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

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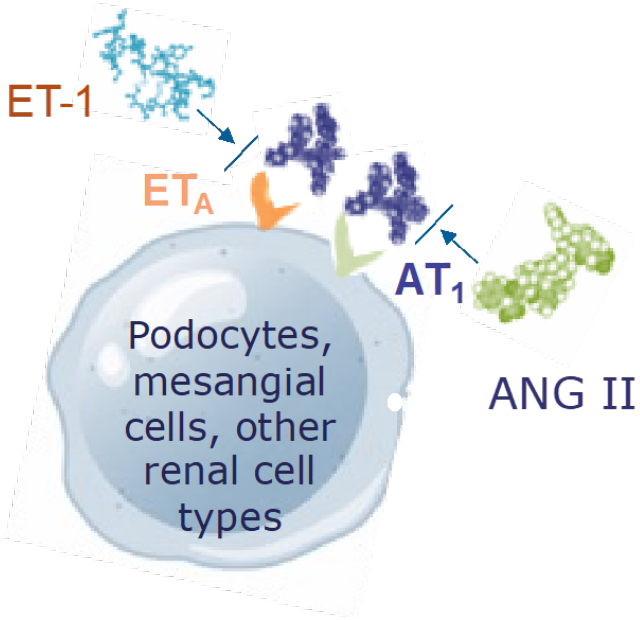
DISCLOSURES

- **HT** has received consulting fees from Aclipse, Boehringer Ingelheim, Maze Therapeutics, Natera, Otsuka, PhaseV, Travere Therapeutics, Inc., and Walden; received speaking honoraria from the National Kidney Foundation; and participated on data safety monitoring or advisory boards for ChemoCentryx, Otsuka, and Travere Therapeutics, Inc.
- **RC** has received consultancy fees from Alnylam, Amgen, argenx, Bayer, Calliditas, Chinook, Menarini, Novartis, Purespring, Otsuka-Visterra, Reata, STADApharm, and Travere Therapeutics, Inc.
- **PH** was an employee of Travere Therapeutics, Inc. at the time of the study
- **KVL** has received consultancy fees and speaker's honoraria from Alexion Pharmaceuticals 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 ENYO Pharma, Visterra, and Walden Biosciences; research funding from Akebia Therapeutics, Chinook Therapeutics, the Department of Defense, NIDDK, 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.
- **RK** is an employee of Travere Therapeutics, Inc.

- Sparsentan is a novel dual endothelin angiotensin receptor antagonist (DEARA) approved to treat adults with immunoglobulin A (IgA) nephropathy in the US[1,2] and in development for focal segmental glomerulosclerosis (FSGS).[3,4] Phase 3 trials are PROTECT and DUPLEX



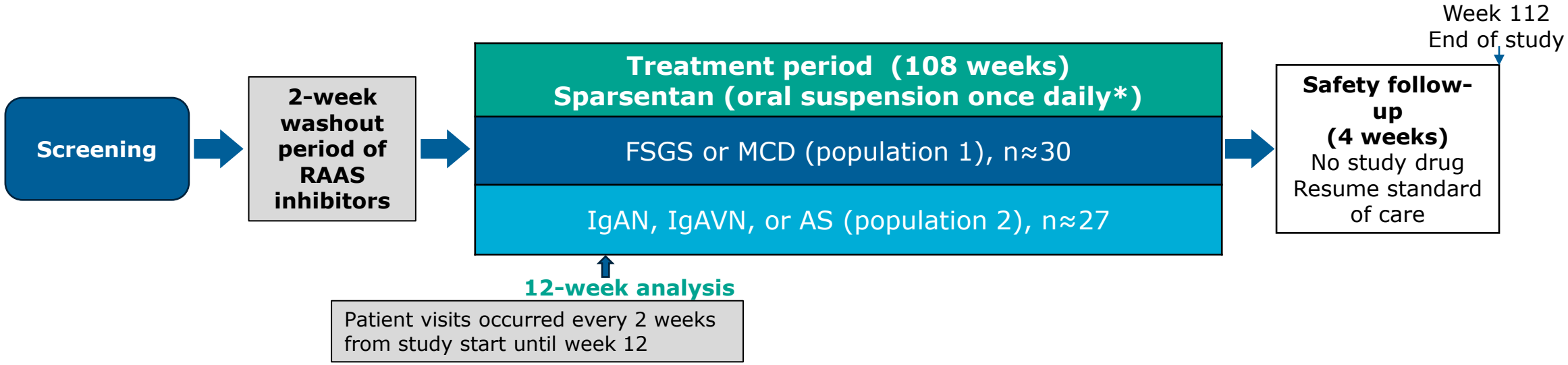
- Dual ET_A and AT_1 receptor antagonism has anti-inflammatory, antiproliferative, and antifibrotic actions of therapeutic potential in addition to hemodynamic benefits
- The ongoing phase 2 open-label EPPIK (Evaluating Problematic Proteinuria in Kids; NCT05003986) study is examining an oral suspension formulation of sparsentan in pediatric patients with:
  - FSGS
  - Minimal change disease (MCD)
  - IgA nephropathy (IgAN)
  - IgA vasculitis nephritis (IgAVN)
  - Alport syndrome (AS)

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

1. Heerspink H, et al. *Lancet.* 2023;401:1584–1594. 2. Rovin BH, et al. *Lancet.* Published online November 3, 2023. 3. Rheault MN, et al. *N Engl J Med.* Published online November 3, 2023. 4. Trachtman H, et al. *J Am Soc Nephrol.* 2018;29(11):2745-2754.

METHODS

- Open-label, single-arm, descriptive, multicenter trial enrolling ≈57 pediatric patients



Key eligibility criteria

- **All patients:** eGFR ≥30 mL/min/1.73 m^2 at screening
- **Population 1 (FSGS or MCD):** ≥1 to <18 years and urine protein-to-creatine ratio (UPCR) ≥1.5 g/g
- **Population 2 (IgAN, IgAVN, or AS):** ≥2 to 18 years andUPCR ≥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)

*Target exposure is equivalent to 800 mg (FSGS or MCD) or 400 mg (IgAN, IgAVN, or AS) in adults.

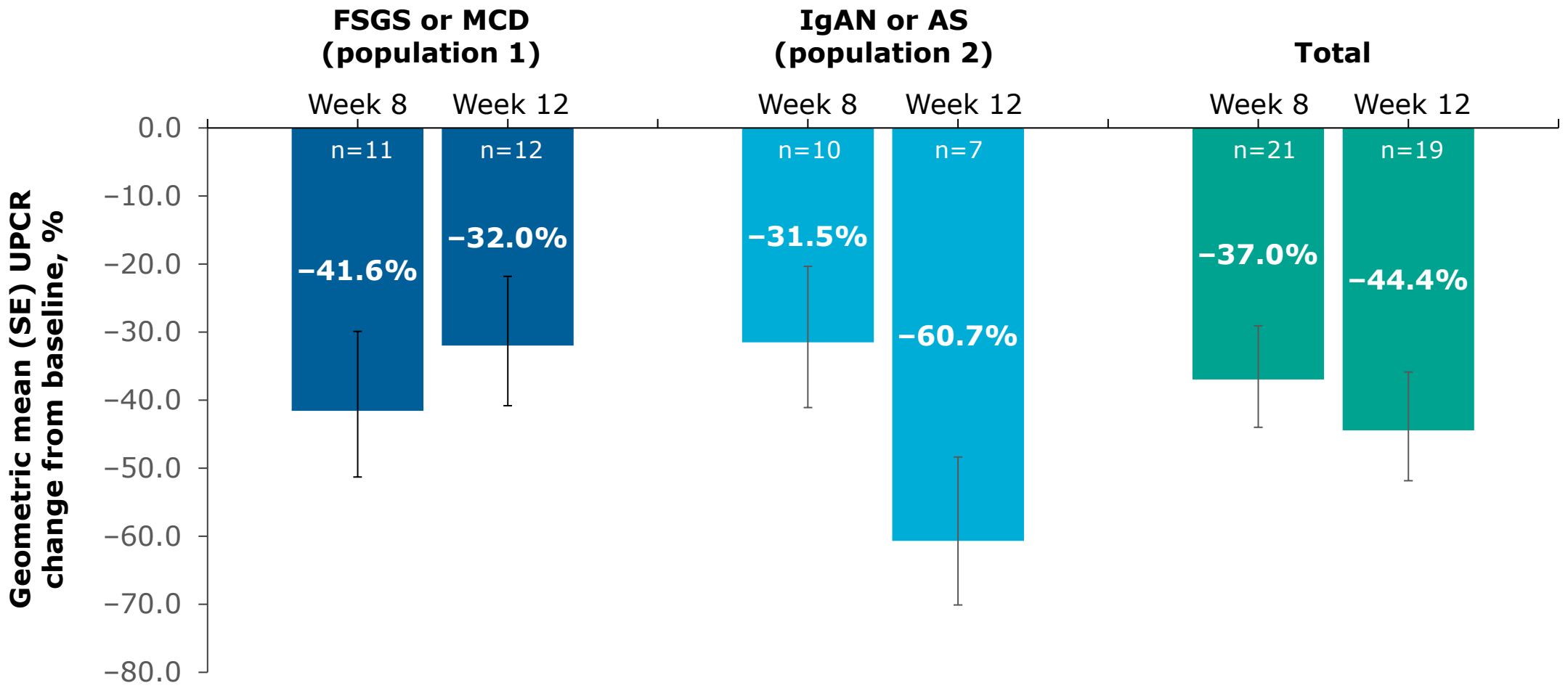
- Baseline characteristics of the 23 patients who had received ≥1 dose of sparsentan at data cutoff (April 5, 2023)

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 sex, n (%)	8 (61.5)	8 (80.0)	16 (69.6)
Age, median (IQR), years*	8 (6-13)	13 (12-14)	12 (7-14)
White race, 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 (16.1)/69.3 (11.3)	116.2 (10.0)/69.1 (8.4)	115.5 (13.5)/69.2 (9.9)

IQR, interquartile range. *At screening.

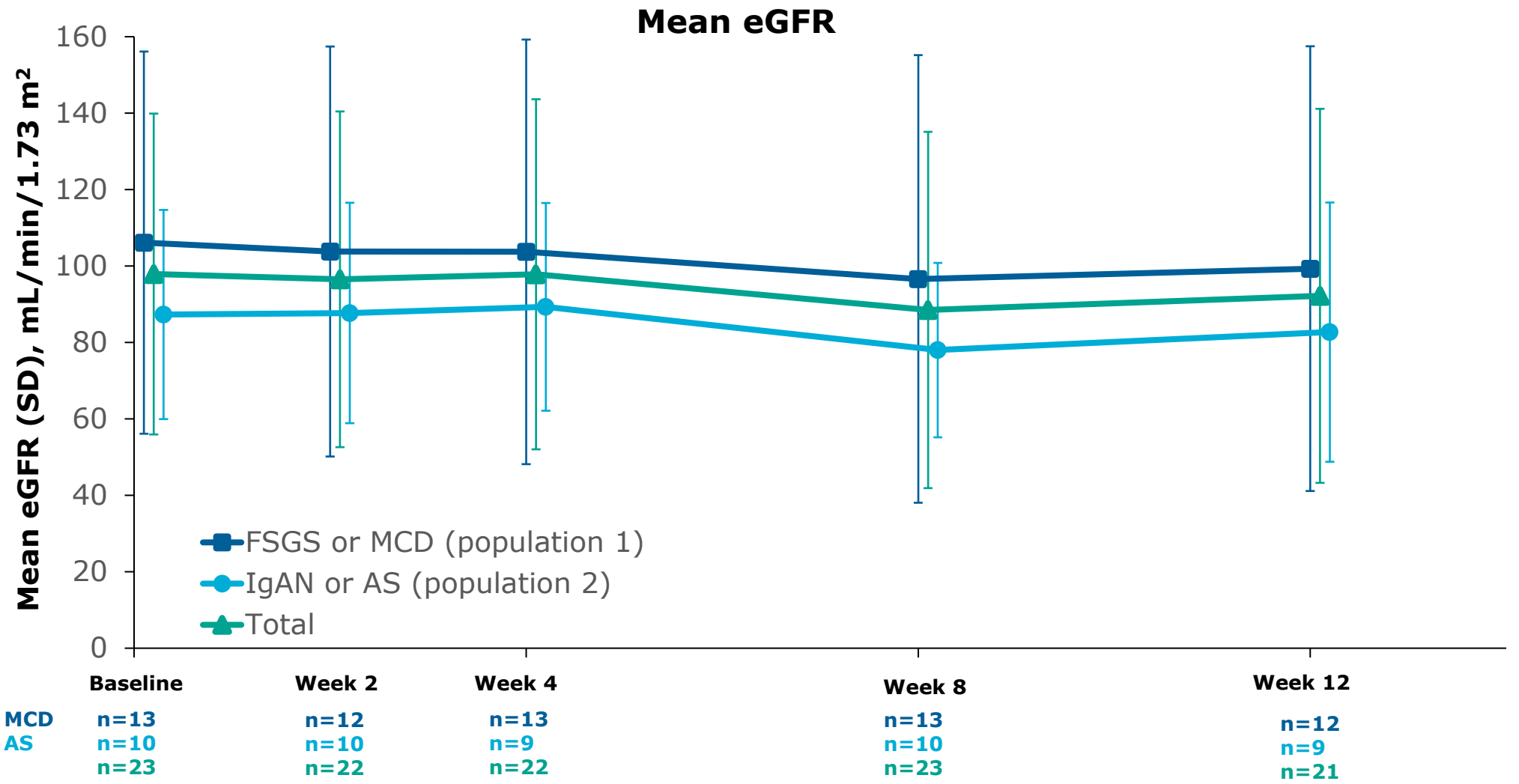
RESULTS

- Proteinuria decreased from baseline over 12 weeks of sparsentan treatment



RESULTS

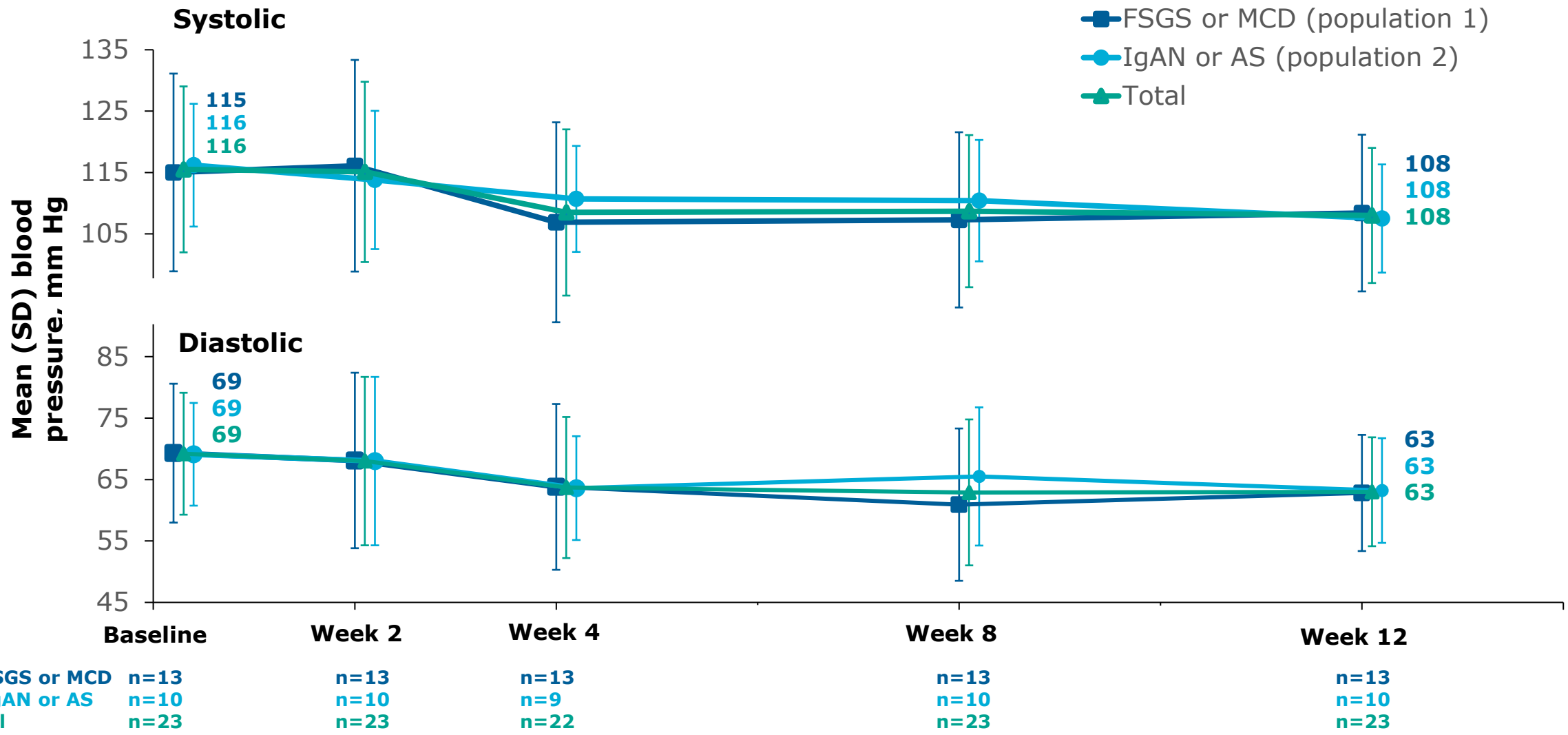
- eGFR was broadly stable during the first 12 weeks of treatment



eGFR determined using the modified Schwartz formula.[1,2]

1. Schwartz GJ, et al. *J Am Soc Nephrol.* 2009;20(3):629-637. 2. Schwartz GJ, et al. *Clin J Am Soc Nephrol*. 2009;4(11):1832-1843.

- Effect of sparsentan on blood pressure during the first 12 weeks of treatment



- Sparsentan was generally well tolerated over the 12-week treatment period
- 1 patient discontinued study treatment due to worsening of nephrotic syndrome

Patients, n (%)	FSGS or MCD population 1 (n=13)	IgAN or AS: population 2 (n=10)	Total (N=23)
Any treatment-emergent adverse event (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)

Occurrences of other TEAEs such as edema, aspartate aminotransferase increase, fluid retention, hyperkalemia, and hypotension each occurred in 1 patient only

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

1. Heerspink H, et al. *Lancet* 2023;401:1584-1594. 2. Rheault MN, et al. *N Engl J Med.* Published online November 3, 2023. 3. Trachtman H, et al. *J Am Soc Nephrol.* 2018;29:2745-2754. 4. Rovin BH, et al. *Lancet.* Published online November 3, 2023.

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Questions?

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