Duvyzat™ (givinostat) – New orphan drug approval

- On March 21, 2024, the FDA announced the approval of Italfarmaco's Duvyzat (givinostat), for the treatment of Duchenne muscular dystrophy (DMD) in patients 6 years of age and older.

- DMD is a rare neurological disorder which causes progressive muscle weakness due to a lack of muscle protein called dystrophin. Over time, the muscles deteriorate causing problems with walking and muscle strength and ultimately problems with breathing leading to early death.

    — DMD incidence is approximately one in every 3,500 to 6,000 male births worldwide.

- 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 is the first nonsteroidal drug approved to treat patients with all genetic variants of DMD.

- The efficacy of Duvyzat was established in a randomized, double-blind, placebo-controlled study in 179 male patients 6 years of age and older with a confirmed diagnosis of DMD who were ambulatory and on a stable dosage of corticosteroids. Patients were randomized to receive either Duvyzat or placebo. The primary endpoint was the change from baseline to month 18 in 4-stair climb (4SC) time. The 4SC is a measure of muscle function that tests the time it takes to climb 4 stairs. A secondary endpoint was change from baseline to month 18 in physical function as assessed by the North Star Ambulatory Assessment (NSAA).

    — Patients treated with Duvyzat showed statistically significant less decline in the 4SC vs. placebo. The mean change from baseline in 4SC was 1.25 seconds with Duvyzat vs. 3.03 seconds with placebo (difference of -1.78, 95% CI: -3.46, -0.11; p = 0.037).
    — Patients treated with givinostat experienced less worsening on the NSAA compared to placebo, which was nominally significant but not statistically significant.

- Warnings and precautions for Duvyzat include hematological changes, increased triglycerides, gastrointestinal disturbances, and QTc prolongation.

- The most common adverse reactions (≥ 10%) with Duvyzat use were diarrhea, abdominal pain, thrombocytopenia, nausea/vomiting, hypertriglyceridemia, and pyrexia.

- The recommended dose of Duvyzat is 22.2 mg to 53.2 mg, based on body weight, and administered orally twice daily with food.

- Italfarmaco's launch plans for Duvyzat are pending. Duvyzat will be available as a 8.86 mg/mL oral suspension.