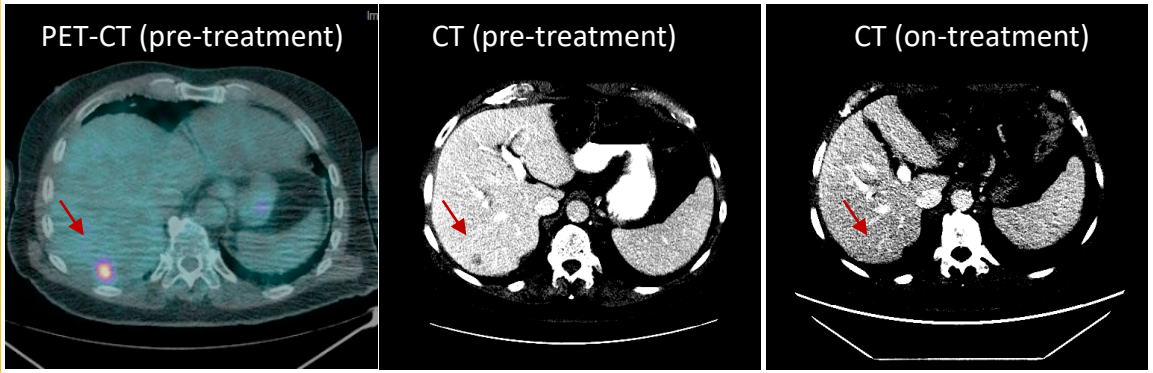
WTX-124 Demonstrated Monotherapy Antitumor Activity in Patients Refractory to ICI Therapy

At 12 mg IV Q2W, WTX-124 shrank treatment-refractory tumor metastatic deposits (3/5 patients); all 12 mg responders remain on study drug

Objective response observed at 12 mg dose

- 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 (*see below*) show complete resolution of a 1.4 cm target lesion in the liver
- Stable non-target bone lesion in the T11 vertebral body



Additional evidence of antitumor activity

Cohort 4 (12 mg):

- 72-year-old man with cutaneous SCC with shrinkage of a premaxillary subcutaneous nodule on ultrasound; at the first restaging scan (8 weeks), investigator interpretation was consistent with a partial response**
- 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, remains on study drug

Cohort 3 (6 mg):

- 65-year-old woman with progressive melanoma at baseline with stable disease (SD) for 4 months

Cohort 1 (1 mg):

- 63-year-old man with refractory NSCLC with SD for 6 months

Abbreviation: ICI-immune checkpoint inhibitor

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

**Staging scan data as of November 1, 2023.

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

Preliminary monotherapy dose escalation data from ongoing Phase 1/1b study establish biologic and clinical activity for WTX-124

- **WTX-124 administered as a monotherapy IV Q2W has been well tolerated and reached exposures associated with intratumoral IL-2 pharmacodynamic activity and clinical responses despite enrollment of a heterogeneous patient population and small patient numbers**
- WTX-124 up to 12 mg IV Q2W was generally well tolerated with no cases of vascular leak syndrome of any grade, no DLTs, no related SAEs, and no treatment discontinuations due to related AEs
- PK data showed extended prodrug exposure in plasma with substantially lower levels of free (active) IL-2 than HD IL-2 therapy (Proleukin®), accounting for the improved therapeutic index and opportunity for continued dose escalation
- WTX-124 6-12 mg IV Q2W achieved biologically relevant IL-2 exposures in the tumor microenvironment as demonstrated by antitumor activity (uPR, SD by RECIST 1.1) and CD8+ T cell and NK cell expansion and activation
- Data support potential of WTX-124 to elicit monotherapy activity from the delivery of a fully potent, wild-type IL-2 to the TME in patients with refractory solid tumors
- Expecting to report additional interim data from monotherapy arm, informing RDE declaration and opening of expansion arms 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; SD-stable disease

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Thank You!