Ctexli™ (chenodiol) – New orphan drug approval

- On February 21, 2025, the FDA announced the approval of Mirum Pharmaceuticals' Ctexli (chenodiol), for **treatment of cerebrotendinous xanthomatosis (CTX) in adults.**

- CTX is a very rare genetic metabolic disorder caused by a mutation in a gene called CYP27A1 resulting in a deficiency of the enzyme that is important in the body's ability to break down fats. Due to reduced bile acid production in the liver, patients with CTX are unable to break down cholesterol in a normal way, resulting in deposition of atypical cholesterol metabolites in various places in the body including the brain, liver, skin and tendons, leading to damage to those organs and tissues.

- **Ctexli is the first FDA approved therapy for CTX**. It works to replace deficient levels of one of the bile acids, reducing the abnormal deposits of cholesterol metabolites thought to be responsible for clinical abnormalities in CTX.

- Chenodiol is also available under the label name **Chenodal®**, which is approved for patients with radiolucent stones in well-opacifying gallbladders, in whom selective surgery would be undertaken except for the presence of increased surgical risk due to systemic disease or age.

- The efficacy of Ctexli was established in a randomized, double-blind, placebo-controlled study in 13 CTX patients ≥ 16 years of age. Patients were randomized and treated in a crossover withdrawal design to receive either Ctexli or placebo for 4 weeks during 2 double-blind treatment periods. Plasma cholestanol and urine 23S-pentol were assessed at multiple time points.

    - For plasma cholestanol, the estimated mean change from baseline at day 29 was -2.3 µg/mL when patients continued Ctexli and 6.2 µg/mL when patients received placebo. The estimated treatment difference was -8.5 µg/mL (95% CI: -13.2, -3.9).
    - For urine 23S-pentol, the estimated mean change from baseline at day 29 was 185 ng/mL when patients continued Ctexli and 29506 ng/mL when patients received placebo. The estimated treatment difference was -29321 ng/mL (95% CI: -45701, -12941).

- A warning and precaution for Ctexli includes **hepatotoxicity**.

- The most common adverse reactions (> 14%) with Ctexli use were diarrhea, headache, abdominal pain, constipation, hypertension, muscular weakness, and upper respiratory tract infection.

- The recommended dose of Ctexli is 250 mg administered orally three times daily.

- Mirum Pharmaceuticals' launch plans for Ctexli are pending. Ctexli will be available as a 250 mg tablet.