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Phase 3 Study Evaluating Efficacy and Safety of ANX005 in Patients with Guillain-Barré Syndrome

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ANX005 is investigational and has not been approved for any indication in any jurisdiction

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Disclosures

Consultancy/advisory role with Annexon Biosciences

GBS is a Neurological Emergency with Long-Term Disability

Requires a Targeted and Effective Intervention to Immediately Block the Classical Complement Pathway

POST-INFECTIOUS COMPLEMENT-MEDIATED DISEASE

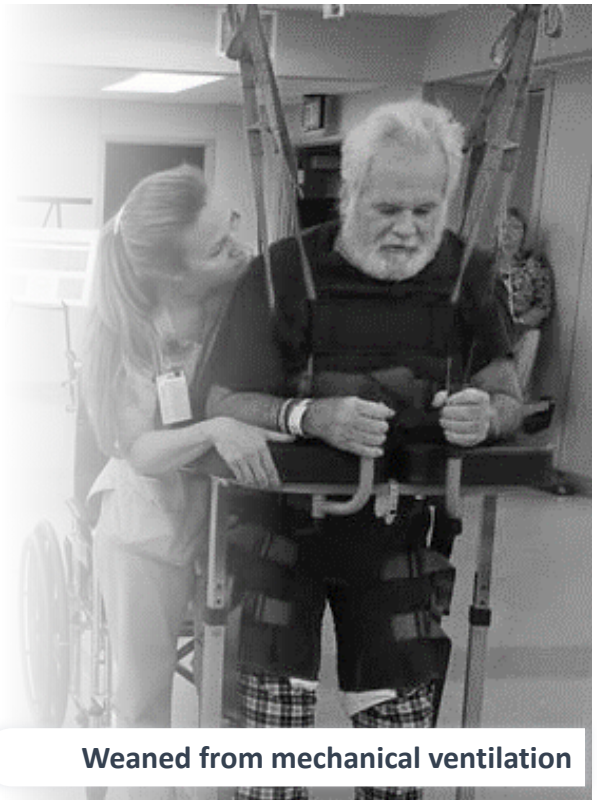
- Following infection, complement-activating autoantibodies attack nerves leading to nerve damage & acute paralysis

HIGH UNMET MEDICAL NEED

- 22,000 patients hospitalized in US & Europe annually
- IVIg not FDA approved, unknown MOA, requires 5-day treatment

SIGNIFICANT MORBIDITY

- Despite IVIg GBS results in:
  - Severe weakness and paralysis
  - Ventilation in 25% of patients
  - Uncertain and incomplete recovery



Weaned from mechanical ventilation

Classical complement drives neuroinflammation and tissue destruction in GBS

ANX005 is an anti-C1q antibody that rapidly shuts down the entire classical complement pathway

1) van Doorn, 2013; Willison et al., 2016 2(van den Berg et al., 2014) 3 Walgaard et al (2021) Lancet Neurology 20(4):275, 4AAN Guidelines "Immunotherapy for GBS", 4Hund EF et al (1993) Crit Care Med 21:433, 454Fletcher D, et al. (2000) Neurology 27;54(12), 46, 5Van den Berg B, et al (2014) *Nat Rev Neurol* Aug;10(8), 6Stephan et al (2012) Neuroscience 35:369, 7Lansita et al (2017) Int. J. Toxicol. 36:449

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Well Designed and Executed Pivotal Phase 3 Trial

Randomized, Double-Blind, Placebo-Controlled Study (Best Supportive Care, no IVIg or PE)

PATIENT SELECTION

- Baseline GBS-DS score 3-5
- <10 days from onset of weakness
- Stratified by baseline prognostic factors: muscle strength and time from onset of weakness

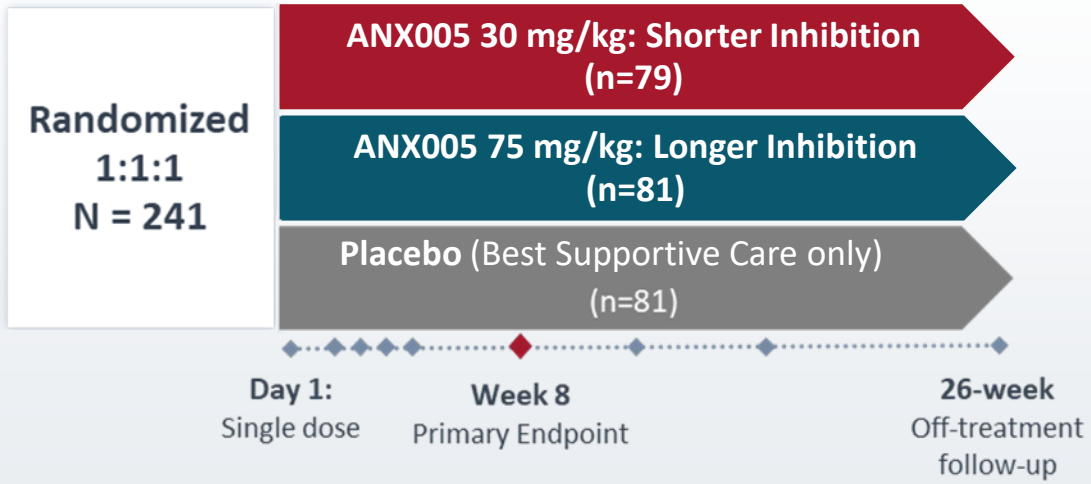
KEY ENDPOINTS

- **Primary Outcome Measure:** GBS-DS at week 8: well-accepted regulatory endpoint assessing functional status
- **Secondary Endpoints:** Muscle strength (MRC sumscore), Motor Disability (ONLS), Duration of Ventilation

KEY LEARNINGS

- **Shorter duration of complement inhibition with 30 mg/kg resulted in better outcomes**
- **Confirms initial observations from Phase 1b study**

2 DOSES SELECTED TO DETERMINE MOST EFFECTIVE DURATION OF INHIBITION



Conducted at Sites in Bangladesh and Philippines

Topline Results Subject to Change

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Baseline Characteristics Similar and Well Balanced Across Treatment Groups

Stratified by Key Prognostic Factors: MRC Sumscore and Time Since Onset of Weakness

Baseline Characteristic	Placebo (N=81)	ANX005 30mg/kg (N=79)	ANX005 75mg/kg (N=81)
Age at Screening (years); mean (SD)	34.2 (12.59)	36.9 (14.88)	37.9 (15.29)
Sex, n (%) Male	57 (70.4)	51 (64.6)	51 (63.0)
Baseline GBS-DS Score, n (%)			
3 Able to walk 10 meters across open space with help	7 (8.6)	12 (15.2)	10 (12.3)
4 Bedridden or chair bound	64 (79.0)	56 (70.9)	60 (74.1)
5 Requiring assisted ventilation for at least part of the day	10 (12.3)	11 (13.9)	11 (13.6)
Baseline MRC Sumscore (range 0-60), n (%)			
21-60 Mild/moderate loss of muscle strength	42 (51.9)	41 (51.9)	44 (54.3)
0 - 20 Severe loss of muscle strength	38 (46.9)	38 (48.1)	37 (45.7)
Time since of onset of weakness to randomization Days, mean (SD)	6.4 (1.7)	6.3 (1.9)	6.5 (2.0)
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 (%)			
Acute Inflammatory Demyelinating Polyneuropathy (AIDP)	18 (22.2)	16 (20.3)	16 (19.8)
Acute Motor Axonal Neuropathy (AMAN)	49 (60.5)	50 (63.3)	50 (61.7)
Other	14 (17.3)	13 (16.5)	15 (18.5)

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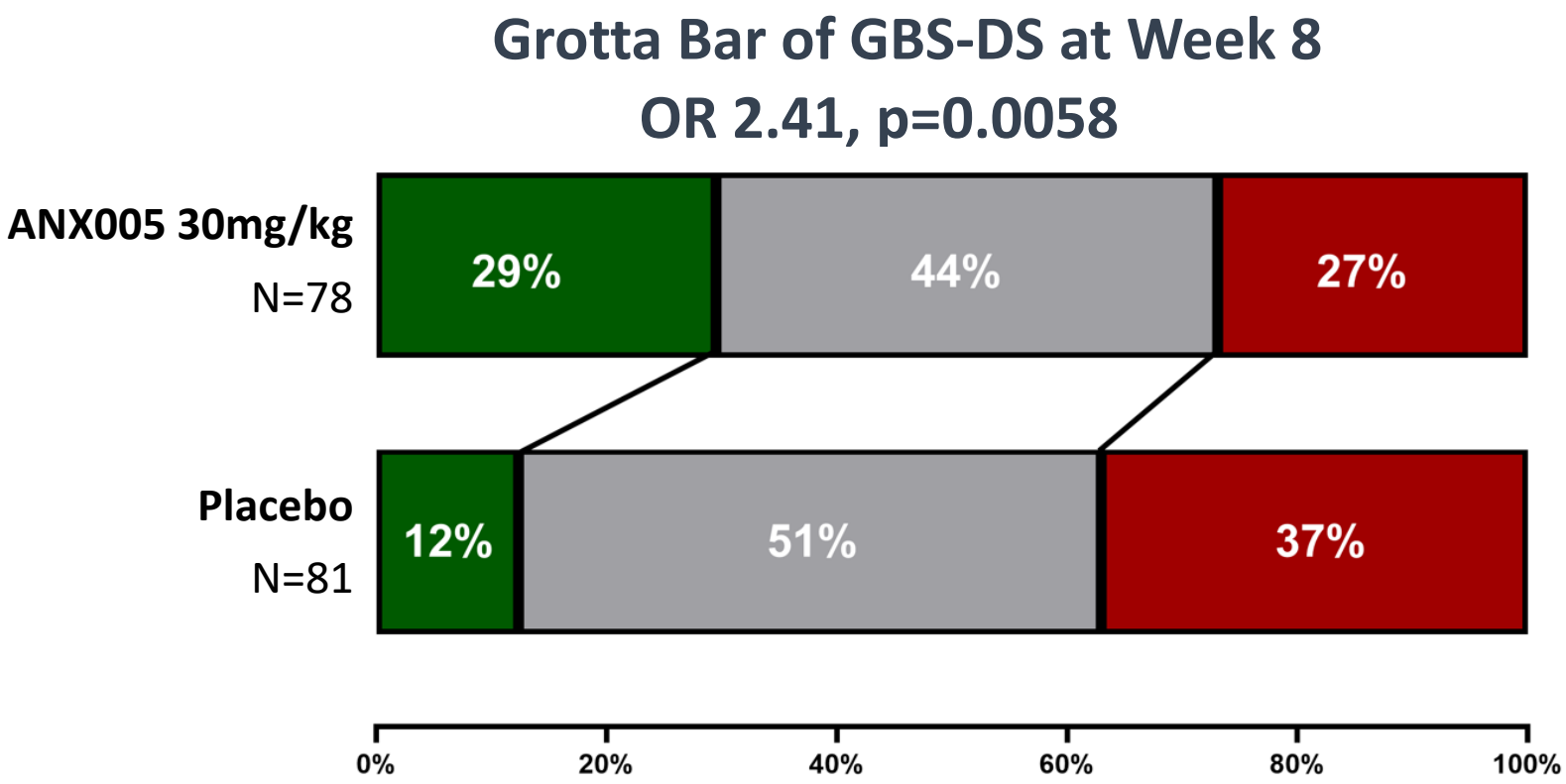
Primary Endpoint: ANX005 30 mg/kg Showed a Highly Significant and Clinically Meaningful Treatment Effect on GBS-DS at Week 8

2.41-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

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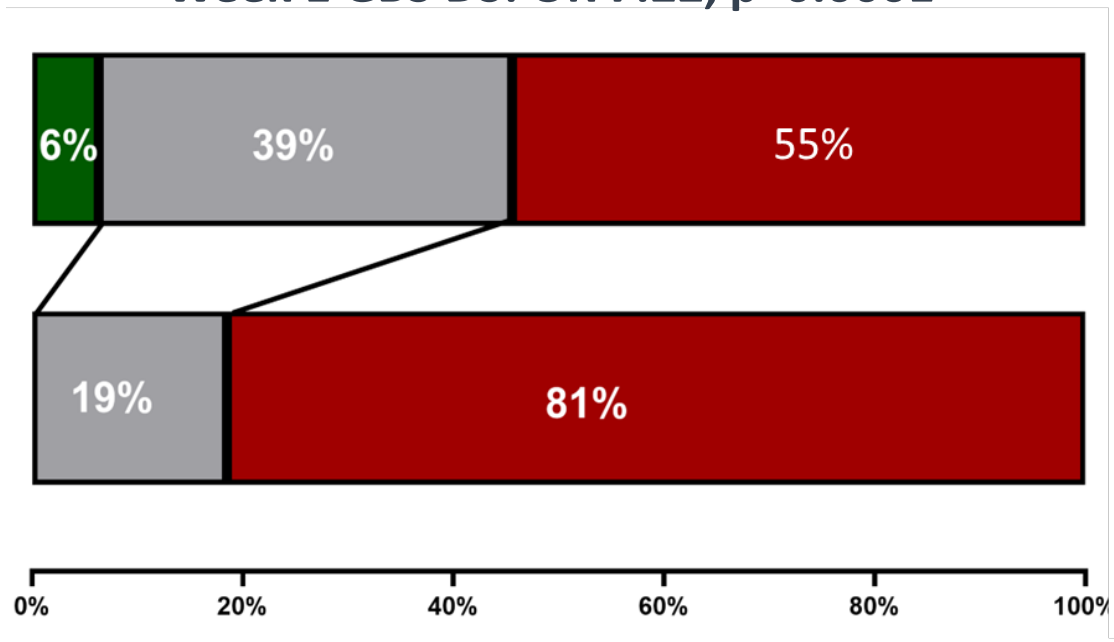
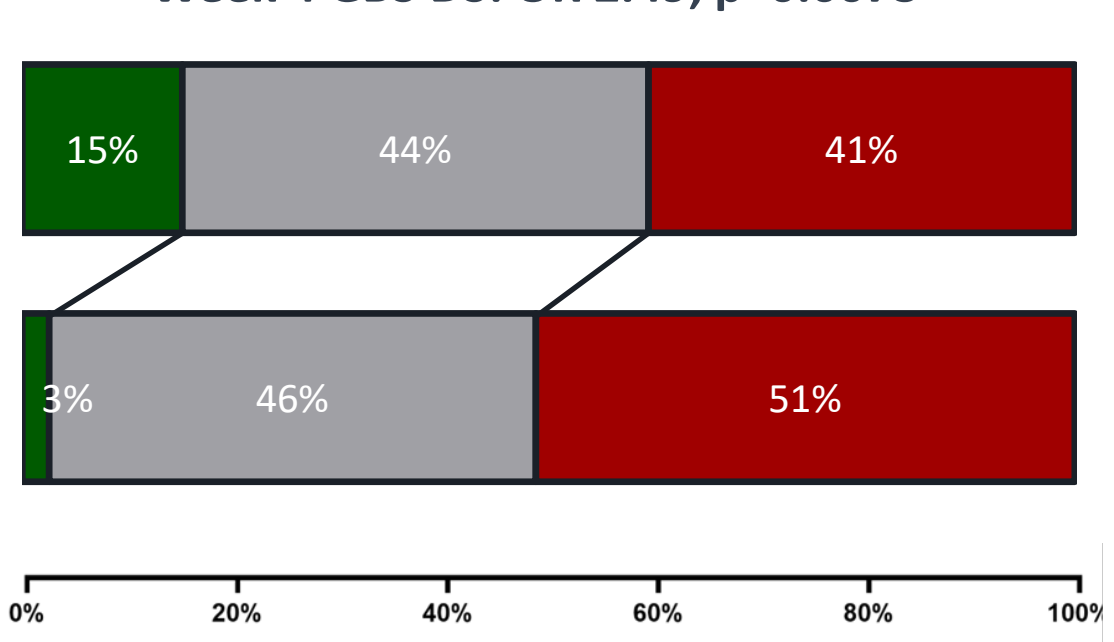
GBS-DS Week 1 and Week 4:
Early and Robust Treatment Effect with ANX005 30 mg/kg

Week 1 GBS DS: OR 7.22, p<0.0001[1]



Week 4 GBS DS: OR 2.49, p=0.0073[1]



0-1: Good State of Health
2-3: Disabled
4-6: Severely Disabled/Death

[1]Nominal

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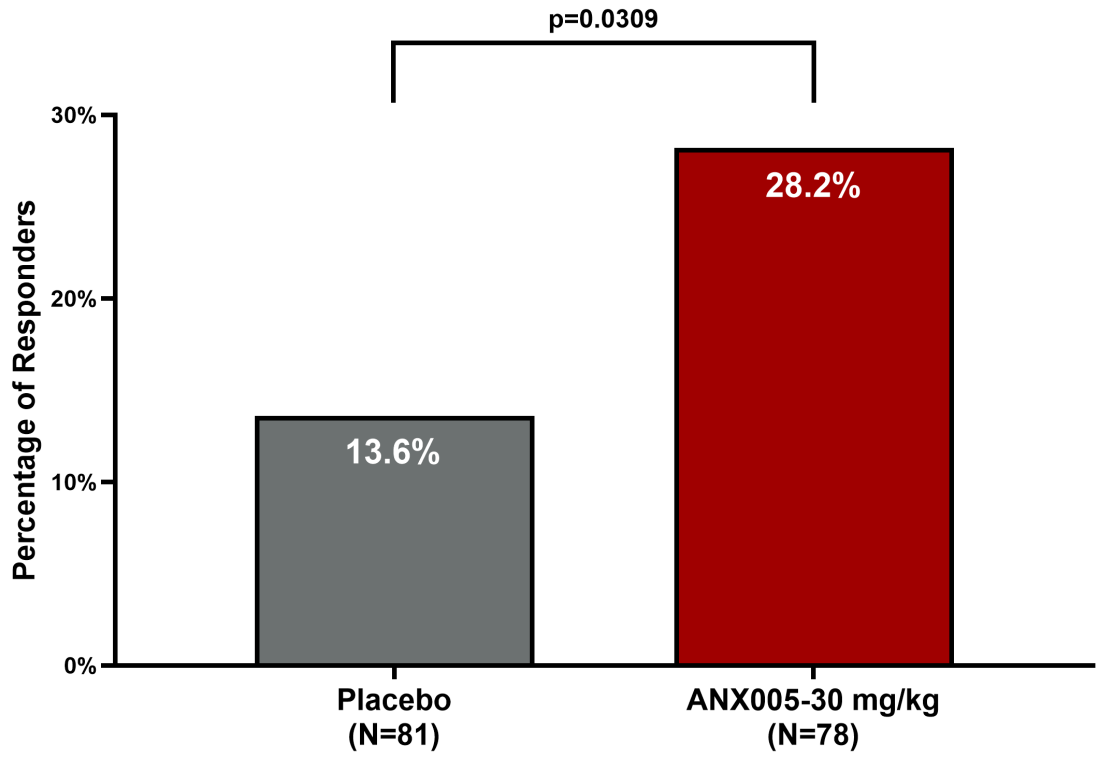
Week 8 Sensitivity Analyses:
Robustness of the Primary Endpoint with ANX005 30 mg/kg

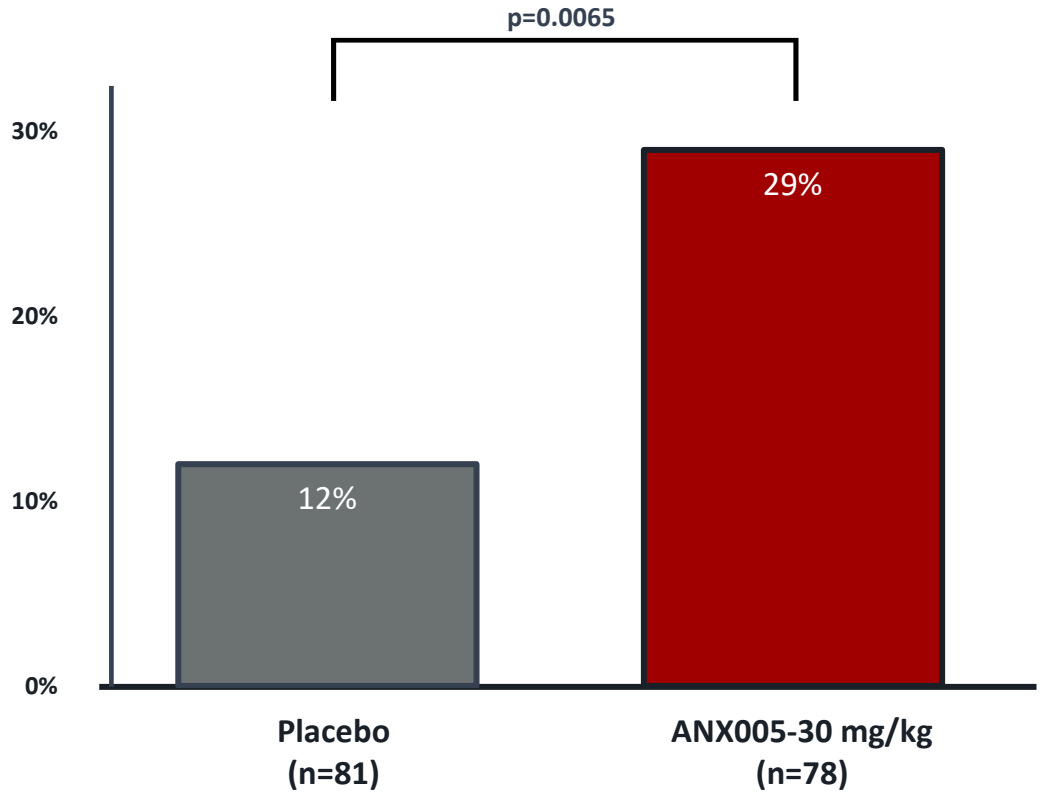
Responder Analysis: ≥3-point at week 8

2x More Patients Improved 3 Points or More



Traditional Dichotomy: (0-1, 2-6) at week 8

2.5x More Patients Were Able to Run or Better (OR 3.34)



[1]Nominal

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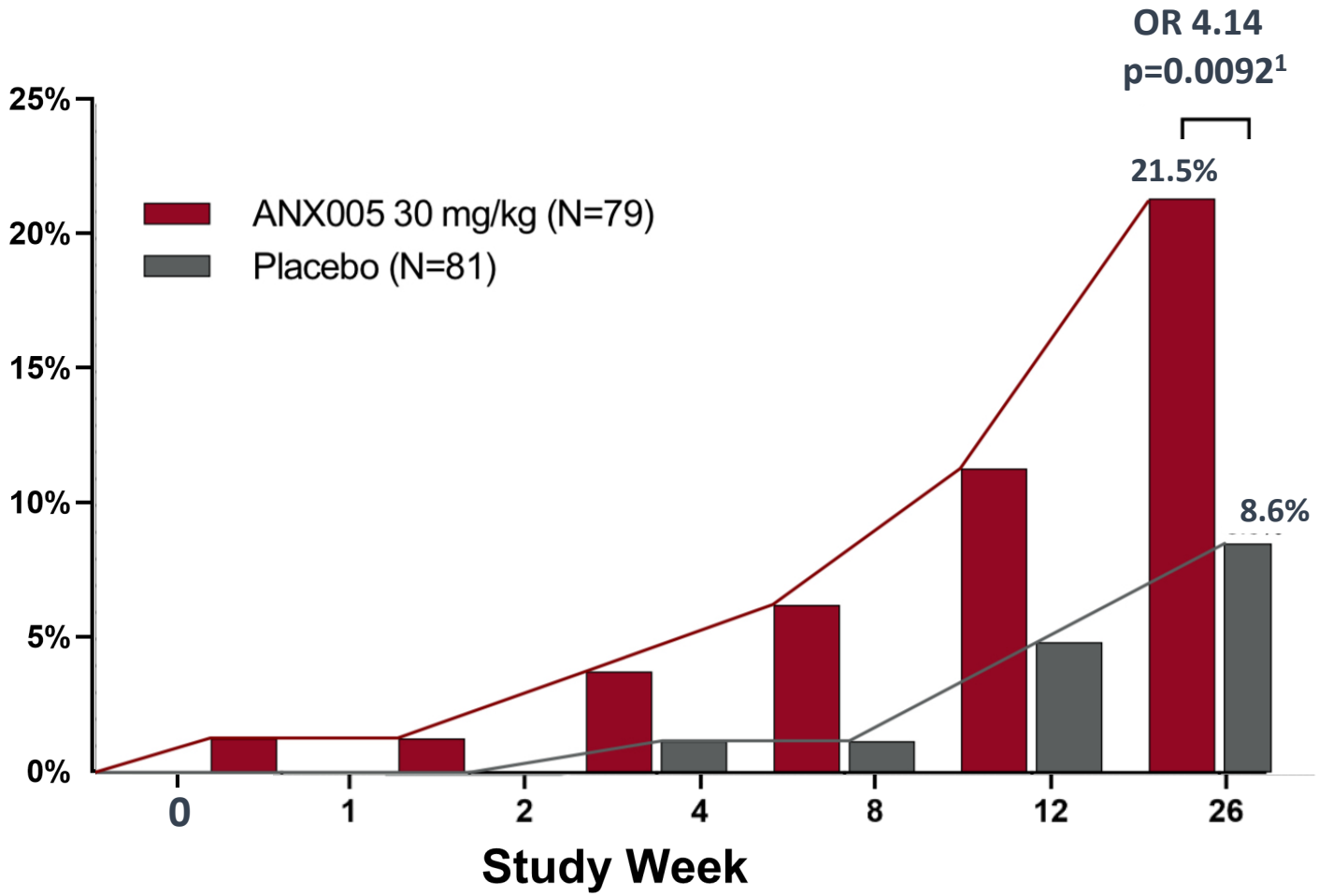
Accelerated Path to Recovery

Significantly more patients reached ‘normal’ by Week 26 in prespecified analysis

2.5 times more treated patients fully recover at Week 26 (GBS-DS = 0)

Effect begins early and grows throughout study



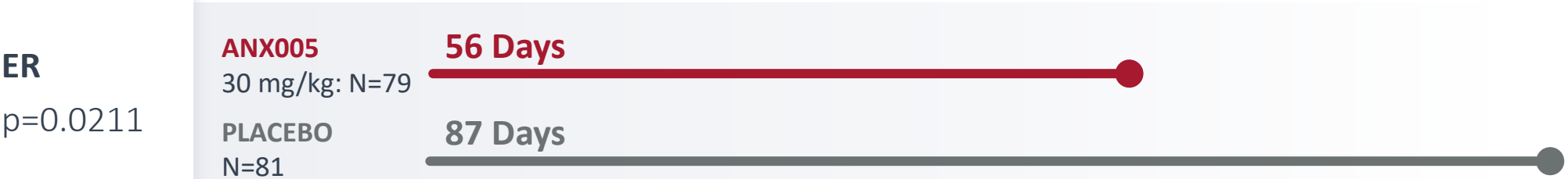
[1]Nominal

Getting Better Sooner: ANX005 30 mg/kg Consistently Showed Faster Recovery Across Clinically Important Measures

Helping patients achieve their independence sooner

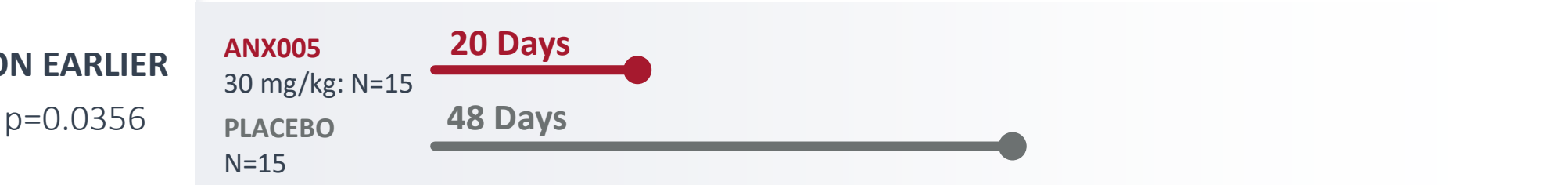
WALKING EARLIER

31 days earlier, p=0.0211



OFF VENTILATION EARLIER

28 days earlier, p=0.0356



[1]Nominal

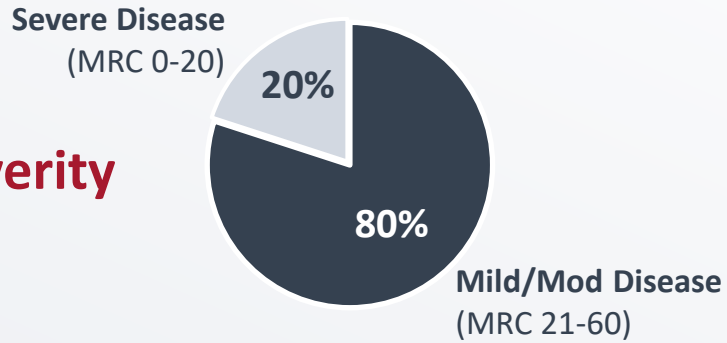
GBS Phase 3 Results are Highly Relevant to US and European Populations

Significant treatment effect in western-world type patients

US and European GBS Demographics

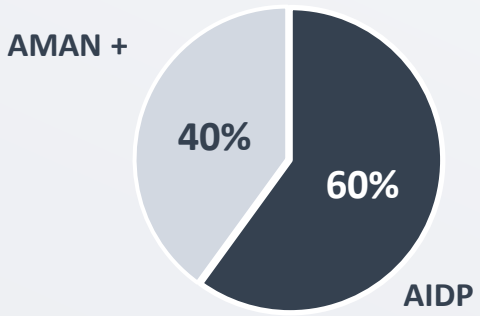
80% have baseline **MRC of >20**

Disease Severity



60% have **AIDP**

Neurotype



IGOS Database

ANX005 Phase 3 Study Results

47% with MRC >20

GBS-DS	**3.03x more likely to be better** vs. pbo at week 8, **p=0.0102**[1]
MRC	**8.8-point improvement** vs. pbo at week 1, **p<0.0001**[1]

21% with AIDP

GBS-DS	**5.31x more likely to be better** vs. pbo at week 8, **p=0.0130**[1]
MRC	**11.9-point improvement** vs. pbo at week 1, p=0.0002[1]

[1]Nominal

Topline Results Subject to Change

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ANX005 Generally Safe and 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
- No autoimmune related adverse events reported
- No increased infection rate while not requiring vaccination or prophylactic antibiotics
- One discontinuation in each dose group
- 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 US and EU
- Deaths occurred in older & more severe subjects

	Placebo N=81	ANX005 30mg/kg N=79	ANX005 75mg/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	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)

Topline Results Subject to Change

ANX005 GBS Phase 3: A Transformational Advancement for the GBS Community

1 **Phase 3 Met Primary Endpoint**

Patients treated with ANX005 30 mg/kg were 2.4x more likely to be in a better health compared to placebo (p=0.0058)

2 **Defined Effective Treatment Window for Acute Disease**

Treatment during active disease phase was effective

3 **ANX005 Helped Patients with GBS Get Better Sooner**

Early, robust, and clinically meaningful benefit on multiple outcome measures
Walking earlier; Less time on mechanical ventilation

4 **Durable Treatment Effects Across Full Course of 26-Week Study**

More patients fully recovered at 26 weeks

5 **Generally Safe and Well Tolerated**

Safety profile similar to placebo – no increased rate of infections, convenient single dose

Topline Results Subject to Change

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GBS-02 Principal Investigators and Study Team	**Bangladesh:** Khan Abul Kalam Azad, Zhahirul Islam, Prof Badrul Alam
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