

**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549**

FORM 8-K

**CURRENT REPORT
Pursuant to Section 13 OR 15(d)
of The Securities Exchange Act of 1934**

Date of Report (Date of earliest event reported): August 29, 2023

CLENE INC.

(Exact name of registrant as specified in its charter)

Delaware

(State or Other Jurisdiction
of Incorporation)

001-39834

(Commission File Number)

85-2828339

(IRS Employer
Identification No.)

6550 South Millrock Drive, Suite G50

Salt Lake City, Utah

(Address of Principal Executive Offices)

84121

(Zip Code)

(801) 676-9695

(Registrant's telephone number, including area code)

N/A

(Former Name or Former Address, if Changed Since Last Report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, \$0.0001 par value	CLNN	The Nasdaq Capital Market
Warrants, to acquire one-half of one share of Common Stock for \$11.50 per share	CLNNW	The Nasdaq Capital Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act.

Item 7.01 Regulation FD Disclosure.

In connection with the press release discussed under Item 8.01 in this Current Report on Form 8-K, on August 29, 2023, Clene Inc. (the “Company”) released an updated corporate presentation (the “Corporate Presentation”) on its website, invest.clene.com. A copy of the Corporate Presentation is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference. The Company plans to use its website to disseminate future updates to the Corporate Presentation and may not file or furnish a Current Report on Form 8-K alerting investors if the Corporate Presentation is updated.

The information furnished in this Item 7.01, including Exhibit 99.1, shall not be deemed to be “filed” for purposes of Section 18 of the Securities Exchange Act of 1934 (the “Exchange Act”), as amended, or otherwise subject to the liabilities of that section, and shall not be deemed to be incorporated by reference into any filing made by the Company under the Exchange Act or the Securities Act of 1933, as amended, regardless of any general incorporation language in any such filings, except as shall be expressly set forth by specific reference in such a filing.

Item 8.01 Other Events.

On August 29, 2023, the Company issued a press release announcing updated data from the open-label extension of its Phase 2 RESCUE-ALS clinical trial in amyotrophic lateral sclerosis. A copy of the press release is filed as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

<u>Exhibit Number</u>	<u>Exhibit Description</u>
99.1	Corporate Presentation.
99.2	Press Release, dated August 29, 2023, announcing significantly improved survival benefit of 19.3 months and significantly delayed clinical worsening in RESCUE-ALS open-label extension two year follow-up.
104	Cover Page Interactive Data File (formatted as Inline XBRL).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, hereunto duly authorized.

CLENE INC.

Date: August 29, 2023

By: /s/ Robert Etherington
Robert Etherington
President and Chief Executive Officer



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,” “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. 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 drugs; 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 the COVID-19 pandemic 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.

Building the Clinical Case for Neuroprotection & Remyelination

RepairPD
RepairMS



RESCUEALS



HEALEY ALS
Platform Trial



VISIONARY-MS
STUDY



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

CNM-Au8 treatment resulted in statistically significant survival benefit of 75% decreased risk of death through 3.5 years

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 global neurological improvement in stable relapsing MS as an **adjunct** to immunomodulatory DMTs



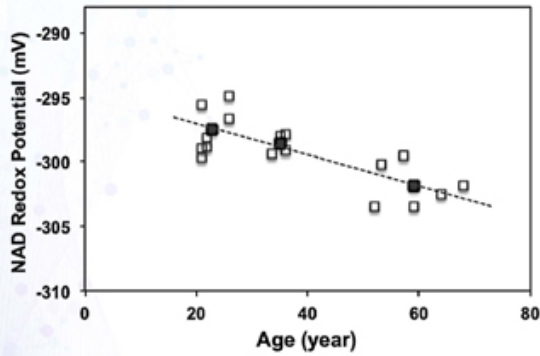
Growing Body of Clinical Evidence Across ALS and MS Supports CNM-Au8 Therapeutic Potential to Treat Neurodegenerative Diseases



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

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

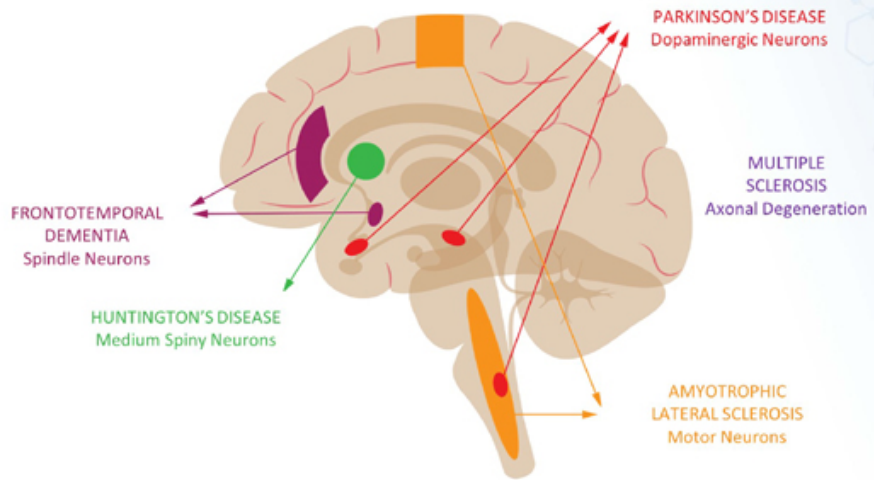
Brain Energy Potential
Declines With Normal Aging



~0.5% NAD⁺/NADH unit decline per decade
(~0.13 mV units per year by ³¹P-MRS Imaging)

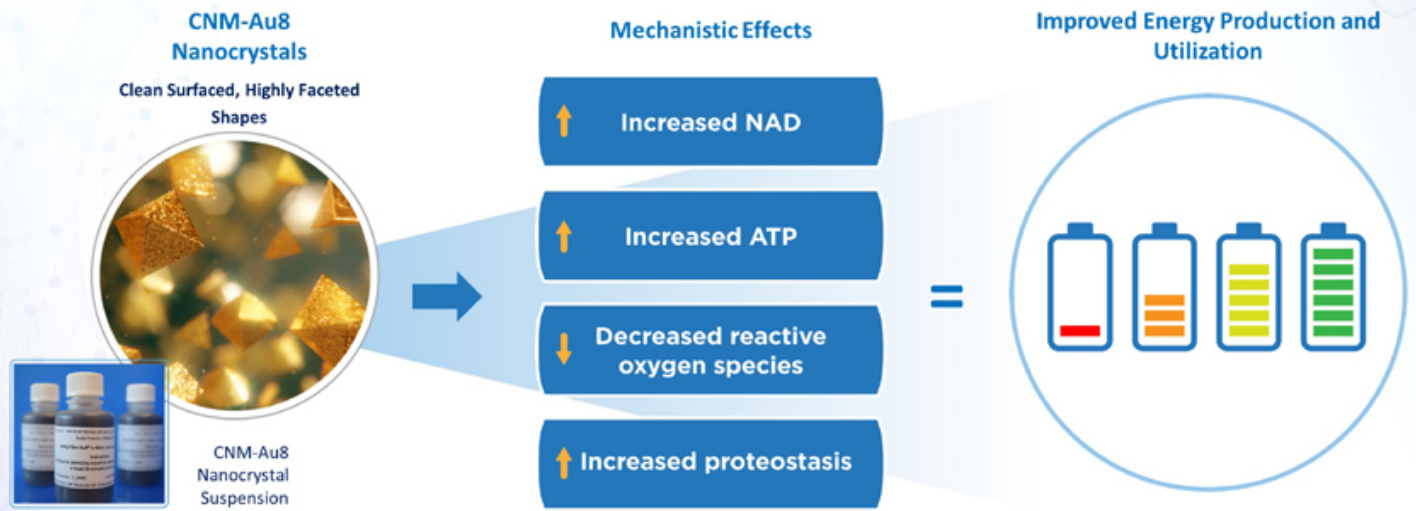
Closed squares = averaged data by age group: 21–26 yrs, 33–36 yrs, and 59–68 yrs old;
Open squares = individual subject values

Specific Neuronal Populations Are Vulnerable to Energetic Failure



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

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



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

Significant Global Opportunity for Treatment in Combination with Standard of Care

Motor Neuron Disease (ALS, Other Orphan Disorders)

ALS PATIENTS IN US & EU **~40K**  **\$1B** GLOBAL SALES BY 2029¹



Current drugs are largely ineffective, mostly generic.

2-5 YEARS LIFE EXPECTANCY  **100%** FATAL

Multiple Sclerosis (MS)

MS PATIENTS GLOBALLY **2.2M**  **\$23B** MARKET²



Existing treatments only target immunomodulation

EMERGING EVIDENCE THAT EARLY MS IS NEURODEGENERATIVE 

Parkinson's Disease (PD)

2ND MOST COMMON DISORDER  **\$6B** PROJECTED BY 2026³



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

30% OF DOPAMINERGIC NEURONS ARE LOST AT DIAGNOSIS⁴ 

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

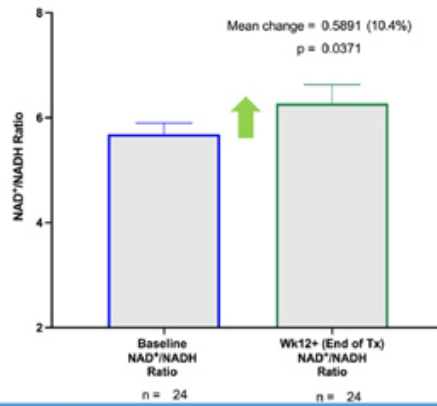
Two REPAIR Trials Demonstrated Target Brain Engagement and Improved Energy Metabolism in Early Parkinson's and Stable Relapsing MS

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)

Results demonstrated a potentially meaningful 10% improvement in NAD^+/NADH ratio, an essential molecule for energy production¹

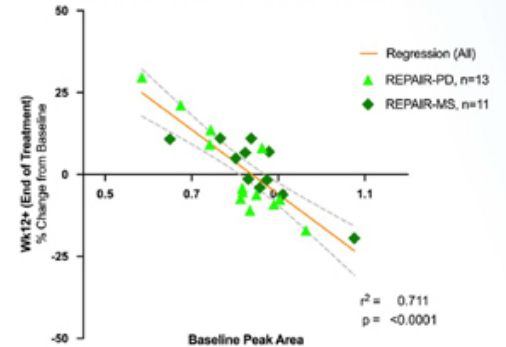
1° Endpoint (Integrated PD & MS)²

^{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 \pm 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



RepairPD
Early Parkinson's Disease

RepairMS
Stable Relapsing MS

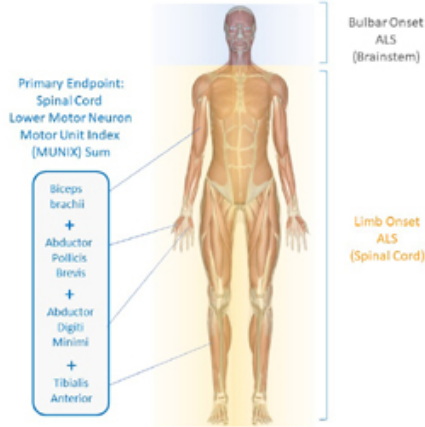
RepairMS
Non-Active Progressive MS
(Ongoing)

Study Objective:

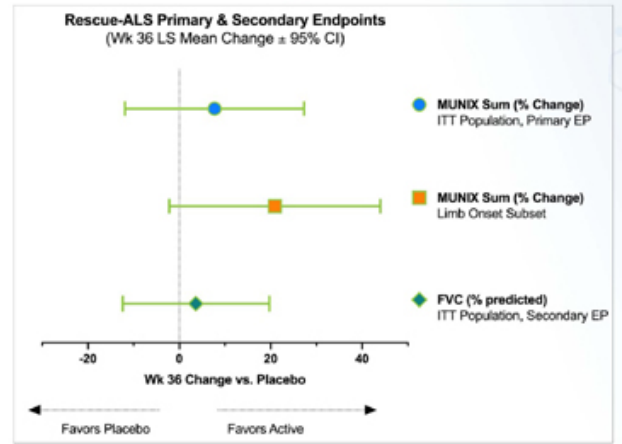
Detect preservation of motor neuron function in people with early ALS as measured by MUNIX

Study Design:

36-week blinded treatment with ongoing long-term open-label follow-up



1° & 2° Endpoints

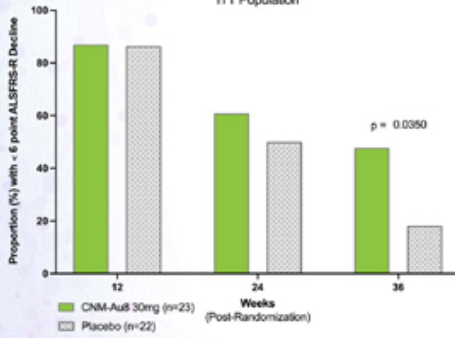


Results favor CNM-Au8 treatment

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

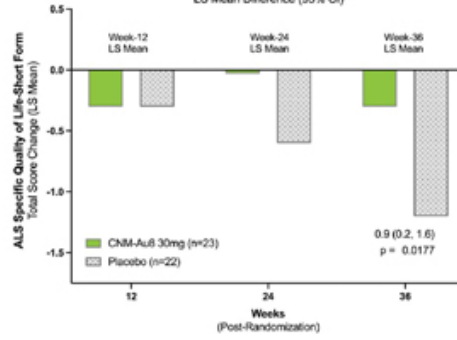
Proportion with <6 point decline

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



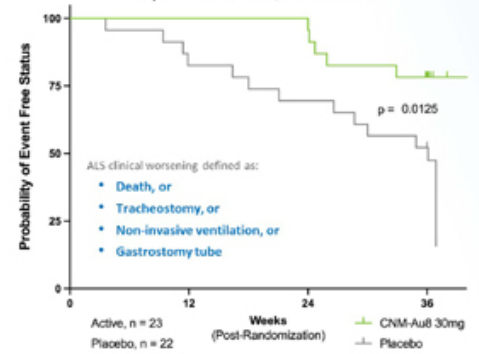
ALS Specific QOL

ALS Specific Quality of Life-Short Form Total Score
RESCUE-ALS Exploratory Endpoint
ITT Population, All Randomized
LS Mean Difference (95% CI)



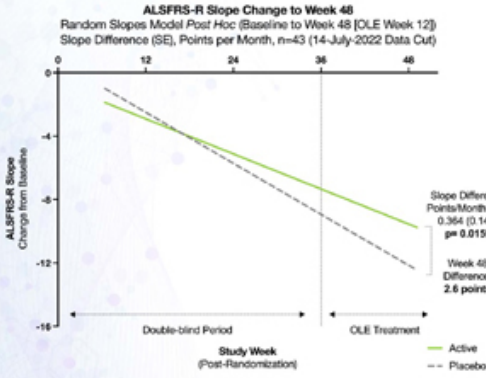
ALS Clinical Worsening

ALS Disease Progression
RESCUE-ALS Exploratory Endpoint
ITT Population, All Randomized
Kaplan-Meier Estimate, Percent Event Free

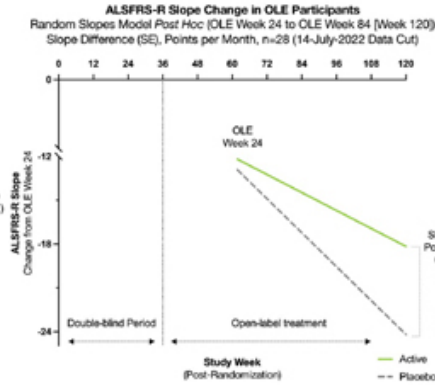


Early CNM-Au8 Treatment Impacts Long-Term Function Compared to Original Placebo

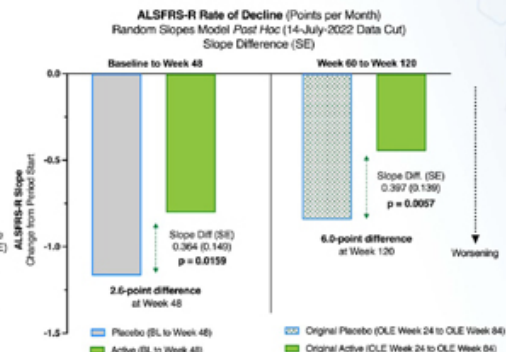
ALSFRS-R Slope
Baseline to Week 48



ALSFRS-R Slope
Week 60 [OLE Week 24] to Week 120

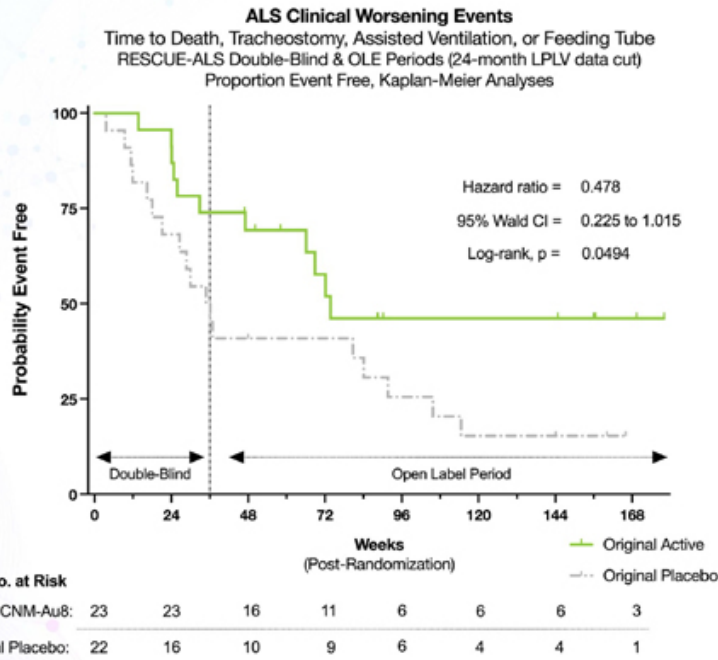


ALSFRS-R Slope
Summary



- CNM-Au8 preserved functional decline: ALSFRS-R of 2.6 points at 48 weeks compared to placebo
- Early CNM-Au8 treatment preserved long-term ALSFRS-R score by 6.0 points vs. OLE original placebo

OLE 12-month LPLV data cut of July 14, 2022.



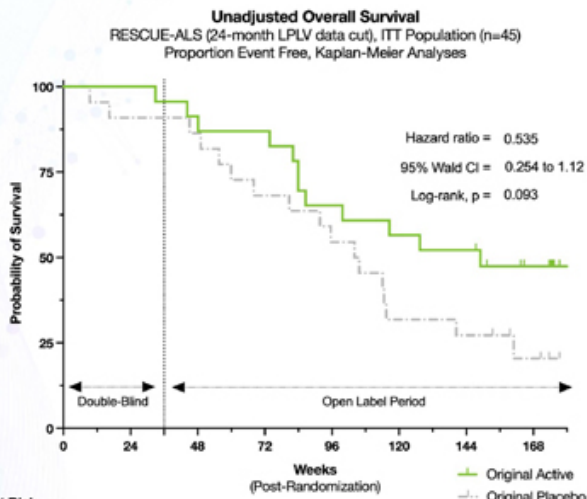
The risk of ALS clinical worsening was decreased 52% for CNM-Au8 compared to placebo in OLE up to 168 weeks

Clinical worsening events included:

- Death,
- Tracheostomy,
- Need for non-invasive ventilatory support, or
- Gastrostomy (feeding) tube placement.

Participants were right-censored at loss of follow-up with OLE withdrawal, as applicable

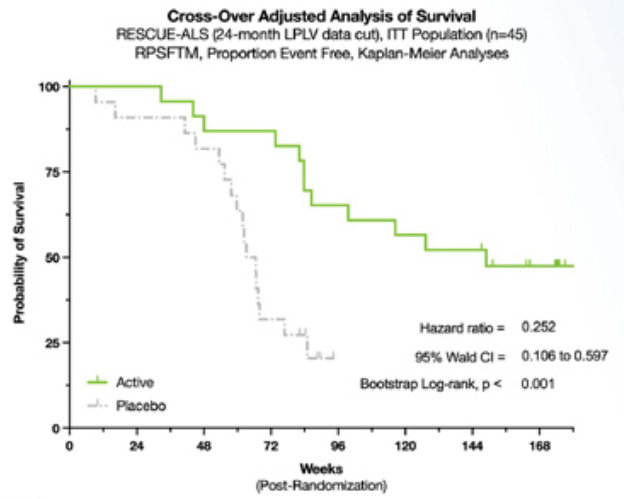
Unadjusted Survival Difference: 10.1 Month



No. at Risk

Original CNM-Au8:	23	23	21	21	16	14	13	8
Original Placebo:	22	21	20	16	13	8	7	7

Cross-Over Adjusted Survival Difference: 19.3 Month



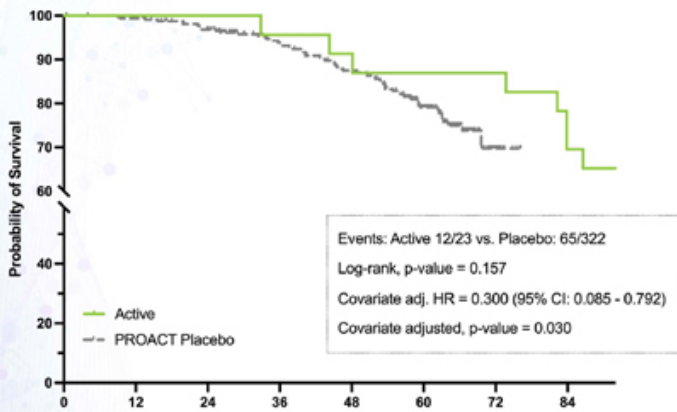
No. at Risk

Original CNM-Au8:	23	23	21	21	16	14	13	8
Original Placebo:	22	21	19	8	1	0	0	0



RESCUE-ALS Long-Term Survival

CNM-Au8 Observed Survival vs. PRO-ACT Matched Placebo Controls



CNM-Au8 treatment demonstrated a significant survival benefit:

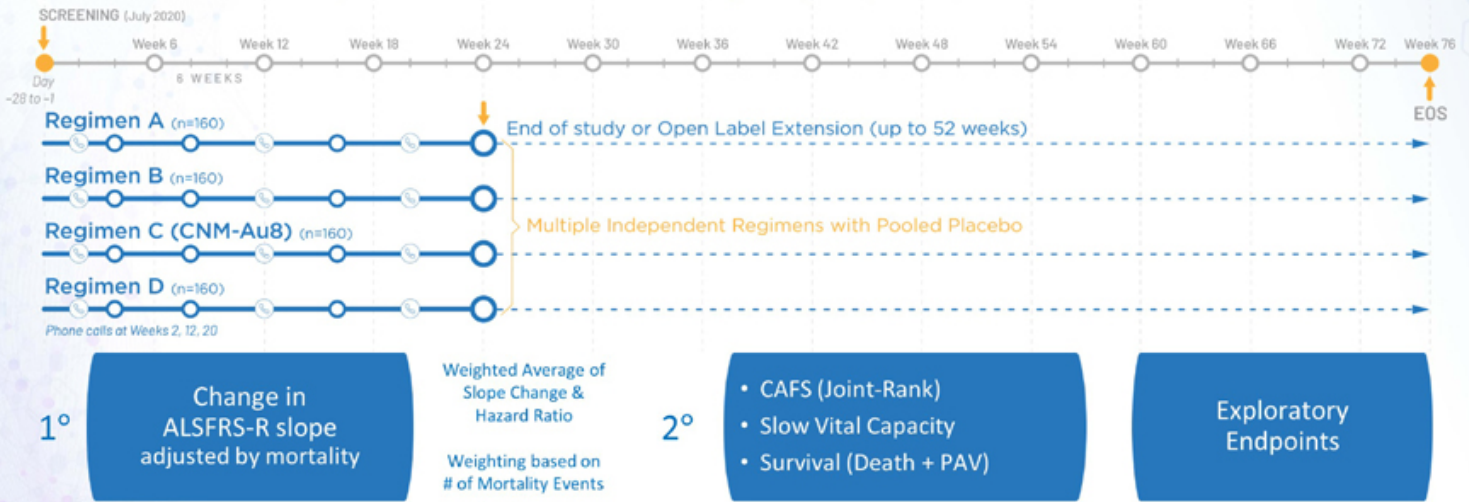
- Follow-up of active compared to matched placebo from PRO-ACT
- 70% decreased risk of death

PRO-ACT contains approximately 12,000 patient records from multiple completed clinical trials. Time to all-cause mortality amongst participants originally randomized to CNM-Au8 compared to propensity matched placebo controls derived from the PRO-ACT database (n=322). Covariates included: Onset Age, Sex, BMI, Pre-Treatment ALSFRS-R Slope (Delta-FS), ALSFRS-R Total Score, Vital Capacity (% predicted), and Diagnostic Delay (Covariates selected by minimizing AICc).

At Risk (n)	Weeks (Post-Randomization)							
	0	12	24	36	48	60	72	84
Active:	23	23	23	23	22	21	21	18
Placebo:	322	317	300	251	231	163	17	0

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

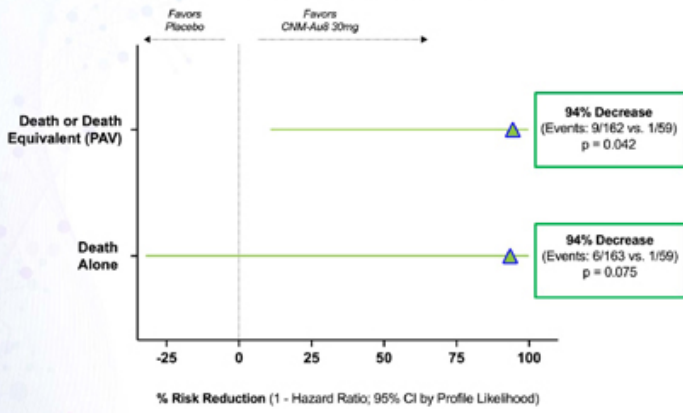
24-Week Treatment Period (3:1 randomization, 120 active [30mg, 60mg]: 40 placebo)



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

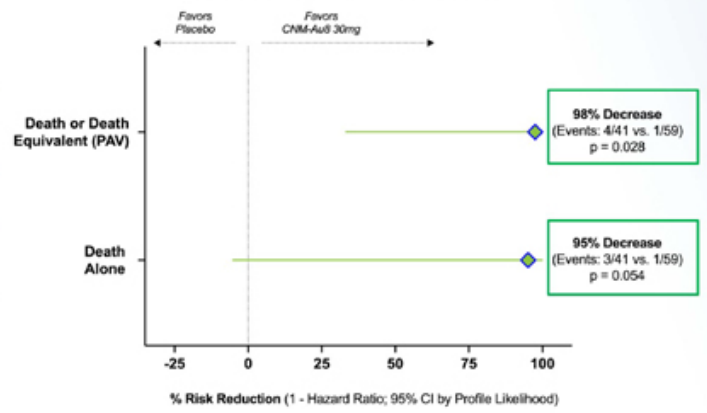
Shared Placebo Across Regimens

CNM-Au8 30mg Survival | Adjusted Cox Proportional Hazard
 Full Analysis Set (All Shared Placebo, Regimens A, B, C, D)
 % Hazard Reduction at Week 24
 (1 - Hazard Ratio, 95% Confidence Interval)



CNM-Au8 Regimen Only (Regimen C)





CNM-Au8 30mg Survival | Adjusted Cox Proportional Hazard
 Efficacy Regimen Only Set (Within Regimen Analysis)
 % Hazard Reduction at Week 24
 (1 - Hazard Ratio, 95% Confidence Interval)



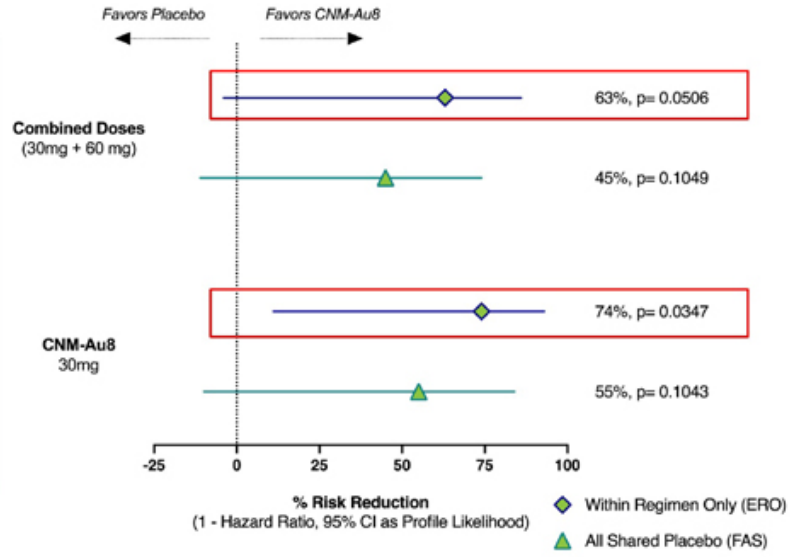
PAV = Permanently Assisted Ventilation; Prespecified covariate adjustments include: (i) time from symptom onset, (ii) pre-baseline ALSFRS-R slope, (iii) riluzole use, (iv) edaravone use, (v) age. Events (placebo vs. active), p-values are not adjusted for multiple comparisons; exploratory analyses by dose.

Delayed Time to ALS Clinical Worsening (Composite)

Clinical Worsening Composite Time to First Instance of:

-  Death
-  Tracheostomy
-  Permanent Assisted Ventilation (NIV >22 hours per day)
-  Feeding Tube Placement

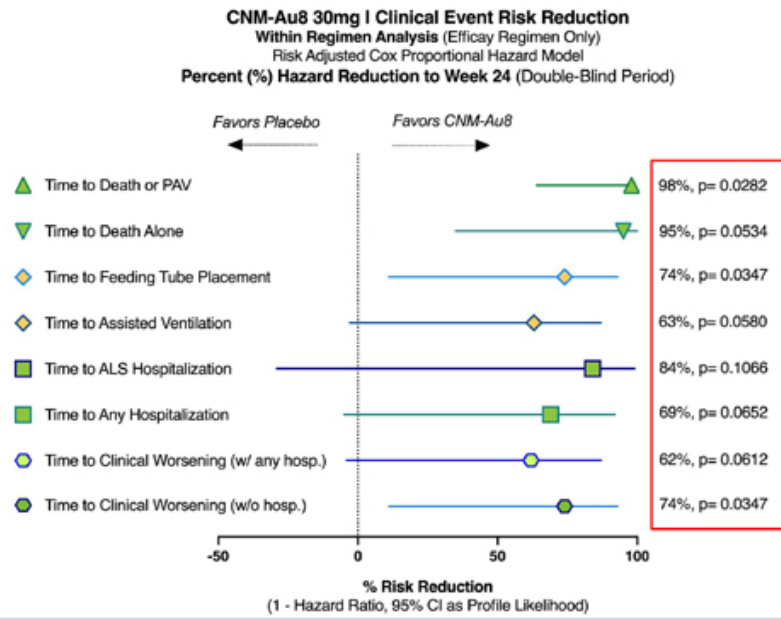
Reduction in Time to ALS Clinical Worsening (Composite) First Instance of Death, Tracheostomy, PAV, or Feeding Tube Risk Adjusted Cox Proportional Hazard Model (Primary Covariate Model) % Hazard Reduction to Week 24 (Double-Blind Period)



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.

For the within regimen (ERO) analysis, feeding tube placement was always the first initiating event for the composite.

CNM-Au8 30mg delayed time to clinical worsening at 6 months

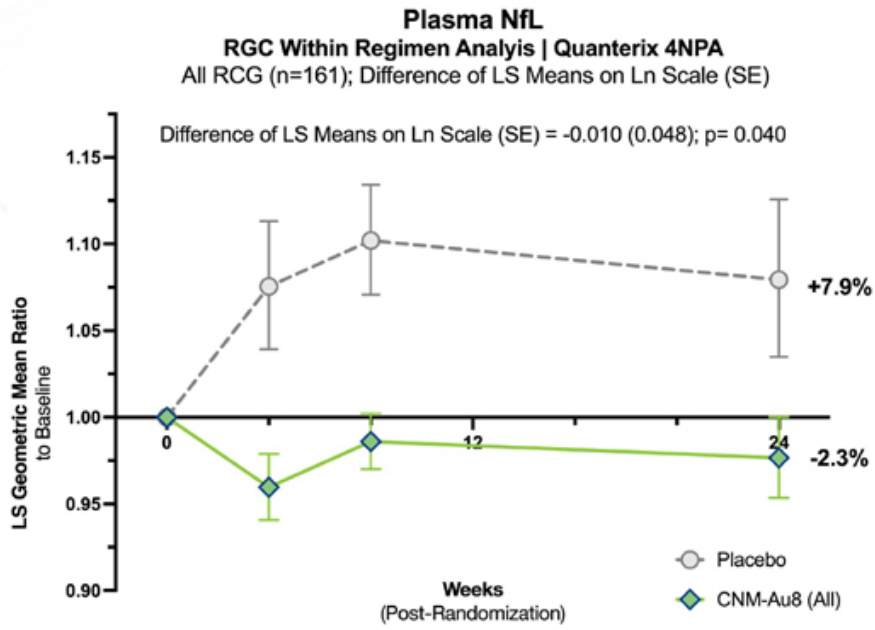


Supportive sensitivity analyses incorporating baseline neurofilament light chain (NfL) levels were similarly robust and resulted in increased effect sizes and smaller nominal p-values.

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.

Plasma NfL Difference | CNM-Au8 vs. Placebo

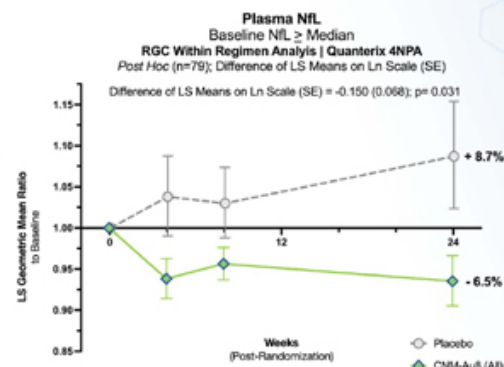
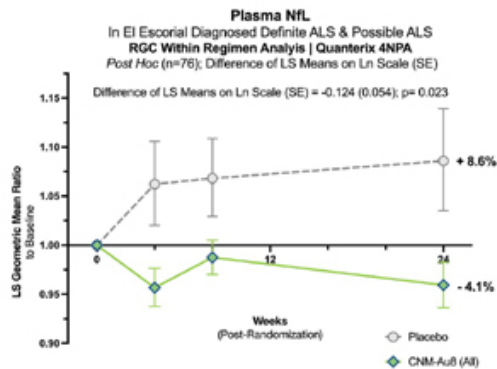
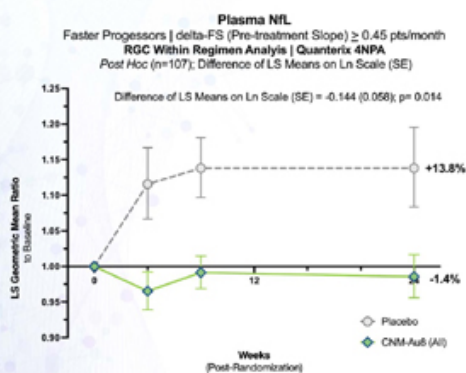
All RGC Participants



MMRM log NfL by group, contrast model; prespecified covariates included: (i) pre-treatment ALSFRS-R slope (delta-FS), (ii) months from symptom onset, (iii) use of riluzole, (iv) use of edaravone; (v) covariate by visit interaction, (vi) treatment by visit interaction

Consistent Plasma NfL Effect in Highest Risk Patients

Sensitivity *Post Hoc* | by Pretreatment delta-FS (ALSFRS-R Slope ≥ 0.45),
El Escorial Criteria, and Baseline NfL Levels



MMRM log NfL by group, contrast model; prespecified covariates included: (i) pre-treatment ALSFRS-R slope (delta-FS), (ii) months from symptom onset, (iii) use of riluzole, (iv) use of edaravone; (v) covariate by visit interaction, (vi) treatment by visit interaction

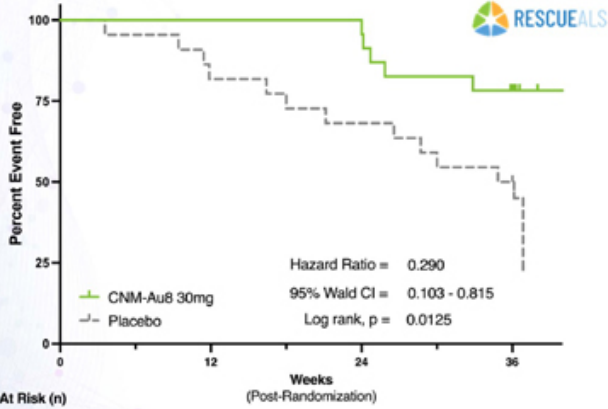
CNM-Au8 | ALS Clinical Worsening Summary

Evidence for Decreased Clinical Worsening Events Across Two Phase 2 Studies

Phase 2 RESCUE-ALS CNM-Au8 30mg
Decreased Time to Clinical Worsening

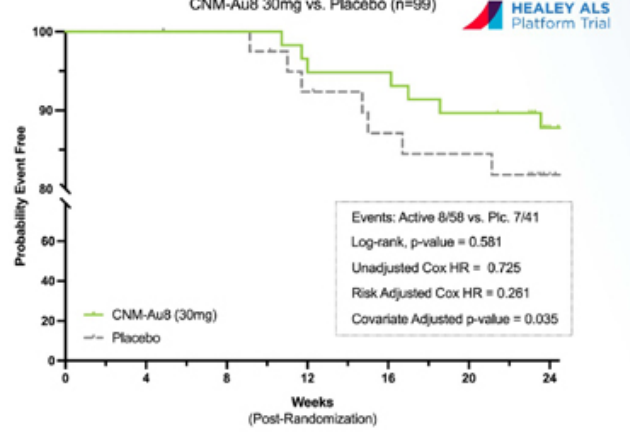
Time to ALS Clinical Worsening

First Occurrence of Death, Tracheostomy, Assisted Ventilation, or Feeding Tube
ITT Population (All Randomized), Kaplan-Meier Estimate



Phase 2 HEALEY ALS Platform CNM-Au8 30mg
Decreased Time to Clinical Worsening

Time to Clinical Worsening | CNM-Au8 30mg
First Occurrence of Death, PAV, Tracheostomy or Feeding Tube
HEALEY ALS Platform Trial | Kaplan-Meier Estimate
Regimen C Population, Efficacy Regimen Only
CNM-Au8 30mg vs. Placebo (n=99)



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

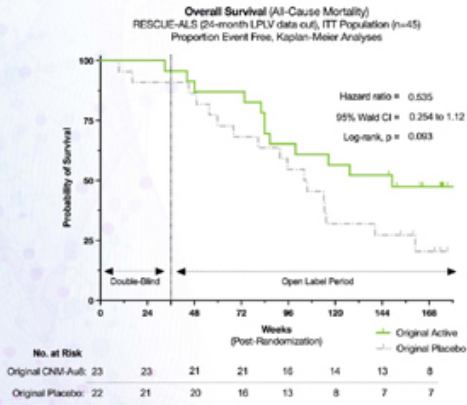


Up to 75% decreased risk of death through 168 weeks

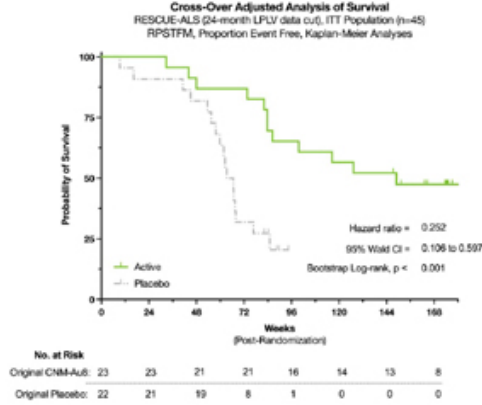


>90% risk reduction of death at 30mg at 24 weeks

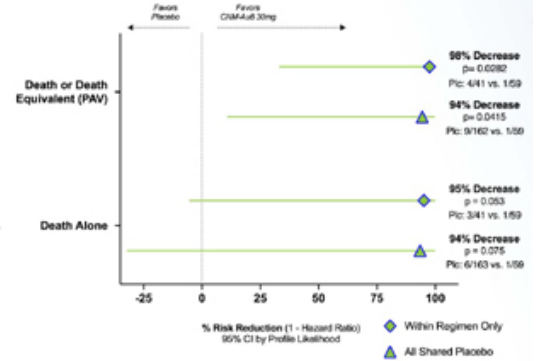
Unadjusted Survival



Cross-Over Adjusted Survival



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



Promising Evidence from Two Phase 2 Trials and Long-Term Data

CNM-Au8 Demonstrated Survival, Delayed Clinical Worsening, and Preserved Function



	RESCUE-ALS	RESCUE-OLE	HEALEY ALS Platform	HEALEY OLE	EAP
ALS Patient Demographics	Early-to-Mid-Stage	Early-to-Mid-Stage	Mid-to-Late-Stage	Mid-to-Late-Stage	Real-World Experience
Duration	36-weeks	Up to 173 weeks	24-weeks	Through April '23	Up to 3.8 years
Survival	--	✓	✓	Pending data 2H 2023	✓
Delayed Time to Clinical Worsening	✓	✓	✓		Not routinely collected
Preserved Function (ALSFRS-R)	--	✓	--		
Progression Biomarkers	p75 trend	UCHL1 ↓*	✓		

Consistent Evidence for CNM-Au8 30mg Dose Across Broad ALS Patient Population

ALS Summary | CNM-Au8 Has Demonstrated Survival Benefit and Delayed Time to Clinical Worsening and Functional Decline



Significant Opportunity

- ALS remains a devastating and fatal disease within ~3 to 5 years of diagnosis—a significant unmet need



CNM-Au8[®] Clinical Results



- Demonstrated significant ALS survival benefit at 30 mg dose in two phase 2 studies
- Preserved ALSFRS-R functional decline with long-term follow-up in RESCUE-ALS OLE:
 - 2.6 points slower decline at 48 weeks vs. placebo (p=0.159)
 - 6.0 points slower decline vs to OLE original placebo (p=0.0057)
- 74% lower risk of time to clinical worsening at 6 months in the Healey ALS Platform Trial (p = 0.035)



Global Phase 3 ALS Trial

- RESCUE-ALS and Healey ALS Platform Trial results support advancement to Phase 3 RESTORE-ALS with the 30 mg dose

HEALEY ALS Platform Safety Summary

- Occurrence of TEAEs were balanced between CNM-Au8 and placebo
- No SAEs were assessed as related to CNM-Au8

Treatment Emergent Adverse Events (TEAEs)	All Shared Placebo (%)	Regimen Placebo (%)	CNM-Au8 30 mg (%)	CNM-Au8 60 mg (%)
Participants with Any TEAE	90%	93%	92%	93%
Participants with Related TEAEs	39%	34%	29%	43%
Participants with SAE	9%	17%	10%	16%
Participants with Related SAEs	1%	2%	0%	0%
Participants Withdrawn due to TEAE	7%	7%	7%	7%

All Shared Placebo (n=164 placebo from Regimens A, B, C, D); Regimen placebo (n=41) includes only concurrent randomization within Regimen C (CNM-Au8)

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 (~50%) study ended prematurely due to COVID-19 pandemic enrollment challenges
- Pre-specified statistical threshold set at p=0.10
- CNM-Au8 Open Label Extension (OLE) for original active and placebo continues for up-to-96 weeks

1°

Change in Low Contrast Letter Acuity (LCLA)



2°

Change in modified MS Functional Composite (mMSFC)



9HPT



SDMT



T25FWT



LCLA

Baseline Demographics and Study Analysis

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

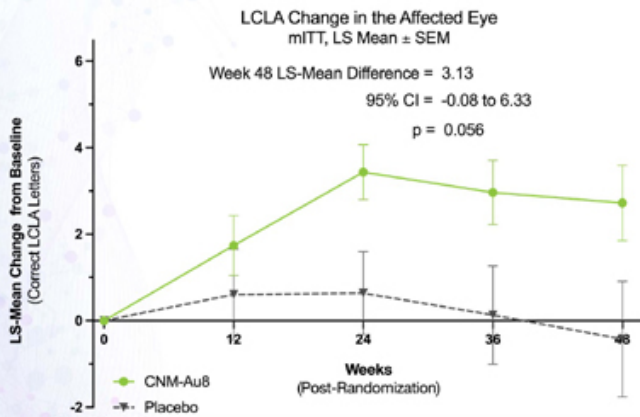
Baseline Value mean (sd)	Age (yrs)	Sex n, (%) Female	Race n, (%) White	Weight (kg)	EDSS Score	Years from Dx	Months Since Relapse
CNM-Au8 15 mg (n=24)	38.4 (10.2)	15 (63%)	23 (96%)	78.0 (17.1)	1.83 (1.3)	6.5 (5.0)	53 (57)
CNM-Au8 30 mg (n=25)	39.6 (7.6)	16 (64%)	24 (96%)	78.6 (17.3)	1.50 (1.1)	3.4 (3.3)	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)

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

Significantly Improved Vision



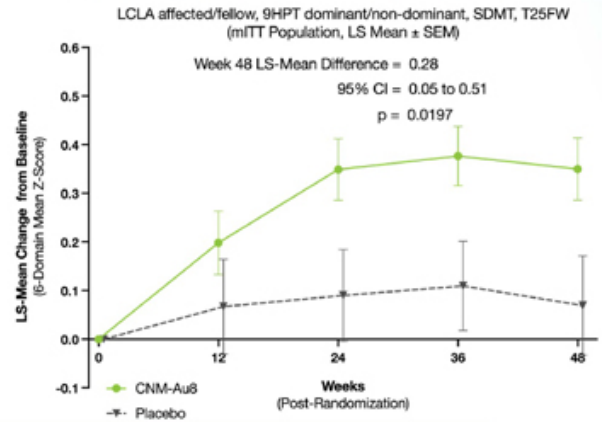
Change in Low Contrast Letter Acuity (LCLA)



Global Neurological Improvement



Change in modified MS Functional Composite (mMSFC)

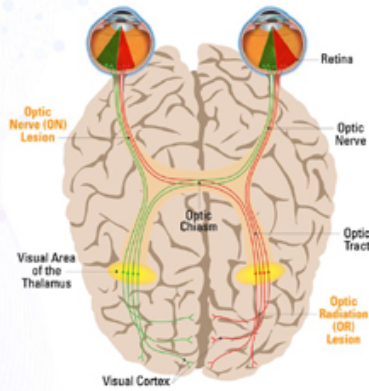


Global neurological clinical improvement was driven by cognition, manual dexterity, and low contrast letter acuity

VISIONARY-MS Measures of Axonal Integrity

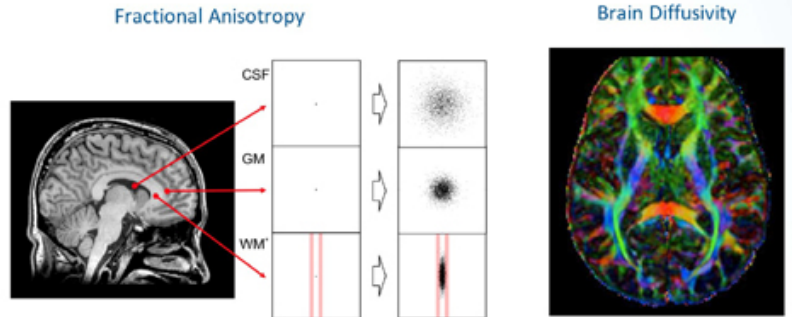
Visual Evoked Potentials (VEP)

Multi-focal Amplitude and Latency Changes



Advanced MRI Techniques

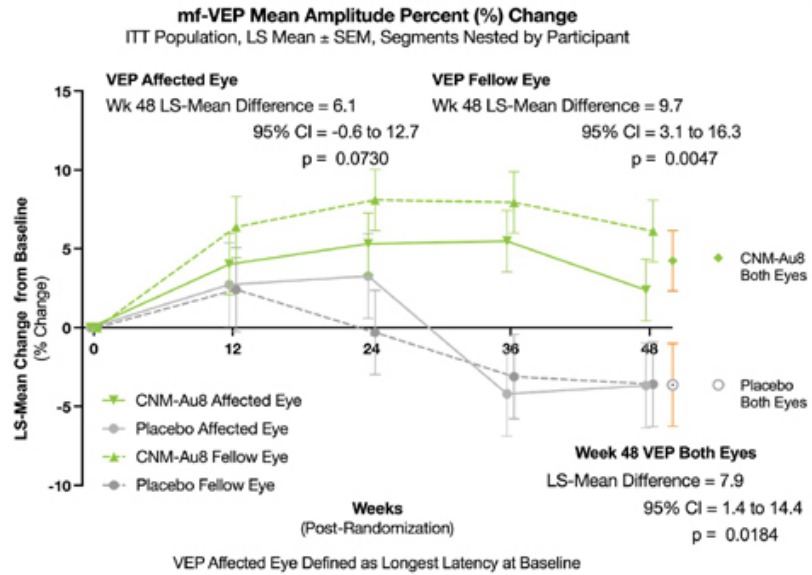
Diffusion Tensor Imaging (DTI) changes



What Happens in the Visual System Happens Throughout the MS Brain

CNM-Au8 Improved Information Signal in the Visual Pathway

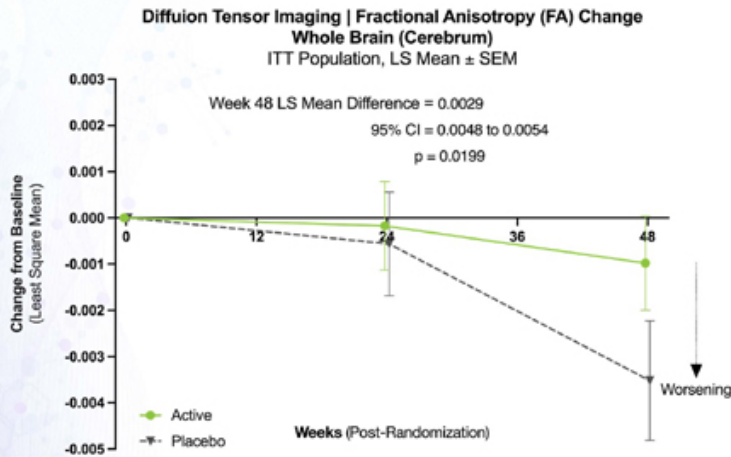
Increased Amplitude
(Signal Strength)
From the Eye to the Brain's
Visual Cortex



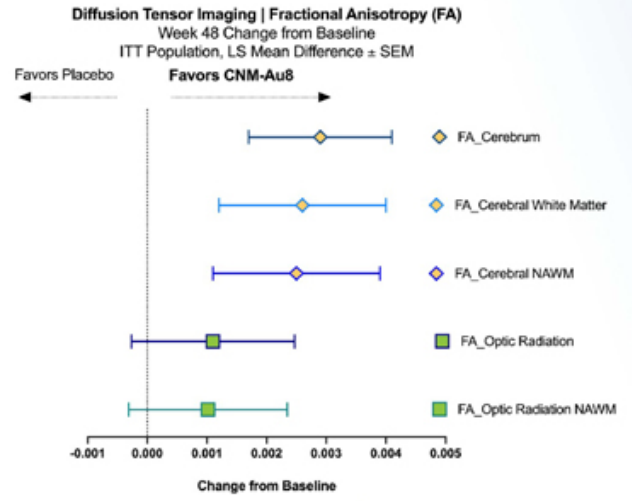
Increased VEP amplitude is associated with improved axonal integrity; provides evidence that previously impaired neurons can contribute to information signaling after treatment

CNM-Au8 Preserved White Matter Integrity Throughout the Brain

Preserved Whole Brain White Matter Integrity



Consistent Effect Across All Brain Regions



Preservation of white matter integrity associated with decreased cognitive and functional decline in MS patients

Summary | Consistent Paraclinical Evidence of Neuroprotective Effects Favoring CNM-Au8 Treatment

Paraclinical Endpoint	Paraclinical Measure LS Mean Change – Week 48	Significance	Key Findings	Implications
Diffusion Tensor Imaging (DTI) measure of Fractional Anisotropy (FA)	FA within the whole brain (Cerebrum)	$p = 0.0199$	Improvements of axonal integrity and neuronal structure across the brain	Neuroprotection and preservation of white matter integrity associated with decreased cognitive and functional decline
	FA within total Cerebral White Matter	$p = 0.0805$		
	FA within total Cerebral Normal Appearing White Matter	$p = 0.0823$		
Multi-focal Visual Evoked Potential (mf-VEP)	Amplitude percent change across both eyes	$p = 0.0184$	Improved information signal along the visual pathway	Neuronal preservation and improved information signal from previously impaired neurons
	Amplitude percent change in the most affected eye at baseline	$p = 0.0730$		
	Amplitude percent change in the least affected eye at baseline	$p = 0.0047$		

Critical unmet need in MS for treatments that protect neuronal function independently of immunomodulation to decrease disease progression

CNM-Au8 treatment was safe and well-tolerated

- Treatment emergent adverse events (TEAEs) were transient and predominantly mild-to-moderate
- No dose limiting adverse events; no related serious adverse events

Treatment Emergent Adverse Events (TEAEs)	Placebo number (%)	CNM-Au8 15 mg number (%)	CNM-Au8 30 mg number (%)
Subjects with any TEAE	22 (92%)	21 (88%)	25 (100%)
Subjects with SAE	2 (8%)	1 (4%)	2 (8%)
Subjects with Related TEAEs	2 (8%)	2 (8%)	5 (20%)
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; **30mg SAEs:** (1) Ketamine infusion for pain and paracetamol overdose; (2) deep vein thrombosis (6-months post-discontinuation)

CNM-Au8



CNM-Au8 is Consistently Favored for Treatment of MS Progression Independent of an Immunomodulatory Effect



Significant Opportunity

- MS patients continue to progress with increasing cognitive and functional deficits accumulating even while receiving disease-modifying therapies—a significant unmet medical need



CNM-Au8® Clinical Results

- Significant improvements in clinical outcomes, brain structure, and visual system on top of immunomodulatory standard of care therapy
- Paraclinical MRI and VEP improvements support clinical benefits, consistently favoring CNM-Au8



Global Phase 3 MS Trial

- Phase 2 VISIONARY-MS safety and efficacy results support advancement to Phase 3

Over 475 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

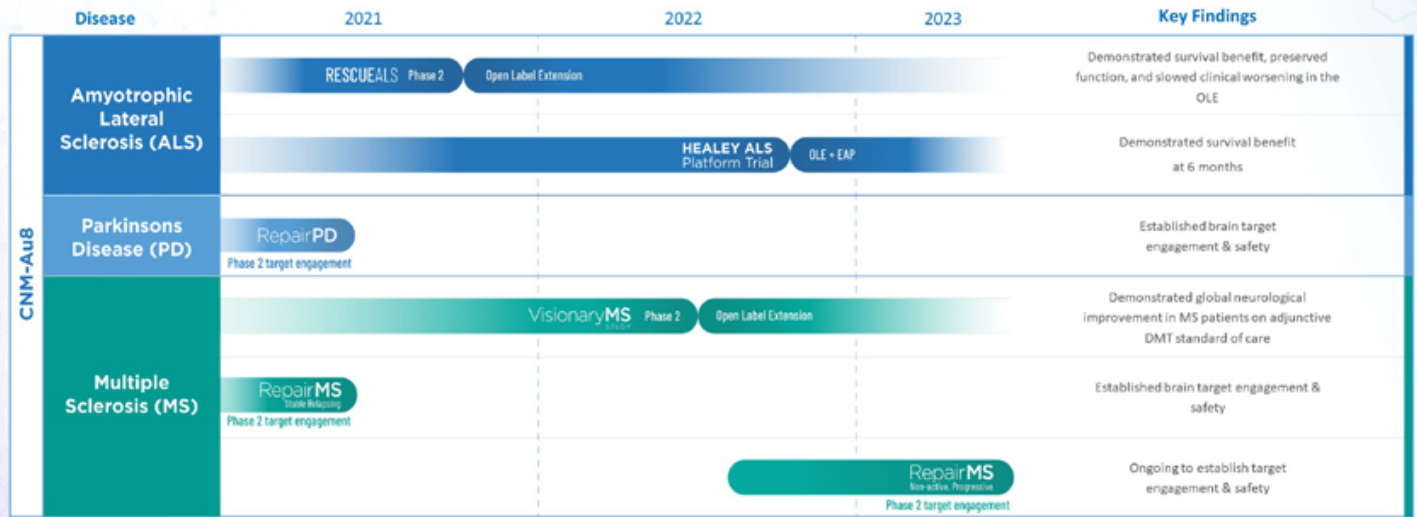
- No SAEs related to CNM-Au8 considered severe, life-threatening, or resulting in death
- AEs transient and predominantly mild-to-moderate severity

Patient Exposure Across ALS, MS & PD

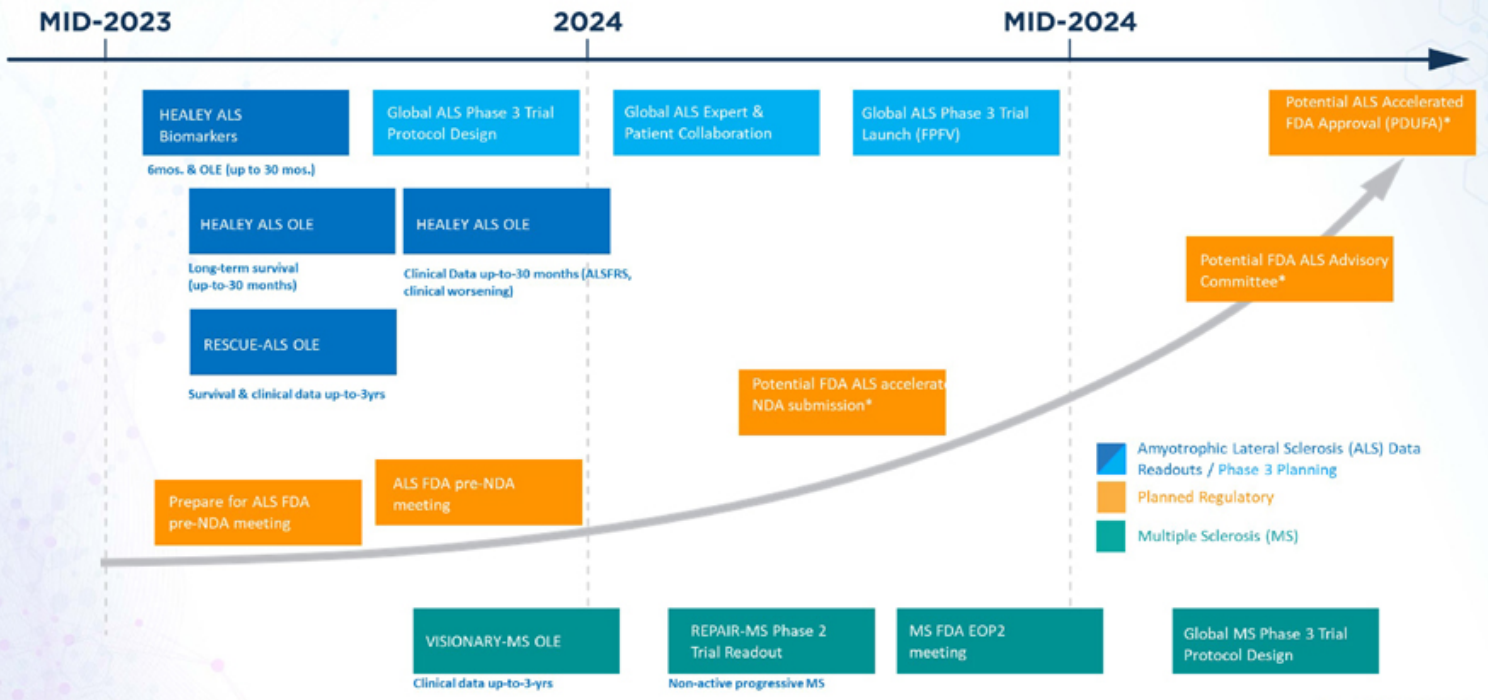
Over 475 Years of Subject Exposure Without Identified Safety Signals

- Long-term dosing experience up to 175 weeks

Growing Body of Evidence for CNM-Au8[®]



Clene | CNM-Au8 Path to Regulatory Approval



Evidence Supports CNM-Au8 Therapeutic Potential to Treat Neurodegenerative Diseases

<p>CNM-Au8[®] a gold nanocrystal suspension, in development as the first cellular energetic catalyst to remyelinate¹ & protect neurological function</p> 	 <p>RESCUEALS</p> <p>75% decreased risk of death in ALS through 168 weeks</p> <p>HEALEY ALS Platform Trial</p> <p>>90% decreased risk of death with 30 mg in ALS</p>	<p>VISIONARY-MS</p> <p>Demonstrated global neurological improvement in MS patients on adjunctive DMT standard of care</p> 	 <p>>475 patient years of CNM-Au8 clinical exposure</p>	<p>Strong IP: 150+ patents on nanotherapeutic platform</p> 	 <p>As of June 30, 2023, cash and equivalents on hand (unaudited):</p> <p>\$49.2M</p>
---	--	--	---	---	---



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

© 2023 Clene Inc.

Version: 29-August-2023

**CLENE REPORTS SIGNIFICANTLY IMPROVED SURVIVAL BENEFIT OF
19.3 MONTHS AND SIGNIFICANTLY DELAYED CLINICAL WORSENING
IN RESCUE-ALS OPEN-LABEL EXTENSION TWO YEAR FOLLOW-UP**

- 19.3 month significant survival difference for CNM-Au8® treated participants versus placebo
- 52% significant decreased risk of ALS clinical worsening events
- Over 475 years of CNM-Au8 treatment exposure without any identified safety signals

SALT LAKE CITY, August 29, 2023 (GLOBE NEWSWIRE) -- Clene Inc. (NASDAQ: CLNN) through its wholly owned subsidiary Clene Nanomedicine, Inc., today announced the 24-month long-term data cut from the Phase 2 RESCUE-ALS ongoing open-label extension (OLE) as of July 2023, which showed a significant median survival benefit of 19.3 months using the rank-preserving structural failure time model (RPSFTM) and a significant 52% decreased risk of ALS clinical worsening events with CNM-Au8® treatment.

RESCUE-ALS was a 36-week double-blind placebo-controlled Phase 2 trial that originally randomized 45 people living with ALS, who were an average of 16 months from symptom onset. Thirty-six participants entered the long-term open-label extension, which included 20 participants originally treated with CNM-Au8 during the blinded period and 16 placebo-treated participants who were subsequently switched to CNM-Au8 during the start of the OLE. Survival status was available for all 45 participants.

Survival Improvement:

- Cross-over adjusted median survival (RPSFTM, all study participants, *post hoc*):
 - 19.3 month median survival benefit (CNM-Au8 median survival of 34.2 months, placebo-adjusted median survival of 14.9 months).
 - 75% decreased risk of long-term all-cause mortality in participants originally randomized to treatment with CNM-Au8 compared to those originally randomized to placebo after adjusting for benefit received by placebo after switching to CNM-Au8 (HR= 0.252, 95% CI: 0.106 to 0.597; bootstrap log-rank $p < 0.001$).

The RPSFTM analysis method estimates the survival gained by receiving active treatment using the data from all study participants and then subtracts the benefit from ex-placebo participants switched to CNM-Au8 during the OLE to provide a comparison of CNM-Au8 versus placebo across the entire study period. This well-recognized method has been used to estimate cross-over treatment effects in a recent ALS trial, and oncology and other rare disease trials.

- Unadjusted median survival (without adjusting for the benefit received in ex-placebo participants; analyses include all study participants):
 - 10.1 month median survival benefit when not accounting for the improvement by ex-placebo treated participants who switched to CNM-Au8 at the start of the OLE (CNM-Au8 median survival of 34.2 months; placebo median survival of 24.1 months).
 - 46% decreased risk of all-cause mortality in participants originally randomized to treatment with CNM-Au8 compared to those originally randomized to placebo (HR: 0.54, 95% CI: 0.25-1.1, log-rank $p = 0.09$).
- Observed survival versus ALS historical placebo controls:
 - 70% decreased risk of long-term mortality in participants originally randomized to treatment with CNM-Au8 compared to matched placebo participants derived from the PRO-ACT database (Cox adjusted HR= 0.300, 95% CI: 0.09 to 0.79; $p = 0.03$).

PRO-ACT contains approximately 12,000 ALS patient records from multiple completed clinical trials.

“This new data include open label participants treated with CNM-Au8—42% of whom remain alive up to 3.5 years from randomization and up to 6.6 years from the onset of ALS symptoms, a profoundly meaningful milestone for people living with this devastating disease,” said Benjamin Greenberg, M.D., Head of Medical at Clene. “A median survival improvement of 19.3 months provides people living with ALS, their families, and caregivers more time that is so invaluable, and adds to the totality of data we are seeing in our ALS clinical program.”

Improved Time to Clinical Worsening (defined as the first occurrence of death, tracheostomy, assisted ventilation, or feeding tube placement):

- 52% decreased risk of ALS clinical worsening events (HR: 0.48, 95% CI: 0.23-1.0, log-rank $p = 0.049$) in the participants originally randomized to CNM-Au8 treatment versus original placebo.
-

Safety:

- Over 475 collective years of exposure across ALS, multiple sclerosis (MS), and Parkinson's disease participants in CNM-Au8 clinical trials and Expanded Access Protocol (compassionate use) programs without any observed safety signals.
- No serious adverse events have been assessed as related to CNM-Au8 treatment; adverse events observed with CNM-Au8 have been characterized as transient and predominantly mild-to-moderate in severity.

"The data that continues to be received from the RESCUE-ALS open label extension study is truly impressive, and now shows consistently significant decreased risk of death greater than 70% using two different long-term analysis models," said Professor Matthew Kiernan, PhD, DSc, Bushell Chair of Neurology, University of Sydney, and one of the trial's clinical advisors. "The survival benefit across treatment arms is linked to less worsening of disease, as experienced by ALS patients. At the same time, the further safety data confirms that CNM-Au8 is well tolerated in ALS patients."

About Clene

Clene Inc. (Nasdaq: CLNN) (along with its subsidiaries, "Clene") and its wholly owned subsidiary Clene Nanomedicine Inc., a late clinical-stage biopharmaceutical company focused on improving mitochondrial health and protecting neuronal function to treat neurodegenerative diseases, including amyotrophic lateral sclerosis, Parkinson's disease, and multiple sclerosis. CNM-Au8® is a federally registered trademark of Clene Nanomedicine, Inc. The company is based in Salt Lake City, Utah, with R&D and manufacturing operations in Maryland. For more information, please visit www.clene.com or follow us on [Twitter](#), [LinkedIn](#) and [Facebook](#).

Forward-Looking Statements

This press release 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," "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. These forward-looking statements represent our views as of the date of this press release 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 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 limited operating history and our ability to obtain additional funding for operations and to complete the development and commercialization of our drug candidates; 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 press release, 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 press release is as of the date of this press release. The information contained in any website referenced herein is not, and shall not be deemed to be, part of or incorporated into this press release.

Media Contact

Ignacio Guerrero-Ros, Ph.D., or David Schull
Russo Partners, LLC
ignacio.guerrero-ros@russopartnersllc.com
David.schull@russopartnersllc.com
(858) 717-2310

Investor Contact

Kevin Gardner
LifeSci Advisors
kgardner@lifesciadvisors.com
617-283-2856