UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of The Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): June 25, 2024

WEREWOLF THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-40366**	**82-3523180**
(State or Other Jurisdiction of Incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

200 Talcott Ave, 2nd Floor **Watertown, Massachusetts** **(Address of Principal Executive Offices)**	**02472** **(Zip Code)**

Registrant's telephone number, including area code: (617) 952-0555

(Former Name or Former Address, if Changed Since Last Report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (*see* General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	HOWL	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☒

Item 7.01. Regulation FD Disclosure.

On June 25, 2024, Werewolf Therapeutics, Inc. (the "Company") issued a press release announcing initial results from the Company's Phase 1 clinical trial evaluating WTX-330, its conditionally activated interleukin-12 ("IL-12") INDUKINE™ molecule. A copy of the press release is furnished as Exhibit 99.1 hereto and is incorporated herein by reference.

The information furnished under this Item 7.01, including Exhibit 99.1, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 8.01. Other Events.

Initial Safety and Efficacy Data from Phase 1 Clinical Trial of WTX-330

On June 25, 2024, the Company announced initial results from the Phase 1 clinical trial evaluating WTX-330 as monotherapy in patients with advanced or metastatic solid tumors or non-Hodgkin lymphoma.

As of the cutoff date of June 12, 2024, the study had dosed eleven patients in dose escalation with solid tumors relapsed or refractory to all standard of care therapies with at least one dose of WTX-330 across three dose escalation cohorts, 0.016 mg/kg (n=3), 0.024 mg/kg (n=3), or 0.032 mg/kg (n=5) and two patients in dose expansion at 0.024 mg/kg.

Preliminary results as of the cutoff date showed:

- Compared to previous IL-12 therapeutic strategies (recombinant human IL-12 at 500 ng/kg (maximum tolerated dose)), at the 0.024 mg/kg dose, WTX-330 demonstrated an approximately 23-fold higher systemic drug concentration of IL-12 prodrug delivered to patients in the outpatient setting, with low free IL-12 levels across all dose levels (<1.6% of prodrug exposure).
- One patient with metastatic melanoma who had previously progressed on adjuvant pembrolizumab was treated with 0.024 mg/kg WTX-330 administered intravenously once every two weeks and achieved an unconfirmed partial response by Response Evaluation Criteria in Solid Tumors ("RECIST") after eight weeks with no evidence of disease on biopsy and marked decreased uptake on positron emission tomography imaging. A confirmatory scan for this patient is pending. Two additional patients with microsatellite stable ("MSS") colorectal cancer ("CRC") were treated with 0.032 mg/kg WTX-330 administered intravenously once every two weeks and achieved RECIST stable disease, one for 24 weeks with evidence of tumor biomarker activity.
- Evidence of increased antitumor CD8+ T and natural killer cell expansion and activation in on-treatment tumor biopsies and/or upregulation of tumor immune gene signatures were observed in the two MSS CRC patients with stable disease.
- All patients exhibited mild to moderate treatment-related toxicities (fever, chills, cytopenias) primarily associated with the first dose, with no Grade 4 or Grade 5 related adverse events. These were correlated with dose-dependent increases in peripheral IFNg and IP-10. Two patients experienced reversible dose-limiting toxicities (Grade 3 mucositis, Grade 3 aspartate aminotransferase increase) at the 0.032 mg/kg dose level, including the MSS CRC patient with prolonged stable disease who remained on therapy for over 6 months after resolution of the mucositis. A maximum tolerated dose has not been established.
- The Company has opened two expansion arms evaluating 0.024 mg/kg of WTX-330. Eligible patients include those with immune checkpoint inhibitor ("ICI")-sensitive solid tumors who demonstrate primary or secondary resistance to immunotherapy and patients with solid tumors or lymphoma for whom ICI blockade is not approved or indicated. Two patients have been enrolled into the expansion arms to date and have received at least one dose of WTX-330.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Press Release, dated June 25, 2024.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

Cautionary Note Regarding Forward-Looking Statements

Any statements in this Current Report on Form 8-K about the Company's future expectations, plans and prospects, as well as any other statements regarding matters that are not historical facts, may constitute "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements are subject to substantial risks and uncertainties and actual results may differ materially from those expressed or implied by such forward-looking statements. Such statements include statements regarding the Company's strategy, future operations, prospects, plans, objectives of management, the expected timeline regarding the clinical development of product candidates, including the announcement of data, the potential activity and efficacy of product candidates in preclinical studies and clinical trials, and the timing and outcome of planned meetings with regulatory authorities. The words "aim," "anticipate," "approach," "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, 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 or preliminary 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 Current Report on Form 8-K represent the Company's views as of the date of this Current Report on Form 8-K. 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 Current Report on Form 8-K.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

WEREWOLF THERAPEUTICS, INC.

By:

Date: June 25, 2024

/s/ Timothy W. Trost
Timothy W. Trost
Chief Financial Officer and Treasurer

Werewolf Therapeutics Highlights Initial Safety and Efficacy Data from its Ongoing Phase 1 Clinical Trial Evaluating WTX-330 in Patients with Advanced or Metastatic Solid Tumors or Non-Hodgkin Lymphoma

- Data demonstrate that administration of WTX-330 reached therapeutically relevant exposure levels of systemically delivered IL-12 prodrug with an improved tolerability profile over historical data for rhIL-12 -

- Early WTX-330 dose-escalation data demonstrated encouraging clinical activity and evidence of immune biomarker activity including an unconfirmed partial response in a metastatic melanoma patient -

- Expansion arms open to checkpoint inhibitor-resistant or -naïve relapsed or refractory advanced tumor patients; additional results anticipated in the fourth quarter of 2024 -

WATERTOWN, Mass., June 25, 2024 — 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 initial results from the Phase 1 clinical trial evaluating WTX-330, its conditionally activated interleukin-12 (IL-12) INDUKINE™ molecule, as monotherapy in patients with immunotherapy insensitive or resistant locally advanced or metastatic solid tumors or non-Hodgkin lymphoma.

"Our focus at Werewolf is grounded in advancing a pipeline of next generation, transformative immuno-stimulatory medicines," said Daniel J. Hicklin, Ph.D., President and Chief Executive Officer of Werewolf. "These preliminary clinical data show promising tolerability and signals of efficacy of WTX-330 in heavily pretreated patients with late-stage solid tumors. We look forward to continued advancement of WTX-330 and further understanding the potential clinical benefit for this molecule."

IL-12 therapy holds tremendous promise for immune-resistant cancer patients but has been historically limited by severe toxicity, like many cytokines. Werewolf is developing a novel, conditionally activated IL-12, WTX-330, in order to overcome this key limitation with its systemically administered, tissue-targeted technology, optimizing its therapeutic index so that efficacious doses can be delivered for clinical impact.

As of the cutoff date of June 12, 2024, the study had dosed eleven patients in dose escalation with solid tumors relapsed or refractory to all standard of care therapies with at least one dose of WTX-330 across three dose escalation cohorts, 0.016 mg/kg (n=3), 0.024 mg/kg (n=3), or 0.032 mg/kg (n=5) and two patients in dose expansion at 0.024 mg/kg.

Preliminary results as of the cutoff date showed:

- **Greatly increased therapeutic window:** Compared to previous IL-12 therapeutic strategies (recombinant human IL-12 (rhIL-12) at 500 ng/kg (maximum tolerated dose)), at the 0.024 mg/kg dose, WTX-330 demonstrated an approximately 23-fold higher systemic drug concentration of IL-12 prodrug delivered to patients in the outpatient setting, with low free IL-12 levels across all dose levels (<1.6% of prodrug exposure).
- **Encouraging signals of clinical activity:** One patient with metastatic melanoma who had previously progressed on adjuvant pembrolizumab was treated with 0.024 mg/kg WTX-330 administered intravenously once every two weeks (IV Q2W) and achieved an unconfirmed partial response by Response Evaluation Criteria in Solid Tumors (RECIST) after eight weeks with no evidence of disease on biopsy and marked decreased uptake on positron emission tomography (PET) imaging. A confirmatory scan for this patient is pending. Two additional patients with microsatellite stable (MSS) colorectal cancer (CRC) were treated with 0.032 mg/kg WTX-330 IV Q2W and achieved RECIST stable disease, one for 24 weeks with evidence of tumor biomarker activity.
- **Robust activation of immune biomarkers:** Evidence of increased antitumor CD8+ T and natural killer (NK) cell expansion and activation in on-treatment tumor biopsies and/or upregulation of tumor immune gene signatures were observed in the two MSS CRC patients with stable disease.
- **Emerging tolerability profile:** All patients exhibited mild to moderate treatment-related toxicities (fever, chills, cytopenias) primarily associated with the first dose, with no Grade 4 or Grade 5 related adverse events. These were correlated with dose-dependent increases in peripheral IFN g and IP-10. Two patients experienced reversible dose-limiting toxicities (Grade 3 mucositis, Grade 3 aspartate aminotransferase (AST) increase) at the 0.032 mg/kg dose level, including the MSS CRC patient with prolonged stable disease who remained on therapy for over 6 months after resolution of the mucositis. A maximum tolerated dose has not been established.
- **Expanded Phase 1 program:** The Company has opened two expansion arms evaluating 0.024 mg/kg of WTX-330. Eligible patients include those with immune checkpoint inhibitor (ICI)-sensitive solid tumors who demonstrate primary or secondary resistance to immunotherapy (Arm A) and patients with solid tumors or lymphoma for whom ICI blockade is not approved or indicated (Arm B). Two patients have been enrolled into the expansion arms to date and have received at least one dose of WTX-330.

“We believe this is the first time that clinical benefit using a full-potency, systemically delivered, IL-12 molecule has been observed at therapeutically relevant doses with fewer severe toxicity-related events in an outpatient setting,” said Randi Isaacs, M.D., Chief Medical Officer of Werewolf. “We are encouraged by these early results and anticipate presenting further safety, biomarker, and antitumor activity from patients enrolled in expansion arms at a medical meeting in the fourth quarter of 2024.”

About IL-12

Interleukin-12 (IL-12) is a cytokine well recognized as a promising antitumoral therapeutic agent due to its range of functions that include activation of natural killer (NK) cells, NK T and CD8+ T cells, promotion of dendritic cell (DC) antigen presentation, and production of IFN-γ. Native IL-12 is highly toxic, and all previous methods of administration of the molecule at potentially efficacious doses have resulted in unmanageable systemic toxicities or lack of efficacy. To leverage the potent therapeutic properties of IL-12, there is a need to develop locally active but systemically blocked IL-12-based treatment approaches.

About WTX-330

WTX-330 was designed to be a systemically dosed prodrug with the ability to deliver fully active IL-12 selectively into the tumor microenvironment via targeted intratumoral activation of the INDUKINE molecule, potentially broadening the therapeutic window and promoting local activation and immune response against the tumor.

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 are advancing 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 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, objectives of management, the expected timeline regarding the clinical development of product candidates, including the announcement of data, the potential activity and efficacy of product candidates in preclinical studies and clinical trials, and the timing and outcome of planned meetings with regulatory authorities, constitute forward-looking statements within the meaning of The Private Securities Litigation Reform Act of 1995. The words "aim," "anticipate," "approach," "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, 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 or preliminary 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.

PREDATOR® is a registered trademark of Werewolf Therapeutics, Inc., Watertown, MA, USA.

Investor Contact:

John Norton
Precision AQ
212.362.1200
John.Norton@precisionaq.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