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# Long-term renal benefit over 2 years with Nefecon verified: The NeflgArd Phase 3 full trial results

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# Introduction

- Nefecon is a targeted-release budesonide formulation specifically designed to treat IgAN[1,2]
- It was the first ever treatment approved by the FDA and EMA for adult patients with primary IgAN at risk of rapid disease progression[2,3]
- In the Phase 3 NefIgArd trial, treatment with Nefecon resulted in a significant reduction in UPCR (27%, p=0.0003) and significant treatment benefit on eGFR compared with placebo after 9 months[3]
- Here, we present primary data from the full long-term data set, comprising 9 months of treatment and 15 months of follow-up (2 years in total)[1,2]

eGFR, estimated glomerular filtration rate; EMA, European Medicines Agency; FDA, Food and Drug Administration; IgA, immunoglobulin A; IgAN, Immunoglobulin A nephropathy; UPCR, urine protein-to-creatinine ratio.

1. Barratt J, et al. *Kidney Int Rep*. 2020;5:1620-1624. 2. Barratt J, et al. *Kidney Int*. 2023;103:391-402. 3. Calliditas Therapeutics press release. March 12, 2023. https://www.calliditas.se/en/calliditas-announces-primary-endpoint-successfully-met-in-phase-3-nefigard-trial-evaluating-nefecon-in-iga-nephropathy/ (accessed May 19, 2023).

# Method

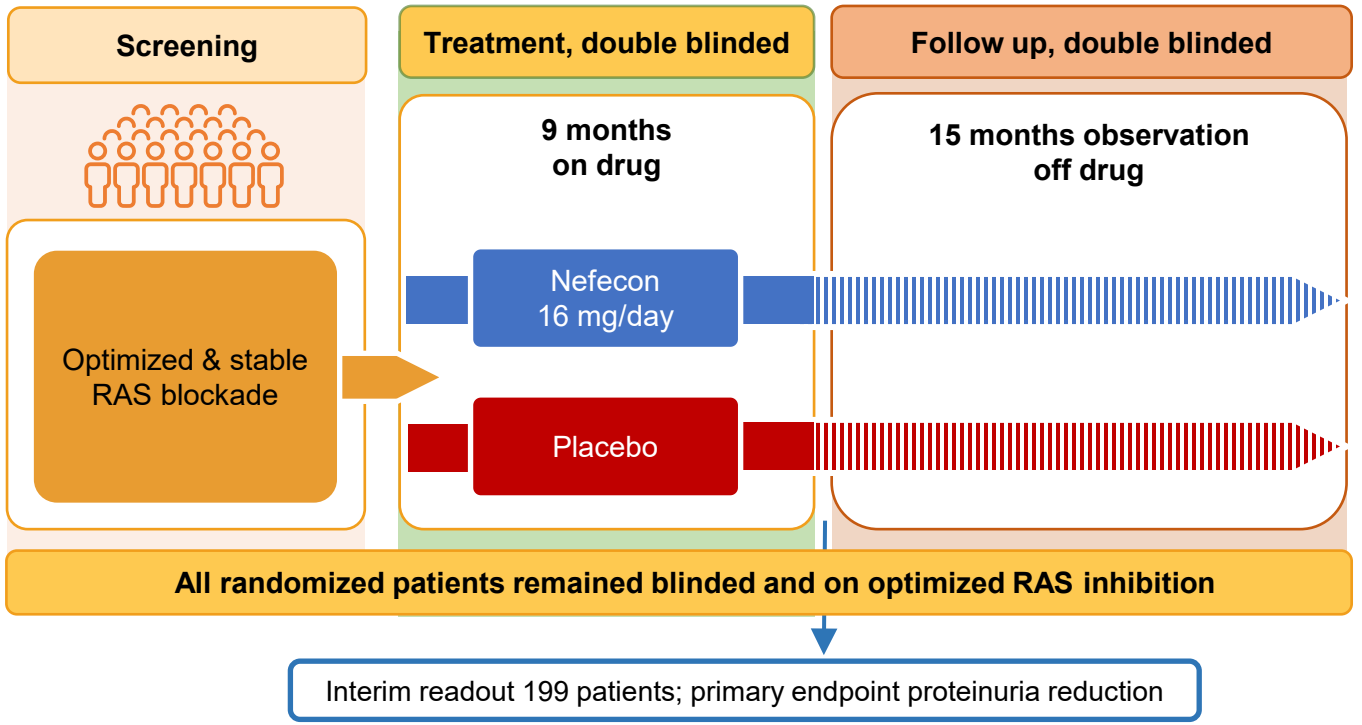
## Interim readout

- November 2020 readout; global study with 199 patients
- Primary endpoint: proteinuria; key secondary endpoint: eGFR
- Basis for accelerated/conditional approval in USA/Europe, respectively

## Full Phase 3 trial

- Designed to confirm the long-term renal benefit of observed proteinuria reduction
- Primary endpoint eGFR
- Read out positive data in March 2023; global study with 364 patients
- Estimated FDA filing July 2023

**NefIgArd: A two-part, global, randomized, double-blind, placebo-controlled study**




**Base inclusion/exclusion criteria:**

- Study included patients ≥18 years old with biopsy-proven IgAN; >1 g of proteinuria; eGFR >35–<90 mL/min/1.73 m², and well-controlled blood pressure of <140/90 mmHg
- Among the exclusion criteria were systemic diseases, having undergone a kidney transplant, and the presence of other glomerulopathies

**Primary efficacy endpoint: Time-weighted average change from baseline in eGFR over the 2-year period**

eGFR, estimated glomerular filtration rate; FDA, Food and Drug Administration; IgAN, immunoglobulin A nephropathy; RAS, renin–angiotensin system.

# Results: Patient overview

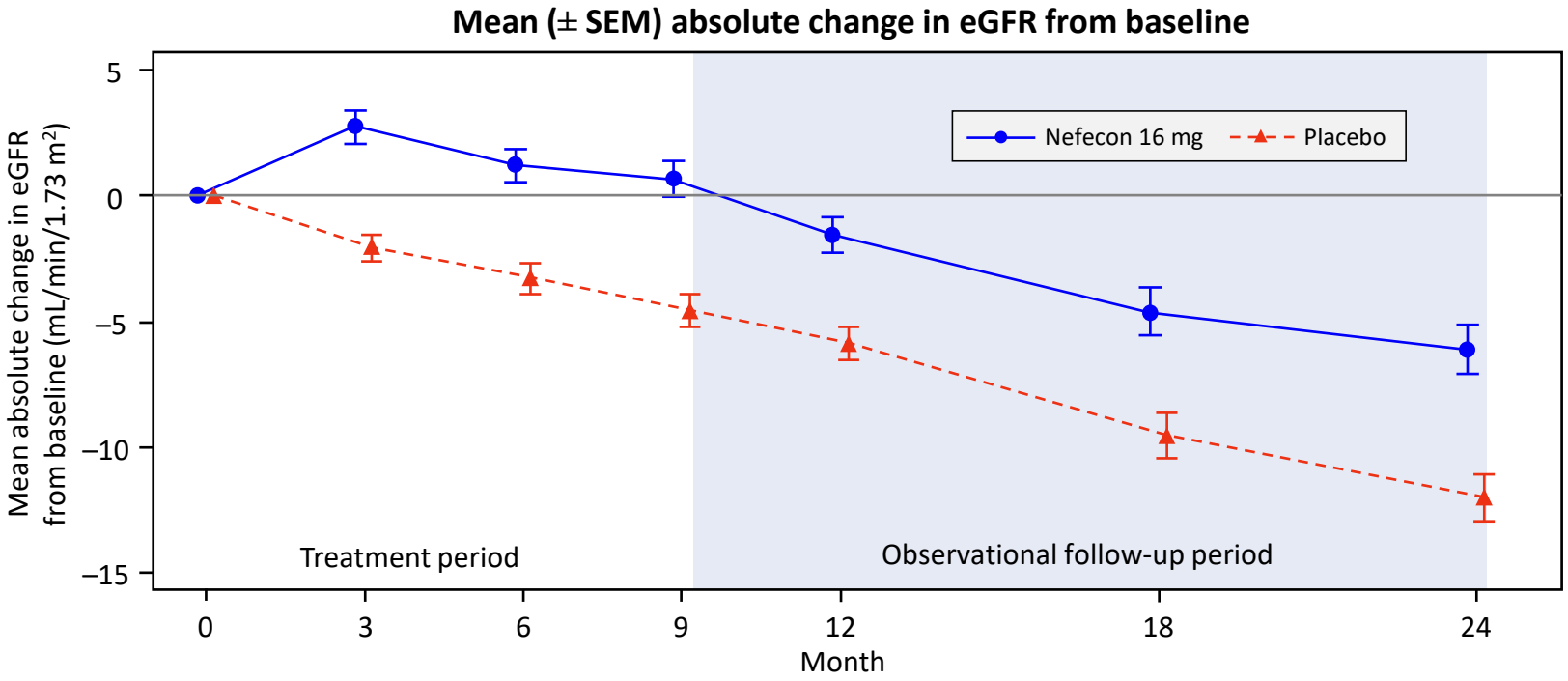
| | Nefecon 16 mg/day (n=182) | Placebo (n=182) |
|---|---|---|
| Median (range) age, years | 43 (21-69) | 42 (20-73) |
| <45 years, n (%) | 98 (53.8) | 104 (57.1) |
| Sex, n (%) | | |
| Male | 117 (64.3) | 123 (67.6) |
| Female | 65 (35.7) | 59 (32.4) |
| Race, n (%) | | |
| White | 138 (75.8) | 137 (75.3) |
| Asian | 43 (23.6) | 40 (22.0) |
| Black or African American | 0 (0.0) | 0 (0.0) |
| Other | 1 (0.5) | 5 (2.7) |
| Median (IQR) blood pressure, mmHg | | |
| Systolic | 126 (121-132) | 124 (117-130) |
| Diastolic | 79 (76-84) | 79 (74-84) |
| Median (IQR) UPCR (g/g) | 1.28 (0.9-1.76) | 1.25 (0.88-1.74) |
| Median (IQR) UACR (g/g) | 0.99 (0.68-1.40) | 0.98 (0.66-1.42) |
| Median (IQR) eGFR CKD-EPI (mL/min/1.73 $m^2$) | 56.14 (45.50-70.97) | 55.11 (45.96-67.74) |
| Microhematuria at randomization, n (%) | | |
| Yes | 123 (67.6) | 127 (69.8) |
| No | 59 (32.4) | 55 (30.2) |
| Median (IQR) years since IgAN diagnosis | 2.4 (0.6-6.9) | 2.6 (0.6-6.5) |
| Systemic CS or immunosuppressant use before randomization, n (%) | | |
| Yes | 15 (8.2) | 19 (10.4) |
| No | 167 (91.8) | 163 (89.6) |

CKD-EPI, Chronic Kidney Disease Epidemiology Collaboration; CS, corticosteroid; eGFR, estimated glomerular filtration rate; IgAN, immunoglobulin A nephropathy; IQR, interquartile range; UACR, urine albumin-to-creatinine ratio; UPCR, urine protein-to-creatinine ratio.

# Results: Efficacy (1)

**Primary endpoint: time-weighted average change from baseline in eGFR over the 2-year period**

- 5.05 mL/min/1.73 $m^2$ eGFR treatment benefit in favor of Nefecon vs placebo over 2 years ($p<0.0001$)
- eGFR benefit at the end of the 9-month treatment period with Nefecon was maintained during the 15-month observational follow-up

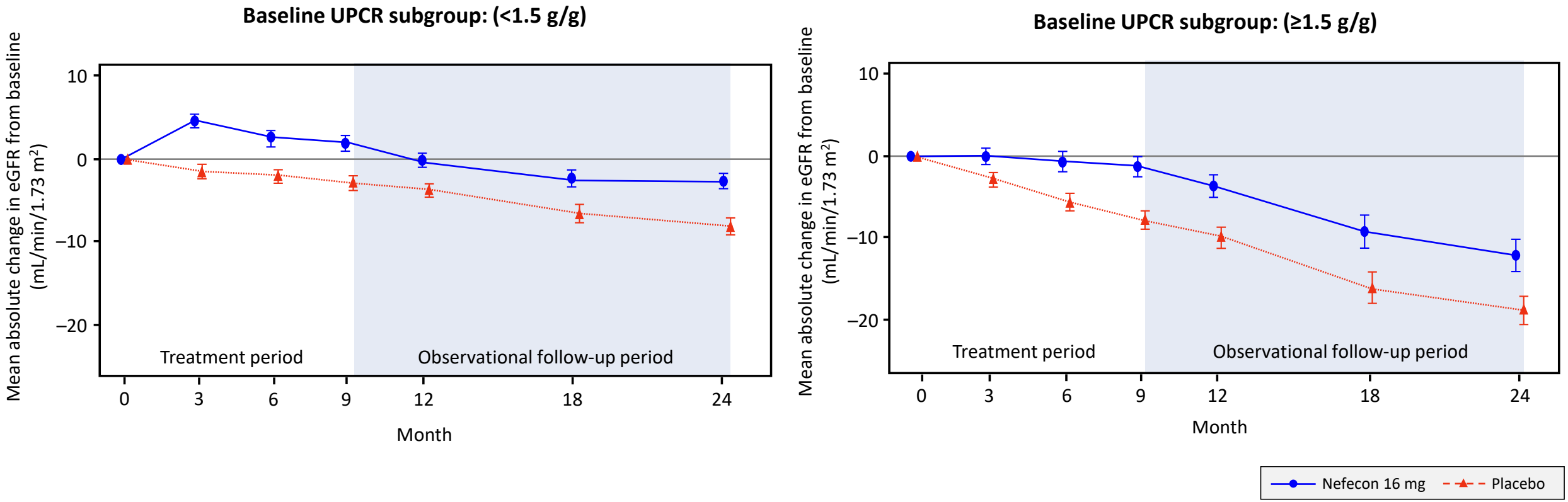



| | | | |
|---|---|---|---|
| Nefecon 16 mg/day, mL/min/1.73 $m^2$ | +0.66 | −1.52 | −6.11 |
| Placebo, mL/min/1.73 $m^2$ | −4.56 | −5.85 | −12.00 |
| Absolute difference, mL/min/1.73 $m^2$ (95% CI) | 5.21 (3.35–7.58) | 4.33 (2.44–6.66) | 5.89 (3.35–9.15) |

CI, confidence interval; eGFR, estimated glomerular filtration rate; SEM, standard error of the mean; UPCR, urine protein-to-creatinine ratio.

# Results: Efficacy (2)

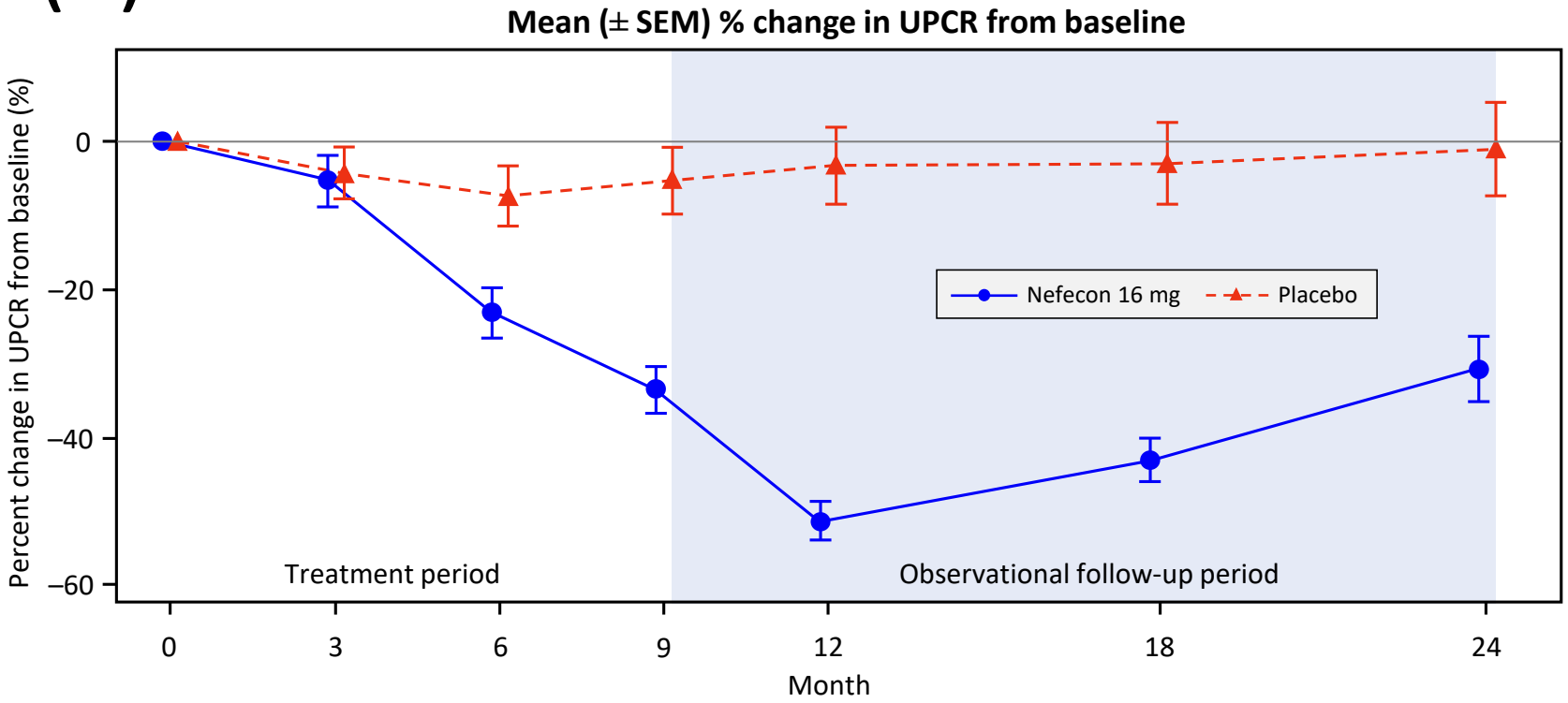
- The eGFR benefit with Nefecon vs placebo was consistent regardless of baseline UPCR




eGFR, estimated glomerular filtration rate; UPCR, urine protein-to-creatinine ratio.

# Results: Efficacy (3)

- At 2 years, the percentage reduction in UPCR in the Nefecon vs placebo arm was similar to the end of the 9-month treatment period




| | | | |
|---|---|---|---|
| Nefecon 16 mg/day, % | –33.6 | –51.3 | –30.7 |
| Placebo, % | –5.2 | –3.2 | –1.0 |
| Corresponding percentage reduction, % (95% CI) | 30 (20–39) | 50 (42–57) | 30 (16–41) |

CI, confidence interval; SEM, standard error of the mean; UPCR, urine protein-to-creatinine ratio.

# Results: TEAEs by preferred term (USPI definition)

**Safety analysis set (≥5% Nefecon-treated patients and ≥2% higher than placebo)**

| Adverse reaction, n (%) | Nefecon 16 mg (n=195) | Placebo (n=194) |
|---|---|---|
| Peripheral edema[a] | 33 (16.9) | 10 (5.2) |
| Hypertension | 23 (11.8) | 6 (3.1) |
| Muscle spasms | 23 (11.8) | 8 (4.1) |
| Acne | 22 (11.3) | 2 (1.0) |
| URTI | 16 (8.2) | 12 (6.2) |
| Face edema[b] | 15 (7.7) | 1 (0.5) |
| Weight increased | 13 (6.7) | 6 (3.1) |
| Dyspepsia | 13 (6.7) | 4 (2.1) |
| Arthralgia | 12 (6.2) | 4 (2.1) |
| WBC increased | 11 (5.6) | 1 (0.5) |

[a]Includes preferred terms of edema peripheral and peripheral swelling. [b]Includes preferred terms of face edema and swelling face.
TEAE, treatment-emergent adverse event; URTI, upper respiratory tract infection; USPI, United States prescribing information; WBC, white blood cell.

# Discussion

- The NefIgArd study met its 2-year primary endpoint, demonstrating that 9 months of treatment with Nefecon on top of optimized SoC provided a statistically significant and clinically relevant preservation of eGFR compared with optimized SoC
- The size of the eGFR benefit was maintained over the 15-month off-drug, observational follow-up period, supporting a disease-modifying effect of Nefecon 16 mg treatment
- Nefecon 16 mg was generally well tolerated, and the AE profile was consistent with that reported in the previous interim analysis

AE, adverse event; eGFR, estimated glomerular filtration rate; SoC, standard of care.

# Acknowledgments

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