New Study Shows Effect of Neupro® (Rotigotine Transdermal System) on Cardiovascular Measures in Patients with Restless Legs Syndrome

Data Showed Reduced Nocturnal Systolic Blood Pressure Elevations and Periodic Limb Movements During Sleep in Restless Legs Syndrome (RLS) Patients

First study of its kind will be presented at the Annual Scientific Meeting of the American Society of Hypertension

Atlanta, May 17, 2013 – UCB today announced data from a double-blind, placebo-controlled study that found that Neupro® (Rotigotine Transdermal System) reduced total nocturnal systolic blood pressure (NSBP) elevations associated with periodic limb movements during sleep (PLMS) and total PLMS in patients with idiopathic moderate-to-severe Restless Legs Syndrome (RLS)/Willis-Ekbom disease.1 The data was presented at the Annual Scientific Meeting of the American Society of Hypertension, May 15-18, 2013.

The data showed that rotigotine reduces PLMS and associated total nocturnal systolic blood pressure (NSBP) elevations in patients with RLS.1 Research has found that episodic nocturnal blood pressure excursions coincide with PLMs, possibly increasing the risk of hypertension and cardiovascular disease.2

Neupro® is approved in the U.S. for the treatment of moderate-to-severe primary RLS.3 Neupro® is also approved in the European Union for the symptomatic treatment of moderate-to-severe idiopathic RLS in adults.4

“Our understanding of the extent to which RLS affects health is broadening. We are increasingly becoming aware of new organ systems that interact with this complex neurological disorder, going beyond symptoms of leg discomfort. The association of RLS with cardiovascular risk suggests that this disorder has unintended bed fellows,” said Dr. David Rye, MD, PhD, Professor of Neurology, Emory University School of Medicine. “The data demonstrate the potential impact of Neupro® upon nocturnal blood pressure elevations that coincide with periodic limb movements, a sign present in nearly all RLS patients. These findings beg for additional research into the pathophysiological underpinnings of this association and the potential new vistas it suggests into the control and treatment of both cardiovascular disease and RLS.”

RLS is an often misdiagnosed and undertreated condition that affects an estimated 23 million Americans.5 PLMS occur in up to 90% of patients with RLS, and autonomic activation, associated with PLMS, has been linked to blood pressure increases in these RLS patients.2

The study randomized 81 RLS patients (1:1) to receive an optimal dose of rotigotine (1mg/24h, 2mg/24hr, or 3mg/24hr) or placebo. Continuous beat-by-beat blood pressure and heart rate assessments were performed at baseline and at the end of 4-week maintenance. The primary outcome was a change from baseline to end of maintenance in the number of NSBP elevations associated with PLMS. Change from baseline in total NSBP elevations and PLM index (PLMI) were also assessed.1

Of the 66 RLS patients who completed the study, 37 received rotigotine and 29 received placebo. Mean (±SD) baseline PLMI was similar between rotigotine (72.9±55.6) and
placebo (69.9±47.9). Patients with PLM-associated NSBP elevations (~300 elevations at baseline) saw greater reductions with rotigotine versus placebo. Total NSBP elevations (~785 elevations) decreased more in patients using rotigotine versus placebo. Rotigotine users also experienced greater decreases from baseline to end of maintenance in PLMI versus placebo. These results indicate that rotigotine reduced PLM-associated and total NSBP elevations in patients with RLS. Adverse events were consistent with dopaminergic stimulation and transdermal application. A total of 15 patients (rotigotine: 4/40; placebo: 11/41) discontinued prematurely.¹

About Restless Legs Syndrome and PLMS

RLS is characterized by unpleasant sensations in the legs and an uncontrollable urge to move to gain relief. Most people with RLS have difficulty falling asleep and staying asleep.⁶ PLMS are described as a rhythmic extension of the big toe and dorsiflexion of the ankle, with occasional flexion at the knee and hip.² Frequent PLMS, often associated with RLS, have also been associated with cardiovascular risks, including left ventricular hypertrophy, high blood pressure and coronary artery disease.²,⁸,⁹

Patients with moderate-to-severe RLS may require long-term treatment for their RLS.⁷ While the underlying pathophysiology of RLS is not fully understood, it is thought to involve central dopamine systems. Recent neuroimaging data suggest that RLS patients may carry an abnormality in dopamine transport.⁶

About Neupro® in the U.S.
Neupro® (Rotigotine Transdermal System) is indicated for the treatment of the signs and symptoms of idiopathic Parkinson’s disease and moderate-to-severe primary Restless Legs Syndrome (RLS). For more information about Neupro visit www.neupro.com.

Neupro® in the U.S. Important Safety Information
Neupro® contains sodium metabisulfite, a sulfite that may cause allergic-type reactions including anaphylactic symptoms and life-threatening or less severe asthmatic episodes in certain susceptible people and is seen more frequently in people with asthma.

Patients treated with Neupro® have reported somnolence and falling asleep without warning signs during activities of daily living, including driving, which sometimes resulted in accidents. Some patients believed they were alert immediately prior to the event. Patients may not recognize or acknowledge increased drowsiness or sleepiness. Therefore, prescribers should directly question patients about these possible occurrences and continually reassess patients, as some events have been reported well after the start of treatment. Patients should be advised to exercise caution while driving, operating heavy machinery, or working at heights during treatment with Neupro®. If patients develop daytime sleepiness or episodes of falling asleep during activities of daily living, Neupro® should be discontinued.

There is an increased risk for hallucinations in patients with advanced-stage Parkinson’s disease treated with Neupro®. Patients also may experience new or worsening mental status and behavioral changes, which may be severe, including psychotic-like behavior during Neupro® treatment or after starting or increasing the dose of Neupro®.

Neupro® may cause symptomatic postural/orthostatic hypotension, and Parkinson’s disease patients appear to have an impaired capacity to respond to postural challenge. Both Parkinson’s and RLS patients treated with dopamine agonists require careful monitoring for signs and symptoms of postural hypotension, especially during dose escalation, and should be informed of this risk. Neupro® may also cause syncope, elevated blood pressure, elevated heart rate, weight gain, and fluid retention. Neupro® should be used with caution in patients with severe cardiovascular disease.
Case reports suggest that patients can experience intense urges to gamble, increased sexual urges, intense urges to spend money, binge eating, and other intense urges, and the inability to control these urges while taking medications, including Neupro®, that increase central dopaminergic tone and that are generally used for the treatment of Parkinson’s disease. Because patients may not recognize these behaviors as abnormal, prescribers should specifically ask patients and their caregivers about the development of new or increased urges while being treated with Neupro®. Dose reduction or discontinuation of Neupro® should be considered if such urges develop.

Neupro® may increase the dopaminergic side effects of levodopa and may cause and/or exacerbate preexisting dyskinesia.

Neupro® can cause application site reactions, and some may be severe. In clinical trials, most reactions were mild or moderate in intensity and were limited to the patch area.

Patients with Parkinson’s disease have a higher risk of developing melanoma than the general population. Patients should be monitored for melanomas frequently when using Neupro®.

Dopaminergic medicinal products, including Neupro®, may cause augmentation and rebound in RLS patients.

Neupro® should be removed before magnetic resonance imaging or cardioversion, because the aluminum backing layer in the patch could cause skin burns. Heat application has been shown to increase absorption several fold with other transdermal products. Therefore, patients should be advised to avoid exposing the application site to sources of direct heat, such as heating pads or electric blankets, heat lamps, saunas, hot tubs, heated water beds, and prolonged direct sunlight.

The most common adverse reactions (≥5% greater than placebo) for the highest recommended doses of Neupro® for treatment of Parkinson’s disease are nausea, vomiting, somnolence, application site reactions, dizziness, anorexia, hyperhidrosis, insomnia, peripheral edema, and dyskinesia. The most common adverse reactions (≥5% greater than placebo) for the highest recommended dose of Neupro® for treatment of Restless Legs Syndrome are application site reactions, nausea, somnolence, and headache.

Additional important safety information for Neupro® can be accessed at www.neupro.com/pi.

**About Neupro® in the European Union**

Neupro® (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 occur (end of dose or on-off fluctuations). Neupro® is also approved in the European Union for the symptomatic treatment of moderate to severe idiopathic Restless Legs Syndrome in adults.

**Neupro® in the European Union Important Safety Information**

Neupro® 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® should be removed if the patient has to undergo MRI or cardioversion to avoid skin burns.

It is recommended to monitor blood pressure, especially at the beginning of treatment, due to the risk of postural/orthostatic hypotension associated with dopaminergic therapy and reported during Neupro® treatment. Neupro® has been associated with somnolence and episodes of sudden sleep onset. Patients treated with dopamine agonists, including Neupro®, have been reported to exhibit behavioural symptoms of impulse control disorders such as hypersexuality, compulsive spending or
buying, increased libido, pathological gambling, punding, aggressive behaviour/aggression, binge eating and compulsive eating. Symptoms suggestive of neuroleptic malignant syndrome have been reported with abrupt withdrawal of dopaminergic therapy. Therefore it is recommended to taper treatment.

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.

Exposure of a skin rash or irritation to direct sunlight could lead to changes in the skin colour. Application site reactions lasting more than a few days, spreading outside the area of the patch, or that increase in severity should lead to risk/benefit balance re-assessment. If a generalised skin reaction (eg, allergic rash) associated with the use of Neupro® is observed, Neupro® 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®.

Neupro® 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.

Neupro® should not be used during pregnancy. Breast-feeding should be discontinued.

In restless legs syndrome augmentation may occur. Augmentation refers to the earlier onset of symptoms in the evening (or even the afternoon), increase in severity of symptoms, and spread of symptoms to involve other body parts.

At the beginning of therapy, dopaminergic adverse reactions, such as nausea and vomiting, may occur. These are usually mild or moderate in intensity and transient, even if treatment is continued.

Adverse drug reactions reported in more than 10% of Parkinson’s patients treated with Neupro® are nausea, vomiting, application site reactions, somnolence, dizziness and headache. The majority of these application site reactions are mild or moderate in intensity.

Adverse drug reactions reported in more than 10% of RLS patients treated with Neupro® are nausea, application site reactions, asthenic conditions (including fatigue, asthenia, malaise) and headache. The majority of these application site reactions are mild or moderate in intensity.


For further information
Andrea Levin, Associate Director, Public Relations and Communications, UCB
T +1.770.970.8352, andrea.levin@ucb.com
Eimear O’Brien, Director, Brand Communications, UCB
T +32.2.559.9271, eimear.obrien@ucb.com
Antje Witte, Investor Relations, UCB
T +32.2.559.9414, antje.witte@ucb.com
France Nivelle, Global Communications, UCB
T +32.2.559.9178, france.nivelle@ucb.com
Laurent Schots, Media Relations, UCB
T +32.2.559.9264, laurent.schots@ucb.com
About UCB
UCB, Brussels, Belgium (www.ucb.com) is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the immune system or of the central nervous system. With 9000 people in approximately 40 countries, the company generated revenue of EUR 3.4 billion in 2012. UCB is listed on Euronext Brussels (symbol: UCB).

Forward looking statements
This press release contains forward-looking statements based on current plans, estimates and beliefs of management. All statements, other than statements of historical fact, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial information, expected legal, political, regulatory or clinical results and other such estimates and results. By their nature, such forward-looking statements are not guarantees of future performance and are subject to risks, uncertainties and assumptions which could cause actual results to differ materially 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, the inability to obtain necessary regulatory approvals or to obtain them on acceptable terms, costs associated with research and development, changes in the prospects for products in the pipeline or under development by UCB, effects of future judicial decisions or governmental investigations, product liability claims, challenges to patent protection for products or product candidates, changes in laws or regulations, exchange rate fluctuations, changes or uncertainties in tax laws or the administration of such laws and hiring and retention of its employees. UCB is providing this information as of the date of this press release and expressly disclaims any duty to update any information contained in this press release, either to confirm the actual results or to report a change in its expectations.

There is no guarantee that new product candidates in the pipeline will progress to product approval or that new indications for existing products will be developed and approved. Products or potential products which are the subject of partnerships, joint ventures or licensing collaborations may be subject to differences between the partners. Also, UCB or others could discover safety, side effects or manufacturing problems with its products after they are marketed.

Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment and the reimbursement policies imposed by third-party payers as well as legislation affecting biopharmaceutical pricing and reimbursement.

###


