RESCUEALS

HEALEY ALS Platform Trial

ALS EXPANDED ACCESS PROTOCOLS (EAP)

Evidence for Survival Benefit in ALS with CNM-Au8 Treatment Across Three Study Populations

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CNM-Au8 | Cellular Energetic Nanocatalyst

CNM-Au8 Oral Suspension

Clean Surfaced, Highly Faceted Nanocrystals

Mechanistic Effects
In Neurons and Glia[1]

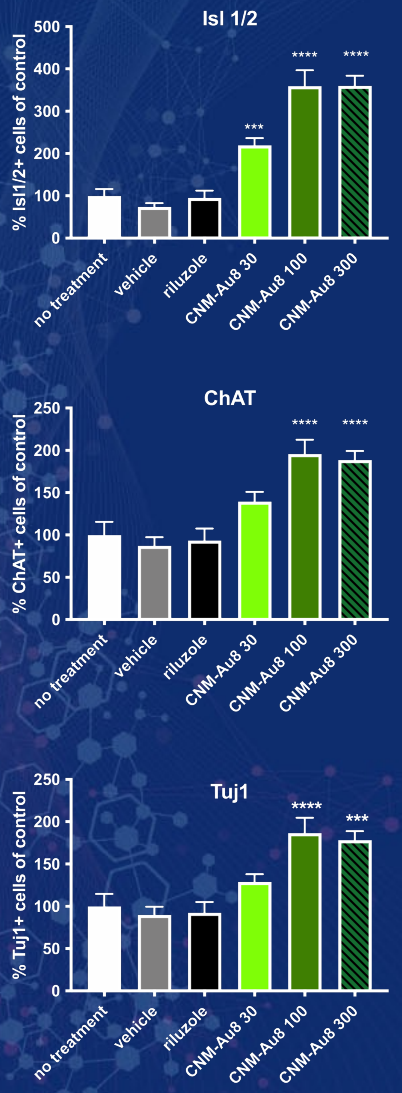
- ↑ Increased NAD
- ↑ Increased ATP
- ↓ Decreased reactive oxygen species
- ↑ Increased proteostasis

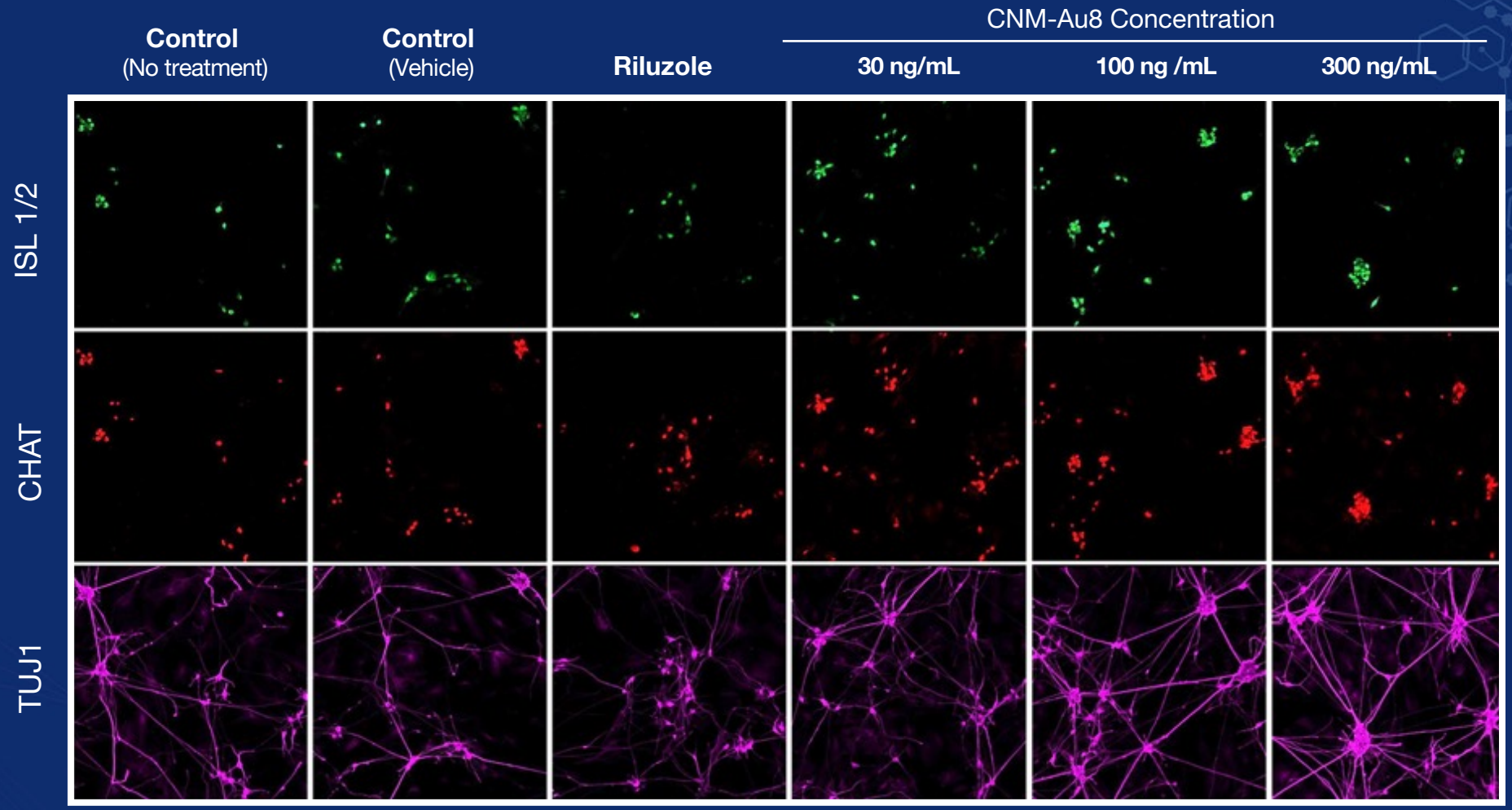
Improved Energy Production and Utilization

[1] Robinson et al. Sci Rep. 2020 Feb 11;10(1):1936

Preclinical | Improved Motor Neuron Survival

iPSC Motor Neuron with *SOD1^{A4V}* Astrocytes





14-day co-incubation of SOD1^{A4V} astrocytes in fully differentiated mature motor neurons

Preclinical | Improved Neuron Survival

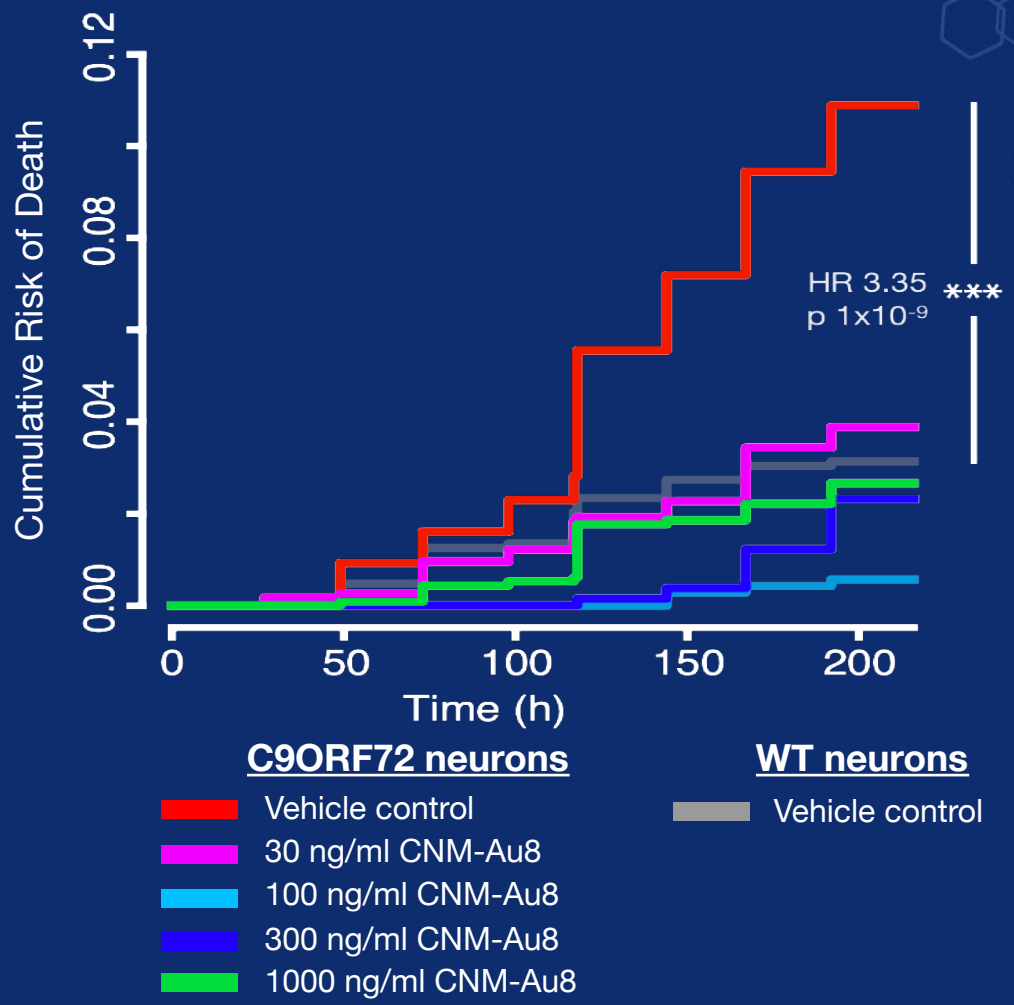
iPSC *C9ORF72* Neuron Model (Cortical Forebrain)

Results vs. *C9ORF72* Neuron Vehicle Control

CNM-Au8 Conc.	Hazard Ratio	Hazard Reduction (%)	p-value
30 ng/mL	0.36	64%	1×10^{-8}
100 ng/mL	0.07	93%	1×10^{-7}
300 ng/mL	0.21	79%	4×10^{-14}
1000 ng/mL	0.26	74%	4×10^{-11}

- Neuronal nutrient deprivation model
- Survival assessed from treatment initiation
- Automated tracking of individual neurons (~1000 neurons per experimental condition)

C9ORF72 Neuronal Death

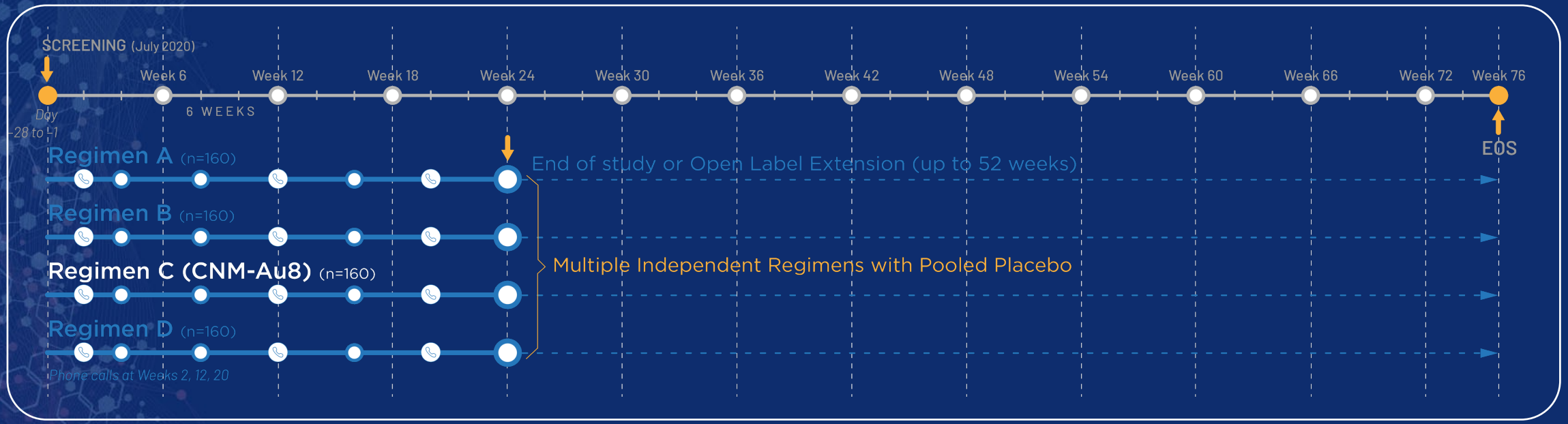


Phase 2

HEALEY ALS Platform Trial

A Multi-center, Randomized Double-Blind, Placebo-Controlled Clinical Trial Assessing the Efficacy, Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of CNM-Au8 in Participants with Amyotrophic Lateral Sclerosis

24-Week Blinded Treatment Period (3:1 randomization, 120 active [30mg, 60mg]: 41 placebo)



1° **Change in ALSFRS-R slope** adjusted by mortality

Weighted Average of Slope Change & Hazard Ratio

Weighting based on # of Mortality Events

2°

- **CAFS** (Joint-Rank)
- **Slow Vital Capacity**
- **Survival** (Death + PAV)

Exploratory Endpoints

PAV (Permanently assisted Ventilation) includes >22 hours/day of noninvasive or invasive mechanical ventilation for more than seven consecutive days

Baseline Characteristics

HEALEY ALS Platform Trial

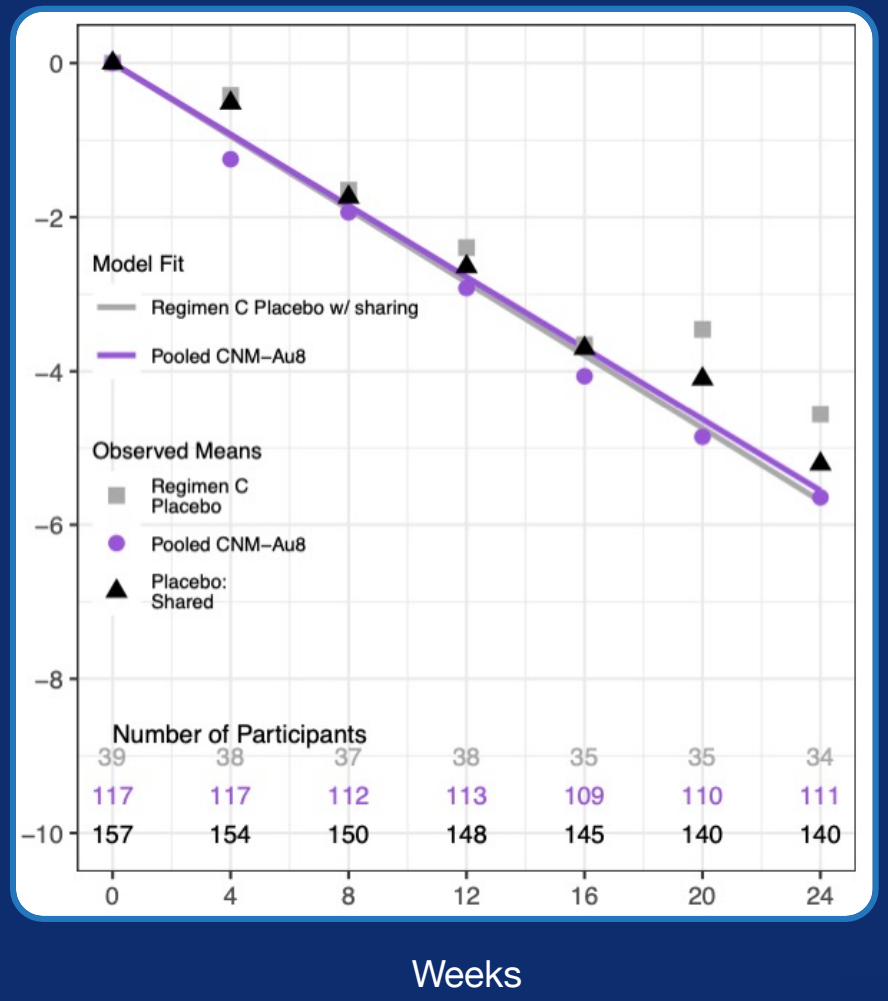
Category Mean (SD), n (%)	All Shared Placebo (n=164)	Regimen Placebo (n=41)	CNM-Au8 30 mg (n=59)	CNM-Au8 60 mg (n=61)
Age (years)	57.2 (11.26)	57.0 (11.72)	57.7 (10.18)	58.6 (9.86)
ALSFRS-R total score	35.1 (6.7)	36.1 (5.9)	34.5 (5.8)	34.0 (7.3)
Pre-baseline delta-FS (points/month)	0.66 (0.43)	0.60 (0.35)	0.77 (0.58)	0.67 (0.49)
Time since symptom onset (months)	21.9 (8.7)	21.9 (8.5)	21.2 (8.6)	24.2 (8.5)
SVC (% predicted)	76.0 (16.5)	76.1 (16.8)	74.4 (16.0)	76.0 (16.3)
Baseline Riluzole use (n, %)	126 (76%)	32 (78%)	45 (76%)	49 (80%)
Baseline Edaravone use (n, %)	41 (25%)	10 (24%)	12 (20%)	16 (26%)
King's Stage 3 or 4 (n, %)	91 (55%)	21 (51%)	38 (64%)	33 (54%)
El Escorial Criteria, Clinically Definite (n, %)	66 (40%)	14 (34%)	28 (48%)	30 (49)%
El Escorial Criteria, Clinically Possible (n, %)	16 (10%)	1 (2%)	1 (2%)	2 (3%)

Primary and Secondary Outcomes

HEALEY ALS Platform Trial

- 1° EP | No effect on ALSFRS-R change (adjusted by mortality) at 24-weeks for combined 30mg and 60mg CNM-Au8 doses (-2%, 95% CI: -20% to 19%)
- 2° EP | Non-significant effect at 24-weeks for combined 30mg and 60mg CNM-Au8 doses for (i) CAFS, (ii) SVC, and (iii) survival (death or PAV)

24-Week ALSFRS-R Progression



EP: endpoint; CI: credible interval; SVC: slow vital capacity; CAFS: combined assessment of function and survival (joint-rank)

Delayed Time to Death or Death Equivalent (PAV) through 24-weeks

HEALEY ALS Platform Trial

Death

or

Permanent Assisted Ventilation

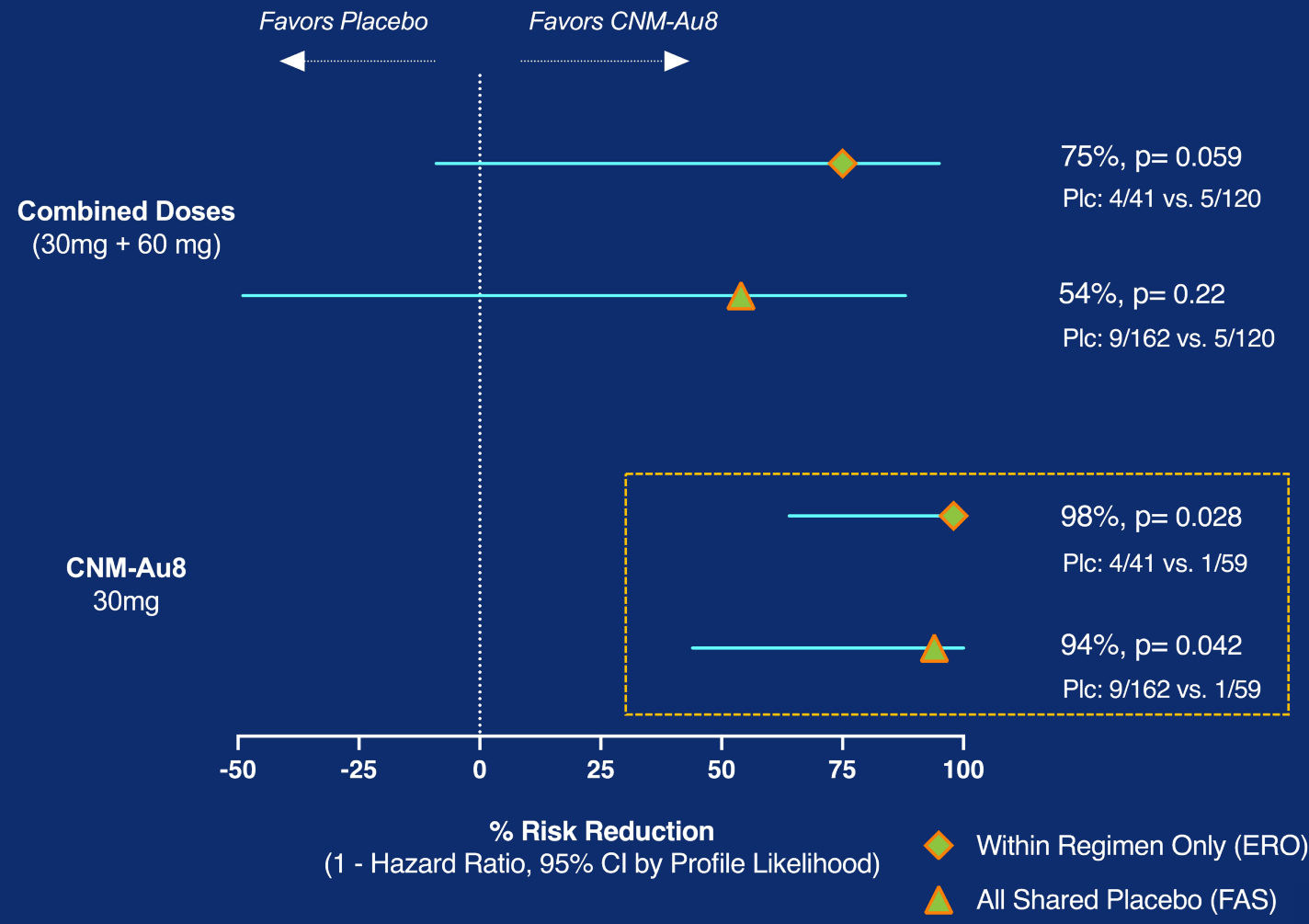
(Tracheostomy or NIV with ventilatory support >22 hours per day over 7 days)

NIV: Non-invasive ventilation

Reduction in Death or Death Equivalent (PAV)

Risk Adjusted Cox Proportional Hazard Model (Primary Covariate Model)

% Hazard Reduction to Week 24 (Double-Blind Period)

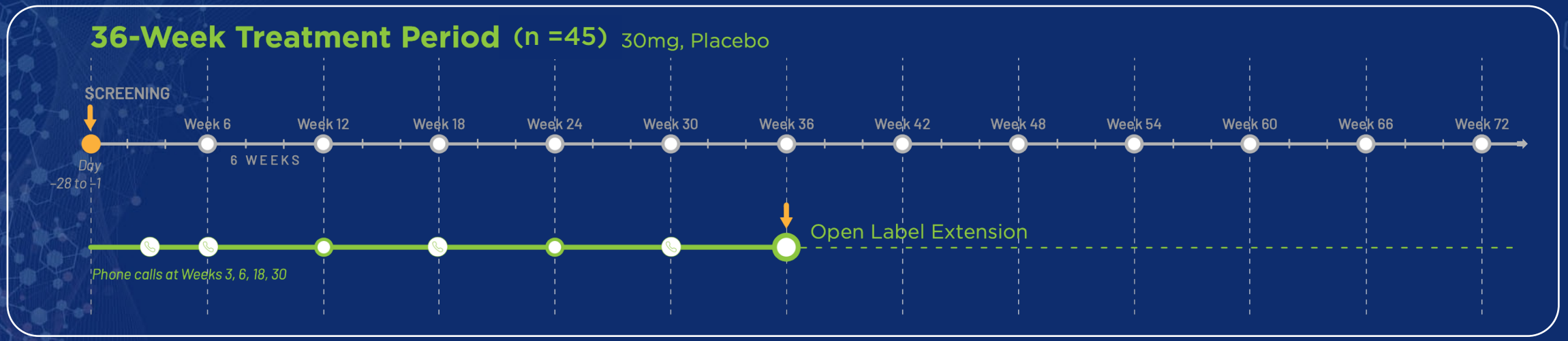


ERO | Efficacy Regimen Only; FAS | Full Analysis Set (all shared placebo); p-values not adjusted for multiple comparisons

Phase 2

RESCUEALS

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



Study Objective:

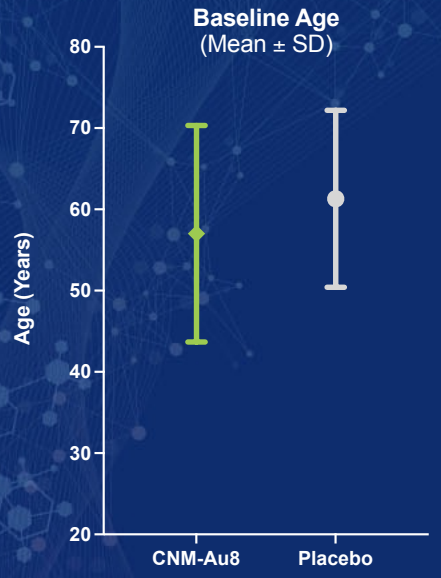
Detect preservation of motor neuron function in people with early ALS as measured by MUNIX

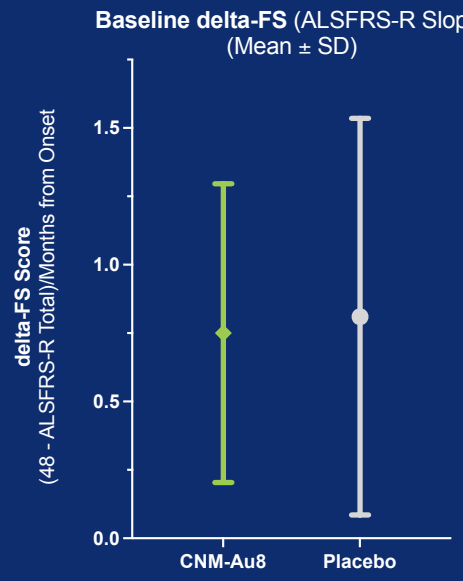
Study Design:

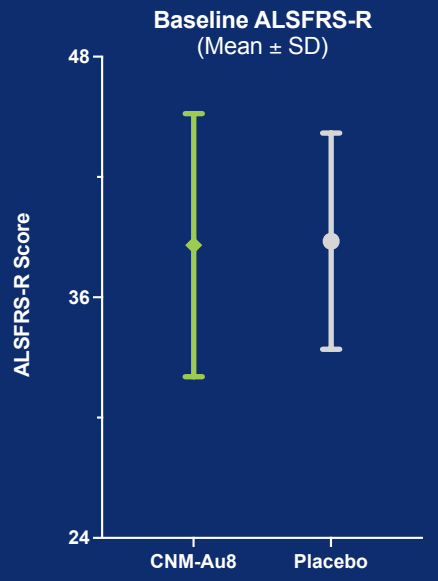
36-week blinded treatment with ongoing long-term open-label follow-up (>120 weeks)

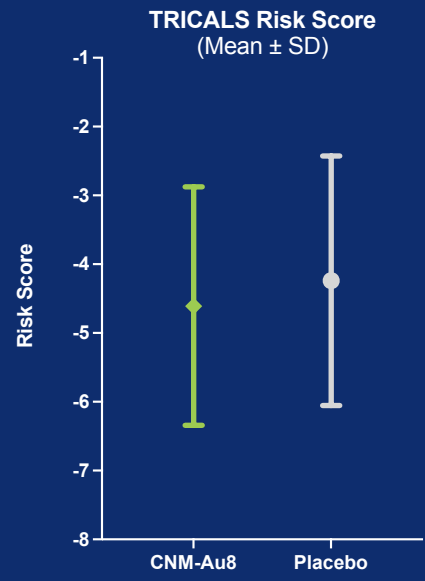
Key Baseline Characteristics

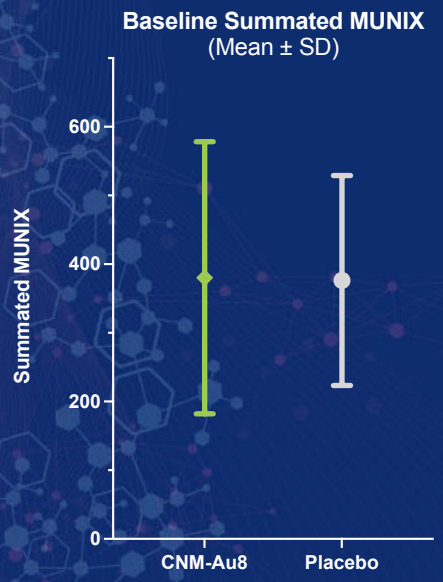
RESCUEALS

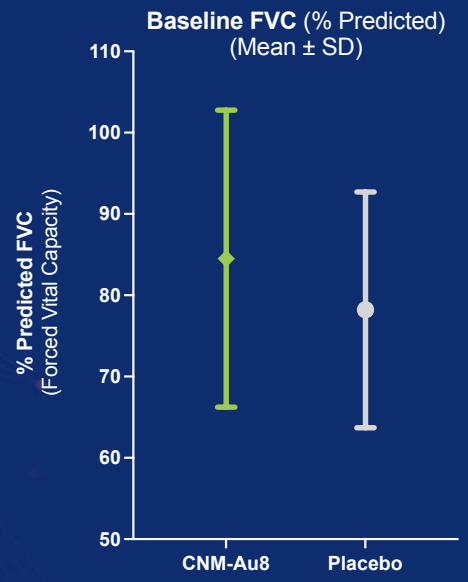


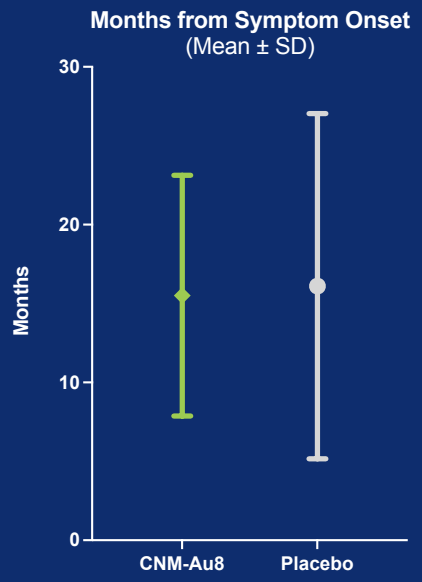


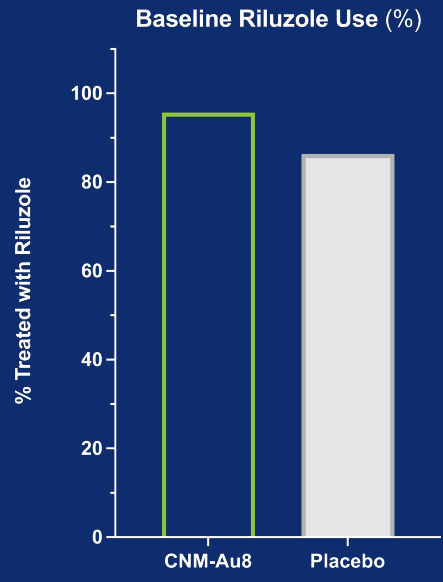








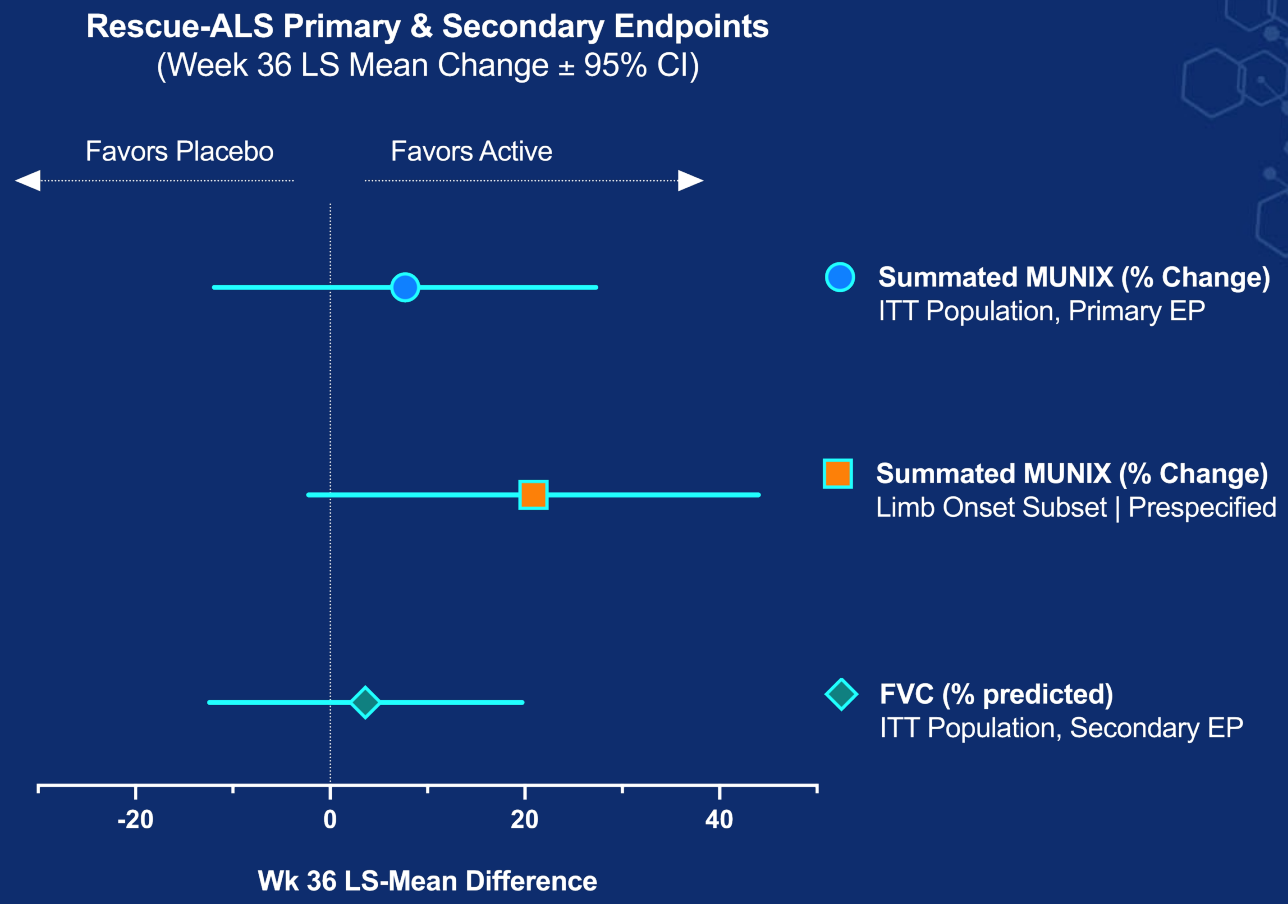




Primary & Secondary Outcomes

- 1st | Non-significant percent change of Motor Unit Index (MUNIX) at 36-weeks for CNM-Au8 30mg dose

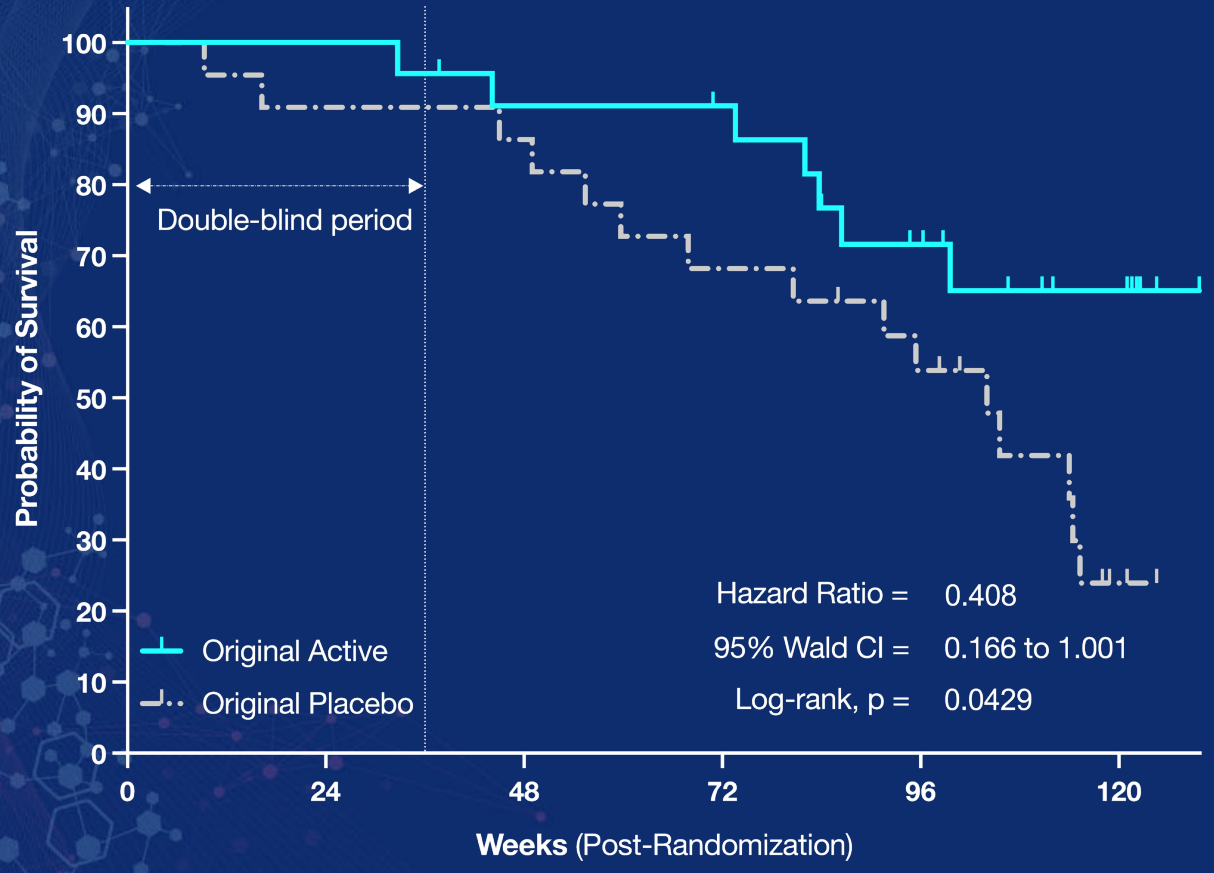
- 2nd | Non-significant change on summated MUNIX (total) and FVC (% predicted)



MUNIX: Motor Unit Index, summed values of 4 spinal cord innervated muscles (ABP, ADM, TA, BB); FVC: forced vital capacity

Delayed Time to All-Cause Mortality in Long-Term Follow-Up

All Cause Mortality During Long-Term Follow-Up
Interim Analysis (14-July-2022), ITT Population
All Participants from Randomization



At Risk (n)

CMM-Au8:	23	23	20	19	13	7
Placebo:	22	20	19	15	11	2

Early CNM-Au8 treatment (30mg) demonstrated a significant survival benefit:

- **60% decreased risk of death through 120-weeks follow-up**
- **Follow-up of original active vs. original placebo randomization (delayed start or no treatment)**

Time to all-cause mortality amongst participants originally randomized to CNM-Au8 compared to participants originally randomized to placebo through at least 12-months following the last-patient last-visit (14-July-2022). Vital status and date of death (as applicable) were captured for all subjects withdrawn from the study. Lost-to-follow-up (active, n=3; placebo, n=1) censored as of the date of last study contact. All OLE ex-placebo CNM-Au8 transitioned participants within the placebo group. All current active OLE subjects are right censored as of 14-July-2022.

Real World Evidence | Expanded Access Protocols

Survival Status vs. ENCALS Predicted Median Survival

ALS EXPANDED ACCESS PROTOCOLS (EAP)

Expanded Access Protocol (EAP) Overview

Compassionate Use Access to CNM-Au8 30mg

(2-sister protocols across 4-sites)

EAP Baseline Characteristics

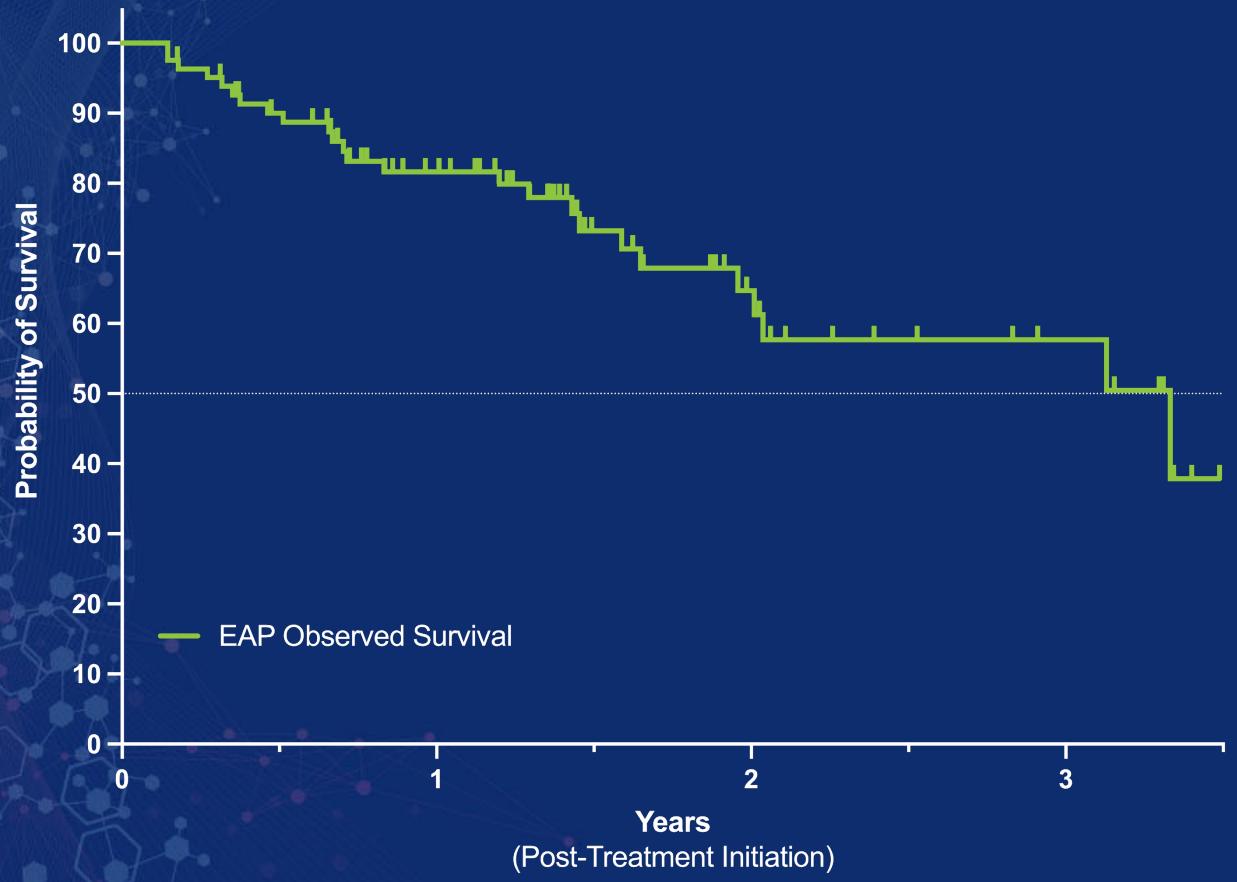
Description mean (SD); [range]	**EAP01** (MGH)	**EAP02** (BNI, HSC, HCH/NVU)
Total Exposed (n)	65	17
Start Date (1st exposure)	Sep-2019	Oct-2021
Treatment Duration (months)	18.3 (11.8) [1.8 to 41.9]	12.2 (4.7) [3.8 to 17.4]
Delta-FS (ALSFRS-R slope)	0.60 (0.49) [0 to 2.6]	0.48 (0.27) [0.06 to 0.9]
ALSFRS-R	31.8 (10.6) [2 to 48]	27.0 (9.6) [9 to 42]
TRICALS Risk Score	-4.7 (2.4) [-0.8 to -12]	-4.5 (2.8) [0.7 to -9]

MGH: Massachusetts General Hospital; BNI: Barrows Neurological Institute; HSC: Hospital for Specialty Care; HCH: Holy Cross Hospital, NVU: Nova Southeastern University

EAP Long Term Survival Status

ALS EXPANDED ACCESS PROTOCOLS (EAP)

CNM-Au8 EAP Long Term Survial Status Estimate
Interim data as of 20-March-2023; All Enrolled EAP Participants (n=82)
Observed Survival from Baseline



At Risk (n):	82	70	52	29	20	13	9

Real World Evidence from compassionate use open-label expanded access protocols

- 82 participants with treatment observations
- Median survival >3 years

Notes: (i) Withdrawals (n=20) censored from date of safety follow-up. (ii) Ongoing participants right-censored as of 20-March-2023.

Conclusion

CNM-Au8 Treatment Associated with Consistent Survival Improvements Across Multiple Populations

RESCUEALS

CNM-Au8 30mg demonstrated statistically significant survival benefit of 60% decreased risk of death through 120-weeks versus original placebo randomization

Early-to-Mid Stage ALS

HEALEY ALS Platform Trial

CNM-Au8 30mg associated with 90% lower hazard of death or death-equivalent through 24 weeks versus placebo

Mid-to-Late-Stage ALS

ALS EXPANDED ACCESS PROTOCOLS (EAP)

CNM-Au8 30mg observed survival suggest potential survival benefit through 3+ years of follow-up

Real World Experience