Werewolf Therapeutics Announces Initiation of Patient Dosing in Phase 1 Study of WTX-330

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WTX-330 is designed as systemically delivered, conditionally activated IL-12 therapy

Phase 1 Study of WTX-330 is intended to evaluate the safety, tolerability, and clinical activity of WTX-330 in Patients with Advanced or Metastatic Solid Tumors or Non-Hodgkin Lymphoma

Second clinical stage program of a new class of systemically delivered, conditionally activated INDUKINE™ therapeutics developed by Werewolf

WATERTOWN, Mass., Feb. 24, 2023 (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 that the first patient has been dosed in a Phase 1 clinical trial evaluating WTX-330, the Company's lead INDUKINE ™ molecule targeting Interleukin-12 (IL-12). The Phase 1 clinical trial is a first-in-human, multi-center, open-label trial that will evaluate WTX-330 in patients with advanced or metastatic solid tumors or lymphoma resistant to checkpoint inhibitors or for which checkpoint inhibitors are not approved.

"Dosing the first patient in our Phase 1 trial of WTX-330 marks the second INDUKINE molecule arising from our PREDATOR ™ protein engineering platform to enter the clinic. Our continued transition into a clinical stage company comes at an exciting time for Werewolf following the initiation of a Phase 1/1b clinical study of WTX-124 last year," said Daniel J. Hicklin, Ph.D., Werewolf's Founder and Chief Executive Officer. "WTX-330 serves as another example of our team's capacity to expand our clinical pipeline and validates our novel approach of developing conditionally activated cytokines as cancer therapies to improve outcomes for patients with hard-to-treat tumors."

"We are pleased to begin patient dosing in our Phase 1 clinical trial with WTX-330, a novel tumor-selective IL-12 therapy with the potential to address the shortcomings associated with recombinant IL-12, including toxicities resulting from off-tumor effects," said Randi Isaacs, M.D., Chief Medical Officer of Werewolf Therapeutics. "WTX-330 has the potential to be the only systemic, conditionally active IL-12 therapy with normal tissue IL-12R receptor blockade to deliver the full potency of IL-12 directly to the tumor microenvironment. We are eager to advance this candidate through the clinic with the goal of delivering a new treatment option for people living with cancer."

IL-12 has historically been an extremely attractive immuno-oncology mechanism, having the ability to regulate antitumor immunity through numerous innate and adaptive immune pathways, but to-date has been undruggable due to serious toxicities when administered systemically. WTX-330 is specifically designed to maximize clinical benefit and minimize the severe toxicities that have been observed with recombinant IL-12 therapy by including high affinity blockade of IL-12 – IL-12R interaction in systemic circulation and non-tumor tissues, half-life extension for optimal tumor exposure and proprietary tumor-selective protease activation.

In preclinical studies, WTX-330 exhibited excellent anti-tumor activity and a favorable pharmacokinetic and tolerability profile. WTX-330 was designed to mediate robust anti-tumor activity through stimulation of innate and adaptive antitumor immune responses, including dendritic cell maturation and cross-presentation, Th1 differentiation and amplification of antitumor T effector cell responses.

For additional information about the trial, please visit www.clinicaltrials.gov using the Identifier: NCT05678998

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 risk and uncertainties. All statements, other than statements of historical facts, contained in this press release, including statements regarding Werewolf's future operations, prospects, plans, the expected timeline for the clinical development of product candidates, and the potential activity and efficacy of product candidates in preclinical and clinical studies constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. The words "aim," "anticipate," "believe," "contemplate," "continue," "could," "design," "designed to," "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; 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; the Company's ability to obtain sufficient cash resources to fund the Company's foreseeable and unforeseeable operating expenses and capital expenditure requirements; the impact of the COVID-19 pandemic on the Company's business and operations; 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 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 press release.

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