**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): **October 13, 2022**

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

| **Nevada** | **001-39082** | **45-5401931** |
|---|---|---|
| (State or other jurisdiction of incorporation) | (Commission File Number) | (IRS Employer Identification No.) |

| **2222 Ponce de Leon Blvd., Floor 3 Coral Gables, FL** | **33134** |
|---|---|
| (Address of principal executive offices) | (Zip Code) |

Registrant's telephone number, including area code **(212) 547-9591**

(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 | Name of exchange on which registered |
|---|---|---|
| **Common stock, $0.001 par value per share** | **RLMD** | **The NASDAQ Stock Market LLC** |

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 October 13, 2022, Relmada Therapeutics, Inc. (the "Company"), issued a press release that provided information regarding top-line results from the Company's Phase 3 RELIANCE III Trial for REL-1017 as a monotherapy for the treatment of major depressive disorder. Pursuant to Regulation FD, the press release is furnished with this Current Report as Exhibit 99.1.

*The information set forth in Item 7.01 of this Current Report on Form 8-K and in the attached Exhibit 99.1 is deemed to be "furnished" and shall not be deemed to be "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. The information set forth in Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1, shall not be deemed incorporated by reference into any filing under the Exchange Act or the Securities Act of 1933, as amended, regardless of any general incorporation language in such filing.*

**Item 8.01 Other Events.**

On October 13, 2022, the Company announced that its RELIANCE III study (REL-1017-303), evaluating REL-1017 in the monotherapy setting for Major Depressive Disorder (MDD), did not achieve its primary endpoint, which was a statistically significant improvement in depression symptoms compared to placebo as measured by the Montgomery-Asberg Depression Rating Scale (MADRS) on Day 28. In the study, the REL-1017 treatment arm showed a MADRS reduction of 14.8 points at Day 28 versus 13.9 points for the placebo arm, a higher than expected placebo response.

REL-1017, which was administered for 28 days to 232 subjects in RELIANCE III, demonstrated very favorable tolerability and safety, with no opioid-like effects, no withdrawal effects, and no psychotomimetic effects. There were no adverse events related to QTcF prolongation.

**Item 9.01 Financial Statements and Exhibits.**

(d) Exhibits.

| Exhibit No. | Description |
|---|---|
| 99.1 | Press release issued on October 13, 2022 |
| 104 | Cover Page Interactive Data File (embedded within the Inline XBRL document) |



**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.

Dated: October 13, 2022

**RELMADA THERAPEUTICS, INC.**

*By:* */s/ Sergio Traversa*
Name: Sergio Traversa
Title: Chief Executive Officer

**Relmada Therapeutics Announces Top-line Results from Phase 3**
**RELIANCE III Trial for REL-1017 as a Monotherapy for the Treatment of Major Depressive Disorder**

***RELIANCE I and II Adjunctive MDD Trials Continue to Advance***

CORAL GABLES, Fla., Oct. 13, 2022 /PRNewswire/ -- Relmada Therapeutics, Inc. (Nasdaq: RLMD), a late-stage biotechnology company addressing diseases of the central nervous system (CNS), today announced that its RELIANCE III study (REL-1017-303), evaluating REL-1017 in the monotherapy setting for Major Depressive Disorder (MDD), did not achieve its primary endpoint, which was a statistically significant improvement in depression symptoms compared to placebo as measured by the Montgomery-Asberg Depression Rating Scale (MADRS) on Day 28. In the study, the REL-1017 treatment arm showed a MADRS reduction of 14.8 points at Day 28 versus 13.9 points for the placebo arm, a higher than expected placebo response. Paradoxical results were observed in certain study sites, where placebo dramatically outperformed REL-1017. Relmada is investigating the nature of these results.

REL-1017, which was administered for 28 days to 232 subjects in RELIANCE III, demonstrated very favorable tolerability and safety, confirming the results of Phase 1 and Phase 2 studies (Fava et al, 2022)[1], with no opioid-like effects, no withdrawal effects, and no psychotomimetic effects. There were no adverse events related to QTcF prolongation.

“While these RELIANCE III results are disappointing for patients, the need for new, safe and effective treatments for MDD continues to exist. We look forward to the data from the ongoing RELIANCE I and II trials of REL-1017, a potential new therapy for the adjunctive treatment of MDD.” said Maurizio Fava, Psychiatrist-In-Chief, Massachusetts General Hospital and Slater Family Professor of Psychiatry, Harvard Medical School.

To better understand the paradoxical results, a post-hoc, exploratory analysis using the band-pass method (Merlo-Pich et al, 2010[2]) was conducted. The band-pass analysis excludes sites with implausibly high or low placebo responses (defined as a mean decrease from baseline in MADRS10 score greater than 14 and less than 3 points) and showed a meaningful difference between REL-1017 and placebo (>4.9 points on the MADRS, $p<0.05$).

Relmada continues to enroll patients in RELIANCE I and RELIANCE II, two ongoing Phase 3, placebo-controlled, pivotal studies evaluating REL-1017 as a potential adjunctive treatment for MDD. The RELIANCE development program also includes RELIANCE-OLS, a long-term open-label safety study that is enrolling rollover participants from all three pivotal studies, as well as de novo participants.

**References**


1 Fava M, Stahl S, Pani L, De Martin S, Pappagallo M, Guidetti C, Alimonti A, Bettini E, Mangano RM, Wessel T, de Somer M, Caron J, Vitolo OV, DiGuglielmo GR, Gilbert A, Mehta H, Kearney M, Mattarei A, Gentilucci M, Folli F, Traversa S, Inturrisi CE, Manfredi PL. REL-1017 (Esmethadone) as Adjunctive Treatment in Patients With Major Depressive Disorder: A Phase 2a Randomized Double-Blind Trial. Am J Psychiatry. 2022 Feb;179(2):122-131. doi: 10.1176/appi.ajp.2021.21020197. Epub 2021 Dec 22. PMID: 34933568.

2 Merlo-Pich E, Alexander RC, Fava M, Gomeni R. A new population-enrichment strategy to improve efficiency of placebo-controlled clinical trials of antidepressant drugs. Clin Pharmacol Ther. 2010 Nov;88(5):634-42. doi: 10.1038/clpt.2010.159. Epub 2010 Sep 22.


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**About REL-1017**

REL-1017, a new chemical entity (NCE) and novel NMDA receptor (NMDAR) channel blocker that preferentially targets hyperactive channels while maintaining physiological glutamatergic neurotransmission, is currently in late-stage development for the treatment of major depressive disorder (MDD). The ongoing Reliance Clinical Research Program is designed to evaluate the potential for REL-1017 as a rapid-acting, oral, once-daily antidepressant treatment. In a Phase 2 trial, REL-1017 demonstrated rapid, robust, and sustained antidepressant effects with statistically significant improvements compared to placebo. The Phase 2 study also showed a favorable pharmacokinetic, safety, and tolerability profile of REL-1017 consistent with results observed in previously completed Phase 1 studies.

**About Relmada Therapeutics, Inc.**

Relmada Therapeutics is a late-stage biotechnology company addressing diseases of the central nervous system (CNS), with focus on major depressive disorder (MDD). Relmada’s experienced and dedicated team is committed to making a difference in the lives of patients and their families. Relmada’s lead program, REL-1017, is a new chemical entity (NCE) and novel NMDA receptor (NMDAR) channel blocker that preferentially targets hyperactive channels while maintaining physiological glutamatergic neurotransmission. REL-1017 has entered late-stage development as an adjunctive treatment for MDD in adults. In addition, Relmada is advancing a clinical-stage program in neurodegenerative diseases based on psilocybin and select derivative molecules. Learn more at www.relmada.com.

**Forward-Looking Statements**

The Private Securities Litigation Reform Act of 1995 provides a safe harbor for forward-looking statements made by us or on our behalf. This press release contains statements which constitute “forward-looking statements” within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934. Any statement that is not historical in nature is a forward-looking statement and may be identified by the use of words and phrases such as “expects,” “anticipates,” “believes,” “will,” “will likely result,” “will continue,” “plans to,” “potential,” “promising,” and similar expressions. These statements are based on management’s current expectations and beliefs and are subject to a number of risks, uncertainties and assumptions that could cause actual results to differ materially from those described in the forward-looking statements, including potential failure of RELIANCE trial results to demonstrate clinically significant evidence of efficacy and/or safety, failure of top-line results to accurately reflect the complete results of the trial, failure to obtain regulatory approval of REL-1017 for the treatment of major depressive disorder, and the other risk factors described under the heading “Risk Factors” set forth in the Company’s reports filed with the SEC from time to time. No forward-looking statement can be guaranteed, and actual results may differ materially from those projected. Relmada undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events, or otherwise. Readers are cautioned that it is not possible to predict or identify all the risks, uncertainties and other factors that may affect future results and that the risks described herein should not be a complete list.


**Investor Contact:**
Tim McCarthy
LifeSci Advisors
tim@lifesciadvisors.com

**Media Inquiries:**
FischTank PR
relmada@fischtankpr.com