Werewolf Therapeutics Announces Initiation of Patient Dosing in Phase 1/1b Clinical Trial of WTX-124 for the Treatment of Patients with Selected Solid Tumors

September 1, 2022

- First clinical candidate of a new class of systemically delivered conditionally activated INDUKINE™ therapeutics developed by Werewolf

- WTX-124 is designed to target delivery of a highly potent, wild-type IL-2 cytokine to the tumor microenvironment

WATERTOWN, Mass., Sept. 01, 2022 (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 1/1b clinical trial evaluating WTX-124, the Company's lead INDUKINE ^{TM} molecule targeting IL-2 for the treatment of solid tumors. The Phase 1/1b clinical trial is a first-in-human, multi-center, open-label trial that will evaluate WTX-124 as a monotherapy and in combination with KEYTRUDA® (pembrolizumab), Merck's anti-PD-1 (programmed death receptor-1) therapy in patients with immunosensitive advanced or metastatic solid tumors who have failed standard of care, including checkpoint inhibitor therapy.

"We are thrilled to share this important milestone for Werewolf of dosing the first patient in our Phase 1/1b trial of WTX-124," shared Daniel J. Hicklin, Ph.D., Werewolf's Founder and Chief Executive Officer. "WTX-124 is the first program from our portfolio of novel INDUKINE molecules to enter the clinic, and its progress into clinical investigation further highlights our team's ability to execute efficiently and move our pipeline forward. We believe WTX-124 presents a tremendous opportunity, not only to improve outcomes for patients with hard-to-treat solid tumors but also to validate our novel approach of developing conditionally activated cytokines as innovative cancer therapy."

The WTX-124 design consists of a wild-type IL-2 cytokine tethered to an inactivation domain to prevent activation in off-target tissue, a tumor protease-sensitive linker to allow for activation in the tumor micro-environment (TME) and a half-life extension domain to improve tumor exposure. The selective release of IL-2 in the TME induces anti-tumor immune responses resulting in tumor regressions in preclinical models while minimizing the toxicities associated with systemic delivery of recombinant IL-2.

"We are pleased to begin patient dosing in our Phase 1/1b clinical trial with WTX-124, a novel tumor-selective IL-2 candidate with the potential to increase the therapeutic benefit of IL-2 while decreasing the systemic toxicities often seen with high-dose IL-2 therapy," said Randi Isaacs, M.D., Chief Medical Officer of Werewolf Therapeutics. "WTX-124 has been designed to be active only within the TME, with the goal of reducing toxicity and enhancing anti-tumor activity. We look forward to advancing this trial to further our understanding of WTX-124 as a potential therapy for the treatment of people living with cancer."

For additional information about the trial, please visit www.clinicaltrials.gov using the identifier NCT05479812.

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 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 both WTX-124 and WTX-330 in multiple tumor types as a single agent and in combination with an immune checkpoint inhibitor.

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 strategy, future operations, prospects, plans, objectives of management, the expected timeline for entering clinical development for product candidates, and the potential activity and efficacy of product candidates in future 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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