Werewolf Therapeutics Publishes Preclinical Data on mWTX-330, an IL-12 INDUKINE™ Molecule, in Cancer Immunology Research

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WATERTOWN, Mass., April 19, 2023 (GLOBE NEWSWIRE) -- Werewolf Therapeutics, Inc. (the "Company" or "Werewolf") (Nasdaq: HOWL), an innovative biopharmaceutical company pioneering the development of conditionally activated therapeutics, announced the publication in *Cancer Immunology Research Online First* of preclinical data for mWTX-330, a systemically delivered Interleukin-12 (IL-12) INDUKINE™ molecule. The article, entitled "mWTX-330, an IL-12 INDUKINE Molecule, Activates and Reshapes Tumor-infiltrating CD8$^+$ T and NK Cells to Generate Antitumor Immunity," includes preclinical data that demonstrates that mWTX-330 delivers IL-12 selectively to the tumor microenvironment, where it stimulates a potent anti-tumor immune response [DOI: 10.1158/2326-6066.CIR-22-0705].

"IL-12 is a cytokine with broad stimulatory effects on various immune cell populations, having the ability to regulate antitumor immunity through numerous innate and adaptive immune pathways, but clinical administration has been limited due to serious toxicities when administered systemically," said Cynthia Seidel-Dugan, Ph.D., Chief Scientific Officer of Werewolf and one of the article's authors. "Our published preclinical data show that mWTX-330 generates potent anti-tumor immunity in mice by activating and restoring the metabolic health of tumor-infiltrating lymphocytes, with the potential to minimize the toxicity previously associated with systemic IL-12 administration."

Other key findings and data outlined in the article include:

- mWTX-330 treatment generates a robust, cleavage-dependent anti-tumor immune response in multiple syngeneic tumor models and is well tolerated.
- mWTX-330 delivery expands the therapeutic window of the IL-12 cytokine.
- mWTX-330 treatment activates various tumor-infiltrating lymphocyte populations in the MC38 mouse model and results in the transcriptional reprogramming of the tumor microenvironment and the subsequent activation of various tumor-infiltrating effector-cell populations.
- mWTX-330 treatment expands unique T-cell receptor (TCR) clones and increases TCR clonality in the tumor microenvironment.
- mWTX-330 treatment substantially increases mitochondrial activity in tumor infiltrating CD8+ T cells and NK Cells while reducing signs of exhaustion on CD8+ T cells.
- The fully human WTX-330 INDUKINE™ molecule is preferentially activated by primary human tumors.

Werewolf is currently recruiting patients for a first-in-human, multi-center, open-label Phase 1 clinical 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. For additional information about the trial, please visit **www.clinicaltrials.gov** using the Identifier: NCT05678998

WTX-330 was 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.

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 clinical studies for 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 the expected efficacy or safety of investigational new drugs based on preclinical data or Werewolf's strategy, future operations, prospects, plans, or objectives of management constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. The words "aim," "anticipate," "believe," "contemplate," "continue," "could," "estimate," "expect," "goal," "intend," "may," "might," "objective," "ongoing," "plan," "potential," "predict," "project," "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 our 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 Company's Annual Report on Form 10-K filed on March 23, 2023, 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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