NEWS RELEASE

Newron TRS Study 6 Months' Results: Evenamide Substantially Improves Patients to an Extent That They No Longer Meet Protocol Entry Criteria

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Ad hoc announcement pursuant to Art. 53 LR

40% of patients no longer met TRS severity criteria

Company presented data from study in treatment resistant schizophrenia (TRS) confirming therapeutic durability and efficacy at the 36th ECNP Congress in Barcelona

Data after six months of treatment with evenamide demonstrate significant, clinically important, sustained and long-lasting improvement on PANSS total, CGI-S and Levels of Functioning (LOF)

Almost all patients benefited from evenamide, with none showing psychotic worsening during the study

Results further validate the use of a selective glutamate inhibitor as an adjunct to antipsychotics in patients with TRS

Company prepares for initiation of potentially pivotal, Phase III, 1-year, randomized, double-blind, placebo-controlled trial to confirm these results

MILAN--(BUSINESS WIRE)-- 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 (CNS), today at 12:35 pm CEST presentednew data from study 014/015

evaluating its investigational drug evenamide for the management of treatment resistant schizophrenia (TRS). The data, which demonstrated that evenamide treatment was associated with an increasing, sustained, and clinically significant improvement of symptoms were presented at the 36th European Clinical Neuropsychopharmacology Congress (ECNP) in Barcelona, Spain.

Results to date show that the addition of evenamide to antipsychotics was well tolerated, with low incidence of treatment-emergent adverse events, or drop out due to intolerance, and no pattern of central nervous system abnormalities. 95% of patients completed six weeks of treatment, 94% of the completers chose to continue with evenamide treatment into the long-term extension study (Study 015) and 92% of them reached six months of treatment.

Key findings and conclusions at six months (full study population):

- Efficacy results based on change from baseline in the Positive and Negative Syndrome Scale (PANSS), the Clinical Global Impression of Severity (CGI-S) as well as the Strauss Carpenter Levels of Functioning (LOF) showed a statistically significant improvement at 6 months (p-value < 0.001: paired t-test, LOCF). All efficacy scales showed gradual and sustained improvement.
- In contrast to common clinical experience, no patients experienced worsening of their psychoses; consequently, no patients relapsed.
- A large proportion of the responders (≥ 20 % reduction compared to baseline on PANSS total score) at week 6 maintained their response at 6 months.
- Review of the efficacy data indicated that treatment with evenamide resulted in approximately 40% of patients, at six months, no longer meeting the protocol severity criteria used to diagnose treatment resistance.

These results have expedited the design of a potentially pivotal, Phase III randomized, double-blind, placebo-controlled study of two doses of evenamide (15 and 30 mg bid) as an add-on treatment in patients with TRS.

Ravi Anand, Newron's Chief Medical Officer, said: "These highly encouraging results from study 014/015 presented today demonstrate the potential benefits of evenamide and its unique glutamatergic mechanism of action. The findings show that the addition of this glutamate modulation to first- and second-generation antipsychotics in patients with TRS potentiates their effects on dopamine dysfunction and can potentially produce a beneficial antipsychotic response."

What is remarkable about the effect of evenamide in this study is that treatment benefits continue to accrue overtime, and many patients who do not respond early achieve clinically important benefits later. Importantly, over the course of the study period, we found that no patients relapsed or experienced worsened psychosis, and a

significant portion of patients improved to the point that they no longer met the criteria to enrol in the study to begin with.

Following these encouraging results, which have been assessed by our international advisory committee, we are preparing to initiate a potentially pivotal, Phase III, multinational, randomized, double-blind, placebo-controlled trial in patients with TRS and are confident that the results from that study will endorse the use of evenamide as an adjunct treatment to any other antipsychotic as a new therapeutic strategy for TRS."

Efficacy and safety results from all 161 patients at the six-week primary endpoint of study 014 were announced in March 2023. All posters presented are available at Newron's **website**.

About treatment-resistant schizophrenia (TRS)

A significant proportion of patients with schizophrenia show virtually no beneficial response to antipsychotics (APs) despite adequate treatment, leading to a diagnosis of treatment-resistant schizophrenia (TRS). TRS is defined as no, or inadequate, symptomatic reliefdespite treatment with therapeutic doses of two APs from two different chemical classes for an adequate period. About 15% of patients develop TRS from illness onset, and about one-third of patients overall. Increasing evidence supports abnormalities in glutamate neurotransmission in TRS, not targeted by current APs, along with normal dopaminergic synthesis, to explain the lack of benefit of most typical and atypical antipsychotics.

About study 014/015

Study 014 was a six-week, randomized, rater-blinded study being conducted at multiple sites in three countries (India, Italy and Sri Lanka). Study 014 has completed the enrollment of 161 patients with TRS on a stable, therapeutic dose of a single antipsychotic other than clozapine. The primary objective of the study was to evaluate the safety and tolerability of evenamide given orally at three fixed doses (7.5, 15 and 30 mg bid). The assessment of preliminary efficacy was based on changes from baseline in the Positive and Negative Syndrome Scale (PANSS). Changes from baseline in Clinical Global Impression of Change (CGI-C), Severity of Illness (CGI-S), and Strauss-Carpenter Level of Functioning (LOF) scale, were secondary objectives. Study 015 is the extension study to determine the long-term benefits of glutamate release inhibition. Seventy-seven (77) of the first 100 patients completed the 1-year of treatment with evenamide, 16 discontinued the study early, two due to adverse events (one patient due to fever, vomiting, and nausea, the other due to somnolence, reduced concentration and increased sweating), the other 14 due to withdrawal of consent or lost to follow up.

About evenamide

Evenamide, an orally available new chemical entity, specifically blocks voltage-gated sodium channels (VGSCs) and is devoid of biological activity at >130 other 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 ineffective doses of evenamide and other APs, including clozapine, were associated with benefit in animal models of psychosis, suggesting synergies in mechanisms that may provide benefit in patients who are poor responders to current APs, including clozapine.

About Newron Pharmaceuticals

Newron (SIX: NWRN, XETRA: NP5) is a biopharmaceutical company focused on the development of novel therapies for patients with diseases of the central and peripheral nervous system. The Company is headquartered in Bresso near Milan, Italy. 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, and is commercialized by Newron's Partner Zambon. Supernus Pharmaceuticals holds the commercialization rights in the USA. Meiji Seika has the rights to develop and commercialize the compound in Japan and other key Asian territories. Newron is also developing evenamide as the potential first add-on therapy for the treatment of patients with symptoms of schizophrenia. For more information, please visit: **www.newron.com**

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For more information:

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 / Caroline Bergmann, MC Services
+49 211 52925222
newron@mc-services.eu

USA
Paul Sagan, LaVoieHealthScience

+1 617 374 8800, Ext. 112

psagan@lavoiehealthscience.com

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