Newron presents six-month interim data from the first 100 patients randomized in study 014/015 at the 31st European Congress of Psychiatry

Study 014/015 is a Phase II trial evaluating evenamide as add-on therapy for patients with treatment-resistant schizophrenia (TRS)

Full data suggest a new strategy for the management of TRS patients in the future

A new definition of TRS patient responders indicated, which integrates three widely accepted scales

Milan, Italy, March 28, 2023, 12:30 pm CET – 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), presented two e-posters at today's ***"Schizophrenia and other psychotic disorders"*** *session* at the 31st European Congress of Psychiatry, taking place at the Palais des Congrès in Paris, France.

New data suggestive of clinically important response in TRS patients

The first poster presented full results from the cohort of the first 100 patients completing six months/endpoint of treatment with evenamide in study 014/015. Study 014/015 is an international, randomized, open label, rater-blinded study of evenamide as an add-on to an antipsychotic (excluding clozapine) in patients with moderate to severe treatment-resistant schizophrenia (TRS) not responding to their current antipsychotic medication.

Top-line six-month results from this cohort of patients were announced in January 2023, and top-line one-year results were announced in February 2023.

Key findings and conclusions at six months:

- Efficacy results based on changes from baseline in the Positive and Negative Syndrome Scale (PANSS) as well as CGI-S showed a statistically significant improvement at six months (p-value < 0.001: paired t-test, LOCF). All other efficacy scales showed gradual and sustained improvement during the same period.
- The PANSS total score improved by approximately 13 points (16%) compared to baseline; the PANSS responder rate was 39%, more than double compared to week six (16%).

- Ratings of the Clinical Global Impression of Change (CGI-C) indicated that 85% of the patients experienced at least a minimal improvement; 36% of the patients were rated as much or very much improved; this represents an increase of approximately 10% from week 6.
- The Clinical Global Impression of Severity (CGI-S) improved (i.e., the disease severity was considered reduced) by 0.9 units from baseline.
- The addition of evenamide to antipsychotics was well tolerated, with low incidence of treatment-emergent adverse events, the most frequent were pyrexia (3%) and insomnia (3%). 97% of patients completed six weeks of treatment, and more than 90% of the completers chose to continue with evenamide treatment into the long-term extension study (study 015).

This was the first international trial of an antipsychotic new chemical entity (NCE) as an add-on to a single antipsychotic in patients with TRS who were not responding to their current medication. These results suggest a new strategy for the management of TRS patients in the future.

The poster is available at Newron's website.

New responder definition indicated for TRS

The second poster detailed the characterization of "Responder" in TRS patients based on data from this study.

Key findings and conclusions:

A widely accepted definition of response in patients with TRS treated with a putative antipsychotic added to their background antipsychotic monotherapy is currently not available.

Following a thorough analysis of the results from this first study evaluating the add-on therapy with evenamide in TRS, the aim was to determine a definition of responder that integrated three of the most accepted scales to evaluate patients with schizophrenia worldwide, the PANSS, the CGI-S and the CGI-C.

The following two definitions resulted from that analysis:

- A **"Full responder"** was defined as PANSS total score improvement of ≥ 20%; the CGI-C to be at least much improved; CGI-S at least 1-point improvement and at most mildly ill.
- A **"Partial responder**" was defined as a PANSS total score improvement of ≥ 15%; the CGI-C rated as any improvement; the CGI-S at least 1-point improvement.

The poster is 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 relief despite 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, explaining the lack of benefit of most typical and atypical APs.

About study 014/015
Study 014 is 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 is 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 is 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, are 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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