



## UCB files VIMPAT<sup>®</sup> (lacosamide) in the US as monotherapy treatment in adult epilepsy patients with partial-onset seizures

- Results from VIMPAT<sup>®</sup> (lacosamide) monotherapy study supporting this filing to be presented at AES 2013

**Brussels (Belgium), November 4<sup>th</sup>, 2013 – 0700 (CEST)** – UCB announced that the US Food and Drug Administration (FDA) has accepted for filing a supplemental new drug application (sNDA) for VIMPAT<sup>®</sup> (lacosamide) C-V as monotherapy in the treatment of partial-onset seizures in patients with epilepsy aged 17 years and older. Investigational data from the phase 3 lacosamide conversion to monotherapy study in adults with partial-onset seizures that support the US filing will be presented by leading clinical researchers at the Annual Meeting of the American Epilepsy Society in Washington DC (6-10 December 2013).<sup>1</sup>

In the US, VIMPAT<sup>®</sup> is approved as adjunctive therapy for the treatment of partial-onset seizures in patients with epilepsy aged 17 years and older. The most common adverse reactions reported in pivotal trials and occurring in 10 percent or more of VIMPAT<sup>®</sup>-treated patients, and greater than placebo, were dizziness, headache, nausea and diplopia. Additional important safety information for VIMPAT<sup>®</sup> in the US is available below. Lacosamide is not currently approved as monotherapy.<sup>2</sup>

“UCB has a strong heritage in epilepsy. The US filing for lacosamide in monotherapy is another important step forward for people living with epilepsy. It underscores our commitment to the treatment of epilepsy and to make lacosamide available to more patients.” said Professor Dr. Iris Loew-Friedrich, Chief Medical Officer and Executive Vice President, UCB.

“The Phase 3, historical-controlled study to be presented at AES 2013 was conducted to assess the efficacy and safety of conversion to lacosamide monotherapy in adult patients continuing to experience partial-onset seizures while taking one to two other anti-epileptic drugs. Results from the study offer important insights and an understanding of the response to lacosamide monotherapy in this patient population.” said Robert T. Wechsler, MD, PhD, FAAN, Medical Director of the Idaho Comprehensive Epilepsy Centre in Boise, Idaho, US.

Data to be presented at AES show that the study met its primary endpoint demonstrating that the predicted exit rate for patients converting to lacosamide 400mg/day (0.300:95% confidence interval [0.246, 0.355]) was significantly lower than the historical control exit rate, used as a comparator (0.653). In the study, a lacosamide 300mg/day arm was added to blind the treatment group and to ensure a study design consistent with the historical control studies. The most common treatment-emergent adverse events reported for lacosamide (300 mg/day and 400 mg/day) were dizziness, nausea and headache.<sup>1</sup> These adverse events were generally similar to those attributed to lacosamide in placebo-controlled adjunctive studies.

Secondary endpoints from the study included both clinician- and patient-reported outcomes including an evaluation of Clinical Global Impression of Change and Patient Global Impression of Change.<sup>1</sup>

### **VIMPAT® in the European Union**

In the European Union, VIMPAT® 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.<sup>3</sup> A non-inferiority monotherapy study is underway to support the potential monotherapy filing with the European Medicines Agency. The study aims to compare the efficacy and safety of lacosamide to carbamazepine controlled-release as monotherapy in newly or recently newly diagnosed patients.<sup>4</sup> Topline results from this study are expected in Q4 2014.

### **Notes to editors**

#### **About the Phase 3 conversion to lacosamide monotherapy study<sup>1,5</sup>**

The Phase 3 study was an international, historical-controlled, multicenter, double-blind, randomized trial evaluating lacosamide (400mg/day) for conversion to monotherapy in 425 patients, aged 16-70 years with partial-onset seizures taking one to two other AEDs. Patients experiencing  $\geq 2$  to  $\leq 40$  partial-onset seizures per 28 days during the 8-week baseline period were randomized 3:1 to lacosamide 400 mg/day or 300 mg/day. During the 3-week titration period, lacosamide was initiated at 200mg/day and increased at 100 mg/day weekly increments, with no dose reductions allowed, to the randomized dose. The maintenance phase included a 6-week period during which previous AEDs were sequentially withdrawn, followed by a 10-week lacosamide monotherapy period. The most common background AEDs for the 300 mg/day and 400 mg/day groups, respectively, were levetiracetam (22.2%, 22.9%), carbamazepine (18.2%, 20.1%) and lamotrigine (14.1%, 15.1%).

Patients were evaluated from the first day of tapering of the background AEDs and required to discontinue the study if they experienced any of the protocol exit events defined by an increase in seizure frequency, duration or severity. The primary efficacy endpoint of the study was the percentage of patients who met at least one of the pre-defined exit criteria by Day 112 relative to the start of withdrawal of background antiepileptic drugs compared with the historical control exit rate.

## About Epilepsy

Epilepsy is a chronic neurological disorder affecting approximately 65 million people worldwide and 3 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.<sup>6,7,8</sup>

## About VIMPAT<sup>®</sup>

VIMPAT<sup>®</sup> 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<sup>®</sup> injection is a short-term replacement when oral administration is not feasible in these patients. VIMPAT<sup>®</sup> oral solution was launched in June 2010. The availability of the oral tablets, oral solution, and intravenous (IV) injection formulations permits flexibility in administration. Important safety information about VIMPAT<sup>®</sup> in the US is available below.<sup>2</sup>

In the European Union, VIMPAT<sup>®</sup> (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.<sup>3</sup>

## Important Safety Information about VIMPAT<sup>®</sup> in the U.S.

### Warnings and Precautions

Antiepileptic drugs (AEDs), including VIMPAT<sup>®</sup>, increase the risk of suicidal behavior and ideation. Patients taking VIMPAT<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup> on their ability to perform such activities.

Dose-dependent PR interval prolongation has been observed in VIMPAT<sup>®</sup> clinical studies in patients and in healthy volunteers. When VIMPAT<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup>, and after VIMPAT<sup>®</sup> is titrated to steady state, is recommended.

VIMPAT<sup>®</sup> 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<sup>®</sup> may cause syncope.

VIMPAT<sup>®</sup> 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<sup>®</sup> should be discontinued.

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

VIMPAT<sup>®</sup> (C-V) is a Schedule V controlled substance.

### **Common Adverse Reactions**

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

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 full prescribing information on VIMPAT<sup>®</sup>, visit [http://www.vimpat.com/PDF/vimpat\\_PI.pdf](http://www.vimpat.com/PDF/vimpat_PI.pdf)

(Accessed 30th September, 2013).

For more information on VIMPAT<sup>®</sup>, <http://www.vimpat.com/> or contact UCB at 800.477.7877.

VIMPAT<sup>®</sup> is a registered trademark used under license from Harris FRC Corporation.

### **Important Safety Information about VIMPAT<sup>®</sup> in the EU and EEA**

VIMPAT<sup>®</sup> (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<sup>®</sup> therapy can be initiated with either oral or IV administration. A loading dose may be initiated in patients in situations when the physician determines that rapid attainment of lacosamide steady state plasma concentration and therapeutic effect is warranted. It should be administered under medical supervision with consideration of the potential for increased incidence of CNS adverse reactions. Administration of a loading dose has not been studied in acute conditions such as status epilepticus. 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<sup>®</sup> 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<sup>®</sup> have been observed in clinical studies. Cases with second- and third-degree AV block associated with VIMPAT<sup>®</sup> treatment have been reported in post-marketing experience. VIMPAT<sup>®</sup> 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<sup>®</sup> is used in combination with products known to be associated with PR prolongation. In the placebo-controlled trials of VIMPAT<sup>®</sup> 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<sup>®</sup> 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. VIMPAT<sup>®</sup> 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<sup>®</sup> may have minor to moderate influence on the ability to drive and use machines. VIMPAT<sup>®</sup> 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<sup>®</sup> on their ability to perform such activities. Undesirable effects: The most common adverse reactions ( $\geq 10\%$ ) 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. Incidence of CNS adverse reactions such as dizziness may be higher after a loading dose. Other common adverse reactions ( $\geq 1\%$  -  $< 10\%$ ) 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), irritation (specific to solution for infusion), fall, and skin laceration. The use of VIMPAT<sup>®</sup> 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<sup>®</sup> in adult patients with partial-onset seizures who were taking 1-3 concomitant antiepileptic drugs. Elevations of ALT to  $\geq 3 \times \text{ULN}$  occurred in 0.7% (7/935) of VIMPAT<sup>®</sup> 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<sup>®</sup> and if multiorgan hypersensitivity reaction is suspected, VIMPAT<sup>®</sup> should be discontinued.

Refer to the European Summary of Product Characteristics for other adverse reactions and full prescribing information. Date of revision: 31<sup>st</sup> July 2013.

[http://www.ema.europa.eu/docs/en\\_GB/document\\_library/EPAR -  
\\_Product\\_Information/human/000863/WC500050338.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000863/WC500050338.pdf) (Accessed 30th September 2013)

#### For further information

- Eimear O'Brien, Global Brand Communications  
T +32.2.559.9271, eimear.obrien@ucb.com
- Andrea Levin, Associate Director, US Communications and Public Relations  
T +1.770.970.8352, andrea.levin@ucb.com  
Antje Witte, Investor Relations UCB  
T +32.2.559.9414, antje.witte@ucb.com
- Alexandra Deschner, Investor Relations, UCB  
T +32 2 559 9683, alexandra.deschner@ucb.com
- France Nivelles, Global Communications UCB  
T +32.2.559.9178, france.nivelles@ucb.com
- Laurent Schots, Media Relations, UCB  
T +32.2.559.9264, laurent.schots@ucb.com

#### References

1. Wechsler R *et al.* Lacosamide conversion to monotherapy for the treatment of partial-onset seizures: results from a historical controlled, multicenter, double-blind, randomized trial. 67th Annual Meeting of the American Epilepsy Society (AES), December 6-10, 2013, Washington, U.S.
2. VIMPAT<sup>®</sup> US Prescribing Information. Accessed 12th October 2013 from [http://www.vimpat.com/PDF/vimpat\\_PI.pdf](http://www.vimpat.com/PDF/vimpat_PI.pdf)
3. VIMPAT<sup>®</sup> EU Summary of Product Characteristics. Accessed 12th October 2013 from [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/EPAR -  
\\_Product\\_Information/human/000863/WC500050338.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000863/WC500050338.pdf)
4. ClinicalTrials.gov. Accessed 12th October 2013 from <http://clinicaltrials.gov/ct2/show/NCT01243177?term=Vimpat+Monotherapy&rank=2>
5. ClinicalTrials.gov. Accessed 12th October 2013 from <http://clinicaltrials.gov/ct2/show/NCT00520741?term=Vimpat+Monotherapy&rank=4>
6. The Epilepsy Foundation of America Accessed 12th October 2013 from <http://www.epilepsyfoundation.org/aboutepilepsy/whatisepilepsy/statistics.cfm>
7. Epilepsy Foundation. About Epilepsy. Accessed 12th October 2013 from <http://www.epilepsyfoundation.org/aboutepilepsy/>
8. NINDS/NIH. Seizures and Epilepsy. Accessed 12th October 2013 from [http://www.ninds.nih.gov/disorders/epilepsy/detail\\_epilepsy.htm#196923109](http://www.ninds.nih.gov/disorders/epilepsy/detail_epilepsy.htm#196923109)

#### About UCB

UCB, Brussels, Belgium ([www.ucb.com](http://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 3.46 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.