UCB Announces New Data to Increase Understanding of Short- and Long-Term Clinical Profile of Antiepileptic Drug VIMPAT® (lacosamide)

Data presented at the 66th Annual Meeting of the American Epilepsy Society

- Post hoc, population-based analysis of pivotal trials explored the efficacy of VIMPAT® relative to placebo starting from the first week of exposure.
- Pooled analysis of open-label extension studies assessed the tolerability and efficacy of VIMPAT® for a period of up to eight years among patients exposed only to approved doses.
- Pooled analysis of open-label extension studies evaluated the safety and efficacy of VIMPAT® among elderly patients.
- Exploratory Phase II study evaluated the safety of lacosamide as adjunctive therapy for patients with primary generalized tonic-clonic seizures (PGTCS). VIMPAT® is not approved for the treatment of PGTCS.

Atlanta, December 4, 2012 – UCB today announced research evaluating safety and efficacy of VIMPAT® (lacosamide) C-V in adults with partial-onset seizures (POS) and in other special populations. An additional study offered preliminary insight into the antiepileptic drug’s (AED) safety as adjunctive therapy for patients with primary generalized tonic-clonic seizures (PGTCS). These and other VIMPAT® data were presented at the 66th Annual Meeting of the American Epilepsy Society (AES) in San Diego, Calif., November 30 - December 4.

“As researchers, our commitment to ongoing clinical investigation of medicines is driven by patient needs,” said Dr. William Rosenfeld, M.D., Director, The Comprehensive Epilepsy Care Center for Children and Adults, St. Louis, Mo. “By better understanding the short-term and long-term profile of VIMPAT® in a variety of patient populations and settings, we can identify appropriate treatment options for patients with epilepsy and where further research is warranted.”

VIMPAT® is indicated as adjunctive therapy for the treatment of partial-onset seizures in adults with epilepsy (ages ≥ 17 years in the U.S., ages ≥ 16 years in the EU). VIMPAT® is not approved for the treatment of PGTCS. The most common adverse reactions reported in pivotal trials and occurring in 10 percent or more of VIMPAT®-treated patients, and greater than placebo, were dizziness, headache, nausea, and diplopia. Additional important safety information for VIMPAT® is available below.

Summary of Lacosamide Data Presented at AES:

Abstract: 1.227 Long-Term Treatment of Partial-Onset Seizures in Adults Exposed Only to Approved Lacosamide Doses: Pooled Analysis of Three Open-label Extension Studies

This sub-group analysis of pooled data from three long-term open-label extension trials studied the long-term tolerability and efficacy of adjunctive lacosamide for up to eight years. Of the 1054 patients who completed a phase II or III trial and entered the open label trials, 363 patients were treated within the approved dose range (≤400 mg/day).

Among those patients, the safety profile of lacosamide was consistent with the findings observed in the controlled clinical trials. The most commonly reported treatment-emergent
adverse events (≥10%) were dizziness (21.5%), headache (14%), and nasopharyngitis (10.7%). Lacosamide exposure was associated with a reduction in seizure frequency during the study period. Further studies are warranted.

Abstract: 3.250 Early Efficacy with Adjunctive Lacosamide Treatment in Patients with Uncontrolled Partial Seizures: Analysis of Mean Percentage of Seizure-Free Days Per Week

This post hoc analysis of pooled data from three randomized, double-blind, placebo-controlled Phase II/III trials studied lacosamide’s efficacy starting from the first week of exposure (100 mg/day). Data from 935 patients with long-standing epilepsy (mean time since diagnosis of >20 years) with a median baseline seizure frequency per 28 days of 11.5 seizures were included in the analysis. All patients in the exposure group received 100 mg/day of lacosamide during the first week, followed by weekly titration of 100 mg increments to three levels of exposure: 200 mg/day, 400 mg/day and 600mg/day. The maximum approved daily dose for lacosamide in the European Union and the U.S. is 400 mg/day.

The study results suggested a greater percentage of seizure-free days during the first week of exposure to lacosamide (all doses combined) relative to placebo. During the treatment period of the study, there was also a difference between lacosamide and placebo. Additional studies are warranted.

Abstract: 3.234 Evaluation of Long-Term Treatment with Lacosamide for Partial-Onset Seizures in the Elderly

The prevalence of new-onset seizures in the elderly is highest among any age group. As the elderly often take concomitant drugs for other chronic conditions, treatment decisions for epilepsy in this patient population can be challenging. Consequently, a sub-group analysis was performed to compare lacosamide’s safety and efficacy profile among elderly patients in three open label trials with the overall patient population. Across three open-label extension trials, which assessed lacosamide exposure for up to eight years, 33 patients were ≥ 65 years of age by study end. The median modal dose of lacosamide in this group was 400 mg/day for a mean duration of 1,563.2 days up to a maximum duration of 2,790 days (~7.6 years). Among these patients, the safety and efficacy profile of lacosamide was consistent with the findings observed in the total population of 1,054 patients who initiated open-label lacosamide treatment. Treatment with lacosamide was associated with a reduction in seizure frequency during the study period.

The most commonly reported treatment-emergent adverse events (≥15%) were dizziness (36.4%), fall (27.3%), contusion or sinusitis (21.2% each), cognitive disorder, tremor, headache, depression or cough (18.2% each), and urinary tract infection, nausea, diplopia, vision blurred, convulsion, balance disorder, or pain in extremity (15.2% each).

Prospective evaluations still need to be conducted.

Abstract 1.228 Open-Label Pilot Study of Adjunctive Lacosamide for Uncontrolled Primary Generalized Tonic-Clonic Seizures

This Phase II multicenter open-label pilot study is the first assessment of the safety of adjunctive lacosamide for uncontrolled PGTCS in adults with idiopathic generalized epilepsy.
The 13-week study included a total of 49 patients, the majority (69.4%) of whom were taking two to three concomitant AEDs at baseline. Lacosamide dose titration started at 100 mg/day (50mg bid) and increased weekly to a maximum of 400 mg/day.

**VIMPAT®** is not approved for the treatment of PGTCS. For more information about this study, please consult the abstract.

**For Further Information**
Andrea Levin, Associate Director, U.S. Communications and Public Relations
770.970.8352, Andrea.Levin@ucb.com

Amy Condon, Cooney/Waters Group
212.886.2212, ACondon@cooneywaters.com

**About Epilepsy**
Epilepsy is a chronic neurological disorder affecting approximately 65 million people worldwide and 2.2 million people in the U.S.—making it more common than autism, cerebral palsy, multiple sclerosis and Parkinson’s disease combined. Anyone can develop epilepsy; it occurs across all ages, races and genders and is defined as two or more unprovoked seizures. More than 1 million patients in the U.S. continue to have seizures despite initial therapy.3,6

**About VIMPAT®**
VIMPAT® tablets and injection were launched in the U.S. in May 2009 as an add-on therapy for the treatment of partial-onset seizures in people with epilepsy who are aged 17 years and older. VIMPAT® injection is a short-term replacement when oral administration is not feasible in these patients. VIMPAT® oral solution was launched in June 2010. The availability of the oral tablets, oral solution, and intravenous (IV) injection allows for consistent treatment in a hospital setting. The most common adverse reactions occurring in greater than or equal to 10 percent of VIMPAT®-treated patients, and greater than placebo, were dizziness, headache, nausea, and diplopia.

In the European Union, VIMPAT® (film-coated tablets, syrup and solution for infusion) is approved as adjunctive therapy for the treatment of partial-onset seizures with or without secondary generalization in adult and adolescent (16-18 years) patients with epilepsy. VIMPAT® solution for infusion may be used when oral administration is temporarily not feasible.

The maximum approved daily dose for VIMPAT® in the European Union and the U.S. is 400 mg/day.

**Important safety information about VIMPAT® in the U.S.**

**Warnings and Precautions**
Antiepileptic drugs (AEDs), including VIMPAT®, increase the risk of suicidal behavior and ideation. Patients taking VIMPAT® should be monitored for the emergence or worsening of depression, suicidal thoughts or behavior, and/or any unusual changes in mood or behavior. Patients and caregivers should also be advised to be alert for these behavioral changes and to immediately report them to the healthcare provider.
Patients should be advised that VIMPAT® may cause dizziness and ataxia. Therefore patients should not drive a car or operate complex machinery until they are familiar with the effects of VIMPAT® on their ability to perform such activities.

Dose-dependent PR interval prolongation has been observed in VIMPAT® clinical studies in patients and in healthy volunteers. When VIMPAT® is given with other drugs that prolong the PR interval, further PR prolongation is possible. Patients should be made aware of the symptoms of second-degree or higher AV block (e.g. slow or irregular pulse, feeling of lightheadedness and fainting) and told to contact their physician should any of these occur. VIMPAT® should be used with caution in patients with known cardiac conduction problems or with severe cardiac disease. In such patients, obtaining an ECG before beginning VIMPAT®, and after VIMPAT® is titrated to steady state, is recommended.

VIMPAT® administration may predispose to atrial arrhythmias (atrial fibrillation or flutter), especially in patients with diabetic neuropathy and/or cardiovascular disease. Patients should be made aware of the symptoms of atrial fibrillation and flutter (e.g. palpitations, rapid pulse, shortness of breath) and told to contact their physician should these symptoms occur.

Patients should be advised that VIMPAT® may cause syncope.

VIMPAT® should be gradually withdrawn (over a minimum of 1 week) to minimize the potential of increased seizure frequency.

Multiorgan hypersensitivity reactions have been reported with antiepileptic drugs. If this reaction is suspected, VIMPAT® should be discontinued.

VIMPAT® oral solution contains aspartame, a source of phenylalanine. A 200 mg dose of VIMPAT® oral solution (equivalent to 20 mL) contains 0.32 mg of phenylalanine.

**Common Adverse Reactions**

In clinical trials, the most frequently seen adverse reaction with VIMPAT® was dizziness (31% vs 8% placebo). Other common adverse reactions occurring in ≥10 percent of VIMPAT®-treated patients, and greater than placebo, were headache, nausea, and diplopia.

VIMPAT® is a Schedule V controlled substance.

Dosage adjustments are recommended for patients with mild or moderate hepatic impairment or severe renal impairment. Use in severe hepatic impairment patients is not recommended. Dose titration should be performed with caution in all renally impaired patients.

In clinical trials, adverse reactions with intravenous administration generally appeared similar to those observed with the oral formulation, although intravenous administration was associated with local adverse events such as injection site pain or discomfort (2.5%), irritation (1%), and erythema (0.5%).


For more information on VIMPAT®, visit www.Vimpat.com or contact UCB at 800.477.7877.
VIMPAT® (C-V) is a Schedule V controlled substance.
VIMPAT® is a registered trademark used under license from Harris FRC Corporation.

**Important safety information about VIMPAT® in the EU and EEA**

VIMPAT® (lacosamide) is indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalization in adult and adolescent (16-18 years) patients with epilepsy. VIMPAT® solution for infusion is an alternative for patients when oral administration is temporarily not feasible. Contraindications: Hypersensitivity to the active substance or any of the excipients; known second- or third-degree atrioventricular (AV) block. Special warnings and precautions for use: Treatment with VIMPAT® has been associated with dizziness which could increase the occurrence of accidental injury or falls. Therefore, patients should be advised to exercise caution until they are familiar with the potential effects of the medicine. Prolongations in PR interval with VIMPAT® have been observed in clinical studies. Cases with second- and third-degree AV block associated with VIMPAT® treatment have been reported in post-marketing experience. VIMPAT® should be used with caution in patients with known conduction problems or severe cardiac disease such as a history of myocardial infarction or heart failure. Caution should especially be exerted when treating elderly patients as they may be at an increased risk of cardiac disorders or when VIMPAT® is used in combination with products known to be associated with PR prolongation. In the placebo-controlled trials of VIMPAT® in epilepsy patients, atrial fibrillation or flutter were not reported; however both have been reported in open-label epilepsy trials and in post-marketing experience. Patients should be made aware of the symptoms of second-degree or higher AV block (e.g. slow or irregular pulse, feeling of lightheaded and fainting) and of the symptoms of atrial fibrillation and flutter (e.g. palpitations, rapid or irregular pulse, shortness of breath). Patients should be counselled to seek medical advice should any of these symptoms occur. Suicidal ideation and behavior have been reported in patients treated with anti-epileptic agents in several indications. Therefore patients should be monitored for signs of suicidal ideation and behaviors and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behavior emerge.

VIMPAT® syrup contains sodium methyl parahydroxybenzoate (E219) which may cause allergic reactions (possibly delayed). It contains 3.7 g sorbitol (E420) per dose (200 mg lacosamide), corresponding to a calorific value of 9.7 kcal. Patients with rare hereditary problems of fructose intolerance should not take this medicine. The syrup contains aspartame (E951), a source of phenylalanine, which may be harmful for people with phenylketonuria. It contains 1.24 mmol (or 28.36 mg) sodium per dose (200 mg lacosamide). VIMPAT® syrup and the solution for infusion contain sodium, which should be taken into consideration for patients on a controlled sodium diet. Effects on ability to drive and use machines: VIMPAT® may have minor to moderate influence on the ability to drive and use machines. VIMPAT® treatment has been associated with dizziness or blurred vision. Accordingly patients should be advised not to drive a car or to operate other potentially hazardous machinery until they are familiar with the effects of VIMPAT® on their ability to perform such activities. Undesirable effects: The most common adverse reactions (≥10%) are dizziness, headache, diplopia, and nausea. They were usually mild to moderate in intensity. Some were dose-related and could be alleviated by reducing the dose. Incidence and severity of CNS and gastrointestinal (GI) adverse reactions usually decreased over time. Other common adverse reactions (≥1% - <10%) are depression, confusional state, insomnia, balance disorder, coordination abnormal, memory impairment, cognitive disorder, somnolence, tremor, nystagmus, hypoesthesia, dysarthria, disturbance in attention, vision
blurred, vertigo, tinnitus, vomiting, constipation, flatulence, dyspepsia, dry mouth, pruritus, rash, muscle spasms, gait disturbance, asthenia, fatigue, irritability, injection site pain or discomfort (specific to solution for infusion), fall, and skin laceration. The use of VIMPAT® is associated with dose-related increase in the PR interval. Adverse reactions associated with PR interval prolongation (e.g. atrioventricular block, syncope, bradycardia) may occur. Laboratory abnormalities: Abnormalities in liver function tests have been observed in controlled trials with VIMPAT® in adult patients with partial-onset seizures who were taking 1-3 concomitant antiepileptic drugs. Elevations of ALT to ≥3XULN occurred in 0.7% (7/935) of VIMPAT® patients and 0% (0/356) of placebo patients. Multiorgan Hypersensitivity Reactions: Multiorgan hypersensitivity reactions have been reported in patients treated with some antiepileptic agents. These reactions are variable in expression but typically present with fever and rash and can be associated with involvement of different organ systems. Potential cases have been reported rarely with VIMPAT® and if multiorgan hypersensitivity reaction is suspected, VIMPAT® should be discontinued.

Refer to the European Summary of Product Characteristics for other adverse reactions and full prescribing information. Date of revision: 24th October 2012.


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 more than 8,500 people in about 40 countries, the company generated revenue of EUR 3.2 billion in 2011. 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.

**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.

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**References**


