ENYO Pharma Announces completion and topline data from Phase 2 ALPESTRIA-1 clinical study in Alport syndrome demonstrating Vonafexor reverses kidney function decline and has sustained therapeutic benefit

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- ***Vonafexor reversed a historical mean eGFR decline of -6.4 mL/min/1.73 m²/yr to a mean functional gain on-treatment of +4.8 mL/min/1.73 m²/yr from baseline***
- ***73% of patients maintained albuminuria reduction three months after treatment cessation consistent with a true disease-modifying effect***
- ***Company plans to advance vonafexor to Phase 3 in Alport Syndrome***

Lyon, France – January 8, 2026 - ENYO Pharma ("ENYO"), a clinical-stage biopharmaceutical company developing innovative therapies for kidney diseases, today confirmed positive results from its Phase 2 Alpestria-1 study of vonafexor in patients with Alport syndrome. The data demonstrates that vonafexor, a highly differentiated FXR agonist, produced clinically meaningful improvements on kidney disease progression markers in a high-risk population already receiving standard of care (SoC) therapy. In addition to significantly reducing albuminuria, vonafexor treatment was associated with a reversal of the expected decline in kidney function with durable effects after treatment discontinuation.

Groundbreaking Clinical Data: Reversing the Slope of Decline

The Alpestria-1 study enrolled (in France, USA and Spain) 26 patients with Alport syndrome at high risk of a rapid loss of kidney function despite stable multiple SoC drugs, including renin–angiotensin system inhibitors, SGLT2 inhibitors, and mineralocorticoid receptor antagonists. Key findings include:

- **eGFR Slope Reversal:** Patients entered the study with a documented historical mean eGFR decline of -6.4 mL/min/1.73 m²/yr. During the 24-week treatment period, vonafexor treatment resulted in a mean functional gain of +4.8 mL/min/1.73 m²/yr, representing an impressive shift from the natural history of disease progression.

- **Sustained eGFR Benefit (Off-Drug):** Following treatment discontinuation, kidney function benefits persisted. At Week 36 (12 weeks off vonafexor), mean eGFR

remained +2.5 mL/min/1.73 m² above the extrapolated natural history trajectory, consistent with a durable effect.

- **Durable Albuminuria Reduction:** 73% of patients maintained a reduction in urine albumin-to-creatinine ratio (UACR) below their baseline levels three months after stopping treatment

"Results from the ALPESTRIA-1 study demonstrate clinically meaningful improvements in eGFR and UACR, along with clear FXR target engagement at low doses. These findings confirm a differentiated mechanism of action consistent with preclinical data and position vonafexor as a promising therapeutic candidate for Alport syndrome, supporting continued clinical development" said Prof. Bertrand Knebelmann, MD, PhD, Principal Investigator of the ALPESTRIA-1 study and Chair of the Scientific Advisory Board having reviewed the results.

"The convergence of sustained eGFR improvement, durable albuminuria reduction, and positive patient-reported experience provides compelling evidence supporting vonafexor's disease-modifying potential in Alport syndrome and beyond" commented Pietro Scalfaro, MD, CMO of ENYO Pharma.

"The Alpestria-1 results represent a pivotal moment for ENYO and are more importantly a watershed moment for patients living with Alport syndrome" added Jacky Vonderscher, PhD, CEO of ENYO Pharma.

Safety and Tolerability

Vonafexor was generally well-tolerated, with a safety profile consistent with previous clinical trials involving over 400 subjects. The most common adverse event was pruritus, which was dose dependent and manageable through dose adjustments while maintaining pharmacological activity and efficacy.

2026 Strategic Milestones

ENYO is entering a catalyst-rich year as it prepares for pivotal development:

- **FDA Engagement**: A Fast Track designation submission is planned for January 2026, with a Type-D-meeting response expected mid-month.
- **Pivotal Phase 3**: an End-of-Phase 2 meeting is planned for Q2 2026, with initiation of a Phase 3 study in Alport syndrome in the second half of 2026.
- **Pipeline Expansion**: ENYO is also considering initiation of a Phase 2 proof-of-concept study of vonafexor in Autosomal Dominant Polycystic Kidney Disease (ADPKD) and of EYP651 in common renal diseases in H2 2026.

ENYO Pharma management will be in San Francisco **during the upcoming 44th Annual J.P. Morgan Healthcare Conference** to discuss these data and the company's 2026–2031 roadmap with potential partners and investors**.**

About Vonafexor

Vonafexor is a once-daily, oral, non-bile acid FXR agonist designed with a unique chemical scaffold that prioritizes delivery to the kidney. By regulating metabolic, inflammatory, and fibrotic pathways, Vonafexor addresses the core drivers of renal injury and extracellular matrix remodeling.

About ENYO Pharma SA:

ENYO is a clinical-stage biopharmaceutical company headquartered in Lyon (France) and developing proprietary drug candidates to improve quality of life and avoid end stage renal disease and dialysis for patients with rare and common kidney diseases.
Since its inception ENYO collected extensive phase I/II clinical data through 9 completed clinical studies with 400+ subjects. The company's pipeline includes vonafexor and EYP651, a next-generation FXR agonist entering Phase 2 studies in 2H 2026 for common renal diseases (CKD/DKD). For more information: ENYO Pharma – Developing therapeutics for diseases with impaired kidney function

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