UCB News

UCB Announces Publication of Data in *Brain Communications* Demonstrating Positive Impact of KYGEVVI®▼ (doxecitine and doxribtimine) in Patients with Thymidine Kinase 2 Deficiency (TK2d)

- Data indicate that KYGEVVI therapy improved survival and functional outcomes in people with TK2d.[1]
- Additional data from the largest pool of information on TK2d illustrates the impact and burden of disease progression[2] and highlights the benefits of early diagnosis.[3]

Brussels (Belgium) June 17, 2026, 6PM (CEST) – UCB, a global biopharmaceutical company, today announced the publication of two manuscripts in *Brain Communications*. One manuscript reports integrated safety and efficacy findings for KYGEVVI® (doxecitine and doxribtimine), the first and only approved treatment for paediatric and adult patients with genetically confirmed thymidine kinase 2 deficiency (TK2d) with an age of symptom onset on or before 12 years, demonstrating improved survival and functional outcomes in treated patients, along with acceptable tolerability.[1,3] A second manuscript features findings from the largest published dataset of untreated patients with TK2d, illustrating the progressive burden of disease and increased risk of early death, thus reinforcing the importance of timely diagnosis and treatment.[2]

"TK2d can have a devastating impact on patients and families if left untreated, which the data compiled and published in *Brain Communications* confirm," said Dr. Caterina Garone, Associate Professor of Medical Genetics, University of Bologna, Italy, and co-author of both studies.

Key findings from the TK2d Integrated Summary of Efficacy (ISE)/ Integrated Summary of Safety (ISS) based on data from 104 treated and 114 untreated patients include:

- Treatment was generally well tolerated and improved survival and functional outcomes, especially in patients who developed symptoms on or before 12 years of age.
- In a subgroup of patients with age of TK2d symptom onset on or before 12 years of age, the risk of death was reduced with treatment by 92%–94% from the time of symptom onset.
- In this same subgroup, patients receiving treatment lived an estimated average of 29.2 years over a 30-year period versus 14.4 years for untreated patients.
- After treatment initiation, most patients in the same subgroup (75%) regained at least one motor milestone and some (22.5%) regained at least four.
- Most treatment-emergent adverse events (TEAEs) did not lead to discontinuation; 13.4% discontinued treatment as a result of a TEAE and 23.9% reported at least one TEAE that led to dose reduction. The most frequent TEAE was diarrhea (86%), which was generally mild or moderate and resolved with dose reduction.

"These results represent an important step forward for this rare genetic mitochondrial disease, offering new hope for patients, particularly those with early-onset TK2d," said Dr. Michio Hirano, Professor of Neurology and Chief of the Division of Neuromuscular Medicine at Columbia University Irving Medical Center.

Key findings from the TK2d Natural Disease Course Study, based on a dataset of 257 untreated patients, one of the largest described to date, confirmed the severe disease burden and high mortality associated with TK2d. Untreated TK2d can have serious effects on daily life and life expectancy, especially for those who develop

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symptoms at an early age, underlining the urgent need for diagnosis (via genetic testing) and treatments for this ultra-rare disease.

- Descriptive analyses of survival indicate that TK2d was associated with early death. Of the patients with age of symptom onset on or before 12 years of age, 56.4% died with a median (Q1, Q3) age at death of 1.9 (1.0, 3.5) years. Approximately two-thirds of patients with age of symptom onset ≤2 years (66.7%) and 22.2% of patients with age of symptom onset >2 to ≤12 years died.
- Loss of previously acquired motor milestones was prevalent in patients with age of symptom onset on or before 12 years of age, with 81.3% losing at least one milestone and 37.3% losing four or more. Most of these patients started to lose milestones within the first few years of symptom onset. Spontaneous regain of lost milestones was rare.
- Both ventilatory and feeding support were commonly required regardless of age at onset, underscoring significant burden of the disease.

Approved by the U.S. Food and Drug Administration (FDA) in November 2025, and the European Medicines Agency (EMA) under exceptional circumstances in March 2026, KYGEVVI is a powder for oral solution for the treatment of TK2d in adults and pediatric patients with an age of symptom onset on or before 12 years.[4,5] KYGEVVI is the first treatment approved for early-onset TK2d.

"Over the years, we have seen first-hand the devastating impact TK2d has, but also how timely diagnosis and treatment help to ease that burden," said Donatello Crocetta, Chief Medical Officer at UCB. "At UCB, we are proud to provide doxecitine and doxribtimine as an option for early-onset TK2d, and we know more must be done to ensure diagnosis and treatment to address the community's unmet needs and help to improve outcomes."

INDICATION

KYGEVVI is indicated for the treatment of thymidine kinase 2 deficiency (TK2d) for paediatric and adult patients with genetically confirmed thymidine kinase 2 deficiency (TK2d) with an age of symptom onset on or before 12 years.[3]

KYGEVVI®▼ (doxecitine and doxribtimine) EU/EEA** Important Safety Information[3]

Increase in Liver Transaminases

Elevated liver enzymes and liver dysfunction/failure have been observed as a clinical manifestation of TK2d. In clinical studies elevations in alanine aminotransferase [ALT] and/or aspartate aminotransferase [AST] have occurred in patients with TK2d following treatment with KYGEVVI. Transaminase levels should be checked prior to initiation of treatment, and changes in liver function monitored periodically during treatment with KYGEVVI and according to routine patient management.

Gastrointestinal disturbances

Gastrointestinal disturbances such as diarrhoea, vomiting, and abdominal pain (including abdominal pain upper) are very commonly reported adverse reactions with doxecitine and doxribtimine treatment. In the pooled safety population 37 out of 50 participants (74%) experienced diarrhoea early after treatment initiation (<3 months). The majority of events of diarrhoea were mild to moderate in severity and were generally self-limiting or improved with temporary dose reduction. Of 133 events of diarrhoea, 12% (16/133) required dose reduction with a median duration of 80 days (Q1, Q3=33.0, 201.5). None of the 50 participants discontinued due to gastrointestinal disturbances, including diarrhoea.

Please consult the summary of product characteristics in relation to other side effects, full safety and prescribing information.

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**EU/EEA means European Union/European Economic Area

▼ *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.*

About thymidine kinase 2 deficiency (TK2d)
TK2d is an ultra-rare, life-threatening, genetic mitochondrial disease characterized by progressive (worsening over time) and severe muscle weakness (myopathy). There previously had been no approved treatment options beyond supportive [palliative] care. TK2d can develop at any point in a patient's life. Because long diagnostic journeys and misdiagnoses are common for patients with mitochondrial diseases, people with TK2d may be diagnosed years after symptom onset. Patients aged ≤12 years at TK2d symptom onset face a high risk of premature death, often occurring within 3 years after symptom onset.[2] It is estimated that the worldwide prevalence of TK2d is 1.64 [0.5, 3.1] cases per 1,000,000 people.[6]

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About UCB
UCB, Brussels, Belgium (www.ucb.com) is a global biopharmaceutical company focused on the discovery and development of innovative medicines and solutions to transform the lives of people living with severe diseases of the immune system or of the central nervous system. With more than 9000 people in approximately 40 countries, the company generated revenue of €7.7 billion in 2025. UCB is listed on Euronext Brussels (symbol: UCB).

Forward-looking statements
This document contains forward-looking statements, including, without limitation, statements containing the words "potential", "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 guaranteeing 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 be materially different from any future results, performance, or achievements expressed or implied by such forward-looking statements contained in this document.

Important factors that could result in such differences include but are not limited to: global spread and impacts of wars, pandemics and terrorism, the general geopolitical environment, climate change, 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, supply chain disruption and business continuity risks; potential or actual data security and data privacy breaches, or disruptions of UCB's information technology systems, product liability claims, challenges to patent protection for products or product candidates, competition from other products including biosimilars or disruptive technologies/business models, changes in laws or regulations, exchange rate fluctuations, changes or uncertainties in laws and/or rules pertaining to tax and duties or the administration of such laws and/or rules, and hiring, retention and compliance of 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'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, the public is cautioned not to place any undue reliance on such forward-looking statements. These forward-looking statements are made only as of the date of this document, and do not reflect any potential impacts from the evolving event or risk as mentioned above as well as any other adversity, unless indicated otherwise. The company continues to follow the development diligently to assess the financial significance of these events, as the case may be, to UCB.

UCB expressly disclaims any obligation to update any forward-looking statements in this document, 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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3. KYGEVVI® (doxecitine and doxribtimine) EU Summary of Product Characteristics.

4. KYGEVVI US Approval Press Release. https://www.ucb.com/newsroom/press-releases/article/us-fda-approves-kygevvitm-doxecitine-and-doxribtimine-the-first-and-only-treatment-for-adults-and-children-living-with-thymidine-kinase-2-deficiency-tk2d. Accessed June 2026.

5. KYGEVVI EU Approval Press Release. https://www.ucb.com/newsroom/press-releases/article/european-commission-approves-kygevvirv-doxecitine-and-doxribtimine-as-first-and-only-treatment-for-thymidine-kinase-2-deficiency-tk2d. Accessed June 2026.

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