



PHYOX2 was a Phase 2 pivotal, placebo-controlled, double-blind, 6-month efficacy, safety and tolerability study of nedosiran in patients with genetically confirmed PH1 and PH2.<sup>1</sup>

## Eligibility Criteria<sup>1</sup>

### Inclusion Criteria

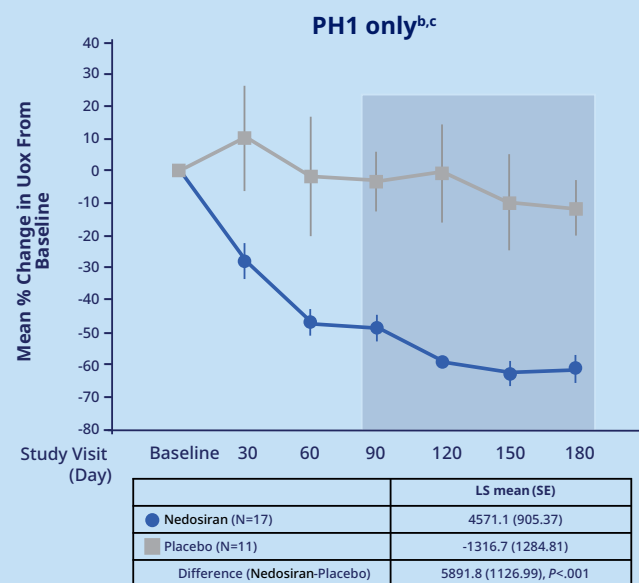
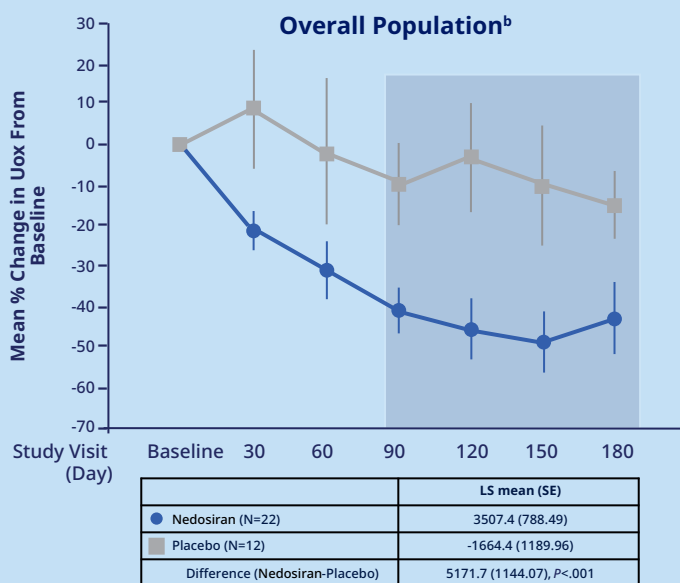
Patients had to be  $\geq 6$  years of age with a 24-hour Uox excretion  $\geq 0.7$  mmol (adjusted per  $1.73 \text{ m}^2$  BSA if  $< 18$  years of age) and an eGFR  $\geq 30$  mL/min per  $1.73 \text{ m}^2$  BSA. Twelve or more patients were required to have  $\geq 1$  24-hour adjusted Uox excretion  $\geq 1.6$  mmol.

### Exclusion Criteria

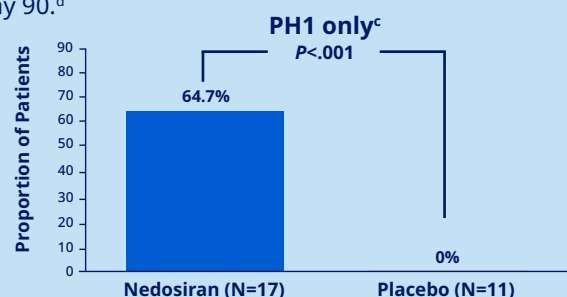
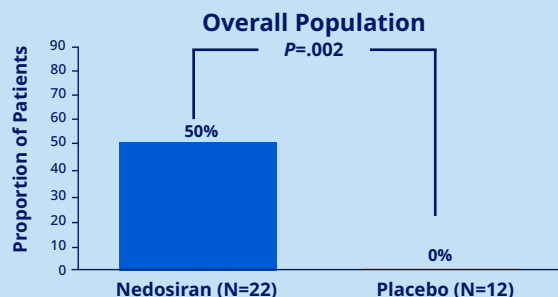
Patients with history of renal or liver transplantation, planned transplant, concurrent or planned dialysis or use of an RNAi drug within 6 months of the trial period were excluded.

## Results<sup>1</sup>

The **primary endpoint** was the 24-hour Uox excretion percent change from baseline as assessed by AUC between Day 90 and Day 180.<sup>a</sup>



The **key secondary endpoint** was proportion of patients reaching normal or near-normal 24-hour Uox excretion on 2 or more consecutive visits starting at Day 90.<sup>d</sup>



<sup>a</sup>mITT population included all patients in the intent-to-treat population who had  $\geq 1$  efficacy assessment after Day 90

<sup>b</sup>Error bars represent  $\pm$  SEM

<sup>c</sup>PH1 subgroup analysis was prespecified for the primary endpoint and post-hoc for all other endpoints

<sup>d</sup>Patients had to meet the following 24-hour Uox excretion criteria on  $\geq 2$  consecutive visits beginning on Day 90: normal 24-hour Uox excretion ( $< 0.46$  mmol per 24 hours ULN) or near-normal ( $\geq 0.46$  to  $< 0.60$  mmol per 24 hours ULN or  $< 1.3$  times ULN)

## Safety<sup>1</sup>



- TEAEs occurred in 19 (83%) patients in the nedosiran arm and 10 (83%) patients in the placebo arm (AE data include patients with PH1 and PH2).
- Majority of AEs were considered mild or moderate in severity.
- ISRs occurred in 2 (9%) patients in the nedosiran arm compared to 0 patients in the placebo arm. All ISRs were grade 1 and resolved by completion of the study.
- No participants in either group experienced muscle pain or weakness.

**References:** 1. Baum MA, Langman C, Cochat P, et al. PHYOX2: a pivotal randomized study of nedosiran in primary hyperoxaluria type 1 or 2. *Kidney Int.* 2023;103(1):207-217.

**Abbreviations:** AE: adverse events; AUC: area under the curve; BSA: body surface area; eGFR: estimated glomerular filtration rate; ISR: injection site reaction; LS: least squares; mITT: modified intent-to-treat; N: number of patients; PH: primary hyperoxaluria; PH1: primary hyperoxaluria type 1; PH2: primary hyperoxaluria type 2; RNAi: ribonucleic acid interference; SE: standard error; SEM: standard error of mean; TEAEs: treatment-emergent adverse events; ULN: upper limit normal; Uox: urinary oxalate.

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