RESCUE-ALS Trial Results: A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study of CNM-Au8 to Slow Disease Progression in ALS

RESCUE ALS

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CONCLUSION: RESCUE-ALS has established safety and suggested efficacy of CNM-Au8, a cellular energetic catalyst, for the treatment of ALS
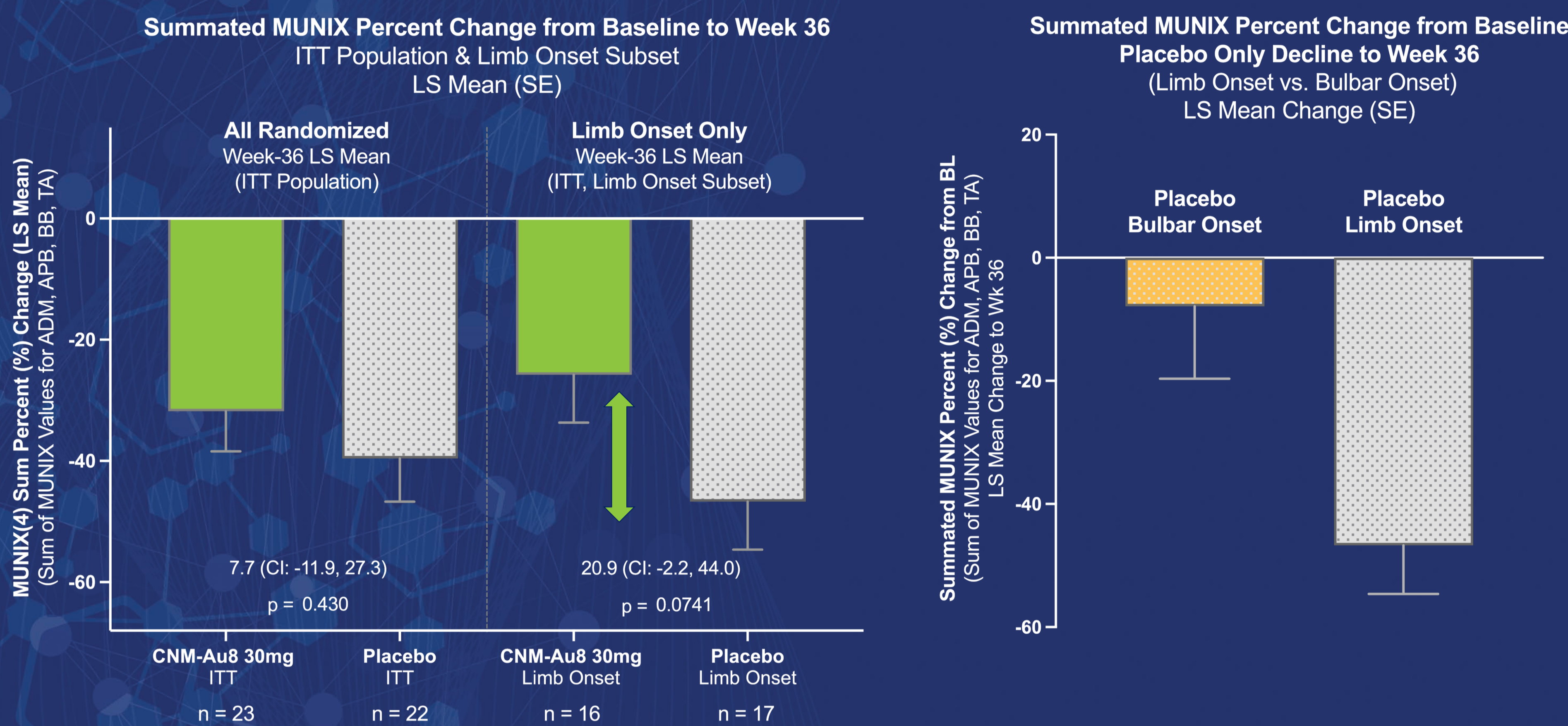
Baseline Demographics

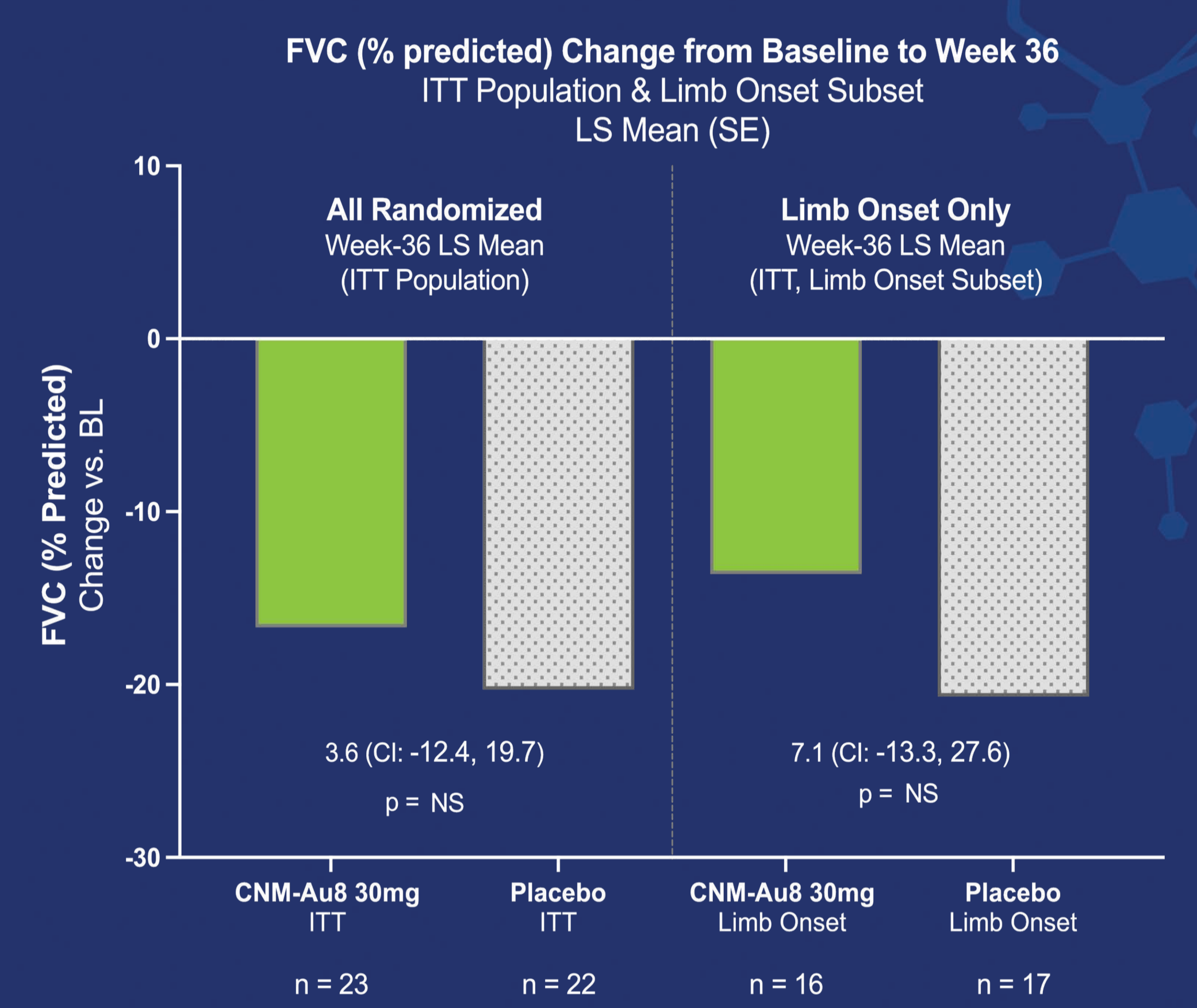| Baseline Value mean (sd)	Age (yrs)	Sex n, (%) Male | Female	Onset Site n, (%) Limb | Bulbar	Months from Onset	FVC (% pred.)	ALSFRS-R Score	ENCALS Risk Profile[1]	MUNIX Sum
All (n=45)	59.1 (12.3)	M: 26 (58%) F: 19 (42%)	L: 33 (73%) B: 12 (27%)	15.8 (9.3)	81.5 (16.7)	38.7 (6.0)	-4.4 (1.8)	378.2 (175.3)
CNM-Au8 30mg (n=23)	57.0 (13.3)	M: 13 (57%) F: 10 (43%)	L: 16 (70%) B: 7 (30%)	15.5 (7.6)	84.5 (18.3)	38.6 (6.6)	-4.6 (1.7)	380.2 (198.0)
Placebo (n=22)	61.3 (10.9)	M: 13 (59%) F: 9 (41%)	L: 17 (77%) B: 5 (23%)	16.1 (10.9)	78.2 (14.5)	38.8 (5.4)	-4.2 (1.8)	376.2 (152.7)

Design Summary

- Early symptomatic ALS
- Randomized (1:1, CNM-Au8 30 mg or placebo)
- 36-week treatment period with open label extension
- 1st EP: MUNIX(4) summed %change of ADM, APB, BB, & TA
- 2nd EPs: absolute MUNIX change, % FVC
- Exploratory EPs: disease progression, 6-pt decline in ALSFRS-R, ALSSQOL-SF, & other neurophysiology endpoints
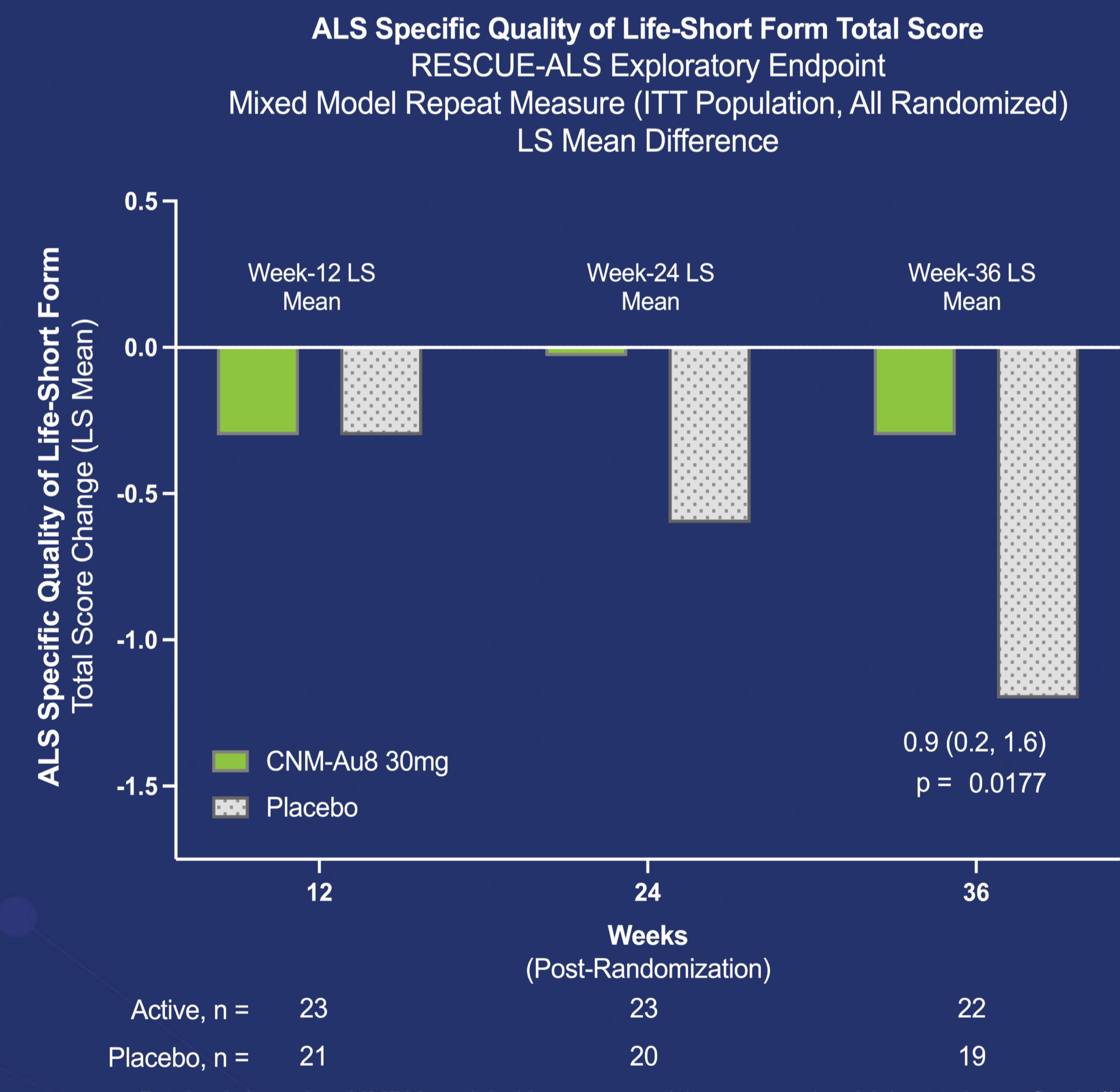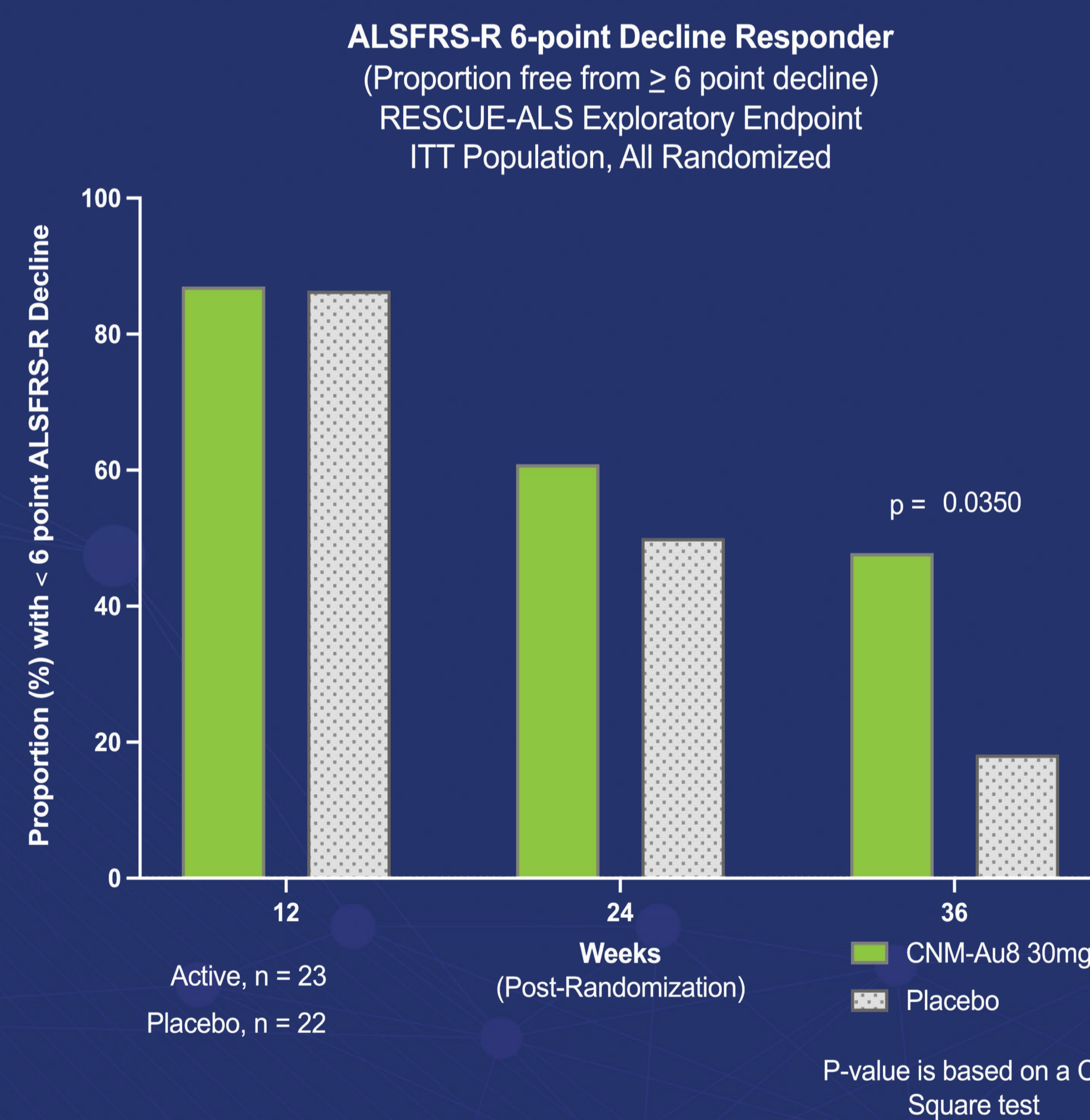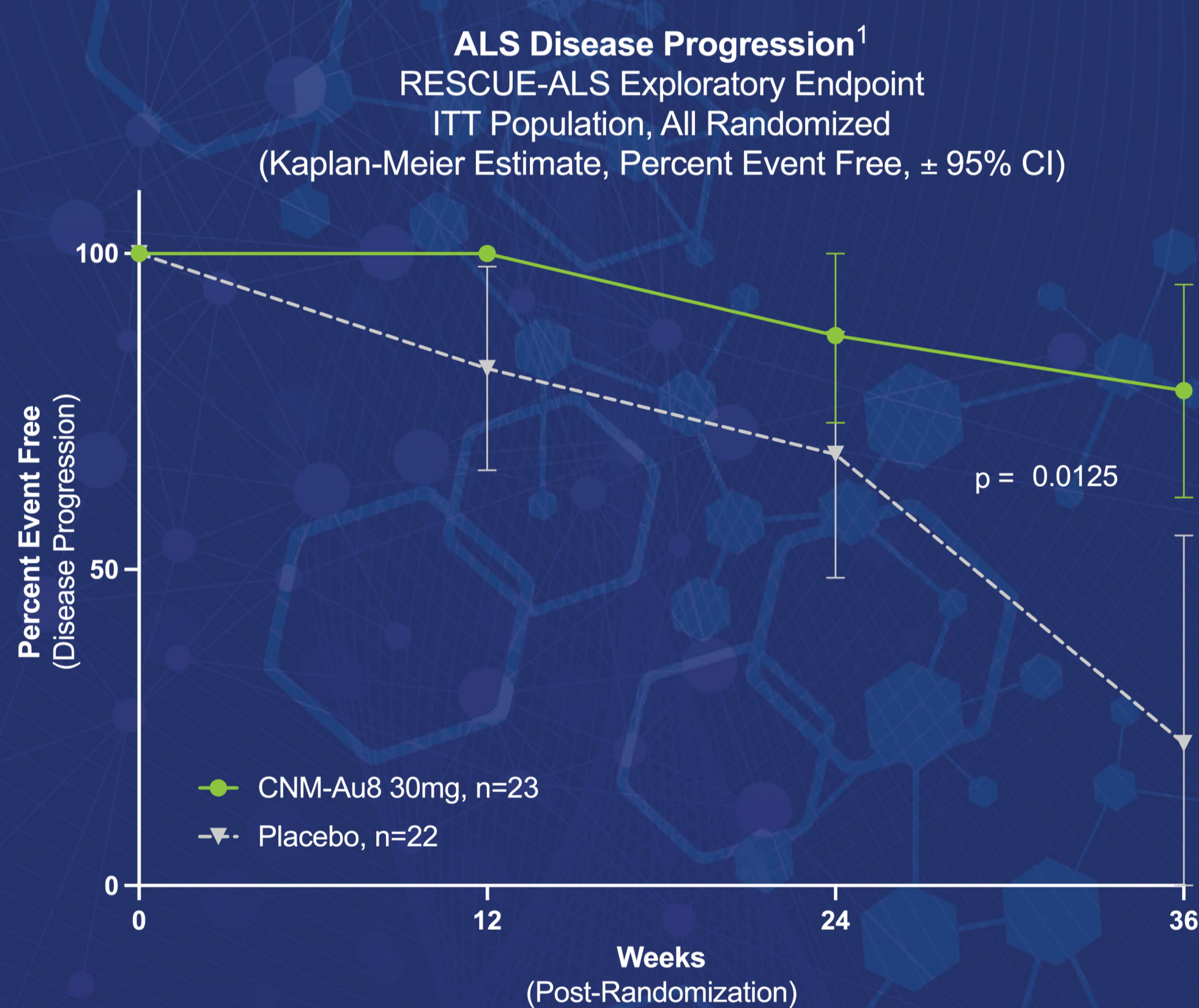
1° Endpoint | Summated MUNIX Change at Week 36

Summated MUNIX Percent Change from Baseline to Week 36
ITT Population & Limb Onset Subset
LS Mean (SE)

All Randomized — Week-36 LS Mean (ITT Population): CNM-Au8 30mg ITT (n = 23), Placebo ITT (n = 22); 7.7 (CI: -11.9, 27.3); p = 0.430

Limb Onset Only — Week-36 LS Mean (ITT, Limb Onset Subset): CNM-Au8 30mg Limb Onset (n = 16), Placebo Limb Onset (n = 17); 20.9 (CI: -2.2, 44.0); p = 0.0741

Summated MUNIX Percent Change from Baseline Placebo Only Decline to Week 36
(Limb Onset vs. Bulbar Onset)
LS Mean Change (SE)
Placebo Bulbar Onset; Placebo Limb Onset

Primary endpoint p-value is based on mixed model repeat measures with treatment, visit, treatment by visit interaction as fixed effects, and baseline value and ENCALS score as covariates. An unstructured covariance model was used.

2° EP | FVC Change at Week 36

FVC (% predicted) Change from Baseline to Week 36
ITT Population & Limb Onset Subset
LS Mean (SE)

All Randomized — Week-36 LS Mean (ITT Population): CNM-Au8 30mg ITT (n = 23), Placebo ITT (n = 22); 3.6 (CI: -12.4, 19.7); p = NS

Limb Onset Only — Week-36 LS Mean (ITT, Limb Onset Subset): CNM-Au8 30mg Limb Onset (n = 16), Placebo Limb Onset (n = 17); 7.1 (CI: -13.3, 27.6); p = NS

Clinical Endpoints | Exploratory

ALS Disease Progression[1]
RESCUE-ALS Exploratory Endpoint
ITT Population, All Randomized
(Kaplan-Meier Estimate, Percent Event Free, ± 95% CI)

CNM-Au8 30mg, n=23; Placebo, n=22; p = 0.0125

[1] Disease progression defined as death, tracheostomy, or need for non-invasive ventilatory support or gastrostomy tube placement.

ALSFRS-R 6-point Decline Responder
(Proportion free from ≥ 6 point decline)
RESCUE-ALS Exploratory Endpoint
ITT Population, All Randomized

Active, n = 23; Placebo, n = 22; p = 0.0350
CNM-Au8 30mg; Placebo
P-value is based on a Chi-Square test

ALS Specific Quality of Life-Short Form Total Score
RESCUE-ALS Exploratory Endpoint
Mixed Model Repeat Measure (ITT Population, All Randomized)
LS Mean Difference

Week-12 LS Mean; Week-24 LS Mean; Week-36 LS Mean
CNM-Au8 30mg; Placebo
0.9 (0.2, 1.6); p = 0.0177

	Week-12	Week-24	Week-36
Active, n =	23	23	22
Placebo, n =	21	20	19

P-value is based on MMRM model with treatment, visit, treatment by visit interaction as fixed effects, and baseline value, and ENCALS score as covariates. An unstructured covariance model was used.
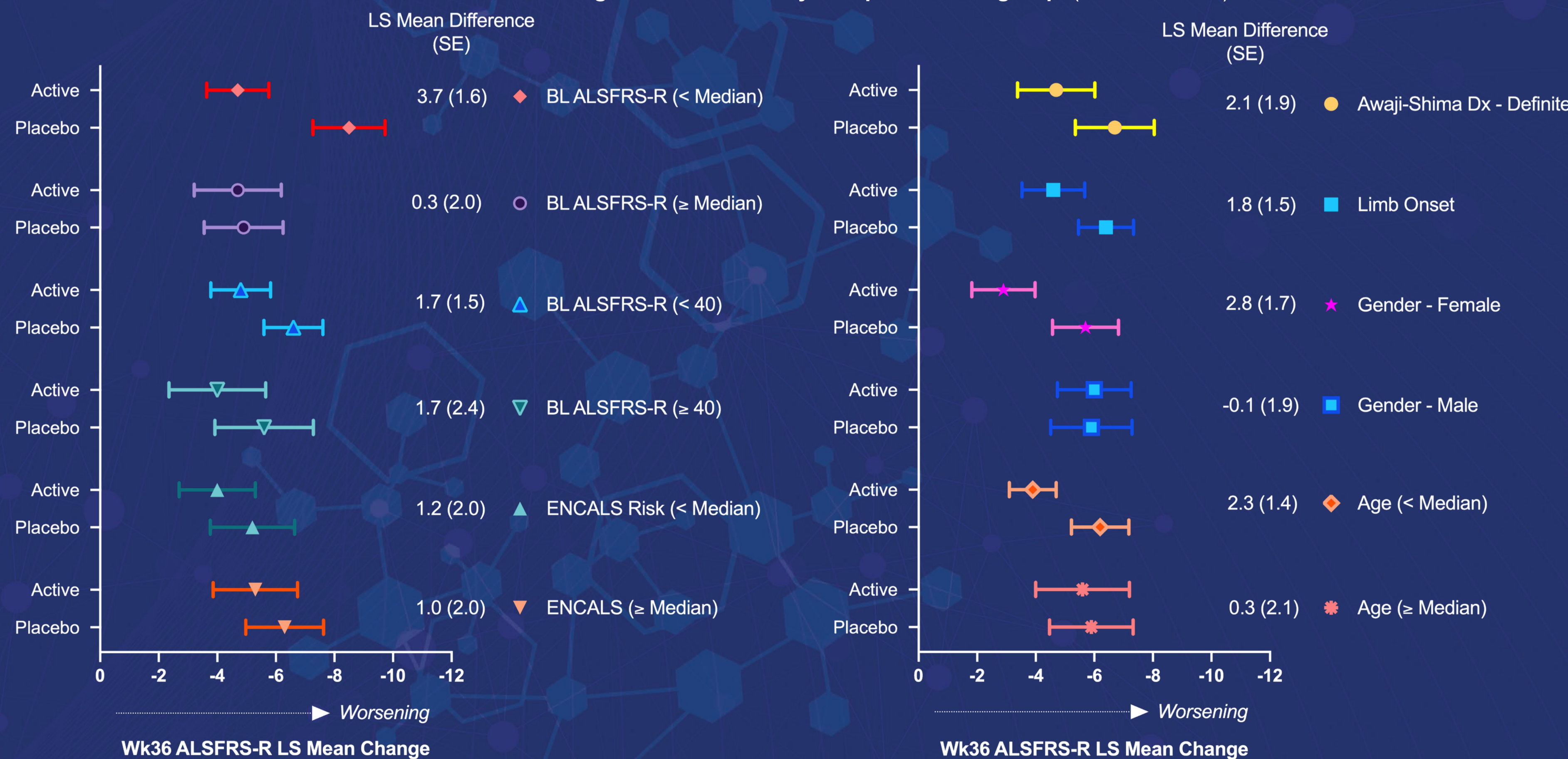
ALSFRS-R Week 36 Change from Baseline by Prespecified Subgroup[1] (LS Mean ± SE)

LS Mean Difference (SE):
- BL ALSFRS-R (< Median): 3.7 (1.6)
- BL ALSFRS-R (≥ Median): 0.3 (2.0)
- BL ALSFRS-R (< 40): 1.7 (1.5)
- BL ALSFRS-R (≥ 40): 1.7 (2.4)
- ENCALS Risk (< Median): 1.2 (2.0)
- ENCALS (≥ Median): 1.0 (2.0)
- Awaji-Shima Dx - Definite: 2.1 (1.9)
- Limb Onset: 1.8 (1.5)
- Gender - Female: 2.8 (1.7)
- Gender - Male: -0.1 (1.9)
- Age (< Median): 2.3 (1.4)
- Age (≥ Median): 0.3 (2.1)

Wk36 ALSFRS-R LS Mean Change — Worsening

[1] Selected subgroups with n ≥ 20 subjects (active + placebo combined)

Safety Summary

- No CNM-Au8 related SAEs, drug discontinuations, or adverse event (AE) imbalance by system organ class.
- AEs predominantly mild-to-moderate & transient.
- The AEs most commonly associated with CNM-Au8 included aspiration pneumonia, n=3; nausea, n=2; abdominal discomfort, n=2.

Acknowledgements

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