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Forward Looking Statements

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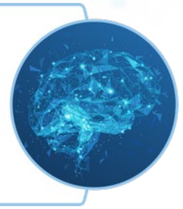
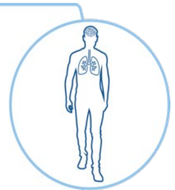
Building the Clinical Case for Neuroprotection & Remyelination

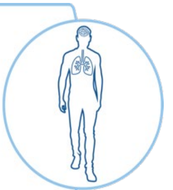
RepairPD
RepairMS



RESCUEALS



HEALEY ALS Platform Trial



VISIONARY-MS STUDY

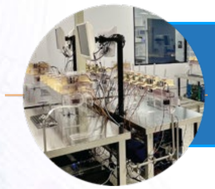
Established brain target engagement in early PD and stable relapsing MS patients

CNM-Au8 demonstrated statistically significant **survival benefit of 60% decreased risk of death** through 120 wks

CNM-Au8 demonstrated a **>90% reduction in risk of death or permanently assisted ventilation** for the 30 mg dose at 24 weeks

CNM-Au8 demonstrated **neurological improvements in stable relapsing MS** as adjunctive therapy to immunomodulatory DMTs

Growing Body of Clinical Evidence Across ALS and MS Supports CNM-Au8 Therapeutic Potential



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

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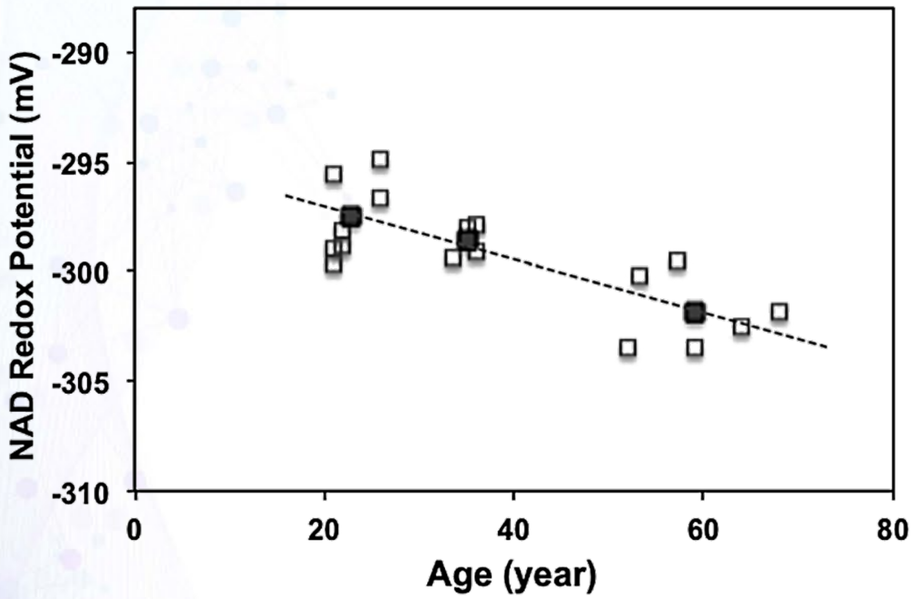
Neurodegenerative Diseases Share A Common Mechanism: A Decline In The Brain's Ability To Produce Energy

Brain Energy Potential Declines With Normal Aging

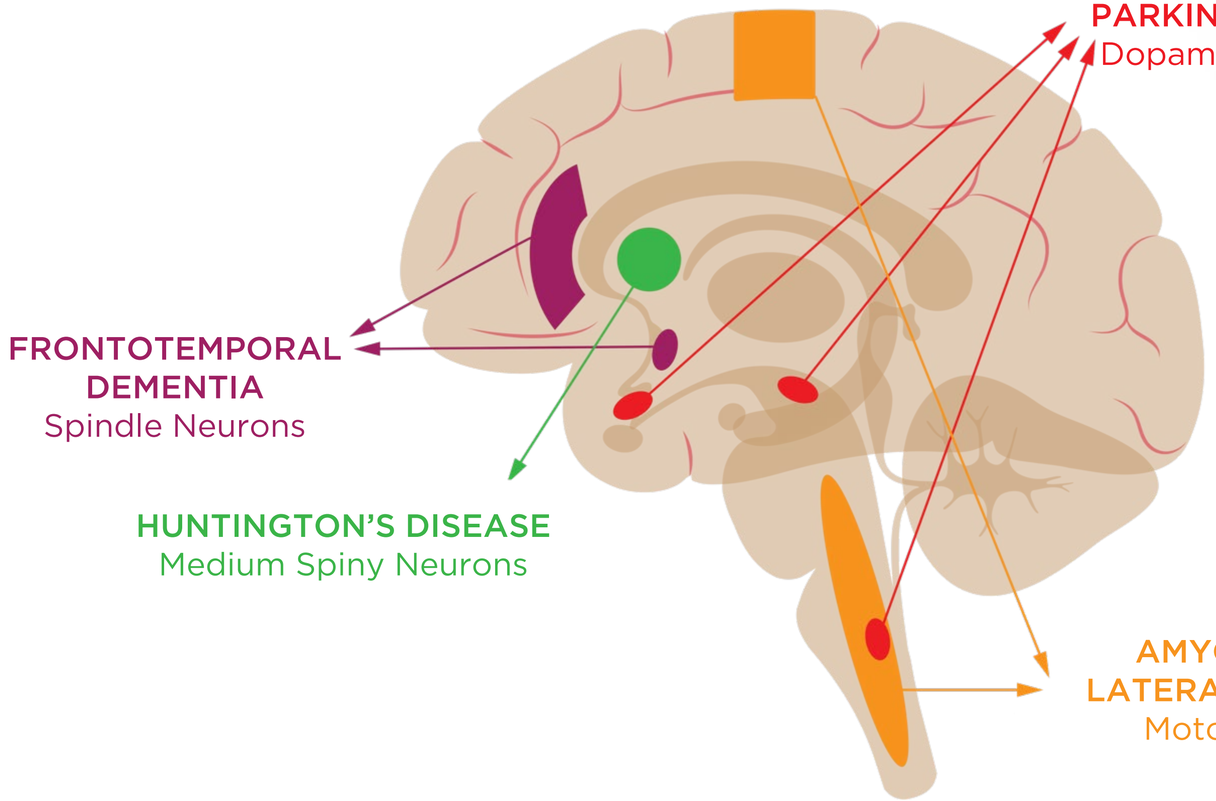


~0.5% NAD^+/NADH unit decline per decade

(~0.13 mV units per year by ^{31}P-MRS Imaging)

Closed squares = averaged data by age group: 21–26 yrs, 33–36 yrs, and 59–68 yrs old; Open squares = individual subject values

Specific Neuronal Populations Are Vulnerable to Energetic Failure



PARKINSON'S DISEASE
Dopaminergic Neurons

MULTIPLE SCLEROSIS
Axonal Degeneration

FRONTOTEMPORAL DEMENTIA
Spindle Neurons

HUNTINGTON'S DISEASE
Medium Spiny Neurons

AMYOTROPHIC LATERAL SCLEROSIS
Motor Neurons

Energetic impairments in the CNS both pre-dispose and drive progression in neurodegenerative diseases

Fu, H., et al; Nature Neuroscience (2018) 21: 1350-1358. Zhu et al. Proc Natl Acad Sci USA 2015 Mar 3;112(9):2876-81. Rone et al. J Neurosci. 2016 Apr 27;36(17):4698-707.

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CNM-Au8® | Pioneering A New Drug Class To Improve Cellular Energy Production And Utilization

CNM-Au8 Nanocrystals

Clean Surfaced, Highly Faceted Shapes

CNM-Au8 Nanocrystal Suspension

Mechanistic Effects

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

=

Improved Energy Production and Utilization

By targeting energy metabolism, CNM-Au8 may protect neuronal health

Robinson et al. Sci Rep. 2020 Feb 11;10(1):1936. Data on File, Clene Nanomedicine, Inc.

Significant Global Opportunity for Treatment in Combination with Standard of Care

Motor Neuron Disease (ALS, Other Orphan Disorders)

ALS PATIENTS IN US & EU ~40K[1]

$1B GLOBAL SALES BY 2029[1]

Current drugs are largely ineffective, mostly generic.

2-5 YEARS[2] LIFE EXPECTANCY

100% FATAL

Multiple Sclerosis (MS)

MS PATIENTS GLOBALLY 2.2M

$23B MARKET[3]

Existing treatments only target immunomodulation

EMERGING EVIDENCE THAT EARLY MS IS NEURODEGENERATIVE

Parkinsons Disease (PD)

2ND MOST COMMON DISORDER

$6B PROJECTED BY 2026[4]

No disease-modifying treatments available, only symptom-targeted options

30% OF DOPAMINERGIC NEURONS ARE LOST AT DIAGNOSIS[5]

Urgent unmet need to develop neuroprotective treatment to support cells' energetic efficiency and resilience

[1] Clarivate, DRG, ALS 2020 2. https://pubmed.ncbi.nlm.nih.gov/17974351/ 3. Westad et al. 2017, doi:10.1038/nrd.2017.107;. 4. Parkinson's Market Data Forecast, April 2021.. 5. Cheng HC, Ulane CM, Burke RE. Clinical progression in Parkinson disease and the neurobiology of axons. Ann Neurol 2010;67:715-725..

Two **REPAIR Trials Demonstrated Target Brain Engagement** and **Improved Energy Metabolism** in Early Parkinson's and Stable Relapsing MS

Results demonstrated a potentially meaningful 10% improvement in NAD+/NADH ratio, an essential molecule for energy production[1]

Study Objective: to demonstrate target engagement for CNM-Au8 on CNS biomarkers related to energetic effects in the brain using Magnetic Resonance Spectroscopy (^{31}P-MRS)

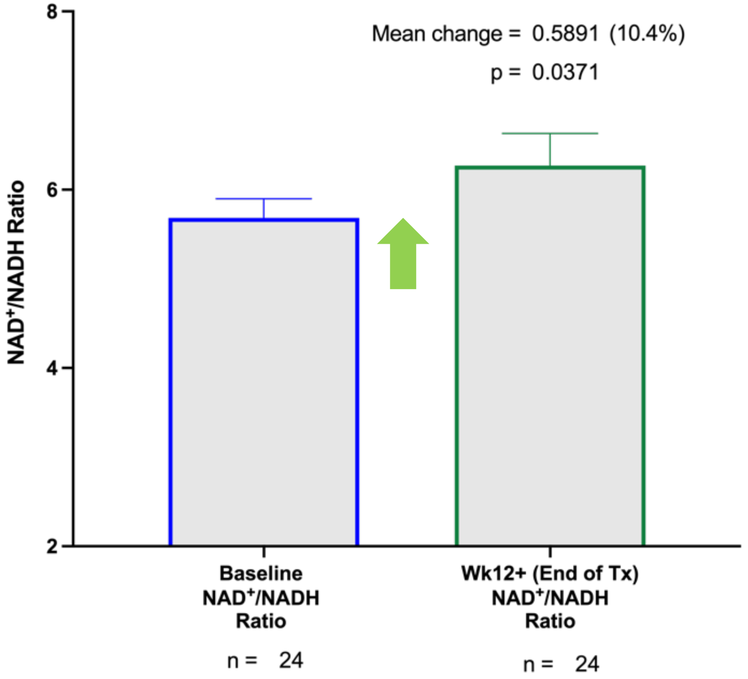
RepairPD
Early Parkinson's Disease

RepairMS
Stable Relapsing MS

RepairMS
Non-Active Progressive MS
(Ongoing)

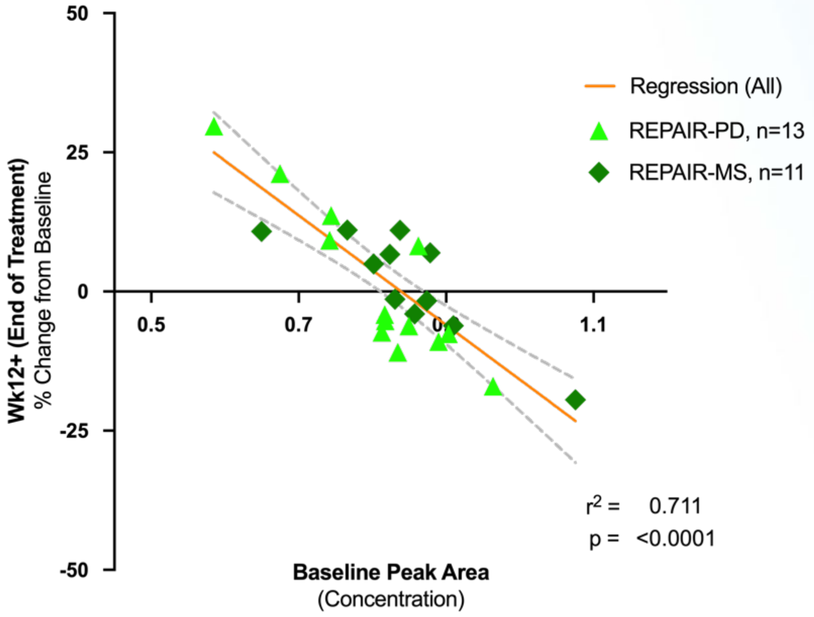
1° Endpoint (integrated PD & MS)[2]

^{31}P-MRS Change in Brain NAD$^+$/NADH Ratio at End of Treatment
Partial Volume Coil; Ratio of NAD$^+$/NADH (% Fraction of NAD$^+$/ % Fraction NADH)
Primary Endpoint, Mean ± SEM (Paired t-test)



Exploratory
(ATP Normalization)

REPAIR Integrated Analysis
^{31}P-MRS Change in β-ATP at End of Treatment
Full Volume Coil ^{31}P Signal Area (Integral)
Exploratory Endpoint, Percent (%) Change vs. Baseline Value



[1] Zhu et al. Proc Natl Acad Sci USA 2015 Mar 3;112(9):2876-81.. 2. Glanzman et al Improvement of Brain Energy Metabolism in Relapsing Multiple Sclerosis Patients - Results from Phase 2 REPAIR-MS Clinical Trial With CNM-Au8, ACTRIMS February 2022

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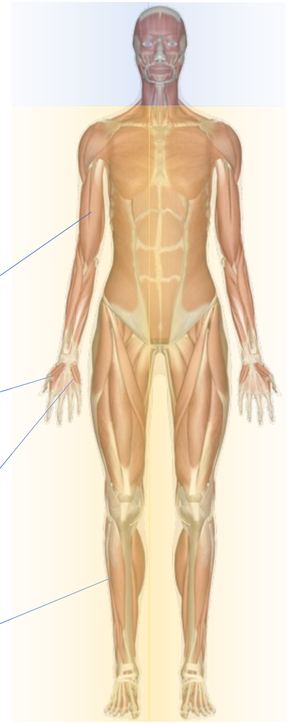
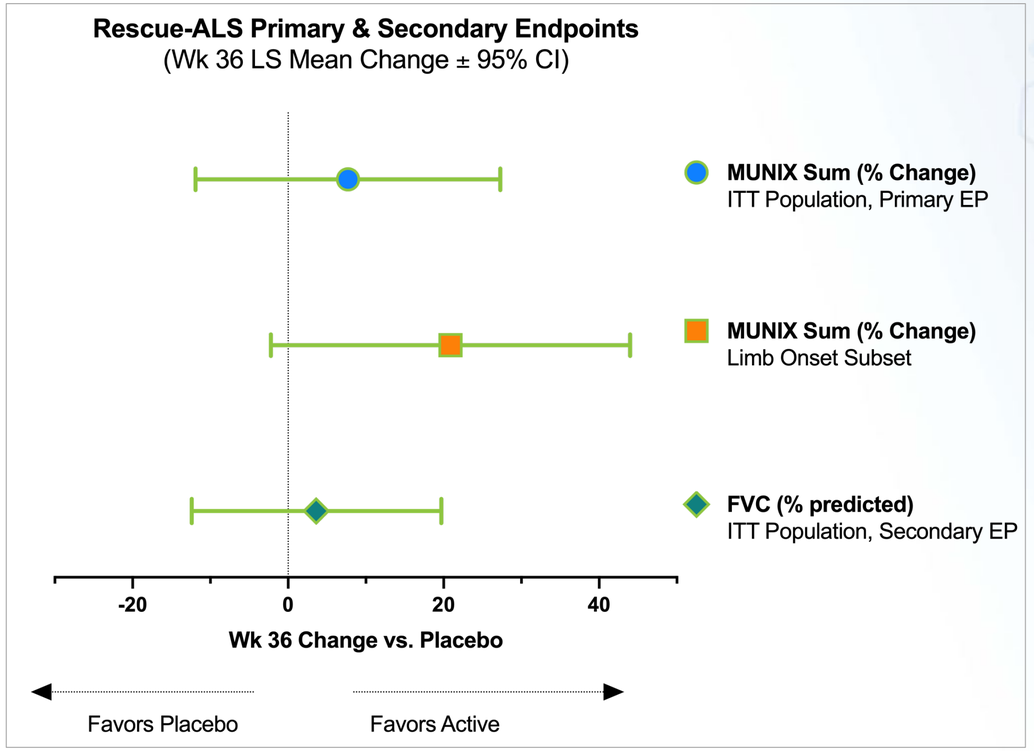
RESCUEALS Encouraging Efficacy Signals in Phase 2 Trial

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



1° & 2° Endpoints



Results in favor of CNM-Au8 treatment but study underpowered

Vucic et al. RESCUE-ALS Trial Results: A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study of CNM-Au8 to Slow Disease Progression in Amyotrophic Lateral Sclerosis; Presented at International Symposium on ALS/MND; 7-10 December 2021.

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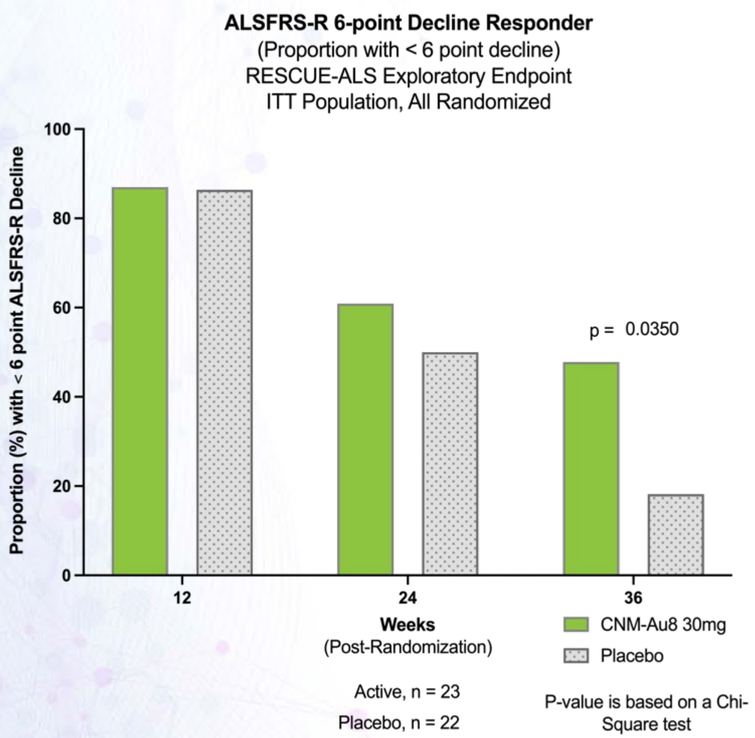
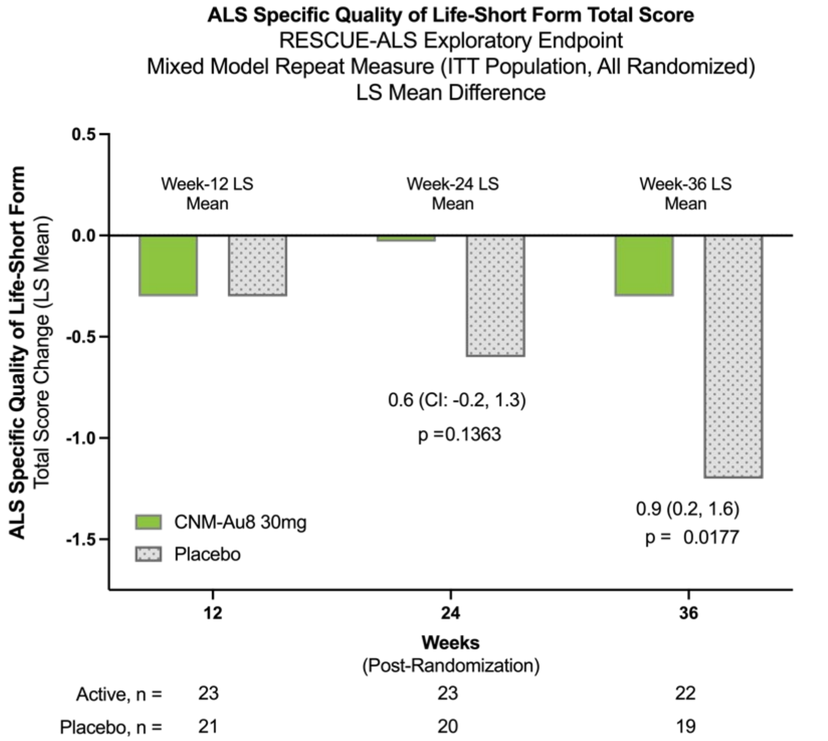
CNM-Au8 Improved Patient Function and QOL, and Slowed ALS Disease Progression

Phase 2 Study: 36-Week Placebo-Control Treatment Period 1:1 Randomization (Active 30 mg: Placebo);
45 enrolled with early ALS

Proportion with <6 point decline

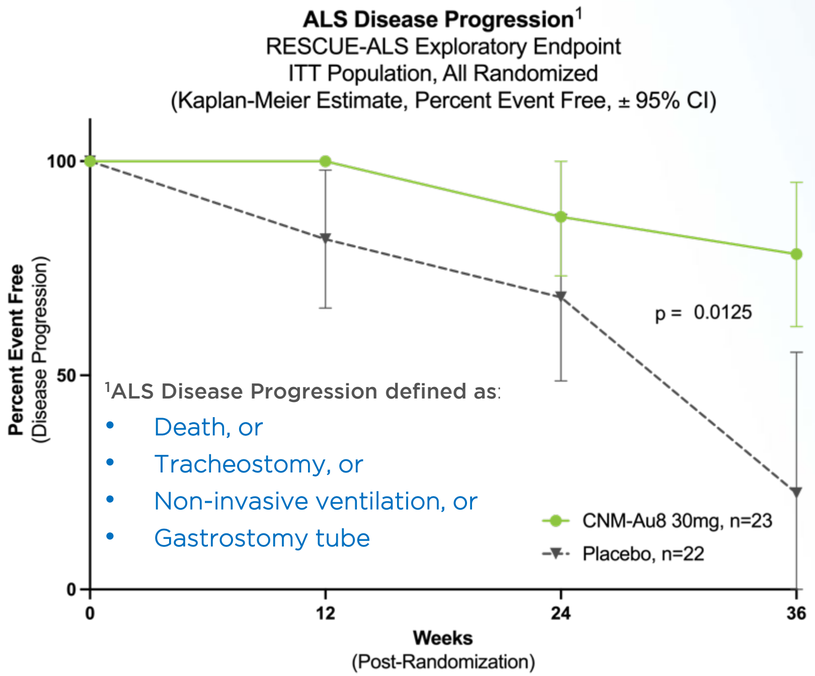


ALS Specific QOL



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.

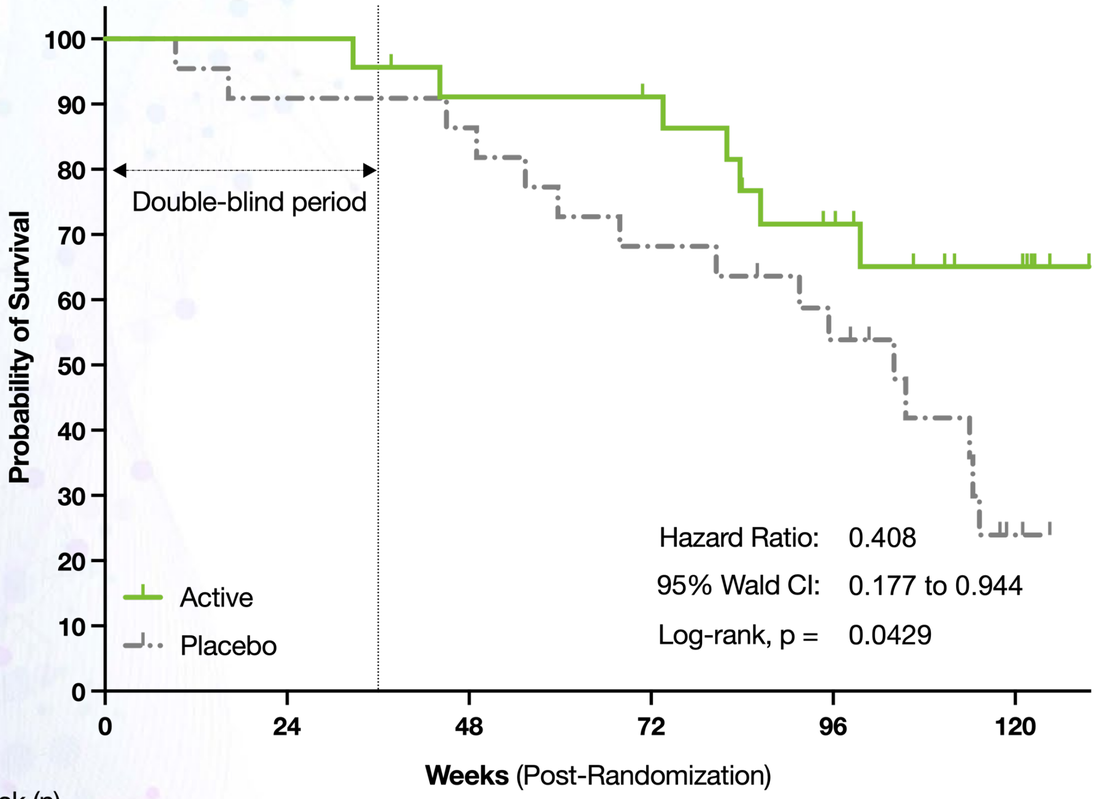
ALS Disease Progression



Vucic et al. RESCUE-ALS Trial Results: A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study of CNM-Au8 to Slow Disease Progression in Amyotrophic Lateral Sclerosis; Presented at International Symposium on ALS/MND; 7-10 December 2021

RESCUEALS Demonstrated Significant Impact on Long-Term Survival — 60% Decreased Risk of Death through 120 weeks

Long-Term Survival (All-Cause Mortality): Originally Randomized Active vs. Placebo
Interim Analysis (12-July-2022), ITT Population, All Subjects from Randomization
(Long-term vital status including all study withdrawals)



At Risk (n)						
CMM-Au8:	23	23	20	19	13	7
Placebo:	22	20	19	15	11	3

Early CNM-Au8 treatment demonstrated a significant survival benefit:

- Follow-up of active compared to initial placebo randomization*
- 60% decreased risk of death

*9-month delayed treatment start (ex-placebo) or no treatment

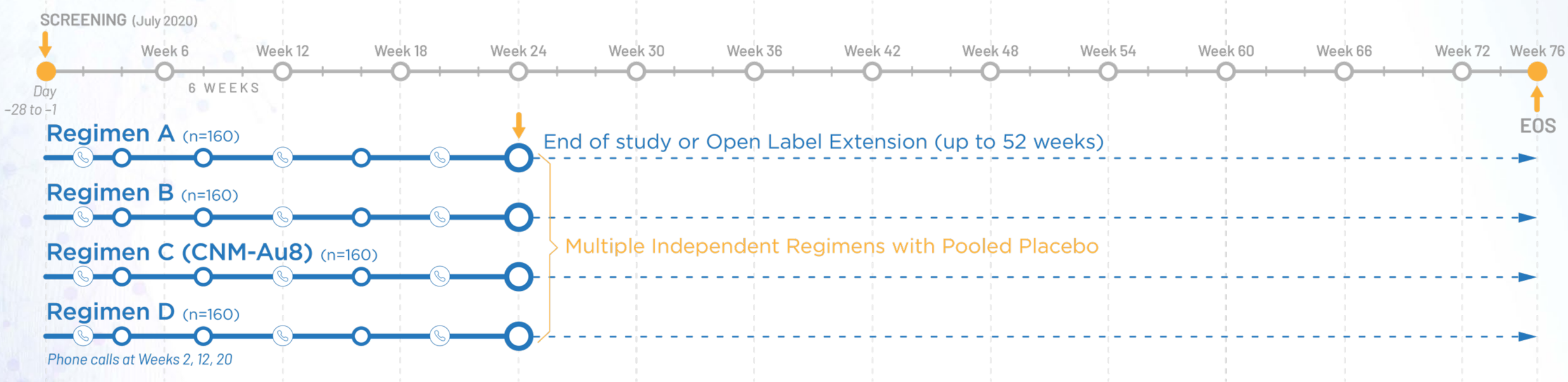
Time to all-cause mortality amongst participants originally randomized to CNM-Au8 compared to participants originally randomized to placebo through at least 12-months following the last patient last visit (12-July-2022). Vital status and date of death (as applicable) were captured for all subjects withdrawn 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 12-July-2022.

Data on File, Clene Nanomedicine, Inc.

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

Registration Study: 24-Week Treatment Period (3:1 randomization, 120 active [30mg, 60mg]: 40 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)

Paganoni et al. Adaptive Platform Trials to Transform Amyotrophic Lateral Sclerosis Therapy Development. Ann Neurol. 2022; 91:165-175.

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Healey ALS Platform Trial CNM-Au8 Results

HEALEY ALS Platform Trial

- No evidence for treatment effect at 24 weeks for either adjusted ALSFRS-R, CAFS, or SVC (combined 30 & 60 mg doses)

- Potential survival signal: > 90% decreased risk of death at 30 mg
  - Mortality/PAV, p=0.028; Mortality = 0.057 (Regimen only)
  - Mortality/PAV, p=0.042; Mortality = 0.075 (Shared placebo)

Data on File, Clene Nanomedicine, Inc.

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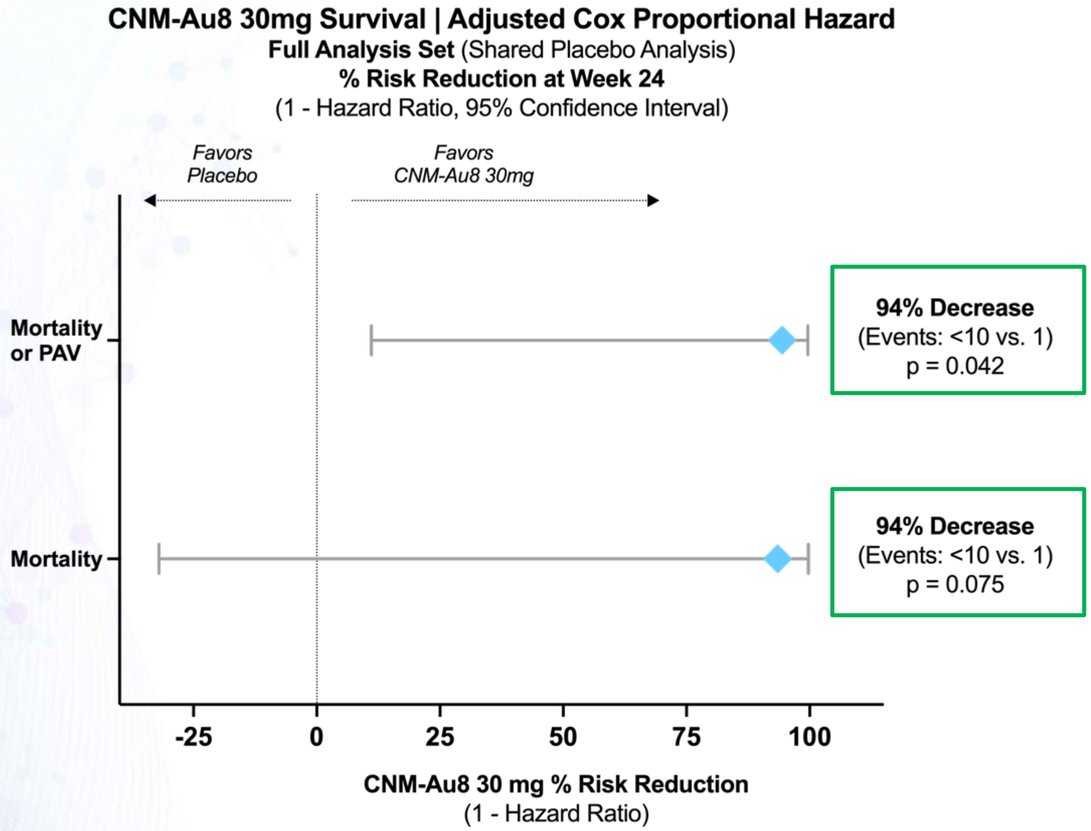
24-Week Survival Signal | >90% Reduced Risk of Death at 30 mg

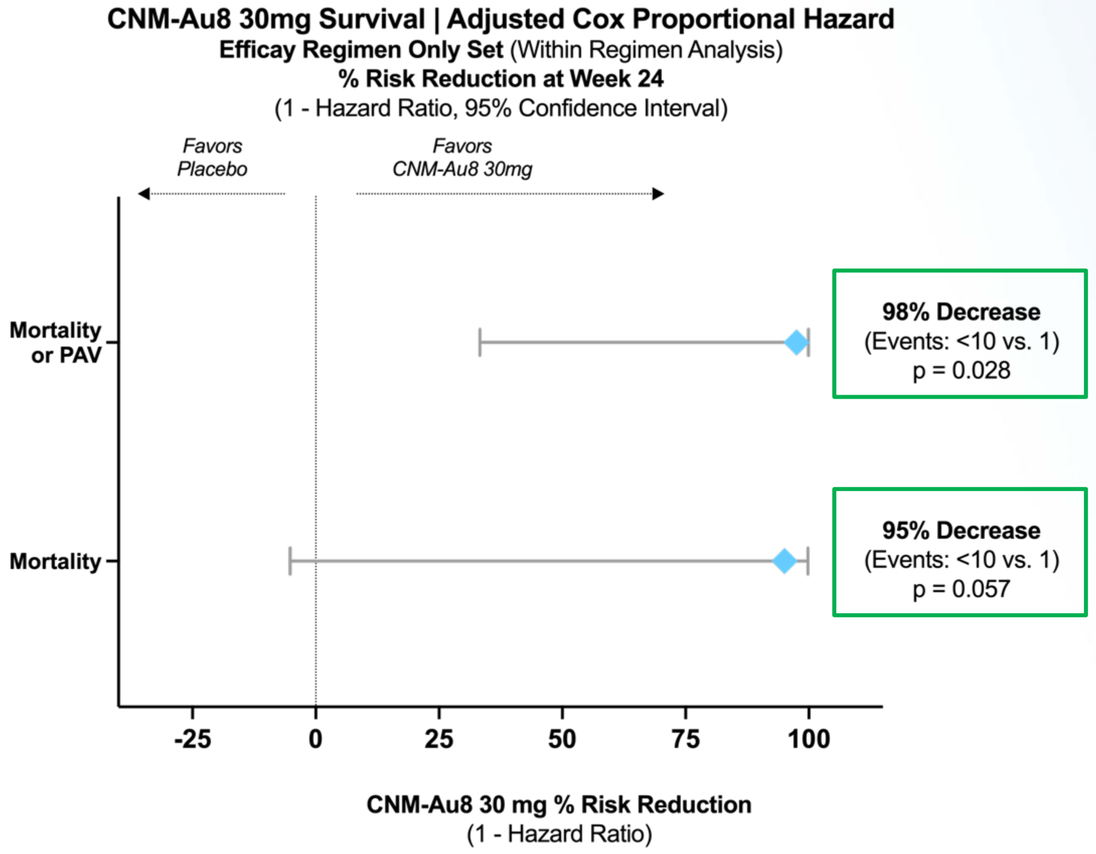
HEALEY ALS Platform Trial

*Shared Placebo Across Regimens



PAV = Permanently Assisted Ventilation; Prespecified covariate adjustments include: (i) time from symptom onset, (ii) pre-baseline ALSFRS-R slope, (iii) riluzole use, (iv) edaravone use, (v) age.

*CNM-Au8 Regimen Only



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* p-values are not adjusted for multiple comparisons; exploratory analyses by dose

Data on File, Clene Nanomedicine, Inc.

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CNM-Au8 Has Demonstrated ALS Survival Benefit at 30 mg Dose in Two Phase 2 Studies

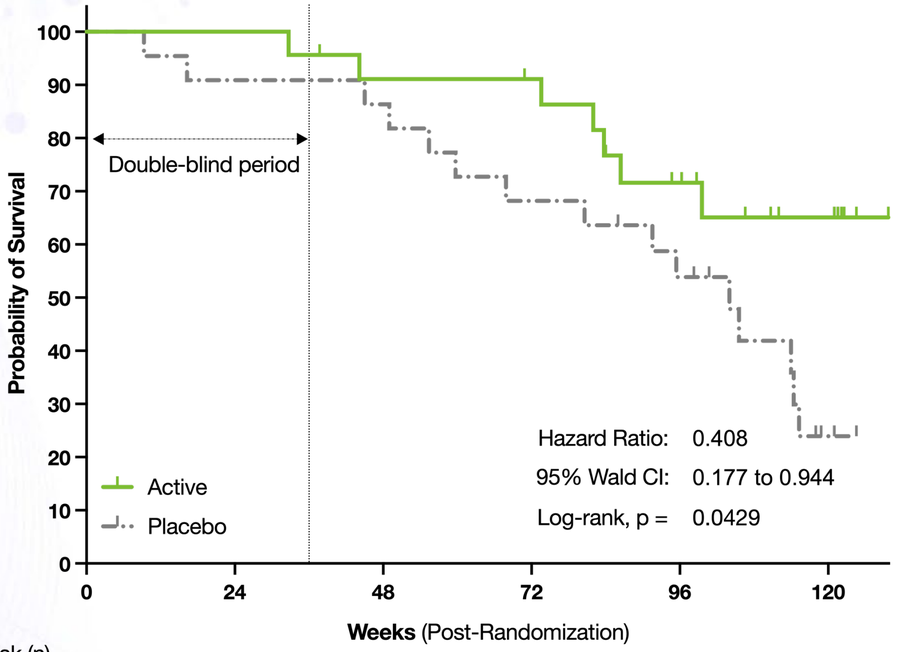
RESCUEALS

CNM-Au8: 60% decreased risk of death through 120 weeks

HEALEY ALS Platform Trial

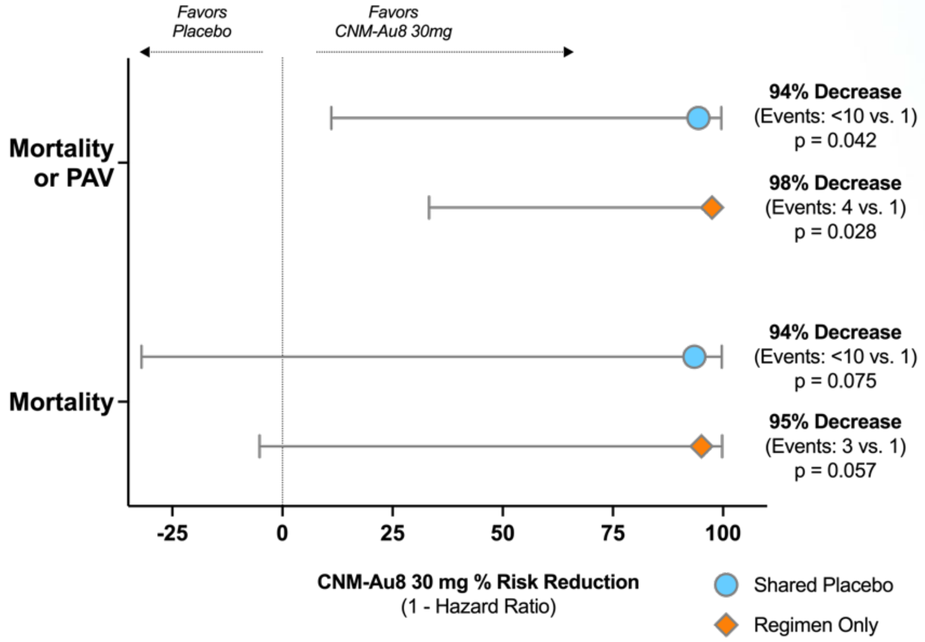
CNM-Au8: >90% risk reduction of death at 30mg at 24 weeks

Long-Term Survival (All-Cause Mortality): Originally Randomized Active vs. Placebo
Interim Analysis (12-July-2022), ITT Population, All Subjects from Randomization
(Long-term vital status including all study withdrawals)



At Risk (n)						
CMM-Au8:	23	23	20	19	13	7
Placebo:	22	20	19	15	11	3

CNM-Au8 30mg | Adjusted Cox Proportional Hazard Ratio
% Risk Reduction at Week 24
(1 - Adjusted Hazard Ratio, 95% Confidence Interval)



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Data on File, Clene Nanomedicine, Inc.

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Healey ALS Safety Summary

- Occurrence of TEAEs were balanced between CNM-Au8 and placebo
- No SAEs were assessed as related to CNM-Au8
- Higher incidence of SAEs at 60mg dose

Treatment Emergent Adverse Events (TEAEs)	Placebo (%)	CNM-Au8 30 mg (%)	CNM-Au8 60 mg(%)
Subjects with Any TEAE	90%	92%	93%
Subjects with Related TEAEs	39%	29%	43%
Subjects with SAE	9%	10%	16%
Subjects Withdrawn due to TEAE	7%	7%	7%

VISIONARY-MS STUDY Core Design Elements

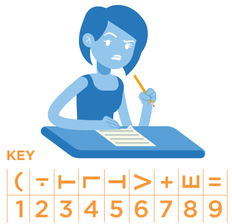
Phase 2 Study: 48-Week Placebo-Control Treatment Period 2:1 Randomization (Active [15mg, 30 mg]: Placebo)

- Enrolled stable relapsing remitting MS participants with chronic optic neuropathy on background DMTs
- n=73 of 150 planned – study ended prematurely due to pandemic-related enrollment challenges

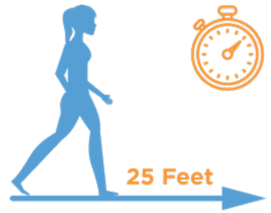
1° **Change in Low Contrast Letter Acuity (LCLA)**

2° **Change in modified MS Functional Composite (mMSFC)**

9HPT



SDMT



T25FWT

LCLA

https://clinicaltrials.gov/ct2/show/NCT03536559, Data on File, Clene Nanomedicine, Inc.

Baseline Demographics and Clinical Profile

VISIONARY-MS STUDY

- All participants were diagnosed with stable relapsing remitting MS with chronic optic neuropathy
- 92% treated with background DMTs (inc 53% monoclonal antibodies, 32% oral)

Baseline Value mean (sd)	**Age** (yrs)	**Sex** n, (%) Female	**Race** n, (%) White	**Weight** (kg)	**EDSS Score**	**Years from Dx**	**Months Since Relapse**
CNM-Au8 15 mg (n=24)	38.4 (10.2)	15 (63%)	23 (96%)	78.0 (17.1)	1.83 (1.3)	6.5 (5.0)	53 (57)
CNM-Au8 30 mg (n=25)	39.6 (7.6)	16 (64%)	24 (96%)	78.6 (17.3)	1.50 (1.1)	3.4 (3.3)	37 (35)
Placebo (n=24)	38.1 (8.3)	20 (83%)	22 (92%)	83.0 (23.3)	1.85 (1.4)	6.6 (3.7)	57 (38)
All Participants (n=73)	38.7 (8.6)	51 (70%)	69 (95%)	79.9 (19.3)	1.75 (1.5)	5.5 (4.3)	49 (45)

Data on File, Clene Nanomedicine, Inc.

Pandemic Significantly Impacted Study Conduct

VISIONARY-MS STUDY

- **Study was ended prematurely—due to COVID enrollment challenges** (as announced February 2022)
  - Enrolled 73 of 150 planned
  - Underpowered due to limited enrollment
  - Pre-specified statistical threshold set at p=0.10
  - COVID restrictions precluded direct Sponsor monitoring

- **Modified ITT (mITT) Analysis Population—2 censored observations**
  - Change in mobility assist device (cane to walker) for T25FW (n=1)
  - Invalid data from 1 of 11 sites (n=9) with LCLA testing execution errors, including multiple testing locations and varying lighting conditions

Data on File, Clene Nanomedicine, Inc.

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

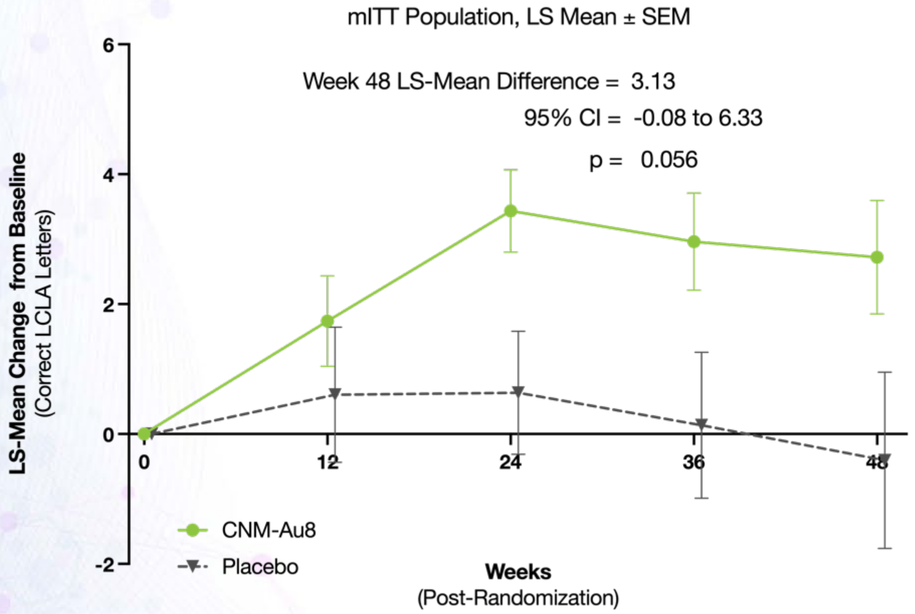
VISIONARY-MS STUDY

Phase 2 Study: 48-Week Placebo-Control Treatment Period 2:1 Randomization (Active [15mg, 30 mg]: Placebo)

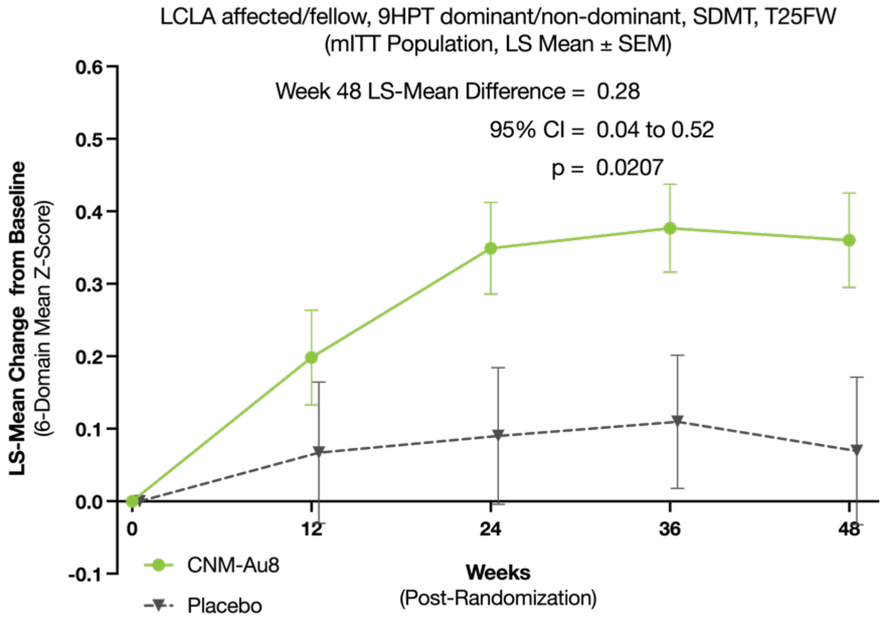
Enrolled stable relapsing remitting MS participants with chronic optic neuropathy on background DMTs

n=73 of 150 planned – study ended prematurely due to COVID-19 pandemic-related enrollment challenges

1° Change in Low Contrast Letter Acuity (LCLA)



2° Change in modified MS Functional Composite (mMSFC)



Data on File, Clene Nanomedicine, Inc.

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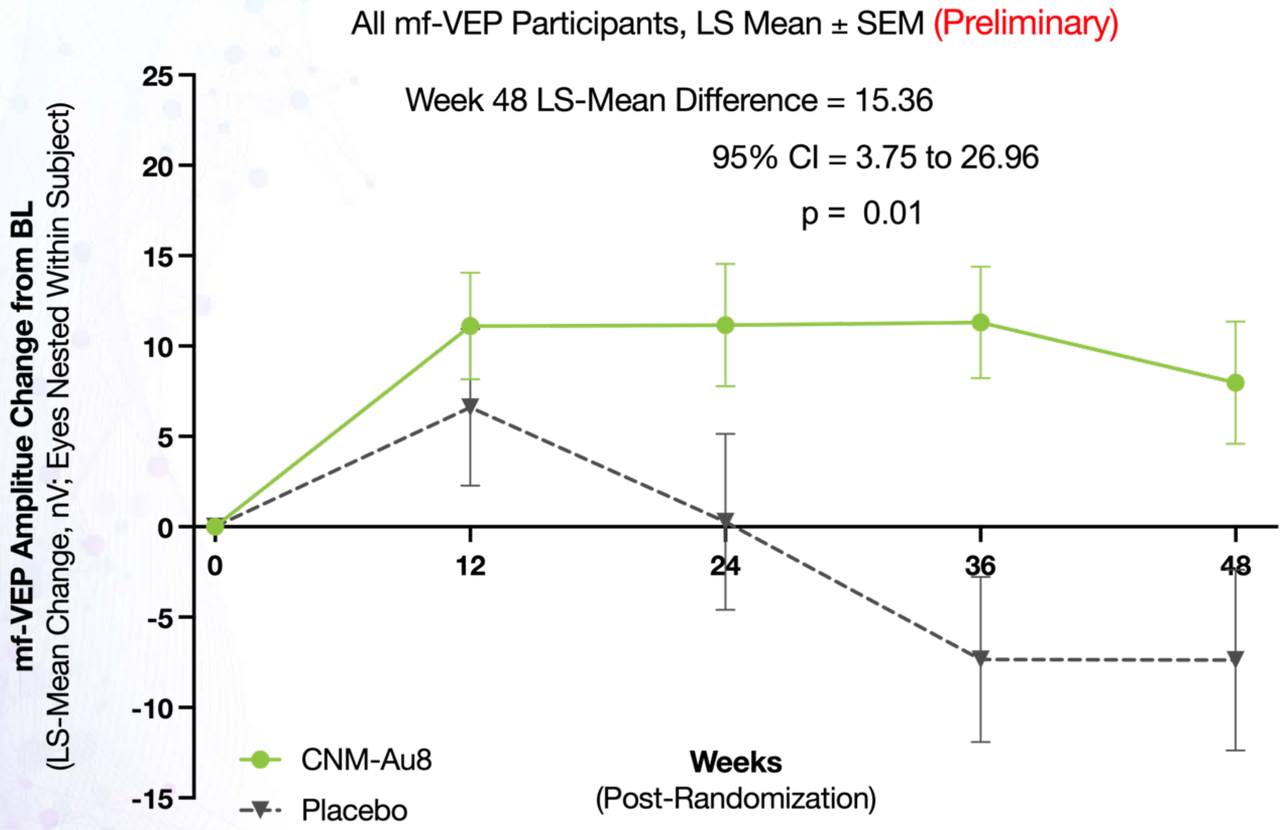
CNM-Au8 Improved Axonal Integrity and Retinal Structure

VISIONARY-MS STUDY

Increased Amplitude (Signal Strength)

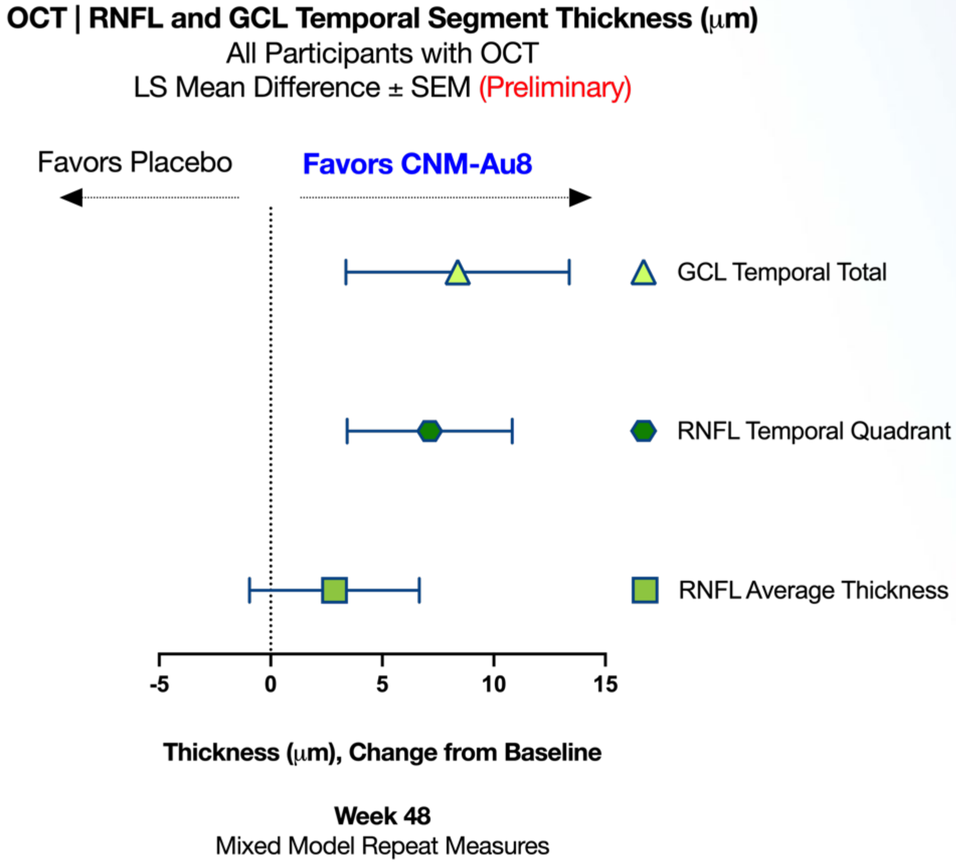
Exploratory Endpoint



mf-VEP amplitude

Improved Temporal Segment GCL & RNFL

Exploratory Endpoint



OCT retinal nerve fiber & ganglion cell layers

Data on File, Clene Nanomedicine, Inc.

CLene NANOMEDICINE

Visionary-MS Safety Summary

VISIONARY-MS STUDY

- **CNM-Au8 treatment was safe and well-tolerated**
  - Treatment emergent adverse events (TEAEs) were predominantly mild-to-moderate and transient
  - No dose limiting adverse events; no related serious adverse events

Treatment Emergent Adverse Events (TEAEs)	**CNM-Au8 15 mg** number (%)	**CNM-Au8 30 mg** number (%)	**Placebo** number (%)
Subjects with any TEAE	21 (88%)	25 (100%)	22 (92%)
Subjects with SAE	1 (4%)	2 (8%)	2 (8%)
Subjects with Related TEAEs	2 (8%)	5 (20%)	2 (8%)
Subjects Discontinued due to TEAE	--	1 (4%)	1 (4%)

Placebo SAEs: (1) Lentigo maligna melanoma, (2) pregnancy; CNM-Au8 15mg SAEs: (1) Pneumonia, bacteremia (staph aureus), endocarditis; CNM-Au8 30mg SAEs: (1) Ketamine infusion for pain and paracetamol overdose; (2) deep vein thrombosis (6-months post-discontinuation)

Data on File, Clene Nanomedicine, Inc.

Over 400 Years of Subject Exposure Without Identified Safety Signals Across ALS, MS, and PD

Clean Toxicology Findings

All Animal Toxicology Studies Resulted in No-Adverse Effect Level (NOAEL) Findings

- Multiple species up to 9-months treatment
- Up to maximum feasible dosing without any toxicology findings related to CNM-Au8

Well Tolerated Adverse Event (AE) Profile

Assessed as Predominantly Mild-to-Moderate Severity and Transient

- No SAEs related to CNM-Au8 considered severe, life-threatening, or resulting in death
- AEs predominantly mild-to-moderate

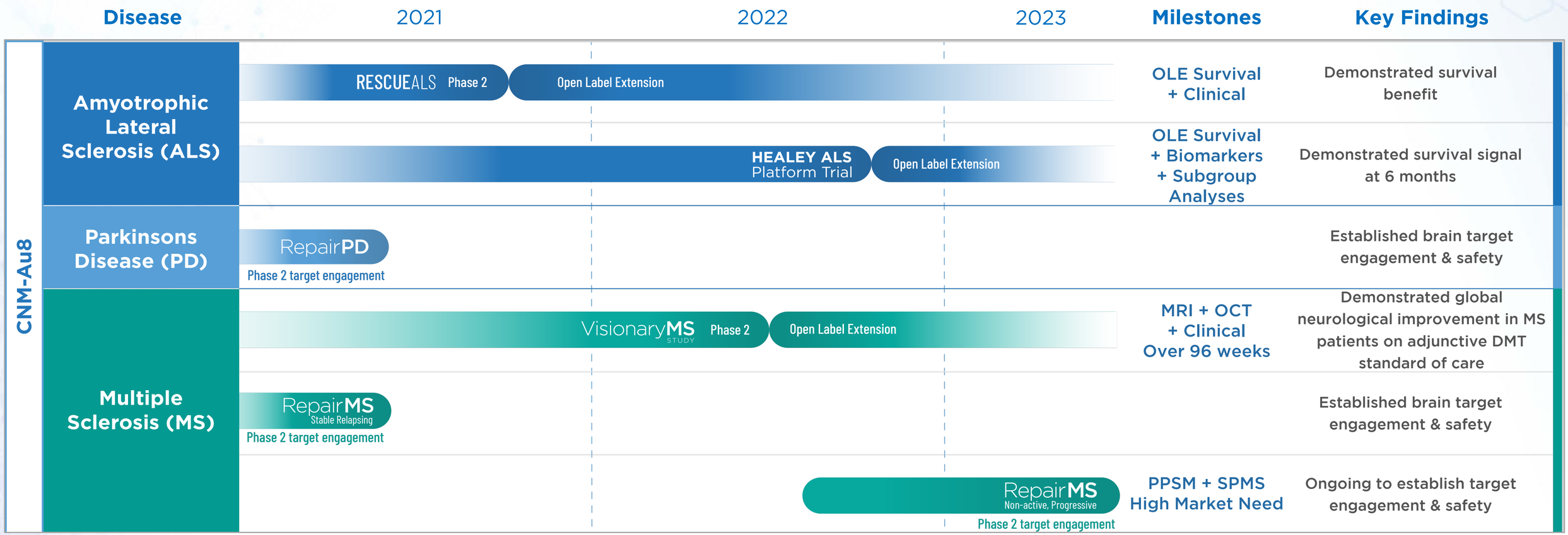
Patient Exposure Across ALS, MS & PD

Over 400 Years of Subject Exposure Without Identified Safety Signals

- Long-term dosing experience up to 150 weeks

Data on File, Clene Nanomedicine, Inc. MS: Multiple Sclerosis, ALS: Amyotrophic lateral sclerosis, and PD: Parkinson's Disease.

Growing Body of Evidence for Clene Nanotherapeutics



Data on File, Clene Nanomedicine, Inc.

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 remyelinate[1] & protect neurological function

RESCUEALS

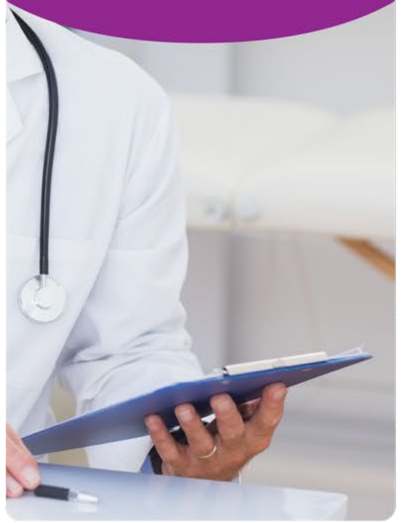
60% decreased risk of death in ALS through 120 weeks

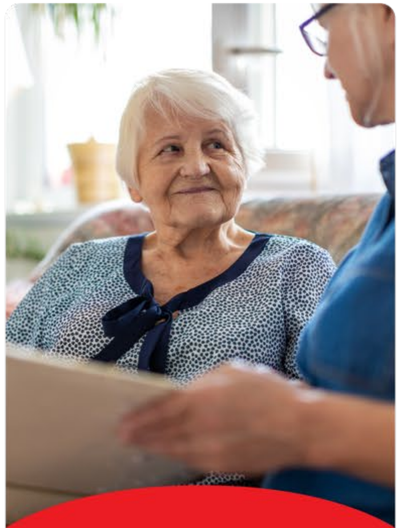
HEALEY ALS Platform Trial

>90% decreased risk of death with 30 mg in ALS

VISIONARY-MS STUDY

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





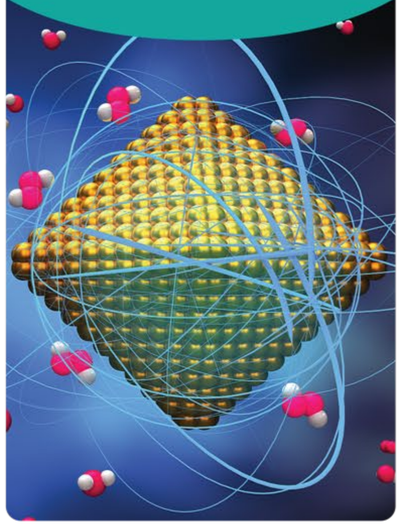
>400

patient years of CNM-Au8 clinical exposure

Strong IP:

150+

patents on nanotherapeutic platform



As of September 30, 2022, adjusted cash and investments on hand (unaudited):

$32.0M*

*Includes cash and investments as of September 30, 2022 of $16.2M + $10.8M November 2022 registered direct offering + $5.0M December 2022 loan with the Maryland Depart of Housing and Community Development

Data on File, Clene Nanomedicine, Inc. [1]Robinson et al. Sci Rep. 2020 Feb 11;10(1):1936.[2]https://clinicaltrials.gov/ct2/show/NCT04414345.

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

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