Werewolf Therapeutics to Present Clinical and Preclinical Data at the Society for Immunotherapy of Cancer's (SITC) 38th Annual Meeting

October 31, 2023

- Interim, first-in-human clinical results from initial monotherapy dose-escalation cohorts in ongoing Phase 1/1b study of WTX-124 including safety and preliminary antitumor activity to be described in poster presentation.
- Additional posters representing an expansive body of data demonstrating the potential of Werewolf's PREDATOR™ platform and INDUKINE™ product candidates will also be presented.
- Company to host conference call and webcast to review WTX-124 initial clinical results November 3, 2023, at 8:30 am ET

WATERTOWN, Mass., Oct. 31, 2023 (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 a poster describing interim first-in-human clinical results from initial monotherapy dose-escalation cohorts in the ongoing Phase 1/1b study of WTX-124 will be presented at the Society for Immunotherapy of Cancer's (SITC) 38 th Annual Meeting, taking place November 1-5, 2023 in San Diego, California. Additional posters with preclinical data supporting the PREDATOR platform and INDUKINE product candidates will also be presented at the meeting.

"At SITC, we look forward to sharing first-in-human clinical results from our lead candidate, WTX-124, including initial assessments of safety, pharmacokinetics, relevant biomarkers and preliminary antitumor activity from the ongoing monotherapy dose-escalation portion of our Phase 1/1b study in solid tumors. These data will provide early insight into the profile of WTX-124 and preferential activation through our INDUKINE design, including additional data since the abstract submission in June," said Randi Isaacs, M.D., Chief Medical Officer of Werewolf. "Several preclinical abstracts were also accepted for poster presentation, collectively reinforcing distinct immune activating potential of our INDUKINE molecules across various mechanisms, including IL-2, and as a complement to other anti-cancer approaches, including checkpoint inhibitors and cell therapy."

All posters will be available at https://investors.werewolftx.com/news-and-events/scientific-resources at 12:00 pm ET on Friday, November 3, 2023. The posters corresponding to the first three abstracts described below will be presented at SITC on Friday November 3rd and the posters corresponding to the second three abstracts described below will be presented on Saturday November 4th.

Abstract Highlights:

Highlights of the abstracts, which are now available on the SITC website, include:

Abstract Title: A Phase 1/1b Study of the Tumor-Activated IL-2 Prodrug WTX-124 Alone or in Combination with Pembrolizumab in Patients with Immunotherapy-Sensitive Locally Advanced or Metastatic Solid Tumors
Abstract Number: 737

- This Phase 1/1b, multi-center, open-label clinical trial is designed to evaluate WTX-124 as a monotherapy and in combination with KEYTRUDA® (pembrolizumab) in patients with immunotherapy sensitive advanced or metastatic solid tumors who have failed standard of care, including prior checkpoint inhibitor therapy.
- As of June 22, 2023, 11 patients with relapsed/refractory solid tumors, including non-small cell lung cancer, cutaneous melanoma and renal cell carcinoma were treated with WTX-124 in three monotherapy dose escalation cohorts of 1, 3 and 6 mg administered intravenously every two weeks.
- WTX-124 was well-tolerated with no dose limiting toxicities at doses up to 6mg.
- Pharmacokinetic data as of June 22, 2023, demonstrated WTX-124 sustained prodrug exposure in plasma with low levels of active IL-2.
- These results support the potential of WTX-124 to deliver a potent, wild-type IL-2 to the tumor microenvironment in patients with solid tumors with limited toxicities.

Abstract Title: Spatial Analysis of Tumor Infiltrating Lymphocyte Populations in Syngeneic Mouse Tumor Models After Treatment with IL-12 (mWTX-330) and IL-2 (WTX-124) INDUKINE™ Molecules
Abstract Number: 1059

- Tumor growth over time was measured in mice bearing syngeneic tumors treated with either mWTX-330 (a chimeric IL-12 containing INDUKINE ™ molecule) or WTX-124 (a human IL-2 containing INDUKINE molecule) using various techniques, including high-plex immunofluorescence, resulting in significant remodeling of immune cell populations found within the tumor tissue and simultaneously increased immune cell infiltration generating a potent activation of effector cells.
- These results were further amplified in combination with PD-1 pathway inhibitors, highlighting the potential for INDUKINE

™ treatments to improve the effects of checkpoint inhibition therapies.

Abstract Title: Development of WTX-712, a Conditionally Activated IL-21 INDUKINE™ Molecule for the Treatment of Cancer
Abstract Number: 1075

- Human IL-21 receptor knock-in (hIL-21R KI) mice bearing syngeneic tumors were treated with WTX-712, an IL-21 INDUKINE™ molecule, or half-life extended human IL-21 to monitor tumor growth and body weight over time via flow cytometry, tissue pharmacokinetics and high-plex immunofluorescence.
- WTX-712 exhibited activity with an expanded therapeutic window compared to half-life extended IL-21 in mouse syngeneic tumor models including complete regressions and protection against tumor growth upon rechallenge.

Title: The Combination of ACT and INDUKINE™ Therapy Leads to Improved Antitumor Immunity in Solid Tumors
Abstract Number: 252

- The ability of INDUKINE molecules to improve the engraftment and antitumor activity of adoptive cell therapy (ACT) products was evaluated using a pmel-1 transgenic mouse model and a human CD19 CAR-T cell model.
- The combination of pmel-1 ACT and INDUKINE™ polypeptides enhanced antitumor activity and animal survival compared to either pmel-1 or INDUKINE treatment alone, including increased donor cell engraftment and persistence of long-term effector memory T cells in both the periphery and the tumor microenvironment.

Title: Optimal Antitumor Immunity Triggered by WTX-124, a Clinical Stage Conditionally Activated INDUKINE™ Molecule that Releases Fully Potent IL-2 in the Tumor Microenvironment
Abstract Number: 1058

- The potential benefits of full activation of IL-2 were evaluated to determine antitumor response in syngeneic tumor models of WTX-124 as compared to non-alpha forms of IL-2 designed to reduce dose limiting toxicities associated with current cytokine therapy.
- Systemic administration of WTX-124 resulted in robust antitumor immunity and preferentially activated tumor-infiltrating immune cells as compared to a non-alpha IL-2 version of the INDUKINE demonstrating that the full activity of IL-2 contained in WTX-124 is required to activate potent antitumor responses.

Title: PK/RO Modeling of WTX-124, a Tumor-Activated IL-2 Prodrug, Highlights the Potential for a Substantially Improved Therapeutic Index Compared to Other IL-2 Molecules
Abstract Number: 1074

- A pharmacokinetic model was developed to evaluate peripheral and tumor lymphocyte IL-2 receptor occupancy for tumor-activated IL-2 molecules such as WTX-124 as compared to non-alpha IL-2 molecules.
- WTX-124 was found to be more likely to improve the therapeutic index by maximizing receptor occupancy on tumor-infiltrating CD8+ T cells than comparable doses of non-alpha IL-2 molecules and substantially higher doses of the non-alpha IL-2 molecule were required to attain the same receptor occupancy.

Conference Call & Webcast Details

Werewolf management will host a conference call and webcast at 8:30 am ET on Friday, November 3, 2023, to review initial clinical results from the ongoing Phase 1/1b study of WTX-124 that will be presented at SITC. The event can be accessed live at https://investors.werewolftx.com/news-and-events/events. An archived replay will be available for approximately 90 days following the event.

About Werewolf Therapeutics:

Werewolf Therapeutics, Inc. is an innovative clinical-stage 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 for the treatment of solid tumors. WTX-124 is in development as a monotherapy and in combination with KEYTRUDA® (pembrolizumab) in multiple solid tumor types. WTX-330 is in development as a single agent in refractory and/or immunotherapy unresponsive or resistant advanced or metastatic solid tumors and non-Hodgkin lymphoma.

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, the expected timeline for the clinical development of product candidates and availability of data from such clinical development, and the potential activity, efficacy and safety 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 and clinical trials; 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; whether interim data from a clinical trial will be predictive of the results of the trial and future 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; 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 press release. 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:
Josh Rappaport Stern IR 212.362.1200
Josh.Rappaport@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