

# OXLUMO™ (lumasiran)

## Product Fact Sheet

- OXLUMO™ (lumasiran) subcutaneous injection is approved by the U.S. Food and Drug Administration (FDA) for the treatment of primary hyperoxaluria type 1 (PH1) to lower urinary oxalate levels in pediatric and adult patients.<sup>1</sup>
  - » OXLUMO is the first and only FDA-approved pharmacologic treatment for this patient population.
  - » OXLUMO is Alnylam's first RNA interference (RNAi) therapeutic approved for use in children (including infants) and third wholly owned RNAi therapeutic to receive regulatory approval in the last three years.
- PH1 is an ultra-rare, inherited disease in which overproduction of oxalate – an unneeded end-product of metabolism – results in the deposition of calcium oxalate crystals in the kidneys and urinary tract and can lead to the formation of painful and recurrent kidney stones, nephrocalcinosis, progression to kidney failure, and systemic organ dysfunction.<sup>2,3</sup>
- In the largest interventional study of PH1, treatment with OXLUMO was shown to result in significant reduction of urinary oxalate levels relative to placebo, with a majority of patients achieving normal\* ( $\leq$  upper limit of normal) or near-normal† ( $\leq 1.5 \times$  the upper limit of normal) levels of urinary oxalate.
- Injection site reactions (ISRs) were the most common drug-related adverse reaction.
- OXLUMO targets the messenger RNA, or mRNA, of the hydroxyacid oxidase 1 (*HAO1*) gene. *HAO1* encodes glycolate oxidase (GO) – the liver enzyme involved in the overproduction of oxalate and upstream of the enzyme deficient in patients with PH1. By degrading the *HAO1* mRNA and reducing the synthesis of GO, OXLUMO inhibits production of oxalate – the metabolite that directly contributes to the pathophysiology of PH1.
- OXLUMO is a subcutaneous injection administered by a healthcare professional. The dose of OXLUMO is determined based on a patient's actual body weight; three starting doses are administered monthly followed by ongoing quarterly or monthly doses (depending on the weight of the patient).
- For more information about OXLUMO, please visit [OXLUMO.com](https://oxlumo.com).

### OXLUMO Research at a Glance

- The FDA approval of OXLUMO was based on the positive results from the ILLUMINATE-A and ILLUMINATE-B Phase 3 studies.<sup>1</sup>
- ILLUMINATE-A was a randomized (2:1; drug to placebo), double-blind, placebo-controlled, multinational Phase 3 study.
  - » The study enrolled 39 patients with PH1, ages six and above, with relatively preserved renal function (an estimated glomerular filtration rate [eGFR]  $\geq 30$  mL/min/1.73m<sup>2</sup>), at 16 study sites, in eight countries around the world.
  - » OXLUMO achieved the ILLUMINATE-A primary endpoint of percent change from baseline, relative to placebo, in 24-hour urinary oxalate excretion averaged across months 3 to 6 and corrected for body surface area.
  - » Specifically, treatment with OXLUMO resulted in a 65% mean reduction in urinary oxalate relative to baseline versus 12% reduction reported in response to placebo, resulting in a mean treatment difference of 53% relative to placebo ( $p=1.7 \times 10^{-14}$ ).
  - » At Month 6, all tested secondary endpoints were met, including the proportion of patients treated with OXLUMO achieving at or below the upper limit of normal\* (13/25 patients or 52%;  $p=0.001$ ) and at or below 1.5x upper limit of normal† (21/25 patients or 84%;  $p=8.3 \times 10^{-7}$ ) levels of urinary oxalate, compared to none (0/13) of the patients receiving placebo.
  - » No serious or severe adverse events were reported. ISRs were the most common drug-related adverse reaction, reported in 10 out of 26, or 38%, of patients receiving OXLUMO. No ISRs were reported in patients receiving placebo. ISRs occurred throughout the study period and included erythema, pain, pruritus, and swelling. These symptoms were generally mild and resolved within one day of the injection and did not lead to discontinuation of treatment.

Please see Important Safety Information and full [Prescribing Information](#) on the next page.

\* Normalization was defined as urinary oxalate levels  $\leq$  upper limit of normal (0.514 mmol/24 hr/1.73 m<sup>2</sup>)

† Near-normalization was defined as urinary oxalate levels  $\leq 1.5 \times$  the upper limit of normal (0.771 mmol/24hr/1.73m<sup>2</sup>)

- ILLUMINATE-B was a single arm, open-label, multinational Phase 3 pediatric study.
  - » The approval was based on an interim analysis, which included 16 of 18 PH1 patients enrolled in the study; patients were under the age of six with an eGFR  $\geq 45$  mL/min/1.73 m<sup>2</sup> or normal serum creatinine, if less than 12 months old.
  - » The primary endpoint of the study was the percent change from baseline to month 6 in spot urinary oxalate:creatinine ratio averaged across months 3 to 6.
  - » In the interim analysis (N=16), patients treated with OXLUMO™ (lumasiran) achieved a 71% mean reduction in spot urinary oxalate:creatinine ratio from baseline (95% CI: 65, 77).
  - » In the 6-month primary analysis (N=18), patients treated with OXLUMO achieved a 72% mean reduction in spot urinary oxalate:creatinine ratio from baseline.<sup>4</sup>
  - » The overall safety and tolerability profile of OXLUMO was consistent with that observed in the ILLUMINATE-A pivotal study.

## RNAi as a Class of Medicines

- Historically, RNA was only thought to be involved in protein synthesis. However, in recent years, RNA has been identified to also play significant roles in regulatory functions within the cell.<sup>5</sup>
- A specific class of RNA, called small-interfering RNA (siRNA), appeared to exert cellular control resulting in gene silencing.<sup>6</sup> In 2001, researchers confirmed that siRNA-mediated gene silencing did occur in human cells.<sup>7</sup> This form of gene silencing has since become widely known as RNA interference, or RNAi for short and has been the subject of a Nobel Prize in Medicine in 2006.
- The FDA approval of OXLUMO reinforces RNAi as a key platform for the development of therapeutics for complex, serious conditions for patients with limited treatment options.

## Access to OXLUMO: Alnylam Assist®

As part of Alnylam's commitment to making therapies available, Alnylam Assist® offers a wide range of services to guide patients through treatment with OXLUMO, including help with understanding insurance coverage, financial assistance programs for eligible patients, educational materials to help facilitate conversations with doctors and family, and assistance with connecting to local resources. Patients will have access to dedicated Case Managers and Patient Education Liaisons throughout their treatment with OXLUMO. The goal of Alnylam Assist® is to provide comprehensive support and guidance to patients prescribed OXLUMO. Visit [AlnylamAssist.com/OXLUMO](https://AlnylamAssist.com/OXLUMO) for more information.

## IMPORTANT SAFETY INFORMATION

### Adverse Reactions

The most common adverse reaction that occurred in patients treated with OXLUMO was injection site reaction (38%). Symptoms included erythema, pain, pruritus, and swelling.

### Pregnancy and Lactation

No data are available on the use of OXLUMO in pregnant women. No data are available on the presence of OXLUMO in human milk or its effects on breastfed infants or milk production. Consider the developmental and health benefits of breastfeeding along with the mother's clinical need for OXLUMO and any potential adverse effects on the breastfed child from OXLUMO or the underlying maternal condition.

**For additional information about OXLUMO, please see the full [Prescribing Information](#)**

1. OXLUMO [package insert]. Cambridge, MA: Alnylam Pharmaceuticals, Inc.  
 2. Cochat P, Rumsby G. Primary hyperoxaluria. N Engl J Med. 2013;369(7):6-658.  
 3. Milliner DS, Harris PC, Cogal AG, et al. Primary Hyperoxaluria Type 1. GeneReviews® [Internet]. 2002 Jun 19.  
 4. Deschenes G, Cochat P, Magen D, et al. ILLUMINATE-B, a Phase 3 Open-Label Study to Evaluate Lumasiran, an RNAi Therapeutic, in Young Children with Primary Hyperoxaluria Type 1 (PH1). Presented at: American Society of Nephrology (ASN) Annual Virtual Meeting, October 22, 2020.

5. Couzin J. Science. 2002;298:2296-7.  
 6. Fire A, Xu S, Montgomery MK, et al. Nature. 1998;391:806-11.  
 7. Elbashir SM, Harborth J, Lendeckel W. Nature. 2001;411:494-8.

