Newron and Zambon sign agreement for potentially pivotal study with *safinamide* in Parkinson's disease patients

Global study to evaluate the reduction of levodopa-induced dyskinesia (PD LID)

Milan, Italy – March 15, 2021 – 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 and its partner, Zambon S.p.A. ("Zambon"), an international pharmaceutical company strongly committed to the central nervous system (CNS) therapeutic area, today announced an agreement regarding a potentially pivotal study to evaluate the efficacy of *safinamide* in Parkinson's disease patients with levodopa induced dyskinesia (PD LID).

Under the agreement, Newron will sponsor the study and be responsible for its development and execution, as well as leading on all related regulatory interactions. Newron and Zambon will evenly share the cost of the study.

The double-blind, placebo-controlled study is intended to be performed in the US, Europe and Asia/Australia, with the aim of a label extension for *safinamide* in key markets. *Safinamide* has previously been approved for the treatment of Parkinson's disease as add-on therapy to levodopa/carbidopa experiencing "off" episodes in 20 markets including: the European Union, Switzerland, the United Kingdom, the United States, Canada, Australia, Latin America, Israel, the United Arab Emirates, Japan and South Korea. *Safinamide* is commercialized by Zambon as well as Meiji Seika/Eisai. Supernus Pharmaceuticals, a biopharmaceutical company focused on the development and commercialization of products for the treatment of CNS diseases, acquired the US commercialization rights for *safinamide* in 2020.

Ravi Anand, CMO of Newron, said: *"Previous pre-clinical and clinical studies have provided preliminary evidence of the efficacy of safinamide in reducing dyskinesia. We will be working with international clinical experts and regulatory authorities to finalize the design of a global trial to demonstrate the benefits of safinamide on dyskinesia in patients with PD*."

Paola Castellani, CMO and R&D Head of Zambon, added: *"Since 2015, thousands of Parkinson's disease patients around the world have benefited from safinamide's safe and efficacious profile and the subsequent improvement in their motor fluctuations. We look forward to working closely with Newron to potentially provide a new treatment option for those living with PD LID, an area of huge medical need."*

Parkinson's disease affects an estimated seven to ten million patients worldwide. More than 40% of Parkinson patients experience PD LID, involuntary, non-rhythmic and often painful movements during waking hours that are purposeless and unpredictable. Dyskinesia can interfere with people's daily living, resulting in functional impairment and disability. People with Parkinson's disease often experience multiple fluctuating periods of OFF time and dyskinesia during any given day, which can impede their movement and daily function. Currently, only one drug has ever received marketing authorization for PD LID in the US.

References:
Two-year, randomized, controlled study of safinamide as add-on to levodopa in mid to late Parkinson's disease. Borgohain, Rupam; Szasz, Jozsef; Stanzione, Paolo; Meshram, Chandrashekhar; Bhatt, Mohit H et al. (2014)
Movement disorders : official journal of the Movement Disorder Society vol. 29 (10) p. 1273-80.
Anand R: Safinamide is associated with clinically important improvement in motor symptoms in fluctuating PD patients as add-on to levodopa (SETTLE). 17th International Congress of Parkinson's Disease and Movement Disorders, Sydney, Australia, June 16-20, 2013.

About Parkinson's disease and Levodopa (L-dopa) Induced Dyskinesia (LID)
PD is the second most common chronic progressive neurodegenerative disorder in the elderly after Alzheimer's disease, affecting 1-2% of individuals aged ≥ 65 years worldwide. The prevalence of the PD market is expected to grow in the next years due to the increase in the global population and advancements in healthcare that contribute to an aging population at increased risk for PD. The diagnosis of PD is mainly based on observational criteria of muscular rigidity, resting tremor, or postural instability in combination with bradykinesia. As the disease progresses, symptoms become more severe. Early-stage patients are more easily managed on L-dopa. L-dopa remains as the most effective treatment for PD, and over 75% of the patients with PD receive L-dopa. However, long term treatment with L-dopa leads to seriously debilitating motor fluctuations, i.e. phases of normal functioning (ON-time) and decreased functioning (OFF-time). Furthermore, as a result of the use of high doses of L-dopa with increasing severity of the disease, more than 40% of patients experience L-dopa-Induced Dyskinesia, involuntary and non-rhythmic movements during waking hours that are purposeless and unpredictable. Dyskinesia can interfere with people's daily living, resulting in functional impairment and disability. People with Parkinson's disease often experience multiple fluctuating periods of OFF time and dyskinesia during any given day, which can impede their movement and daily function. As the disease progresses, more drugs are used as an add-on to what the patient already takes, and the focus is to treat symptoms while managing LID and the "off-time" effects of L-dopa. Most current therapies target the dopaminergic system that is implicated in the pathogenesis of PD, and most current treatments act by increasing dopaminergic transmission that leads to amelioration of motor symptoms.

References:
BMC Oertel. European Handbook of Neurological Management, Vol 1, Chapter 14 & 15, 2011.
NICE PD guideline, 2006.

About safinamide
Safinamide is a new chemical entity with a unique mode of action including selective and reversible MAO-B-inhibition and blocking of voltage dependent sodium channels which leads to modulation of abnormal glutamate release. Clinical trials have established its efficacy in controlling motor symptoms and motor complications in the short term, maintaining this effect over 2 years. Results from 24-month double-blind controlled studies suggest that safinamide shows statistically significant effects on motor fluctuations (ON/OFF time) without increasing the risk of developing troublesome dyskinesia. This effect may be related to its dual mechanism acting on both the dopaminergic and the glutamatergic pathways. Safinamide is a once-daily dose and has no diet restrictions due to its high MAO-B/MAO-A selectivity. Zambon has the rights to develop and commercialize *Safinamide* globally, excluding Japan and other key Asian territories where Meiji Seika has the rights to develop and commercialize safinamide. The rights to develop and commercialize *Safinamide* in the USA have been acquired by Supernus Pharmaceuticals.

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. *Safinamide* has received marketing authorization for the treatment of Parkinson's disease in the European Union, Switzerland, the USA, Australia, Canada, Brazil, Colombia, 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 positive symptoms of schizophrenia. For more information, please visit: **www.newron.com**

About Zambon
Zambon is a multinational pharmaceutical company that focuses on innovation and development with the aim to improve patients' lives. Based on a valuable heritage and strongly focused on the future, its goal is to improve people's health through the development of innovative health care solutions. Zambon products are commercialized in 87 countries. The company has 20 subsidiaries in three different continents – Europe, America and Asia – and owns manufacturing units in Italy, Switzerland, China and Brazil. The company today has a strong focus on the treatment of rare diseases and specialties, on top of respiratory, pain management and women's care. Zambon was established in 1906 in Italy and today counts around 2,500 employees all over the world. For further information please visit www.zambon.com

For more information, please contact

Newron
Stefan Weber – CEO
+39 02 6103 46 26 - pr@newron.com

UK/Europe: Simon Conway / Natalie Garland-Collins
FTI Consulting
+44 20 3727 1000 SCnewron@fticonsulting.com

Germany/Europe: Anne Hennecke, MC Services
+49 211 52925222 - anne.hennecke@mc-services.eu

Switzerland: Valentin Handschin, IRF Reputation
+41 43 244 81 54 - handschin@irf-reputation.ch

USA- Paul Sagan, LaVoieHealthScience
+1 617 374 8800, Ext. 112 - psagan@lavoiehealthscience.com

Zambon
Valentina Saffioti - Global Pharma Communication
+39 0266524508 - valentina.saffioti@zambongroup.com

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