**A multicenter phase 1/2b dose escalation study of WTX-124 as a monotherapy and in combination with selected advanced or metastatic solid tumors**

**WTX-124**

An IL-2 INDUKINE™ molecule to address the limitations of recombinant human IL-2

**STUDY OBJECTIVES AND ENDPOINTS**

**OBJECTIVES**

1. **MonoTherapy (WTX-124)**
   - Evaluate safety and tolerability
   - Determine the maximum tolerated dose (MTD) and/or recommended dose for expansion (RD)

2. **Dose Expansion (N~70 patients)**
   - Safety must be established in the first three monotherapy cohorts
   - Determination of the highest safe dose as monotherapy
   - Evaluation of changes in immunological naïve

**ENDPOINTS**

- Safety
- Tumor effects
- Incidence of treatment emergent adverse events
- Antitumor activity
- PK/PD
- Proinflammatory cytokine toxicity limits therapeutic index

**PATIENT POPULATIONS**

**Cancer indications**

- Melanoma
- Renal cell carcinoma
- Non-squamous lung cancer
- Pancreatic ductal adenocarcinoma
- Cutaneous melanoma
- Thyroid cancer
- Severe chronic immune mediated inflammatory disorders

**Dose escalation**

<table>
<thead>
<tr>
<th>Dose Escalation (N=70 patients)</th>
<th>Dose Expansion (N~70 patients)</th>
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</thead>
<tbody>
<tr>
<td><strong>Monotherapy (WTX-124)</strong></td>
<td><strong>Dose Expansion (N~70 patients)</strong></td>
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<tr>
<td>WTX-124 100, 200, and 400 mcg (3-day “QW” cycle)</td>
<td>WTX-124 800 mcg (3-day “QW” cycle)</td>
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<tr>
<td>Only 1 prior line (L) maximum</td>
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<td>Prior ICI is mandatory</td>
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<tr>
<td>No dose above 400 mcg (Q3W) due to toxicity</td>
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**Dose Expansion**

<table>
<thead>
<tr>
<th>Dose Expansion for WTX-124 in monotherapy and combination therapy with pembrolizumab</th>
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<tbody>
<tr>
<td><strong>Arm A[CC1] and Arm B[Melanoma]</strong></td>
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<tr>
<td><strong>Melanoma (MM, wild type)</strong></td>
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<tr>
<td><strong>Melanoma (MM, mutant)</strong></td>
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<td><strong>Renal Cell Carcinoma</strong></td>
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**Clinical study sites**

1. **Cancer Institute of Emory University, Atlanta, GA**
2. **Providence Cancer Institute, Portland, OR**
3. **HonorHealth Research and Innovation Institute, Scottsdale, AZ**
4. **ProInflammatory Therapeutics, Providence Cancer Institute, (Portland, OR)**
5. **Next Oncology, San Antonio, TX**
6. **Werewolf Therapeutics, Inc., Watertown, MA**

**CLINICAL TRIAL PAGE**

http://www.werewolftx.com

**Summary and conclusions**

- Recombinant human IL-2 is an approved treatment for advanced melanoma and renal cell carcinoma, but its use is limited by a narrow therapeutic index
- WTX-124 is a novel INDUKINE™ molecule rationally engineered to optimize the therapeutic index for IL-2 therapy
- WTX-124 incorporates a wild type cytokine anticipated to leverage the full biology and potency of IL-2 to stimulate antitumor immune responses
- Enrollment in monotherapy dose escalation of the WTX-124a2101 first-in-human study is presently ongoing
- Guiding towards data package in Q4 2023