Topline Data from the Two-Year Endpoints in the Phase 3 DUPLEX Study of Sparsentan in Focal Segmental Glomerulosclerosis

May 1, 2023

Forward-Looking Statements

This presentation contains forward-looking statements, including statements about the efficacy, safety and tolerability profile of sparsentan based on the topline data from the DUPLEX Study which is based on a preliminary analysis of the data and subject to more comprehensive analyses, including with respect to secondary and topline exploratory endpoints, including renal outcomes; our plan and timing for engaging with regulators to explore a potential path for a regulatory submission of sparsentan for FSGS; predictive modeling of Proteinuria Reduction and Preservation of Kidney Function in FSGS; the potential ability to submit a supplemental NDA for sparsentan for FSGS in the U.S. and the potential for a submission for a subsequent variation to the Conditional Marketing Authorization (CMA) of sparsentan for the treatment of FSGS in Europe, subject to a review decision on the pending application for CMA of sparsentan in IgA nephropathy; and plans for further analysis of the results from the DUPLEX Study. These forward-looking statements may be accompanied by such words as “anticipate,” “believe,” “estimate,” “expect,” “forecast,” “intend,” “may,” “plan,” “potential,” “project,” “schedule,” “target,” “will,” and other words and terms of similar meaning. You should not place undue reliance on these statements.

These statements involve risks and uncertainties that could cause actual results to differ materially from those reflected in such statements. Specifically, we face the risk that the results from the Phase 3 DUPLEX Study of sparsentan in FSGS will not serve as a basis for a regulatory submission for approval of sparsentan for FSGS. There is no guarantee that we will be able to establish a pathway to a potential submission of sparsentan for FSGS based on the results from the DUPLEX Study, that the FDA and/or EMA will support an application for sparsentan in FSGS, or that sparsentan will be approved for FSGS. We face additional risks, including risks and uncertainties associated with regulatory review and product approvals, the safety and efficacy of our products and product candidates, product competition, market acceptance, the occurrence of adverse safety events with our products or product candidates, clinical trials risk, adverse market and economic conditions, regulatory uncertainty, our dependence on collaborations and other third parties over which we may not always have full control, failure to comply with government regulation, our ability to protect our intellectual property rights, and have sufficient rights to market our products and services together with the cost of doing so, problems with our manufacturing processes and our reliance on third parties, the potential impact of a resurgence of COVID-19 or other health epidemic or pandemic, our ability to attract and retain qualified personnel, our level of indebtedness, environmental risks, change of control provisions in our collaborations, and the other risks and uncertainties that are described in the Risk Factors section of our most recent annual or quarterly report and in other reports we have filed with the SEC.

These statements are based on our current beliefs and expectations and speak only as of the date of this presentation. We do not undertake any obligation to publicly update any forward-looking statements.

Travere Therapeutics Presenters

Opening Remarks

Eric Dube, Ph.D.
President and Chief Executive Officer

Topline Results from the Phase 3 DUPLEX Study of Sparsentan in FSGS

Jula Inrig, M.D.
Chief Medical Officer

Q&A session

William Rote, Ph.D.
Senior Vice President, Research & Development

TRAVERE™ THERAPEUTICS

We are in rare for life.

At Travere Therapeutics, we are a biopharmaceutical company that comes together every day to help patients, families, and caregivers of all backgrounds as they navigate life with a rare disease. On this path, we know the need for treatment options is urgent — that is why our global team works with the rare disease community to identify, develop, and deliver life-changing therapies.

Overview of the Topline Results from Two-Year Primary Efficacy Endpoint in Pivotal Phase 3 DUPLEX Study of Sparsentan in FSGS

Key Findings

- The DUPLEX Study did not achieve the primary efficacy eGFR slope endpoint over 108 weeks of treatment
- Secondary and topline exploratory endpoints trended favorably for sparsentan
- Treatment with sparsentan resulted in a reduction of proteinuria that was sustained through 108 weeks of treatment
- Sparsentan was well-tolerated with a consistent safety profile across all clinical trials conducted to date and comparable to irbesartan

Next Steps

- Complete a full evaluation of the data from the DUPLEX Study
- The Company will engage with regulators to explore a potential path forward for a supplemental New Drug Application (sNDA) in the US
- With our collaborator, CSL Vifor, the Company will engage with the EMA to determine the potential for a variation submission in Europe*

sNDA; supplemental new drug application. *Conditional Marketing Authorization (CMA) of sparsentan for the treatment of FSGS, subject to a review decision on the pending application for a CMA of sparsentan in IgA nephropathy.

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Focal Segmental Glomerulosclerosis (FSGS) is a Rare Glomerular Disease

A complex and heterogenous disease with a high unmet need

- Caused by continuous and sustained glomerular injury to podocytes, leading to elevated and persistent proteinuria
- Reduction of proteinuria to remission and partial remission thresholds can significantly improve outcomes[1,2,3,4]
- 30-60% of FSGS patients progress to kidney failure within 5-10 years[5]

Treatment options are limited, ineffective, and associated with significant complications

- 47% of children and 38% of adults do not respond to currently available therapies[1,6,7]
- 40% of transplant patients develop recurrent disease
- No FDA-approved drugs indicated for treatment of FSGS

[1]Kidney Disease: Improving Global Outcomes (KDIGO) Glomerulonephritis Work Group. KDIGO Clinical Practice Guideline for Glomerulonephritis. *Kidney Inter., Suppl.* 2012; 2: 139–274; [2]Troyanov S, et al. *J Am Soc Nephrol.* 2005;16:1061-1068;[3]Troost JP, et al. *Clin J Am Soc Nephrol.* 2018;13:414-421; [4]Saleem MA, et al. American Society of Nephrology (ASN) Kidney Week virtual, November 4-7, 2021. PO1529; [5]Kiffel et al. *Adv Chronic Kidney Dis.* 2011;18:332-338; [6]Gipson D. *Semin Nephrol.* 2016; 36(6):453-459; [7]Gipson D, et al. *Pediatr Nephrol.* 2006;21:344–349

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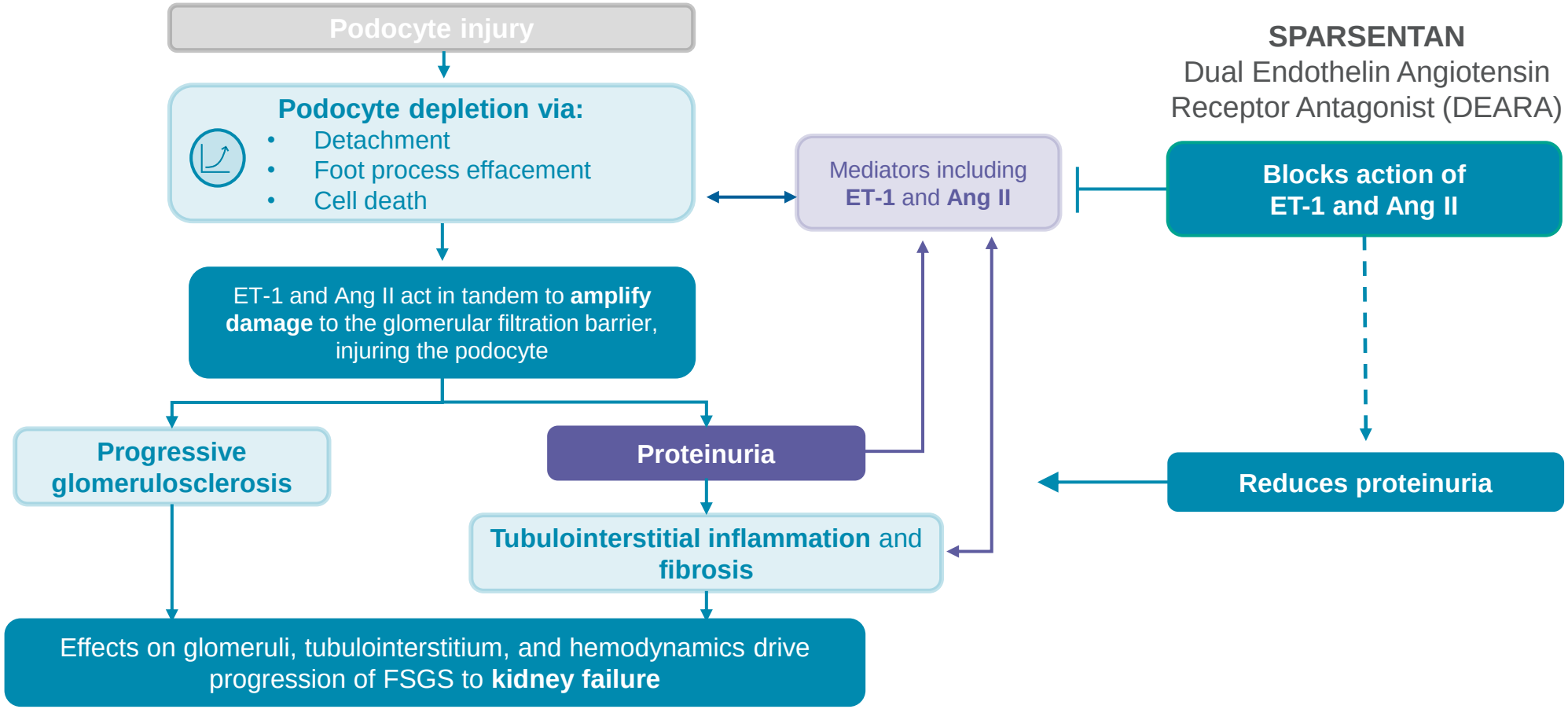
Sparsentan Targets the Pathways Known to Cause Kidney Failure in FSGS



Sparsentan is a potential first-in-class Dual Endothelin Angiotensin Receptor Antagonist (DEARA) for FSGS designed to selectively inhibit the ET-1 and Ang II receptors

Ang II: angiotensin II; AT1: angiotensin II type 1 receptor; ET-1: endothelin-1; ETAR: endothelin type A receptor; FSGS: focal segmental glomerulosclerosis.

Abbate M, et al. *Am J Pathol* 2002; 161:2179–2193; Abbate M, et al. *J Am Soc Nephrol* 2006; 17:2974–2984; De Vriese AS, et al. *J Am Soc Nephrol* 2018; 29:759–774; Jefferson JA & Shankland SJ. *Adv Chronic Kidney Dis* 2014; 21:408–416; Kohan DE & Barton M. *Kidney Int* 2014; 86:896–904; Komers R & Plotkin H. *Am J Physiol Regul Integr Comp Physiol* 2016; 310:R877–R884.

Figure adapted from: Jefferson JA & Shankland SJ. *Adv Chronic Kidney Dis* 2014; 21:408–416.

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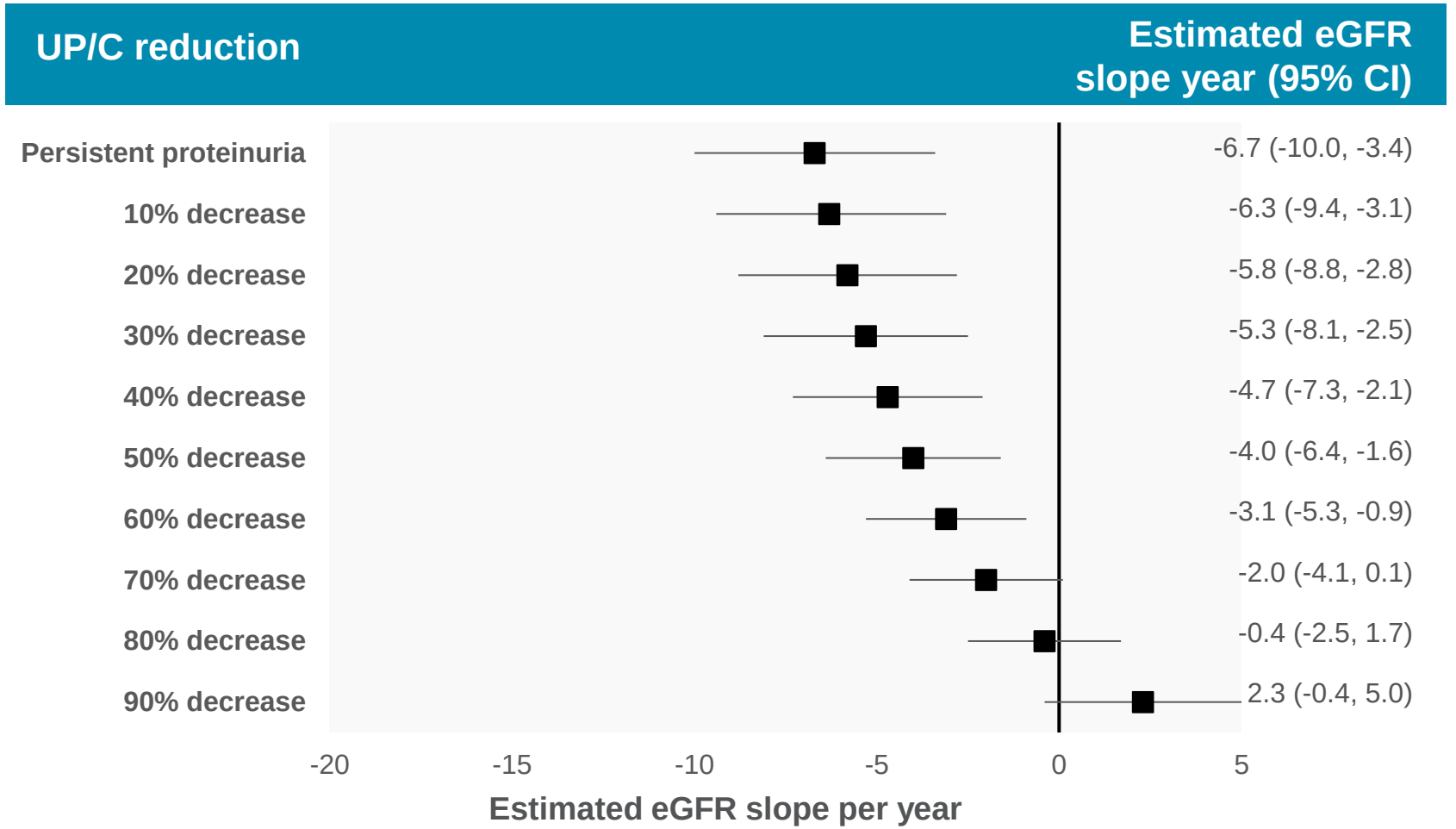
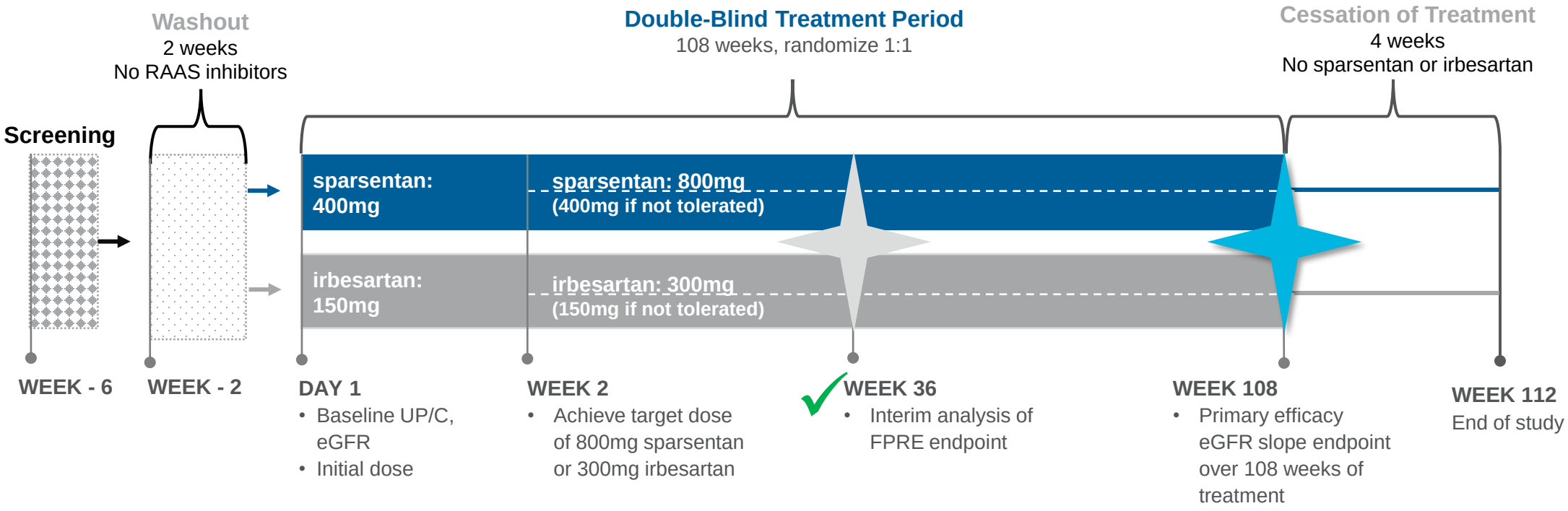
Proteinuria Reduction and Preservation of Kidney Function in FSGS*



Reduction in proteinuria from baseline to week-26 associated with slower rate of eGFR decline from week-26 onward. Results of adjusted linear mixed effects models (n=138 participants; n=752 observations) Model adjusted for *APOL1* genotype, log-baseline UP:C, baseline eGFR, and treatment arm.

*Troost et al, *Am J Kidney Dis* 2021; J Am 77; 216-225

The DUPLEX Study is the Largest Interventional Phase 3 Trial in FSGS



Efficacy: To determine the long-term nephroprotective potential of treatment with sparsentan as compared to irbesartan in patients with primary and genetic focal segmental glomerulosclerosis (FSGS). N=371 patients (ages 8 to 75 years US and UK, ages 18 to 75 ROW)

Primary Efficacy eGFR Slope Endpoint: estimated glomerular filtration rate (eGFR) over 108 weeks of treatment
- **eGFR total slope:** From day 1 to week 108 of treatment (US Primary)
- **eGFR chronic slope:** From week 6 to week 108 of treatment, following the initial acute effect of randomized treatment (EU primary)

Interim endpoint: Proportion of patients achieving a urine protein/creatinine (UP/C) ≤1.5 g/g and a >40% reduction (FPRE) at week 36

UP/C: urine protein/creatinine ratio, g/g: grams per gram, eGFR: estimated glomerular filtration rate, ROW: rest of world

DUPLEX Study: Patient Selection

Key inclusion criteria

Patient characteristics
- Male or female aged 8 to 75 years inclusive, weighing ≥20 kg at screening (US and UK sites)
- Male or female aged 18 to 75 years inclusive, weighing ≥20 kg at screening (outside US or UK)

Histology
- Biopsy-proven FSGS or documentation of a genetic mutation in a podocyte protein associated with FSGS

Laboratory parameters
- UP/C ≥1.5 g/g (170 mg/mmol) at screening
- eGFR ≥30 mL/min/1.73 m^2
- Mean seated BP ≥100/60 mmHg (patients ≥18 years of age) or above the 5th percentile for sex and height (patients <18 years of age)

Contraception
- Women of child-bearing potential must agree to use contraception

Key exclusion criteria

Disease characteristics
- FSGS secondary to another condition

Medical history/concomitant medication
- Treatment with rituximab, cyclophosphamide, or abatacept within ≤3 months prior to screening. For other chronic immunosuppressive medications, dosage must be stable ≥1 month prior to screening
- Any previous organ transplantation, with the exception of corneal transplants

Comorbidities
- Significant medical conditions related to cardiac, hepatic, or immune function
- Documented history of heart failure
- Type 1 DM, uncontrolled Type 2 DM (HbA1c >8% [>64 mmol/mol], or non-fasting blood glucose >180 mg/dL [>10 mmol/L])
- Positive for HIV or markers indicating acute or chronic HBV/HCV infection

Laboratory parameters
- Hematocrit <27% or hemoglobin <9 g/dL at screening
- Potassium >5.5 mEq/L at screening

DUPLEX clinicaltrials.gov ID: NCT03493685; DUPLEX clinicaltrialsregister.eu number: 2016-005141-23; DUPLEX Protocol ID: 021FSGS16010. . BP, blood pressure; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; FSGS, focal segmental glomerulosclerosis; HbA1c, hemoglobin A1c; HBV, hepatitis B virus; HCV, hepatitis C virus; HIV, human immunodeficiency virus; UP/C, urinary protein-to-creatinine ratio.

Komers R et al. *Kidney Int Rep*. 2020;5:494-502.

DUPLEX Characteristics are Balanced and Representative of the Heterogenous FSGS Population

	Irbesartan (N=187)	Sparsentan (N=184)	Total (N=371)
Age at informed consent, years, mean (SD)	41.5 (17.3)	41.7 (16.5)	41.6 (16.9)
Age group,			
9 years to <18 years, n (%)	19 (10.2)	16 (8.7)	35 (9.4)
≥18 years	168 (89.8)	168 (91.3)	336 (90.6)
Sex (n, % Female)	88 (47)	83 (45)	171 (46)
Race, n (%)			
White	138 (74)	137 (74)	275 (74)
Asian	28 (15)	23 (13)	51 (14)
Black or African American	12 (6)	17 (9)	29 (8)
Not Hispanic or Latino, n (%)	135 (72)	147 (80)	282 (76)
Systolic / diastolic blood pressure, mmHg, mean±SD	130.9±14.6 / 82.4±10.1	133.1±14.8 / 85.5±10.6	132.0±14.8 / 83.9±10.5
UP/C, g/g, median (IQR)	3.0 (2.1, 4.7)	3.1 (2.3, 4.5)	3.0 (2.2, 4.6)
eGFR, mL/min/1.73m^2, mean±SD/median (IQR)	64.1±31.7 / 55.0 (40.0, 79.0)	63.3±28.6 / 55.5 (42.0, 81.5)	63.7±30.1 / 55.0 (41.0, 80.0)
Pre-treatment RAASi use, n (%)	143 (76)	152 (83)	295 (80)

Internal data on file
IQR: interquartile range

Sparsentan Shows Activity on eGFR Slopes – Did Not Achieve Primary Endpoints

Primary Efficacy Endpoints:

- The DUPLEX Study did not achieve the primary efficacy eGFR slope over 108 weeks of treatment
- **Total Slope:** Sparsentan showed a 0.3 mL/min/1.73m^2 per year favorable difference versus irbesartan
  - 0.6 mL/min/1.73m^2, predicted difference in eGFR at 2 years
- **Chronic Slope:** Sparsentan showed a 0.9 mL/min/1.73m^2 per year favorable difference versus irbesartan
  - 1.8 mL/min/1.73m^2, predicted difference in eGFR at 2 years

	Irbesartan (N=187)	Sparsentan (N=184)	Difference (Sparsentan - Irbesartan)
Total slope, mL/min/1.73m^2 per year[a] (95% CI)	**-5.7** (-7.2, -4.3)	**-5.4** (-6.9, -3.9)	**0.3,** p=0.7491 (-1.7, 2.4)
Chronic slope, mL/min/1.73m^2 per year[b] (95% CI)	**-5.7** (-7.2, -4.2)	**-4.8** (-6.3, -3.3)	**0.9,** p=0.4203 (-1.3, 3.0)
Acute effect[c] (change from baseline at week 6) (95% CI)	**-0.8** (-2.5, 0.9)	**-4.1** (-5.8, -2.4)	**-3.3** (-5.7, -0.9)

[a]Random coefficient analysis with 1 slope including available on-treatment eGFR data through week 108; mL/min/1.73m^2 per year
[b]Random coefficient analysis with 2 slopes (change point at week 6) including available on-treatment eGFR data through week 108; mL/min/1.73m^2 per year
[c]MMRM analysis including data through week 108; mL/min/1.73m^2
Results are LS Means and 95% Confidence Intervals

Treatment with Sparsentan Reduces Proteinuria

The secondary and topline exploratory endpoints in the study trended favorably for sparsentan.

- **UP/C**: The change from baseline UP/C was 50% for sparsentan versus. 32% for irbesartan, following 108 weeks of treatment
- **Complete Remission:** Patients on sparsentan were 2x more likely to achieve complete remission
  - 34 (18%) of patients on sparsentan versus 14 (7%) on irbesartan achieved complete remission of proteinuria (UP/C <0.3 g/g) at any time during the double-blind period

	Week	Irbesartan (N=187)	Sparsentan (N=184)
UP/C % change from baseline by visit week (95% CI)	36	**-36.2** (43.44, -28.03)	**-51.0** (-56.61, -44.67)
	108	**-32.3** (42.56, -20.21)	**-50.0** (-57.73, -40.81)
FPRE UP/C ≤ 1.5 g/g and a >40% reduction from baseline (95% CI)	36	**26.8** (19.70, 38.87)	**45.9** (38.32, 53.54)
	108	**22.6** (15.31, 29.94)	**37.5** (29.14, 45.82)

Composite Renal Endpoints Trended Favorably for Sparsentan

	Irbesartan (N=187), n (%)	Sparsentan (N=184), n (%)	Sparsentan vs. Irbesartan
Confirmed 40% Reduction in eGFR, ESRD, or Death during the Study - Events	**43** (23.0)	**37** (20.1)	**RR: 0.87** (0.60, 1.26)[a]
Confirmed 50% Reduction in eGFR, ESRD, or Renal death during the Study - Events	**31** (16.6)	**21** (11.4)	**RR: 0.68** (0.43, 1.10)[a]
End-stage Renal Disease (ESRD)	21 (11)	12 (7)	
Confirmed eGFR < 15 mL/min/1.73m^2	11 (6)	5 (3)	
Renal Replacement Therapy	13 (7)	10 (5)	
Death	3 (2)	4 (2)	
Renal Death	0 (0)	0 (0)	

[a]Relative risk (RR) of events and 95% CI from CMH Test

Sparsentan was Well-tolerated and Comparable to Irbesartan

Adverse Reactions	Irbesartan (n=184), N, (%), [Events]	Sparsentan (n=187), N, (%), [Events]	Total (n=371), N, (%), [Events]
Any TEAEs[a]	174 (93) [1,316]	172 (93) [1,535]	346 (93) [2,851]
Any related TEAEs[b]	88 (47) [174]	88 (48) [262]	176 (47) [436]
Any severe TEAEs	41 (22) [79]	44 (24) [101]	85 (23) [180]
Any SAEs	82 (44) [166]	68 (37) [147]	150 (40) [313]
Any AEOIs: Abnormal liver function tests[c]	5 (3) [8]	7 (4) [13]	12 (3) [21]
Any TEAEs leading to treatment discontinuation	22 (12) [25]	26 (14) [30]	48 (13) [55]
Any TEAEs leading to death	3 (2) [3]	4 (2) [4]	7 (2) [7]

- No new safety signals emerged
- No Hy's law or drug-induced liver injury with sparsentan
- No SAEs due to congestive heart failure.
- SAEs due to peripheral edema were 3% with irbesartan and 0% with sparsentan

TEAE: treatment-emergent adverse event, SAE: serious adverse event, AEOI: adverse event of interest, ULN: upper limit of normal
[a]Treatment-emergent adverse event (TEAE) is defined as any AE that newly appear, increase in frequency, or worsen in severity following initiation of study medication.
[b]Related TEAEs are defined as TEAEs that are deemed to be 'possibly related' or 'related' to the study medication by the investigator.
[c]Adverse event of interest (AEOI) are those abnormal liver function tests that meet the following criteria: (1) new elevation in ALT or AST >3 x ULN with or without elevation of total serum bilirubin >2 x ULN; (2) 2-fold increase in ALT or AST above the baseline value in patients who had elevated values prior to starting study medication.

Review of the Phase 3 DUPLEX Study Results and Next Steps

Key Findings

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