Ad hoc announcement pursuant to Art. 53 LR

Newron begins enrollment in pivotal Phase III ENIGMA-TRS program with evenamide as add-on therapy in patients with treatment-resistant schizophrenia (TRS)

ENIGMA-TRS 1 is an international, one-year, double-blind, placebo-controlled Phase III study in at least 600 patients; 12-week study results expected in Q4 2026

Evenamide, a first-in-class glutamate modulator, has the potential to be the first add-on therapy for TRS patients and for poorly responding patients with schizophrenia

Unique glutamatergic modulation mechanism of action offers new therapeutic option for this patient population

Milan, Italy, and Morristown, NJ, USA, August 12, 2025, 07:00 am CEST – Newron Pharmaceuticals S.p.A. ("Newron") (SIX: NWRN, XETRA: NP5), a biopharmaceutical company focused on the development of novel therapies for patients with diseases of the central and peripheral nervous system, today announced that following the completion of a 42 day-screening period and the review of the patients by the Independent Eligibility Committee, it has successfully randomized the first patients in its pivotal ENIGMA-TRS 1 Phase III development program. ENIGMA-TRS 1 will evaluate evenamide as an add-on therapy to current antipsychotics, including clozapine, in patients with treatment-resistant schizophrenia (TRS).

"Today's announcement marks an important milestone for the clinical advancement of evenamide for treatment-resistant schizophrenia patients who urgently need more effective therapeutic options," said **Ravi Anand, CMO, Newron Pharmaceuticals**. "We look forward to advancing evenamide through this pivotal Phase III study and delivering an important benefit to patients in need."

ENIGMA-TRS 1 is an international, 52-week, randomized, double-blind, placebo-controlled Phase III study evaluating the efficacy, tolerability, and safety of the 15mg BID and 30mg BID therapeutic doses of evenamide compared to placebo. Patients on second-generation antipsychotics (SGAs), including clozapine, need to meet Treatment Response and Resistance Psychosis (TRRIP) international consensus criteria for TRS.

ENIGMA-TRS 1 will enroll at least 600 patients at study centers in Europe, Asia, Latin America and Canada. Prior to randomization, patients undergo a 42-day screening period, during which their TRS diagnosis, antipsychotic plasma levels (background medication), and conformance to protocol selection criteria will be evaluated by an Independent Eligibility Assessment Committee (IEAC) of three leading international schizophrenia experts.

The primary assessment of efficacy and safety will be performed 12 weeks after randomization to treatment. The study will continue double-blind and placebo-controlled until the 52-week time point. The 12-week results from the study are expected in Q4 2026.

Results from previous Phase II (study 014/015) and Phase III (study 008A) studies have demonstrated evenamide's significant and increasing efficacy as an add-on therapy on multiple measures of psychopathology in patients with TRS and inadequate responders, respectively. These results also confirmed a favorable safety and tolerability profile, adding to the growing evidence that evenamide's glutamatergic inhibition mechanism of action offers an innovative therapeutic option to schizophrenia patients who are not benefiting from current antipsychotic treatments.

ENIGMA-TRS 2, the second study of Newron's pivotal Phase III ENIGMA-TRS program, has been approved by the US Food and Drug Administration (FDA), and will be performed at centers in the US and selected additional countries. It will include at least 400 patients in a 12-week, randomized, double-blind, placebo-controlled Phase III study, designed to evaluate the efficacy, tolerability, and safety of the 15mg BID dose of evenamide. Patients will meet selection criteria and be reviewed by the above-mentioned IEAC. The analysis for determination of efficacy and safety will be performed after patients complete 12 weeks of participation in the trial. US investigational centers are expected to initiate the study by October 2025.

About schizophrenia

Approximately 25 million people worldwide are affected by schizophrenia. Despite more than 60 different types of atypical and typical antipsychotics used to treat schizophrenia globally, a considerable number of patients remain severely ill or resistant to treatment. Overall, 30-50% of patients do not respond to the available medications and are defined as treatment resistant. In addition to the patients with treatment-resistant schizophrenia (TRS), another 20-30% are described as "poor responders to antipsychotic medication", even if not meeting the criteria for TRS. New findings indicate that patients with TRS have abnormalities in the glutamatergic system, but not in dopaminergic transmission, so there is a significant unmet medical need for treatments with a glutamatergic mechanism of action, efficacious both in TRS patients and in those who are poor responders to the current treatments.

About evenamide

Evenamide is the first new chemical entity that has demonstrated significant benefits in this difficult-to-treat patient population, as seen in the potentially pivotal Phase III study 008A trial, as an add-on treatment to second generation antipsychotics including clozapine, in 291 poorly responding patients with chronic schizophrenia. The primary endpoint, the Positive and Negative Syndrome Scale (PANSS)[1], and the key secondary endpoint, the Clinical Global Impressions Scale – Severity (CGI-S), were met and showed statistical significance compared to placebo. Importantly, evenamide treatment was associated with statistically significant increases in the proportion of patients who experienced "clinically meaningful benefit" on the outcome variables. Evenamide was extremely well tolerated, without any of the usual side effects of available antipsychotics.

About Newron Pharmaceuticals

Newron (SIX: NWRN, XETRA: NP5) is a biopharmaceutical company focused on developing novel therapies for patients with diseases of the central and peripheral nervous system.

Headquartered in Bresso, near Milan, Italy, Newron is advancing its lead compound, evenamide, a first-in-class glutamate modulator, which has the potential to be the first add-on therapy for treatment-resistant schizophrenia (TRS) and for poorly responding patients with schizophrenia. Evenamide is currently in Phase III development and clinical trial results to date demonstrate the benefits of this drug candidate in the TRS patient population, with significant improvements across key efficacy measures increasing over time, as well as a favourable safety profile, which is uncommon for available antipsychotic medications.

Newron has signed development and commercialization agreements for evenamide with EA Pharma (a subsidiary of Eisai) for Japan and other Asian territories, as well as Myung In Pharm for South Korea.

Newron has a proven track record in bringing CNS therapies to market. Its Parkinson's disease treatment, Xadago® (safinamide), is approved in over 20 markets, including the USA, UK, EU, Switzerland, and Japan, and commercialized in

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1 Positive and Negative Syndrome Scale (PANSS) is widely used in clinical trials of schizophrenia and is considered the "gold standard" for assessment of antipsychotic treatment efficacy (Innvo Clin Neurosci, 2017: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5788255/)

partnerships with Zambon and Meiji Seika.

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