Phase 2 Results

RESCUE ALS

Randomized, Double-Blind, Placebo-Controlled Study in Early Symptomatic Amyotrophic Lateral Sclerosis Patients on Stable Background Therapy to Assess Bioenergetic Catalysis with CNM-Au8 to Slow Disease Progression in ALS

Disclosures & Acknowledgements

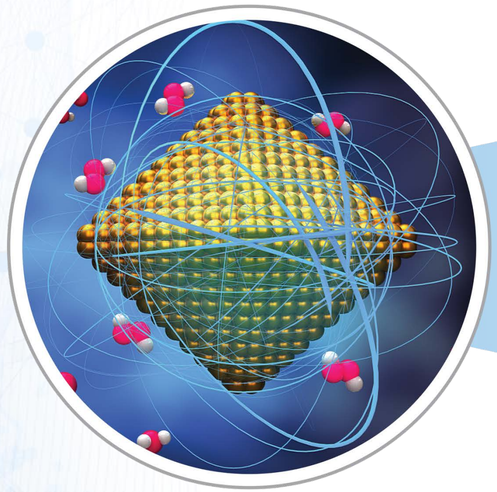
- Robert Glanzman, MD FAAN is an employee of Clene Nanomedicine, Inc.
- Funding support from FightMND Australia is gratefully acknowledged
- We thank ALS patients and their caregivers for participating in RESCUE-ALS
- Presenting on behalf of trial investigators

FIGHT MND. IT TAKES PEOPLE

RESCUEALS

Oral CNM-Au8 | Improves Energy Production to Promote Neuroprotection and Remyelination

CNM-Au8 Nanocrystal



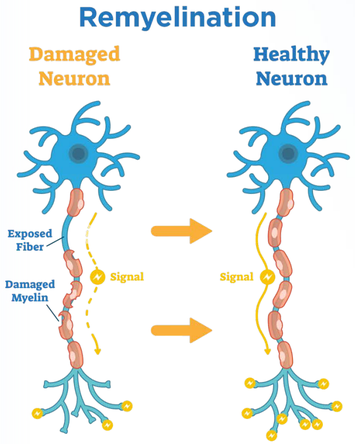
Mechanistic Effects

- ↑ Increased NAD
- ↑ Increased ATP
- ↓ Decreased reactive oxygen species
- ↑ Increased proteostasis

Improved Energy Production and Utilization

- ↑ Increased energetic potential
- ↑ Improved resistance to oxidative, mitochondrial, and excitotoxic stressors
- ↓ Reduction in levels of misfolded proteins

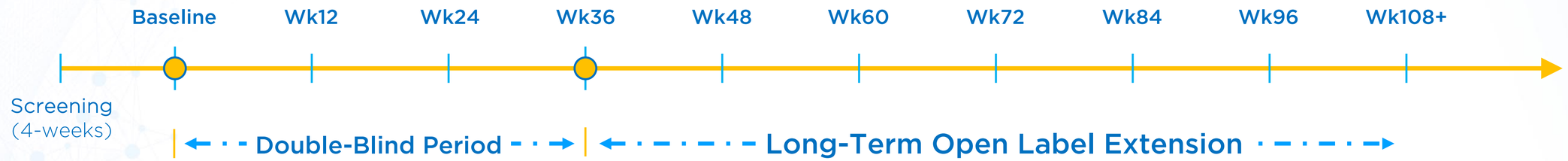
Promotes Neuroprotection and Remyelination



Neuroprotection

RESCUE-ALS | Design & Baseline Demographics

36-Week Blinded Treatment Period with Long-Term Open-Label Extension



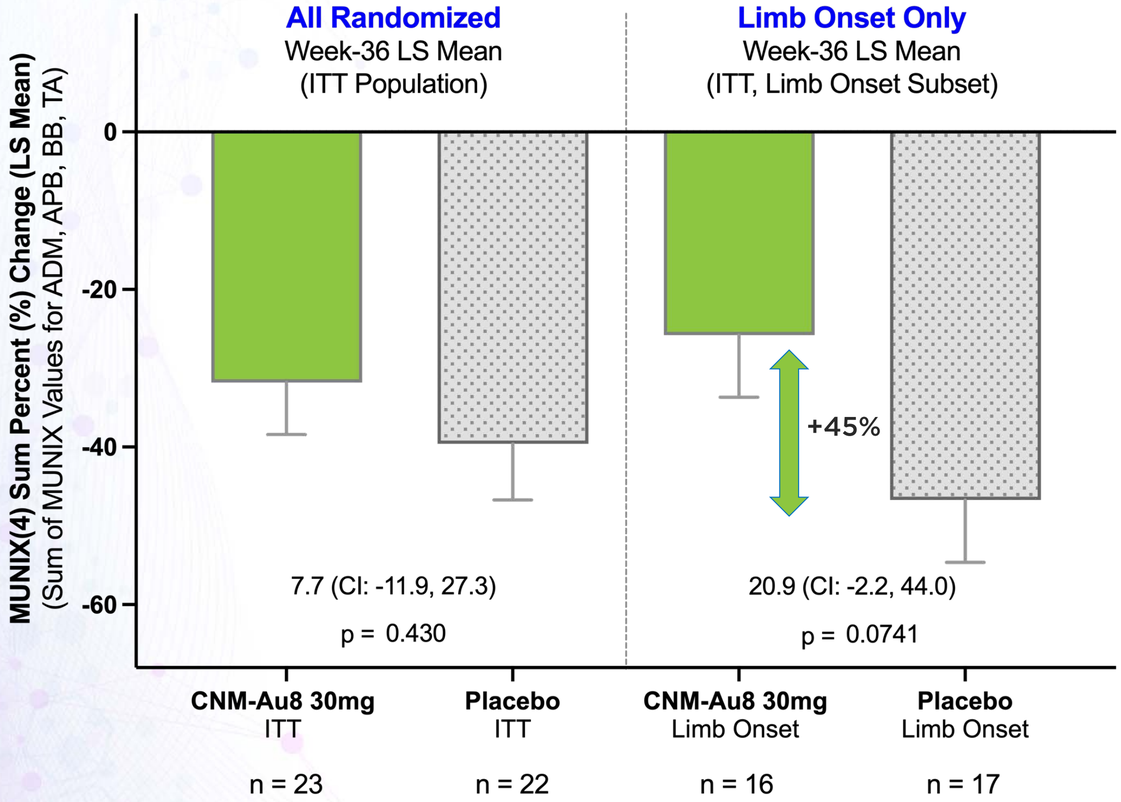
Baseline Value mean (sd)	**Age** (yrs)	**Sex** n, (%) Male | Female	**Onset Site** n, (%) Limb | Bulbar	**Months from Onset**	**FVC** (% pred.)	**ALSFRS-R Score**	**ENCALS Risk Profile**[1]	**MUNIX Sum**
All (n=45)	59.1 (12.3)	M: 26 (58%) F: 19 (42%)	L: 33 (73%) B: 12 (27%)	15.8 (9.3)	81.5 (16.7)	38.7 (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)

Evidence for Motor Neuron Protection

Primary Endpoint (MUNIX %, LS Mean Change)

All Randomized

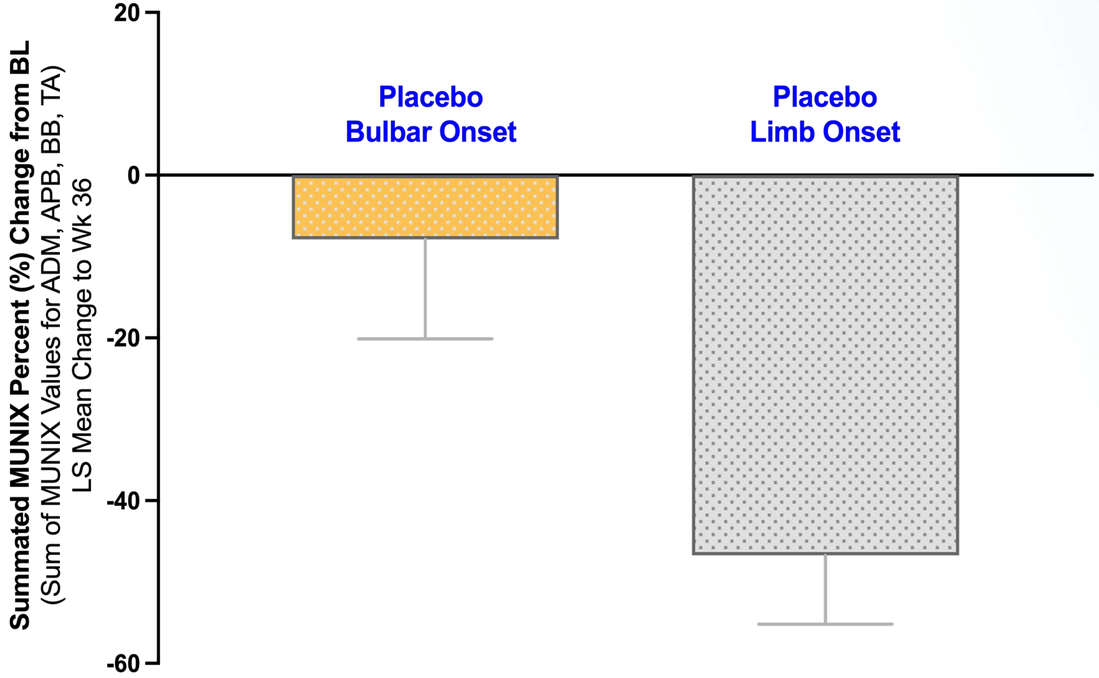
Summated MUNIX Percent Change from Baseline to Week 36
RESCUE-ALS Primary Endpoint
Mixed Model Repeat Measure (ITT Population & Limb Onset Subset)
LS Mean (SE)



All Placebo

Limited Rate of MUNIX Decline in Bulbar Onset

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



Insufficient Spinal Cord Lower Motor Neuron Progression in Early Bulbar Trial Participants

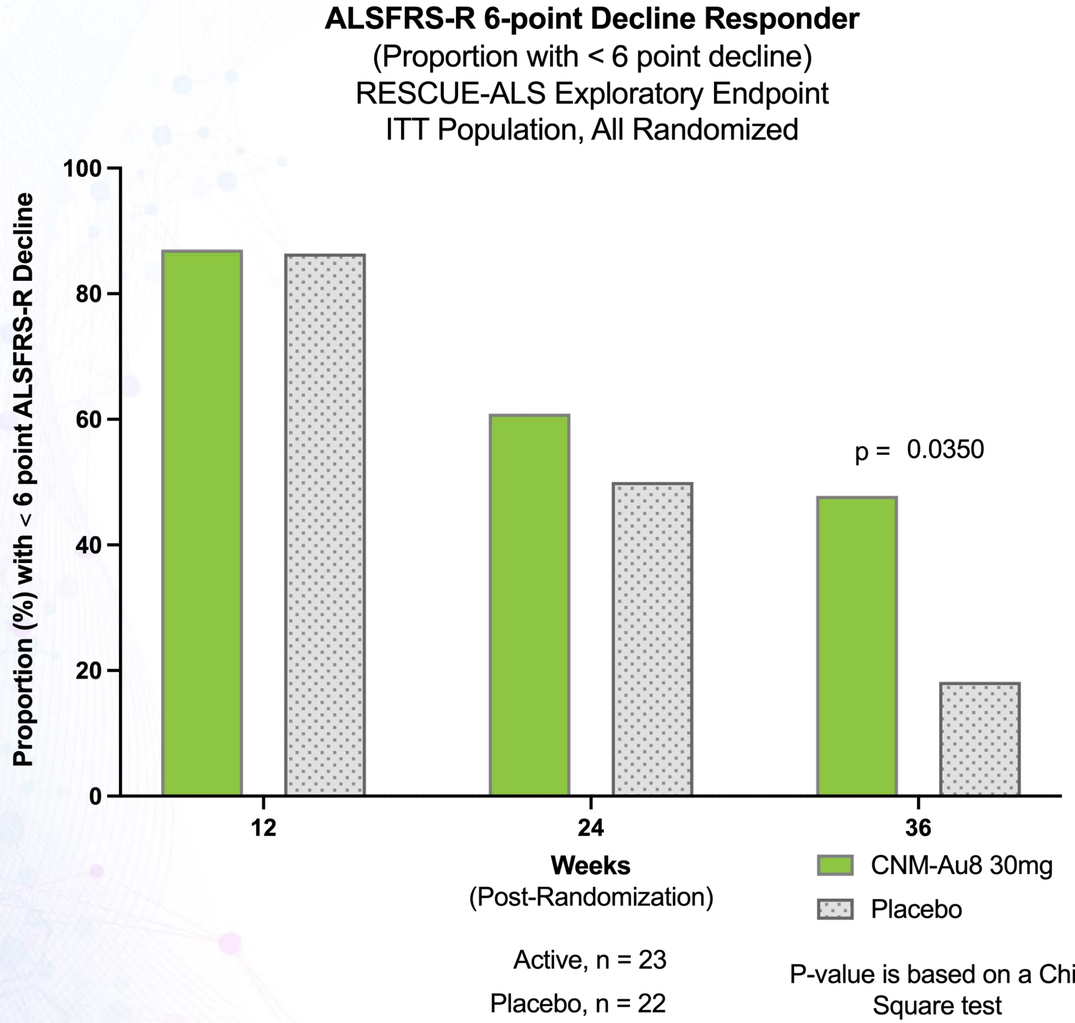
RESCUE-ALS: A Phase 2, randomized, double-blind, placebo-controlled study of CNM-Au8 to slow disease progression in ALS. MNDA Virtual Symposium, 2021 Data on File, Clene Nanomedicine, Inc.

RESCUEALS

Significant Impact on ALSFRS-R Decline

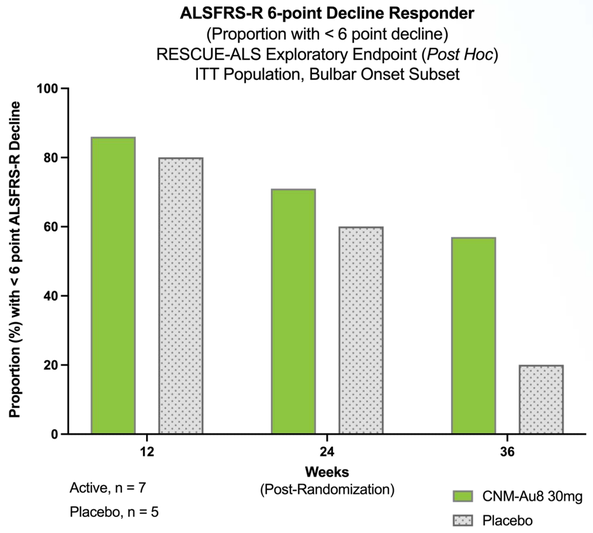
Exploratory (ALSFRS-R Responder Analysis, < 6-point decline)

All Randomized

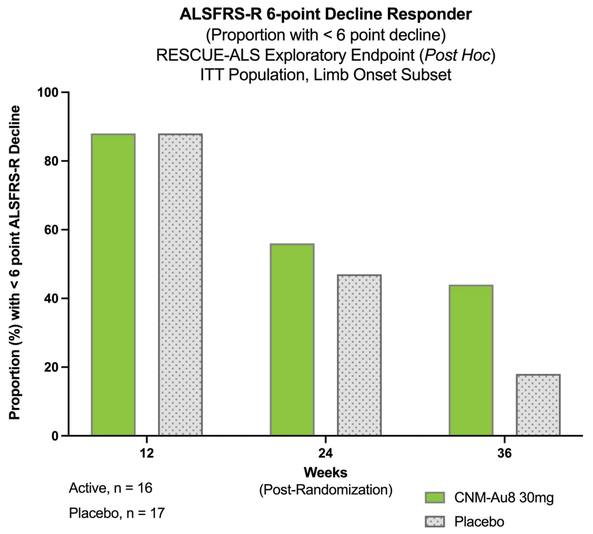


Sensitivity Analysis

All Bulbar



All Limb



RESCUE-ALS: A Phase 2, randomized, double-blind, placebo-controlled study of CNM-Au8 to slow disease progression in ALS. MNDA Virtual Symposium, 2021 Data on File, Clene Nanomedicine, Inc.

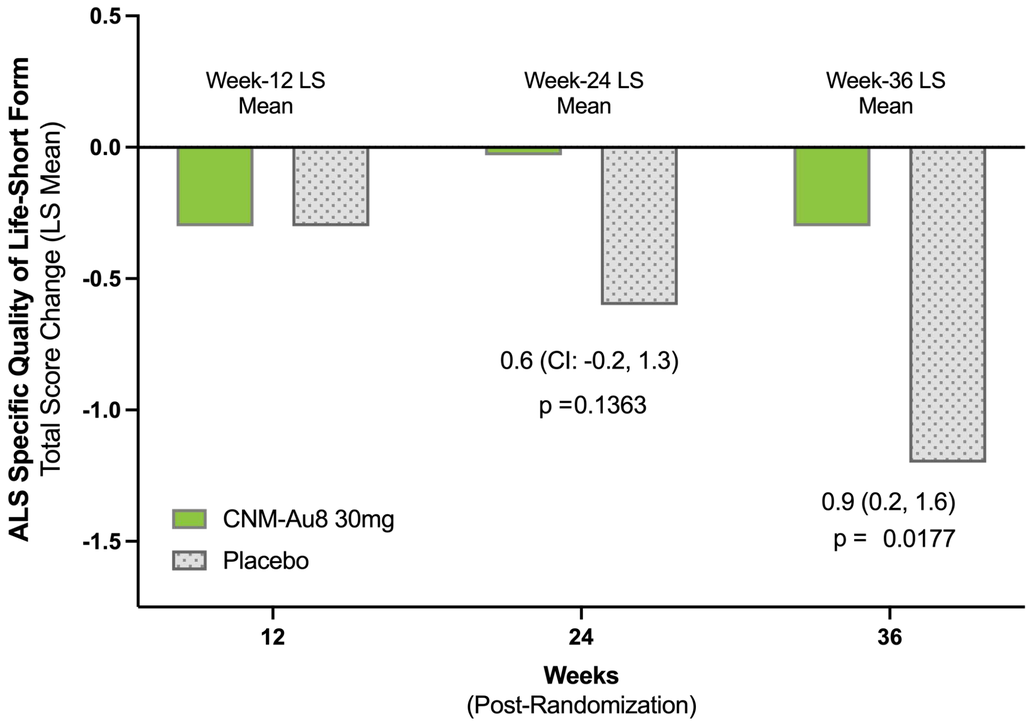
RESCUEALS

Significant Quality of Life Improvement

Exploratory (ALS Specific QOL-SF)

All Randomized

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



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.

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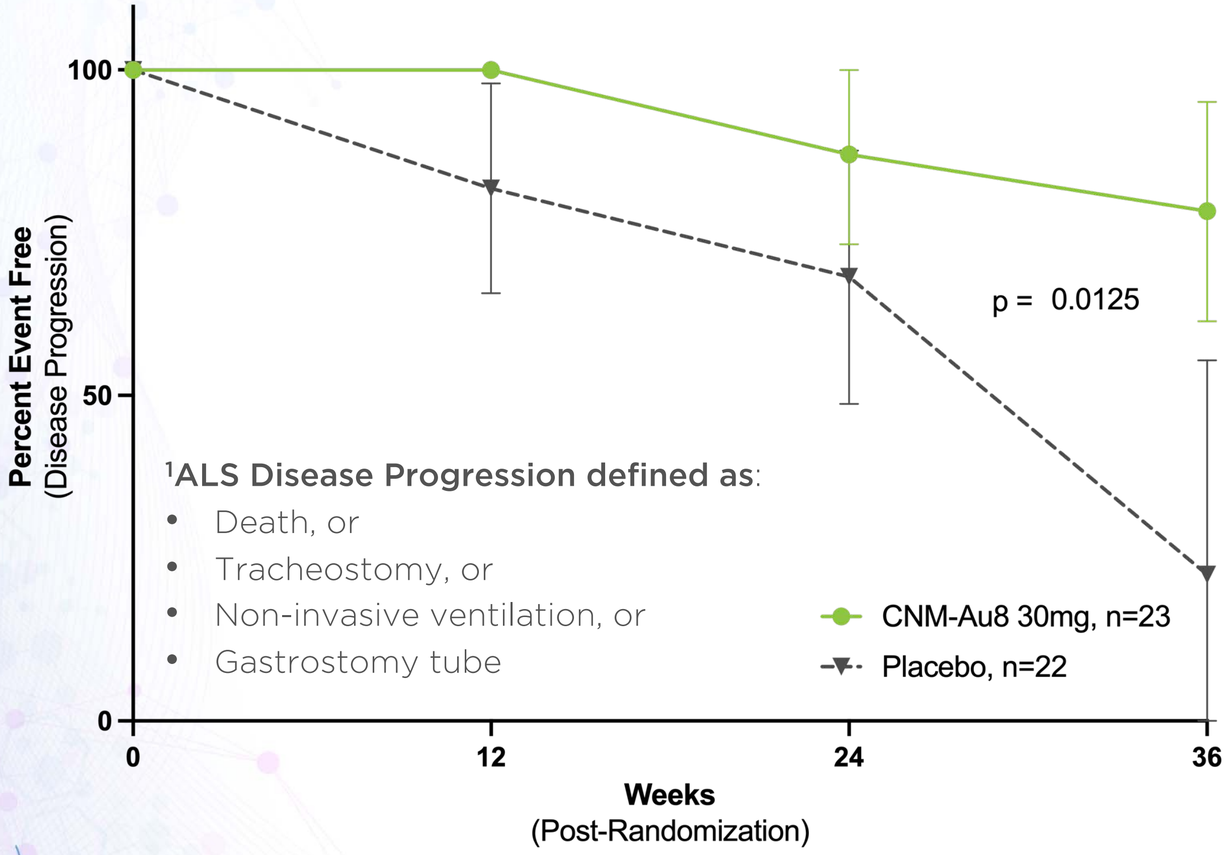
RESCUEALS

Significant Impact on Disease Progression

Exploratory Endpoint (Disease Progression)

All Randomized

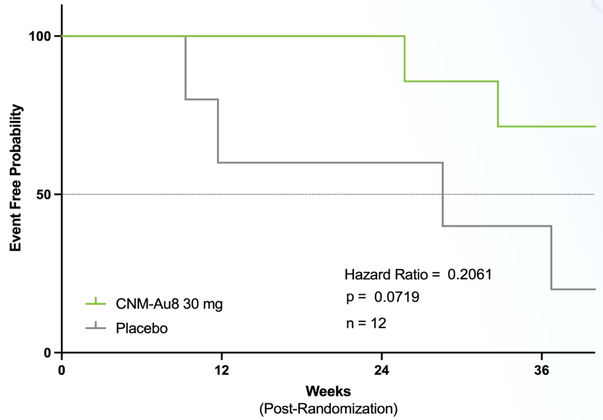
ALS Disease Progression[1]
RESCUE-ALS Exploratory Endpoint
ITT Population, All Randomized
(Kaplan-Meier Estimate, Percent Event Free, ± 95% CI)



Sensitivity

All Bulbar

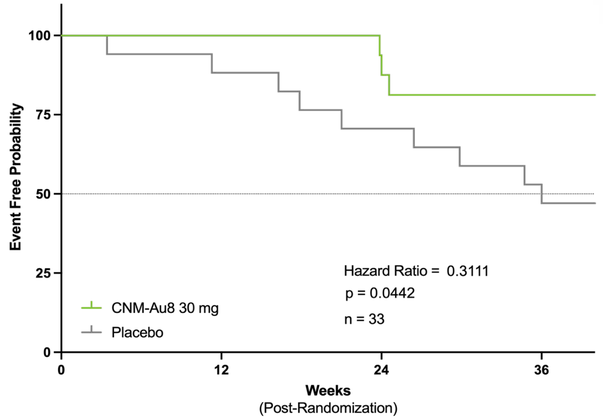
Bulbar Onset ALS Disease Progression[1]
RESCUE-ALS Exploratory Endpoint (Post Hoc)
ITT Population, Bulbar Onset Subset
Kaplan-Meier Estimates, Proportion Event Free



[1] Disease progression defined as death, tracheostomy, use of non-invasive ventilatory support, or insertion of gastrostomy tube.

All Limb

Limb Onset ALS Disease Progression[1]
RESCUE-ALS Exploratory Endpoint (Post Hoc)
ITT Population, Limb Onset Subset
Kaplan-Meier Estimates, Proportion Event Free



RESCUE-ALS: A Phase 2, randomized, double-blind, placebo-controlled study of CNM-Au8 to slow disease progression in ALS. MNDA Virtual Symposium, 2021 Data on File, Clene Nanomedicine, Inc.

Joint Rank Trend | Survival & ALSFRS-R

Exploratory Endpoint Pre-specified (Combined Assessment of Survival and Function [CAFS])

Score participants based on relative function or time of death

Scoring

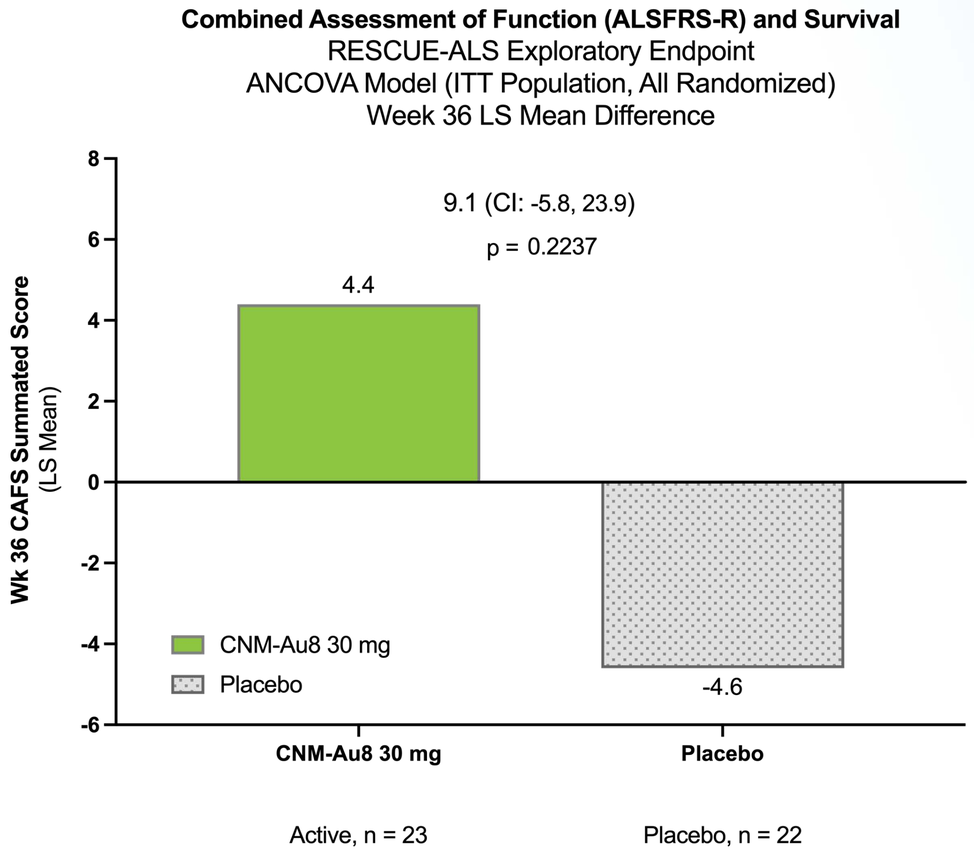
If...	Score
Better function or died later than comparison	+1
Same function or died at the same time as comparison	0
Worse function or died before comparison subject	-1

CAFS

Survival

ALSFRS-R Decline

All Randomized



P-value is based on ANCOVA model with baseline ENCALS score as a covariate. Change in ALSFRS-R total score and date of death were combined to determine the CAFS score.

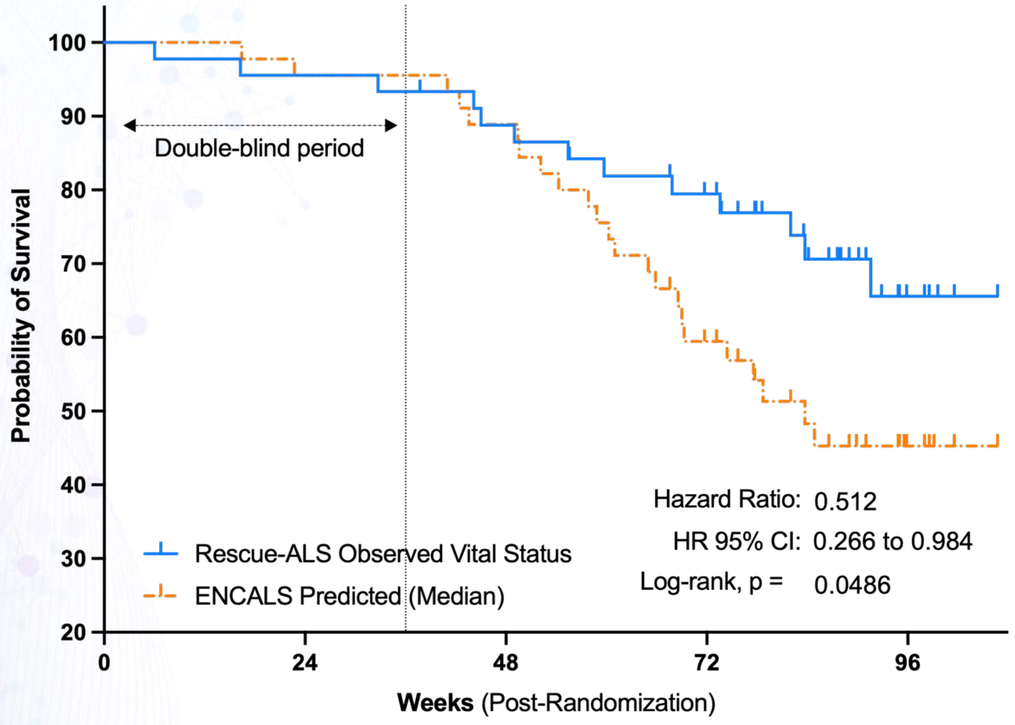
Berry et al. Amyotroph Lateral Scler Frontotemporal Degener. 2013 Apr;14(3):162-8.

RESCUEALS

Impact on Long-Term Survival

All Randomized

RESCUE-ALS Long-Term Observed Survival (All Randomized)
vs. ENCALS Predicted Median Survival
ITT Population, All Subjects from Randomization (Active & Placebo)

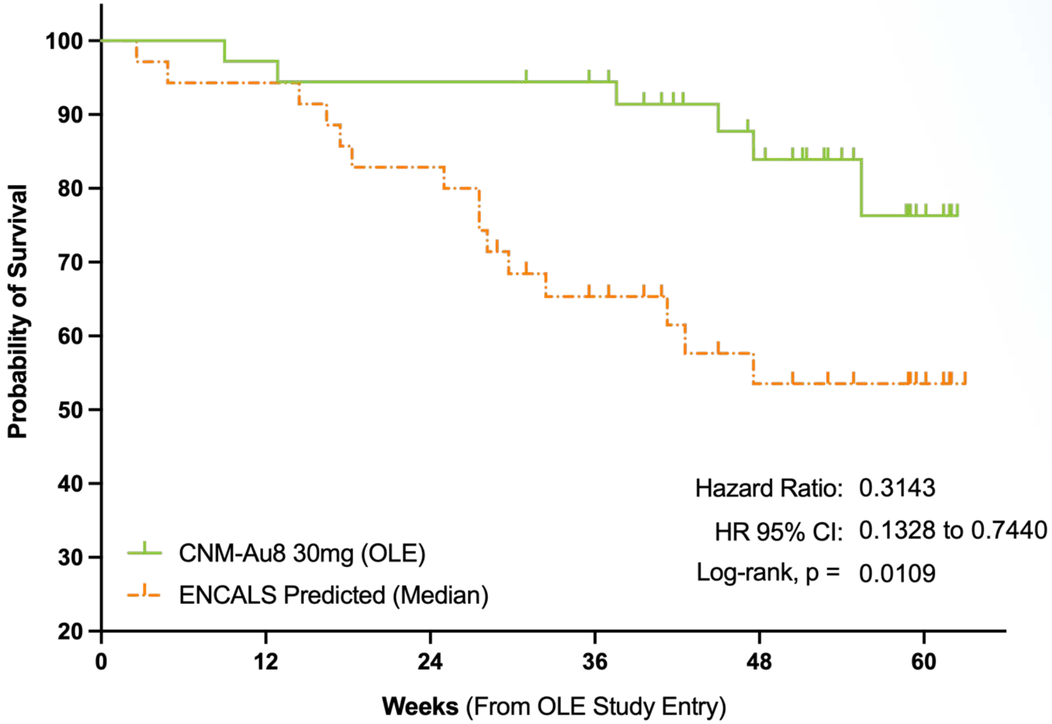


At Risk (n):					
	45	43	39	39	8

All randomized subjects censored as of 1-February-2022. Vital status and date of death captured for all subjects withdrawn from the study through Dec 2021. Lost-to-follow-up (n=1) censored as of the last date of last study contact.

All OLE Participants (CNM-Au8 Treated)

RESCUE-ALS Long-Term Observed Survival (OLE Participants)
vs. ENCALS Predicted Median Survival
All Open Label Extension Participants



At Risk (n):						
	36	35	34	32	21	6

All OLE subjects censored as of 1-February-2022. Vital status and date of death (as applicable) captured for all subjects withdrawn from the study through December 2021.
ENCALS median survival estimate from baseline characteristics.

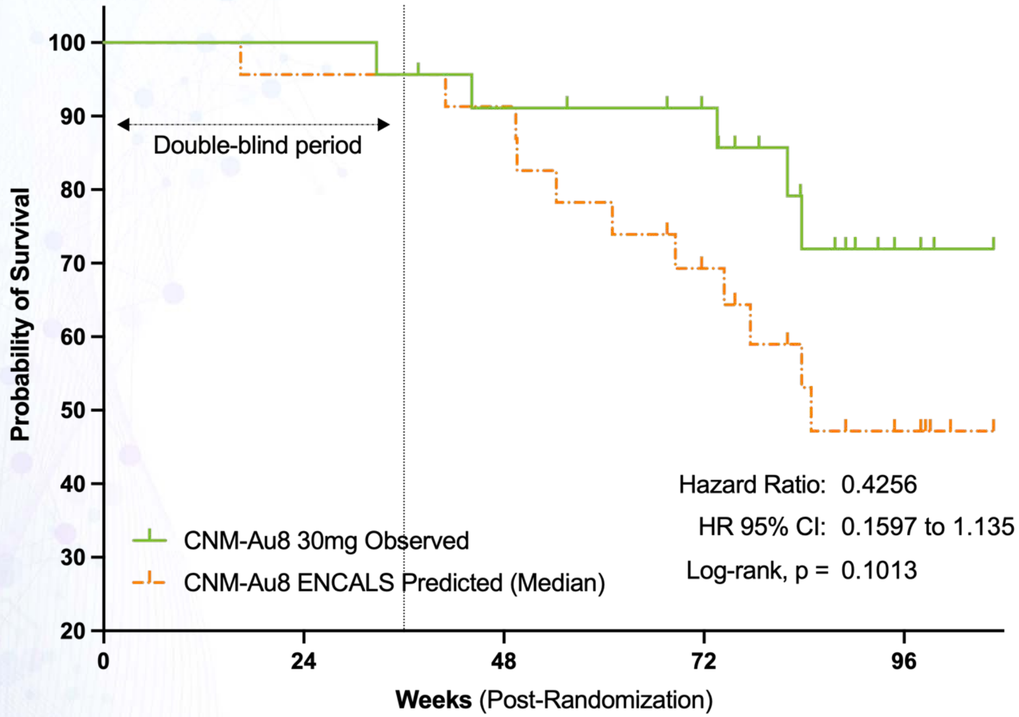
RESCUEALS

Impact on Long-Term Survival | by Randomization Group

All CNM-Au8 Randomized

RESCUE-ALS Original CNM-Au8 Randomized Long Term Observed Survival vs. ENCALS Predicted Median Survival

All CNM-Au8 Treated Subjects, Survival from Randomization, ITT Population



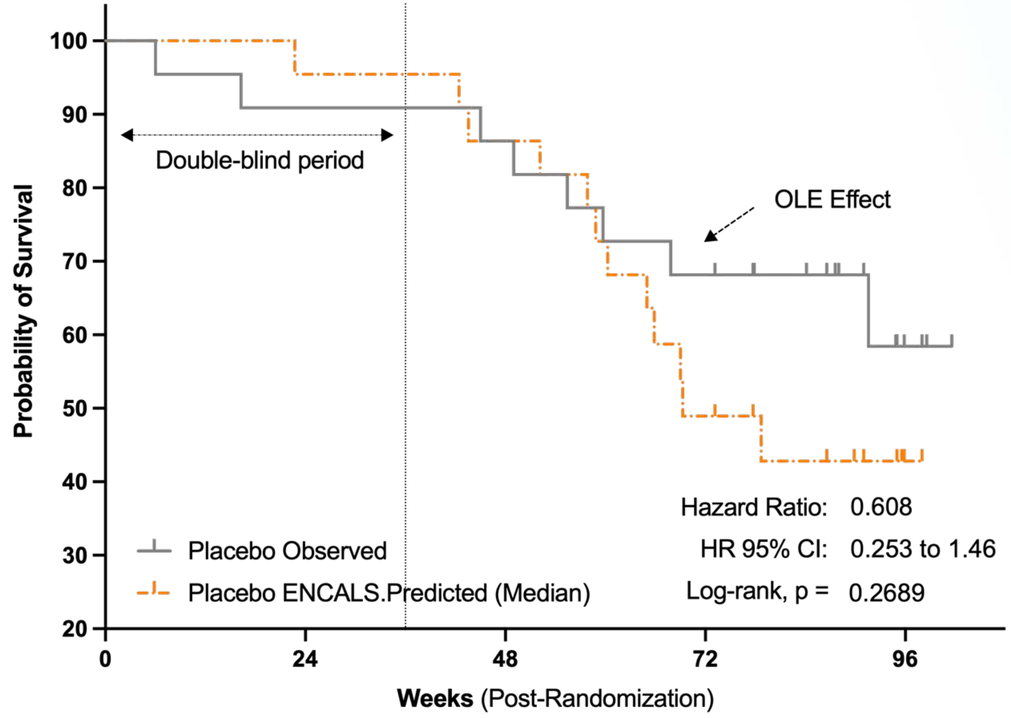
At Risk (n):					
	23	23	20	17	6

All current OLE subjects censored as of 1-February-2022. Vital status and date of death (as applicable) captured for all subjects withdrawn from the study through December 2021. Lost-to-follow-up (n=1) censored as of the last date of last study contact.

All Placebo Randomized

RESCUE-ALS Original Placebo Randomized Long-Term Observed Survival vs. ENCALS Predicted Median Survival

All Placebo Treated Subjects, Survival from Randomization, ITT Population



At Risk (n):					
	22	20	19	14	2

All current OLE subjects censored as of 1-February-2022. Vital status and date of death (as applicable) captured for all subjects withdrawn from the study through December 2021.

RESCUEALS

Safety Summary | Well Tolerated & No Safety Signals

- No CNM-Au8 related serious adverse events (SAEs)
- No CNM-Au8 related drug discontinuations
- No imbalances in treatment emergent adverse event (TEAEs) by system organ classification
- TEAEs were predominantly mild-to-moderate and transient
- Most common TEAEs associated with CNM-Au8
  (aspiration pneumonia, n=3; nausea, n=2; abdominal discomfort, n=2)

Data on File, Clene Nanomedicine, Inc.

Conclusions

- **<u>Evidence of CNM-Au8 therapeutic efficacy</u>**
  - ✓ Improved survival
  - ✓ Significant slowing in disease progression
  - ✓ Significant reduction in functional decline
  - ✓ Significant improvement in quality of life
  - ✓ Preservation of lower motor neurons
- **CNM-Au8, well tolerated and safe in ALS**
- **Larger clinical trial underway**

RESCUEALS