Company Announcement

Italfarmaco Receives FDA Approval for Duvyzat™ (givinostat) in Duchenne Muscular Dystrophy

Orally administered treatment for DMD approved in patients 6 years and older

EPIDYS trial met primary endpoint demonstrating statistically and clinically meaningful treatment benefit in one of the largest DMD phase 3 trials to date

Median follow-up of over 3 additional years in open label long-term safety and tolerability study

Italfarmaco also announces establishment of new U.S.-based subsidiary ITF Therapeutics to expand company focus on rare diseases and lead commercial launch for Duvyzat™

MILAN, Italy, March 22, 2024 – Italfarmaco S.p.A. announced today that the U.S. Food and Drug Administration (FDA) has approved Duvyzat™ (givinostat), a novel histone deacetylase (HDAC) inhibitor, for the treatment of patients 6 years or older with Duchenne muscular dystrophy (DMD), a rare X-linked progressive and life-limiting neuromuscular condition with symptoms from early childhood.

"The FDA's approval of Duvyzat for DMD, based on our robust and successful clinical development program, reflects Italfarmaco's commitment to providing a safe and proven-effective therapy that can have a meaningful impact for people living with DMD," **said Paolo Bettica, MD, PhD, Chief Medical Officer at Italfarmaco Group.** "We are grateful for the support of those living with DMD and their dedicated caregivers, which played a central role in helping us reach this landmark FDA approval. Our focus now is to make Duvyzat available as a treatment for DMD management in the U.S. as quickly as possible."

Dr Francesco De Santis, President of Italfarmaco Holding and Chairman of Italfarmaco Group added, "Duchenne muscular dystrophy is a disease with significant unmet medical need and Duvyzat has the potential to benefit a broad DMD patient population independent of the underlying gene mutation that causes the disease. The FDA approval highlights the dedication of Italfarmaco's research and clinical teams to achieve this milestone for the company."

The approval is based on the results of the pivotal multicentre, randomised, double-blind, placebo-controlled phase 3 EPIDYS 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 glucocorticosteroid treatment. The EPIDYS study met its primary endpoint demonstrating that patients on Duvyzat showed 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. The majority of adverse effects observed with Duvyzat were mild to moderate in severity. Results from this study were published in *The Lancet Neurology* in March 2024.

"There is a tremendous unmet need for novel therapies in DMD that can achieve meaningful benefits for a broad range of patients. Duvyzat's unique mechanism of action has shown a positive risk/benefit profile and the ability to delay disease progression, supporting its potential to become a key component of the standard of care for people living with DMD," **added Craig M. McDonald, MD, Professor at the Department of Pediatrics and Physical Medicine**

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Rehabilitation at the University of California Davis Health and investigator for the EPIDYS trial. "I would like to thank all patients and their families for participating in the clinical trials and for making this approval possible."

"We are thrilled with the FDA's approval of Duvyzat, a new therapy for DMD. It is an oral medication that will be available to every person 6 years and older with DMD. This brings great hope for the Duchenne community, and we believe this will be a key therapy to prevent disease progression in Duchenne," said **Pat Furlong, Founding President & CEO at Parent Project Muscular Dystropy (PPMD).**

Italfarmaco has significantly expanded its U.S. presence through the formation of a new fully owned subsidiary, ITF Therapeutics LLC. ITF Therapeutics will be responsible for the commercialisation of Duvyzat in the U.S. and the company is working closely with healthcare providers, patient advocacy groups and payors to make Duvyzat available to patients.

Duvyzat received priority review, orphan drug and rare pediatric disease designations from the FDA. A Marketing Authorisation Application (MAA) for givinostat as a potential treatment for DMD has been submitted to the European Medicine Agency (EMA) and is currently under review. Italfarmaco has a global presence and is also working with other regulatory agencies.

About Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is a severe neuromuscular genetic disease characterised by progressive muscle weakness and degeneration and is the most common type of muscular dystrophy globally. DMD is caused by mutations in the dystrophin gene that result in the absence of a functional dystrophin protein. Without dystrophin, muscle fibres are highly susceptible to injury and this continuous muscle injury leads to chronic inflammation, impairment of muscle regeneration and muscle replacement by fibrotic and fat tissue. The disease primarily affects boys, with symptoms usually first seen between two and five years of age. Symptoms worsen over time affecting the ability to walk. Eventually, heart and respiratory muscles are affected, which are the two main causes of premature death. DMD incidence is approximately one in every 3500 - 6000 male births worldwide.

About Duvyzat™

Duvyzat is an investigational drug discovered through Italfarmaco's research and development efforts in collaboration with Telethon and Duchenne Parent Project (Italy). Duvyzat is a histone deacetylase (HDAC) inhibitor that modulates the deregulated activity of HDACs in the dystrophic muscle, which is a major consequence of the lack of dystrophin associated with DMD. Duvyzat's mechanism of action has the potential to inhibit HDAC pathological overactivity in an effort to address the cascade of events leading to muscle damage, thereby counteracting the disease pathology and slowing down muscle deterioration.

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.

Indication and Important Safety Information

What is DUVYZAT?

DUVYZAT is a prescription medicine that is used 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 6 years of age.

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, and a decrease in their numbers can lead to an increased risk of bleeding or bruising. Your healthcare provider will check your blood count before you start DUVYZAT and regularly during treatment for any signs of thrombocytopenia. Call your healthcare provider right away if you notice any unusual bleeding or small red or purple spots on the skin called petechiae. Your healthcare provider may change your dose of DUVYZAT if your blood platelet counts continue to be low or may stop your treatment with DUVYZAT.
- **Increased levels of fat (triglycerides) in your blood.** You may not have any symptoms, so your healthcare provider will do blood tests before you start DUVYZAT and regularly during treatment to check your triglyceride levels. Your healthcare provider may change your dose of DUVYZAT if your triglyceride levels continue to be high or may stop your treatment with DUVYZAT.
- **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 diarrhea symptoms, drink plenty of fluids, and contact your healthcare provider. Your healthcare provider may change your dose of DUVYZAT if the diarrhea cannot be managed or does not go away. Your healthcare provider may also stop your treatment with DUVYZAT.

Before taking DUVYZAT, tell your healthcare provider about all of your medical conditions, including if you:

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

Tell your healthcare provider about all of the medicines you take, including prescription and over-the-counter medicines, vitamins, and herbal supplements.

Taking DUVYZAT with certain other medicines may affect each other. Taking DUVYZAT with other medicines can cause serious side effects. Do not start or stop other medicines without talking to your healthcare provider.

DUVYZAT can cause serious side effects, including:

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- **See "What is the most important information I should know about DUVYZAT?"**
- **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 healthcare provider right away if you feel faint, have an irregular heartbeat, feel dizzy, or lose consciousness.

The most common side effects of DUVYZAT included diarrhea, nausea, vomiting, stomach pain, low platelet counts in the blood, increased fat level in the blood and fever.

These are not all of the possible side effects of DUVYZAT. For more information, ask your healthcare provider or pharmacist.

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.

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