Livmarli™ (maralixibat) – New orphan drug approval

- On September 29, 2021, Mirum Pharmaceuticals announced the FDA approval of Livmarli (maralixibat), for the treatment of cholestatic pruritus in patients with Alagille syndrome (ALGS) 1 year of age and older.

- ALGS is a rare genetic disorder which leads to bile accumulation in the liver and ultimately progressive liver disease. Pruritus experienced by patients with ALGS is among the most severe in any chronic liver disease and is present in most affected children by the third year of life.

    — The estimated incidence of ALGS is one in every 30,000 people and an estimated 2,000 to 2,500 children are affected in the U.S.

- Livmarli, an ileal bile acid transporter (IBAT) inhibitor, is the first approved treatment for ALGS.

- The efficacy of Livmarli was established in a single trial in 31 pediatric ALGS patients with cholestasis and pruritus. The study consisted of an 18-week open-label treatment period; a 4-week randomized, double-blind, placebo-controlled drug-withdrawal period; a subsequent 26-week open-label treatment period; and a long-term open-label extension period. A single-item observer-reported outcome was used to measure patients' pruritus symptoms as observed by their caregiver twice daily (once in the morning and once in the evening) on the Itch Reported Outcome Instrument (ItchRO[Obs]). Pruritus symptoms were assessed on a 5-point scale, with scores ranging from 0 (none observed or reported) to 4 (very severe).

    — Weekly average of worst daily ItchRO(Obs) pruritus severity scores were 1.6 and 3.0 for Livmarli and placebo, respectively. The mean change from week 18 to week 22 (placebo-controlled period) was 0.2 and 1.6, respectively (mean difference -1.4, 95% CI: -2.1, -0.8).

- Warnings and precautions for Livmarli include liver test abnormalities, gastrointestinal adverse reactions, and fat-soluble vitamin deficiency.

- The most common adverse reactions (≥ 5%) with Livmarli use were diarrhea, abdominal pain, vomiting, fat-soluble vitamin deficiency, liver test abnormalities, gastrointestinal bleeding, and bone fractures.

- The recommended dosage of Livmarli is 380 mcg/kg orally once daily, taken 30 minutes before the first meal of the day. The starting dosing is 190 mcg/kg administered orally once daily; after one week, the dose can be increased to 380 mcg/kg once daily, as tolerated. The maximum daily dose volume for patients above 70 kg is 3 mL or 28.5 mg per day.

    — Refer to drug label for the complete dosing by weight guidelines.

- Mirum Pharmaceuticals plans to launch Livmarli immediately. Livmarli will be available as a 9.5 mg/mL oral solution.