UCB News

UCB reinforces its leadership in epilepsy at the 2014 Annual Meeting of the American Epilepsy Society (AES)

- 24 UCB-sponsored presentations including new data on VIMPAT® (lacosamide)
- First presentation of primary data from the latest Phase 3 study evaluating the Company's investigational medicine brivaracetam as adjunctive treatment of partial-onset seizures in adults with epilepsy

Brussels (Belgium), 3rd December 2014 – 0700 (CET) – UCB, a global biopharmaceutical company with a focus on epilepsy treatment and research, announced today that there will be 24 UCB-sponsored presentations at the 68th Annual Meeting of the American Epilepsy Society (AES) in Seattle, Washington, US, (December 5th – 9th, 2014).

Presentations will include 12 scientific posters on UCB's marketed product VIMPAT® (lacosamide) CV, including new post-hoc analyses from the conversion to lacosamide monotherapy study that was published earlier this year.[1] In addition, an accepted late-breaking abstract will share primary data from the most recent Phase 3 study evaluating the investigational medicine brivaracetam as adjunctive treatment of partial-onset seizures in adults with epilepsy.

"UCB has a rich heritage in epilepsy with over 20 years of experience in the research and development of antiepileptic drugs [AEDs]. Data to be presented at this year's AES highlight the role of UCB's approved AEDs, as well as our dedication to investigational medicines for the future," said Professor Dr. Iris Loew Friedrich, Chief Medical Officer and Executive Vice President, UCB. "In addition, our goal is to address unmet medical needs and to contribute to advances in the understanding of epilepsy. Together with our partners, we are very pleased to share a number of abstracts reporting data from surveys and studies offering new insights on epilepsy care."

In the US, VIMPAT® is indicated as monotherapy or adjunctive therapy in the treatment of partial-onset seizures in people with epilepsy aged 17 years and older.[2] In the European Union, VIMPAT® is indicated 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.[3] In placebo-controlled

adjunctive trials the most common adverse reactions reported and occurring in 10 percent or more of VIMPAT®-treated patients, and greater than placebo, were dizziness, headache, nausea, and diplopia.[2,3] In the monotherapy clinical trial, adverse reactions were generally similar to those observed and attributed to drug in adjunctive placebo controlled trials, with the exception of insomnia (observed at a higher rate of ≥2%).[2] Important safety information for VIMPAT® is available below.

Brivaracetam is an investigational medicine for the adjunctive treatment of partial-onset seizures in adults with epilepsy and is not approved by any regulatory authority worldwide.

Following is a guide to UCB-sponsored data presentations at the 68th Annual Meeting of the AES, being held December 5th – 9th, 2014:

Lacosamide:

1. **[3.292]: Conversion to lacosamide monotherapy: post-hoc analysis on responder and seizure freedom rates**
   Ryvlin P, *et al.*
   - Date/Time: Monday December 8th; 8.00-15.00
   - Session Info: Poster session 3, Exhibit Hall 4B

2. **[3.291]: Focal seizure frequency by study phase and seizure type in conversion to lacosamide monotherapy study: a post-hoc analysis**
   Stern J, *et al.*
   - Date/Time: Monday December 8th; 8.00-15.00
   - Session Info: Poster session 3, Exhibit Hall 4B

3. **[3.299]: Tolerability of lacosamide 200 mg/day starting dose: post-hoc analysis of conversion to lacosamide monotherapy study**
   Werhahn K, *et al.*
   - Date/Time: Monday December 8th; 8.00-15.00
   - Session Info: Poster session 3, Exhibit Hall 4B

4. **[2.320]: Randomized crossover study comparing neuropsychological effects of lacosamide versus carbamazepine immediate release in healthy subjects**
   Meador K, *et al.*
   - Date/Time: Sunday December 7th; 8.00-18.00
   - Session Info: Poster session 2, Exhibit Hall 4B

5. **[3.293]: Lacosamide added to a baseline monotherapy in patients with partial-onset seizures (POS): efficacy and safety across center types in the VITOBA study**
   Brandt C, *et al.*
   - Date/Time: Monday December 8th; 8.00-15.00
   - Session Info: Poster session 3, Exhibit Hall 4B

6. **[3.297]: Lacosamide added to an existing monotherapy in epilepsy patients with partial-onset seizures: a subgroup analysis of the elderly population in the VITOBA study (VImpat added To One Baseline AED)**
   Runge U, *et al.*
   - Date/Time: Monday December 8th; 8.00-15.00
   - Session Info: Poster session 3, Exhibit Hall 4B

7. **[2.297]: Lacosamide monotherapy treatment pathways in epilepsy patients in a US managed care population**
   Durgin TL, *et al.*
   - Date/Time: Sunday December 7th; 8.00-18.00
   - Session Info: Poster session 2, Exhibit Hall 4B

8. **[3.298]: An open-label trial evaluating the efficacy and safety of lacosamide as first add-on treatment of partial-onset seizures**
   Tzvetanov P, *et al.*
   - Date/Time: Monday December 8th; 8.00-15.00
   - Session Info: Poster session 3, Exhibit Hall 4B

9. **[3.290]: Immediate steady state concentrations in plasma after oral or intravenous lacosamide loading dose**
   Cawello W, *et al.*
   - Date/Time: Monday December 8th; 8.00-15.00
   - Session Info: Poster session 3, Exhibit Hall 4B

10. **[2.283]: High predictability of plasma lacosamide and no differences by different age and gender through normalization processes**
    Schaefer C, *et al.*
    - Date/Time: Sunday December 7th; 8.00-18.00
    - Session Info: Poster session 2, Exhibit Hall 4B

11. **[3.295]: Efficacy and safety of lacosamide as adjunctive treatment for partial-onset seizures in Hispanic/Latino patients from Mexico: post hoc analysis of an open-label trial**
    Ceja Moreno H, *et al.*
    - Date/Time: Monday December 8th; 8.00-15.00
    - Session Info: Poster session 3, Exhibit Hall 4B

12. **[3.294]: Safety and tolerability of lacosamide monotherapy in elderly: a subgroup analysis from lacosamide trials in diabetic neuropathic pain***
    Sirven J, *et al.*
    - Date/Time: Monday December 8th; 8.00-15.00
    - Session Info: Poster session 3, Exhibit Hall 4B

**VIMPAT® (lacosamide) is not approved for the treatment of diabetic neuropathic pain*

Brivaracetam:

13. **[2.417]: A randomized, double-blind, placebo-controlled, multicenter, parallel-group study to evaluate the efficacy and safety of brivaracetam in adult patients with partial-onset seizures**
    Klein P, *et al.*
    - Date/Time: Sunday December 7th; 8.00-17.00
    - Session Info: Poster session 2, Exhibit Hall 4B

14. **[3.300]: Reduction of treatment-limiting non-psychotic behavioral adverse events associated with levetiracetam: an open-label, prospective study of patients with epilepsy switching from levetiracetam to brivaracetam treatment**
    Yates S, *et al.*
    - Date/Time: Monday December 8th; 8.00-15.00
    - Session Info: Poster session 3, Exhibit Hall 4B

15. **[2.332]: Brivaracetam achieves brain SV2A occupancy faster than levetiracetam**
    Mercier J, *et al.*
    - Date/Time: Sunday December 7th; 8.00-18.00
    - Session Info: Poster session 2, Exhibit Hall 4B

16. **[1.298]: Consistent seizure suppression by brivaracetam in animal models of partial epilepsy includes protection against pilocarpine- and kainic acid induced partial seizures in rats**
    Matagne A, *et al.*
    - Date/Time: Saturday December 6th; 12.00-18.00
    - Session Info: Poster session 1, Exhibit Hall 4B

17. **[2.307]: Interaction study between brivaracetam and ethanol in healthy subjects**
    Stockis A, *et al.*
    - Date/Time: Sunday December 7th; 8.00-18.00
    - Session Info: Poster session 2, Exhibit Hall 4B

18. **[2.310]: In vitro pharmacokinetic profile of brivaracetam reveals low risk of drug-drug interaction and unrestricted brain permeability**
    Chanteux H, *et al.*
    - Date/Time: Sunday December 7th; 8.00-18.00
      Session Info: Poster session 2, Exhibit Hall 4B

Levetiracetam:

19. **[2.277]: Safety of levetiracetam among infants younger than 12 months – results from a European multicenter observational study**
    Arzimanoglou A, *et al.*
    - Date/Time: Sunday December 7th; 8.00-18.00
    - Session Info: Poster session 2, Exhibit Hall 4B

Epilepsy:

20. **[3.130]: A study of epilepsy prevalence and incidence in the US using administrative claims data**
    Helmers S, *et al.*
    - Date/Time: Monday December 8th; 8.00-15.00
    - Session Info: Poster session 3, Exhibit Hall 4B

21. **[2.047]: Improving the standard of care for patients with epilepsy: factors influencing hospitalization rates**
    Begley C, *et al.*
    - Date/Time: Sunday December 7th; 8.00-18.00
    - Session Info: Poster session 2, Exhibit Hall 4B

22. **[2.033]: Antiepileptic drug therapy and model predictions of treatment success**
    Dilley C, *et al.*
    - Date/Time: Sunday December 7th; 8.00-18.00
    - Session Info: Poster session 2, Exhibit Hall 4B

23. **[2.031]: Survey of online patient communities to analyze perceptions of healthcare value**
    Cohen G, *et al.*
    - Date/Time: Sunday December 7th; 8.00-18.00
    - Session Info: Poster session 2, Exhibit Hall 4B

24. **[2.058]: The POEM Study: patient usage and satisfaction with an online health management platform for epilepsy**
    Hixson, J, *et al.*
    - Date/Time: Sunday December 7th; 8.00-18.00
    - Session Info: Poster session 2, Exhibit Hall 4B

About Epilepsy[4-6]

Epilepsy is a chronic neurological disorder affecting approximately 65 million people worldwide and more than 2 million people in the US. It is the fourth most common neurological disorder in the US. Although epilepsy may be linked to factors such as health conditions, race and age, it can develop in anyone at any age. In the US, approximately 1 in 26 people will develop epilepsy in their lifetime.

Epilepsy is considered to be a disease of the brain defined by any of the following conditions: (1) at least two unprovoked (or reflex) seizures occurring >24 hours apart; (2) one unprovoked (or reflex) seizure and a probability of further seizures similar to the general recurrence risk (at least 60%) after two unprovoked seizures, occurring over the next 10 years; (3) diagnosis of an epilepsy syndrome.

About VIMPAT®[2,3]

VIMPAT® is approved in the US as tablets, injection and oral solution as monotherapy or adjunctive therapy in the treatment of partial-onset seizures in people with epilepsy ages 17 years and older. VIMPAT® injection is a short-term replacement when oral administration is not feasible in these patients. The availability of the oral tablets, oral solution, and intravenous (IV) injection formulations permits flexibility in administration.

A single loading dose (200 mg) administration option is also approved in the U.S. for all formulations of VIMPAT® when used as monotherapy or adjunctive therapy in the treatment of partial-onset seizures in patients with epilepsy aged 17 years and older.

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® is also approved in the European Union for initiation as a single loading dose of 200 mg, followed approximately 12 hours later by a 100 mg twice-daily maintenance dose regimen.

Important safety information about VIMPAT® in the US and the European Union is available below.

IMPORTANT SAFETY INFORMATION ABOUT VIMPAT® IN THE US[2]

Warnings and Precautions

- **Suicidal Behavior and Ideation**: 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.
- **Dizziness and Ataxia**: VIMPAT® may cause dizziness and ataxia. Accordingly, patients should be advised not to drive a car or to operate other complex machinery until they are familiar with the effects of VIMPAT® on their ability to perform such activities.
- **Cardiac Rhythm and Conduction Abnormalities**:

  PR interval prolongation

  Dose-dependent prolongations in PR interval with VIMPAT® have been observed in clinical studies in patients and in healthy volunteers. Second degree and complete AV block have been reported in patients in pain studies and in patients with seizures. When VIMPAT® is given with other drugs that prolong the PR interval, further PR prolongation is possible.

  VIMPAT® should be used with caution in patients with known cardiac conduction problems (e.g., marked first-degree AV block, second-degree or higher AV block and sick sinus syndrome without pacemaker), sodium channelopathies (e.g., Brugada Syndrome), or with severe cardiac disease such as myocardial ischemia or heart failure, or structural heart disease. VIMPAT® should be used with caution in patients on concomitant medications that prolong PR interval, because of a risk of AV block or bradycardia, e.g., beta-blockers and calcium channel blockers. In such patients, obtaining an ECG before beginning VIMPAT®, and after VIMPAT® is titrated to steady-state, is recommended. In addition, these patients should be closely monitored if they are administered VIMPAT® through the intravenous route.

  Atrial fibrillation and Atrial flutter

  VIMPAT® administration may predispose to atrial arrhythmias (atrial fibrillation or flutter), especially in patients with diabetic neuropathy and/or cardiovascular disease.
- **Syncope**: Patients should be advised that VIMPAT® may cause syncope.
- **Withdrawal of Antiepileptic Drugs**: VIMPAT® should be gradually withdrawn (over a minimum of 1 week) to minimize the potential of increased seizure frequency.
- **Multiorgan Hypersensitivity Reactions**: Multiorgan hypersensitivity reactions (also known as Drug Reaction with Eosinophilia and Systemic Symptoms, or DRESS) have been reported with antiepileptic drugs. If this reaction is suspected, VIMPAT® should be discontinued and alternative treatment started.
- **Phenylketonurics**: 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.

Adverse Reactions

- **Adjunctive therapy**: In the placebo controlled 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.

- **Monotherapy :** In the clinical trial, adverse reactions were generally similar to those observed and attributed to drug in adjunctive placebo controlled trials, with the exception of insomnia (observed at a higher rate of ≥2%).
- **Injection**: In adjunctive therapy clinical trials, adverse reactions with intravenous administration generally were 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%). When administering a loading dose, the incidence of CNS adverse reactions, such as dizziness, somnolence, and paresthesia may be higher with 15-minute administration than over a 30-to 60-minute period.

Dosing Considerations

The loading dose should be administered with medical supervision considering the VIMPAT® pharmacokinetics and increased incidence of CNS adverse reactions.

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

VIMPAT® is a Schedule V controlled substance.

Please refer to full Prescribing Information provided by the sales representative and visit www.VIMPAT.com/hcp

For more information on VIMPAT® contact 844-599-CARE (2273).

VIMPAT® is a registered trademark used under license from Harris FRC Corporation.

IMPORTANT SAFETY INFORMATION ABOUT VIMPAT® IN THE EU AND EEA[3]

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® therapy can be initiated with either oral or IV administration. A single 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® 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 counseled to seek medical advice should any of these symptoms occur. Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic agents in several indications. Therefore patients should be monitored for signs of suicidal ideation and behaviours and appropriate treatment should be considered. Patients (and caregivers of patients) should be advised to seek medical advice should signs of suicidal ideation or behaviour 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. 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. Incidence of CNS adverse reactions such as dizziness may be higher after a loading dose. 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, paraesthesia, vision blurred, vertigo, tinnitus, vomiting, constipation, flatulence, dyspepsia, dry mouth, diarrhoea, pruritus, rash, muscle spasms, gait disturbance, asthenia, fatigue, irritability, feeling drunk, injection site pain or discomfort (local adverse events associated with intravenous administration), irritation (local adverse events associated with intravenous administration), fall, and skin laceration, contusion.

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 (also known as Drug Reaction with Eosinophilia and Systemic Symptoms, DRESS) 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. 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: 23rd October 2014. http://www.ema.europa.eu/

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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 8500 people in approximately 40 countries, the company generated revenue of € 3.4 billion in 2013. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news

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.