Company Announcement

ITF Therapeutics Announces Publication of Positive Long-Term Data Reinforcing Givinostat Efficacy and Safety as a Treatment for Duchenne Muscular Dystrophy

- New data published in *Annals of Clinical and Translational Neurology* show that long-term treatment with givinostat can significantly delay loss of key mobility functions in patients with Duchenne muscular dystrophy
- Meaningful clinical benefit was observed across treatment groups, regardless of disease stage at initiation
- Givinostat remained well-tolerated during extended use, consistent with previous clinical trials
- Average follow-up in the extension study exceeded 36 treatment months, with some patients receiving treatment for over eight years since initiating givinostat treatment.

Please see **Important Safety Information** below and the full **Prescribing Information**.

CONCORD, Mass., August 25, 2025 – ITF Therapeutics LLC, the U.S. affiliate of Italfarmaco, today announced publication of positive long-term safety and efficacy data for givinostat as a treatment for Duchenne muscular dystrophy (DMD) from the company's open-label extensions of its Phase 2 and Phase 3 (EPIDYS) trials. The results, published in *Annals of Clinical and Translational Neurology,* show that long-term treatment with givinostat, a novel histone deacetylase (HDAC) inhibitor, in combination with corticosteroids, delayed disease progression in ambulant patients aged six years and older with DMD. Importantly, clinical benefit was observed across treatment groups receiving givinostat, with positive impact on key mobility functions such as rising from the floor, climbing stairs, and the ability to walk (ambulation). Givinostat has received marketing authorization in the U.S., E.U. and U.K.

"These data represent an important step in building a robust body of evidence for the long-term use of givinostat in DMD," said **Paolo Bettica, MD, PhD, Chief Medical Officer at Italfarmaco**. "The sustained benefit observed across functional outcomes reinforces the potential of givinostat to meaningfully alter the course of the disease. With its well-established safety profile and ease of administration, givinostat continues to emerge as a valuable treatment option for patients affected by DMD and their families."

The study included multiple cohorts of boys with DMD all of whom received givinostat over various durations. Some had previously taken part in the Phase 2 or Phase 3 EPIDYS studies - either on active treatment or placebo - before entering the extension study. Others enrolled directly into the extension study after meeting eligibility criteria while not participating in the main trial. The total treatment exposure for some patients exceeded eight years.

Using propensity matching methods, 142 patients receiving givinostat and 142 from the natural history cohort were included in the analyses. In individuals who began treatment with givinostat in EPIDYS or the long-term extension study, patients treated with givinostat experienced a delay in disease progression compared to the matched natural history cohort. The data suggest that givinostat may delay the loss of the ability to rise from the floor by a median of 2.0 years, loss of the ability to climb four stairs (4SC) by 3.3 years, and loss of the ability to walk by 2.9 years. These findings further support the potential of givinostat to provide clinical benefit to patients with DMD. Givinostat was generally well-tolerated across all cohorts in this open-label extension study, and no new safety signals emerged during long-term treatment.

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"For patients and families affected by Duchenne, maintaining motor function for as long as possible can mean more independence, more participation, and more time doing everyday activities that matter," said **Scott Baver, PhD, Vice President, Medical Affairs at ITF Therapeutics.** "Our new long-term data further reinforce the potential of our treatment option to make a real difference for patients."

"These new findings show that treatment with givinostat continues to have a positive impact by addressing symptoms that patients are most concerned about, and that these long-term benefits are achieved over several years while treatment remains safe and tolerable," added **Craig M. McDonald, Chair, Department of Physical Medicine & Rehabilitation, Professor, Departments of Pediatrics and Physical Medicine & Rehabilitation, University of California Davis Health, Sacramento, CA**.

Duvyzat was approved by the US Food and Drug Administration (FDA) in March 2024 for the treatment of DMD patients six years and older. The European Commission (EC) also granted Duvyzat conditional marketing authorisation in the EU in June 2025 for ambulant DMD patients 6 years and older. In December 2024, the UK's Medicines and Healthcare products Regulatory Agency (MHRA) approved Duvyzat for patients aged six years and older who are ambulatory and granted conditional marketing approval for non-ambulatory patients.

Indication

What is DUVYZAT?

DUVYZAT is a prescription medicine for the treatment of Duchenne muscular dystrophy (DMD) in people 6 years of age and older. It is not known if DUVYZAT is safe and effective in children under age 6.

Important Safety Information

What is the most important information I should know about DUVYZAT?

- **Low platelet counts in your blood (thrombocytopenia)**. Platelets are important for blood clotting, so having fewer can increase your risk of bleeding or bruising. Your doctor will check your blood count before you start DUVYZAT and regularly during treatment for signs of thrombocytopenia. Call your doctor right away if you notice unusual bleeding or small red or purple spots on the skin.
- **Increased levels of fat (triglycerides) in your blood**. You may not have any symptoms, so your doctor will do blood tests before you start DUVYZAT and regularly during treatment to check your triglyceride levels.
- **Frequent watery loose stools (diarrhea) and vomiting**. DUVYZAT can cause vomiting and moderate to severe diarrhea. If diarrhea occurs, you should keep track of the frequency and severity of your symptoms, drink plenty of fluids, and contact your doctor.
- If thrombocytopenia, increased triglycerides, or diarrhea cannot be managed, your doctor may change your dose or stop your treatment with DUVYZAT, if needed.

Before taking DUVYZAT, tell your doctor about all of your medical conditions, including:

- any heart problems or medicines you take that could increase your chance for irregular heart rhythms.
- any bleeding problems.

What are the possible side effects of DUVYZAT?

- **DUVYZAT can cause serious side effects, including changes in the electrical activity of your heart called QT prolongation**. QT prolongation can increase the risk of developing a type of irregular heart rhythm known as Torsades de Pointes. Call your doctor right away if you feel faint, have an irregular heartbeat, feel dizzy, or lose consciousness. **See the section titled "What is the most important information I should know about DUVYZAT?" for more information about side effects**.

The most common side effects (occurring in >5% of DUVYZAT-treated patients) included diarrhea, abdominal pain, low platelet levels, nausea/vomiting, high triglyceride levels, elevated temperature/fever, muscle aches, rash, joint pain, fatigue, constipation and decreased appetite.

Call your doctor for medical advice about side effects. You may report side effects to FDA at 1- 800-FDA-1088.

Please see full Prescribing Information and Medication Guide

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.[1-4] 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.[5] 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.[6]

About Duvyzat®

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. [7, 8]

About ITF Therapeutics LLC

ITF Therapeutics was launched in January 2024 as the U.S. affiliate of Italfarmaco focused on the development and commercialization of products to treat rare diseases. Building on a legacy grounded in collaboration and innovation, ITF Therapeutics strives to partner with leaders from the patient advocacy and treatment communities to ensure that our programs reflect and support their unique needs and goals. The establishment of ITF Therapeutics reflects Italfarmaco's goal to build a world-class team of experts who share a passion to make a positive impact for rare disease communities. For more information visit www.itftherapeutics.com.

About ITALFARMACO

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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 90 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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