Werewolf Therapeutics Announces Pipeline and Business Updates

December 18, 2025

- WTX-124 initial Phase 1b expansion arm data showed 30% overall response rate as a monotherapy in a defined subset of post-ICI advanced or metastatic cutaneous melanoma patients, with potential best-in-class tolerability profile
- WTX-330 Phase 1b/2 trial initial data demonstrated additional evidence of antitumor activity and highly favorable tolerability profile, building upon monotherapy activity demonstrated in first-in-human Phase 1 clinical trial
- Additional Phase 1/1b data update for WTX-124 and completion of Part A of Phase 1b/2 clinical trial for WTX-330 are both expected in the first half of 2026
- WTX-1011, Werewolf's first nominated INDUCER™ T cell engager development candidate targeting advanced, relapsed/refractory STEAP1-expressing cancers, continues to progress towards IND; with the announcement of Werewolf's second INDUCER development candidate, WTX-2022, targeting CDH6-expressing cancers, Werewolf is now planning for two INDs by mid-2027

WATERTOWN, Mass., Dec. 18, 2025 (GLOBE NEWSWIRE) -- Werewolf Therapeutics, Inc. (Nasdaq: HOWL) (the "Company" or "Werewolf"), 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, today announced a pipeline update, including a review of recent data for its INDUKINE™ programs, and a business overview of its priorities for 2026 that includes a focus on the Company's highly differentiated INDUCER T cell engager platform. The Company is seeking strategic partnerships for further development of the promising WTX-124 and WTX-330 INDUKINE programs, informed by additional data from ongoing studies.

Dan Hicklin, PhD, President and CEO of Werewolf said, "Werewolf is dedicated to developing novel, tumor activated immunotherapies for the treatment of cancer. We are encouraged by the unprecedented clinical responses in conjunction with tolerability demonstrated by WTX-124 as a monotherapy and in combination with pembrolizumab in patients with cancers refractory to standard of care. We believe these data provide a rationale for further development of WTX-124 in the refractory setting as well as potential development in earlier lines of therapy. We are also pleased that recent WTX-330 data further demonstrated a very favorable tolerability profile and additional evidence of monotherapy activity in particularly difficult to treat immunotherapy resistant cancers. These clinical data from our WTX-124 and WTX-330 INDUKINE programs have provided important validation for our core PREDATOR® platform technology. We are excited to apply this validated technology to our new INDUCER T cell engager platform where preclinical studies have demonstrated potentially best-in-class silencing and reduction of off-tumor toxicity that has the potential to address the challenges and gaps of current T cell engagers."

Recent preliminary data for the INDUKINE programs:

- Compelling data from the Phase 1/1b clinical trial for WTX-124 as of October 30, 2025, included objective, durable responses as a monotherapy in melanoma, cutaneous squamous cell carcinoma, and gastroesophageal junction cancer, and in combination with pembrolizumab in cutaneous melanoma, non-small cell lung cancer, and renal cell carcinoma.
    - Monotherapy objective response rate of 21% seen in heavily pretreated patients with advanced or metastatic cutaneous melanoma is consistent with historic high-dose IL-2 activity.
    - For patients in this same melanoma population who had a prior response to any immunotherapy regimen (i.e., were not primary resistant to immunotherapy), a 30% objective response rate was observed.
    - Among patients treated on study with either 12 or 18 mg of WTX-124, tumor regression was seen in approximately 33% of tumors, including renal cell carcinoma, cutaneous squamous cell carcinoma, non-small cell lung cancer, and additional solid tumor indications.
    - There was no evidence of vascular leak syndrome or recurrence of prior immune-related adverse events, and with Grade 3 and 4 related TEAEs seen in 25.5% (27/106) and 1.9% (2/106), based on clinical data as of October 20, 2025.
    - In addition, at a recent End of Phase 1 meeting with the FDA, 18 mg was accepted as the recommended dose to move forward in development, and the FDA provided initial guidance for a monotherapy WTX-124 registration path in post-ICI advanced or metastatic relapsed/refractory melanoma.
- In the Phase 1b/2 clinical trial of WTX-330, additional evidence of highly favorable tolerability and antitumor activity in

challenging tumor types was observed in the first twelve patients treated as of the data cutoff date of October 31, 2025. These results build upon data from the first-in-human Phase 1 clinical trial completed in the first quarter of 2025.

- An optimized manufacturing process for WTX-330 was introduced in this study, which further improved the safety profile, pharmacokinetics, and therapeutic index.
- At a dose of 0.024 mg/kg IV Q2W, WTX-330 had a 17-fold higher Cmax than the published Cmax of rhIL-12, and at all dose levels, free IL-12 levels were 0.12% of prodrug exposure.
- As of December 2, 2025, there was one confirmed partial response in metastatic gall bladder cancer failing prior standard of care with a 45% reduction in tumor target lesions by RECIST 1.1.

Key Updates and 2026 Priorities

The Phase 1/1b clinical trial of WTX-124 is expected to be completed in the first half of 2026, with an additional data update planned to be provided at that time. Additional funding will be required to initiate any further development, which could include a registration-enabling trial. An update from the dose- and regimen-determining Part A of the Phase 1b/2 clinical trial of WTX-330 is expected in the first half of 2026. Additional funding will be required to further develop WTX-330, which could include sequential administration of WTX-330 and WTX-124 that may provide a novel development path in poorly immunogenic tumors. The Company is seeking strategic partners for its INDUKINE programs.

Werewolf's INDUCER molecules incorporate several differentiating features to address the limitations of other T-cell engager approaches by improving the therapeutic index, enhancing INDUCER exposure in the target tissue, and careful selection of tumor associated antigens that have the potential for preferential tumor association compared to normal tissue. We believe these qualities could establish Werewolf as the leading T cell engager company. INDUCER molecules utilize a proprietary masking approach and the same novel linker technology that has been clinically validated in the WTX-124 and WTX-330 programs. The preliminary preclinical data on the Company's first development candidate, WTX-1011, targeting STEAP1 were consistent with preclinical data from the second, newly announced development candidate, WTX-2022, that targets the CDH6 tumor associated antigen. Preclinical data for each candidate demonstrated the power of the INDUCER technology with robust silencing, reversible masking and highly efficient activation in human tumor tissue. Additionally, these data showed potent, consistent and compelling preclinical anti-tumor activity in murine models of human tumor xenografts and excellent prevention of cytokine release in initial non-human primate studies. Cell line development has been initiated for each program and IND-enabling studies are underway, with IND filings planned for mid-2027, pending additional funding.

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 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, and its second INDUCER candidate, WTX-2022, targets CDH6 for ovarian and kidney cancer.

To learn more visit www.werewolftx.com or follow us on LinkedIn.

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, including potential strategic partnerships; the projection of the cash runway; the expected timeline for the preclinical and clinical development of product candidates and the availability of data from such preclinical and clinical development; the timing of anticipated regulatory engagement; 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; 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 preliminary or interim data from a clinical trial will be predictive of the future results of the trial and future 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 has made and 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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