UCB News

UCB to present latest epilepsy scientific data and research perspectives at EILAT Conference

Brussels (Belgium), 11 May, 07:00 (CET): UCB is set to present the latest preclinical and clinical data on its in-market and developmental epilepsy portfolio and to describe new discovery avenues for drug resistance and disease modification during numerous presentations at the 14th EILAT Conference on New Antiepileptic Drugs and Devices. The meeting takes place from 13 to 16 May in Madrid, Spain.

Data from VIMPAT® (lacosamide) and BRIVIACT® (brivaracetam) clinical development programmes will be presented which will include an update on UCB's pediatric epilepsy programmes for both medicines. For lacosamide, this will include results from a large randomly controlled efficacy and safety trial in children with partial onset seizures (POS).[1] Separately, new data from a long-term extension trial, investigating tolerability of lacosamide as monotherapy treatment in adults with newly-diagnosed epilepsy will be described.[2] Brivaracetam human PET data, describing speed of brain penetration by brivaracetam compared to other racetam molecules will also be presented.[3]

UCB will also present data on its promising developmental medicine candidate padsevonil including results of a Phase II proof-of-concept trial.[4] Padsevonil is the first rationally designed AED candidate that inhibits seizures through both pre- and post-synaptic activity.

Senior scientists from UCB's New Medicines Group have been invited to present their perspectives on new discovery approaches for both drug resistance and disease modification. A key topic is to debate whether we are now at a stage where measuring disease modification in a clinical setting could be a new and beneficial reality.

"Despite the introduction of many new anti-epilepsy drugs, approximately one third of epilepsy patients remain without seizure control - which is completely unacceptable. We believe there is a substantial patient value in investigating new compounds that target the disease pathology of specific sub-groups with drug resistance", explained Henrik Klitgaard, Ph.D., Vice President and Fellow, Neurosciences Therapeutic Area, UCB. *"We also believe that progress in genetic and biomarker research could advance the date where promising preclinical findings may be translated successfully to potentially alter the course*

of acquired epilepsies. For that reason, we're very excited to share our perspectives and discuss the potential for disease modification with epilepsy experts from around the world. We are confident this will strengthen UCB's ability to deliver on our commitment to address remaining unmet needs in epilepsy and thereby improve the lives of patients living with epilepsy".

Details about the EILAT conference, including the agenda and scientific programme, are available online: https://www.eilatxiv.com/program-outline

About Epilepsy [5,6]

Epilepsy is a disease of the brain affecting approximately 65 million people worldwide. It is defined as either the occurrence of two or more unprovoked seizures >24 hours apart or one unprovoked (or reflex) seizure and a probability of further seizures occurring over the next 10 years that is similar to the general recurrence risk (at least 60%) after two unprovoked seizures or diagnosis of an epilepsy syndrome. Although epilepsy may be linked to factors such as health conditions, race and age, it can develop in anyone at any age, and approximately 1 in 26 people will develop epilepsy in their lifetime.

About UCB in Epilepsy

UCB has a longstanding commitment to improving the lives of people with epilepsy around the world. With over 20 years of experience in the research and development of antiepileptic drugs, our goal is to become a preferred partner for the global epilepsy community, improving knowledge about and access to effective solutions to help patients better manage their individual epilepsy journeys. We strive to 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 people with epilepsy.

About VIMPAT® [7, 8]

In the U.S., VIMPAT® is indicated for the treatment of partial-onset seizures in patients 4 years of age and older. As the safety of VIMPAT® injection in pediatric patients has not been established, VIMPAT® injection is indicated for the treatment of partial-onset seizures only in adult patients (17 years of age and older). VIMPAT® was approved in the U.S. in 2008 as an add-on therapy for adult patients. VIMPAT® was approved as monotherapy for adults in August 2014. VIMPAT® is available in three formulations: oral tablets, oral solution, and intravenous (IV) injection. Important safety information about VIMPAT® in the U.S. is available below.

VIMPAT® (lacosamide) was first launched in the European Union in September 2008, as adjunctive therapy for the treatment of partial-onset seizures with or without secondary generalisation in adult and adolescent (16-18 years) patients with epilepsy. In September 2017 the use of VIMPAT® was expanded to adolescents and children from 4 years of age. In countries of the EU, VIMPAT® is available as film-coated tablets, syrup and solution for infusion. VIMPAT® solution for infusion is an alternative for patients when oral administration is temporarily not feasible. The availability of the oral tablets, oral syrup, and intravenous (IV) injection allows for consistent patient

treatment. In Asia, VIMPAT® is available in Korea, Hong Kong, Malaysia, Philippines and Thailand, and was approved for use in Japan in 2016, where the product will be jointly commercialised by Daiichi Sankyo. VIMPAT® is not approved in China. Important safety information about VIMPAT® is available below.

Important Safety Information about VIMPAT® in the EU and EEA[8]

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 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. A maximum dose of 300 mg/day is recommended for paediatric patients weighing 50 kg or more and for adult patients with mild to moderate hepatic impairment. 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. 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, severe cardiac disease (e.g. history of myocardial infarction or heart failure), in elderly patients, or when VIMPAT® is used in combination with products known to be associated with PR prolongation. 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. 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 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). 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. The safety profile of lacosamide in open-label studies in adjunctive therapy in children from 4 years to less than 16 years was consistent with the safety profile observed in adults. In the paediatric population the most frequently reported adverse reactions were vomiting (17.1 %), dizziness (16.7 %), somnolence (12.1 %), headache (11.7 %) and convulsion (10.1 %). Additional adverse reactions reported in children were decreased appetite (6.6 %), lethargy (4.3 %) and abnormal behaviour (1.9 %). 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 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: 14th September 2017 http://www.ema.europa.eu/.

About BRIVIACT® [9,10]

BRIVIACT® (brivaracetam) is a new molecular entity that was rationally designed and developed by UCB.

In the U.S., BRIVIACT® is approved for the treatment of partial-onset seizures in patients 16 years of age and older with epilepsy.[5]

In the EU, BRIVIACT® is indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adult and adolescent patients from 16 years of age with epilepsy.[6]

BRIVIACT® was approved in the EU and the U.S. in 2016 as an add-on therapy for adult patients.

BRIVIACT® is available in three formulations (film-coated tablets, oral solution, and injection).

Important Safety Information about BRIVIACT® in the EU and EEA[10]

BRIVIACT® (brivaracetam) is indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adult and adolescent patients from 16 years of age with epilepsy. Contraindications Hypersensitivity to the active substance, other pyrrolidone derivatives or any of the excipients. Special warnings and precautions for use Suicidal ideation and behaviour have been reported in patients treated with anti-epileptic drugs (AEDs) in several indications, including BRIVIACT®. Patients should be monitored for signs of suicidal ideation and behaviour and appropriate treatment should be considered. Patients (and caregivers) should be advised to seek medical advice should any signs of suicidal ideation or behaviour emerge. Dose adjustments are recommended for patients with hepatic impairment (50 mg/day starting dose should be considered, up to maximum daily dose of 150 mg administered in 2 divided doses). BRIVIACT® film-coated tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, the Lapp lactase deficiency or glucose-galactose malabsorption should not take BRIVIACT®. Both the solution for injection/infusion and the oral solution contain sodium – to be taken into consideration for patients on a controlled sodium diet. The oral solution contains sorbitol (E420). Patients with rare hereditary problems of fructose intolerance should not take this medicine. The oral solution contains methyl parahydroxybenzoate (E218), which may cause allergic reactions (possibly delayed). Interaction with other medicinal products and other forms of interaction With co-administration of BRIVIACT® 200 mg single dose and ethanol 0.6 g/L continuous infusion in healthy subjects there was no pharmacokinetic interaction, but the effect of alcohol on psychomotor function, attention and memory was doubled. Intake of BRIVIACT® with alcohol is not recommended. In healthy subjects, co-administration with rifampicin, a strong enzyme-inducer (600 mg/day for 5 days), decreased BRIVIACT® area under the plasma concentration curve (AUC) by 45%. Prescribers should consider adjusting the dose of BRIVIACT® for patients starting or ending treatment with rifampicin. Other strong enzyme-inducers (such as St John´s wort [Hypericum perforatum]) may also decrease the systemic exposure of BRIVIACT®.

Therefore, starting or ending treatment with St John's wort should be done with caution. In vitro interaction studies have shown that BRIVIACT® can inhibit CYP2C19, therefore BRIVIACT® may increase plasma concentrations of medicinal products metabolised by CYP2C19 (e.g., lanzoprazole, omeprazole, diazepam). CYP2B6 induction has not been investigated in vivo and BRIVIACT® may decrease plasma concentrations of medicinal products metabolised by CYP2B6 (e.g. efavirenz). In vitro studies have also shown that BRIVIACT® has inhibitory effects on OAT3. BRIVIACT® 200 mg/day may increase plasma concentrations of medicinal products transported by OAT3. BRIVIACT® plasma concentrations are decreased when co-administered with strong enzyme inducing antiepileptic drugs (carbamazepine, phenobarbital, phenytoin) but no dose adjustment is required. Effects on ability to drive and use machines BRIVIACT®, has minor or moderate influence on the ability to drive and use machines. Patients should be advised not to drive a car or to operate other potentially hazardous machines until they are familiar with the effects of BRIVIACT®, on their ability to perform such activities. Undesirable effects The most frequently reported adverse reactions with BRIVIACT® (reported by >10% of patients) were somnolence (14.3%) and dizziness (11.0%). They were usually mild to moderate in intensity. Somnolence and fatigue (8.2 %) were reported at higher incidences with increasing dose. Other common adverse reactions (≥1% to <10%) were influenza, decreased appetite, depression, anxiety, insomnia, irritability, convulsion, vertigo, upper respiratory tract infections, cough, nausea, vomiting and constipation. Neutropenia has been reported in 0.5% (6/1,099) BRIVIACT® - patients and 0% (0/459) placebo-treated patients. Four of these patients had decreased neutrophil counts at baseline, and experienced additional decrease in neutrophil counts after initiation of BRIVIACT®. None of the six cases were severe, required any specific treatment, led to BRIVIACT® discontinuation or had associated infections. Suicidal ideation was reported in 0.3 % (3/1099) of BRIVIACT® -treated patients and 0.7 % (3/459) of placebo-treated patients. In short-term clinical studies of BRIVIACT® in patients with epilepsy, there were no cases of completed suicide and suicide attempt, however both were reported in the long-term open-label extension studies. In patients who were followed up in the open-label extension studies for up to 8 years, the safety profile was similar to that observed in the short-term, placebo-controlled studies. Overdose There is limited clinical experience with BRIVIACT® overdose in humans. Somnolence and dizziness were reported in a healthy subject taking a single dose of 1,400 mg of BRIVIACT®. There is no specific antidote. Treatment of an overdose should include general supportive measures. Since less than 10% of BRIVIACT® is excreted in urine, haemodialysis is not expected to significantly enhance BRIVIACT® clearance.

Refer to the European Summary of Product Characteristics for other adverse reactions and full prescribing information. Date of revision: April 2017. 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 7500 people in approximately 40 countries, the company generated revenue of € 4.2 billion in 2016. 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.

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