Ztalmy® (ganaxolone) – New orphan drug approval

- On March 18, 2022, Marinus Pharmaceuticals announced the FDA approval of Ztalmy (ganaxolone), for the treatment of seizures associated with cyclin-dependent kinase-like 5 (CDKL5) deficiency disorder (CDD) in patients 2 years of age and older.

- CDD is a rare genetic disorder characterized by early-onset, difficult-to-control seizures and severe neuro-developmental impairment. It's caused by a mutation of the *CDKL5* gene, located on the X chromosome. The *CDKL5* gene produces a protein that is important for normal brain development and function.

- Ztalmy is the first FDA approved treatment for CDD. The precise mechanism by which Ztalmy exerts its therapeutic effects in the treatment of seizures associated with CDD is unknown, but its anticonvulsant effects are thought to result from positive allosteric modulation of the gamma-aminobutyric acid type A ($GABA_A$) receptor in the central nervous system (CNS).

- The efficacy of Ztalmy was established in a double-blind, randomized, placebo-controlled study in 100 patients 2 to 19 years of age with seizures associated with CDD. Overall, 96% of patients were taking between 1 to 4 concomitant antiepileptic drugs. The primary endpoint was the percentage change in the 28-day frequency of major motor seizures from a 6-week prospective baseline phase during the 17-week double-blind phase.

    — Patients treated with Ztalmy had a significantly greater reduction in the 28-day frequency of major motor seizures vs. patients receiving placebo. The median percent change was -7 and -31 with placebo and Ztalmy, respectively (p = 0.0036).

- Warnings and precautions for Ztalmy include somnolence and sedation; suicidal behavior and ideation; and withdrawal of antiepileptic drugs.

- The most common adverse reactions (≥ 5% for Ztalmy and at least twice the rate of placebo) with Ztalmy use were somnolence, pyrexia, salivary hypersecretion, and seasonal allergy.

- Ztalmy is administered orally three times daily and must be taken with food. Refer to the Ztalmy drug label for complete dosing and titration schedule information.

- Ztalmy will be priced at about $133,000 per patient per year.

- Marius Pharmaceuticals plans to launch Ztalmy in July following scheduling by the Drug Enforcement Administration (DEA). Ztalmy will be available as a 50 mg/mL oral suspension.