How the study works

REL-1017 is an oral tablet taken once daily at home.

The Relight Clinical Research Study is for patients who are currently taking antidepressants.

Participants in the clinical studies continue their current antidepressant and the investigational medication (REL-1017 or placebo, the inactive comparison pill) is taken in addition to their current medication.

There are no costs associated to participating in the study

Participants do not have to pay for participation in a clinical research study. The Investigational medication, study supplies, study visits, and any test costs are covered as part of the study.

Participants in the Relight studies may receive reimbursements for travel expenses.

Study duration

Relight will compare REL-1017 to placebo (inactive comparison pill) over 28 days.

Participants who are enrolled in the trial receive REL-1017 or placebo for 28 days. Prior to receiving REL-1017 or placebo, participants undergo a screening period to ensure that they meet all study requirements.

The overall duration of the study, including screening and intervention period, will be approximately 50 days.

The study is expected to enroll over 300 patients.

What happens when the clinical trial is over?

Participants have the opportunity to enroll in an Expanded Access Program if recommended by the treating physician.

Participants can decide to withdraw from the study at any time.

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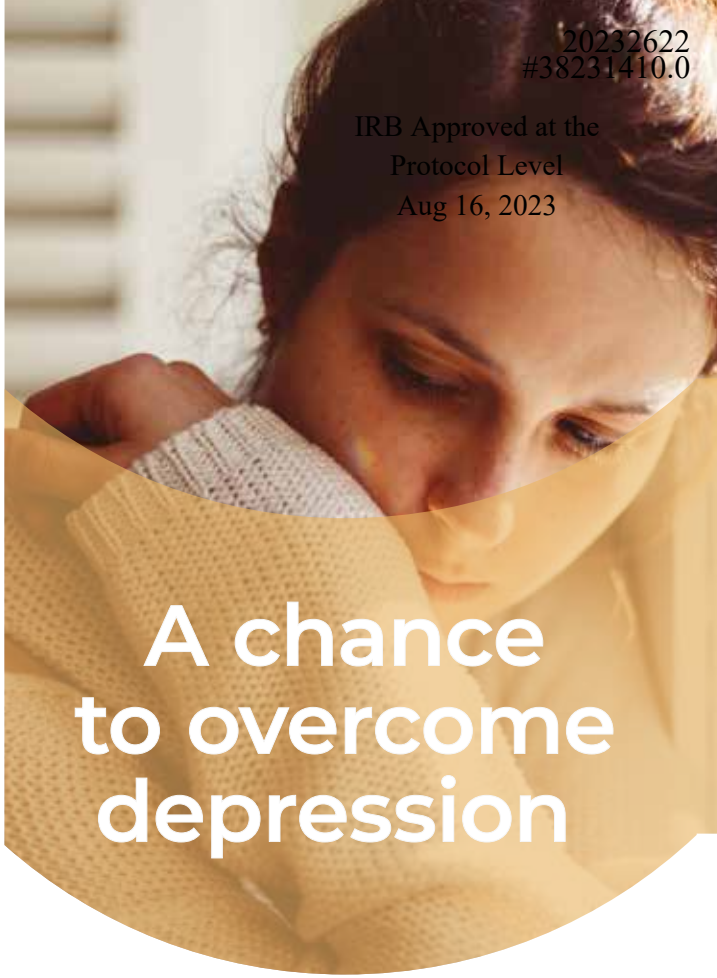
IRB Approved at the
Protocol Level
Aug 16, 2023



A chance to overcome depression

You may be eligible to participate as a volunteer if you:

- **Are 18-65 years of age**
- **Have been diagnosed with depression (Major Depressive Disorder)**
- **Are currently feeling depressed and are taking an antidepressant**

The Relight clinical research study is currently testing an investigational medication for people living with depression, or Major Depressive Disorder (MDD)

Relight

Even with treatment, depression may continue to be challenging. That is why researchers are exploring how an investigational medication, when added to existing antidepressants, may help manage MDD. If you are currently taking antidepressants but find that they are not fully managing your symptoms, participating in the Relight clinical research study may be an option for you.

REL-1017 is an investigational medicine * currently under evaluation in Phase III clinical trials in the United States for the treatment of MDD (Major Depressive Disorder). REL-1017 is not currently approved for any condition.

* An investigational medication is a substance that is being tested in clinical research studies and may or may not be approved by the Food and Drug Administration for treatment of this condition. A placebo looks like the investigational medication but has no active drug in it. Researchers compare the results of the investigational medication to those of the placebo.

The active ingredient in REL-1017 is esmethadone

REL-1017 interacts with a family of brain receptors called N-methyl-D-aspartate (NMDA) receptors, which are unique and distinct from other brain receptors[1]. By interacting with NMDA receptors, REL-1017 may relieve depression[2]. The active ingredient in REL-1017 tablets is esmethadone. Esmethadone is also sometimes referred to as dextro-methadone or d-methadone. Opioid effects, such as dissociation, withdrawal symptoms and drug likability, have not been seen with esmethadone.

Phase I and II results

The Phase I and Phase II studies of REL-1017 caused no serious adverse events[3,4]. One of the purposes of Phase III clinical trials is to evaluate the potential for adverse events.

Human Abuse Potential (HAP) study

A recently completed dedicated study called the Human Abuse Potential (HAP) study showed that REL 1017 does not have addictive potential[5].

1. Bettini E, Stahl SM, De Martin S, et 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. Published 2022 Aug 13. doi:10.3390/ph15080997
2. Mathews DC, Henter ID, Zarate CA. Targeting the glutamatergic system to treat major depressive disorder: rationale and progress to date. Drugs. 2012;72(10):1313-1333
3. Bernstein G. 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. J Clin Psychopharmacol. 2019;39: 226-237
4. 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
5. Shram MJ, Henningfield JE, Apseloff G, et al. The novel uncompetitive NMDA receptor antagonist esmethadone (REL-1017) has no meaningful abuse potential in recreational drug users. Transl Psychiatry. 2023;13(1):192. Published 2023 Jun 7. doi:10.1038/s41398-023-02473-8

Thank you

We appreciate your interest in the Reliance Clinical Research Program

You can learn more about the Reliance study by contacting:

clinicaltrials@relmada.com

Or by contacting the Clinical Research Coordinator:

Name
Clinic
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Relight