Ad hoc announcement pursuant to Art. 53 LR

Newron notes the publication of new preclinical research suggesting evenamide ameliorates schizophrenia-related dysfunction

New findings published in Neuropsychopharmacology are the first to demonstrate that evenamide targets the key site of schizophrenia pathology in the hippocampus, and so could be an ideal therapeutic agent for treatment of the disorder

Systemic, acute administration of evenamide in the neurodevelopment MAM model of schizophrenia improved positive, negative and cognitive symptoms of schizophrenia

Time-course analysis indicates effects of a single dose of evenamide last long after elimination of drug, suggesting effect on neuronal plasticity

Evenamide's glutamate modulation may improve overall outcomes in poorly responding or treatment resistant patients with schizophrenia on current antipsychotics, offering a novel strategy for managing the disorder

Milan, Italy and Morristown, NJ, USA – August 11 , 2025, 7:00 am CET – Newron Pharmaceuticals S.p.A. ("Newron") (SIX: NWRN, XETRA: NP5), a biopharmaceutical company focused on the development of novel therapies for diseases of the central and peripheral nervous system, notes the publication of new preclinical research in the peer-reviewed journal *Neuropsychopharmacology* on the unique mechanism and site of action of evenamide as a potential treatment for schizophrenia.[1] The findings by researchers at the University of Pittsburgh, using the neurodevelopmental methylazoxymethanol acetate (MAM) animal model, indicated that evenamide, Newron's first-in-class glutamate modulator, could offer a novel therapeutic strategy capable of addressing positive, cognitive, and negative symptoms of schizophrenia.

Schizophrenia is a neurodevelopmental disorder affecting approximately 1% of the world's population, and is characterized by positive, negative, and cognitive symptoms. However, current dopamine D2 antagonist-based antipsychotic drugs only address primarily positive symptoms. It is known that limbic hippocampus hyperexcitability is a key pathological state of schizophrenia and therefore represents an ideal therapeutic target. This newly published research shows how evenamide, a selective voltage-gated sodium channel blocker, uniquely targets hippocampal hyperexcitability and selectively inhibits hyperactive neurons. Additionally, time-course analysis indicates effects of a single dose of evenamide last long after its elimination, suggesting evenamide may have an effect on neuronal plasticity. Studies to date suggest evenamide is devoid of activity at any other central nervous system target, and it normalizes excessive synaptic glutamate induced by NMDA hypofunction.

"The study examined the effect of acute evenamide treatment on the hyperdopaminergic state, hippocampal hyperexcitability, social deficits, and recognition memory in the methylazoxymethanol acetate (MAM) neurodevelopmental model", explained Daniela L. Uliana, first author of the study, from the Departments of Neuroscience, Psychiatry and Psychology of the University of Pittsburgh. "The MAM model consists of injecting MAM during gestational day 17 into pregnant rats at a time that approximates the human second trimester; a

[1] Uliana DL, Walsh RA, Fabris D and Grace AA. Evenamide reverses schizophrenia-related dysfunction in a neurodevelopmental animal model, *Neuropsychopharmacology* (2025); https://doi.org/10.1038/s41386-025-02188-y

period of vulnerability in pregnancy during which prenatal disruptions can result in increased schizophrenia incidence in adults. The MAM-treated rats show multiple anatomical, behavioral, neurochemical, and physiological changes consistent with schizophrenia."

"The study findings suggest that evenamide has high therapeutic potential for treating multiple symptom domains of schizophrenia," **said Senior study author Dr. Anthony A. Grace of the University of Pittsburgh.** "Evenamide is a unique NCE agent in acting at the site of the deficit in schizophrenia by reducing hippocampal hyperexcitability. This represents a significant advancement in treatment, as evenamide can downregulate the hyperdopaminergic state without producing D2 blockade-related side effects while also improving behavioral deficits that are not properly treated by D2 blocking antipsychotic agents."

"The recognition memory improvement induced by evenamide in the study's MAM model may indicate that it may also enhance cognitive function in patients with schizophrenia and ultimately lead to a better functional outcome," continued Grace. "Current D2-based antipsychotic agents do not effectively address cognitive symptoms, which limits their overall efficacy and produces a significant functional burden on patients. Therefore, evenamide would offer advantages over existing antipsychotic drugs by targeting positive symptoms, cognitive deficits and social isolation."

"This study provides important learnings, which explain the results of our earlier Phase II and Phase III trials in patients with chronic schizophrenia. The prolonged effect in the MAM model explains the continuing improvement in symptoms even one year after starting treatment with evenamide in TRS patients in our phase 2 trial. In the Phase 3 trial in patients who were not responding to their current 2nd-generation antipsychotic drugs, including clozapine, the addition of evenamide led to significant improvements on the primary efficacy measure (PANSS total) as well as a clinically and statistically significant increases in responder rates", said Ravi Anand, Newron's CMO. "The preclinical and clinical results suggest high likelihood of success for our ongoing pivotal Phase III program and to potentially offering a completely new treatment paradigm to patients with schizophrenia."

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)[2], 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.

---

2 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/)

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 partnerships with Zambon and Meiji Seika.

For more information, please visit: www.newron.com

For more information, please contact:

Newron
Stefan Weber – CEO; +39 02 6103 46 26, pr@newron.com

UK/Europe
Simon Conway / Ciara Martin / Natalie Garland-Collins, FTI Consulting; +44 20 3727 1000, SCnewron@fticonsulting.com

Switzerland
Valentin Handschin, IRF; +41 43 244 81 54, handschin@irf-reputation.ch

Germany/Europe
Anne Hennecke / Maximilian Schur, MC Services; +49 211 52925227, newron@mc-services.eu

USA
Paul Sagan, LaVoieHealthScience; +1 617 865 0041, psagan@lavoiehealthscience.com

###