



Ad hoc announcement pursuant to Art. 53 LR

Newron Provides Update on FDA Clinical Hold and Phase 3 ENIGMA-TRS Development Program

Management call today at 3.30 pm CEST

Newron received the anticipated FDA written communication on clinical hold at U.S. study centers and is reviewing feedback and preparing its response

ENIGMA-TRS 1 enrollment expected to be completed by mid-October; topline 12-week data expected in Q1 2027

ENIGMA-TRS 2 enrollment continuing outside the U.S., with additional clinical sites being added as planned

FDA clinical hold remains in place at U.S. study centers; Newron intends to respond upon thorough review and analysis of FDA feedback

Milan, Italy, and Morristown, NJ, USA – October 8, 2026, 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, further to its press release on September 25 2026, the Company has in the meantime received written communication from the U.S. Food and Drug Administration (FDA) regarding the clinical hold at U.S. study centers in its Phase 3 ENIGMA-TRS 2 study with evenamide. Newron is conducting a thorough review of the FDA’s feedback and the available data and intends to submit its response upon completion.

Newron continues to advance the Phase 3 ENIGMA-TRS development program. ENIGMA-TRS 1 enrollment is expected to be completed by mid-October, with topline 12-week data expected in Q1 2027. ENIGMA-TRS 2 enrollment continues outside the U.S. Additional clinical sites are being added as planned.

FDA Clinical Hold and ENIGMA-TRS Program Update

The FDA’s concern relates to the known risk that certain members of the class of sodium channel blockers may trigger arrhythmias which in turn can lead to serious cardiovascular events or seizures. Evenamide is a glutamate modulator via its action as a selective voltage-gated sodium channel blocker.

In its written communication, the FDA notes four deaths among patients treated with evenamide across all clinical studies with evenamide to date, compared with one death among patients receiving placebo. Of the four deaths among patients receiving evenamide, three were considered unrelated to evenamide by the study investigators, while one was considered



“possibly related” because two autopsies could not identify a definitive cause of death. The four deaths have been characterized by the FDA as a potential safety signal based on the possibility of a fatal arrhythmic mechanism, which cannot be definitively excluded through post hoc adjudication. Evenamide is also known to result in a very small shortening of the QTc interval on an electrocardiogram (ECG). Unlike QTc prolongation, there is no established risk or intervention threshold for QTc shortening, and a standard screening ECG does not reliably exclude latent sodium-channel disorders in asymptomatic patients.

Newron is reviewing the FDA's feedback and the full body of safety data generated across the evenamide development program, which includes more than 10,000 ECGs from approximately 700 evenamide-treated subjects and input from independent cardiac electrophysiologists. Newron has not observed a pattern of cardiac abnormalities or arrhythmias in the preclinical and clinical safety data generated with evenamide to date. This includes a thorough QT study and more than 5,000 ECGs from over 700 patients with schizophrenia. As part of its response, Newron is also evaluating additional cardiac screening and monitoring measures for ENIGMA-TRS 2.

“We remain confident in the ENIGMA-TRS studies and encouraged by the program's progress. Our belief in the potential of evenamide and its novel mechanism for patients with treatment-resistant schizophrenia remains strong,” said Ravi Anand, MD, Chief Medical Officer of Newron. “Patient safety is our utmost priority. Our team is working with high commitment to complete a thorough review of the FDA's feedback and the available data, and to submit our response upon its completion. Our assessment is supported by the substantial body of preclinical and clinical safety data generated with evenamide. To date, we have not observed a pattern of cardiac abnormalities or arrhythmias. The four deaths among patients treated with evenamide represent an incidence of 0.56%, compared with one death and an incidence of 0.27% among patients receiving placebo. When adjusted for duration of treatment, the mortality rate was 1.31 per 100 patient-years for evenamide compared with 1.81 per 100 patient-years for placebo.”

Professor Dr. Peter Falkai, Chair Department of Psychiatry and Psychotherapy, LMU University of Munich, stated: *“Schizophrenia is a tragic disease that affects patients in the teenage (males) and early twenties (females) and has a devastating effect on their lives. In addition to multiple episodes of psychosis and hospitalization, patients need to take antipsychotic medication with debilitating side-effects that makes them suffer from cardiac, hormonal, metabolic and motor disorders. Furthermore, schizophrenia reduces life-expectancy by about 10 years. TRS, a more severe form of the disease in which patients do not respond to any medication, reduces longevity by about 20 years.”*

Investor Update Conference Call

Management will provide a brief update on the FDA clinical hold and ENIGMA-TRS development program. The call will be recorded and take place today at 3.30 pm CEST.

The access details:

Switzerland / Europe	+41 (0) 58 310 50 00
United Kingdom	+44 (0) 203 059 58 63
United States	+1 (1) 631 570 56 13

Other international numbers available [here](#).



About ENIGMA-TRS

ENIGMA-TRS 1 is an ongoing, international, 52-week, randomized, double-blind, placebo-controlled Phase 3 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, including clozapine, will meet Treatment Response and Resistance Psychosis international consensus criteria for TRS. The study is expected to have enrolled at least 600 patients in the study by mid-October 2026, at study centers in 20 countries in Europe, Asia, Latin America, and Canada.

The primary assessment of efficacy and safety of ENIGMA-TRS 1 will be performed 12 weeks after randomization to treatment. Following this initial period, the study will continue to be double-blind and placebo-controlled until the 26- and 52-week time points. The primary efficacy endpoint of the trial will be the change from baseline in the Positive and Negative Syndrome Scale (PANSS) scores at 12 weeks. Newron expects to announce results from the 12-week primary endpoint assessment in Q1 2027.

ENIGMA-TRS 2 is taking place at centers in the U.S. and selected additional countries with the same screening procedure as the ENIGMA-TRS 1 trial. ENIGMA-TRS 2 will include at least 400 patients in a 12-week, randomized, double-blind, placebo-controlled Phase 3 study, designed to evaluate the efficacy, tolerability, and safety of the 15mg BID dose of evenamide compared to placebo. In December 2025, ENIGMA-TRS 2 was initiated in the U.S., following approvals from the U.S. Food and Drug Administration (FDA) and the Institutional Review Board (IRB). The efficacy and safety analysis will be performed at the 12-week point following successful completion of the study. On April 29, 2026, Newron reported a hold by the FDA on the enrollment of new patients in the U.S. sites of the study. While U.S. patients entered screening, no U.S. patients have been dosed with evenamide, in the study.

About Newron Pharmaceuticals

Newron (SIX: NWRN, XETRA: NP5) is a biopharmaceutical company focused on the development of innovative therapies for patients with diseases of the central and peripheral nervous system. Headquartered in Bresso near Milan, Italy, the Company has a strong track record of advancing neuroscience-based treatments from discovery to market. Newron's lead compound, evenamide, is a first-in-class glutamate modulator and 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 developed in the global pivotal ENIGMA-TRS Phase 3 development program. Clinical trial results to date demonstrate the benefits of this drug candidate in TRS as well as poorly responding patient population, with significant improvements across key efficacy measures increasing over time, as well as a favorable 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's first marketed product, Xadago®/safinamide has received marketing authorization for the treatment of Parkinson's disease in the European Union, Switzerland, the UK, the USA, Australia, Canada, Latin America, Israel, the United Arab Emirates, Japan and South Korea. The product is commercialized by Newron's partner Zambon, with Supernus Pharmaceuticals holding marketing rights in the U.S., and Meiji Seika responsible for development and commercialization in Japan and other key Asian territories. For more information, please visit: <https://www.newron.com> and connect with us on [LinkedIn](#).

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