UCB News

UCB's strong presence at International Epilepsy Congress reinforces value to epilepsy patients

- Studies spanning from preclinical to clinical investigations of *brivaracetam,* UCB's new epilepsy portfolio candidate, will be presented alongside post-hoc and pooled analyses of Phase 2/3 clinical trial data.
- Data presentations evaluate the use of VIMPAT® (*lacosamide*) for the treatment of epilepsy in patients with diverse therapeutic needs.

Brussels (Belgium), 4 September, 2015 – 0700 (CEST) – UCB is pleased to present a total of 17 accepted abstracts at the upcoming 31st International Epilepsy Congress (IEC) in Istanbul, Turkey, including three best posters and an oral presentation. The accepted abstracts span two anti-epileptic drugs; the investigational drug *brivaracetam*[1-11] and the approved drug VIMPAT® (*lacosamide*),[12-16] with an additional presentation reporting data from an interim assessment of the International League Against Epilepsy (ILAE) drug-resistant epilepsy criteria[17] in real-world clinical practice.[18]

Jeffrey Wren, Head of UCB's Neurology Patient Value Unit said: 'The UCB data presentations at this year's IEC reinforce our foundational approach to help address the unmet needs of people with epilepsy. We are proud to present the latest clinical findings for our anti-epileptic drug VIMPAT®; which is approved in Europe as an adjunctive therapy for partial-onset seizures in adults with epilepsy, and shows increasing promise for the treatment of epilepsy in patients with diverse therapeutic needs. We are also pleased to share results which expand the known profile of *brivaracetam,* our investigational anti-epileptic drug, which we hope will achieve FDA and EMA approval in the near future."

Brivaracetam is currently under review by the FDA and EMA for approval as an adjunctive treatment for partial-onset seizures in adults with epilepsy aged 16 years or older. Presentations at the 2015 IEC extend the current knowledge of the preclinical, therapeutic and pharmacokinetic profile of *brivaracetam*. New data confirm the efficacy of *brivaracetam* in a pre-clinical disease model,[1] its mechanism of action,[2] and show the differential interaction of *brivaracetam* and *levetiracetam* at the synaptic vesicle glycoprotein 2A protein.[3] Several clinical datasets will also be presented, including an

evaluation of the interaction potential with other anti-epileptic drugs,[4-6] results from pooled analyses of previously completed Phase 2/3 clinical trials,[7,8] and a feasibility assessment for a novel Phase 3 study design.[9] Further presentations report on clinical aspects of *brivaracetam* therapy, including results from an open-label study evaluating the change in health-related quality of life in patients switching to *brivaracetam* from *levetiracetam* without up-titration,[10] and from a post-hoc analysis evaluating the predictors of treatment response.[11]

For VIMPAT®, UCB presentations at the 2015 IEC will report new data from studies conducted in several epilepsy patient subgroups. Posters will present clinical pharmacokinetic data in adults converting from adjunctive therapy to VIMPAT® monotherapy,[12] and will provide preliminary evaluations of VIMPAT® pharmacokinetics in pediatric patients.[13] Additionally, findings on seizure control in relatively difficult-to-treat patients cross-titrating from a concomitant sodium-channel blocking anti-epileptic drug to VIMPAT®, when taking a stable dose of *levetiracetam*, will be presented.[14] An oral presentation will communicate clinical data on the differential neuropsychological effects between VIMPAT® and *carbamazepine* in healthy subjects.[15] Looking to the future, the rationale behind a novel endpoint in an ongoing clinical trial evaluating the efficacy and safety of VIMPAT® for the adjunctive treatment of primary generalized tonic-clonic seizures in both adult and pediatric patients with idiopathic generalized epilepsy will be presented.[16]

The following is a guide to 17 UCB-sponsored data presentations at the 31st IEC, held September 5-9th 2015 in Istanbul, Turkey:

***Brivaracetam*:**

1. POSTER PRESENTATION
   [P0185] Anticonvulsant effects of brivaracetam in the 6 Hz fully-kindled mice
   K. Leclercq and R-M Kaminski
   Date & Time: Sunday 6 September 2015, 13:30-14:30

2. POSTER PRESENTATION
   [P0787] Brivaracetam does not modulate the major ionic conductances in neurons
   I. Niespodziany *et al.*
   Date & Time: Tuesday 8 September 2015, 13:30-14:30

3. BEST POSTER PRESENTATION
   [P0879] Evidence for a differential interaction of brivaracetam and levetiracetam with the SV2A protein
   M. Wood *et al.*
   Date & Time: Tuesday 8 September 2015, 13:30-14:30

4. BEST POSTER PRESENTATION
   [P0859] Brivaracetam and carbamazepine interaction study in adult patients with epilepsy

A. Stockis *et al.*
Date & Time: Tuesday 8 September 2015, 13:30-14:30

5. POSTER PRESENTATION
[P0857] Brivaracetam and topiramate interaction study in healthy subjects
A. Stockis and S. Watanabe
Date & Time: Tuesday 8 September 2015, 13:30-14:30

6. POSTER PRESENTATION
[P0858] Brivaracetam and lamotrigine interaction study in healthy subjects
A. Stockis, *et al.*
Date & Time: Tuesday 8 September 2015, 13:30-14:30

7. POSTER PRESENTATION
[P0851] Efficacy and safety of adjunctive brivaracetam for partial-onset (focal) seizures: pooled results from three fixed-dose, randomised, double-blind, placebo-controlled Phase III studies
P. P. Quarato *et al.*
Date & Time: Tuesday 8 September 2015, 13:30-14:30

8. POSTER PRESENTATION
[P0870] Safety and tolerability of long-term treatment with adjunctive brivaracetam for partial-onset seizures
M. Toledo *et al.*
Date & Time: Tuesday 8 September 2015, 13:30-14:30

9. POSTER PRESENTATION
[P0183] Analysis of adjunctive brivaracetam in adults with partial-onset (focal) seizures according to pathological substrate: methodology from a Phase III study
A. Beydoun *et al.*
Date & Time: Sunday 6 September 2015, 13:30-14:30

10. POSTER PRESENTATION
[P0104] Health-related quality of life (HRQoL) in patients with epilepsy switching from levetiracetam (LEV) to brivaracetam (BRV): an open-label prospective study
S. Borghs *et al.*
Date & Time: Sunday 6 September 2015, 13:30-14:30

11. POSTER PRESENTATION
[P0435] Predictors of response in patients with epilepsy in a double-blind, placebo-controlled study of brivaracetam
P. Klein et al.
Date & Time: Monday 7 September 2015, 13:30-14:30

VIMPAT® (*lacosamide*):

12. POSTER PRESENTATION
[P0188] Exposure to lacosamide in blood plasma during adjunctive therapy and monotherapy: pharmacokinetic analysis of data from a conversion to lacosamide monotherapy study
W. Cawello

Date & Time: Sunday 6 September 2015, 13:30-14:30

13. BEST POSTER PRESENTATION
[P0724] Lacosamide population pharmacokinetics in children from 6 months to 17 years of age
J. Winkler *et al.*
Date & Time: Monday 7 September 2015, 13:30-14:30

14. POSTER PRESENTATION
[P0182] Seizure control with lacosamide (≤400 mg/day) following cross-titration from a sodium channel blocker in patients with partial-onset seizures receiving stable doses of levetiracetam
M. Baulac *et al.*
Date & Time: Sunday 6 September 2015, 13:30-14:30

15. ORAL PRESENTATION
[0066] Differential neuropsychological and EEG effects of lacosamide versus carbamazepine in healthy subjects
K. Meador *et al.*
Date & Time: Clinical Trials Session 2, Tuesday 8 September 2015, 15:00-15:10

16. POSTER PRESENTATION
[P0878] Rationale and study design for a novel Phase 3, randomized, double-blind trial of adjunctive lacosamide in patients with idiopathic generalized (genetic) epilepsy and uncontrolled primary generalized tonic-clonic seizures
R. Warnock *et al.*
Date & Time: Tuesday 8 September 2015, 13:30-14:30

Epilepsy:

18. POSTER PRESENTATION
[P0544] PROMETEO: Interim analysis of a PRospective Observational study to assess the treatMent Effect after introduction of a different AED in paTients with partial Epilepsy fulfilling the 2010 ILAE criteria Of drug-resistant epilepsy
R. Michelucci *et al.*
Date & Time: Monday 7 September 2015, 13:30-14:30

About UCB in Epilepsy

UCB has a rich heritage in epilepsy with over 20 years of experience in the research and development of antiepileptic drugs. As a company with a long-term commitment to epilepsy research our goal is to address unmet medical needs. Our scientists are proud to contribute to advances in the understanding of epilepsy and its treatment. We partner and create super-networks with world-leading scientists and clinicians in academic institutions, pharmaceutical companies and other organizations who share our goals. At UCB, we are inspired by patients and driven by science in our commitment to support patients with epilepsy.

About VIMPAT® [19, 20]

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.

VIMPAT® is approved in the U.S. as film-coated tablets, injection for intravenous use 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 indicated as short-term replacement when oral administration is not feasible in these patients.

A single loading dose 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.

The availability of the oral tablets, oral solution, and formulation for intravenous administration permits flexibility in administration.

Important Safety Information about VIMPAT® in the European Union and EEA

VIMPAT® (*lacosamide*) is marketed as Benvida® in Turkey.

VIMPAT® 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® 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. VIMPAT® syrup and the solution for infusion contain sodium, which should be taken into consideration for patients on a controlled sodium diet. 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. 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, paresthesia, vision blurred, vertigo, tinnitus, vomiting, constipation, flatulence, dyspepsia, dry mouth, diarrhea, 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, skin laceration, and 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. 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 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: October 2014. http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000863/WC500050338.pdf. (Accessed 12th August 2015)

For further information

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References

1-11. *Brivaracetam* presentations at IEC 2015, see above for times.

12-16. VIMPAT® presentations at IEC 2015, see above for times.

17. Kwan P, Arzimanoglou A, Berg AT, et al. Definition of drug resistant epilepsy: Consensus proposal by the ad hoc Task Force of the ILAE Commission on Therapeutic Strategies. *Epilepsia*. 2010; 51: 1069-77.

18. Epilepsy presentation at IEC 2015, see above for times.

19. UCB Pharma. Vimpat® (*lacosamide*) EMA Summary of Product Characteristics. Accessed 12th August 2015 from http://www.ema.europa.eu/docs/en_GB/document_library/EPAR_-_Product_Information/human/000863/WC500050338.pdf. Last updated October 2014

20. UCB Pharma.Vimpat® (*lacosamide* tablets, injection, oral solution) [U.S. prescribing

information]. Smyrna: UCB. Accessed 12th August from http://www.vimpat.com/pdf/vimpat_PI.pdf. Last updated June 2015

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 about 40 countries, the company generated revenue of EUR 3.3 billion in 2014. 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.