Two Phase 3 Trial Designs Evaluating Riliprubart, a C1s-Complement Inhibitor, in CIDP

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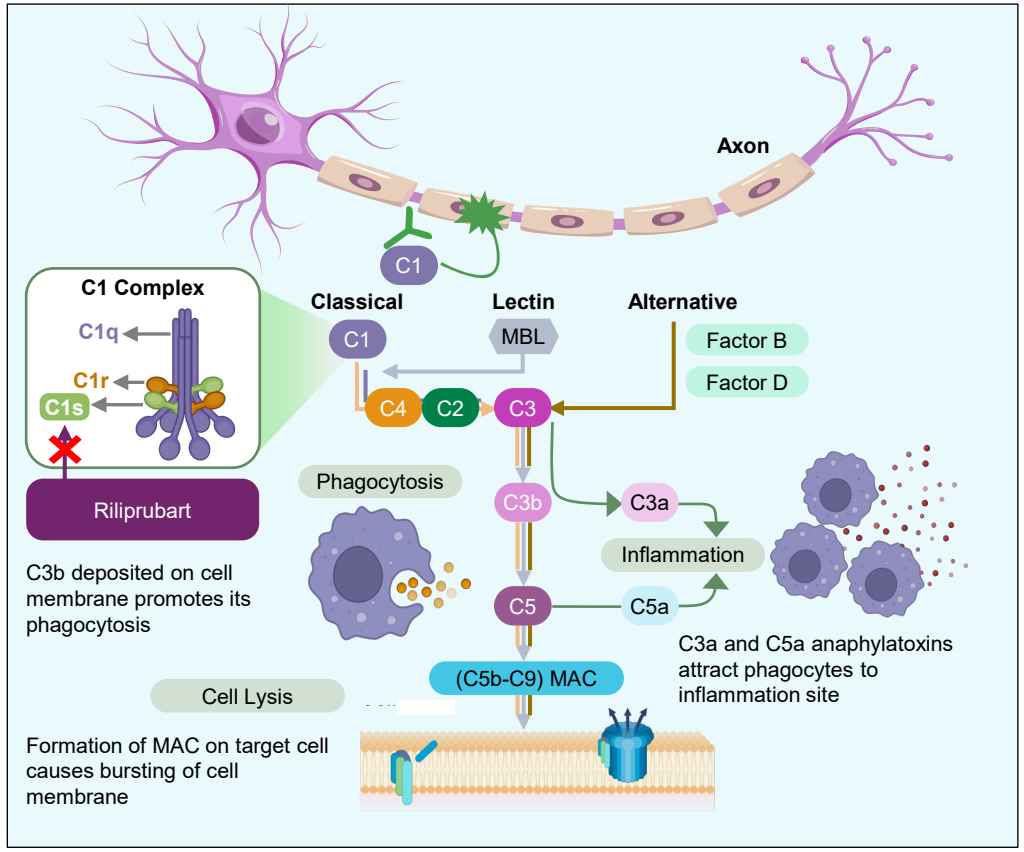
Riliprubart Targets Activated C1s in the Classical Complement Pathway

Figure 1. Riliprubart targets activated C1s in the classical complement pathway



Current SoC therapies (immunoglobulins/corticosteroids) are often unable to address the needs of people living with CIDP[1]

Riliprubart is a first-in-class, humanized IgG4 monoclonal antibody that selectively inhibits activated C1s in the classical complement pathway[2,3] (Figure 1)

In an ongoing open-label, Phase 2 trial with 48 SoC-treated and 18 SoC-refractory participants (NCT04658472), riliprubart demonstrated encouraging efficacy and favorable safety[4]:

- 87% (42/48) SoC-treated participants improved or remained stable after switching from SoC to riliprubart (52% improved). 50% (9/18) SoC-refractory participants improved on riliprubart
- Strong inhibition of complement activity by riliprubart reduced NfL levels, which may be associated with less neuroaxonal damage in CIDP[4]

These data support the development of riliprubart in two different Phase 3 trials:

- **MOBILIZE** (NCT06290128) includes **participants with failure or inadequate response to SoC treatments (SoC-refractory)**
- **VITALIZE** (NCT06290141) includes participants treated with **IVIg with residual disability**

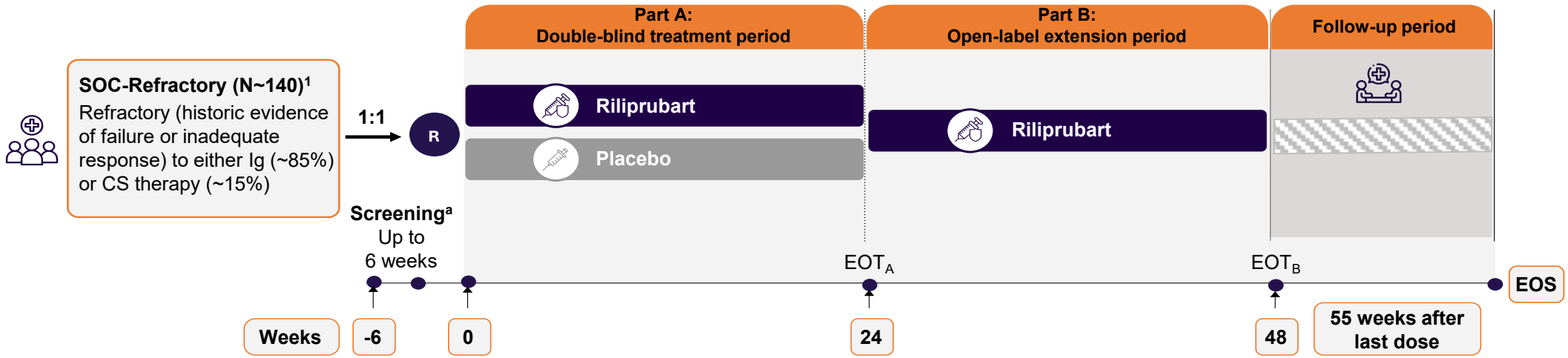
Objective: To describe the designs of two Phase 3 trials, **MOBILIZE** and **VITALIZE**

1. Cocito, et al. *Eur J Neurol*. 2010;17(2):289-94. 2. Gorson, et al. *J Peripheral Nervous System*. 2010;15(4):326-333. 3. Bus, et al. *J Neurol*. 2022;269(2):945-955. 4. Querol, et al. Presented at the Peripheral Nerve Society (PNS) Annual Meeting 2024, June 22–25, Montréal, Canada. C1, complement component 1, s subcomponent; CIDP, chronic inflammatory demyelinating polyneuropathy; IgG4, immunoglobulin G4; MAC, membrane attack complex; MBL, mannose-binding lectin; NfL, neurofilament light chain; SoC, standard of care.

MOBILIZE Trial: Targeting Patients with Refractory CIDP – Study Design and Endpoints

Mobilize Clinical Trial

- Global, multicentre, randomized, double-blind Phase 3 trial (NCT06290128) in **SoC-refractory participants** with CIDP
- Eligible participants will be randomized (1:1) to receive riliprubart or placebo



Primary endpoint

- Percentage of **SoC-refractory** participants achieving ≥ 1 point decrease in adjusted INCAT disability score at Week 24 (Part A) and Week 48 (Part B), compared to baseline

Key secondary endpoints

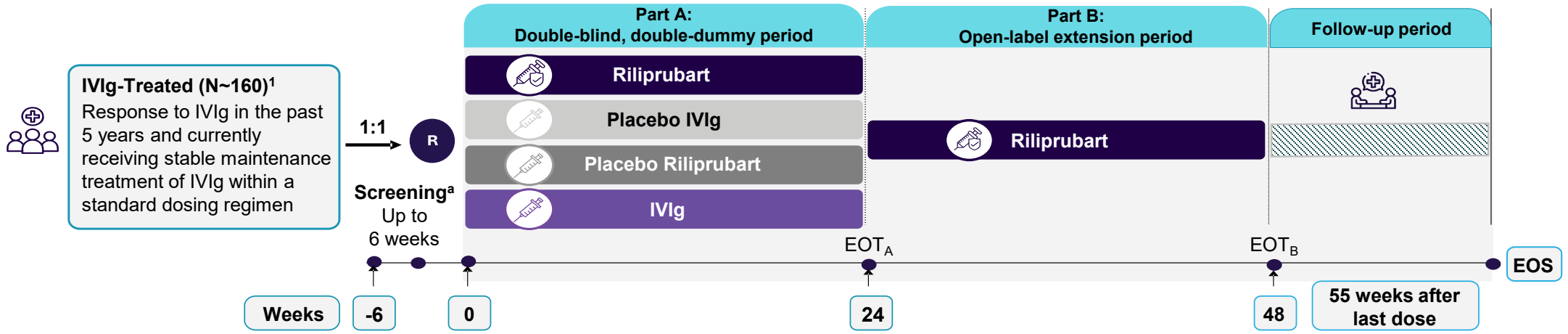
- Additional efficacy at Week 24 (Part A) and Week 48 (Part B) in the following domains:
  - Functional disability: I-RODS, INCAT
  - Muscle impairment: Grip strength, MRC-SS
  - Quality of life: EQ-5D-5L
  - Fatigue: R-FSS
- Safety and Immunogenicity: TEAEs, ADA at Week 24 (Part A) and during open-label treatment period (Part B)

*Sample sizes will be re-estimated based on a pre-defined interim analysis during Part A. [a]For patients who had not received required vaccinations prior to study, vaccinations were initiated on Day 42, or as early as possible during the screening period, but no later than 14 days before the first dose of riliprubart. 1. ClinicalTrials.gov. NCT06290128. A Study to Test the Effects and Safety of Riliprubart in People With Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) for Which the Usual Treatments do Not Work (MOBILIZE). ADA, anti-drug antibodies; CIDP, chronic inflammatory demyelinating polyneuropathy; CS, corticosteroid; EoS, end-of-study; EoT$_{A/B}$, end-of-treatment Part A/B; EQ-5D-5L, EuroQol 5 Dimension 5-Level health scale; Ig, immunoglobulin; INCAT, Inflammatory Neuropathy Cause and Treatment; I-RODS, Inflammatory Rasch-built Overall Disability Scale; MRC-SS, Medical Research Council - Sum Score; R-FSS, Rasch-built Modified Fatigue Severity Scale; SoC, standard-of-care; TEAE, treatment-emergent adverse events.

VITALIZE Trial: Targeting IVIg-Treated CIDP Patients with Residual Disability - Study Design and Endpoints

Vitalize Clinical Trial

- Global, multicentre, randomized, double-blind Phase 3 trial (NCT06290141) in **IVIg-treated participants** with residual disability
- Eligible participants will be randomized (1:1) to receive riliprubart plus IVIg-placebo or IVIg plus riliprubart-placebo §



Primary endpoint

- Percentage of **IVIg-treated** participants achieving ≥ 1 point decrease in adjusted INCAT disability score at Week 24 (Part A) and Week 48 (Part B) versus baseline relative to IVIg continuation

Key secondary endpoints

- Additional efficacy at Week 24 (Part A) and Week 48 (Part B) in the following domains:
  - Functional disability: I-RODS, INCAT
  - Muscle impairment: Grip strength, MRC-SS
  - Quality of life: EQ-5D-5L
  - Fatigue: R-FSS
- Safety and Immunogenicity: TEAEs, ADA at Week 24 (Part A) and during open-label treatment period (Part B)

*Sample sizes will be re-estimated based on a pre-defined interim analysis during Part A. [a]For patients who had not received required vaccinations prior to study, vaccinations were initiated on Day 42, or as early as possible during the screening period, but no later than 14 days before the first dose of riliprubart. § There is no IVIg wash-out (withdrawal) period. 1. ClinicalTrials.gov. NCT06290141. A Study to Test the Efficacy and Safety of Riliprubart Against the Usual Treatment of Intravenous Immunoglobulin (IVIg) in People With Chronic Inflammatory Demyelinating Polyneuropathy (CIDP) (VITALIZE). ADA, anti-drug antibodies; CIDP, chronic inflammatory demyelinating polyneuropathy; EoS, end-of-study; EoT$_{A/B}$, end-of-treatment Part A/B; EQ-5D-5L, EuroQol 5 Dimension 5-Level health scale; INCAT, Inflammatory Neuropathy Cause and Treatment; I-RODS, Inflammatory Rasch-built Overall Disability Scale; IVIg, intravenous immunoglobulin; MRC-SS, Medical Research Council - Sum Score; R-FSS, Rasch-built Modified Fatigue Severity Scale; SoC, standard-of-care; TEAE, treatment-emergent adverse events.

Study Population

Key Inclusion Criteria

Both Trials

- Age ≥18 years old
- Diagnosis of CIDP or possible CIDP (typical, motor, or multifocal) based on 2021 PNS/EAN guidelines (Adjudication Committee)
- Active disease, defined by a CDAS of ≥2 points at screening

Mobilize Clinical Trial

- **Historic evidence of failure or inadequate response (SoC- refractory) to either Ig or corticosteroid therapy***
- INCAT score of 2–9 (2 should be exclusively from the legs)

Vitalize Clinical Trial

- **Response to IVIg in the past 5 years and currently receiving stable maintenance treatment of IVIg within a standard dosing regimen****
- Residual disability, defined as INCAT disability score of 2–9 (2 should be exclusively from the legs)

Key Exclusion Criteria

Both Trials

- Poorly controlled diabetes (HbA1c >7%)
- Recent serious infection with hospitalization
- Clinical diagnosis of systemic lupus erythematosus
- Treatment with B-cell-depleting agents such as rituximab and highly immunosuppressive/chemotherapeutic medications with sustained effects

Mobilize Clinical Trial

- **Treatment with Igs (IVIg or SCIg) or plasma exchange within 8 weeks prior to screening**
- Treatment with highly immunosuppressive/chemotherapeutic medications within 6 months prior to dosing (azathioprine, cyclosporine, or mycophenolate mofetil are allowed)

Vitalize Clinical Trial

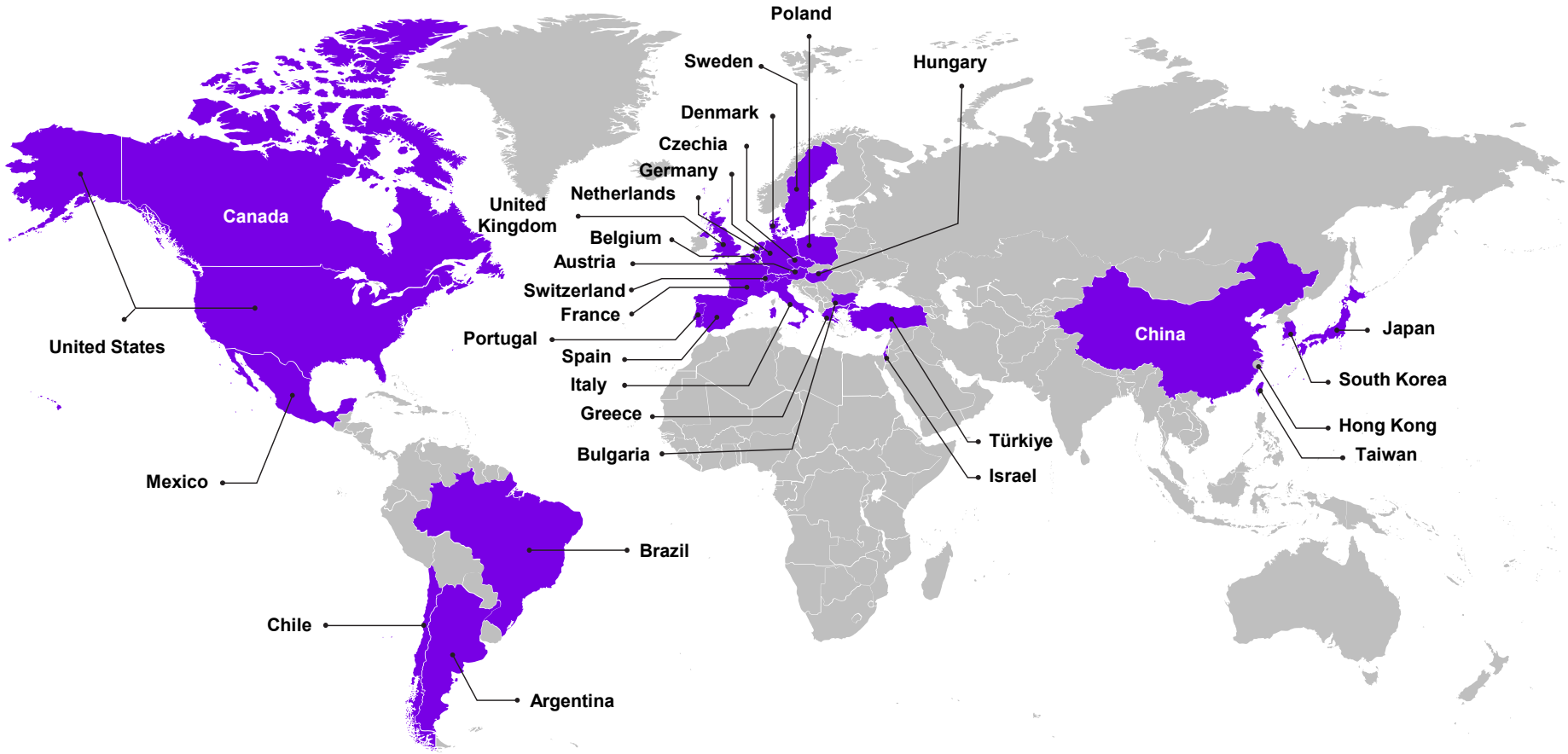
- Contraindication related to the administration of immunoglobulins
- Treatment with plasma exchange within the 8 weeks prior to screening
- Treatment within 3 months prior to dosing with immunosuppressive/immunomodulator medication or corticosteroids

*See ClinicalTrials.gov. NCT06290128 for more details on these criteria. **See ClinicalTrials.gov. NCT06290141 for more details on these criteria. CDAS, CIDP disease activity score; CIDP, chronic inflammatory demyelinating poly neuropathy; EAN, European Academy of Neurology; INCAT, Inflammatory Neuropathy Cause and Treatment; IVIg, intravenous immunoglobulin; PNS, peripheral nerve society; SC, subcutaneous; SoC, standard-of-care.

Planned Trial Sites

World map depicting planned enrollment for both MOBILIZE and VITALIZE trials

Both trials are expected to begin enrollment in 2024 across 28 countries worldwide



Conclusions

The MOBILIZE and VITALIZE Phase 3 trials aim to confirm the efficacy and safety of riliprubart, addressing key unmet needs in people living with CIDP who have experienced an inadequate response or failure to at least one treatment (SoC-refractory), and those with residual disability (SoC-treated) despite SoC treatment

MOBILIZE is the first global controlled clinical trial for people living with CIDP with failure or inadequate response to SoC treatments

VITALIZE is the first clinical trial in CIDP evaluating a new therapy versus an active comparator (IVIg)

These Phase 3 trials will also assess the effects of riliprubart on biomarkers related to complement and neuroaxonal damage, safety, and quality of life

CIDP, chronic inflammatory demyelinating poly neuropathy; IVIg, intravenous immunoglobulin; SoC, standard-of-care.