



Werewolf Therapeutics Presents Preclinical and Clinical Data at the Society for Immunotherapy of Cancer's (SITC) 39th Annual Meeting

November 7, 2024

- Interim phase 1 clinical trial update reveals the clinical potential of the tumor-activated IL-12 prodrug WTX-330, with favorable tolerability profile and encouraging efficacy signals -

- Additional preclinical data demonstrate INDUKINE™ molecules' anti-tumor potency with distinct immune activation profiles across four cytokines -

WATERTOWN, Mass., Nov. 07, 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 and other immune mediated conditions, today shared clinical and preclinical data at the 2024 Society for Immunotherapy of Cancer's (SITC) 39th Annual Meeting, taking place November 6-10 in Houston, Texas.

WTX-330, a potential first-in-class systemically delivered IL-12 therapy selectively activated in the tumor microenvironment, is currently being evaluated in a Phase 1 clinical trial: [NCT05678998](#). This is Werewolf's second clinical program to validate the INDUKINE design, delivering potent immune mechanisms to the tumor with improved tolerability and evidence of clinical efficacy. Preliminary clinical findings presented at SITC demonstrate WTX-330's promising therapeutic potential as a monotherapy, exhibiting a favorable tolerability profile and inducing tumor shrinkage in patients with treatment-resistant solid tumors, including those tumors that are less sensitive to immunotherapy. A Phase 1/2 dose- and regimen-finding clinical trial, designed to optimize WTX-330 exposure in the tumor microenvironment and explore activity in selected indications, is expected to begin enrolling in the first half of 2025.

"The data from this first-in-human trial of WTX-330 combined with the observed monotherapy activity seen in both immunotherapy sensitive and resistant solid tumors in heavily pretreated patients, reinforces our belief in WTX-330's potential to address critical unmet needs in oncology," said Randi Isaacs, M.D., Chief Medical Officer. "We are excited to advance the development of this novel therapeutic and explore its full clinical potential for the benefit of patients."

As of October 7, 2024, the study had enrolled twenty-five patients with diverse solid tumors, including microsatellite stable colorectal cancer (MSS CRC), cholangiocarcinoma, metastatic cutaneous melanoma, and non-small cell lung cancer (NSCLC), with more than 70% of patients having received at least two prior lines of therapy for metastatic disease. Key findings include:

- **Favorable tolerability profile:** Treatment-related adverse events (AEs) were primarily mild to moderate (most commonly fatigue, increased aspartate transaminase/alanine transaminase (AST/ALT), pyrexia, and neutropenia); severe AEs occurred but were manageable and reversible.
- **Pharmacokinetic improvements over rhIL-12:** WTX-330 had 22-fold greater plasma exposure than the reported maximum tolerated dose of rhIL-12 but with low levels of active IL-12 (<1.6% of prodrug).
- **IL-12 activity and tumor immune activation:** Evidence of IL-12 activity in the tumor microenvironment with four patients with MSS CRC showing evidence of tumor immune activation in on-treatment tumor biopsies.
- **Antitumor activity:** A 76 year old patient with diffuse in-transit metastatic melanoma who had progressed on adjuvant pembrolizumab achieved a Response Evaluation Criteria in Solid Tumors (RECIST) confirmed partial response.

Additionally, Werewolf presented preclinical data demonstrating the ability of INDUKINE molecules containing IL-2, IL-12, IL-21, or IL-18 cytokines to generate cytokine-specific antitumor immunity as monotherapy in mice bearing syngeneic tumors. These data revealed unique pharmacological profiles for each cytokine, underscoring the strategic rationale to develop each as an INDUKINE molecule for targeted therapeutic applications.

About WTX-330

WTX-330 was designed to be a systemically dosed prodrug with the ability to deliver fully active IL-12 selectively into the tumor microenvironment via targeted intratumoral activation of the INDUKINE molecule, potentially broadening the therapeutic window and promoting local activation and immune response against the tumor.

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 and other immune-mediated conditions. The Company is leveraging its 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. Werewolf's INDUKINE molecules are intended to remain inactive in peripheral tissue yet activate selectively in the tumor microenvironment. The Company's 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. Werewolf is advancing 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.werewolfx.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, and objectives of management; the expected timeline for the preclinical and clinical development of product candidates, and the availability of data from such preclinical and clinical development; the potential activity and efficacy of product candidates in preclinical studies and clinical trials; the anticipated safety profile of product candidates; and the upcoming presentations at SITC, 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 and 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 or interim data from a clinical trial will be predictive of the results of the trial and future clinical trials; the Company's ability to manage cash resources and obtain additional 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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