ILLUMINATE: Lumasiran Clinical Development Program

Lumasiran is an investigational, subcutaneously administered RNA interference (RNAi) therapeutic that targets hydroxyacid oxidase 1 (HAO1) gene, encoding glycolate oxidase (GO) enzyme. It is in development for the treatment of primary hyperoxaluria type 1 (PH1), an ultra-rare, life-threatening disease caused by a genetic defect in the liver, resulting in oxalate overproduction and a progressive decline in kidney function that often culminates in end-stage renal disease.[1,2]

ILLUMINATE-A:

ILLUMINATE-A is a Phase 3 randomized, double-blind, placebo-controlled study with an extended dosing period to evaluate the efficacy and safety of lumasiran in children (age six or older) and adults with PH1.

Study Objective

To evaluate the safety and efficacy of lumasiran in children and adults with a documented diagnosis of PH1.

Trial Design

- The global, multicenter trial enrolled PH1 patients, age six or older, with preserved renal function (estimated glomerular filtration rate [eGFR] not less than 30 mL/min/1.73m^2),[3] at clinical centers worldwide.
- Study participants were randomized 2:1 to receive three monthly loading doses of lumasiran or placebo at 3 mg/kg, followed by quarterly maintenance doses.[3]
- All patients completing the treatment period, with either lumasiran or placebo, may continue to an open-label extension (OLE) study for long-term follow-up.

Endpoints

- The primary endpoint of the study is percent change in 24-hour urinary oxalate excretion from baseline to Month 6.
- Key secondary and exploratory endpoints will evaluate additional measures of urinary and plasma oxalate, eGFR, safety, tolerability, and clinical outcomes.

Timelines

- **September 2019:** Study initiated
- **June 2019:** Study enrollment completed
- **Late 2019:** Topline results
- **Early 2020:** Intended New Drug Application (NDA) filing in the U.S.

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ILLUMINATE-B:

ILLUMINATE-B is an open-label Phase 3 study in infants and young children with PH1.

Study Objective

To evaluate the safety, efficacy, pharmacokinetics (PK), and pharmacodynamics (PD) of lumasiran in infants and young children with a documented diagnosis of PH1.

Trial Design

- The open-label, multicenter trial is enrolling PH1 patients, under the age of six, with relatively preserved renal function (eGFR greater than 45 mL/min/1.73m^2),[3] at clinical centers worldwide.
- Dosing regimen will be based on weight with three monthly loading doses followed by monthly or quarterly maintenance doses.[3]

Endpoints

- The primary endpoint of the study is percent change in urinary oxalate excretion from baseline to Month 6.
- Key secondary and exploratory endpoints will evaluate additional measures of urinary and plasma oxalate, eGFR, safety, tolerability, and clinical outcomes.

Timelines

- **April 2019:** Study initiated
- **Mid-2020:** Topline results

ILLUMINATE-C:

ILLUMINATE-C is a single arm study to evaluate the efficacy and safety of lumasiran in patients with advanced PH1.

Study Objective

To evaluate the safety, efficacy, PK, and PD of lumasiran in PH1 patients with advanced renal disease, including patients on dialysis.

Trial Design

- The open-label, multicenter trial is enrolling PH1 patients of all ages with advanced renal disease (eGFR of less than or equal to 45 mL/min/1.73m^2),[3] at clinical centers worldwide.
- Dosing regimen will be based on weight with three monthly loading doses followed by monthly or quarterly maintenance doses.[3]

Endpoints

- The primary endpoint of the study is the percent change in plasma oxalate from baseline to Month 6.
- Key secondary endpoints will evaluate additional measures of plasma oxalate and changes in: urinary oxalate, renal function, frequency and mode of dialysis, frequency of renal stone events, and measures of systemic oxalosis.

Timelines

- **November 2019:** Study initiated
- **Late 2020:** Topline results

For more information on ILLUMINATE-A (NCT03681184), ILLUMINATE-B (NCT03905694), and ILLUMINATE C (NCT04152200), please visit www.clinicaltrials.gov or contact media@alnylam.com.

1. Cochat P and Rumsby G. Primary hyperoxaluria. N Engl J Med. 2013;369:649-658
2. Hoppe B., Beck BD., Milliner DS. The primary hyperoxalurias. Kidney International. 2009;75:1264-1271.
3. Data on file. Alnylam Pharmaceuticals.

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