REL-1017-202: A Phase 2 Study of REL-1017 at Two Doses in Subjects with Treatment Resistant Depression

Cl=Check-In; CRU=Clinical Research Unit; FU=Follow-Up
# Study REL-1017-202 Was Designed to Provide Data on Safety, PK and Efficacy of REL-1017 in Treatment Resistant Depression

## Primary Objectives

- Safety and tolerability of 25 mg and 50 mg of REL-1017 vs Placebo as adjunctive treatment

## Secondary Objectives

- To characterize pharmacokinetic (PK) profile of REL-1017 25 mg and 50 mg x 7 days
- To explore the efficacy of 25 mg and 50 mg of REL-1017 as adjunctive treatment in patients with TRD [Note: Maged, original says TRD]

## Primary Endpoints

- PE, Laboratory studies, ECG, AEs
- CADSS (dissociative symptoms)
- 4-item PSRS (psychotomimetic symptoms)
- COWS (opiate withdrawal symptoms)
- C-SSRS (suicidality)

## Secondary Endpoints

- PK parameters for both 25 and 50 mg qday
- Change from BSL at Day 2, 4, 7 and 14 on:
  - MADRS
  - SDQ
  - CGI-S
- Difference in CGI-I score placebo vs treatment groups Day 2 to 14

---

**PE**=Physical exam; **ECG**=Electrocardiogram; **AEs**=Adverse Events; **CADSS**=Clinician Administered Dissociative States Scale; **PSRS**=Positive Symptom Rating Scale; **COWS**=Clinical Opiate Withdrawal Scale; **C-SSRS**=Columbia Suicide Severity Rating Scale; **MADRS**=Montgomery Asberg Depression Rating Scale; **SDQ**=Symptoms of Depression Questionnaire; **CGI-S** and **CGI-I**=Clinical Global Impression Severity and Improvement
Subjects’ Disposition, Demographic Characteristics and Depression Severity Were Homogeneously Distributed Across Arms

<table>
<thead>
<tr>
<th></th>
<th>Placebo</th>
<th>REL-1017 25 mg</th>
<th>REL-1017 50 mg</th>
<th>All Subjects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Randomized Subjects</td>
<td>22</td>
<td>19</td>
<td>21</td>
<td>62</td>
</tr>
<tr>
<td>Completed All Visits (Day 21)</td>
<td>20</td>
<td>18</td>
<td>19</td>
<td>57</td>
</tr>
<tr>
<td>Received All Doses</td>
<td>21</td>
<td>19</td>
<td>21</td>
<td>61</td>
</tr>
<tr>
<td>Age: Mean Years (SD)</td>
<td>49.7 (11.1)</td>
<td>49.4 (12.4)</td>
<td>48.6 (10.9)</td>
<td>49.2 (11.3)</td>
</tr>
<tr>
<td>Females</td>
<td>11 (50%)</td>
<td>8 (42.1%)</td>
<td>9 (42.9%)</td>
<td>28 (45.2%)</td>
</tr>
<tr>
<td>Subjects ITT</td>
<td>22</td>
<td>19</td>
<td>21</td>
<td>62</td>
</tr>
<tr>
<td>Subjects PPP</td>
<td>21</td>
<td>19</td>
<td>21</td>
<td>61</td>
</tr>
<tr>
<td>Screening HAMD – Mean (SD)</td>
<td>25.6 (3.5)</td>
<td>25.1 (3.5)</td>
<td>25.0 (3.8)</td>
<td>25.3 (3.6)</td>
</tr>
<tr>
<td>Baseline MADRS – Mean (SD)</td>
<td>33.8 (4.0)</td>
<td>32.9 (6.0)</td>
<td>35.2 (3.9)</td>
<td>34.0 (4.7)</td>
</tr>
</tbody>
</table>

ITT=Intent-To-Treat; PPP=Per-Protocol-Population; HAMD=Hamilton Depression Rating Scale; MADRS=Montgomery-Asberg Depression Rating Scale
Study REL-1017-202 Key Safety Findings

REL-1017-202 results confirm the favorable tolerability and safety profile observed in the Phase 1 SAD and MAD studies

• Only Mild and Moderate AEs – no SAEs

• No increased prevalence of specifically relevant organ group AEs in treatment groups vs placebo

• No evidence of treatment induced dissociative symptoms in the treatment groups vs placebo

• No evidence of treatment induced psychotomimetic symptoms in treatment groups vs placebo

• No evidence of opiate withdrawal symptoms in treatment groups vs placebo

AE=adverse event; SAE=serious adverse event
Source: Relmada Phase 2 Top Line Data Presentation at Relmada.com
Study REL-1017 Key Efficacy Findings

REL-1017 25 mg and 50 mg show rapid onset and sustained antidepressant efficacy with statistically significant differences compared to placebo on all efficacy measures

- Solid efficacy results on MADRS with P values <0.03 and large effect sizes (0.7-1.0) from Day 4 to Day 14
- CGI-S and CGI-I solid findings consistent with MADRS results with P values and effect sizes of similar magnitude
- SDQ scores with moderate effect size differences (d=0.4 and 0.5) from Day 4 to Day 7 and with both statistically significant differences and large effect size for both 25 mg (P=0.0066; d=0.9) and 50 mg (P=0.0014; d=1.1) arms at Day 14
- Study demonstrates rapid onset and long-lasting antidepressant efficacy
- Findings support continuing clinical development and larger pivotal study
MADRS Scores in the Treatment Groups Achieved Statistically Significant Difference vs Placebo from Day 4 through Day 14

MADRS Change from Baseline – ITT Population

Least-Square Mean Change

Day 2
Day 4
Day 7
Day 14

Placebo
REL-1017 25 mg
REL-1017 50 mg

P=0.0087; d=0.9
P=0.0096; d=0.8
P=0.0122; d=0.8
P=0.0308; d=0.7
P=0.0103; d=0.9
P=0.0039; d=1.0

MADRS=Montgomery-Asberg Depression Rating Scale; ITT=Intent-To-Treat; Error Bars=Standard Errors; P and d values as Treatment vs Placebo
CGI-S Scores Achieved Statistically Significant Difference vs Placebo from Day 4 for REL-1017 50 mg and for both Doses on Day 7 and Day 14

CGI-S Change from Baseline – ITT Population

- Least-Square Mean Change
  - Placebo
  - REL-1017 25 mg
  - REL-1017 50 mg

P-values and effect sizes:
- REL-1017 25 mg:
  - Day 4: P=0.0951; d=0.5
  - Day 7: P=0.0253; d=0.7
  - Day 14: P=0.0245; d=0.7

- REL-1017 50 mg:
  - Day 4: P=0.0272; d=0.7
  - Day 7: P=0.0253; d=0.7
  - Day 14: P=0.0454; d=0.7
  - Day 14: P=0.0043; d=0.9

CGI-S=Clinical Global Impression of Severity; ITT=Intent-To-Treat; Error Bars=Standard Errors; P and d values as Treatment vs Placebo