# Newron to re-submit US NDA for Xadago® (safinamide)

## FDA agrees no additional evaluation of abuse liability or dependence/withdrawal effects in humans is required

**Milan, Italy – July 26, 2016 –** Newron Pharmaceuticals S.p.A. ("Newron") (SIX: NWRN), a biopharmaceutical company focused on the development of novel therapies for patients with diseases of the central nervous system (CNS) and pain, and its partners Zambon S.p.A. and US WorldMeds announced today that the US Food and Drug Administration (FDA) and the Controlled Substance Staff (CSS) in the Center for Drug Evaluation and Research (CDER) at the Food and Drug Administration no longer require Newron to perform any studies to clinically evaluate the potential abuse liability or dependence/withdrawal effects of Xadago®. The FDA decision was communicated during a meeting with Newron that was scheduled following the March 29, 2016 Complete Response Letter (CRL).

The CRL did not require submission of any additional new data/studies/analyses for efficacy or safety in patients with Parkinson's disease, thus Newron will now expedite re-submission of the New Drug Application (NDA) to the FDA.

Ravi Anand, MD, Newron's CMO, said: "*We thank the FDA and CSS for their help over the last months. Newron's submission of additional pre-clinical abuse liability studies and additional analyses of the clinical data requested by the CSS led the FDA and CSS to conclude that no further evaluation of the abuse liability or dependence/withdrawal effects of Xadago® were required. Newron and the FDA agreed on the contents of the NDA re-submission which Newron expects to complete by November of this year."*

"*We appreciate the exciting development which will allow us to advance the introduction of this potential new treatment option to the one million Americans living with Parkinson's disease*", said P. Breckinridge ("Breck") Jones, CEO of US WorldMeds.

"*We are very pleased that the FDA has allowed the re-submission of* Xadago® *in the next months. This reinforces once more our commitment in finding innovative therapies for patients suffering from PD and other Central Nervous System diseases",* said Elena Zambon, President of Zambon.

**About Xadago® (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 Xadago® globally, excluding Japan and other key territories where Meiji Seika has the rights to develop and commercialize the compound. The rights to develop and commercialize Xadago® in the USA have been granted to US WorldMeds, by Zambon.

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**
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, many patients experience involuntary movements known as L-dopa-Induced Dyskinesia (LID). 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, Vol1, Chapter 14 & 15, 2011.
NICE PD guideline, 2006.

**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 NW-3509 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 US WorldMeds**
US WorldMeds is a specialty pharmaceutical company dedicated to developing, licensing and commercializing unique and significant specialty pharmaceuticals that address unmet medical needs or overcome limitations of existing products. Through sound science and targeted commercialization, the Kentucky-based company continually strives to identify specialty and orphan products for diseases with limited patient populations. US WorldMeds' portfolio includes Revonto® (dantrolene sodium for injection) for the treatment of malignant hyperthermia, MYOBLOC® (rimabotulinumtoxinB) Injection for the treatment of cervical dystonia in adults and APOKYN® (apomorphine hydrochloride injection) for the acute, intermittent treatment of hypomobility, "off" episodes associated with advancing Parkinson's disease. In addition, US WorldMeds is working on the development of a non-narcotic drug product (Lofexidine) for the treatment of opiate withdrawal symptoms. For more information about US WorldMeds, visit www.usworldmeds.com.

**About Zambon**
Zambon is a leading Italian pharmaceutical and fine-chemical multinational company that has earned a strong reputation over the years for high quality products and services. Zambon is well-established in 3 therapeutic areas: respiratory, pain and woman care, and is very strongly committed to its entry into the CNS space. Zambon SpA produces high quality products thanks to the management of the whole production chain which involves Zach (Zambon chemical), a privileged partner for API, custom synthesis and generic products. The Group is strongly working on the treatment of the chronic respiratory diseases as asthma and BPCO and on the CNS therapeutic area with Xadago® (safinamide) for the Parkinson treatment. Zambon is headquartered in Milan and was established in 1906 in Vicenza. Zambon is present in 19 countries with subsidiaries and almost 2,700 employees with manufacturing units in Italy, Switzerland, France, China and Brazil. Zambon products are commercialized in 84 countries.
For details on Zambon please see: **www.zambongroup.com**

**For more information**

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