

clene.com



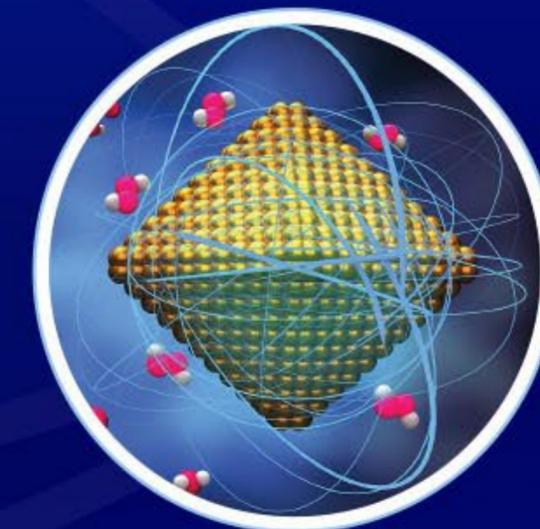
clene™

NASDAQ: CLNN

Forward Looking Statements

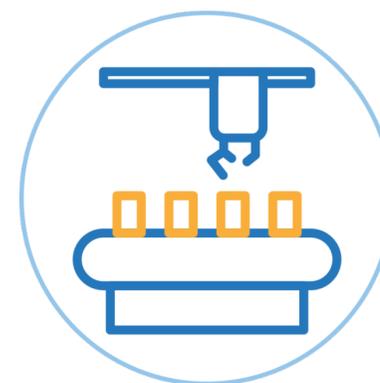
This presentation contains “forward-looking statements” within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended, which are intended to be covered by the “safe harbor” provisions created by those laws. Clene’s forward-looking statements include, but are not limited to, statements regarding our or our management team’s expectations, hopes, beliefs, intentions or strategies regarding our future operations. In addition, any statements that refer to projections, forecasts or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking statements. The words “anticipate,” “believe,” “contemplate,” “continue,” “could,” “estimate,” “expect,” “intends,” “may,” “might,” “plan,” “possible,” “potential,” “predict,” “project,” “should,” “will,” “would,” and similar expressions may identify forward-looking statements, but the absence of these words does not mean that a statement is not forward-looking. Forward-looking statements in this presentation may include, for example, statements about our drug candidate’s trial results and potential impact on disease states, and other factors detailed under “Risk Factors” in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q. These forward-looking statements represent our views as of the date of this presentation and involve a number of judgments, risks and uncertainties. We anticipate that subsequent events and developments will cause our views to change. We undertake no obligation to update forward-looking statements to reflect events or circumstances after the date they were made, whether as a result of new information, future events or otherwise, except as may be required under applicable securities laws. Accordingly, forward-looking statements should not be relied upon as representing our views as of any subsequent date. As a result of a number of known and unknown risks and uncertainties, our actual results or performance may be materially different from those expressed or implied by these forward-looking statements. Some factors that could cause actual results to differ include our substantial dependence on the successful commercialization of our drug candidates, if approved, in the future; our inability to maintain the listing of our common stock on Nasdaq; our significant net losses and net operating cash outflows; our ability to demonstrate the efficacy and safety of our drug candidates; the clinical results for our drug candidates, which may not support further development or marketing approval; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials and marketing approval; our ability to achieve commercial success for our drug candidates, if approved; our ability to obtain and maintain protection of intellectual property for our technology and drug candidates; our reliance on third parties to conduct drug development, manufacturing and other services; our limited operating history and our ability to obtain additional funding for operations and to complete the licensing or development and commercialization of our drug candidates; the impact of epidemics, pandemics, and the ongoing conflicts between Ukraine and Russia and Israel and Hamas on our clinical development, commercial and other operations; changes in applicable laws or regulations; the effects of inflation; the effects of staffing and materials shortages; the possibility that we may be adversely affected by other economic, business, and/or competitive factors; and other risks and uncertainties set forth in “Risk Factors” in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q. In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this presentation, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain, and you are cautioned not to rely unduly upon these statements. All information in this presentation is as of the date of this presentation. The information contained in any website referenced herein is not, and shall not be deemed to be, part of or incorporated into this presentation.

Focused on Improving Mitochondrial Health and Protecting Neuronal Function to Treat Neurodegenerative Diseases



THE PROBLEM

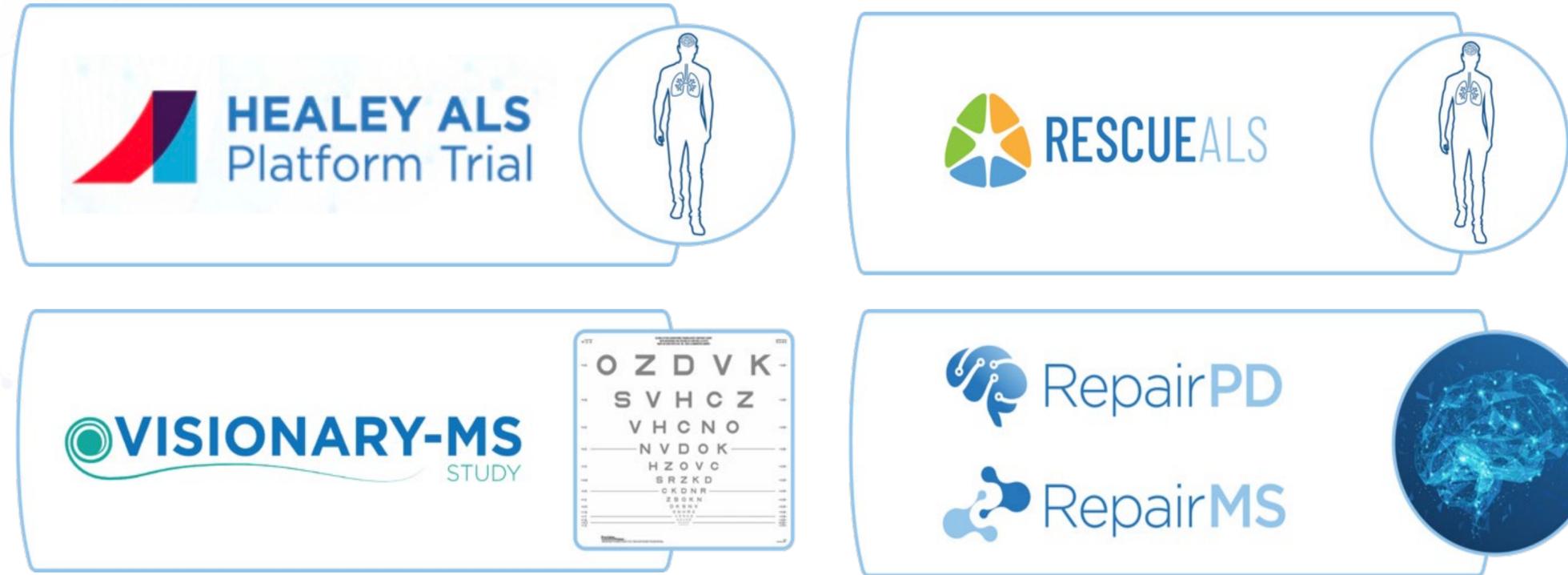
- The World Health Organization predicts **neurodegenerative diseases will become the second-most prevalent cause of death** within the next 20 years.
- A therapeutic breakthrough is urgently needed.
- In neurodegenerative diseases, **impaired mitochondrial activity and compromised cellular metabolism can lead to neuronal death.**



A NEW APPROACH

- Clene is **pioneering catalytic nanotherapeutics** to treat neurodegenerative diseases, such as amyotrophic lateral sclerosis, Parkinson's disease and multiple sclerosis.
- By **targeting the improvement of mitochondrial function** via the nicotinamide adenine dinucleotide pathway, Clene's first-in-class drug, CNM-Au8, is **pioneering a new way to restore and protect neuronal function.**

Building the Clinical Case for Neuroprotection & Remyelination



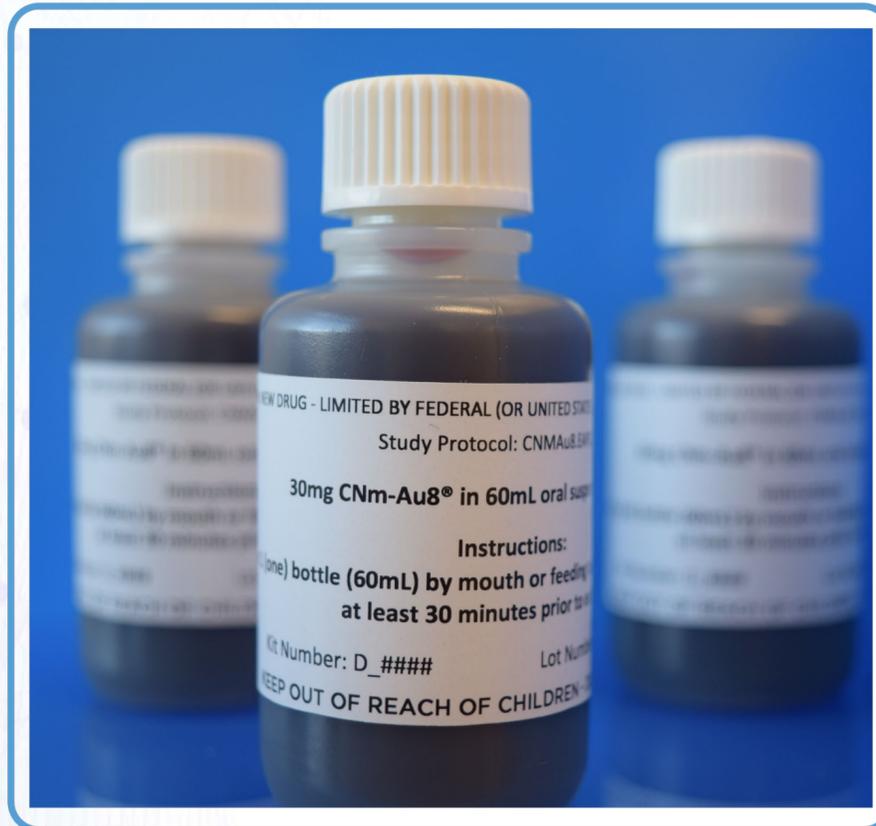
**Growing Body of Clinical Evidence Across ALS and MS Supports CNM-Au8
Therapeutic Potential to Treat Neurodegenerative Diseases**



**Proprietary Nanotherapeutic Manufacturing
Strong IP: 150+ granted patents PLUS Trade Secrets**

What is CNM-Au8® ?

CNM-Au8 Nanocrystal Suspension
60 mL per bottle (once daily)

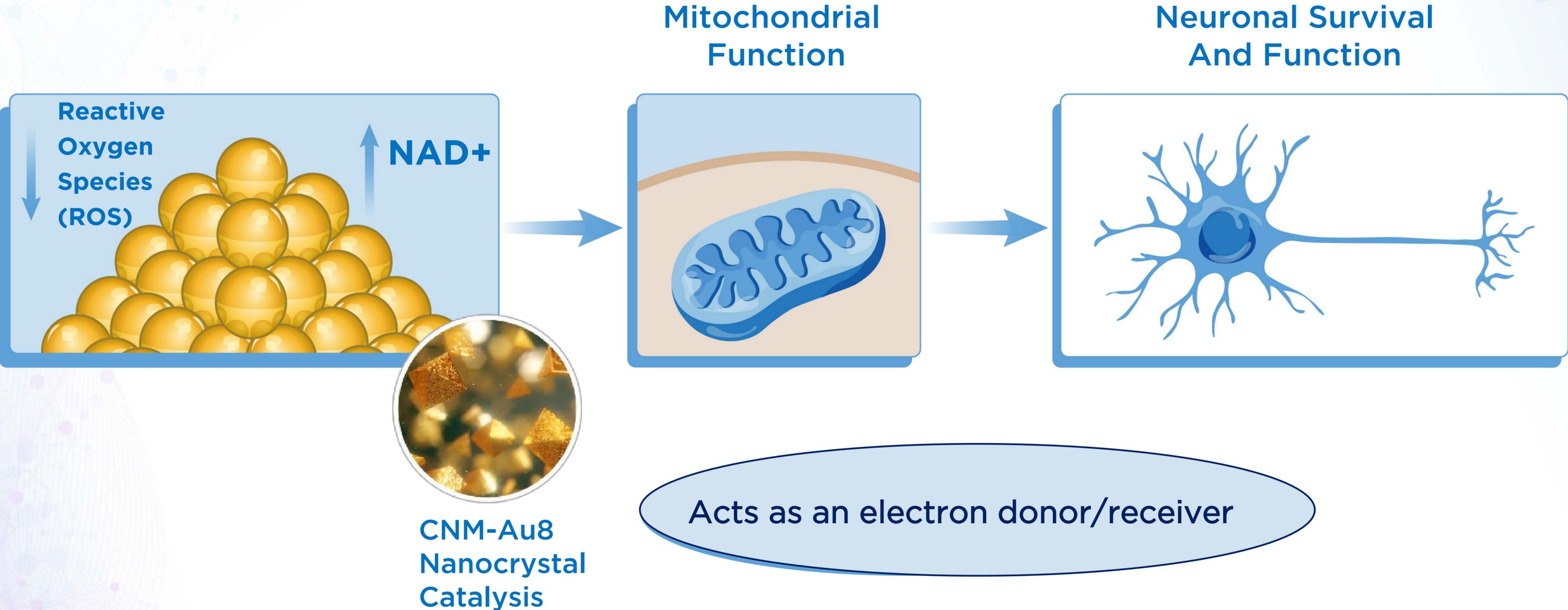


>100 Trillion Nanocrystals per
60 mL dose (at 30 mg)

CNM-Au8 Attributes:

- ✓ Nanocrystal suspension
- ✓ Orally administered (or by feeding tube)
- ✓ Targets energy metabolism and oxidative stress
- ✓ Blood-brain-barrier penetrant

CNM-Au8[®] | Surface Catalysis Supports Mitochondrial Function



Safety Review

- Over **700 participant-years** of exposure to CNM-Au8
- CNM-Au8 long-term **treatment duration up to 5.1 years**
- TEAEs (treatment-emergent adverse events) predominantly assessed as **mild-to-moderate severity, and transient**
- **No related SAEs** (serious adverse events) related to CNM-Au8 across all clinical programs
- No temporal association of increasing TEAE or SAE incidence based on exposure duration
- ‘No Adverse Effect Level’ (**NOAEL**) **findings across all toxicology studies** up to maximum feasible dose



Despite Missed Primary Endpoints, Concordant Survival Outcomes with CNM-Au8 Treatment in ALS are Promising



	RESCUE-ALS	RESCUE-OLE	HEALEY ALS Platform	HEALEY OLE	Expanded Access Protocols
ALS Participant Demographics	Early-to-Mid-Stage (n=45)	Early-to-Mid-Stage (n=36)	Mid-to-Late-Stage (n=161; Regimen C)	Mid-to-Late-Stage (n=134)	Real-World Experience (~300)
Duration	36-weeks	Up to 234 weeks	24-weeks	Up to 133 weeks	Over 5.0 years
Primary/Secondary Endpoints	1. MUNIX % change 2. MUNIX total change 2. FVC (% predicted)	NA	1. ALSFRS-R adj. by death 2. CAFS 2. SVC (% predicted) 2. Time to Death or PAV	NA	NA
Survival	--	✓	✓	✓ vs. ALS natural history controls	✓ vs. ALS natural history controls
Delayed Time to Clinical Worsening	✓	✓	✓	✓	Not routinely collected
Preserved Function (ALSFRS-R)	--	✓	--	✓ in NfL Responders	
Progression Biomarkers	↓ p75 (trend)	Not routinely collected	✓ NfL ↓	✓ NfL ↓ ✓ GSH, GSH/GSSG ↑ ✓ NAD, NAD ⁺ /NADH ↑	
Safety	>700 Years of Participant Exposure without Identified Safety Signals across ALS, MS, and PD				

Time to Event | Survival During the Double-Blind Period

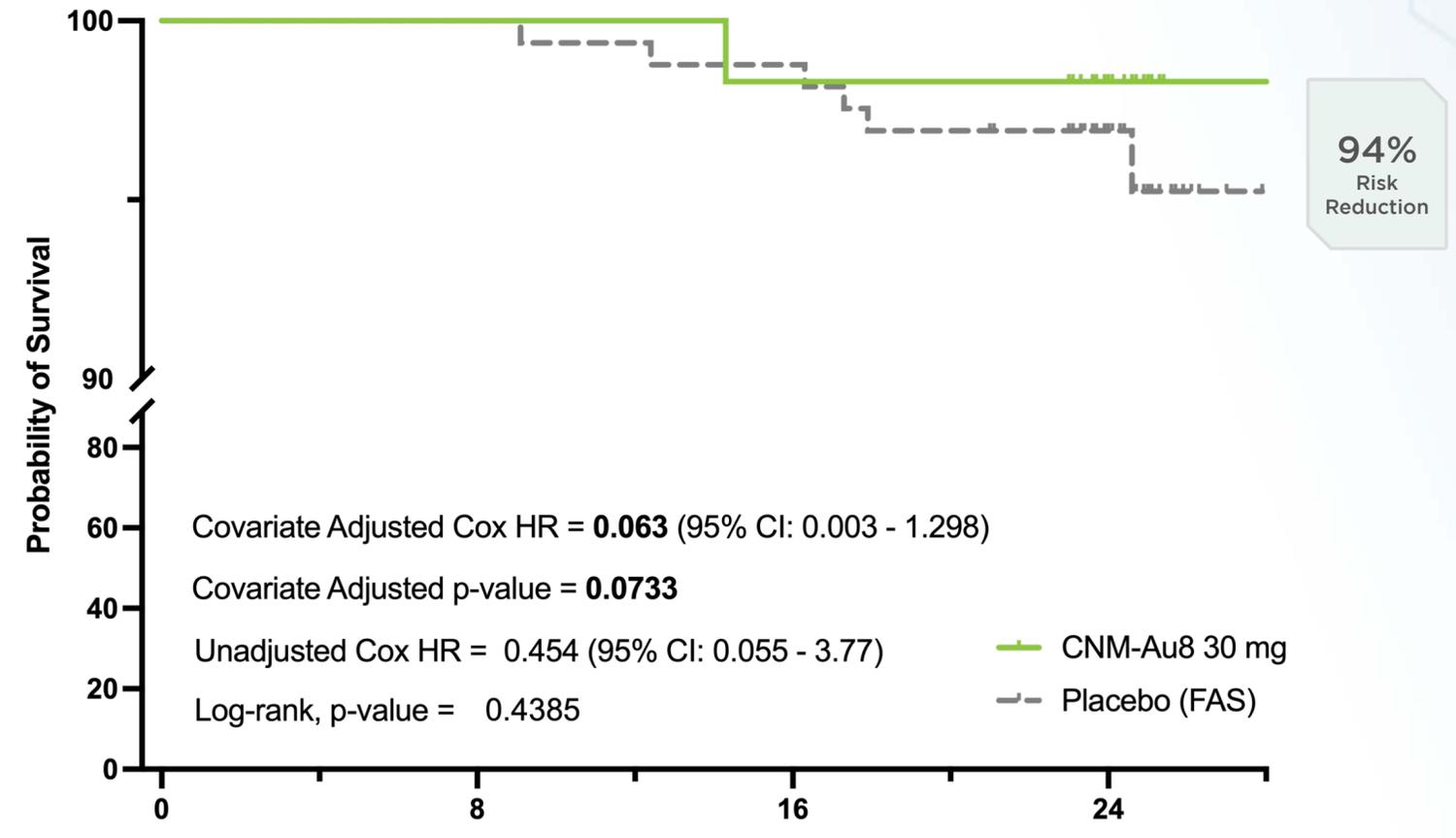
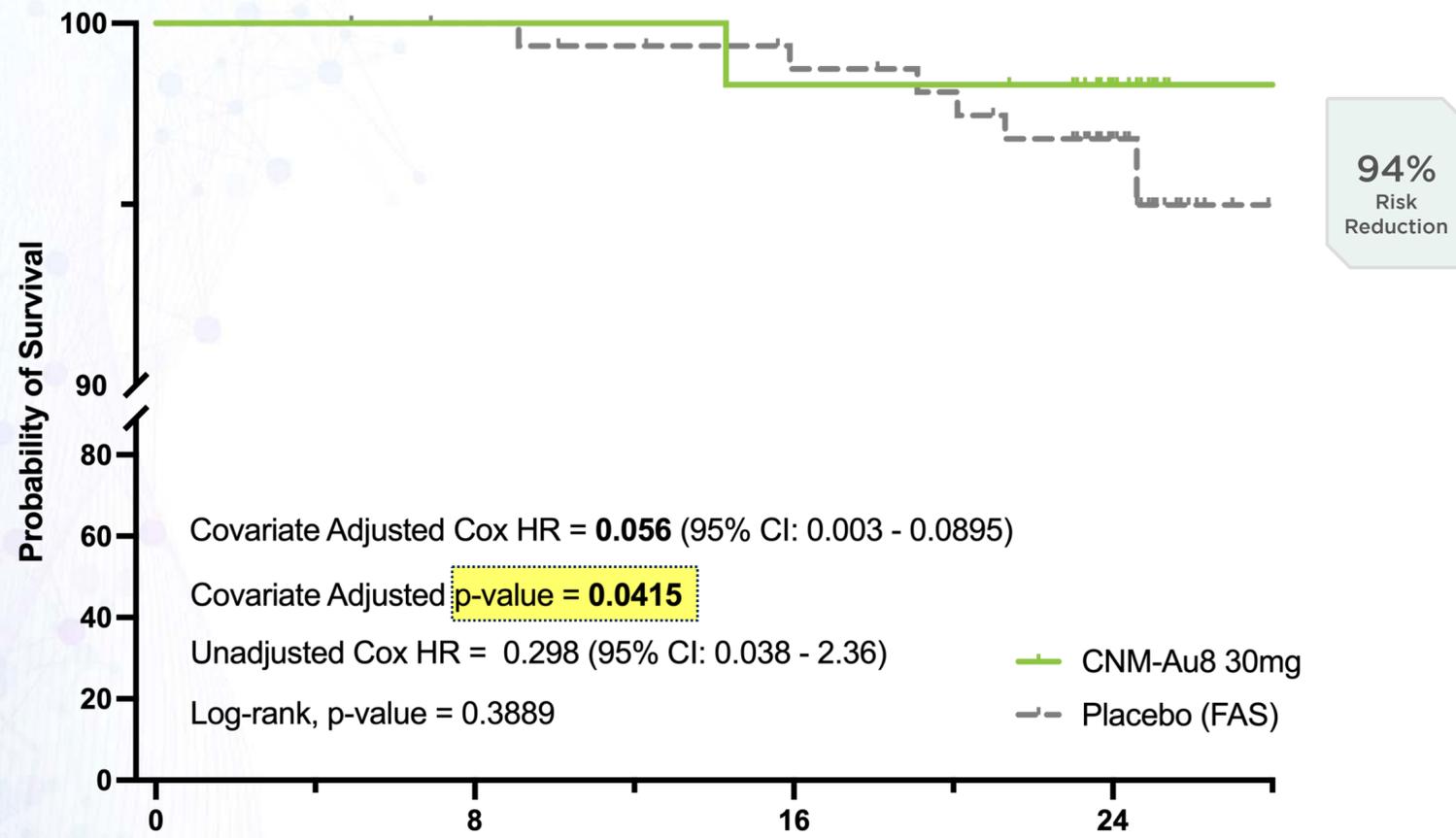
HEALEY ALS Platform Trial CNM-Au8 30 mg (Full Analysis Set | All Shared Placebo)

Time to Death or PAV*

Time to Death

HEALEY ALS Platform Trial | Double-Blind Period | Kaplan-Meier Estimator
CNM-Au8 30 mg (n=59) vs. Placebo Full Analysis Set (n=162)

HEALEY ALS Platform Trial | Double-Blind Period | Kaplan-Meier Estimator
CNM-Au8 30 mg (n=59) vs. Placebo Full Analysis Set (n=163)



*PAV=Permanently Assisted Ventilation

At Risk	Weeks (Post Baseline)	0	8	16	24
CNM-Au8 30mg:	59	59	58	45	
Placebo:	162	162	159	116	

At Risk	Weeks (Post-Baseline)	0	8	16	24
CNM-Au8 30mg:	59	59	58	45	
Placebo:	163	163	161	119	

Time to Event | Improved Survival During the OLE to Month 12

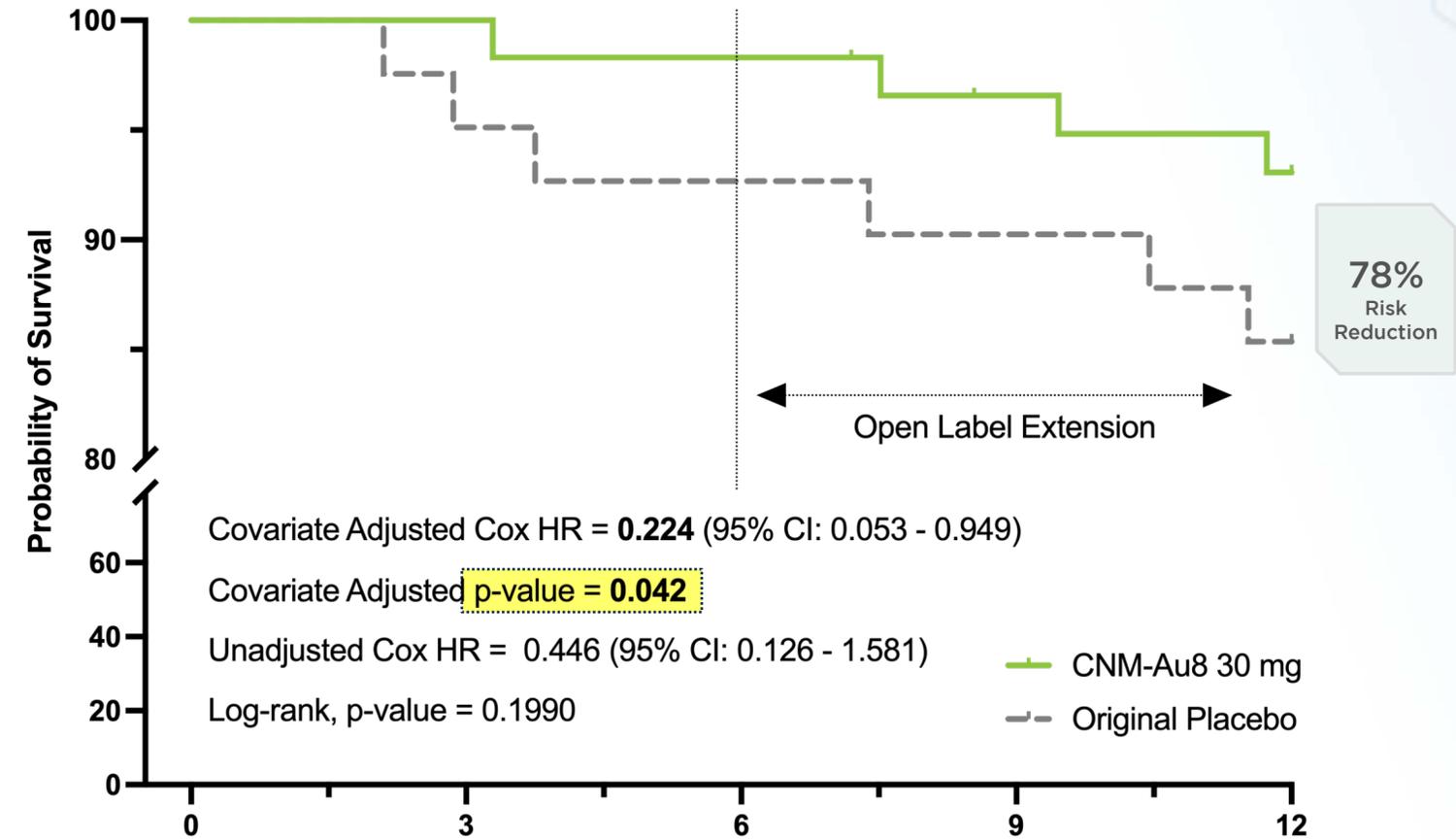
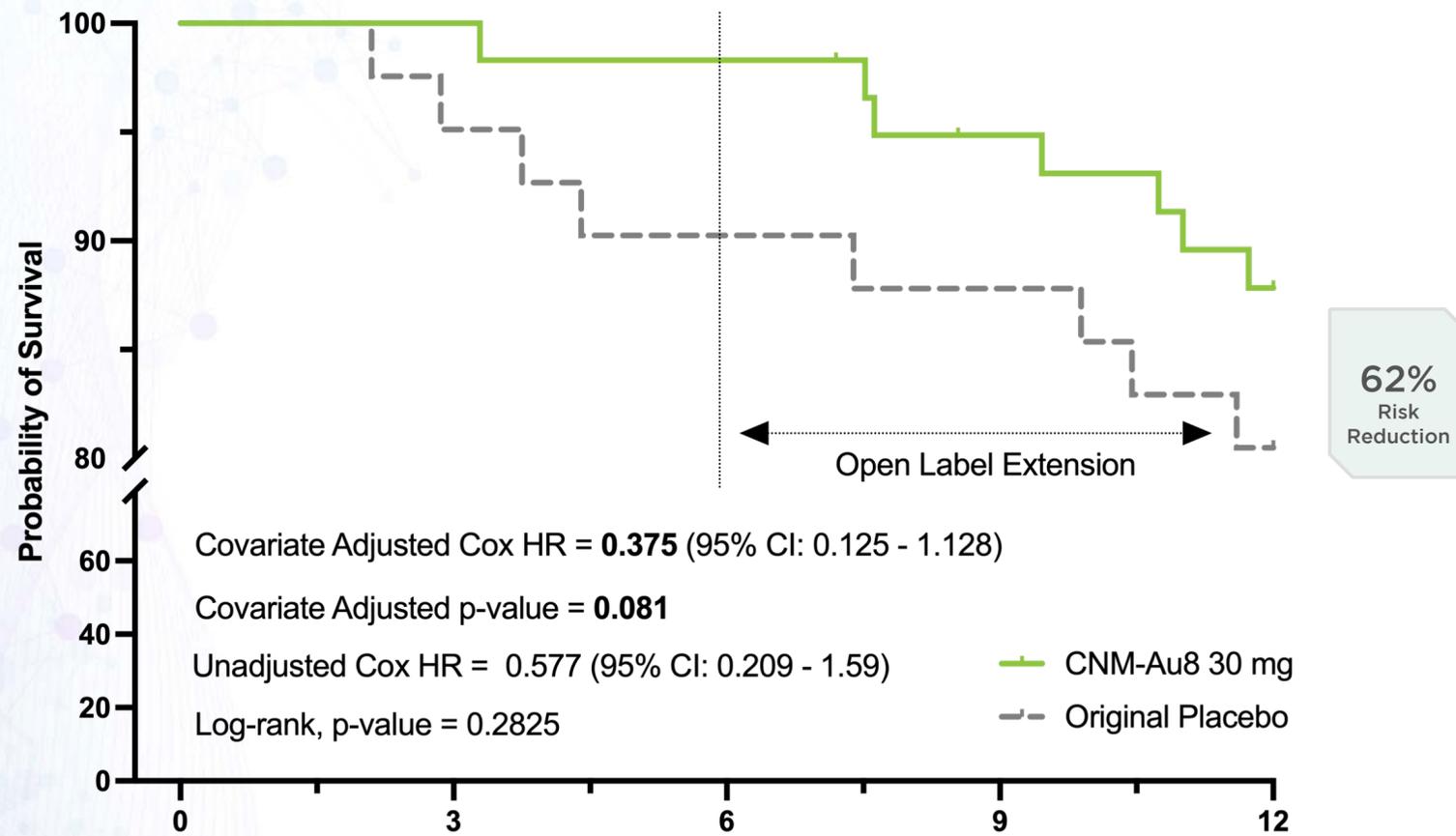
HEALEY ALS Platform Trial CNM-Au8 30 mg

Time to Death or PAV

Time to Death

HEALEY ALS Platform Trial | Kaplan-Meier Estimator | Open Label Extension
 Prespecified Covariate Adjusted Hazard Model at Week 52
 CNM-Au8 30 mg (n=59) vs. Placebo Within Regimen (n=41)

HEALEY ALS Platform Trial | Kaplan-Meier Estimator | Open Label Extension
 Prespecified Covariate Adjusted Hazard Model at Week 52
 CNM-Au8 30 mg (n=59) vs. Placebo Within Regimen (n=41)



	0	3	6	9	12
At Risk					
CNM-Au8:	59	59	58	54	50
Placebo:	41	39	37	36	33

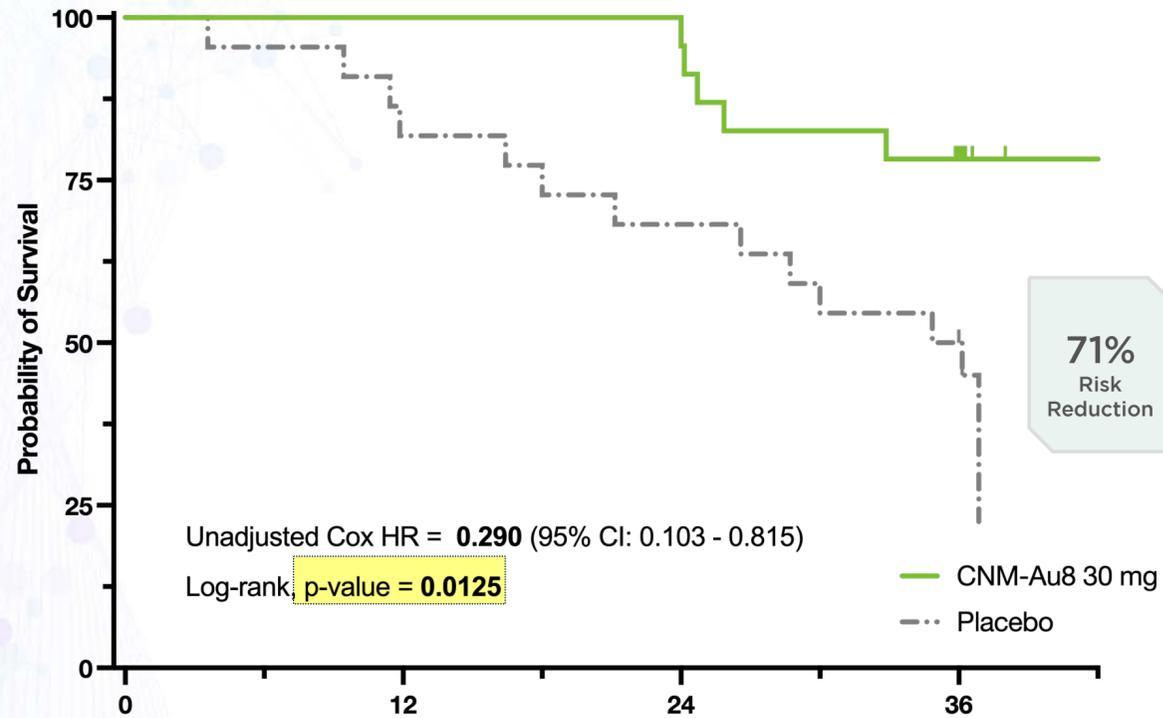
	0	3	6	9	12
At Risk					
CNM-Au8:	59	59	58	55	53
Placebo:	41	39	38	37	35

CNM-Au8 | Delayed Time to Clinical Worsening Events Concordant in Double-Blind Periods of Two Independent Phase 2 Trials

Delayed Time to Clinical Worsening

Prespecified Exploratory Clinical Composite Endpoint

Time to ALS Clinical Worsening | CNM-Au8 30mg
First Occurrence of Death, Tracheostomy, Feeding Tube, or NIV Initiation
 RESCUE-ALS | Kaplan-Meier Estimate
 CNM-Au8 30mg vs. Placebo (n=45)



At Risk	Weeks (Post-Baseline)			
	0	12	24	36
CNM-Au8 30mg:	23	23	23	17
Placebo:	22	18	15	11

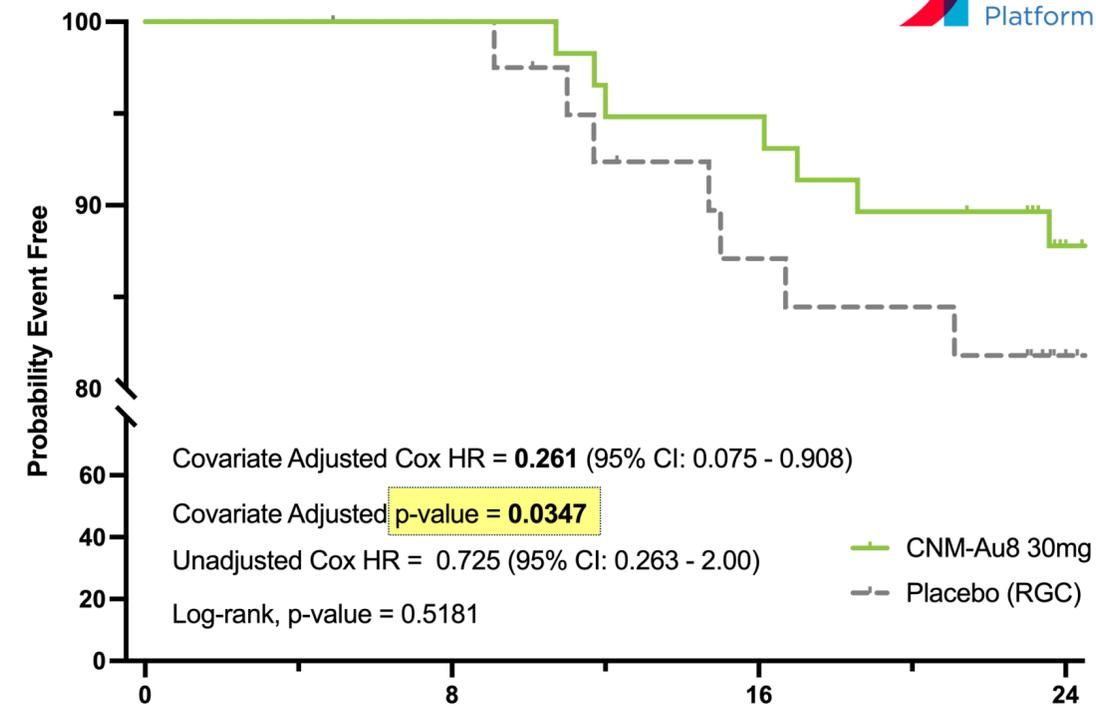
1st Occurrence of:

- Death
- Tracheostomy
- Feeding Tube Placement
- Non-Invasive Ventilation

Delayed Time to Clinical Worsening

Prespecified Exploratory Clinical Composite Endpoint

Time to ALS Clinical Worsening | CNM-Au8 30mg
First Occurrence of Death, PAV, Tracheostomy or Feeding Tube
 HEALEY ALS Platform Trial Within Regimen | Kaplan-Meier Estimator
 CNM-Au8 30mg (n=58) vs. Placebo (n=41)



At Risk	Weeks (Post-Baseline)			
	0	8	16	24
CNM-Au8 30mg:	58	58	55	40
Placebo:	41	40	33	25

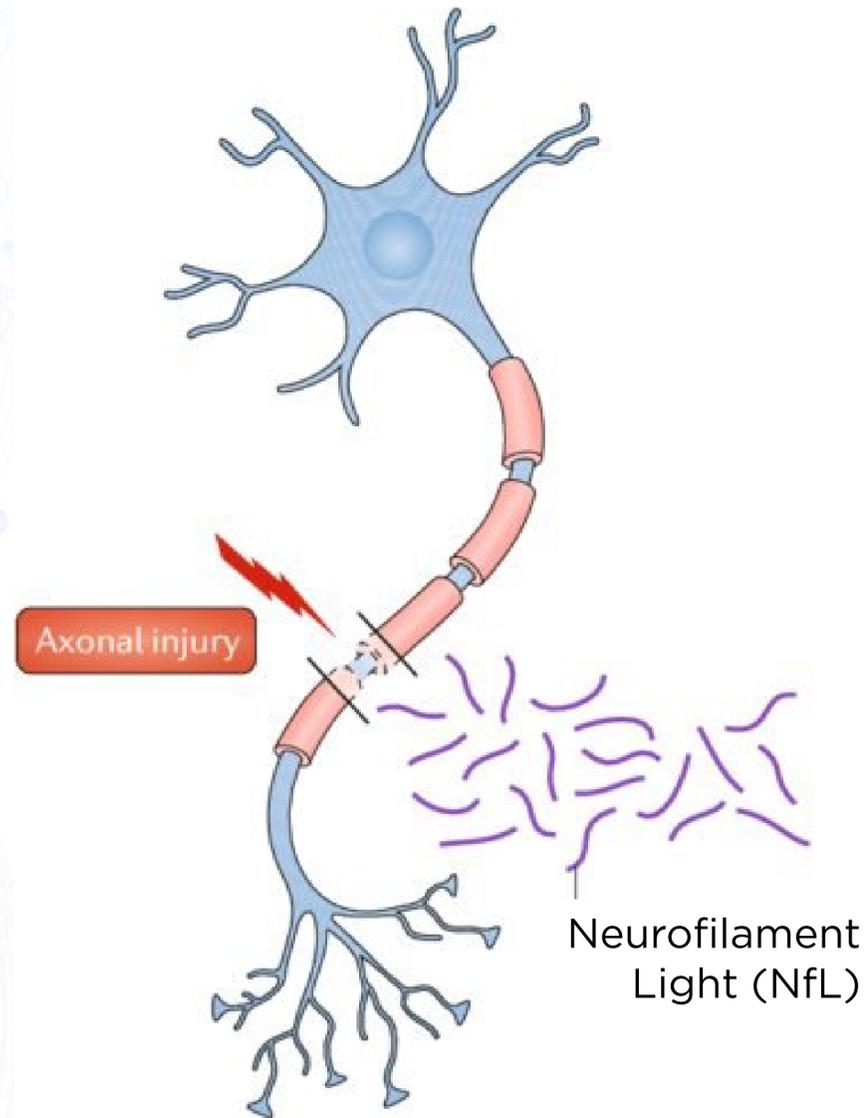
1st Occurrence of:

- Death
- PAV
- Tracheostomy
- Feeding Tube Placement

PAV defined as continuous ventilatory support (>23 hr/day) by tracheostomy or NIV for at least 7-days

Prespecified covariate risk adjustments included: (i) time from symptom onset, (ii) pre-baseline ALSFRS-R slope, (iii) riluzole use, (iv) edaravone use, and (v) age.

NfL is a Key Biomarker of Disease Progression in ALS Patients



Neurofilament Light Chain (NfL) Protein

Cytoskeletal proteins that provide structure and support for the cell and are highly specific for neurons

Axonal damage: high NfL levels are associated with axonal damage

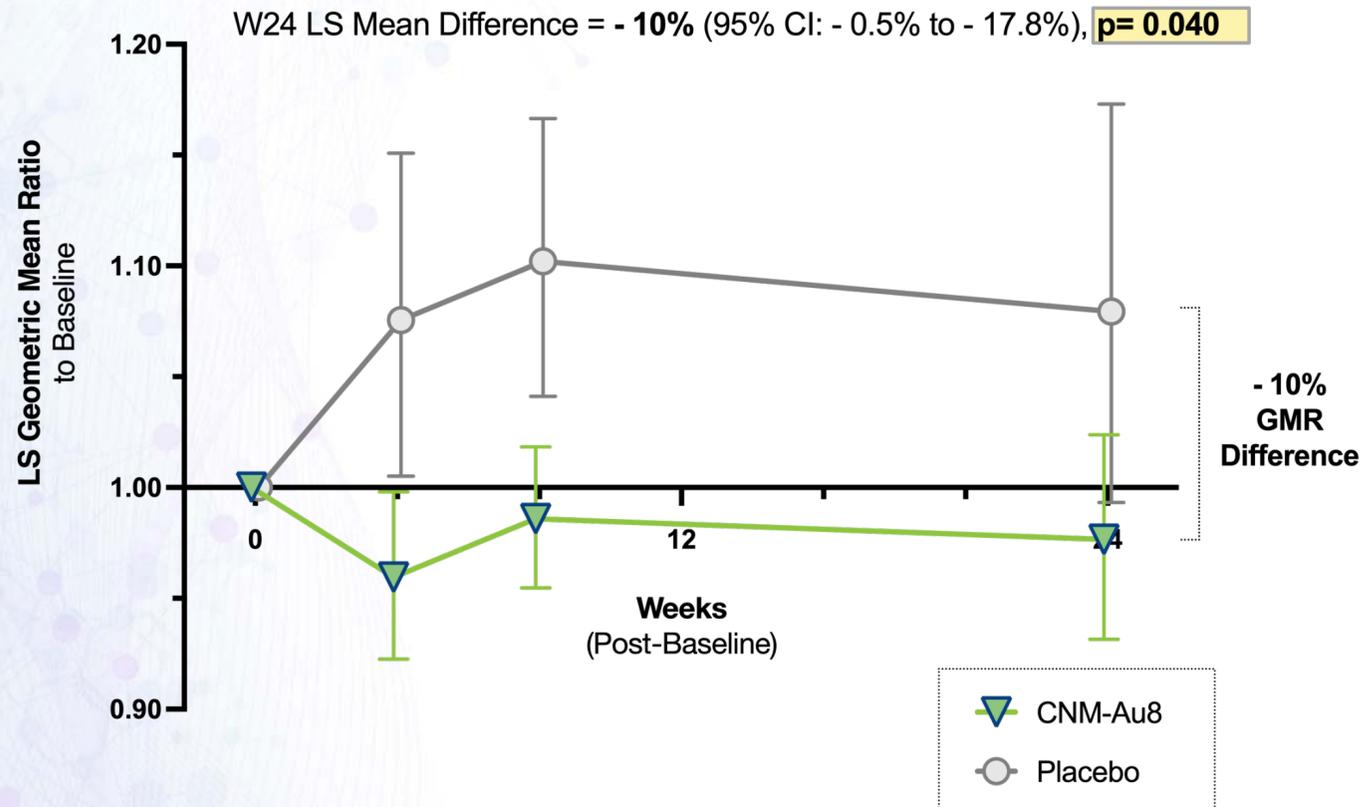
High NfL in ALS: predicts greater risk of disease progression

Plasma NfL Decline During Double-Blind & Long-Term Treatment

HEALEY ALS Platform Trial Double-Blind & Open Label Extension

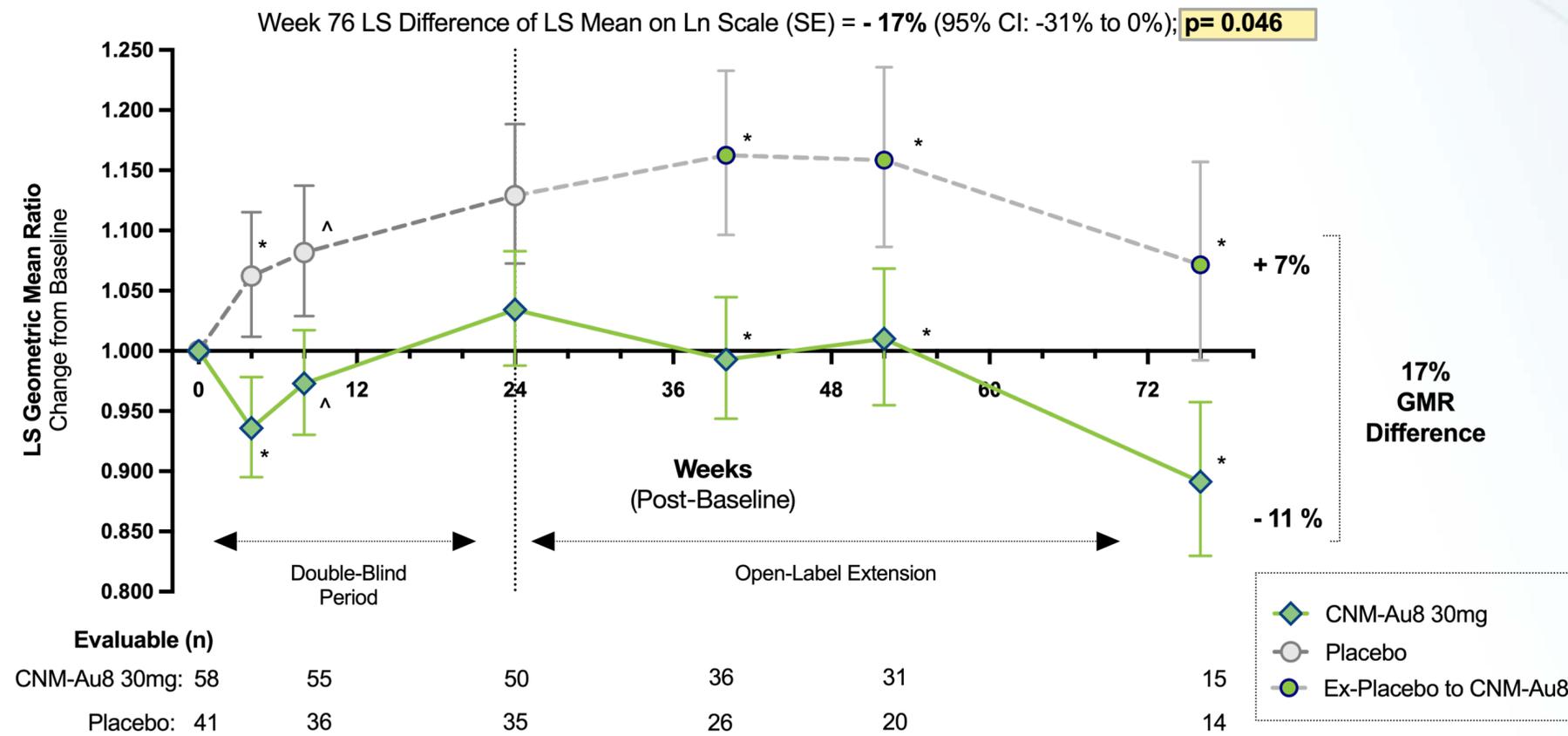
Double-Blind Period

**Plasma Neurofilament Light Chain (NfL)
Regimen C Within Regimen Analysis | Quanterix 4NPA**
All RCG Participants (n=161)
LS Means on Ln Scale ± 95% CI (Exponentiated)



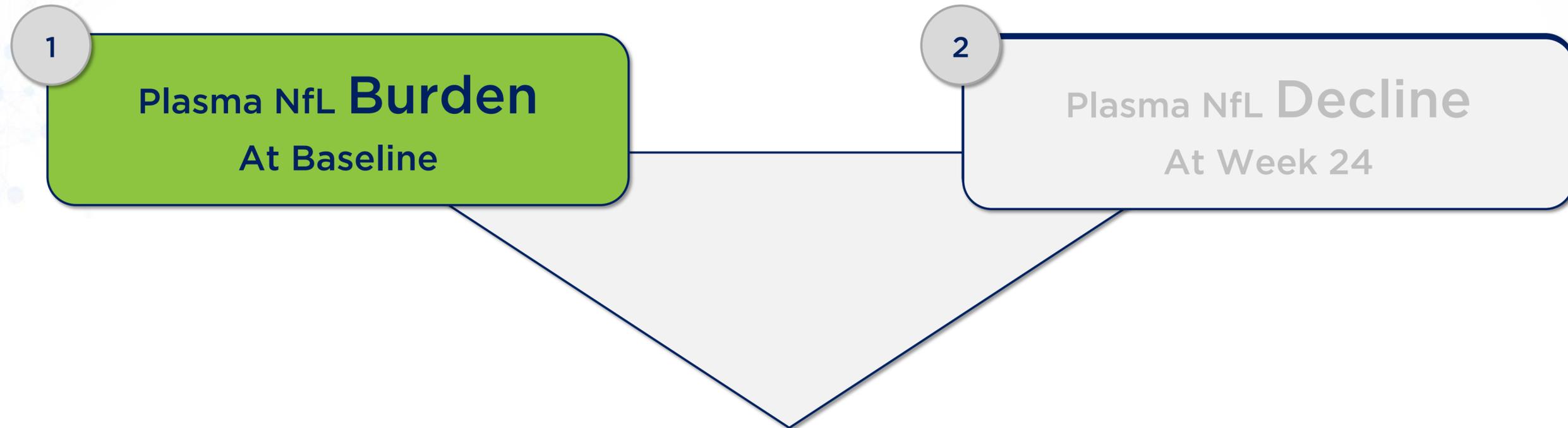
Open Label Extension

CNM-Au8 30mg Plasma NfL Geometric Mean Change
All Evaluable with Baseline, n=99; LS Geometric Mean Difference ± SEM



MMRM includes all evaluable clinical visits. All visits with ≥ 10 participants (for either group) are graphed.
 LS Geometric mean difference: *** p<0.001, ** p<0.01, * p < 0.05, ^ p<0.10

Evidence Linking Plasma NfL with CNM-Au8 Clinical Benefit



Time to Death or PAV to Month 12

Week 52 post-baseline was a prespecified time point for OLE analyses

Greatest Benefit in Participants with Highest Baseline NfL Burden | Death or PAV

HEALEY ALS Platform (Through Month 12) | Upper Tertile & \geq Median

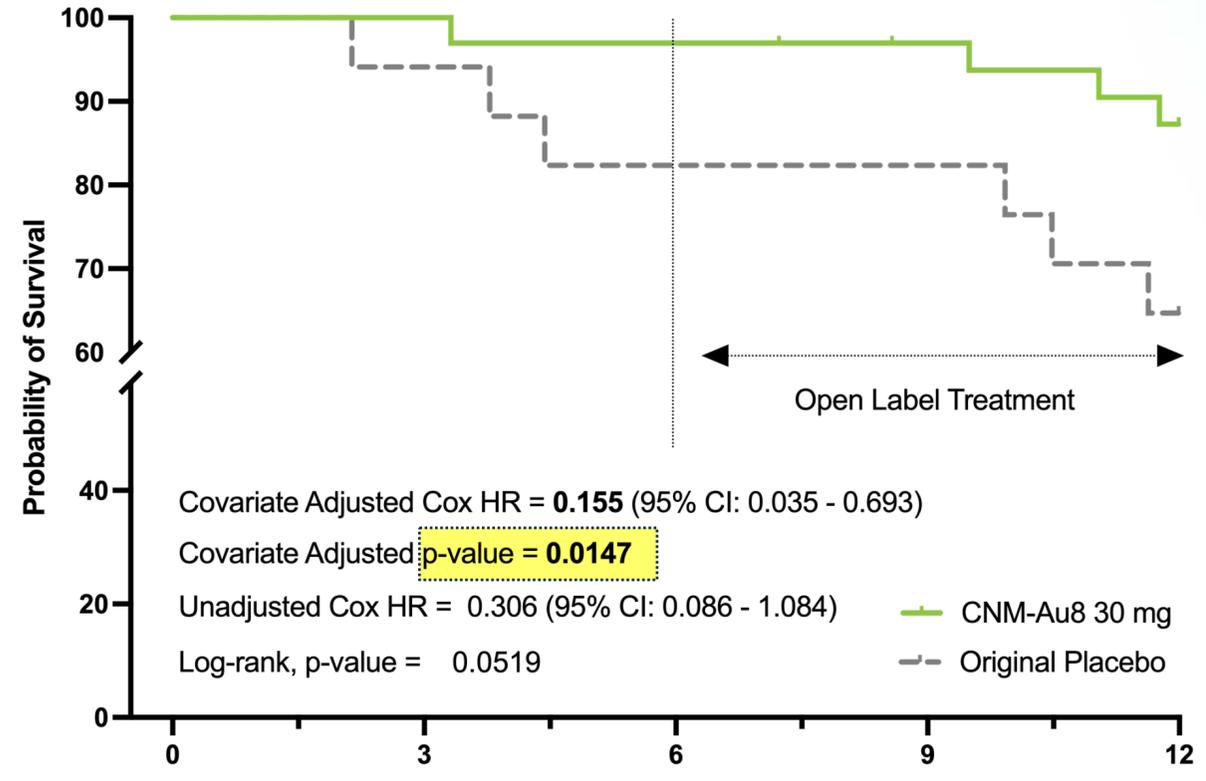
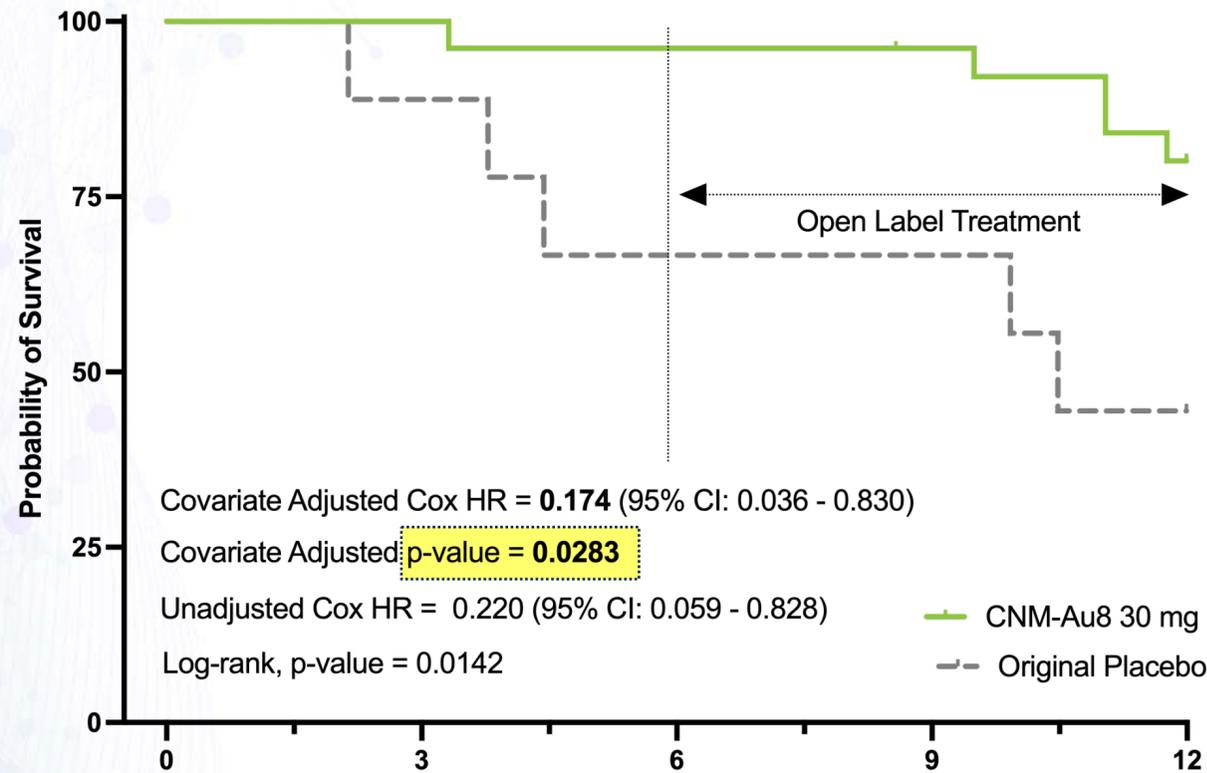


HEALEY | Upper NfL Tertile By Baseline Plasma NfL

HEALEY | NfL > Median By Baseline Plasma NfL

Time to Death or PAV (Through Month 12)
In Participants with the Highest Baseline Plasma NfL (Upper Tertile)
HEALEY ALS Platform Trial | Kaplan-Meier Estimator
CNM-Au8 30 mg (n=29) vs. Placebo Within Regimen (n=13)

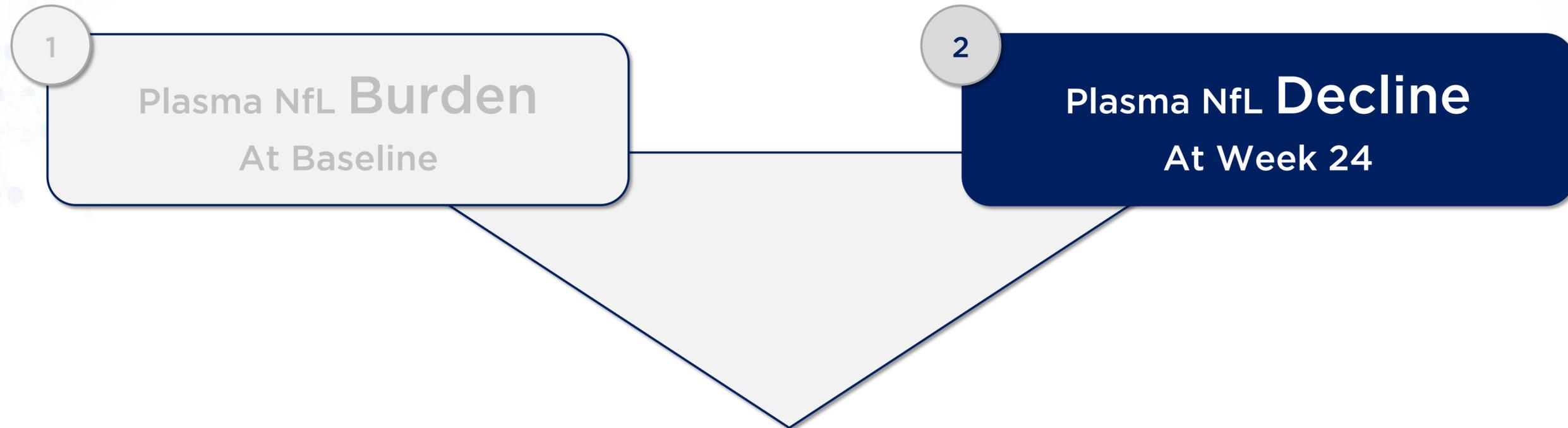
Time to Death or PAV (Through Month 12)
In Participants with the Baseline Plasma NfL (\geq Median)
HEALEY ALS Platform Trial | Kaplan-Meier Estimator
CNM-Au8 30 mg (n=32) vs. Placebo (n=17)



At Risk	Months (Post-Baseline)				
	0	3	6	9	12
CNM-Au8:	24	24	23	22	19
Placebo:	9	8	6	6	4

At Risk	Months (Post-Baseline)				
	0	3	6	9	12
CNM-Au8:	32	32	31	29	26
Placebo:	17	16	14	14	11

Evidence Linking Plasma NfL with CNM-Au8 Clinical Benefit



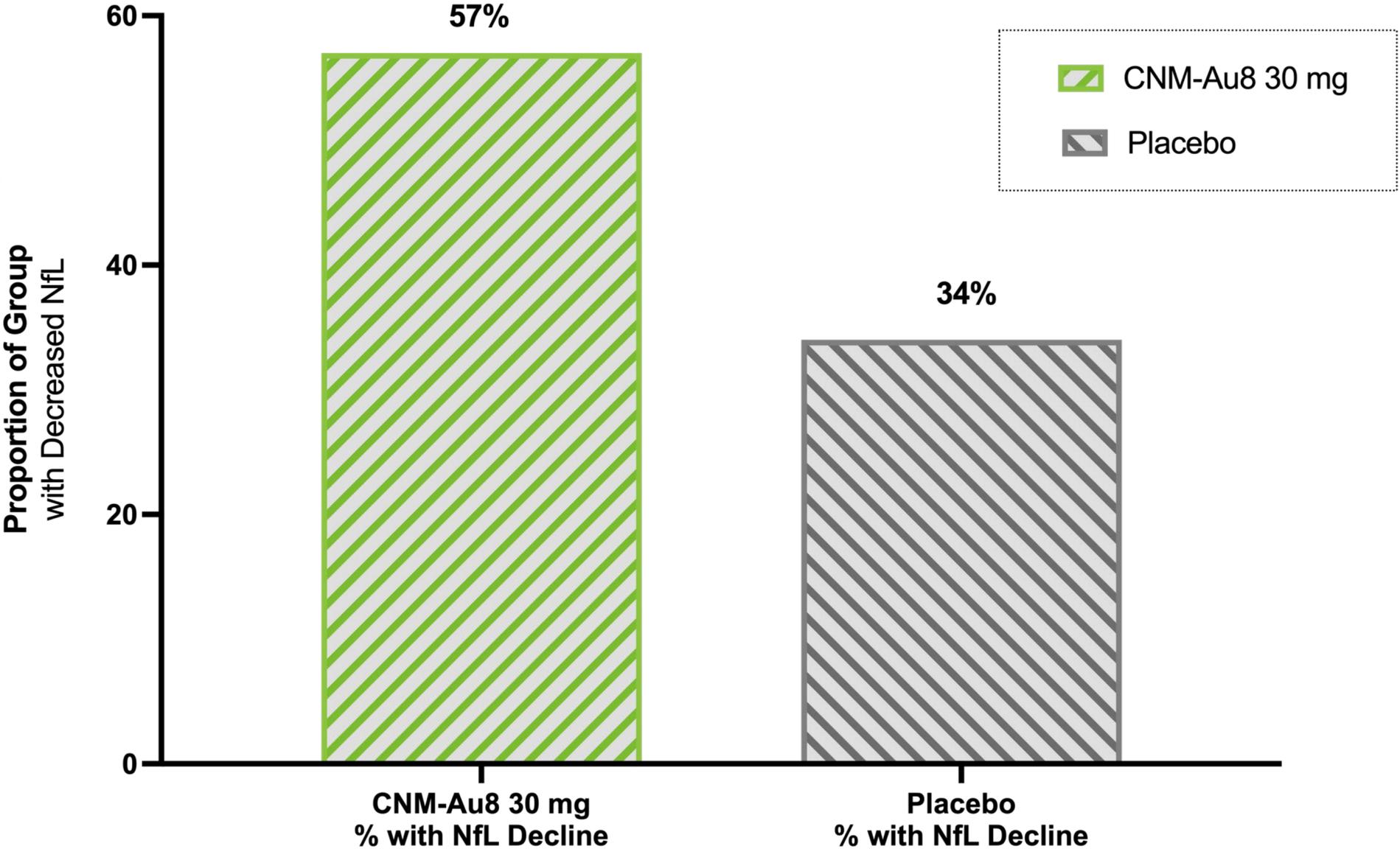
Time to Death or PAV to Month 12

Week 52 post-baseline was a prespecified time point for OLE analyses

Proportion of Participants Demonstrating NfL Decline at Week 24

End of Double-Blind

CNM-Au8 30 mg Plasma NfL Change at Week 24 (End of Double-Blind)
Proportion of Evaluable with NfL Decline



Long-Term Survival Benefit in Participants with Any NfL Decline at 24-Weeks

HEALEY ALS Platform (Through Month 12) | Time to Death or PAV

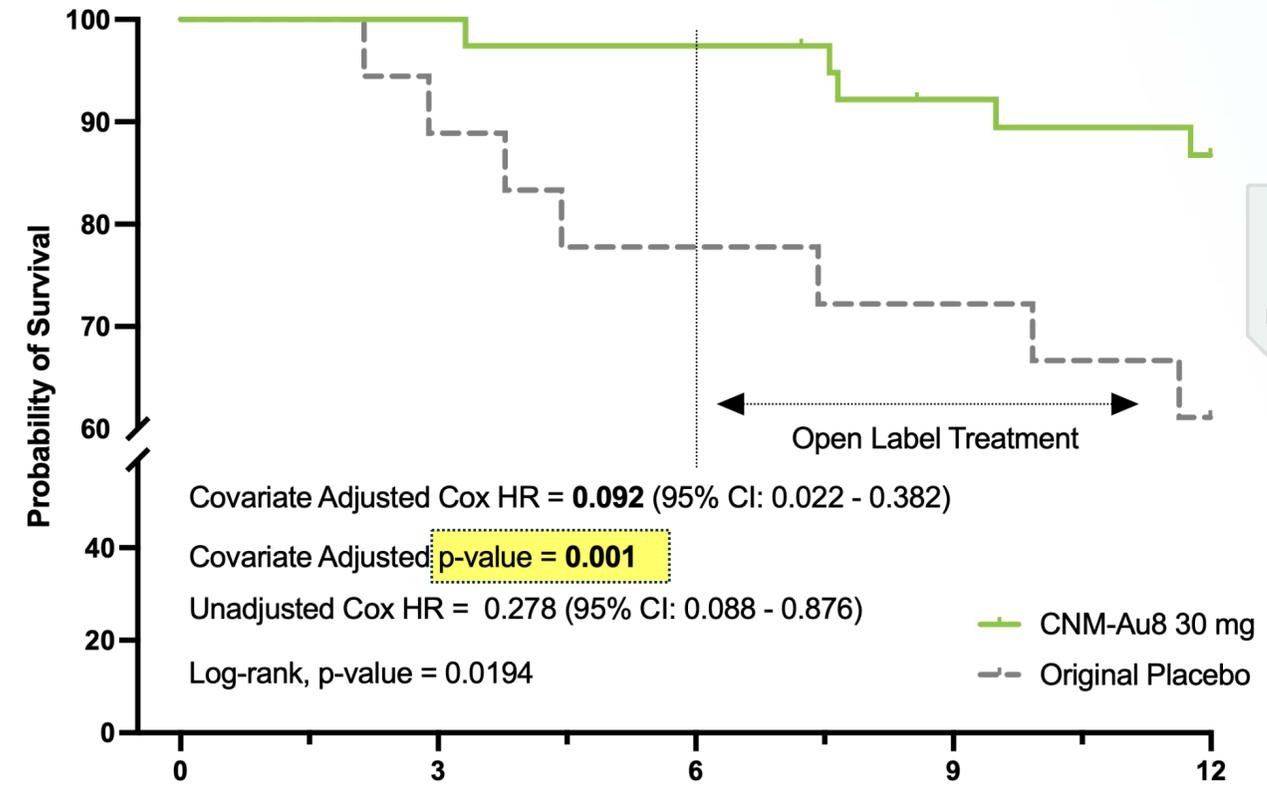
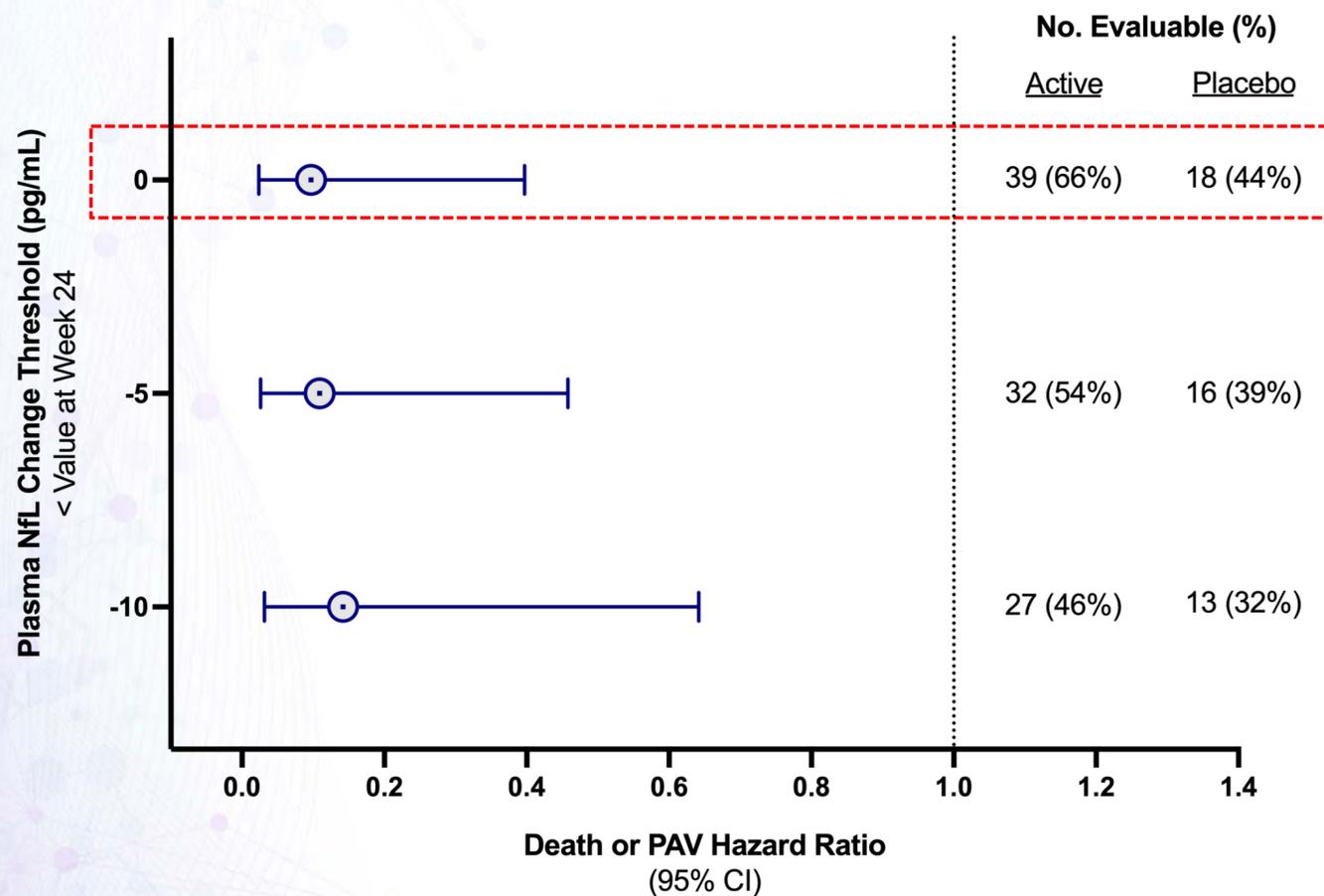


Hazard Ratio for Death or PAV At 12 Months Post-Baseline

Time to Death or PAV In Participants with NfL Decline at Week 24

Hazard Ratio for Time to Death or PAV Through Month 12
by Plasma NfL Change from Baseline Threshold (pg/mL) and Missing at **Week 24**
CNM-Au8 30 mg Treated vs. Original Placebo | HEALEY ALS Platform Trial
Prespecified Covariate Adjusted Cox Proportional Hazard Model

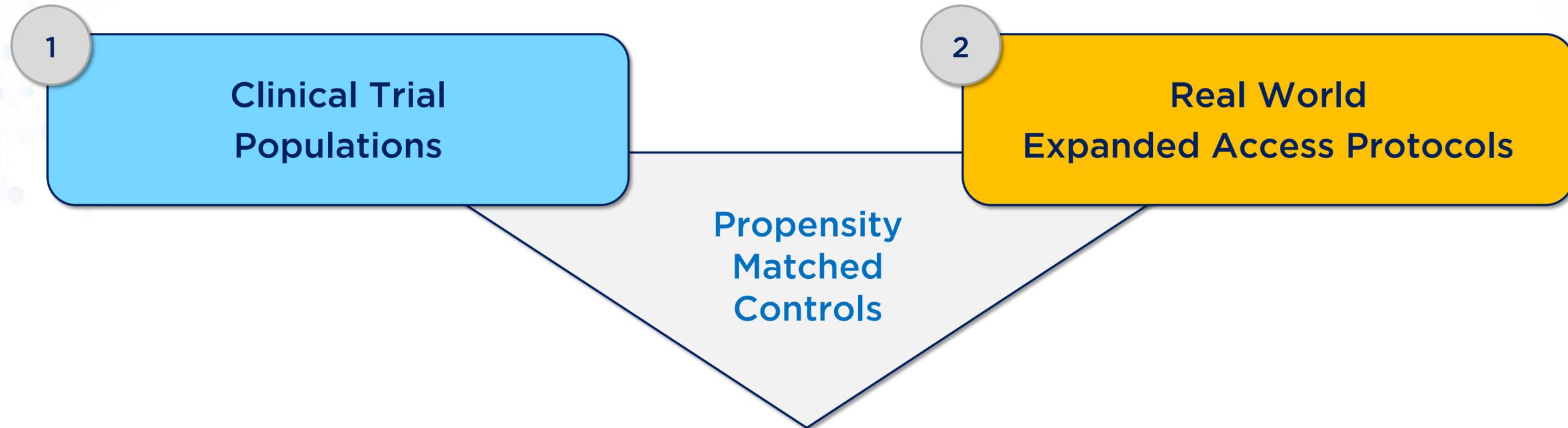
Time to Death or PAV (Through Month 12)
HEALEY ALS Platform Trial | Kaplan-Meier Estimator | Open Label Extension
All Evaluable with Week 24 Plasma NfL Decline < 0 pg/mL (or Missing Week 24)
CNM-Au8 30 mg (n=39) vs. Placebo Within Regimen (n=18)



	0	3	6	9	12
At Risk					
CNM-Au8:	39	39	38	34	32
Placebo:	18	16	14	13	11

Participants with missing W24 NfL Values are included across groups

Evidence Supporting Long-Term Survival Benefit



PRO-ACT, ALS Natural History Consortium (ALS NHC), ANSWER-ALS

**Long-Term
All-Cause Mortality**

Improved Long-Term Survival | HEALEY ALS Platform & Pooled ALS Trials

CNM-Au8 30 mg Original Randomization vs. Propensity Matched Controls



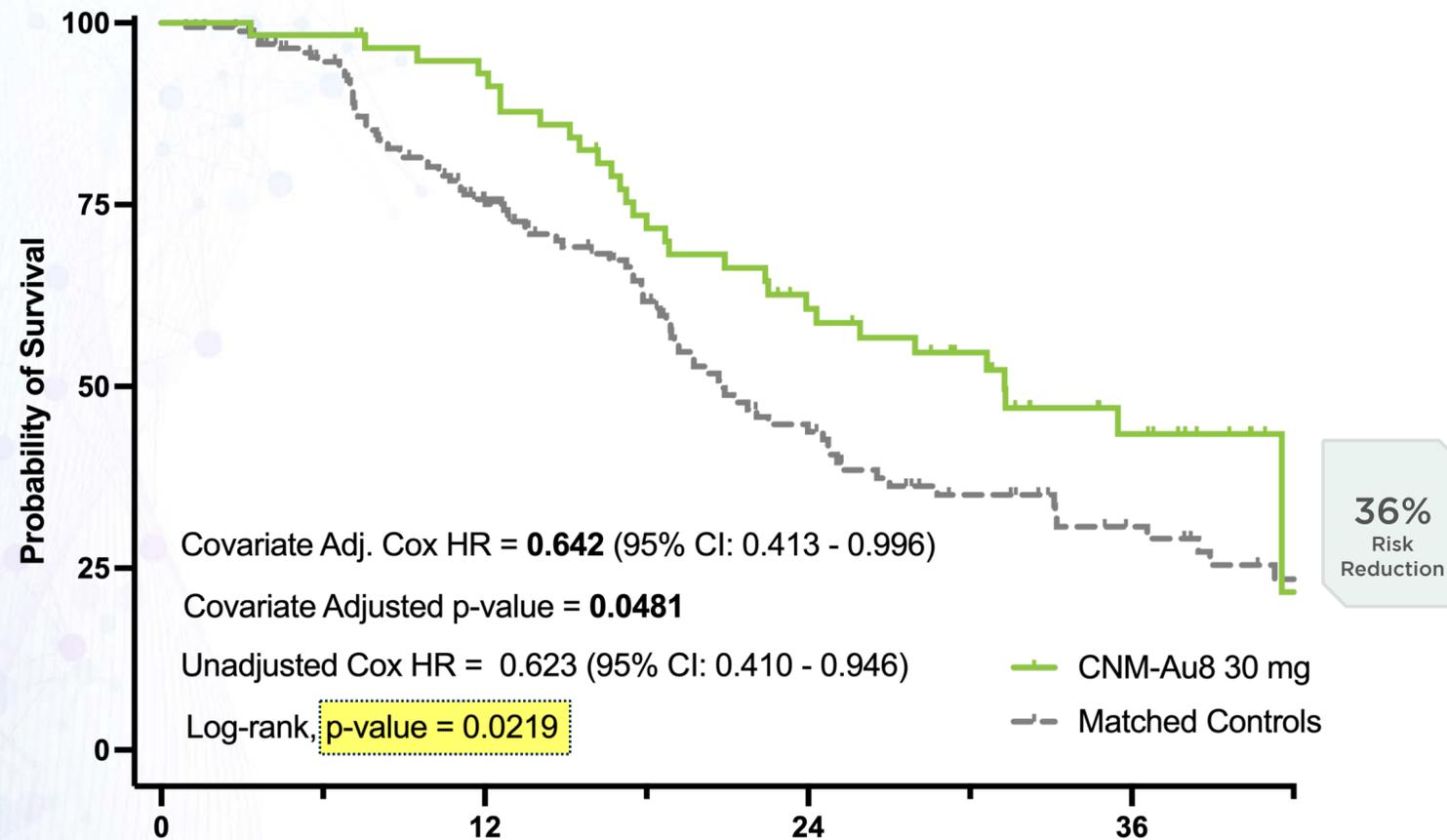
HEALEY | Optimal Variable Ratio Matching
Prespecified Matching Methodology



Pooled ALS Trials | Optimal Variable Ratio Matching

Original CNM-Au8 30 Randomized mg vs. Propensity Matched Controls

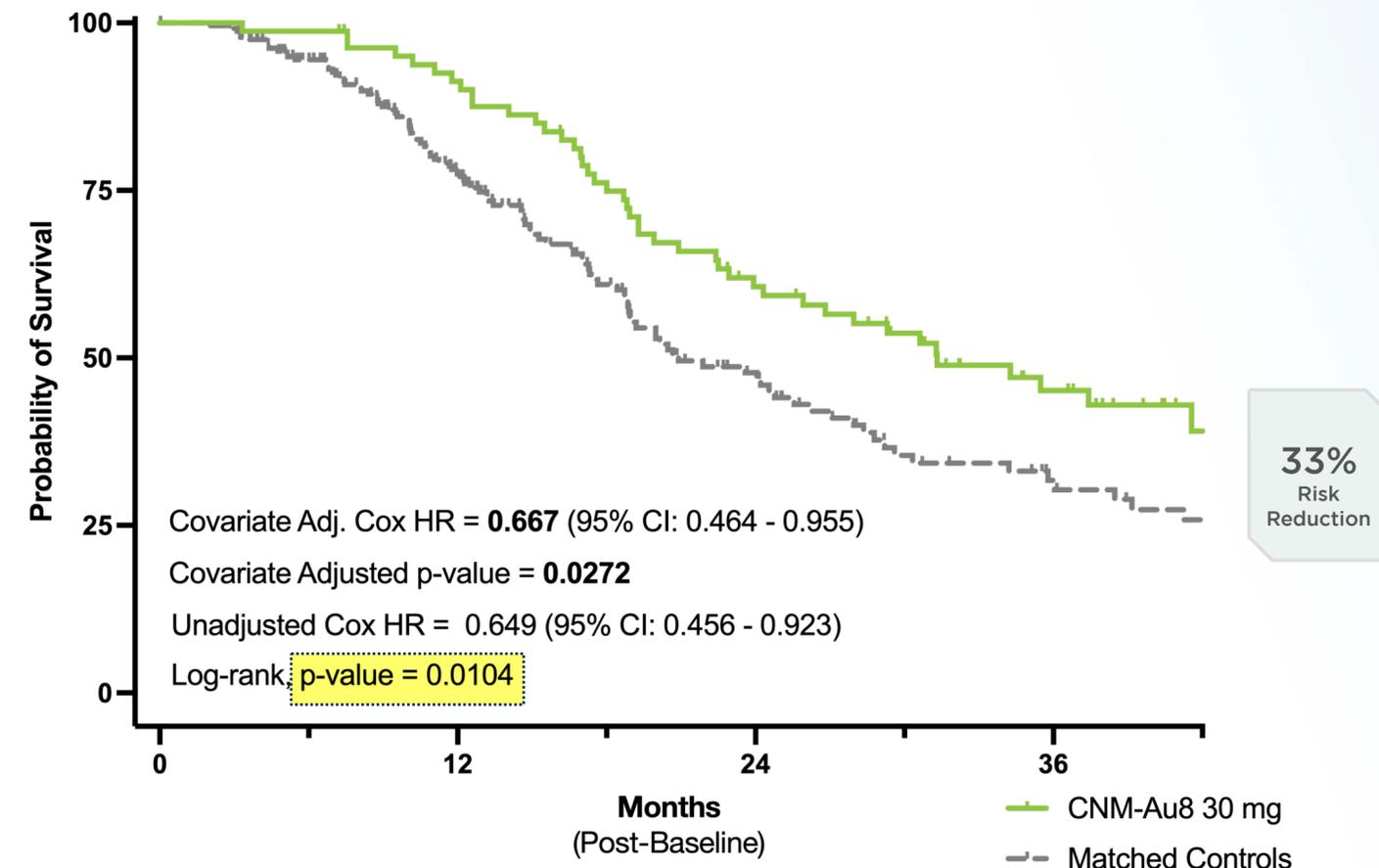
HEALEY ALS Platform Trial | Optimal Variable Matching
Pooled Matched Controls (PRO-ACT, ALS NHC, ANSWER-ALS)



At Risk	Months (Post-Baseline)							
	0	12	24	36	48	60	72	84
CNM-Au8 30 mg:	59	58	53	41	31	23	12	1
Placebo:	177	153	112	65	43	28	19	12

Original CNM-Au8 30 Randomized mg vs. Propensity Matched Controls

Pooled HEALEY ALS Platform Trial & RESCUE-ALS | Optimal Variable Matching
Pooled Matched Controls (PRO-ACT, ALS NHC, ANSWER-ALS)



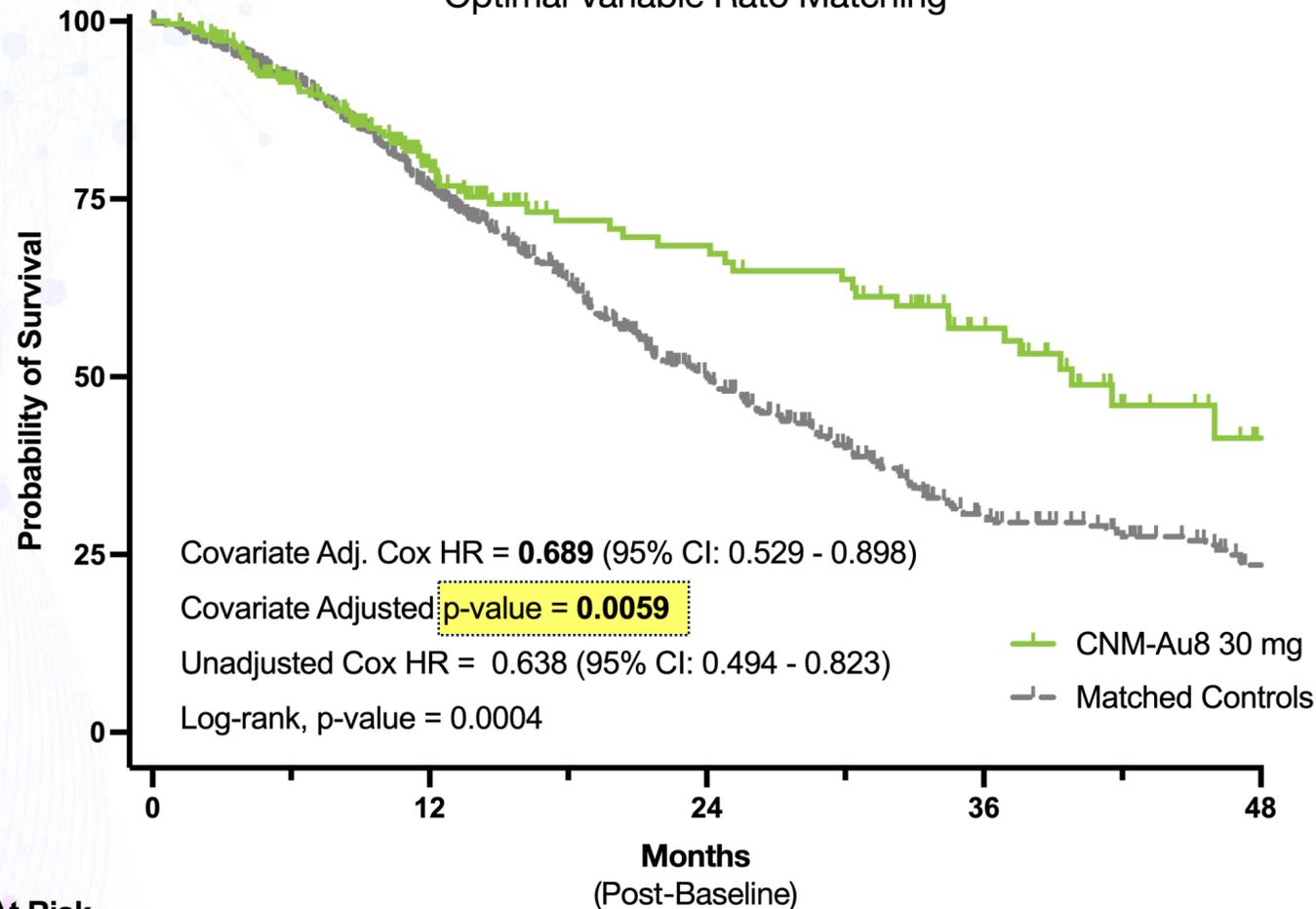
At Risk	Months (Post-Baseline)							
	0	12	24	36	48	60	72	84
CNM-Au8 30 mg:	82	81	73	60	45	35	23	10
Placebo:	246	211	147	78	52	31	23	17

Long-Term Survival | Real-World Expanded Access Protocols

CNM-Au8 30 mg vs. Propensity Matched Controls (Pooled PRO-ACT, ALS NHC, ANSWER-ALS)

EAP Matching | Optimal Variable Ratio (Prespecified)

CNM-Au8 30 mg EAP Participants vs. Propensity Matched Controls
 CNM-Au8 30 mg (EAP01 & EAP02) All Evaluable with Baseline Covariates vs.
 Pooled Matched Controls (PRO-ACT, ALS NHC, ANSWER-ALS)
 Optimal Variable Ratio Matching



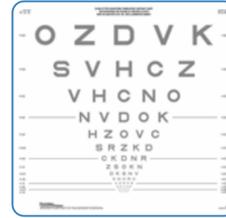
31%
Risk
Reduction

At Risk	0	12	24	36	48				
CNM-Au8 30 mg:	258	206	112	61	58	53	33	15	6
Matched Controls:	774	656	485	280	186	126	76	55	11

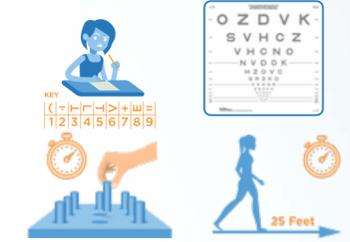
- **Propensity Matching: Variable Optimal Ratio Matching**
 Minimizes global distance of the logit score by assessing the overall set of matches when choosing individual matches
- **Pooled Control Set:** PRO-ACT, ALS Natural History Consortium (ALS NHC), ANSWER-ALS
 - Widest possible universe for control matches
 - 1:3 (active:control) match
- **Narrow Logit Caliper Width:** 0.1
- **Matching Covariates:**
 BMI, Sex, Bulbar Onset, Months from Symptom Onset, Onset Age, Diagnostic Delay (Months), ALSFRS-R Pre-Treatment Slope, ALSFRS-R Total Score, Vital Capacity (% predicted), VC (% predicted) Pre-Treatment Slope, TRICALS Risk Score
- **Survival Cox Proportional HR Model Covariates:**
 Bulbar Onset, (ii) Onset Age, (iii) Sex, (iv) BMI, (v) Pre-treatment ALSFRS-R slope, (vi) ALSFRS-R Total Score, (vii) Diagnostic Delay (in months), (viii) Vital Capacity (% predicted), (ix) Pre-Treatment Vital Capacity Slope, and (x) TRICALS Risk Score

CNM-Au8 Demonstrated Vision and Global Neurological Improvement in Stable MS patients on DMTs

Significantly Improved Vision



Global Neurological Improvement

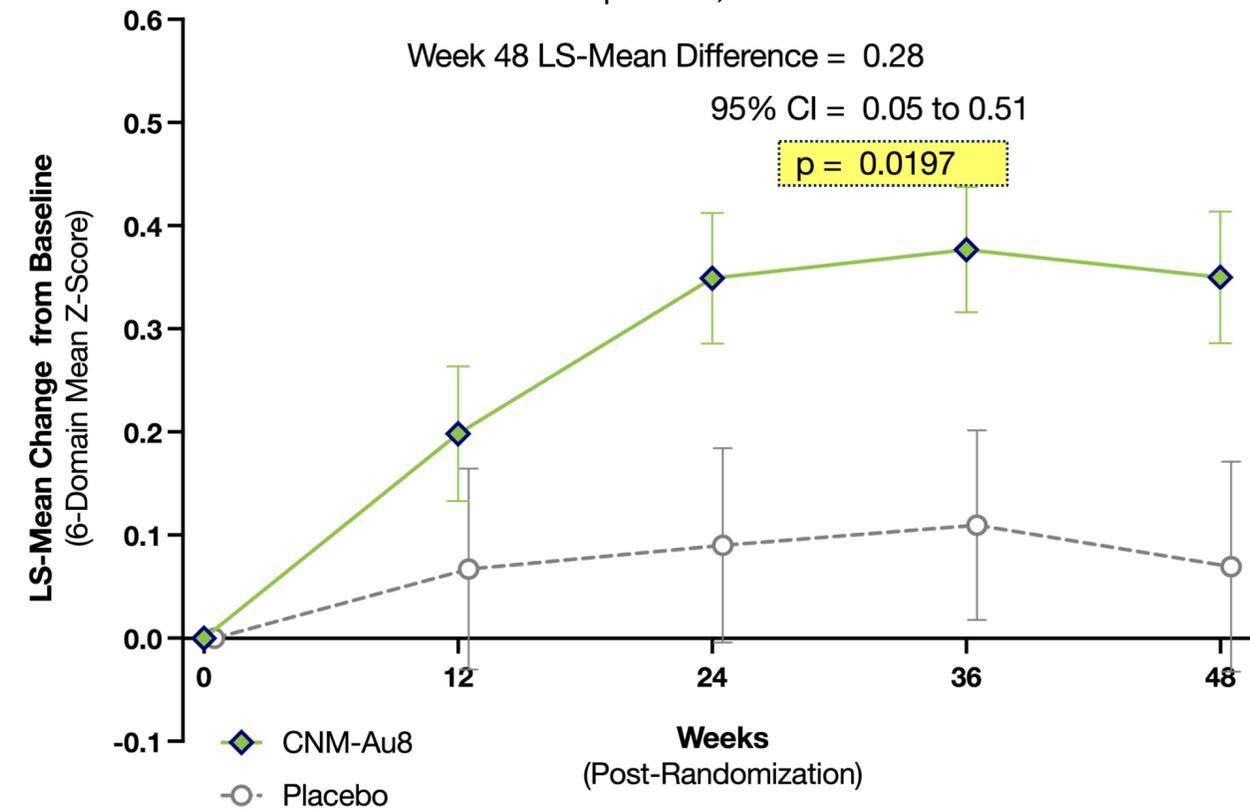
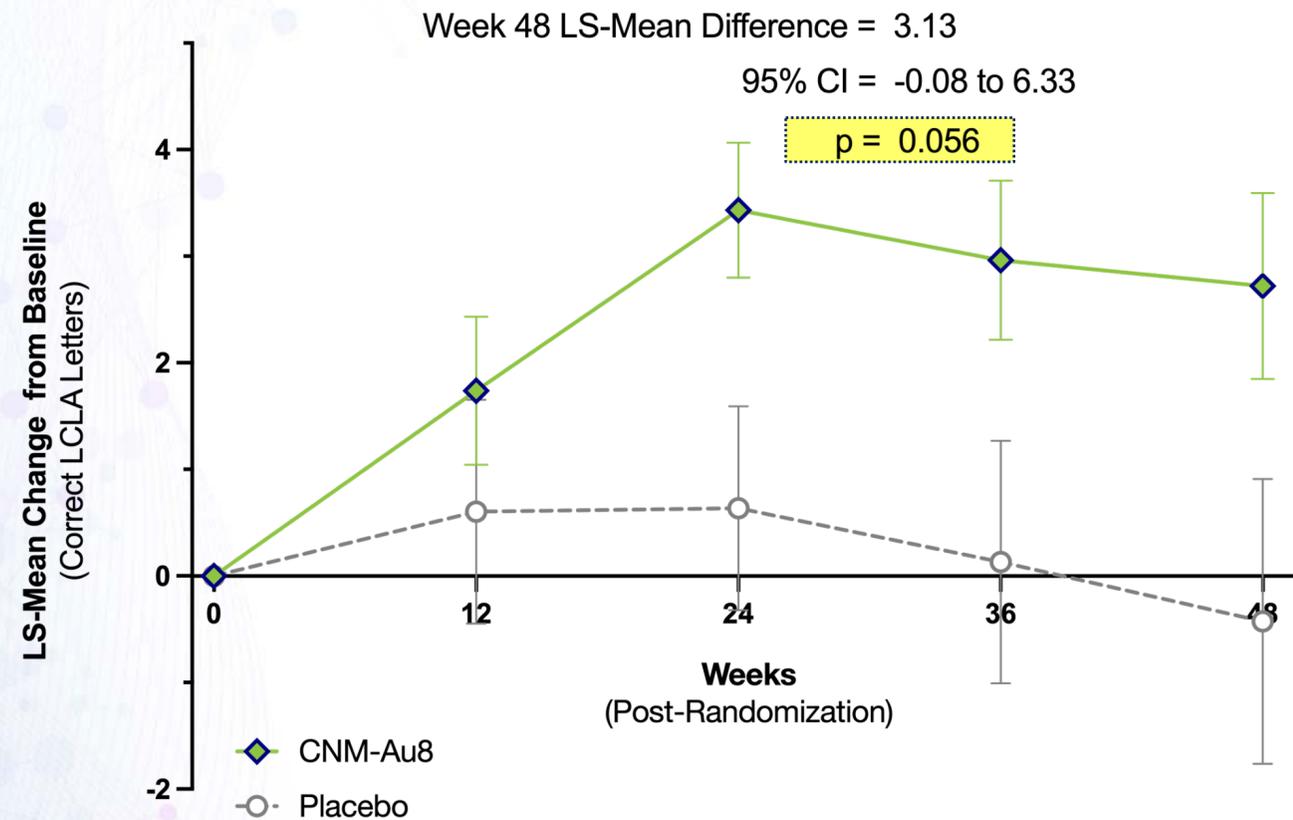


Change in Low Contrast Letter Acuity (LCLA)

LCLA Change in the Affected Eye
mITT, LS Mean ± SEM

Change in modified MS Functional Composite (mMSFC)

Average mMSFC Z-Score Change
LCLA affected/fellow, 9HPT dominant/non-dominant, SDMT, T25FW
mITT Population, LS Mean ± SEM



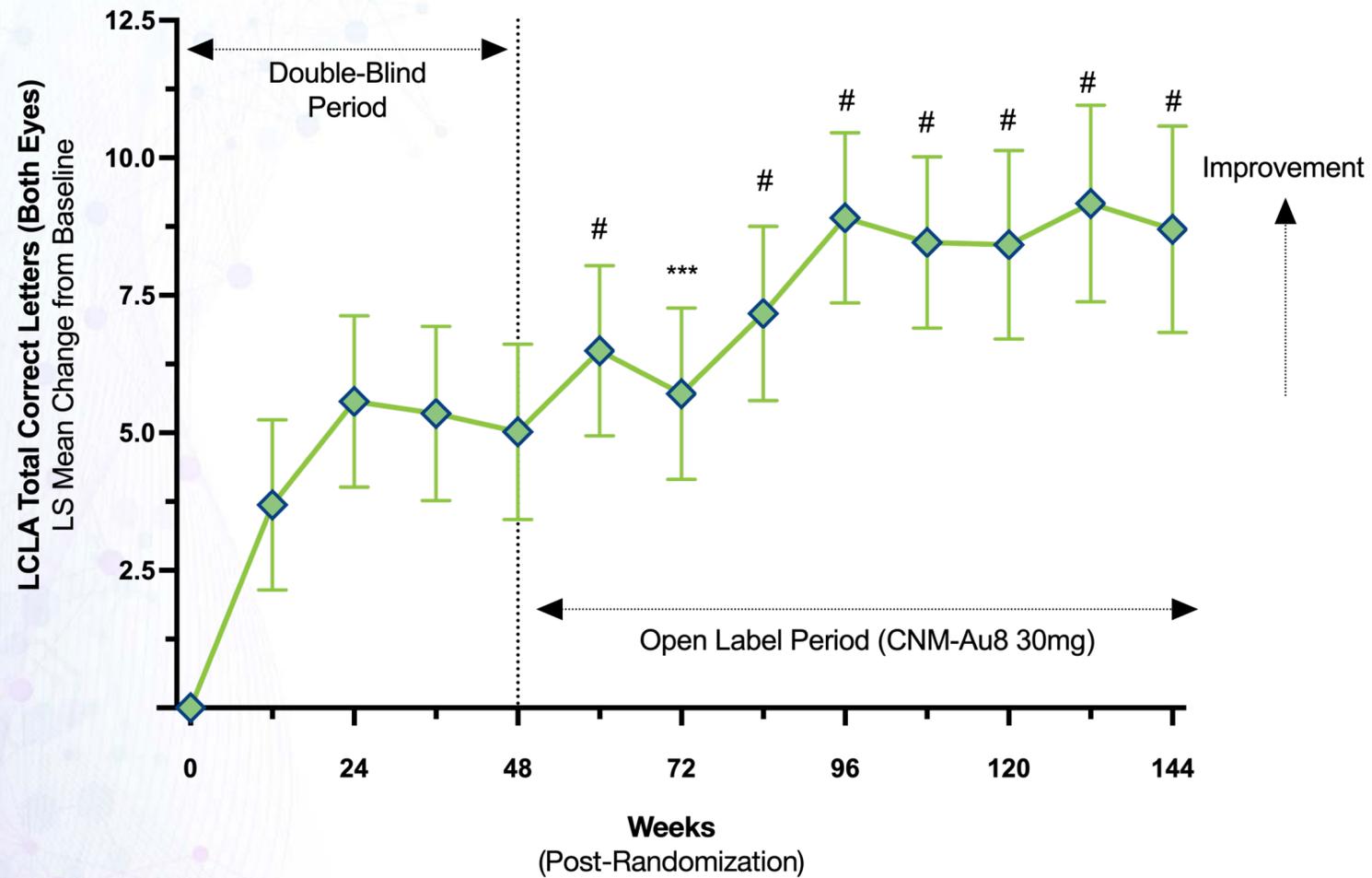
Global neurological clinical improvement was driven by cognition, manual dexterity, and low contrast letter acuity

Long-Term LCLA Improvement in LTE Participants

Low Contrast Letter Acuity

Original Active (CNM-Au8)

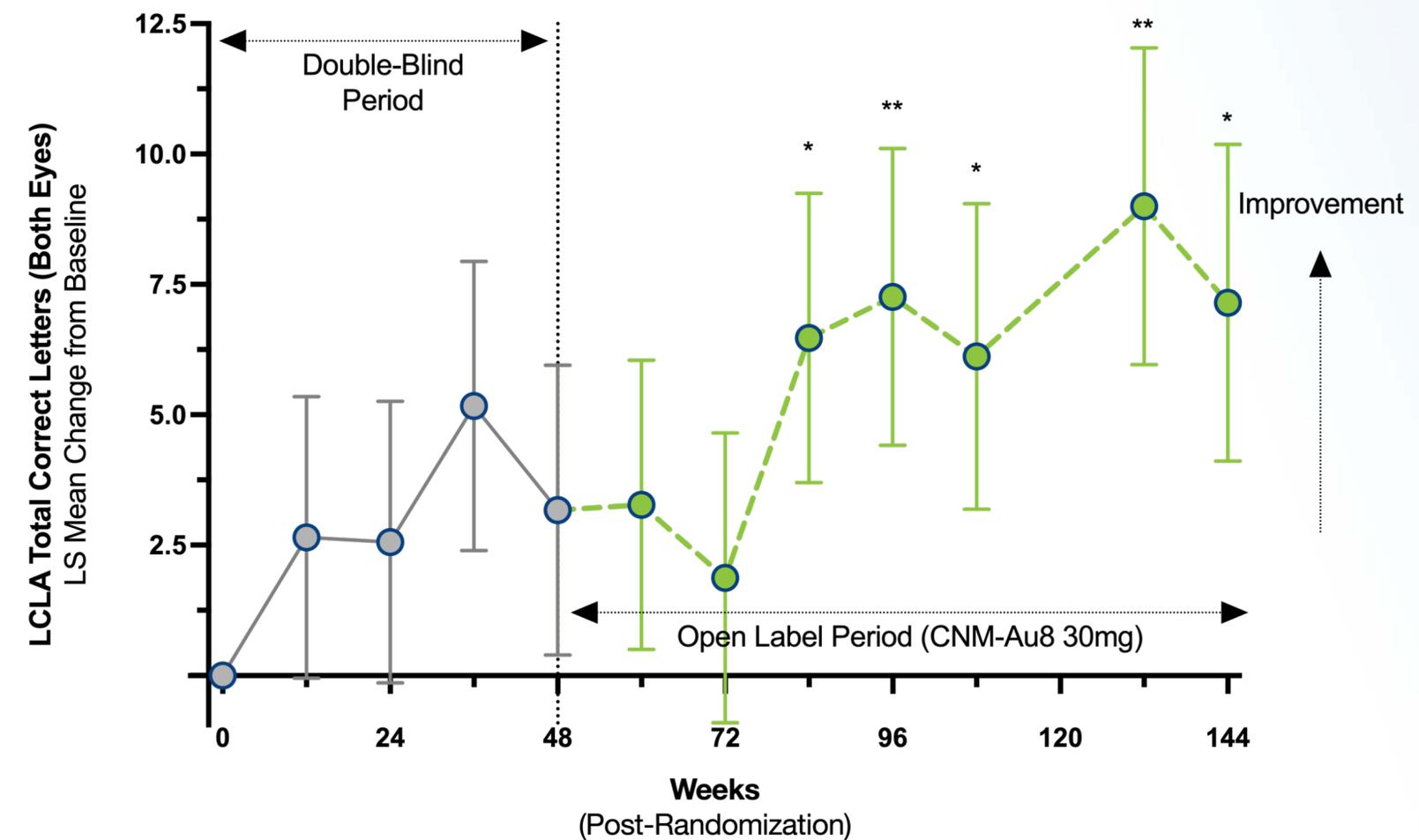
Longitudinal LCLA | Change from Baseline (Total Correct, Both Eyes) | All Active
 In LTE Participants Originally Randomized to CNM-Au8 (n=35), mITT Population
 LS Mean ± SEM, Change from Baseline (Preliminary)



LTE: LS mean difference vs. randomization baseline: # p≤0.0001, *** p≤0.001, ** p≤0.01, *p≤0.05

Original Placebo

Longitudinal LCLA | Change from Baseline (Total Correct, Both Eyes)
 In LTE Participants Originally Randomized to Placebo (n=11), mITT Population
 LS Mean ± SEM, Change from Baseline (Preliminary)

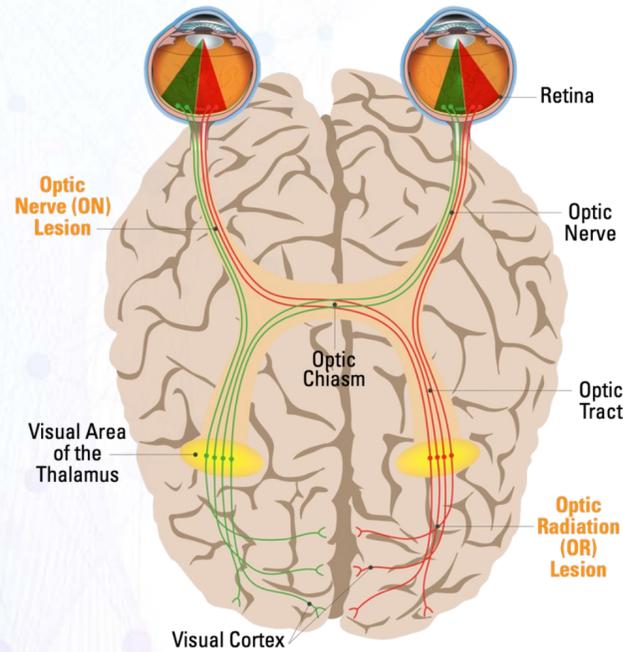


MMRM accounts for missing data; all visits with ≥ 60% participant values are graphed.

LTE: LS mean difference vs. randomization baseline: # p≤0.0001, *** p≤0.001, ** p≤0.01, *p≤0.05

CNM-Au8 Improved Information Signal Strength & Speed in the Visual Pathway

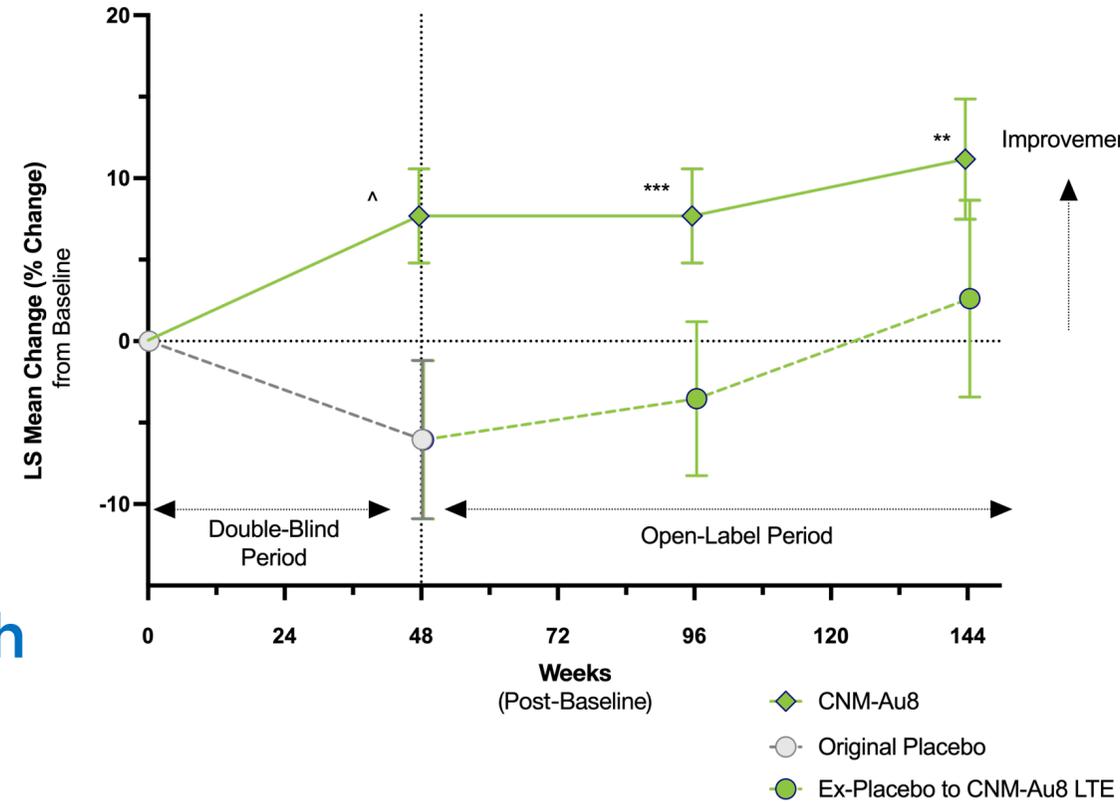
Visual Evoked Potentials



Amplitude = Signal Strength
Latency = Signal Speed
 From the Eye to Visual Cortex

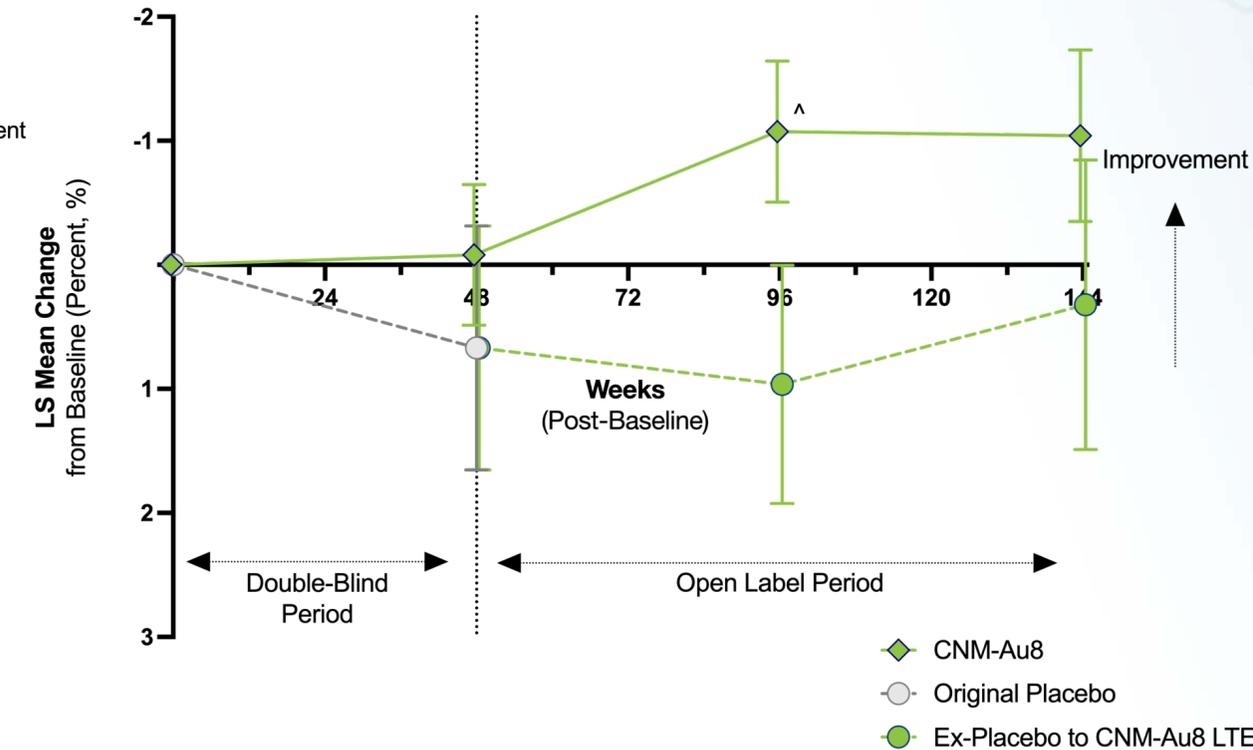
Improved Amplitude

mf-VEP Amplitude | Longitudinal Percent (%) Change
 In LTE Participants (n=43; 31 active, 12 ex-placebo), All Evaluable, ITT Population
 Percent Change from Baseline [A6], LS Mean ± SEM



Improved Latency

mf-VEP Average Latency | Longitudinal Percent (%) Change
 In LTE Participants (n=42; 30 active, 12 ex-placebo), All Evaluable, ITT Population
 Percent Change from Baseline [A6], LS Mean ± SEM (Preliminary)



LTE: LS mean difference vs. randomization baseline: # p≤0.0001, *** p≤0.001, ** p≤0.01, *p≤0.05, ^p≤0.10

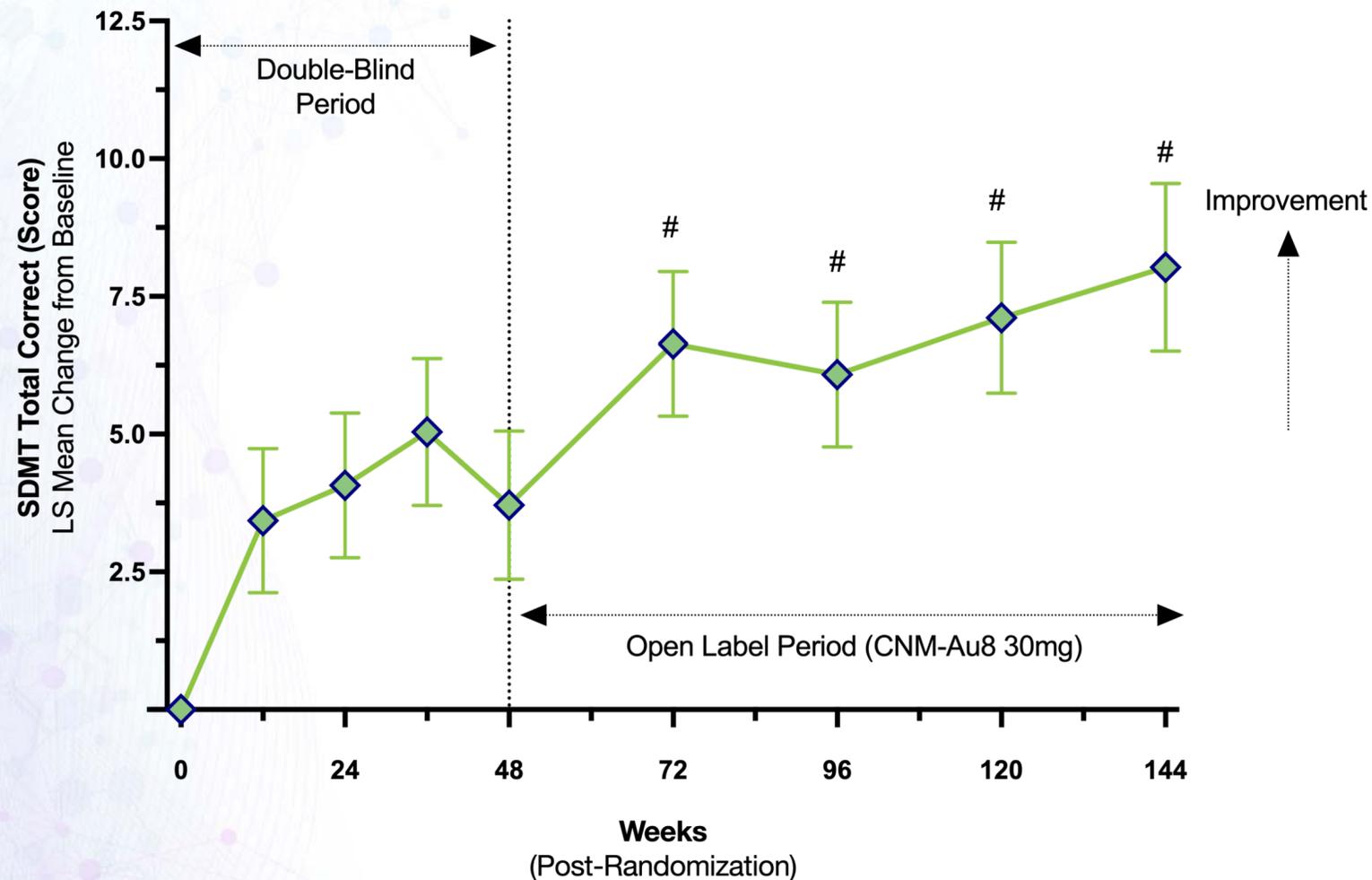
Increased VEP amplitude is associated with improved axonal integrity (more signal); Improved latency is associated with evidence of remyelination (faster conduction velocity)

Long-Term SDMT Improvement in LTE Participants

Symbol Digit Modality Test | Working Memory & Cognition

Original Active (CNM-Au8)

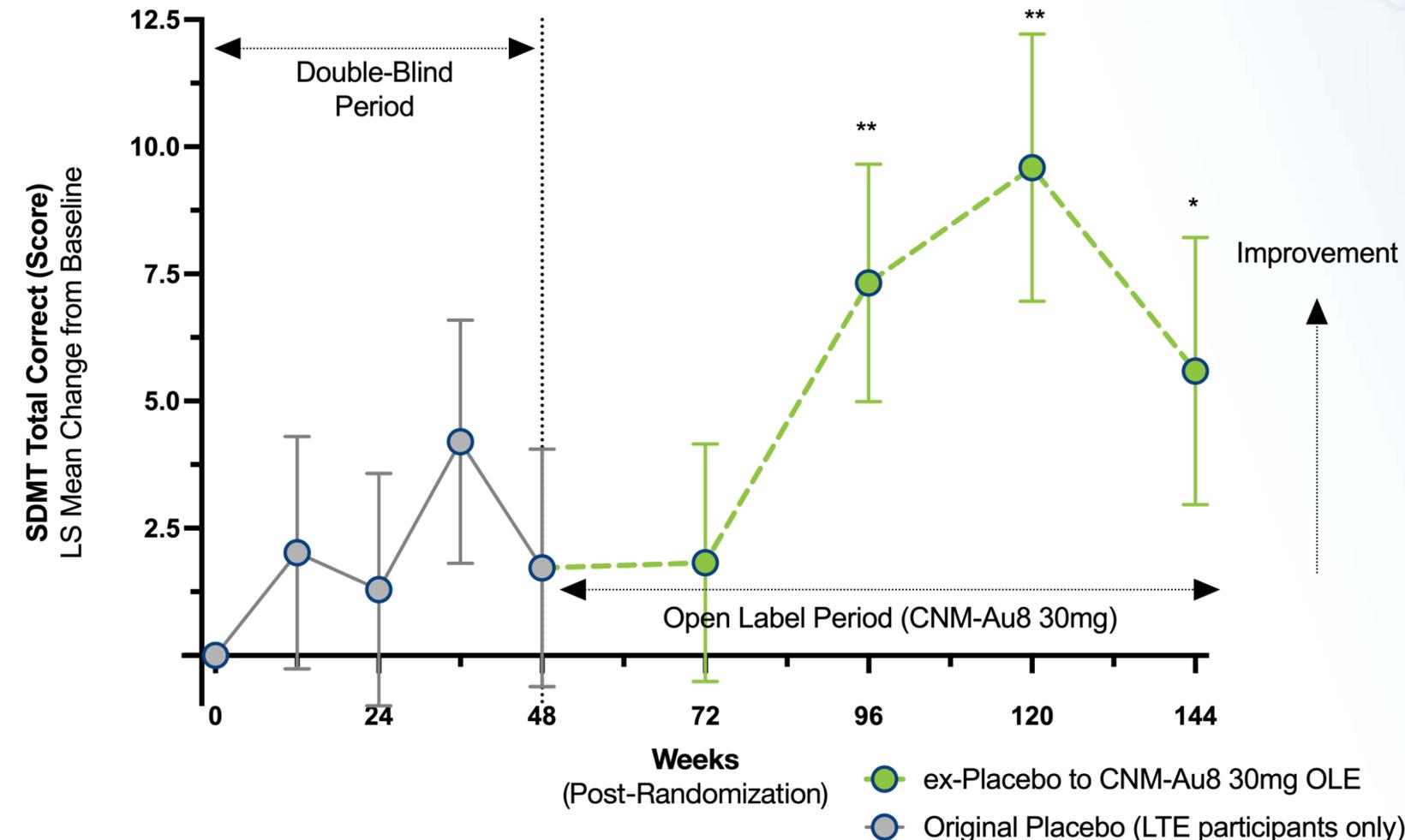
Longitudinal SDMT | Change from Baseline (Total Score) | All Active
 In LTE Participants Originally Randomized to CNM-Au8 (n=35), mITT Population
 LS Mean ± SEM, Change from Baseline (Preliminary)



LTE: LS mean difference vs. randomization baseline: # p<0.0001, *** p<0.001, ** p<0.01, *p<0.05

Original Placebo

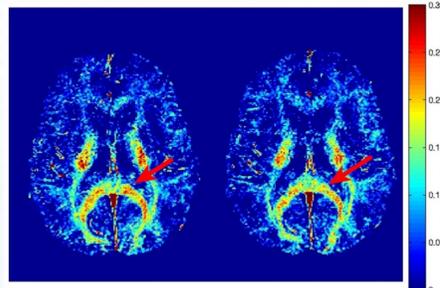
Longitudinal SDMT | Change from Baseline (Total Score)
 In LTE Participants Originally Randomized to Placebo (n=11), mITT Population
 LS Mean ± SEM, Change from Baseline (Preliminary)



LTE: LS mean difference vs. randomization baseline: # p<0.0001, *** p<0.001, ** p<0.01, *p<0.05

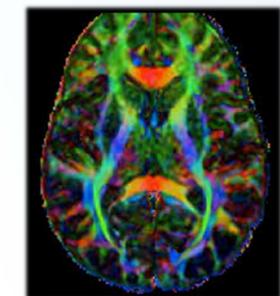
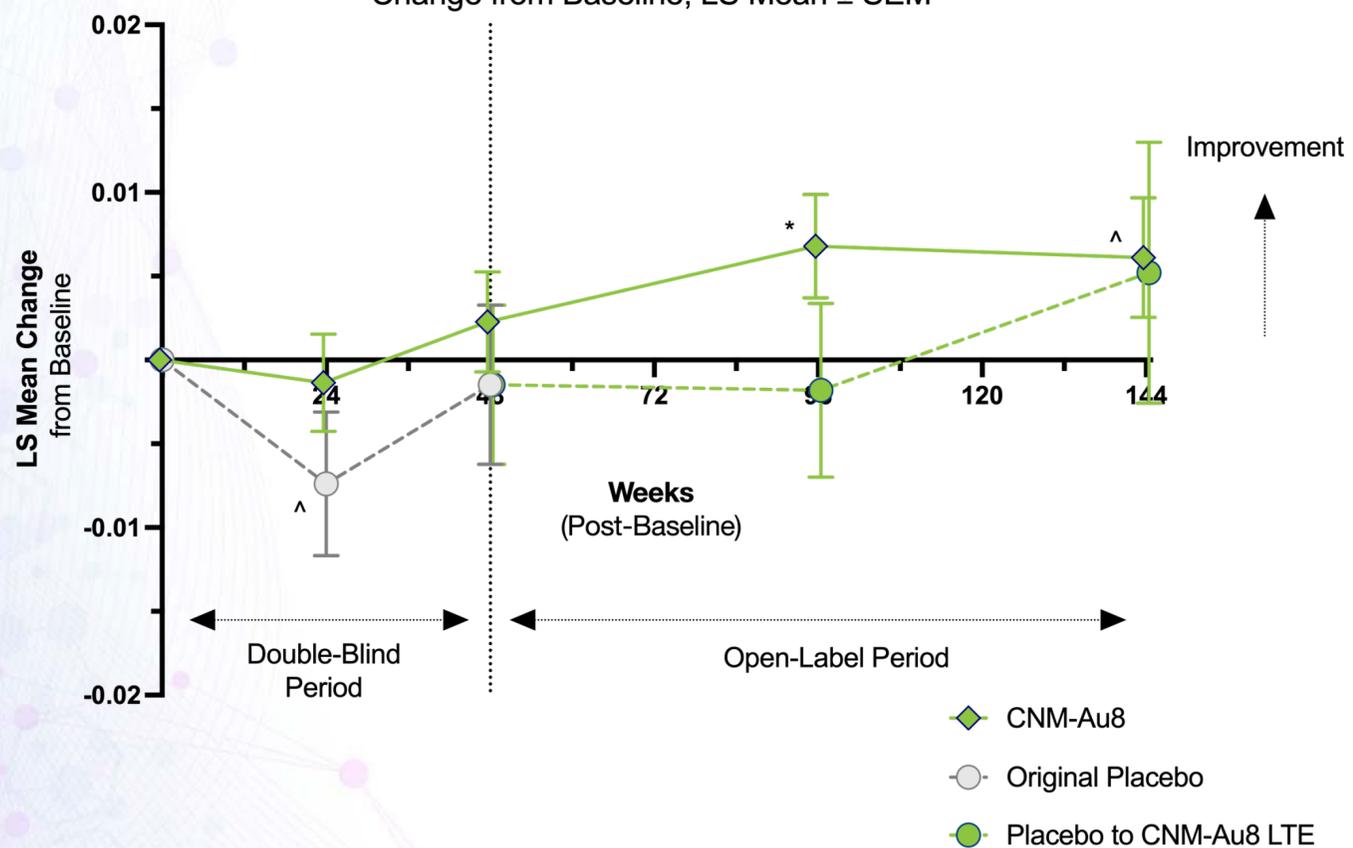
CNM-Au8 Treatment Demonstrated MS Lesion Repair and Promoted Remyelination

Advanced MRI Techniques



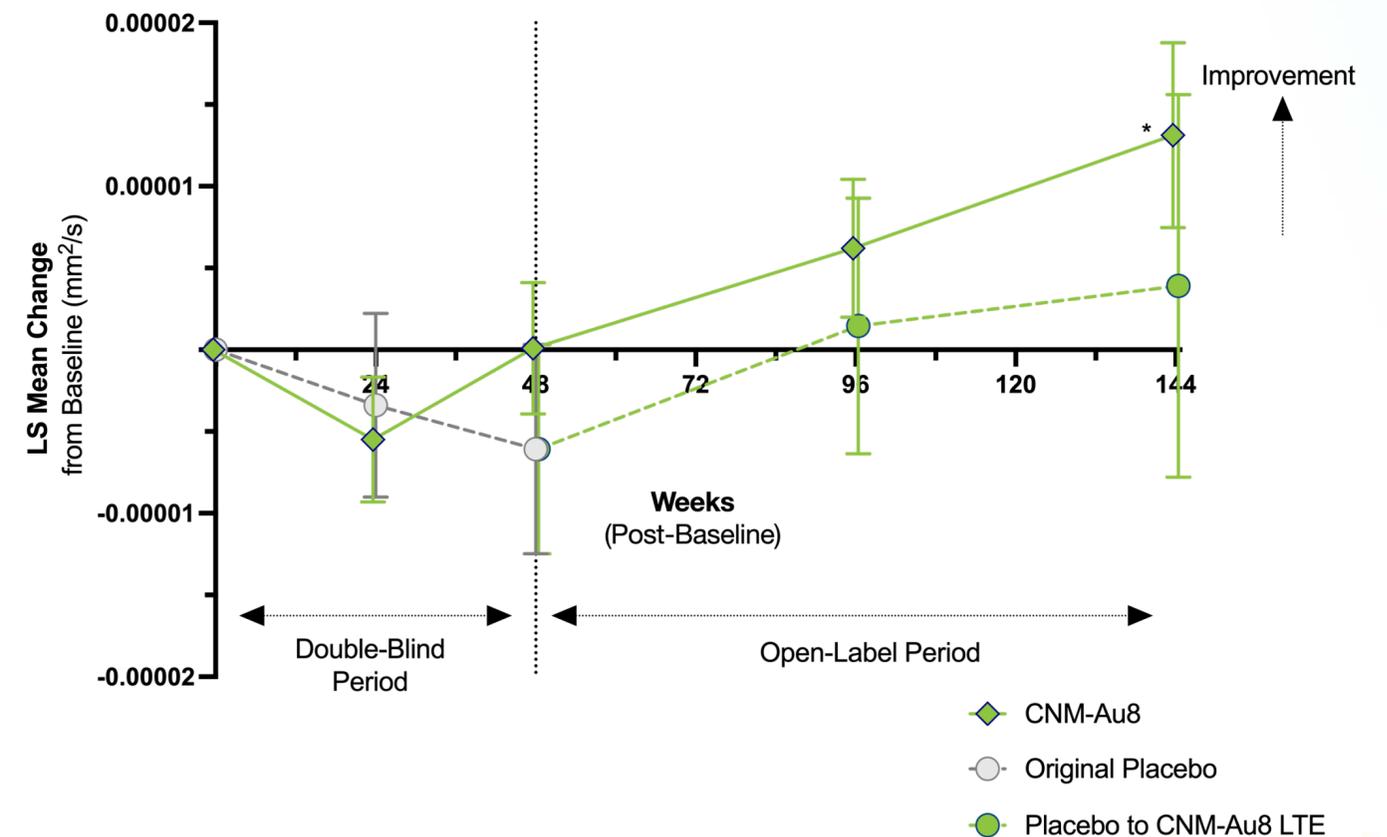
T2 Lesion Myelin Water Fraction (Remyelination)

T2 Lesion Myelin Water Fraction in the Cerebrum
MRI Longitudinal Analyses (n=69), All Evaluable, ITT Population
Change from Baseline, LS Mean ± SEM

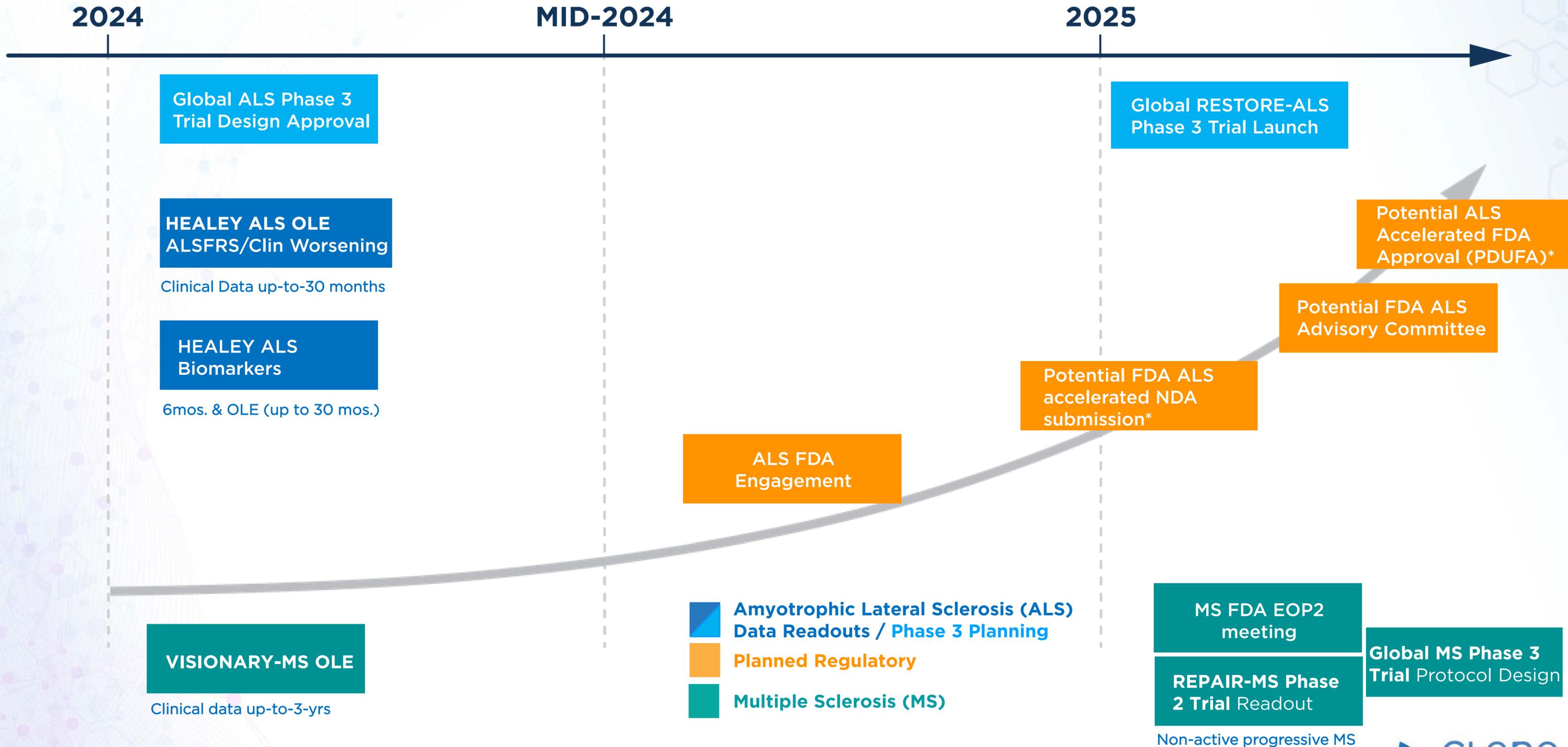


T2 Lesion Axial Diffusivity (Axonal Integrity)

T2 Lesion Axial Diffusivity in the Cerebrum
MRI Longitudinal Analyses (n=69), All Evaluable, ITT Population
Change from Baseline, LS Mean ± SEM



Clene | CNM-Au8 Path to Regulatory Approval



Evidence Supports CNM-Au8 Therapeutic Potential to Treat Neurodegenerative Diseases

CNM-Au8[®]
a gold nanocrystal suspension, in development as the first cellular energetic catalyst to remyelinate¹ & protect neurological function



 **HEALEY ALS**
Platform Trial

 **RESCUEALS**

Concordant Survival in two Phase 2 trials, with NfL Biomarker in HEALEY

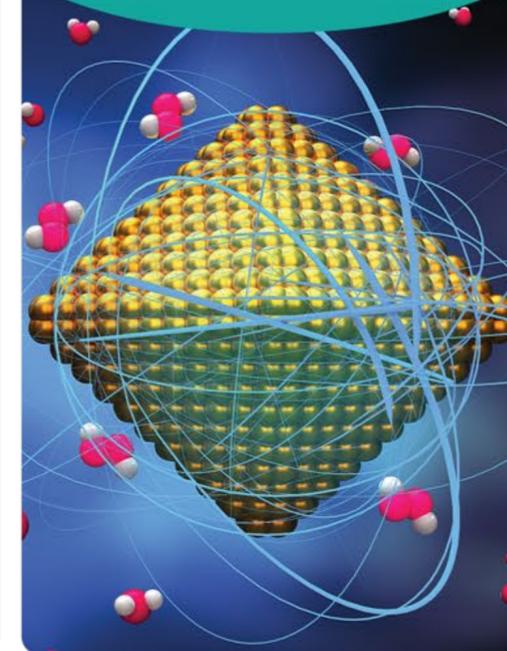
 **VISIONARY-MS**
STUDY

Demonstrated global neurological improvement in MS patients on adjunctive DMT standard of care



>700
participant years of CNM-Au8 clinical exposure

Strong IP:
150+ patents on nanotherapeutic platform, plus trade secret protection



As of September 30 2024, cash and equivalents on hand (unaudited):

\$14.6

+ \$3.5

Raised in an RDO on 10/1/2024



CLene
NANOMEDICINE

Clene Inc.

HQ & Clinical Development

6550 South Millrock Drive, Suite G50
Salt Lake City, UT 84121

R&D and Manufacturing

500 Principio Parkway, Suite 400
North East, MD 21901

©2024 Clene Inc.

Version: 10 Dec 2024