Newron announces encouraging preliminary results of its Phase IIa study with Evenamide in patients with schizophrenia

Evenamide met study objectives of good tolerability, safety, and preliminary evidence of efficacy as an add-on therapy for the treatment of schizophrenia

Unique mechanism: glutamate modulation and voltage-gated sodium channel blockade

Milan, Italy and Morristown, NJ, USA, January 3, 2017 – Newron Pharmaceuticals S.p.A. ("Newron"), a biopharmaceutical company focused on the development of novel therapies for patients with diseases of the central nervous system (CNS) and pain, announced today preliminary results of a Phase IIa study with its unique sodium channel blocker, Evenamide (NW-3509), in patients with schizophrenia. The new chemical entity is orally available and specifically targets voltage-gated sodium channels by a unique mechanism of action.

Detailed results will be presented at the 16th International Congress on Schizophrenia Research, 24-28 March 2017, in San Diego.

Ravi Anand, M.D., Newron's Chief Medical Officer, stated: "The results of this study are very encouraging. Evenamide was not associated with any dose-limiting toxicities, or the extrapyramidal, sexual, endocrine, and metabolic side effects associated with dopamine-blocking antipsychotics. The addition of Evenamide, which acts by attenuating glutamate release, to patients showing a worsening of their symptoms while on their current atypical antipsychotic, was not only well-tolerated, but showed a consistent pattern of benefit on all efficacy measures assessed. These preliminary results warrant further investigation in larger and longer trials in patients with more severe symptoms."

The four-week, Phase IIa, double-blind, placebo-controlled randomized study was designed to investigate tolerability, safety and preliminary evidence of efficacy of Evenamide as an add-on treatment in 89 patients with schizophrenia. Patients included in the study were experiencing break-through psychotic symptoms while on stable and adequate doses of risperidone (mean dose: 4.2 ± 2.0 mg/day; n=70) or aripiprazole (mean dose: 19.7 ± 7.0 mg/day; n=19), the atypical antipsychotic to which they had responded previously. The study was held in two U.S (n=61) and three Indian (n=28) study centers, and enrolled schizophrenia patients with a mean duration of illness of approximately 18 years and an average of 3 hospitalizations. Patients were randomized to receive twice daily Evenamide (15-25 mg) or placebo, in addition to their current antipsychotic. The study protocol, including doses and study design, was finalized with FDA input and guidance, and received approval from the Drug Controller General of India (DCGI), as well as the institutional review board (IRB) at each center.

The results of the study indicate that patients treated with Evenamide showed improvement on the symptoms of schizophrenia assessed by (the Positive and Negative Syndrome Scale) PANSS, as well as functioning assessed by the Strauss-Carpenter Level of Functioning scale, compared to their standard antipsychotic. In addition, a global assessment of change from baseline in the patient's overall condition (Clinical Global Impression of Change), performed by a clinician, showed a greater proportion of Evenamide-treated patients rated as improved (54%), compared to placebo (36%).

Evenamide in the range of 15-25 mg *bid* (30-50 mg/day) was well tolerated. The most frequent (>5% of patients in any group) adverse events (AEs) (Evenamide vs. placebo), were somnolence [8 (16.0%) vs. 5 (12.8%)], insomnia [5 (10.0% vs. 1 (2.6%)], overdose [3 (6.0%) vs. 1 (2.6%)], dry mouth [3 (6.0%) vs. 2 (5.1%)], and headache [3 (6.0%) vs 0]. The incidence of AEs classified as 'skin and subcutaneous disorders' was higher in the Evenamide group [5 (10.0%) vs. 0], while the incidence of 'respiratory, thoracic and mediastinal disorders' was higher for placebo [1 (2.0%) vs. 3 (7.7%)]. Most AEs were of mild severity [Evenamide, 58 of 69 (84%); placebo, 30 of 34 (88%)]; 9 of 69 (13%) AEs for Evenamide and 4 of 34 (12%) for placebo were assessed as moderate.

Two patients in the Evenamide group discontinued treatment due to AEs: seizure (n=1) and atrial fibrillation (n=1). There was no evidence of any worsening of extrapyramidal symptoms, abnormal ECG findings, or clinically notable changes in laboratory values or vital signs (blood pressure, pulse or body weight) with Evenamide treatment, compared to placebo.

About schizophrenia

Schizophrenia is a long-term mental health condition that causes a range of different psychological symptoms. It is one of the most common serious mental health conditions. About 1 in 100 people will experience schizophrenia in their lifetime, with many continuing to lead normal lives. Schizophrenia is most often diagnosed between the ages of 15 and 35. Men and women are affected equally. There is no single test for schizophrenia. It is most often diagnosed after an assessment by a mental health care professional, such as a psychiatrist. It is important to diagnose schizophrenia as early as possible, as the chances of recovery improve the earlier it is treated. Schizophrenia is often described in terms of positive and negative (or deficit) symptoms. Positive symptoms are those that most individuals do not normally experience but are present in people with schizophrenia. They can include delusions, disordered thoughts and speech, and tactile, auditory, visual, olfactory and gustatory hallucinations, typically regarded as manifestations of psychosis. Hallucinations are also typically related to the content of the delusional theme. Positive symptoms generally respond well to medication. Negative symptoms are deficits of normal emotional responses or of other thought processes, and are less responsive to medication.

About Evenamide (NW-3509)

Evenamide is an orally available new chemical entity that specifically targets voltage-gated sodium channels. The compound modulates sustained repetitive firing, without inducing impairment of normal neuronal excitability. Evenamide normalizes glutamate release induced by aberrant sodium channel activity. The potential benefits of the compound have been demonstrated in numerous preclinical models predictive of efficacy in psychiatric diseases, including models of psychosis such as amphetamine-induced hyperactivity, sensorimotor gating and information processing deficits (pre-pulse inhibition impairment induced by different stimuli), mania and depression. Efficacy of Evenamide has also been demonstrated in models of aggression and compulsive behavior, as well as in short- and long-term memory tests. Sub-threshold doses of the compound increased the activity of inactive doses of both typical and atypical antipsychotics in models of schizophrenia, psychosis and mania. Moreover, given its neuronal stabilization properties, Evenamide may reduce relapses and prevent or treat episodes of psychosis due to established super-sensitivity psychosis (SSP) induced by antipsychotics. As it is devoid of the risk of drug-induced movement disorders or weight gain, Evenamide can be given in combination for extended periods of time.

About Newron Pharmaceuticals

Newron (SIX: NWRN) is a biopharmaceutical company focused on the development of novel therapies for patients with diseases of the Central Nervous System (CNS) and pain. 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 and Switzerland and is commercialized by Newron's Partner Zambon. US WorldMeds holds the commercialization rights in the US. Meiji Seika has the rights to develop and commercialize the compound in Japan and other key Asian territories. In addition to Xadago® for Parkinson's disease, Newron has a strong pipeline of promising treatments for rare disease patients at various stages of clinical development, including sarizotan for patients with Rett syndrome and ralfinamide for patients with specific rare pain indications. Newron is also developing Evenamide as the potential first add-on therapy for the treatment of patients with positive symptoms of schizophrenia. **www.newron.com**

For further information

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