

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): **November 11, 2022**

RELMADA THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Nevada
(State or other jurisdiction
of incorporation)

001-39082
(Commission File Number)

45-5401931
(IRS Employer
Identification No.)

2222 Ponce de Leon Blvd, Floor 3
Coral Gables, FL
(Address of principal executive offices)

33134
(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 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 8.01 Other Events.

On November 11, 2022, the Company updated its corporate presentation, a copy of which is filed herewith as Exhibit 99.1 and is incorporated herein by reference.

Item 9.01. Financial Statements and Exhibits.

(d) Exhibits

Exhibit No.	Description
99.1	Corporate Presentation dated November 11, 2022
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

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: November 11, 2022

RELMADA THERAPEUTICS, INC.

By: /s/ Sergio Traversa

Name: Sergio Traversa

Title: Chief Executive Officer



Targeting Major Advances in Treatment of CNS Disorders

November 11th, 2022 | Nasdaq: RLMD



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

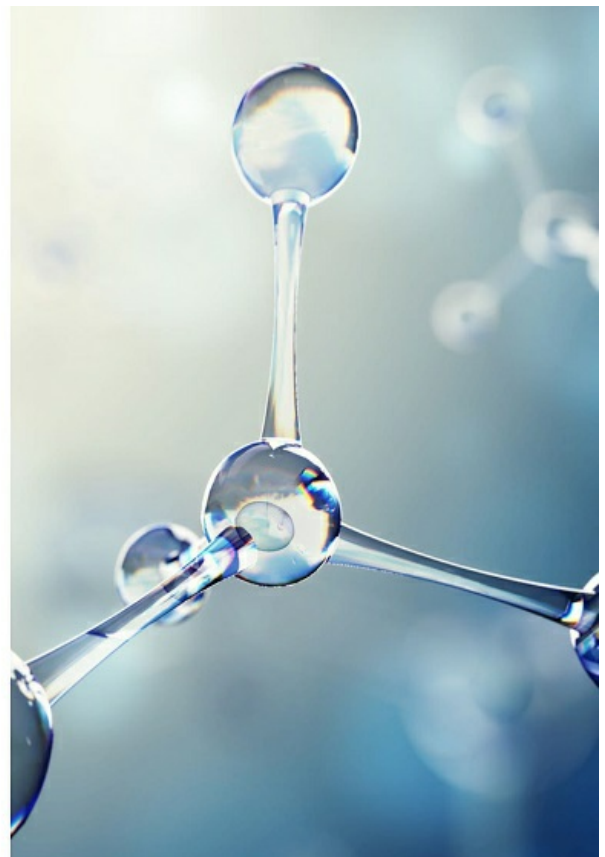
Multiple Catalysts Expected Over the Next 12 Months

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

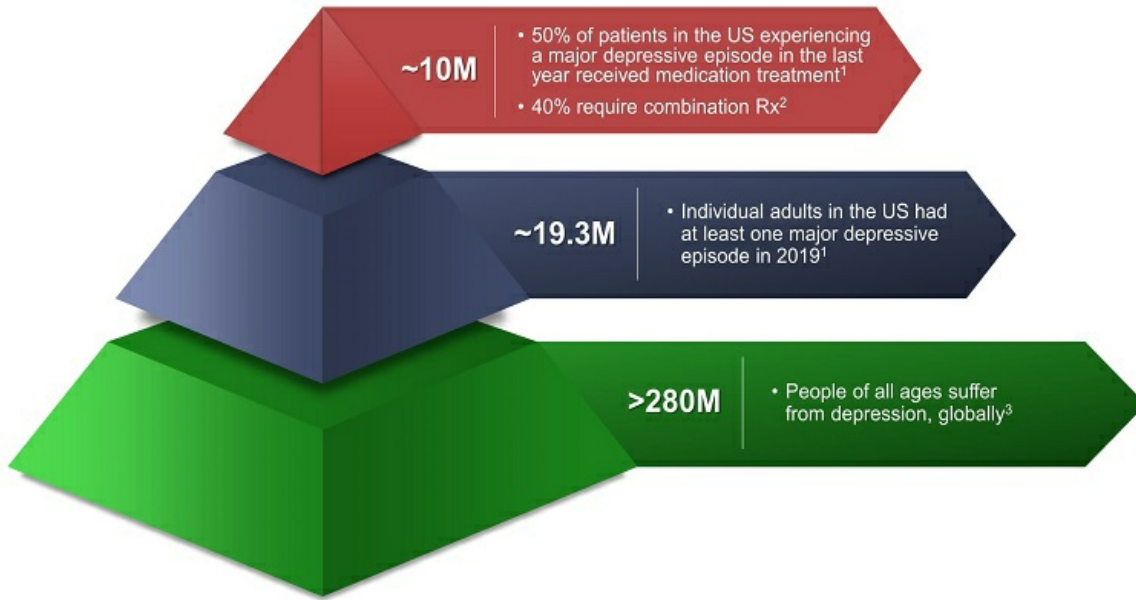
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Major Depressive Disorder & REL-1017



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

Limitations of Current Treatments for MDD



Limited Efficacy

~65% MDD patients do not respond to first antidepressant treatment¹



Slow Onset of Action

Standard antidepressants, even when effective, may take up to 8 weeks to reach efficacy¹



Safety & Tolerability Challenges

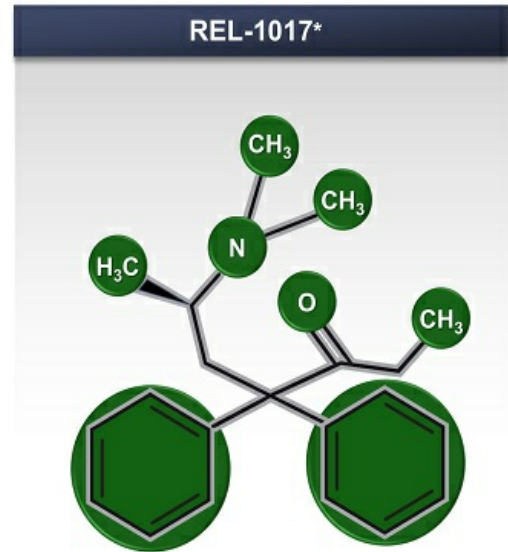
Side effects of atypical antipsychotics approved as adjunctive treatments for MDD include tardive dyskinesia, metabolic syndrome, cognitive impairment and stroke²

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):97-106;
2. US Prescribing Information, brexpiprazole, quetiapine, aripiprazole

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 MDD¹
- Available clinical data demonstrated:
 - Robust, rapid, and sustained statistically significant antidepressant effects on all tested scales²
 - Rapid onset: significant efficacy effects by Day 4²
 - Favorable safety and tolerability profile consistent across Phases 1 & 2 studies: no opioid and no psychotomimetic adverse events^{2,3} and no metabolic side effects
 - Orally administered, once-daily tablet



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

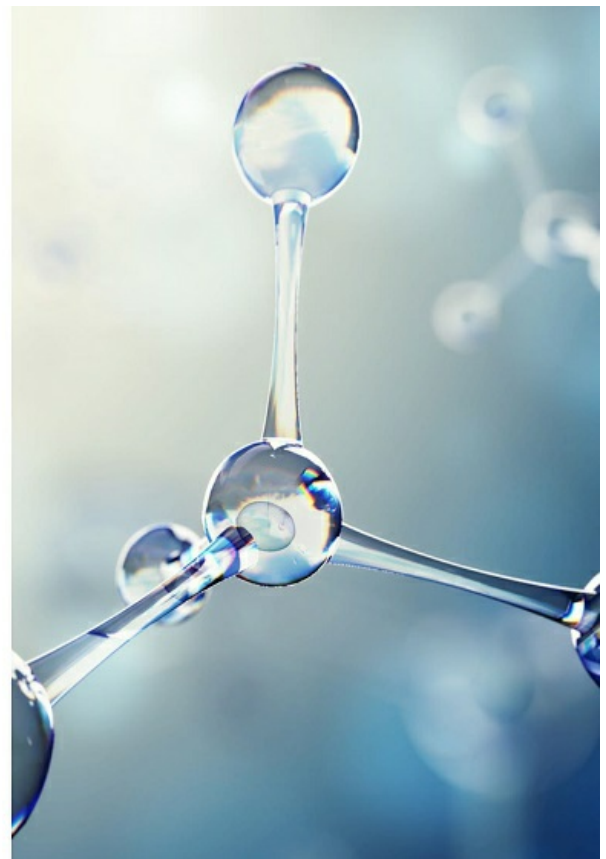
*Diagram reflects chemical structure of REL-1017 (esmethyladone), molecules are CH₃ = Methyl Group, O = Oxygen, N = Nitrogen

1. Bellini et al. Esmethyladone (REL-1017) Reduces Glutamate-Induced Currents in NMDA Receptors With the GluN2D Subunit. *Biological Psychiatry*, 89(9), S198-S199. 2. Fava et al. Rapid and Sustained Antidepressant Effects of REL-1017 (dextromethyladone) as an Adjunctive Treatment for Major Depressive Disorder: A Phase 2 Trial. 2021. Poster presented at: American Psychiatric Association Annual Meeting. 3. Bernstein, et al. 2019 *Journal of Clinical Psychopharmacology*.

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REL-1017 Ph 1 & 2 Efficacy & Safety Data



Phase 1 SAD & MAD Studies for REL-1017, Data Published 2019

Single Ascending Dose (SAD) Study Design

Parallel group, double-blind, placebo controlled

Objectives

Establish PK, PD, and safety of single dose administration

Treatment Administration

- 6 Cohorts: 5, 20, 60, 100, 150, 200 mg
- N = 42

Study Conclusions

- Maximum Tolerated Dose (MTD) = 150 mg
- PK demonstrated linear proportionality of C_{max} , AUC_{0-inf} vs. dose
- No clinically significant opioid or NMDA AESI signal

Multiple Ascending Dose (MAD) Study Design

Parallel group, double-blind, placebo controlled

Objectives

Establish PK, PD, and safety of once daily, 10-day administration

Treatment Administration

- 3 Cohorts: 25, 50, 75 mg
- N = 24

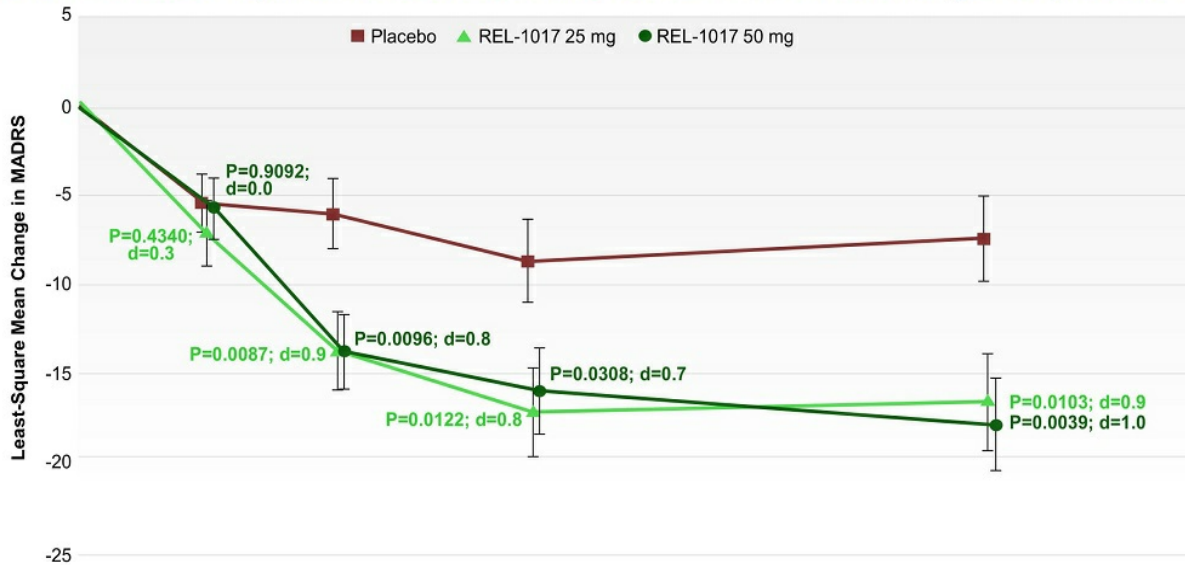
Study Conclusions

- The highest dose studied, 75mg daily, was well tolerated
- Favorable safety and tolerability profile
- No clinically significant opioid or NMDA AESI signal

PK = pharmacokinetics; PD = pharmacodynamics; MTD = maximum tolerated dose; C_{max} = maximum plasma concentration; AUC_{0-inf} = area under the curve 0 to infinite time; AUC_C = 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/June; 39(3):226-237.

Phase 2 Study REL-1017: Primary Efficacy Endpoint

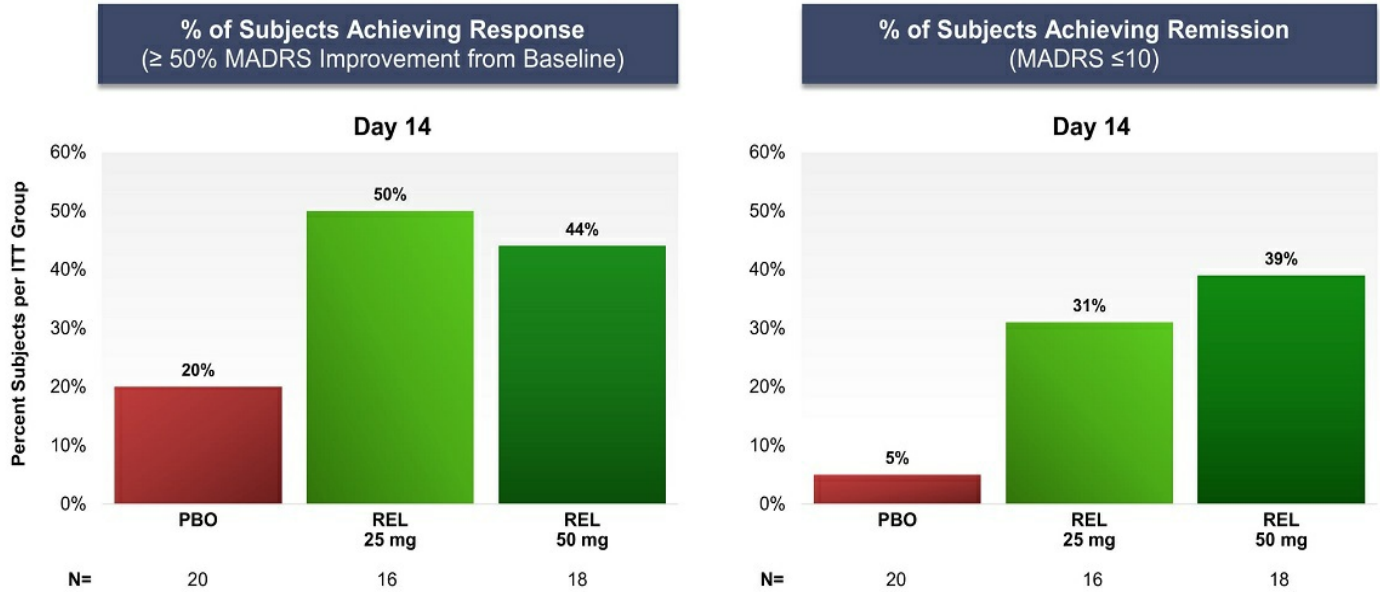
REL-1017 showed rapid and sustained differences in MADRS change vs. placebo



Δ MADRS REL-1017 vs Placebo	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

REL-1017 Phase 2 Study Efficacy: Response & Remission



Day 14: last efficacy assessment, 7 days after last dose of study drug
MADRS=Montgomery-Asberg Depression Rating Scale
Source: Reimada Data on File

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. Poster presented at: American Psychiatric Association Annual Meeting 12

REL-1017 Phase 2 Study Safety: Treatment Emergent Adverse Events

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

Variable	Placebo (N = 23)		REL-1017 25 mg (N=19)		REL-1017 50 mg (N=21)		All Patients (N = 62)	
	N	%	N	%	N	%	N	%
Patients with a serious adverse event	0	0.0	0	0.0	0	0.0	0	0.0
Patients with a severe treatment-emergent adverse event	0	0.0	0	0.0	0	0.0	0	0.0
Patients with at least one adverse event	12	54.5	9	47.4	15	71.4	36	58.1
Treatment-emergent adverse events occurring in three or more patients								
Constipation	3	13.6	1	5.3	3	14.3	7	11.3
Nausea	2	9.1	1	5.3	2	9.5	5	8.1
Diarrhea	3	13.6	0	0.0	0	0.0	3	4.8
Headache	3	13.6	2	10.5	3	14.3	8	12.9
Somnolence	2	9.1	1	5.3	1	4.8	4	6.5
Dizziness	1	4.5	1	5.3	1	4.8	3	4.8
Back Pain	0	0.0	1	5.3	2	9.5	3	4.8

Source: Fava et al. 2021 *American Journal of Psychiatry*

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

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The results of experimental studies predictive of human abuse potential¹ and the results of human abuse potential studies in recreational opioid users² and in recreational ketamine users³ 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 2019⁴



1. Henningfield, J., Gauvin, D., Bifari, F. 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, Henningfield J, Apseloff G, Gorodetzky C, De Martin S, Vocci F, Sapienza F, Kosten T, Huston J, Buchhalter A, Ashworth J, Lanier R, Folli F, Traversa S, Inturnisi CE, Manfredi P, & Pappagallo M. 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

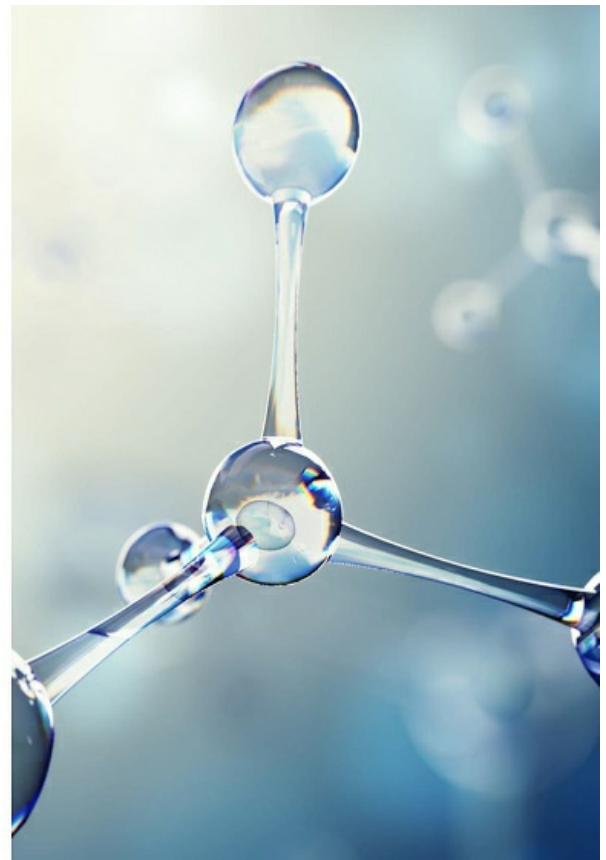
3. Shram M, Henningfield J, Apseloff G, Gorodetzky C, De Martin S, Vocci F, Sapienza F, Kosten T, Huston J, Buchhalter A, Ashworth J, Lanier R, Folli F, Traversa S, Inturnisi CE, Manfredi P, & Pappagallo M. No meaningful abuse potential in recreational ketamine users of REL-1017 (esmethadone hydrochloride), a new NMDAR antagonist and potential rapid-acting antidepressant. *American Society of Clinical Psychopharmacology (ASCP)* 2022

4. US DEA Statement on Methadone, December 2019 https://www.deadiversion.usdoj.gov/drug_chem_info/methadone/methadone.pdf#search=methadone last access February 2022

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Reliance: The Phase 3 Program for REL-1017



REL-1017 Phase 3 Program for the Treatment of MDD

Reliance I

Reliance II

Two sister two-arm, placebo-controlled pivotal studies in patients with MDD and inadequate response to ongoing standard antidepressant treatment:

- In MDD patients with inadequate response to 1-3 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

Pivotal Phase 3 Trial Design for patients with MDD and inadequate response to ongoing standard antidepressant treatment:

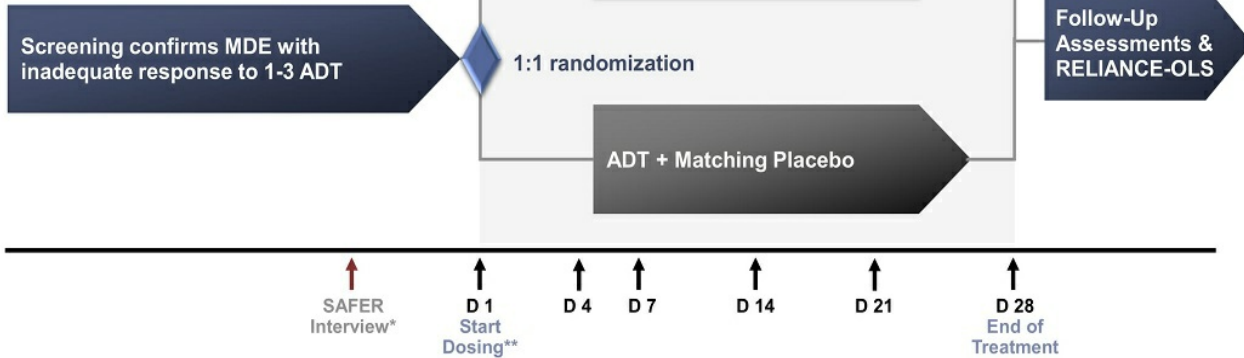


Primary Endpoint:

- 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

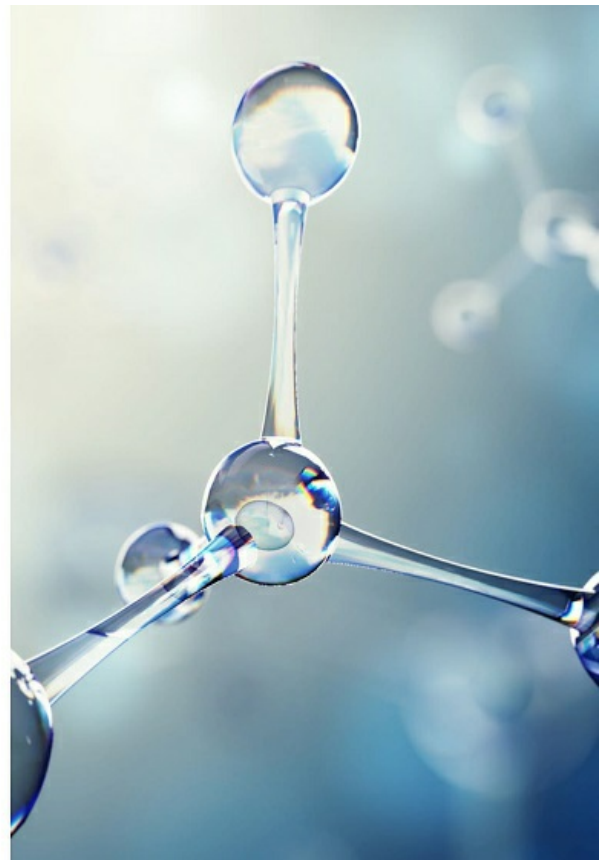
Relmada Development Programs & Timeline*

Program	1Q 22	2Q 22	3Q 22	4Q 23	1H 23
REL-1017	RELIANCE I: 1st Pivotal Adjunctive MDD trial				
	RELIANCE II: 2nd Pivotal Adjunctive MDD trial				
	RELIANCE-OLS: Long-Term, Open-Label Study in MDD				

MDD = Major Depressive Disorder; OLS = Open Label Study
 *Subject to FDA feedback **Our fiscal year end is December 31. The periods referred to in this slide are calendar years and quarters



Neuroplastogen™ Program



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

Novel esmethadone derivatives

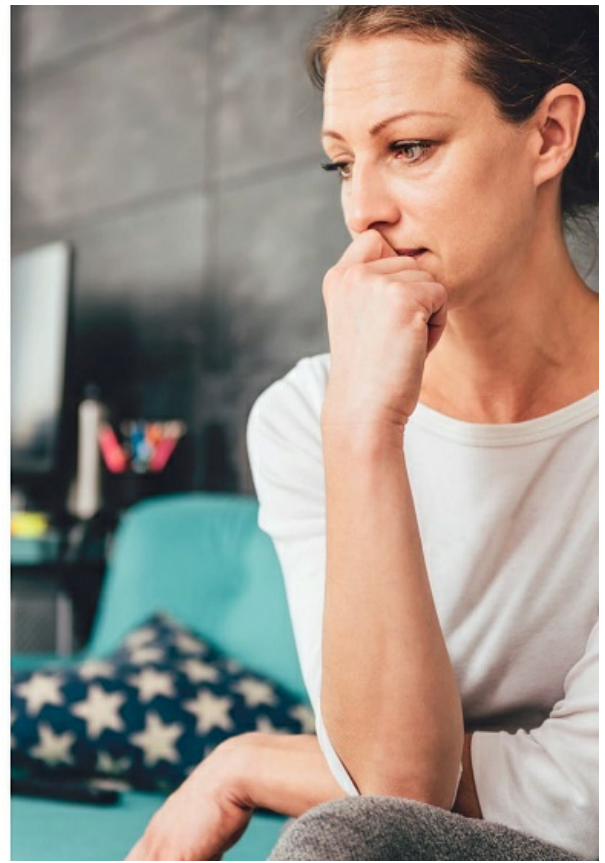
We have synthesized a series of novel esmethadone derivatives with NMDAR regulating activity. We are in the process of selecting the most promising candidates for advancing their development in the treatment of CNS disorders

Novel psilocybin formulation and novel psilocybin derivatives

We are developing a novel psilocybin formulation and we are synthesizing psilocybin derivatives with promising therapeutic activity



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 (MDD)

- REL-1017, lead candidate, is in Phase 3 for depression, a leading cause of disability worldwide¹
- 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 medication²
- Standard antidepressants can take 2-8 weeks to work and have significant side-effects

Highly Compelling Lead Product 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 profile³
- **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

Key Catalysts Expected Over the Next 12 Months

- Completion of RELIANCE I adjunctive MDD trial expected 4Q 2022
- Completion of RELIANCE II adjunctive MDD trial expected in 2023
- Completion of RELIANCE – OLS (Long-term, Open-label study in MDD) expected in 1H 2023

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. Poster presented at: American Psychiatric Association Annual Meeting