Werewolf Therapeutics to Present Data from Ongoing Phase 1/1b Clinical Trial of WTX-124 as Monotherapy and in Combination with Pembrolizumab in Solid Tumors

June 1, 2024

- WTX-124 was shown to be clinically active and generally well-tolerated in patients who were relapsed/refractory to immune checkpoint inhibitor therapy -

- Encouraging single agent clinical activity with three objective responses, including a durable confirmed complete response -

- Monotherapy recommended dose for expansion selected and expansion arms open for enrollment -

- Preliminary data on WTX-124 administered to patients in combination with pembrolizumab showed that the combination was generally well-tolerated with enhanced immune activation in tumors -

- Company to host webcast to review these data on Monday, June 3, 2024, at 8:00 am ET -

WATERTOWN, Mass., June 01, 2024 (GLOBE NEWSWIRE) -- Werewolf Therapeutics, Inc. (the "Company" or "Werewolf") (Nasdaq: HOWL), an innovative biopharmaceutical company pioneering the development of conditionally activated therapeutics engineered to stimulate the body's immune system for the treatment of cancer, today announced new clinical data from the Phase 1/1b trial evaluating WTX-124, its conditionally activated Interleukin-2 (IL-2) INDUKINE™ molecule, in patients with locally advanced or metastatic solid tumors after checkpoint inhibitor therapy. The data will be presented today, on June 1, 2024, in a poster session at the 2024 American Society of Clinical Oncology (ASCO) Annual Meeting in Chicago, Illinois, and in a webcast on June 3, 2024.

"Approved high-dose IL-2 (HD IL-2) has been known to be effective in creating durable responses for some patients, however the toxicity of the drug has meant that many patients are not eligible for the treatment," said Justin Moser, M.D., WTX-124 study investigator and Associate Clinical Investigator, HonorHealth Research Institute, Scottsdale, AZ. "The emerging data from the Phase 1/1b clinical trial of WTX-124 suggest that we may potentially achieve durable objective responses with a favorable safety profile for patients in the outpatient setting, some of whom would not have been candidates for HD IL-2."

"We are pleased to share these findings from our ongoing Phase 1/1b clinical trial of WTX-124 that build on the promise of our INDUKINE hypothesis that potent cytokine-based immunotherapies could address difficult-to-treat tumors while minimizing toxicities typical of IL-2 therapy," added Randi Isaacs, M.D., Chief Medical Officer. "We have selected our recommended dose for expansion (RDE) and opened three monotherapy expansion arms in more homogenous and less heavily pre-treated populations to better assess clinical activity in each while we continue to explore additional doses in dose escalation. In addition, the combination of WTX-124 with pembrolizumab was generally well-tolerated, which alongside compelling biomarker activity, suggests the potential for combination efficacy. Altogether, these results reinforce our conviction in WTX-124 as a potential best-in-class IL-2 therapy, and we look forward to providing additional updates as the program progresses."

The ongoing Phase 1/1b study is evaluating WTX-124 as a monotherapy and in combination with pembrolizumab in patients with immunotherapy sensitive advanced or metastatic solid tumors who have failed standard of care treatment, including checkpoint inhibitor therapy. The presentation at ASCO captures data from 47 heavily pretreated patients: 35 patients treated with at least one monotherapy dose of WTX-124, ranging from 1 mg to 28 mg; 12 patients treated with WTX-124 at doses ranging from 3 mg to 12 mg in combination with pembrolizumab.

Data as of the May 1, 2024, cutoff date are summarized as follows:

- WTX-124 as a monotherapy produced three objective clinical responses including one durable confirmed complete response (CR) and two partial responses (PRs) in patients who are relapsed/refractory to immune checkpoint inhibitor therapy.
- Responding patients had 100% regression of target lesions with responses occurring within the first two cycles of therapy and showing durability at RDE.
- Related treatment emergent adverse events (TEAEs) were primarily mild to moderate in severity, manageable and reversible; no new safety signals were identified when WTX-124 was combined with pembrolizumab.
- Analysis of paired tumor biopsies by NanoString suggests that WTX-124 robustly activated/expanded effector T cells preferentially over Tregs.
- Increased T cell activation signature for the combination suggests a potential for improved antitumor activity by combining WTX-124 with pembrolizumab.
- WTX-124 was clinically active and generally well tolerated in patients, not all of whom would be eligible for HD IL-2 based on age, indication or other factors.

These findings are summarized in a poster titled, *"A phase 1/1b trial of the IL-2 prodrug WTX-124 in patients with locally advanced or metastatic solid tumors after checkpoint inhibitor therapy: Updated results of the monotherapy dose escalation and initial results of the combination therapy dose*

escalation with pembrolizumab." The poster can be viewed in person from 9:00 am-12:00 pm CT on Saturday, June 1, 2024, on board number 102 and is available on the Company's website at https://investors.werewolftx.com/news-and-events/scientific-resources.

Next Steps for WTX-124 Development

Based on these results, Werewolf has selected a WTX-124 monotherapy dose of 18 mg administered intravenously every two weeks (IV Q2W), as the RDE to progress into the Phase 1b dose-expansion portion of the trial. The Company has thus far opened three expansion arms in advanced or metastatic renal cell carcinoma, cutaneous melanoma and cutaneous squamous cell carcinoma. Werewolf also continues to dose-escalate WTX-124 in combination with pembrolizumab and expects to select an RDE to open the combination dose-expansion portion of the study in the third quarter of 2024. In parallel, the Company also plans to engage regulators to discuss potential registrational pathways for WTX-124, including strategies for monotherapy accelerated approval in immune-checkpoint inhibitor relapsed/refractory indications.

Webcast Details

Werewolf will host a webcast at 8:00 am ET on Monday, June 3, 2024, to review these clinical results presented at ASCO. Werewolf management will be joined by study investigator Justin Moser, M.D., Associate Clinical Investigator, HonorHealth Research Institute, Scottsdale, AZ, who will present the updated data. The event can be accessed live at https://investors.werewolftx.com/news-and-events/events. An archived replay will be available for approximately 90 days following the event.

About Werewolf Therapeutics

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

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements that involve substantial risks and uncertainties. All statements, other than statements of historical facts, contained in this press release, including statements regarding Werewolf's strategy, future operations, prospects, plans, objectives of management, the expected timeline regarding the clinical development of product candidates, including the announcement of data, the potential activity and efficacy of product candidates in 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," "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 press release represent the Company's views as of the date of this press release. The Company anticipates that subsequent events and developments will cause its views to change. However, while the Company may elect to update these forward-looking statements at some point in the future, it specifically disclaims any obligation to do so. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date of this press release.

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