

# CAPTIVATE Trial Design: A Pivotal Phase 3 Study of Claseprubart in Chronic Inflammatory Demyelinating Polyneuropathy

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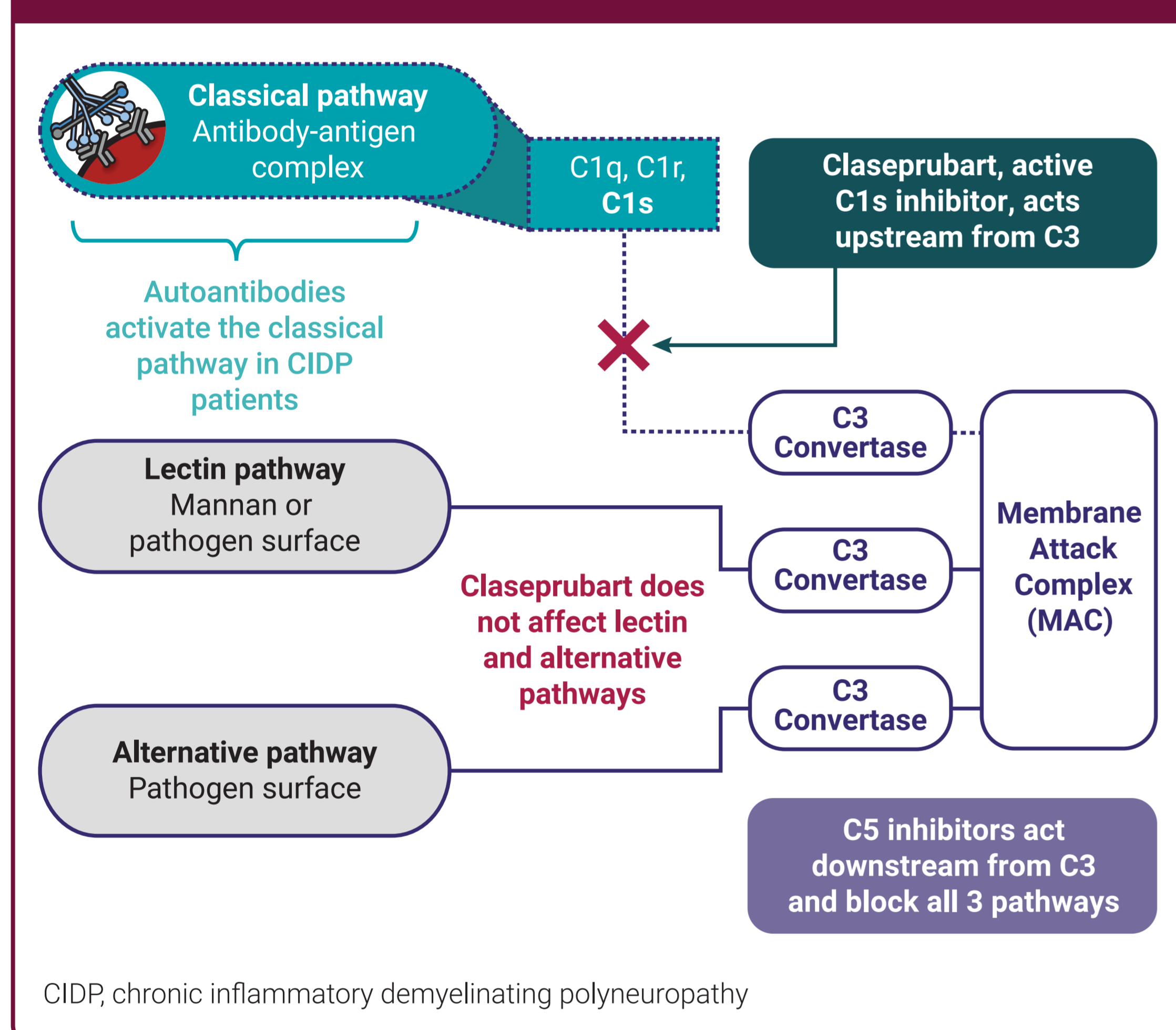
## MAIN FINDINGS

- CAPTIVATE is an innovative, rigorous phase 3 study evaluating claseprubart, an active C1s inhibitor administered as a convenient subcutaneous biweekly injection, in CIDP.
- CAPTIVATE features a relapse-prevention design, commonly used in studies of interventions in CIDP.
- CAPTIVATE prioritizes patient safety, avoids complete washout of standard of care, minimizes exposure to ineffective therapy, and provides continued access as part of an optional open-label extension.

## INTRODUCTION

- Chronic inflammatory demyelinating polyneuropathy (CIDP) is a chronic, progressive, acquired autoimmune disease targeting peripheral nerves, resulting in demyelination.
- Current standard of care for CIDP includes intravenous (IV) or subcutaneous (SC) immunoglobulins (Ig), corticosteroids, and plasmapheresis, all of which are associated with limited long-term efficacy or burdensome administration.<sup>1</sup>
- Several complement inhibitors are in development for the treatment of CIDP and increasing evidence suggests that activation of the classical complement pathway (CCP) plays a crucial role in the pathophysiology of CIDP.<sup>2</sup>
- Claseprubart (DNTH103) is an investigational, clinical-stage, potent monoclonal antibody engineered to selectively target the CCP by inhibiting the active form of the C1s protein, a clinically validated complement target (Figure 1). Claseprubart is designed to enable a more convenient SC, infrequently dosed, self-administered injection.

Figure 1. Claseprubart Mechanism of Action.



- In the phase 2 MaGic Study, SC Q2W claseprubart demonstrated clinically meaningful improvements in patients with generalized myasthenia gravis with a well-tolerated safety profile,<sup>3</sup> supporting the therapeutic potential of active C1s blockade in complement-mediated autoimmune neurological disorders such as CIDP.
- Here, we describe the design of the ongoing CAPTIVATE study, evaluating the efficacy and safety of claseprubart in patients with CIDP.

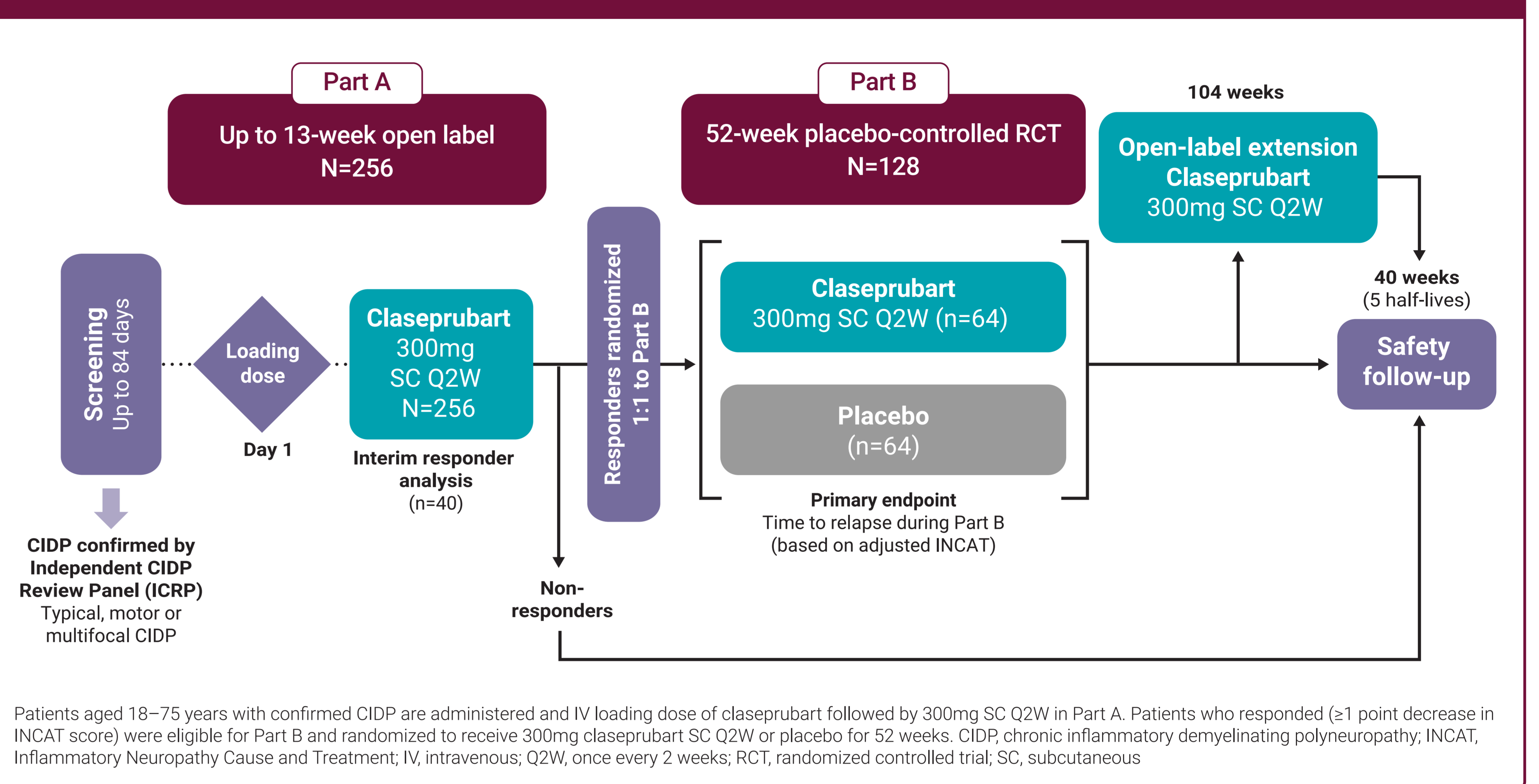
## STUDY DESIGN AND DOSING

- CAPTIVATE is a global, multicenter, randomized, double-blind, placebo-controlled phase 3 study (NCT06858579) that is evaluating claseprubart in a broad population of adults with a diagnosis of CIDP.

### Part A Design

- Part A is a 13-week open-label period in which patients are administered SC 300mg claseprubart Q2W for 13 weeks following an IV loading dose (Figure 2).
  - Beginning at Week 5, patients will be assessed for a response, defined as a  $\geq 1$  point decrease in the adjusted INCAT (Inflammatory Neuropathy Cause and Treatment) score compared to Part A baseline. If the response is confirmed at the next consecutive visit, the participant will enter Part B (if the patient continues to meet the definition for response at Day 1 Part B). Non-responders will enter the safety follow-up.
  - It is anticipated that approximately 256 participants will be enrolled into Part A. An interim responder analysis was planned with the first 40 patients completing Part A.

Figure 2. CAPTIVATE Study Design.



### Part B Design

- Part B is a randomized, placebo-controlled, double-blind treatment period of up to 52 weeks for participants who respond to claseprubart in Part A.
  - Approximately 128 participants identified as responders in Part A will be randomized 1:1 in Part B to receive 300mg claseprubart or placebo given SC once every 2 weeks.

### Open-Label Extension and Safety Follow-up

- Patients who complete Part B are permitted to enter a 104-week open-label extension (OLE). Additionally, patients who have a relapse in Part B (increase of  $\geq 1$  point in adjusted INCAT score) are also eligible for the OLE, including those who received Ig, corticosteroid, or PLEX rescue therapy.
- All patients are eligible for a 40-week safety follow-up period following their last dose of claseprubart or placebo. Patients can resume standard of care treatment for CIDP per the investigator's judgment.

### Study Population

- Adults aged 18–75 years (inclusive) with a diagnosis of CIDP or possible CIDP per the 2021 EAN/PNS guidelines.<sup>4</sup> Participants must have either typical, motor or multifocal CIDP.
- At screening, patients must have a CIDP Disease Activity Status (CDAS) score  $\geq 3$ , and INCAT score between 2 and 9 (inclusive) and be neurologically stable.
- Patients on prior standard of care (SoC) therapy were eligible if they are SoC-refractory (worsening or inadequate response to SoC) or SoC-treated (current or past treatment with SoC). If applicable, oral corticosteroids (after tapering) and allowed immunosuppressants are continued in Parts A and B. Treatment-naïve patients are also eligible.
- For patients on IV or SC Ig, the last dose for both must occur 1 week prior to Day 1 of Part A. Patients who received complement inhibitors or anti-CD20 treatments within the previous 6 months are not eligible.

## References

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### Assessments

- The primary objective of CAPTIVATE is to evaluate the efficacy of claseprubart compared to placebo, assessed as the time from first dose in Part B to relapse ( $\geq 1$  point increase in adjusted INCAT) (Table 1).
- Safety and tolerability will be assessed throughout the study and OLE.

Table 1. Assessments and Endpoints

Efficacy assessments	
<b>Primary</b>	• Evaluate efficacy of claseprubart compared to placebo, assessed as the time from first dose in Part B to relapse ( $\geq 1$ point increase in adjusted INCAT)
<b>Secondary</b>	• Time from first dose in Part B to a decrease from Part B baseline of $\geq 4$ points (centile metric) in I-RODS score during Part B • Time from first dose in Part B to a decrease from Part B baseline of $\geq 8$ kPa in grip strength in the dominant hand during Part B • Health-related quality of life outcomes
Other assessments	
	• Safety and tolerability, including adverse events • Pharmacokinetics and pharmacodynamics • Immunogenicity of claseprubart • Assess effect of claseprubart on biomarkers of disease activity
INCAT, Inflammatory Neuropathy Cause and Treatment; I-RODS, Rasch-built Overall Disability Scale	

## INTERIM RESPONDER ANALYSIS

- CAPTIVATE was launched in 2024 and is actively enrolling participants in North America, South America, Europe, and Asia.
  - In March 2026, a planned interim responder analysis was conducted on currently enrolled patients in Part A.<sup>5</sup> The target was a response rate of 50% or greater (i.e.,  $\geq 20$  confirmed responders out of first 40 participants to complete Part A) based on precedent set with aC1s inhibition.
  - The decision to continue to Part B of the study was reached early, after 20 confirmed responders were achieved with less than 40 planned participants completing open-label Part A of the trial.

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## Disclosures

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