Werewolf Therapeutics Presents Promising Preclinical Data on its Two Lead INDUKINE™ Molecules at AACR 2022 Annual Meeting

April 8, 2022

WTX-124 demonstrated high tumor selectivity and generated significant anti-tumor activity in a CD8+ T cell-dependent manner

WTX-330 surrogate demonstrated significant expansion of the therapeutic window, compared to recombinant IL-12, and generated potent anti-tumor immunity in multiple syngeneic tumor models

Werewolf CSO Cynthia Seidel-Dugan, Ph.D., to discuss the PREDATOR™Protein Engineering Platform During AACR Session

CAMBRIDGE, Mass., April 08, 2022 (GLOBE NEWSWIRE) -- Werewolf Therapeutics, Inc. (the "Company" or "Werewolf") (Nasdaq: HOWL), an innovative biopharmaceutical company pioneering the development of conditionally activated therapeutics, today announced it presented promising preclinical data on its IL-2 and IL-12 INDUKINE™ molecules, WTX-124 and WTX-330, respectively, in posters at the American Association for Cancer Research (AACR) Annual Meeting, taking place April 8-13, 2022, at the Ernest N. Morial Convention Center in New Orleans.

"Our conditionally activated, novel prodrug INDUKINE molecules continue to demonstrate targeted anti-tumor responses that reflect their design and engineering, remaining inactive in peripheral tissue, then unleashing an immune response within the tumor microenvironment," said Cynthia Seidel-Dugan, Ph.D., Chief Scientific Officer of Werewolf. "IL-2 and IL-12 are proinflammatory cytokines with great potential to treat people with cancer, but systemic toxicities and poor pharmaceutical properties have limited their clinical application. These data suggest our approach may overcome these limitations and address the shortcomings associated with current cytokine treatments."

Dr. Seidel-Dugan will discuss Werewolf's innovative PREDATOR™ protein engineering platform, in a talk entitled, "Transforming Powerful Proinflammatory Mechanisms Into Novel Therapies for Cancer Patients," during AACR session "New Developments in Immunotherapy: Targeting and Localizing Cytokine Activity," on Tuesday, April 12 at 12:30 PM CDT, in the Great Hall AD, Convention Center.

Both data posters are now available online to AACR Annual Meeting attendees, and can be viewed in person between 1:30-5:00 PM CDT on Monday, April 11, during the AACR session PO.IM02.13, "Immune Response to Therapies 1", Poster Section 37.

The WTX-124 data are summarized in a poster entitled, "WTX-124 is a Novel IL-2 Prodrug that is Conditionally Activated in Tumors and Drives Anti-Tumor Immunity by Activating Tumor Infiltrating CD8+ T Cells" (Abstract #2054). These preclinical data demonstrate WTX-124:

- is tumor-selective and generates significant anti-tumor activity in a CD8+ T Cell-dependent manner;
- has a better therapeutic window than recombinant human IL-2 (rhIL-2) or half-life extended rhIL-2;
- significantly shifts the transcriptional profile of the tumor microenvironment towards activation of various immune cell populations in both the MC38 and B16F10 models; and
- preferentially activates tumor infiltrating CD8+ and CD4+ T cells, with limited evidence of systemic T cell activation.

The WTX-330 data are summarized in a poster entitled, "WTX-330 is a Conditionally Activated IL-12 Prodrug that Fundamentally Reprograms Tumor Infiltrating CD8+ T Cells and Drives Tumor Regression" (Abstract #2055). These preclinical data demonstrate that a surrogate WTX-330:

- generates potent anti-tumor immunity in multiple syngeneic tumor models in a cleavage-dependent manner;
- displays a significant expansion of the therapeutic window compared to recombinant IL-12;
- induces an anti-tumor immune memory response;
- fundamentally shifts the transcriptional profile within the tumor and activates tumor infiltrating cytolytic effector cells in the MC38, B16-F10, and EMT6 tumor models

WTX-124 and WTX-330 INDUKINE molecules consist of wild-type IL-2 and IL-12 cytokines, respectively, tethered to an inactivation domain to prevent activation in peripheral tissue, a tumor protease-sensitive linker to allow for activation in the tumor microenvironment, and a half-life extension domain to improve tumor exposure.

Werewolf is developing WTX-124 as a potential monotherapy or in combination with checkpoint inhibitors in multiple tumor types. The Company has entered into a clinical trial collaboration agreement with Merck, known as MSD outside the United States and Canada, to 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 solid tumors.

Werewolf is developing WTX-330 as a single agent for the treatment of relapsed or refractory advanced or metastatic solid tumors, or lymphoma failing standard of care.

The Company expects to file an Investigational New Drug Application (IND) for WTX-124 in the second quarter of 2022, and for WTX-330 in the third quarter of 2022.

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 are continuing preclinical studies for both WTX-124 and WTX-330 and expect to advance each candidate in multiple tumor types as a single agent and in combination with an immune checkpoint inhibitor.

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 strategy, future operations, prospects, plans, objectives of management, the expected timeline for submitting investigational new drug applications and the potential activity 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," "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 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 "Risk Factors" section of the Company's Annual Report on Form 10-Q for the year ended December 31, 2021, 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.

Investor Contact:
Jonathan M. Nugent
Stern IR
212.698.8698
jonathan.nugent@sternir.com

Media Contact:
Amanda Sellers
VERGE Scientific Communications
301.332.5574
asellers@vergescientific.com

Company Contact:
Ellen Lubman
Chief Business Officer
Werewolf Therapeutics
elubman@werewolftx.com