



**TRAVERE**<sup>®</sup>  
THERAPEUTICS

# **Topline Confirmatory Data from the Phase 3 PROTECT Study of FILSPARI<sup>®</sup> (sparsentan) in IgAN**

September 21, 2023

# Forward-Looking Statements

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This presentation contains forward-looking statements, including, but not limited to, statements about: our expectations regarding planned future engagement with FDA regarding the filing of an sNDA for full approval of FILSPARI for patients with IgAN in the U.S. and the timing and outcome thereof; statements regarding the potential long-term benefit of FILSPARI as a foundational treatment for patients with IgAN and the potential for preservation of long-term kidney function in patients with IgAN; statements regarding our further evaluation of the data from the PROTECT Study and work with the study investigators on future presentations and publications; expectations related to the regulatory approval pathway; and the expected addressable IgAN patient population of FILSPARI. These forward-looking statements may be accompanied by such words as “anticipate,” “believe,” “estimate,” “expect,” “forecast,” “intend,” “may,” “plan,” “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. Among the factors that could cause actual results to differ materially from those indicated in the forward-looking statements are risks and uncertainties associated with the commercial launch of a new product, the regulatory review and approval process, including traditional approval in the United States and the CMA and subsequent variation pathway in the European Union, our business and finances in general, success of our commercial products and our preclinical and clinical stage pipeline. Specifically, we face risks associated with market acceptance of FILSPARI and our other products, including efficacy, safety, price, reimbursement and benefit over competing therapies; the risk that the results of the Phase 3 PROTECT Study of sparsentan in IgAN will not be deemed sufficient by the FDA to serve as the basis for an sNDA submission for traditional approval of sparsentan. There is no guarantee that the FDA will grant traditional approval of sparsentan for IgAN. We also face additional risks, including risks relating to our dependence on contractors for clinical drug supply and commercial manufacturing; uncertainties relating to patent protection and exclusivity periods and intellectual property rights of third parties; risks associated with regulatory interactions; risks and uncertainties relating to competitive products, including current and potential future generic competition with certain of our products, and technological changes that may limit demand for our products. We also face additional risks associated with global and macroeconomic conditions, including health epidemics and pandemics, including risks related to potential disruptions to clinical trials, commercialization activity, supply chain, and manufacturing operations, 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.

# Presenters



Opening Remarks

**Eric Dube, Ph.D.**

President and Chief Executive Officer

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PROTECT Study Phase 3  
Confirmatory Results

**Jula Inrig, M.D.**

Chief Medical Officer

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A Nephrologist's Experience with  
FILSPARI® for Patients with IgA  
Nephropathy

**Dr. Brad Rovin, M.D., FACP, FASN**

The Lee A. Hebert Professor of Nephrology;  
Director of the Division of Nephrology;  
Director, Center for Clinical Research  
Management, Ohio State University Wexner  
Medical Center





## We are in rare for life.

At Traverre 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.

# FILSPARI® Demonstrated Long-Term Kidney Function Preservation in IgA Nephropathy; Narrowly Missing eGFR Total Slope Endpoint versus Active Control, Irbesartan

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## Key Findings

- FILSPARI (sparsentan) achieved a clinically meaningful difference vs. irbesartan in eGFR total slope (1.0 mL/min/1.73m<sup>2</sup> per year) [p= 0.058] and eGFR chronic slope (1.1 mL/min/1.73m<sup>2</sup> per year) [p=0.037]
  - Patients treated with FILSPARI over two years exhibited one of the slowest annual rates of kidney function decline seen in a clinical trial of IgAN patients (-2.7 to -2.9 mL/min/1.73m<sup>2</sup> per year)
  - eGFR chronic slope was statistically significant with respect to the confirmatory endpoint for the EU
  - All topline efficacy endpoints favored FILSPARI
  - FILSPARI was well-tolerated with a consistent safety profile comparable to irbesartan across all clinical trials conducted to date, supporting long-term use
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## Next Steps

- The Company will meet with regulators and expects to submit a supplemental New Drug Application (sNDA) in 1H 2024 for full approval in the U.S.
- Together with its partner CSL Vifor, the Company anticipates a review opinion by the Committee for Medicinal Products for Human Use (CHMP) on the CMA application for sparsentan for the treatment of IgAN in the EU around year-end





# IgA Nephropathy (IgAN) is a Serious Unmet Rare Kidney Disease

- IgAN, a rare kidney disease (RKD), is the most prevalent primary glomerulonephritis worldwide<sup>1</sup>
- Often uncontrolled, progressive IgAN is a major cause of kidney failure<sup>2,3</sup>

30k-50k

Addressable IgAN population for FILSPARI<sup>®7</sup>

~11 years

is the median time to kidney failure in high-risk adult patients<sup>5</sup>

25-39

peak incidence age of IgAN<sup>4</sup>

30-40%

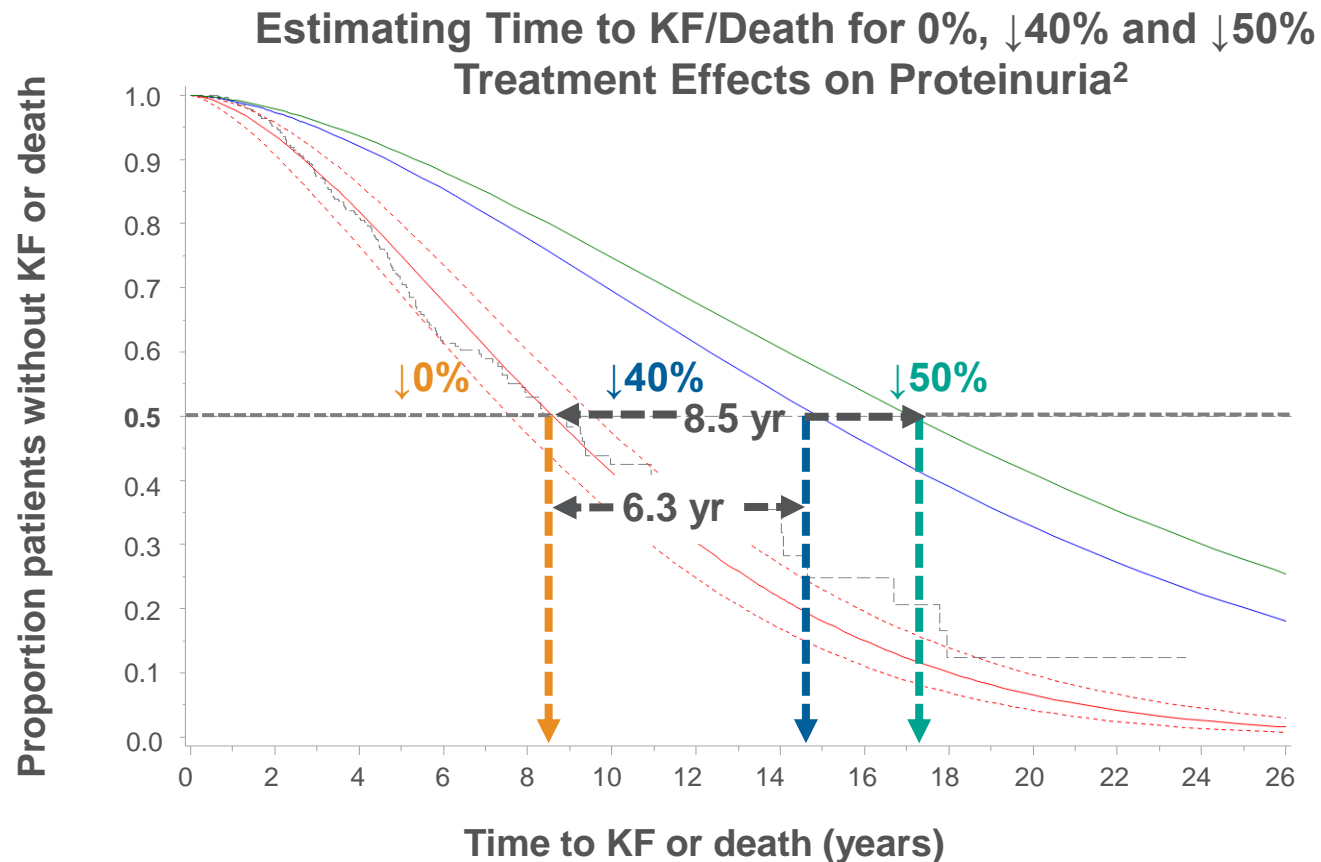
of transplant fail due to disease recurrence<sup>6</sup>

<sup>1</sup>Le W, et al. *Nephrol Dial Transplant* 2012; 27:1479–1485; <sup>2</sup>McGrogan A, et al. *Nephrol Dial Transplant*. 2011;26:414-430; <sup>3</sup>Nasri H, et al. *J Nephrol*. 2015; 4:1-5; <sup>4</sup>Nair R & Walker PD. *Kidney Int* 2006; 69:1455–1458; <sup>5</sup>Barratt J, et al. "Natural History of IgA Nephropathy: Analysis of a UK National RaDaR IgA Nephropathy Cohort." ASN 2021; Poster presentation (Abstract P01577); <sup>6</sup>Uffing A et al. *Clin J Am Soc Nephrol*. 2021 Aug;16(8):1247-1255; <sup>7</sup>addressable population numbers are estimates sourced from McGrogan et al. *Nephrol Dial Transplant* (2011); Sim et al., *AJKD* (2016); Simon et al., 2004; Zara et al. *Nephrol Dial Transplant* (2013); Braun et al., *Int Urol Nephrol* (2011), and data on file.

# Persistent Proteinuria is the Single Strongest Modifiable Prognostic Indicator for Disease Progression in IgAN<sup>1</sup>

## Proteinuria reduction lowers the risk of progression to kidney failure (KF):

- Achieving a 40% reduction of proteinuria substantially lowers risk of kidney failure and death, as demonstrated in the RaDaR Registry (The UK Kidney Association)



RaDaR IgAN cohort: Phase 3 representative population (N=535, events=171)

Median (IQR) UP/C: 1.5 (1.1–2.2) g/g

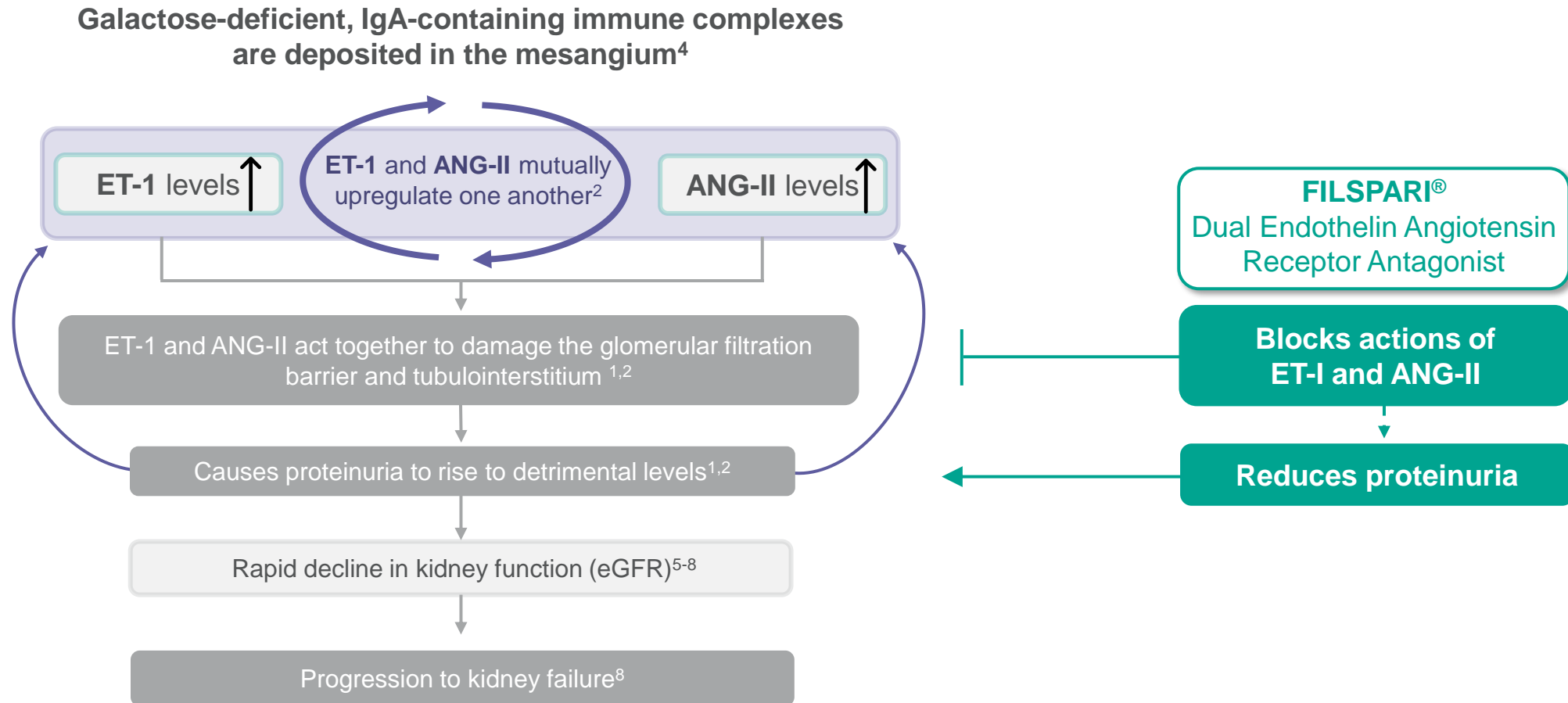
Mean (SD) eGFR: 61 (26) mL/min/1.73m<sup>2</sup>

eGFR: estimated glomerular filtration rate, HR: hazard ratio, IgAN: IgA nephropathy, IQR: interquartile range, KF: kidney failure, SD: standard deviation, UP/C: urine protein/creatinine ratio

1. Reich HN, et al. *J Am Soc Nephrol.* 2007;18:3177-3183

2. Image reprinted from Mercer A, et al. *Nephrology Dialysis Transplantation.* 2023;38(Suppl 1):4503. Copyright © 2023, Oxford University Press. Mercer A, et al. Oral presentation at 60th ERA congress; Milan, IT; June 15-18, 2023.

# The Progression of IgA Nephropathy to Kidney Failure is Driven by Two Critical Pathways - Endothelin-1 (ET-1) and Angiotensin II (ANG-II)<sup>1-3</sup>



Ang II: angiotensin II; ET-1: endothelin-1; IgAN: Immunoglobulin A Nephropathy.

Figure adapted from Lai K, et al. *Nat Rev Dis Primers*. 2016;16001

<sup>1</sup>Komers R, et al. *Am J Physiol Regul Integr Comp Physiol*. 2016;310(10):R877-R884. <sup>2</sup>Kohan DE, et al. *Kidney Int*. 2014;86(5):896-904. <sup>3</sup>Raina R, et al. *Kidney Dis*. 2020;6(1):22-34. <sup>4</sup>Ebefors K, Bergwall L, Nyström J. *Front Med (Lausanne)*. 2022;8:740527. doi:10.3389/fmed.2021.740527. <sup>5</sup>Zoja C, Morigi M, Figliuzzi M, et al. *Am J Kidney Dis*. 1995;26(6):934-941. <sup>6</sup>Morigi M, Buelli S, Angioletti S, et al. *Am J Pathol*. 2005;166(5):1309-1320. <sup>7</sup>Tejera N, Gómez-Garre D, Lázaro A, et al. *Am J Pathol*. 2004;164(5):1817-1826. <sup>8</sup>Lai K, et al. *Nat Rev Dis Primers*. 2016;2:160001.

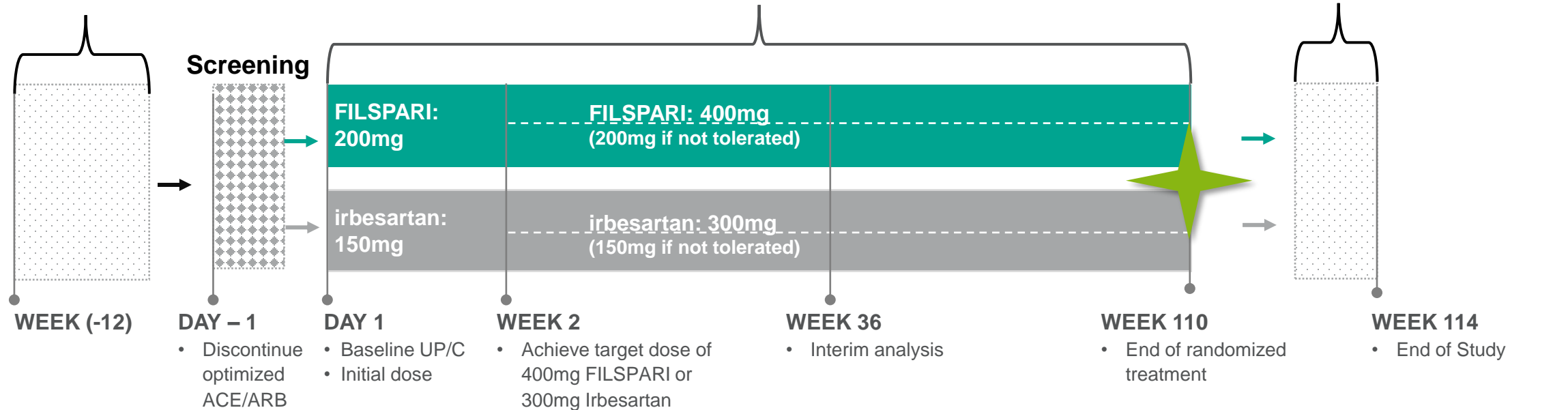


# Phase 3 PROTECT Study Design - Largest and Only Head-to-Head, Active-Controlled Trial in IgAN to Date

**Optimized ACE/ARB**  
12 weeks prior to screening

**Double-Blind Treatment Period**  
110 Weeks, Randomize 1:1

**Resume ACE/ARB**  
4 weeks post cessation of randomized treatment



**Trial Design:** A global, multicenter, double-blind, randomized, active-controlled trial that enrolled 404 patients with IgAN, ages 18 and up, evaluating the efficacy and safety of FILSPARI® (sparsentan)

### Primary and Key Secondary Efficacy Endpoints

- Primary endpoint (U.S. and EU): UP/C change from baseline<sup>a</sup> at week 36
- Secondary confirmatory endpoints: eGFR total slope<sup>b</sup> (U.S.) eGFR chronic slope<sup>c</sup> (EU) at week 110

### Prespecified Other Secondary Efficacy and Exploratory Endpoints

- UP/C (g/g)
- Absolute change in eGFR – mean change from baseline at week 110
- Absolute change in eGFR – mean change from baseline at week 114<sup>b</sup> following 4 weeks post treatment (patients who completed blinded treatment period)
- Confirmed 40% reduction in eGFR, ESRD, or death during the study

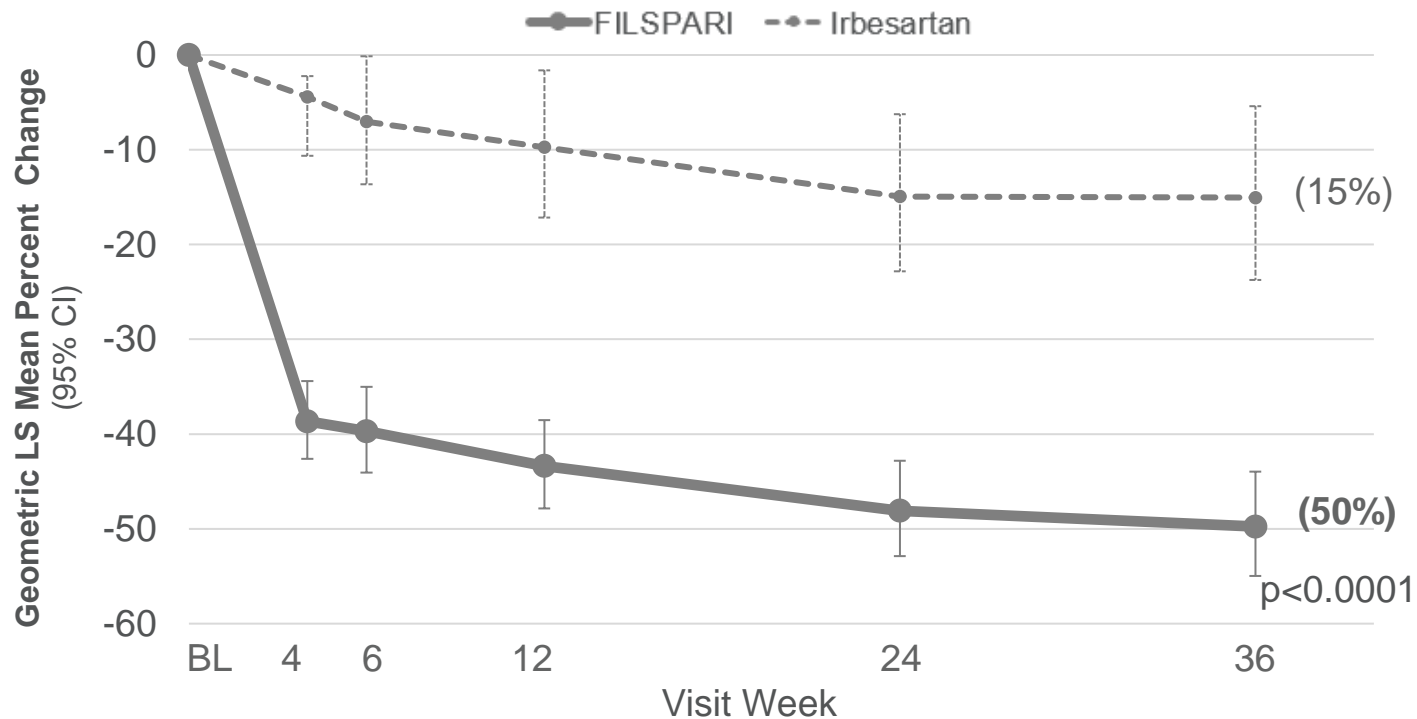
<sup>a</sup>change from baseline (day 1) in the urine protein/creatinine ratio (UP/C), based on a 24-hour urine sample, at week 36, <sup>b</sup>eGFR total slope measures day 1 to 110 weeks of treatment, post randomization, <sup>c</sup>eGFR chronic slope measures week 6 to 110 weeks of treatment, following the initial acute effect of randomized treatment

# PROTECT Study Demographics are Balanced and Representative of the IgAN Population

	FILSPARI® (N=202)	Irbesartan (N=202)	Total (N=404)
Age at informed consent, years, mean	46.6	45.4	46.0
Sex (n, % Female)	63 (31)	59 (29)	122 (30) <sup>-</sup>
<b>Race, n (%)</b>			
White	130 (64)	142 (70)	272 (67)
Asian	67 (33)	48 (24)	115 (28)
Black or African American	1 (<1)	3 (1)	4 (1)
Other	4 (2)	9 (4)	13 (3)
<b>Not Hispanic or Latino, n (%)</b>	<b>185 (92)</b>	<b>183 (91)</b>	<b>368 (91)</b>
Systolic / diastolic blood pressure, mm Hg, mean	128.0 / 81.6	129.9 / 83.2	129.0 / 82.4
UP/C, g/g median	1.25	1.23	1.24
UP/E, g/day median	1.76	1.82	1.80
eGFR, mL/min/1.73m <sup>2</sup> , mean	56.8	57.1	56.9

# Phase 3 PROTECT Study at 36 Week Interim Analysis Achieved Statistical Significance and Supported FDA Accelerated Approval of FILSPARI®

## Pre-specified Primary Analysis (PAS)\*



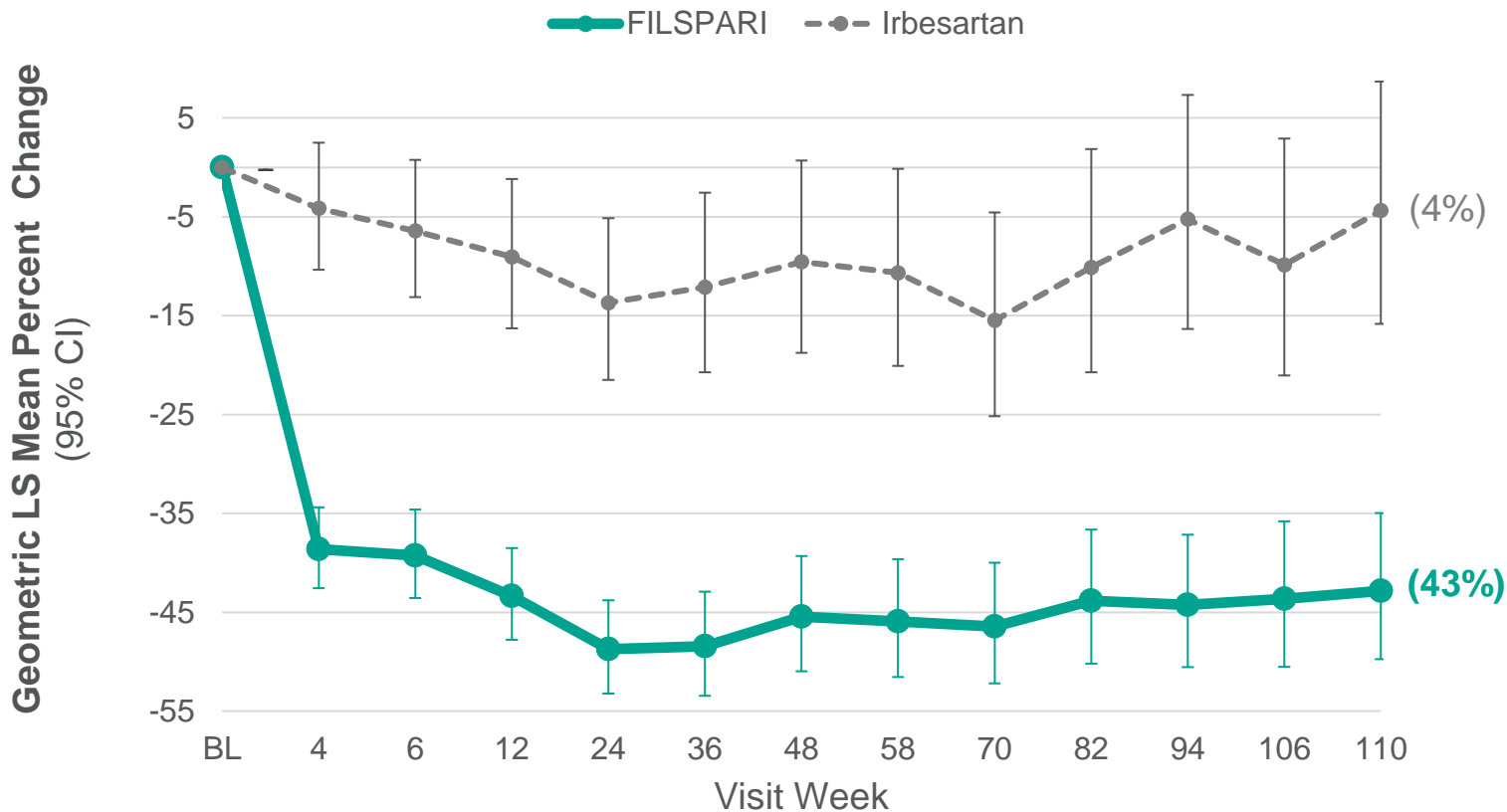
- **49.8% proteinuria reduction:** compared to a mean reduction from baseline of 15.1% for irbesartan-treated patients
  - Consistent treatment effect across subgroups including age, sex, race, and baseline proteinuria and eGFR
- Differentiated profile to support FILSPARI as the new treatment standard to reduce proteinuria in IgAN patients at risk of rapid disease progression

PAS: Pre-specified Primary Analysis

\*The FDA has not approved inclusion of the PAS data on the FILSPARI label

# FILSPARI® Shows Largest Magnitude of Sustained Proteinuria Reduction in Pivotal, Phase 3 PROTECT Trial

## UP/C % Change from Baseline by Visit (FAS)



- **43% proteinuria reduction with FILSPARI** compared to a mean reduction from baseline of 4% for irbesartan-treated patients over two-years
- FILSPARI provides a rapid and sustained antiproteinuric effect over two years
- Confirmatory Phase 3 PROTECT Study results build upon the interim analysis and continue to demonstrate that FILSPARI has a durable treatment effect on proteinuria over two years of treatment



# FILSPARI<sup>®</sup> Demonstrates Long-Term Kidney Function Preservation in IgAN

## Confirmatory Secondary Endpoints:

- All topline efficacy endpoints favored FILSPARI as compared to irbesartan; study narrowly missed achieving statistical significance on eGFR total slope endpoint
- IgAN patients treated with FILSPARI over two years exhibited one of the slowest annual rates of kidney function decline seen in a pivotal clinical trial in IgAN
- **eGFR total slope:** FILSPARI showed a 1.0 mL/min/1.73m<sup>2</sup> per year favorable difference as compared to irbesartan
- **eGFR chronic slope:** FILSPARI showed 1.1 mL/min/1.73m<sup>2</sup> per year favorable difference as compared to irbesartan

eGFR Slope	FILSPARI (N=202)	Irbesartan (N=202)	Difference (FILSPARI - Irbesartan) (95% CI)
<b>eGFR total slope,</b> mL/min/1.73m <sup>2</sup> per year <sup>a</sup>	<b>-2.9</b>	<b>-3.9</b>	<b>1.0, p=0.058</b> (-0.03, 1.94)
<b>eGFR chronic slope,</b> mL/min/1.73m <sup>2</sup> per year <sup>b</sup>	<b>-2.7</b>	<b>-3.8</b>	<b>1.1, p=0.037</b> (0.07, 2.12)

<sup>a</sup>LS Means and 95% CI from a random coefficient analysis including available on-treatment eGFR data through week 110 with multiple imputation; mL/min/1.73m<sup>2</sup> per year

<sup>b</sup>LS Means and 95% CI from a random coefficient analysis including available on-treatment eGFR data from week 6 through week 110 with multiple imputation; mL/min/1.73m<sup>2</sup> per year

# FILSPARI® Shows Favorable Kidney Function Benefit in ITT Population and Sensitivity Analyses in Phase 3 PROTECT Study

Favorable and consistent kidney function trends when considering imbalances in patients treated with irbesartan compared to patients treated with FILSPARI

- Higher rates of early treatment discontinuations (driven by patient and physician decision to stop treatment) and initiation of rescue immunosuppression were observed with patients on irbesartan as compared to patients on FILSPARI

All Randomized Patients (irrespective of early treatment discontinuations - mITT Analysis)	FILSPARI (N=202)	Irbesartan (N=202)	Treatment Difference (FILSPARI - Irbesartan) (95% CI)
<b>eGFR total slope,</b> mL/min/1.73m <sup>2</sup> per year	-3.0	-4.2	<b>1.2</b> (0.23, 2.16)
<b>eGFR chronic slope,</b> mL/min/1.73m <sup>2</sup> per year	-2.9	-4.2	<b>1.3</b> (0.36, 2.32)
<b>Exclusion of Assessments After Initiation of Immunosuppression for Renal Disease</b>			
<b>eGFR total slope,</b> mL/min/1.73m <sup>2</sup> per year	-2.9	-3.9	<b>1.0</b> (0.03, 1.99)
<b>eGFR chronic slope,</b> mL/min/1.73m <sup>2</sup> per year	-2.8	-3.9	<b>1.2</b> (0.16, 2.15)

# FILSPARI® Shows Favorable Treatment Benefit on Pre-specified Kidney Function Endpoints and Hard Outcomes, in Phase 3 PROTECT Study

Patients treated with FILSPARI maintain more of their kidney function over time as compared to irbesartan

Absolute Overall Change in Kidney Function	FILSPARI (N=202)	Irbesartan (N=202)	Difference (FILSPARI - Irbesartan) (N=404)
<b>Absolute change in eGFR</b> Mean change from baseline at week 110 <sup>a</sup>	<b>-5.8</b>	<b>-9.5</b>	<b>3.7</b> (1.45, 5.99)
<b>Absolute change in eGFR</b> Mean change from baseline to 4 weeks post-cessation of randomized treatment week 114 <sup>b</sup> (Patients who completed the blinded treatment period)	(n=174) <b>-6.1</b>	(n=154) <b>-9.0</b>	<b>2.9</b> (0.45, 5.25)
	<b>FILSPARI (N=202)</b>	<b>Irbesartan (N=202)</b>	<b>Difference (FILSPARI - Irbesartan)</b>
<b>Confirmed 40% Reduction in eGFR, ESRD, or Death during the Study, n (%)</b>	<b>18</b> (8.9)	<b>26</b> (12.9)	<b>RR: 0.68</b> (0.37, 1.24) <sup>c</sup>

<sup>a</sup>LS Means and 95% CI from MMRM analysis including on-treatment data through Week 110; mL/min/1.73m<sup>2</sup>

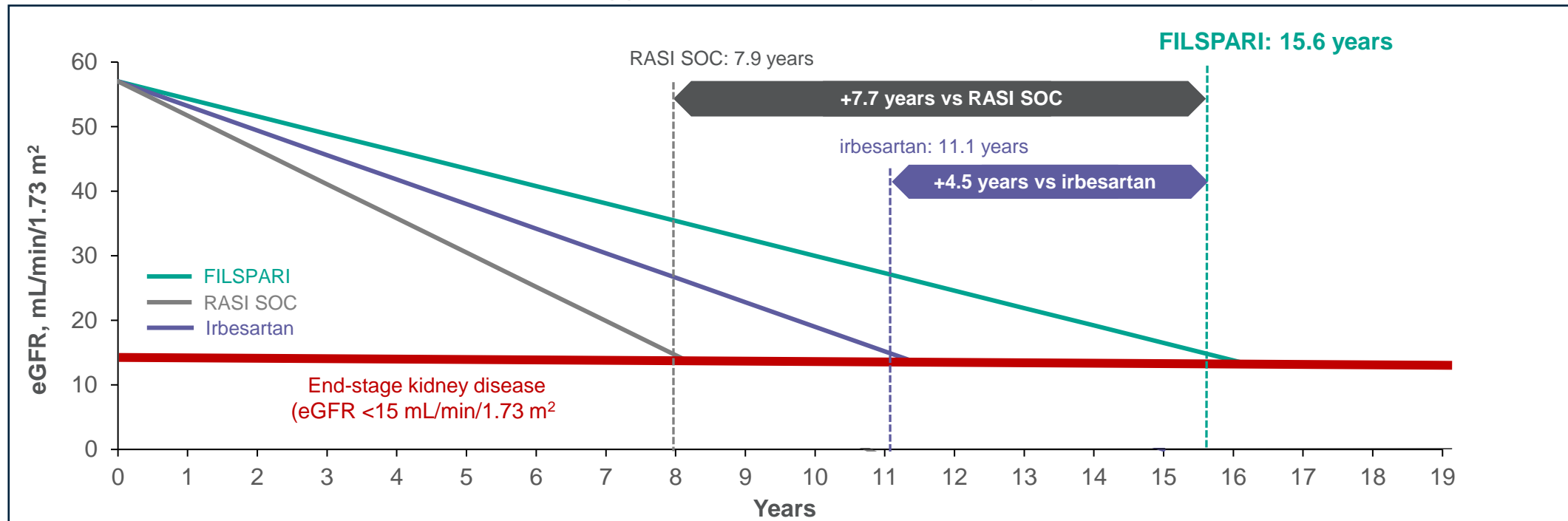
<sup>b</sup>LS Means and 95% CI from ANCOVA adjusted for eGFR at baseline; mL/min/1.73m<sup>2</sup>

<sup>c</sup>Relative risk (RR) of events and 95% CI from Poisson regression model

# eGFR Slope Results from Phase 3 PROTECT Study Project Delay in Time to Kidney Failure with FILSPARI® Treatment

	FILSPARI	Irbesartan	RASI SOC (ACEi/ARB)
eGFR chronic slope, mL/min/1.73 m <sup>2</sup>	- 2.7	- 3.8	- 5.3 <sup>a</sup>
Difference in eGFR slope vs. FILSPARI	-	1.1	2.6

## Improved eGFR slope suggests FILSPARI delays end-stage kidney disease



ACEi: angiotensin-converting enzyme inhibitor, ARB: angiotensin receptor blocker, eGFR: estimated glomerular filtration rate, RASI: renin-angiotensin system inhibitor, SOC: standard of care  
 eGFR = 57 mL/min/1.73m<sup>2</sup> at baseline (0 years) based on the mean eGFR of the FILSPARI group in the PROTECT study at the interim analysis.<sup>1</sup>

<sup>a</sup>Mean of observed slopes for maximized ACEi/ARB as reported in 5 clinical trials.<sup>2-6</sup>

<sup>1</sup>Heerspink HJL, et al. *Lancet*. 2023;401(10388):1584-1594. <sup>2</sup>Lafayette R, et al. *Lancet*. 2023;402(10405):859-870. <sup>3</sup>Lv J, et al. *JAMA*. 2022;327(19):1888-1898. <sup>4</sup>Wheeler DC, et al. *Kidney Int*. 2021;100:215-225. <sup>5</sup>Manno C, et al. *Nephrol Dial Transplant*. 2009;24(12):3694-3701. <sup>6</sup>Li PK-T, et al. *Am J Kidney Dis*. 2006;47(5):751-760.



# FILSPARI® Was Well-Tolerated in Two-Year Phase 3 PROTECT Study with a Consistent Safety Profile Comparable to Irbesartan, Supporting Long-Term Use

Adverse Reactions	FILSPARI (N=202), N (%)	Irbesartan (N=202), N (%)	Total (N=404), N (%)
Any TEAEs <sup>a</sup>	187 (93)	177 (88)	364 (90)
Any related TEAEs <sup>b</sup>	93 (46)	70 (35)	163 (40)
Any severe TEAEs	24 (12)	29 (14)	53 (13)
Any SAEs	75 (37)	71 (35)	146 (36)
Any AEOIs: Abnormal liver function tests <sup>c</sup>	5 (2)	7 (3)	12 (3)
Any TEAEs leading to treatment discontinuation	21 (10)	18 (9)	39 (10)
Any TEAEs leading to death	0 (0)	1 (<1)	1 (<1)

- No new safety signals emerged
- No new AEs of interest of 3x ULN AST or ALT with FILSPARI
- No Hy's law or drug-induced liver injury with FILSPARI

TEAE: treatment-emergent adverse event, SAE: serious adverse event, AEOI: adverse event of interest, ULN: upper limit of normal

<sup>a</sup>Treatment-emergent adverse event (TEAE) is defined as any AE that newly appear, increase in frequency, or worsens in severity following initiation of study medication.

<sup>b</sup>Related TEAEs are defined as TEAEs that are deemed to be 'possibly related' or 'related' to the study medication by the investigator.

<sup>c</sup>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.

# A Prescribers Experience with FILSPARI® for Patients with IgA Nephropathy

**Dr. Brad Rovin, M.D., FACP, FASN**



**The Lee A. Hebert Professor of Nephrology  
Director of the Division of Nephrology  
Director, Center for Clinical Research Management,  
Ohio State University Wexner Medical Center**

Dr. Rovin has had several leadership roles in the American Society of Nephrology, including running the Glomerular Diseases Pre-Course and Co-Editing NephSAP-Glomerular Diseases, a continuing education program of the Society. Most recently he was appointed Deputy Editor of Kidney International, the flagship journal of the International Society of Nephrology. He also is Co-Chair for glomerular disease guideline development for the Kidney Disease Improving Global Outcomes effort.

Dr. Rovin is a founding member of NephroNet, a grass-roots nephrology community clinical trial organization, and the Lupus Nephritis Clinical Trials Network. He is and has been the Principal Investigator on several trials of novel therapeutics for glomerular diseases.

# Phase 3 PROTECT Data Further Support FILSPARI® As Promising Treatment for IgAN Patients In Need

## Positioning FILSPARI to become the foundational therapy in IgAN

### Clinical Conclusions

- FILSPARI (sparsentan) achieved a clinically meaningful difference vs. irbesartan in eGFR total slope (1.0 mL/min/1.73m<sup>2</sup> per year) [p= 0.058] and eGFR chronic slope (1.1 mL/min/1.73m<sup>2</sup> per year) [p=0.037]
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### Next Steps

- The Company is engaging with regulators with the expectation of sNDA submission in 1H 2024
- Together with its partner CSL Vifor, the Company anticipates a review opinion by the Committee for Medicinal Products for Human Use (CHMP) on the CMA application for sparsentan for the treatment of IgAN in the EU around year-end



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