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): **December 7, 2022**

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 December 7, 2022, Relmada Therapeutics, Inc. (the "Company"), issued a press release that provided information regarding top-line results from the Company's Phase 3 RELIANCE I Trial for REL-1017 as an adjunctive treatment for major depressive disorder. The Company also announced that it would conduct a conference call and audio webcast on December 7, 2022, at 5:00 PM EST, to discuss the study results. 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 December 7, 2022, the Company announced that its RELIANCE I study (REL-1017-301), evaluating REL-1017 as an adjunctive treatment for Major Depressive Disorder (MDD), did not achieve its primary endpoint, which was a statistically significant improvement in depression symptoms compared to placebo as measured by the Montgomery-Asberg Depression Rating Scale (MADRS) on Day 28. RELIANCE I evaluated the use of REL-1017 in addition to a standard antidepressant for patients who had inadequate response to at least one and up to three standard antidepressant therapies.

REL-1017, as it did in the Company's RELIANCE III monotherapy trail, demonstrated very favorable tolerability and safety in RELIANCE I, with no opioid-like effects, no withdrawal effects, and no psychotomimetic effects. There were no adverse events related to QTcF prolongation.

On December 7, 2022, the Company also issued a slide presentation that provided additional information regarding top-line results from the RELIANCE I Trial. The slide presentation is filed with this Current Report as Exhibit 99.2 and is incorporated into this Item 8.01 by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1*	Press release issued on December 7, 2022
99.2	Presentation dated December 7, 2022— Reliance I Topline: REL-1017 for Major Depressive Disorder (MDD)
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: December 7, 2022

RELMADA THERAPEUTICS, INC.

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

Exhibit 99.1

Relmada Therapeutics Announces Top-line Results from Phase 3 RELIANCE I Trial for REL-1017 as an Adjunctive Treatment for Major Depressive Disorder

Company to Host Conference Call Today, December 7, 2022, at 5:00 PM ET

CORAL GABLES, Fla., December 7, 2022 /PRNewswire/ -- Relmada Therapeutics, Inc. (Nasdaq: RLMD), a late-stage biotechnology company addressing diseases of the central nervous system (CNS), today announced results of the RELIANCE I study (REL-1017-301), evaluating REL-1017 as an adjunctive treatment for Major Depressive Disorder (MDD). The same factors that negatively affected the previously announced results from the RELIANCE III study, a limited number of high enrolling sites with unplausible placebo response, also affected RELIANCE I and the study did not achieve its primary endpoint, which was a statistically significant improvement in depression symptoms compared to placebo as measured by the Montgomery-Asberg Depression Rating Scale (MADRS) on Day 28. RELIANCE I evaluated the use of REL-1017 in addition to a standard antidepressant for patients who had inadequate response to at least one and up to three standard antidepressant therapies.

In the study, the REL-1017 treatment arm (n= 113) showed a MADRS reduction of 15.1 points at Day 28 versus 12.9 points for the placebo arm (n=114), which is a clinically meaningful difference of 2.2 points on the MADRS, as well as a statistically significant difference in the response rate, with a response rate of 27.2% on placebo vs 39.8% in the REL1017 arm ($p<0.05$).

As was observed in the monotherapy study RELIANCE III (Study 303), implausible results were again observed in two of the same high enrolling RELIANCE I (Study 301) study centers, where placebo dramatically outperformed REL-1017. While the patient population in RELIANCE I was different than RELIANCE III in that subjects enrolled should already have been diagnosed with depression and did not respond adequately to at least one, and up to three courses of antidepressant therapy, a limited number of the same high enrolling centers had implausible rapid and sustained placebo response rates that outperformed REL1017.

In a post-hoc analysis of RELIANCE 1 (301 Study) that excluded the same two high enrolling centers that showed implausible placebo response in both REL-1017 studies, the REL-1017 treatment arm (n=97) showed a MADRS reduction of 16.7 points at Day 28 versus 12.6 points for the placebo arm (n=88), a 4.1 point difference, with a p=0.02.

A second post-hoc confirmatory analysis, using the well-established band-pass method (Merlo-Pich et al, 2010[1]), that excludes patients from those centers with implausible responses in the placebo arm (centers with a placebo response less than 3% from baseline and more than 33% from baseline) showed a robust difference between REL-1017 and placebo.

REL-1017, as it did in RELIANCE III, demonstrated very favorable tolerability and safety in RELIANCE I, again confirming the results of Phase 1 and Phase 2 studies (Fava et al, 2022[2]), with no opioid-like effects, no withdrawal effects, and no psychotomimetic effects.

Relmada continues to enroll patients in RELIANCE II, the second ongoing Phase 3, two-arm, placebo-controlled, pivotal study evaluating REL-1017 as a potential adjunctive treatment for MDD. Based on the results of RELIANCE I and RELIANCE III, Relmada is applying several protocol and operational changes to RELIANCE II and making certain improvements to how the trial is being conducted. The RELIANCE development program also includes RELIANCE-OLS, a long-term open-label safety study that is evaluating rollover participants from all three pivotal studies, as well as de novo participants.

Conference Call and Webcast Information

Relmada will host a conference call and webcast presentation today, December 7, 2022, at 5:00 PM Eastern Time to discuss the study results, which can be accessed with the information below:

Wednesday, December 7, 2022, at 5:00 PM ET

Domestic: 1-877-407-0792
International: 1-201-689-8263
Conference ID: 13734757
Webcast: https://viavid.webcasts.com/starthere.jsp?ei=1586761&tp_key=6ce3a6bfd7

The subsequent archived recording will be available on the Investors section of the Relmada website at www.relmada.com.

References

[1]Merlo-Pich E, Alexander RC, Fava M, Gomeni R. A new population-enrichment strategy to improve efficiency of placebo-controlled clinical trials of antidepressant drugs. Clin Pharmacol Ther. 2010 Nov;88(5):634-42. doi: 10.1038/clpt.2010.159. Epub 2010 Sep 22.

[2]Fava M, Stahl S, Pani L, De Martin S, Pappagallo M, Guidetti C, Alimonti A, Bettini E, Mangano RM, Wessel T, de Somer M, Caron J, Vitolo OV, DiGuglielmo GR, Gilbert A, Mehta H, Kearney M, Mattarei A, Gentilucci M, Folli F, Traversa S, Inturrisi CE, Manfredi PL. REL-1017 (Esmethadone) as Adjunctive Treatment in Patients With Major Depressive Disorder: A Phase 2a Randomized Double-Blind Trial. Am J Psychiatry. 2022 Feb;179(2):122-131. doi: 10.1176/appi.ajp.2021.21020197. Epub 2021 Dec 22. PMID: 34933568.

About REL-1017

REL-1017, a new chemical entity (NCE) and novel NMDA receptor (NMDAR) channel blocker that preferentially targets hyperactive channels while maintaining physiological glutamatergic neurotransmission, is currently in late-stage development for the treatment of major depressive disorder (MDD). The ongoing Reliance Clinical Research Program is designed to evaluate the potential for REL-1017 as a rapid-acting, oral, once-daily antidepressant treatment. In a Phase 2 trial, REL-1017 demonstrated rapid, robust, and sustained antidepressant effects with statistically significant improvements compared to placebo. The Phase 2 study also showed a favorable pharmacokinetic, safety, and tolerability profile of REL-1017 consistent with results observed in previously completed Phase 1 studies.

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 is in 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 RELIANCE 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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relmada@fischtankpr.com

Exhibit 99.2

Reliance I Topline

REL-1017 for Major Depressive Disorder (MDD)

Dec 07, 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.

Topline Data Reliance I

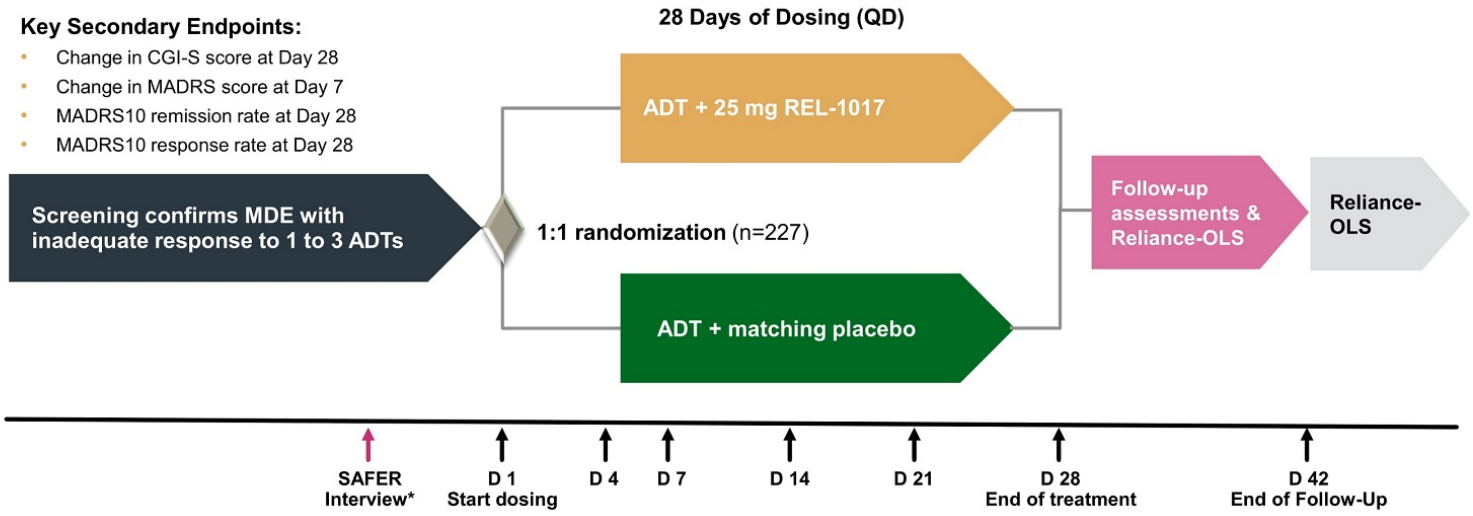
Phase 3 trial (Reliance I) was designed to assess efficacy and safety of REL-1017 as treatment for MDD in subjects with inadequate response to ongoing antidepressant treatment

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
- MADRS10 remission rate at Day 28
- MADRS10 response rate at Day 28



ADT=antidepressant treatment; CGI-S=Clinical Global Impression–Severity of Illness; MADRS=Montgomery-Asberg Depression Rating Scale; MDE=major depressive episode; OLS=open-label study; QD=once daily
*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. *Harv Rev Psychiatry*. 2013;21(5):269-274.

Key Inclusion/ Exclusion Criteria

Key Inclusion Criteria

- Adults 18 to 65 years.
- Diagnosis of **MDD.**
- **HAM-D-17 (≥19) and** Montgomery-Åsberg Depression Rating Scale-**MADRS10 (≥24).**
- Duration of current **MDE** 8 weeks-36 months.
- Stabilized for at least 6 weeks prior to Baseline on an approved dosing regimen of ADT.

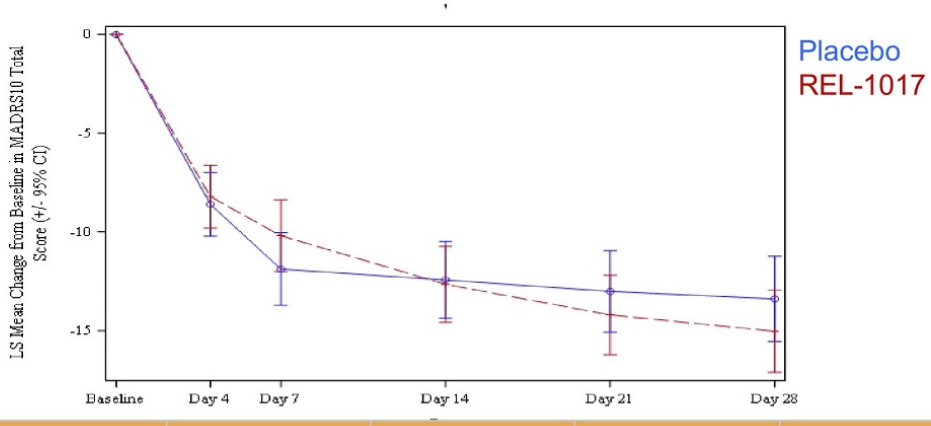
Key Exclusion Criteria

- Any current and primary psychiatric disorder other than MDD.
- Severe alcohol or substance use disorder.
- History of bipolar I and II disorder, psychosis, and/or mania.
- Prior use of ketamine, esketamine, dextromethorphan or NMDAR-antagonists

Demographics

Characteristics	Placebo (N=114)		REL-1017 25 mg (N=113)		All patients (N=227)	
	Mean	SD	Mean	SD	Mean	SD
Age (years)	43.6	14.2	43.3	15.1	43.5	14.6
Body Mass Index	26.3	3.3	25.8	2.8	26.0	3.0
	N	%	N	%	N	%
Sex						
Male	27	23.7	31	27.4	58	25.6
Female	87	76.3	82	72.6	169	74.4
Ethnicity						
Hispanic or Latino	23	20.2	29	25.7	52	22.9
Not Hispanic or Latino	85	74.6	79	69.9	164	72.2
Not reported	6	5.3	3	2.7	9	4.0
Unknown	0	0.0	2	1.8	2	0.9
Race						
Asian	7	6.1	6	5.3	13	5.7
Black or African American	14	12.3	16	14.2	30	13.2
Caucasian	90	78.9	85	75.2	175	77.1
Multiracial	2	1.8	4	3.5	6	2.6
Other	1	0.9	2	1.8	3	1.3

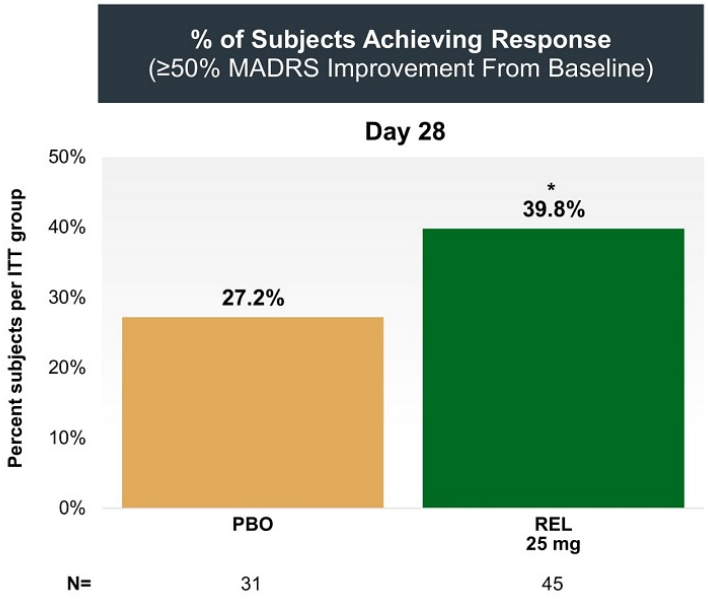
Primary efficacy endpoint: REL-1017 showed a -2.2 MADRS point non-significant difference vs. placebo at Day 28.

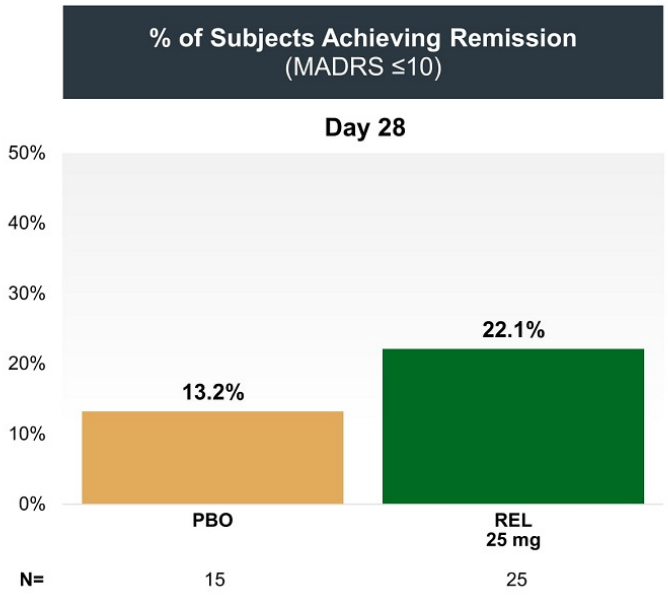


ΔMADRS (N=227) Placebo N=114, 25 mg N=113, 43 sites	Day 4	Day 7	Day 14	Day 21	Day 28 – End of Treatment
Placebo Mean (SD)	-9.3 (7.3)	-11.8 (9.9)	-12.2 (10.9)	-13.0 (11.2)	**-12.9** (10.4)
25 mg Mean (SD)	-8.3 (8.9)	-10.2 (9.5)	-12.4 (9.4)	-14.4 (10.4)	**-15.1** (11.3)
Placebo LSMean (SE), MMRM	-8.6 (0.8)	-11.9 (0.9)	-12.4 (1.0)	-13.0 (1.0)	-13.4 (1.1)
25 mg LSMean (SE), MMRM	-8.2 (0.8)	-10.2 (0.9)	-12.7 (1.0)	-14.2 (1.0)	-15.0 (1.1)
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

Reliance I achieved a statistically significant response rate of 39.8%, and 22.1% achieved remission with 25 mg REL-1017

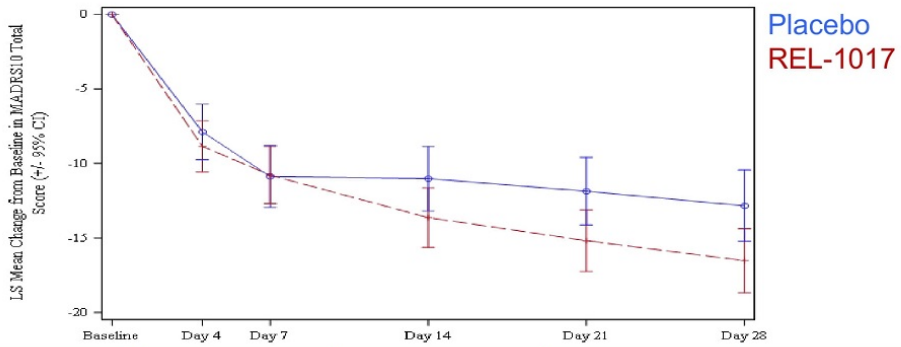




Day 28: last efficacy assessment
Total N=227; * p= <0.05
MADRS=Montgomery-Asberg Depression Rating Scale
Source: Relmada Data on File.

REL-1017 vs placebo Day 28 MADRS with post-hoc removal of two high enrolling centers with non-plausible results across Relmada studies: modified analysis of 41 of 43 centers and 185 of 227 subjects*

*These same two centers produced non-plausible results in study 303



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)
Placebo LSMean (SE), MMRM	-7.9 (1.0)	-10.9 (1.1)	-11.0 (1.1)	-11.9 (1.2)	-12.8 (1.2)
25 mg LSMean (SE), MMRM	-8.9 (0.9)	-10.8 (1.0)	-13.6 (1.0)	-15.2 (1.0)	-16.5 (1.1)
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

No serious treatment related treatment-emergent adverse event (TEAE) was observed in Reliance I. Placebo-like adverse event profile.

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 in one 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
Diarrhoea	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 robust safety profile— Reliance I confirmed no evidence for abuse potential or dissociative effects

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 COWs[3] and PWC-20[4] scales

Abuse Potential MADDERS® reports[1]

- **No** evidence of abuse potential as reported in the **MADDERS®** reports[5]

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

Summary

Efficacy

- REL-1017 shows a -2.2 MADRS point non-significant difference to placebo
- Statistically significant MADRS response rate of REL-1017 compared to placebo
- A post-hoc analysis with the exclusion of 2 non-plausible high enrolling centers, previously identified in Reliance III, results in a statistically significant 4.1 difference from placebo (p=0.02)

Safety

- Placebo-like adverse event profile.
- No evidence for abuse potential or dissociative effects

Thank you!