



Traverse Therapeutics Corporate Overview

March 2022

Forward-Looking Statements

This presentation contains forward-looking statements, including statements about our prospects, products, growth projections, competitive position, potential regulatory filings and agency actions, and the anticipated development, timing, data readouts and therapeutic scope of programs in our clinical pipeline. These forward-looking statements may be accompanied by such words as “anticipate,” “believe,” “estimate,” “expect,” “forecast,” “intend,” “may,” “plan,” “project,” “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, including the safety and efficacy of our 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 the ongoing COVID-19 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.



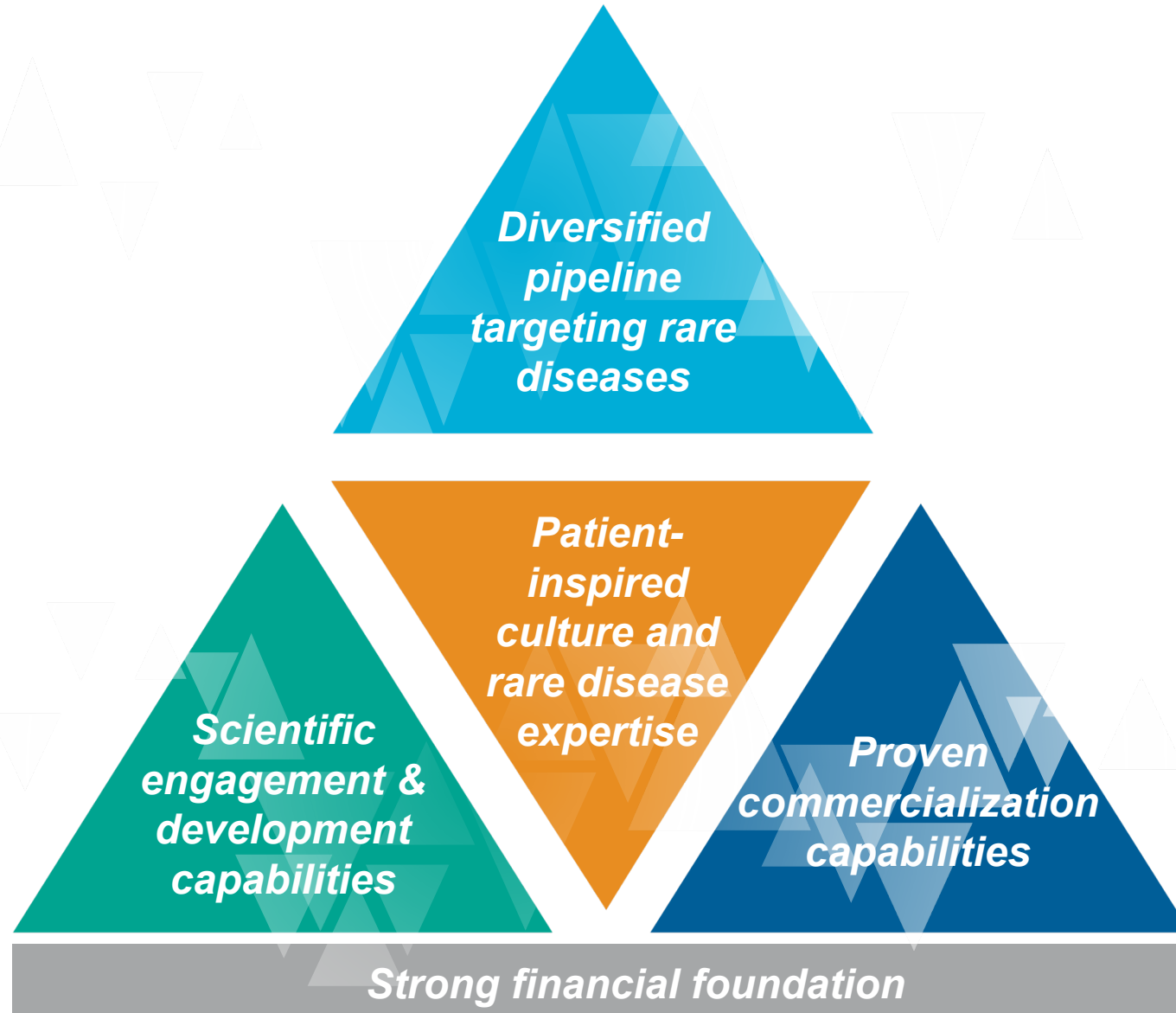


We are in rare for life.

At Traveře 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.



Key Strengths of Traverre Therapeutics



Financial Snapshot

GAAP Reported Financials	FY2021	FY2020	FY2019	FY2018
Net Product Sales	\$210.8mm	\$198.3mm	\$175.3mm	\$164.2mm
Operating Expenses	\$389.3mm	\$374.5mm	\$312.7mm	\$244.3mm
Operating Income / (Loss)	(\$161.8mm)	(\$176.2mm)	(\$137.4mm)	(\$80.0mm)
Net Income / (Loss)	(\$180.1mm)	(\$169.4mm)	(\$146.4mm)	(\$102.7mm)
Cash, Cash Equivalents and Marketable Debt Securities	\$552.9mm	\$361.6mm	\$398.5mm	\$471.5mm

- Shares outstanding as of December 31, 2021: basic ~62mm, diluted ~73mm
- Convertible notes: \$69 million due 2025, \$316 million due March 2029



Pipeline of Potential First-in-Class Programs Targeting Rare Diseases

PROGRAM	THERAPEUTIC AREA	PRECLINICAL	PHASE 1	PHASE 2	PHASE 3
Sparsentan	<i>FSGS</i>				
Sparsentan	<i>IgAN</i>				
CDCA*	<i>CTX</i>				
Pegtibatinase (TVT-058)**	<i>HCU</i>				
NGLY1 Collaboration	<i>NGLY1 Deficiency</i>				
ALGS Collaboration	<i>ALGS</i>				

*CDCA is not indicated for CTX but has received a medical necessity determination in the US by the FDA for CTX. Traverre Therapeutics is conducting a Phase 3 clinical trial to examine the safety and efficacy of CDCA (Chenodal®) for the treatment of CTX.

**Pegtibatinase is currently in a Phase 1/2 clinical study.

Key Milestones for Traverre Therapeutics

February 2021 Topline data from proteinuria endpoint* in DUPLEX Study in FSGS ✓

December 2021 Preliminary data from ongoing Phase 1/2 COMPOSE Study evaluating pegtibatase (TVT-058) ✓

Mid-2022 Potential NDA (Subpart H) submission in U.S. for FSGS**

2022 Engagement with regulators on pivotal program for pegtibatase; Continued advancement of COMPOSE Study in HCU

Advancement of CRADA research collaborations and continue to access external innovation

August 2021 Topline data from proteinuria endpoint* in PROTECT Study in IgAN ✓

1Q 2022 NDA (Subpart H) submission in U.S. for IgAN

Mid-2022 Potential MAA submission in EU for sparsentan in IgAN + FSGS

Late 2022/Early 2023 Potential first commercial launches of sparsentan in IgAN and FSGS

*Interim endpoint; confirmatory endpoint is slope of eGFR ** Pending additional supportive eGFR data from DUPLEX Study



Sparsentan - A Potential New Treatment Standard for FSGS and IgAN

Progressive Kidney Disease Has A Devastating Impact on Patients, Caretakers and Society

The devastating impact of progressive kidney disease:

- Kidney disease is one of the leading causes of death
- About 1-in-4 patients die within first year of dialysis
- High mortality rate prior to ESKD due to kidney related vascular events

Progressive kidney disease has a dramatic impact on healthcare cost:

- CKD accounts for ~20% in traditional Medicare spending upwards of \$114B/year
- Total Medicare expenditures \$49.2B for beneficiaries with ESKD in the US
- >125,000 patients start dialysis each year in the US; this number is growing

Results in disproportional number of patients with FSGS and IgAN in ESKD due to progressive nature of disease

ESKD = End Stage Kidney Disease

Xu et. al, NCHS Data Brief No. 355, January 2020; USRDS 2020 Annual Report; HHS Press Office, 2019;



The Burden of FSGS and IgA Nephropathy

FSGS

- ▼ **Primary FSGS generally affects patients in their mid-forties to fifties**
- ▼ **High proteinuria levels in (sub)nephrotic range is hallmark of disease**
- ▼ **Majority of patients relapse, many within 20-36 months**
- ▼ **30-60% progress to ESKD with 5-10 years; Recurrent disease develops in 40% of transplant patients**



▼ **Growing incidence and prevalence**

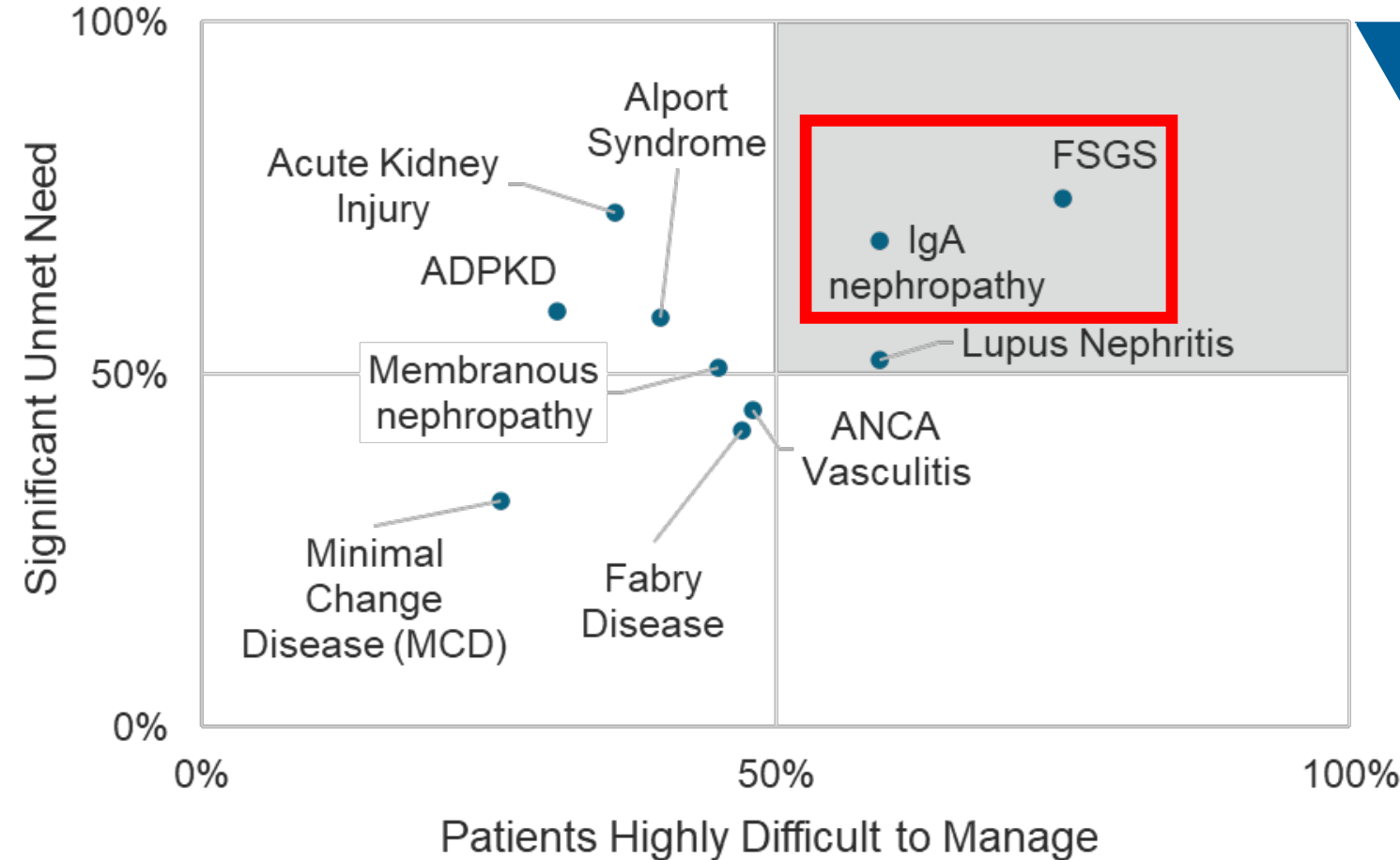
IgAN

- ▼ **Most commonly reported primary glomerulonephritis**
- ▼ **Affects young adults, often leading to dialysis or transplant in their 40s or early 50s**
- ▼ **~30-40% of patients have a progressive course to ESKD**
- ▼ **The prognosis is worse for those with persistent proteinuria >1gr/day**

Sources: Gipson et al. *Kidney Int.* (2011); Healthagen 2007 – 2019; Korbet et al., *J Am Soc Nephrol.* (2012); Market Dynamix 2020; USRDS (2019); Rauen et al. *Kidney Int.* (2020); Moranne et al., *Q J Med* (2008) Jarrick et al., *JASN* (2019); Le et al., *Nephrol Dial Transplant* (2011); Selvaskandan et al., *Clin and Exp Nephrol* (2019); proprietary market research

Nephrologists Rate FSGS & IgAN as Most Challenging to Manage, Given Limited or No Indicated Treatment Options Available

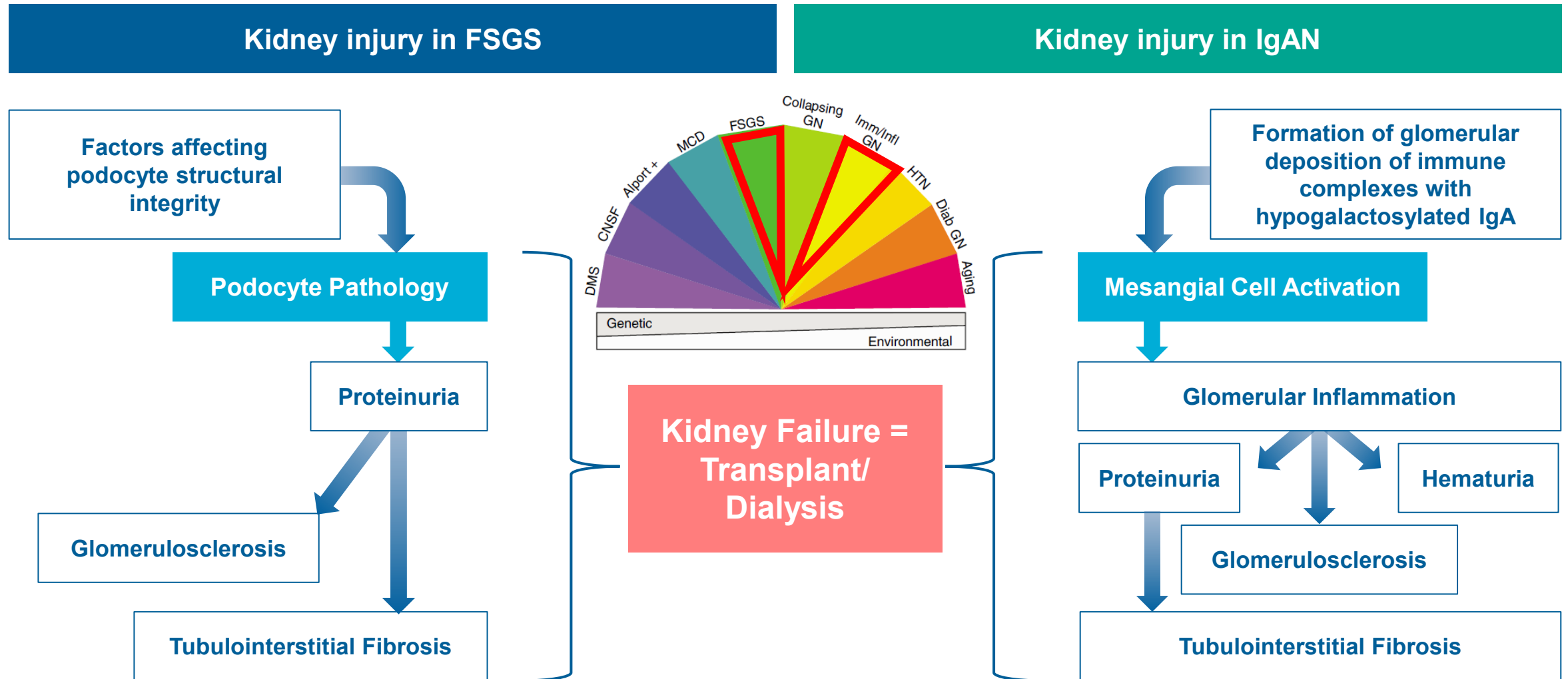
Unmet Needs Vs. Difficulty to Manage Patients
(Percentage respondents)



Surveyed nephrologists: *only 8% of their FSGS patients are “optimally managed”*

Surveyed nephrologists: *only 19% of IgAN patients are “optimally managed”*

FSGS and IgAN Share Common Renal Injury Pathways

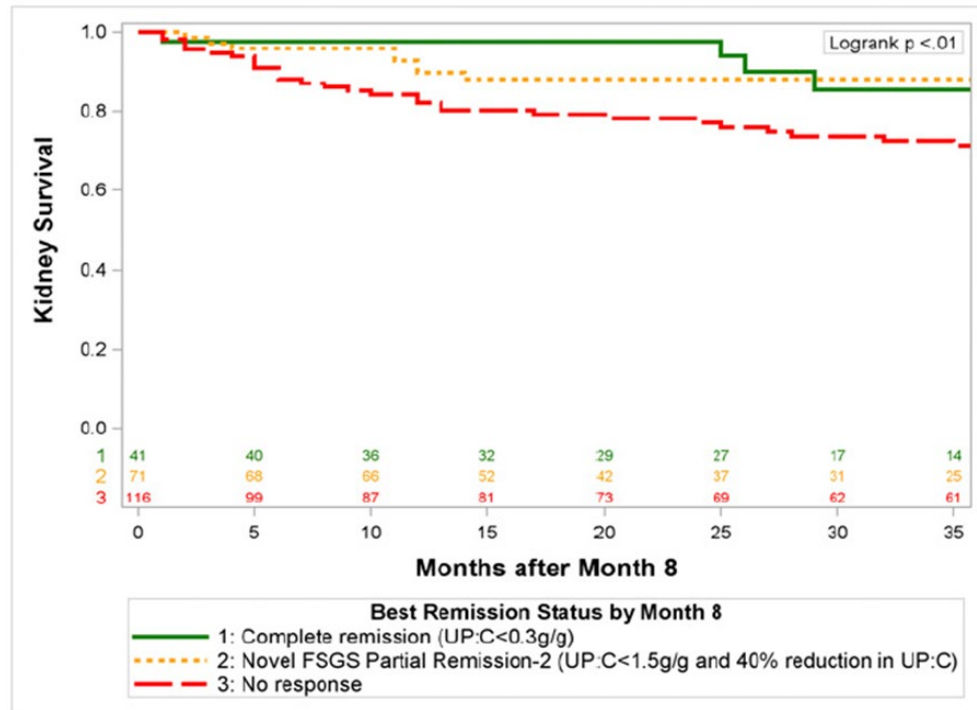


Source: Wiggins, Kidney International (2007)

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Reductions in Proteinuria Have Been Tied to Improved Kidney Outcomes in Third-Party Studies Evaluating Patients with Both FSGS and IgAN

FSGS Partial Remission of Proteinuria Endpoint (FPRE)¹



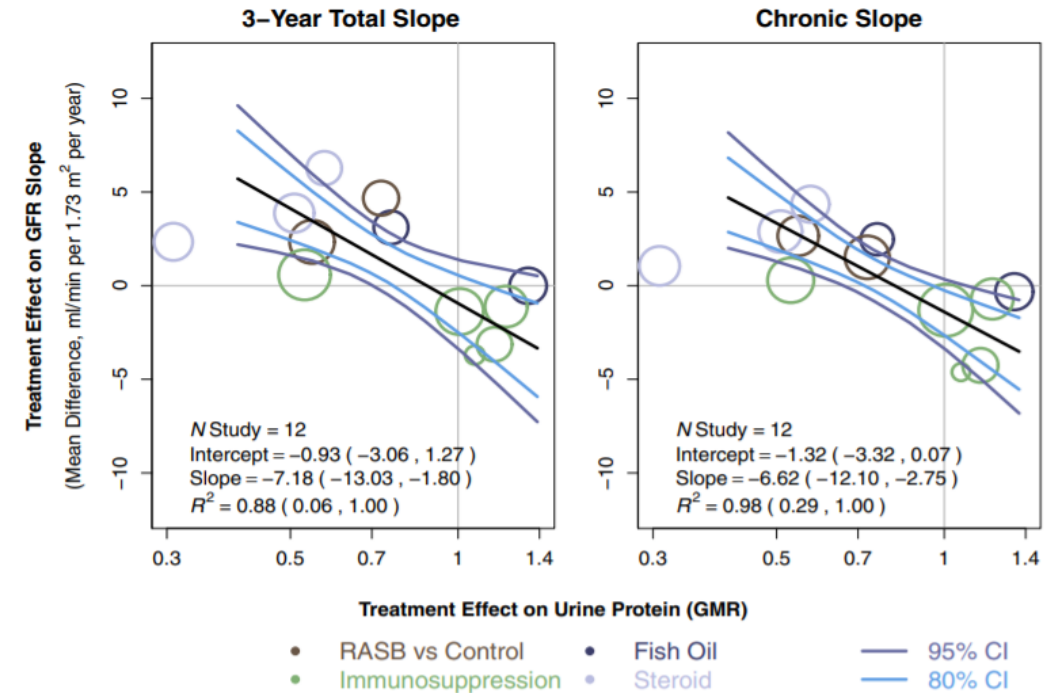
Data from five independent cohorts totaling 466 patients with primary FSGS showed that achieving a modified partial remission of proteinuria endpoint of <1.5 g/g accompanied with at least a 40% reduction in proteinuria was a robust correlate of kidney survival

UP/C = urinary protein-to-creatinine ratio.

1. Troost JP, et al. *Clin J Am Soc Nephrol* 2018; **13**:414–421

2. Inker, et al. *Am J Kidney Dis*. 2021

Proteinuria Reduction in IgAN²



Individual-patient meta-analysis including data from 1,037 patients with IgAN across 12 trials showed that treatment effects on urine protein accurately predicted treatment effects on the total GFR slope at 3 years and on chronic GFR slope

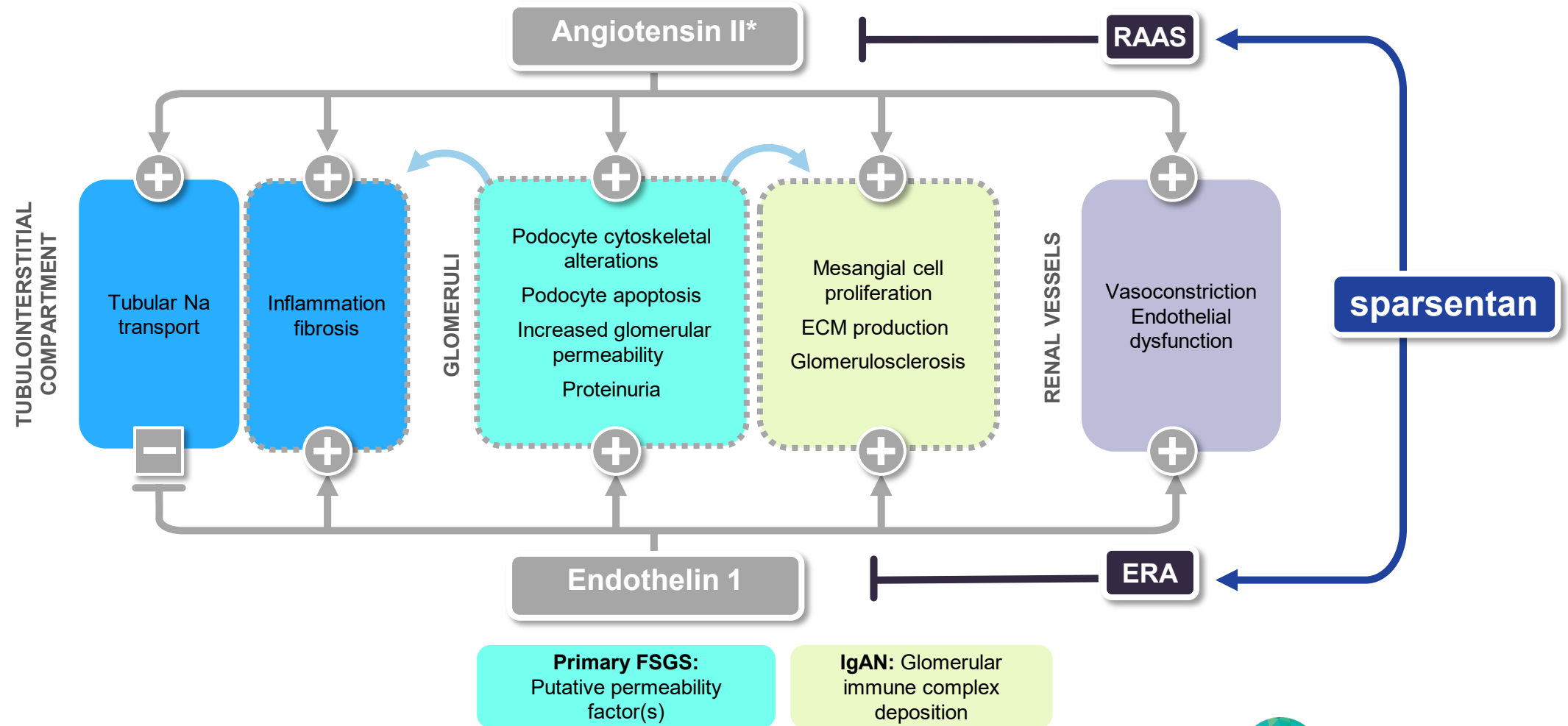
Sparsentan is a Potential First-in-Class Molecule Designed to Selectively Inhibit the Endothelin Receptor and Angiotensin II Receptor

- Sparsentan is an investigational product candidate designed to inhibit both endothelin receptor type A (ET_A) and angiotensin II receptor type 1 (AT_1) in a single molecule¹⁻³
- Distinct selectivity profile: high affinity selective antagonist at both the ET_A and AT_1 receptors; highly selective ET_A/ET_B
- Has shown nephroprotective properties across pre-clinical and non-clinical studies in both FSGS and IgAN
- Sparsentan is expected to have exclusivity until 2033 with potential for further extension
 - Orphan Drug Designations for FSGS and IgAN in the U.S. and Europe
 - Methods of use patents expiring March 2030 with potential for extension



Source: 1. Kowala MC, et al. *J Pharmacol Exp Ther*. 2004;309:275–284., 2. Komers R, et al. *Am J Physiol Regul Integr Comp Physiol*. 2016; 310 (10): R877-884., 3. Benigni A, et al. *Pediatr Nephrol* 2020. <https://doi.org/10.1007/s00467-020-04518-2>

Sparsentan Acts by Inhibiting the Signaling Pathways Present in FSGS and IgAN



*Also applies to aldosterone. Image adapted from Komers R. et al. *Am J Physiol Regul Integr Comp Physiol.* 2016;310:R877–R884.
ECM, extracellular matrix; ERA, endothelin receptor antagonist; RAAS, renin-angiotensin-aldosterone system.

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Robust Clinical Experience Across FSGS and IgAN to Support the Potential Profile of Sparsentan

Ongoing Pivotal Phase 3 PROTECT Study in IgAN

- 404 patients
- 1:1 vs active control (irbesartan)
- Interim proteinuria endpoint evaluated at 36 weeks
- eGFR confirmatory endpoint will be evaluated at 110 weeks of treatment

Ongoing Pivotal Phase 3 DUPLEX Study in FSGS

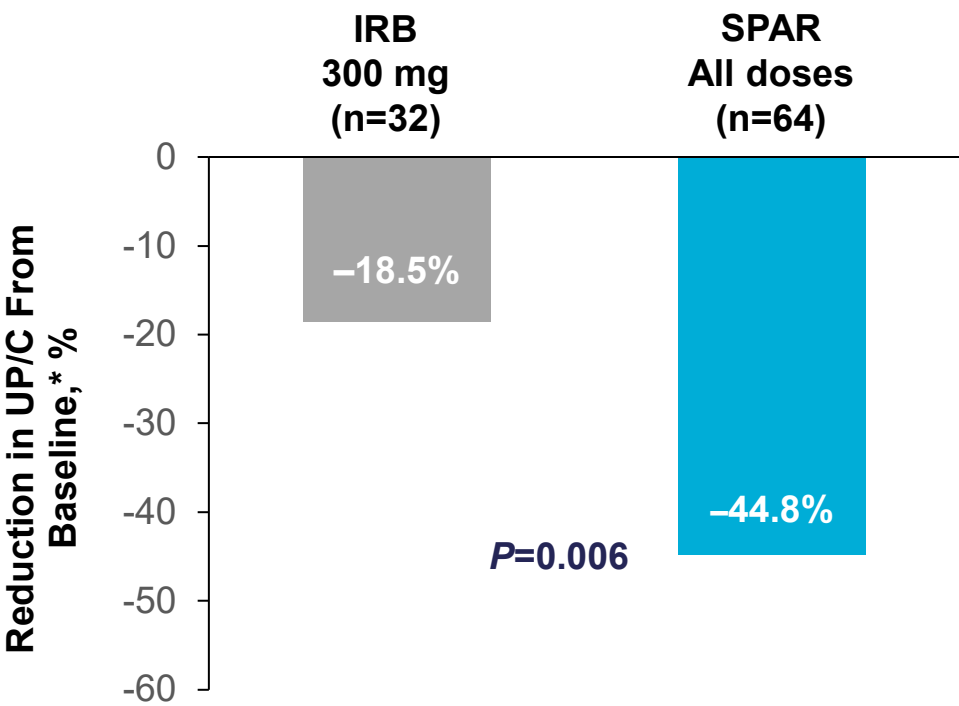
- 371 patients
- 1:1 vs active control (irbesartan)
- Interim proteinuria endpoint evaluated at 36 weeks
- eGFR confirmatory endpoint will be evaluated at 108 weeks of treatment

Phase 2 DUET Study in FSGS

- 109 patients
- 2:1 vs active control (irbesartan)
- Proteinuria endpoint at 8 weeks
- eGFR observed throughout OLE (ongoing)

- More than 500 patients with FSGS and IgAN have received sparsentan in clinical trials
- Several patients in the DUET OLE have been on sparsentan for more than seven years

Phase 2 DUET Study: Overall Sparsentan Treatment Group Met Primary Endpoint; More Than Doubled Reduction of Proteinuria vs. Irbesartan



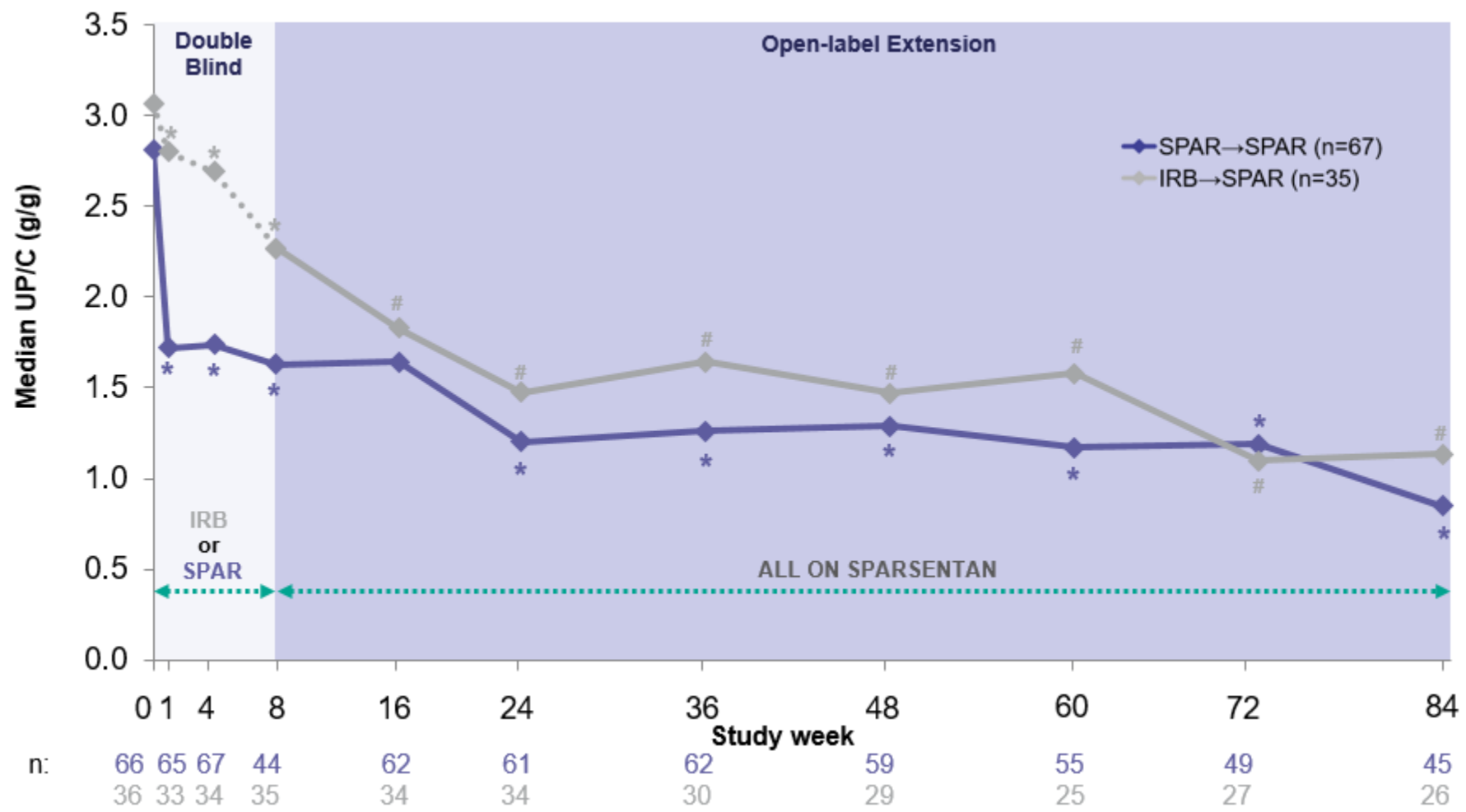
Significant reduction in proteinuria after 8 weeks of sparsentan vs irbesartan treatment in primary and genetic FSGS patients

TEAE	Patients with TEAEs During the Double-Blind Period, %	
	IRB (n = 36)	SPAR, All Doses (n = 73)
Any	72.2	76.7
Drug-related	36.1	43.8
Serious	2.8	2.7
Leading to dose change or interruption	8.3	23.3
Leading to drug discontinuation	2.8	4.1
Leading to study withdrawal	2.8	2.7
Death	0	0

Similar incidence of TEAEs between irbesartan and sparsentan-treated patients

*Geometric least squares mean reduction. P values from analysis of covariance. Analyses based on the efficacy evaluable set. UP/C based on 24-hour urine. Individual dose cohorts showed clear signals of relative improvement, but did not reach statistical significance; H Trachtman, *et al. J Am Soc Nephrol* 2018; 29:2745–2754. Loreto G, *et al. ERA-EDTA* 2017 Oral presentation TO042

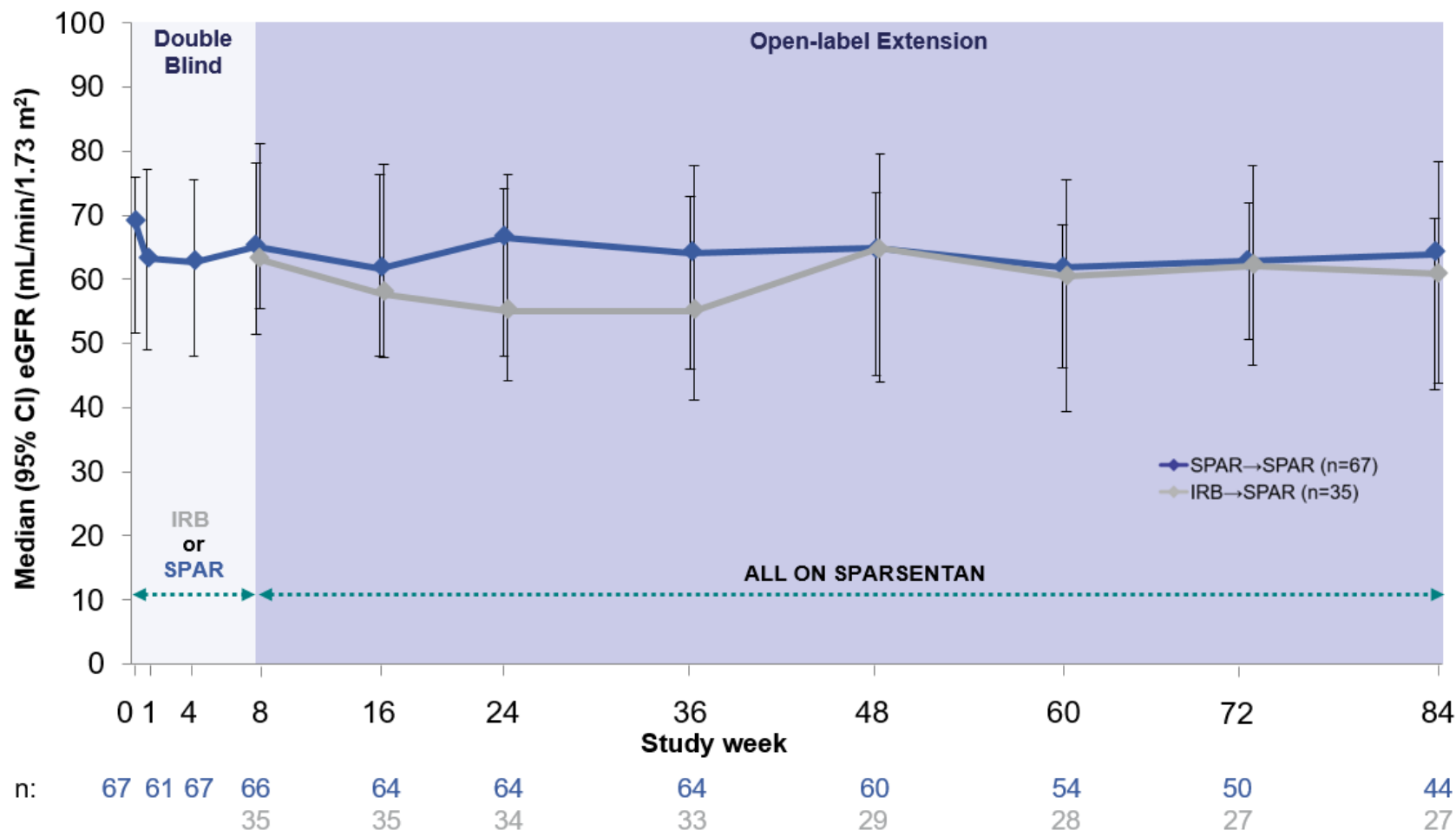
Phase 2 DUET Study OLE: Sustained Long-Term Proteinuria Reduction over 84 Weeks



95% confidence interval of the mean change from baseline (* Week 0; # Week 8) excludes 0.
Based on the full analysis set. UP/C based on first morning void.
UP/C = urinary protein-to-creatinine ratio; OLE = open-label extension



Phase 2 DUET Study OLE: eGFR Remained Stable in Sparsentan-Treated Patients Over 84 Weeks



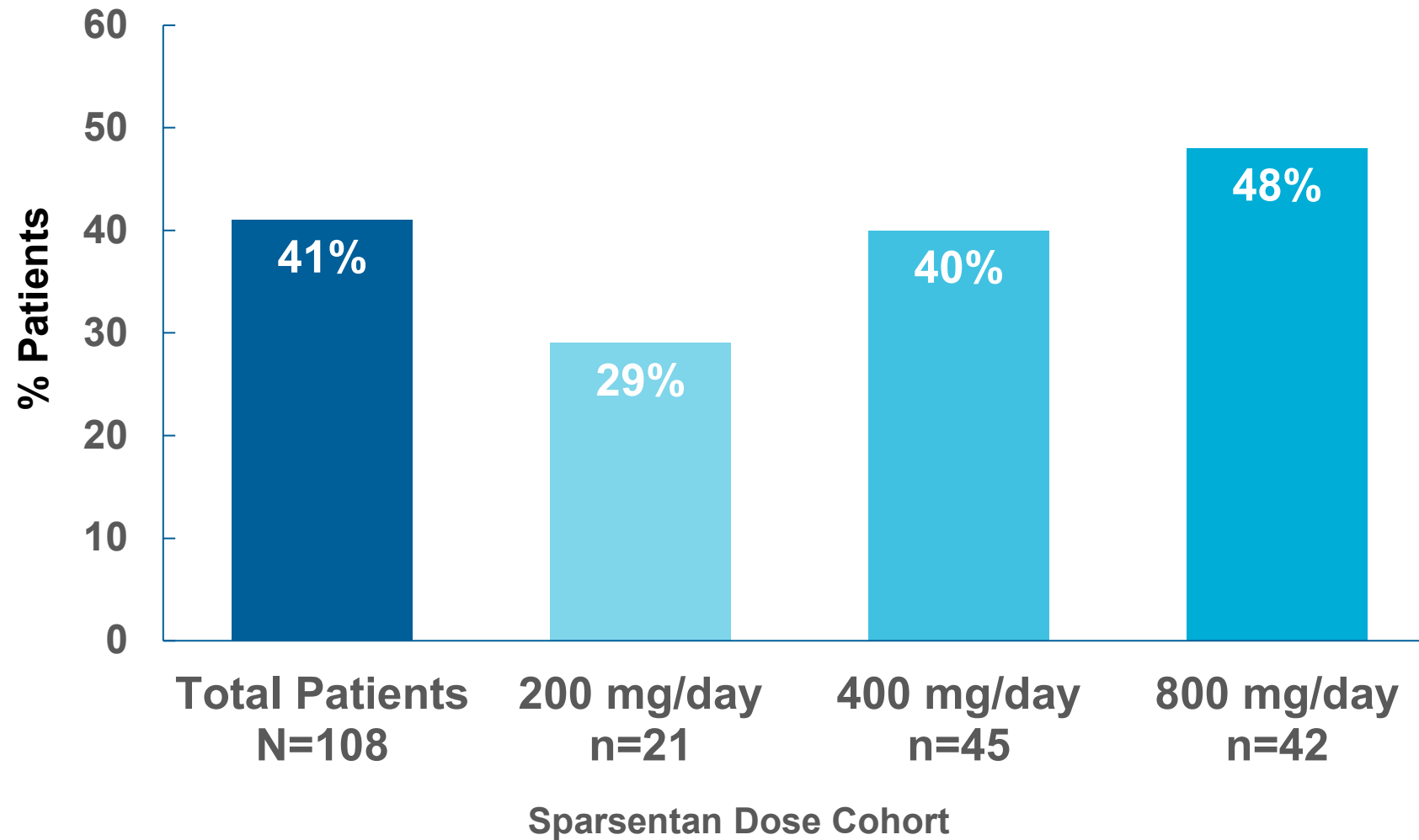
- Treatment with sparsentan resulted in an acute reduction in eGFR followed by long-term stabilization
- This dynamic is mechanism-driven and similar to the well-documented effects of other RAAS inhibitors and in recent SGLT2 inhibitor publications - where additional acute effects were seen when these therapies were added on top of ARBs

Based on the full analysis set. 95% CIs were calculated for the median value at each time point. Note: There were 9 study withdrawals due to renal causes during the follow-up period, including 1 case of end-stage renal disease.

CI = confidence interval; eGFR = estimated glomerular filtration rate; IRB:SPAR = patients randomized to irbesartan who then transitioned to sparsentan in the OLE; OLE = open-label extension; SPAR:SPAR = patients randomized to sparsentan who also received sparsentan in the OLE. Hogan J, et al. Long-Term Effects of Sparsentan, a Dual Angiotensin and Endothelin Receptor Antagonist in Primary FSGS: Interim 84-Week Analysis of the DUET Trial (Abstract FR-OR087). *J Am Soc Nephrol*. 2018;29:61. Accessed at <https://www.asn-online.org/education/kidneyweek/archives>



Phase 2 DUET Study OLE: Post hoc analysis – A High Percentage of Patients Achieved UP/C ≤ 0.3 g/g at Any Visit in a Dose-related Manner

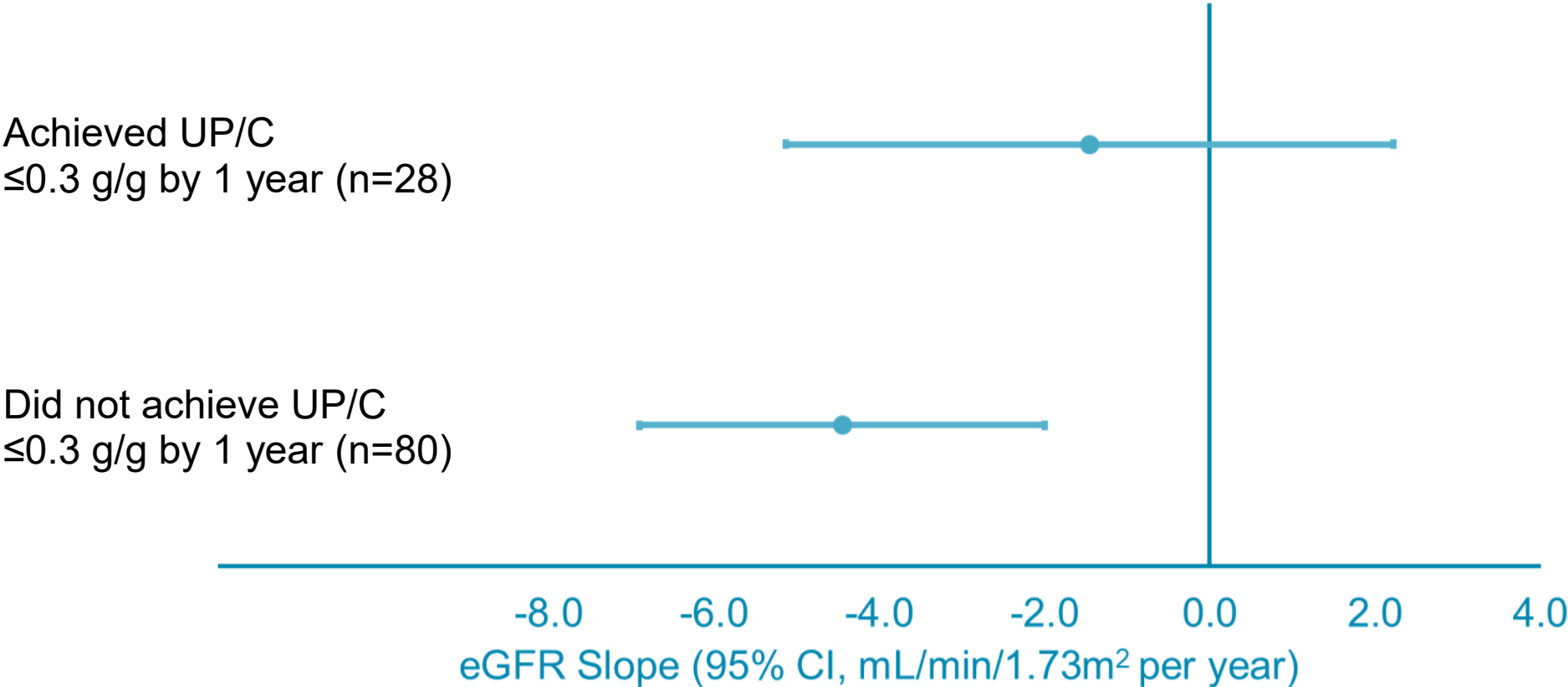


Hogan J, *et al.* ASN 2020 [oral presentation]

109 patients were randomized in DUET; 108 patients received at least one dose of sparsentan and were eligible for evaluation of UP/C while on sparsentan.

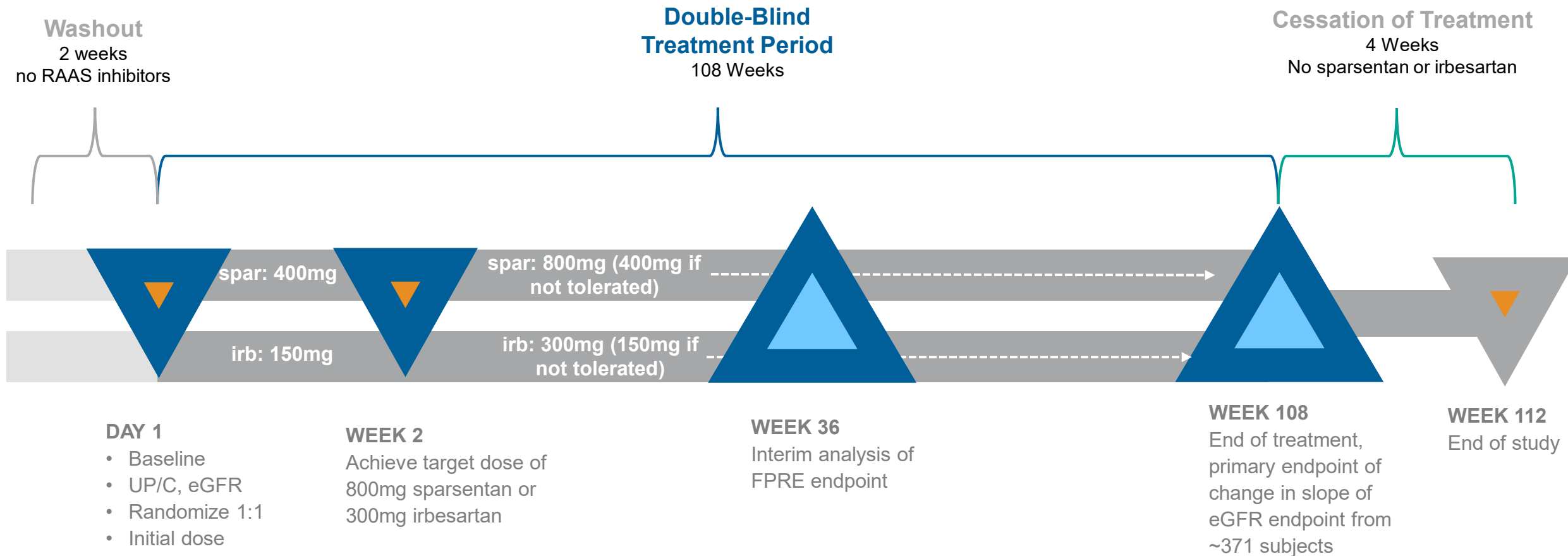
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Phase 2 DUET Study OLE: Achieving Complete Remission With Sparsentan in the First Year was Associated w/ Slower eGFR Decline Over Two Years



Hogan J, *et al.* ASN 2020 [oral presentation]

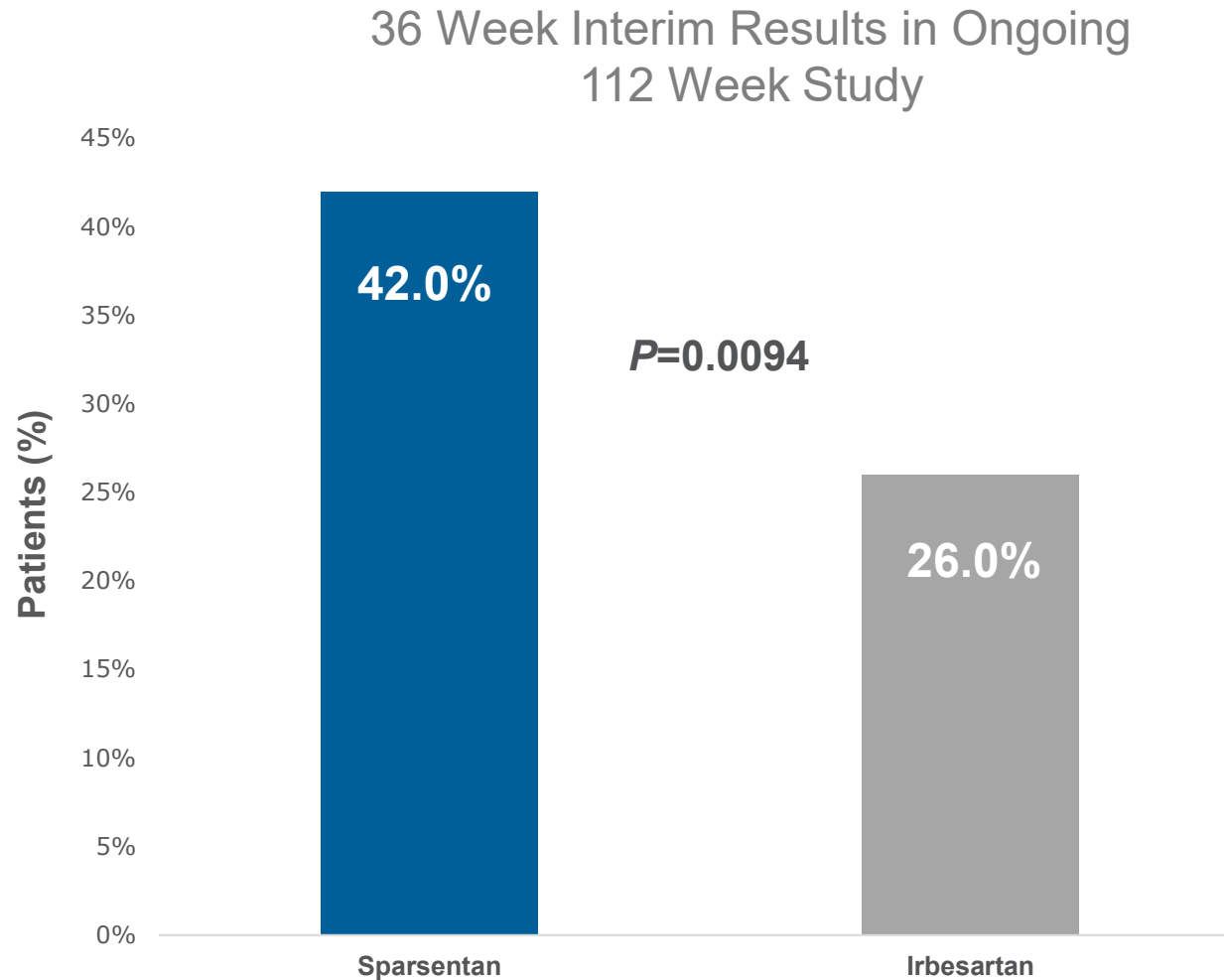
Phase 3 DUPLEX Study Designed to Support NDA & MAA Submissions for FSGS



- Fully enrolled with 371 patients; largest controlled study to-date in FSGS
- DUPLEX is scheduled to continue as planned on a blinded basis to assess the confirmatory eGFR endpoint after 108 weeks of treatment

Ongoing Phase 3 DUPLEX Study Achieved Interim FPRE Proteinuria Endpoint

The FSGS partial remission endpoint (FPRE) is defined as >40% reduction in proteinuria to a UP/C ≤ 1.5 g/g



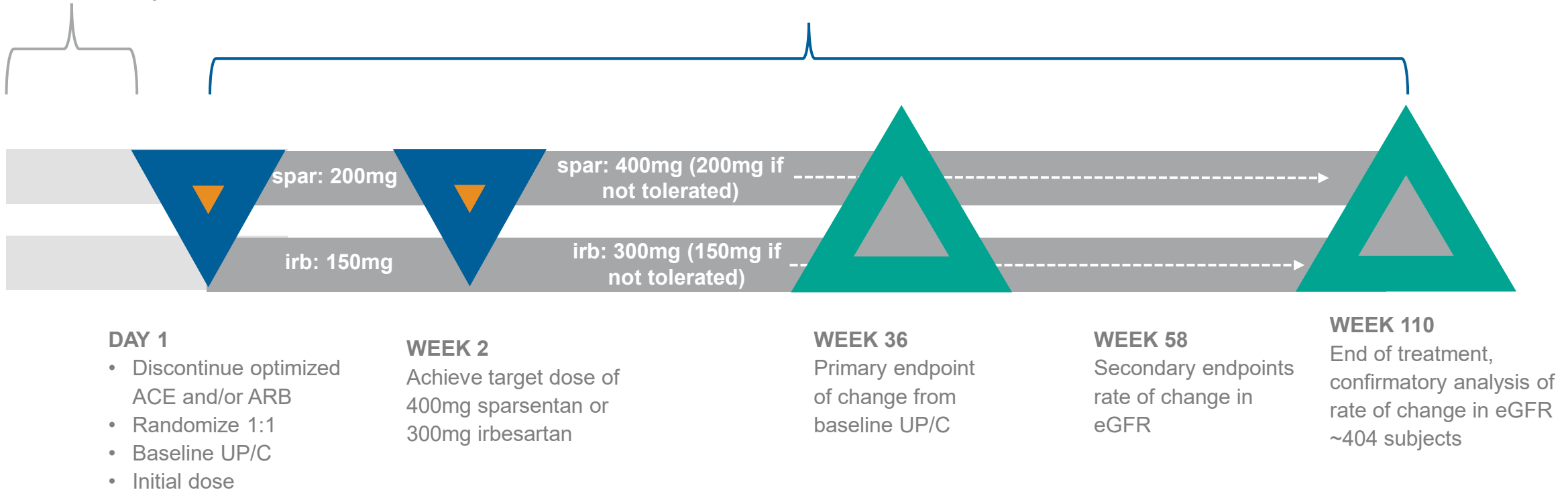
- Treatment with sparsentan resulted in a 60% greater relative likelihood of achieving FPRE when compared to irbesartan
- At the time of the interim assessment, sparsentan was generally well-tolerated and had shown a comparable safety profile to irbesartan

Phase 3 PROTECT Study Designed to Support Potential NDA & MAA Submissions for IgAN

Optimized ACE/ARB

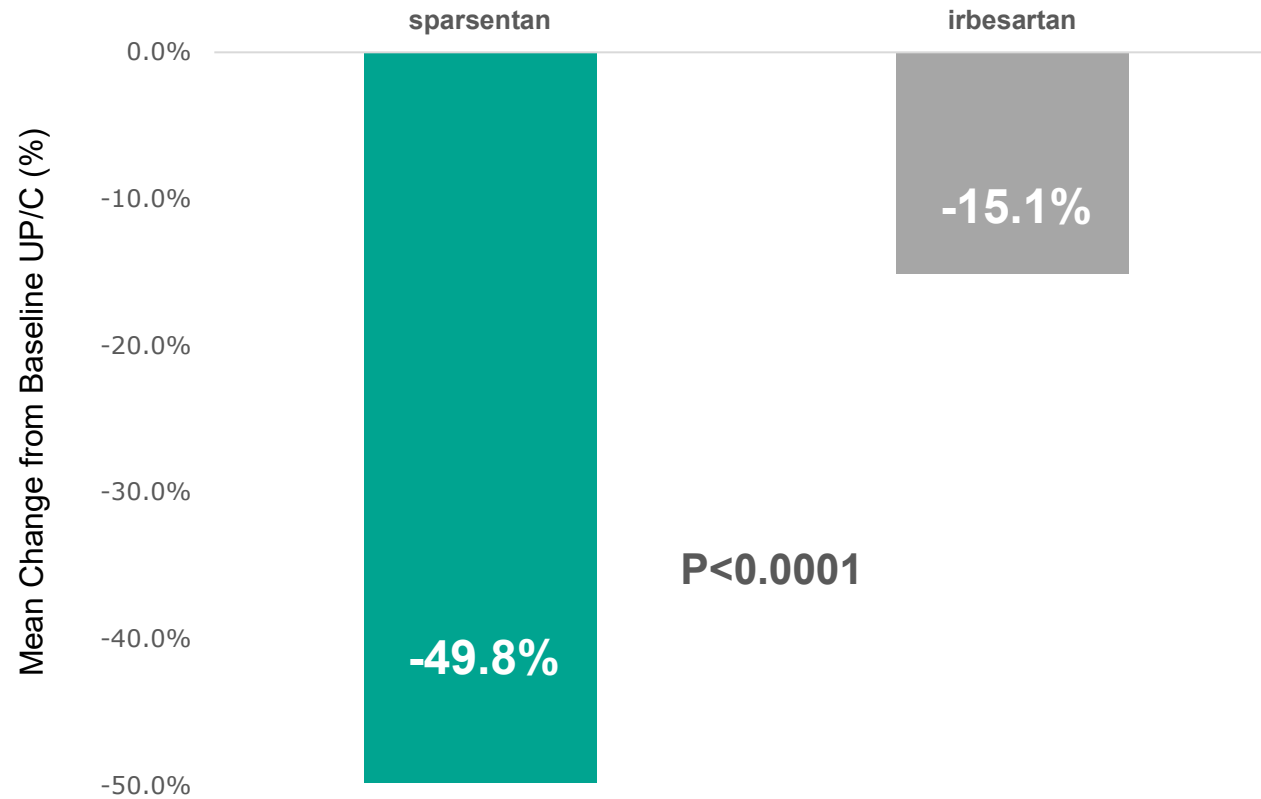
12 weeks
prior to screening

Double-Blind
Treatment Period
108 Weeks



- Patients treated in the PROTECT study are those at high risk of progressing to renal failure; believed to be largest controlled study to date in IgAN
- PROTECT is fully enrolled and is scheduled to continue on a blinded basis to assess the confirmatory eGFR endpoint after 110 weeks of treatment

Ongoing Phase 3 PROTECT Study Met its Interim Reduction of Proteinuria Endpoint



36 Week Interim Results in Ongoing
110 Week Study

- Sparsentan demonstrated a greater than 3x reduction of proteinuria from baseline after 36 weeks of treatment, compared to the active control irbesartan
- PROTECT Study was designed to detect a 30% difference in the geometric mean ratio (GMR) of proteinuria reduction between sparsentan and irbesartan; topline results demonstrated a 41% difference in GMR
- Preliminary eGFR data available at the time of the interim analysis are believed to be indicative of a potential clinically meaningful treatment effect after two years of treatment
- At the time of the interim assessment, sparsentan was generally well tolerated, and appeared consistent with the previously observed safety results with no new safety signals emerging

Sparsentan has Demonstrated Consistent Anti-proteinuric Responses Across Phase 2 and Phase 3 Clinical Trials



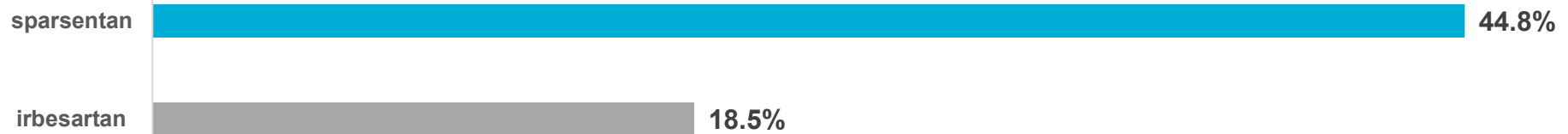
IgAN, mean change from baseline UP/C (%) at 36 weeks
 $P < 0.0001$



FSGS, FPRE response at 36 weeks
 $P = 0.0094$



FSGS overall treatment group, mean change from baseline UP/C (%) at 8 weeks
 $P = 0.006$

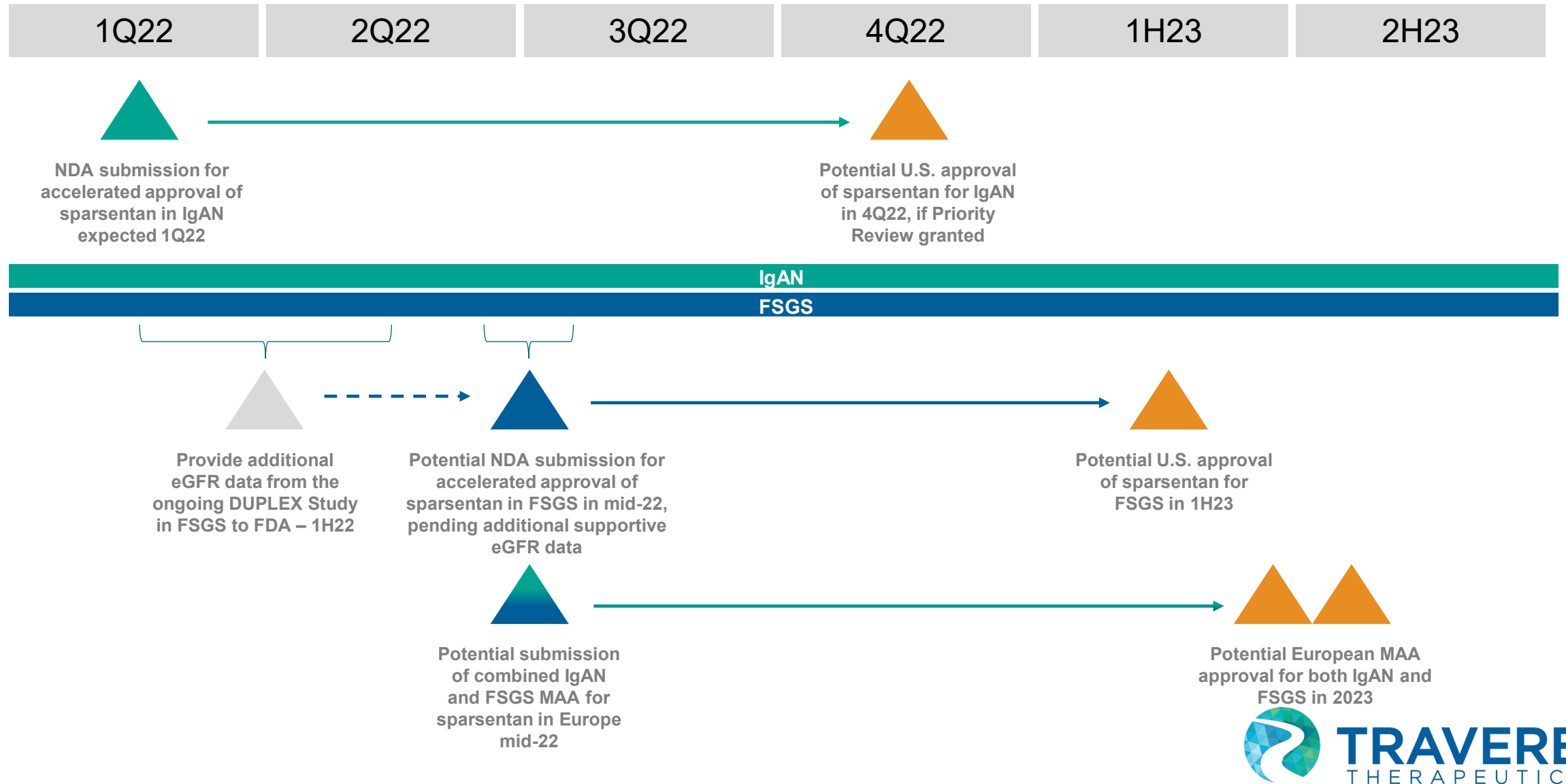


0.0% 5.0% 10.0% 15.0% 20.0% 25.0% 30.0% 35.0% 40.0% 45.0% 50.0%

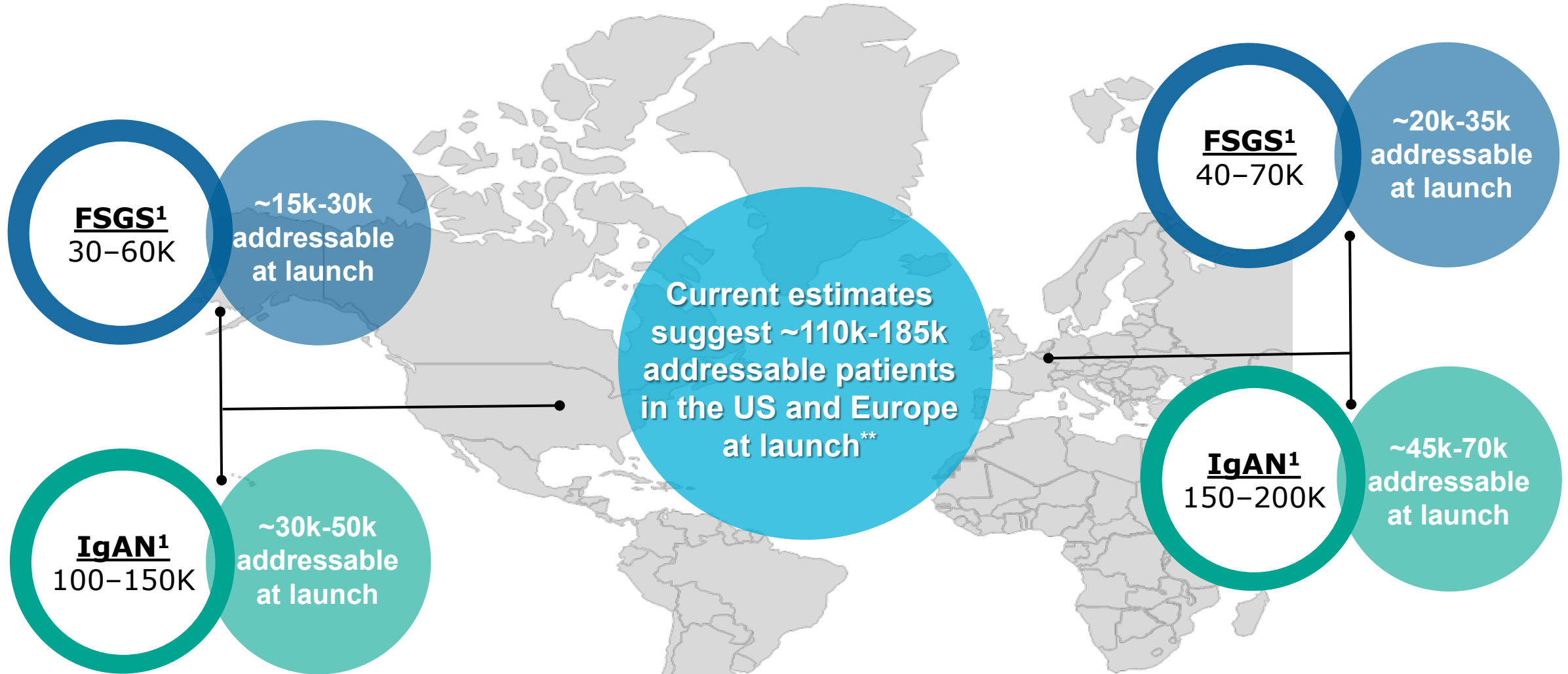
FDA granted its first drug approval based upon proteinuria reduction in 4Q21



Expected Regulatory Pathways to Potential Submissions and Approvals of Sparsentan in the U.S. and Europe



Significant Opportunity to Increase the Number of Patients Treated in the Coming Years if Sparsentan is Approved*



*Pending Phase 3 data and if approved **Aggregate both FSGS and IgAN – FSGS expected to launch prior to IgAN. Sources: ¹Estimated based on 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); data on file. Additional sources: Korbet et al., *J Am Soc Nephrol* (2012); Kitiyakara et al., *Am J Kidney Dis.* (2004); USRDS (2019); KDIGO, *Kidney Int Suppl* (2011);
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Joint Collaboration and Licensing Agreement with Vifor Pharma; Two Leaders in Rare Nephrology to Deliver Sparsentan in the U.S. and Europe, if Approved



Proven U.S. commercial capabilities and infrastructure; organic y-o-y growth for last six years

Established nephrology network, Patient Hub and expertise in the U.S.

Field-force currently calling on ~2,000 nephrologists in U.S.

U.S.

Shared vision to make sparsentan a new treatment standard for IgAN and FSGS, if approved

EU/AUS/NZ

Exclusive commercialization rights for sparsentan in Europe, Australia and New Zealand

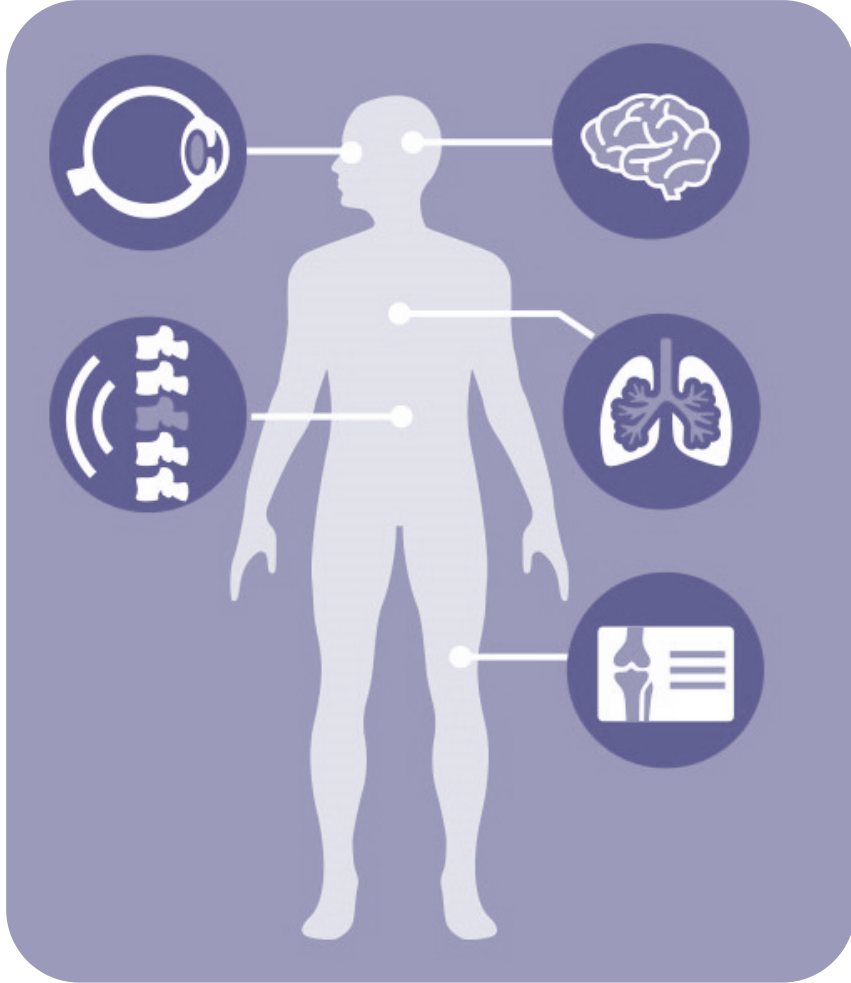
Global leader in nephrology w/ established commercialization expertise in EU, AUS and NZ

Dedicated nephrology sales force currently calling on nephrologists across Europe

Traverse to receive up to \$845 million in total milestone and upfront payments + tiered double-digit royalties up to 40% on net sales of sparsentan in Europe, Australia and New Zealand

Pegtibatinase (TVT-058) – The Potential First Disease Modifying Therapy for Classical Homocystinuria (HCU)

Classical Homocystinuria (HCU) is a Rare Disorder that can Lead to Life-Threatening Complications



- **Rare autosomal recessive disorder caused by mutations in cystathionine beta-synthase (CBS) gene, leading to deficient activity of CBS**
 - Metabolic deficiency of CBS leads to bodily buildup of toxic homocysteine (Hcy)
- **Toxic levels of Hcy can lead to serious complications for people living with classical HCU**
 - Continuous risk of developing life-threatening thrombotic events including heart attack and stroke
 - Other symptoms of classical HCU include dislocation of the eye lens and extreme nearsightedness, skeletal complications including osteoporosis, and developmental delay
- **There are no approved treatments that address the underlying genetic cause of HCU**
 - Current standard of care includes vitamin B6, low-protein diet + supplements, betaine
- **Estimates suggest at least 3,500 patients in US, similar number in Europe**

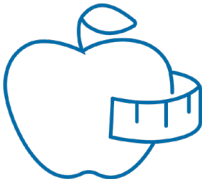
With Largely Ineffective Treatment Options, a Significant Unmet Need Remains for People Living with HCU



Generally accepted therapeutic goal is to reduce total homocysteine (tHcy) levels but current treatment options rarely sustain reductions in tHcy



Significant challenges for patients to maintain compliance; periods of poor metabolic control have a cumulative deleterious effect



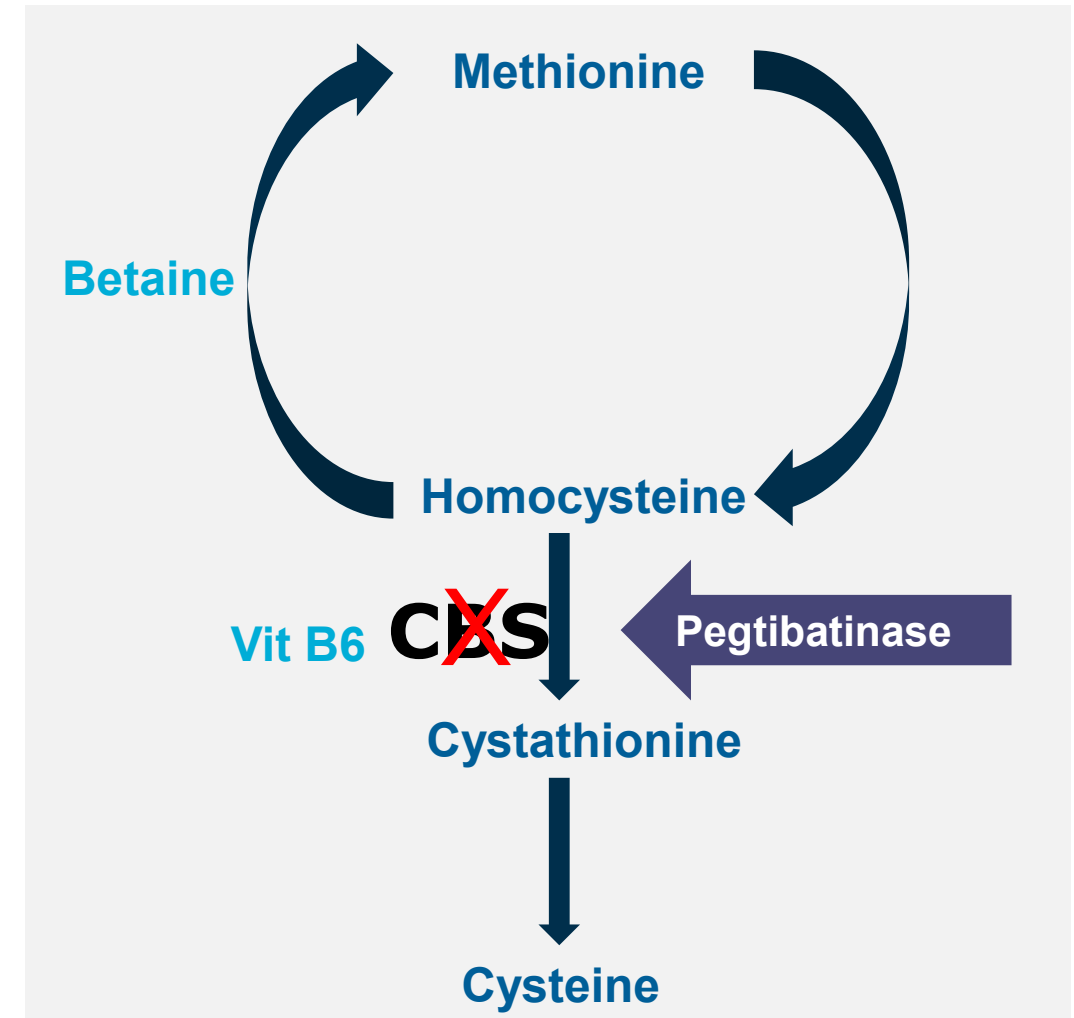
Patients struggle with severe dietary protein restrictions as they age; liberalized diet is amongst top needs



Inability to sustain reductions in Hcy results in life-long risk of thrombotic and cardiac events + cognitive impairment

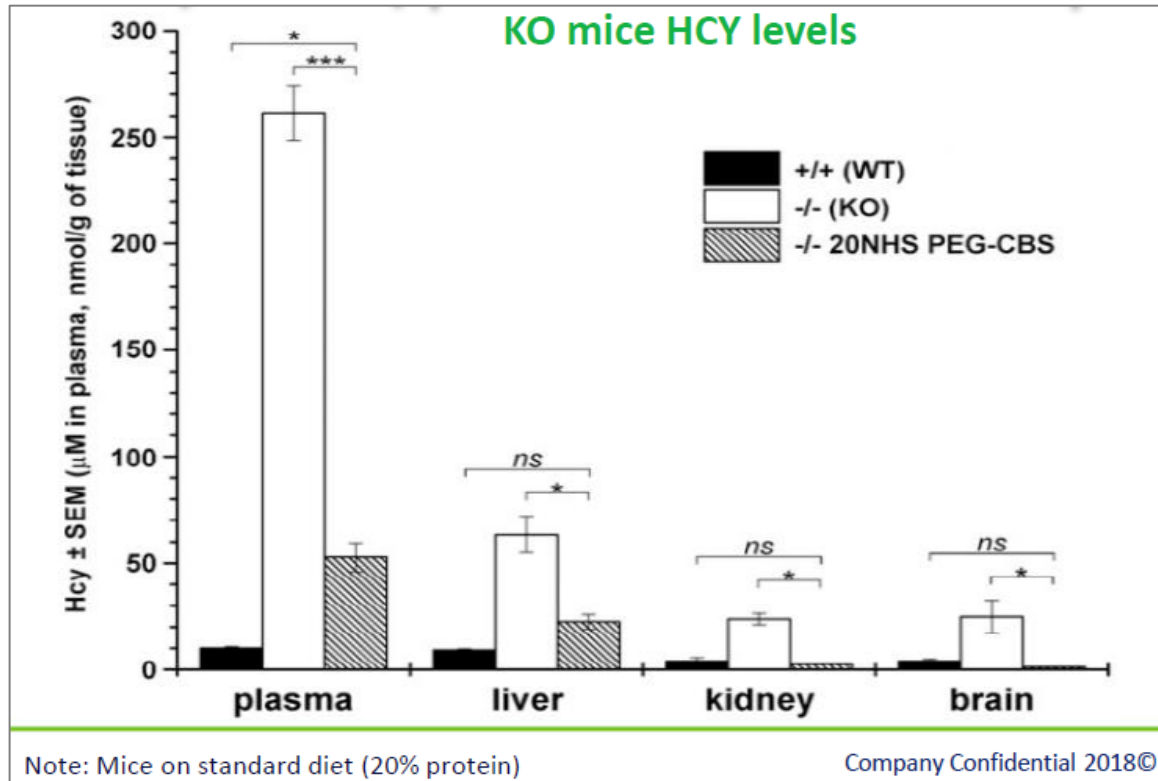
Pegtibatinase (TVT-058) is an Investigational, Modified Recombinant CBS Human Enzyme Therapy

- Pegtibatinase (TVT-058) is a pegylated, modified recombinant truncated human enzyme, designed to address the underlying genetic cause of HCU
 - Mechanism of action is pathology agnostic
- Pegtibatinase is administered subcutaneously and designed to be active and stable in plasma unlike native CBS
- Designed to introduce the CBS enzyme into circulation and reduce intracellular and plasma Hcy levels
- Pegtibatinase has been granted multiple regulatory designations for the treatment of classical HCU:
 - FDA Rare Pediatric Disease designation
 - FDA Fast Track designation
 - Orphan Drug designation in the US and Europe.



Administration of Pegtibatinase Resulted in Up To 70-90% Reduction of Plasma and Tissue Hcy Levels in Mouse Models

Dosing with pegtibatinase resulted in a decrease of extracellular Hcy



“Metabolic Sink”

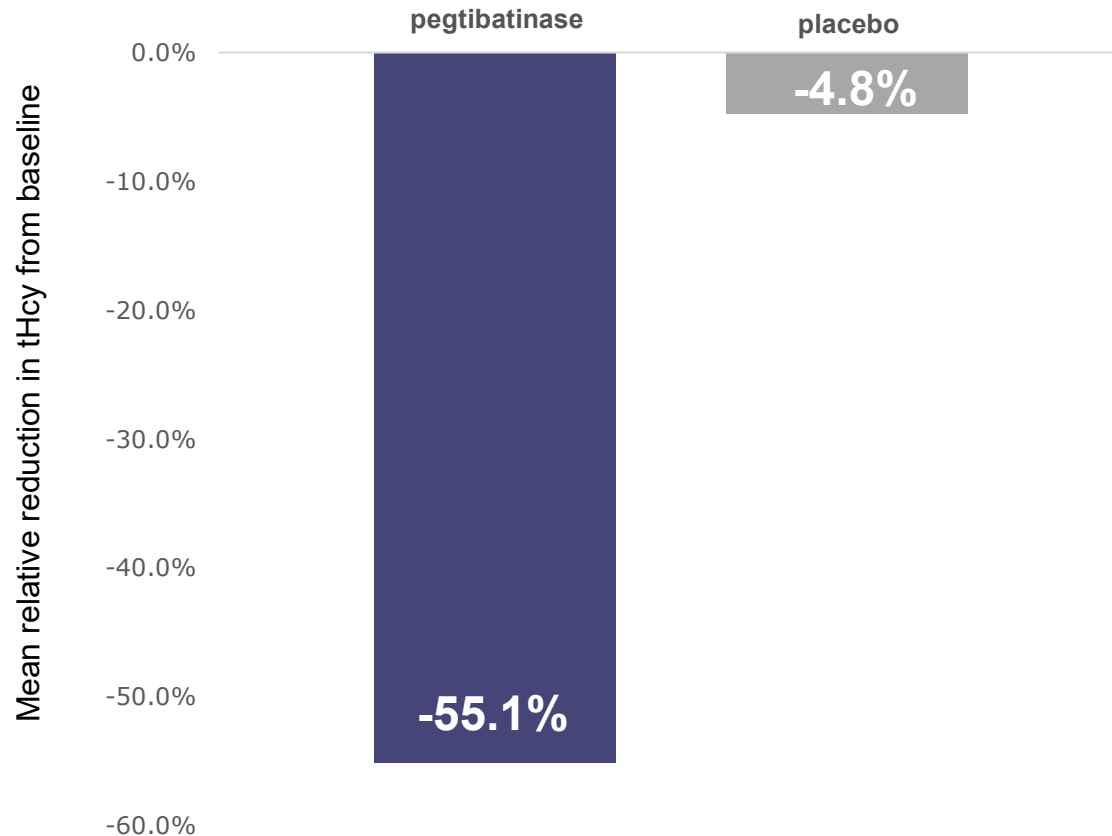
By lowering the Hcy levels in the blood, pegtibatinase has been shown to create a concentration gradient that causes excess Hcy in tissues to move to plasma, where it is metabolized

Pegtibatinase is Advancing in the Phase 1/2 COMPOSE Study in HCU

- Pegtibatinase is advancing in the Phase 1/2 COMPOSE Study – a double blind, randomized, placebo-controlled study in patients with HCU
- Cohorts are enrolled in a dose escalating fashion; following completion of each cohort, unblinded safety data are reviewed by DMC prior to activating next cohort
- Primary endpoint
 - Incidence of treatment-emergent adverse events
- Secondary endpoints
 - Total plasma homocysteine (tHcy)
 - Cognitive function changes
 - Ocular assessment
 - Bone mineral density
 - Patient QoL scales: Neuro-QoL, EQ-5D & SF-36



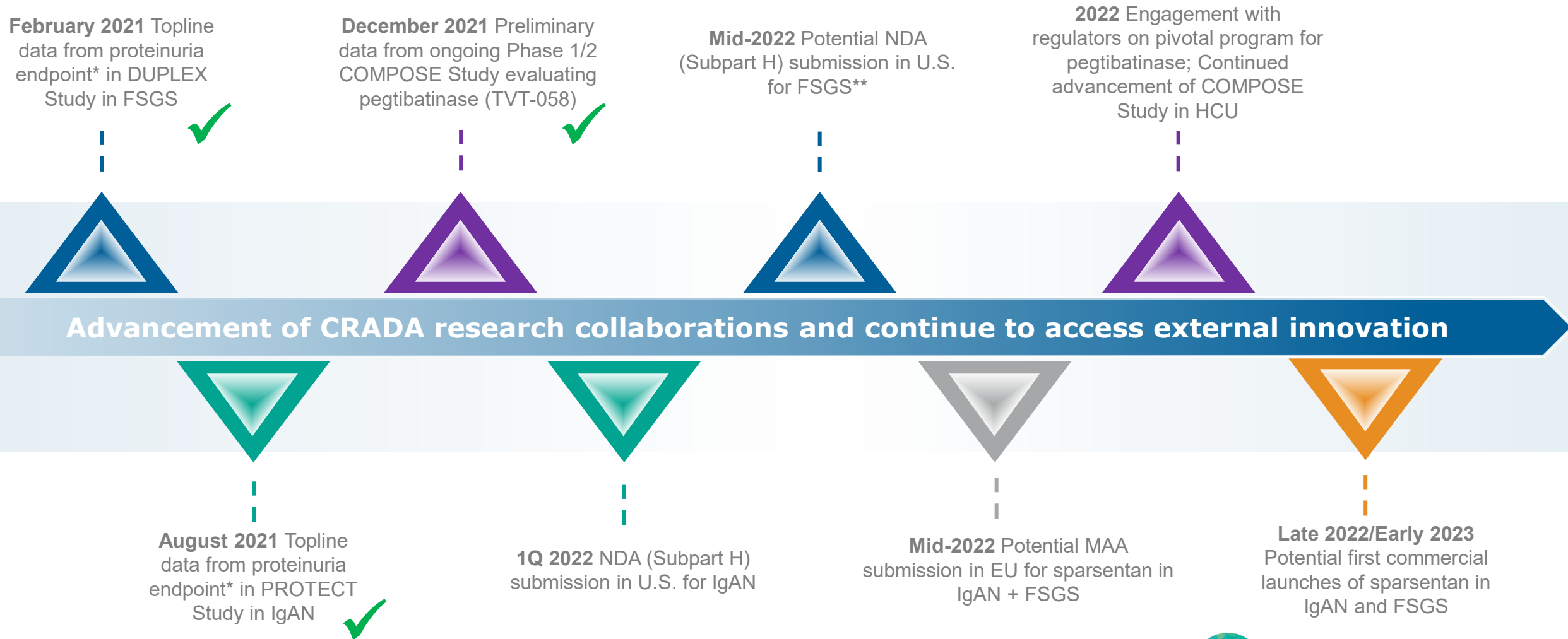
Positive Topline Results from the Ongoing Phase 1/2 COMPOSE Study Provide Clinical Proof of Concept for Pegtibatinase



12 Week Results from 1.5mg/kg BIW Dose Cohort vs All Placebo Pts in Ongoing Study

- Pegtibatinase demonstrated dose-dependent reductions in tHcy during 12 weeks of treatment in the Phase 1/2 COMPOSE Study
- In the 1.5mg/kg BIW dose cohort, treatment with pegtibatinase resulted in a mean relative reduction from baseline of 55.1% (n=3, mean baseline tHcy = 187.0 μ mol), compared to a mean relative reduction from baseline of 4.8% for all patients receiving placebo in the study (n=5, mean baseline tHcy = 131.1 μ mol)
- In the 1.5mg/kg BIW dose cohort, treatment with pegtibatinase resulted in rapid and sustained reductions in tHcy, resulting in a maintenance of tHcy below a clinically meaningful threshold of 100 μ mol from week 2 through week 12 of treatment
- In a dose-dependent manner, methionine levels were substantially reduced, and cystathionine levels were substantially elevated following treatment with pegtibatinase, suggesting that pegtibatinase acts in a manner similar to the native CBS enzyme
- The topline results suggested pegtibatinase had been generally well-tolerated

Key Milestones for Traverre Therapeutics



*Interim endpoint; confirmatory endpoint is slope of eGFR ** Pending additional supportive eGFR data from DUPLEX Study



TRAVERETM
THERAPEUTICS

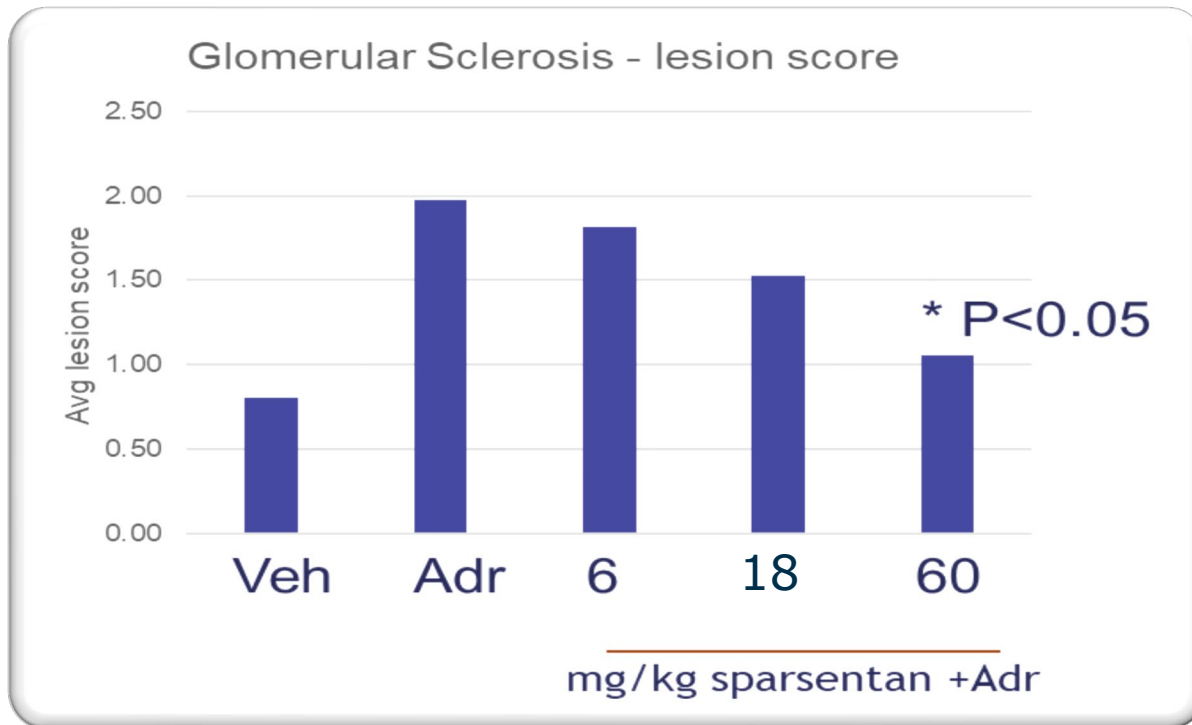
In Rare For Life.



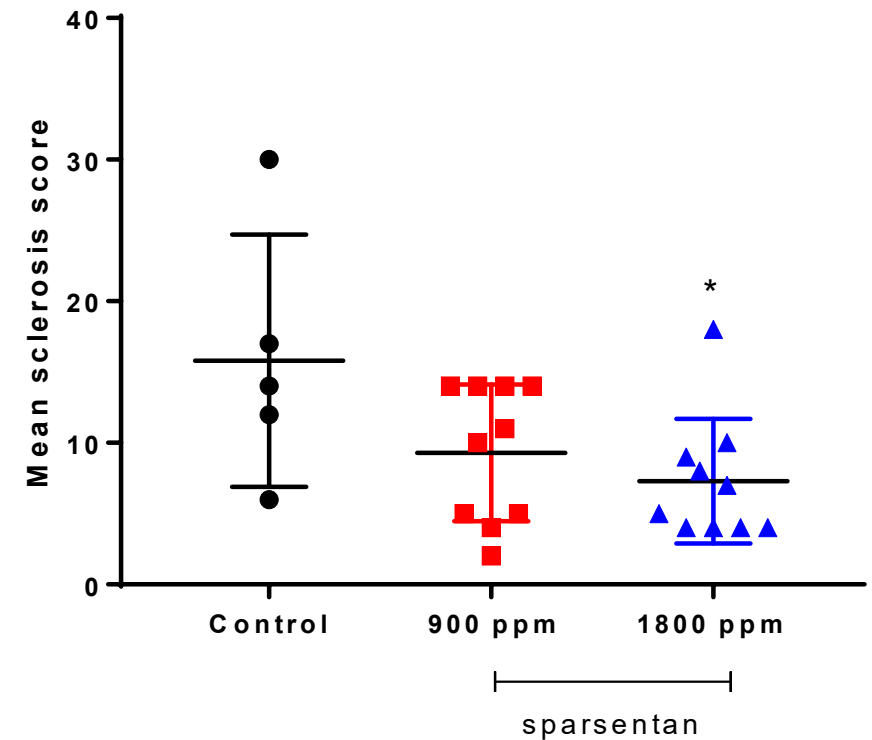
Appendix

Sparsentan Preclinical Demonstration of Prevention of Glomerulosclerosis in FSGS and IgAN

FSGS Rat Model



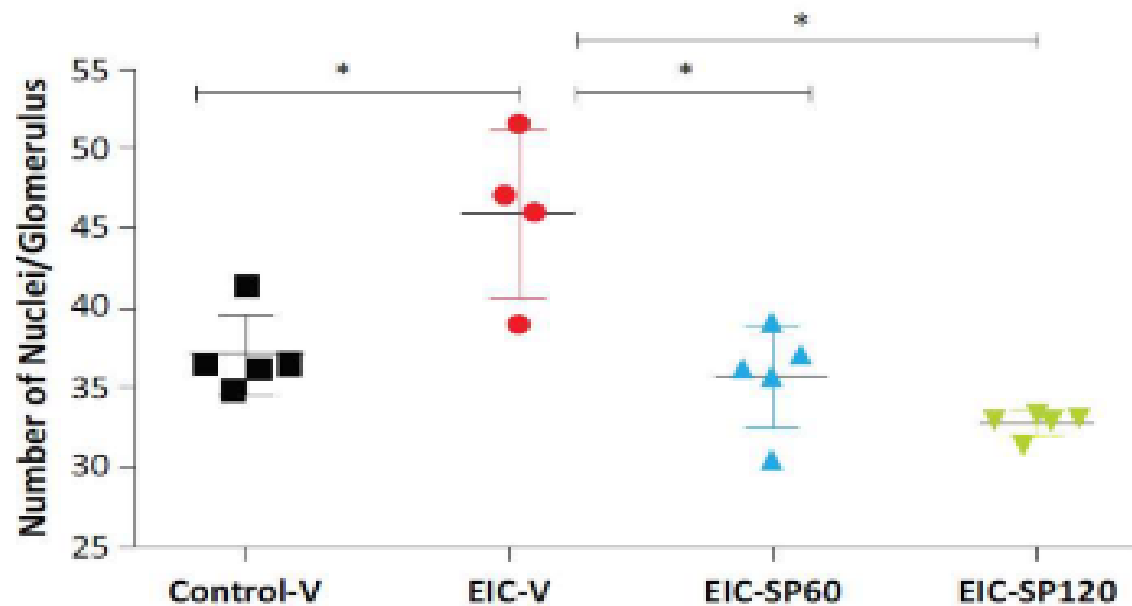
IgAN gddY Mouse Model



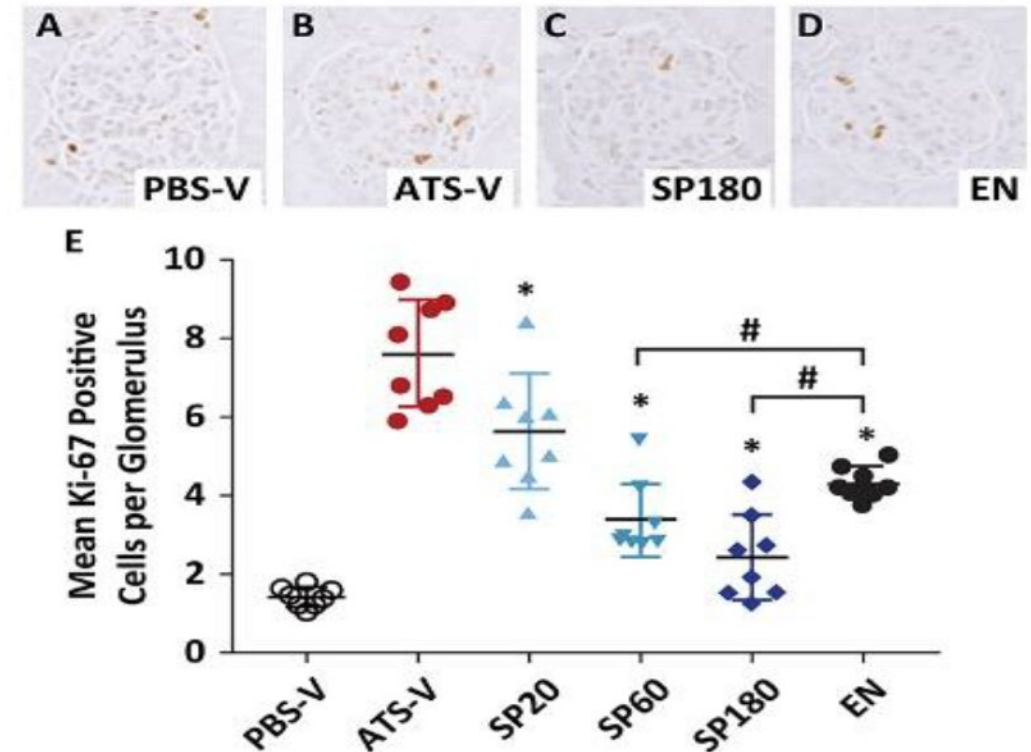
Source: Adriamycin rat FSGS model: RE-021-Report0034-PHARM; gddY Model: RE-021-Report054-2018-PHARM; presented as e-poster ERA-EDTA 2020

Sparsentan Preclinical Demonstration of Prevention of Mesangial Cell Proliferation

Engineered Immune Complex (EIC) - induced IgAN Model



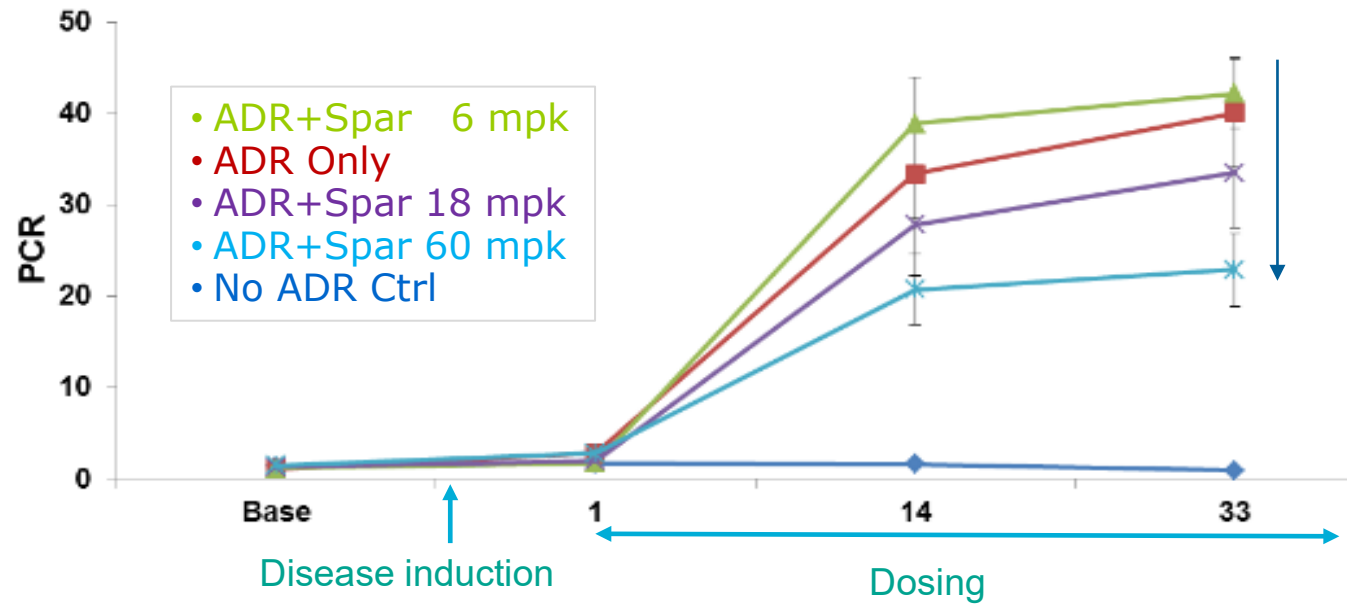
Anti-Thy1 Model



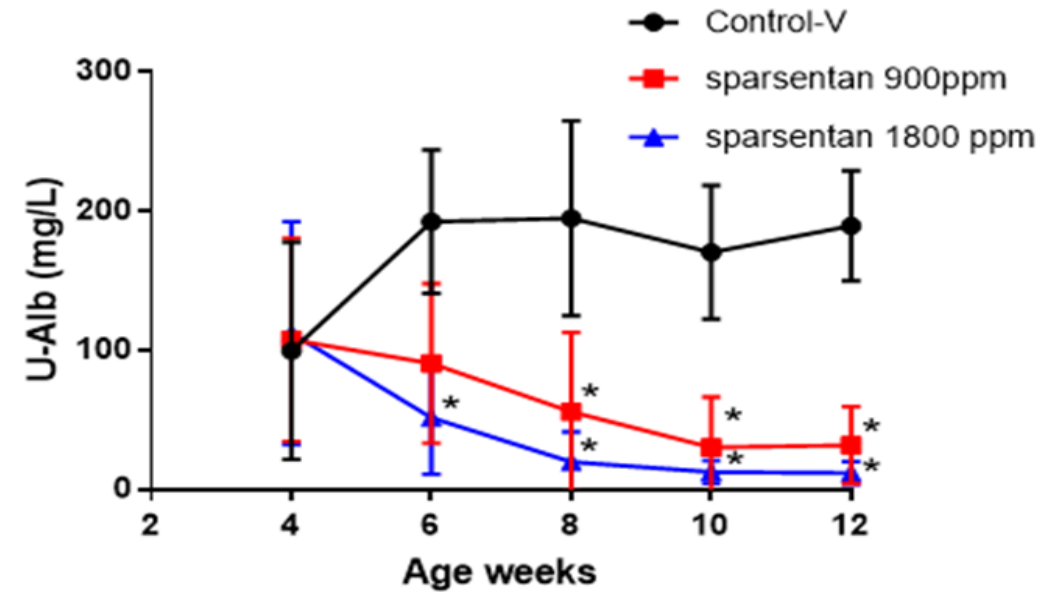
Source: EIC Model: RE-021-Report004-2018-PHARM; presented as poster WCN 2019
Anti-Thy1 Model: Jenkinson, et.al. (2018) 15th International Symposium on IgA Nephropathy, Buenos Aires, Argentina

Sparsentan Preclinical Demonstration of Proteinuria Reduction in FSGS and IgAN

FSGS Rat Model

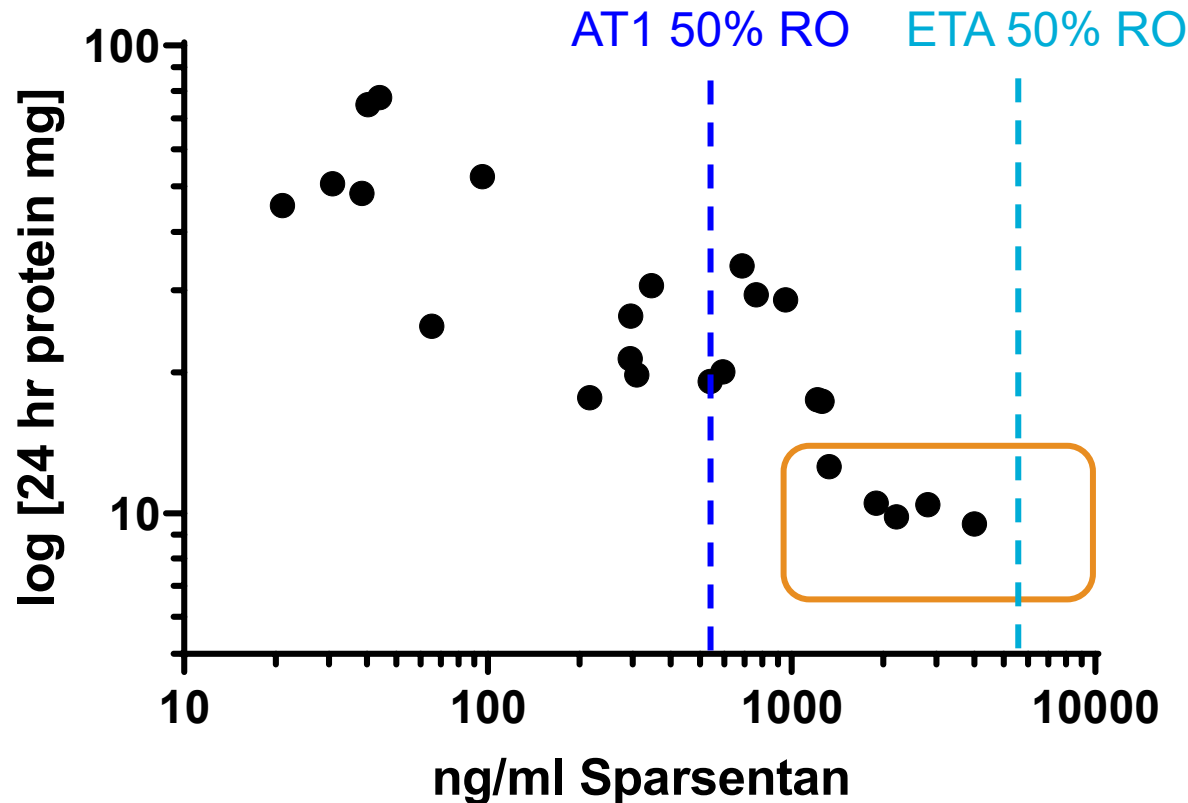


IgAN gddY Mouse Model



Source: Adriamycin rat FSGS model: RE-021-Report0034-PHARM; gddY Model: RE-021-Report054-2018-PHARM; presented as e-poster ERA-EDTA 2020

Non-clinical Evidence: Inhibition of Both AT₁ and ET_a Together with Sparsentan Resulted in Further Proteinuria Reduction in Rat Models



- In vitro receptor binding in Rats
 - AT1 Ki = 11 nM
 - ETA Ki = 110 nM
- Sparsentan circulates bound to protein, hence 10x Ki concentration results in ~50% receptor occupancy
- **Maximum efficacy is observed with significant inhibition of ETA receptors**

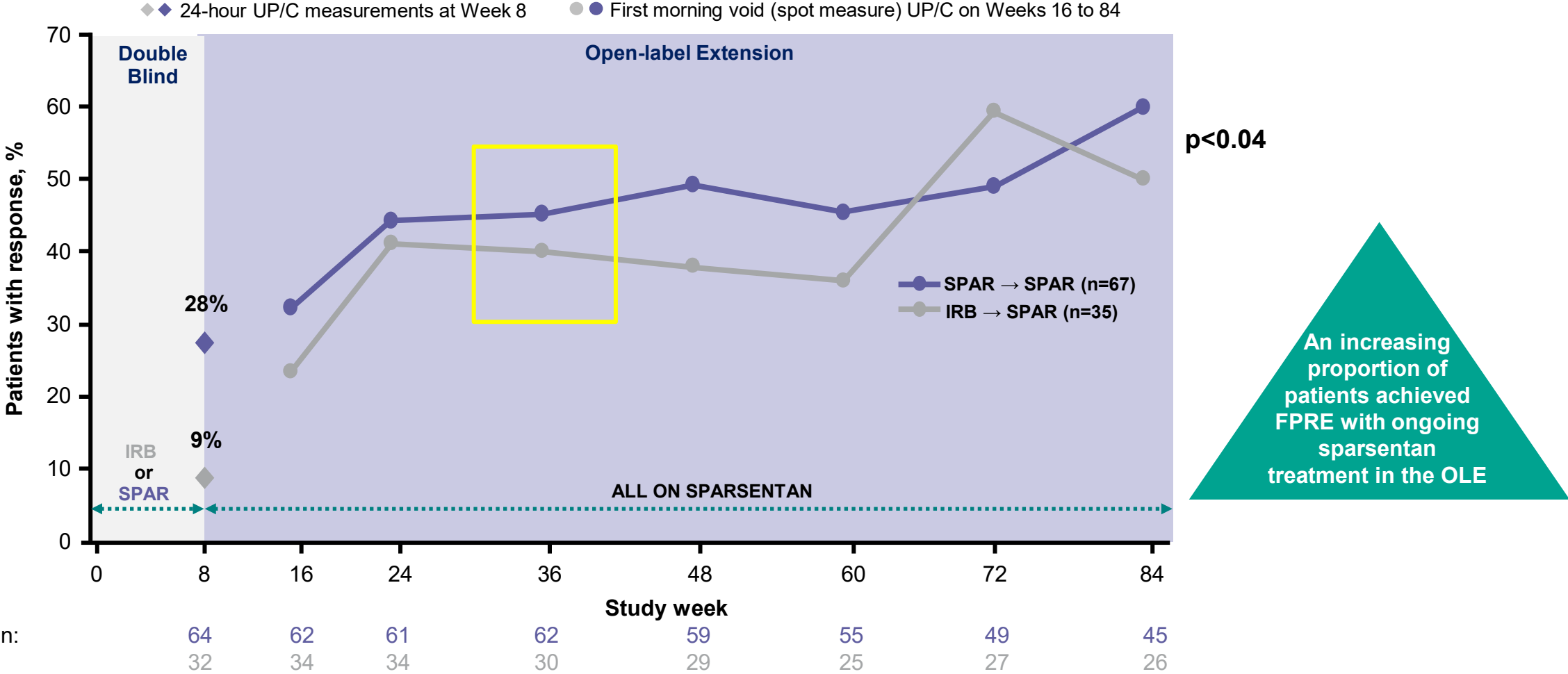
Source: RE-021-0045; RE-021-0057, RE-021-Report003-2018-PHARM; RE-021-Report007-2018-BIOA

Phase 2 DUET Study: A Closer Look at Edema

TEAEs with Incidence >5%	Patients n (%)			
	Irbesartan		Sparsentan	
	All	Drug Related	All	Drug Related
Headache	7 (19.4)	1 (2.8)	14 (19.2)	9 (12.3)
Hypotension/orthostatic hypotension	3 (8.3)	3 (8.3)	12 (16.4)	11 (15.1)
Dizziness	4 (11.1)	3 (8.3)	10 (13.7)	8 (11.0)
Edema/edema peripheral	1 (2.8)	0	9 (12.3)	2 (2.7)
Nausea	3 (8.3)	0	9 (12.3)	6 (8.2)
Diarrhea	1 (2.8)	0	6 (8.2)	2 (2.7)
Vomiting	1 (2.8)	0	6 (8.2)	4 (5.5)
Upper abdominal pain	2 (5.6)	0	4 (5.5)	2 (2.7)
Cough	2 (5.6)	0	3 (4.1)	0
Fatigue	4 (11.1)	1 (2.8)	3 (4.1)	2 (2.7)
Nasal congestion	4 (11.1)	0	2 (2.7)	0
Upper respiratory tract infection	2 (5.6)	0	2 (2.7)	0
Hyperkalemia	2 (5.6)	2 (5.6)	1 (1.4)	1 (1.4)
Muscle spasms	2 (5.6)	0	0	0

- Edema is common in people living with FSGS
- Adverse event of interest given potential ERA class effect
- Treatment related edema events in DUET were well managed with diuretics
- OLE findings are consistent with double blind portion of study

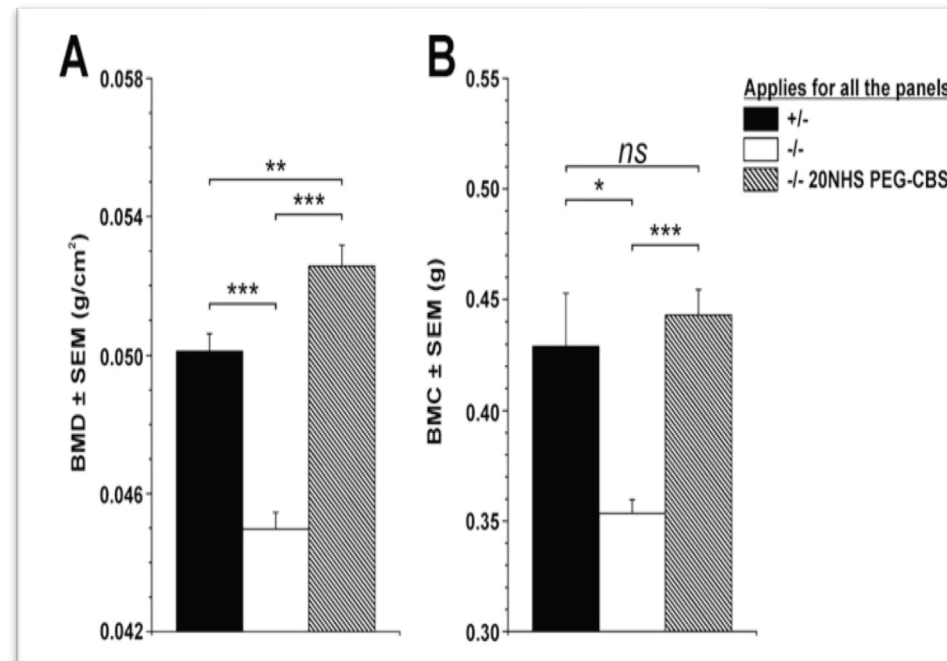
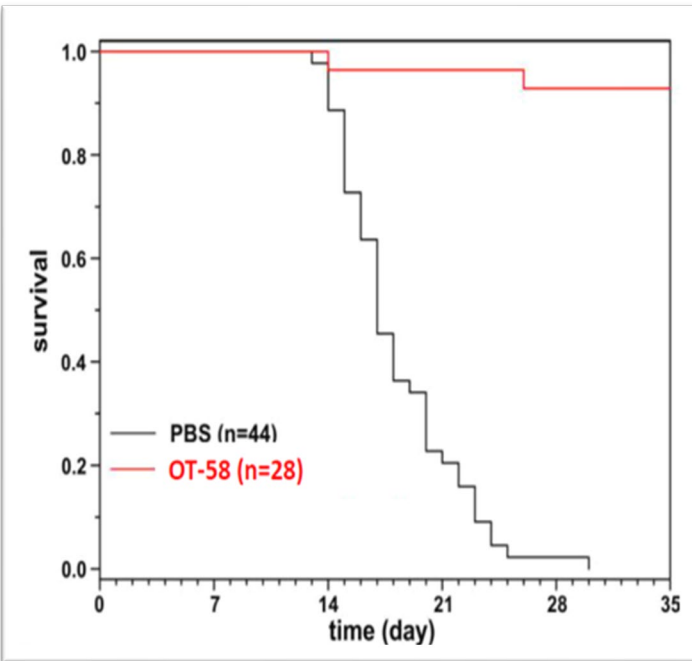
Interim FPRE Response in Phase 3 DUPLEX Study is Consistent with Phase 2 DUET Study OLE



FPRE is defined as UP/C ≤ 1.5 g/g and $>40\%$ reduction in UP/C from baseline. Baseline in the double-blind period defined as Week 0; baseline for the open-label period defined as last observation before start of open-label sparsentan treatment (i.e. Week 8). Data for Week 8 are based on the EES. Data for Weeks 16 to 84 are based on the full analysis set. EES = efficacy evaluable set; FPFE = FSGS partial remission endpoint; IRB:SPAR = patients randomized to irbesartan who then transitioned to sparsentan in the OLE; OLE = open-label extension; SPAR:SPAR = patients randomized to sparsentan who also received sparsentan in the OLE; UP/C = urinary protein-to-creatinine ratio. 1. Hogan J, et al. *J Am Soc Nephrol* 2018; 29:61 (Abstract FR-OR087); 2. Trachtman H, et al. *J Am Soc Nephrol* 2018; 29:2745–2754; DUET ClinicalTrials.gov Identifier: NCT01613118.



Treatment with Pegtibatinase Appeared to Prolong Survival, Prevent Osteoporosis and Rescue Ocular Structure in Mouse Models



Treatment with pegtibatinase appeared to prolong survival in KO mouse models¹

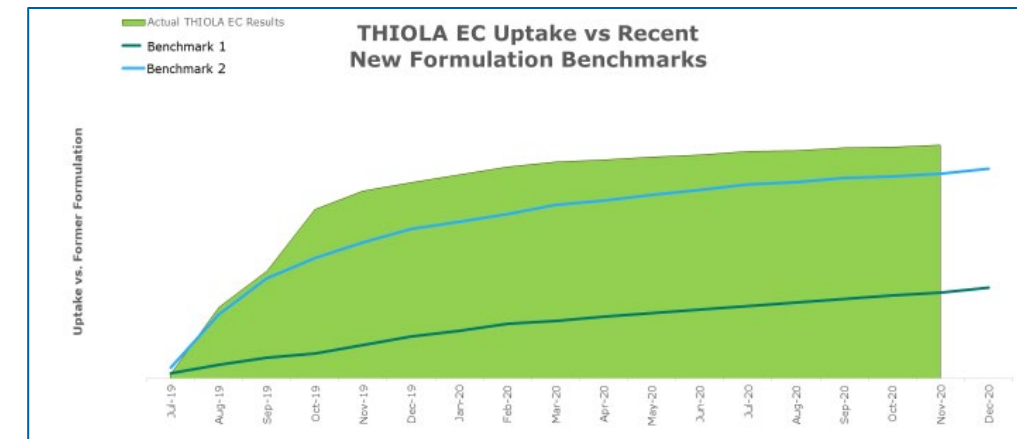
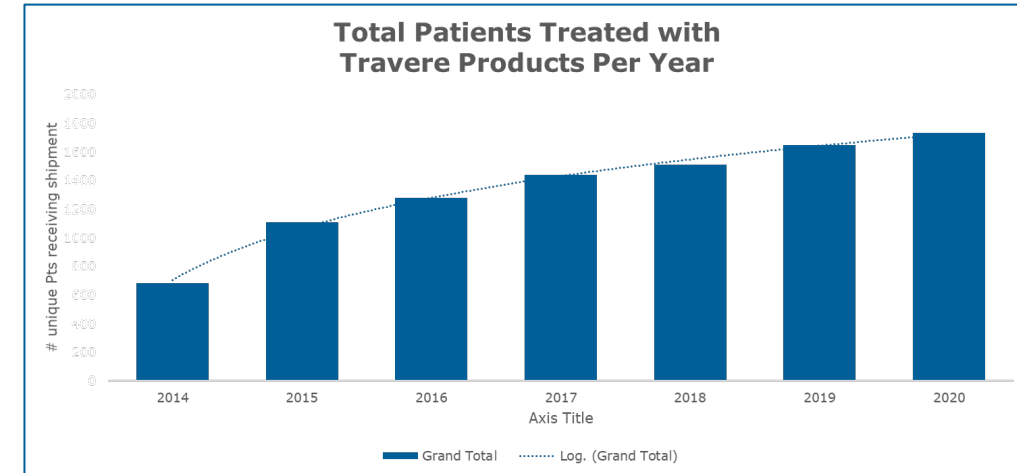
Untreated KO mouse models resulted in significant liver damage and death within 20-30 days

Early treatment with pegtibatinase appeared to prevent loss of bone mineralization and fat content in KO mice¹

Treatment with pegtibatinase appeared to preserve fiber integrity and prevent the degradation of the structure that secures the lens in the eye²

Commercial Infrastructure: Utilizing Established Commercial Rare Disease Capabilities and Nephrology Footprint to Deliver Approved Products*

- **Proven commercial capabilities and infrastructure**
 - Organic year-over-year growth for last six years
 - FY 2021 net products sales of ~\$211 million, ~6% growth over 2020
- **Experience planning and executing new product launches in rare disease**
 - Recent Thiola EC launch outperformed benchmarks
- **Established nephrology network, Patient Hub and expertise**
 - Field-force currently calling on ~2,000 nephrologists in US
 - Ability to build upon established customer support services
 - Experienced central distribution capabilities to meet the needs of rare patients



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*Pending Phase 3 data and if approved

