# 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): April 17, 2023**

# CLENE INC.
(Exact name of registrant as specified in its charter)

| **Delaware** | **001-39834** | **85-2828339** |
|---|---|---|
| (State or Other Jurisdiction of Incorporation) | (Commission File Number) | (IRS Employer Identification No.) |

| **6550 South Millrock Drive, Suite G50**<br>**Salt Lake City, Utah**<br>(Address of Principal Executive Offices) | **84121**<br>(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.**

On April 17, 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 9.01 Financial Statements and Exhibits.**

(d) Exhibits

| Exhibit Number | Exhibit Description |
|---|---|
| 99.1 | Corporate Presentation. |
| 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: April 17, 2023

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

**Exhibit 99.1**

# 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

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 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



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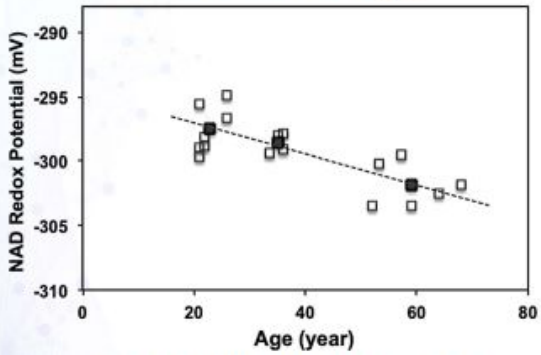
# Neurodegenerative Diseases Share A Common Mechanism: A Decline In The Brain's Ability To Produce Energy

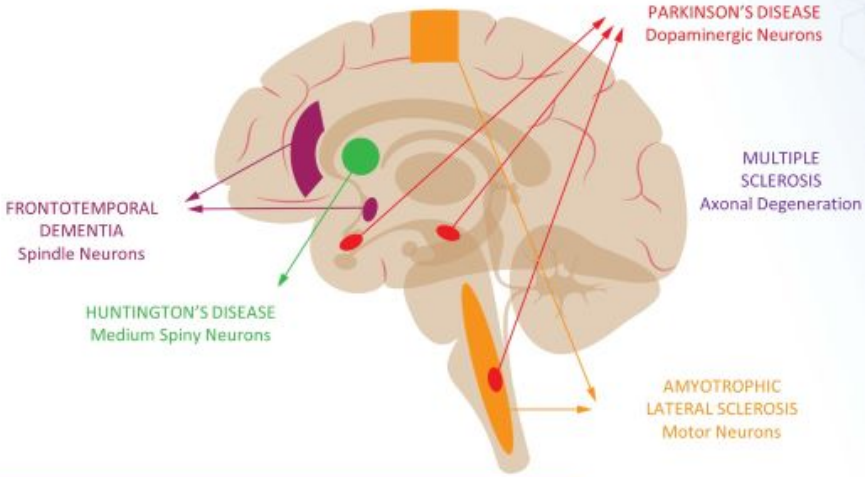
Brain Energy Potential
Declines With Normal Aging




~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




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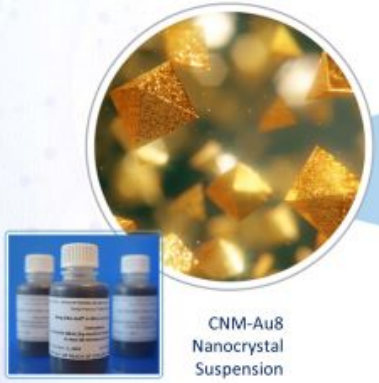
# CNM-Au8® | Pioneering A New Drug Class To Improve Cellular Energy Production And Utilization

**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.

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# 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

## Parkinson's 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..

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# 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)

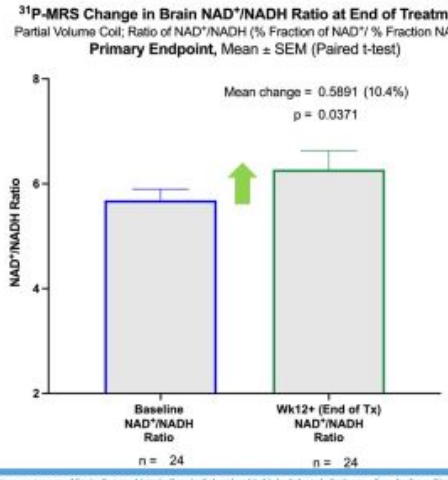
RepairPD
Early Parkinson's Disease

RepairMS
Stable Relapsing MS

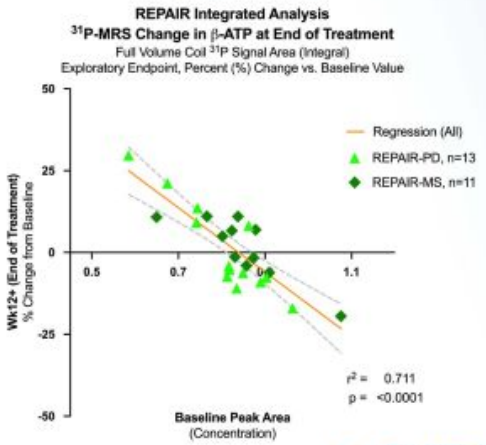
RepairMS
Non-Active Progressive MS
(Ongoing)

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

1° Endpoint (integrated PD & MS)[2]




Exploratory
(ATP Normalization)






[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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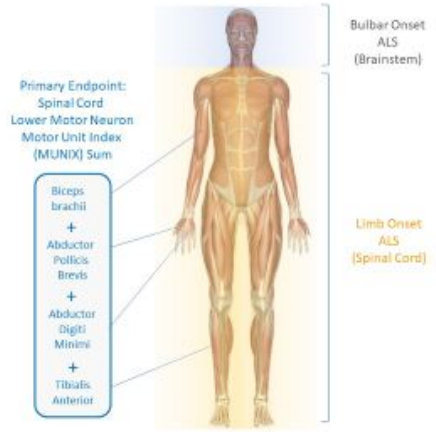
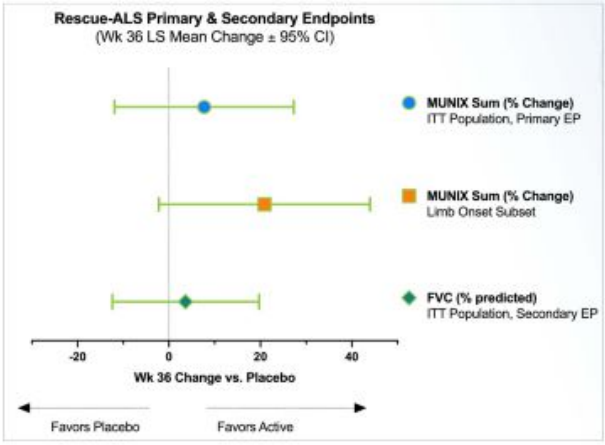
# RESCUEALS Encouraging Efficacy Signals in Phase 2 Trial

**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 favor CNM-Au8 treatment


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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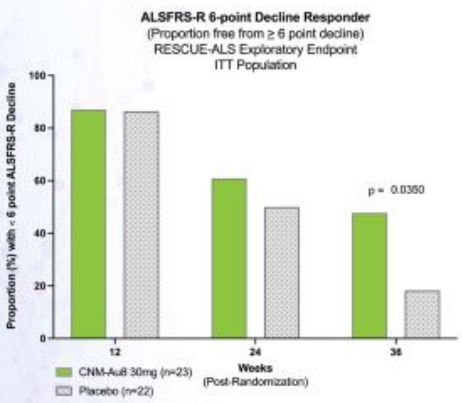
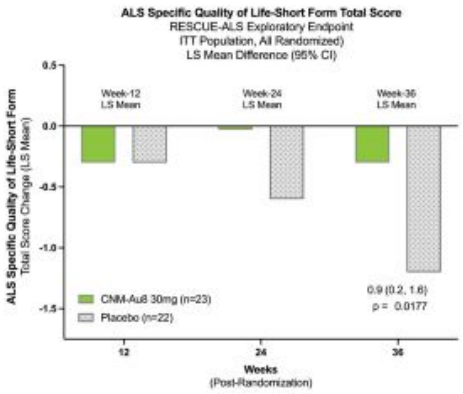
# CNM-Au8 Improved Patient Function, QOL, and Slowed Time to ALS Clinical Worsening

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

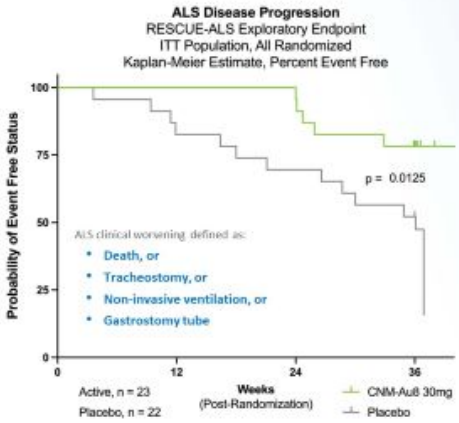
Proportion with <6 point decline




ALS Specific QOL




ALS Clinical Worsening



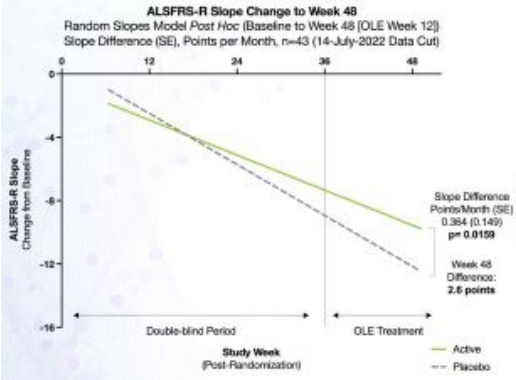



Vucic et al. RESCUE-ALS Trial Results: A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study of CNM-Au8 to Slow Disease Progression in Amyotrophic Lateral Sclerosis; Presented at International Symposium on ALS/MND; 7-10 December 2021

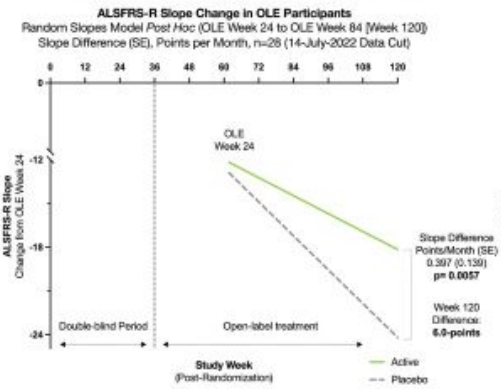
# RESCUEALS OLE | Preserved ALSFRS-R Functional Decline

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

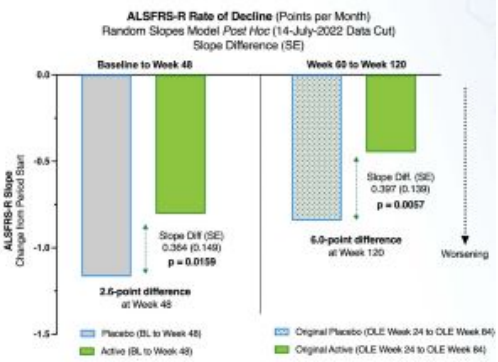
### ALSFRS-R Slope Baseline to Week 48




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




### ALSFRS-R Slope Summary



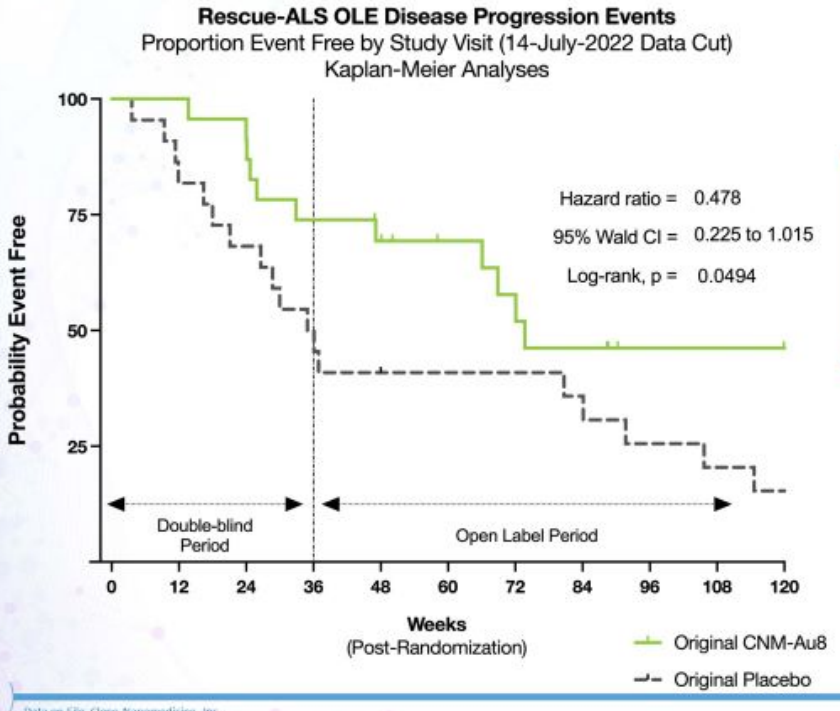

- **CNM-Au8 preserved functional decline: ALSFRS-R of 2.6 points at 48 weeks compared to placebo**
- **Early CNM-Au8 treatment preserved long-term ALSFRS-R score by 6.0 points vs. OLE original placebo**

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



Data on File, Clene Nanomedicine, Inc.

# RESCUEALS OLE | Decreased ALS Time to Clinical Worsening




The risk of ALS clinical worsening was decreased ~50% for CNM-Au8 compared to placebo in OLE up-to-120 weeks

Clinical worsening events included:

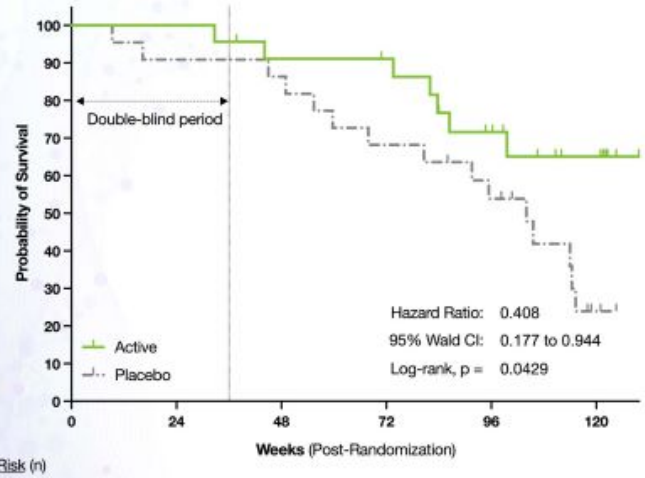
- Death,
- Tracheostomy,
- Need for non-invasive ventilatory support, or
- Gastrostomy (feeding) tube placement.



Data on File, Clene Nanomedicine, Inc.

# 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 (14-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 (14-July-2022). Vital status and date of death (as applicable) were captured for all subjects withdrawn from the study. Lost-to-follow-up (active, n=3; placebo, n=1) censored as of the date of last study contact. All OLE ex-placebo CNM-Au8 transitioned participants within the placebo group. All current active OLE subjects are right censored as of 14-July-2022.


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

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)

Exploratory Endpoints



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

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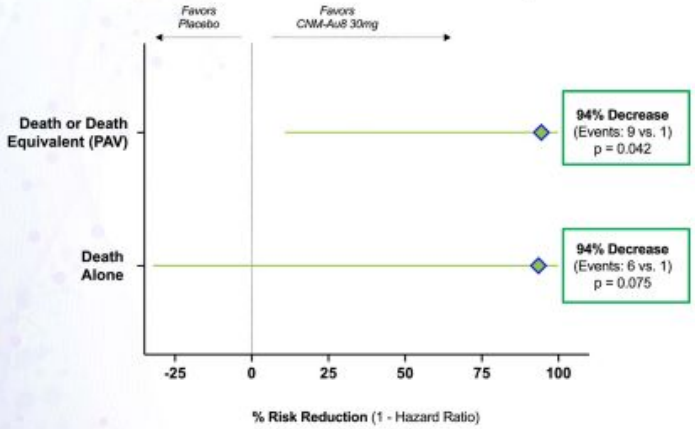
# Survival Signal | >90% Reduced Risk of Death with 30mg

HEALEY ALS Platform Trial

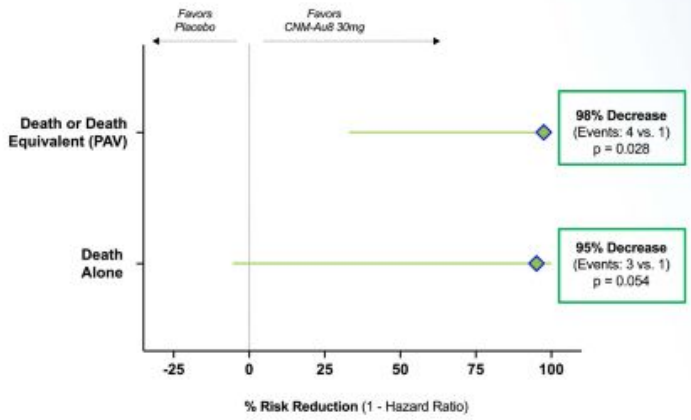
## Shared Placebo Across Regimens

**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**
Efficay 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.

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



Data on File, Clene Nanomedicine, Inc.

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# Time to Clinical Worsening Events

HEALEY ALS Platform Trial

Death

Permanent Assisted Ventilation


Hospitalization
ALS-Related and All-Cause

Feeding Tube Placement

Assisted Ventilation

- Time to clinical worsening events were prespecified in the protocol and analysis plan
- p-values provided are uncorrected for multiple comparisons
- Since the primary outcome was negative, the results are hypothesis generating and not confirmatory
- Combined analyses of the 30mg and 60mg doses were prespecified for primary & secondary outcomes



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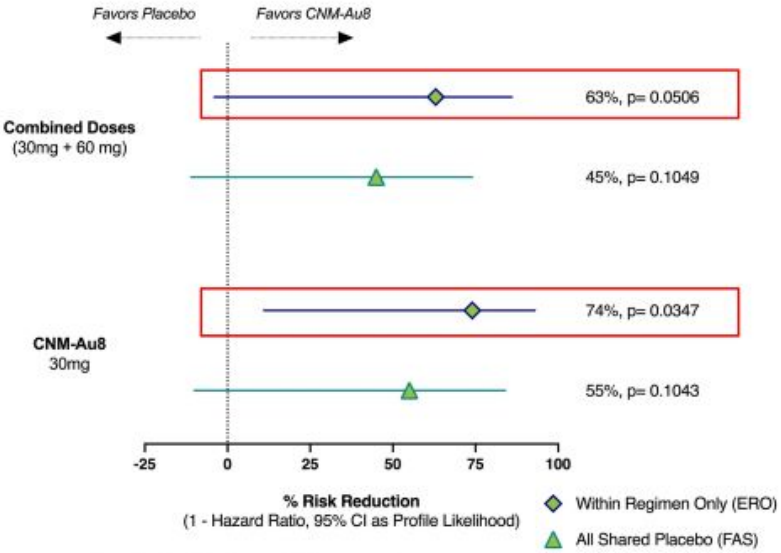
# Delayed Time to ALS Clinical Worsening (Composite)

HEALEY ALS Platform Trial

## Clinical Worsening Composite (Time to First Instance)

- 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.

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



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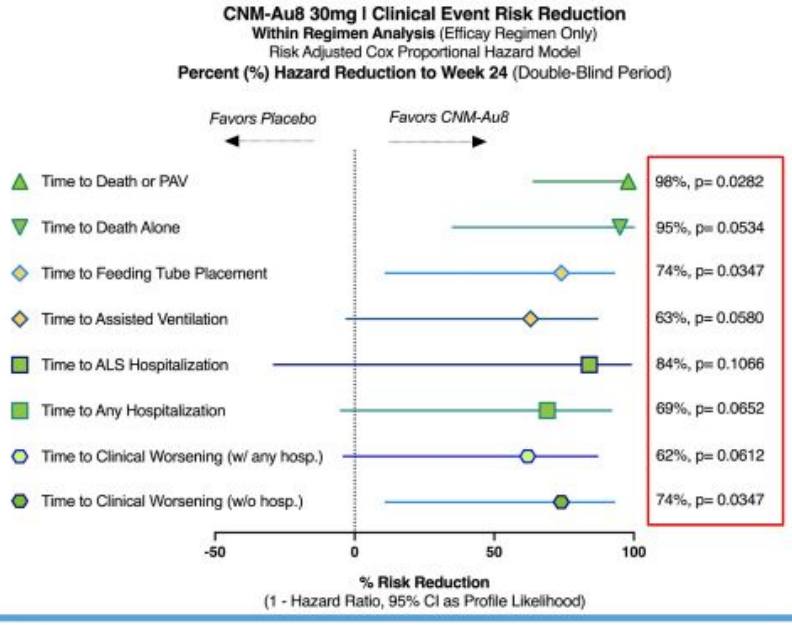
# Delayed Time to Clinical Event Summary

## CNM-Au8 30mg | Within Regimen Analysis (Primary Model)

HEALEY ALS Platform Trial

### 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.



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# 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**

RESCUEALS

HEALEY ALS Platform Trial

- 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



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# 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)

# 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 (~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



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

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# Baseline Demographics and Study Analysis

VISIONARY-MS STUDY

- 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) |



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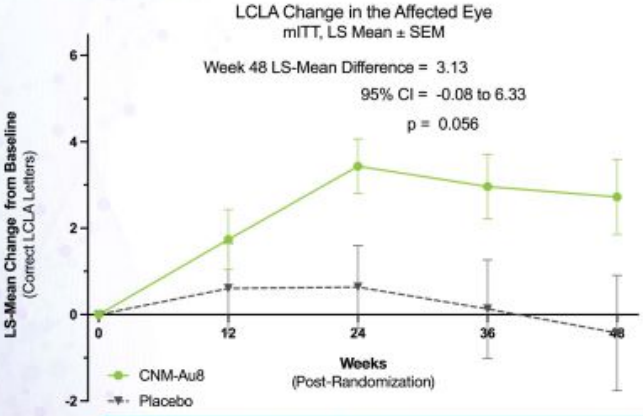
# CNM-Au8 Demonstrated Vision and Global Neurological Improvement in Stable MS patients on DMTs

VISIONARY-MS STUDY

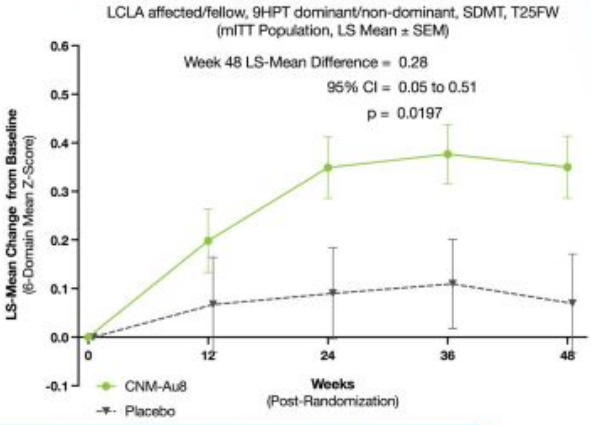
## Significantly Improved Vision


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



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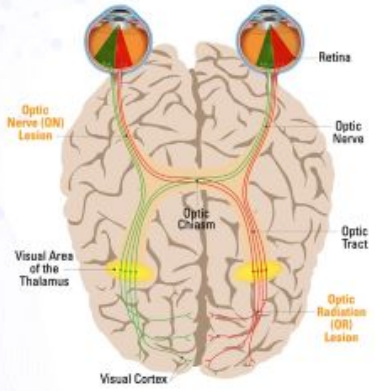
# VISIONARY-MS Measures of Axonal Integrity

VISIONARY-MS STUDY

## Visual Evoked Potentials (VEP)

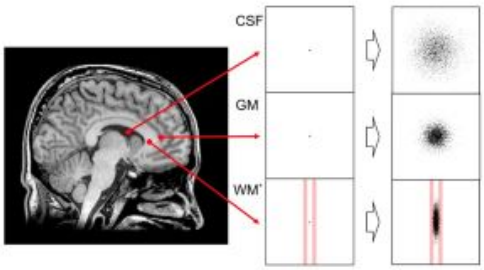
Multi-focal Amplitude and Latency Changes



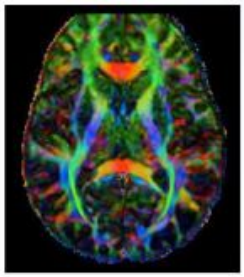

## Advanced MRI Techniques

Diffusion Tensor Imaging (DTI) changes

Fractional Anisotropy




Brain Diffusivity



**What Happens in the Visual System Happens Throughout the MS Brain**



Balcer et la. Mult Scler. 2017 Apr;23(5):734-747.

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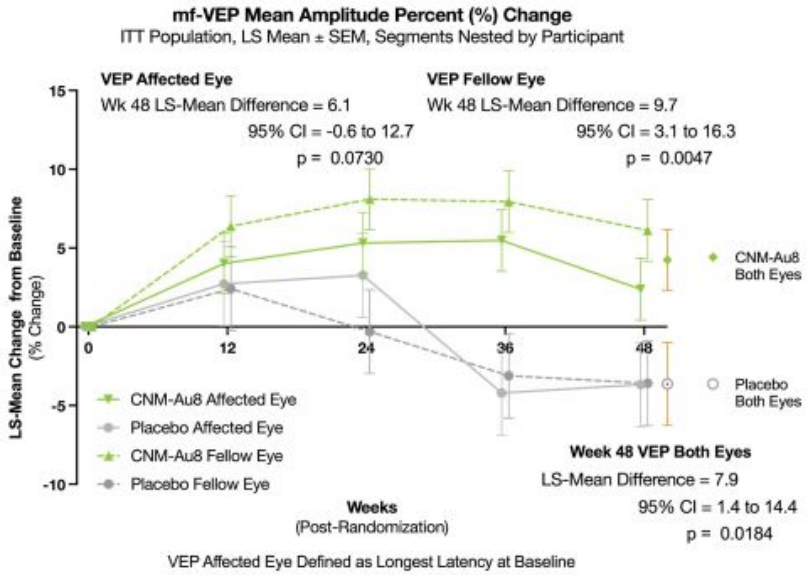
# CNM-Au8 Improved Information Signal in the Visual Pathway

VISIONARY-MS STUDY

Increased Amplitude (Signal Strength)

From the Eye to the Brain's Visual Cortex




VEP Affected Eye Defined as Longest Latency at Baseline

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



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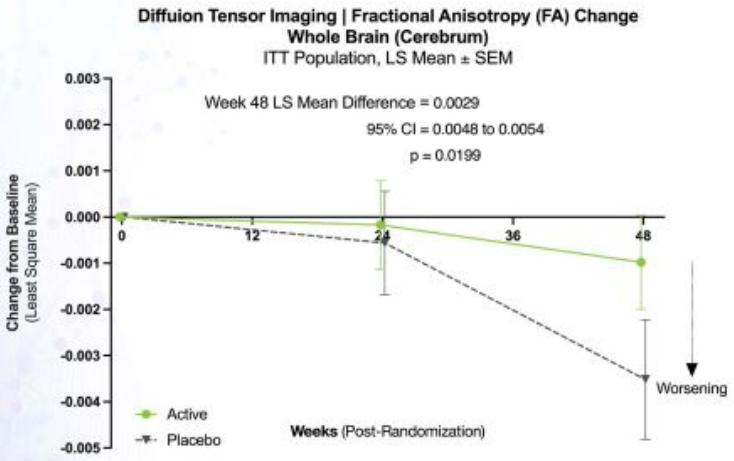
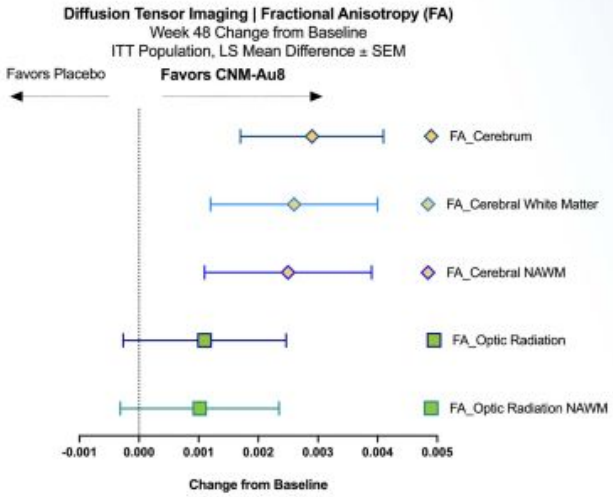
# CNM-Au8 Preserved White Matter Integrity Throughout the Brain

VISIONARY-MS STUDY

## 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



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# 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



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# VISIONARY-MS Safety Summary

VISIONARY-MS STUDY

## 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



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

VISIONARY-MS STUDY

**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



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# 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 transient and predominantly mild-to-moderate severity

## Patient Exposure Across ALS, MS & PD

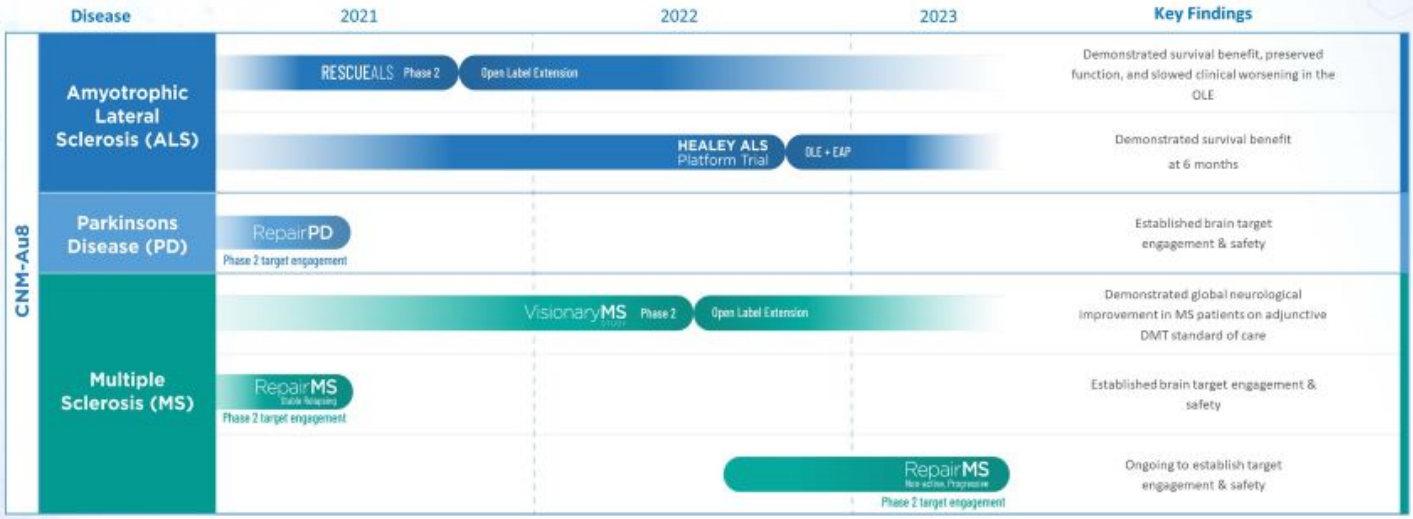
Over 400 Years of Subject Exposure Without Identified Safety Signals

- Long-term dosing experience up to 175 weeks



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

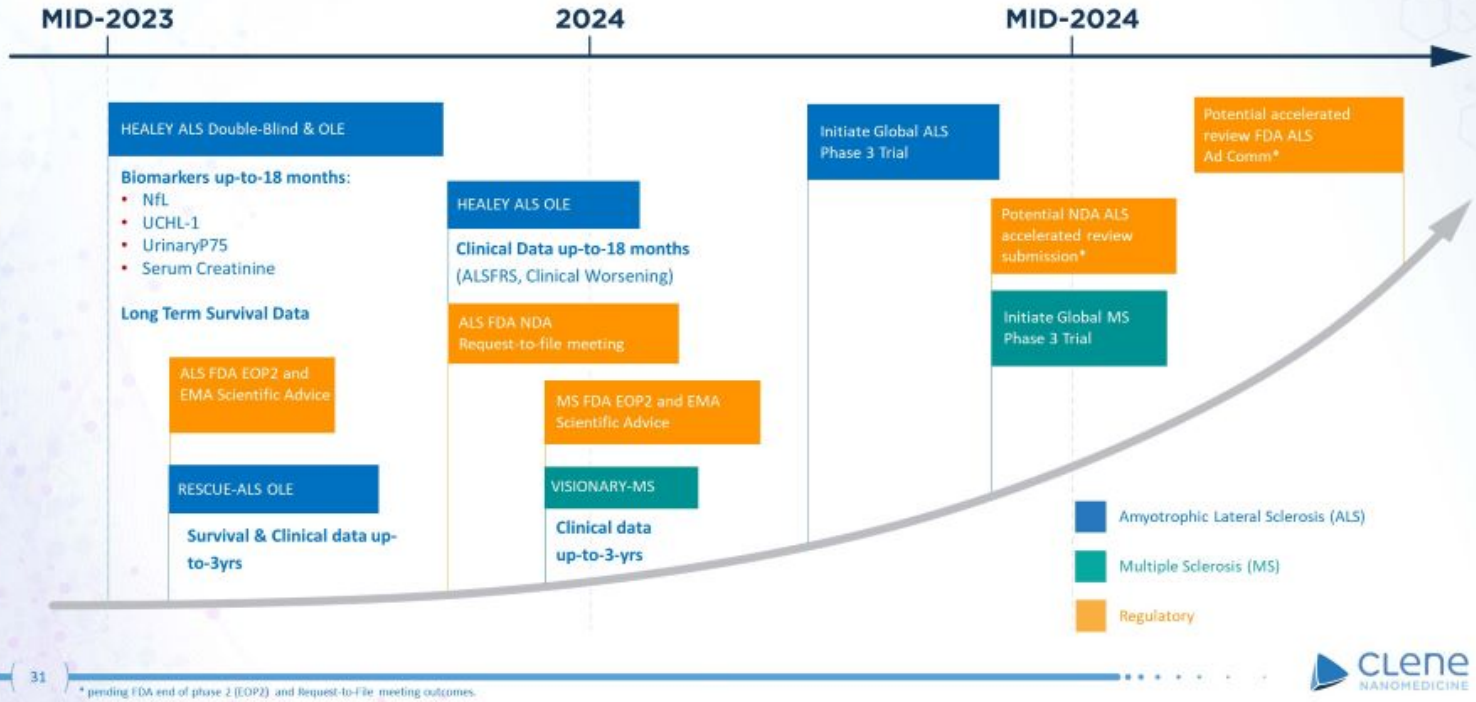
# Growing Body of Evidence for CNM-Au8®






Data on File, Clene Nanomedicine, Inc.

# Clene | Anticipated Catalysts Over the Next Year






* pending FDA end of phase 2 (EOP2) and Request-to-File meeting outcomes.

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# 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

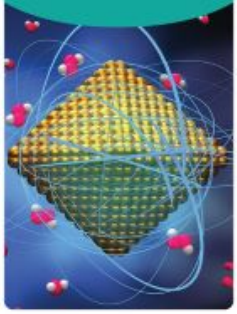
>90% decreased risk of death with 30 mg in ALS

VISIONARY-MS

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 December 31, 2022, cash and investments on hand (audited):

**$23.3M**



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.

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