June 18, 2024

Relmada Therapeutics Announced Publication of Results from the Phase 3 Reliance I Study of REL-1017 in The Journal of Clinical Psychiatry

CORAL GABLES, Fla., June 18, 2024 /PRNewswire/ -- Relmada Therapeutics, Inc. (Nasdaq: RLMD), a late-stage biotechnology company addressing diseases of the central nervous system (CNS), today announced the publication of REL-1017 clinical data from the Reliance I Study in the peer-reviewed journal, *The Journal of Clinical Psychiatry*. The article is titled, "*Efficacy and Safety of Esmethadone (REL-1017) in Patients with Major Depressive Disorder and Inadequate Response to Standard Antidepressants: A Phase 3 Randomized Controlled Trial*", and is available online at *Link To Title*.

"The overall results from this trial are clearly consistent with the evidence, produced by the prior phase 2 trial, for the efficacy, safety, and tolerability of esmethadone as a promising antidepressant for the adjunctive treatment of major depressive disorder. The side-effect profile of esmethadone compares quite favorably with the side effects of the currently FDA-approved adjunctive treatments for MDD.," said Maurizio Fava, MD, the Principal Investigator of Reliance I.

About Reliance I

Reliance I was a 28-day, Phase 3, randomized, double-blind, placebo-controlled study to evaluate REL-1017 (75 mg on day 1, followed by 25 mg daily on days 2 through 28) compared to placebo as adjunctive treatment in patients with major depressive disorder (MDD). The intent-to-treat (ITT) population comprised 227 randomized patients; the per protocol (PP) population comprised 198 patients completing treatment. The primary efficacy measure was mean difference (MD) between REL-1017 and placebo in change from baseline (CFB) through day 28 in the Montgomery-Asberg Depression Rating Scale (MADRS) score.

As reported in December 2022, Reliance I did not meet the primary endpoint in the ITT analysis, yet, REL-1017 showed a statistically significant improvement in response rate compared to placebo (P = .044) and an encouraging nonsignificant trend for improvement in remission rate (P = .076). In the PP prespecified supportive analysis that excluded protocol noncompliant patients for reasons unrelated to REL-1017 adverse events (AE), results trended toward a more favorable outcome (MD CFB = 3.1; P =.051, ES = 0.29). Further, in

post hoc analyses of patients with severe depression (MADRS score ≥35 at baseline), significant improvement as measured occurred with REL-1017 vs. placebo in both the ITT and PP populations (MD CFB 6.9 and 7.9; P =.0059 and P = .0015; ES = 0.57 and 0.68, respectively)

The side effect profile of REL-1017 was consistent with previous phase 1 and phase 2 studies of REL-1017, with no observations of treatment-related serious AEs and no observed signal for abuse potential and compares favorably with the side effects of the currently FDA-approved adjunctive treatments for MDD.

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 adjunctive treatment of major depressive disorder (MDD). Relmada's ongoing clinical research program is designed to evaluate the potential for REL-1017 as a rapid-acting, oral, once-daily antidepressant treatment. The development program for REL-1017 as an adjunctive treatment for MDD includes two Phase 3 randomized, double-blind, placebo-controlled studies, Reliance II (Study 302) and Relight (Study 304). Reliance II and Relight have the same key study design parameters.

Relmada continues to enroll patients in both ongoing REL-1017 trials including Reliance II (Study 302), with top-line data anticipated in the second half of 2024, and Relight (Study 304) with top-line data anticipated approximately six months after the completion of Study 302.

About Relmada Therapeutics, Inc.

Relmada Therapeutics is a late-stage biotechnology company addressing diseases of the central nervous system (CNS), with a 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 is in late-stage development as an adjunctive treatment for MDD in adults. 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 clinical trial results to demonstrate statistically and/or clinically significant evidence of efficacy and/or safety, failure of top-line results to accurately reflect the complete results of the trial, failure of the 310 open-label study to accurately reflect the results of the ongoing 302 and 304 blinded, randomized and controlled studies, failure of the planned psilocybin Phase 1 and Phase 2a trials to be successfully carried out, 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:
Corporate Communications
media@relmada.com

View original content to download multimedia:https://www.prnewswire.com/news-releases/relmada-therapeutics-announced-publication-of-results-from-the-phase-3-reliance-i-study-of-rel-1017-in-the-journal-of-clinical-psychiatry-302175451.html

SOURCE Relmada Therapeutics, Inc.