UCB News

UCB announces positive preliminary results for major brivaracetam (Briviact®) study in Asia

- *Positive topline results from a Phase 3 study investigating the efficacy and safety of adjunctive brivaracetam in participants across Asia (≥16 to 80 years of age) with partial seizures with or without secondary generalization*[1]
- *Study met primary and all secondary endpoints*
- *UCB plans regulatory submissions for Briviact in Japan in Q3 2023*

Brussels, 10 October 2022 – 0700 (CEST) – UCB, a global biopharmaceutical company, announced today positive top-line results from the latest Phase 3 study of brivaracetam (Briviact). The study was a randomized, double-blind, placebo-controlled, multi-center, parallel-group trial, designed to evaluate the efficacy and safety of adjunctive brivaracetam in participants from Asia (≥16 to 80 years of age) with partial seizures with or without secondary generalization.[2]

The study efficacy and safety outcomes will support the regulatory submission of brivaracetam in Japan in Q3, 2023.

A preliminary analysis of the unblinded data concludes that the trial met its primary efficacy endpoint; a significant percent reduction in 28-day partial onset seizure (POS) frequency was observed in both brivaracetam groups over placebo [24.6% (p=0.0004) in the brivaracetam 50 mg/day group and 33.3% (p<0.0001) in the brivaracetam 200 mg/day group].[1]

All key secondary endpoints were also met:

- A total of 41.1% of participants in the brivaracetam 50 mg/day group and 49.3% of participants in the brivaracetam 200 mg/day group achieved at least a 50% reduction in POS frequency compared with 19.0% of participants on placebo (p<0.0001 for both groups).[1]
- Significant median percent reductions in POS frequency from baseline were observed in both brivaracetam groups compared with placebo [38.9% (p= 0.0011) in the brivaracetam 50 mg/day group and 46.7% (p<0.0001) in the brivaracetam 200 mg/day group].[1]

In addition, the study safety data suggest that brivaracetam was well-tolerated, and no new safety signals were observed. The most common (≥5%) treatment emergent adverse events were somnolence (14.4%), dizziness (12.7%), headache (6.0%), upper respiratory tract infection (6.0%), and nasopharyngitis (5.7%).[1]

"Today's positive results with brivaracetam represent a significant milestone in our ambition to deliver new solutions for people living with epilepsy," said Mike Davis, Global Head of Epilepsy, UCB. "We are proud to provide new treatment options for the epilepsy community and remain committed to addressing the unmet needs of adult patients who continue to experience uncontrolled seizures."

"The positive data from this trial, demonstrating robust and clinically relevant seizure reduction, were consistent with previous brivaracetam trials," said Kanako Kikuchi, Head of UCB Japan. "This study was

the largest Phase 3 study conducted in epilepsy patients with partial-onset seizures in Asia, and we look forward to discussing the data with the regulatory authorities and the scientific community."

A total of 449 participants took part in the study (Japan = 98; Thailand = 145; China = 86; Philippines = 62; Malaysia = 47; Singapore = 6; Taiwan = 5). Participants were assigned either brivaracetam 50 or 200 mg/day vs. placebo, for a 12-week treatment period.[1]

Detailed data from this study will be submitted for presentation at upcoming epilepsy congresses and for publications in peer-reviewed journals.

About Epilepsy

Epilepsy is a chronic neurological disorder affecting approximately 65 million people worldwide. It 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. [3]

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. Partial seizures begin with an electrical discharge in one area of the brain. Different things can cause partial seizures, for example head injury, brain infection, stroke, tumour, and changes in the way an area of the brain was formed before birth, called cortical dysplasias. Many times, no known cause is found, but genetic factors may be important in some partial seizures.[4,5]

About BRIVIACT® (brivaracetam)

Important Safety Information about BRIVIACT® in the EU and EEA[6]

BRIVIACT® (brivaracetam) is indicated as adjunctive therapy in the treatment of partial-onset seizures with or without secondary generalisation in adults, adolescents and children from 2 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. BRIVIACT® film-coated tablets contain lactose. Patients with rare hereditary problems of galactose intolerance, total lactase deficiency or glucose-galactose malabsorption should not take BRIVIACT®. Brivaracetam film-coated tablets, solution for injection/infusion and oral solution contain less than 1 mmol sodium (23mg) per tablet/vial/ml respectively, that is to say essentially 'sodium free'. The oral solution contains 168 mg sorbitol (E420) in each ml. Patients with hereditary fructose intolerance (HFI) should not take this medicinal product. The oral solution contains methyl parahydroxybenzoate (E218), which may cause allergic reactions (possibly delayed). Brivaracetam oral solution contains propylene glycol (E1520). **Posology** No dose adjustment is needed in adults with impaired renal function. Based on data in adults, no dose adjustment is necessary neither in paediatric patients with impaired renal function. No clinical data are available in paediatric patients with

Date of Preparation: September 2022
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renal impairment. In patients with hepatic impairment, the following adjusted doses, administered in 2 divided doses, approximately 12 hours apart, are recommended for all stages of hepatic impairment: In adults, adolescents and children weighing ≥50 kg, a 50 mg/day starting dose is recommended, with a maximum daily dose of 150 mg/day. For adolescents and children weighing from 20 kg to <50 kg, a 1 mg/kg/day starting dose is recommended, with a maximum daily dose of 3 mg/kg/day. For children weighing from 10 kg to <20 kg, a 1 mg/kg/day starting dose is recommended, with a maximum daily dose of 4 mg/kg/day. No clinical data are available in paediatric patients with hepatic impairment. **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. Limited clinical data are available implying that coadministration of cannabidiol may increase the plasma exposure of brivaracetam, possibly through CYP2C19 inhibition, but the clinical relevance is uncertain. 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* studies have shown that brivaracetam exhibits little or no inhibition of CYP450 isoforms except for CYP2C19. Brivaracetam may increase plasma concentrations of medicinal products metabolised by CYP2C19 (e.g., lansoprazole, 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 were reported at higher incidences with increasing dose. Very common adverse reactions (≥1% to <10%) were influenza, decreased appetite, depression, anxiety, insomnia, irritability, convulsion, vertigo, upper respiratory tract infections, cough, nausea, vomiting, constipation and fatigue. 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. Reactions suggestive of immediate (Type I) hypersensitivity have been reported in a small number of BRIVIACT® patients (9/3022) during clinical development. The safety profile of brivaracetam observed in children from 1 month of age was consistent with the safety profile observed

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in adults. In the open label, uncontrolled, long-term studies suicidal ideation was reported in 4.7 % of paediatric patients assessed from 6 years onwards (more common in adolescents) compared with 2.4 % of adults and behavioural disorders were reported in 24.8 % of paediatric patients compared with 15.1 % of adults. The majority of events were mild or moderate in intensity, were non-serious, and did not lead to discontinuation of study drug. An additional adverse reaction reported in children was psychomotor hyperactivity (4.7 %). No specific pattern of adverse event (AE) was identified in children from 1 month to < 4 years of age when compared to older paediatric age groups. No significant safety information was identified indicating the increasing incidence of a particular AE in this age group. As data available in children younger than 2 years of age are limited, brivaracetam is not indicated in this age range. No clinical data are available in neonates. **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®. The following adverse reactions were reported with brivaracetam overdose: nausea, vertigo, balance disorder, anxiety, fatigue, irritability, aggression, insomnia, depression, and suicidal ideation in the post-marketing experience. In general, the adverse reactions associated with brivaracetam overdose were consistent with the known adverse reactions. 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.
https://www.ema.europa.eu/en/documents/product-information/briviact-epar-product-information_en.pdf

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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 approximately 8 600 people in approximately 40 countries, the company generated revenue of €5.8 billion in 2021. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news

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