Ad hoc announcement pursuant to Art. 53 LR

Newron reports striking one-year interim efficacy results from its Phase II clinical trial evaluating evenamide as add-on therapy for patients with treatment-resistant schizophrenia

Highly compelling, statistically significant, clinically meaningful improvement in assessments of symptoms of psychosis, disease severity and global evaluation at one year; increase in magnitude of these measures over time

Evenamide could be a potential breakthrough treatment in the management of treatment-resistant schizophrenia (TRS) patients

Initiation of a pivotal, international, randomized, placebo-controlled study in TRS patients expected in 2023

Investor and analyst conference call today at 3 pm CET/ 9 am ET

Milan, Italy, February 16, 2023, 07:00 am 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), announces very exciting new results from the first 100 randomized patients who have completed one year (52 weeks) of treatment in its international, randomized, open label, rater-blinded study of evenamide (study 014/015) 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. Results from these same 100 patients at six weeks and six months in study 014/015 have been reported previously.

Results in patients completing one year of treatment with evenamide provide further striking new evidence of the sustained efficacy of evenamide as an add-on to antipsychotics (excluding clozapine) in TRS patients, by demonstrating substantially greater benefit at one year than noted at the six-week and six-month datapoints.

The efficacy results, based on changes over baseline at one year in the Positive and Negative Syndrome Scale (PANSS), showed more than a 50% increase over the statistically significant benefit noted at the six-week datapoint (p-value < 0.001: paired t-test). Furthermore, the proportion of patients experiencing a clinically meaningful PANSS improvement ("responders") at one year was almost three times higher than the proportion responding at week six (16%).

In addition, the mean change for the severity of illness (as measured by Clinical Global Impression of Severity (CGI-S)) showed a statistically significant improvement at one year compared to baseline. The proportion of patients who experienced highly meaningful (at least two categories) improvement in the severity of disease as assessed by the CGI-S more than doubled compared to the proportion of patients improving at week six (10%).

The proportion of patients experiencing clinically meaningful improvement (i.e., patients rated at least "much improved") on the Clinical Global Impression of Change (CGI-C) increased by an additional 10% at one year from the proportion at week six (27%). Further evidence of the progressive benefit over time was evident from the growing proportion of patients rated "very much improved" at one year.

Jean-Pierre Lindenmayer, M.D., Director of Research, Psychopharmacology Research Unit - Nathan Kline Institute for Psychiatric Research at Manhattan Psychiatric Center, commented: "*Clozapine is the treatment of choice for the management of treatment-resistant schizophrenia (TRS). However, more than half of patients with TRS do not respond to clozapine, which makes it extremely urgent to find new and effective treatments for TRS. These Phase II, open-label data of evenamide in patients with TRS, obtained with blinded raters, are very promising. The pattern of improvement is particularly unusual as it occurs gradually over a year and is sustained. We rarely see such a pattern of improvement with current treatments. In addition, the mechanism of action of evenamide appears to be completely novel, which may open up new pathways for treatment for TRS. Of course, these results need to be confirmed by a planned randomized, placebo-controlled study in TRS patients*."

The interim results are based on the first 100 patients randomized to receive evenamide (7.5, 15 or 30 mg bid) in study 014. Ninety of these entered the long-term treatment period (study 015) and 77 of these reached the 52-week endpoint. Most of the first 100 patients were randomized to receive either the 7.5 or 15 mg bid doses, as patients were initially randomized to treatment with these doses before an Independent Safety Monitoring Board reviewed the safety data from the first 50 patients completing the trial and agreed with the initiation of the randomization to the 30 mg bid dose.

The addition of evenamide to the current antipsychotic medication continued to be well tolerated, only two patients discontinued for adverse events (flu-like symptoms and headache) after one year of treatment.

Ravi Anand, M.D., Newron's Chief Medical Officer, said: *"These striking results, at the end of one year, from the first 100 patients randomized to this study are markedly better than could have been expected. While recognizing this study has no control arm, such statistically significant, clinically meaningful improvements over baseline in key efficacy measures after one year are, to our knowledge, unprecedented in patients with diagnosed treatment-resistant schizophrenia. We are particularly struck by data suggesting there is a continued improvement over time in these measures. We eagerly await the full results from the trial, which will include six- and twelve-month data from many more patients on the higher 30 mg dose. These results validate the role of this glutamate release inhibitor in repairing disturbed neural connectivity in a treatment-refractory patient population and should help us to expedite the start of our placebo-controlled Phase III study in patients with TRS that we plan in 2023."*

Newron will be presenting the results of the previously announced six-month endpoint at the 31st European Congress of Psychiatry taking place March 25-28, 2023, in Paris, France, and the one-year data at the Congress of the Schizophrenia International Research Society taking place May 11-15, 2023, in Toronto, Canada.

The enrollment of patients in study 014 has been completed, with 161 subjects randomized. Newron anticipates announcing the full results from the study in March 2023. The extension study 015 is ongoing and is expected to provide results of evenamide treatment for up to one year from all patients by Q1 2024.

Newron expects to initiate a potentially pivotal, multinational, randomized, placebo-controlled trial in patients with TRS (study 003) in 2023, as part of its ongoing Phase II/III development plan for evenamide. The first potentially pivotal study of this development program, study 008A, with evenamide as add-on therapy in patients with chronic schizophrenia experiencing inadequate response to their current antipsychotics (but not diagnosed as having TRS), is enrolling patients, and results are expected in 2023.

The company continues its dialogue with industry partners around potential future collaboration opportunities for the development of evenamide.

Conference call
Newron's CEO Stefan Weber and CMO Ravi Anand will host a conference call today, February 16, 2023, at 3 pm CET/ 9 am ET.

The call can be accessed via the following dial-in numbers:

Switzerland/Europe:	+41 (0) 58 310 5000
United Kingdom:	+44 (0) 207 107 0613
United States:	+1 (1) 631 570 5613

The presentation for this conference call can be downloaded as of today, February 16, 2023, at 7 am CET, on Newron's website (https://www.newron.com/investors/reports-and-presentation/year/2023#reports,-presentations-&-webcasts).

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 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 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 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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