# Long-term safety and efficacy of pegcetacoplan in patients with C3 glomerulopathy or primary immune-complex membranoproliferative glomerulonephritis: The long-term VALE extension study



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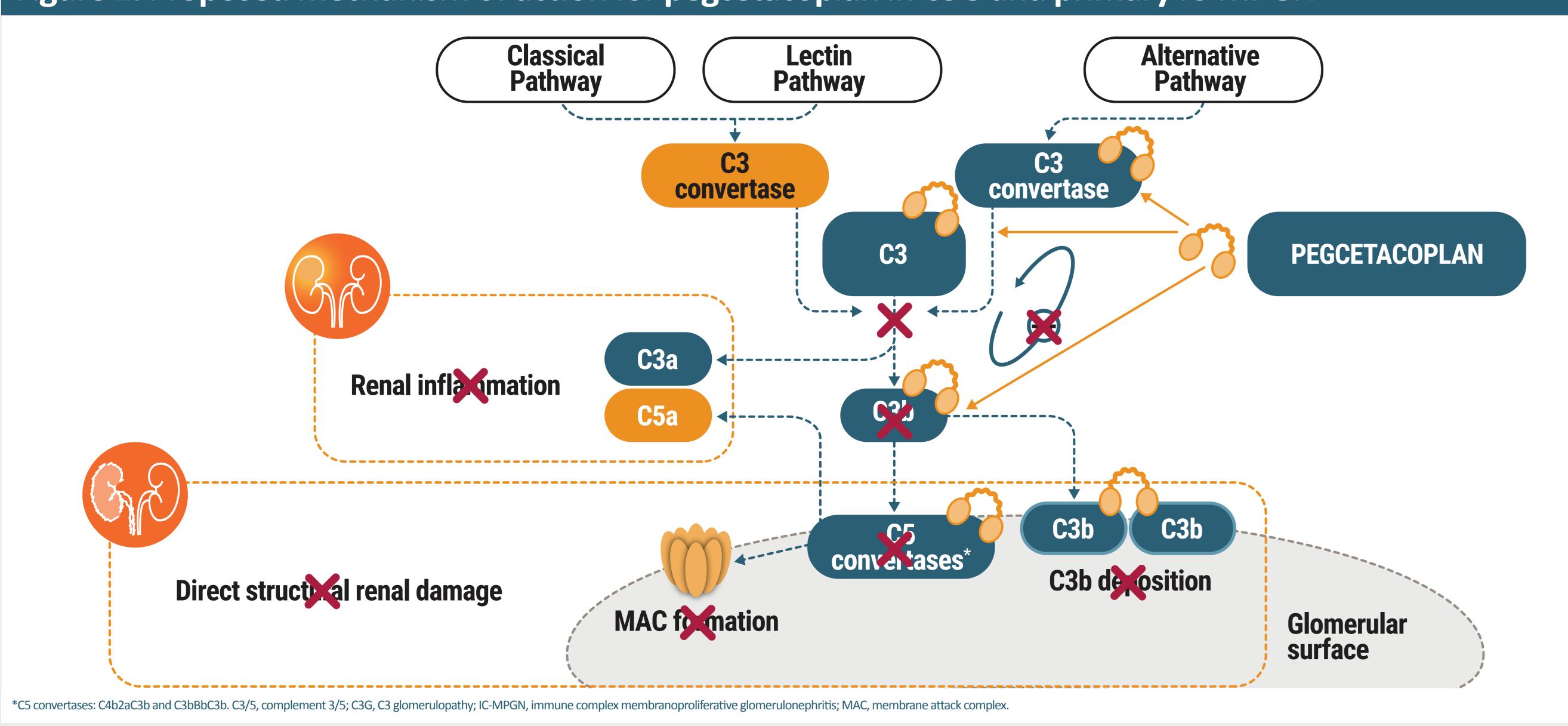
### CONCLUSIONS

✓ The VALE extension study will establish the long-term efficacy and safety of pegcetacoplan in C3G and primary IC-MPGN

### BACKGROUND

- C3G and primary IC-MPGN are rare glomerular conditions characterized by C3 dysregulation/overactivation leading to excessive deposition of C3 breakdown products in the kidney, causing inflammation, renal damage, and renal failure<sup>1-5</sup>
- Pegcetacoplan, a C3 and C3b inhibitor, blocks overactivation of the alternative and classical complement pathway by inhibiting both C3 and C5 convertases<sup>5,6</sup> (Figure 1)

Figure 1. Proposed mechanism of action for pegcetacoplan in C3G and primary IC-MPGN<sup>5–11</sup>



- In the phase 2 trials, pegcetacoplan demonstrated clinical benefit for participants with C3G and was well tolerated<sup>5,12</sup>
- The phase 3 VALIANT (NCT05067127) trial, in participants with C3G or primary IC-MPGN in native kidney or post transplant, is further evaluating the safety and efficacy of pegcetacoplan<sup>13</sup>

### **OBJECTIVE**

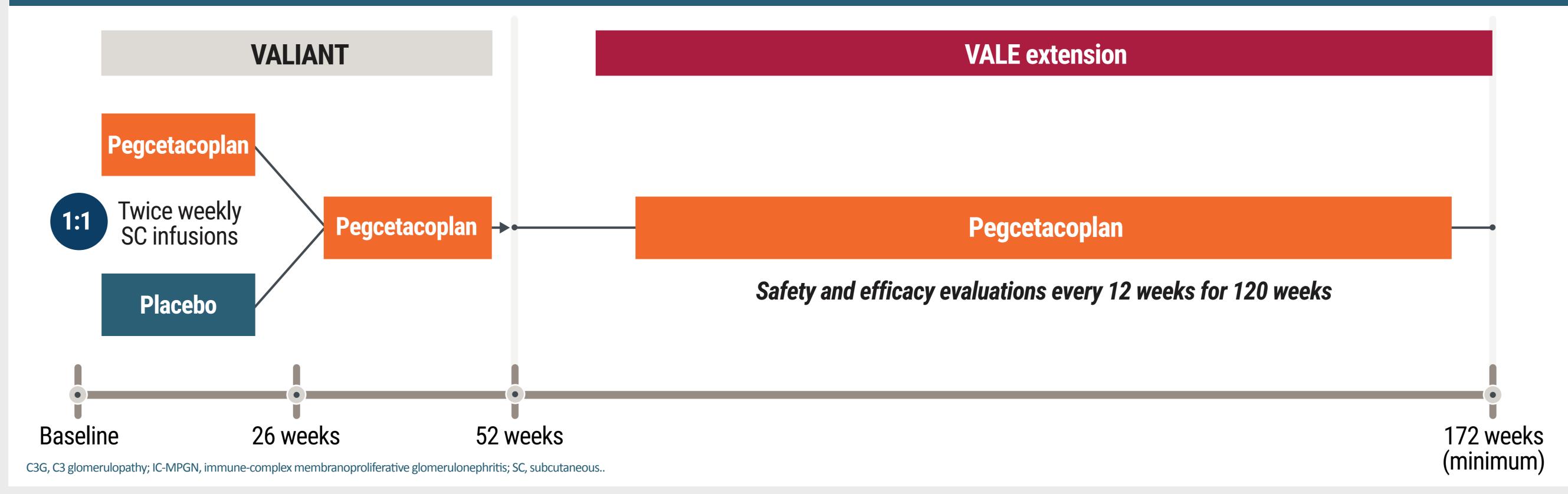
Here we describe VALE (NCT05809531), a phase 3 extension study designed to establish the long-term efficacy and safety of pegcetacoplan in participants with C3G or primary IC-MPGN

### METHODS

■ In the open-label, nonrandomized VALE extension study, participants ≥12 years old who completed VALIANT through Week 52 and achieved clinical benefit, per investigator opinion, will continue to receive twiceweekly doses of pegcetacoplan for a minimum of approximately 2.5 years (Figure 2)

## METHODS (continued)

Figure 2. Study design for VALIANT phase 3 trial and subsequent VALE extension trial of long-term pegcetacoplan treatment for participants with C3G or primary IC-MPGN



 Key VALIANT inclusion and exclusion criteria and additional inclusion criteria for VALE participants are shown in **Table 1** 

### Table 1. Key inclusion and exclusion criteria for VALIANT and key inclusion criteria for VALE

### **VALIANT**

**VALE** 

**Key inclusion criteria** 

Key inclusion criteria	Key exclusion criteria
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Experienced clinical benefit from pegcetacoplan in the VALIANT trial, per investigator opinion

Must remain on a stable regimen for treatment according to the requirements of the VALIANT trial

• Vaccinated per VALIANT requirements and agreed to receive additional vaccinations recommended by ACIP or other similar local

applicable guidelines for adults or children with complement deficiencies and/or immunocompromising conditions

- Age of ≥18 years or, where approved, 12–17 years weighing
- Diagnosis of primary C3G or IC-MPGN (with or without previous renal transplant)
- Evidence of active renal disease
- For male participants, agreement to use protocol-defined contraception methods for the duration of the study through ≥90 days after the last dose of pegcetacoplan
- For female participants of childbearing potential, a negative pregnancy test and agreement to use protocol-defined contraception methods for the duration of the study through ≥90 days after the last dose of pegcetacoplan
- Willingness and ability to self-administer pegcetacoplan or have a specified caregiver available to administer pegcetacoplan

ACIP, Advisory Committee on Immunization Practices; C3G, C3 glomerulopathy; IC-MPGN, immune-complex membranoproliferative glomerulonephritis

 Vaccination against Streptococcus pneumoniae, Neisseria meningitidis (types A, C, W, Y, and B), and Haemophilus *influenzae* (type B)

Completed the VALIANT trial through Week 52

### Previous exposure to pegcetacoplan

- Evidence of improving renal disease in the 8 weeks prior to screening or during the screening period
- C3G or IC-MPGN secondary to another condition in the opinion of the investigator
- Inability or unwillingness to follow the study protocol
- Evidence of ongoing drug or alcohol abuse or dependence, per investigator opinion
- Presence of a condition that creates an undue risk for the participant or will confound interpretation of the study, per investigator opinion
- For female participants who are breastfeeding or planning to become pregnant, unwillingness to discontinue for the study duration and through at least ≥90 days after the last dose of pegcetacoplan

93% of eligible patients have entered VALE as of June 2024

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METHODS (continued)

Pegcetacoplan dosages were determined based on participant age, with adjustments for body weight in adolescent participants (Table 2)

Pegcetacoplan dosage	
1080 mg twice weekly	
1080 mg twice weekly	
810 mg twice weekly	
648 mg twice weekly	
	1080 mg twice weekly 810 mg twice weekly

• Key primary and secondary efficacy endpoints and the safety endpoint are shown in Table 3

### Table 3. Key outcomes to be assessed in the VALE extension trial

### **Primary efficacy endpoint**

Log-transformed ratio of uPCR over time versus pretreatment baseline

### Secondary efficacy endpoints

- Change from pretreatment in eGFR values over time
- Proportion of participants with a uPCR reduction of ≥50% from the pretreatment value over time
- Proportion with eGFR values that are stable or improved from pretreatment values over time
- Proportion reaching proteinuria of <1 g/day over time</li>
- Change from pretreatment in the FACIT-Fatigue Scale score
- Time to progression to a composite clinical outcome (≥1 of the following: sustained doubling of serum creatinine, progression to chronic kidney disease stage 5 or ESRD, renal transplant, death from renal or cardiovascular disease)

### **Key safety endpoints**

- Incidence and severity of TEAEs and changes from baseline in vital signs, clinical laboratory tests, and ECG results
- CG, electrocardiogram; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy Fatigue; TEAEs, treatment-emergent adverse events; uPCR, urine protein-to-creatinine ratio...

# RESULTS

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Results are not yet available for this ongoing study

Estimated completion: 2027

ACIP, Advisory Committee on Immunization Practices; C3G, C3 glomerulopathy; eGFR, estimated glomerular filtration rate; ESRD, end-stage renal disease; FACIT-Fatigue, Functional Assessment of Chronic Illness Therapy – Fatigue Scale; IC-MPGN, immune-complex membranoproliferative glomerulonephritis; MAC, membrane attack complex; MASP, MBL-associated serine protease; MBL, mannose-binding lectin; SC, subcutaneous; TEAEs, treatment-emergent adverse events; uPCR, urine protein-to-creatinine ratio.

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