# Preliminary Findings From the Phase 2 EPPIK Study of Sparsentan in Pediatric Patients With Selected Proteinuric Glomerular Diseases

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TRAVERE THERAPEUTICS

## RESULTS

- Baseline characteristics of the 23 patients who had received ≥1 dose of sparsentan at data cutoff (April 5, 2023) are shown in **Table 1**

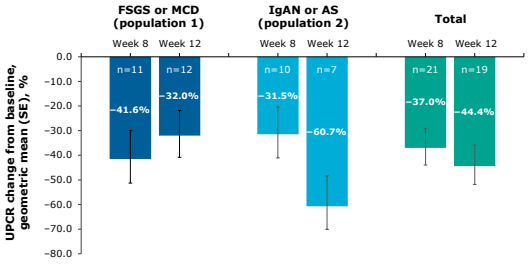
**Table 1. Baseline Characteristics**

| Characteristic | Population 1: MCD or FSGS (n=13) | Population 2: IgAN or AS (n=10) | Total (N=23) |
|---|---|---|---|
| **Diagnosis, n (%)** | | | |
| MCD | 8 (61.5) | 0 | 8 (34.8) |
| FSGS | 5 (38.5) | 0 | 5 (21.7) |
| IgAN | 0 | 3 (30.0) | 3 (13.0) |
| AS | 0 | 7 (70.0) | 7 (30.4) |
| IgAVN | 0 | 0 | 0 |
| **Male, n (%)** | 8 (61.5) | 8 (80.0) | 16 (69.6) |
| **Age, median (IQR), years[a]** | 8 (6-13) | 13 (12-14) | 12 (7-14) |
| **White, n (%)** | 12 (92.3) | 6 (60.0) | 18 (78.3) |
| **UPCR, median (IQR), g/g** | 3.0 (2.5-5.7) | 2.5 (2.1-3.2) | 2.8 (2.3-5.0) |
| **Nephrotic-range proteinuria (UPCR ≥2 g/g), n (%)** | 12 (92.3) | 8 (80.0) | 20 (87.0) |
| **eGFR, mean (SD), mL/min/1.73 m²** | 106.1 (50.0) | 87.3 (27.4) | 97.9 (42.0) |
| **Immunosuppressant use at baseline, n (%)** | 8 (61.5) | 1 (10.0) | 9 (39.1) |
| **Blood pressure, systolic/diastolic, mean (SD), mm Hg** | 115.0 (61.1)/ 69.3 (11.3) | 116.2 (10.0)/ 69.1 (8.4) | 115.5 (13.5)/ 69.2 (9.9) |

AS, Alport syndrome; eGFR, estimated glomerular filtration rate; FSGS, focal segmental glomerulosclerosis; IgAN, immunoglobulin A nephropathy; IgAVN, immunoglobulin A vasculitis nephritis; MCD, minimal change disease; UPCR, urine protein-to-creatinine ratio.
[a]At screening.

- Proteinuria decreased from baseline over 12 weeks of treatment (**Figure 3**)

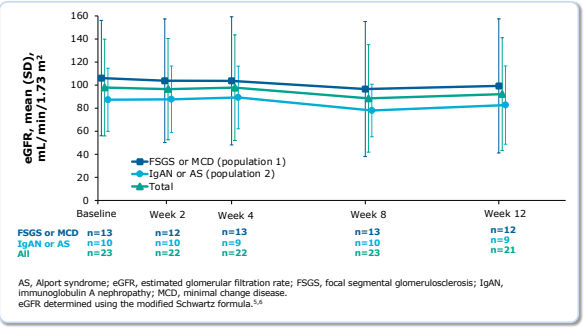
**Figure 3. Geometric Mean Percent Change From Baseline in UPCR Over 12 Weeks of Sparsentan Treatment**




AS, Alport syndrome; FSGS, focal segmental glomerulosclerosis; IgAN, immunoglobulin A nephropathy; MCD, minimal change disease; UPCR, urine protein-to-creatinine ratio.

- Estimated glomerular filtration rate (eGFR) was broadly stable during the first 12 weeks of treatment (**Figure 4**)

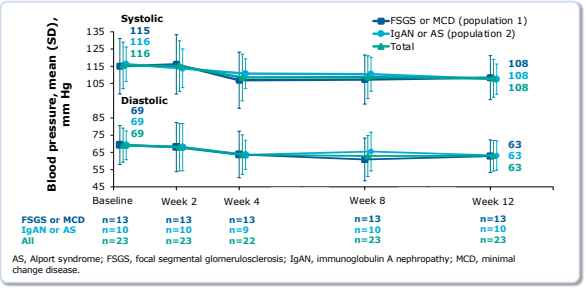
**Figure 4. Mean eGFR Change From Baseline Over 12 Weeks of Sparsentan Treatment**




AS, Alport syndrome; eGFR, estimated glomerular filtration rate; FSGS, focal segmental glomerulosclerosis; IgAN, immunoglobulin A nephropathy; MCD, minimal change disease.
eGFR determined using the modified Schwartz formula.[5,6]

- Effect of sparsentan on blood pressure during the first 12 weeks of treatment is shown in **Figure 5**

**Figure 5. Mean Blood Pressure Change From Baseline Over 12 Weeks of Sparsentan Treatment**




AS, Alport syndrome; FSGS, focal segmental glomerulosclerosis; IgAN, immunoglobulin A nephropathy; MCD, minimal change disease.

- Sparsentan was generally well tolerated over the 12-week treatment period (**Table 2**)
  - Occurrences of other treatment-emergent adverse events such as edema, aspartate aminotransferase increase, fluid retention, hyperkalemia, and hypotension each occurred in 1 patient only
  - 1 patient discontinued study treatment due to worsening of nephrotic syndrome

**Table 2. TEAEs Over 12 Weeks of Sparsentan Treatment**

| Patients, n (%) | FSGS or MCD: population 1 (n=13) | IgAN or AS: population 2 (n=10) | Total (N=23) |
|---|---|---|---|
| **TEAE** | **11 (85)** | **7 (70)** | **18 (78)** |
| Most common TEAEs (≥3 patients in either population) | | | |
| Pyrexia | 3 (23) | 1 (10) | 4 (17) |
| Vomiting | 3 (23) | 1 (10) | 4 (17) |
| Headache | 3 (23) | 1 (10) | 4 (17) |
| Blood creatinine increase | 3 (23) | – | 3 (13) |
| **Any serious TEAE** | **4 (31)** | **2 (20)** | **6 (26)** |
| Acute kidney injury | 0 | 1 (10.0) | 1 (4.0) |
| Nephrotic syndrome | 1 (8.0) | 0 | 1 (4.0) |
| Hypotension | 1 (8.0) | 0 | 1 (4.0) |
| Fluid retention | 1 (8.0) | 0 | 1 (4.0) |

AS, Alport syndrome; FSGS, focal segmental glomerulosclerosis; IgAN, immunoglobulin A nephropathy; MCD, minimal change disease; TEAE, treatment-emergent adverse event.

## CONCLUSIONS

- In pediatric patients with a range of proteinuric glomerular diseases, sparsentan treatment resulted in proteinuria reductions over the initial 12 weeks
- Sparsentan had a safety profile consistent with that observed in studies of adults with IgAN or FSGS,[1-4] and the oral suspension formulation was generally well tolerated
- Enrollment for the EPPIK trial (NCT05003986) is ongoing, and further follow-up over the full study period will evaluate the long-term efficacy and safety, as well as pharmacokinetics and palatability, in children with rare proteinuric glomerular diseases

## DISCLOSURES

**RK and NAMA** are employees of Travere Therapeutics, Inc. **RC** has participated on data safety monitoring or advisory boards for Amgen and Bayer; has received consultancy fees from Alnylam, argenx, Calliditas, Chinook, Menarini, Novartis, Purespring, Otsuka-Visterra, Reata, STADApharm, and Travere Therapeutics, Inc.; and serves as an UpToDate Session Editor. **KVL** has received consultancy fees and speaker's honoraria from Alexion and Calliditas. **AM** is an employee of Travere Therapeutics, Inc. and JAMCO Pharma Consulting; and has received consultancy fees from HI-Bio, Travere Therapeutics, Inc., and Vera Therapeutics. **MR** has received consultancy fees from ELOXX, ENYO Pharma, Visterra, and Walden Biosciences; has received research funding from Akebia Therapeutics, Chinook Therapeutics, the Department of Defense, the National Institute of Diabetes and Digestive and Kidney Diseases, Reata Pharmaceuticals, River 3 Renal, and Sanofi; and participated on data safety monitoring/advisory boards for Advicenne. **MAS** has received consultancy fees and speaker's honoraria from Travere Therapeutics, Inc., Purespring Therapeutics, and ProteinQure. **TS** is an employee of and owns stock or stock options in Travere Therapeutics, Inc. **HT** has received consultancy fees from Aclipse, Boehringer Ingelheim, Maze Therapeutics, Natera, Otsuka, PhaseV, Travere Therapeutics, Inc., and Walden; has received speaking honoraria from the National Kidney Foundation; has participated on data safety monitoring or advisory boards for ChemoCentryx, Otsuka, and Travere Therapeutics, Inc.; and serves on the board of Kidney Health Initiative and on the editorial board of *Pediatric Nephrology* and *Glomerular Diseases*.

These data were previously presented at the American Society of Nephrology (ASN) Kidney Week 2023; November 2-5, 2023; Philadelphia, PA, USA

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## REFERENCES

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*For more information about the EPPIK trial, please visit https://www.clinicaltrials.gov/study/NCT05003986*

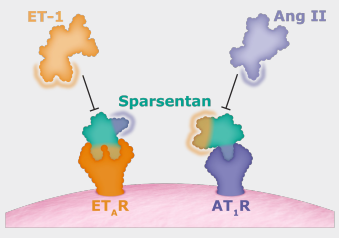
## INTRODUCTION

- Sparsentan, a novel dual endothelin angiotensin receptor antagonist (DEARA), is approved to treat adults with immunoglobulin A (IgA) nephropathy (IgAN) in the US based on data from the phase 3 PROTECT trial[1,2]
  - The ongoing DUPLEX phase 3 trial is studying sparsentan treatment for focal segmental glomerulosclerosis (FSGS)[3,4]
- Dual endothelin type A receptor and angiotensin II type 1 receptor antagonism has anti-inflammatory, antiproliferative, and antifibrotic actions of therapeutic potential in addition to hemodynamic benefits (**Figure 1**)
- The ongoing, phase 2, open-label EPPIK (Evaluating Problematic Proteinuria in Kids; NCT05003986) study is examining an oral suspension formulation of sparsentan in pediatric patients with IgAN, FSGS, minimal change disease, IgA vasculitis nephritis, or Alport syndrome

### OBJECTIVE

- To assess the preliminary efficacy, safety, and tolerability of the oral suspension formulation of sparsentan after 12 weeks of treatment in the EPPIK study

**Figure 1. Sparsentan Mechanism of Action**

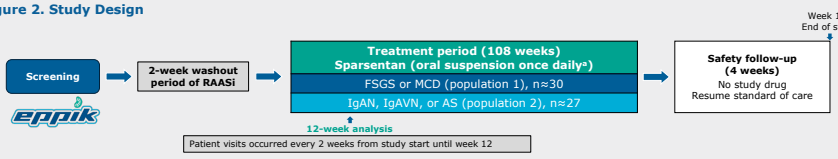



Ang II, angiotensin II; $AT_1R$, angiotensin II type 1 receptor; $ET_AR$, endothelin type A receptor; ET-1, endothelin-1.

## METHODS

- EPPIK is an open-label, single-arm, descriptive, multicenter trial enrolling ≈57 pediatric patients (**Figure 2**)

**Figure 2. Study Design**




**Key eligibility criteria**

- **All patients:** eGFR ≥30 mL/min/1.73 m² at screening
- **Population 1 (FSGS or MCD):** ≥1 to <18 years and UPCR ≥1.5 g/g
- **Population 2 (IgAN, IgAVN, or AS):** ≥2 to 18 years and UPCR ≥0.6 g/g
- Patients taking any chronic immunosuppressive medication without a stable dose for ≥1 month were excluded

**Endpoints**

**Primary**
- Safety (adverse events)
- UPCR changes from baseline through week 108

**Other**
- eGFR changes from baseline through week 112
- Changes in vital signs (eg, blood pressure)

AS, Alport syndrome; eGFR, estimated glomerular filtration rate; FSGS, focal segmental glomerulosclerosis; IgAN, immunoglobulin A nephropathy; IgAVN, immunoglobulin A vasculitis nephritis; MCD, minimal change disease; RAASi, renin-angiotensin-aldosterone system inhibitor; UPCR, urine protein-to-creatinine ratio.
[a]Target exposure is equivalent to 800 mg (FSGS or MCD) or 400 mg (IgAN, IgAVN, or AS) in adults.

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