Werewolf Therapeutics Presents Preclinical Results Demonstrating Anti-Tumor Effects of Pro-Inflammatory Cytokine Therapeutics WTX-518 and WTX-712 at AACR 2024 Annual Meeting

April 5, 2024

WTX-518, a conditionally activated IL-18 INDUKINE™ molecule that resists suppression by IL-18BP, led to complete tumor regressions in preclinical models

WTX-712, a conditionally activated IL-21 INDUKINE™ molecule has potent antitumor activity in preclinical models with a differentiated immune activation mechanism

WATERTOWN, Mass., April 05, 2024 (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, is presenting preclinical data on development candidates WTX-518 and WTX-712 in posters at the American Association for Cancer Research (AACR) Annual Meeting, taking place April 5-10 in San Diego, California.

"We are excited to share that both WTX-518 and WTX-712 demonstrate powerful immunotherapeutic effects in preclinical models," said Daniel J. Hicklin, Ph.D., President and Chief Executive Officer of Werewolf. "WTX-518 exhibits remarkable tumor-selective activation, resistance to IL-18BP and robust immune activation, overcoming key hurdles in the use of this promising cytokine in cancer therapy. WTX-712 acts through a unique mechanism that robustly activates tumor-specific T lymphocytes with an expanded therapeutic window through its selective release of wild-type IL-21 in the TME. These data collectively highlight the innovative strategies we are pursuing to further expand the repertoire of unique immune stimulating cytokine mechanisms in the fight against cancer."

Results highlighting WTX-518 findings are summarized in a poster titled, "Discovery of WTX-518, an IL-18 pro-drug that is conditionally activated within the tumor microenvironment and induces regressions in mouse tumor models" (Abstract # 4074). Key takeaways reveal that WTX-518:

- is inducible, and its in vitro activity is not impeded by IL-18BP;
- selectively delivers active binding protein resistant (BPR) IL-18 to the tumor microenvironment (TME); and
- promotes increased influx and activation of NK cells and polyfunctional CD8 T cells in the TME, and demonstrates complete tumor regression in the MC38 mouse tumor model.

The WTX-712 data are summarized in a poster titled, "WTX-712, a conditionally active IL-21 INDUKINE™ molecule, induces a strong anti-tumor phenotype through a differentiated mechanism" (Abstract # 4078). Key takeaways reveal that:

- WTX-712 demonstrates inducibility and antitumor activity with regressions in the MC38 mouse tumor model;
- IL-21 HLE (half-life extended) has superior anti-tumor efficacy compared to IL-2 HLE therapy in mouse tumor models that are highly resistant to anti-PD-1/PD-L1 treatment, in part due to the activation of type-I IFN pathways; and
- IL-21 HLE promotes sustained expansion and activation of tumor infiltrating CD8 T cells with increased polyfunctionality and induces expression of cytotoxic effector molecules (Granzyme A, Granzyme B, and perforin).

Both posters can be viewed in person from 9:00 a.m. to 12:30 p.m. PDT on Tuesday, April 9, during the session category "Immunology" at Poster Section 4, and will be available on our website at https://investors.werewolftx.com/news-and-events/scientific-resources.

Werewolf plans to develop WTX-518 and WTX-712 as potential immunotherapies in refractory and/or immunologically unresponsive tumors.

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, and the potential activity and efficacy of product candidates in preclinical 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-K 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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