



Newron Pharmaceuticals reports on its 2024 Investor Day in New York City

Clinical results and new findings of mechanism of action indicate evenamide would be uniquely effective in patients with treatment resistant schizophrenia

Leading schizophrenia experts predict earlier use of evenamide would benefit patients with inadequate response

Evenamide's unique mechanism of action targets the core abnormalities in patients with schizophrenia and reduces hippocampal dopaminergic activity, improving symptoms of psychosis, social interactions and cognition

Long-term benefits of evenamide as an add-on therapy were presented: 25% of treated patients met the criteria for remission suggesting evenamide may positively affect the long-term course of schizophrenia in TRS patients

Milan, Italy and Morristown, NJ, USA – June 25, 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), welcomed investors, analysts and media today to its well-attended investor day in New York City. The event focused on the Company's clinical, scientific and commercial plans for evenamide, its investigational drug candidate in Phase III clinical development for the potential treatment of patients with chronic and TRS.

The event featured three leading schizophrenia experts who presented on the unmet medical needs in schizophrenia, as well as new concepts and recent neurobiological findings for treating poor responders and patients with TRS. An outline of Newron's Phase III clinical development plan in TRS was also presented.

Breakthrough pre-clinical data supporting evenamide in the treatment of TRS

Anthony Grace, Ph.D., Editor-in-Chief, International Journal of Neuropsychopharmacology, Distinguished Professor of Neuroscience, and Professor of Psychiatry and Psychology at the University of Pittsburgh, stated, "The hippocampal hyper dopaminergic activity in patients with schizophrenia contributes to the development of symptoms of psychosis, loss of functioning, decreased social interactions and deterioration of cognition."

Dr. Grace further stated, "Evenamide's glutamate modulation has produced dramatic effects in the MAM model of schizophrenia, which closely mimics the changes observed in patients with schizophrenia. In this model, evenamide reversed abnormal hippocampal neuronal activity, normalized dopamine neuron population activity, improved cognition and normalized social interactions. Its effects on neuronal firing, which persisted well beyond its half-life, indicated that it induces neuronal plasticity and may help with neuronal repair. Furthermore, by acting at the site of pathology, evenamide might also be effective for negative symptoms and cognitive dysfunction."



Data from first evenamide placebo-controlled randomized study

John Kane, M.D., Co-Director and Professor, Institute of Behavioural Science, Feinstein Institutes for Medical Research, and Professor of Psychiatry, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell stated: “A substantial proportion of patients with schizophrenia do not respond well to first line medications, and this is true even at the onset of illness. This may be because there are biological changes in the brains of patients that show reduced benefit and non-response to treatments, compared with patients who respond adequately to treatment.”

“Patients who are poor responders are likely to relapse more than patients who respond to medication,” stated Kane. “To date, there are no studies which have demonstrated that the addition of one antipsychotic to another, or switching antipsychotics, has produced any benefit to inadequate responders and TRS patients.”

Dr Kane continued, “The evenamide 008A study is unique in demonstrating a significant benefit in patients who were moderately to severely psychotic, while being compliant with their antipsychotic medication. This therapeutic benefit may derive from evenamide’s glutamate modulation activity. The drug was extremely well tolerated, without any of the usual side effects of available antipsychotics.”

Results from an open label, long-term study of evenamide as add-on therapy in TRS

Stephen R. Marder, M.D., Distinguished Professor of Psychiatry, Semel Institute of Neuroscience & Human Behavior, and Director, Section on Psychosis, UCLA Neuropsychiatric Institute stated: “One-third of patients with schizophrenia are treatment resistant and the only drug available, clozapine, is used in less than 5% of patients. The use of higher doses, the addition of another antipsychotic, or switching to another drug is unsuccessful in patients with TRS.”

Dr. Marder continued, “The one-year results from studies where evenamide was added to antipsychotics are noteworthy, as the sustained and continuous improvement across all efficacy measures is virtually unknown in patients with TRS. Similarly, the conversion of TRS patients to a non-resistant state, as well as the finding that 25% of patients met criteria for remission, is remarkable and unprecedented.”

A new placebo controlled, one-year trial in patients with TRS who are receiving other antipsychotics is in planning with Dr. Marder as the Principal Investigator.

An outline of the late-stage clinical development for evenamide in TRS

Ravi Anand, MD, Newron’s Chief Medical Officer, provided an update on evenamide’s clinical program, outlining that evenamide’s promising results will be evaluated in a Phase III randomized, double-blind, one-year trial. The trial will compare evenamide to placebo as add-on treatments in at least 400 TRS patients. The primary efficacy endpoint will be change



from baseline in PANSS¹ scores at 12 weeks. Following this initial period, subjects will continue on their assigned treatment until week 26, for the second, maintenance efficacy endpoint, and then on to 1 year for read-out of the third (one-year, long term) efficacy endpoint. The long-term extension will also serve to evaluate the long-term safety and tolerability of evenamide.

Stefan Weber, Chief Executive Officer of Newron Pharmaceuticals, commented: “As highlighted by the three world-leading KOLs, evenamide has enormous potential, if approved, in addressing the significant unmet medical needs of patients with chronic and treatment-resistant schizophrenia. We continue to explore all options, including partnering, that could enable us to complete the Phase III clinical development of evenamide, which we believe could have blockbuster potential.”

A replay of the event is available on the Company’s website for one month after the date of the event: <https://www.newron.com/investors/reports-and-presentation/year/2024#reports,-presentations-&-webcasts>

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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¹ Positive and Negative Syndrome Scale (PANSS) is widely used in clinical trials of schizophrenia and is considered the “gold standard” for assessment of antipsychotic treatment efficacy (Innvo Clin Neurosci, 2017: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5788255/>)



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