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Relmada Therapeutics Announces Top-Line Results from REL-1017 Phase 2 Study in Individuals with Treatment Resistant Depression

Findings show that REL-1017 has rapid onset and sustained antidepressant efficacy with statistically significant differences compared to placebo on all efficacy measures

NEW YORK, Oct. 15, 2019 /PRNewswire/ -- Relmada Therapeutics, Inc. (NASDAQ: RLMD), a clinical-stage company developing novel therapies for the treatment of central nervous system (CNS) diseases, today reported top-line data from REL-1017-202, a double-blind, placebo-controlled Phase 2 clinical study evaluating the safety, tolerability and efficacy of two doses of REL-1017 (dextromethadone), 25 mg once a day and 50 mg once a day, as an adjunctive treatment in patients with treatment resistant depression.

Subjects were adults with major depressive disorder (MDD) who did not respond to one to three courses of antidepressant treatment in their current episode. 62 subjects, average age 49.2 years, with an average Hamilton Depression Rating Scale score of 25.3 and an average Montgomery-Asberg Depression Rating Scale (MADRS) score of 34.0 (severe depression), were randomized. Other demographic characteristics were balanced across all arms. After an initial screening period, subjects were randomized to one of three arms: placebo, REL-1017 25 mg or REL-1017 50 mg, in addition to stable background antidepressant therapy. Subjects in the REL-1017 treatment arms received one loading dose of either 75 mg (25 mg arm) or 100 mg (50 mg arm) of REL-1017. Subjects were treated inpatient for 7 days and discharged home at Day 9. They returned for follow-up visits at Day 14 and Day 21. Efficacy was measured on Days 2, 4 and 7 in the dosing period and on Day 14, one week after treatment discontinuation. 61 subjects received all treatment doses and were included in the per-protocol population (PPP) treatment analysis; 57 subjects completed all visits. All 62 randomized subjects were part of the intention-to-treat population (ITT) analysis. No differences were observed between the ITT and PPP analyses and results.

Key findings:

- Subjects in both the REL-1017 25 mg and 50 mg treatment groups experienced statistically significant improvement of their depression compared to subjects in the placebo group on all efficacy measures, including: the Montgomery-Asberg Depression Rating Scale (MADRS); the Clinical Global Impression – Severity (CGI-S) scale; the Clinical Global Impression – Improvement (CGI-I) scale; and the Symptoms of Depression Questionnaire (SDQ).
- The improvement on the MADRS appeared on Day 4 in both REL-1017 dose groups and continued through

Day 7 and Day 14, seven days after treatment discontinuation, with P values < 0.03 and large effect sizes (a measure of quantifying the difference between two groups), ranging from 0.7 to 1.0. Similar findings emerged from the CGI-S and CGI-I scales.

MADRS: Analysis of Change from Baseline to Day 7 and to Day 14 ITT Population

	Day 2			Day 4			Day 7			Day 14		
	LS Means Difference	P-value	d	LS Means Difference	P-value	d	LS Means Difference	P-value	d	LS Means Difference	P-value	d
REL-1017 25mg vs Placebo	-1.9	0.4340	0.3	-7.9	0.0087	0.9	-8.7	0.0122	0.8	-9.4	0.0103	0.9
REL-1017 50mg vs Placebo	-0.3	0.9092	0.0	-7.6	0.0096	0.8	-7.2	0.0308	0.7	-10.4	0.0039	1.0

LS = Least Squares; d = Cohen's effect size

- The study also confirmed the favorable safety and tolerability profile of REL-1017, which was also observed in the Phase 1 studies. Subjects experienced mild and moderate adverse events (AEs), and no serious adverse events, without significant differences between placebo and treatment groups. There was no evidence of either treatment induced psychotomimetic and dissociative AEs or withdrawal signs and symptoms upon treatment discontinuation.

"We are very pleased to announce these highly compelling results," said Dr. Ottavio Vitolo, Relmada Head of R&D and CMO. "This is the first clinical evidence that REL-1017 exerts a rapid and robust antidepressant effect, which continues even after treatment discontinuation. These findings replicate what was previously observed in animal studies and support a potentially neurotrophic effect of REL-1017. We would like to thank the participating investigators, our collaborators at Syneos Health and our colleagues at the Massachusetts General Hospital (MGH) Clinical Trials Network and Institute, whose contribution was critical to controlling the placebo response. We look forward to continuing the development of REL-1017 with the goal of bringing a new effective treatment to the millions of patients suffering from depression."

"The results of this Phase 2 study demonstrate a solid and rapid antidepressant effect and overall favorable tolerability and safety profile of REL-1017," said Maurizio Fava, M.D., Chief of the Department of Psychiatry, Massachusetts General Hospital. "Ultimately, the goal is to improve the lives of individuals with serious depression who have not responded to standard therapies. These data suggest that REL-1017 could offer a treatment option to such patients, and I am hopeful that the results of ongoing studies will continue to show great promise."

"We are delighted to report these data that we believe represent a critical step forward in the effort to bring a new and potentially treatment paradigm changing option to patients who suffer from major depression," said Sergio Traversa, CEO of Relmada. "These results confirm for the first time in severely depressed patients that REL-1017 is showing rapid, statistically and clinically meaningful antidepressant activity, in conjunction with a favorable tolerability and safety profile, and a simple oral administration regime. We look forward to discussing with the U.S. Food and Drug Administration the next steps to enable us to rapidly advance the clinical development of this important clinical program."

About dextromethadone (REL 1017)

Relmada is currently developing dextromethadone as a rapidly acting oral agent for the treatment of depression. Working as an NMDA receptor antagonist and on the same binding site as ketamine but having shown no ketamine psychotomimetics side effects, dextromethadone is fundamentally differentiated from all currently FDA-approved antidepressants, as well as all atypical antipsychotics used adjunctively. In April 2017, the FDA granted Fast Track designation for dextromethadone for the adjunctive treatment of major depressive disorder.

About Relmada Therapeutics, Inc.

Relmada Therapeutics is a clinical-stage, publicly traded biotechnology company developing novel medicines that potentially address areas of high unmet medical need in the treatment of central nervous system (CNS) diseases. The Company has a diversified portfolio of products at various stages of development. Relmada's lead program, dextromethadone (REL-1017), is an N-methyl-D-aspartate (NMDA) receptor antagonist. NMDA receptor antagonists may have potential in the treatment of a range of psychiatric and neurological disorders associated with a variety of cognitive, neurological and behavioral symptoms. For more information, please visit Relmada's website 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. We may from time to time make written or oral statements in this letter, the proxy statements filed with the SEC communications to stockholders and press releases 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. These forward-looking statements are based upon management's current expectations, estimates, assumptions and beliefs concerning future events and conditions and may discuss, among other things, anticipated future performance, expected product development, product potential, future business plans and costs. 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" and similar expressions. 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 of the risks, uncertainties and other factors that may affect future results and that the risks described herein should not be considered to be a complete list.

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