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): November 7, 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 **Salt Lake City, Utah**	**84121**
(Address of Principal Executive Offices)	(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 2.02 Results of Operations and Financial Condition.

On November 7, 2023, Clene Inc. (the "Company") issued a press release announcing its third quarter 2023 financial results and operating highlights for its quarter ended September 30, 2023. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

The information furnished in this Item 2.02, 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 (the "Securities Act"), 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 7.01 Regulation FD Disclosure.

In connection with the November 7, 2023 press release announcing the Company's third quarter 2023 financial results and operating highlights for its quarter ended September 30, 2023, 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 99.2 to this Current Report 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 99.2, shall not be deemed to be "filed" for purposes of Section 18 of 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, 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	Press Release, dated November 7, 2023, announcing the Company's third quarter 2023 financial results and operating highlights.
99.2	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: November 7, 2023

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

Exhibit 99.1

CLENE REPORTS THIRD QUARTER 2023 FINANCIAL RESULTS AND OPERATING HIGHLIGHTS

- *Reported statistically significant improved survival benefit of 19.3 months and significantly delayed clinical worsening in patients treated with CNM-Au8® in the RESCUE ALS open-label extension trial*
- *Reported statistically significant long-term survival benefit of 70% decreased risk of death associated with CNM-Au8 treatment in the HEALEY ALS Platform Trial compared to PRO-ACT historical controls*
- *Awarded $45.1 million NINDS grant to support research and expanded access of CNM-Au8 in people living with ALS*
- *Announced peer-reviewed publication characterizing CNM-Au8 neuroprotective mechanism of action in the nanotechnology-focused journal, Small*
- *Cash and cash equivalents of $42.1 million as of September 30, 2023, which includes gross proceeds of $40 million from a public offering in June and that may provide additional capital of up to $130 million through future warrant exercises based on regulatory milestones*

SALT LAKE CITY, November 7, 2023 -- 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 (ALS), Parkinson's disease and multiple sclerosis (MS), today announced its third quarter 2023 financial results and provided recent operating highlights for its ALS clinical program.

"We are pleased to be approaching a meaningful regulatory discussion with the U.S. Food and Drug Administration (FDA) later in the fourth quarter to elucidate key next steps in our ALS regulatory submission of CNM-Au8," said Rob Etherington, President and CEO of Clene. "We are hopeful that the consistent survival, delayed time to clinical worsening and strong safety profile with CNM-Au8 treatment from two phase 2 independent trials is sufficiently compelling for FDA to consider an accelerated path forward. The unmet need remains high for treatments to improve and extend life for patients living with this highly debilitating and rapidly progressive condition."

Third Quarter 2023 and Recent Operating Highlights

CNM-Au8, a gold nanocrystal suspension, for the treatment of ALS

- In August, Clene reported 24-month data from the open-label extension of the Phase 2 RESCUE ALS study which showed a significant median survival benefit of 19.3 months, a 75% decreased risk of long-term all-cause mortality and a significant 52% decreased risk (p=0.049) of ALS clinical worsening events in patients originally randomized to CNM-Au8 treatment.
- In September, Clene announced long-term follow-up data for patients treated with CNM-Au8 for up to 133 weeks in the HEALEY ALS Platform Trial. These post hoc data demonstrate significantly improved survival with a 49% decreased risk of death compared to a group of historical controls, who were included in the largest U.S. clinical database of previous ALS trials (PRO-ACT).
- In October, Clene, in collaboration with Columbia University and Synapticure, was awarded a four-year grant totaling $45.1 million from the National Institute of Neurological Disorders and Stroke (NINDS), a division of the National Institutes of Health (NIH), to support an Expanded Access Protocol (EAP) for the Company's investigational drug, CNM-Au8, in ALS.

Corporate Update

In September, the Company announced the publication of a scientific paper describing the catalytic mechanism of action (MOA) of its investigational drug, CNM-Au8 in the journal *Small*, a top nanotechnology-focused journal at the interface of materials science, chemistry, physics, engineering, medicine, and biology. The publication titled "A Mechanism Underpinning the Bioenergetic Metabolism-Regulating Function of Gold Nanocatalysts" characterizes the robust neuroprotective properties of CNM-Au8, which are related to the compound's therapeutic catalytic activity. Because of the unique MOA of CNM-Au8 and the wide applicability of its neuroprotective activities, the drug is being studied across multiple neurodegenerative diseases including ALS, MS and Parkinson's Disease.

The publication is available via Open Access at https://onlinelibrary.wiley.com/doi/10.1002/smll.202304082.

Third Quarter 2023 Financial Results

Clene's cash, cash equivalents and marketable securities totaled $42.1 million as of September 30, 2023, compared to $23.3 million as of December 31, 2022. Clene expects that its resources as of September 30, 2023, will be sufficient to fund its operations into the third quarter 2024.

Research and development expenses were $6.0 million for the quarter ended September 30, 2023, compared to $6.4 million for the same period in 2022. The year-over-year decrease was primarily related to a decrease in expenses related to our lead drug candidate, CNM-Au8, due to a decrease in clinical trial expenses in our HEALEY ALS Platform Trial and our RESCUE-ALS, REPAIR-MS, REPAIR-PD, and VISIONARY-MS clinical trials due to the completion of the blinded period of each trial, partially offset by increased expenses related to our ongoing EAPs and increased facility costs related to our newly-leased facility in Elkton, Maryland.

General and administrative expenses were $3.7 million for the quarter ended September 30, 2023, compared to $3.6 million for the same period in 2022. General and administrative expenses have remained flat year over year although directors' and officers' insurance fees and legal fees have decreased year over year while finance and accounting expenses related to fees from auditors, consultants and other financial vendors have increased and personnel fees have increased.

Total other income was $7.1 million for the quarter ended September 30, 2023, compared to total other expense of $1.2 million for the same period in 2022. The year-over-year increase in other income was primarily attributable to the changes in the fair value of common stock warrant liabilities and contingent earn-out liabilities as well as an increase in interest income.

Clene reported a net loss of $2.4 million, or $0.02 per share, for the quarter ended September 30, 2023, compared to a net loss of $11.0 million, or $0.17 per share, for the same period in 2022.

About Clene

Clene Inc., (Nasdaq: CLNN) (along with its subsidiaries, "Clene") and its wholly owned subsidiary Clene Nanomedicine Inc., is 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 an investigational first-in-class therapy that improves central nervous system cells' survival and function via a mechanism that targets mitochondrial function and the NAD pathway while reducing oxidative stress. 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 X (formerly Twitter) and LinkedIn.

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.

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CLENE INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS
(In thousands, except share and per share amounts)
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2023	2022	2023	2022
Revenue:				
Product revenue	$ 65	$ 130	$ 355	$ 139
Royalty revenue	43	44	129	100
Total revenue	108	174	484	239
Operating expenses:				
Cost of revenue	12	19	83	19
Research and development	5,972	6,403	19,982	24,149
General and administrative	3,666	3,557	11,029	12,807
Total operating expenses	9,650	9,979	31,094	36,975
Loss from operations	(9,542)	(9,805)	(30,610)	(36,736)
Other income (expense), net:				
Interest income	546	59	931	144
Interest expense	(1,188)	(857)	(3,358)	(2,390)
Gain on termination of lease	—	—	—	420
Commitment share expense	—	—	(402)	—
Issuance costs for common stock warrant liability	—	—	(333)	—
Loss on initial issuance of equity	—	—	(14,840)	—
Change in fair value of common stock warrant liabilities	6,341	149	5,958	151
Change in fair value of Clene Nanomedicine contingent earn-out liability	1,004	(1,591)	2,114	6,662
Change in fair value of Initial Stockholders contingent earn-out liability	129	(205)	272	849
Research and development tax credits and unrestricted grants	247	1,346	902	2,001
Other income (expense), net	45	(72)	35	35
Total other income (expense), net	7,124	(1,171)	(8,721)	7,872
Net loss before income taxes	(2,418)	(10,976)	(39,331)	(28,864)
Income tax benefit	—	—	—	—
Net loss	(2,418)	(10,976)	(39,331)	(28,864)
Other comprehensive loss:				
Unrealized gain (loss) on available-for-sale securities	(4)	33	16	(54)
Foreign currency translation adjustments	(81)	(39)	(130)	(99)
Total other comprehensive loss	(85)	(6)	(114)	(153)
Comprehensive loss	$ (2,503)	$ (10,982)	$ (39,445)	$ (29,017)
Net loss per share – basic and diluted	$ (0.02)	$ (0.17)	$ (0.41)	$ (0.46)
Weighted average common shares used to compute basic and diluted net loss per share	128,405,483	63,508,928	97,026,964	63,234,757

CLENE INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(In thousands, except share and per share amounts)
(Unaudited)

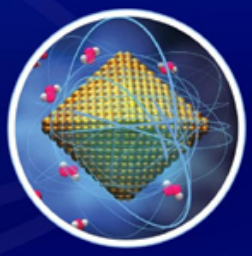
	September 30, 2023	December 31, 2022
ASSETS		
Current assets:		
Cash and cash equivalents	$ 42,113	$ 18,332
Marketable securities	—	4,983
Accounts receivable	64	189
Inventory	104	43
Prepaid expenses and other current assets	4,165	5,648
Total current assets	46,446	29,195
Restricted cash	58	58
Operating lease right-of-use assets	4,287	4,602
Property and equipment, net	9,642	10,638
TOTAL ASSETS	$ 60,433	$ 44,493
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 1,889	$ 3,014
Accrued liabilities	3,194	3,863
Operating lease obligations, current portion	553	488
Finance lease obligations, current portion	44	74
Notes payable, current portion	9,588	6,418
Total current liabilities	15,268	13,857
Operating lease obligations, net of current portion	5,080	5,557
Finance lease obligations, net of current portion	—	34
Notes payable, net of current portion	6,675	9,483
Convertible notes payable	9,975	9,770
Common stock warrant liabilities	1,860	—
Clene Nanomedicine contingent earn-out liability	150	2,264
Initial Stockholders contingent earn-out liability	19	291
TOTAL LIABILITIES	39,027	41,256
Commitments and contingencies		
Stockholders' equity:		
Common stock, $0.0001 par value: 300,000,000 and 150,000,000 shares authorized at September 30, 2023 and December 31, 2022, respectively; 128,411,981 and 74,759,591 shares issued and outstanding at September 30, 2023 and December 31, 2022, respectively	13	7
Additional paid-in capital	253,854	196,246
Accumulated deficit	(232,550)	(193,219)
Accumulated other comprehensive income	89	203
TOTAL STOCKHOLDERS' EQUITY	21,406	3,237
TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY	$ 60,433	$ 44,493

Exhibit 99.2

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.

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



THE PROBLEM

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

A NEW APPROACH

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

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Building the Clinical Case for Neuroprotection & Remyelination

HEALEY ALS Platform Trial

RESCUEALS

VISIONARY-MS STUDY

RepairPD

RepairMS

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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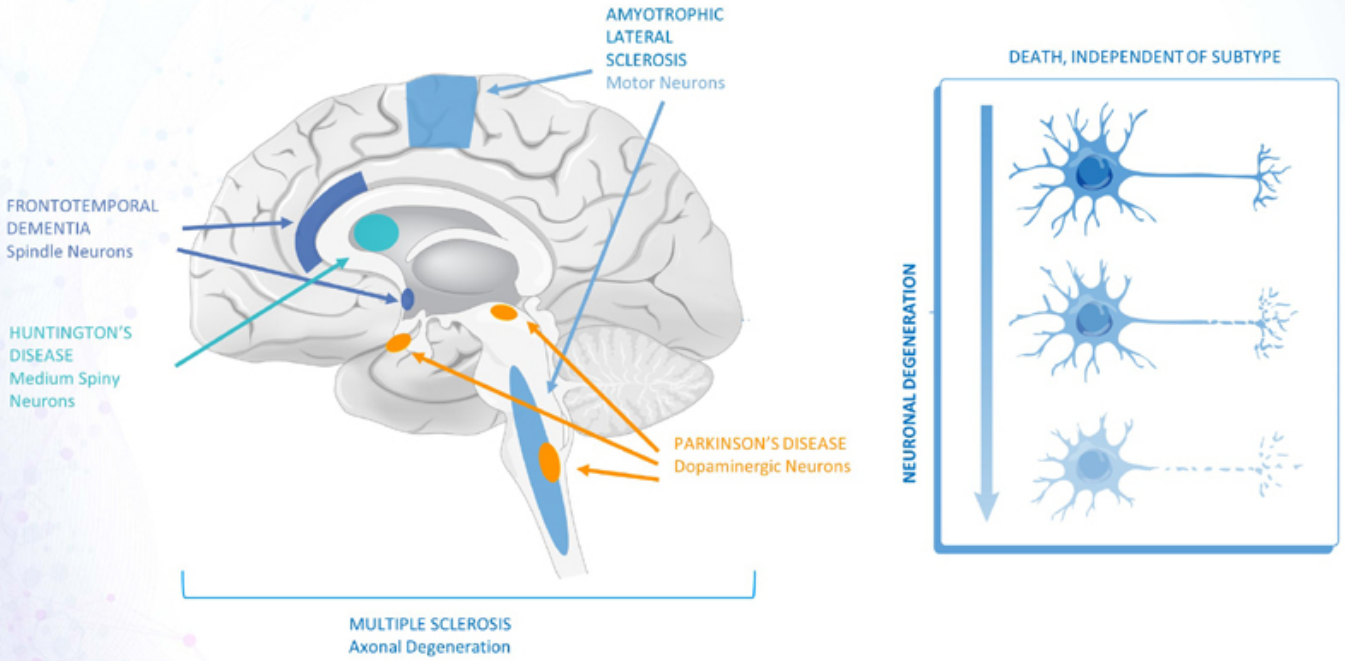
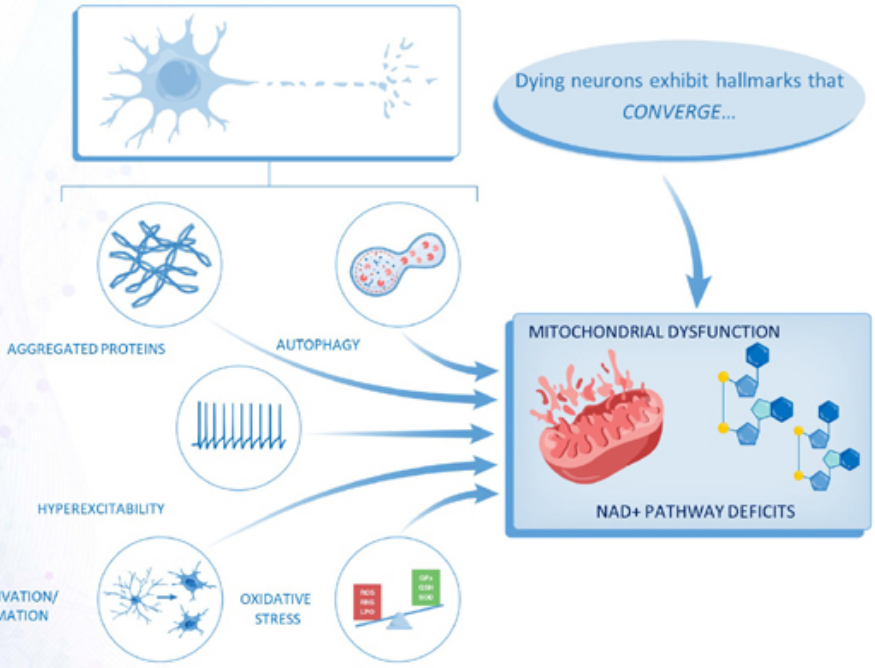
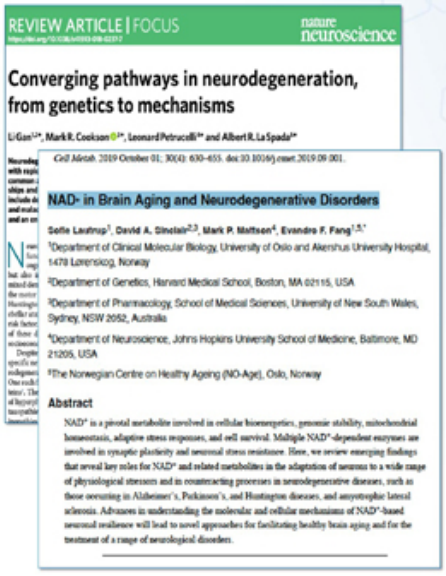
All Neurodegenerative Diseases Involve Neuronal Death



Fu, H., et al; Nature Neuroscience (2018) 21: 1350-1358. Rone et al. J Neurosci. 2016 Apr 27;36(17):4698-707.

Hallmarks of Neuronal Death Converge on ***Mitochondrial Dysfunction*** and ***NAD+ Pathway Deficits***





REVIEW ARTICLE | FOCUS

nature neuroscience

Converging pathways in neurodegeneration, from genetics to mechanisms

Li Gan[1,2*], Mark R. Cookson[3*], Leonard Petrucelli[4*] and Albert R. La Spada[5*]

Cell Metab. 2019 October 01; 30(4): 630–655. doi:10.1016/j.cmet.2019.09.001.

NAD+ in Brain Aging and Neurodegenerative Disorders

Sofie Lautrup[1], David A. Sinclair[2,3], Mark P. Mattson[4], Evandro F. Fang[1,5,*]

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[3]Department of Pharmacology, School of Medical Sciences, University of New South Wales, Sydney, NSW 2052, Australia

[4]Department of Neuroscience, Johns Hopkins University School of Medicine, Baltimore, MD 21205, USA

[5]The Norwegian Centre on Healthy Ageing (NO-Age), Oslo, Norway

Abstract

NAD+ is a pivotal metabolite involved in cellular bioenergetics, genomic stability, mitochondrial homeostasis, adaptive stress responses, and cell survival. Multiple NAD+-dependent enzymes are involved in synaptic plasticity and neuronal stress resistance. Here, we review emerging findings that reveal key roles for NAD+ and related metabolites in the adaptation of neurons to a wide range of physiological stressors and in counteracting processes in neurodegenerative diseases, such as those occurring in Alzheimer's, Parkinson's, and Huntington diseases, and amyotrophic lateral sclerosis. Advances in understanding the molecular and cellular mechanisms of NAD+-based neuronal resilience will lead to novel approaches for facilitating healthy brain aging and for the treatment of a range of neurological disorders.

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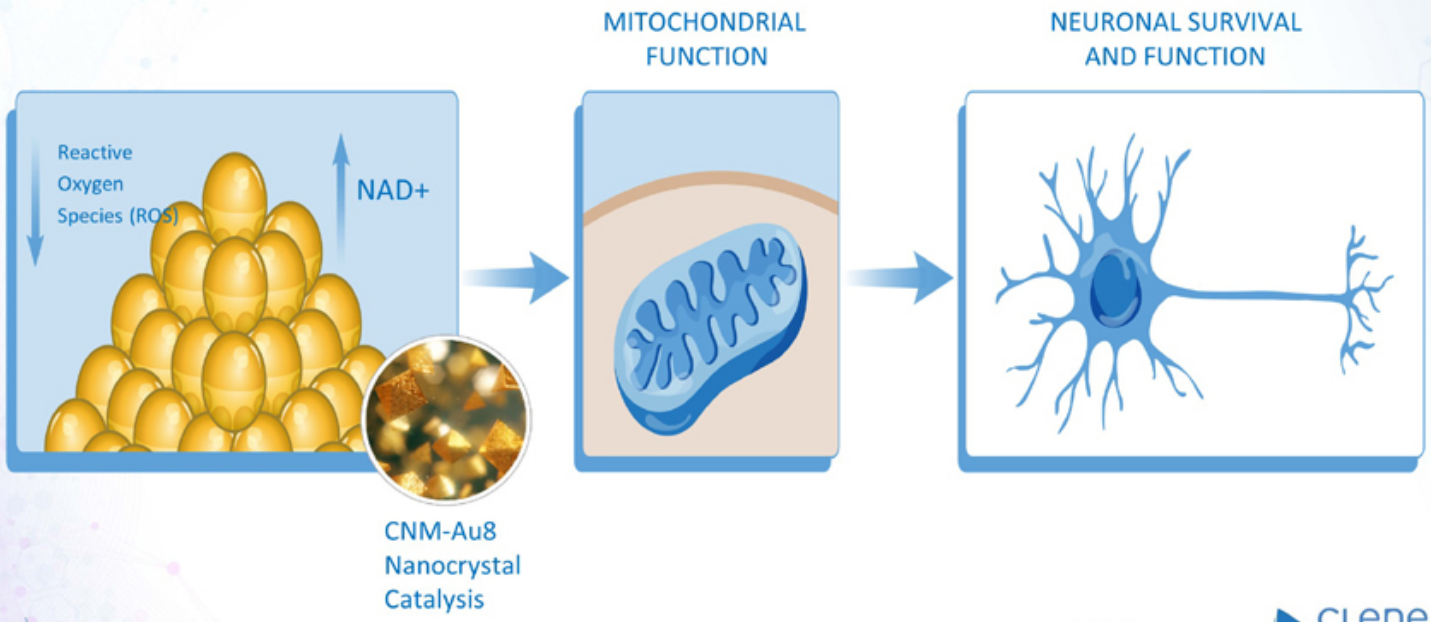
CNM-Au8® | Surface Catalysis Improves Mito Function



Robinson et al. Sci Rep. 2020 Feb 11;10(1):1936. Wang et al 2023, https://doi.org/10.1101/2023.05.08.539856.

clene NANOMEDICINE

Over 500 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/mild-to-moderate** severity (GI/Headache)

Patient Exposure Across ALS, MS & PD

Over 500 Years of Subject Exposure Without Identified Safety Signals

- Long-term dosing experience **over 4 years**

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

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

Study Objective: Demonstrate target engagement & Blood-Brain penetration 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

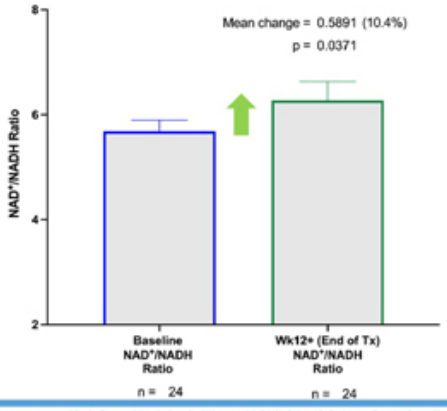
RepairMS
Stable Relapsing MS

RepairMS
Non-Active Progressive MS
(Ongoing)

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

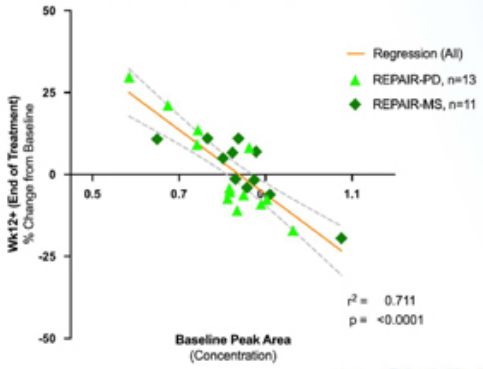
1° Endpoint (integrated PD & MS)[2]

^{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

CLENE NANOMEDICINE

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 (45)	Early-to-Mid-Stage	Mid-to-Late-Stage (161 Regimen C)	Mid-to-Late-Stage	Real-World Experience (>200)
Duration	36-weeks	Up to 173 weeks	24-weeks	Through April '23	Over 4.0 years
Survival	--	✓	✓	✓ PRO-ACT	✓
Delayed Time to Clinical Worsening	✓	✓	✓	Pending data 1Q 2024 Or earlier	Not routinely collected
Preserved Function (ALSFRS-R)	--	✓	--		
Progression Biomarkers	p75 trend	UCHL1 ↓*	NfL ✓		

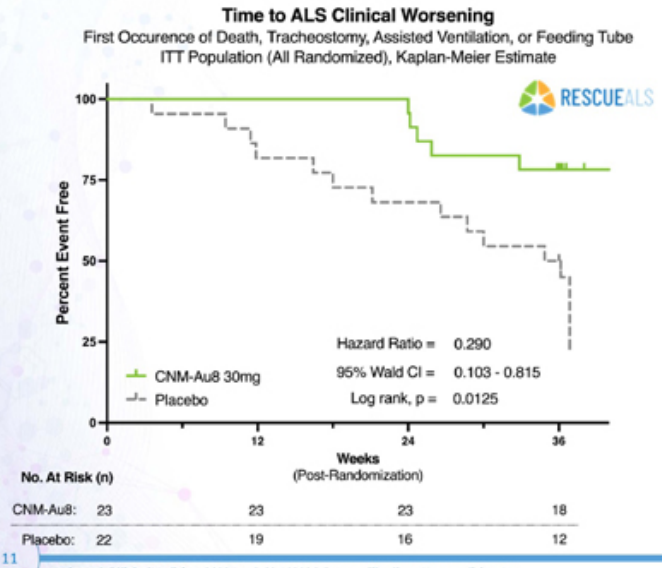
Consistent Evidence for CNM-Au8 30mg Dose Across Broad ALS Patient Population

Data on File, Clene Nanomedicine, Inc. *Small sample available for analyses in RESCUE OLE

CNM-Au8 | Clinical Worsening Concordant in Two Phase 2 Trials

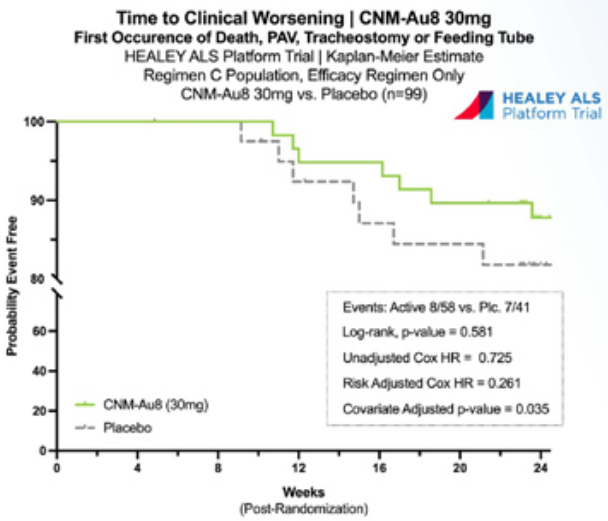
Evidence for Decreased Clinical Worsening Events Across Two Phase 2 Studies

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



No. At Risk (n)				
CNM-Au8:	23	23	23	18
Placebo:	22	19	16	12

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



Vucic et al. EClinicalMedicine. 2023 Jun 8;60:102036. Data on File, Clene Nanomedicine, Inc.

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CNM-Au8 | ALS Survival at 30mg Concordant in Two Phase 2 Trials

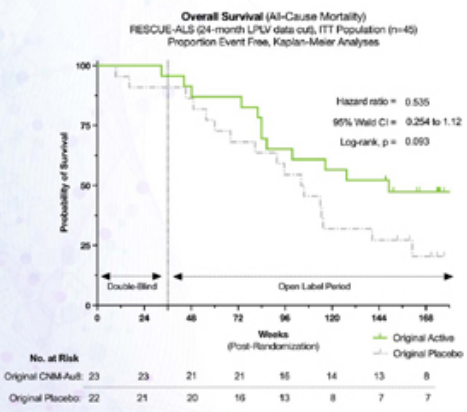
RESCUEALS

Up to 75% decreased risk of death through 168 weeks

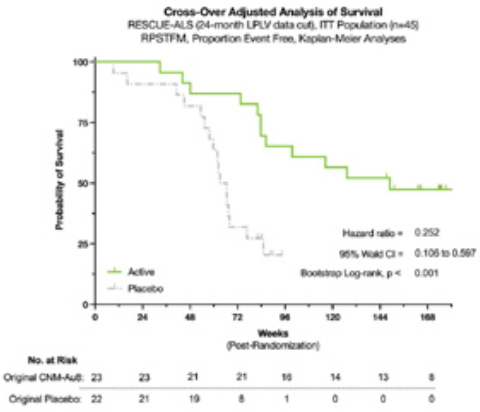
HEALEY ALS Platform Trial

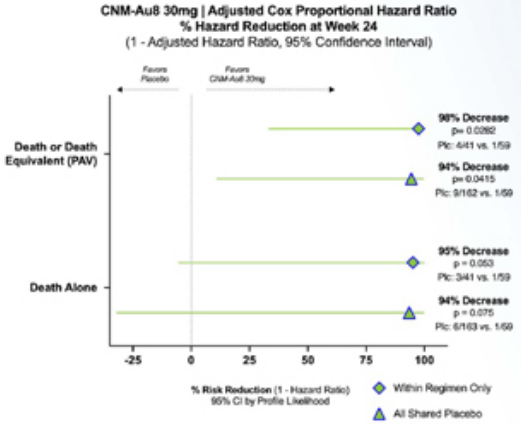
>90% risk reduction of death at 30mg at 24 weeks

Unadjusted Survival



Cross-Over Adjusted Survival





Data on File, Clene Nanomedicine, Inc.

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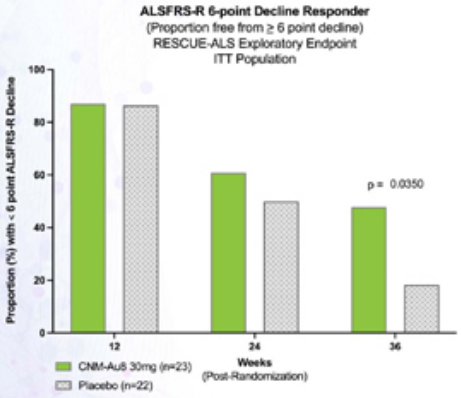
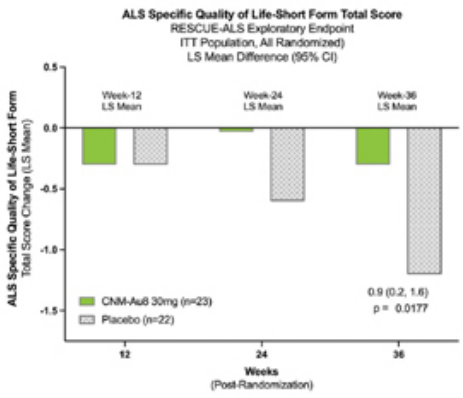
Improved Exploratory Endpoints: Patient Function, QOL, and Slowed Time to ALS Clinical Worsening

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

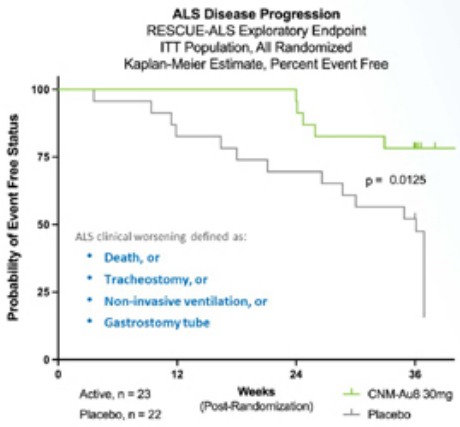
Proportion with <6 point decline



ALS Specific QOL



ALS Clinical Worsening

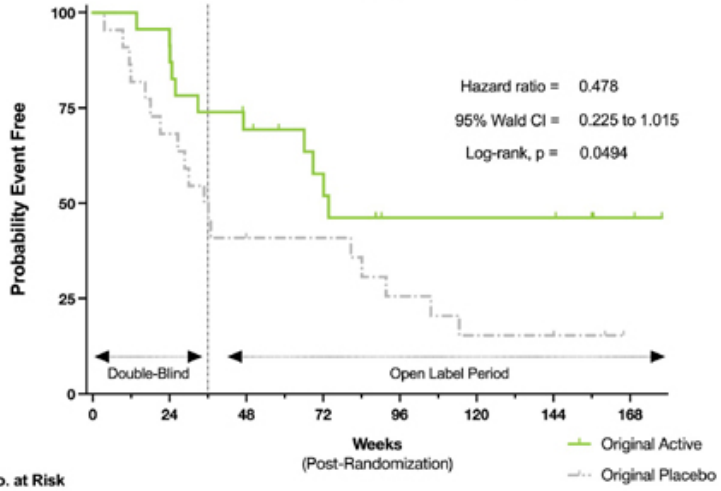


Vucic et al. EClinicalMedicine. 2023 Jun 8;60:102036.

RESCUEALS OLE | 52% Reduced Risk of ALS Clinical Worsening

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

ALS Clinical Worsening Events
Time to Death, Tracheostomy, Assisted Ventilation, or Feeding Tube
RESCUE-ALS Double-Blind & OLE Periods (24-month LPLV data cut)
Proportion Event Free, Kaplan-Meier Analyses



No. at Risk								
Original CNM-Au8:	23	23	16	11	6	6	6	3
Original Placebo:	22	16	10	9	6	4	4	1

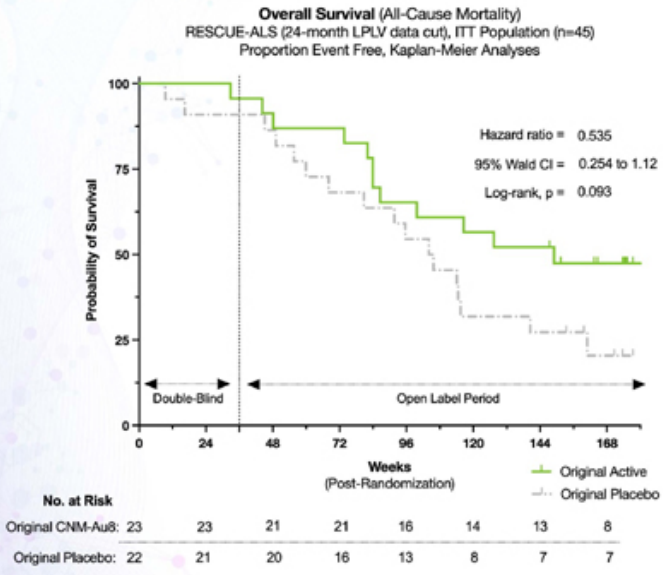
Participants were right-censored at loss of follow-up with OLE withdrawal, as applicable

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

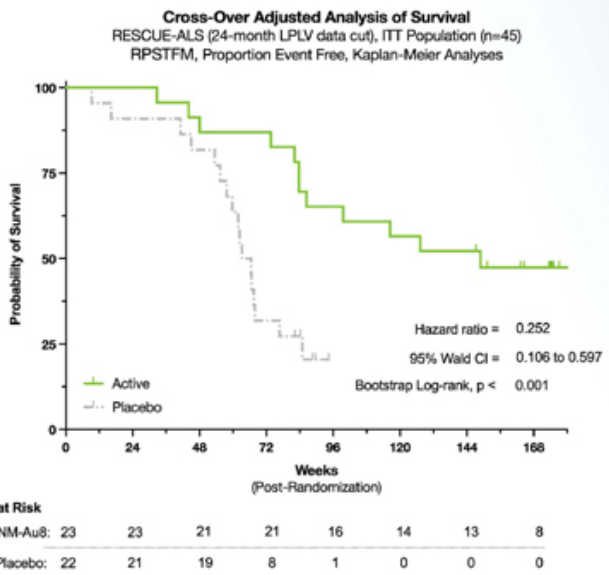
Data on File, Clene Nanomedicine, Inc.

RESCUEALS Up to 19.3 Month Survival Benefit vs. Original Placebo

Unadjusted Survival Difference: 10.1 Months



Cross-Over Adjusted Survival Difference: 19.3 Months



Data on File, Clene Nanomedicine, Inc.

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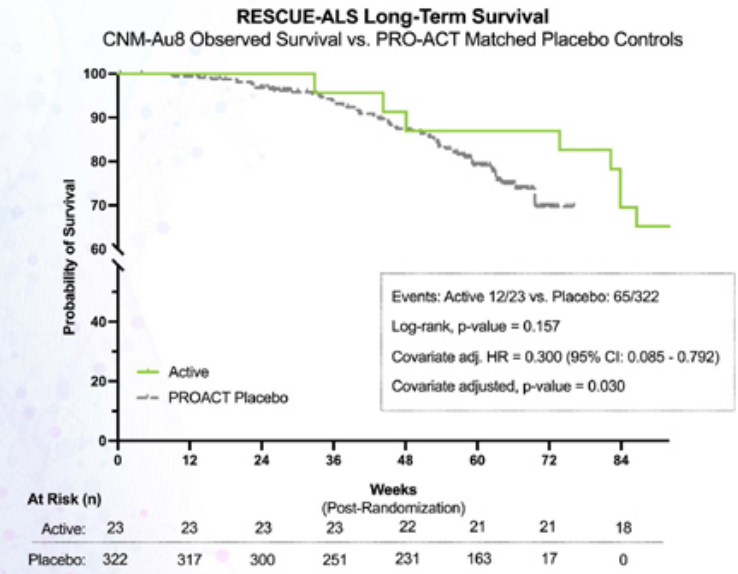
Long-Term Survival Benefit Compared to Historical Matched PRO-ACT Placebo Controls



At Risk (n)								
Active:	23	23	23	23	22	21	21	18
Placebo:	322	317	300	251	231	163	17	0

CNM-Au8 treatment demonstrated a significant survival benefit:

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

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

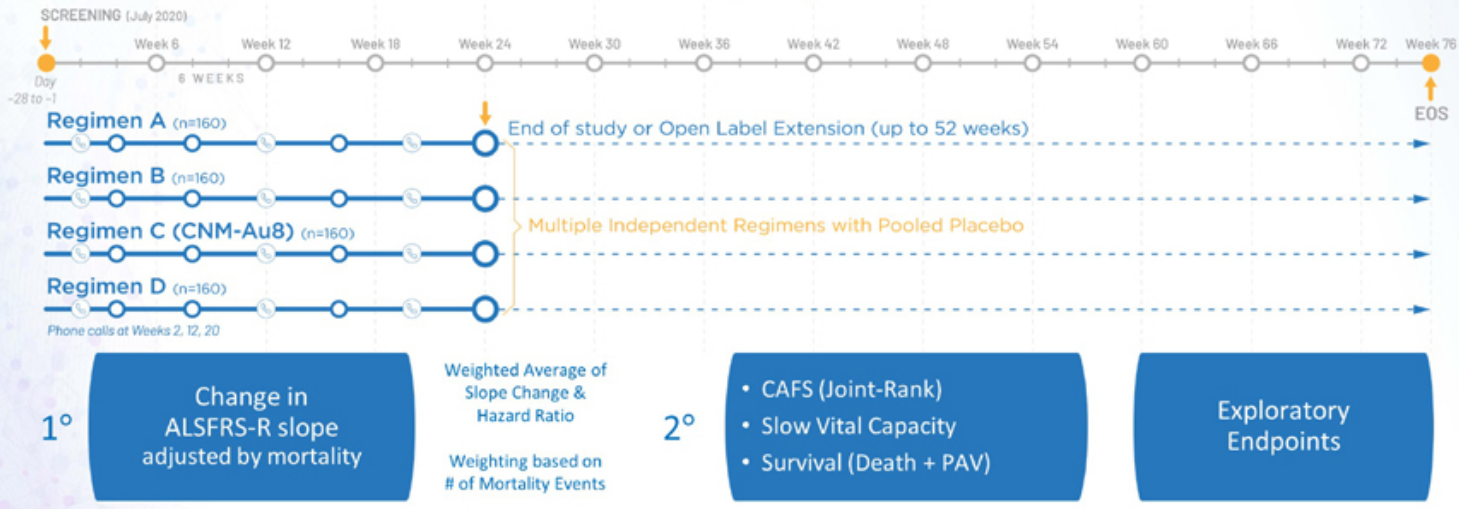
Time to all-cause mortality amongst participants originally randomized to CNM-Au8 compared to propensity matched placebo controls derived from the PRO-ACT database (n=322). Covariates included: Onset Age, Sex, BMI, Pre-Treatment ALSFRS-R Slope (Delta-FS), ALSFRS-R Total Score, Vital Capacity (% predicted),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

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

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

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

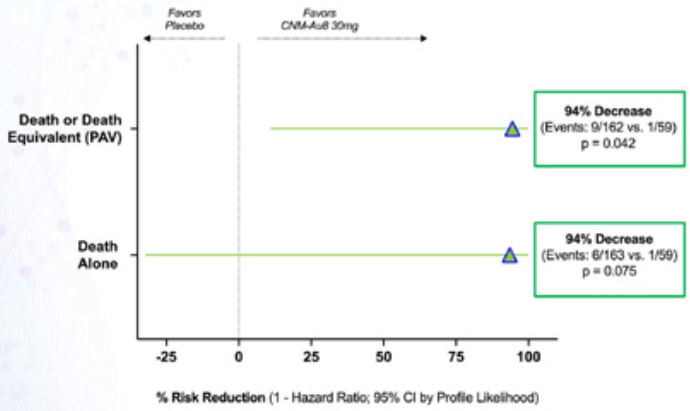
CLENE NANOMEDICINE

Survival Signal | >90% Reduced Risk of Death with CNM-Au8 30mg

HEALEY ALS Platform Trial

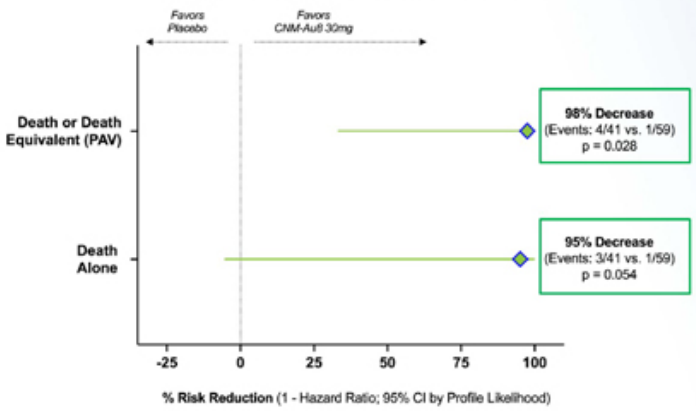
Shared Placebo Across Regimens

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.

Data on File, Clene Nanomedicine, Inc.

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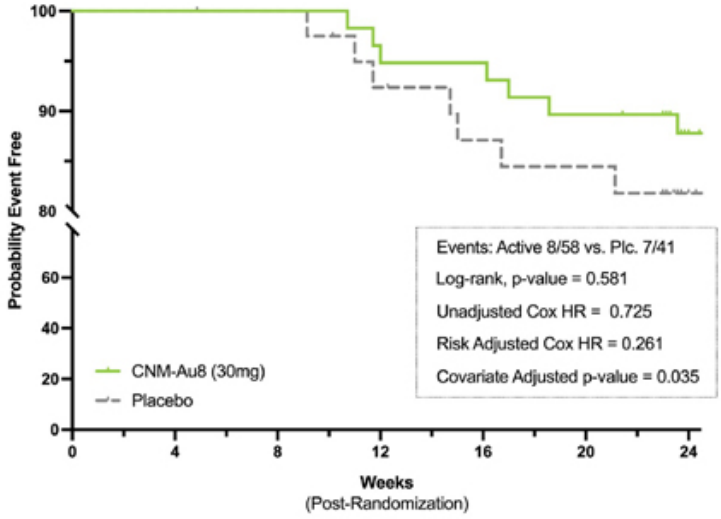
Delayed Time to ALS Clinical Worsening

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

HEALEY ALS Platform Trial

Time to Clinical Worsening | CNM-Au8 30mg
First Occurence 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)



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.

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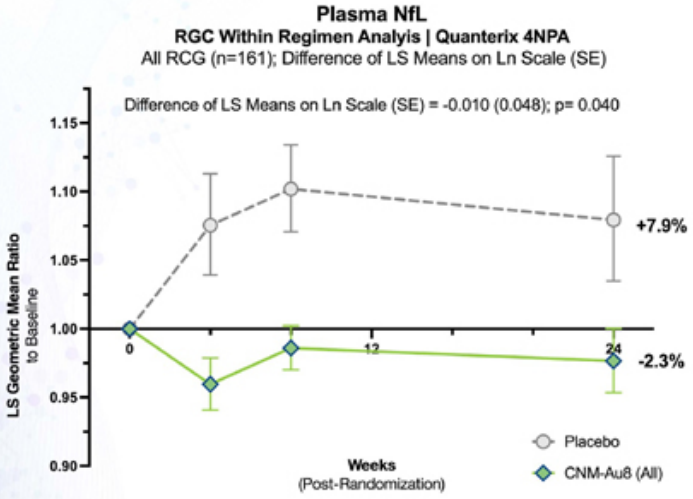
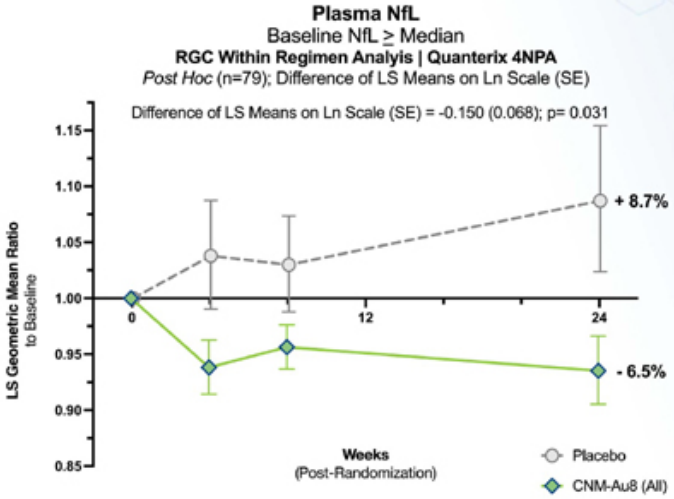
Significant Biomarker Plasma NfL Difference

CNM-Au8 vs. Placebo | All RGC Participants During Double-Blind Period

HEALEY ALS Platform Trial





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

Data on File, Clene Nanomedicine, Inc.

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Long-Term Survival | Propensity Matched Placebo

PRO-ACT Placebo Matching vs. Regimen C CNM-Au8 30mg

HEALEY ALS Platform Trial

Baseline Values Mean (SD) or Percent (%)	HEALEY Regimen C		Integrated Meta-Analysis	
	CNM-Au8 30mg (n=59)	PRO-ACT Placebo Matches (i) (n=322)	CNM-Au8 30mg (n=82)	PRO-ACT Placebo Matches (ii) (n=322)
Onset Age	55.4 (10.4)	55.5 (11.0)	55.4 (11.1)	55.0 (11.4)
Sex (Male, %)	56%	62%	56%	65%
BMI (kg/m²)	27.4 (5.3)	26.5 (4.9)	27.2 (5.2)	26.6 (5.0)
ALSFRS-R (Total Score)	34.5 (5.8)	37.7 (5.5)	35.7 (6.3)	37.9 (5.5)
Delta-FS (Pre-treatment slope)	0.77 (0.58)	0.75 (0.50)	0.76 (0.57)	0.74 (0.51)
Vital Capacity (% predicted)	74.4 (16.0)	89.2 (17.0)	77.3 (17.1)	89.3 (16.9)
Diagnostic Delay (months)	9.8 (5.2)	8.8 (5.2)	10.6 (6.1)	8.9 (5.4)
Site of Onset (Bulbar, %)	17%	20%	21%	20%
Riluzole Treatment (%)	76%	98%	82%	98%

Source(s): Data on File, Cene Nanomedicine, Inc. (Table 14.1.4.1.1 Pooled vs. PROACT; Table 14.1.4.1.2 Healey vs. PROACT)
Notes: Vital capacity reported as SVC or FVC based on individual study characteristics.

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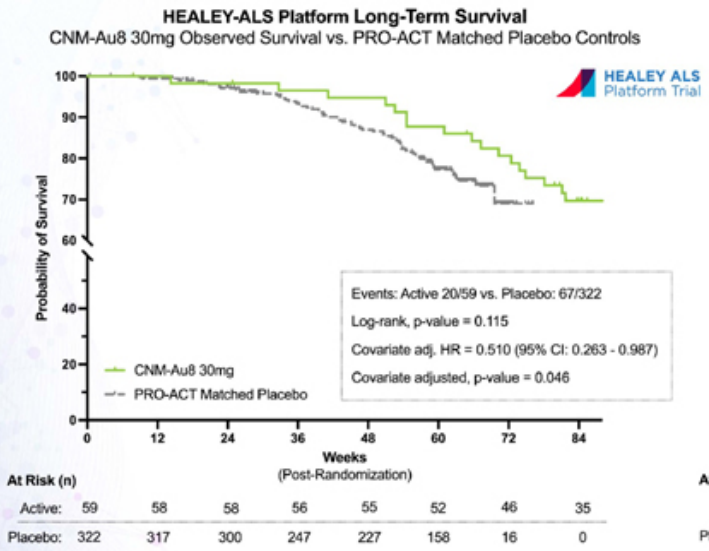
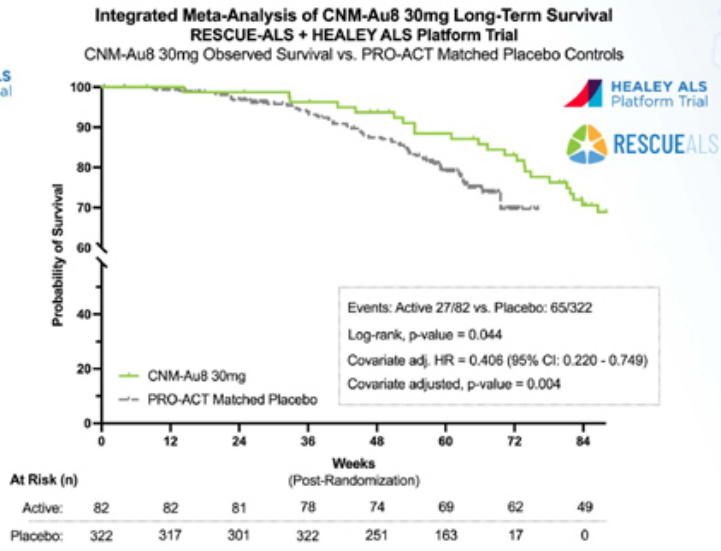
Long-Term Survival | Propensity Matched Placebo

PRO-ACT Placebo vs. CNM-Au8 30mg

CNM-Au8 30mg HEALEY



CNM-Au8 30mg Integrated Meta-Analysis



Covariates: Onset Age, Sex, BMI, Pretreatment ALSFRS-R Slope, ALSFRS-R Total at Baseline, Vital Capacity % at Baseline, Diagnostic Delay

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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
- 92% treated with background DMTs (inc 53% monoclonal antibodies, 32% oral)
- n=73 of 150 planned (~50%) study ended prematurely due to COVID-19 pandemic enrollment challenges
- Modified ITT (mITT) Analysis Population; 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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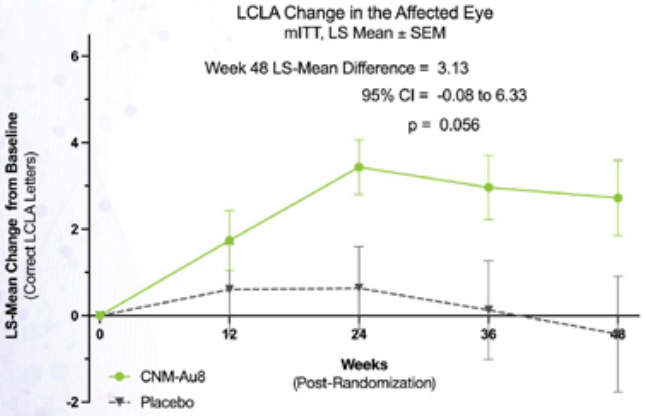
CNM-Au8 Demonstrated Vision and Global Neurological Improvement in Stable MS patients on DMTs

VISIONARY-MS STUDY

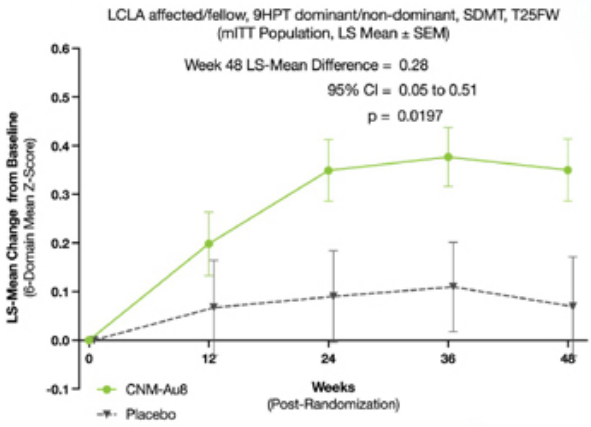
Significantly Improved Vision

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

Data on File, Clene Nanomedicine, Inc.

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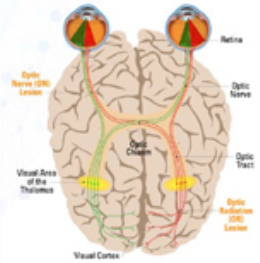
CNM-Au8 Improved Information Signal in the Visual Pathway

VISIONARY-MS STUDY

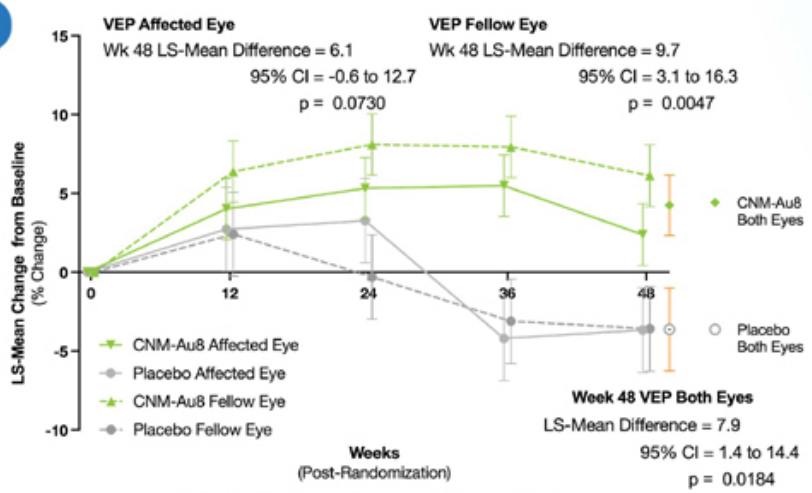
Visual Evoked Potentials (VEP)



Increased Amplitude (Signal Strength)

From the Eye to the Brain's Visual Cortex

mf-VEP Mean Amplitude Percent (%) Change
ITT Population, LS Mean ± SEM, Segments Nested by Participant



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

Data on File, Clene Nanomedicine, Inc.

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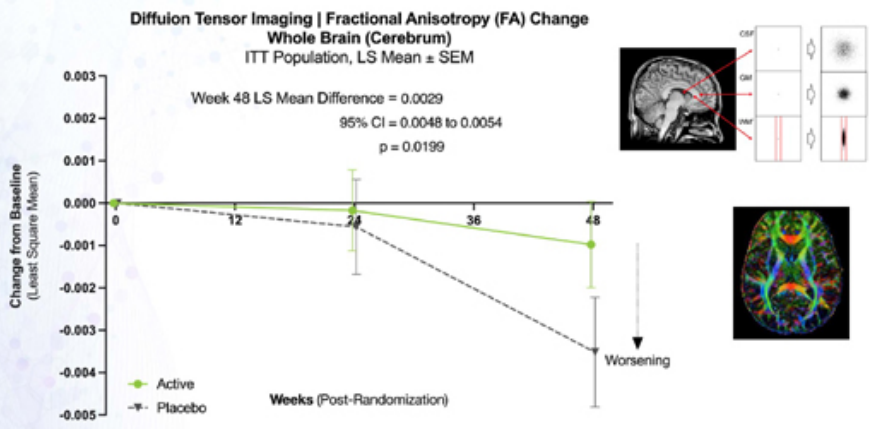
CNM-Au8 Preserved White Matter Integrity Throughout the Brain

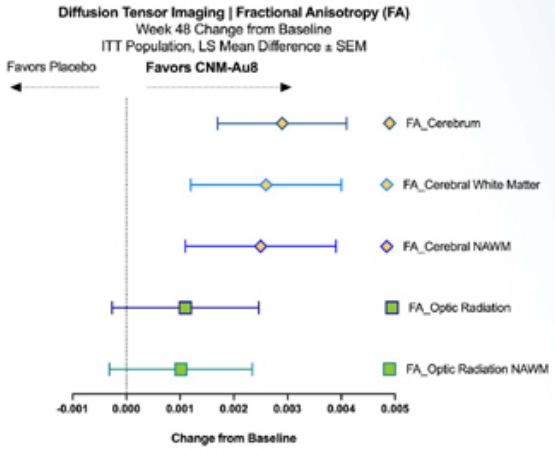
VISIONARY-MS STUDY

Advanced MRI Techniques

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

Data on File, Clene Nanomedicine, Inc.

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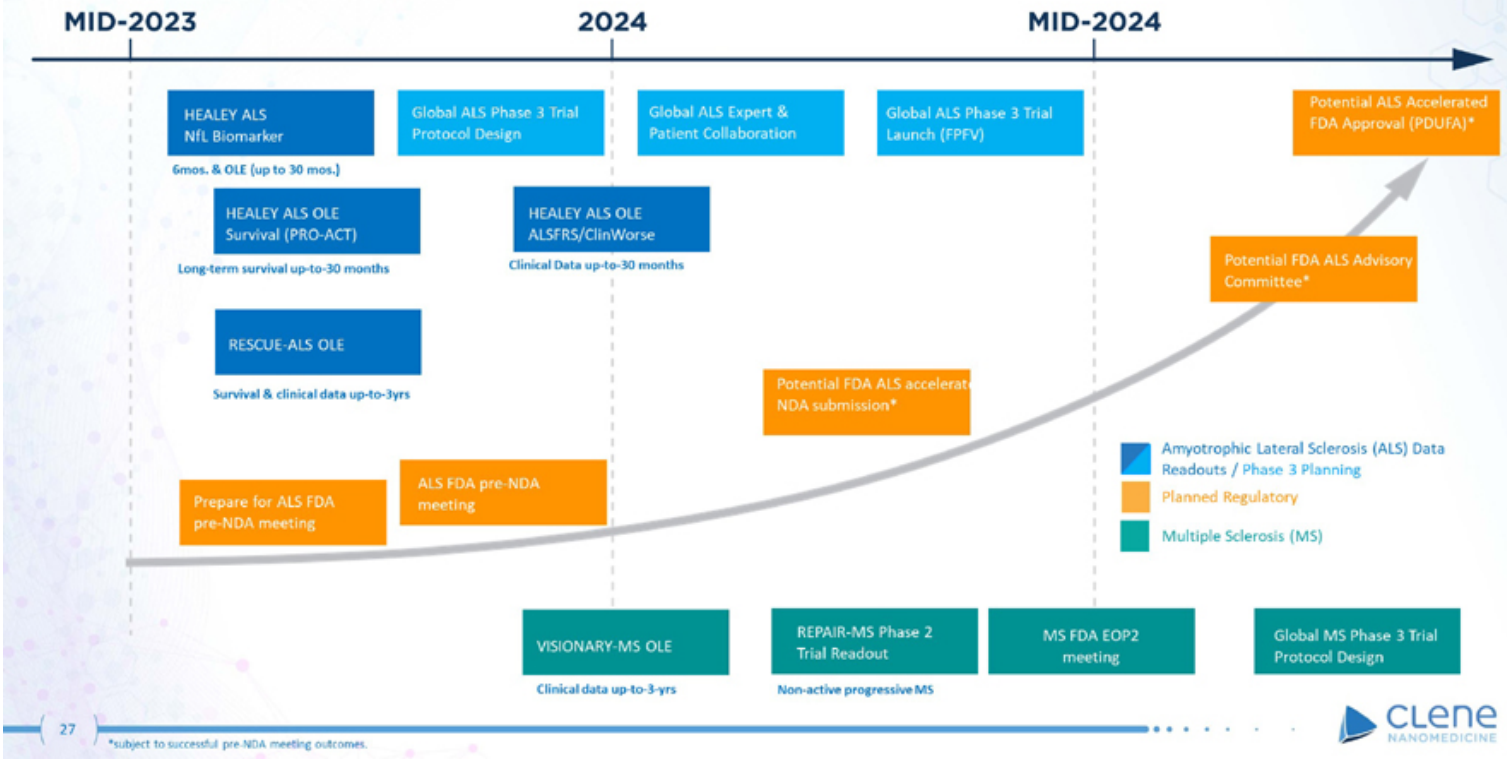
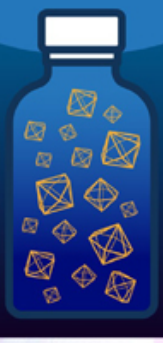
Clene | CNM-Au8 Path to Regulatory Approval



Evidence Supports CNM-Au8 Therapeutic Potential to Treat Neurodegenerative Diseases

CNM-Au8®
a gold nanocrystal suspension, in development as the first cellular energetic catalyst to remyelinate[1] & protect neurological function



RESCUEALS

75% decreased risk of death in ALS through 168 weeks

HEALEY ALS Platform Trial

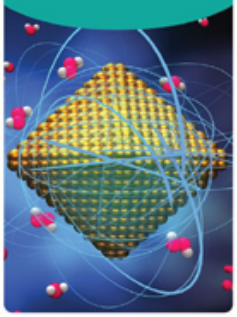
>90% decreased risk of death with 30 mg in ALS

VISIONARY-MS STUDY

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

>500
patient years of CNM-Au8 clinical exposure

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



As of Sept 30, 2023, cash and equivalents on hand (unaudited):

$42.1M

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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Version: 7-November-2023