Company Announcement

CHMP recommends EU approval for Duvyzat to treat Duchenne muscular dystrophy

- Recommendation is based on Phase 3 EPIDYS trial data that demonstrated Duvyzat (givinostat) provides statistically and clinically meaningful treatment benefits in individuals with Duchenne muscular dystrophy (DMD)
- If approved by the European Commission, Duvyzat will be available for individuals with DMD aged six years and older who are able to walk; adding to the existing authorisations, already granted in the US and UK
- European Commission decision on marketing authorisation is expected in July 2025

MILAN, Italy, April 25, 2025 – Italfarmaco S.p.A. announced today that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) has adopted a positive opinion recommending the granting of a conditional marketing authorisation for Duvyzat® (givinostat), a novel histone deacetylase (HDAC) inhibitor. The recommended marketing authorisation is for the treatment of patients with Duchenne muscular dystrophy (DMD) aged six years and older who are able to walk (ambulant), when taken together with corticosteroids. Conditional approval would make Duvyzat available to patients while Italfarmaco continues to generate additional clinical evidence to further strengthen and expand upon the compelling results observed to date. The European Commission (EC) will review the CHMP's recommendation and is expected to make a final decision in July 2025. Pending authorisation, Italfarmaco will work closely with local authorities to facilitate rapid access, ensuring Duvyzat is made available across the European Union (EU).

"The CHMP's recommendation is a validation of Duvyzat's therapeutic potential," said **Paolo Bettica, MD, PhD, Chief Medical Officer at Italfarmaco Group**. "This milestone reflects our unwavering commitment to advancing innovative treatments that can provide life-changing benefits to individuals living with DMD. We are profoundly grateful to the families, caregivers, and patient communities whose engagement and advocacy have been instrumental in reaching this significant achievement."

"The urgent need for disease-modifying therapies in Duchenne cannot be overstated, and this CHMP recommendation marks a critical step forward. Through years of rigorous research, Duvyzat has consistently demonstrated a favourable risk-benefit profile and the potential to significantly delay disease progression across a broad range of patients. Its unique mechanism of action represents an important addition to the treatment landscape, offering new hope that Duvyzat could become a foundational therapy for those living with Duchenne," said **Prof Eugenio Mercuri, MD, Professor of Paediatric Neurology at the Catholic University, Rome, Italy.**

"Together with the DMD community, we welcome the CHMP's opinion, which moves us closer to making Duvyzat available to eligible patients living with Duchenne in the EU," said **Dr. Francesco De Santis, President of Italfarmaco Holding and Chairman of Italfarmaco Group at Italfarmaco**. "The positive decision supports bringing this novel treatment to patients while we continue to generate additional clinical evidence. Our focus remains clear: to improve outcomes and quality of life for individuals affected by Duchenne."

The positive CHMP decision is based on the results of the EPIDYS Phase 3 multicentre, randomised, double-blind, placebo-controlled trial (NCT02851797). In the EPIDYS study, a

total of 179 ambulant boys six years of age or older received either Duvyzat twice daily or placebo, in addition to corticosteroid treatment. The EPIDYS study met its primary endpoint demonstrating a statistically significant and clinically meaningful difference in time to complete the four-stair climb assessment. Duvyzat also showed favourable results on key secondary endpoints including North Star Ambulatory Assessment (NSAA) and fat infiltration evaluation by magnetic resonance imaging. Specifically, Duvyzat treatment was associated with 40% less decline in cumulative loss of NSAA items, indicating Duvyzat's potential to delay disease progression in affected individuals. Most adverse effects observed with Duvyzat were mild to moderate in severity. Results from this study were published in *The Lancet Neurology* in March 2024.[1] Long-term data from the ongoing EPIDYS extension study was presented at the MDA conference, showing that givinostat may delay disease progression. Using propensity score matching, the median age at loss of ambulation was 18.1 years in the givinostat group versus 15.2 years in controls.[2]

In March 2024, the US Food and Drug Administration (FDA) approved Duvyzat for the treatment of patients aged six years and older independent of ambulation status, and in December 2024, the UK Medicines and Healthcare Products Regulatory Agency (MHRA) granted full approval for ambulant patients six years and older, while conditional approval was given for non-ambulant patients.

In compliance with the paediatric investigational plan (PIP), Italfarmaco is conducting two additional clinical studies to determine the safety and efficacy in non-ambulant patients with DMD nine years of age and older (NCT 05933057), and to assess the safety and potential benefits of early treatment in patients with DMD two to five years of age (NCT 06769633). These studies are an integral part of Italfarmaco's efforts to generate additional evidence and to expand the understanding of Duvyzat's full therapeutic potential across the broad spectrum of disease progression with the goal of ensuring access for all individuals affected by DMD, regardless of age or functional status.

About Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is a rare, progressive neuromuscular disorder caused by mutations in the *DMD* gene. Mutations in the *DMD* gene prevent the production of functional dystrophin, causing the dystrophin-associated protein complex (DAPC) to break down. This makes muscle fibres more vulnerable to damage and increases histone deacetylase (HDAC) levels in the muscle cells, blocking the activation of important genes needed for muscle maintenance and repair. As a result, muscle fibres experience ongoing damage, leading to chronic inflammation and poor regeneration. Over time, muscle cells die and are replaced by scar tissue and fat.[3, 4-6] DMD primarily affects males, with symptoms typically appearing between the ages of two and five. As the condition progresses, muscle weakness worsens, leading to difficulty walking and eventually to loss of ambulation. Over time, the heart and respiratory muscles are also affected, which are the leading causes of premature death.[7] DMD is one of the most severe and common forms of childhood muscular dystrophy, with a global birth incidence of approximately 1 in 5,050 boys.[8]

About Duvyzat®

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Duvyzat was discovered through Italfarmaco's research and development efforts in collaboration with Telethon and Duchenne Parent Project (Italy). Duvyzat is an orally administered histone deacetylase (HDAC) inhibitor that regulates the excessive HDAC activity characteristic of DMD muscles. By doing so, it helps restore the expression of key genes and biological processes essential for muscle maintenance and repair. Its mechanism of action is independent of the specific dystrophin gene mutation causing the disease.[9,10]

About ITALFARMACO

Founded in 1938 in Milan, Italy, Italfarmaco is a private global pharmaceutical company that has led the successful development and approval of many pharmaceutical products around the world. The Italfarmaco group has operations in more than 60 countries through directly controlled or affiliated companies. The company is a leader in pharmaceutical research, product development, production and commercialisation with proven success in many therapeutic areas including immuno-oncology, gynaecology, neurology, cardiovascular disease and rare diseases. Italfarmaco's rare disease unit includes programmes in Duchenne muscular dystrophy, Becker muscular dystrophy, amyotrophic lateral sclerosis and polycythaemia vera.

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