GBS-02: A Phase 3 Study to Evaluate Efficacy, Safety, Pharmacokinetics, and Pharmacodynamics of ANX005 in Patients with Guillain-Barré Syndrome (GBS)

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PRESENTED AT THE AMERICAN ACADEMY OF NEUROLOGY ANNUAL MEETING | APRIL 5-9, 2025, SAN DIEGO, CA

Data originally presented at the 2024 Peripheral Nerve Society Annual Scientific Meeting, June 22-25, 2024, Montreal, QC

Disclosures: JA: Honoraria, consultation fees, advisory board: Alexion, Alnylam, Akcea therapeutics, Argenx SE, Annexon, Dianthus, CSL Behring, Hansa, Grifols, Immunovant, Immunopharm, ImmunoAbs, Sanofi, Johnson & Johnson, Pfizer, Takeda HAK: employee and shareholder of Annexon Bioscience; ZI: research funding from Fogarty International Center, National Institute of Neurological Disorders and Stroke of the National Institutes of Health, USA, and Annexon Biosciences; PC: employee of Annexon Biosciences; BH: employee of Annexon Biosciences; EH: former employee and shareholder of Annexon Biosciences; PL: employee and shareholder of Annexon Biosciences; GM: employee and shareholder of Annexon Biosciences; JN: consultancy/advisory role with Annexon Biosciences; KAKA: no relevant disclosures; DRA: employee of Annexon Biosciences; TY: employee of Annexon Biosciences and holds equity ownership in Annexon Biosciences; QDM: consultancy/advisory role with Annexon Biosciences

Acknowledgement: The study was sponsored by Annexon Biosciences (Brisbane, CA, USA). Medical writing and editing assistance were provided by MedVal Scientific Information Services, LLC (Princeton, NJ, USA), and were funded by Annexon Biosciences.

Complement Inhibition With Tanruprubart (ANX005) Leads to Rapid, Robust Benefit Across Multiple Endpoints in Patients With GBS

GBS is a complement mediated neuromuscular emergency with significant unmet need despite current treatment options

Tanruprubart Inhibits C1q to rapidly and completely shut down the classical complement pathway and subsequent neuroinflammation and nerve damage

In a Phase 3 pivotal trial, **tanruprubart met the primary endpoint** and **showed consistent clinically meaningful and statistically significant benefit** on GBS outcomes

Tanruprubart has been generally well tolerated with a safety profile comparable to placebo

GBS is a Neuromuscular Emergency with Significant Long-Term Disability With No FDA Approved Therapies

Significant unmet need exists[1]

GBS is a rare, life-threatening post infectious neuromuscular emergency[2]

~7,000 hospitalized and treated in the US per year[3] and **150,000** worldwide[1]

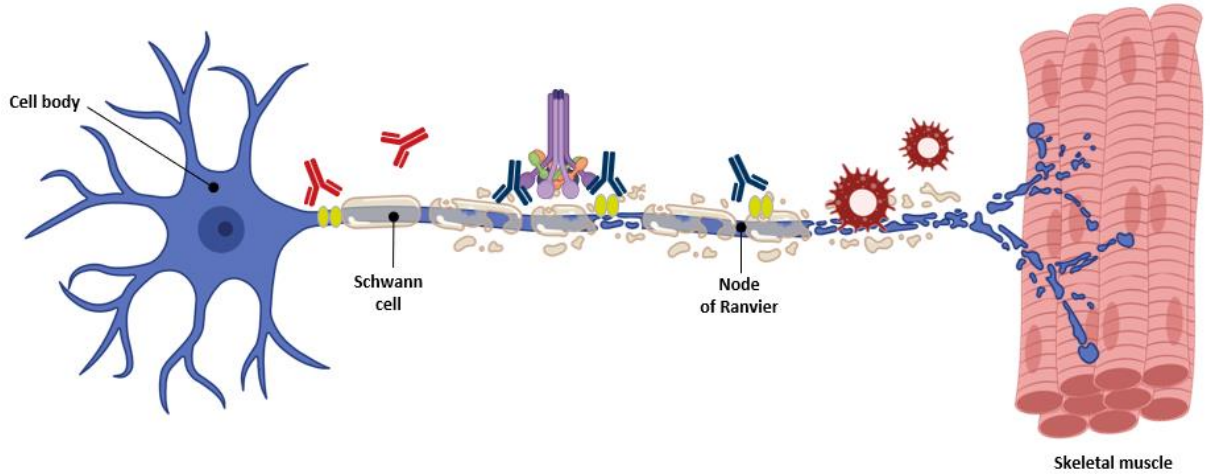
No FDA-approved therapies[4]

Despite current treatment:

~1 in 4 patients requires mechanical ventilation[5,6]

Global 1-year mortality rate[7] is **2-17%**

GBS is a complement mediated neuromuscular emergency[1,8]

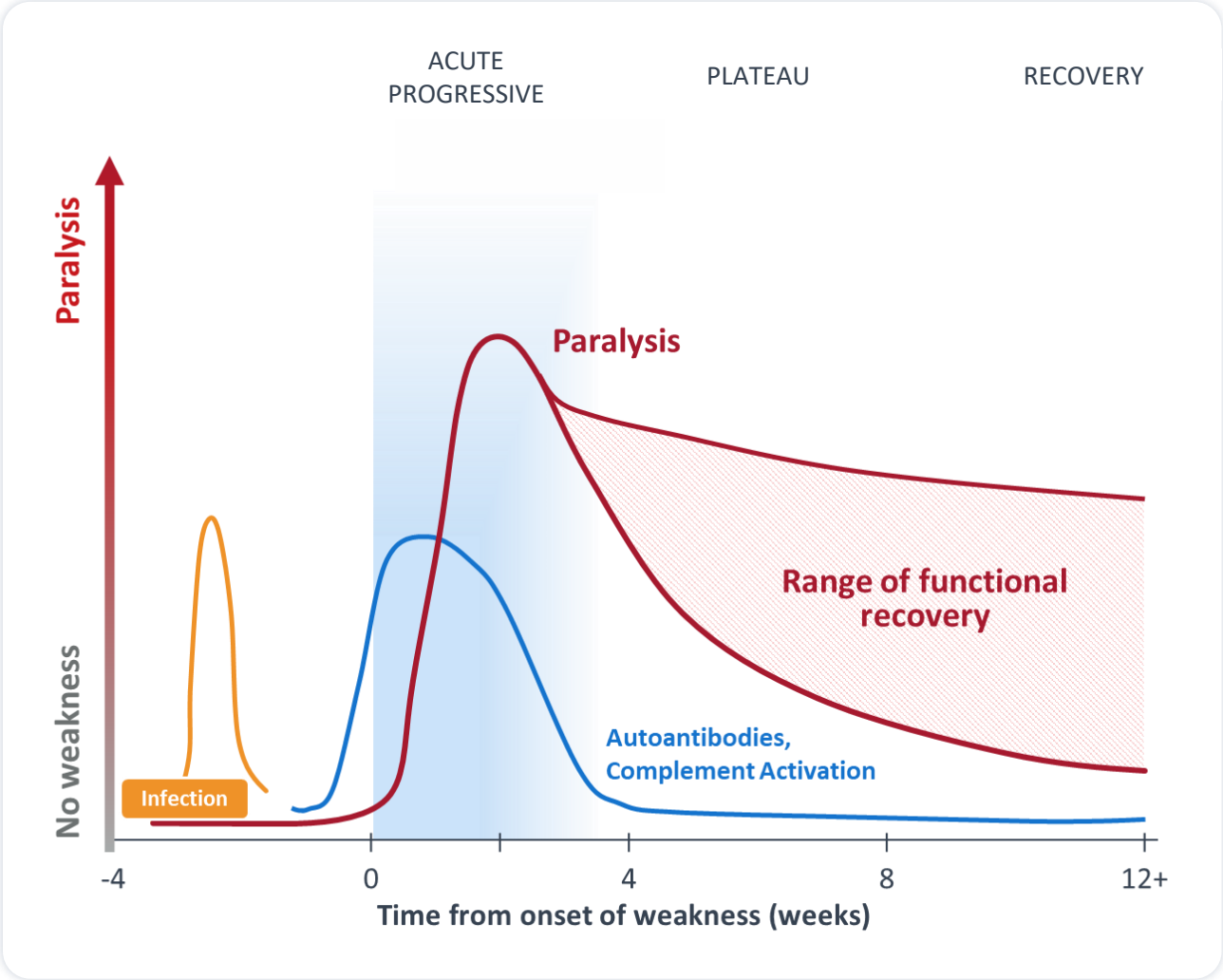


*On the GBS-DS scale

GBS, Guillain-Barré syndrome; IVIg, intravenous immunoglobulin; MOA, mechanism of action.

1. van Doorn PA. *Presse Med*. 2013;42(6 Pt 2):e193-201; 2. Willison HJ, et al. *Lancet*. 2016;388(10045):717-27; 3. Annexon, data on file. 4. Hughes RA, et al. *Cochrane Database Syst Rev*. 2014;2014(9):Cd002063; 5. Martic V, et al. *Can J Neurol Sci.* 2018 May;45(3):269-74. 6. van den Berg B, et al. *Nat Rev Neurol*. 2014;10(8):469-82; 7. Doets AY, et al. Regional variation of Guillain-Barré syndrome. *Brain*. 2018;141(10):2866-77. 8. Dalakas MC et al. *Nat Rev Neurol*. 2020;16(11):601-17.

Complement Rapidly Drives Neuroinflammation and Nerve Damage During the Acute Progressive Phase of GBS Leading to Disability



Acute progressive phase:

- Rapidly progressive bilateral muscle weakness peaking by 1 week in most cases and lasting up to 4 weeks

Plateau phase:

- May include extended period of ventilation in ICU and intensive support care lasting weeks to months

Recovery phase:

- Gradual muscle strength and functional improvement occurring over weeks to years as nerves repair

Adapted from van den Berg B et al. *Nat Rev Neurol*. 2014;10(8):469-482. and Leonhard SE et al. *Nat Rev Neurol*. 2019;15(11):671-683.

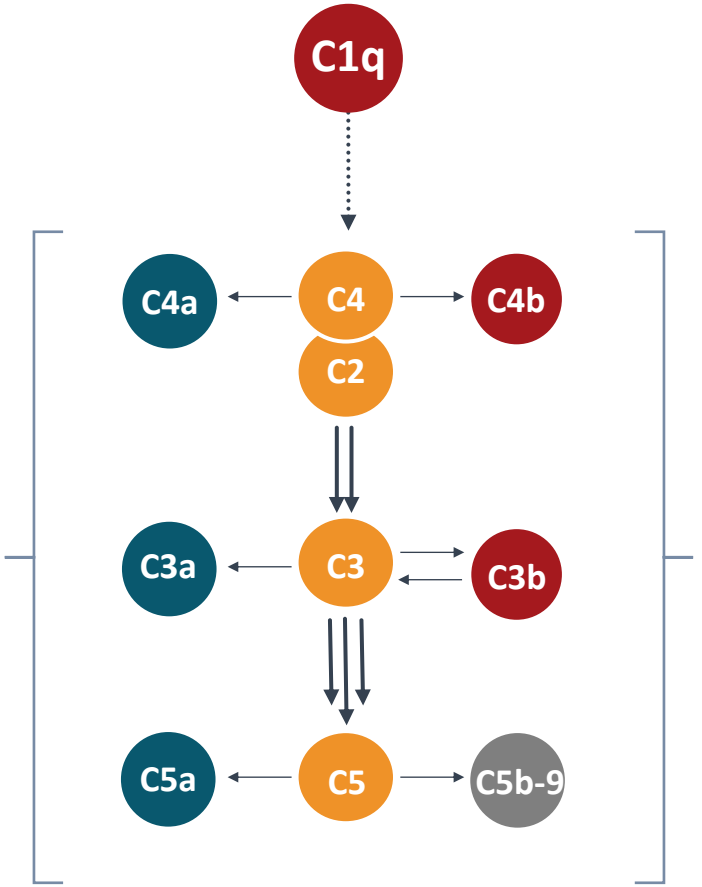
Tanruprubart (ANX005) Is A Monoclonal Antibody Targeting C1q To Block The Classical Complement Pathway At the Start

C1q Is the Initiating Molecule of the Classical Complement Pathway

C1q anchors to auto-antibodies on nerve surface and activates the pathway

INFLAMMATION AND EDEMA

Local, immediate, complement and '1st responder' driven



NERVE DAMAGE & DESTRUCTION

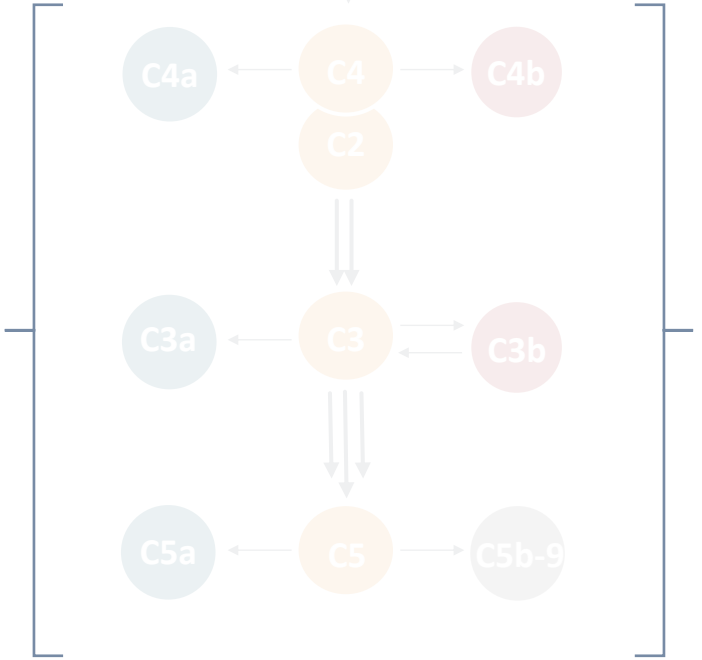
Recruitment of destructive cells including macrophages

1. Lansita, et al., 2017; DOI: 10.1177/1091581817740873

Tanruprubart (ANX005) Is A Monoclonal Antibody Targeting C1q To Block The Classical Complement Pathway At the Start

Tanruprubart Rapidly Shuts Down Activation of the *ENTIRE* Classical Complement Pathway on the Nerve

Tanruprubart



IMMEDIATE CESSATION OF INFLAMMATION AND EDEMA

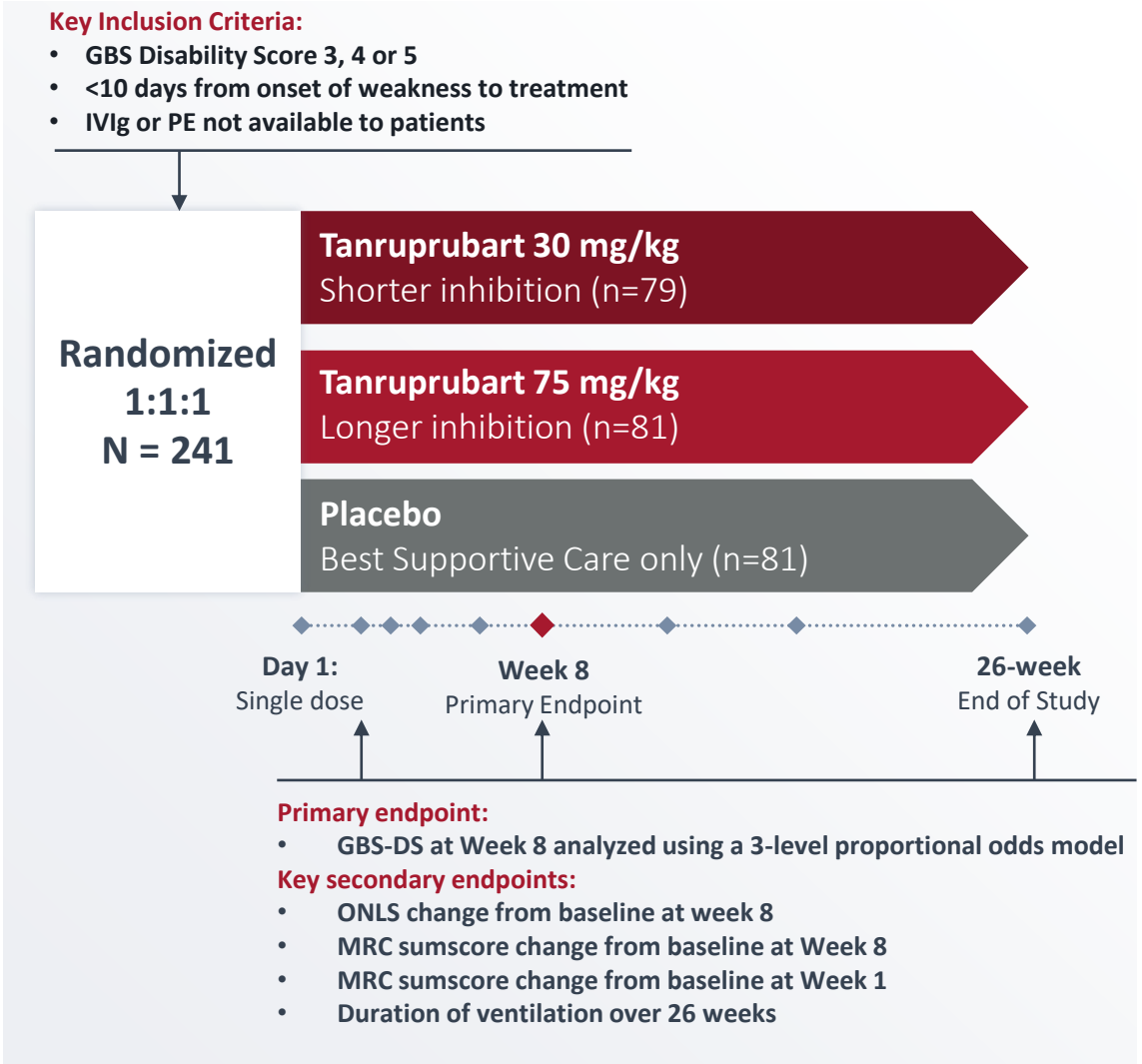
HALT NERVE DAMAGE & DESTRUCTION

Allow for recovery phase and repair of damaged nerves

1. Lansita, et al., 2017; DOI: 10.1177/1091581817740873

GBS-02 Was A Phase 3 Randomized, Double-blind, and Placebo-controlled Study Of Tanruprubart (ANX005) In Patients With GBS

Two doses selected to determine most effective duration of C1q inhibition

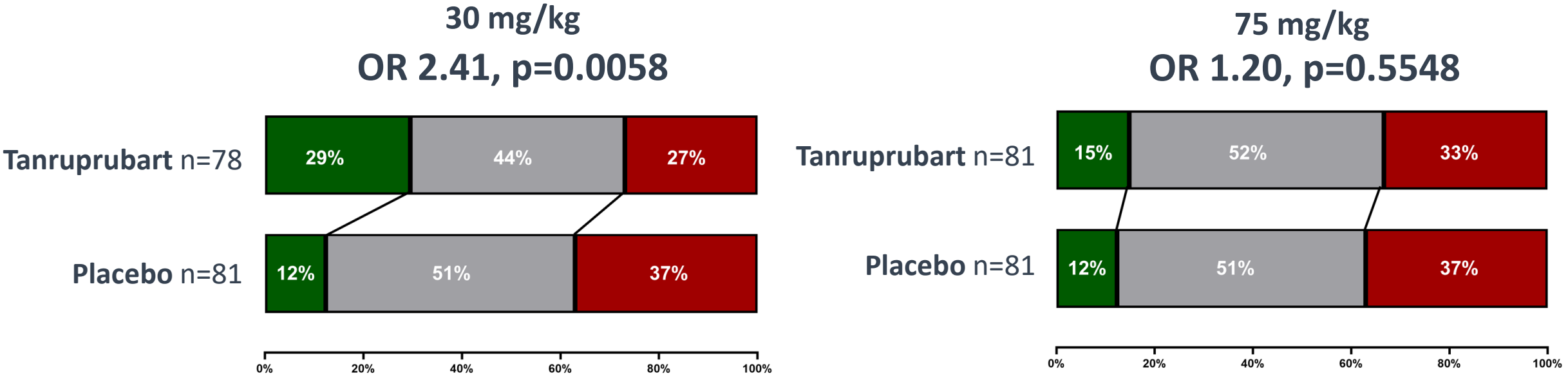


Baseline Characteristic	Placebo (n=81)	Tanruprubart 30mg/kg (n=79)	Tanruprubart 75mg/kg (n=81)
Age, years, mean (SD)	34.2 (12.59)	36.9 (14.88)	37.9 (15.29)
Male sex, n (%)	57 (70.4)	51 (64.6)	51 (63.0)
Baseline GBS-DS score, n (%)			
3	7 (8.6)	12 (15.2)	10 (12.3)
4	64 (79.0)	56 (70.9)	60 (74.1)
5	10 (12.3)	11 (13.9)	11 (13.6)
Baseline MRC sumscore, n (%)			
0-20	38 (46.9)	38 (48.1)	37 (45.7)
21-60	42 (51.9)	41 (51.9)	44 (54.3)
Time since of onset of weakness to treatment			
Days, mean (SD)	6.5 (1.7)	6.3 (1.9)	6.6 (2.0)
Electrophysiology by Hadden criteria, n (%)			
AIDP	18 (22.2)	16 (20.3)	16 (19.8)
AMAN	49 (60.5)	50 (63.3)	50 (61.7)
Other	14 (17.3)	13 (16.5)	15 (18.5)

AIDP, acute inflammatory demyelinating polyneuropathy; AMAN, acute motor axonal neuropathy; GBS-DS, Guillain-Barré Syndrome Disability Score; IVIg, intravenous immunoglobulin; MRC, Medical Research Council; ONLS, Overall Neuropathy Limitations Scale; PE, plasma exchange.

Shorter Duration of Complement Inhibition Showed Significant and Clinically Meaningful Treatment Effect on GBS-DS at Week 8

Primary Endpoint: 2.4-Fold Higher Likelihood of Being in a Better State of Health Relative to Placebo



APPROACH: Collapse 7-grade scale to a 3-grade scale (trichotomy)

0-1: Good state of health **2-3:** Disabled **4-6:** Severely disabled/death

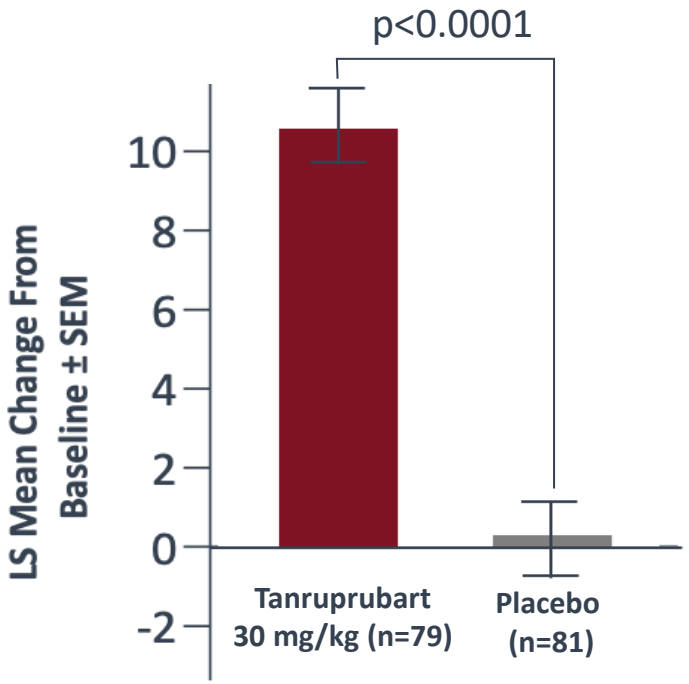
GBS-DS, Guillain-Barré Syndrome Disability Score; OR, odds ratio.

Tanruprubart (ANX005) 30 mg/kg Provided Rapid Recovery of Muscle Strength and Motor Function

Rapid Recovery in Muscle Strength Is A Critical Prognostic Factor Of Clinically Meaningful Improvement

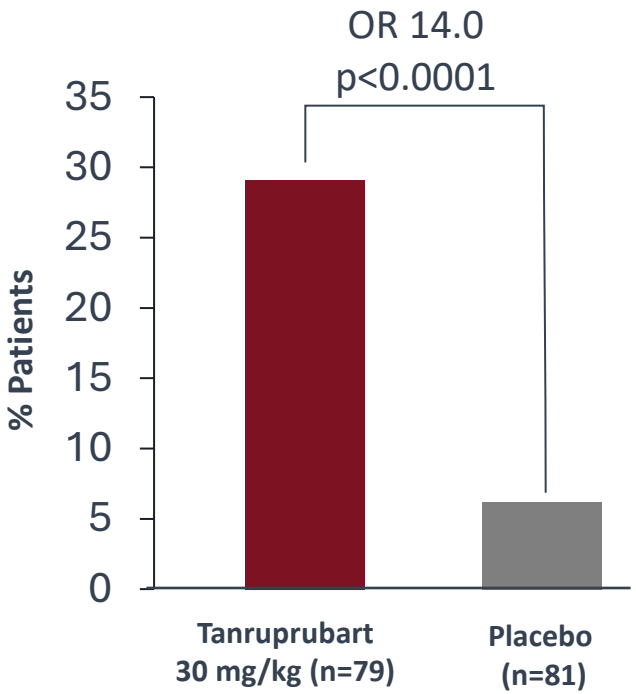
Key Secondary Endpoint:
More Than A 10-point Improvement In Muscle Strength (MRC Sum Score)[1] Over Placebo At Week 1

MUSCLE STRENGTH



14 Times More Likely To Perform Timed Up And Go (TUG) At Week 1

MOTOR FUNCTION

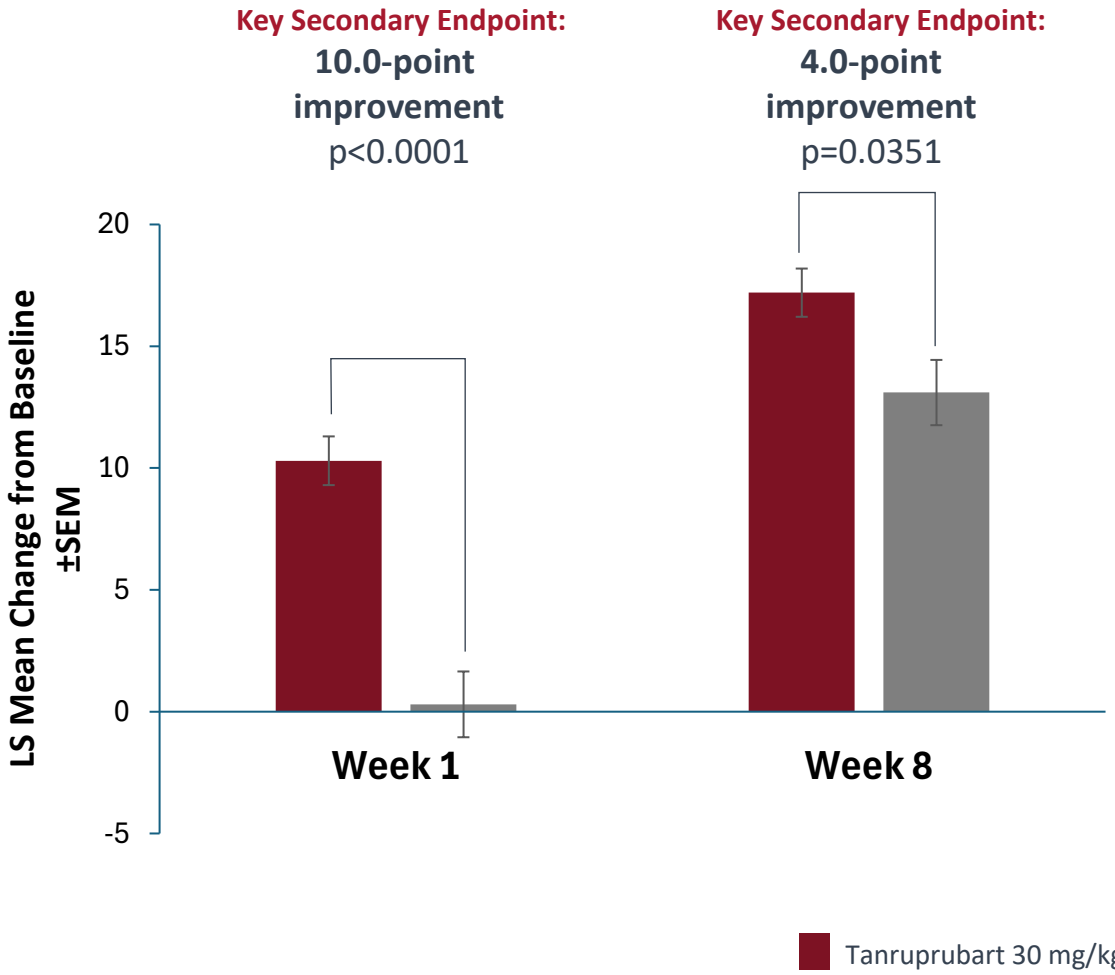


[1]LS mean point improvement relative to placebo

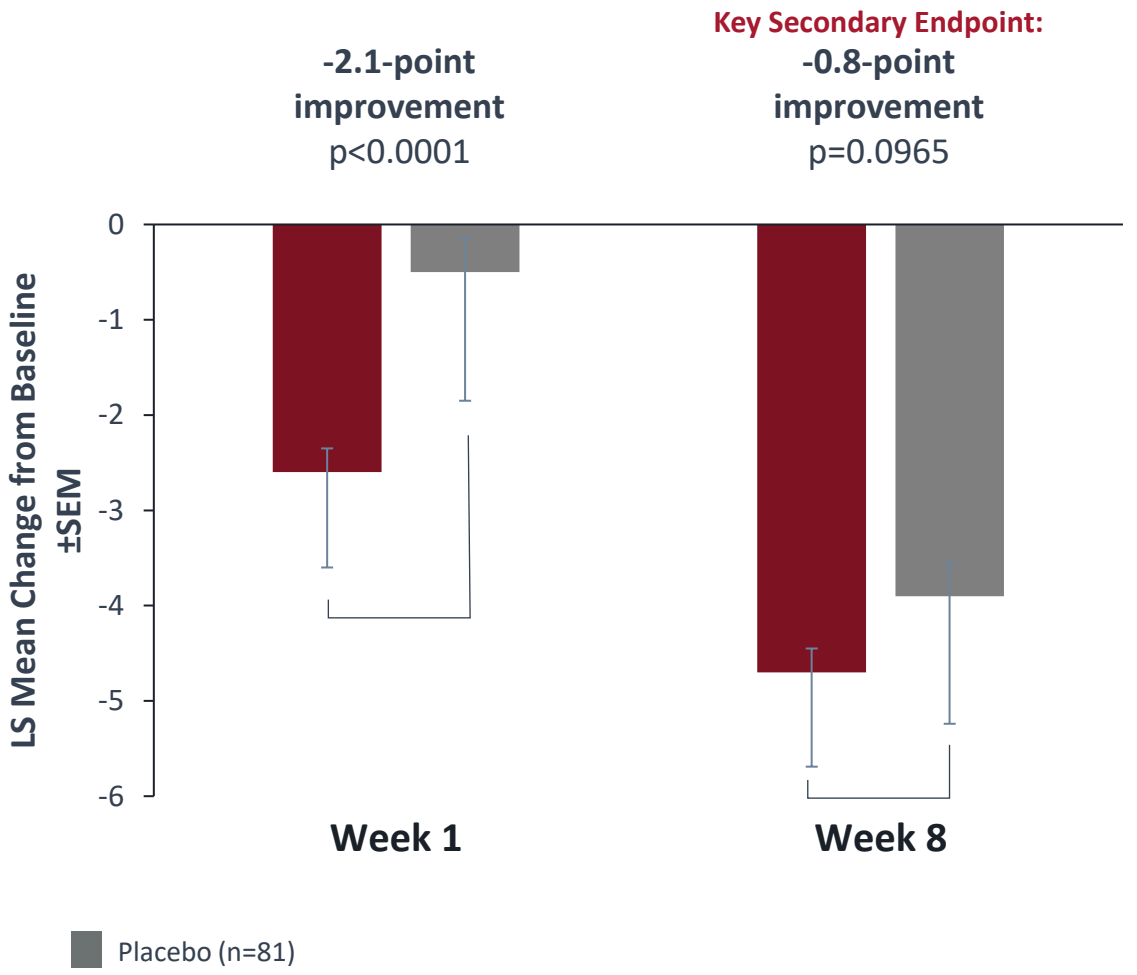
Rapid and Immediate Impact To Disease Trajectory

Other Key Secondary Endpoints Demonstrated Treatment Benefit

RAPID IMPROVEMENT IN MUSCLE STRENGTH (MRC SUM SCORE)



REDUCED MOTOR DISABILITY (ONLS)



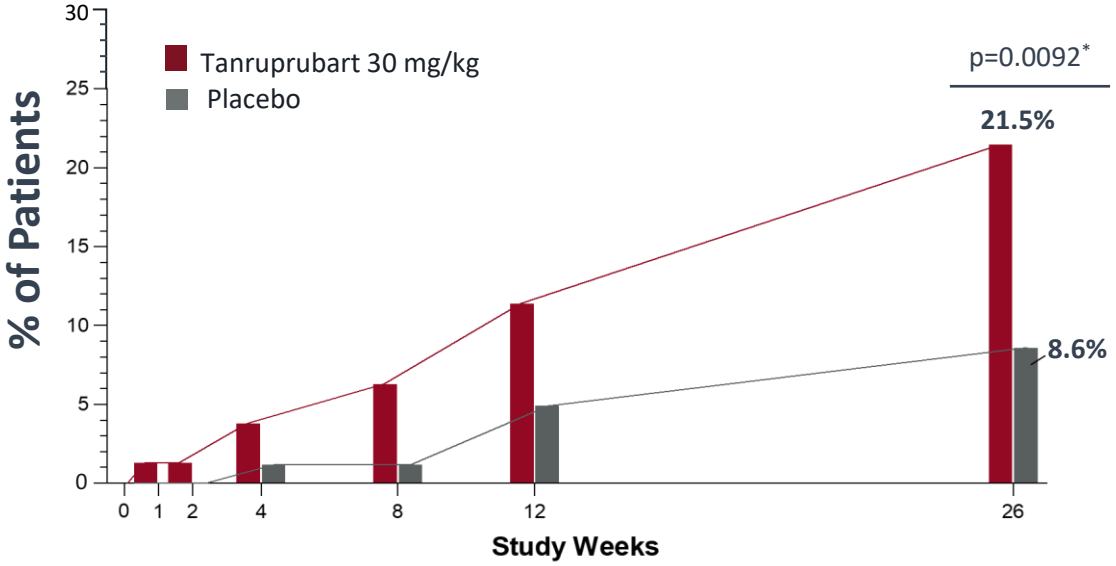
Tanruprubart 30 mg/kg (n=79) Placebo (n=81)

 MRC, Medical Research Council; ONLS, Overall Neuropathy Limitation Scale

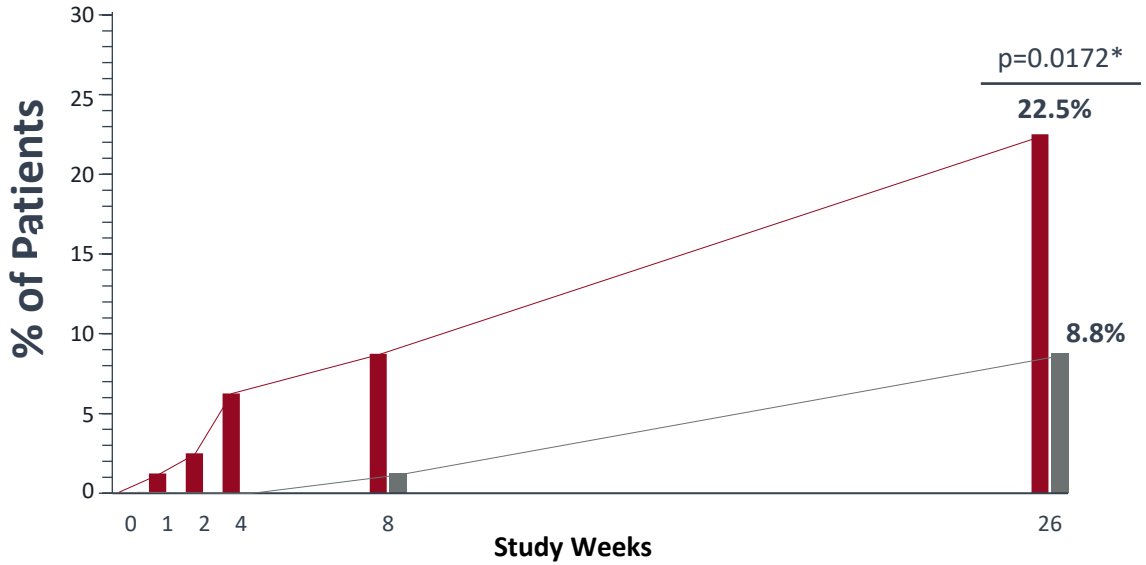
Tanruprubart (ANX005) Treatment Benefit is Durable, Leading to Increased Return to Normal Function Across Multiple Measures of Function and Mobility

~2X+ times more treated patients fully recover on multiple measures at week 26

FULL RECOVERY
GBS-DS=0



NO LIMITATIONS
ONLS (TOTAL SCORE=0)



*Nominal

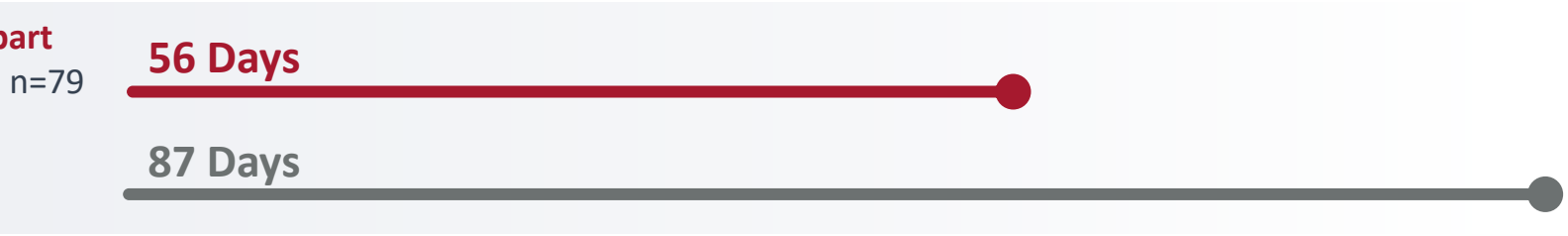
GBS-DS, Guillain-Barré syndrome Disability Score; ONLS, Overall Neuropathy Limitations Scale

Tanruprubart (ANX005) Consistently Showed Faster Recovery Across Clinically Important Measures

Helping Patients Achieve Their Independence Sooner

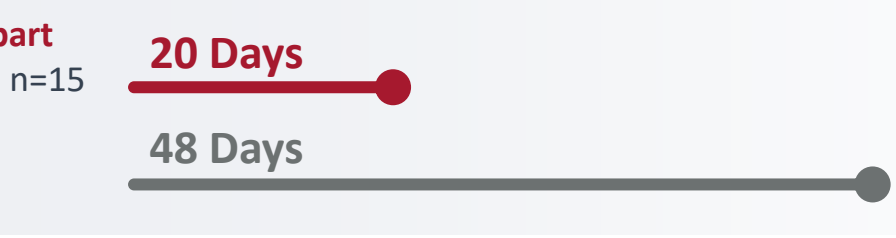
WALKING INDEPENDENTLY EARLIER

31 days earlier[1], p=0.0211



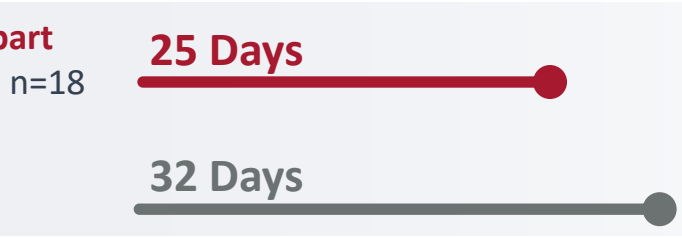
OFF VENTILATION EARLIER

28 days earlier[2], p=0.0356



FEWER DAYS IN ICU

7 fewer days[3], p=ns



ICU, intensive care unit; ns, not significant.

[1]Based on first scheduled visit of recording [2]Among patients ventilated [3]Among patients requiring ICU

Tanruprubart (ANX005) Was Generally Well-Tolerated

MAJORITY OF AES WERE MILD (GRADE 1) TO MODERATE (GRADE 2)

- Most common related events were infusion-related reactions
  - Majority were mild transient rashes
- SAEs and Grade 3 AEs balanced across groups, characteristic of disease morbidity

DEATHS

- No difference observed in incidence of all-cause mortality — 3 deaths in each dose group
  - Mortality rate of 3.7% consistent with rates seen in clinical trials

	Placebo n=81	Tanruprubart 30 mg/kg n=79	Tanruprubart 75 mg/kg n=81
	All Grades	All Grades	All Grades
Number of subjects reporting TEAEs, n (%)	79 (97.5)	79 (100.0)	80 (98.8)
Number of subjects with infusion-related reaction, n (%)	4 (4.9)	24 (30.4)	32 (39.5)
Rash (most common with IRR)	2 (2.5)	20 (25.3)	25 (30.9)
Most common TEAEs (non-IRR), n (%)			
Blood CPK increased	46 (56.8)	44 (55.7)	35 (43.2)
Musculoskeletal pain	35 (43.2)	36 (45.6)	26 (32.1)
ALT increased	23 (28.4)	21 (26.6)	23 (28.4)
Urinary tract infection	18 (22.2)	19 (24.1)	18 (22.2)
Hypokalemia	24 (29.6)	16 (20.3)	11 (13.6)
Constipation	10 (12.3)	15 (19.0)	17 (21.0)
AST increased	16 (19.8)	11(13.9)	17 (21.0)

AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; CPK, creatinine phosphokinase; IRR, infusion-related reaction; SAE, serious adverse event; TEAE, treatment-emergent adverse event; UTI, urinary tract infection.

Tanruprubart (ANX005) 30 mg/kg Single Dose Led to Rapid, Robust, and Consistent Benefit Across Multiple Endpoints

First targeted immunotherapy in GBS

- **Single dose rapidly blocks C1q** and complement-mediated neuroinflammation and nerve damage

Clinically meaningful improvement throughout the study

- **10-point point improvement** in muscle strength at week 1
- **Earlier gains in function** and reductions in disability
- **~2x more complete recovery** at the end of the 26-week study

Generally well tolerated

- **Safety data similar to placebo**
- **No increased infection rate** while not requiring vaccination or prophylactic antibiotics