

## Case Report: REL-1017 Reduces Abnormal Clinician Administered Dissociative States Scale Scores in Patients with Major Depressive Disorder

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### Abstract

**Background.** Dissociative symptoms may be found in a subset of patients with major depressive disorders (MDD). The Clinician-Administered Dissociative States Scale (CADSS) is a 23-item scale for the measurement of present-state dissociative symptoms with good inter-rater reliability and construct validity that can discriminate patients with dissociative disorders. The total CADSS score is derived by adding the score for each of the 23 items. A score of 4 or more on the CADSS is considered abnormal and clinically meaningful. Uncompetitive *N*-methyl-D-aspartic acid receptor (NMDAR) channel blockers have been proposed as a treatment for post-traumatic stress disorder (PTSD). REL-1017 is a novel, low potency, NMDAR channel blocker currently in Phase 3 studies for MDD.

**Methods.** This retrospective case series describes a subset of patients from a double-blind, randomized, placebo-controlled, in-patient 7-day, phase 2 trial of oral, once daily, 25 mg (75 mg loading dose on day 1, first dose) and 50 mg REL-1017 (100 mg loading dose on day 1, first dose) as an adjunctive treatment for MDD. This subset of patients was selected based on abnormal CADSS score at baseline, pre-treatment with the study drug. As part of REL-1017 safety evaluation, the CADSS was administered at four timepoints to all study patients: (a) 30 to 60 minutes pre-treatment at baseline on day 1; (b) 2 hours post-treatment on day 1 (after the first dose of study drug); (c) 2 hours post-treatment on day 7 (after the last dose); and (d) prior to discharge on day 9 (2 days after the last dose).

**Results.** Among the 62 randomized patients, four patients had a CADSS score of at least 4 on day 1 before study drug administration (2 patients in the 25 mg arm [CADSS score 22 and 4]; 1 patient in the 50 mg arm [CADSS score 35]; 1 patient in the placebo arm [CADSS score 6]). Among these 4 patients, starting on day 1, 2 hours post-treatment, the 2 subjects in the 25 mg subgroup (75 mg loading dose) and 1 subject in the 50 mg subgroup (100 mg loading dose) showed a clinically meaningful decrease in their CADSS score, while the single patient in the placebo group showed no change. CADSS scores on Day 1 pre-treatment, day 1 post-treatment, day 7 post last treatment, and on

day 9 prior to discharge were 22-2-6-0; 4-0-0-0; 35-14-9-0, and 6-6-n/a-n/a, for the two patients in the 25 mg REL-1017 subgroup, the single patient in the 50 mg REL-1017 subgroup, and the single patient in the placebo group, respectively.

**Conclusions.** These retrospective case report data potentially signal that REL-1017 may determine rapid and sustained improvement in patients with MDD and concurrent clinically meaningful dissociative symptoms assessed by a CADSS score of 4 or above. Ongoing phase 3 trials with REL-1017 are expected to enroll a total of 1200 outpatients with MDD. These studies will potentially generate additional data that may support the initiation of controlled studies with REL-1017 for the treatment of PTSD.

**Funding.** Relmada Therapeutics

## Predicting Potential Drug-Drug-Gene Interactions in a Population of Individuals Utilizing a Community-Based Pharmacy

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### Abstract

**Introduction.** Adverse drug reactions (ADRs) are associated with increased morbidity, mortality, and resource utilization. Drug interactions (DDIs) are among the most common causes of ADRs, and estimates have cited that up to 22% of patients take interacting medications. DDIs are often due to the propensity for agents to induce or inhibit enzymes responsible for the metabolism of concomitantly administered drugs. However, this phenomenon is further complicated by genetic variants of such enzymes. The aim of this study is to quantify and describe potential drug-drug, drug-gene, and drug-drug-gene interactions in a community-based patient population.

**Methods.** A regional pharmacy with retail outlets in Arkansas provided deidentified prescription data from March 2020 for 4761 individuals. Drug-drug and drug-drug-gene interactions were assessed utilizing the logic incorporated into GenMedPro, a commercially available digital gene-drug interaction software program that incorporates variants of 9 pharmacokinetic (PK) and 2 pharmacodynamic (PD) genes to evaluate DDIs and drug-gene interactions. The data were first assessed for composite drug-drug interaction risk, and each individual was stratified to a risk category using the logic incorporated in GenMedPro. To calculate the frequency of potential drug-gene interactions, genotypes were imputed and allocated to the cohort according to each gene's frequency in the general population. Potential genotypes were randomly allocated to the population 100 times in a Monte