UCB News

U.S. FDA approves KYGEVVI® (doxecitine and doxribtimine), the first and only treatment for adults and children living with thymidine kinase 2 deficiency (TK2d)

- **Approved indication:** KYGEVVI® (doxecitine and doxribtimine) powder for oral solution (2g/2g) is approved for the treatment of thymidine kinase 2 deficiency (TK2d) in adults and pediatric patients with an age of symptom onset on or before 12 years.[1]
- **Survival benefit:** Treatment reduced the overall risk of death from the start of treatment by approximately 86% (95% CI: 61%, 96%).[1]
- **Burden of disease:** TK2d is an ultra-rare, life-threatening, genetic mitochondrial disease characterized by progressive and severe muscle weakness (myopathy).[2]

Brussels (Belgium) 03 November 2025, 22:00: (CET) – UCB (Euronext Brussels: UCB), a global biopharmaceutical company, today announced that KYGEVVI® has been granted approval by the U.S. Food and Drug Administration (FDA) for the treatment of adults and pediatric patients living with thymidine kinase 2 deficiency (TK2d), with an age of symptom onset on or before 12 years.[1] It is the first and only approved treatment for these patients living with TK2d.

TK2d is an ultra-rare, life-threatening, genetic mitochondrial disease characterized by progressive (worsening over time) and severe muscle weakness (myopathy) with no approved treatment options beyond supportive care until now.[2,3,4,5] It is often fatal, with those experiencing initial symptoms on or before the age of 12 years facing a high risk of premature death (often occurring within 3 years after symptom onset).[6] It is estimated that the worldwide prevalence of TK2d is 1.64 [0.5, 3.1] cases per 1,000,000 people.[7]

"The approval of doxecitine and doxribtimine represents a pivotal moment for the TK2d community who previously had no FDA-approved treatment options for this rare genetic mitochondrial disease beyond supportive [palliative] care," said Donatello Crocetta, Chief Medical Officer at UCB. "We extend heartfelt thanks to the patients, families and friends, advocates, healthcare providers and dedicated clinical trial teams who have partnered with us on this important journey."

"It's hard to overstate the importance of this FDA approval for those diagnosed with TK2d. This is an ultra-rare disease community in dire need of treatment options. For too long, caregivers and their families have had to endure the burden of this disease," said Kristen Clifford, United Mitochondrial Disease Foundation President and CEO. "Having the first-ever FDA-approved therapy for TK2d in this patient population not only meets a critical medical need - it represents something greater - hope for the future."

"I've been studying mitochondrial diseases for more than three decades and have witnessed firsthand the impact TK2d has on patients and their families. We have been waiting for an approved treatment for many years, and this approval marks a significant milestone in how we can support and manage this debilitating condition," said Dr. Michio Hirano, Professor of Neurology and Chief of the Division of Neuromuscular Medicine at Columbia University Irving Medical Center.

GL-MT-2500027 Date of preparation: November 2025

Supporting data
The KYGEVVI approval is supported by safety and efficacy data from one Phase 2 clinical study, two retrospective chart review studies, and an expanded access use program*.[1,8,9,10,11] These studies included a total of 82 unique patients treated with KYGEVVI or pyrimidine nucleosides with an age of TK2d symptom onset ≤12 years. Efficacy was assessed by comparing overall survival in these pediatric and adult treated patients to an external control group of untreated patients who were matched to treated patients using age of TK2d symptom onset (≤ 2 years or >2 to ≤ 12 years).[1] A total of 78 matched pairs were identified. The results showed that survival time from treatment start was improved; treatment reduced the overall risk of death from treatment start by approximately 86% (95% CI: 61%, 96%).[1] Of the 78 treated patients included in the survival analysis, the median age of TK2d symptom onset was 1.5 years (range: 0.01 to 12 years).[1] The median duration of treatment was 4 years (range: 1 day to 12 years) and the median dose received was 762 mg/kg/day (range: 260 to 800 mg/kg/day).[1]

The most common adverse reactions (incidence ≥5%) are diarrhea, abdominal pain (including abdominal pain upper), vomiting, alanine aminotransferase increased (ALT), and aspartate aminotransferase increased (AST).[1]

A regulatory review of doxecitine and doxribtimine is currently underway by the EMA (European Medicines Agency), and further regulatory submissions are planned. KYGEVVI is currently not approved for use in any indication by any regulatory authority outside of the U.S. UCB expects KYGEVVI to be commercially available in the U.S. in Q1, 2026. To further its mission of equitable care, UCB will provide a personalized support program for KYGEVVI that places the needs of patients and caregivers at the forefront.

In the U.S., KYGEVVI received Orphan Drug, Breakthrough, Priority Review and Rare Pediatric Disease designations from the FDA.[12,13] With this approval by FDA, UCB was awarded a Rare Pediatric Disease Priority Review Voucher (RPDPRV) redeemable for a priority review for a future marketing application.

About KYGEVVI
KYGEVVI is a combination of doxecitine and doxribtimine, both pyrimidine nucleosides, indicated for the treatment of thymidine kinase 2 deficiency (TK2d) in adults and pediatric patients with an age of symptom onset on or before 12 years.[1] Administration of KYGEVVI is intended to incorporate the pyrimidine nucleosides, deoxycytidine and deoxythymidine, into skeletal muscle mitochondrial DNA.**Error! Bookmark not defined.** This action restores mitochondrial DNA copy number in TK2d mutant mice.[1]

Important safety information for KYGEVVI[1]

Increase in Liver Transaminases

Elevated liver transaminase [alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST)] levels were reported in patients treated with KYGEVVI. Obtain baseline liver transaminase (ALT, AST) and total bilirubin levels in patients prior to treatment initiation with KYGEVVI. If signs or symptoms consistent with liver injury are observed, interrupt treatment with KYGEVVI until liver transaminase (ALT, AST) and total bilirubin levels have either returned to baseline or stabilized at a new baseline value. Consider permanently discontinuing KYGEVVI if signs or symptoms consistent with liver injury persist or worsen. Monitor liver transaminases and total bilirubin levels yearly and as clinically indicated.

Gastrointestinal Adverse Reactions

Diarrhea and vomiting leading to hospitalization, dose reduction, and permanent discontinuation were reported in patients treated with KYGEVVI. Based on the severity of the diarrhea and/or vomiting, reduce the dosage of

GL-MT-2500027 Date of preparation: November 2025

KYGEVVI or interrupt treatment until diarrhea and/or vomiting improves or returns to baseline. Consider restarting KYGEVVI at the last tolerated dose, and increase the dose as tolerated. For persistent or recurring diarrhea and/or vomiting, consider discontinuing KYGEVVI permanently and provide supportive care with electrolyte repletion as clinically indicated.

Please see the full U.S Prescribing Information for additional information. Talk to your healthcare provider about your condition or your treatment.

**The KYGEVVI® approval is supported by safety and efficacy data from one Phase 2 clinical study (Trial 1, (NCT03845712), two retrospective chart review studies (Study 1 and Study 2, NCT03701568 and NCT05017818 respectively), and an expanded access use program (NCT06590493).*

For more information about the trial visit: https://clinicaltrials.gov/study/NCT03845712 *(NCT03845712);* https://clinicaltrials.gov/study/NCT03701568 *(NCT03701568);* https://clinicaltrials.gov/study/NCT05017818 *(NCT05017818);* https://clinicaltrials.gov/study/NCT06590493 *(NCT06590493).*

For further information, contact UCB:

Global Communications
Nick Francis
T: +44 7769 307745
nick.francis@ucb.com

US Rare Diseases Communications
Daphne Teo
T: +1 770.880.7655
daphne.teo@ucb.com

Corporate Communications, Media Relations
Laurent Schots
T +32.2.559.92.64
laurent.schots@ucb.com

Investor Relations
Antje Witte
T +32.2.559.94.14
antje.witte@ucb.com

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 9 000 people in approximately 40 countries, the company generated revenue of € 6.1 billion in 2024. UCB is listed on Euronext Brussels (symbol: UCB). Follow us on Twitter: @UCB_news

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

GL-MT-2500027 Date of preparation: November 2025

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.

References:

1. KYGEVVI® U.S. Prescribing Information
2. Berardo A, et al. Advances in Thymidine Kinase 2 Deficiency: Clinical Aspects, Translational Progress, and Emerging Therapies. J Neuromuscul Dis. 2022;9(2):225-235.
3. Wang J, et al. eds. GeneReviews®. [Internet]. Seattle (WA): University of Washington, Seattle; 1993-2024.
4. Domínguez-González C, et al. Late-onset thymidine kinase 2 deficiency: a review of 18 cases. Orphanet J Rare Dis. 2019;14(1):100.
5. National Institute of Health. TK2-related mitochondrial DNA depletion syndrome, myopathic form. https://medlineplus.gov/genetics/condition/tk2-related-mitochondrial-dna-depletion-syndrome-myopathic-form/#genes. Accessed October 2025.
6. Hirano M, et al. The Disease Course of Untreated Patients with Thymidine Kinase 2 Deficiency (TK2d) Aged ≤12 Years at TK2d Symptom Onset: Findings from the Largest International TK2d Dataset. 2025 AAN.
7. Ma Y. 2023 ISPOR Europe. EPH140.
8. ClinicalTrials.gov.NCT03701568. https://clinicaltrials.gov/study/NCT03701568. Accessed October 2025.
9. ClinicalTrials.gov.NCT03845712. https://clinicaltrials.gov/study/NCT03845712. Accessed October 2025.
10. ClinicalTrials.gov.NCT05017818. https://clinicaltrials.gov/study/NCT05017818. Accessed October 2025.
11. ClinicalTrials.gov. NCT06590493. https://clinicaltrials.gov/study/NCT06590493. Accessed October 2025.
12. U.S. FDA Orphan Drug Designations and Approvals.https://www.accessdata.fda.gov/scripts/opdlisting/oopd/detailedIndex.cfm?cfgridkey=532716. Accessed October 2025.
13. UCB Press Release. https://www.ucb.com/newsroom/press-releases/article/on-growth-path-for-a-decade-plus-strong-launch-execution-driving-company-growth. Accessed October 2025.

