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![Relmada Therapeutics logo]

Relmada Therapeutics Announces Publication of REL-1017 Preclinical Data in Frontiers in Pharmacology

CORAL GABLES, Fla., April 29, 2022 /PRNewswire/ -- Relmada Therapeutics, Inc. (Nasdaq: RLMD), a late-stage biotechnology company addressing diseases of the central nervous system (CNS), announced today the publication of REL-1017 preclinical data in the peer-reviewed journal, *Frontiers in Pharmacology.* The article is titled, "*REL-1017 (Esmethadone), A Novel NMDAR Blocker for the Treatment of MDD is Not Neurotoxic in Sprague-Dawley Rats*," and is available online at: [Frontiers | REL-1017 (Esmethadone), A Novel NMDAR Blocker for the Treatment of MDD is Not Neurotoxic in Sprague-Dawley Rats | Pharmacology (frontiersin.org)](#).

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"These compelling previously presented data confirm that REL-1017 does not produce Olney's lesions, unlike what has been seen in other NMDAR blockers," said Paolo L. Manfredi, M.D., Chief Scientific Officer of Relmada. "The results further contribute to our understanding of the safety profile of REL-1017."

The aim of the study was to determine whether the novel, low affinity, low potency, NMDAR channel blocker, REL-1017, administered once daily *via* oral gavage for 1–4 days to male and female Sprague-Dawley rats, would induce transient (Olney's lesions) and irreversible (necrosis) pathomorphological changes to the posterior cingulate and retrosplenial brain cortical neurons as compared with animals treated with another NMDAR channel blocker, dizocilpine (MK-801), a positive control.

In REL-1017 treated rats, early Olney's lesions, which usually appear one day after MK-801 treatment, were not observed. Similarly, REL-1017 treated rats did not show necrotic neurons both at the cingulate and olfactory bulb cortex at later time points (Day 3 and 5). This effect is statistically different from what was observed in cortical neurons by using MK-801. Additionally, in contrast with MK-801 treated rats, REL-1017 treated rats did not show evidence of impaired behavior.

These preclinical data, in addition to clinical data to date, have been encouraging to the development of REL-1017 as a potentially safe and effective treatment option 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 treatment of 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 robust, rapid, 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 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 has entered late-stage development as an adjunctive treatment and monotherapy 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, including but not limited to statements regarding the expected use of the proceeds from the offering. 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 the 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.

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