PRESS RELEASE

Italfarmaco Group Announces Positive Topline Data from Phase 3 Trial Showing Beneficial Effect of Givinostat in Patients with Duchenne Muscular Dystrophy

-- Study meets primary endpoint with secondary and exploratory endpoints showing consistency with primary endpoint --

-- Data reinforces previously observed safety profile for Givinostat; treatment in boys with DMD continues to show a good tolerability profile --

-- The company is planning to discuss the potential for marketing application submission with regulatory authorities for Givinostat in DMD --

-- Results were presented at the Annual PPMD Conference on June 25, 2022 --

MILAN, Italy, June 25, 2022 – Italfarmaco Group announced today positive topline data from its completed Phase 3 EPIDYS trial with Givinostat, the company's proprietary histone deacetylase (HDAC) inhibitor, in boys with Duchenne Muscular Dystrophy (DMD). The primary objective of the study was to evaluate the effects of Givinostat on slowing disease progression in ambulant DMD boys aged 6 years and above on chronic steroids. The study compared Givinostat to placebo and met the primary endpoint (change from baseline in the time to climb 4 stairs) following 18 months of treatment in the target population[1] with key secondary endpoints consistent with the functional primary endpoint. Givinostat continued to demonstrate a tolerability profile in line with previous studies. The topline data were presented by Italfarmaco Group's Chief Medical Officer, Dr. Paolo Bettica on June 25, 2022, at the hybrid Parent Project Muscular Dystrophy (PPMD) Annual Conference.

In October 2020, the U.S. Food and Drug Administration (FDA) granted a Rare Pediatric Disease designation to Givinostat for the treatment of DMD. Earlier, the company also received an Orphan Drug Designation from the FDA and EMA, and a Fast Track designation from the FDA. Based on the study results, which show that the addition of Givinostat to steroid treatment leads to clinical benefits for the individuals in the study, the company plans to meet with US and EU regulators to discuss the potential for marketing application submission and seek input on a future submission of the application for regulatory approval. The company intends to submit the complete results of the EPIDYS study for publication in a peer-reviewed journal in due course.

"These topline Phase 3 results in DMD add to the growing dataset we have collected over the last years which have shown positive outcomes with our investigational therapeutic candidate, Givinostat, when taken together with steroids in patients with DMD, providing new hope for boys with DMD, their families and the medical community," said **Paolo Bettica, MD, PhD, Chief Medical Officer at the Italfarmaco Group**. "There is a tremendous unmet medical need for additional drugs to treat this

[1] Target population: Individuals with a baseline vastus lateralis muscle fat fraction (VL MFF) assessed by magnetic resonance spectroscopy (MRS) in the range >5% and ≤ 30%

debilitating rare disease and with these positive results, we intend to meet with regulatory agencies to share these findings and discuss a path forward to submit the complete dataset in a marketing application for potential approval. We are extremely excited to share these new positive analyses from the EPIDYS trial with the community and would like to thank all the stakeholders involved."

The EPIDYS Phase 3 clinical trial is a randomized, double-blind, placebo-controlled, multicenter study evaluating the efficacy and safety of Givinostat in individuals with DMD (Cinicaltrials.gov: NCT02851797). The trial enrolled 179 male ambulant individuals with a mean age of 9 years and on stable steroids for at least 6 months. Boys were randomized 2:1 and treated chronically with an oral suspension of Givinostat or placebo for a period of 18 months. Of these, 120 boys formed the target population[1].

Overview of Clinical Results

Primary Endpoint: The mean change from baseline to climb 4 stairs was selected as the primary endpoint to assess the efficacy of Givinostat compared to placebo. The results demonstrated a slower decline to perform this functional task in the Givinostat-treated group (difference vs Placebo of 1.78 seconds, p=0.0345).

Key Secondary Endpoints: A variety of secondary endpoints were analyzed that showed results consistent with the functional primary endpoint. These included functional tests such as the North Star Ambulatory Assessment (NSAA) and the time to rise (TTR) test along with muscle strength analyses. Fat infiltration in the vastus lateralis (VL) muscle of the thigh is a characteristic of disease progression in DMD patients and was measured using a non-invasive objective imaging method called Magnetic Resonance Spectroscopy (MRS) to assess the efficacy of Givinostat. The data indicated that treatment with Givinostat delayed fat infiltration by approximately 30% (difference vs Placebo, -2.9%, nominal p=0.035). Additional exploratory endpoints were also analyzed in the clinical study. These results further support the potential of Givinostat in providing a clinical benefit for boys with DMD.

Safety and Tolerability: The majority of Adverse Events (AE) were mild to moderate in severity (95%). Three (2.5%) boys treated with Givinostat withdrew from the trial because of an AE. Similar to what had been previously observed, the AE occurring in at least 1/10 subjects were diarrhea, abdominal pain, thrombocytopenia, hypertriglyceridemia, platelet decrease and triglyceride increase. Givinostat tolerability was managed with appropriate monitoring and dose adjustments. No other safety concerns were observed.

Prof. Eugenio Mercuri, Professor of Paediatric Neurology at the Catholic University, Rome, Italy, commented, "These results show Givinostat's beneficial effect in DMD boys providing evidence of its ability to slow down disease progression."

"I believe the EPIDYS study results are clinically meaningful, are consistent with previous findings and further demonstrate that Givinostat can slow down muscle deterioration leading to a reduction in the decline of muscle function," **added Prof. Craig McDonald, Professor at the Department of Pediatrics and Physical Medicine & Rehabilitation at the University of California Davis.**

[1] Target population: Individuals with a baseline vastus lateralis muscle fat fraction (VL MFF) assessed by magnetic resonance spectroscopy (MRS) in the range >5% and ≤ 30%

About Duchenne Muscular Dystrophy

Duchenne muscular dystrophy (DMD) is a severe neuromuscular genetic disease characterized by progressive muscle weakness and degeneration and is the most common type of muscular dystrophy globally. DMD is caused by mutations in the DMD gene that results in an absence of a functional dystrophin protein, which plays a crucial role in maintaining the structural and membrane stability of muscle fibers. The disease primarily affects boys with symptoms usually seen between two and five years of age that worsen over time with individuals losing their ability to walk. Eventually, heart and respiratory muscles get affected leading to premature death. DMD incidence is approximately 1 in every 3500 - 6000 male births worldwide.

About Givinostat

Givinostat is an investigational drug discovered through Italfarmaco Group's internal research and development efforts in collaboration with Lorenzo Puri (Sanford Burnham Prebys Medical Research Institute, San Diego, formerly Santa Lucia Foundation, Rome) and his team, and partnerships with Telethon and Parent Project aps. It is being evaluated for safety and efficacy for the treatment of Duchenne- and Becker- Muscular Dystrophy. Givinostat inhibits histone deacetylases (HDACs). HDACs are enzymes that prevent gene translation by changing the three-dimensional folding of DNA in the cell. Studies show that higher than normal HDAC activity in individuals with DMD may prevent muscle regeneration and also trigger inflammation. In the company's clinical study in DMD, boys aged 7 to less than 11 years, Givinostat was observed to slow disease progression, significantly increase muscle mass and reduce the amount of fibrotic tissue. In this study, Givinostat treatment also significantly reduced muscle tissue necrosis and fatty replacement, two additional parameters related to disease progression (Bettica *et al*., Neuromuscular Disorders 2016).

About Italfarmaco Group

Italfarmaco Group is a specialty pharmaceutical company engaged in the discovery, development, manufacturing and marketing of branded prescription and nonprescription products in more than 60 countries on 5 continents. Italfarmaco Group's research and development expertise is best demonstrated through its HDAC inhibitor development programs, addressing new therapeutic treatments of specialty and rare diseases. Through both marketed drugs and compounds in development, Italfarmaco Group is dedicated to serving patients whose needs remain largely unmet.

Contact:
For media enquiries:
Trophic Communications
Jacob Verghese, PhD or Laura Mittmann, PhD
+49 (0) 89 2070 89831 or +49 (0) 151 5798 4222
italfarmaco@trophic.eu