

UCB presents final open-label extension FINTEPLA[®] ▼ (fenfluramine)¹ data at International Child Neurology Congress (ICNC) Annual Meeting

- **Data demonstrated long-term efficacy of adjunctive fenfluramine in people living with Dravet syndrome aged between 2 and 32 years^{2,3}**
- **Additional caregiver and clinical CGI-I ratings complement seizure reduction measures, providing positive effectiveness endpoint encompassing parent/caregiver assessment of non-seizure outcomes in Lennox-Gastaut syndrome and Dravet syndrome⁴**

Brussels (Belgium), 8 May 2024 - 7.00 am - UCB (Euronext Brussels: UCB), a global biopharmaceutical company, today announced the final three-year open-label extension (OLE) study results of FINTEPLA[®] (fenfluramine) in Dravet syndrome are being presented at the International Child Neurology Congress (ICNC), May 6-10, 2024, in Cape Town, South Africa.

As of January 2023, 375 patients were enrolled in the OLE; 92 were 2 to <6 years old and received ≥ 1 dose of fenfluramine. The data demonstrated that treatment with fenfluramine for up to 3 years in people living with Dravet syndrome was generally well tolerated, with no new or unexpected safety signals identified, and patients experiencing clinically significant, durable reductions in monthly convulsive seizure frequency (MCSF).

- In the modified intent-to-treat (mITT) population (n=324), the median percent MCSF change from baseline over the entire OLE was -66.8%, $P < 0.001$.²
- In the mITT population of patients 2 to <6 years old (n=85), median MCSF change from baseline during the overall OLE was -74.2%, $P < 0.001$.³

In addition, global functioning scores – as measured by the Clinical Global Impression (CGI) scale - were “much improved” or “very much improved” from fenfluramine treatment by 61.4% and 62.5% of caregivers and investigators, respectively.² In patients under 6 years of age, clinically meaningful improvement was reported by 69.0% and 66.7% of caregivers and investigators, respectively.³

No new or unexpected treatment-emergent adverse events were observed in the studies, and there were no cases of valvular heart disease or pulmonary arterial hypertension.^{2,3} The most common (occurring in $\geq 15\%$ of patients during the OLE) treatment-emergent adverse events were pyrexia, nasopharyngitis, decreased appetite, decreased blood glucose diarrhea, upper respiratory tract infection and seizure.^{2,3}

“The final analyses from the open-label extension (OLE) studies being presented at this year’s ICNC meeting reinforce the long-term treatment potential and efficacy of fenfluramine for up to three years, showing profound, durable reductions in median monthly convulsive seizure frequency in people living with Dravet syndrome,” commented Dr Elaine C. Wirrell, principal investigator. “The ultimate goals are reducing seizure frequency for the patient and maximizing developmental potential and quality of life.”

“The data being presented at ICNC highlight the seizure, non-seizure, and improved survival outcomes of fenfluramine as well as our unwavering commitment to transforming care and improving the quality of life for people living with epilepsies,” said Konrad Werhahn, Global Head of Medical Affairs, Epilepsy & Rare Syndromes, UCB. “Hosting this essential gathering on African soil marks a momentous occasion. Approximately 25 million people in Africa are living with epilepsy, and yet more needs to be done to improve patient care and support. Everything we do is centered around providing treatment



options to people and families across the world living with seizure disorders and helping them to maximize their life opportunities.”

UCB data presented at the 18th International Child Neurology Congress

- A phase 3 and interim open-label extension (OLE) study on the median monthly convulsive seizure frequency (MCSF) in patients with Dravet syndrome treated with fenfluramine.²
- A phase 3 and interim OLE study on the MCSF in children under 6 years of age with Dravet syndrome treated with fenfluramine.³
- A comparison study of CGI-I ratings given by caregivers and investigators from the phase 3 and OLE studies in Dravet syndrome and Lennox-Gastaut syndrome.⁴

Symposium

In addition to the poster presentations, UCB will host a symposium on 8 May (12:30–13:30, SAST) entitled 'Navigating the Challenges of Developmental and Epileptic Encephalopathies: Exploring the Window of Opportunity'. At the symposium, we will discuss the importance of an early and accurate diagnosis of DEEs to stop the diagnostic odyssey for patients and families, facilitate timely treatment, and improve outcomes. Through sharing complex case studies, practical steps will be discussed to help navigate some of the diagnostic challenges. The session will also cover the management of seizure and non-seizure outcomes in Dravet syndrome and Lennox-Gastaut syndrome, using illustrative cases.

The symposium is for healthcare professionals only.

*general e-poster display schedule

7, May 2024 & 8 May 2024

1:30 PM – 2:00 PM

4:00 PM – 4:30 PM

9, May 2024

1:30 PM – 2:00 PM

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Important Safety Information about FINTEPLA[®] ▼ (fenfluramine) in the EU¹

▼ *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.*

Indications: 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.





Dosage and Administration: Please refer to SmPC for full information. Should be initiated and supervised by physicians with experience in the treatment of epilepsy. Fintepla is prescribed and dispensed according to the Fintepla controlled access programme. *Dravet syndrome: Patients who are **not** taking stiripentol:* Starting dose is 0.1 mg/kg twice daily (0.2 mg/kg/day). After 7 days, if tolerated, can increase dose to 0.2 mg/kg twice daily (0.4 mg/kg/day). After an additional 7 days, if tolerated and further seizure reduction required, can increase dose to a maximum of 0.35 mg/kg twice daily (0.7 mg/kg/day), which is the recommended maintenance dose. Patients requiring more rapid titration may increase the dose every 4 days. Do not exceed maximum daily dose of 26 mg (13 mg twice daily). *Patients who are taking stiripentol:* Starting dose is 0.1 mg/kg twice daily (0.2 mg/kg/day). After 7 days, if tolerated, can increase dose to 0.2 mg/kg twice daily (0.4 mg/kg/day), which is the recommended maintenance dose. Patients requiring more rapid titration may increase the dose every 4 days. Do not exceed a total dose of 17 mg (8.6 mg twice daily). *Lennox-Gastaut syndrome:* Starting dose is 0.1 mg/kg twice daily (0.2 mg/kg/day). After 7 days, the dose should be increased to 0.2 mg/kg twice daily (0.4 mg/kg/day), if tolerated. After an additional 7 days, if tolerated, dose should be increased to 0.35 mg/kg twice daily (0.7 mg/kg/day), which is the recommended maintenance dose. Do not exceed maximum daily dose of 26 mg (13 mg twice daily). *Discontinuation:* When discontinuing treatment, decrease the dose gradually. As with all anti-epileptic medicines, avoid abrupt discontinuation when possible to minimize the risk of increased seizure frequency and status epilepticus. A final echocardiogram should be conducted 3-6 months after the last dose of treatment with fenfluramine. *Renal impairment:* Generally, no dose adjustment is recommended when administered to patients with mild to severe renal impairment, however, a slower titration may be considered. If adverse reactions are reported, a dose reduction may be needed. Has not been studied in patients with end-stage renal disease. Not known if fenfluramine or its active metabolite, norfenfluramine, is dialyzable. *Hepatic impairment:* Generally, no dose adjustment is recommended when Fintepla is administered without concomitant stiripentol to patients with mild and moderate hepatic impairment (Child-Pugh Class A and B). In patients with severe hepatic impairment (Child-Pugh C) not receiving concomitant stiripentol, the maximum dosage is 0.2mg/kg twice daily, and the maximal total daily dose is 17 mg. There are limited clinical data on the use of Fintepla with stiripentol in patients with mild impaired hepatic function. A slower titration may be considered in patients with hepatic impairment and a dose reduction may be needed if adverse reactions are reported. No clinical data is available on the use of Fintepla with stiripentol in moderate and severe hepatic impairment, therefore not recommended for use. *Elderly:* No data available. *Pediatric population:* Safety and efficacy in children below 2 years of age not yet established. No data available. **Contraindications:** Hypersensitivity to active substance or any excipients. Aortic or mitral valvular heart disease and pulmonary arterial hypertension. Within 14 days of the administration of monoamine oxidase inhibitors due to an increased risk of serotonin syndrome.

Warnings and Precautions: *Aortic or mitral valvular heart disease and pulmonary arterial hypertension:* Prior to starting treatment, patients must undergo an echocardiogram to establish a baseline and exclude any pre-existing valvular heart disease or pulmonary hypertension. Conduct echocardiogram monitoring every 6 months for the first 2 years and annually thereafter. If an echocardiogram indicates pathological valvular changes, consider follow-up earlier to evaluate whether the abnormality is persistent. If pathological abnormalities seen on echocardiogram, evaluate the benefit versus risk of continuing fenfluramine treatment with the prescriber, caregiver and cardiologist. Once treatment is discontinued for any reasons, a final echocardiogram should be conducted 3-6 months after the last dose of treatment with fenfluramine. If echocardiogram findings suggestive of pulmonary arterial hypertension, perform a repeat echocardiogram as soon as possible and within 3 months to confirm these findings. If echocardiogram finding is confirmed suggestive of an increased probability of pulmonary arterial hypertension defined as intermediate probability, conduct a benefit-risk evaluation of continuation of Fintepla by the prescriber, carer and cardiologist. If echocardiogram suggests a high probability, it is recommended fenfluramine treatment should be stopped. *Decreased appetite and weight loss:* Fenfluramine can cause decreased appetite and weight loss - an additive effect can occur in combination with other anti-epileptic medicines such as stiripentol. Monitor the patient's weight. Undertake risk-benefit evaluation before starting treatment if 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 which could be potentiated by other central nervous system depressants. *Suicidal behaviour and ideation:* Suicidal behaviour and ideation have been reported in patients treated with anti-epileptic medicines in several indications. Advise patients and caregivers to seek medical advice should any signs of suicidal behaviour and ideation emerge. *Serotonin syndrome:* Serotonin syndrome, a potentially life-threatening condition, may occur with fenfluramine treatment, particularly with concomitant use of other serotonergic agents; with agents that impair metabolism of serotonin such as MAOIs; or with antipsychotics that may affect the serotonergic





neurotransmitter systems. Carefully observe the patient, particularly during treatment initiation and dose increases.

Increased seizure frequency: A clinically relevant increase in seizure frequency may occur during treatment, 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, monitor patient 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 ocular pain of unknown origin.

Effect of CYP1A2 or 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 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.

Excipients: Contains sodium ethyl para-hydroxybenzoate (E 215) and sodium methyl para-hydroxybenzoate (E 219) - 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 medicine. The product contains less than 1 mmol sodium (23 mg) per the maximum daily dose of 12 mL; essentially 'sodium-free'. Contains glucose - may be harmful to teeth.

Interactions: Pharmacodynamic interactions with other CNS depressants increase the risk of aggravated central nervous system depression. An increase in dose may be necessary when coadministered with rifampicin or a strong CYP1A2 or CYP2B6 inducer. In in vitro studies co-administration with a strong CYP1A2 or CYP2D6 inhibitor may result in higher exposure (see section 4.4 of the SmPC). Co-administration with CYP2D6 substrates or MATE1 substrates may increase their plasma concentrations. Co-administration with CYP2B6 or CYP3A4 substrates may decrease their plasma concentrations.

Pregnancy and lactation: Limited data in pregnant women. As a precaution, avoid use of Fintepla in pregnancy. It is unknown whether fenfluramine/metabolites are excreted in human milk. Animal data have shown excretion of fenfluramine/metabolites in milk. A decision must be made whether to discontinue breast-feeding or to discontinue/abstain from Fintepla taking into account the benefit of breast-feeding for the child and the benefit of therapy for the woman.

Drive and use machines.: Fintepla has moderate influence on the ability to drive/ use machines as it may cause somnolence and fatigue. Advise patients not to drive or operate machinery until they have sufficient experience to gauge whether it adversely affects their abilities.

Adverse effects:

Dravet syndrome: Very common ($\geq 1/10$): Upper respiratory tract infection, decreased appetite, somnolence, diarrhoea, pyrexia, fatigue, blood glucose decreased, echocardiogram abnormal (Consisted of trace and mild mitral regurgitation, and trace aortic regurgitation, which are considered physiologic).

Common ($\geq 1/100$ to $< 1/10$): Bronchitis, abnormal behaviour, aggression, agitation, insomnia, mood swings, ataxia, hypotonia, lethargy, seizure, status epilepticus, tremor, constipation, salivary hypersecretion, weight decreased and blood prolactin increased.

Not known (cannot be estimated from the available data): Pulmonary arterial hypertension.

Lennox-Gastaut syndrome: Very common ($\geq 1/10$): Upper respiratory tract infection, decreased appetite, somnolence, diarrhoea, vomiting, fatigue.

Common ($\geq 1/100$ to $< 1/10$): Bronchitis, influenza, pneumonia, aggression, seizure, status epilepticus, lethargy, tremor, constipation, salivary hypersecretion, blood prolactin increased, weight decreased, fall. Refer to SmPC for other adverse reactions.

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/fintepla-epar-product-information_en.pdf

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 9,000 people in approximately 40 countries, the company generated revenue of €5.3 billion in 2023. 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. 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 it does not reflect any potential impact from the evolving COVID-19 pandemic, unless indicated otherwise. UCB is following the worldwide developments diligently to assess the financial significance of this pandemic to UCB. UCB 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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buy any securities, nor shall there be any offer, solicitation or sale of securities in any jurisdiction in which such offer, solicitation or sale would be unlawful prior to the registration or qualification under the securities laws of such jurisdiction.

References:

1. FINTEPLA® EU SmPC. https://www.ema.europa.eu/en/documents/product-information/fintepla-epar-product-information_en.pdf. (Accessed April 2024).
2. Scheffer I, Nabbout R, Lagae L, et al. 2024. Poster presented at: International Child Neurology Congress (ICNC); Cape Town, South Africa. Safety and Effectiveness of Adjunctive Fenfluramine in an Open-Label Extension Study of Patients With Dravet Syndrome. #667.
3. Scheffer I, Nabbout R, Lagae L, et al. 2024. Poster presented at: International Child Neurology Congress (ICNC); Cape Town, South Africa. Safety and Effectiveness of Adjunctive Fenfluramine in an Open-Label Extension Study of Children (Under 6 Years Old) With Dravet Syndrome. #663.
4. Lagae L, Knupp K, Cross H, et al. 2024. International Child Neurology Congress (ICNC), Cape Town, South Africa. Caregiver versus Investigator Clinical Global Impression-Improvement Ratings in Fenfluramine Clinical Trials. Oral platform session.

