**ILLUMINATE-C: A Phase 3 Single-Arm Study to Evaluate Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of Lumasiran in Patients with Advanced Primary Hyperoxaluria Type 1**

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**Background**

**Primary Hyperoxaluria Type 1 (PH1)**

- PH1 is a rare autosomal recessive disease that is characterized by excessive hepatic oxalate, which is excreted almost entirely by the kidney, and that is caused by mutations in the alanine-glyoxylate aminotransferase (AGT) gene (Figure 1).

- Patients with PH1 with specific mutations, pyroxidine (vitamin B6) is the only therapeutic known to lower urinary and plasma oxalate to normal or near-normal levels.15

- The only potentially curative treatment is dual liver/kidney transplant,6,7 a complicated procedure that is limited by organ availability and accompanied by serious risks, including graft dysfunction and death.10-13

- Lumasiran is a investigational RNAi therapeutic for PH1 targeting glycolate oxidase (GO), a key enzyme involved in the formation of oxalate (Figure 2). Lumasiran is designed to reduce hepatic oxalate production by inhibiting GO activity.

**Methods**

**Trial Design**

- **ILLUMINATE-C** (NCT04152200; EudraCT 2019-001346-17) is a single-arm study designed to evaluate the efficacy, safety, pharmacokinetics (PK), and pharmacodynamics of lumasiran in patients with advanced PH1 (Figure 3).

**Inclusion Criteria**

- Infants to adults
- Estimated glomerular filtration rate ≥45 mL/min/1.73 m² in patients ≥12 months of age, elevated serum creatinine ≥2× of normal in patients ≥12 months of age
- Plasma oxalate ≥30 μmol/L
- Stable pyridoxine therapy regimen (if applicable)

**Exclusion Criteria**

- Presence of evidence of current or chronic hepatitis C or hepatitis B virus infection
- Peritoneal dialysis or combination hemodialysis/peritoneal dialysis
- Nephrocalcinosis as assessed by renal ultrasound
- Frequency of renal stone events
- Renal function by eGFR

**Table 1. Primary and Secondary Study Outcomes**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Primary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Percentage change in plasma oxalate</td>
<td>-55% or greater</td>
</tr>
<tr>
<td>Percentage change in plasma oxalate</td>
<td>-25% or greater</td>
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</tbody>
</table>

**Table 2. Secondary Study Outcomes**

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Secondary</th>
</tr>
</thead>
<tbody>
<tr>
<td>Frequency of renal stone events</td>
<td>≤2 events per year</td>
</tr>
<tr>
<td>Renal function by eGFR</td>
<td>≤25% decrease from baseline</td>
</tr>
<tr>
<td>Plasma PK parameters of lumasiran</td>
<td>-50% decrease from baseline</td>
</tr>
<tr>
<td>Frequency of AEs</td>
<td>Change from baseline</td>
</tr>
<tr>
<td>Change in the following:</td>
<td>-50% decrease from baseline</td>
</tr>
<tr>
<td>Nephrocalcinosis as assessed by renal ultrasound</td>
<td>-50% decrease from baseline</td>
</tr>
</tbody>
</table>

**Key Inclusion Criteria:**

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**Patient Eligibility**

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**Table 3. Primary and Secondary Study Endpoints**

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<tr>
<th>Endpoint</th>
<th>Primary</th>
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<tbody>
<tr>
<td>Percentage change in plasma oxalate during dialysis sessions</td>
<td>-55% or greater</td>
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</tbody>
</table>

**Abbreviations**

- AGT, alanine-glyoxylate aminotransferase; GO, glycolate oxidase; GR, glyoxylate reductase; LDH, lactate dehydrogenase

**Figure 2. Lumasiran Is an Investigational RNAi Therapeutic for PH1**

- Lumasiran will be administered subcutaneously monthly during the loading doses and either monthly or every 3 months during maintenance dosing; doses will be determined by weight.

**References**


**Acknowledgments**

- Medical writing and editorial assistance provided by the sponsor (Alnylam Pharmaceuticals)
- Medical writing and editorial assistance provided by John Mitchell, PhD, Sheetal Varade, PhD, Joyalika Saha, and Audrey Lockett of Ashfield Healthcare Communications (Walden, CT)

**Funding**

This study is sponsored by Alnylam Pharmaceuticals

**Additional Information**

For more information, please contact us at clinicaltrials@alnylam.com or visit our website at https://www.alnylam.com/alnylam-rnai-pipeline/clinical-trials/