Sobi's Aspaveli® and Phase 3 VALIANT data in Nephrology

VALIANT Phase 3 results after presentation at ASN

Conference call for investors and analysts

29 October 2024

Forward-looking statements

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Agenda - speakers

Introduction C3G and IC-MGN

Michael Lai
Medical development leader, Pegcetacoplan

VALIANT study

Fadi Fakhouri
MD PhD Professor of Nephrology

Summary and Q&A

Guido Oelkers
Chief Executive Officer

Lydia Abad-Franch
Head of R&D and Chief Medical Officer

Pegcetacoplan in C3G and primary IC-MPGN

Michael Lai, MBBS FFPM MBA
Medicine Development Leader, Pegcetacoplan, Sobi

C3G and primary IC-MPGN are **rare, chronic and heterogeneous** kidney diseases[1–5]

A

Clinical background

A group of complement driven renal diseases that typically present with proteinuria and/or haematuria, with symptoms overlapping with other glomerulopathies

B

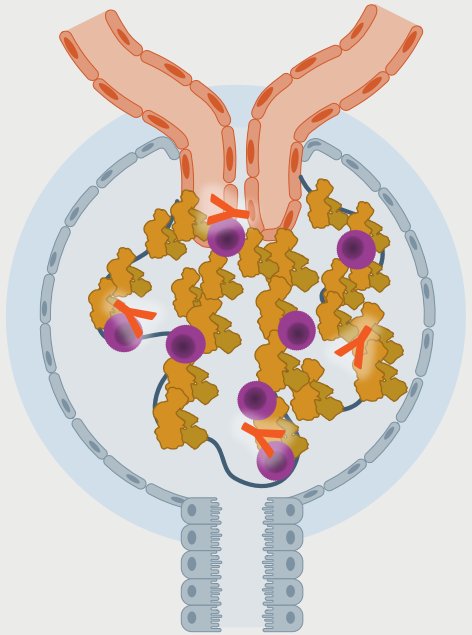
Pathophysiology

C3 overactivation drives accumulation of C3 breakdown products in the glomeruli

This leads to progressive damage that can result in ESKD if left untreated

Key

- Myeloid cell
- C3 deposit
- Immune deposit

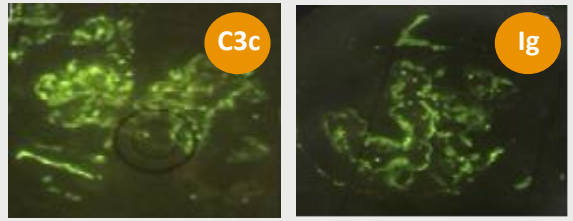


C

Diagnosis

C3 glomerulopathy (C3G)
No or few Igs | **C3 dominant***

C3/Ig deposits (IC-MPGN)
Ig positive | **Not C3 dominant**



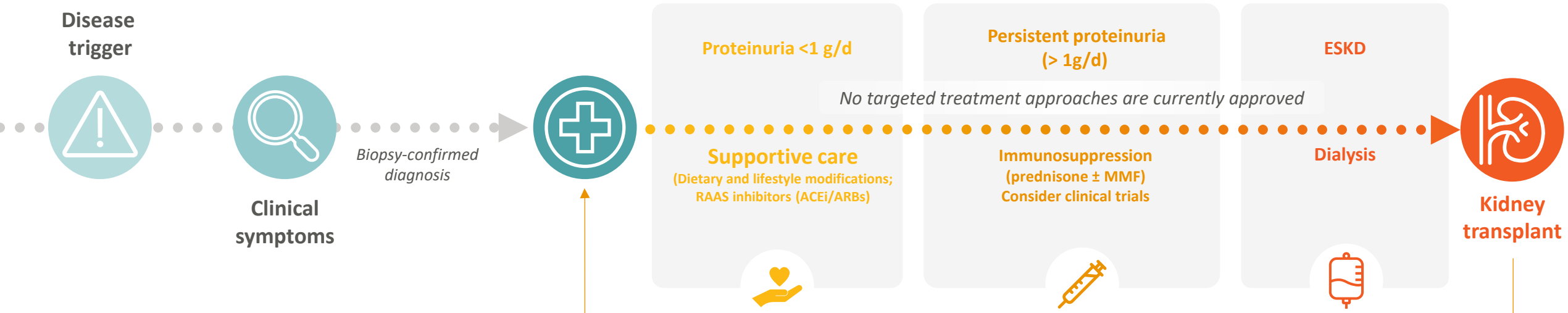
*C3 dominant: C3 is ≥2 orders of magnitude stronger than for any other common immune reactant.

C3/3c, complement 3/3c; ESKD, end-stage kidney disease; IC-MPGN, immune complex-mediated membranoproliferative glomerulonephritis; Ig, immunoglobulin.

References: 1. Smith RJH, et al. Nat Rev Nephrol 2019;15:129–43. 2. Zipfel PF, et al. Mol Immunol 2015;67:21–30. 3.Cook HT & Pickering MC. Nat Rev Nephrol 2015;11:14–22. 4. Noris M & Remuzzi R. Nephrol Dial Transplant 2024;39:202–14. 5.Mastrangelo A, et al. Front Pediatr 2020;8:205.

Despite the current treatment algorithm in C3G and primary IC-MPGN, **patients continue to progress to ESKD**[1–6]

50% of patients progress to ESKD within 10 years of diagnosis despite treatment



Post-transplant patients have impaired eGFR and require further immunosuppressive treatment

Up to 80% of patients experience clinical disease recurrence after transplantation, with a **76% greater risk of mortality** vs other nephropathies

ACEi, angiotensin-converting enzyme inhibitor; ARB, angiotensin II receptor blocker; C3G, complement 3 glomerulopathy; d, day; eGFR, estimated glomerular filtration rate; ESKD, end-stage kidney disease; IC-MPGN, immune complex-mediated membranoproliferative glomerulonephritis; MMF, mycophenolate mofetil; RAAS, renin-angiotensin-aldosterone system.

References: 1. Caravaca-Fontán F, et al. Nephron 2020;144:272–80. 2. Michels MAHM, et al. Pediatr Nephrol 2022;37:601–12. 3. Vivarelli M, et al. Pediatr Nephrol 2021;37:521–35. 4.Jefferson JA. Clin J Am Soc Nephrol 2018;13:1264–75. 5. O'Shaughnessy MM, et al. J Am Soc Nephrol 2017;28:632–44. 6. Heiderscheit AK, et al. Am J Med Genet C Semin Med Genet 2022;190C:344–57.

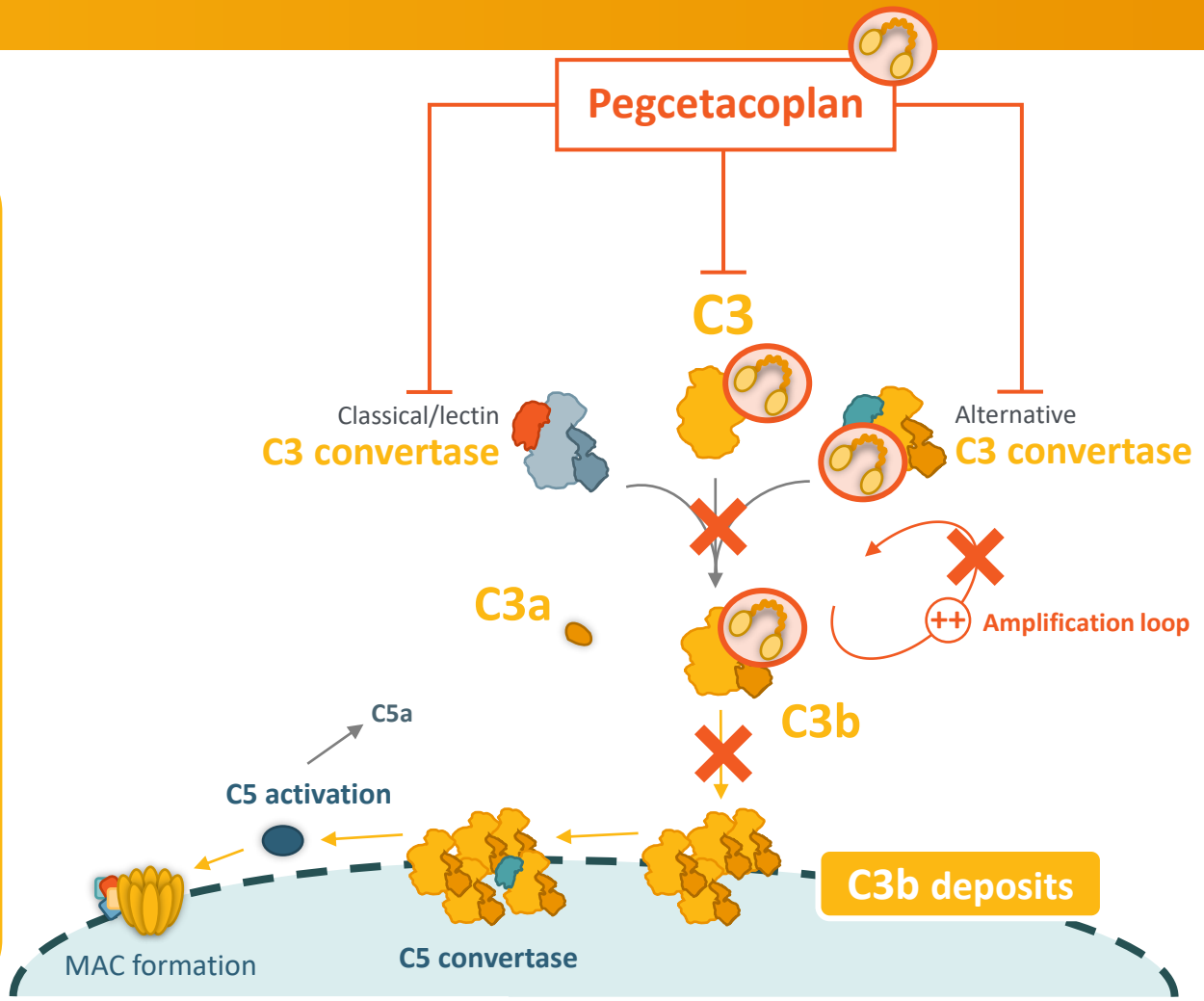
Pegcetacoplan, a C3 and C3b inhibitor, targets C3 dysregulation to preserve kidney function and prevent disease progression

Pegcetacoplan

Selectively binds to **C3** and **C3b**, blocking C3 cleavage by all convertases and downstream effectors of complement activation[1–5]

Assessed in patients with C3G and IC-MPGN in Phase 2 studies[6,7]

Under **Phase 3 investigation in adults and adolescents with C3G and primary IC-MPGN**, either in native kidneys or post-transplant[8,9]



Pegcetacoplan in C3G and primary IC-MPGN is investigational and has not been reviewed or approved for C3G/primary IC-MPGN by any regulatory authority.

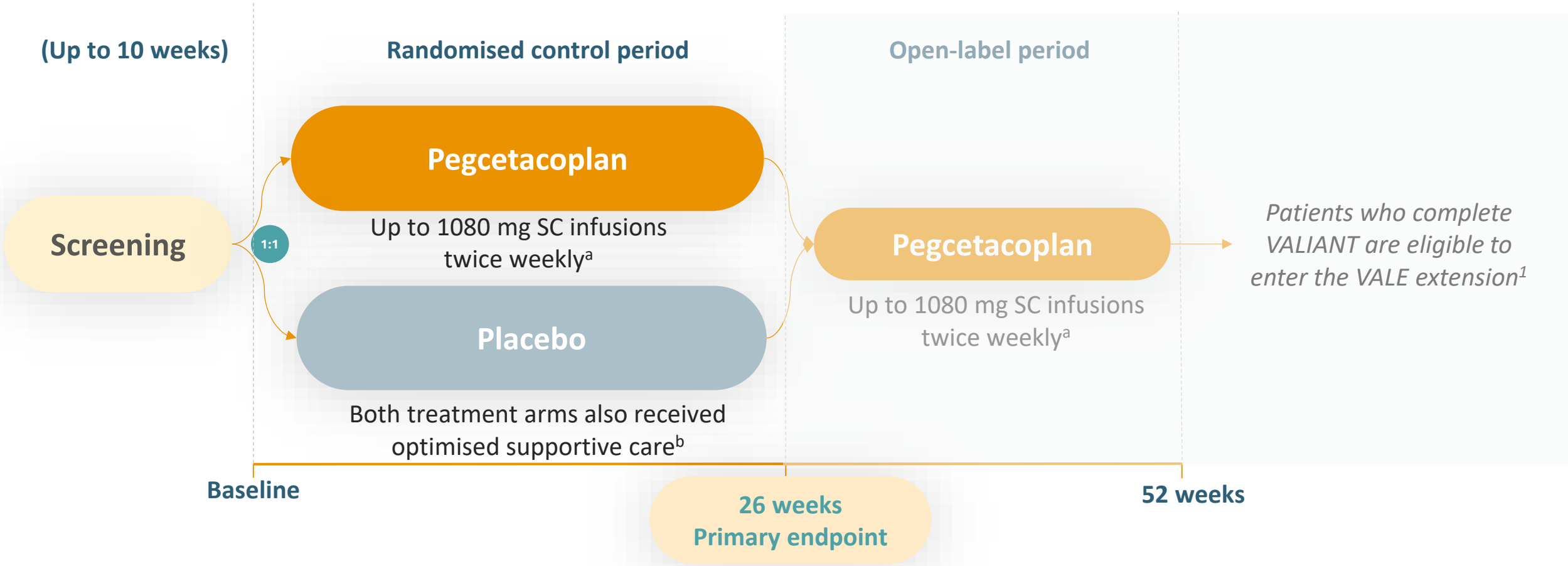
C3/3a/3b/5/5a, complement 3/3a/3b/5/5a; C3G, C3 glomerulopathy; IC-MPGN, immune complex-mediated membranoproliferative glomerulonephritis; MAC, membrane attack complex.

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. US Prescribing Information: EMPAVELI® (pegcetacoplan) injection, for subcutaneous use, 02/2024. Accessed 12 September 2024; 5. EMA Summary of Product Characteristics: ASPAVELI 1 080 mg solution for infusion, 12/2021. Accessed 12 September 2024; 6. Dixon BP, *et al. Kidney Int Rep* 2023;8:2284–93; 7. Bomback A, et al. Presented at American Society of Nephrology Kidney Week 2023 (Poster SA-PO923); 8. Dixon BP, et al. Presented at American Society of Nephrology Kidney Week 2023 (Poster 048); 9. ClinicalTrials.gov identifier: NCT05809531. Last update posted 12 March 2024. Accessed 12 September 2024.

VALIANT: Phase 3 Trial of Pegcetacoplan for Patients With Native or Post-Transplant Recurrent C3G or Primary IC-MPGN

Fadi Fakhouri, MD PhD
Professor of Nephrology
Centre Hospitalier Universitaire Vaudois
Lausanne, Vaud, Switzerland

VALIANT: a double-blind, randomised, placebo-controlled Phase 3 trial



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

[a]All adults and adolescents weighing ≥50 kg self administered 1080 mg/20 mL. Adolescent patients weighing 30–34 kg received 540 mg/10 mL for the first 2 doses, then 648 mg/12 mL. Adolescent patients weighing 35–49 kg received 648 mg/12 mL for the first dose, then 810 mg/15 mL.

[b]Stable, optimized antiproteinuric regimens: ACEis, ARBs, SGLT2is; MMF and corticosteroids (prednisone ≤20 mg/day or equivalent) were permitted.

1. ClinicalTrials.gov. VALIANT. clinicaltrials.gov/study/NCT05067127. Accessed Sep 18, 2024.

VALIANT: eligibility criteria

Inclusion

- **Adolescents** (12–17 yrs) **or adults** (≥18 yrs)
- **Diagnosis of C3G or primary IC-MPGN (with or without previous renal transplant)**
- **MMF and corticosteroids (prednisone ≤20 mg/day) permitted**

Exclusion

- **>50% global glomerulosclerosis or interstitial fibrosis on renal biopsy**

Other eligibility criteria

Inclusion

- Evidence of active disease
- ≥1 g/day of proteinuria on screening urine collection and uPCR ≥1 g/g in 2 or more first-morning spot urine samples
- eGFR ≥30 mL/min/1.73 m^{2}[a]
- Mandatory vaccination against *Streptococcus pneumoniae*, *Neisseria meningitidis* (types A, C, W, Y, and B), and *Haemophilus influenzae* (type B)
- Stable, optimised antiproteinuric regimens: ACEis, ARBs, SGLT2is

Exclusion

- Evidence of transplant rejection
- Diagnosis of secondary C3G or IC-MPGN
- Severe infection within 14 days prior to first dose
- Recurrent or chronic severe infections or history of meningococcal disease
- Previous exposure to pegcetacoplan or another complement inhibitor
- Evidence of improving renal disease

ACEi, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor blockers; C3, complement protein 3; C3G, C3 glomerulopathy; eGFR, estimated glomerular filtration rate; IC-MPGN, immune complex membranoproliferative glomerulonephritis; MMF, mycophenolate mofetil; SGLT2is, sodium-glucose cotransporter-2 inhibitors; uPCR, urine protein-to-creatinine ratio; yrs, years.

[a]Calculated using the CKD-Epi equation for adults or the Bedside Schwartz equation for adolescents.

VALIANT: primary and key secondary endpoints

Primary

- **Log-transformed ratio of uPCR at Week 26** compared to baseline

Key Secondary

- **Proportion of participants who met the criteria for achieving a composite renal endpoint** (i.e., a stable or improved eGFR compared to the baseline visit [≤15% reduction in eGFR] and a ≥50% reduction in uPCR compared to the baseline visit) at Week 26
- **Proportion of participants with a reduction of ≥50% in uPCR** from baseline to Week 26
- For participants with evaluable renal biopsies, **change in the activity score of the C3G histologic index score** from baseline to Week 26
- Proportion of participants with evaluable renal biopsies showing **decreased C3c staining on renal biopsy** from baseline to Week 26
- **Change in eGFR** from baseline to Week 26

C3c, complement protein 3c; eGFR, estimated glomerular filtration rate; uPCR, urine protein-to-creatinine ratio.

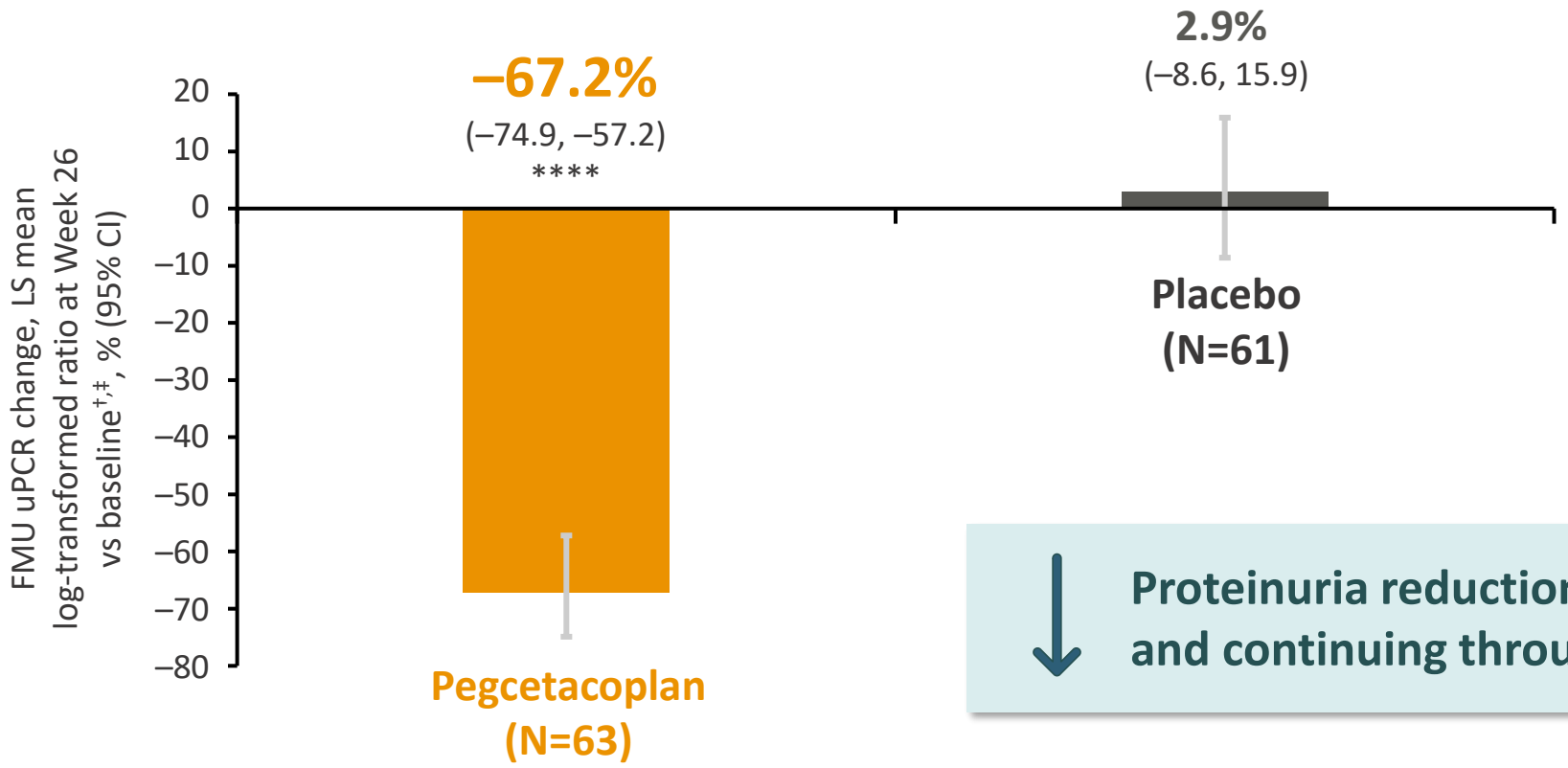
VALIANT included a broad patient population:
≥12 years, pre- and post-transplant, C3G and primary IC-MPGN

Characteristic*	Pegcetacoplan (N=63)	Placebo (N=61)
Age, mean (SD), years	28.2 (17.08)	23.6 (14.26)
Adolescents (12–17 years) / adults (≥18 years), n (%)	**28 (44.4)** / 35 (55.6)	**27 (44.3)** / 34 (55.7)
Gender, female, n (%)	37 (58.7)	33 (54.1)
Race, white†, n (%)	45 (71.4)	46 (75.4)
Baseline 24 hr uPCR, mean (SD), g/g	3.95 (2.888)	3.29 (2.357)
Baseline triplicate first morning spot uPCR, mean (SD), g/g	3.12 (2.408)	2.54 (2.015)
Baseline eGFR, mean (SD), mL/min/1.73 m^2	78.5 (34.12)	87.2 (37.15)
Underlying disease based on screening biopsy, n (%)		
C3G	**51 (81.0)**	**45 (73.8)**
C3GN	45 (71.4)	41 (67.2)
DDD	4 (6.3)	4 (6.6)
Undetermined	2 (3.2)	0
Primary IC-MPGN	**12 (19.0)**	**16 (26.2)**
Time since diagnosis, mean (SD), years	3.6 (3.47)	3.8 (3.62)
Post-transplant recurrent disease, n (%)	**5 (7.9)**	**4 (6.6)**

*Intent-to-treat population (all randomised patients). †Additional race categories included Asian (PEG: 9 [14.3%]; PBO: 9 [14.8%]); American Indian or Alaskan Native (PEG: 1 [1.6%]; PBO: 0); Black or African American (PEG: 1 [1.6%]; PBO: 0); and Other (PEG: 7 [11.1%]; PBO: 6 [9.8%]).
C3G, complement 3 glomerulopathy; C3GN, complement 3 glomerulonephritis; DDD, dense deposit disease; eGFR, estimated glomerular filtration rate; hr, hour;
IC-MPGN, immune complex-mediated membranoproliferative glomerulonephritis; PBO, placebo; PEG, pegcetacoplan; SD, standard deviation; uPCR, urine protein-to-creatinine ratio.

Highly statistically and clinically significant proteinuria reduction of 68.1% with pegcetacoplan vs placebo

Change in proteinuria (Week 26 vs baseline)[†,‡]



Primary endpoint

Relative reduction[‡] (95% CI) in pegcetacoplan vs placebo arms

68.1%

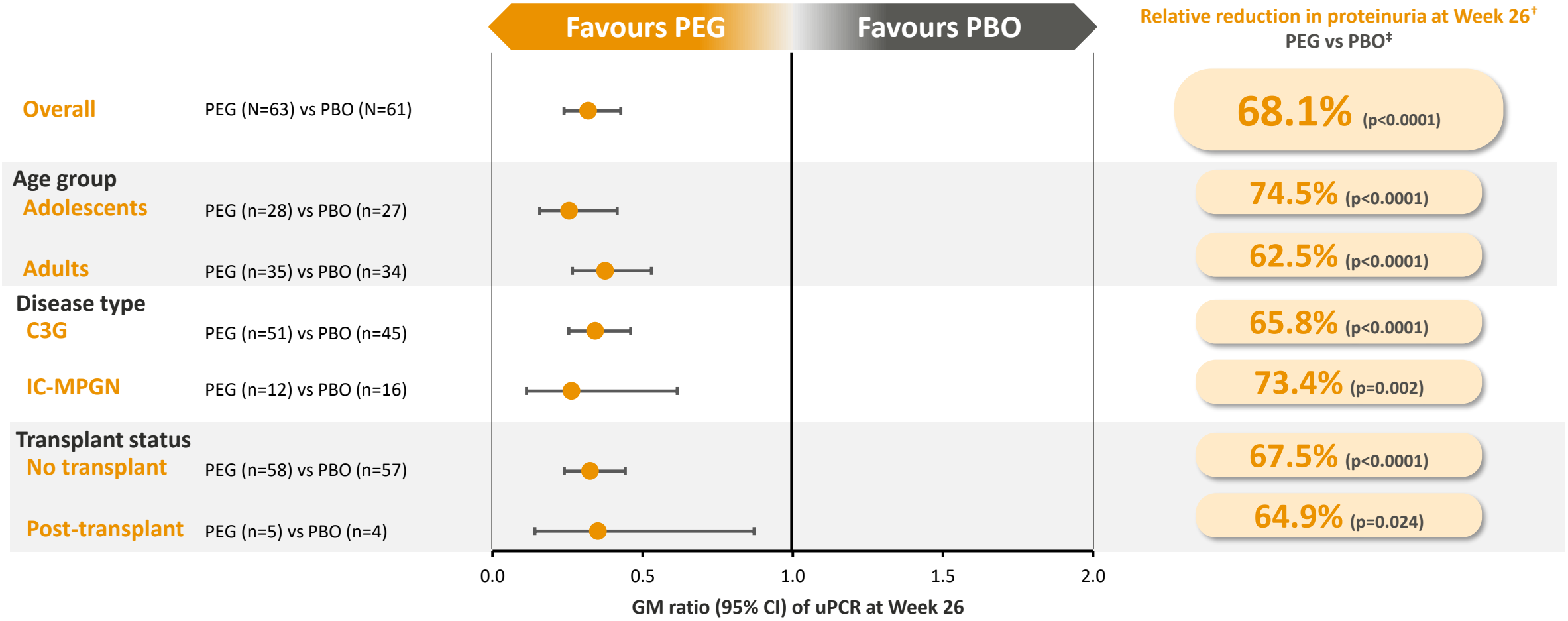
(57.3, 76.2)

p<0.0001

Proteinuria reduction observed as early as Week 4 and continuing through Week 26

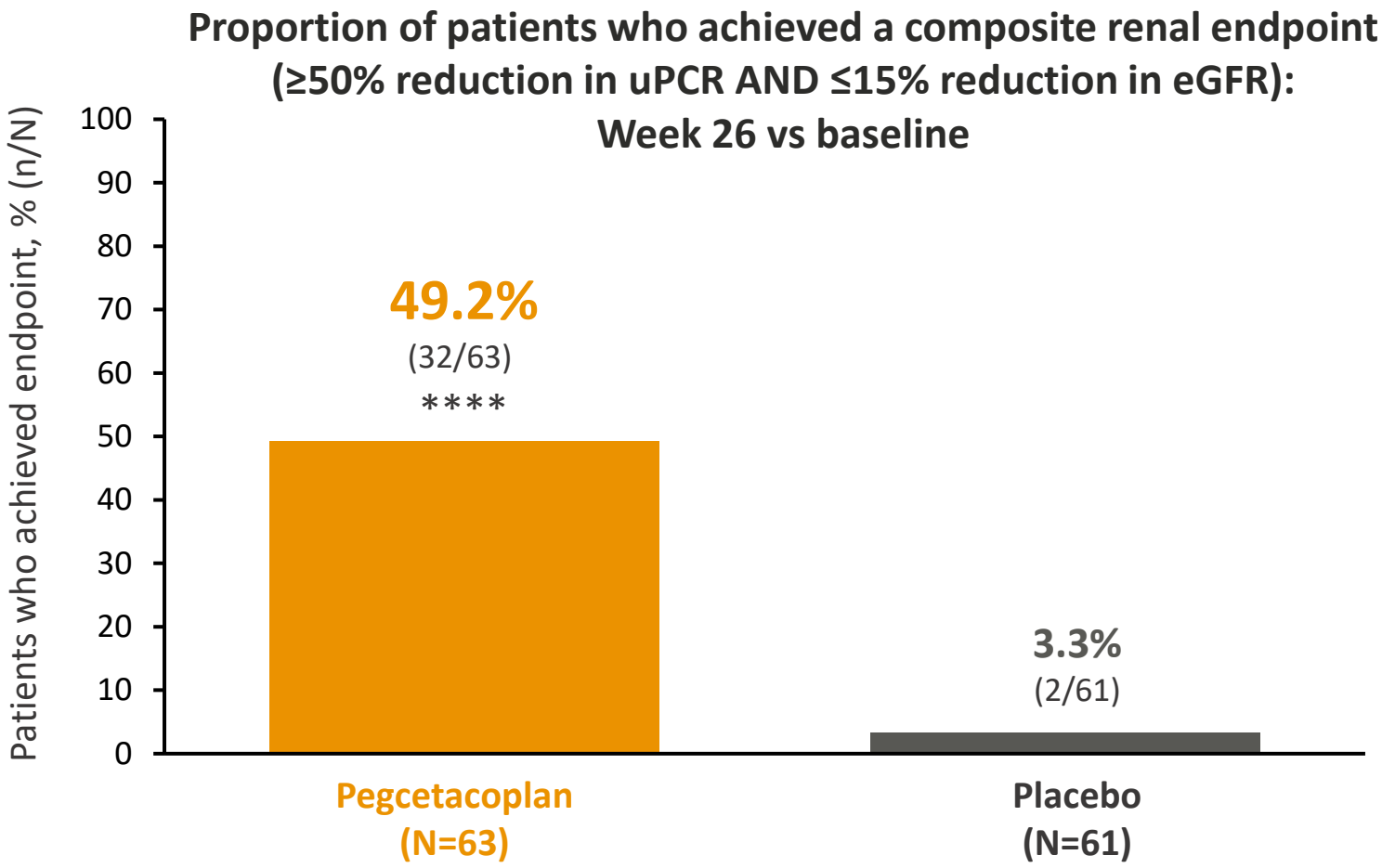
****p≤0.0001. Intention-to-treat population (all randomised patients).
[†]Using an equal-weighted average from FMU over Weeks 24, 25 and 26. [‡]Percentages calculated by converting the ratio of geometric means to percentages.
CI, confidence interval; FMU, first-morning spot urine; LS, least squares; uPCR, urine protein-to-creatinine ratio.

Consistent, clinically meaningful proteinuria reductions with pegcetacoplan vs placebo were observed across broad patient subgroups



Intention-to-treat population (all randomised patients).
†Using an equal-weighted average over Weeks 24, 25, and 26 compared with baseline. ‡Percentages calculated by converting the ratio of geometric means to percentages.
C3G, complement 3 glomerulopathy; CI, confidence interval; GM, geometric mean; IC-MPGN, immune complex-mediated membranoproliferative glomerulonephritis; PBO, placebo; PEG, pegcetacoplan; uPCR, urine protein-to-creatinine ratio.

Pegcetacoplan resulted in **significantly more patients achieving the positive composite renal endpoint**



Key secondary endpoint

Odds ratio
pegcetacoplan vs placebo

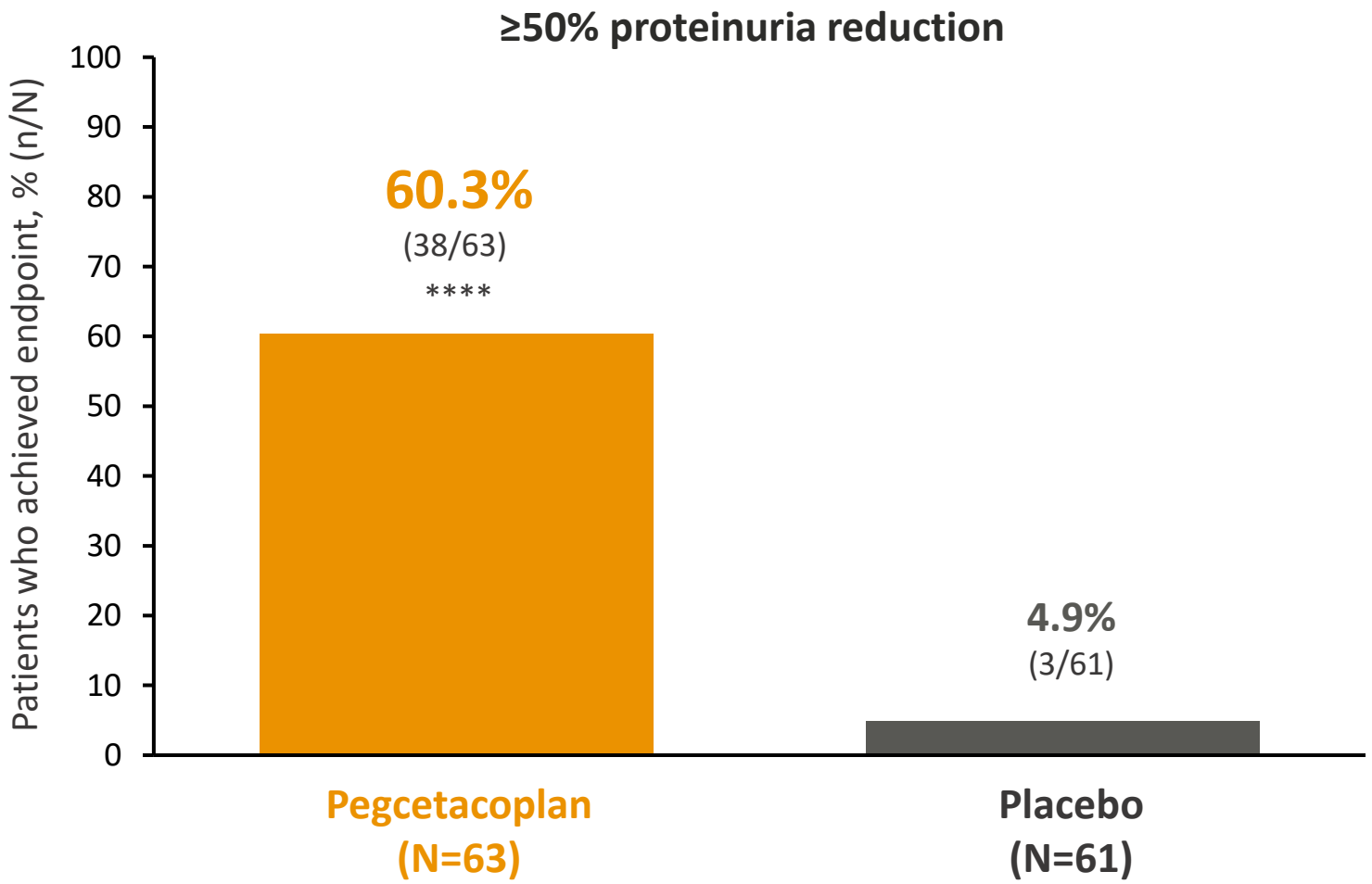
27x

higher odds of achieving composite renal endpoints vs placebo

p<0.0001

****p≤0.0001. Intention-to-treat population (all randomised patients). 2-sided p values.
eGFR, estimated glomerular filtration rate; uPCR, urine protein-to-creatinine ratio.

Significantly more patients achieved ≥50% proteinuria reduction with pegcetacoplan vs placebo



Key secondary endpoint

Odds ratio
pegcetacoplan vs placebo arms

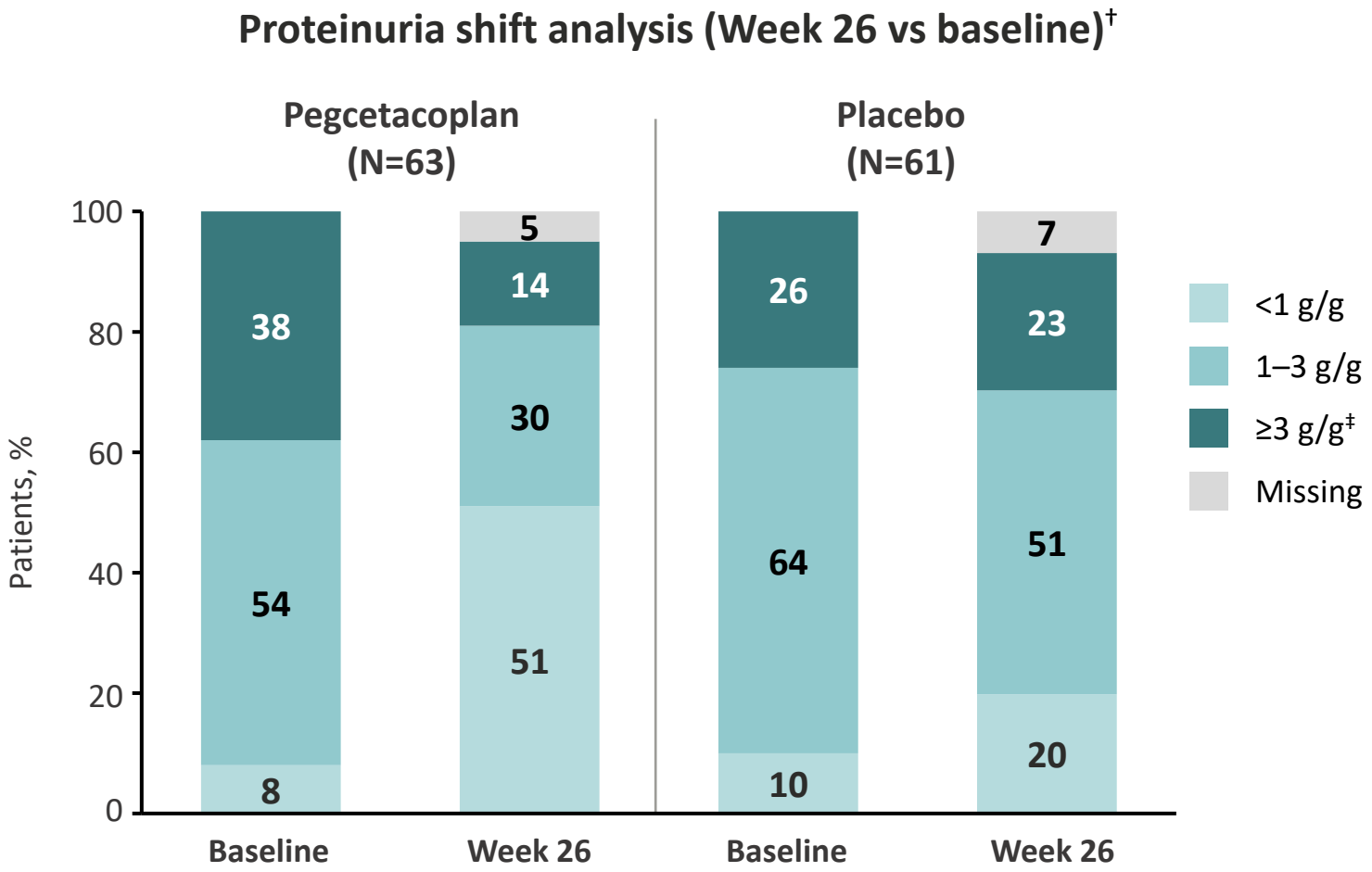
31x

higher odds of achieving ≥50% proteinuria reduction

p<0.0001

****p≤0.0001. Intention-to-treat population (all randomised patients). 2-sided p values.

Substantial improvement in the proportion of patients with proteinuria <1 g/g and decrease in percentage in nephrotic range (≥3 g/g) following pegcetacoplan treatment



Post-hoc analysis

Proportion of pegcetacoplan-treated patients with

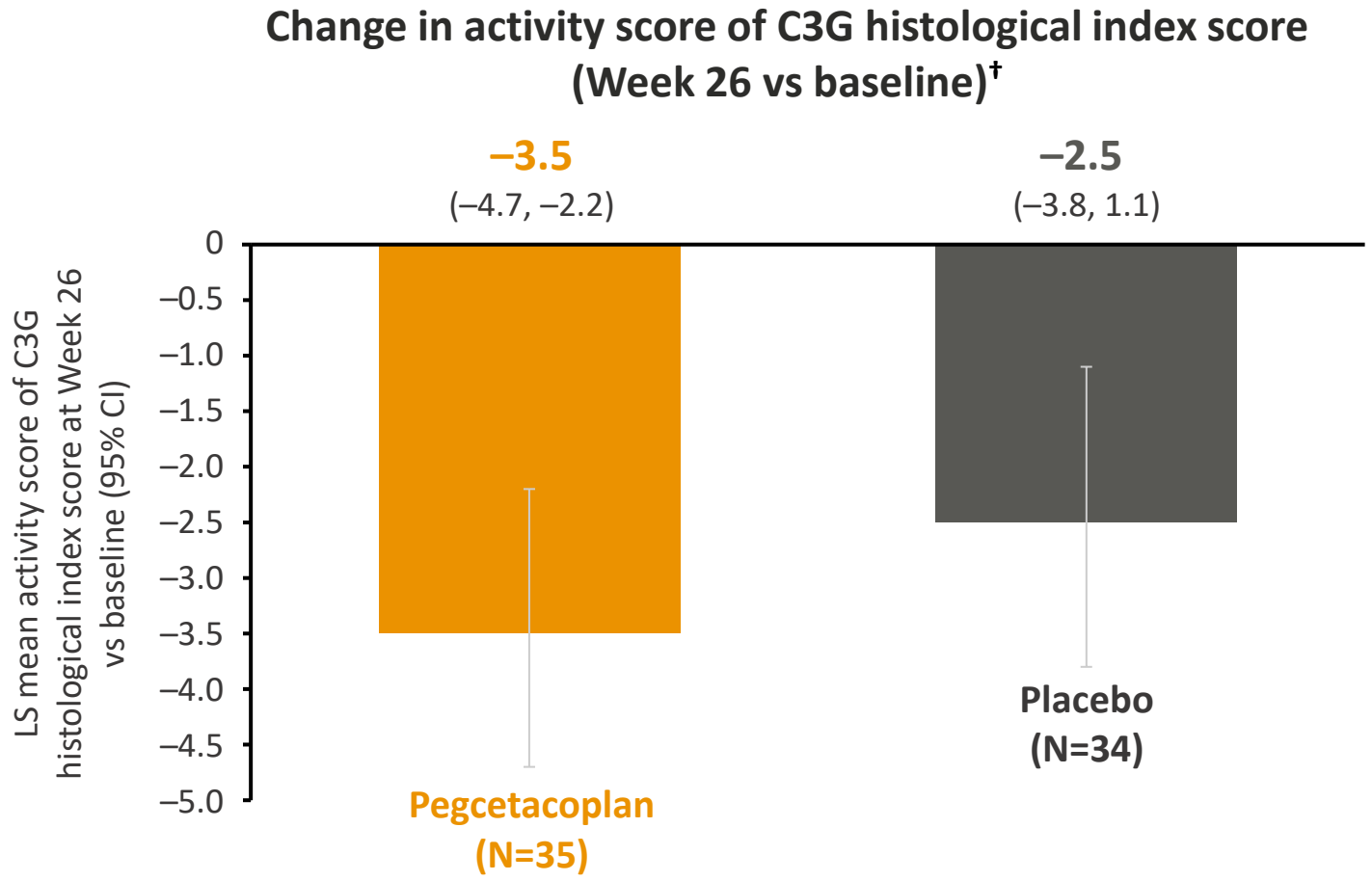
<1 g/g proteinuria

after 26 weeks

50.8%

†Based on FMU uPCR. ‡Nephrotic range
FMU, first morning urine; uPCR, urine protein-to-creatinine ratio.

Reduction in activity score of C3G histologic index score with pegcetacoplan



Key secondary endpoint

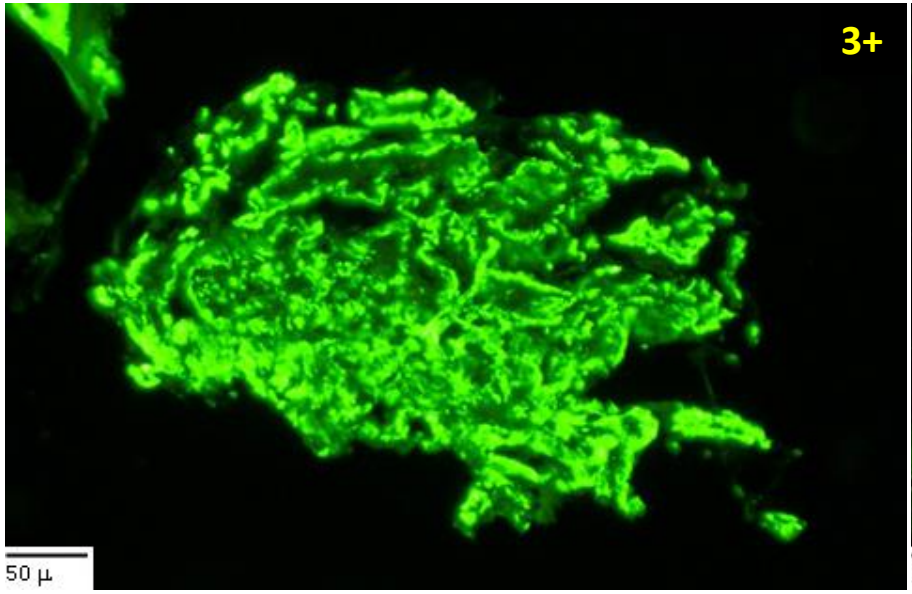
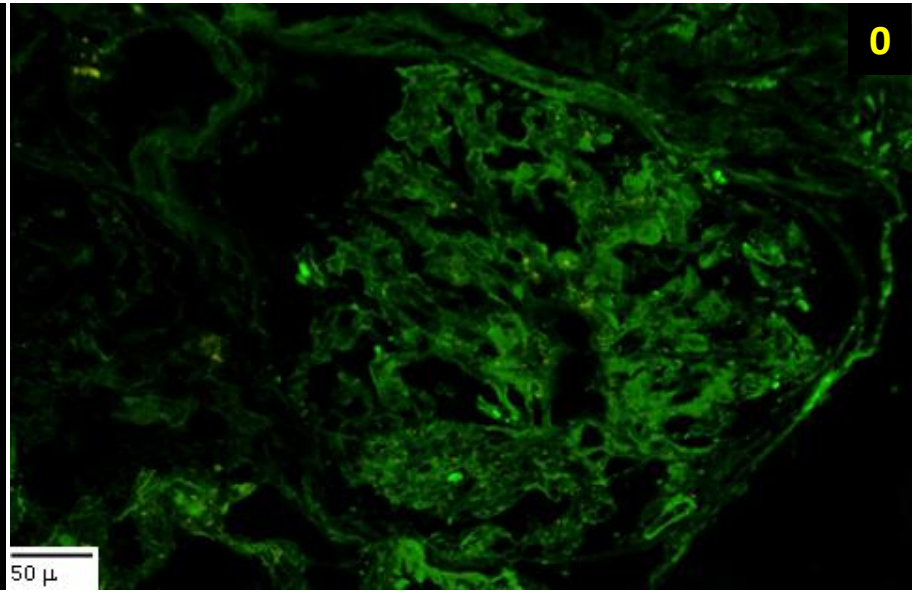
Adjusted LS mean (95% CI) difference in pegcetacoplan vs placebo

–1.0 (–2.8, 0.8); p=0.28

Non-statistically significant p>0.05.
†In adult patients.
CI, confidence interval; C3G, complement 3 glomerulopathy; LS, least squares.

Pegcetacoplan treatment resulted in **clinically significant clearance of C3c** from renal biopsies

Renal biopsies from a pegcetacoplan-treated C3G native kidney patient:

Baseline	Week 26
	

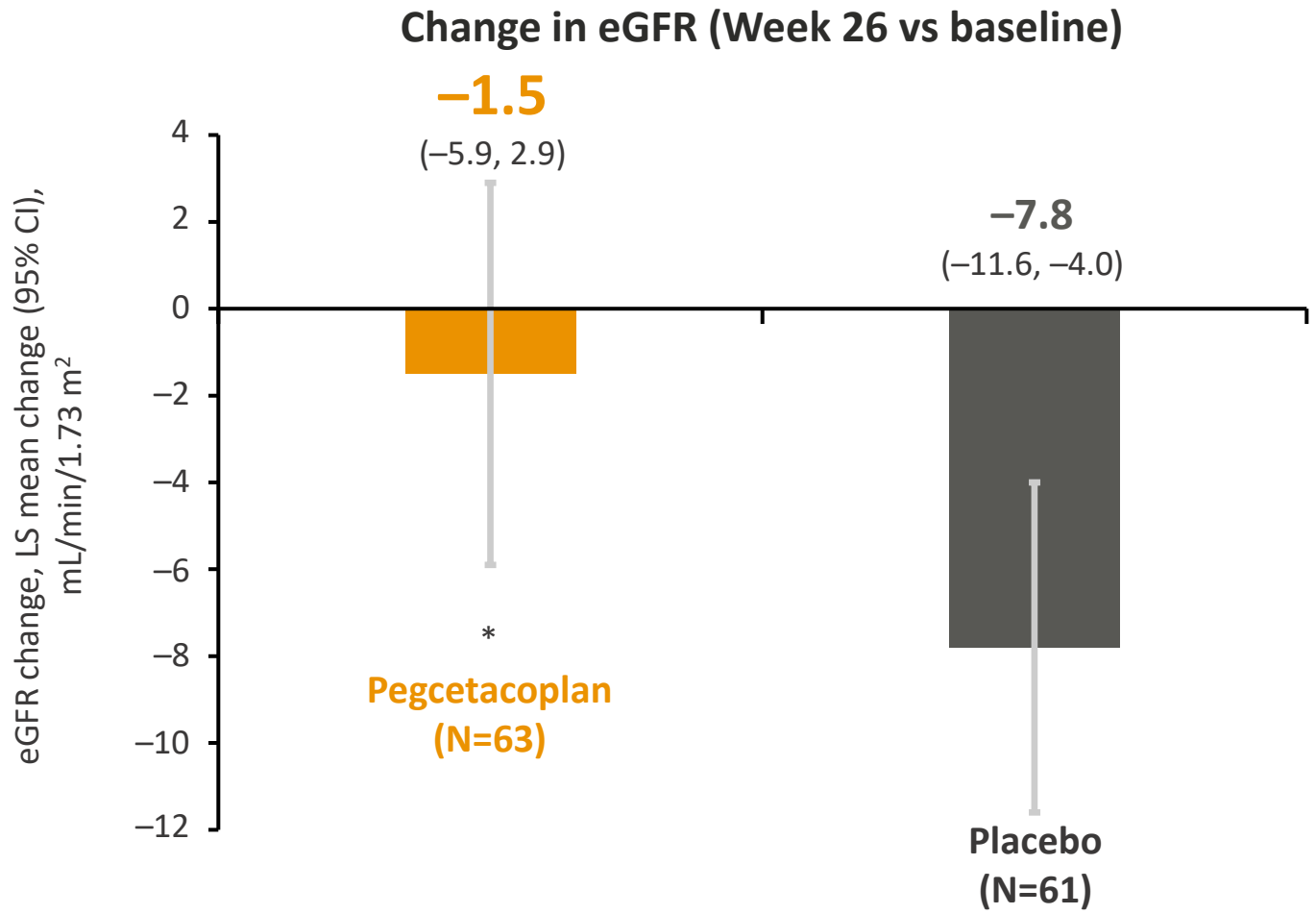
71.4% (25/35) of pegcetacoplan-treated patients achieved 0 intensity staining

Key secondary endpoint	
Proportion with reduced C3c renal biopsy staining[†]	
Pegcetacoplan	74.3% (26/35)
Placebo	11.8 (4/34)

27x higher odds of achieving ≥2 OOM reduction
(6.5, 115.9); nominal[‡]
p<0.0001

[†]Difference defined as ≥2 OOM at Week 26 vs baseline; in all adults. Baseline renal biopsies were not required for adolescent participants.
[‡]Statistical testing stopped after first endpoint to not reach significance between treatment arms (i.e., change in activity score of C3G histological index score at Week 26 vs baseline).
C3c, complement 3c; C3G, C3 glomerulopathy; CI, confidence interval; OOM, orders of magnitude.

Pegcetacoplan **significantly stabilised eGFR** compared with placebo



Key secondary endpoint

Difference in pegcetacoplan vs placebo

+6.3 mL/min/1.73 m²

P=0.03

nominal†

*p≤0.05. Intention-to-treat population (all randomised patients). †Statistical testing stopped after first endpoint to not reach significance between treatment arms (i.e., change in activity score of C3G histologic index score at Week 26 vs baseline).
CI, confidence interval; eGFR, estimated glomerular filtration rate; LS, least squares..

TEAE frequency and severity were similar between treatment arms

Patients, n (%)	Pegcetacoplan (N=63)	Placebo (N=61)
TEAEs	53 (84.1)	57 (93.4)
Treatment-related TEAEs	25 (39.7)	26 (42.6)
Severe TEAEs	3 (4.8)	4 (6.6)
Serious TEAEs	6 (9.5)	6 (9.8)
Serious infections		
COVID-19 pneumonia	1 (1.6)	0 (0.0)
Influenza	1 (1.6)	0 (0.0)
Pneumonia	1 (1.6)	0 (0.0)
Viral infection	0 (0.0)	1 (1.6)
TEAEs leading to study discontinuation	1 (1.6)	1 (1.6)
Deaths (COVID-19 pneumonia, unrelated to pegcetacoplan)	1 (1.6)	0 (0.0)

No encapsulated *N. meningitidis* cases among the four reported serious infections (pegcetacoplan, n=3; placebo, n=1)

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

Safety population (all randomised 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; TEAE, treatment-emergent AE.

Pegcetacoplan demonstrated marked efficacy in the phase 3 VALIANT trial

Proteinuria reduction of 68.1%

- Highly statistically significant and clinically meaningful
- Consistent across subgroups of age, disease type and transplant status
- Among pegcetacoplan-treated patients, **50.8% achieved <1 g/g** at Week 26

Statistically significant stabilisation of eGFR, +6.3mL/min/1.73 m^2 pegcetacoplan vs placebo

Zero intensity staining of C3c achieved in **>70%** of pegcetacoplan-treated patients

Pegcetacoplan has been **well tolerated** with **no encapsulated meningitis** reported, consistent with previous trials and with more than **2000 patient-years of pegcetacoplan exposure**

C3, complement 3; eGFR, estimated glomerular filtration rate.

Summary and concluding remarks

Guido Oelkers

CEO Sobi

Sobi's view on pegcetacoplan in C3G – IC-MPGN

#1 We are confident in pegcetacoplan's blockbuster potential

We remain confident in a diagnosed patient population of at least 8k patients with C3G or IC-MPGN in Europe. Additional potential opportunity in Japan and selected international markets.

#2 Increasing opportunity – today's numbers are more a reflection of today's options

Unlocking the potential requires understanding the individual complete patient journey

#3 The data support pegcetacoplan's use in a number of patient subgroups

pegcetacoplan is the only investigational product with phase 3 results in C3G and IC-MPGN including adolescent and adult patients, as well as pre and post transplant patients

#4 Pegcetacoplan shown to reduce proteinuria by 68%

The Spanish Group for the Study of Glomerular Diseases (GLOSEN) establish 50% as the threshold for being clinically meaningful – and pegcetacoplan is the only product that clearly surpasses that threshold

Device partnership with Enable Injections, Inc.

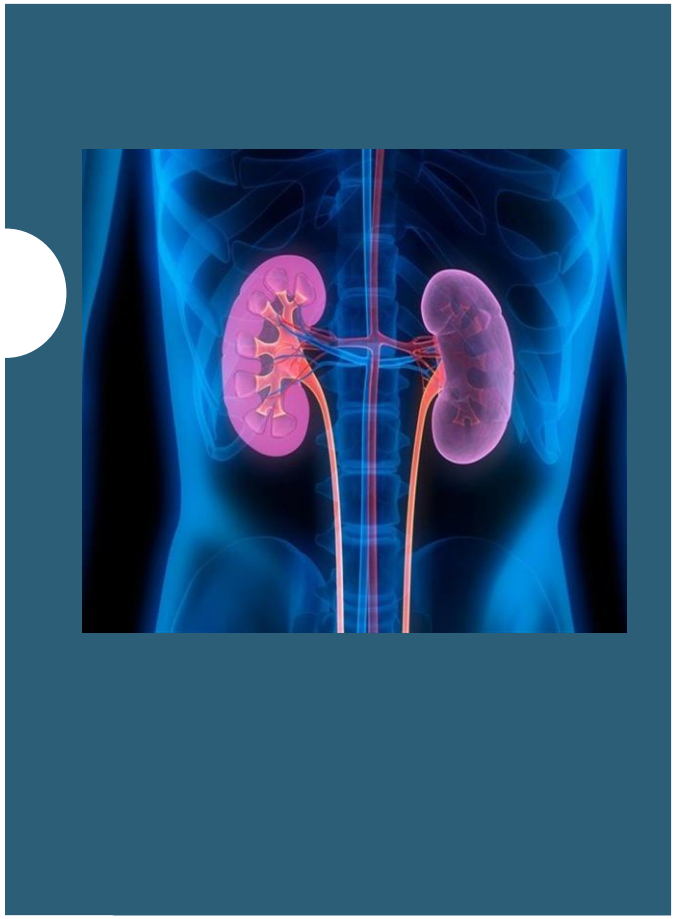
- **enFuse® Injector** for subcutaneous delivery of pegcetacoplan
- Goals: enhance patient experience, support adherence, expand choice
- International development and distribution agreement across Sobi territories
- Aim to be available in Europe for PNH, C3G and IC-MPGN

Empaveli Injector® commercialized by Apellis Pharmaceuticals, Inc. in the US

enFuse is a trademark of Enable Injections, Inc.

Pegcetacoplan a potential new treatment in C3G and IC-MPGN

- Devastating diseases with no approved targeted treatments
- Large market potential – 8K diagnosed patients in Europe
- Pegcetacoplan has show best in class efficacy in both C3G and IC-MPGN with a clinically meaningful 68% reduction in proteinuria and consistent data across key subgroups
- Regulatory filing planned with EMA and Japanese health authorities in 2025




Q&A