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): **January 9, 2023**

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: **(786) 629 1376**

(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 each 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 January 9, 2023, Relmada Therapeutics, Inc. (the "Company"), issued a press release announcing the appointment of Cedric O'Gorman MD as the Company's Chief Medical Officer. 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 (the "Securities Act"), regardless of any general incorporation language in such filing.

Item 8.01 Other Events.

On January 9, 2023, the Company updated its corporate presentation, a copy of which is filed herewith as Exhibit 99.2 and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	**Description**
99.1*	Press release issued on January 9, 2023
99.2	Corporate Presentation dated January 9, 2023
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

* *This Exhibit attached to this Form 8-K shall not be deemed "filed" for purposes of Section 18 of the Exchange Act or otherwise subject to liability under that section, nor shall it be deemed incorporated by reference in any filing under the Securities Act or the Exchange Act, except as expressly set forth by specific reference in such filing.*

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: January 9, 2023

RELMADA THERAPEUTICS, INC.

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

Exhibit 99.1

Relmada Therapeutics Appoints CNS Therapeutic Expert Cedric O'Gorman MD as Chief Medical Officer

CORAL GABLES, Fla., January 9, 2023 /PRNewswire/ -- Relmada Therapeutics, Inc. (Nasdaq: RLMD), a late-stage biotechnology company addressing diseases of the central nervous system (CNS), today announced the appointment of Cedric O'Gorman MD as the Company's Chief Medical Officer. Dr. O'Gorman will lead medical, clinical and regulatory functions in support of the Company's late-stage REL-1017 development program.

Dr. O'Gorman brings to Relmada more than two decades of life sciences experience in clinical development, medical affairs and medical strategy, with significant expertise in the CNS therapeutics field. Most recently, he served as Chief Medical Officer at Alpha Cognition, where he led clinical development programs for the company's Alzheimer's disease targets. Prior to Alpha Cognition, he served as Senior Vice President, Clinical Development and Medical Affairs, at Axsome Therapeutics, where Dr. O'Gorman led clinical development programs for therapeutic indications, which included major depressive disorder (MDD), agitation associated with Alzheimer's disease, narcolepsy and migraine. Prior to Axsome, he was Vice President of Medical Affairs at Intra-Cellular Therapies, and before that, Dr. O'Gorman was the U.S. Medical Lead for Psychiatry at Genentech/Roche. Prior to Genentech/Roche, he spent five years at Pfizer representing medical affairs on several branded neuroscience products for schizophrenia, bipolar disorder, and MDD.

"Dr. O'Gorman adds important depth to our management team given his extensive CNS medical and research experience, and his demonstrated leadership acumen," stated Sergio Traversa, Relmada's Chief Executive Officer. "Importantly, he has significant expertise that correlates directly with our ongoing REL-1017 development program, and successfully developed a recently approved antidepressant with a similar mechanism of action to our promising product candidate. As we approach key regulatory discussions with the U.S. Food and Drug Administration and consider additional potential clinical trials for REL-1017, we look forward to leveraging Dr. O'Gorman's substantial clinical development and regulatory experience. We welcome his energy and insights as we continue to move forward with our late-stage REL-1017 program for MDD."

"I am excited to be joining Relmada at this critical juncture and look forward to collaborating with the outstanding leadership team," said Dr. O'Gorman. "Based on the promising data generated to date, which I have reviewed thoroughly, I am highly confident in the potential of REL-1017 to be an important, safe and effective new therapy for the treatment of MDD."

Dr. O'Gorman received his medical degree from the National University of Ireland in Galway, trained at the Institute of Psychiatry in London, England, and earned his MBA from the New York University Stern School of Business.

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 REL-1017 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.

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Disclosures

Certain statements contained in this presentation or in other documents of Relmada Therapeutics, Inc. (the "Company"), along with certain statements that may be made by management of the Company orally in presenting this material, may contain "forward-looking statements." These statements can be identified by the fact that they do not relate strictly to historic or current facts. They use words such as "estimate," "expect," "intend," "believe," "plan," "anticipate," "projected" and other words and terms of similar meaning in connection with any discussion of future operating or financial performance or condition. These statements are based upon the current beliefs and expectations of the Company's management and are subject to significant risks and uncertainties. Statements regarding future action, future performance and/or future results, those relating to the timing for completion, and results of, scheduled or additional clinical trials and the FDA's or other regulatory review and/or approval and commercial launch and sales results (if any) of the Company's formulations and products and regulatory filings related to the same may differ from those set forth in the forward-looking statements. Peak sales and market size estimates have been determined on the basis of market research and comparable product analysis, but no assurances can be given that such sales levels will be achieved, if at all, or that such market size estimates will prove accurate.

Because actual results are affected by these and other potential risks, contingencies and uncertainties, the Company cautions investors that actual results may differ materially from those expressed or implied in any forward-looking statement. It is not possible to predict or identify all such risks, contingencies and uncertainties. The Company identifies some of these factors in its Securities and Exchange Commission ("SEC") filings on Forms 10-K, 10-Q and 8-K, and investors are advised to consult the Company's filings for a more complete listing of risk factors, contingencies and uncertainties affecting the Company and its business and financial performance.

The Company assumes no obligation to update forward-looking statements as circumstances change. Investors are advised to consult further disclosures that the Company makes or has made on related subjects in the Company's Form 10-K, 10-Q and 8-K reports.

Investment highlights

- CNS focus with lead program in major depressive disorder (MDD)
- Highly compelling opportunity in REL-1017
- Lessons learned provide strong confidence in the path to NDA

CNS= Central Nervous System
**Our fiscal year end is December 31. The periods referred to in this slide are calendar years and quarters.

Major Depressive Disorder and REL-1017's Novel Mechanism of Action

Limitations of current treatments for MDD

Limited efficacy

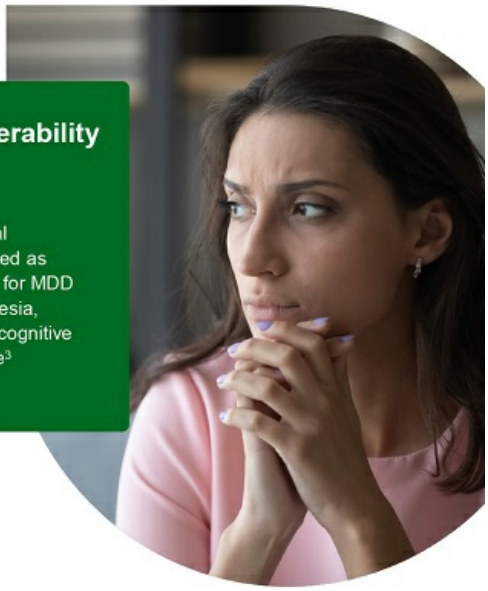
~65% MDD patients do not respond to first antidepressant treatment[1]

Slow onset of action

Standard antidepressants, even when effective, may take up to 8 weeks to reach efficacy[2]

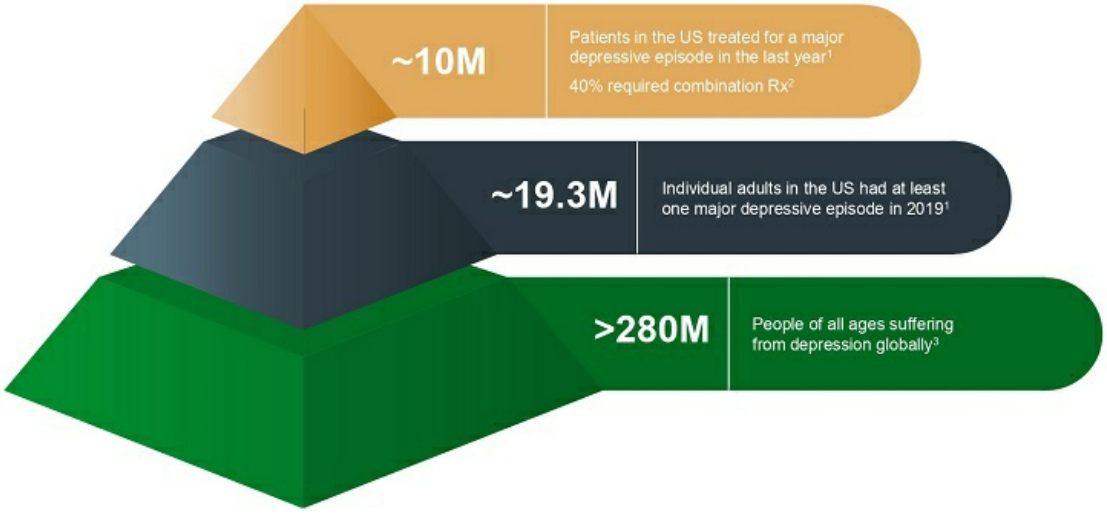
Safety and tolerability challenges

Side effects of atypical antipsychotics approved as adjunctive treatments for MDD include tardive dyskinesia, metabolic syndrome, cognitive impairment and stroke[3]



MDD = major depressive disorder
1.) Trivedi MH, et al. Am J Psychiatry. 2006;163:28-40; 2.) Ashton AK, et al. Curr Ther Res. 2005;66(2):97-108; 3.) US Prescribing Information, brexpiprazole, quetiapine, aripiprazole

Prevalence of depression



Rx = prescription
1.) Substance Abuse and Mental Health Services Administration (SAMHSA), U.S. Department of Health and Human Services (HHS) 2019 National Survey on Drug Use and Health; 2.) Decision Resources Group Unipolar Depression 2020 report; 3.) WHO Depression Fact Sheet

Unique profile of REL-1017

Potential as a rapid, oral, once-daily antidepressant for MDD, if approved

Novel Mechanism of Action: preferential targeting of NMDAR channels potentially associated with MDD[1,2,3]

Clinical data demonstrated:

- Robust, rapid, and sustained statistically significant antidepressant effects on all tested scales[4]
- Rapid onset: significant efficacy effects by Day 4[4]
- Favorable safety and tolerability profile consistent across all studies[4,5,6]: no opioid and no psychotomimetic adverse events and no metabolic side effects[4,5,6]
- Orally administered, once-daily tablet

MDD = major depressive disorder; NMDAR = N-methyl-D-aspartate receptor

1.) Bettini E al. Pharmacological Comparative Characterization of REL-1017 (Esmethadone-HCl) and Other NMDAR Channel Blockers in Human Heterodimeric N-Methyl-D-Aspartate Receptors. Pharmaceuticals (Basel). 2022;15(8):997; 2.) Bettini E et al. The N-Methyl-D-Aspartate Receptor Blocker REL-1017 (Esmethadone) Reduces Calcium Influx Induced by Glutamate, Quinolinic Acid, and Gentamicin. Pharmaceuticals (Basel). 2022;15(7):882; 3.) Stahl SM et al. Esmethadone (REL-1017) and Other Uncompetitive NMDAR Channel Blockers May Improve Mood Disorders via Modulation of Synaptic Kinase-Mediated Signaling. Int J Mol Sci. 2022;23(20); 4.) Fava M et al. REL-1017 (Esmethadone) as Adjunctive Treatment in Patients With Major Depressive Disorder: A Phase 2a Randomized Double-Blind Trial. Am J Psychiatry. 2022;179(2):122-131; 5.) Bernstein et al. Characterization of the Safety and Pharmacokinetic Profile of D-Methadone, a Novel N-Methyl-D-Aspartate Receptor Antagonist in Healthy, Opioid-Naive Subjects: Results of Two Phase 1 Studies. J Clin Psychopharmacol. 2019;39(3):226-237; 6.) Relmada data on file

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REL-1017 Phase 1 & 2 Efficacy and Safety Data

Phase 1 SAD & MAD studies for REL-1017

Safety & tolerability comparable to placebo

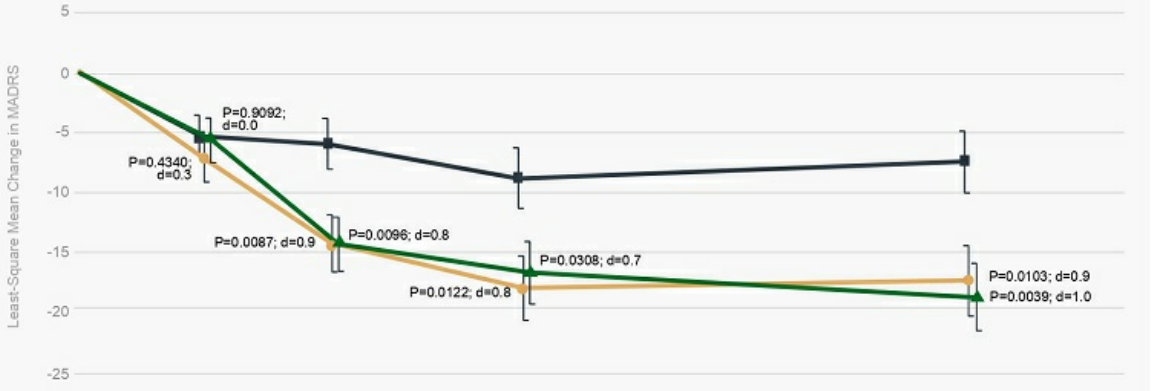
	APPROACH	OBJECTIVES	STUDY CONCLUSIONS
Multiple Ascending Dose (MAD) study design	Parallel group, double-blind, placebo controlled	Establish PK, PD, and safety of single dose administration	• **Maximum Tolerated Dose (MTD) = 150 mg** • **PK demonstrated linear proportionality of Cmax, AUC0-inf vs. dose** • **No clinically meaningful opioid or NMDA AESI signal**
Single Ascending Dose (SAD) study design	Parallel group, double-blind, placebo controlled	Establish PK, PD, and safety of once daily, 10-day administration	• **The highest dose studied, 75mg daily, was well tolerated** • **Favorable safety and tolerability profile** • **No clinically meaningful opioid or NMDA AESI signal**

PK = pharmacokinetics; PD = pharmacodynamics; MTD: =maximum tolerated dose; Cmax = maximum plasma concentration; AUC0-inf = area under the curve 0 to infinite time; AUCt = area under the curve to the end of dosing period; N = number of patients; NMDA = N-methyl-D-aspartate receptor antagonist; AESI = adverse event of special interest

Source: Bernstein, G. et al., J. Clin. Psychopharmacology 2019 May/Jun; 39(3) 226-237.

Phase 2 study REL-1017: primary efficacy endpoint

REL-1017 25 and 50 mg (Day 1 loading dose 75 and 100 mg, respectively) showed rapid and sustained differences in MADRS change vs. placebo

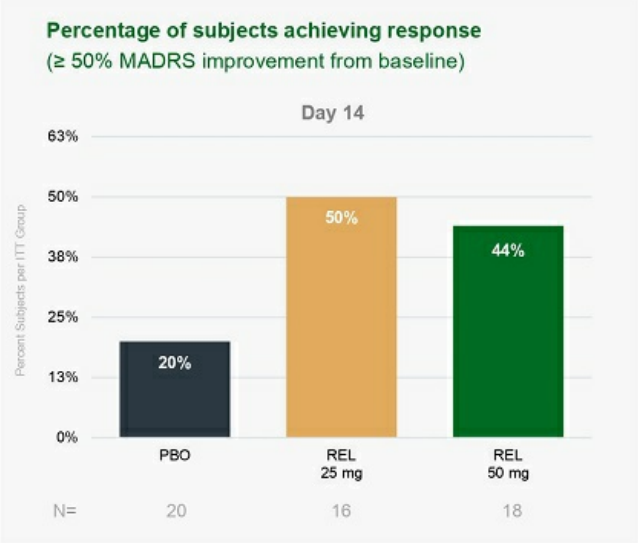


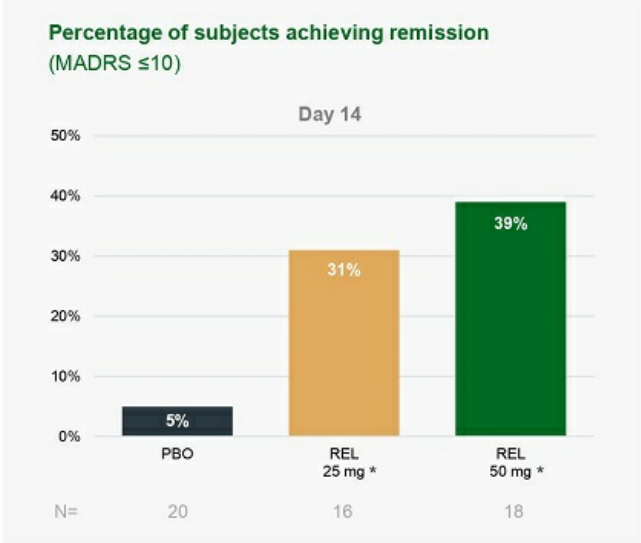
ΔMADRS	Day 2	Day 4	Day 7	Day 14
25mg	-1.9	-7.9*	-8.7*	-9.4*
50mg	-0.3	-7.6*	-7.2*	-10.4*

*P-value < .05

MADRS=Montgomery-Asberg Depression Rating Scale

REL-1017 phase 2 study efficacy: response & remission



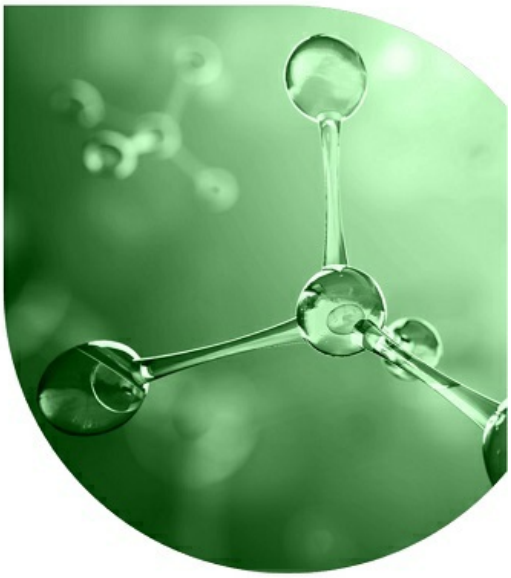


Day 14: last efficacy assessment, 7 days after last dose of study drug
* p = < .05
MADRS=Montgomery-Asberg Depression Rating Scale
Source: Fava et al. Rapid and Sustained Antidepressant Effects of REL-1017 (dextromethadone) as an Adjunctive Treatment for Major Depressive Disorder

Safety & tolerability findings from phase 2

Safety & tolerability comparable to placebo

- Only Mild and Moderate transient AEs—no SAEs
- No increased prevalence of specifically relevant organ group AEs in treatment groups vs placebo
- No evidence of opiate effects or withdrawal symptoms in treatment groups vs placebo
- No evidence of treatment-induced dissociative or psychotomimetic symptoms in the treatment groups vs placebo



AE = adverse event; SAE = serious adverse event
Source: Fava et al. Rapid and Sustained Antidepressant Effects of REL-1017 (dextromethadone) as an Adjunctive Treatment for Major Depressive Disorder: A Phase 2 Trial. 2021

The results of experimental studies predictive of human abuse potential [1] and the results of human abuse potential studies in recreational opioid users [2] and in recreational ketamine users [3] indicate no meaningful abuse potential and support the DEA statement below:

"The *d*-isomer lacks significant respiratory depressant action and addiction liability..."

US Drug Enforcement Administration
December 2019 [4]

1.) Henningfield, et al. REL-1017 (esmethadone; D-methadone) does not cause reinforcing effect, physical dependence and withdrawal signs in Sprague Dawley rats. Sci Rep 12, 11389 (2022); 2.) Shram M, et al., No meaningful abuse potential in recreational opioid users of REL-1017 (esmethadone hydrochloride), a new NMDAR antagonist and potential rapid-acting antidepressant American Society of Clinical Psychopharmacology (ASCP) 2022; 3.) Shram M, et al., No meaningful abuse potential in recreational ketamine users of REL-1017 (esmethadone hydrochloride), a new NMDAR antagonist and potential rapid-acting antidepressant. American Society of Clinical Psychopharmacology (ASCP) 2022; 4.) US DEA Statement on Methadone, December 2019 February 2022

Reliance: The Phase 3 Program for REL-1017

REL-1017 phase 3 program for the treatment of MDD

Reliance I + II

Randomized two-arm, placebo-controlled pivotal studies in patients with MDD and inadequate response to ongoing standard antidepressant treatment. These are two studies conducted one after the other.

In MDD patients with inadequate response to 1-3 ADT in the current MDE

Primary Endpoint: Change in MADRS at Day 28

Key Secondary Endpoints:

- Change in CGI-S score at Day 28
- Change in MADRS score at Day 7

Reliance III

Randomized, two-arm, placebo-controlled pivotal study as a monotherapy treatment for patients with MDD.

In patients experiencing an untreated MDE (patients receiving no ADT)

Primary Endpoint: Change in MADRS at Day 28

Key Secondary Endpoints:

- Change in CGI-S score at Day 28
- Change in MADRS score at Day 7

Reliance OLS

Long-term, open-label safety study.

Patients continuing from Reliance I, II & III

Patients new to REL-1017

Reliance

Additional phase 3 MDD trials in preparation.

MDD = major depressive disorder; ADT = antidepressant treatment ; OLS = open label study;
MADRS = Montgomery-Asberg Depression Rating Scale; CGIs = Clinical Global Impression scales; MDE = major depressive episode

Reliance I and Reliance III results overview

- Reliance I and Reliance III did not reach primary endpoint
- Reliance I showed a significant 40% response rate compared to placebo (p=0.044)
- Reliance I and Reliance III confirmed very favorable safety and lack of abuse potential
- In Reliance I and Reliance III, post-hoc analyses excluding 2-4 common top-enrolling centers* show a positive efficacy signal

* Center-specific factors in these top-enrolling centers yielded paradoxical results: placebo robustly outperformed REL-1017. The top enrolling center in Reliance III had a mean placebo response of 23 MADRS points

Pivotal phase 3 trial design for monotherapy

Reliance III
MONOTHERAPY

Primary endpoint:

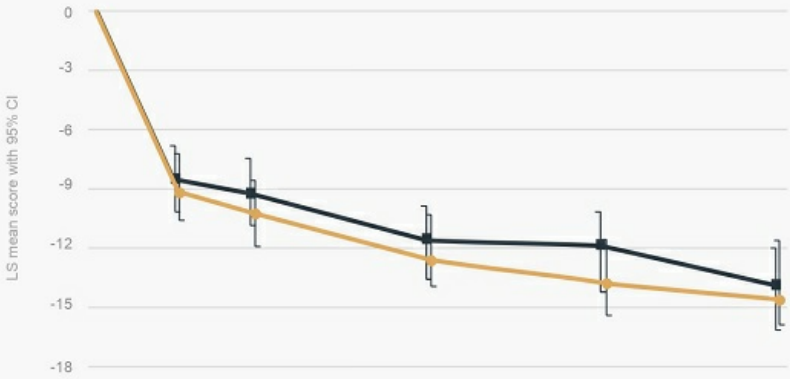
- Change in MADRS at Day 28

Key secondary endpoints:

- Change in MADRS score at Day 7
- Change in CGI-S score at Day 28

MADRS = Montgomery-Asberg Depression Rating Scale; CGIs = Clinical Global Impression scales; MDE = major depressive episode; QD = once daily; OLS = open label study
*SAFER interview confirms that the illness is a specific state and excludes patients with any symptoms that are nonspecific or not readily assessable. Desseilles M, et al 2013. Massachusetts General Hospital SAFER criteria for clinical trials and research. Harv Rev Psychiatry. Sep-Oct;21(5):269-74.
**75mg loading dose on Day 1 of REL-1017

Reliance III primary efficacy endpoint: REL-1017 showed non-significant difference in MADRS vs placebo at Day 28



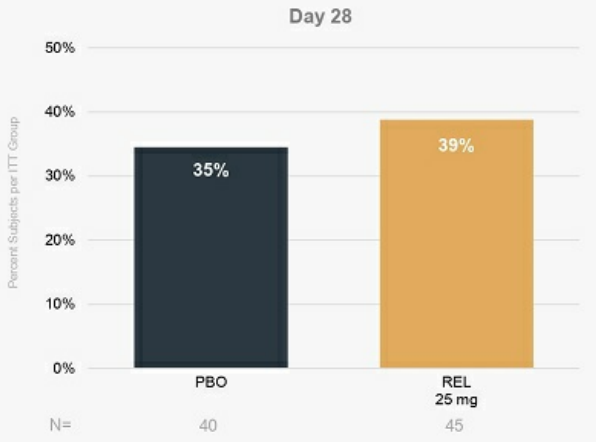
ΔMADRS (N=232) Placebo N=116, 25 mg N=116, 45 sites	Day 4	Day 7	Day 14	Day 21	Day 28 End of treatment
Placebo Mean (SD)	-8.5, (8.9)	-9.2 (9.5)	-11.7 10.1)	-11.9 (9.9)	**-13.9** (10.8)
25 mg Mean (SD)	-9.7 (9.1)	-10.7 (10.2)	-12.9 (10.4)	-14.5 (11.9)	**-14.8** (12.4)
REL-1017 vs Placebo LS Mean Diff (SE); p-value, MMRM	-0.45 (1.26) 0.7228	-0.84 (1.30) 0.5176	-0.31 (1.39) 0.8215	-1.34 (1.48) 0.3683	0.3 (1.58) 0.8466

-0.9 diff. REL-1017 vs. placebo

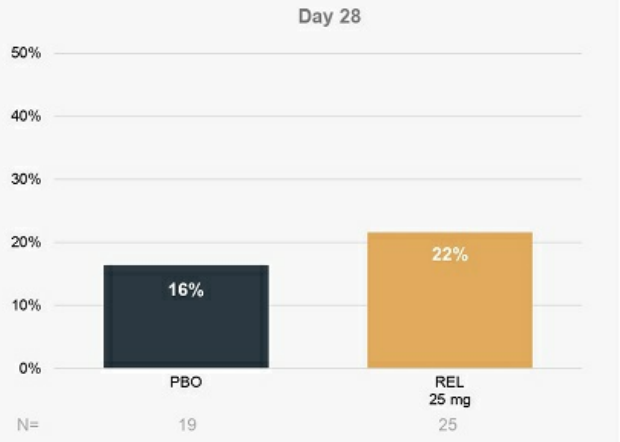
Day 28: last efficacy assessment
Total N=232
MADRS=Montgomery-Asberg Depression Rating Scale; Source: Relmada Data on File

In Reliance III 39% of subjects achieved response and 22% achieved remission with 25 mg REL-1017 in the full analysis set

Percentage of subjects achieving response
(≥ 50% MADRS improvement from baseline)



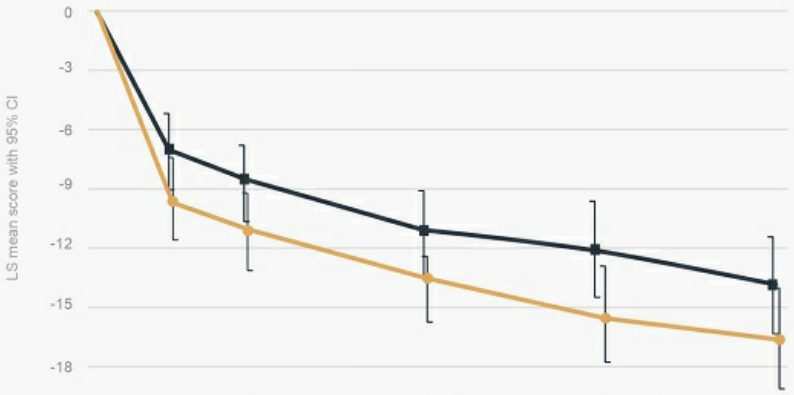
Percentage of subjects achieving remission
(MADRS ≤10)



Day 28: last efficacy assessment
Total N=232
MADRS=Montgomery-Asberg Depression Rating Scale; Source: Relmada Data on File

Reliance III: REL-1017 showed a meaningful -4.1 MADRS point difference vs. placebo at Day 28 with removal of four sites with paradoxical results

Modified analysis of 41 of 45 centers and 164 of 232 subjects*



Placebo
REL-1017 25mg

ΔMADRS (N=164) Placebo N=85, 25 mg N=79, 41 sites	Day 4	Day 7	Day 14	Day 21	Day 28 End of treatment
Placebo Mean (SD)	-6.6 (7.5)	-8.3 (8.2)	-10.6 (9.6)	-11.4 (10.5)	**-13.0** (10.4)
25 mg Mean (SD)	-9.8 (9.4)	-11.4 (10.1)	-13.4 (10.6)	-16.2 (11.4)	**-17.1** (12.1)
REL-1017 vs Placebo LSMean Diff (SE); p-value, MMRM	-2.2 (1.5); 0.14	-2.5 (1.5); 0.093	-2.3 (1.6); 0.18	-3.4 (1.8); 0.062	-2.7 (1.8); **0.14**

-4.1 diff. REL-1017 vs. placebo

*These same two centers produced non-plausible results in Reliance I
Day 28: last efficacy assessment
Total N=164
MADRS=Montgomery-Asberg Depression Rating Scale; Source: Relmada Data on File

Pivotal phase 3 trial design for adjunctive therapy

Reliance I

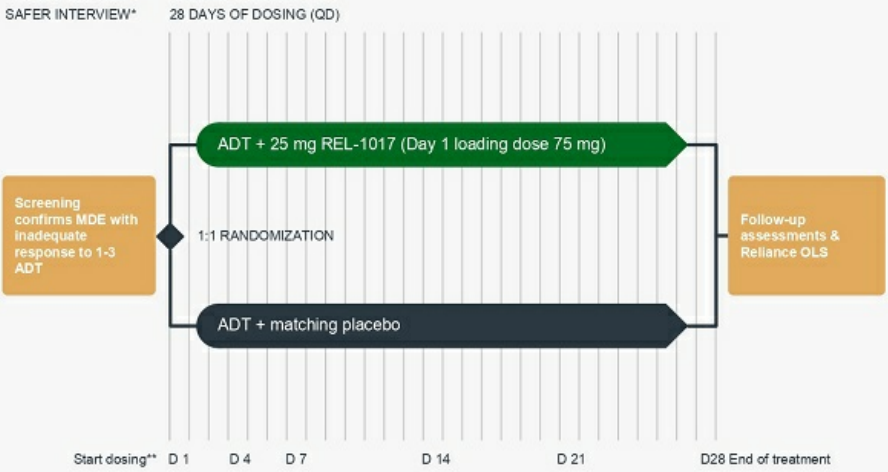
ADJUNCTIVE THERAPY

Primary endpoint:

- Change in MADRS at Day 28

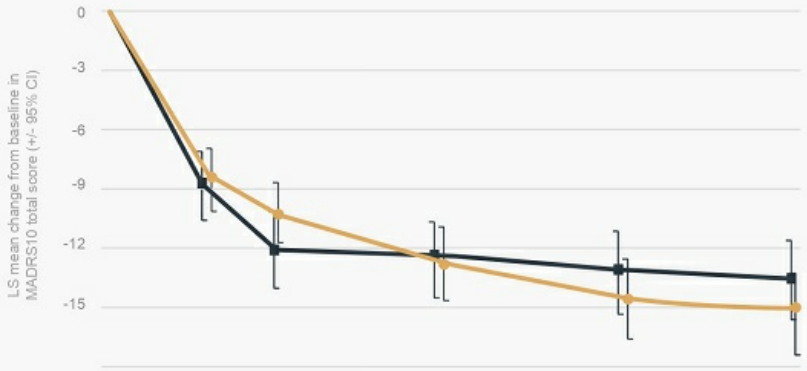
Key secondary endpoints:

- Change in MADRS score at Day 7
- Change in CGI-S score at Day 28



MADRS = Montgomery-Asberg Depression Rating Scale; CGIs = Clinical Global Impression scales; MDE = major depressive episode; ADT = antidepressant treatment; QD = once daily; OLS = open label study
*SAFER interview confirms that the illness is a specific state and excludes patients with any symptoms that are nonspecific or not readily assessable. Desseilles M, et al 2013. Massachusetts General Hospital SAFER criteria for clinical trials and research. Harv Rev Psychiatry. Sep-Oct;21(5):269-74.
**75mg loading dose on Day 1 of REL-1017

Reliance I primary efficacy endpoint: REL-1017 showed a -2.2 MADRS point clinically meaningful difference vs. placebo at Day 28 in the full analysis set

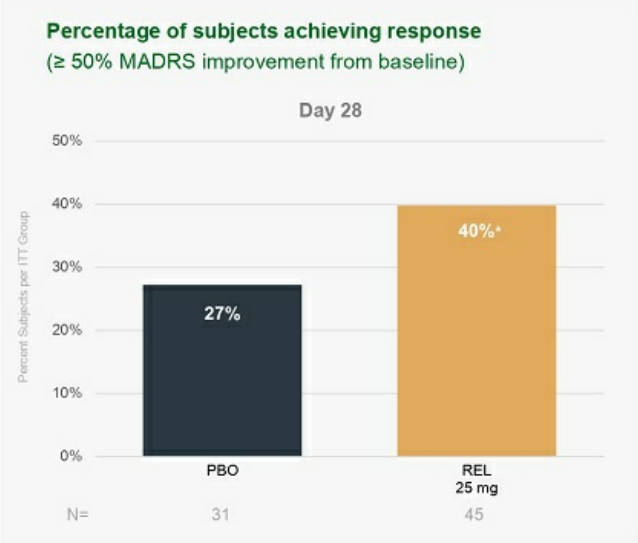


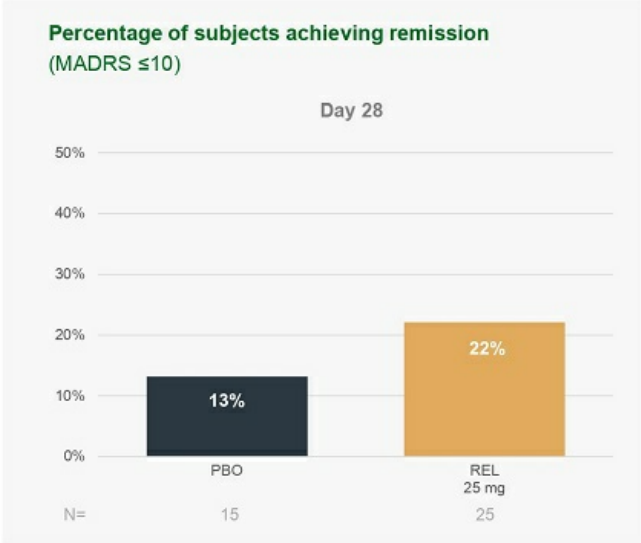
ΔMADRS (N=227) Placebo N=114, 25 mg N=113, 43 sites	Day 4	Day 7	Day 14	Day 21	Day 28 End of Treatment
Placebo Mean (SD)	-9.3 (7.3)	-11.8 (9.9)	-12.2 (10.9)	-13.0 (11.2)	**-12.9** (10.4)
25 mg Mean (SD)	-8.3 (8.9)	-10.2 (9.5)	-12.4 (9.4)	-14.4 (10.4)	**-15.1** (11.3)
REL-1017 vs Placebo LSMean Diff (SE); p-value, MMRM	0.4 (1.2); 0.74	1.7 (1.3); 0.20	-0.2 (1.4); 0.88	-1.2 (1.5); 0.41	-1.6 (1.5); 0.28

-2.2 diff. REL-1017 vs. placebo

Day 28: last efficacy assessment
Total N=227; * p= <0.05
MADRS=Montgomery-Asberg Depression Rating Scale; Source: Relmada Data on File

Reliance I achieved a statistically significant response rate of 40% (p=0.044), and achieved remission rate of 22% (p=0.076) at Day 28 in the full analysis set

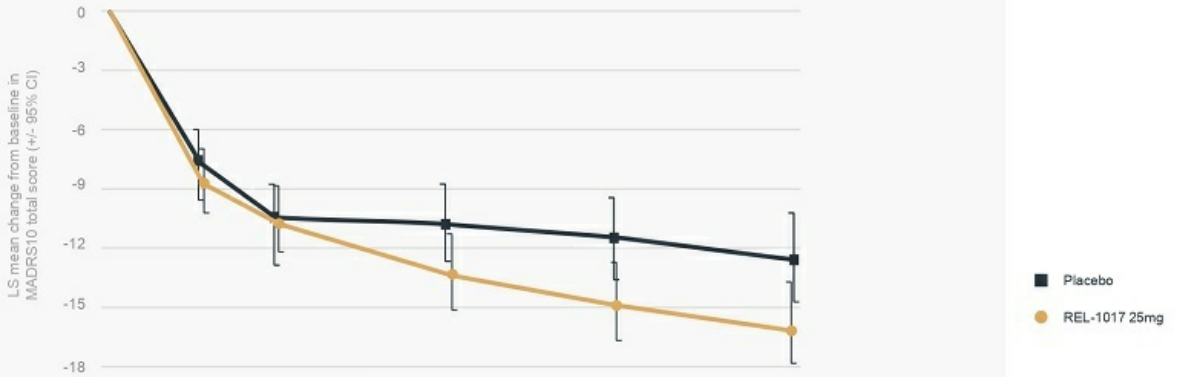




Day 28: last efficacy assessment
Total N=227; * p= <0.05
MADRS=Montgomery-Asberg Depression Rating Scale; Source: Relmada Data on File

Reliance I: REL-1017 vs placebo with post-hoc removal of two sites with paradoxical results

Modified analysis of 41 of 43 centers and 185 of 227 subjects*



ΔMADRS (N=185) Placebo N=88, 25 mg N=97, 41 sites	Day 4	Day 7	Day 14	Day 21	Day 28 End of Treatment
Placebo Mean (SD)	-8.5 (7.0)	-11.0 (9.6)	-11.0 (10.8)	-11.8 (10.5)	**-12.6** (9.8)
25 mg Mean (SD)	-8.8 (9.1)	-10.7 (9.6)	-13.4 (9.1)	-15.3 (10.1)	**-16.7** (11.1)
REL-1017 vs Placebo LSMean Diff (SE); p-value, MMRM	-1.0 (1.3); 0.45	0.1 (1.4); 0.95	-2.6 (1.5); 0.08	-3.3 (1.6); **0.03**	-3.7 (1.6); **0.02**

-4.1 diff. REL-1017 vs. placebo

*These same two centers produced non-plausible results in Reliance III
Day 28: last efficacy assessment
Total N=185; * p= <0.05
MADRS=Montgomery-Asberg Depression Rating Scale; Source: Relmada Data on File

REL-1017 displays a robust safety profile and confirms no evidence for abuse potential or dissociative effects across studies

Cardiac safety

No AE related to QTcF prolongation

Suicidality

No evidence of increased suicidal ideation/behavior measured with C-SSRS[1] scales

Dissociative effects and withdrawal symptoms

No evidence of drug-induced dissociation based on CADDS[2]

No evidence of withdrawal symptoms based on the SOWS[3], COWS[4] and PWC-20[5] scales

Abuse potential MADDERS® reports[1]

No signal of abuse potential as assessed in the **MADDERS®** reports[5]

1.) C-SSRS: Columbia Suicide Severity Rating Scale; 2.) CADDS: Clinician-Administered Dissociative States Scale; 3.) SOWS: Subjective Opioid Withdrawal Scale; 4.) COWS: Clinical Opiate Withdrawal Scale; 5.) PWC-20: Physician Withdrawal Checklist; 5.) MADDERS®: Misuse, Abuse, and Diversion Drug Event Reporting System

In Reliance I no serious treatment related treatment-emergent adverse event (TEAE) and no opioid like effects were observed

Treatment-emergent adverse events by preferred term in patients with MDD in the safety analysis set

Variable	Placebo (N=114)		REL-1017 25 mg (N=113)		All patients (N=227)	
	N	%	N	%	N	%
Patients with at least one TEAE	61	53.5	55	48.7	116	51.1
Patients with at least one treatment related TEAE	28	24.6	30	26.5	58	25.6
Patients with at least one serious treatment related TEAE	0	0.0	0	0.0	0	0.0
Treatment-emergent adverse events* occurring in 5% or more patients per treatment arm						
Headache	9	7.9	13	11.5	22	9.7
COVID19	10	8.8	6	5.3	16	7.0
Upper respiratory tract infection	6	5.3	8	7.1	14	6.2
Nausea	5	4.4	8	7.1	13	5.7
Diarrhea	7	6.1	5	4.4	12	5.3
Constipation	7	6.1	3	2.7	10	4.4
Dizziness	2	1.8	7	6.2	9	4.0

*Treatment-emergent adverse event was defined as an adverse event that started or worsened after treatment with the trial drug

In Reliance III no serious treatment related treatment-emergent adverse event (TEAE) and no opioid like effects were observed

Treatment-emergent adverse events by preferred term in patients with MDD in the safety analysis set

Variable	Placebo (N=116)		REL-1017 25 mg (N=116)		All patients (N=232)	
	N	%	N	%	N	%
Patients with at least one TEAE	56	48.3	62	53.4	118	50.9
Patients with at least one treatment related TEAE	37	31.9	39	33.6	76	32.8
Patients with at least one serious treatment related TEAE	0	0.0	0	0.0	0	0.0
Treatment-emergent adverse events* occurring in 5% or more patients per treatment arm						
Headache	11	9.5	13	11.2	24	10.3
Nausea	6	5.2	11	9.5	17	7.3
Dizziness	5	4.3	10	8.6	15	6.5
COVID19	3	2.6	11	9.5	14	6.0
Fatigue	4	3.4	6	5.2	10	4.3
Dry mouth	3	2.6	6	5.2	9	3.9

*Treatment-emergent adverse event was defined as an adverse event that started or worsened after treatment with the trial drug

Focus and action for ongoing and new studies

Clinical trial management

- New clinical trial leadership with MDD Phase 3 NMDAR antagonist-specific experience
- Closer engagement of sites (PIs & research coordinators)

Patient selection

- Requirement for medical/pharmacy records to confirm an existing depression diagnosis and ongoing ADT
- Exclusion of patients with prior life-time history of participation in clinical trials
- Exclusion of patients with positive drug screen

Site selection

- Favor research sites with clinical practice over centers without clinical practice
- Cap the number of patients that can be enrolled per site

Quality raters

- Improve rater qualification process and rater quality
- Real time quality assessments to look for discrepancies in ratings

MADRS=Montgomery-Asberg Depression Rating Scale
ADT =Antidepressant

Path to NDA

- ✓ All non-clinical & phase 1 studies completed
- ✓ All Human Abuse Potential studies (HAPs) completed
- ✓ ~40% NDA submission readiness
- ✓ Stability testing of primary packaging completed and production at scale validated
- ✓ Considerable safety data collected from two phase 3 studies

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Neuroplastogen™ Program

We have a pipeline of molecules with neural plasticity modulating activity for the treatment of CNS disorders

Novel esmethadone derivatives

We have synthesized a series of novel esmethadone derivatives with NMDAR regulating activity. We are in the process of selecting the most promising candidates for advancing their development in the treatment of CNS disorders.

Novel psilocybin formulation and novel psilocybin derivatives

We are developing a novel psilocybin formulation and we are synthetizing psilocybin derivatives with promising activity for the treatment of CNS disorders.

CNS = Central Nervous System; NMDAR = N-methyl-D-aspartate receptor

Corporate Information

Financial overview

*As converted share count of 43.8 MM share as of 11/7/2022

Investment highlights

Focus on CNS diseases and lead program in major depressive disorder

- REL-1017 is in Phase 3 clinical trials for depression, a primary cause of disability worldwide[1]
- CNS focus, with expertise in developing novel therapeutics that show potential for neuroplasticity
- 50%–66% of patients with depression do not fully recover on an antidepressant medication[2]
- Standard antidepressants can take 2-8 weeks to work and have significant side-effects

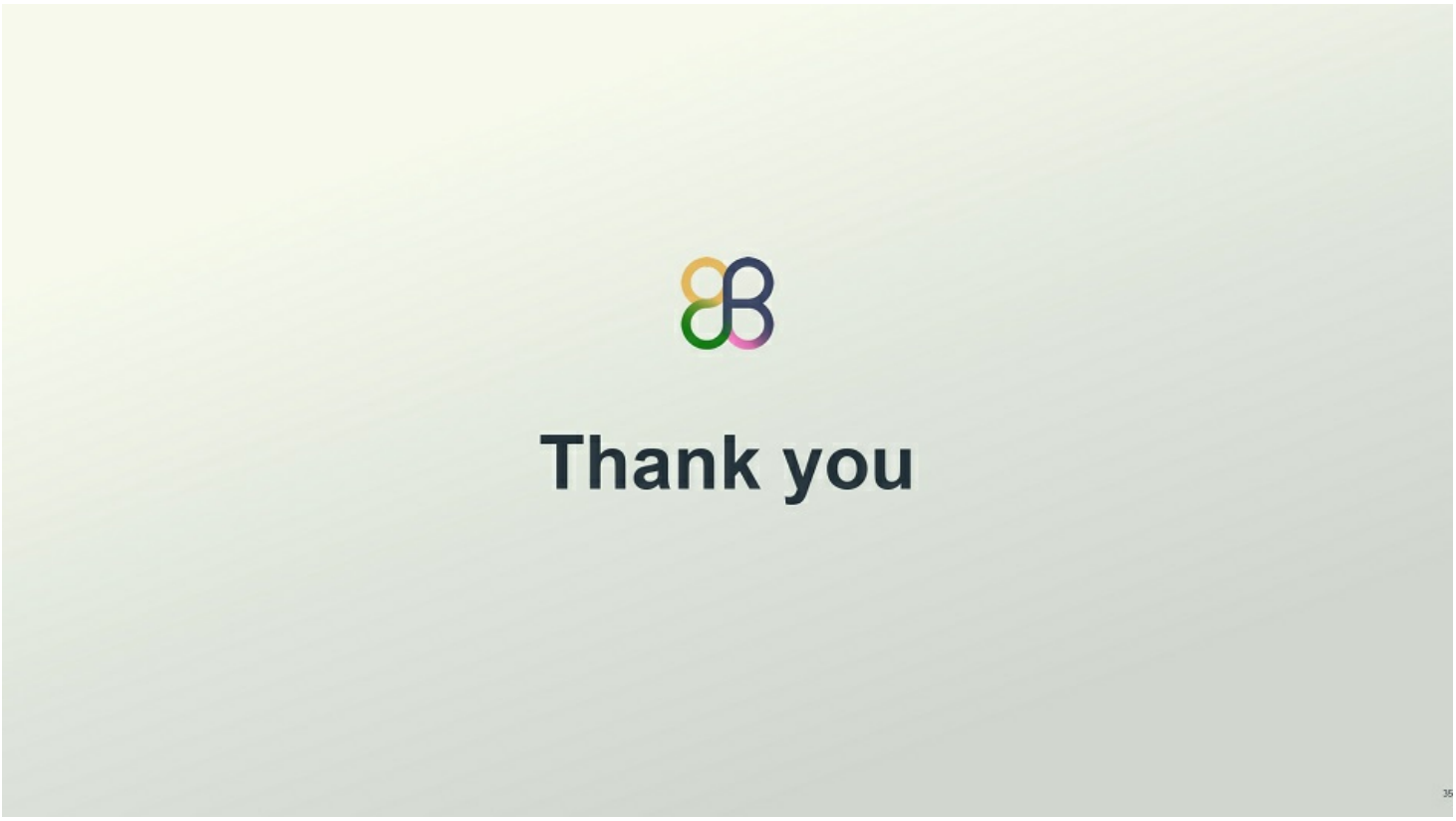
Highly compelling opportunity in REL-1017

- Novel MOA with successful Phase 2 trial in adjunctive MDD that showed statistically significant, robust, rapid, and sustained antidepressant effects with favorable safety and tolerability profile[3]
- **Phase 3 program underway** following successful end of Phase 2 Meeting with the FDA
- Strong intellectual property position around REL-1017 with expirations through the mid/late-2030s

Lessons learned provide strong confidence in the path to NDA

- Improved clinical trial management
- Quality patient selection
- Careful site selection
- Quality raters

CNS= Central Nervous System; MDD = major depressive disorder; MOA = mechanism of action\
**Our fiscal year end is December 31. The periods referred to in this slide are calendar years and quarters.
1.) WHO Depression Fact Sheet; 2.) Al-Harbi K.S. 2012 *Patient Preference and Adherence*; 3.) Fava et al. Rapid and Sustained Antidepressant Effects of REL-1017 (dextromethadone) as an Adjunctive Treatment for Major Depressive Disorder: A Phase 2 Trial. 2021


Thank you