An Open-Label Study Evaluating the Pharmacokinetics, Pharmacodynamics, Efficacy, and Safety of Tanruprubart (ANX005) Single Dose in Participants from North America and Europe with Guillain-Barré Syndrome

Shafeeq Ladha[1], Rafid Mustafa[2], Thomas Ragole[3], Kavita Grover[4], Glenn Morrison[5], Ping Lin[5], Henk-André Kroon[5], Jeffrey A. Allen[6]

[1]Barrow Neurological Institute, Phoenix, AZ; [2]Mayo Clinic College of Medicine & Science, Rochester, MN; [3]University of Colorado Anschutz Medical Campus, Aurora, CO; [4]Henry Ford Hospital and Wayne State University, Detroit, MI; [5]Annexon Biosciences, Brisbane, CA; [6]University of Minnesota, Minneapolis, MN

SCAN ME
For more information on GBS-FORWARD

Introduction

- Guillain-Barré syndrome (GBS) is a rare, acute-onset, life-threatening neuromuscular condition that occurs worldwide and requires immediate intervention.[1]
- Tanruprubart (ANX005), a monoclonal antibody, is a targeted immunotherapy that selectively and fully blocks C1q, the initiating molecule of the classical complement pathway, thus providing rapid and complete inhibition of classical complement activity to halt neuroinflammation and nerve damage.[2,3]
- The primary goal of this open-label study (GBS-FORWARD) is to characterise the pharmacokinetics (PK), pharmacodynamics (PD), efficacy, and safety of tanruprubart in participants with GBS in North America and Europe (**Figure 1**). Clinicaltrials.gov: NCT07020819.

Previous findings

GBS-02

- GBS-02 (NCT04701164) was a Phase 3, multi-center, double-blind, placebo-controlled study of tanruprubart in patients with GBS in Bangladesh and the Phillipines.[4]
- This study met the primary endpoint and demonstrated that patients treated with tanruprubart 30 mg/kg had a 2.4-fold higher likelihood of being in a better state of health relative to placebo at Week 8 on the GBS-disability scale (GBS-DS; **Figure 2**), alongside significantly reducing the duration of ventilation over time (p=0.0356)[4].
- Tanruprubart 30 mg/kg provided rapid recovery of muscle strength and motor function, with >10-point improvement in muscle strength based on the Medical Research Council sumscore (MRCss: **Figure 3**), and 87% of participants treated with tanruprubart achieving a ≥1-point increase in MRCss from baseline, versus 46% with placebo (p<0.0001).
- GBS-DS and MRCss were significantly improved in a broad spectrum of patients, including those with axonal (acute motor axonal neuropathy; AMAN) or demyelinating (acute inflammatory demyelinating polyneuropathy) nerve conduction study classification.[5]
- In study GBS-02, tanruprubart was well tolerated, and most adverse events were mild to moderate in severity, due to GBS and not considered related to study drug. Rash was the most common infusion-related reaction; cases were mostly mild to moderate and resolved without sequalae.[4]

Figure 2. GBS-02 Primary endpoint: Change in GBS-DS at Week 8

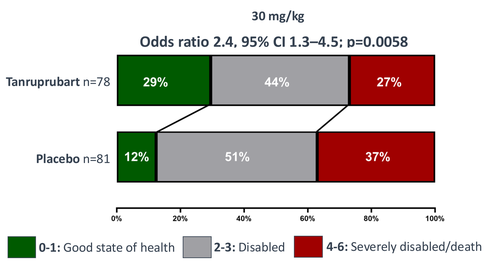
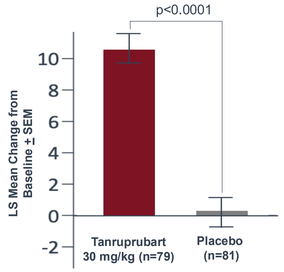
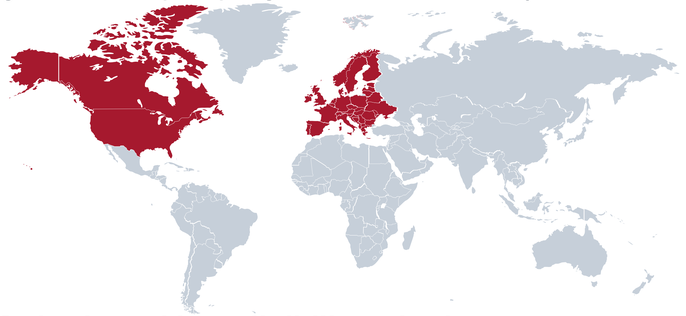


Figure 3: Recovery in muscle strength (MRCss) at Week 1



LS: Mean point improvement relative to placebo

Figure 1. Countries participating in the GBS-FORWARD study



Methods and key eligibility criteria

- GBS-FORWARD is a multi-center, open-label, single-arm, PK, PD, efficacy, and safety study of a single intravenous (IV) administration of tanruprubart 30 mg/kg in participants recently diagnosed with GBS.
- 30 participants between the ages of 12 and 85 will be recruited.
- All participants will receive best supportive care.
- IV immunoglobulin or plasma exchange may be administered in the event of clinical deterioration judged by the investigator and considering these criteria:
  - An unanticipated development of respiratory failure
  - A ≥5 point worsening from baseline in MRCss
  - A worsening in GBS-DS ≥ 1 point from prior visit.

Inclusion criteria

- Diagnosis of GBS according to the National Institute of Neurological Disorders and Stroke Diagnostic Criteria for GBS, including AMAN, or acute motor and sensory axonal neuropathy.
- Onset of GBS-related weakness ≤10 days before start of infusion on Day 1.
- GBS-DS score of 3, 4, or 5 at screening and before start of infusion on Day 1.

Exclusion criteria

- Previous or intended treatment with either IVIG or plasma exchange for GBS.
- Diagnosis of a variant of GBS, including Miller Fisher syndrome, Bickerstaff's encephalitis, and overlap syndromes.

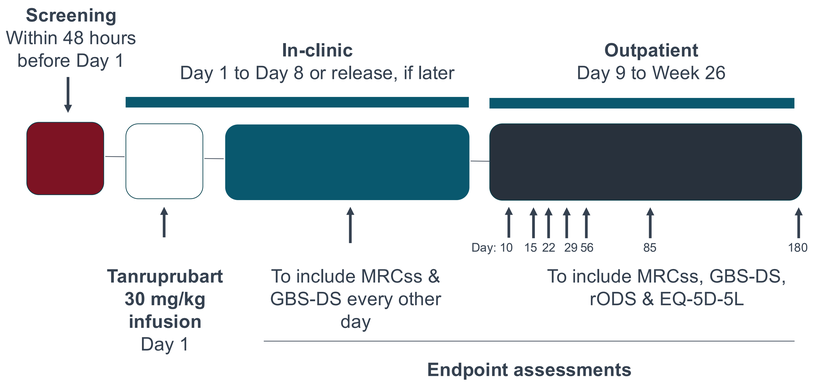
Study design

- Patients who meet the eligibility criteria during screening will be enrolled and receive an IV infusion of tanruprubart (30 mg/kg).
- Participants will remain in the clinic for the completion of study assessments either until Day 8 or until they are cleared to be released, depending on which occurs later. Participants will return for follow-up visits until the end of the study on Week 26 (**Figure 4**).
- The study is powered to compare MRCss at Week 1 with an IVIg-treated, external control group from the International GBS Outcome Study database.[6]

Outcome measures

- In addition to PK and PD analyses, the efficacy, safety and tolerability of tanruprubart will also be assessed in this cohort.
- Efficacy and participant quality of life will be assessed using the MRCss, GBS-DS scale, Rasch-built Overall Disability Scale (rODS) and EuroQol five-dimensional, five-level questionnaire (EQ-5D-5L).

Figure 4. GBS-FORWARD Study Design



CONCLUSIONS

- In study GBS-02, C1q inhibition with tanruprubart significantly improved the odds of being in a better state of health in participants from Bangladesh and the Philippines[4].
- This open-label study (GBS-FORWARD) will recruit participants with recently diagnosed GBS in North America and Europe, to confirm the generalizability of previous study findings.
- This study aims to add to the current body of evidence demonstrating the efficacy, safety and tolerability of tanruprubart (30 mg/kg) in patients with GBS.

References
1.Willison HJ, et al. *Lancet*. 2016;388:717–27. 2. Lansita JA, et al. *Int J Toxicol*. 2017;36:449–62. 3. Suri P. et al. *Neurology*. 2022;98(18 Suppl):3867. 4. Kroon H-A, et al. Presented at the Neuromuscular Study Group Annual Scientific Meeting, 20–22 September 2022, Tarrytown, NY, USA. 5. Kroon H-A et al. Poster presented at the Peripheral Nerve Society Annual Meeting, 17–20 May 2025, Edinburgh, UK. 6. Leonhard SE et al. *Neurology*. 2022;99:e1299-e1313.

Acknowledgments
The study was sponsored by Annexon Biosciences (Brisbane, CA, USA). Medical writing and editing assistance were provided by Envision Ignite, an Envision Medical Communications agency, a part of Envision Pharma Group and were funded by Annexon Biosciences.

Disclosures
TR: Received grants or contracts from Alexion and argenx for investigator-initiated research projects, received payment as a panellist for the 2024 American Journal of Managed Care – Institute for Value-Based Medicine, provided support for a myasthenia gravis scientific advisory committee for Alexion, provided support for a Guillain-Barré scientific advisory committee for Annexon, and received payment to participate on advisory boards for Alexion and UCB. GM, H-AK: Employment with and shareholder of Annexon Biosciences. PL: Employee of Annexon Biosciences at the time of the study. JA: Honoraria, consultation fees, advisory board: Alexion, Almylam, Akcea therapeutics, argenx SE, Annexon, Dianthus, CSL Behring, Hansa, Grifols, Immunovant, Immunopharm, ImmunoAbs, Sanofi, Johnson & Johnson, Pfizer, Takeda. SL, RM, KG: No relevant disclosures.

For additional information, please reach out to Glenn Morrison: gmorrison@annexonbio.com