Oxlumo® (lumasiran) – New orphan drug approval

- On November 23, 2020, the FDA announced the approval of Alnylam's Oxlumo (lumasiran), for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric and adult patients.

- Primary hyperoxalurias (PHs) are caused by excess production of oxalate. PH1 affects an estimated 1 to 3 individuals per million in North America and Europe and accounts for approximately 80% of PH cases. In patients with PH1, excess oxalate can combine with calcium to cause kidney stones and deposits in the kidneys. Patients can experience progressive kidney damage, which can lead to kidney failure and the need for dialysis. Oxalate can also build up and damage other organs (eg, heart, bones, and eyes)

- Oxlumo is the first FDA approved therapy for the treatment of PH1.

    — Oxlumo is an RNA interference (RNAi) therapeutic targeting *hydroxyacid oxidase 1 (HAO1)*. *HAO1* encodes glycolate oxidase (GO), an enzyme upstream of the disease-causing defect in PH1. Oxlumo works by degrading *HAO1* messenger RNA and reducing the synthesis of GO, which inhibits hepatic production of oxalate.

- The efficacy of Oxlumo was established in ILLUMINATE-A, a randomized, placebo controlled, double-blind study in 39 patients 6 years of age and older with PH1. Patients received 3 loading doses of 3 mg/kg Oxlumo or placebo administered once monthly, followed by quarterly maintenance doses of 3 mg/kg Oxlumo or placebo. The primary endpoint was the percent reduction from baseline in 24-hour urinary oxalate excretion corrected for body surface area (BSA) averaged over months 3 through 6.

    — The least squares (LS) mean percent change from baseline in 24-hour urinary oxalate in the Oxlumo group was -65% vs. -12% in the placebo group (between-group LS mean difference of 53%, 95% CI: 45, 62; $p < 0.0001$).
    — By month 6, 52% of patients treated with Oxlumo achieved a normal 24-hour urinary oxalate corrected for BSA vs. 0% placebo-treated patients ($p = 0.001$).

- In addition, the efficacy of Oxlumo was evaluated in ILLUMINATE-B, a single-arm study in 18 patients < 6 years of age with PH1. Efficacy analyses included the first 16 patients who received 6 months of treatment with Oxlumo and dosing was based on body weight. The primary endpoint was the percent reduction from baseline in spot urinary oxalate:creatinine ratio averaged over months 3 through 6.

    — Patients treated with Oxlumo achieved a reduction in spot urinary oxalate:creatinine ratio from baseline of 71% (95% CI: 65, 77).

- The most common adverse reaction (≥ 20%) with Oxlumo use was injection site reactions.

- The recommended dosing regimen of Oxlumo consists of loading doses followed by maintenance doses administered subcutaneously by a healthcare professional. Dosing is based on actual body weight.

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Body weight	Loading dose	Maintenance dose (begin 1 month after the last loading dose)
Less than 10 kg	6 mg/kg once monthly for 3 doses	3 mg/kg once monthly
10 kg to less than 20 kg	6 mg/kg once monthly for 3 doses	6 mg/kg once every 3 months
20 kg and above	3 mg/kg once monthly for 3 doses	3 mg/kg once every 3 months

- The average annual list price for Oxlumo is expected to be $493,000.
- Alnylam plans to launch Oxlumo by year-end. Oxlumo will be available as 94.5 mg/0.5 mL single-dose vials.