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): **August 10, 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 Global Select Market**

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 August 10, 2023, 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 August 10, 2023
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: August 10, 2023

RELMADA THERAPEUTICS, INC.

By: */s/ Sergio Traversa*

Name: Sergio Traversa
Title: Chief Executive Officer

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.

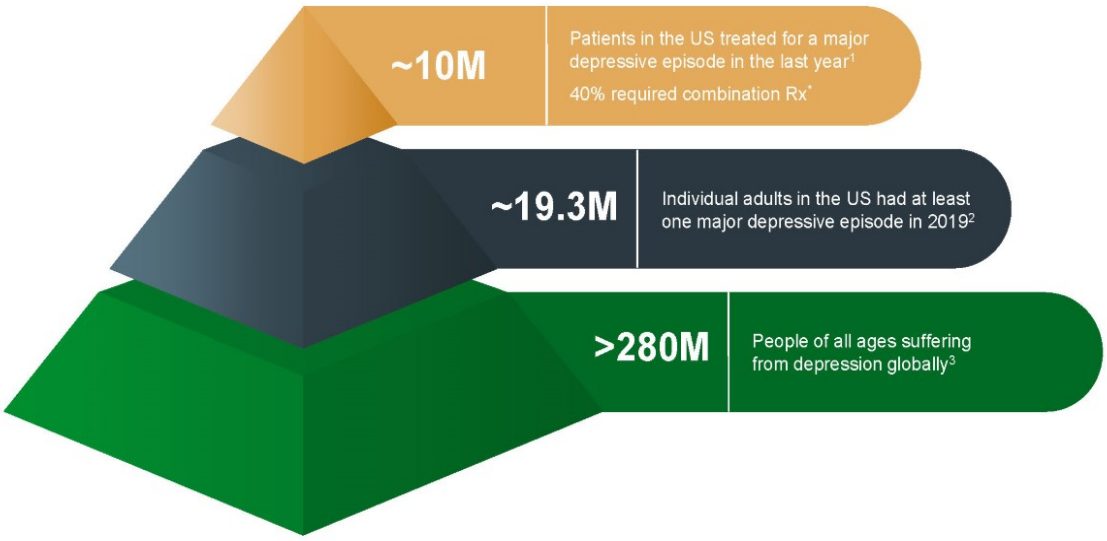
Investment highlights

- CNS focused, with lead program for REL-1017, a novel MOA, in Phase 3 for Major Depressive Disorder (MDD)
- Compelling Phase 2 data indicating the robust therapeutic effect of REL-1017 for MDD
- Efficacy and safety profile of REL-1017 potentially address limitations of current MDD treatments options
- Phase 3 program underway with two ongoing Phase 3 trials for REL-1017 as Adjunctive Treatment for MDD
- Highly experienced clinical team with a successful track record advancing CNS programs through NDA approval

CNS= Central Nervous System

The unique profile of esmethadone (REL-1017) addresses the limitations of current treatment options for MDD

The 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

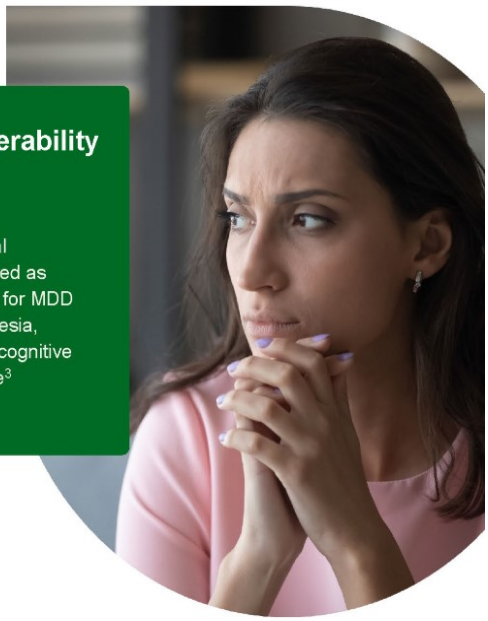
~65% MDD patients do not respond to first antidepressant treatment[1]

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):97-106; 3. US Prescribing Information, brexpiprazole, quetiapine, aripiprazole

Unique profile of esmethadone (REL-1017) addresses limitations of current treatments

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 has 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

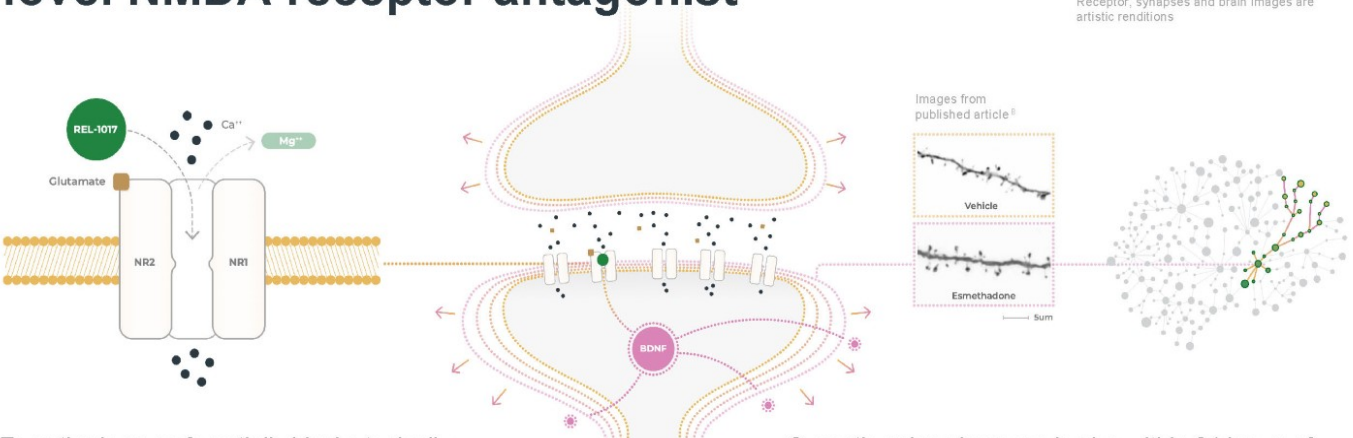
MDD = major depressive disorder; NMDAR = N-methyl-D-aspartate receptor

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

Esmethadone [1] (REL-1017) is a novel NMDA receptor antagonist

NMDA: N-methyl-D-aspartate
GluN2D: Glutamate NMDA receptor with 2D subunits
BDNF: brain-derived neurotrophic factor
MDD: major depressive disorder

Receptor, synapses and brain images are artistic renditions



Esmethadone preferentially blocks tonically hyperactive GluN2D receptor subtypes [2], potentially increasing BDNF [3], decreasing neuroinflammation [4] and restoring physiological neuroplasticity [5,6,7].

Synaptic spines increase in size within 24 hours of administration [8]. Esmethadone is devoid of dissociative effects [9], has no meaningful abuse potential [10] and is administered orally once-daily.

1. Esmethadone is a promising non-dissociative NMDAR antagonist antidepressant (Fava 2023)
2. Esmethadone preferentially targets tonically hyperactive GluN2D receptors (Bettini 20222A)
3. Esmethadone increases BDNF release (Fogaca 2019; De Martin 2021)
4. Esmethadone reduces calcium influx induced by quinolinic acid (Bettini 2022B)
5. Esmethadone restores impaired neuroplasticity (Fogaca 2019; Stahl 2022)
6. Impaired neuroplasticity and neuroinflammation may be central to the pathophysiology of MDD (Cooper 2023)
7. Esmethadone is a promising neuroplastogen® that could transform the current treatment of MDD (Cooper 2023)
8. A single dose of esmethadone increases synaptic spines (Fogaca 2019)
9. Esmethadone does not cause dissociative effects (Shram 2023)
10. Esmethadone differs pharmacologically from levomethadone because it is devoid of clinically relevant opioid activity. Esmethadone has no meaningful abuse potential in healthy subjects (Bernstein 2019), patients with MDD (Fava 2022) and recreational substance users (Shram 2023)

The clinical development of esmethadone (REL-1017) is steadily progressing as Adjunctive Treatment for MDD

Esmethadone (REL-1017) clinical development status

- All non-clinical studies have been successfully completed
- All Phase 1 studies and Human Abuse Potential studies (HAPs) have been successfully completed
- The open-label 12-month study has been successfully completed
- The Phase 3 development program is ongoing; Reliance I (study 301) has been completed, Reliance II (study 302) and Relight (study 304) are currently in progress
- Stability testing of primary packaging has been completed, and production at scale has been validated

Data from the Phase 1, Phase 2, and Human Abuse Potential studies indicate favorable safety and tolerability of esmethadone (REL-1017)

All Phase 1 studies have been successfully completed

- Multiple Ascending Dose (MAD) study
- Single Ascending Dose (SAD) study
- Oxycodone Human Abuse Potential (HAP) study
- Intravenous Ketamine Human Abuse Potential (HAP) study
- Renal Impairment study and Hepatic Impairment study
- Drug-Drug Interaction (DDI) study
- Absorption, distribution, metabolism, excretion (ADME) study

The Human Abuse Potential studies have been successfully completed and indicate no abuse potential of REL-1017

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:

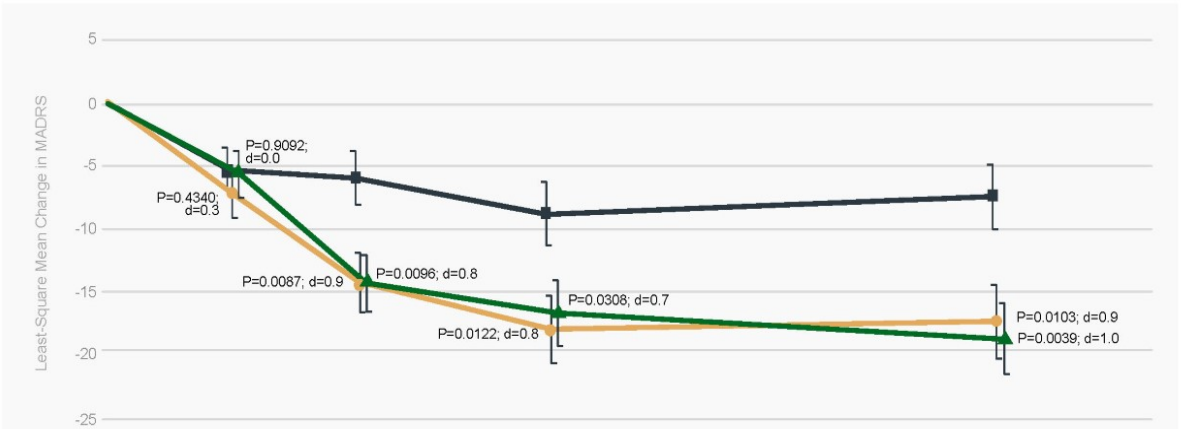
"The *d*-isomer lacks significant respiratory depressant action and addiction liability..."

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

Phase 2 study results: 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



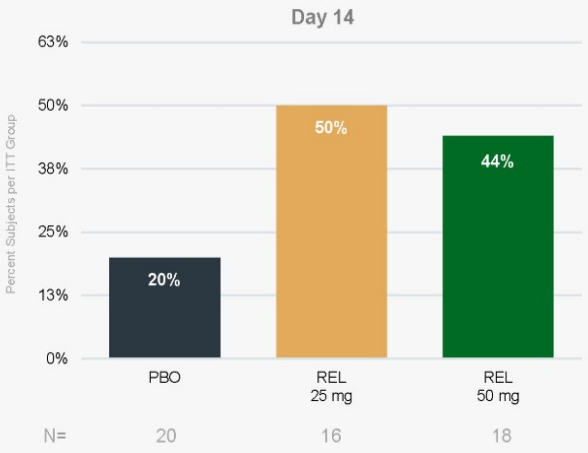
Mean drug-placebo difference

MADRS	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*

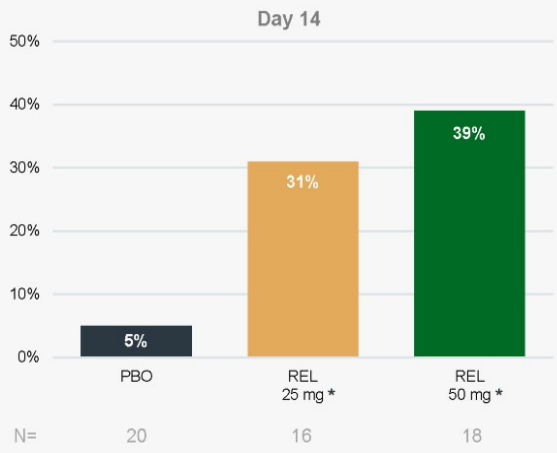
*P-value <.05
MADRS=Montgomery-Asberg Depression Rating Scale

Phase 2 study efficacy results: response & remission

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



Percentage of subjects achieving remission
(MADRS ≤10)



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

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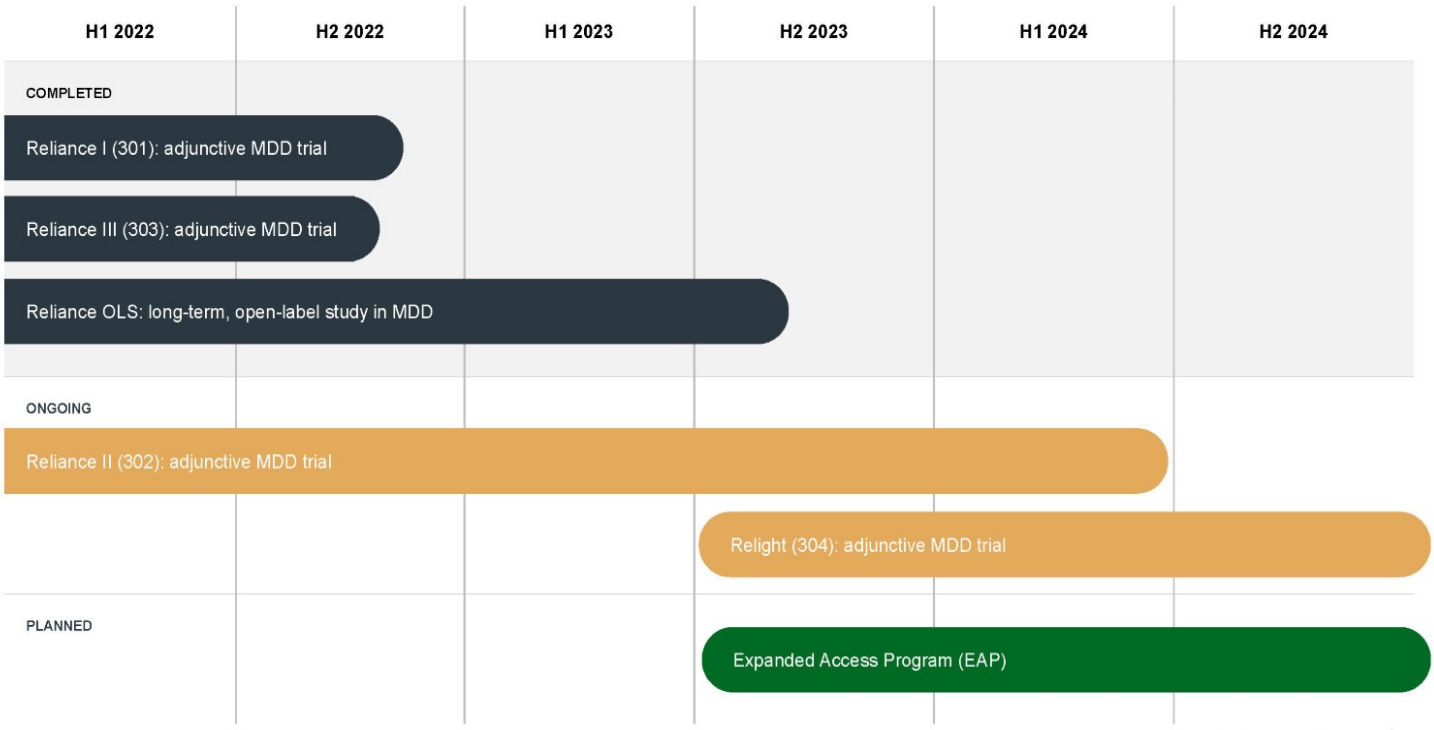
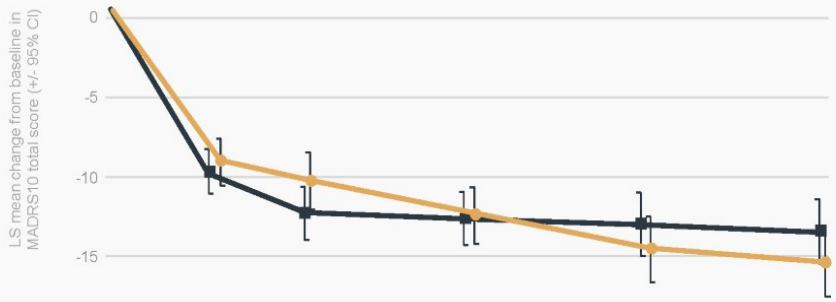
The Phase 3 program as Adjunctive Treatment for MDD is currently ongoing

Esmethdadone (REL-1017) Phase 3 development program



Reliance I primary efficacy endpoint: REL-1017 showed a clinically meaningful -2.3 MADRS point difference vs. placebo at Day 28 in the full analysis set



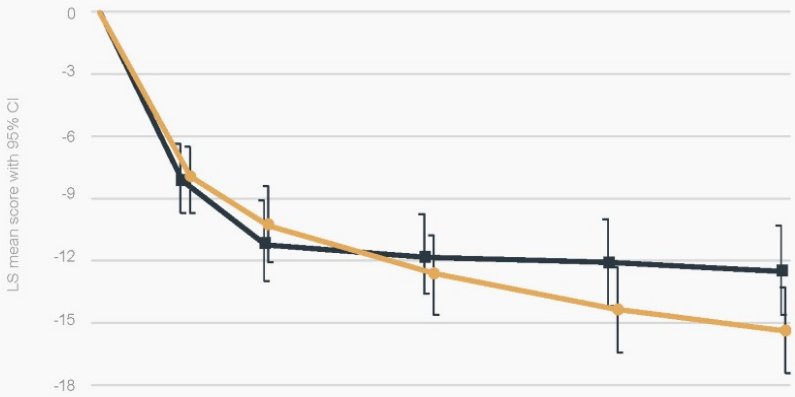
Placebo
REL-1017 25mg

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)
Placebo LSMean (SE), MMRM	-8.5 (0.8)	-11.9 (0.9)	-12.4 (1.0)	-13.0 (1.0)	-13.4 (1.1)
25 mg LSMean (SE), MMRM	-8.3 (0.8)	-10.2 (0.9)	-12.6 (1.0)	-14.2 (1.0)	-15.1 (1.1)
REL-1017 vs Placebo LSMean Diff (SE); p-value, MMRM	0.2 (1.2); 0.85	1.7 (1.3); 0.20	-0.2 (1.4); 0.88	-1.2 (1.5); 0.42	-1.7 (1.5); 0.26

-2.3 diff. REL-1017 vs. placebo p=0.15 ES=-0.21

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

In Reliance I REL-1017 showed a clinically meaningful -3.1 MADRS point difference vs. placebo at Day 28 in the Reliance I per protocol set* (p=0.051)



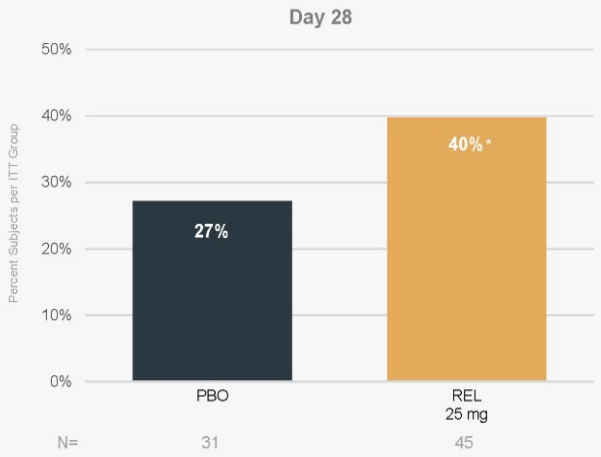
ΔMADRS (N=198) Placebo N=97, 25 mg N=101	Day 4	Day 7	Day 14	Day 21	Day 28 End of treatment
Placebo Mean (SD)	-9.0 (7.4)	-11.2 (9.7)	-11.8 (10.2)	-12.5 (10.8)	**-12.5** (9.9)
25 mg Mean (SD)	-8.3 (8.7)	-10.4 (9.5)	-12.6 (9.5)	-15.0 (10.5)	**-15.6** (11.2)
Placebo LSMean (SE), MMRM	-8.2 (0.9)	-11.2 (1.0)	-11.9 (1.0)	-12.3 (1.1)	-12.7 (1.1)
25 mg LSMean (SE), MMRM	-8.3 (0.8)	-10.4 (1.0)	-12.9 (1.0)	-14.6 (1.1)	-15.6 (1.1)
REL-1017 vs Placebo LSMean Diff (SE); p-value, MMRM	-0.8 (1.2); 0.95	0.8 (1.4); 0.56	-1.0 (1.4); 0.50	-2.3 (1.5); 0.12	-2.9 (1.5); 0.057

-3.1 diff. REL-1017 vs. placebo p= 0.051 ES=-0.29

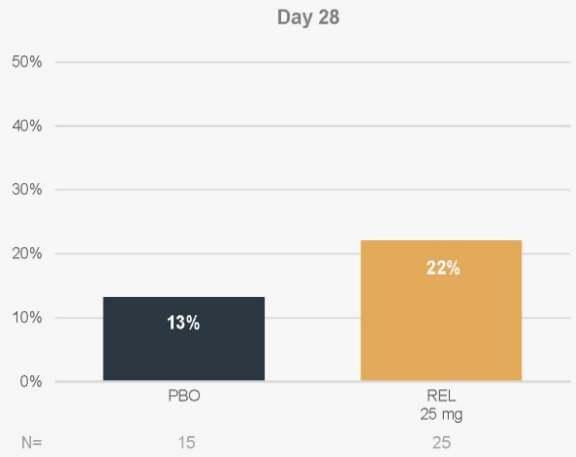
*Per-Protocol Set: Valid completer, i.e, participants who completed the 28-day treatment and did not have any major protocol deviations impacting the efficacy assessments. This set was analyzed according to the treatment actually received.
Day 28: End of treatment and primary efficacy endpoint
MADRS=Montgomery-Asberg 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

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



Percentage of subjects achieving remission
(MADRS ≤10)



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

Patient sources: verifiable vs. unverifiable

Verifiable sources

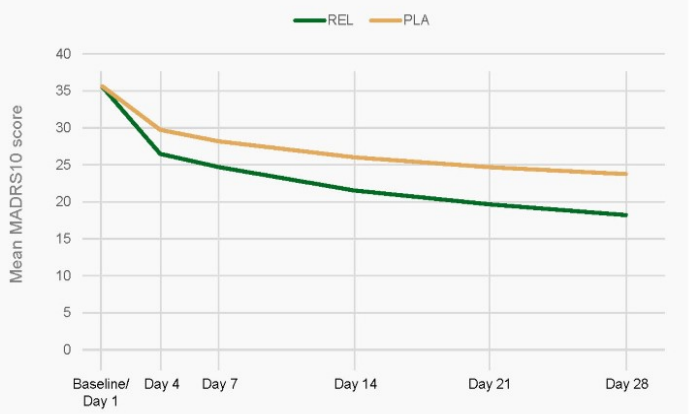
- Past patient at site
- Current patient
- Site database
- HCP referral

Unverifiable sources

- Radio/TV AD
- Banner/Pop AD
- Social media
- Internet search
- Friend
- Recruitment company
- Referral from other patients

Reliance I MADRS10 results for patients from verifiable sources vs unverifiable sources

Patients from verifiable sources

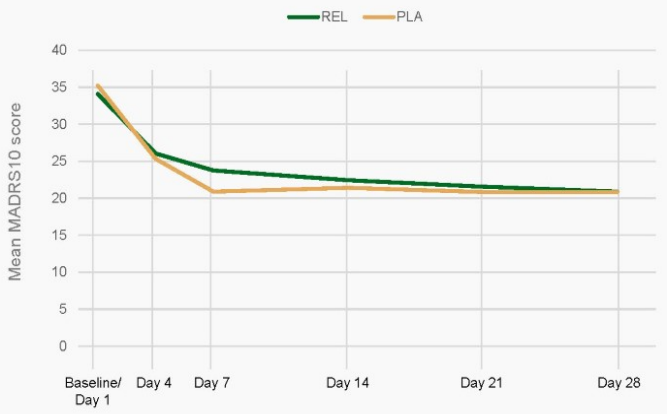


REL	52	50	50	50	49	49
PLA	40	39	39	39	37	37

Average change from baseline on Day 28	REL-1017	-17.22	p = 0.01614
	PLACEBO	-11.76	

-5.5 diff. REL-1017 vs. placebo

Patients from unverifiable sources



REL	61	61	60	60	59	60
PLA	74	70	70	66	65	70

Average change from baseline on Day 28	REL-1017	-13.22	p = 0.58911
	PLACEBO	-14.31	

P-values are calculated using Student's Two-sample equal variance t-Test, with a two-tailed distribution

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

REL-1017 displays a favorable safety & tolerability profile and confirms no evidence for meaningful abuse potential across studies

Cardiac safety

No AE related to QTcF prolongation

No increase in suicidality

No signal of drug induced suicidal ideation/behavior measured with C-SSRS[1]

No dissociative effects

No signal of drug-induced dissociation measured with CADDS[2]

No abuse potential

No "drug liking" VAS differences from placebo

No signal of withdrawal measured with SOWS[3], COWS[4] and PWC-20[5]

No MADDERS® reports of concern[6]

These Phase 3 results are consistent with safety and tolerability findings from the Phase 2 study

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; 6. MADDERS®: Misuse, Abuse, and Diversion Drug Event Reporting System

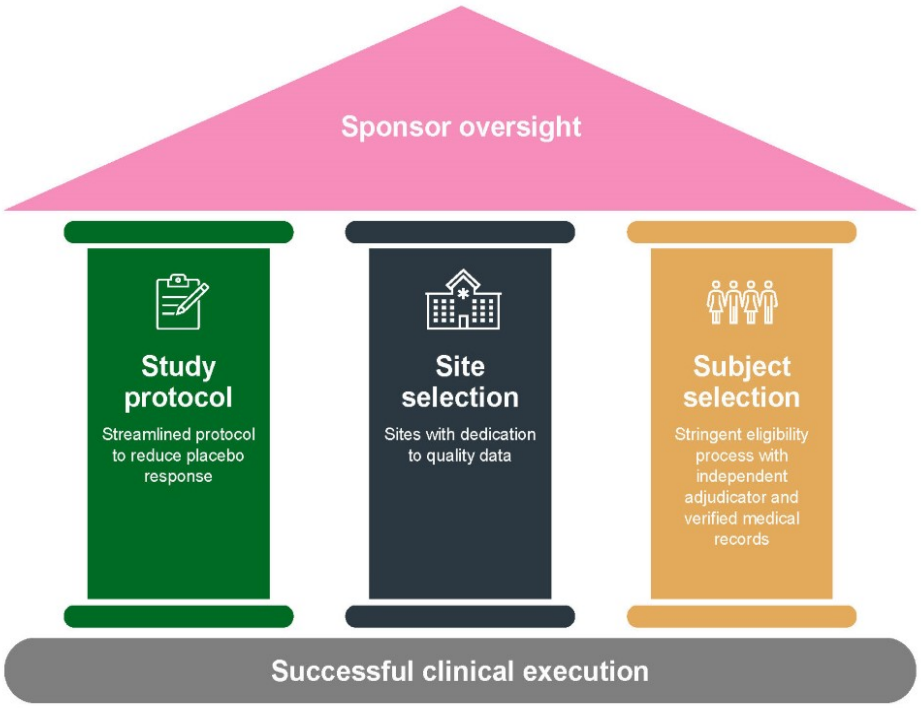
Relmada is conducting two Phase 3 trials

Reliance II

Relight

Phase 3 studies, currently ongoing in the United States, to evaluate the efficacy and safety of REL-1017 as an adjunctive treatment for MDD.

Three pillars for successful clinical execution



Reliance II (study 302) trial design for Adjunctive Treatment of MDD

Reliance II

ADJUNCTIVE THERAPY

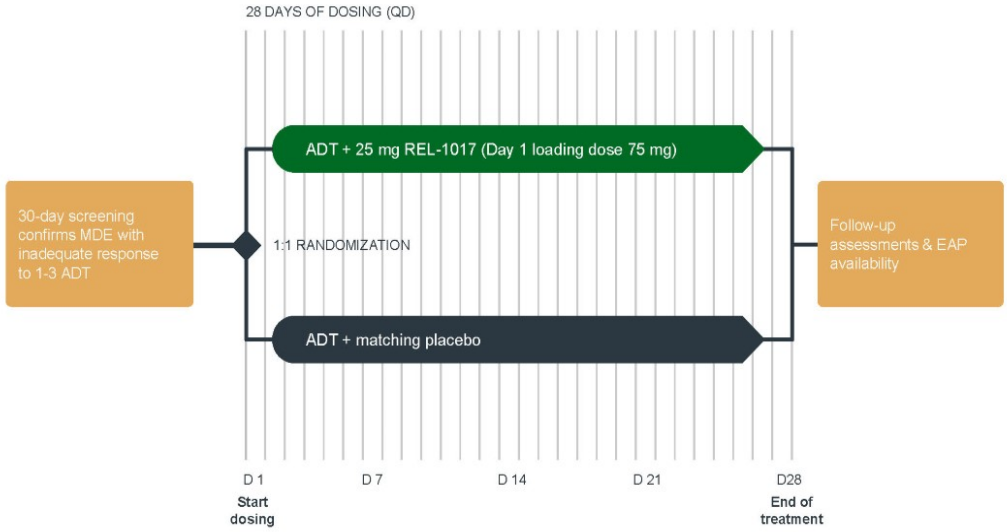
Primary endpoint:

- Change in MADRS at Day 28

Secondary endpoints:

- Change in MADRS score at Day 7
- Change in CGI-S score at Day 28
- Response Rate at Day 28
- Remission Rate at Day 28

Safety and tolerability assessments



MADRS = Montgomery-Asberg Depression Rating Scale; EAP = expanded access program; MDE = major depressive episode; QD = once daily

Relight (study 304) trial design for Adjunctive Treatment of MDD

Relight

ADJUNCTIVE THERAPY

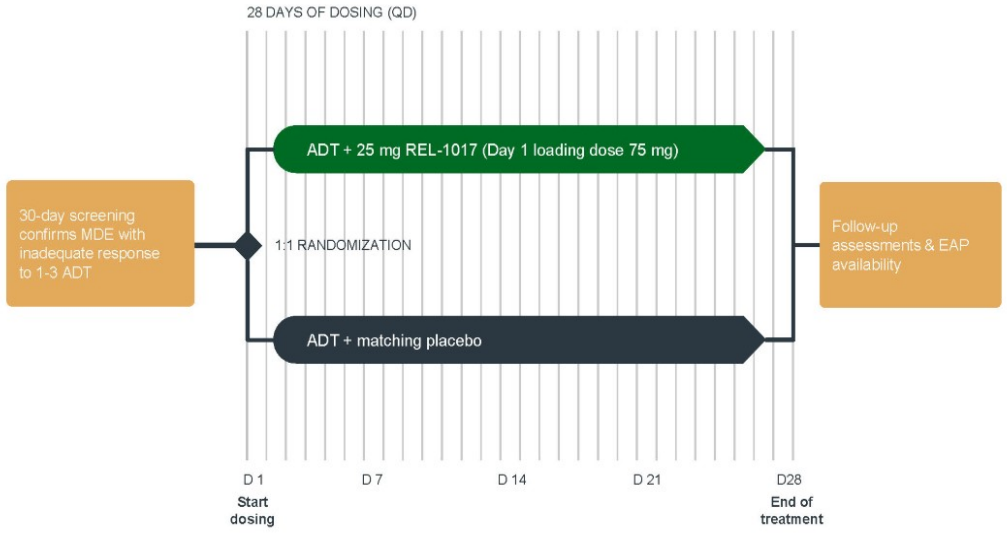
Primary endpoint:

- Change in MADRS at Day 28

Secondary endpoints:

- Change in MADRS score at Day 7
- Change in CGI-S score at Day 28
- Response Rate at Day 28
- Remission Rate at Day 28

Safety and tolerability assessments



MADRS = Montgomery-Asberg Depression Rating Scale; MDE = major depressive episode; ADT = antidepressant treatment; QD = once daily; EAP = expanded access program

Data generated for esmethadone (REL-1017) support efficacy, safety, and tolerability for adjunctive treatment of depression

- Phase 2 trial reached significance p= 0.0122 (25 mg) for the primary endpoint in the Intent-to-treat (ITT) analysis
- Reliance I, the first adjunctive Phase 3 trial, showed a 40% response rate (p = 0.044) in the ITT analysis and 3.1 MADRS-points CFB difference compared with placebo (p = 0.0510) in the Per Protocol (PP) analysis
- All studies to date have shown a consistent favorable safety and tolerability profile with no evidence of abuse potential or withdrawal
- Reliance II (study 302) and Relight (study 304) are currently ongoing in the US to evaluate the efficacy of REL-1017 25mg

MADRS = Montgomery-Asberg Depression Rating Scale; CFB = change from baseline

Corporate information

Financial overview

$118.5 million

Cash, cash equivalents & short-term investments

As of 06/30/2023

~3.0 million

Warrants outstanding

As of 06/30/2023, weighted average exercise price, $17.02

$13.3 million

Operating cash burn

2Q23

~30.1 Million

Common shares outstanding*

As of 06/30/2023

*As converted share count of 45.6 MM share as of 06/30/2023

Through our Neuroplastogen™ Program we are developing a pipeline of molecules with neuroplastic modulating activity for a variety of indications

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 to advance into development for 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

Summary

Focus on CNS diseases and lead program in Major Depressive Disorder

- REL-1017 is in Phase 3 for depression, a primary cause of disability worldwide[1]
- REL-1017 potentially addresses the limitations of current MDD treatments where 50%–66% of patients do not fully recover on an antidepressant medication[2], take 4-8 weeks to work, and have significant side effects
- Highly experienced clinical team with CNS focused backgrounds and successful track record of advancing programs through NDA approval

Highly compelling opportunity with esmethadone (REL-1017)

- **Phase 3 program underway** with positive efficacy signals and safety data
- 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]
- Strong intellectual property estate around REL-1017 with expirations through the mid/late-2030s

Ongoing Phase 3 trials are operationally improved

- Improved clinical trial management
- Quality patient selection
- Careful site selection
- Protocol simplification

CNS= Central Nervous System; MDD = major depressive disorder; MOA = mechanism of action\
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