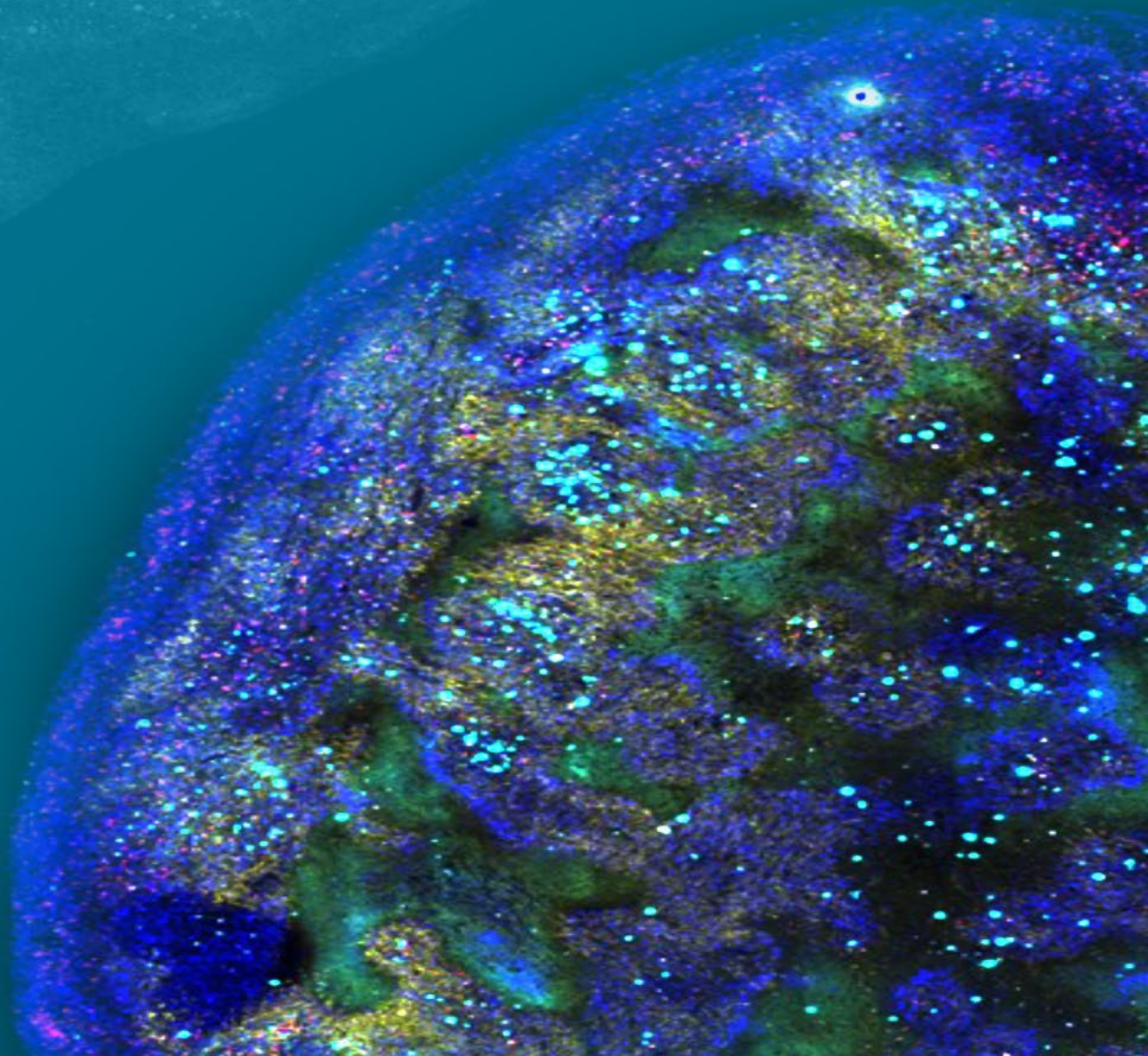
Werewolf THERAPEUTICS

Shifting the Balance in Cytokine Therapeutics



ASCO 2024

WTX-124 Phase 1/1b Clinical Trial Update

Investor Webcast

June 3, 2024

Cautionary Note Regarding Forward-Looking Statements and Disclaimer

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 timing and outcome of planned meetings with regulatory authorities, 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," "opportunity," "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 interim or 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.

Agenda

- Introductory Remarks and Program Overview – Dan Hicklin, Ph.D., CEO
- Walk-through of WTX-124 Data – Justin Moser, M.D.
- Closing Remarks – Randi Isaacs, M.D., CMO
- Q&A

Overview of WTX-124 Program Objectives

A cytokine prodrug engineered to improve 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

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 to patients ineligible for HD IL-2 based on age, performance status, and/or comorbidities
- Address an urgent unmet medical need for patients relapsed/refractory to all SOC therapies including CPIs
- Safely combine IL-2 therapy with SOC agents including CPIs in earlier lines of therapy
- Explore the potential benefit of IL-2 therapy in other IO-sensitive solid tumor indications

Abbreviations: SOC-standard of care; CPI-checkpoint inhibitors; IO-immunotherapy

Werewolf THERAPEUTICS

WTX-124: Summary of Data to Date

Establishes potential for a best-in-class IL-2 therapy

SITC - Nov 2023

Initial monotherapy dose-escalation data; 16 patients (1-12 mg)

- Generally **well tolerated** by IO-refractory patients in the outpatient setting, many ineligible for HD IL-2 based on age, comorbidities, or indication
- **Wide therapeutic index** established demonstrating proof of concept for the INDUKINE platform
- Demonstrated **Teff cell activation** and **monotherapy clinical activity (2 PRs at 12 mg dose level)**
- Proof of concept established for WTX-124

ASCO - June 2024

Updated monotherapy and initial combination dose-escalation data; 47 patients (1-28 mg)

- **Monotherapy antitumor activity further demonstrated** – durable complete response in patient with CSCC (earlier PR)
- **100% target lesion reduction** noted in responding patients
- Data support **selection of monotherapy RDE and opening of expansion arms**
- Combination dose escalation data demonstrated a **favorable safety profile with strong biomarker signals supportive of combination antitumor activity**

Abbreviations: PR-partial response; CSCC-cutaneous squamous cell carcinoma; RDE-recommended dose for expansion; IO-immunotherapy; ICI-immune checkpoint inhibitor
Note: SITC data as of November 1, 2023; ASCO data as of May 1, 2024, each for an ongoing, open label Phase 1/1b clinical trial.

Werewolf THERAPEUTICS

Justin Moser, MD

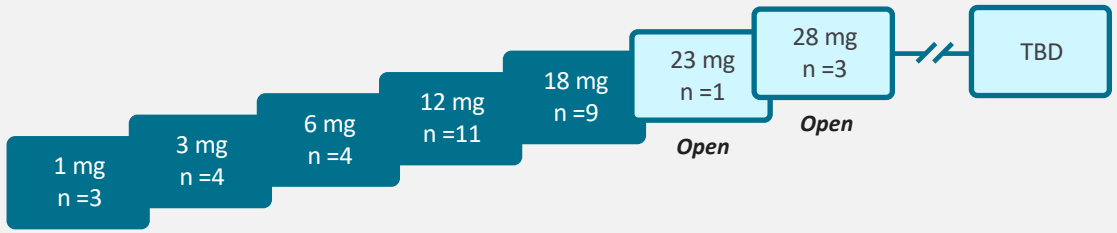
Associate Clinical Investigator

HonorHealth Research Institute

WTX-124 FIH Study Monotherapy Expansion Arms are now Open and Enrolling

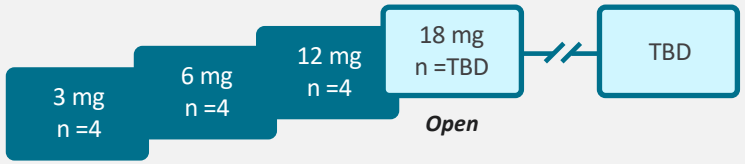
Forty-seven patients have received at least one dose of WTX-124 (35 in monotherapy, 12 in combination)

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 renal cell carcinoma
- Advanced or metastatic cutaneous melanoma
- **Advanced or metastatic cutaneous squamous cell carcinoma (monotherapy only)**
- Other advanced or metastatic IO-sensitive tumor types TBD

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: FIH-first in human; IV-intravenous; Q2W-once every two weeks; Q6W-once every six weeks; RDE-recommended dose for expansion; MTD-maximum tolerated dose; TBD-to be determined; IO-immunotherapy; ADA-antidrug antibody; PD-pharmacodynamic

Note: Preliminary clinical data as of May 1, 2024, of an ongoing, open label Phase 1/1b clinical trial. Monotherapy expansion arms opened and enrolling as of May 20, 2024.

Werewolf THERAPEUTICS

WTX-124 Phase 1 Patient Population was Heterogeneous and Heavily Pretreated

All 47 patients (monotherapy, combination) progressed on standard-of-care ICI regimens

Demographics

AGE (years)	**Mean** (SD)	**63.9** (10.9)
	Median	**65.0**
SEX, n (%)	**Female**	**20** (42.6%)
	Male	**27** (57.4%)
RACE, n (%)	**Black/African-American**	**2** (4.3%)
	White	**39** (83.0%)
	Other/ Unknown	**6** (12.7%)

Tumor Types

Enrollment restricted to solid tumor indications for which immunotherapy with ICIs is standard-of-care

	n (%)
Melanoma*	**24** (51.1%)
NSCLC	**8** (17.0%)
Renal cell carcinoma	**4** (8.5%)
Cutaneous SCC	**2** (4.3%)
GEJ adenocarcinoma	**1** (2.1%)
Hepatocellular	**1** (2.1%)
Urothelial (bladder)	**1** (2.1%)
Other	**6** (12.8%)

Prior Therapies

All prior lines of therapy

	n (%)
1	**10** (21.3%)
2	**11** (23.4%)
3	**15** (31.9%)
≥4	**11** (23.4%)

Prior lines of immunotherapy

	n (%)
1	**20** (42.6%)
2	**15** (31.9%)
3	**9** (19.1%)
≥4	**3** (6.4%)

*Includes patients with cutaneous, mucosal and uveal melanoma.

Abbreviations: ICI-immune checkpoint inhibitor; NSCLC-non-small cell lung cancer; SCC-squamous cell carcinoma; GEJ-gastroesophageal junction

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

Werewolf THERAPEUTICS

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

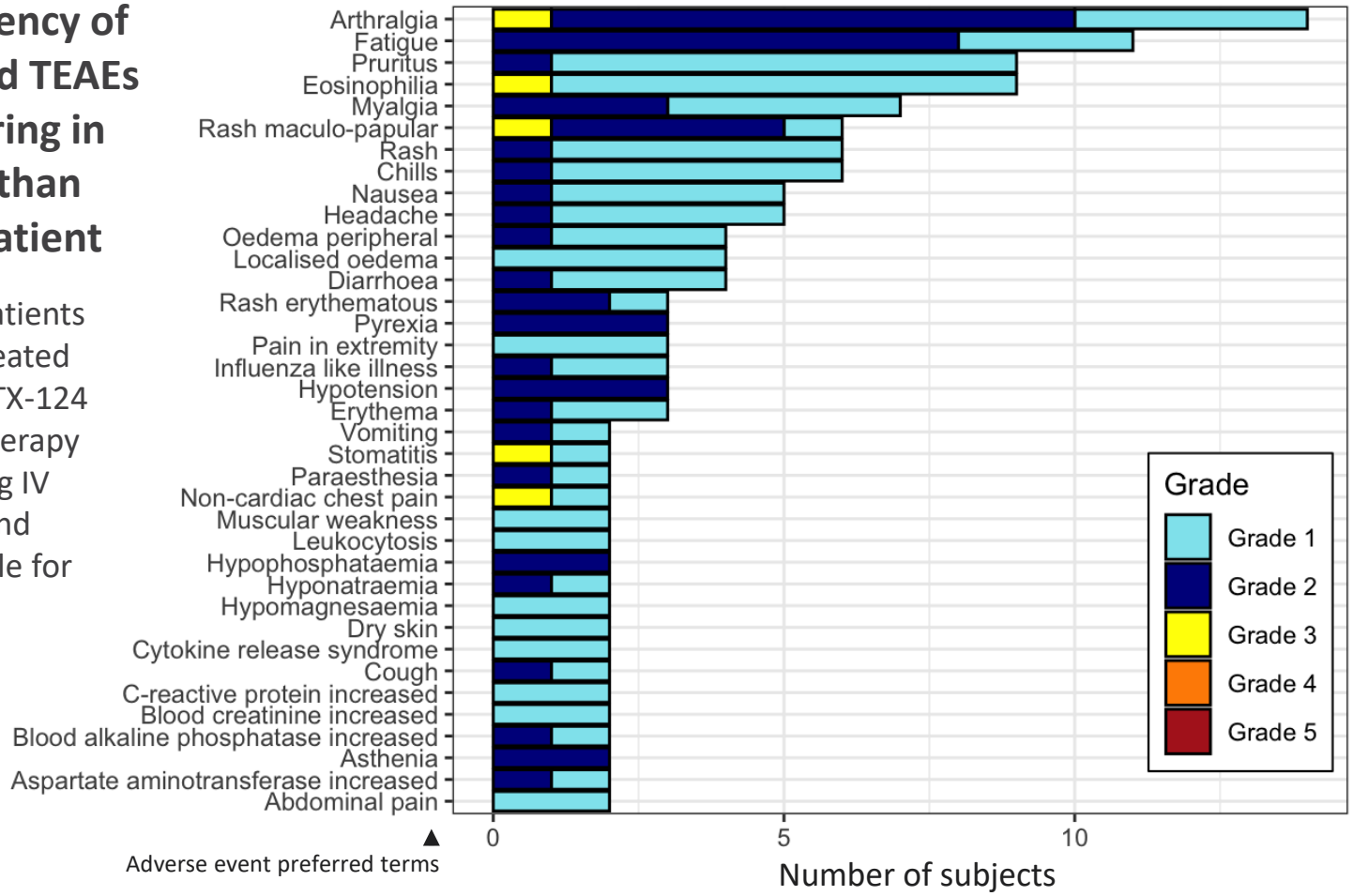
Treatment-related adverse events were primarily mild to moderate including at clinically active doses

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 ≥18 mg were manageable, reversible
- No Grade 4 or 5 related TEAEs
- No evidence of vascular leak syndrome, ≥ Grade 2 cytokine release syndrome, or infusion reactions
- No recurrence to date of irAEs that had previously occurred on ICI therapy

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; HD-high dose; IV-intravenous; Q2W-once every two weeks; irAEs-immune related adverse events; ICI-immune checkpoint inhibitor

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

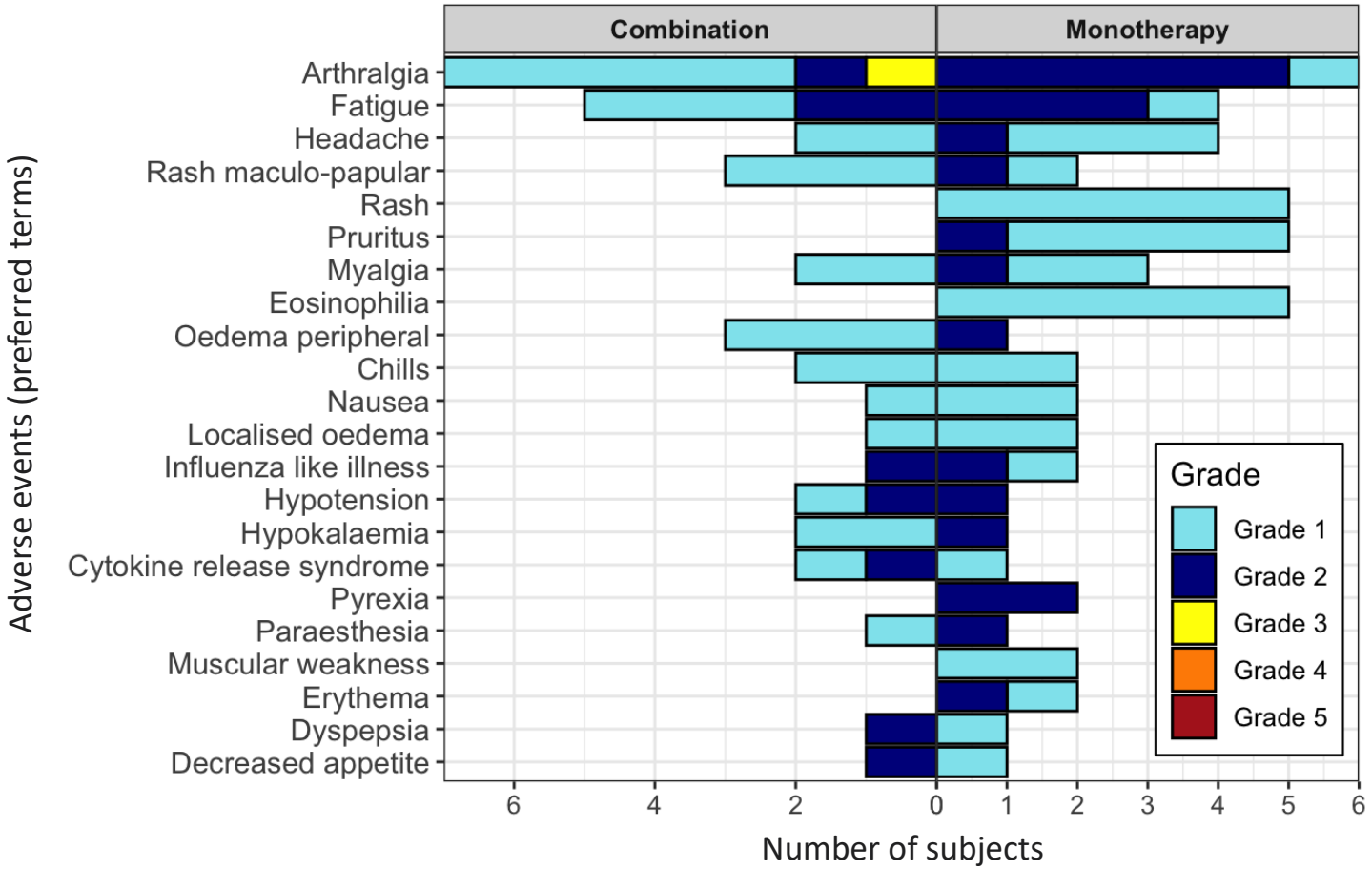
Werewolf THERAPEUTICS

No New Safety Signals were Observed for WTX-124 Combined with Pembrolizumab

Addition of pembrolizumab did not change the character of related adverse events

Frequency of related TEAEs occurring more than once for patients at 3-12 mg WTX-124 monotherapy (N=19) or combination therapy (N=12)

- Majority of related TEAEs for combination therapy were mild to moderate
- Combination therapy did not show an increase in the frequency and/or severity of TEAEs seen with WTX-124 monotherapy (e.g., arthralgia, rash, pruritis, fatigue, eosinophilia)



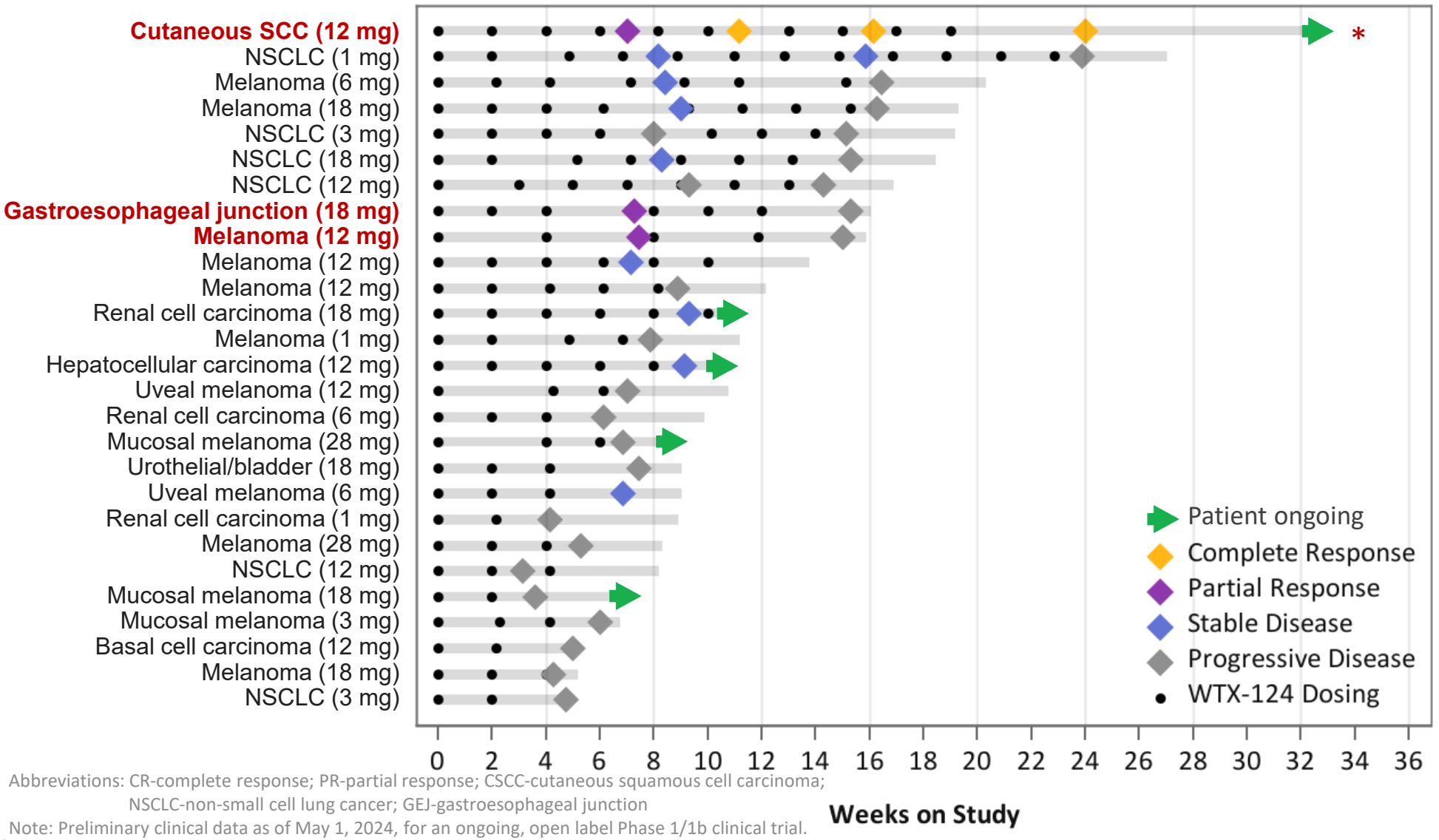
Abbreviation: TEAEs-treatment-emergent adverse events

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

Werewolf THERAPEUTICS

WTX-124 Demonstrated Monotherapy Antitumor Activity at Doses ≥12 mg

Durable CR (8+ months) in a patient with CSCC; PRs in patients with melanoma and GEJ cancer



*Patient being followed off study drug

Note that patients could be treated beyond progression (PD) if clinically indicated.

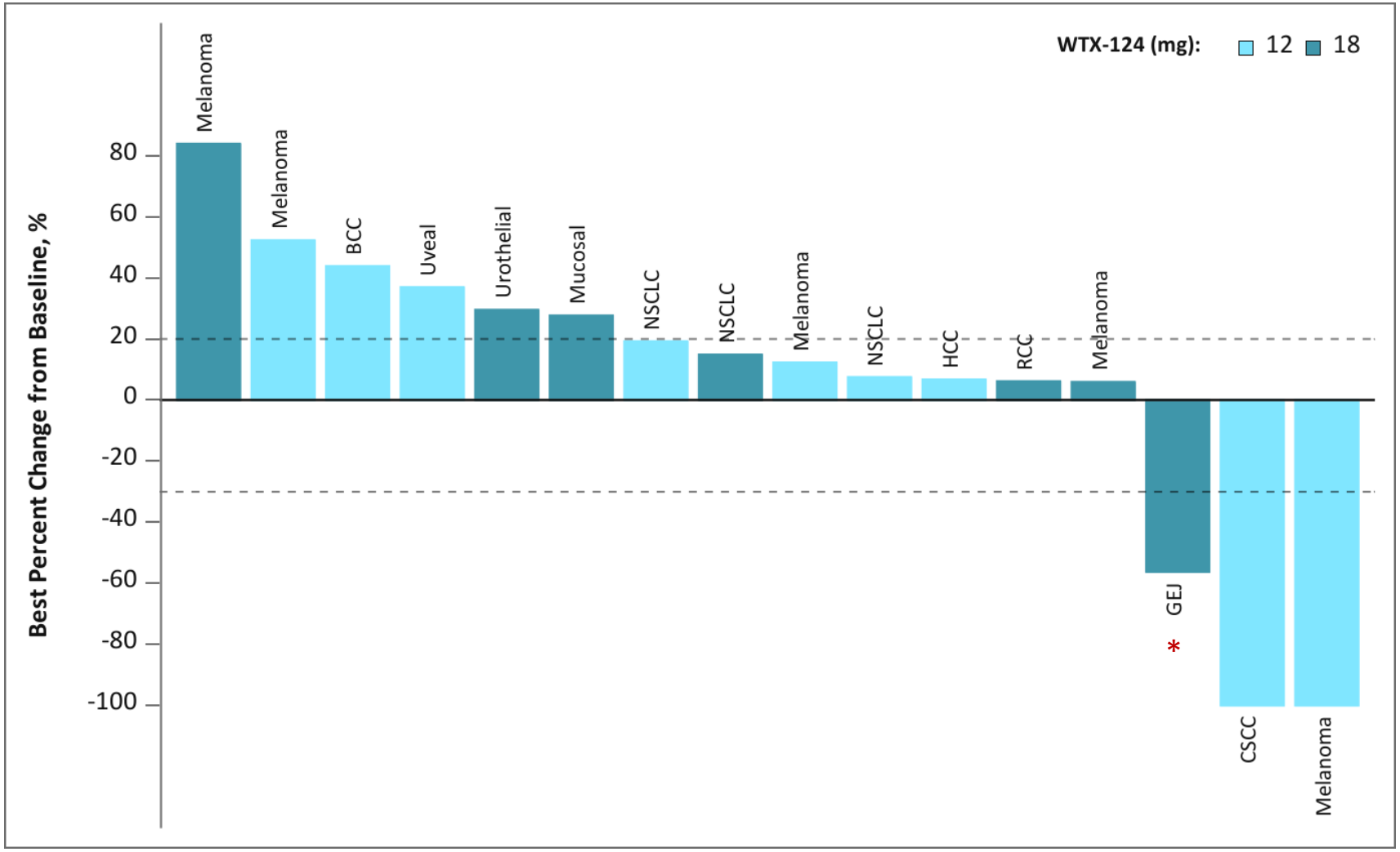
Abbreviations: CR-complete response; PR-partial response; CSCC-cutaneous squamous cell carcinoma; NSCLC-non-small cell lung cancer; GEJ-gastroesophageal junction

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

Werewolf THERAPEUTICS

Complete Regression of Target Lesions in Patients Responding to WTX-124

Three patients had objective responses and an additional seven had stable target lesions at potential RDE doses (n=16)



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

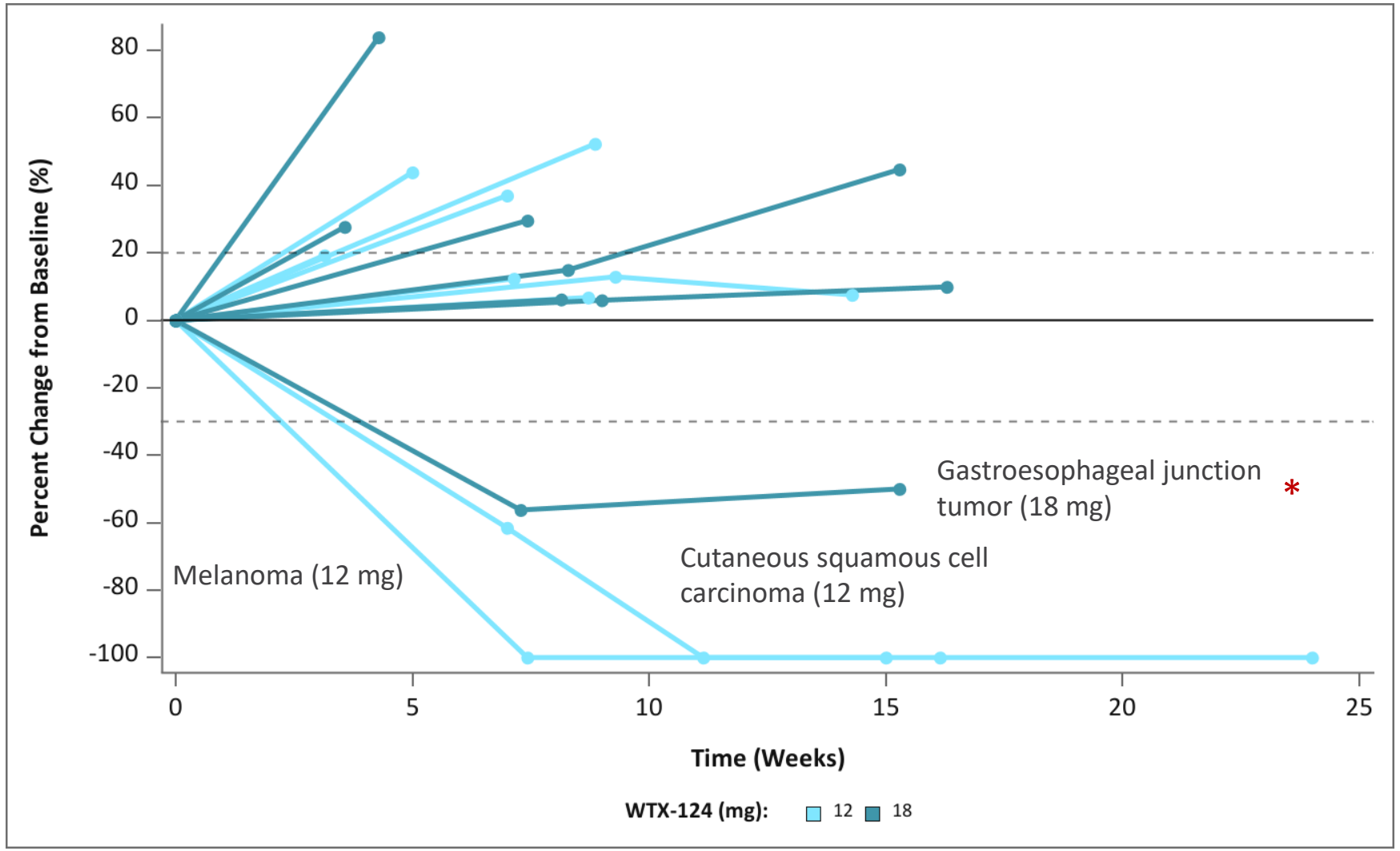
Abbreviations: RDE- recommended dose for expansion; BCC-basal cell carcinoma, NSCLC-non-small cell lung cancer, HCC-hepatocellular carcinoma, RCC-renal cell carcinoma, GEJ-gastroesophageal junction tumor, CSCC-cutaneous squamous cell cancer

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

Werewolf THERAPEUTICS

Responses at Target Lesions Occurred Rapidly and were Durable at Potential RDE Doses

All three objective responses to WTX-124 monotherapy occurred within two cycles (~8 weeks)



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

Abbreviations: RDE- recommended dose for expansion

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

Werewolf THERAPEUTICS

Confirmed Complete Response (CR) Ongoing at 8+ 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*

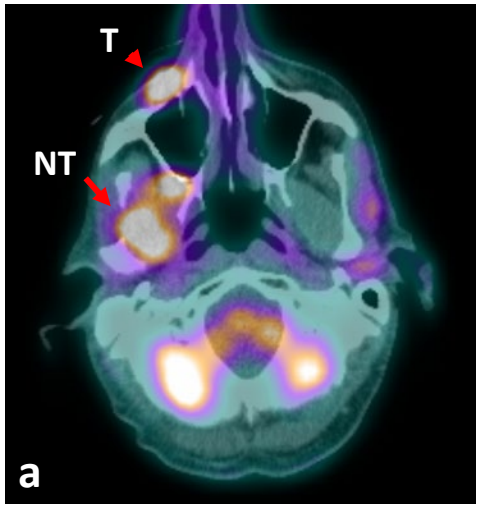
WTX-124 TREATMENT RESPONSE

- **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*

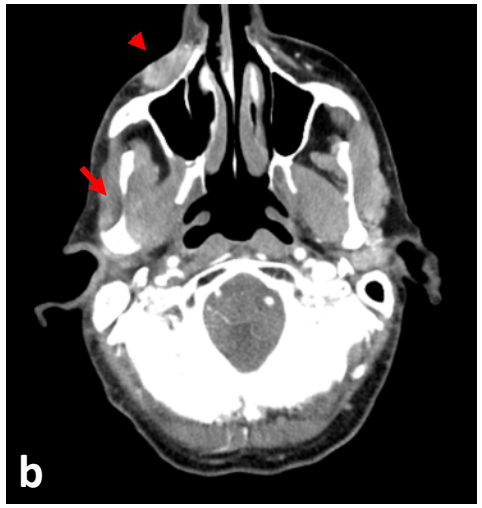
Patient tolerated therapy well with only Grade 2 arthralgias, Grade 2 rash

WTX-124 treatment stopped at 21 weeks in the setting of confirmed CR (ongoing at 8+ months)

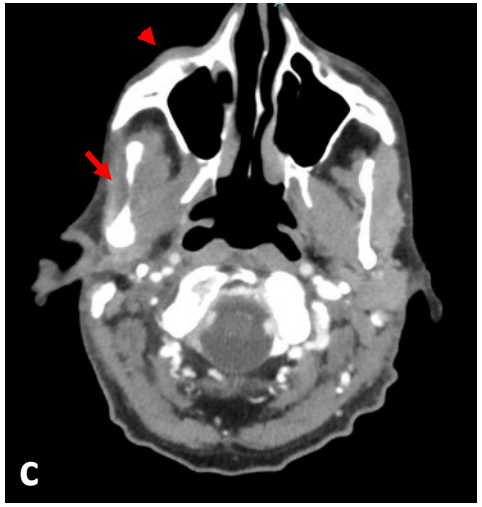
June 2023: PET-CT at time of progression on cemiplimab



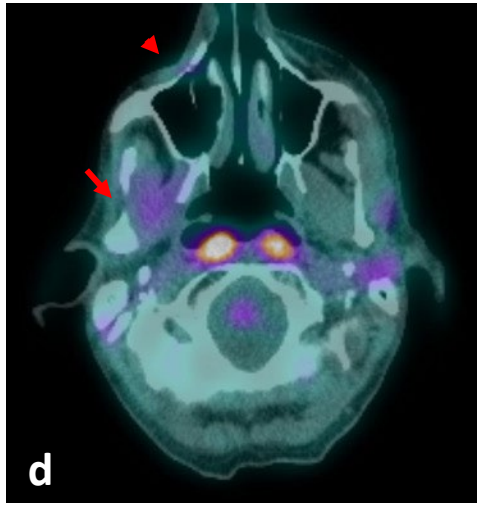
September 2023: Baseline CT performed at study entry



November 1, 2023: First restaging CT at 8 weeks



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



Abbreviations: IO-immunotherapy; SCC-squamous cell carcinoma; IV-intravenous; Q2W-once every two weeks; CT-computed tomography scan; PET-positron emission tomography

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

Werewolf THERAPEUTICS

Partial Response (PR) in a Cutaneous Malignant Melanoma Patient with Secondary ICI Resistance

78-year-old man with metastatic *BRAF* wild type cutaneous melanoma who discontinued adjuvant nivolumab due to toxicity, then progressed on nivolumab/relatlimab (Opdualag™; anti-PD-1, anti-LAG3; *panel a*) as first line therapy for metastatic disease (best overall response PR)

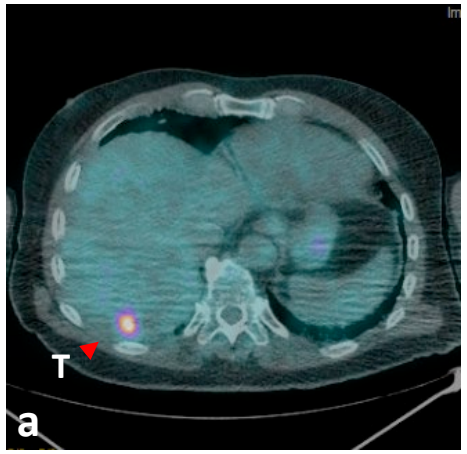
Initiated treatment with **12 mg WTX-124 IV Q2W**

Baseline CT (*panel b*) showed a 1.4 cm liver target lesion (T) and a T11 vertebral non-target lesion (NT). A lesion in the right humerus was demonstrated on PET-CT - *panel d*

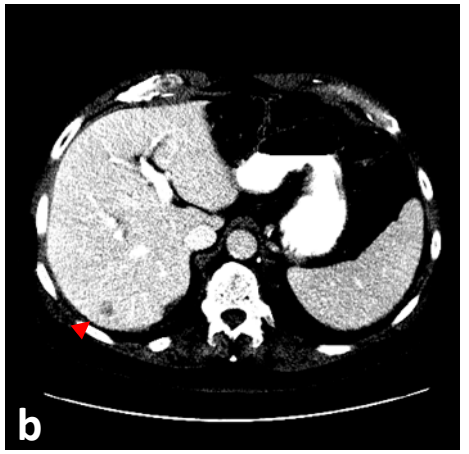
WTX-124 TREATMENT RESPONSE

- **5 weeks:** target lesion biopsied at baseline could not be reidentified for repeat biopsy
- **8 weeks:** restaging CT showed a **100% reduction** of target lesion and no increase of non-target lesion, consistent with a PR – *panel c*
- **16 weeks (CT):** target lesion remained absent, but non-target T11 bone lesion increased. New lesions identified in sternum and periportal lymph nodes – *not shown*
- **16 weeks (PET-CT):** Right humeral bone lesion present at baseline had completely resolved – *panel d*

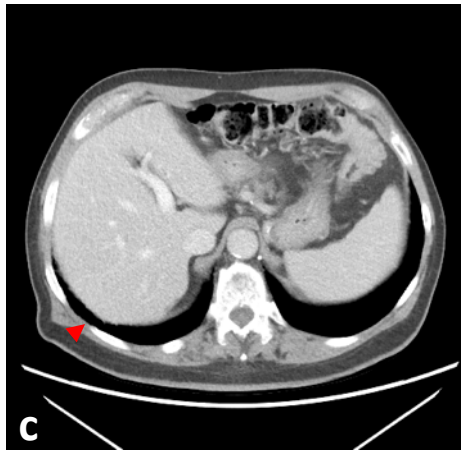
July 2023: Baseline PET-CT at time of progression on Opdualag



July 2023: Baseline CT shows the 1.4 cm target liver lesion

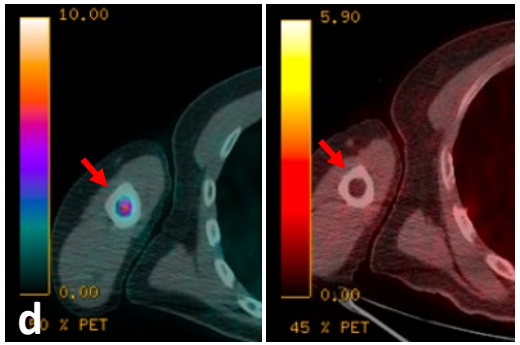


September 2023: First restaging CT at 8 weeks shows complete resolution of target liver lesion



Patient also had complete resolution of a right upper humeral metastasis on PET-CT

July 2023 **November 2023**



Abbreviations: IO-immunotherapy; IV-intravenous; Q2W-once every two weeks; CT-computed tomography; PET-positron emission tomography

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

Werewolf THERAPEUTICS

Partial Response (PR) in a Gastroesophageal Junction Tumor Patient with Secondary ICI Resistance

63-year-old man with a metastatic gastroesophageal junction (GEJ) adenocarcinoma who previously progressed on FOLFOX/nivolumab and nivolumab/BMS986253 (anti-IL-8). BOR for each line was SD.

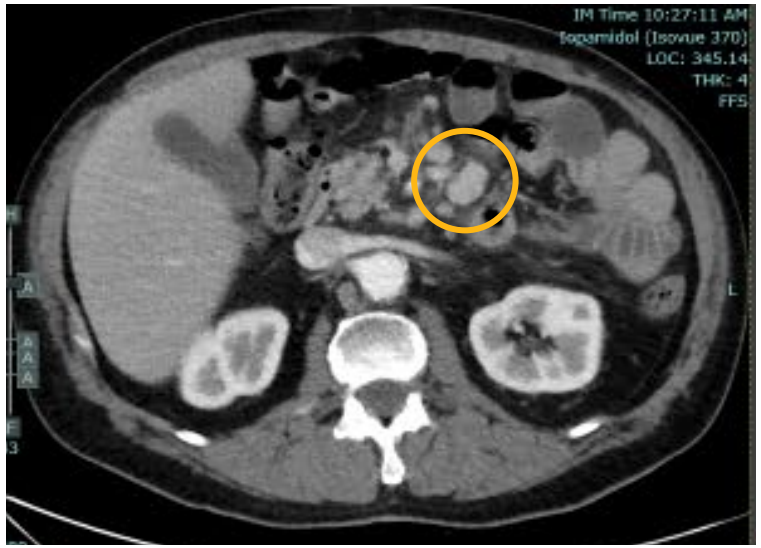
Initiated treatment with **18 mg WTX-124 IV Q2W** three months after discontinuing nivolumab/BMS986253.

Baseline CT showed a 1.6 cm mesenteric lymph node target lesion and four lymph node non-target lesions.

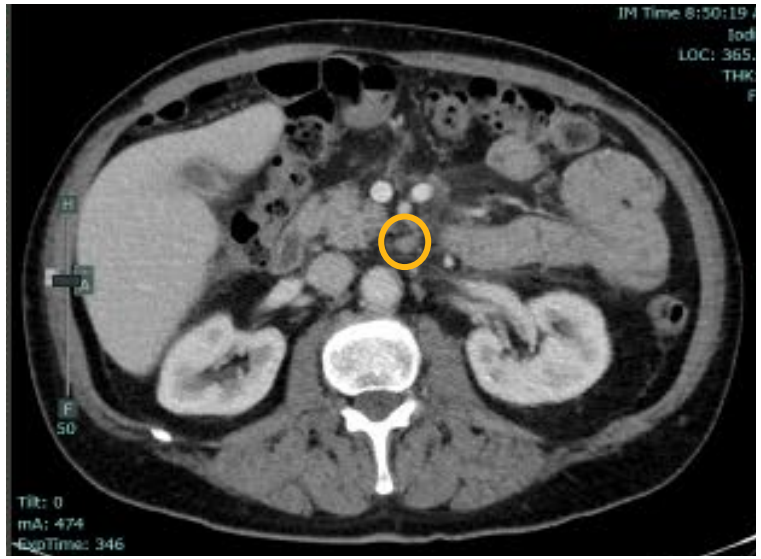
TREATMENT RESPONSE

- **3 weeks:** metastatic L axillary lymph node biopsied at baseline could not be reidentified
- **8 weeks:** restaging CT showed a **56% reduction** of target lesion (complete normalization to <1 cm) and no increase of non-target lesions, consistent with a PR
- **16 weeks:** ongoing response observed at target lesion. Progression seen at one of four non-target lymph nodes, per radiology report.

Patient discontinued WTX-124 but has neither progressed nor needed any additional anticancer therapy for 3 months.



October 2023: Baseline CT shows a 1.6 cm mesenteric lymph node target lesion



January 2024: First restaging CT at 8 weeks shows a 56% reduction of mesenteric lymph node target lesion (normalization of size to <1 cm)

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

Werewolf THERAPEUTICS

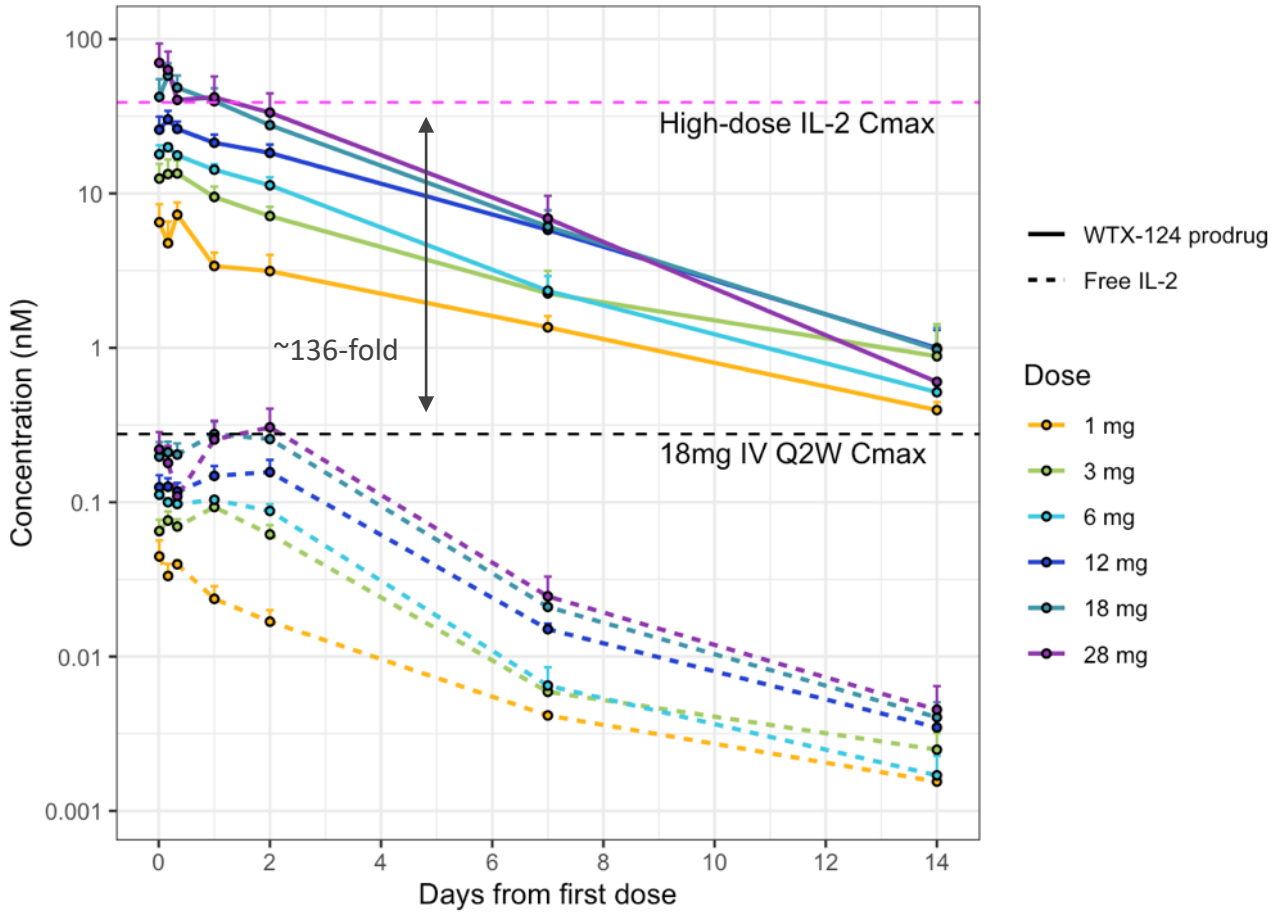
PK Data Continue to Demonstrate Proof of Concept for the INDUKINE Strategy

Data support the improved safety profile and therapeutic index 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)
- WTX-124 PK is approximately dose-proportional up to 18 mg IV Q2W
- Repeat dosing does not cause accumulation of WTX-124 or free IL-2
- ADA are transient, primarily low titer, and have no apparent impact on repeat dose exposure
- Pembrolizumab did not affect WTX-124 PK

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



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

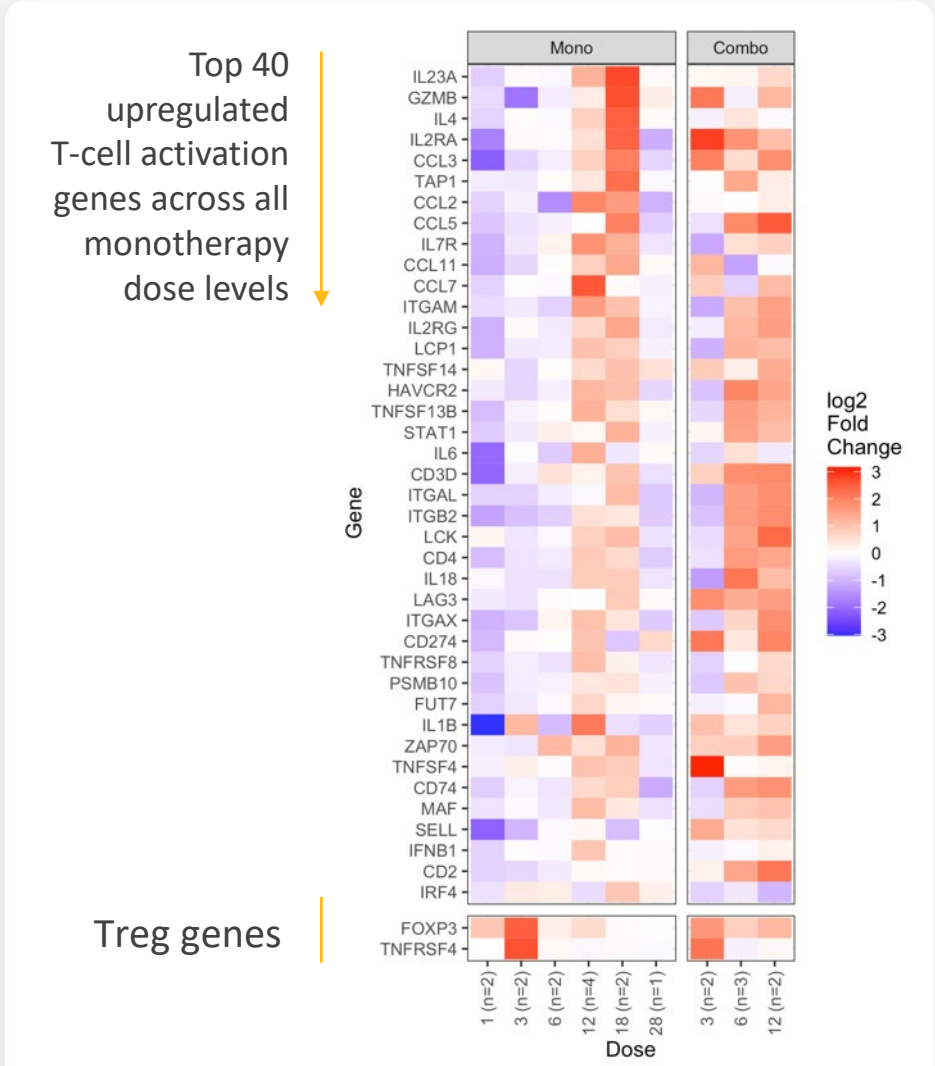
Note: Preliminary clinical data as of May 1, 2024, for an ongoing, open label Phase 1/1b clinical trial.

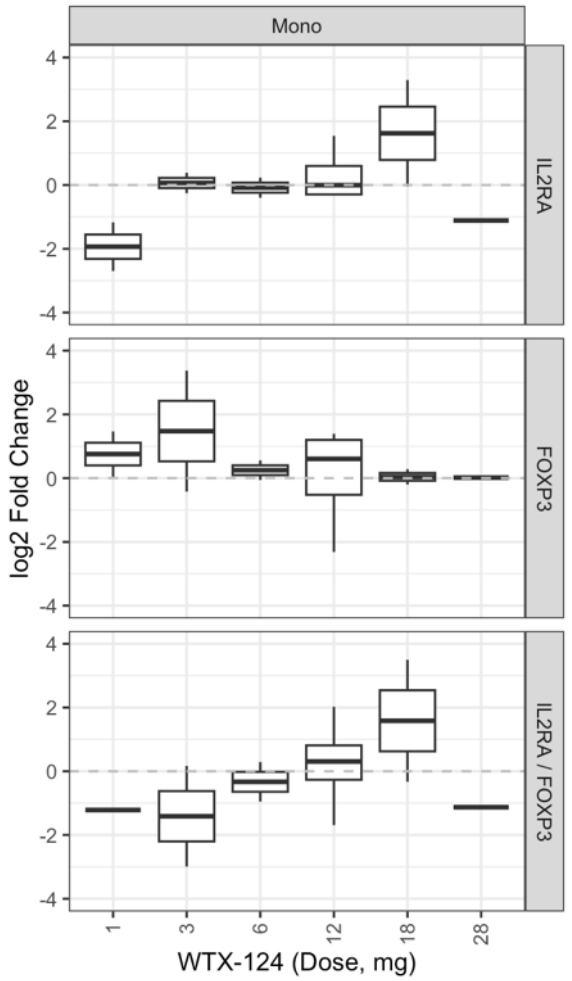
Werewolf THERAPEUTICS

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 suggest preferential activation and 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





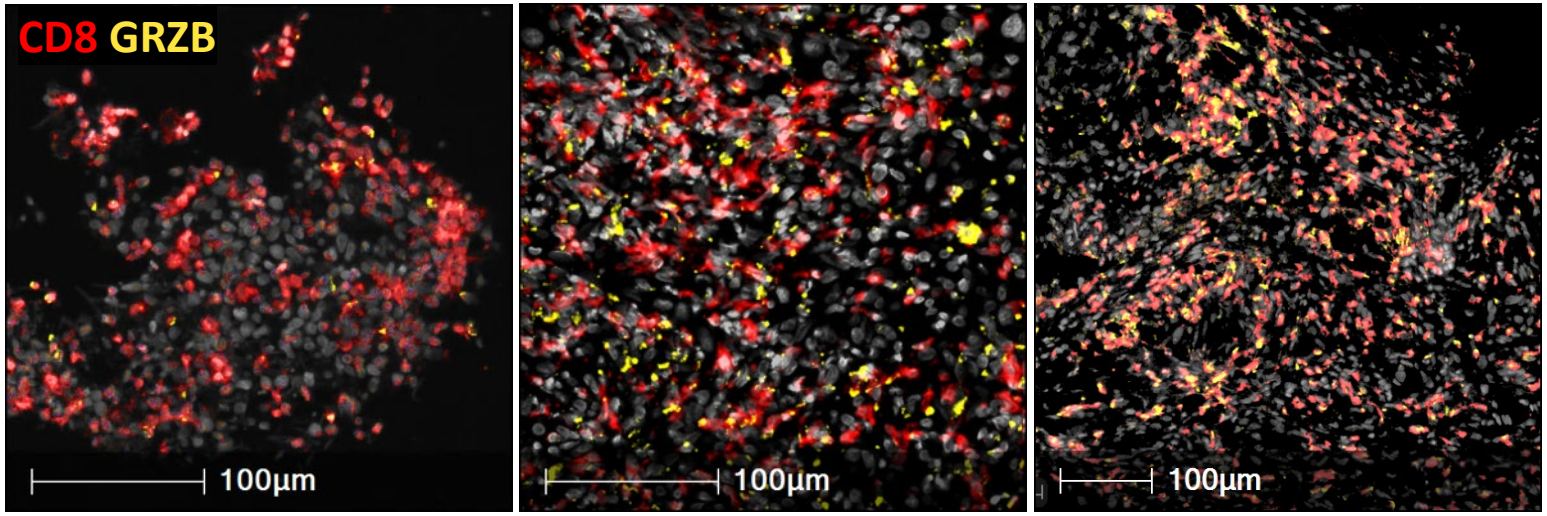
Note: Data presented for patients for whom on-treatment biopsies were available as of May 1, 2024.

Werewolf THERAPEUTICS

T-cell Inflamed Tumor Microenvironment Associated with WTX-124 Clinical Activity

Findings in baseline tumor biopsies were consistent with the known mechanism of action of IL-2

Fresh tumor biopsies acquired prior to starting WTX-124 treatment

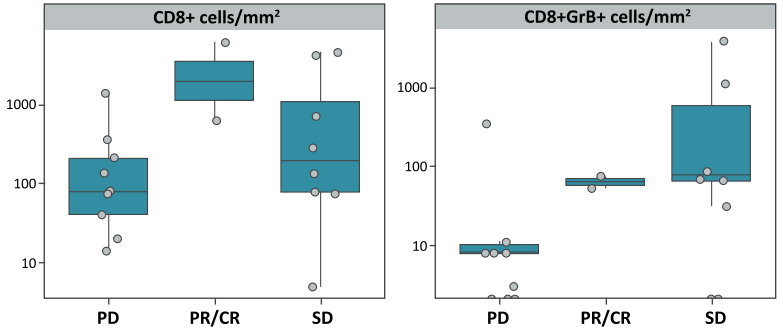


Tumor:	Cutaneous SCC	Melanoma	RCC
Prior IO:	Cemiplimab (1° resistance)	Opdualag (2° resistance)	Pembrolizumab/axitinib (2° resistance)
WTX-124 dose:	12 mg (DL4)	12 mg (DL4)	18 mg (DL4)
Biopsied lesion:	Complete regression	Complete regression	8.5% increase
RECIST	CR (confirmed)	PR (non-confirmed)	SD (awaiting confirmation)

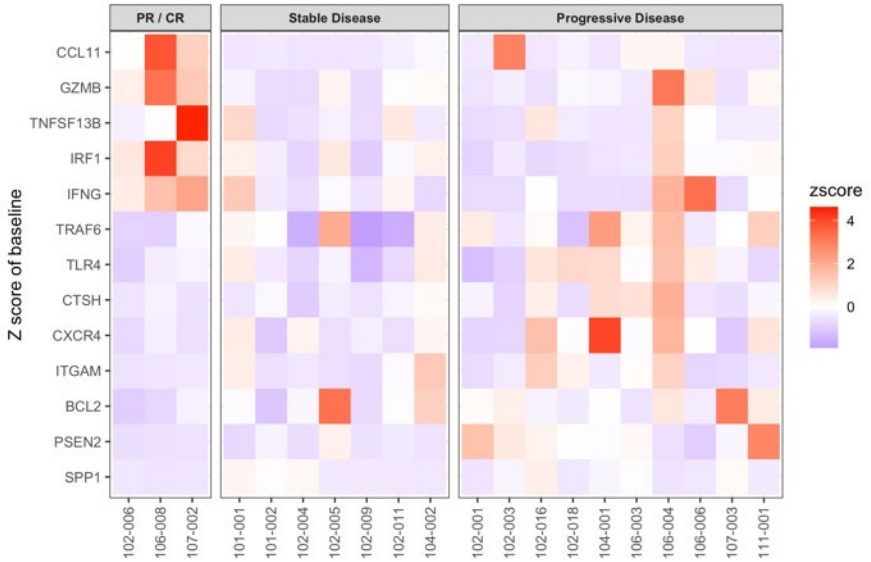
Abbreviations: PR-partial response; CR-complete response; SD-stable disease; PD-progressive disease; CSCC-cutaneous squamous cell carcinoma; RCC-renal cell carcinoma; IO-immunotherapy; DL-dose level

Note: Based on biopsies and preliminary clinical data available as of May 1, 2024.

Baseline biopsies showed trends toward greater CD8+ T cell density in patients with PR/CR/SD versus those with PD (multiplexed IF)



DESeq2 analysis of NanoString data showed that responders have a unique baseline signature



Summary of Data from Ongoing WTX-124 Phase 1/1b Study

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

- Objective responses at monotherapy doses ≥12 mg
  - Confirmed, durable CR in patient with CSCC
  - Two PRs in patients with melanoma, gastroesophageal junction tumor
- 100% regression of target lesions in responding patients
- 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 and no new safety signals when combined with pembrolizumab at clinically active doses

Abbreviations: TEAE-treatment-emergent adverse events; IV-intravenous; Q2W-once every two weeks; CR-complete response; CSCC- cutaneous squamous cell carcinoma; PR-partial response;
Note: Preliminary clinical data as of May 1, 2024, for an ongoing, open label Phase 1/1b clinical trial.

Werewolf THERAPEUTICS

Randi Isaacs, MD

Chief Medical Officer

Werewolf Therapeutics, Inc.

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

- ✓ Monotherapy activity demonstrated in heavily pretreated patients who were refractory to all SOC therapies including checkpoint inhibitors
- ✓ Clinical activity observed in patients ineligible for approved HD IL-2 therapy
- ✓ WTX-124 18 mg IV Q2W was selected as the monotherapy RDE based on clinical activity and outpatient safety profile
- ✓ Combination with pembrolizumab was generally well-tolerated with AE profile similar to monotherapy
- ✓ Increased T cell activation signature for the combination suggests a potential for improved antitumor activity by combining WTX-124 with pembrolizumab
- ✓ Opportunity to explore activity of monotherapy or combination therapy in IO-sensitive indications beyond melanoma and renal cell carcinoma and in earlier lines of therapy

Abbreviations: SOC-standard of care; HD-high dose; IV-intravenous; Q2W-once every two weeks; RDE-recommended dose for expansion; AE-adverse event; IO-immunotherapy
Note: Preliminary clinical data as of May 1, 2024, for an ongoing, open label Phase 1/1b clinical trial. Monotherapy expansion arms opened and enrolling as of May 20, 2024.

Werewolf THERAPEUTICS

WTX-124 program next steps

- ✓ WTX-124 dose of 18 mg IV Q2W has been selected as recommended dose for expansion (RDE)
- ✓ Monotherapy expansion arms in advanced or metastatic renal cell carcinoma (n=20), cutaneous melanoma (n=20), and cutaneous squamous cell carcinoma (n=10) now open for enrollment
- ✓ Dose escalation continuing for WTX-124 combination with pembrolizumab; selection of RDE and opening of combination expansion arms expected in 3Q24
- ✓ Next potential milestone in 4Q24/1Q25
    - Evaluation of monotherapy clinical activity in more homogeneous, less heavily pre-treated patient populations
    - FDA meeting to discuss potential registration pathways, including strategy for monotherapy accelerated approval in ICI relapsed/refractory indications

Abbreviations: IV-intravenous; Q2W-once every two weeks; ICI-immune checkpoint inhibitor

Werewolf THERAPEUTICS

Thank You