UCB News

# *JAMA Neurology* Publishes Phase 3 Study Results on the Efficacy and Safety of FINTEPLA® ▼ (fenfluramine) Oral Solution for the treatment of seizures associated with Lennox-Gastaut Syndrome (LGS)

- *Primary endpoint was met demonstrating that fenfluramine, as adjunctive treatment, is effective in significantly reducing the frequency of drop seizures in LGS patients compared to placebo* [1]
- *LGS is a severe childhood-onset developmental and epileptic encephalopathy characterized by drug-resistant seizures with high morbidity*[2]
- *Fenfluramine was recently approved by the U.S. Food and Drug Administration (FDA), as a treatment option for the treatment of seizures associated with LGS, a rare and devastating lifelong childhood-onset epilepsy*[5]

Brussels (Belgium) and Atlanta, GA (USA)., May 2, 2022 – 7:00 PM (CEST) – UCB (Euronext: UCB), a global biopharmaceutical company, today announced the publication in JAMA Neurology of its multi-center, double-blind, placebo-controlled, parallel-group, randomized Phase 3 trial demonstrating that fenfluramine 0.7 mg/kg/day, when added to a patient's current anti-epileptic treatment regimen for seizures associated with LGS, is effective in reducing the frequency of drop seizures.[1] Drop seizures cause a person to suddenly lose muscle tone, become limp, and fall to the ground, with a high likelihood of injury.[6] Within the study, drop seizures were further defined as generalized tonic-clonic (GTC), secondary GTC [focal to bilateral tonic clonic], tonic, atonic, or tonic and atonic.[1]

LGS is a severe childhood-onset developmental and epileptic encephalopathy characterized by drug-resistant seizures with high morbidity[2] as well as serious impairment of neurodevelopmental, cognitive and motor functions.[3] LGS has far-reaching effects beyond seizures, including issues with communication, psychiatric symptoms, sleep, behavioral challenges and mobility.[7]

The trial met its primary efficacy endpoint. Patients taking fenfluramine 0.7 mg/kg/day experienced an estimated mean difference in the reduction of drop seizure frequency by 19.9% from placebo (P=.001). The median percent reduction in the frequency of drop seizures in the 0.7 mg/kg/day

group was 26.5%, compared with 14.2% in the 0.2mg/kg/day group, and 7.6% in patients taking placebo (P=.09). In key secondary outcomes, the trial demonstrated that a greater proportion of patients taking fenfluramine experienced a 50% or greater reduction in drop seizure frequency, compared to patients in the placebo group.[1]

"Our trial data and the clinical evidence demonstrate the safety and efficacy of fenfluramine for the treatment of seizures associated with LGS and especially for patients where generalized tonic-clonic seizures are the predominant seizure type, where there is a greater risk of mortality," said Kelly Knupp, M.D., MSCS, FAES, Associate Professor, Children's Hospital Colorado, Principal Investigator of the study. "LGS is a highly treatment-resistant developmental and epileptic encephalopathy and we need differentiated treatment options, such as fenfluramine, which has a unique mechanism of action different from and complementary to current seizure medications."

The study also included seizure-type subgroup analyses that demonstrated that fenfluramine 0.7mg/kg/day was highly effective in reducing the frequency of GTCs in nearly 50% of patients. During the maintenance and titration period, patients experienced a decrease in frequency of 45.7% in the fenfluramine 0.7mg/kg/day group, a decrease in frequency of 58.2% in the 0.2 mg/kg/day fenfluramine group, compared with an increase in frequency of 3.7% in the placebo group (P=.001 and P<.001 respectively). The percentage reduction in tonic or atonic seizure frequency was 46.7% in the fenfluramine 0.7mg/kg/day group, compared with 6.8% in the placebo group (P=.046).[1]

The reason these data are compelling is because GTCs are commonly observed in patients with LGS.[9] Moreover, GTCs may result in bodily injury.[10,11] Sudden unexpected death in epilepsy (SUDEP) is a major concern for people living with LGS and patients with a history of GTCs have an estimated 10-fold greater risk of SUDEP.[4]

Fenfluramine was generally well-tolerated in this study. The most common treatment-emergent adverse events included decreased appetite (22%), somnolence (13%), and fatigue (13%).[1] The fenfluramine safety database includes long-term cardiovascular safety data for patients treated for up to three years in DS and LGS.[5]

"This study further validates the importance of fenfluramine as a new treatment option for seizures associated with LGS, including generalized tonic-clonic seizures," said Mike Davis, Global Head of Epilepsy, UCB. "Through our close connection with the LGS community, we know the challenges they face go beyond treatment resistant seizures to include difficulty with behavior and cognition, and we hope that fenfluramine can provide relief for people living with LGS."

Site investigators and caregivers also rated patients as significantly much or very much improved on the Clinical Global Impression of Improvement (CGI-I) scale (investigators 26% vs. 20% vs. 6% and caregivers 34% vs. 27% vs. 5% for 0.7 mg/kg vs. 0.2 mg/kg vs. placebo, respectively).[1]

Fenfluramine was approved by the U.S. Food and Drug Administration (FDA) for the treatment of LGS in patients aged 2 and older in March 2022.[5] Fenfluramine was also approved for the treatment of Dravet Syndrome in patients aged 2 and older in June 2020[5] and by the EU Commission in December 2020 as an add-on treatment for seizures associated with Dravet syndrome in patients aged 2 and older.[12] UCB acquired Zogenix, Inc. and FINTEPLA® on March 7, 2022. The acquisition is consistent with UCB's sustainable patient value strategy and continued commitment to providing world-leading patient value to all people living with epilepsy, with an increasing focus on creating value and new solutions that address the unmet needs of people with certain specialized or rare types of epilepsy, where few or no options exist.

**Study Design**
The multi-center, double-blind, placebo-controlled, parallel-group, randomized Phase 3 clinical trial was conducted from 27 November 2017 to 25 October 2019, and had a 20-week trial duration. Patients were enrolled at 65 study sites in North America, Europe, and Australia.

A total of 263 patients were randomly assigned to receive either fenfluramine 0.7mg/kg/day (n=87) or fenfluramine 0.2mg/kg/day (n=89) or placebo (n=87). After titration (2-week period), patients were maintained on their randomized dose for 12 additional weeks. The median age was 13 years.

Children and adults, aged 2 to 35 years, with a confirmed LGS diagnosis who were using stable anti-seizure medication (ASM) regimens (≥1 and ≤4 concomitant ASMs) were eligible for enrollment if these criteria were met: onset of seizures at age 11 years or younger; multiple seizure types, including tonic and tonic or atonic seizures; stable 4-week seizure baseline with 2 or more drop seizures per week of GTC, or secondary GTC (i.e., focal to bilateral tonic-clonic seizures), tonic, atonic, or tonic or atonic seizure; abnormal cognitive development; and medical history showing electroencephalogram evidence of abnormal background activity with slow spike-and-wave pattern (<2.5Hz). Key exclusion criteria were degenerative neurological disease, history of hemiclonic seizures in the first year of life, only drop seizure clusters, previous or current exclusionary cardiovascular or cardiopulmonary abnormality or concomitant cannabidiol use (not FDA approved at time of study).

This study was funded by Zogenix, Inc., now part of UCB.

**About FINTEPLA® (fenfluramine) C-IV**
FINTEPLA® (fenfluramine) oral solution is a prescription medication approved by the FDA and

authorized by the EU Commission, and under regulatory review with the PMDA (Japan), for the treatment of seizures associated with Dravet syndrome in patients two years of age and older.[12,13] FINTEPLA is also approved in the U.S. for the treatment of seizures associated with Lennox-Gastaut syndrome.[5] Application has also been submitted and is currently under assessment by the European Medicines Agency (EMA) for the treatment of seizures associated with LGS.[14]

In the United States, FINTEPLA is available only through a restricted distribution program called the FINTEPLA REMS program. FINTEPLA is available in Europe under a controlled access program requested by the EMA to prevent off-label use for weight management and to confirm that prescribing physicians have been informed of the need for periodic cardiac monitoring in patients taking FINTEPLA. Further information is available at www.FinteplaREMS.com or by telephone at +1 877 964 3649.

Please see full Prescribing Information, including Boxed Warning, for additional important information on FINTEPLA.

**INDICATIONS AND USAGE**

FINTEPLA is indicated for the treatment of seizures associated with Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS) in patients 2 years of age and older.

**IMPORTANT SAFETY INFORMATION**

**BOXED WARNING: VALVULAR HEART DISEASE and PULMONARY ARTERIAL HYPERTENSION**

**• There is an association between serotonergic drugs with 5-HT2B receptor agonist activity, including fenfluramine (the active ingredient in FINTEPLA), and valvular heart disease and pulmonary arterial hypertension.**

**• Echocardiogram assessments are required before, during, and after treatment with FINTEPLA.**

**• FINTEPLA is available only through a restricted program called the FINTEPLA REMS.**

**CONTRAINDICATIONS**

FINTEPLA is contraindicated in patients with hypersensitivity to fenfluramine or any of the excipients in FINTEPLA and with concomitant use, or within 14 days of the administration of monoamine oxidase inhibitors because of an increased risk of serotonin syndrome.

**WARNINGS AND PRECAUTIONS**

**Valvular Heart Disease and Pulmonary Arterial Hypertension (see Boxed Warning):** Because of the association between serotonergic drugs with 5–HT2B receptor agonist activity, including fenfluramine (the active ingredient in FINTEPLA), and valvular heart disease (VHD) and pulmonary arterial hypertension (PAH), cardiac monitoring via echocardiogram is required prior to starting treatment, during treatment, and after treatment with FINTEPLA concludes. Cardiac monitoring via echocardiogram can aid in early detection of these conditions. In clinical trials for DS and LGS of up to 3 years in duration, no patient receiving FINTEPLA developed VHD or PAH.

Monitoring: Prior to starting treatment, patients must undergo an echocardiogram to evaluate for VHD and PAH. Echocardiograms should be repeated every 6 months, and once at 3-6 months post treatment with FINTEPLA.

The prescriber must consider the benefits versus the risks of initiating or continuing treatment with FINTEPLA if any of the following signs are observed via echocardiogram: valvular abnormality or new abnormality; VHD indicated by mild or greater aortic regurgitation or moderate or greater mitral regurgitation, with additional characteristics of VHD (eg, valve thickening or restrictive valve motion); PAH indicated by elevated right heart/pulmonary artery pressure (PASP >35mmHg).

**FINTEPLA REMS Program (see Boxed Warning):** FINTEPLA is available only through a restricted distribution program called the FINTEPLA Risk Evaluation and Mitigation Strategy (REMS) Program. Prescribers must be certified by enrolling in the FINTEPLA REMS. Prescribers must counsel patients receiving FINTEPLA about the risk of valvular heart disease and pulmonary arterial hypertension, how to recognize signs and symptoms of valvular heart disease and pulmonary arterial hypertension, the need for baseline (pretreatment) and periodic cardiac monitoring via echocardiogram during FINTEPLA treatment, and cardiac monitoring after FINTEPLA treatment. Patients must enroll in the FINTEPLA REMS and comply with ongoing monitoring requirements. The pharmacy must be certified by enrolling in the FINTEPLA REMS and must only dispense to patients who are authorized to receive FINTEPLA. Wholesalers and distributors must only distribute to certified pharmacies. Further information is available at www.FinteplaREMS.com or by telephone at 1-877-964-3649.

**Decreased Appetite and Decreased Weight:** FINTEPLA can cause decreases in appetite and weight. Decreases in weight appear to be dose related. Approximately half of the patients with LGS and most patients with DS resumed the expected measured increases in weight during the open-label extension studies. Weight should be monitored regularly during treatment with FINTEPLA, and dose modifications should be considered if a decrease in weight is observed.

**Somnolence, Sedation, and Lethargy:** FINTEPLA can cause somnolence, sedation, and lethargy. Other central nervous system (CNS) depressants, including alcohol, could potentiate these effects of FINTEPLA. Prescribers should monitor patients for somnolence and sedation and should advise patients not to drive or operate machinery until they have gained sufficient experience on FINTEPLA to gauge whether it adversely affects their ability to drive or operate machinery.

**Suicidal Behavior and Ideation:** Antiepileptic drugs (AEDs), including FINTEPLA, increase the risk of suicidal thoughts or behaviors in patients taking these drugs for any indication. Patients treated with an AED for any indication should be monitored for the emergence or worsening of depression, suicidal thoughts or behaviors, or any unusual changes in mood or behavior.

Anyone considering prescribing FINTEPLA or any other AED must balance the risk of suicidal thoughts or behaviors with the risks of untreated illness. Epilepsy and many other illnesses for which AEDs are prescribed are themselves associated with morbidity and mortality and an increased risk of suicidal thoughts and behaviors. Should suicidal thoughts and behaviors emerge during treatment, consider whether the emergence of these symptoms in any given patient may be related to the illness being treated.

**Withdrawal of Antiepileptic Drugs:** As with most AEDs, FINTEPLA should generally be withdrawn gradually because of the risk of increased seizure frequency and status epilepticus. If withdrawal is needed because of a serious adverse reaction, rapid discontinuation can be considered.

**Serotonin Syndrome:** Serotonin syndrome, a potentially life-threatening condition, may occur with FINTEPLA, particularly during concomitant administration of FINTEPLA with other serotonergic drugs, including, but not limited to, selective serotonin-norepinephrine reuptake inhibitors (SNRIs), selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), bupropion, triptans, dietary supplements (eg, St. John's Wort, tryptophan), drugs that impair metabolism of serotonin (including monoamine oxidase inhibitors [MAOIs], which are contraindicated with FINTEPLA), dextromethorphan, lithium, tramadol, and antipsychotics with serotonergic agonist activity. Patients should be monitored for the emergence of signs and symptoms of serotonin syndrome, which include mental status changes (eg, agitation, hallucinations, coma), autonomic instability (eg, tachycardia, labile blood pressure, hyperthermia), neuromuscular signs (eg, hyperreflexia, incoordination), and/or gastrointestinal symptoms (eg, nausea, vomiting, diarrhea). If serotonin syndrome is suspected, treatment with FINTEPLA should be stopped immediately and symptomatic treatment should be started.

**Increase in Blood Pressure:** FINTEPLA can cause an increase in blood pressure. Rare cases of significant elevation in blood pressure, including hypertensive crisis, has been reported in adult patients treated with fenfluramine, including patients without a history of hypertension. In clinical trials for DS and LGS of up to 3 years in duration, no pediatric or adult patient receiving FINTEPLA developed hypertensive crisis. Monitor blood pressure in patients treated with FINTEPLA.

**Glaucoma:** Fenfluramine can cause mydriasis and can precipitate angle closure glaucoma. Consider discontinuing treatment with FINTEPLA in patients with acute decreases in visual acuity or ocular pain.

**ADVERSE REACTIONS**

The most common adverse reactions observed in DS studies (incidence at least 10% and greater than placebo) were decreased appetite; somnolence, sedation, lethargy; diarrhea; constipation;

abnormal echocardiogram; fatigue, malaise, asthenia; ataxia, balance disorder, gait disturbance; blood pressure increased; drooling, salivary hypersecretion; pyrexia; upper respiratory tract infection; vomiting; decreased weight; fall; status epilepticus.

The most common adverse reactions observed in the LGS study (incidence at least 10% and greater than placebo) were diarrhea; decreased appetite; fatigue; somnolence; vomiting.

**DRUG INTERACTIONS**

Strong CYP1A2, CYP2B6, or CYP3A Inducers: Coadministration with strong CYP1A2, CYP2B6, or CYP3A inducers will decrease fenfluramine plasma concentrations. If coadministration of a strong CYP1A2, CYP2B6, or CYP3A inducer with FINTEPLA is necessary, monitor the patient for reduced efficacy and consider increasing the dosage of FINTEPLA as needed. If a strong CYP1A2, CYP2B6, or CYP3A inducer is discontinued during maintenance treatment with FINTEPLA, consider gradual reduction in the FINTEPLA dosage to the dose administered prior to initiating the inducer.

Strong CYP1A2 or CYP2D6 Inhibitors: Coadministration with strong CYP1A2 or CYP2D6 inhibitors will increase fenfluramine plasma concentrations. If FINTEPLA is coadministered with strong CYP1A2 or CYP2D6 inhibitors, the maximum daily dosage of FINTEPLA is 20 mg. If a strong CYP1A2 or CYP2D6 inhibitor is discontinued during maintenance treatment with FINTEPLA, consider gradual increase in the FINTEPLA dosage to the dose recommended without CYP1A2 or CYP2D6 inhibitors. If FINTEPLA is coadministered with stiripentol and a strong CYP1A2 or CYP2D6 inhibitor, the maximum daily dosage of FINTEPLA is 17 mg.

**USE IN SPECIFIC POPULATIONS**

Administration to patients with hepatic impairment is not recommended.

**To report SUSPECTED ADVERSE REACTIONS, contact Zogenix Inc. at 1-866-964-3649 (1-866-Zogenix) or FDA at 1-800-FDA-1088 or www.fda.gov/medwatch.**

**Please see full Prescribing Information, including Boxed Warning, for additional important information on FINTEPLA.**

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**Important Safety Information about FINTEPLA® ▼ in the EU and EEA[12]**

**Contraindications**

Hypersensitivity to the active substance or any of the excipients of Fintepla®. Aortic or mitral valvular heart disease. Pulmonary arterial hypertension. Within 14 days of the administration of monoamine oxidase inhibitors due to an increased risk of serotonin syndrome

**Summary of the safety profile**

The most commonly reported adverse reactions are decreased appetite (44.2%), diarrhoea (30.8%), pyrexia (25.6%), fatigue (25.6%), upper respiratory tract infection (20.5%), lethargy (17.5%), somnolence (15.4%), and bronchitis (11.6%)

**Special warnings and precautions for use**

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, 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. 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 (see section 4.8). 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

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.

Strong CYP1A2 or CYP2B6 inducers
Co-administration with strong CYP1A2 inducers or CYP2B6 inducers may decrease fenfluramine plasma concentrations .
An increase in fenfluramine dosage should be considered when co-administered with a strong CYP1A2 or CYP2B6 inducer; the maximum daily dose should not be exceeded.

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.

Refer to the European Summary of Product Characteristics for other adverse reactions and full prescribing information. Date of revision: 04 Nov 2021.
https://www.ema.europa.eu/en/documents/product-information/fintepla-epar-product-information_en.pdf

▼ *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.*

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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.

**Forward looking statements**

This press release contains 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 but not limited to, the ability of UCB to successfully integrate the operations of Zogenix as planned or at all, 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, 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.

UCB is providing this information, including forward-looking statements, only 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 or reflect any change in its forward-looking statements with regard thereto or any change in events, conditions or circumstances on which any such statement is based, unless such statement is required pursuant to applicable laws and regulations.

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