

Administration of Tanruprubart

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EVP & Chief Medical Officer

ICD-10 Coordination & Maintenance Committee Update
Fall 2026

Guillain-Barré Syndrome (GBS) is a Devastating Neuromuscular Disease That Can Result in Sudden Paralysis

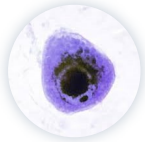
GBS IS A POST-INFECTIOUS IMMUNE-MEDIATED POLYRADICULONEUROPATHY^{1,2}

Campylobacter jejuni

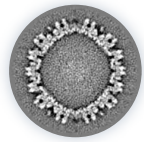


Leading cause
of GBS

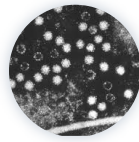
Cytomegalovirus



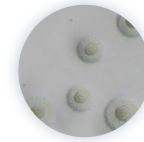
Epstein-Barr virus



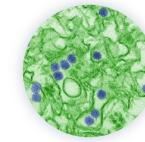
Hepatitis E virus



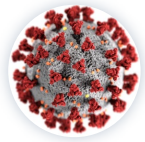
Mycoplasma pneumoniae



Zika virus



SARS-CoV-2 virus



POST-INFECTIOUS COMPLEMENT-MEDIATED DISEASE

Complement-activating antibodies generated in response to the antecedent infection **cross react to nerves leading to nerve damage**^{1,2}

GBS is the **most common cause of acute paralytic inflammatory disease** of the peripheral nervous system¹

Nerve damage can lead to a range of symptoms including **muscle weakness, numbness, pain, fatigue, and in severe cases acute paralysis**¹

GBS develops rapidly, with patients typically presenting within a few days to weeks of symptom onset

GBS is Associated with Significant Morbidity and Mortality in US



~2.5x longer GBS-related hospital length of stay (13 days), compared to US average length of stay

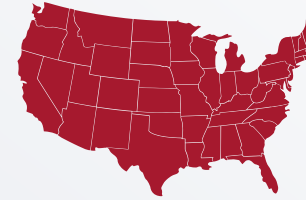


~30% of patients hospitalized with GBS require **ICU care** and **20-25% mechanical ventilation**, substantially increasing the mortality risk



~55% received **other inpatient care** (e.g., SNF, inpatient rehab, LTC) during the 12 months following the hospitalization

1-YEAR MORTALITY



~1 in 4 Medicare (24%) and ~1 in 20 (5.1%) commercially insured patients died during the 12 months following hospitalization

Tanruprubart Is A Monoclonal Antibody Targeting C1q To Block The Classical Complement Pathway At the Start to Halt Nerve Damage & Destruction

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

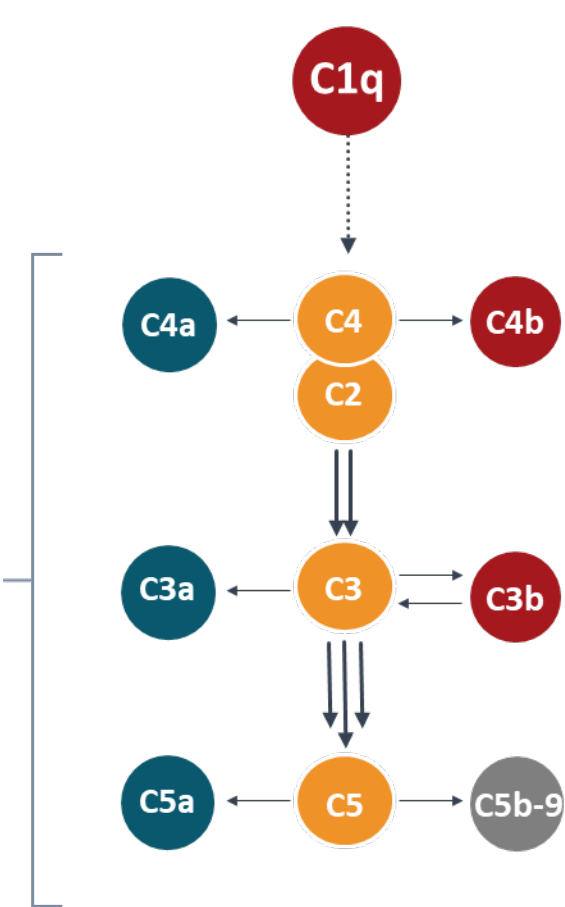
Tanruprubart targets C1q to block the classical complement pathway at the start to halt nerve damage and destruction

INFLAMMATION AND EDEMA

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

NERVE DAMAGE & DESTRUCTION

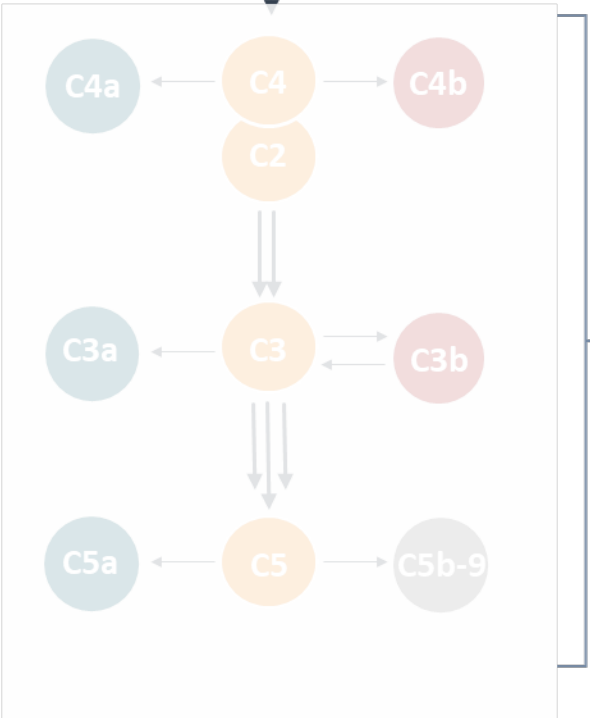
Recruitment of destructive cells including macrophages



RAPID EFFECT ON INFLAMMATION AND EDEMA

HALTING C1 MEDIATED NERVE DAMAGE & DESTRUCTION

Allow for recovery phase and repair of damaged nerves



Target Indication: Tanruprubart, for the Treatment of GBS in Adult Patients and in Pediatric Patients

RECOMMENDED DOSE IS A SINGLE ADMINISTRATION AT 30 MG/KG OF BODY WEIGHT (BW), ADMINISTERED AS AN INTRAVENOUS (IV) INFUSION OVER 18 HOURS

Dosing IV Bag Number	Dose	Volume tanruprubart (20 mg/mL*)	Infusion rate per bag**	Duration of infusion	Infusion rate (mg/kg/hour)
Bag 1	9.0 mg/kg	(BW in kg) x 0.45 mL/kg	44 mL/hour	12 hours	0.75
Bag 2	6.0 mg/kg	(BW in kg) x 0.30 mL/kg	131 mL/hour	4 hours	1.5
Bag 3	15.0 mg/kg	(BW in kg) x 0.75 mL/kg	263 mL/hour	2 hours	7.5

*Each 20 mL single-use vial contains 400 mg of tanruprubart (20 mg/mL). ** A 500 mL bag of sodium chloride 9 mg/ML (0.9%) solution for injection is used..

- Patients are to be adequately hydrated prior to the infusion and must be monitored for infusion-related reactions (IRRs) during infusion.
- Each infusion of the 3-bag single-dose treatment is documented in the medical record and healthcare professional notes in the same manner as other IV-administered therapies.

Pivotal Phase 3 Trial Design (GBS-02)

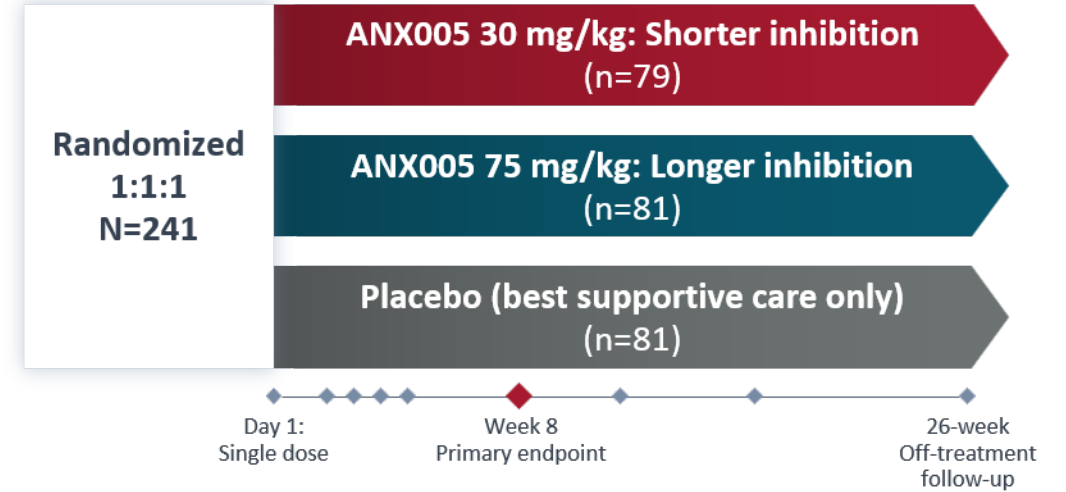
Randomized, double-blind, placebo-controlled study

PATIENT SELECTION

- GBS Disability Score (GBS-DS) 3, 4 or 5
- ≤ 10 days from onset of weakness
- Have not received IVIg or PLEX
- Stratified by baseline prognostic factors: muscle strength and time from onset of weakness

KEY ENDPOINTS

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



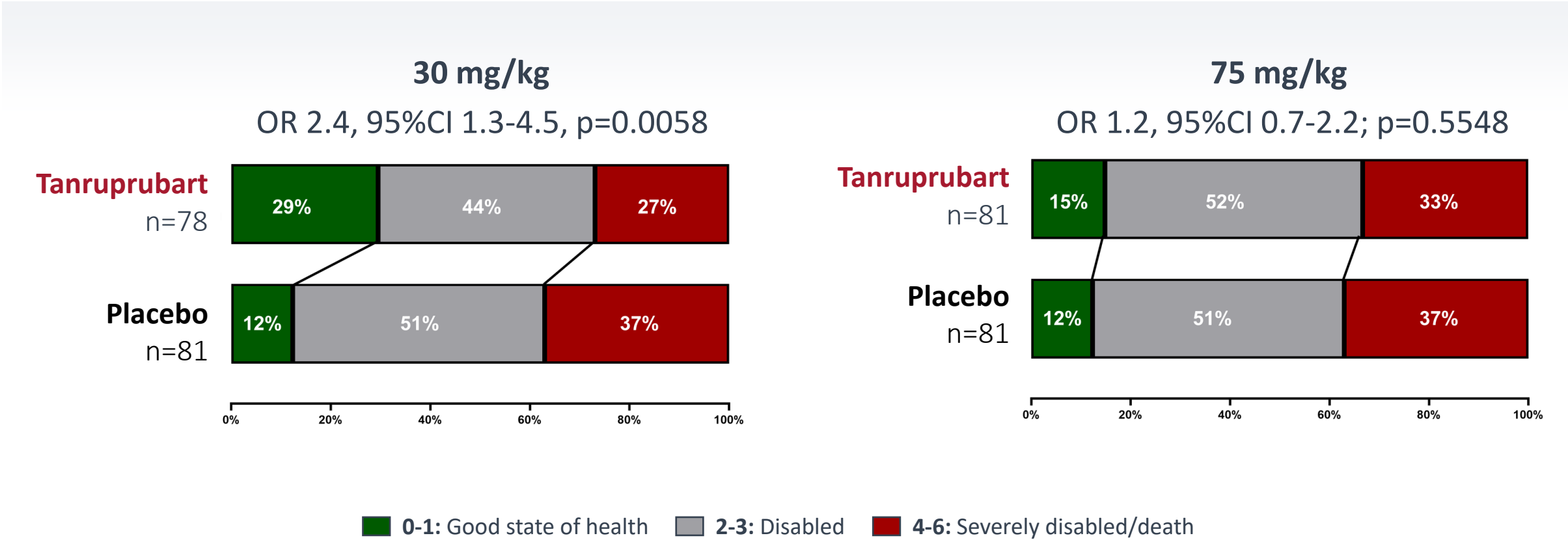
Conducted at sites in Bangladesh and the Philippines

KEY LEARNINGS

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

Phase 3 Primary Endpoint: Tanruprubart 30 mg/kg Showed Statistically Significant and Clinically Meaningful Treatment Effect on GBS-DS at Week 8

More likely to be in a better state of health relative to placebo with shorter duration of complement inhibition. Improvement in muscle strength drives early functional gain at weeks 1 and 4.



Phase 3: Tanruprubart Patients Achieved Clinical Milestones Sooner



**WALKING
INDEPENDENTLY EARLIER**
31 days earlier¹, $p=0.0211$ ²

Tanruprubart
30 mg/kg: n=79

56 Days

Placebo
n=81

87 Days



OFF VENTILATION EARLIER
28 days earlier³, $p=0.0356$ ²

Tanruprubart
30 mg/kg: n=15

20 Days

Placebo
n=15

48 Days



FEWER DAYS IN ICU
7 fewer days⁴, $p=ns$

Tanruprubart
30mg/kg: n=18

25 Days

Placebo
n=19

32 Days

ICU, intensive care unit; ns, not significant.

¹Based on first scheduled visit of recording. ²Nominal. ³Among patients ventilated. ⁴Among patients requiring ICU.

*Phase 3 data reported on the 30 mg/kg dose

Phase 3 Safety Profile Supports a Positive Benefit Risk Assessment for Single Administration in GBS

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

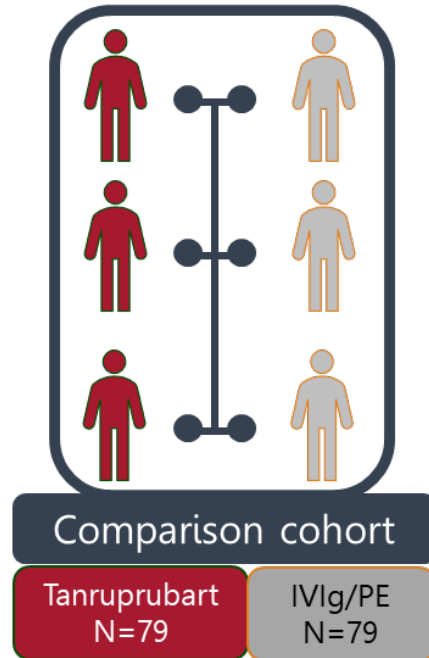
	Placebo n=81	Tanruprubart 30 mg/kg n=79	Tanruprubart 75 mg/kg n=81
	All Grades	All Grades	All Grades
Number of subjects reporting TEAEs, n (%)	79 (97.5)	79 (100.0)	80 (98.8)
Number of subjects with infusion related reaction, n (%)	4 (4.9)	24 (30.4)	32 (39.5)
Rash (most common with IRR)	2 (2.5)	20 (25.3)	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)

GBS-04: A Matched-Cohort Study Comparing Phase 3 & IGOS Data

Annexon and **IGOS (Largest global prospective GBS registry)** partnered on the design and conduct of GBS-04, a matched-cohort study comparing outcomes between IVIG/PLEX-treated IGOS patients (2,000 across 140+ sites in 21 countries) and tanruprubarb treated Phase 3 patients

1:1 matched cohorts

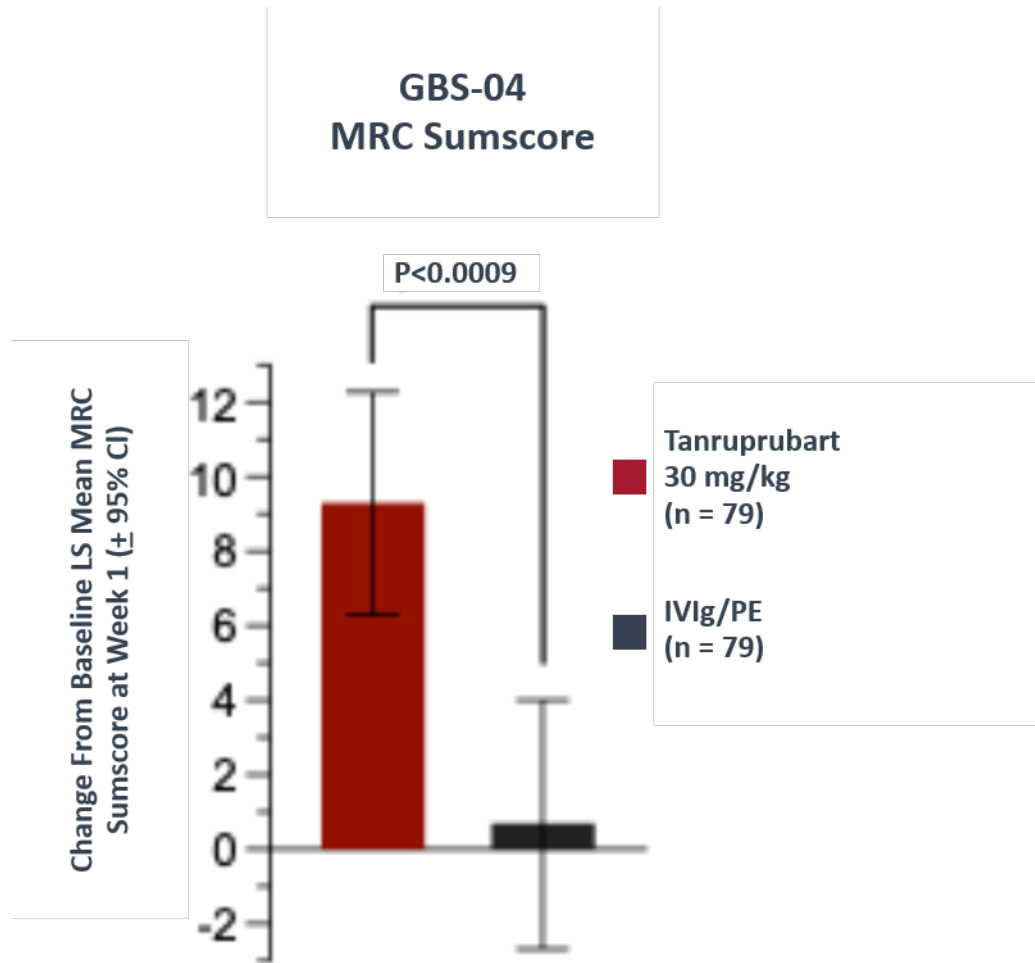
PH3 PATIENTS
MATCHED WITH
IGOS PATIENTS



Tanruprubarb Phase 3 patients matched 1:1 with IGOS on prespecified criteria

- ✓ Propensity score matching based on key prognostic factors of muscle strength and GBS disability
- ✓ Matched cohorts demonstrate Phase 3 population is represented within global GBS patient spectrum

GBS-04: At Week 1, Tanruprubart Treated Patients Improved More Than 8-Points in MRC Sumscore Compared To IVIG/Plex



8.6-POINT IMPROVEMENT IN MRC SUMSCORE¹ OVER IVIG/PLEX

Muscle weakness is a hallmark of GBS

MRC at week 1 is a sensitive measure of the 'acute disease process' of neuroinflammation, nerve damage and destruction²

Time is nerve

Early improvement in muscle strength is important for halting disease progression and highly prognostic of functional improvement on disability, ICU and ventilation

GBS-04: Fewer Tanruprubart Patients Required Ventilation or ICU vs. Matched IVIg/PLEX Patients

Measures of Decreased Burden of Care



FEWER SUBJECTS VENTILATED

Half as many patients, $p = 0.0168$

Tanruprubart 30mg/kg

N = 15 of 79

IGOS IVIG/PE

N = 34 of 79

19%

43%

FEWER DAYS ON VENTILATION

Median 26 fewer days, $p = \text{n.s.}$

Tanruprubart 30mg/kg

N = 15

IGOS IVIG/PE

N = 34

20 Days

46 Days



FEWER SUBJECTS IN ICU

Half as many patients, $p = 0.0242$

Tanruprubart 30mg/kg

N = 18 of 79

IGOS IVIG/PE

N = 38 of 79

23%

48%

FEWER DAYS IN ICU

Median 20 fewer days, $p = \text{n.s.}$

Tanruprubart 30mg/kg

N = 18

IGOS IVIG/PE

N = 38

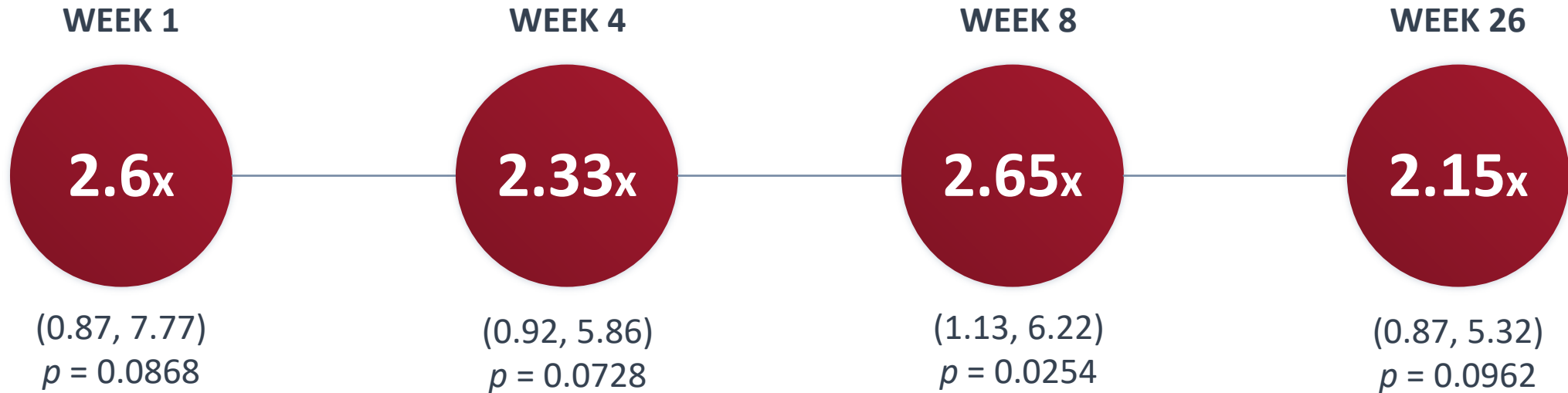
25 Days

45 Days

GBS-04: Tanruprubart 30mg/kg Patients Demonstrated Improvement in Disability Scores vs. IVIg/PLEX Patients

~2X MORE LIKELY TO BE IN A BETTER STATE OF HEALTH

GBS-DS Odds Ratios (OR)



**Primary Endpoint
for Phase 3 Trial**

Tanruprubart 30 mg/kg Single Dose Led to Early and Durable Response Across Multiple Endpoints

POTENTIAL TO BE FIRST TARGETED IMMUNOTHERAPY IN GBS

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

CLINICAL IMPROVEMENT VS. PLACEBO AND IVIG/PE

Substantial improvement in muscle strength at Week 1

Earlier gains in function and reductions in disability

2x More patients with complete recovery at the end of the Week 26

SAFETY PROFILE IN PHASE 3 STUDY

Safety data similar to placebo

No increased infection rate while not requiring vaccination or prophylactic antibiotics