Ad hoc announcement pursuant to Art. 53 LR

Newron reports compelling additional data documenting the efficacy of evenamide in pivotal study 008A in poorly responding schizophrenia patients

Further study analysis reveals significant multi-domain benefits in PANSS and Clinical Global Impression of Change (CGI-C) ratings

Benefit on efficacy measures increased over time, suggesting larger and enduring patient effects to be expected during long-term treatment

Milan, Italy, May 13, 2024, 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 (CNS), presents additional results from the international, randomized, double-blind, placebo-controlled study 008A that evaluated the efficacy and safety of evenamide (30 mg bid) as add-on treatment in 291 patients not benefitting from their second-generation antipsychotic medication, including clozapine. Initial top line data announced on 30th April 2024 demonstrated that the study met its primary endpoint, an improvement of the Positive and Negative Syndrome Scale (PANSS) Total Score as well as the key secondary endpoint, an improvement of the Clinical Global Impression of Severity (CGI-S), in the a-priori defined regulatory analysis.

Additional analyses for the secondary endpoints indicate significant effects achieved at the endpoint (Day 29), on all the following measures:

- PANSS total: Proportion of patients with a clinically relevant improvement (more than 20% improvement from baseline); p-value < 0.05;
- Clinical Global Impression of Change (CGI-C): Mean rating at endpoint; evenamide 3.3 versus placebo 3.5; p-value < 0.001;
- Clinical Global Impression of Change (CGI-C): Proportion of patients rated as showing any improvement; p-value < 0.05;
- Clinical Global Impression of Change (CGI-C): Proportion of patients rated as at least "much improved"; evenamide: 31.3% versus placebo: 17.3%; p-value = 0.006;
- PANSS Positive subscale: Mean change from baseline; p-value < 0.05;
- PANSS Negative subscale: Mean change from baseline; p-value < 0.05.

The sensitivity analyses for the PANSS total (primary endpoint) and CGI-S (secondary endpoint) confirmed a statistically significant improvement for evenamide irrespective of the population analyzed and the statistical methods used; some examples are provided below:

- PANSS total worst observation carried forward (WOCF) ANCOVA p-value = 0.008;
- PANSS total Multiple Imputation (MI) ANCOVA: p-value = 0.006;
- CGI-S Multiple Imputation (MI) ANCOVA: p-value = 0.014.

In the study, the addition of 30 mg (bid) of evenamide to the patients' current antipsychotic medication was very well tolerated, with a similar profile to placebo with no increases in EPS, weight gain, blood glucose, metabolic syndrome, sexual dysfunction, CNS or cardiac effects, or laboratory abnormalities.

Study 008A is the first well-designed study demonstrating efficacy of an adjunctive treatment in benefiting patients who do not respond to their current antipsychotic. Evenamide also is the first glutamate modulator to demonstrate efficacy in inadequately responding patients with schizophrenia in a placebo-controlled study.

Ravi Anand, MD, Chief Medical Officer of Newron, stated: "*These new efficacy results from study 008A attest to the clinical relevance of the benefits for patients, based on the primary and key secondary endpoints. The results for the CGI-C rated by an experienced psychiatrist who assesses not only the symptoms of psychosis, but also the impact of treatment on social interactions, insight, and functioning, indicated a significant proportion of evenamide patients were considered as at least 'much improved'. Significant improvement was also noted on both positive and negative symptoms of schizophrenia.* ***Most importantly, the benefits noted on the efficacy measures increased up to Day 29, thus suggesting larger and enduring effects during longer term treatment.*** *These findings, along with those noted in study 014/015, where patients with treatment resistant schizophrenia treated with evenamide for 1-year experienced progressive, sustained and long-lasting clinically significant important benefits, further highlight the growing importance of glutamate modulation for the development of novel treatments for patients with schizophrenia."*

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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