UCB News

Phase 3 data on VIMPAT® (lacosamide) in primary generalized tonic-clonic seizures published in Journal of Neurology, Neurosurgery & Psychiatry

- **Study met primary and secondary endpoints of significantly lowering the risk of developing a second primary generalized tonic-clonic seizure (PGTCS) during a 24-week treatment and a significantly higher rate of freedom from PGTCS during the treatment period compared with placebo**
- **Lacosamide was generally tolerated by patients enrolled in the study**
- **Regulatory reviews, based, in part, on these data, are currently underway in the U.S., EU, Japan, and Australia**
- **VIMPAT® is currently not approved for PGTCS in any country in the world**

BRUSSELS, BELGIUM (31st August 2020, 7am CEST) - UCB, a global biopharmaceutical company, today announced the publication of the Phase 3 study results of VIMPAT® (lacosamide) as adjunctive treatment for uncontrolled primary generalized tonic-clonic seizures (PGTCS), in the Journal of Neurology, Neurosurgery & Psychiatry.[1]

The Phase 3 study enrolled 242 patients (≥4 years of age) with idiopathic generalized epilepsy (IGE) who were randomised 1:1 to receive lacosamide or placebo (twice daily) in addition to their current epilepsy treatment. The primary endpoint was time to second primary generalized tonic-clonic seizure (PGTCS) during the 24-week (166-day) treatment period.

Treatment with lacosamide resulted in a significantly lower risk of developing a second PGTCS during the 24-week treatment (HR 0.540; p<0.001) and a significantly higher rate of freedom from PGTCS during the treatment period compared with placebo (31.3% vs 17.2%, p=0.011). Lacosamide was generally tolerated in patients with IGE and PGTCS. The most common treatment-emergent adverse events (≥10%) with lacosamide were dizziness (23.1%), somnolence (16.5%) and headache (14.0%). The incidences of dizziness and headache were numerically higher with lacosamide than placebo.

VIMPAT® is currently not approved for PGTCS in any country in the world. Regulatory reviews for use of VIMPAT® as adjunctive therapy in the treatment of **primary generalized tonic-clonic seizures in patients with idiopathic generalized epilepsy four years of age and older compared to placebo** are currently underway in the U.S., EU, Japan, and Australia.

"This Phase 3 trial demonstrated that by adding lacosamide to existing anti-seizure medications, IGE patients with uncontrolled primary generalized tonic-clonic seizures experienced a higher rate of seizure freedom, suggesting lacosamide could be a valuable adjunctive therapy in this patient population," said David Vossler, MD, FAAN FACNS FAES, Department of Neurology, University of Washington, USA.

IGEs account for 20%–40% of all epilepsies[2] and are characterised by different generalized seizure types (absence, myoclonic and PGTCS).[3] Patients living with generalized tonic-clonic seizures have an increased risk

of injury[4] and those who experienced three or more in one year had a fifteen-fold increased risk of sudden unexpected death in epilepsy.[5]

"*UCB remains committed to strengthening our leadership in epilepsy and to investigating new approaches and innovative solutions to deliver improved outcomes and experiences to the global epilepsy community. This applies equally to our current expansive in-market epilepsy portfolio as well as to our exciting pipeline,*" explained Charl van Zyl, Executive Vice President & Head of Neurology Solutions, UCB.

About the Study[1]
The study (SP0982; NCT02408523) was a Phase 3, double-blind, randomized, placebo-controlled, multicenter study in patients with IGE and PGTCS taking 1–3 concomitant anti-epileptic drugs (AEDs). The primary outcome was time to second PGTCS during 24-week treatment. 242 eligible patients were randomised 1:1 to receive lacosamide or placebo (twice daily). Patients were eligible if they were ≥4 years of age with a confirmed diagnosis of IGE experiencing classifiable PGTCS. The treatment period continued until one of the following occurred: completion of ≥6 weeks of the treatment period and occurrence of two or more PGTCS, completion of the 24 week treatment period without occurrence of two PGTCS, or the 125th event occurred in the trial.

About VIMPAT® in the EU and Asia
VIMPAT® was first launched in the European Union in September 2008, 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.

In countries of the EU, VIMPAT® is available as film-coated tablets, syrup and solution for infusion. Lacosamide solution for infusion is an alternative for patients when oral administration is temporarily not feasible.

In Asia, VIMPAT® is available in Japan, China, Hong Kong, Philippines and Thailand.

Important Safety Information about VIMPAT® in the EU and EEA[6]
VIMPAT® is indicated as monotherapy and adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 4 years of age with epilepsy. VIMPAT® therapy can be initiated with either oral or IV administration. For the paediatric population, the physician should prescribe the most appropriate formulation and strength according to weight and dose. 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 serious cardiac arrhythmia and CNS adverse reactions. Administration of a loading dose has not been studied in acute conditions such as status epilepticus. Use of a loading dose is not recommended in adolescents and children weighing less than 50 kg. Administration of a loading dose has not been studied in children. A maximum dose of 300 mg/day is recommended for paediatric patients with mild to moderate hepatic impairment weighing 50 kg or more and for adult patients with mild to moderate hepatic impairment as well. Based on data in adults, in paediatric patients weighing less than 50 kg with mild to moderate hepatic impairment, a reduction of 25 % of the maximum dose should be applied. Lacosamide should be administered to adult and paediatric patients with severe hepatic impairment only when the expected therapeutic benefits are anticipated to outweigh the possible risks. The dose may need to be adjusted while carefully observing disease activity and potential side effects in the patient. In adolescents and adults weighing 50 kg or more with mild to moderate hepatic impairment a loading dose of 200mg may be considered, but further dose titration (>200 mg daily) should be performed with caution. In paediatric patients weighing 50 kg or more and in adult patients with mild or moderate renal impairment a loading dose of 200 mg may be considered, but further dose titration (> 200 mg daily) should be performed with caution. In paediatric patients weighing 50 kg or more and in adult patients with severe renal impairment (CLCR ≤ 30 ml/min) or with end-stage renal disease, a maximum dose of 250 mg/day is recommended and the dose titration should be performed with caution. In paediatric patients weighing less than 50 kg with severe renal impairment (CLCR ≤ 30 ml/min) and in those with end-stage renal disease, a reduction of 25 % of the maximum dose is recommended. 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. Dose-related prolongations in PR interval with VIMPAT® have been observed in clinical studies. VIMPAT® should be used with caution in patients with underlying

proarrhythmic conditions such as patients with known cardiac conduction problems or severe cardiac disease (e.g. myocardial ischaemia/infarction, heart failure, structural heart disease or cardiac sodium channelopathies) or patients treated with medicinal products affecting cardiac conduction, including antiarrhythmics and sodium channel blocking antiepileptic medicinal products, as well as in elderly patients. In these patients it should be considered to perform an ECG before a Vimpat dose increase above 400mg/day and after Vimpat is titrated to steady-state. 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. In post-marketing experience, AV block (including second degree or higher AV block) has been reported. In patients with proarrhythmic conditions, ventricular tachyarrhythmia has been reported. In rare cases, these events have led to asystole, cardiac arrest and death in patients with underlying proarrhythmic conditions. Patients should be made aware of the symptoms of cardiac arrhythmia (e.g. slow, rapid or irregular pulse, palpitations, shortness of breath, feeling lightheaded, fainting). Patients should be counselled to seek immediate medical advice if these symptoms occur. Suicidal ideation and behaviour have been reported in patients treated with antiepileptic medicinal products 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. The safety and efficacy of lacosamide in paediatric patients with epilepsy syndromes in which focal and generalised seizures may coexist have not been determined. VIMPAT® syrup contains sodium methyl parahydroxybenzoate (E219) which may cause allergic reactions (possibly delayed). Vimpat Syrup contains sorbitol (E420). Patients with rare hereditary problems of fructose intolerance should not take this medicine. Sorbitol may cause gastrointestinal discomfort and mild laxative effect.The syrup contains aspartame (E951), a source of phenylalanine, which may be harmful for people with phenylketonuria. Vimpat syrup contains propylene glycol (E1520). VIMPAT® syrup contains 1.42 mg sodium per ml, equivalent to 0.07 % of the WHO recommended maximum daily intake of 2 g sodium for an adult. VIMPAT® solution for infusion contains 59.8 mg sodium per vial, equivalent to 3% of the WHO recommended maximum daily intake of 2 g sodium for an adult. 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, 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. The safety profile of lacosamide in placebo-controlled and in open-label studies (n=408) in adjunctive therapy in children from 4 years of age was consistent with the safety profile observed in adults although the frequency of some adverse reactions (somnolence, vomiting and convulsion) was increased and additional adverse reactions (nasopharyngitis, pyrexia, pharyngitis, decreased appetite, lethargy and abnormal behaviour) have been reported in paediatric patients: nasopharyngitis (15.7 %), vomiting (14.7 %), somnolence (14.0 %), dizziness (13.5 %), pyrexia (13.0 %), convulsion (7.8 %), decreased appetite (5.9 %), pharyngitis (4.7 %), lethargy (2.7 %) and abnormal behaviour (1.7 %).
Laboratory abnormalities: Abnormalities in liver function tests have been observed in placebo-controlled trials with VIMPAT® in adult patients with partial-onset seizures who were taking 1-3 concomitant antiepileptic medicinal products. 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 medicinal products. 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: 03 Sept 2019. http://www.ema.europa.eu/

About Epilepsy
Epilepsy is the main symptom of a variety of chronic disorders of the brain. It is the fourth most common neurological condition worldwide and affects approximately 65 million people.[7] Anyone can develop epilepsy; it occurs across all ages, races and genders, and is defined as one or more unprovoked epileptic seizures with a risk of further seizures.[8]

About UCB in Epilepsy
UCB has a rich heritage in epilepsy with over 30 years of experience in the research and development of anti-epileptic 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 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 7 600 people in approximately 40 countries, the company generated revenue of € 4.9 billion in 2019. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news

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the actual results, financial condition, performance or achievements of UCB, or industry results, to differ materially from those that may be expressed or 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 or within expected timing, 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, safety, quality, data integrity or manufacturing issues; potential or actual data security and data privacy breaches, or disruptions of our information technology systems, product liability claims, challenges to patent protection for products or product candidates, competition from other products including biosimilars, 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. There is no guarantee that new product candidates will be discovered or identified in the pipeline, or that new indications for existing products will be developed and approved. Movement from concept to commercial product is uncertain; preclinical results do not guarantee safety and efficacy of product candidates in humans. So far, the complexity of the human body cannot be reproduced in computer models, cell culture systems or animal models. The length of the timing to complete clinical trials and to get regulatory approval for product marketing has varied in the past and UCB expects similar unpredictability going forward. Products or potential products which are the subject of partnerships, joint ventures or licensing collaborations may be subject to disputes between the partners or may prove to be not as safe, effective or commercially successful as UCB may have believed at the start of such partnership. UCB' efforts to acquire other products or companies and to integrate the operations of such acquired companies may not be as successful as UCB may have believed at the moment of acquisition. Also, UCB or others could discover safety, side effects or manufacturing problems with its products and/or devices after they are marketed. The discovery of significant problems with a product similar to one of UCB's products that implicate an entire class of products may have a material adverse effect on sales of the entire class of affected products. Moreover, sales may be impacted by international and domestic trends toward managed care and health care cost containment, including pricing pressure, political and public scrutiny, customer and prescriber patterns or practices, and the reimbursement policies imposed by third-party payers as well as legislation affecting biopharmaceutical pricing and reimbursement activities and outcomes. Finally, a breakdown, cyberattack or information security breach could compromise the confidentiality, integrity and availability of UCB's data and systems.

Given these uncertainties, you should not place undue reliance on any of such forward-looking statements. There can be no guarantee that the investigational or approved products described in this press release will be submitted or approved for sale or for any additional indications or labelling in any market, or at any particular time, nor can there be any guarantee that such products will be or will continue to be commercially successful in the future.

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