



## **Neupro<sup>®</sup> (rotigotine transdermal system) significantly improved wellbeing and daily activities impaired due to limb pain associated with Restless Legs Syndrome**

- Data presented at major international congress
- Additional five year open-label data provided evidence for long-term safety and efficacy of Neupro<sup>®</sup> (rotigotine transdermal system) in Restless Legs Syndrome (RLS)

**Brussels (Belgium), 18th June 2010, 1430 CET** – The first data to show that Neupro<sup>®</sup> (rotigotine transdermal system) significantly improved wellbeing and daily activities that are often impaired by pain related to Restless Legs Syndrome (RLS) were presented this week at the 14th International Congress of Parkinson’s Disease and Movement Disorders in Buenos Aires, Argentina. Additional data from an open-label extension study showed that the efficacy of rotigotine remained stable over five years of follow up with over a third of patients remaining symptom free during that time and 96% categorized as “very much improved” or “much improved”.

“Pain has been reported by up to 60% of RLS patients. These new data showed that by improving the core symptoms of RLS, rotigotine provided relief from pain and significantly improved patient wellbeing and daily activities impaired due to RLS-related pain. Therefore these data may be relevant for RLS patients with painful symptoms that are not currently being treated effectively” said Professor Ralf Kohnen, University of Erlangen-Nuremberg, Germany.

In the 6-month, double-blind study, 458 patients with moderate to severe RLS were randomised to receive either placebo or rotigotine (1,2,3 mg/24hrs) by transdermal administration. Patient impairment of daily activities due to pain was assessed using Item 8 of the Quality of Life Questionnaire for RLS patients (QoL-RLS; additional exploratory endpoint). At baseline, 456 patients (99.6%) were assessed and 433 patients (94.5%) were assessed at the end of the maintenance period.



At each visit, patients were asked to what degree pain in their arms or legs impaired their wellbeing or normal daytime activities on a scale of 0-5 points (“not at all” to “extremely”). The mean value for pain decreased from 2.41 to 1.85 in the placebo group, and from 2.61 to 1.39 in the rotigotine group ( $p=0.0003$ ). The average change was 0 points in the placebo group, and -1 point in the rotigotine group.

Additionally, at baseline, 55.6% of the placebo group reported moderate to extreme pain, compared with 61.9% of patients in the rotigotine group. At the end of maintenance, these figures had changed to 38.2% and 22.9%, respectively.

*Abstract: Rotigotine reduced impairment of daily activities due to pain in patients with idiopathic Restless Legs Syndrome*

*Stiasny-Kolster K, Trenkwalder C, Garcia-Borreguero D, Bauer L, Grieger F, Schollmayer E, Kohnen R, on behalf of the SP790 study group*

*Poster Session IV, June 17<sup>th</sup> 2010, 0900-1600*

## **Other rotigotine in RLS presentations at the Congress:**

### **5-year results from an open-label follow-up study**

Final results of the longest ever open label prospective follow-up of a placebo-controlled phase II trial in RLS have shown the safety and efficacy of rotigotine seen at previous interim analyses.

This study looked at improvement in symptoms based on the International Restless Legs Syndrome Study Group Rating Scale (IRLS)\*. The total IRLS score ranges from 0 (no symptoms) to 40 (very severe symptoms). A score of  $>20$  indicates severe RLS. Of the 295 patients with moderate to severe RLS who entered the study, 126 (43%) completed the 5-year follow up. At the end of the study, 59% of patients were classified as remitters (IRLS score  $\leq 10$ ), and 39% as symptom-free (IRLS score =0).

*\* The International Restless Legs Syndrome Study Group Rating Scale (IRLS) is a ten-item scale developed and validated by The International Restless Legs Syndrome Study Group and considered to be the best scale for evaluating the severity and frequency of RLS symptoms and the degree to which they affect sleep and daily life. It is administered by clinicians and includes questions related to the severity of sensory and motor symptoms, sleep disturbance, daytime somnolence and impact of RLS on activities of daily living and mood.*



Additionally, the Clinical Global Impression (CGI) Improvement scale was used to assess how much the patient's illness had improved or worsened relative to baseline. The change in the condition from baseline to the end of the study was categorized as "very much improved" or "much improved" in 96% of patients. At the end of the study 85% of patients were in a less severe illness category (normal, borderline ill or mildly ill) compared with 3% at baseline.

The mean dose of rotigotine was 2.43 mg/24 hours after initial titration and 3.09 mg/24 hours at the end of the study. Most adverse events (AEs) were mild to moderate in intensity. The most common AEs were application site reactions (58%), nasopharyngitis (19%), back pain (14%), nausea (12%) and fatigue (11%)†. Thirty per cent of patients discontinued the study due to an AE.

*Abstract: Long-term safety and efficacy of rotigotine in patients with idiopathic RLS: 5-year results from a prospective multinational open-label follow-up study*

*Högl B, Trenkwalder C, Garcia-Borreguero D, Kohnen R, Poewe W, Stiasny-Kolster K, Bauer L, Fichtner A, Schollmayer E, Oertel W, on behalf of the SP710 study group  
Poster Session IV, June 17<sup>th</sup> 2010, 0900-1600*

### **12-month results from an open-label extension study**

The long term safety and efficacy of rotigotine have also been shown in an additional 12-month open label extension study of two earlier placebo-controlled trials of rotigotine in idiopathic RLS.

Of 341 patients who entered the study, 91 (27%) discontinued, 58 (17%) due to adverse events and 17 (5%) due to lack of efficacy. The most common AEs were application site reaction (33%), nausea (7%), fatigue (7%), nasopharyngitis (6%) and headache (6%)†. Mean daily dose at the start of 12-month maintenance was 2.08 mg/24hrs; after initial dose titration, 70% of patients required no further dose adjustment; 5% decreased and 25% increased their dose.

*† Please consult the Neupro® Summary of Product Characteristics for a full listing of adverse events*



At the end of maintenance, mean IRLS score was 10.6, and 65% of patients were classified as IRLS responders (IRLS score reduced by  $\geq 50\%$ ), 55% were IRLS remitters (IRLS score of  $\leq 10$  points), and 30% had no RLS symptoms (IRLS score of 0).

*Abstract: Safety and efficacy of long-term treatment with transdermal rotigotine in patients with idiopathic restless legs syndrome: a 12 month open-label extension study*  
Benes H, Oertel WH, Garcia-Borreguero D, Fichtner A, Schollmayer E, Trenkwalder C, on behalf of the SP791 study group

Poster Session IV, June 17<sup>th</sup> 2010, 0900-1600

#### **For further information**

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#### **Notes to Editors**

##### **About Restless Legs Syndrome**

Restless Legs Syndrome (RLS) is a neurological disorder characterized by unpleasant sensations in the legs and an uncontrollable urge to move when at rest in order to relieve these feelings. It affects between 3 and 10% of the population to some extent. Some researchers estimate that RLS affects as many as 12 million Americans. However, others estimate a much higher occurrence because RLS is thought to be under-diagnosed and in some cases mis-diagnosed. Most people with RLS have difficulty falling asleep and staying asleep. Left untreated the condition causes exhaustion and daytime fatigue. Many people with RLS report that their job, personal relations and activities of daily living are strongly affected as a result of their exhaustion. They are often unable to concentrate, have impaired memory, or fail to accomplish daily tasks. Most than 80% of people with RLS also experience a more common condition known as periodic limb movement disorder (PLMD)

##### **About Neupro<sup>®</sup> in Europe**

Neupro<sup>®</sup> (rotigotine) is approved in the European Union for the treatment of the signs and symptoms of early-stage idiopathic Parkinson's disease, as monotherapy (i.e. without levodopa) or in combination with levodopa, i.e. over the course of the disease, through to late stages when the effect of levodopa wears off or becomes inconsistent and fluctuations of the therapeutic effect occurs. Neupro<sup>®</sup> is also approved in the European Union for the symptomatic treatment of moderate to severe idiopathic restless legs syndrome in adults.

##### **Neupro<sup>®</sup> in Europe Important Safety Information**

Neupro<sup>®</sup> is contraindicated in case of hypersensitivity to the active substance or to any of its excipients, and in case of magnetic resonance imaging (MRI) or cardioversion. Neupro<sup>®</sup> should be removed if the patient has to undergo MRI or cardioversion.

It is recommended to monitor blood pressure, especially at the beginning of treatment, due to the general risk of orthostatic hypotension associated with dopaminergic therapy.



Neupro<sup>®</sup> has been associated with somnolence episodes of sudden sleep onset episodes. Patients treated with dopamine agonists including Neupro<sup>®</sup>, have been reported as exhibiting signs of pathological gambling, increased libido and hypersexuality.

Symptoms suggestive of neuroleptic malignant syndrome have been reported with abrupt withdrawal of dopaminergic therapy. Therefore it is recommended to taper treatment.

Neupro<sup>®</sup> contains sodium metabisulphite, a sulphite that may cause allergic-type reactions including anaphylactic symptoms and life threatening or less severe asthmatic episodes in certain susceptible people.

Hallucinations have been reported, and patients should be informed that hallucinations can occur.

Cases of cardiopulmonary fibrotic complications have been reported in some patients treated with ergot-derived dopaminergic agents. Neuroleptics given as antiemetic should not be given to patients taking dopamine agonists. Ophthalmologic monitoring is recommended at regular intervals or if vision abnormalities occur.

External heat, from any source should not be applied to the area of the patch. Exposure of a skin rash or irritation to direct sunlight could lead to changes in the skin color. If a generalized skin reaction (e.g. allergic rash) associated with the use of Neupro<sup>®</sup> is observed, Neupro<sup>®</sup> should be discontinued.

Caution is advised when treating patients with severe hepatic impairment or acute worsening of renal function, a dose reduction might be needed.

The incidence of some dopaminergic adverse events, such as hallucinations, dyskinesia, and peripheral oedema generally is higher when given in combination with L-dopa. This should be considered when prescribing Neupro<sup>®</sup>.

Neupro<sup>®</sup> should not be used during pregnancy. Breast-feeding should be discontinued.

Augmentation may occur in Restless Legs Syndrome patients. Augmentation refers to the earlier onset of symptoms in the evening (or early afternoon), increase in severity of symptoms, and spread of symptoms to involve other body parts.

Adverse drug reactions reported in more than 10% of Parkinson's patients treated with Neupro<sup>®</sup> are nausea, vomiting, application site reactions, somnolence, dizziness and headache.

Adverse drug reactions reported in more than 10% of RLS patients treated with Neupro<sup>®</sup> are nausea, application site reactions, asthenic conditions and headache.

All Neupro<sup>®</sup> supply should be stored in a refrigerator. There is no need for patients to transport Neupro<sup>®</sup> patches in special containers and they must not be stored in a freezer compartment.

Please refer to the European Summary of Product Characteristics for full prescribing information (Approved 15<sup>th</sup> March 2010): <http://www.emea.europa.eu/humandocs/PDFs/EPAR/neupro/emea-combined-h626en.pdf>

### **About Neupro<sup>®</sup> in the U.S.**

Neupro<sup>®</sup> (rotigotine) is indicated in the U.S. for the treatment of the signs and symptoms of early-stage idiopathic Parkinson's disease. In April 2008, UCB recalled Neupro<sup>®</sup> from the U.S. market after ongoing monitoring revealed that specific batches of Neupro<sup>®</sup> had deviated from their approved specification. Recently the U.S. Food and Drug Administration (FDA) has recommended that UCB reformulate Neupro<sup>®</sup> patches and UCB is working on the development of a new formulation. Patients and physicians with questions about the status of Neupro<sup>®</sup>, or about UCB's Patient Access program for Neupro<sup>®</sup>, may contact UCB Medical Information at 1-866-822-0068 (option 9).

**Important Safety Information – U.S.**

Some patients treated with Neupro<sup>®</sup> reported falling asleep while engaged in activities of daily living, including operation of motor vehicles, which sometimes resulted in accidents. Some patients perceived no warning signs, such as excessive drowsiness. Hallucinations were reported in 2.0% of patients treated with Neupro<sup>®</sup> compared to 0.7% of patients on placebo. Neupro<sup>®</sup> contains metabisulfite. Neupro<sup>®</sup> should be used with caution in patients, especially those at risk for cardiovascular disease, because of the potential for symptomatic hypotension, syncope, elevated heart rate, elevated blood pressure, fluid retention, and/or weight gain. All Parkinson's disease patients are at a higher risk for melanoma and should be monitored regularly. The most commonly reported side effects in clinical trials were nausea, application site reactions, somnolence, dizziness, headache, vomiting, and insomnia. Some subjects who received Neupro<sup>®</sup> experienced a decline in blood hemoglobin levels (about 2% relative to subjects who received placebo). It is not known whether this change is readily reversible with discontinuation of Neupro<sup>®</sup>.

Neupro<sup>®</sup> is a registered trademark of the UCB Group of companies.

Neupro<sup>®</sup> is not approved or available in Argentina for the treatment of Restless Legs Syndrome.

**About UCB**

*UCB, Brussels, Belgium ([www.ucb.com](http://www.ucb.com)) is a biopharmaceutical company dedicated to the research, development and commercialization of innovative medicines with a focus on the fields of central nervous system and immunology disorders. Employing more than 9 000 people in over 40 countries, UCB produced revenue of EUR 3.1 billion in 2009. UCB is listed on Euronext Brussels (symbol: UCB).*

**Forward looking statement**

*This press release contains forward-looking statements based on current plans, estimates and beliefs of management. Such statements are subject to risks and uncertainties that may cause actual results to be materially different from those that may be implied by such forward-looking statements contained in this press release. Important factors that could result in such differences include: changes in general economic, business and competitive conditions, effects of future judicial decisions, changes in regulation, exchange rate fluctuations and hiring and retention of its employees.*