Ad hoc announcement pursuant to Art. 53 LR

Newron announces completion of screening for enrollment in pivotal Phase 3 ENIGMA-TRS 1 study with evenamide as add-on therapy in patients with treatment-resistant schizophrenia (TRS)

ENIGMA-TRS 1 is Phase 3 international, one-year, randomized, double-blind, placebo-controlled study in 600+ patients; 12-week study results expected in Q1 2027

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

Evenamide's unique glutamatergic modulation mechanism of action offers a new therapeutic option for this patient population

Milan, Italy, and Morristown, NJ, USA, September 2, 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 it has completed screening for enrollment in its pivotal ENIGMA-TRS 1 Phase III study. With final patients progressing through the well-defined screening process, Newron expects to complete target enrollment of at least 600 patients around mid-October. Topline data from the 12-week treatment period are expected in Q1 2027. ENIGMA-TRS 1 evaluates evenamide as an add-on therapy to current antipsychotics, including clozapine, in patients with treatment-resistant schizophrenia (TRS).

As of today, 996 patients have entered screening, 411 patients have been randomized to treatment, and 352 patients continue to undergo screening. Based on the stringent selection criteria applied by the International Independent Eligibility Committee, it is expected that at least an additional 200 patients meeting the eligibility criteria from those currently in-screening will be randomized at the end of the 42-day screening period, thus meeting the protocol requirement of at least 600 patients randomized in the study.

"For patients with TRS, the unmet medical need remains compelling. Enthusiasm among investigators worldwide for evenamide and its novel glutamate-modulating mechanism, together with the well-designed ENIGMA-TRS 1 study, has contributed to the strong pace of enrollment," said **Ravi Anand, CMO, Newron Pharmaceuticals**. *"We look forward to receiving the first results from 12-week treatment in Q1 2027."*

ENIGMA-TRS 1 is a pivotal Phase 3, international, one year, randomized, double-blind, placebo-controlled study evaluating the efficacy, tolerability, and safety of the 15mg twice daily (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. Following this initial period, the study will continue 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.

Results from previous Phase 2 (study 014/015) and Phase 3 (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.

About treatment-resistant schizophrenia (TRS)

A significant proportion of patients with schizophrenia show virtually little to no beneficial response to currently available antipsychotic (AP) treatments, leading to a diagnosis of treatment-resistant schizophrenia (TRS). TRS is defined as no or inadequate symptom relief despite treatment with therapeutic doses of two APs from two different chemical classes for an adequate period. It is estimated that approximately 15% of patients develop TRS from the onset of illness, and about one-third to 50% of patients with schizophrenia overall. Emerging scientific evidence supports abnormalities in glutamate neurotransmission in TRS, not targeted by current APs, along with normal dopaminergic synthesis, to explain the lack of clinical benefit of most typical and atypical antipsychotics, which act primarily on dopamine receptors. These insights underline the need for novel therapeutic approaches that target the underlying glutamatergic dysfunction in schizophrenia, offering hope for patients who currently have limited or no effective treatment options.

About evenamide

Evenamide is a novel, orally available new chemical entity with a unique mechanism of action distinct from all currently marketed antipsychotics. It acts by selectively blocking voltage-gated sodium channels (VGSCs) and exhibits no biological activity at more than 130 other central nervous system (CNS) targets. It normalizes glutamate release induced by aberrant sodium channel activity (veratridine-stimulated), without affecting basal glutamate levels, due to inhibition of VGSCs. Combinations of subtherapeutic doses of evenamide and other APs, including clozapine, were associated with benefit in animal models of psychosis, suggesting synergies in mechanisms that may provide meaningful benefits for patients who do not adequately respond to current APs, including those on clozapine. Importantly, the benefits seemed to persist for a substantial time after evenamide had been degraded, explaining the long-term effects seen in clinical studies. Through its novel glutamatergic modulation, evenamide represents a first-in-class approach aimed at addressing the unmet needs of patients with schizophrenia who are resistant to existing treatments.

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 pivotal Phase 3 development program. Clinical trial results to date demonstrate the benefits of this drug candidate in the 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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