Data from Newron's study 014/015 and an evenamide clinical development outlook presented at the 2024 Annual Congress of the Schizophrenia International Research Society (SIRS)

Data from study 014/015, a phase II trial evaluating evenamide as add-on therapy for patients with treatment-resistant schizophrenia (TRS) for up to one year

Presentation of study design for potentially pivotal phase III trial for TRS patients

Information on potentially pivotal study 008A in non-TRS patients presented, with results expected in late April 2024

Milan, Italy, April 8, 2024 – 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 four posters and two oral presentations at the 2024 Annual Congress of the Schizophrenia International Research Society (SIRS) from 3-7 April in Florence, Italy. The data presented were detailing previously reported scientific results of study 014/015, the future clinical development outlook for evenamide and information on study 008A.

Study 014/015 was 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 adequately to their current antipsychotic medication.

As previously announced by Newron, the study showed that the addition of evenamide to antipsychotics was well tolerated, with low incidence of treatment-emergent adverse events. Treatment with evenamide was associated with sustained, clinically significant benefit that increased throughout the one-year course of treatment. Gradual and sustained improvement was demonstrated across all efficacy scales used. More than 70% of patients experienced clinically important reduction in disease severity at one-year. Review of the efficacy data indicated that treatment with evenamide resulted in approximately 50% of patients at one-year no longer meeting any of the protocol severity criteria used to diagnose treatment resistance. Importantly, 25% of all patients achieved "remission" (no/minimal symptoms for at least six months), not reported before in TRS patients. Moreover, in contrast to common clinical experience, no patient relapsed during the one-year treatment period.

Also previously announced, in their totality, the results from study 014/015 support the initiation of a potentially pivotal phase III, randomized, double-blind, placebo-controlled study of evenamide as an add-on treatment in patients with TRS, which will hopefully confirm the benefit of evenamide observed so far. If approved, the compound would be the first add-on drug that improves the symptoms of TRS, offering a much-needed new therapeutic option for

those who are not responding to existing antipsychotics. A poster outlining the design of this potentially pivotal study was presented at SIRS.

Newron is also investigating evenamide in a potentially pivotal study (study 008A) in a separate indication: in patients with chronic schizophrenia currently being treated with a second-generation antipsychotic, but who demonstrate an inadequate response to that treatment. Study 008A is a four-week, randomized, double-blind and placebo-controlled study assessing the efficacy, tolerability, and safety of evenamide (30 mg bid). Patient enrollment has completed and results from this study are expected in late April 2024. Additional information on this study was outlined in an oral presentation at SIRS.

The posters presented at the SIRS conference were titled:

- Pharmaceutical pipeline: Glutamate modulation by evenamide as an add on to TRS patients not responding to current antipsychotics is associated with clinically important improvement across outcome measures: results from 1-year, open-label trial
- Treatment with evenamide for 1 year in TRS patients not benefitting to current antipsychotics is associated with sustained, clinically important benefit: Results from a prospective, pilot, 1-year, randomized, open-label trial
- Addition of evenamide for 1 year to antipsychotics in TRS patients results in increasing clinically important benefit to an extent that a substantial proportion no longer meet international criteria for treatment resistance
- Design of a potentially pivotal, phase 3, international, randomized, double-blind, placebo-controlled clinical trial evaluating evenamide as add-on treatment for treatment-resistant schizophrenia (TRS) patients

The presentations made at SIRS were titled:

- Glutamate modulation by evenamide as an add-on to TRS patients not responding to current antipsychotics is associated with clinically important improvement across outcome measures; results from a pilot, 1-year, open-label trial in treatment resistant schizophrenia (TRS)
- Study 008A: Add-on treatment with evenamide in patients with chronic schizophrenia not responding adequately to their current antipsychotic – Patient disposition and characteristics, challenges/issues in enrolling patients and study conduct

All posters and presentations 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 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, 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 enrolled 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 was the extension study to determine the long-term benefits of glutamate release inhibition, up to 1 year of treatment with evenamide.

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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