Werewolf Therapeutics Presents Data Expanding Its PREDATOR® Platform at the Society for Immunotherapy of Cancer's (SITC) 40th Annual Meeting

November 7, 2025

Novel INDUCER™ T Cell Engager Platform designed to mitigate systemic toxicities

Sequential dosing of INDUKINE™ molecules in preclinical model showed potent antitumor activity with improved safety

First-in-kind real-time pharmacokinetic data in a mouse tumor model confirmed WTX-124 selective activation in tumors, sparing healthy tissue

WATERTOWN, Mass., Nov. 07, 2025 (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 and other immune-mediated conditions, today shared preclinical data at the 2025 Society for Immunotherapy of Cancer's (SITC) 40th Annual Meeting, taking place November 5-9, 2025, in National Harbor, Maryland.

Werewolf's proprietary PREDATOR platform uses clinically validated protease-cleavable linkers for tumor-selective activation to improve the therapeutic index. This technology has already produced three clinical-stage INDUKINE candidates. The new preclinical data presented at SITC expand on this foundation by demonstrating two novel therapeutic strategies: a sequential regimen designed to safely harness the complementary immune mechanisms of IL-12 and IL-2, and the development of masked, conditional T cell engagers (INDUCER molecules) designed to mitigate systemic toxicities. These strategies are supported by first-in-kind pharmacokinetic data that provided a real-time assessment of WTX-124's selective activation and immune engagement within the tumor.

"These data significantly expand the value of our PREDATOR platform by presenting a compelling sequential administration strategy for our INDUKINE molecules and extending our unique approach to the T cell engager modality," said Randi Isaacs, M.D., Chief Medical Officer, Werewolf Therapeutics. "Critically, we are now able to show tumor-selective activation of our technology in real time, validating the same core mechanism that is currently being tested in our clinical trials for WTX-330 and WTX-124. This reinforces our conviction that this technology has the potential to deliver potent medicines while overcoming the challenge of systemic toxicities."

Key findings include:

- **INDUCER Platform mitigated T Cell Engager toxicity with a novel masking strategy**
  Abstract # 964
  - INDUCER molecules use a differentiated masking approach on the anti-CD3 domain that prevents systemic T cell activation and cytokine release in preclinical models.
  - The mask was efficiently removed only in the presence of human tumor tissue, unleashing potent T cell activation and anti-tumor activity, demonstrating the platform's potential to improve the safety and efficacy of this powerful class of cancer drugs.
- **Sequential IL-12 and IL-2 dosing enhanced antitumor activity with improved tolerability**
  Abstract # 861
  - In mice bearing poorly immunogenic EMT6 tumors, a sequential regimen of mWTX-330 (IL-12) followed by WTX-124 (IL-2) was well tolerated and demonstrated superior tumor-killing ability compared to either drug alone.
  - These data suggest that mWTX-330 (IL-12) primes the immune response, and WTX-124 (IL-2) subsequently amplifies it, leveraging their complementary mechanisms of action to create a potent and translatable therapeutic strategy.
- **Real-time spatiotemporal dynamics confirmed WTX-124's tumor-selective activity**
  Abstract # 862
  - Using microdialysis in live animals to monitor IL-2 INDUKINE pharmacology in a syngeneic murine model, WTX-124 was shown to release active IL-2 selectively in the tumor, with minimal active cytokine released in the plasma, validating the prodrug design.
  - This localized IL-2 release drove a robust immune response, increasing the infiltration of NK and CD8+ T cells in the tumor, as well as selective production of effector cytokines like IFNg.

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 and other immune-mediated conditions. The Company is leveraging its proprietary PREDATOR ® platform to design conditionally activated INDUKINE™ and INDUCER™ molecules that stimulate both adaptive and innate immunity with the goal of addressing the limitations of conventional proinflammatory immune therapies. Werewolf's INDUKINE molecules are intended to remain inactive in

peripheral tissue yet activate selectively in the tumor microenvironment. The Company's 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. Werewolf is evaluating WTX-124 in multiple tumor types as a single agent and in combination with an immune checkpoint inhibitor and WTX-330 in multiple solid tumor types as a single agent. Werewolf is leveraging positive data from its INDUKINE molecules to advance the development of INDUCER molecules. Werewolf's first INDUCER development candidate, WTX-1011, targets STEAP1 for prostate cancer. To learn more visit www.werewolftx.com.

Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements that involve substantial risks 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, and objectives of management; the expected timeline for the preclinical and clinical development of product candidates and the availability of data from such preclinical and clinical development; the potential activity and efficacy of product candidates in preclinical studies and clinical trials; and the anticipated safety profile of product candidates 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," "engineered," "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, and 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; whether results from preclinical studies will be predictive of the results of later preclinical studies and clinical trials; the Company's ability to manage cash resources and obtain additional 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.

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