UCB News

UCB presents new data at 35th International Epilepsy Congress (IEC) highlighting important advancements across Fintepla® ▼(fenfluramine) oral solution and broader epilepsies portfolio

- 9 abstracts showcase new data for fenfluramine[1] in rare epilepsies (including late-breaking data on safety profile and efficacy of fenfluramine in adults living with Dravet syndrome) and brivaracetam[2] in the treatment of focal onset seizures of different aetiologies as well as when switching from other anti-seizure medications
- Data presented from the *Seizure Termination Project* – an expert group developing recommendations on rapid and early seizure termination
- UCB will host two symposia: 'Rapid Early Seizure Termination – Time is brain and more' (September 3, 18.00-19.30 CET), and 'Making a difference together for patients with developmental and epileptic encephalopathies' (September 4, 09.00-10.30 CET)

Brussels, Belgium, 31 August 2023 – 07.00 AM CET – Nine abstracts, including one late-breaker and two oral presentations, will be presented at the 35th International Epilepsy Congress (IEC) taking place from September 2-6, 2023. Presentations span multiple forms of epilepsy, as well as rare epileptic conditions such as Dravet syndrome (DS), Lennox-Gastaut syndrome (LGS) and CDKL5 (cyclin-dependent kinase-like 5) deficiency disorder.

Mike Davis, Head of Global Epilepsy & Rare Syndromes, UCB, said: "Utilizing our experience and expertise, we continuously challenge the status quo in our drive to do more for people living with a variety of seizure types and rare syndromes – from innovative early research, to research in conditions where we have considerable history and heritage, as well as in new therapy areas where we are addressing important unmet needs in Dravet and Lennox-Gastaut syndrome – our data at IEC really underlines where we are working to have a positive impact. Our ambition is to do more to improve the lives of patients and families now, and in the future."

Data to be presented at the 35th International Epilepsy Congress (IEC)

Fenfluramine impact in children and adults living with Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS)

A review of published studies where patients were treated with fenfluramine to manage convulsive seizures - including generalized tonic-clonic seizures (GTCS) or tonic-clonic seizures (TCS) - was conducted to examine the efficacy of fenfluramine on GTCS reduction in various types of Developmental and Epileptic Encephalopathies (DEEs) or rare epilepsy conditions. Data from 13 studies (4 randomized-controlled trials (RCTs), 4 observational studies, 4 open-label studies, and 1 case series) were included in the review. [3]

In total 561 patients were included in the review (including 360 patients with Dravet syndrome and 176 with Lennox-Gastaut syndrome). Not all patients in these studies experienced GTCS or TCS. Eight studies (N=117) reported the proportion of patients experiencing ≥75% and/or 100% reduction in GTCS or TCS;

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70% and 55% of patients reported ≥75% and 100% reduction in GTCS or TCS, respectively. 5 studies reported more than half of patients were GTCS-free after fenfluramine treatment.[3]

Lead author and Professor Helen Cross, the Prince of Wales's Chair of Childhood Epilepsy & Director of UCL Great Ormond Street Institute of Child Health, London, and Young Epilepsy, Lingfield, UK commented: "These data demonstrated striking levels of GTCS control, setting new standards for what can be achieved in Dravet syndrome, but also providing important insights into treatment for other developmental and epileptic encephalopathies. These seizures are one of our main concerns because of the risk of SUDEP (Sudden Unexpected Death in Epilepsy)."

Orrin Devinsky, MD, Director of NYU Langone Health's Comprehensive Epilepsy Center, US, said: "The impact of Dravet and Lennox-Gastaut syndromes are far reaching, with many emotional and practical consequences for parents, siblings, relatives and loved ones. These data are raising the bar in what can be achieved in advancing the care for both children and adults living with these difficult to treat conditions."

Late-breaking data presented at IEC also provide additional new evidence on the safety profile and efficacy of fenfluramine in adults living with Dravet syndrome.[4]

In LGS, data include an evaluation of the impact of age and weight on the reduction of seizures associated with a fall, in patients in the phase 3 randomized clinical trial and open-label extension study (NCT03355209). These data suggest that fenfluramine treatment results in effective, sustained reductions in frequency of seizures associated with a fall in adults with LGS, comparable to results in children and adolescents with LGS, and in patients with LGS weighing ≥37.5kg, comparable to results in patients weighing <37.5kg.[5]

Focal-Onset Seizures

Data presented on brivaracetam will look at the effectiveness and tolerability profile of this treatment in adults with epilepsy of different aetiology, including people with brain tumor-related epilepsy, post-stroke epilepsy, and traumatic brain injury-related epilepsy.[6] Additionally, data from the EXPERIENCE analysis will assess effectiveness and tolerability profile of brivaracetam in patients switching from levetiracetam and patients switching from other antiseizure medications.[7]

Rapid and Early Seizure Termination

Expert consensus recommendations will also be presented from the *Seizure Termination Project**, discussing best practice for rapid termination of seizure episodes to prevent progression to a higher-level emergency. The advisors unanimously agreed that an ideal acute seizure termination treatment would start to act within 2 minutes of administration to terminate ongoing seizure activity. Consensus was also reached on goals and potential benefits of rapid seizure termination and specific patient and seizure types that could benefit most from rapid termination.[8] The project aims to fill the gap which exists in guidelines for seizure emergencies.

Pipeline programs**

In CDKL5 deficiency disorder (CDD), a poster describes the design of an ongoing, two-part, multi-center trial of fenfluramine in people with CDD and uncontrolled seizures, outlining how the study will characterize efficacy and safety of the treatment.[9]

Symposia

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UCB-supported symposia aim to increase knowledge and awareness of the different seizure emergencies and the importance of rapid termination of certain ongoing seizures, and the impact of DEEs on seizure and non-seizure outcomes, with focus on adult patients:

1. *Prolonged seizures - Time is brain and more:* Sunday, 3rd September 18.00-19.30 CET, will differentiate the different seizure emergencies and describe the clinical relevance and burden of prolonged seizure duration and progression to more severe seizure types.

2. *Making a difference together for patients with developmental and epileptic encephalopathies:* Monday, 4th September 09:00-10.30 CET, will increase the knowledge of DEEs with focus on the awareness of the impact of seizure and non-seizure outcomes along the patient lifetime, advancing collaboration between specialists in the transition of patients from pediatric to adult care and sharing best practice on complex clinical cases in DS and LGS.

UCB presentations during IEC 2023

Lead Author	Abstract title	Presentation Details (Timings)
Sanchez-Carpintero R	Safety and Efficacy of Fenfluramine in Adult Patients Enrolled De Novo in an Open-Label Extension Study	Digital poster Will be available on virtual platform
Strzelczyk A	12-Month Effectiveness and Tolerability of Brivaracetam in Patients With Epilepsy Stratified by Etiology at Baseline in the Real-World: Subgroup Data From the International EXPERIENCE Pooled Analysis	Sunday, September 3, 16:00-16:10, Platform Session: Drug Therapy 1 The Liffey B
Villanueva V	12-Month Effectiveness and Tolerability of Brivaracetam in Patients With Epilepsy Switching From Levetiracetam Vs Other Antiseizure Medications in the Real-World: Subgroup Data From the International EXPERIENCE Pooled Analysis	Digital poster Will be available on virtual platform
Ma Y	Rescue medication for seizure emergency management in the UK community: A CPRD retrospective database study	Sunday, September 3, Poster Session: Epidemiology, 09:00-17:00
Trinka E	The Seizure Termination Project: Expert Consensus Recommendations for the Rapid Termination of Seizure Emergencies	Digital poster Will be available on virtual platform
Scheffer IE	Impact of Fenfluramine on Drop Seizure Frequency in Adults or Dose-Capped Patients With Lennox-Gastaut Syndrome: Comparative Analysis of Clinical Trial Data	Monday, September 4, 16:50-17:00, The Auditorium
Devinsky O	Design of a Phase 3 Clinical Study to Examine the Efficacy and Safety of Fenfluramine in Subjects With CDKL5 Deficiency Disorder Followed by an Open-Label Extension	Digital poster Will be available on virtual platform
Cross H	Effect of Fenfluramine on Generalized Tonic-Clonic Seizures in Rare Epilepsy Syndromes: A Review of Published Studies	Digital poster Will be available on virtual platform
Arzimanoglou A	Healthcare Resource Utilisation in Lennox-Gastaut Syndrome: Interim results from a European real-world point-in-time study	Digital poster

		Will be available on virtual platform

About FINTEPLA® ▼ (fenfluramine) oral solution in EU[1]

Fintepla is indicated for the treatment of seizures associated with Dravet syndrome and Lennox-Gastaut syndrome as an add-on therapy to other anti-epileptic medicines for patients 2 years of age and older. Fenfluramine is a serotonin releasing agent, and thereby stimulates multiple 5-HT receptor sub-types through the release of serotonin. Fenfluramine may reduce seizures by acting as an agonist at specific serotonin receptors in the brain, including the 5-HT1D, 5-HT2A, and 5-HT2C receptors, and also by acting on the sigma-1 receptor. The precise mode of action of fenfluramine in Dravet syndrome and Lennox-Gastaut syndrome is not known.

Fenfluramine oral solution is available under a controlled access program to ensure regular cardiac monitoring and to mitigate potential off-label use.

Refer to the European Summary of Product Characteristics (SmPC) for other adverse reactions and full prescribing information.

▼ *This medicinal product is subject to additional monitoring. This will allow quick identification of new safety information. Healthcare professionals are asked to report any suspected adverse reactions.*

Important Safety Information about FINTEPLA▼ in EU

Aortic or mitral valvular heart disease and pulmonary arterial hypertension

Because of reported cases of valvular heart disease that may have been caused by fenfluramine at higher doses used to treat adult obesity, cardiac monitoring must be performed using echocardiography. In the controlled clinical studies of fenfluramine for the treatment of Dravet syndrome and Lennox-Gastaut syndrome, no valvular heart disease was observed. Prior to starting treatment, patients must undergo an echocardiogram to establish a baseline prior to initiating treatment and exclude any pre-existing valvular heart disease or pulmonary hypertension. Echocardiogram monitoring should be conducted every 6 months for the first 2 years and annually thereafter. If an echocardiogram indicates pathological valvular changes, a follow-up echocardiogram should be considered at an earlier timeframe to evaluate whether the abnormality is persistent. If pathological abnormalities on the echocardiogram are observed, it is recommended to evaluate the benefit versus risk of continuing fenfluramine treatment with the prescriber, caregiver, and cardiologist. If treatment is stopped because of aortic or mitral valvular heart disease, appropriate monitoring and follow-up should be provided in accordance with local guidelines for the treatment of aortic or mitral valvular heart disease. With past use in higher doses to treat adult obesity, fenfluramine was reported to be associated with pulmonary arterial hypertension. Pulmonary arterial hypertension was not observed in the clinical programme, but because of the low incidence of this disease, the clinical trial experience with fenfluramine is inadequate to determine if fenfluramine increases the risk for pulmonary arterial hypertension in patients with Dravet syndrome and Lennox-Gastaut syndrome. If echocardiogram findings are suggestive of pulmonary arterial hypertension, a repeat echocardiogram should be performed as soon as possible and within 3 months to confirm these findings. If the echocardiogram finding is confirmed suggestive of an increased probability of pulmonary arterial hypertension defined as "intermediate probability" by the 2015 European Society of Cardiology (ESC) and the European Respiratory Society (ERS) Guidelines, it should lead to a benefit-risk evaluation of continuation of Fintepla by the prescriber, carer, and cardiologist. If the echocardiogram finding, after confirmation, suggests of a high probability of pulmonary arterial hypertension, as defined by the 2015 ESC and ERS Guidelines, it is recommended fenfluramine treatment should be stopped.

Decreased appetite and weight loss

Fenfluramine can cause decreased appetite and weight loss. An additive effect on decreased appetite can occur when fenfluramine is combined with other anti-epileptic medicines, for example stiripentol. The decrease in weight appears to be dose related. Most subjects resumed weight gain over time while continuing treatment. The patient's weight should be monitored. A benefit risk evaluation should be undertaken prior to commencing treatment with fenfluramine in patients with a history of anorexia nervosa or bulimia nervosa.

Fintepla controlled access programme

A controlled access programme has been created to 1) prevent off-label use in weight management in obese patients and 2) confirm that prescribing physicians have been informed of the need for periodic cardiac monitoring in patients taking Fintepla.

Somnolence

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Fenfluramine can cause somnolence. Other central nervous system depressants, including alcohol, could potentiate the somnolence effect of fenfluramine.

Suicidal behaviour and ideation
Suicidal behaviour and ideation have been reported in patients treated with anti-epileptic medicines in several indications. A meta-analysis of randomised placebo-controlled trials with anti-epileptic medicines that did not include fenfluramine has shown a small increased risk of suicidal behaviour and ideation. The mechanism of this risk is not known, and the available data do not exclude the possibility of an increased risk for fenfluramine. Patients and caregivers of patients should be advised to seek medical advice should any signs of suicidal behaviour and ideation emerge.

Serotonin syndrome
As with other serotonergic agents, serotonin syndrome, a potentially life-threatening condition, may occur with fenfluramine treatment, particularly with concomitant use of other serotonergic agents (including SSRIs, SNRIs, tricyclic antidepressants, or triptans); with agents that impair metabolism of serotonin such as MAOIs; or with antipsychotics that may affect the serotonergic neurotransmitter systems. Serotonin syndrome symptoms may include mental status changes (eg, agitation, hallucinations, coma), autonomic instability (eg, tachycardia, labile blood pressure, hyperthermia), neuromuscular aberrations (eg, hyperreflexia, incoordination), and/or gastrointestinal symptoms (eg, nausea, vomiting, diarrhoea). If concomitant treatment with fenfluramine and other serotonergic agents that may affect the serotonergic systems is clinically warranted, careful observation of the patient is advised, particularly during treatment initiation and dose increases.

Increased seizure frequency
As with other anti-epileptic medicines, a clinically relevant increase in seizure frequency may occur during treatment with fenfluramine, which may require adjustment in the dose of fenfluramine and/or concomitant anti-epileptic medicines, or discontinuation of fenfluramine, should the benefit-risk be negative.

Cyproheptadine
Cyproheptadine is a potent serotonin receptor antagonist and may therefore decrease the efficacy of fenfluramine. If cyproheptadine is added to treatment with fenfluramine, patients should be monitored for worsening of seizures. If fenfluramine treatment is initiated in a patient taking cyproheptadine, fenfluramine's efficacy may be reduced.

Glaucoma
Fenfluramine can cause mydriasis and can precipitate angle closure glaucoma. Discontinue therapy in patients with acute decreases in visual acuity. Consider discontinuation if there is ocular pain and another cause cannot be determined.

Effect of CYP1A2 and CYP2B6 inducers
Co-administration with strong CYP1A2 inducers or CYP2B6 inducers will decrease fenfluramine plasma concentrations, which may lower the efficacy of fenfluramine. If co-administration of a strong CYP1A2 or CYP2B6 inducer with fenfluramine is considered necessary, the patient should be monitored for reduced efficacy and a dose increase of fenfluramine could be considered provided that it does not exceed twice the maximum daily dose (52 mg/day). If a strong CYP1A2 or CYP2B6 inducer is discontinued during maintenance treatment with fenfluramine, consider gradual reduction of the fenfluramine dosage to the dose administered prior to initiating the inducer.

Effect of CYP1A2 or CYP2D6 inhibitors
Initiation of concomitant treatment with a strong CYP1A2 or CYP2D6 inhibitor may result in higher exposure and, therefore, adverse events should be monitored, and a dose reduction may be needed in some patients.

Coadministration of a single 0.35 mg/kg dose of fenfluramine with fluvoxamine (a strong CYP1A2 inhibitor) at steady state (50 mg once daily) in healthy volunteers increased the AUC0-t of fenfluramine by a ratio of 2.1-fold and the Cmax by a ratio of 1.2-fold, and decreased the AUC0-t of norfenfluramine by a ratio of 1.3-fold and the Cmax by a ratio of 1.4-fold, as compared to fenfluramine administered alone.

Coadministration of a single 0.35 mg/kg dose of fenfluramine with paroxetine (a strong CYP2D6 inhibitor) at steady state (30 mg once daily) in healthy volunteers increased the AUC0-t of fenfluramine by a ratio of 1.8-fold and the Cmax by a ratio of 1.1-fold, and decreased the AUC0-t of norfenfluramine by a ratio of 1.2-fold and the Cmax by a ratio of 1.3-fold, as compared to fenfluramine administered alone.

Excipients

This medicinal product contains sodium ethyl para-hydroxybenzoate (E 215) and sodium methyl para hydroxybenzoate (E 219) which may cause allergic reactions (possibly delayed). It also contains sulfur dioxide (E 220) which may rarely cause severe hypersensitivity reactions and bronchospasm. Patients with rare glucose-galactose malabsorption should not take this medicinal product. This medicinal product contains less than 1 mmol sodium (23 mg) per the maximum daily dose of 12 mL, that is to say essentially 'sodium-free'. This medicinal product contains glucose which may be harmful to the teeth.

About BRIVIACT® (brivaracetam) in the EU[2]

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.

Refer to the European Summary of Product Characteristics for other adverse reactions and full prescribing information.

Important Safety Information about BRIVIACT in the EU

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 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

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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 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.

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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 €5.5 billion in 2022. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news.

Forward looking statements
This press release may contain forward-looking statements including, without limitation, statements containing the words "believes", "anticipates", "expects", "intends", "plans", "seeks", "estimates", "may", "will", "continue" and similar expressions. These forward-looking statements are based on current plans, estimates and beliefs of management. All statements, other than statements of historical facts, are statements that could be deemed forward-looking statements, including estimates of revenues, operating margins, capital expenditures, cash, other financial information, expected legal, arbitration, political, regulatory or clinical results or practices and other such estimates and results. By their nature, such forward-looking statements are not guarantees of future performance and are subject to known and unknown risks, uncertainties and assumptions which might cause 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: the global spread and impact of COVID-19, 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, will progress to product approval 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 differences 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's 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. 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3. Cross H, Devinsky O, Gil-Nagel A. Effect of Fenfluramine on Generalized Tonic-Clonic Seizures in Rare Epilepsy Syndromes: A Review of Published Studies. Poster presented at: International Epilepsy Congress (IEC); 2023, September 2-6; Dublin, Ireland.
4. Sanchez-Carpintero R, Devinsky O, Gil-Nagel A. Safety and Efficacy of Fenfluramine in Adult Patients with Dravet Syndrome Enrolled De Novo in an Open-Label Extension Study. Poster presented at: International Epilepsy Congress (IEC); 2023, September 2-6; Dublin, Ireland.
5. Scheffer IE, Ceulemans B, Sullivan J, et al. Impact of Fenfluramine on Drop Seizure Frequency in Adults or Dose-Capped Patients With Lennox-Gastaut Syndrome: Comparative Analysis of Clinical Trial Data. Poster presented at: International Epilepsy Congress (IEC); 2023, September 2-6; Dublin, Ireland.
6. Strzelczyk A, D'Souza W, Faught E, et al. 12-Month Effectiveness and Tolerability of Brivaracetam in Patients With Epilepsy Stratified by Etiology at Baseline in the Real-World: Subgroup Data From the International EXPERIENCE Pooled Analysis. Poster presented at: International Epilepsy Congress (IEC); 2023, September 2-6; Dublin, Ireland.
7. Steinhoff BJ, D'Souza W, Faught E, et al. 12-Month Effectiveness and Tolerability of Brivaracetam in Patients With Epilepsy Switching From Levetiracetam Vs Other Antiseizure Medications in the Real-World: Subgroup Data From the International EXPERIENCE Pooled Analysis. Poster presented at: International Epilepsy Congress (IEC); 2023, September 2-6; Dublin, Ireland.
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9. Devinsky O, Olsen HE, Rajaraman RR, et al. Design of a Phase 3 Clinical Study to Examine the Efficacy and Safety of Fenfluramine in Subjects With CDKL5 Deficiency Disorder Followed by an Open-Label Extension. Poster presented at: International Epilepsy Congress (IEC); 2023, September 2-6; Dublin, Ireland.

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**The safety and efficacy of fenfluramine for the treatment of CDD has not been established and it is not currently approved for use in this indication by any regulatory authority worldwide

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