October 11, 2023

Relmada Therapeutics to Present New Preclinical Data on its Psilocybin Program at AASLD The Liver Meeting® 2023

- *Low-dose psilocybin generated statistically significant reductions in liver fat content, plasma glucose levels and body weight gain in a mice model with high-fat-high-fructose diet (HFHFD)-induced metabolic dysfunction-associated steatotic liver disease (MASLD) without detrimental CNS effects*
- *Mechanism of action of psilocybin distinct from that of GLP-1 drugs and could be complementary*
- *Company intends to initiate the single-ascending dose Phase 1 trial in patients in early 2024*

CORAL GABLES, Fla., Oct. 11, 2023 /PRNewswire/ -- Relmada Therapeutics, Inc. (Nasdaq: RLMD), a late-stage biotechnology company addressing diseases of the central nervous system (CNS), today announced that new preclinical data on its novel psilocybin will be highlighted in a poster presentation at the American Association for the Study of Liver Diseases (AASLD) The Liver Meeting® 2023, being held November 10-14, 2023, in Boston, MA.

The data demonstrate the beneficial effect of non-psychedelic/low dose psilocybin on multiple metabolic parameters in a rodent model of metabolic dysfunction-associated steatotic liver disease (MASLD). Mice were fed a high fructose, high fat diet (HFHFD) for 17 weeks to induce MASLD, along with hyperglycemia, hyperlipidemia and significant weight gain. One group of MASLD mice (N=10) was treated with low-dose (0.05 mg/Kg) psilocybin daily and a second (N=10) with vehicle daily by oral gavage while continuing on HFHFD. Standard diet-fed mice (N=10) were used as controls. Body-weight and food intake were assessed weekly.

Key statistically significant results in psilocybin-treated mice relative to HFHFD vehicle-treated mice include:

- Significantly reduced hepatic steatosis;
- 12% reduction in body weight gain with no reduction in food intake;
- Significant decrease in fasting blood glucose level and AUC in an Oral Glucose Tolerance Test (OGTT);

Additionally, 0.05 mg/Kg psilocybin resulted in:

- Restoration of plasma and liver triglyceride levels to those of the standard-diet fed mice
- Reduced anxiety-like behavior ($p<0.05$) with no detrimental central nervous system (CNS) effects;
- Modulation of hepatic genes involved in de novo lipogenesis, glycolysis, ß-oxidation, i.e., SREBP1 (2-fold decrease, $p<0.05$), ChREBP (2-fold increase, $p<0.05$ vs. controls) and CPT-1 (3-fold increase, $p<0.05$)

These pleiotropic metabolic effects were demonstrated to be due, in part, to the 5-HT-2A serotonin receptor agonist activity of psilocybin, a mechanism distinct from, and potentially complementary to, the incretin (GLP-1) class of agents.

Additionally, the results show that low-dose psilocin, the pharmacologically active metabolite of psilocybin, reduces lipid accumulation in HepG2 cells in vitro in a 5-HT-2A dependent manner.

Relmada intends to enter human studies of its proprietary, non-psychedelic/low dose modified-release formulation of psilocybin for metabolic indications. Leveraging the large amount of safety data already publicly available on psilocybin, the Company plans to commence a single-ascending dose Phase 1 trial in obese patients with steatotic liver disease in early 2024 to define the pharmacokinetic, safety and tolerability profile of Relmada's modified-release psilocybin formulation in this population, followed by a Phase 2a trial in the same patient population to establish clinical proof-of-concept.

"These initial animal data are quite compelling and warrant further evaluation in the clinic," said Stephen Harrison, M.D., Founder and Chairman of Pinnacle Clinical Research, and a world-renowned non-alcoholic steato-hepatitis (NASH) and metabolic disease expert. "There are currently no approved drugs for MASLD, and these initial pre-clinical results support the therapeutic potential of non-psychedelic/low dose psilocybin. Based on these data, non-psychedelic/low dose psilocybin could improve lipids and glucose with potential for fewer side effects over other investigative treatment approaches such as GLP-1, glucagon, and GIP. A significant opportunity exists to treat MASLD and associated metabolic disorders for a product with this profile"

Relmada acquired the development and commercial rights to a novel psilocybin and derivative program from Arbormentis LLC in July of 2021. The original focus of the program was limited to neurodegenerative diseases. Psilocybin has neuroplastogen™ effects that have the potential to ameliorate the consequences of multiple neurodegenerative conditions. The pleiotropic metabolic effects of low-dose psilocybin were discovered while studying its neuroplastogen™ potential in a rodent model deficient in neurogenesis – obese rodents maintained on a HFHFD. "Although the neurodegenerative program continues according to plan, this new discovery opens a large opportunity to expand the program in the obesity and metabolic disease area, potentially increasing the scope and diversification of Relmada's pipeline," said Sergio Traversa, Chief Executive Officer of Relmada. The Company has a robust portfolio of patent applications covering the proprietary synthesis, the methods-of-use of psilocybin to treat metabolic diseases, as well as patent applications covering the composition of matter of various formulations of psilocybin and psilocin".

Presentation Details

Abstract Number: 2468-C, *THE SEROTONIN RECEPTOR AGONIST PSILOCYBIN AS A NOVEL THERAPEUTIC APPROACH FOR NAFLD: PRECLINICAL STUDIES.*

Presentation Type: Abstract Poster

Presentation Date and Time: *Saturday, November 11, 2023, 8:00 AM*

Presentation Location: Poster Hall C

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 to obtain regulatory approval of REL-1017 for the treatment of major depressive disorder, failure of the psilocybin program to advance to later stages of development, 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.

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