

CAPTIVATE Interim Analysis: A Pivotal Phase 3 Study of Claseprubart in Chronic Inflammatory Demyelinating Polyneuropathy

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MAIN FINDINGS

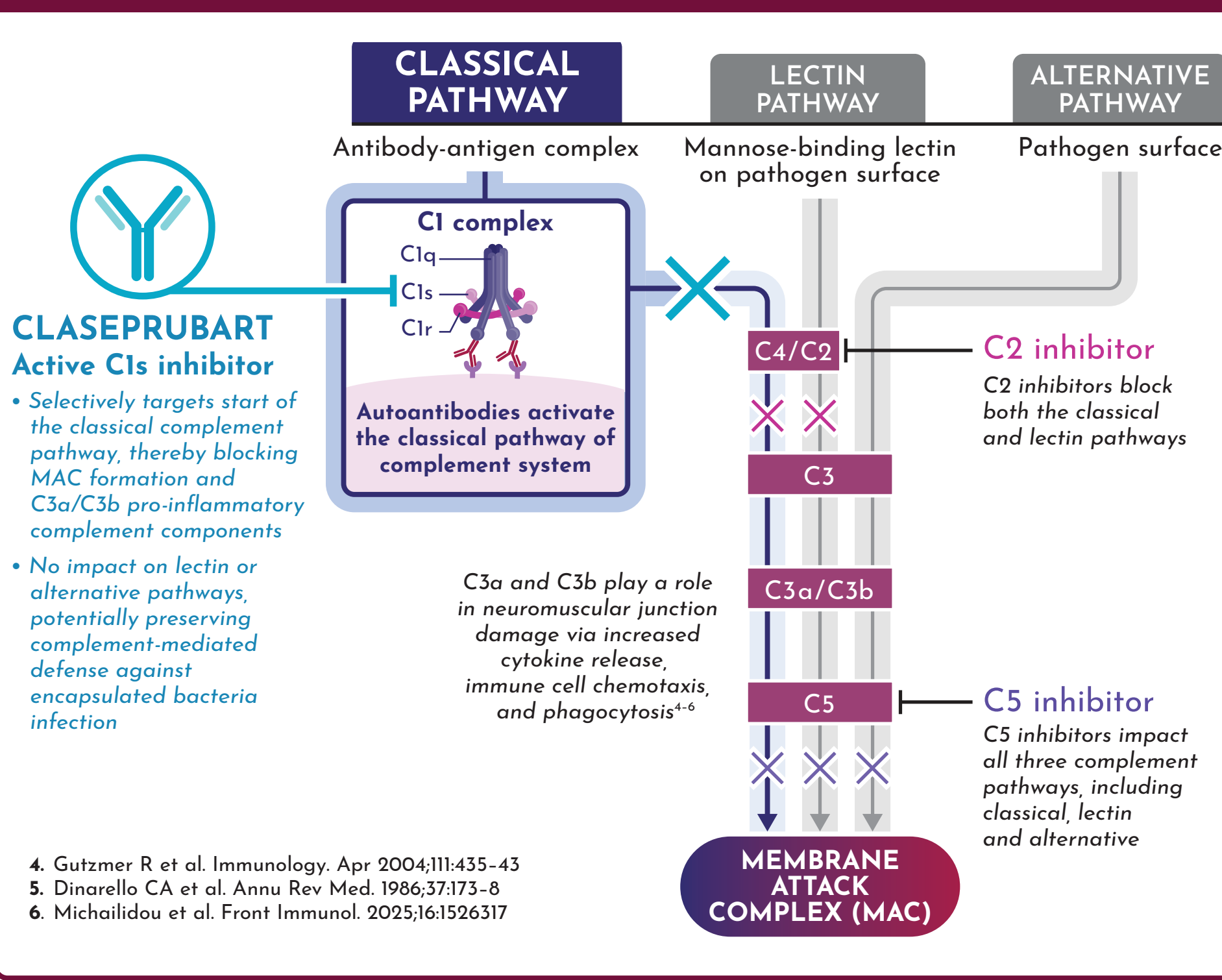
- CAPTIVATE is enrolling a broad, globally diverse CIDP patient population spanning disease severity and prior treatment experience
- 75% of the futility cohort achieved at least a 1-point confirmed INCAT response above clinical baseline on maintenance therapy with a meaningful mean improvement of 1.6

- The INCAT response was supported by meaningful mean improvement in every secondary efficacy metric
- Safety profile remains benign and consistent with claseprubart experience in other indications
- The interim CAPTIVATE findings support the therapeutic potential of classical pathway inhibition and continued evaluation of claseprubart in CIDP

INTRODUCTION

- Chronic inflammatory demyelinating polyneuropathy (CIDP) is a chronic, progressive, acquired autoimmune disease targeting peripheral nerves, resulting in demyelination.
- The current standard of care for CIDP includes intravenous (IV) or subcutaneous (SC) immunoglobulins (Ig), corticosteroids, and plasmapheresis (PLEX), all of which are associated with limited long-term efficacy or burdensome administration.¹
- Several complement inhibitors are in development for the treatment of CIDP and increasing evidence suggests that activation of the classical complement pathway plays a crucial role in the pathophysiology of CIDP.²
- Claseprubart (DNTH103) is an investigational, clinical stage, potent monoclonal antibody engineered to selectively target the classical pathway by inhibiting the active form of the C1s protein (**Figure 1**). Claseprubart is designed to enable a more convenient SC, infrequently dosed, self-administered injection.
- Targeting active C1s in patients with CIDP is supported by positive proof-of-concept results with riliprubart (an active C1s inhibitor) across broad patient groups.³
- Here, we present an interim analysis of the CAPTIVATE study, a global, multicenter, randomized, double-blind, placebo-controlled phase 3 study (NCT06858579) to evaluate the efficacy and safety of claseprubart in a broad population of adults with CIDP.

Figure 1. Claseprubart Mechanism of Action.



OBJECTIVE

- To assess interim efficacy and safety of claseprubart in patients in Part A of the CAPTIVATE study.

METHODS

Study Population

- Adults aged 18–75 years (inclusive) with a diagnosis of CIDP or possible CIDP per the 2021 EAN/PNS guidelines.⁷ Participants must have typical, motor or multifocal CIDP. At screening, patients must have a CIDP Disease Activity Status (CDAS) score ≥ 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.

Part A Design and Interim Analysis

- 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 ≥ 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.
- An interim futility analysis was conducted on the first 40 patients who completed Part A with evaluable efficacy.

Figure 2. CAPTIVATE Study Design.

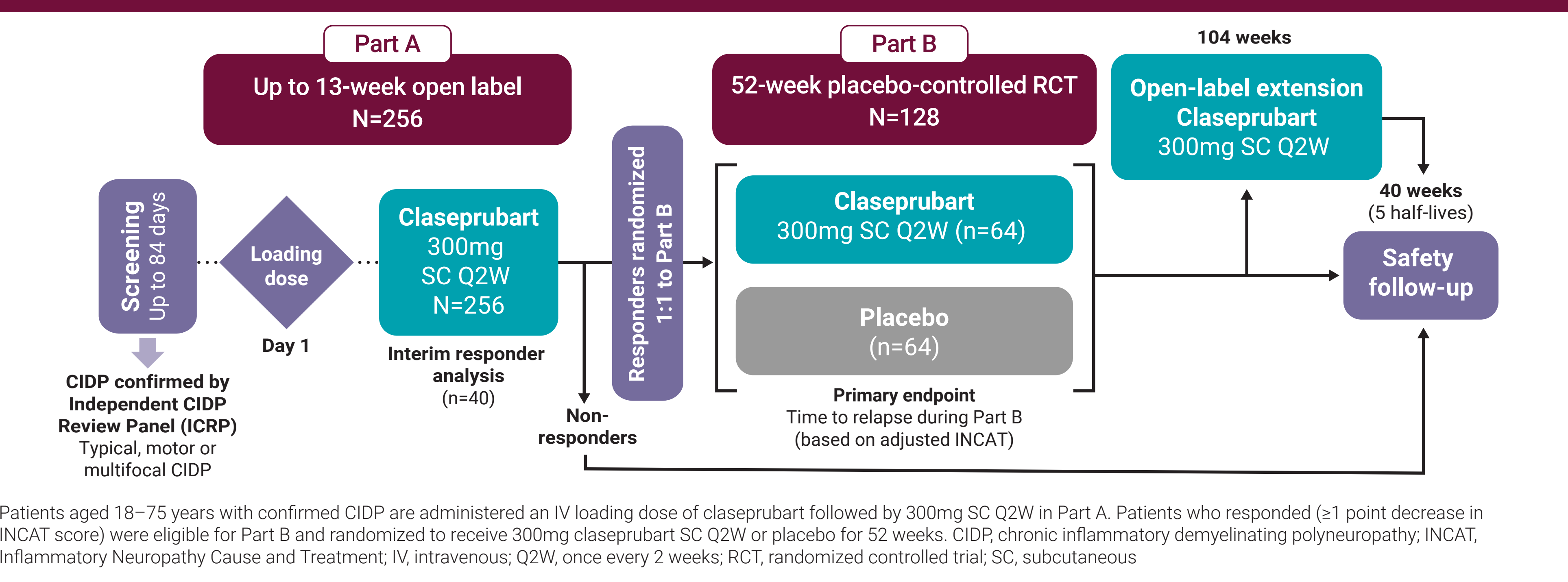
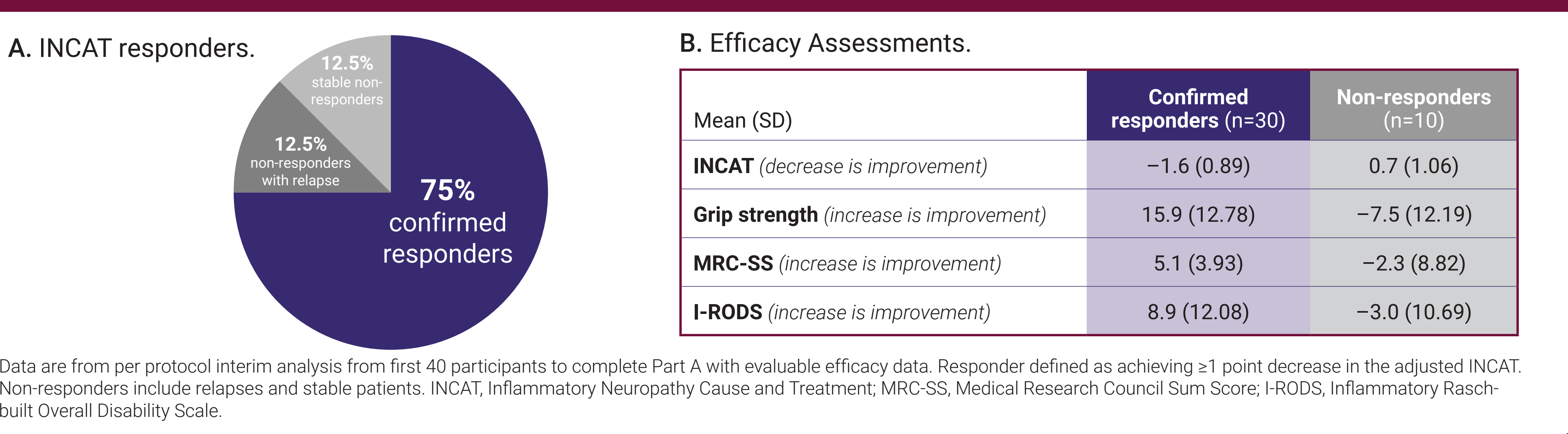


Figure 3. Part A Interim Efficacy Analysis.



Part B: Placebo-controlled, Relapse-Prevention 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.
- Responders from Part A will be randomized 1:1 in Part B to receive 300mg claseprubart or placebo given SC once every 2 weeks.
- 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 (≥ 1 point increase in adjusted INCAT).
- Other efficacy assessments include time to a decrease of ≥ 4 points in I-RODS score, time to a decrease in ≥ 8 kPa in grip strength, and health-related quality of life outcomes.
- 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 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.

Interim Responder Analysis (Part A)

Baseline Demographics

- The pre-planned Part A interim analysis included the first 40 claseprubart-treated patients with evaluable efficacy data.
- Most patients presented with typical CIDP with a mean (SD) time from diagnosis of 4.2 (6.1) years and were receiving immunoglobulins or oral corticosteroids at study entry (**Table 1**).

Interim Efficacy Analysis

- Seventy-five percent (n=30) of the first 40 SC Q2W 300mg claseprubart-treated patients in Part A were confirmed responders (≥ 1 point decrease in the adjusted INCAT) (**Figure 3A**). Of the 10 non-responders, five had stable CIDP and five had a relapse.
- Confirmed responders also demonstrated clinically-meaningful improvements in grip strength, MRC-SS, and I-RODS after 13 weeks of Q2W claseprubart treatment (**Figure 3B**).

Interim Safety Analysis

- Claseprubart was generally well-tolerated. All but one adverse event (AE; unrelated grade 3) were mild or moderate in severity with no treatment-related or serious infections, no related serious AEs, or discontinuations due to safety (**Table 2**).
- One grade 3 serious AE of ureterolithiasis (not treatment-related) was reported in a patient with a history of ureterolithiasis prior to enrollment. The patient continued in the study.

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