RE104: A Novel Serotonergic Psychedelic 4-OH-DiPT Prodrug

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SUBMISSION DETAILS

Request for Proposals Psychedelics

Abstract RE104, a unique, proprietary 4-OH-DiPT prodrug, is a novel psychedelic investigational compound being developed for the treatment of postpartum depression (PPD) and other mental health conditions. Preclinical and clinical characterization confirmed similar pharmacology of 4-OH-DiPT to the well-characterized psychedelic active form of psilocybin (4-OH-DMT), while in vivo studies demonstrated a significantly shorter and reproducible psychedelic experience. Here we present the results of the first-in-human (FIH) phase 1 study characterizing the safety, pharmacokinetics (PK) and pharmacodynamics (PD) of RE-104, as well as an update of an ongoing Phase 2 randomized, active-dose controlled trial in women with moderate to severe PPD.
Methods:
A phase 1, FIH, double-blind, parallel group trial was conducted with 6 ascending dose cohorts of 8 psychedelic experienced health volunteers (randomized 6 active, 2 placebo). Predefined dose escalation ranged from 5 mg to 47.9 mg RE104 administered subcutaneously as a single injection,. Adequate set and setting included one preparatory session followed by a dosing session with a qualified and trained session monitor,. Follow-up study visits occurred on days 2 and 10. Study objectives included assessing safety and tolerability, PK and PD (Drug Effect Questionnaire (DEQ) and Mystical Effect Questionnaire 30 (MEQ)). A "complete" mystical experience (CME) was defined as >/=60% max value in total MEQ score. DEQ</= 1 represented a subjective end of the psychoactive experience.
Results:
A total of 48 subjects with a mean age of 36 years, 27% female and 88% white were enrolled across 6 cohorts. There were no serious AEs and no clinically significant vital signs, clinical laboratory, or electrocardiogram findings at doses up to and including 40 mg RE104. PK demonstrated dose-proportionality. At 30 mg RE104, mean experience duration was 3.7 hours, with all participants having a score off </=1 at 5 hours post-dose. 66.7% of participants in the RE104 30 mg treatment group had a CME predictive of clinical efficacy. This data informed the dose selection of RE104 at 30 mg for the phase 2 trial.
The PPD trial is a multi-center, randomized, double-blind parallel group, active dose-controlled study evaluating the safety and efficacy of a single dose of RE104 in participants aged 18-45 with PPD. The primary endpoint is MADRS at day 7.

Conclusions: *
A single dose of RE104 was found to be safe and generally well-tolerated with robust PD effects and a short induced psychoactive state (approximately 4 hours). RE104 has the potential to be an accessible, fast-acting, single dose treatment for PPD..

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