62nd ERA CONGRESS
VIENNA & VIRTUAL
JUNE 4-7, 2025
Beyond Nephrology

in collaboration with

Österreichische Gesellschaft für Nephrologie

Pegcetacoplan Demonstrates Clinically Significant Responses in C3G and Primary (Idiopathic) IC-MPGN Patients with or without Concomitant Immunosuppression in VALIANT

David Kavanagh[1], Andrew S Bomback[2], Gema Ariceta[3], Antonio Mastrangelo[4], Carla M Nester[5], Giuseppe Remuzzi[6], Marina Vivarelli[7], Zhongshen Wang[8], Johan Szamosi[9], Dima Decker[8], Lucia Quintana-Gallardo[9], Fadi Fakhouri[10]

[1]National Renal Complement Therapeutics Centre, Newcastle University, Newcastle; [2]New York-Presbyterian/Columbia University Irving Medical Center, New York, New York, United States; [3]Hospital Universitari Vall d'Hebron, Barcelona, Catalunya, Spain; [4]Fondazione IRCCS Ca' Granda Ospedale Maggiore Policlinico, Milan, Lombardia, Italy; [5]University of Iowa, Stead Family Children's Hospital, Iowa City, Iowa, United States; [6]Istituto di Ricerche Farmacologiche Mario Negri IRCCS, Bergamo, Italy; [7]Ospedale Pediatrico Bambino Gesu IRCCS, Rome, Italy; [8]Apellis Pharmaceuticals, Inc., Waltham, MA, USA; [9]Swedish Orphan Biovitrum AB, Stockholm, Stockholm, Sweden; [10]Centre Hospitalier Universitaire Vaudois, Lausanne, Vaud, Switzerland

Disclosures

62nd ERA CONGRESS
VIENNA & VIRTUAL
JUNE 4-7, 2025
Beyond Nephrology
in collaboration with
Österreichische Gesellschaft für Nephrologie

- **DK** has received advisory board payments from Idorsia, Novartis, Chemocentryx, Alexion Pharmaceuticals, Samsung, Sobi, Gyroscope Therapeutics, Purespring, and Apellis
- **ASB** has received consulting fees from Amgen, Apellis, Catalyst, Genentech, Kezar, Novartis, Q32, Silence Therapeutics, and Visterra
- **GA** received honoraria for lectures, educational events, or advisory boards for Astra Zeneca (Alexion), Recordati Rare Disease, Advicenne, Chiesi, Kyowa Kirin, Alnylam, and Dicerna; and served as site investigator for Apellis
- **AM** has received consultant and speaker fees from Sobi
- **CMN** is Associated Director of the Molecular Otolaryngology and Renal Research Laboratory; participates as site investigator and serves on advisory boards for Novartis, Achillion, Apellis, and BioCryst; serves on advisory boards for AstraZeneca and Alexion; serves on a data safety monitoring board for Kira; serves on a steering committee for Vertex; participates as site investigator for Retrophin; serves as Chair of a data safety monitoring board for FIT4KID; and received author royalties from UpToDate
- **GR** has had consultancy agreement with Alexion Pharmaceuticals Inc, Janssen Pharmaceutical, Akebia Therapeutics, Biocryst Pharmaceuticals, Menarini Ricerche SpA, AstraZeneca; speaker honoraria/travel reimbursement from Boehringer Ingelheim, Novartis
- **MV** received consultancy fees from Novartis, SOBI, Travere, Roche, Apellis, Alexion, BioCryst, Purespring, Bayer, and WebMD; participates in clinical trials sponsored by Alexion, Bayer, Novartis, Roche, Chinook, Apellis and Travere; and serves on speaker bureaus for Novartis, Roche, Vifor, Travere, SOBI and Glaxo Smith Klyne
- **ZW** and **DD** are employees of Apellis Pharmaceuticals and hold stock or stock options
- **JS** and **LQG** are employees of Swedish Orphan Biovitrum AB and may hold stock or stock options
- **FF** has received consultancy honorarium from Alexion, Astra Zeneca, Apellis, Novartis, Sobi and Roche

C3G and primary IC-MPGN are **rare, chronic, and heterogeneous complement-mediated diseases** with a **high unmet need**

62nd ERA CONGRESS
VIENNA & VIRTUAL
JUNE 4-7, 2025
Beyond Nephrology
in collaboration with
Österreichische Gesellschaft für Nephrologie

Diseases are driven by C3 dysregulation, resulting in the accumulation of **C3 downstream effectors in the glomeruli** (with addition of **immunoglobulins in IC-MPGN**), leading to inflammation and progressive **kidney damage** and **ultimately kidney failure**[1,2]

Immunosuppression is administered to **patients whose disease cannot be controlled with standard of care** (e.g. RAASi, diet), but is associated with **adverse events** and **lack evidence of efficacy from randomized controlled clinical trials**[3-6]

Up to **50% of patients progress to kidney failure within 10 years**.[6]

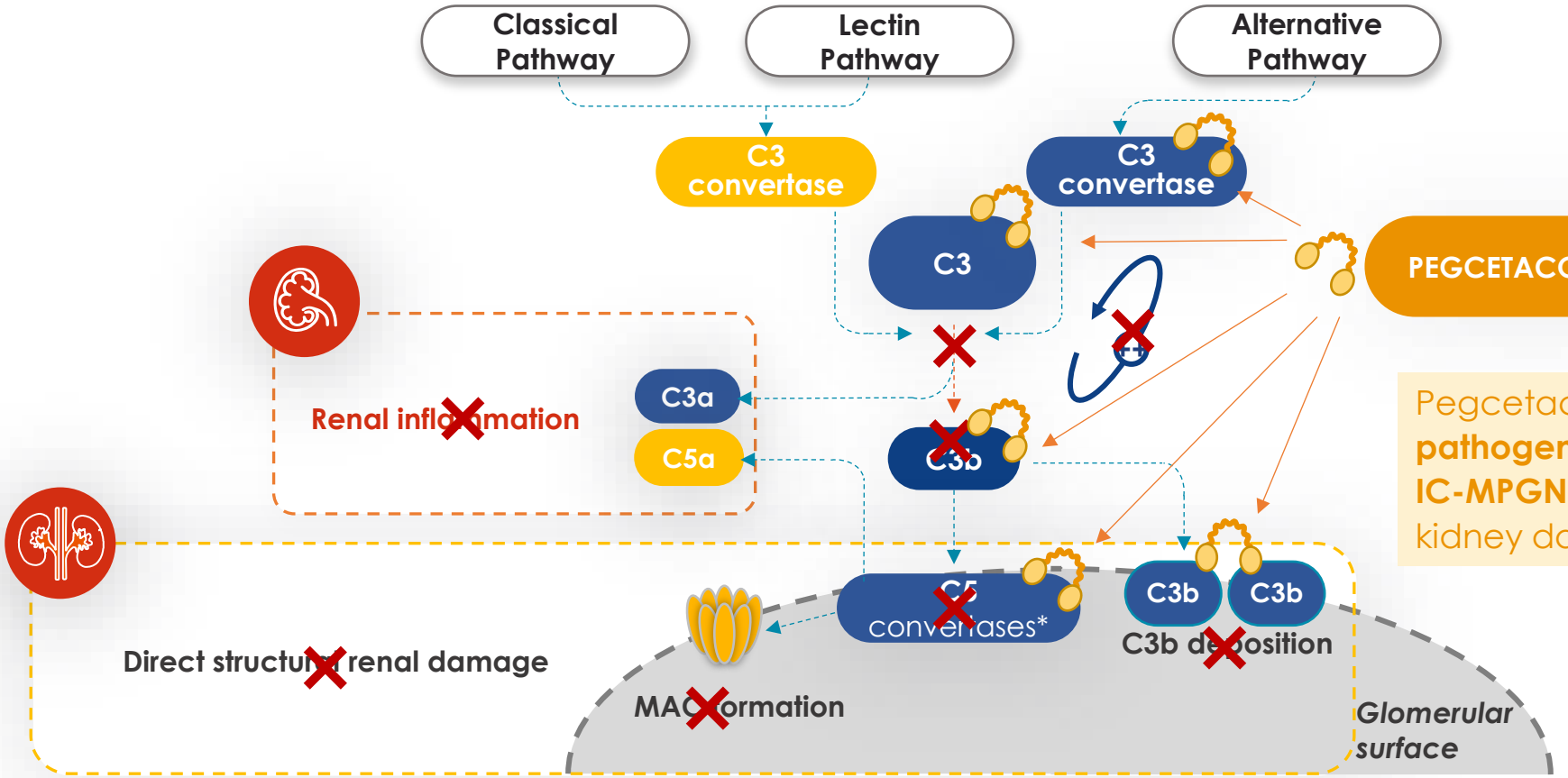
Up to **89% likelihood of recurrence after transplantation**[3,7,8]

C3, complement 3 protein; C3G, C3 glomerulopathy; IC-MPGN, immune-complex membranoproliferative glomerulonephritis; RAASi, renin-angiotensin-aldosterone system inhibition.

1. Bomback AS, et al. *Kidney Int Rep* 2024;10:17-28 **2.** Mastrangelo A, et al. *Front Pediatr* 2020;8:205 **3.** Caravaca-Fontán F, et al. *Nephron* 2020;144(6):272-280
4. Heiderscheit AK, et al. *Am J Med Genet C Semin Med Genet* 2022;190C:344–57. **5.** Jefferson JA. *CJASN* 2018;13(8):1264-1275 **6.** Kidney Disease: Improving Global Outcomes (KDIGO) Glomerular Diseases Work Group. Kidney Int 2021;100:S1–276 **7.** Smith RJH, et al. *Nat Rev Nephrol* 2019;15:129–43
8. O'Shaughnessy MM, et al. *J Am Soc Nephrol* 2017;28:632–44.

Pegcetacoplan, a C3 and C3b inhibitor, **blocks C3 dysregulation and downstream complement activation** in C3G and primary IC-MPGN[1–7]

62nd ERA CONGRESS
VIENNA & VIRTUAL
JUNE 4-7, 2025
Beyond Nephrology
in collaboration with
ÖGN Österreichische Gesellschaft für Nephrologie

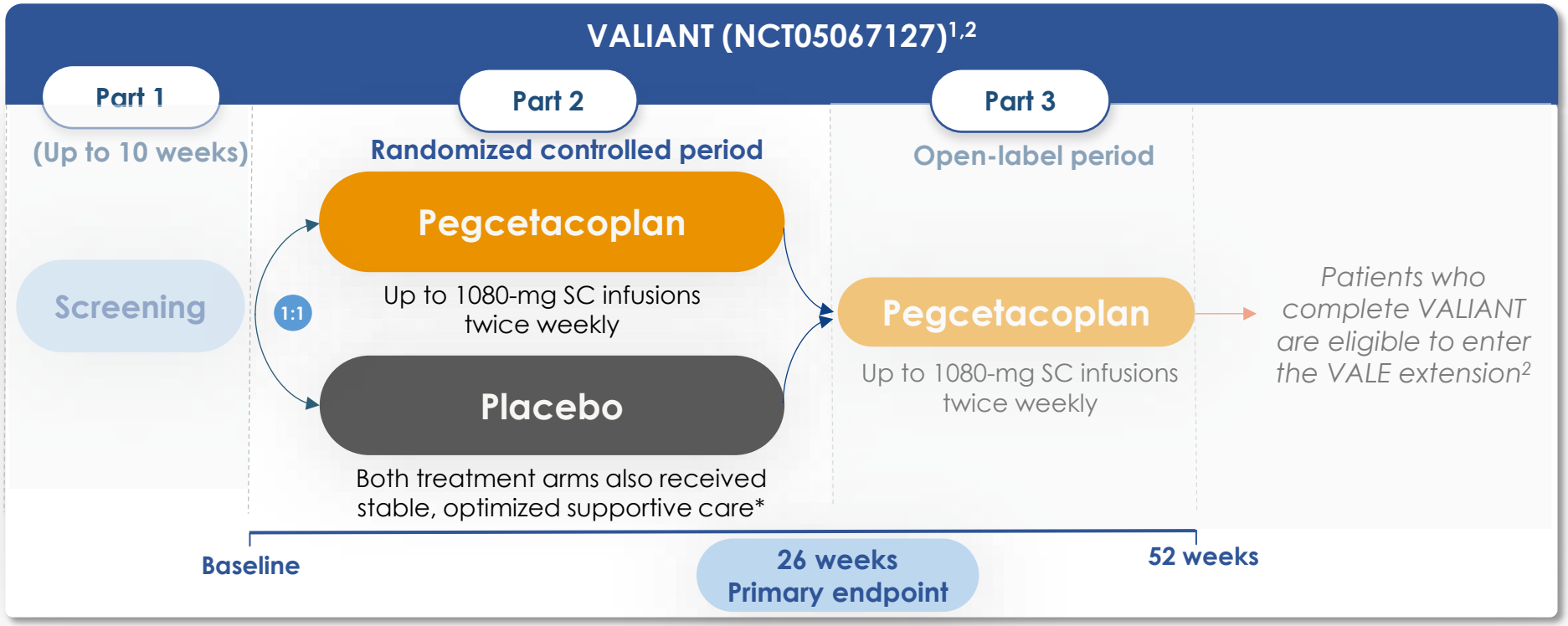


Pegcetacoplan **targets the pathogenic process in C3G/primary IC-MPGN** with the aim of stopping kidney damage

* C5 convertases: C4b2aC3b and C3bBbC3b.
C3/5, complement 3/5; C3G, C3 glomerulopathy; IC-MPGN, immune complex membranoproliferative glomerulonephritis; MAC, membrane attack complex.
1. Smith RJH, et al. *Nat Rev Nephrol* 2019;15:129–43 **2.** Zipfel PF, et al. *Front Immunol* 2019;10:2166 **3.** Meuleman MS, et al. *Semin Immunol* 2022;60:101634
4. Dixon BP, et al. *Kidney Int Rep* 2023;8:2284–93 **5.** EMPAVELI® (pegcetacoplan) US PI 2024 **6.** ASPAVELI Summary of Product Characteristics 2024
7. Lamers C, et al. *Nat Commun* 2022;13:5519.

VALIANT: Double-blind, randomized, placebo-controlled phase 3 study

62nd ERA CONGRESS
VIENNA & VIRTUAL
JUNE 4-7, 2025
Beyond Nephrology
in collaboration with
Österreichische Gesellschaft für Nephrologie



Objective of the post-hoc analysis: Evaluate efficacy and safety of pegcetacoplan in VALIANT patients **with and without concomitant immunosuppressants** (includes immunosuppressant and/or corticosteroids for systemic use) at Week 26

* Stable, optimized antiproteinuric regimens: ACEis, ARBs, SGLT2is, MMF, and corticosteroids (prednisone ≤20 mg/d or equivalent) were permitted, provided doses were stable 12 weeks prior and throughout randomized controlled period.

ACEis, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; MMF, mycophenolate mofetil; SC, subcutaneous; SGLT2is, sodium-glucose cotransporter-2 inhibitors.

1. Dixon BP, et al. ASN Kidney Week 2023. Nov. 2–5, 2023. Abstract INFO12-SA **2.** ClinicalTrials.gov. VALIANT. clinicaltrials.gov/study/NCT05067127. Accessed April 16, 2025.

VALIANT overall study results (26 weeks): **Pegcetacoplan's efficacy** in C3G and primary IC-MPGN[1]

62nd ERA CONGRESS
VIENNA & VIRTUAL
JUNE 4-7, 2025
Beyond Nephrology
in collaboration with
Österreichische Gesellschaft für Nephrologie

Kidney Health Initiative (KHI) consensus[2]:
Favorable treatment effect on **histopathology, proteinuria and eGFR**

68%
significant proteinuria reduction
vs placebo*

Proteinuria reduction

Stabilization of eGFR
+6.3 mL/min/1.73 m²
vs placebo

eGFR stabilization/ improvement

Histopathology improvement

Glomerular C3 clearance in
71% of patients
(zero staining)

* Consistent across subgroups (age, disease type, transplant status).
C3G, C3 glomerulopathy; eGFR, estimated glomerular filtration rate; IC-MPGN, immune complex membranoproliferative glomerulonephritis.
1. Nester CM et al. Presented at American Society of Nephrology Kidney Week 2024 (Oral SA-OR92) **2.** Nester C, et al. *Clin J Am Soc Nephrol* 2024;19:1201–8.

VALIANT: **73% of participants received concomitant immunosuppressive therapy at baseline**

62nd ERA CONGRESS
VIENNA & VIRTUAL
JUNE 4-7, 2025
Beyond Nephrology
in collaboration with
ÖGN Österreichische Gesellschaft für Nephrologie

Concomitant medications for randomized controlled period	Pegcetacoplan (N=63)	Placebo (N=61)	Overall (N=124)
Agents acting on the renin-angiotensin system	57 (90.5)	56 (91.8)	113 (91.1)
Immunosuppressants and/or corticosteroids for systemic use	48 (76.2)	42 (68.9)	90 (72.6)
Immunosuppressants	47 (74.6)	42 (68.9)	89 (71.8)
Mycophenolate and mycophenolic acid	42 (66.7)	39 (63.9)	81 (65.3)
Tacrolimus	12 (19.0)	12 (19.7)	24 (19.4)
Azathioprine	2 (3.2)	0	2 (1.6)
Ciclosporin	0	1 (1.6)	1 (0.8)
Tocilizumab	1 (1.6)	0	1 (0.8)
Corticosteroids for systemic use	25 (39.7)	24 (39.3)	49 (39.5)

Patients had to receive **stable doses for 12 weeks prior and throughout** the randomized controlled period

Use of immuno-suppressive therapy was **balanced** between the **pegcetacoplan and placebo arms**

VALIANT: **Baseline characteristics of patients with and without concomitant immunosuppressants were similar**

62nd ERA CONGRESS
VIENNA & VIRTUAL
JUNE 4-7, 2025
Beyond Nephrology
in collaboration with
ÖGN Österreichische Gesellschaft für Nephrologie

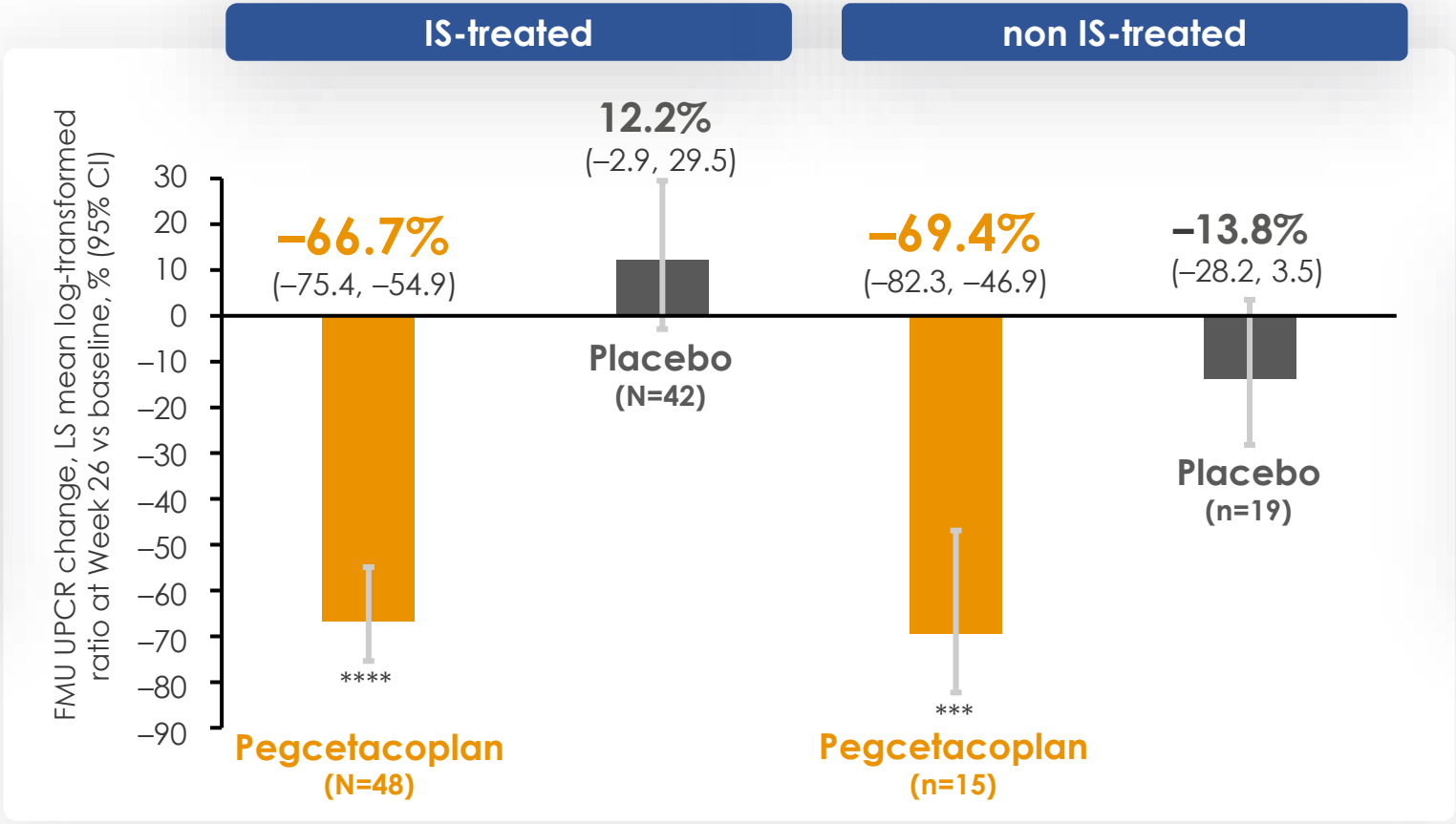
Baseline characteristic	IS-treated patients		Non IS-treated patients	
	Pegcetacoplan (N=48)	Placebo (N=42)	Pegcetacoplan (N=15)	Placebo (N=19)
Age, mean (SD), years	27.1 (16.8)	22.7 (15.0)	31.8 (18.2)	25.7 (12.6)
Adolescents (12–17 years)/adults (≥18 years), n (%)	22 (45.8)/26 (54.2)	21 (50.0)/21 (50.0)	6 (40.0)/9 (60.0)	6 (31.6)/13 (68.4)
Sex, female, n (%)	29 (60.4)	20 (47.6)	8 (53.3)	13 (68.4)
Baseline triplicate first-morning spot UPCR, mean (SD), g/g	3.0 (2.2)	2.4 (2.1)	3.4 (3.0)	2.8 (1.9)
Baseline eGFR, mean (SD), mL/min/1.73 m²	78.8 (31.2)	89.1 (38.3)	77.6 (43.5)	83.2 (35.1)
Underlying disease based on screening biopsy, n (%)				
C3G	**38 (79.2)**	**30 (71.4)**	**13 (86.7)**	**15 (78.9)**
Primary IC-MPGN	**10 (20.8)**	**12 (28.6)**	**2 (13.3)**	**4 (21.1)**
Time since diagnosis, mean (SD), years	3.2 (3.5)	3.4 (3.9)	5.0 (3.3)	4.5 (2.9)

IS-treated refers to patients treated with immunosuppressants and/or corticosteroids for systemic use.
C3G, complement 3 glomerulopathy; eGFR, estimated glomerular filtration rate; IC-MPGN, immune complex-mediated membranoproliferative glomerulonephritis; IS, immunosuppressant; SD, standard deviation; UPCR, urine protein-to-creatinine ratio.

Pegcetacoplan treatment resulted in **clinically meaningful proteinuria reduction** irrespective of IS status

62nd ERA CONGRESS
VIENNA & VIRTUAL
JUNE 4-7, 2025
Beyond Nephrology
in collaboration with
ÖGN Österreichische Gesellschaft für Nephrologie

Relative reduction (95% CI) in pegcetacoplan vs placebo
70.3%
(58.3, 78.8)
p<0.0001
nominal

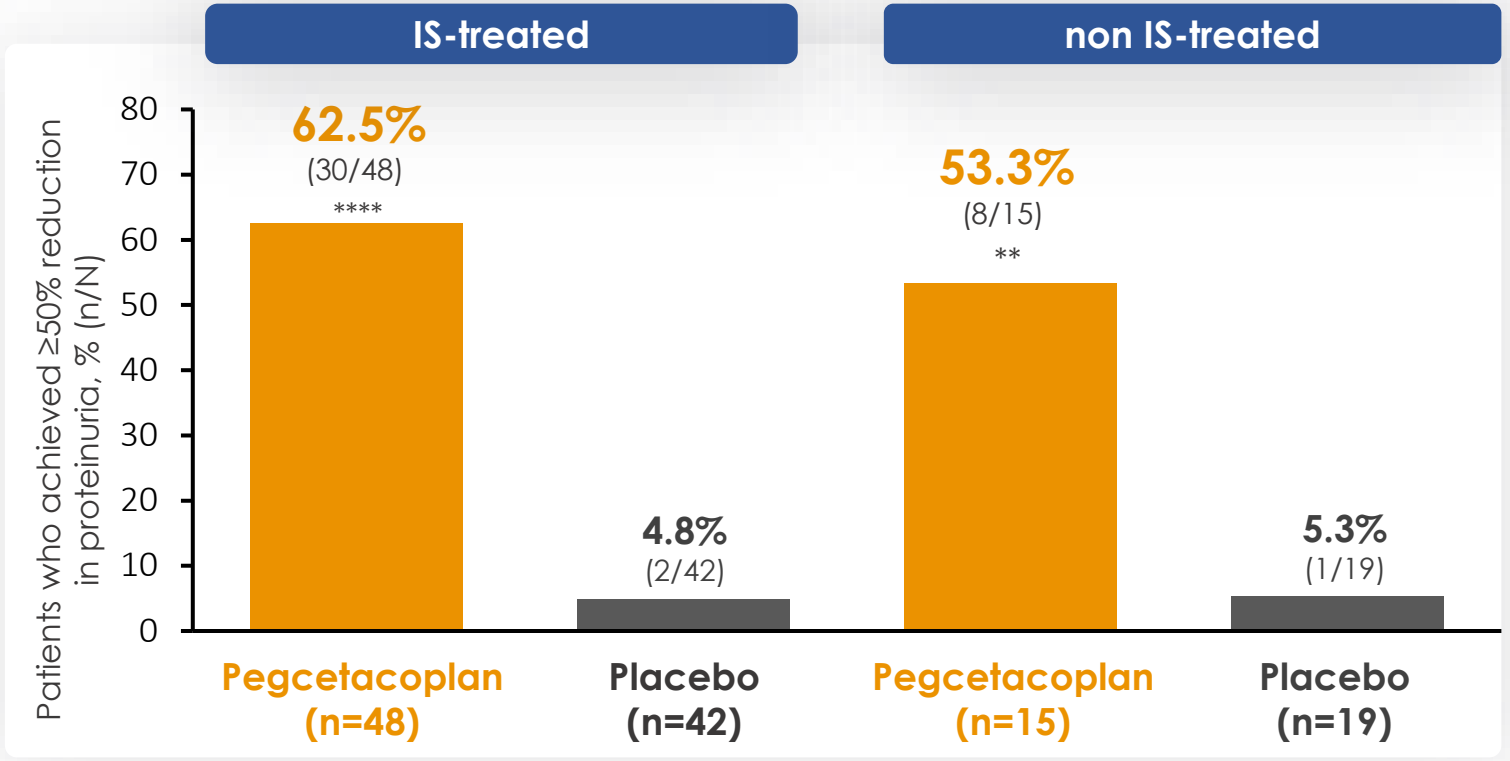


Relative reduction (95% CI) in pegcetacoplan vs placebo
64.5%
(36.6, 80.1)
p=0.0005
nominal

**** p≤0.0001 (nominal). *** p≤0.001 (nominal).
CI, confidence interval; FMU, first-morning spot urine; IS, immunosuppressant; LS, least squares; UPCR, urine protein-to-creatinine ratio.

>50% of patients in both groups **achieved ≥50% reduction in proteinuria with pegcetacoplan**

62nd ERA CONGRESS
VIENNA & VIRTUAL
JUNE 4-7, 2025
Beyond Nephrology
in collaboration with
ÖGN Österreichische Gesellschaft für Nephrologie

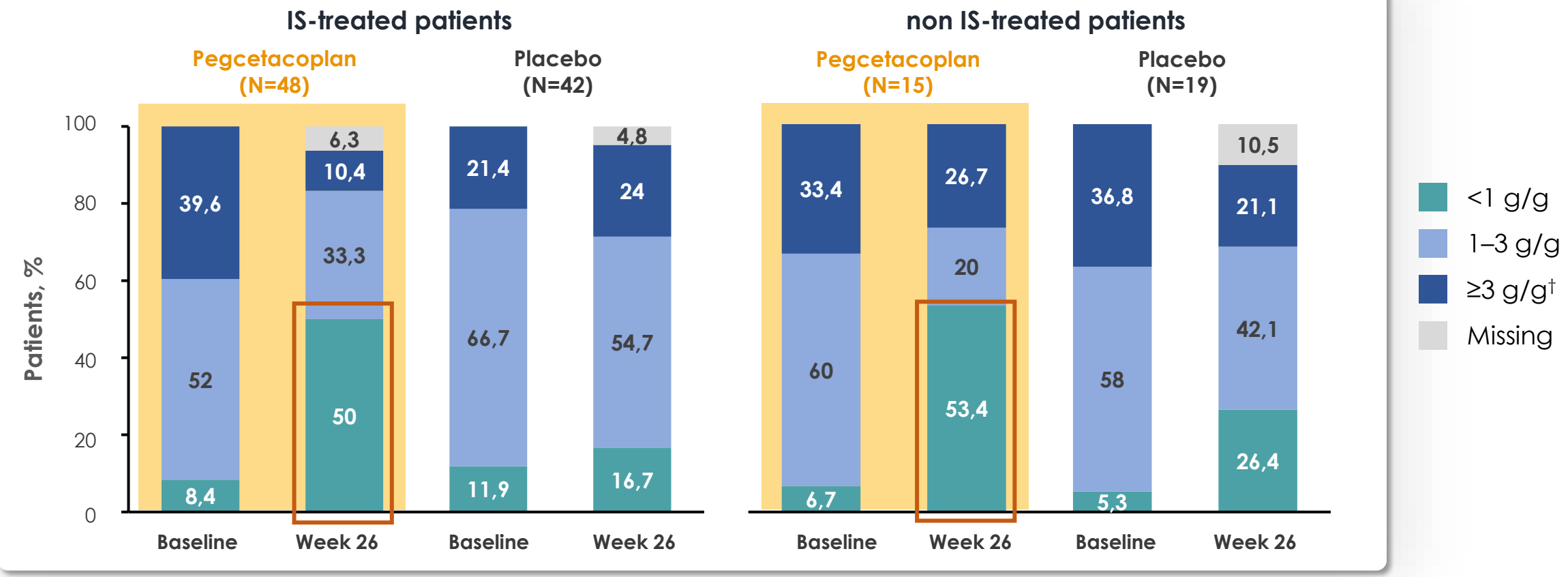


Registry data show that a **≥50% reduction in proteinuria** at 6 or 12 months correlated with a **significantly lower risk of kidney failure** in C3G and primary IC-MPGN patients[1,2]

**** p≤0.0001 (nominal). ** p≤0.01 (nominal).
IS, immunosuppressant. **1.** Masoud S, et al. medRxiv 2024;DOI:10.1101/2024.02.03.24301605v2 **2.** Caravaca-Fontán F et al. *Nephrol Dial Transplant* 2022;37:1270–80.

≥50% of patients in both groups achieved proteinuria <1 g/g with pegcetacoplan

Proteinuria shift analysis

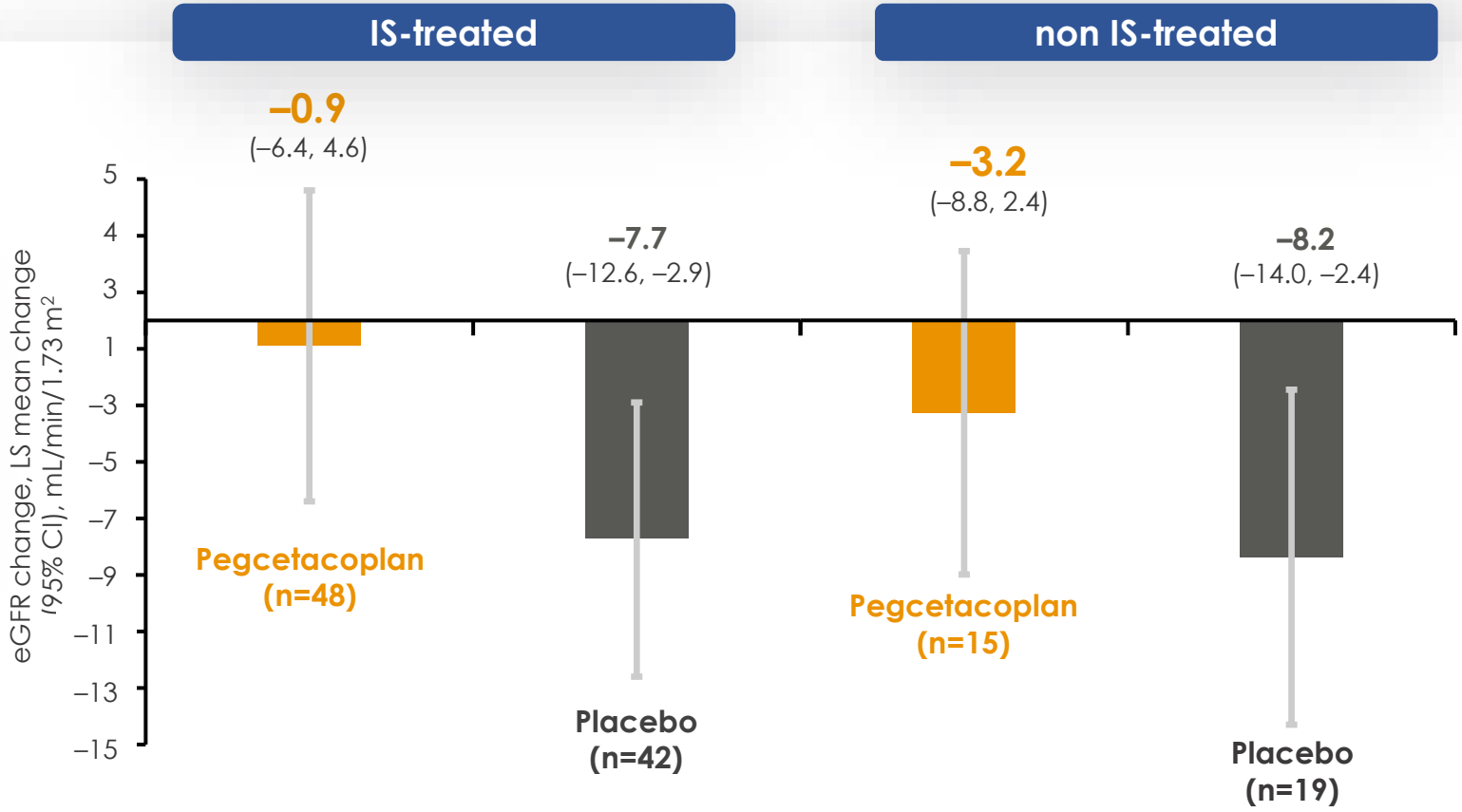


† Nephrotic range
FMU, first morning urine; UPCR, urine protein-to-creatinine ratio.

Pegcetacoplan resulted in **eGFR stabilization** in both groups

62nd ERA CONGRESS
VIENNA & VIRTUAL
JUNE 4-7, 2025
Beyond Nephrology
in collaboration with
ÖGN Österreichische Gesellschaft für Nephrologie

Difference in pegcetacoplan vs placebo
+6.8
mL/min/1.73 m²
p=0.07, nominal



Difference in pegcetacoplan vs placebo
+5.0
mL/min/1.73 m²
p=0.2, nominal

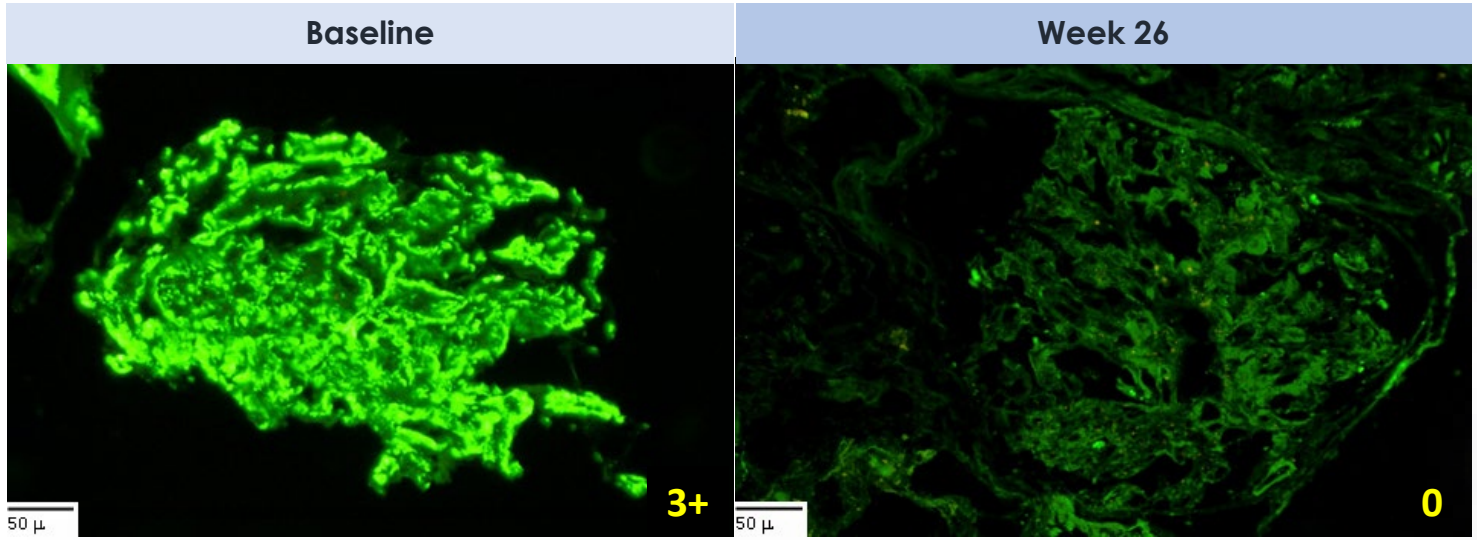
CI, confidence interval; eGFR, estimated glomerular filtration rate; IS, immunosuppressant; LS, least squares.

Pegcetacoplan resulted in a **substantial reduction in glomerular C3 staining** in both groups

62nd ERA CONGRESS
VIENNA & VIRTUAL
JUNE 4-7, 2025
Beyond Nephrology
in collaboration with
ÖGN Österreichische Gesellschaft für Nephrologie

Reduction in C3 staining in renal biopsy

Renal biopsies from a pegcetacoplan-treated C3G native kidney patient



65.4% of IS-treated and **88.9%** of non-IS treated patients achieved **zero C3 staining** in renal biopsy with **pegcetacoplan**

Proportion of patients with reduced C3 staining†

IS-treated	
Pegcetacoplan	**69.2%** (18/26)
Placebo	9.5% (2/21)

non IS-treated	
Pegcetacoplan	**88.9%** (8/9)
Placebo	15.4% (2/13)

† Difference defined as ≥2 OOM at Week 26 vs baseline; in all adults.
C3G, complement 3 glomerulopathy; IS, immunosuppressant; OOM, orders of magnitude.

Pegcetacoplan was **well-tolerated** and the **safety profile was consistent with previous reports**

62nd ERA CONGRESS
VIENNA & VIRTUAL
JUNE 4-7, 2025
Beyond Nephrology
in collaboration with
ÖGN Österreichische Gesellschaft für Nephrologie

Patients, n (%)	IS-treated patients		Non IS-treated patients	
	Pegcetacoplan (N=48)	Placebo (N=42)	Pegcetacoplan (N=15)	Placebo (N=19)
TEAEs	41 (85.4)	40 (95.2)	12 (80.0)	17 (89.5)
Treatment-related TEAEs	19 (39.6)	18 (42.9)	6 (40.0)	8 (42.1)
Severe TEAEs	3 (6.3)	3 (7.1)	0	1 (5.3)
Serious TEAEs	6 (12.5)	5 (11.9)	0	1 (5.3)
Serious infections				
COVID-19 pneumonia	1 (2.1)	0	0	0
Influenza	1 (2.1)	0	0	0
Pneumonia	1 (2.1)	0	0	0
Viral infection	0	0	0	1 (5.3)
TEAEs leading to study discontinuation	1 (2.1)	1 (2.4)	0	0
Deaths (COVID-19 pneumonia, unrelated to pegcetacoplan)	1 (2.1)	0	0	0

No infections caused by ***N. meningitidis***

Consistent with >2,000 patient-years of pegcetacoplan exposure*

Safety population (all randomized and treated patients). TEAEs defined as any new AE that began, or any preexisting condition that worsened in severity, after the first dose of study drug and ≤56 days beyond the last dose of study drug. * Includes exposure in clinical trials and post marketing across multiple indications.
AE, adverse event; COVID-19, coronavirus disease 2019; IS, immunosuppressant; TEAE, treatment-emergent AE.

Pegcetacoplan demonstrated favorable safety and efficacy in both IS-treated and non IS-treated patients

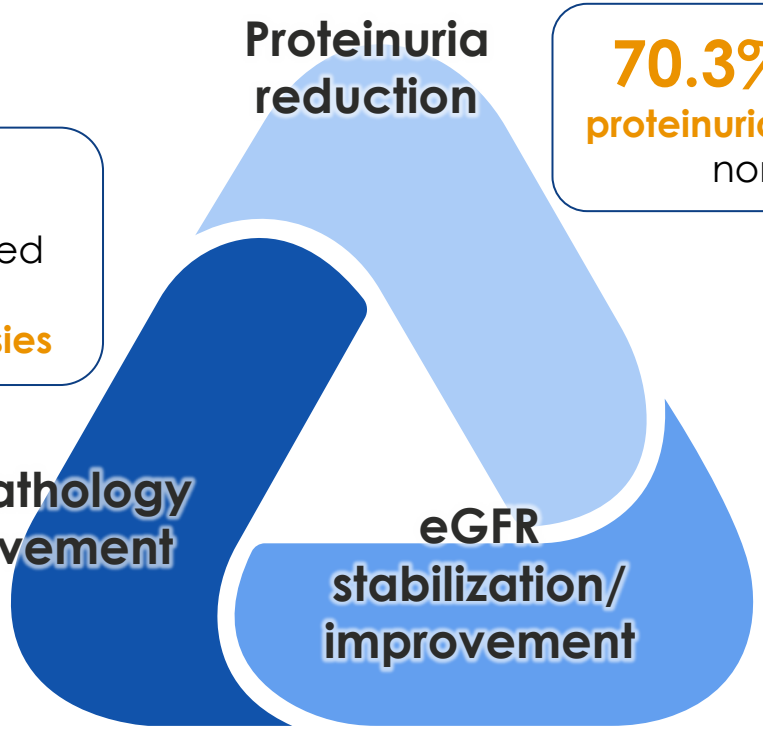
62nd ERA CONGRESS
VIENNA & VIRTUAL
JUNE 4-7, 2025
Beyond Nephrology

in collaboration with

Österreichische Gesellschaft für Nephrologie

70.3% and **64.5%** **clinically meaningful** **proteinuria reduction** vs placebo in IS-treated and non IS-treated patients, respectively

65.4% and **88.9%** of IS-treated and non IS-treated patients **achieved** **zero C3 staining in renal biopsies**



eGFR stabilization
+6.8 and **+5.0 mL/min/1.73 m²** vs placebo in IS-treated and non IS-treated patients, respectively

Pegcetacoplan has been well tolerated with no new safety signals

eGFR, estimated glomerular filtration rate; IS, immunosuppressant.

The authors thank the patients, investigators, and all other collaborators

This study was funded by Sobi (Swedish Orphan Biovitrum AB) and Apellis Pharmaceuticals, Inc.

Writing assistance was provided by Cactus Life Sciences® (Meggen, Switzerland), and was funded by Sobi (Swedish Orphan Biovitrum AB) and Apellis Pharmaceuticals, Inc.

Scan to obtain a digital copy of the presentation

Copies obtained through this QR code are for personal use only

62nd ERA CONGRESS
VIENNA & VIRTUAL
JUNE 4-7, 2025
Beyond Nephrology

in collaboration with

Österreichische Gesellschaft für Nephrologie