Werewolf Therapeutics Presents Preclinical Data on mWTX-330, a Surrogate IL-12 INDUKINE™ Molecule, at the Society for Immunotherapy of Cancer Annual Meeting

November 10, 2022

- mWTX-330 is designed as a systemically delivered, conditionally activated IL-12 therapy and is a member of a novel class of INDUKINE™ therapeutics -

- Preclinical data supports the development of WTX-330, Werewolf's product candidate, for the potential treatment of selected advanced or metastatic solid tumors or lymphoma -

WATERTOWN, Mass., Nov. 10, 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 it will present preclinical data on mWTX-330, a mouse surrogate of its interleukin-12 ("IL-12") INDUKINE™ product candidate, WTX-330, at the 37th Annual Meeting of the Society for Immunotherapy of Cancer ("SITC") being held November 8-12, 2022, in Boston, and virtually.

Details will be presented in a poster titled, "mWTX-330, an IL-12 INDUKINE™ Molecule, Selectively Activates Tumor Infiltrating Lymphocytes and Reprograms the Tumor Microenvironment in Murine Syngeneic Tumor Models" (Abstract #1096) on Friday, November 11, 11:55 am - 1:25 pm, in Hall C. The full abstract is available on the SITC website.

Study data demonstrate that systemic administration of mWTX-330, a mouse surrogate INDUKINE molecule, generates potent anti-tumor activity in a cleavage-dependent manner and protective memory against re-challenge in multiple murine syngeneic tumor models. Additionally, the data showed substantial infiltration and robust IL-12 signaling in intratumoral CD8+ T cells.

"These promising preclinical data add to a growing body of evidence demonstrating the potential of WTX-330 to drive targeted anti-tumor immune responses selectively in the tumor microenvironment (TME)," said Cynthia Seidel-Dugan, Ph.D., Chief Scientific Officer of Werewolf Therapeutics. "This morning, in our Third Quarter 2022 release, we announced that the FDA has granted clearance of the investigational new drug (IND) application for WTX-330. We are excited to advance WTX-330 into the clinic and to continue developing a pipeline of novel proinflammatory cytokine therapies that have the potential to change the lives of cancer patients."

INDUKINE molecules are intended to remain inactive in peripheral tissue yet activate selectively in the TME through a unique combination of molecular components, including: (1) a fully potent wild-type cytokine; (2) a high affinity blockade element that allows for systemic circulation among non-tumor tissues in a "prodrug" state; (3) half-life extension for maximal tumor exposure; and (4) proprietary tumor-selective proteases for selective activation in the TME.

Systemic therapy with proinflammatory interleukin-12 ("IL-12") immune modulators is a validated approach for the treatment of cancer, as the cytokine is a potent inducer of innate and adaptive anti-tumor immunity, but potentially severe toxicities associated with systemic administration of IL-12 has prevented IL-12 treatment strategies from successful clinical application.

WTX-330 is a systemically delivered, conditionally activated IL-12 INDUKINE molecule designed to minimize toxicities and maximize clinical benefit that have been observed with recombinant IL-12 therapy, which Werewolf is developing as a potential first-in-class treatment for selected advanced or metastatic solid tumors or lymphoma resistant to checkpoint inhibitors or for which checkpoint inhibitors are not approved.

Data from the SITC poster presentation demonstrate that mWTX-330:

- generates robust anti-tumor immunity following activation in the tumor microenvironment;
- activates multiple immune cell populations, including CD8+ T cells, CD4+ T cells, and NK cells;
- protects against later rechallenge with the same tumor cell line in mice that rejected primary tumors;
- selectively activates various tumor infiltrating effector cells, with little evidence of immune cell activation in the peripheral blood or secondary lymphoid tissues;
- is better tolerated than chimeric IL-12, significantly expanding the therapeutic window of this cytokine due to the INDUKINE molecule design;
- increases the frequency of polyfunctional CD8+ T cells, skewed CD4+ non-Tregs towards a TH1 phenotype, and drives robust NK cell production of effector cytokines within the tumor; and
- metabolically reinvigorates effector cells in the tumor microenvironment, significantly increasing mitochondrial respiration by tumor infiltrating CD8+ T cells as well as NK cells.

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. 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 regarding preclinical and clinical development for product candidates, and the potential activity and efficacy of product candidates in preclinical studies and clinical trials 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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