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 15, 2022

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** **(Address of Principal Executive Offices)**	**84121** **(Zip Code)**

Registrant's telephone number, including area code: (801) 676-9695

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 August 15, 2022, Clene Inc. (the "Company") issued a press release announcing its second quarter financial results and recent operating highlights for its quarter ended June 30, 2022. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K (the "Current Report") 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.

Corporate Presentation

In connection with the press release announcing the Company's second quarter operating and financial results for its quarter ended June 30, 2022, 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.

VISIONARY-MS Clinical Trial Topline Results

On August 15, 2022, the Company issued a press release announcing positive topline results for CNM-Au8® in the Phase 2 VISIONARY-MS trial in multiple sclerosis ("MS"). The Company also hosted a conference call and webcast on August 15, 2022 to discuss the VISIONARY-MS topline results. A copy of the press release and presentation are furnished as Exhibit 99.3 and Exhibit 99.4, respectively, to this Current Report and are incorporated herein by reference.

The information furnished in this Item 7.01, including Exhibit 99.2, Exhibit 99.3, and Exhibit 99.4, 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 August 15, 2022, announcing the Company's operating and financial results for its quarter ended June 30, 2022.
99.2	Corporate Presentation.
99.3	Press Release dated August 15, 2022, announcing positive topline results for CNM-Au8 in the Phase 2 VISIONARY-MS trial in multiple sclerosis.
99.4	VISIONARY-MS presentation dated August 15, 2022.
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 15, 2022

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

Clene Reports Second Quarter 2022 Financial Results and Recent Operating Highlights

- ***Topline results from the Phase 2 VISIONARY-MS clinical trial with CNM-Au8® met the primary and secondary endpoints of Low Contrast Letter Acuity (LCLA) and modified Multiple Sclerosis Functional Composite (mMSFC) compared to placebo over 48 weeks in the mITT population***
- ***Updated data from RESCUE-ALS demonstrate a statistically significant decrease in mortality in participants who entered open-label extension study (5 CNM-Au8 deaths vs. 14 placebo deaths, HR=0.301, p=0.0143)***
- ***Topline results from HEALEY ALS Platform Trial expected this quarter***
- ***Cash, cash equivalents and marketable securities of $26.3 million as of June 30, 2022***
- ***Entered into a $3.0 million loan facility from State of Maryland to support development of commercial manufacturing facility***

SALT LAKE CITY, August 15, 2022 -- Clene Inc. (Nasdaq: CLNN) (along with its subsidiaries, "Clene") and its wholly owned subsidiary Clene Nanomedicine Inc., a clinical-stage biopharmaceutical company focused on revolutionizing the treatment of neurodegenerative disease, today reported its second quarter 2022 and recent operating highlights.

"We are on the cusp of a transformative period for the Company as we await a key data readout in ALS for our lead asset, CNM-Au8®," said Rob Etherington, President and CEO of Clene. "The ALS patient population is desperate for new treatments to help mitigate the disease course and following the statistically significant survival benefits demonstrated in our open label trial, we are hopeful that we can deliver an effective therapy for people living with ALS."

Second Quarter 2022 and Recent Operating Highlights

CNM-Au8®, a gold nanocrystal suspension, for the treatment of amyotrophic lateral sclerosis (ALS)

- Topline data from the HEALEY ALS Platform Trial, led by the Sean M. Healey & AMG Center for ALS at Massachusetts General Hospital, are expected this quarter.
- Demonstrated statistically significant reduction in mortality in the open-label extension of the RESCUE-ALS trial. As of the July 5, 2022, data cutoff, early CNM-Au8 treatment resulted in a significant survival benefit (5 CNM-Au8 deaths vs. 14 placebo deaths, HR=0.301, p=0.0143). CNM-Au8 was well-tolerated, and the safety profile was consistent with previously reported data.
- Received European Orphan Drug Designation for CNM-Au8 in amyotrophic lateral sclerosis (ALS) from the European Medicines Agency (EMA) Committee for Orphan Medicinal Products (COMP).
- Presented five posters from the RESCUE-ALS trial at the European Network to Cure ALS (ENCALS) conference on June 1-3, 2022. The data included information on the neuroprotective efficacy and survival benefits of CNM-Au8 in ALS as well as on patient quality of life and biomarker data. The posters are available in the Scientific Posters & Presentations section of the Clene website.
- Clene continues to support expanded access programs, providing CNM-Au8 treatment at five clinical sites for up to 55 total participants with ALS.

CNM-Au8 for the treatment of multiple sclerosis (MS)

- Reported topline results from the Phase 2 VISIONARY-MS clinical trial with CNM-Au8 that met the primary and secondary endpoints of LCLA and mMSFC compared to placebo over 48 weeks in a modified intent to treat (mITT) population.
  - o Primary endpoint: LCLA letter change in the clinically affected eye (least squares [LS] mean difference, 3.13; 95% CI: -0.08 to 6.33, p = 0.056)
  - o Secondary outcomes:

        - mMSFC mean standardized change (LS mean difference, 0.28; 95% CI: 0.04 to 0.52, p = 0.0207)
        - mMSFC average rank score (LS mean difference, 13.38; 95% CI: 2.83 to 23.94, p = 0.0138)
        - Time to first repeated clinical improvement to Week 48 (45% vs. 29%, log-rank p=0.3991)
    - CNM-Au8 treatment was well-tolerated and there were no significant safety findings reported.
    - Results provide support to advance CNM-Au8 into Phase 3 clinical development.
- As announced in February 2022, the trial was stopped prematurely due to COVID-19 pandemic operational challenges, limiting enrollment to 73 out of the 150 planned participants. Due to the limited enrollment, the threshold for significance was pre-specified at p=0.10 prior to database lock. The primary analysis was conducted in a modified intent to treat (mITT) population, which censored invalid data. The mITT population excluded data from a single site (n=9) with LCLA testing execution errors and the timed 25-foot walk data from one subject with a change in mobility assist device. The ITT results were directionally consistent with the mITT results, although the ITT results were not significant.
- Clene has initiated a second cohort of the more severe non-active, progressive MS population in the REPAIR-MS Phase 2 clinical trial to confirm target engagement following the target engagement demonstrated in the first cohort of relapsing MS patients.

CNM-ZnAg for the treatment of COVID-19

- Topline results for the ZnAg COVID Phase 2 clinical trial in acutely symptomatic, non-hospitalized COVID-19 patients in Brazil are expected this quarter.

Second Quarter 2022 Financial Results

Clene's cash, cash equivalents and marketable investments securities totaled $26.3 million as of June 30, 2022, compared to $50.3 million as of December 31, 2021.

Research and development expenses were $9.2 million for the quarter ended June 30, 2022, compared to $6.5 million for the same period in 2021. The year-over-year increase is primarily attributable to the development of CNM-Au8 and CNM-ZnAg (including the rapid completion of the COVID study due to a viral wave leading to increased patient recruitment), rent expense for the newly-leased facility in Elkton, Maryland, and personnel expenses due to increased headcount as a result primarily of increased manufacturing hours, partially offset by decreased stock-based compensation expense.

General and administrative expenses were $4.5 million for the quarter ended June 30, 2022, compared to $6.9 million for the same period in 2021. The year-over-year decrease is primarily attributable to a decrease in directors' and officers' insurance costs, stock-based compensation expense and other general and administrative costs, including decreases in investor relations, accounting and consulting fees. These decreases were offset by increases in personnel compensation due to increased headcount as well as increases on other miscellaneous general and administrative expenses.

Clene reported a net loss of $4.5 million, or $0.07 per share, for the quarter ended June 30, 2022, compared to a net loss of $3.4 million, or $0.05 per share, for the same period in 2021. Included in net loss for the quarter ended June 30, 2022, is an unrealized gain from the change in fair value of contingent earn-out liabilities of $9.4 million, compared to an unrealized gain of $9.9 million in the prior year period.

About Clene
Clene is a clinical-stage biopharmaceutical company focused on revolutionizing the treatment of neurodegenerative disease by targeting energetic failure, an underlying cause of many neurological diseases. 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.

About CNM-Au8®
CNM-Au8 is an oral suspension of gold nanocrystals developed to restore neuronal health and function by increasing energy production and utilization. The catalytically active nanocrystals of CNM-Au8 drive critical cellular energy producing reactions that

enable neuroprotection and remyelination by increasing neuronal and glial resilience to disease-relevant stressors. CNM-Au8® is a federally registered trademark of Clene Nanomedicine, Inc.

About CNM-ZnAg

CNM-ZnAg, a proprietary zinc-silver ionic solution, has demonstrated broad antiviral and antimicrobial activity.

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

Source: Clene Inc.

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

	Three Months Ended June 30,		Six Months Ended June 30,	
	2022	2021	2022	2021
Revenue:				
Product revenue	$ 2	$ 138	$ 9	$ 337
Royalty revenue	33	63	56	77
Total revenue	35	201	65	414
Operating expenses:				
Cost of revenue	—	555	—	798
Research and development	9,166	6,472	17,746	12,747
General and administrative	4,464	6,949	9,250	12,339
Total operating expenses	13,630	13,976	26,996	25,884
Loss from operations	(13,595)	(13,775)	(26,931)	(25,470)
Other income (expense), net:				
Interest expense	(751)	(26)	(1,533)	(577)
Gain on extinguishment of notes payable	—	—	—	647
Gain on termination of lease	—	—	420	—
Change in fair value of common stock warrant liability	20	133	2	133
Change in fair value of Clene Nanomedicine contingent earn-out	8,310	8,640	8,253	(16,970)
Change in fair value of Initial Stockholders contingent earn-out	1,066	1,232	1,054	(1,729)
Australia research and development credit	356	375	655	714
Other income (expense), net	60	(2)	192	1
Total other income (expense), net	9,061	10,352	9,043	(17,781)
Net loss before income taxes	(4,534)	(3,423)	(17,888)	(43,251)
Income tax benefit	—	72	—	144
Net loss	(4,534)	(3,351)	(17,888)	(43,107)
Other comprehensive loss:				
Unrealized loss on available-for-sale securities	(37)	—	(87)	—
Foreign currency translation adjustments	(110)	(61)	(60)	(37)
Total other comprehensive loss	(147)	(61)	(147)	(37)
Comprehensive loss	$ (4,681)	$ (3,412)	$ (18,035)	$ (43,144)
Net loss per share-- basic and diluted	$ (0.07)	$ (0.05)	$ (0.28)	$ (0.71)
Weighted average common shares used to compute basic and diluted net loss per share	63,335,271	61,165,018	63,095,400	60,919,340

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

	June 30, 2022	December 31, 2021
ASSETS		
Current assets:		
Cash and cash equivalents	$ 7,253	$ 50,288
Marketable securities	19,033	—
Accounts receivable	—	49
Inventory	107	41
Prepaid expenses and other current assets	5,194	4,205
Total current assets	31,587	54,583
Restricted cash	58	58
Right-of-use assets	4,808	3,250
Property and equipment, net	8,089	5,172
TOTAL ASSETS	$ 44,542	$ 63,063
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 4,526	$ 1,923
Accrued liabilities	2,566	3,610
Operating lease obligations, current portion	440	347
Finance lease obligations, current portion	123	146
Total current liabilities	7,655	6,026
Operating lease obligations, net of current portion	5,858	4,370
Finance lease obligations, net of current portion	55	97
Notes payable	15,551	14,484
Convertible notes payable	4,709	4,598
Common stock warrant liability	167	474
Clene Nanomedicine contingent earn-out	9,847	18,100
Initial Stockholders contingent earn-out	1,263	2,317
TOTAL LIABILITIES	45,105	50,466
Commitments and contingencies		
Stockholders' equity (deficit):		
Common stock, $0.0001 par value: 150,000,000 shares authorized; 63,421,908 and 62,312,097 shares issued and outstanding at June 30, 2022 and December 31, 2021, respectively	6	6
Additional paid-in capital	180,534	175,659
Accumulated deficit	(181,189)	(163,301)
Accumulated other comprehensive income	86	233
TOTAL STOCKHOLDERS' EQUITY (DEFICIT)	(563)	12,597
TOTAL LIABILITIES AND STOCKHOLDERS' EQUITY	$ 44,542	$ 63,063

Exhibit 99.2


Corporate Presentation
August 2022
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.

CLENE | Entering a Transformative Period

Significant Opportunity

- Targeting neurodegenerative diseases such as ALS and Multiple Sclerosis
- >$1B commercial opportunity in each indication

CNM-Au8® Emerging Clinical Results

- Long-term follow-up of RESCUE-ALS Phase 2 participants demonstrated statistically significant survival benefit; 70% decreased risk of death in ALS
- Positive Topline Results from the Phase 2 VISIONARY-MS Trial;CNM-Au8 demonstrated neurological improvements in stable relapsing MS as adjunctive therapy to immunomodulatory DMTs
- HEALEY ALS Platform Trial Phase 2/3 topline results expected in 3Q 2022

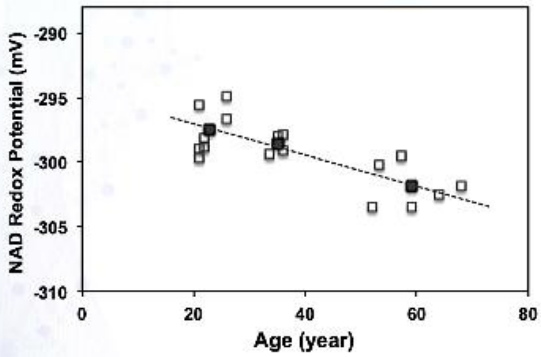
Proprietary Platform

Strong IP

- Proprietary nanotherapeutic manufacturing, scalable to commercialization
- Strong IP, including 150+ granted patents and manufacturing trade secrets

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

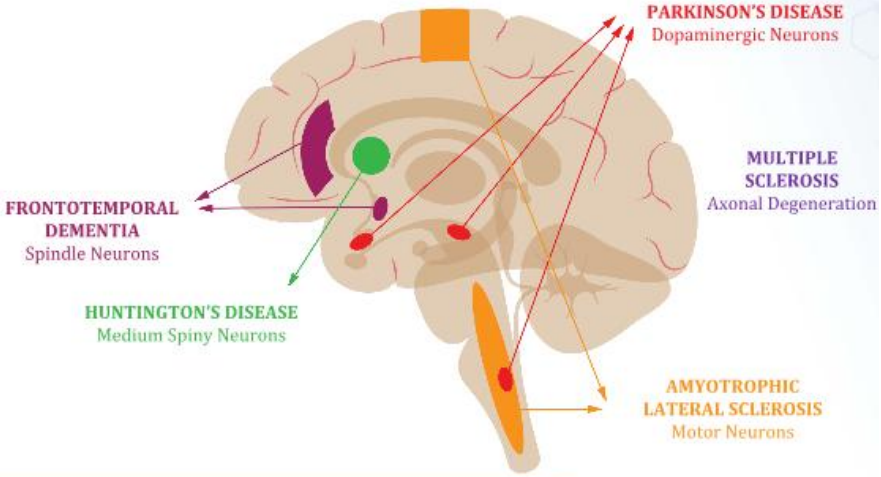
Brain Energy Potential Declines With Normal Aging



~0.5% NAD^+/NADH unit decline per decade
(~0.13 mV units per year by ^{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



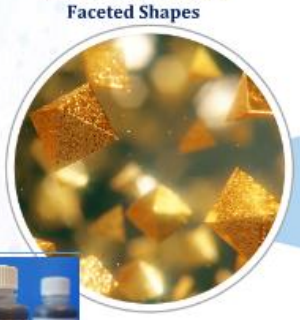
Energetic impairments in the CNS both pre-dispose and drive progression in neurodegenerative diseases

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.

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 and restore neuronal function.

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

clene NANOMEDICINE

Preclinical Evidence of Remyelination and Neuroprotection

Remyelination

CNM-Au8 Supports Remyelination

www.nature.com/scientificreports

SCIENTIFIC REPORTS
nature research

OPEN

Nanocatalytic activity of clean-surfaced, faceted nanocrystalline gold enhances remyelination in animal models of multiple sclerosis

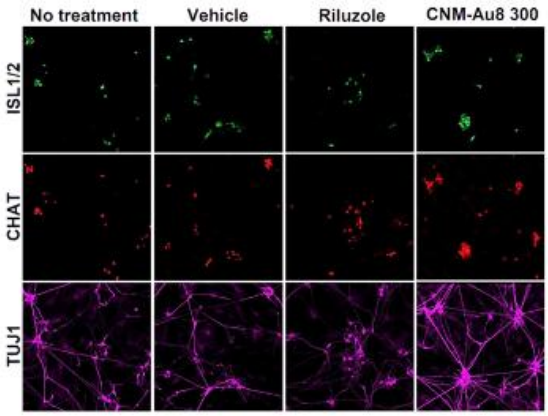
Andrew P. Robinson[1,2], Joanne Zhongyan Zhang[1,2], Haley E. Titus[1], Molly Karl[1], Mikhail Merzliakov[1], Adam R. Dorfman[1], Stephen Karlik[3], Michael G. Stewart[1], Richard K. Watt[1], Benjn D. Facer[1], Jan D. Facer[1], Noah D. Christon[1], Karen S. Ho[1,2], Michael T. Hotchkin[1,2], Mark G. Mortenson[1,2], Robert H. Miller[1,4] & Stephen D. Miller[1,4]

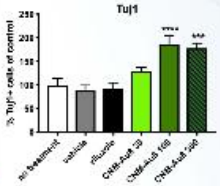
Robinson et al. Sci Rep. 2020 Feb 11;10(1):1936.

Neuroprotection

CNM-Au8 Improves ALS Motor Neuron Function & Survival

Induced Pluripotent Stem Cell *In Vitro* Results – Motor Neuron Markers





Karen S. Ho et al. "Redox-enhancing nanocatalysis improves motor neuron survival in vitro and SOD1 mouse motor function and survival in vivo." Presented at 30th International Symposium on ALS/MND 2019. December 4-6, 2019.

CNM-Au8 novel MOA may be complementary to existing therapies to enable better disease control

CLene NANOMEDICINE

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 2028[1]

Current drugs are largely ineffective, mostly generic.

2-5 YEARS[2] LIFE EXPECTANCY

100% FATAL

Multiple Sclerosis (MS)

MS PATIENTS GLOBALLY 2.2M

$23B MARKET[3]

Existing treatments only target immunomodulation

EMERGING EVIDENCE THAT EARLY MS IS NEURODEGENERATIVE

Parkinsons Disease (PD)

2ND MOST COMMON DISORDER

$6B PROJECTED BY 2026[4]

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

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

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

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

Building the Case for Neuroprotection & Remyelination

RepairPD
RepairMS

RESCUEALS
HEALEY ALS Platform Trial

VISIONARY-MS

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

RESCUE-ALS trial supports CNM-Au8 slowed disease progression in ALS

Demonstrated statistically significant survival benefit; 70% decreased risk of death

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

REPAIR-MS Phase 2 in non-active progressive MS underway

HEALEY ALS Platform Trial topline results expected 3Q 2022

Results provide support to advance CNM-Au8 into Phase 3 clinical development

Growing Body of Evidence from Multiple Trials Supports CNM-Au8 Clinical Potential

CLene NANOMEDICINE

Over 350 Years of Subject Exposure Without Identified Safety Signals Across ALS, MS & PD

Clean Toxicology Findings

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

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

Well Tolerated Adverse Event (AE) Profile

Assessed as Predominantly Mild-to-Moderate Severity and Transient

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

Patient Exposure Across ALS, MS & PD

Over 350 Years of Subject Exposure Without Identified Safety Signals

- Long-term dosing experience up to 125 weeks

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 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)

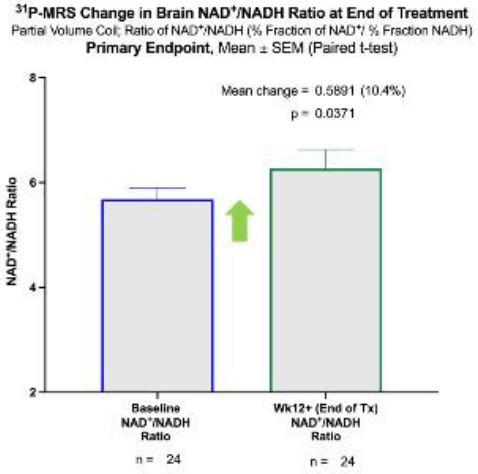
RepairPD
Early Parkinson's Disease

RepairMS
Stable Relapsing MS

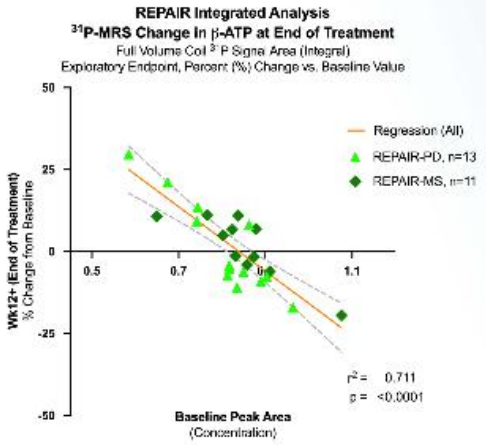
RepairMS
Non-Active Progressive MS
(Ongoing)

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)



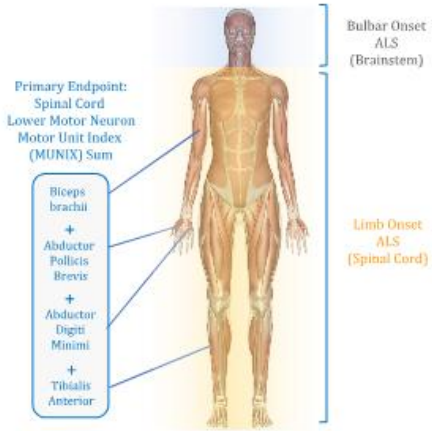
1. Zhu et al. Proc Natl Acad Sci USA 2015 Mar 3;112(9):2876-81. 2. Glanzman et al Improvement of Brain Energy Metabolism in Relapsing Multiple Sclerosis Patients - Results from Phase 2 REPAIR-MS Clinical Trial With CNM-Au8. ACTRIMS February 2022

CLene NANOMEDICINE

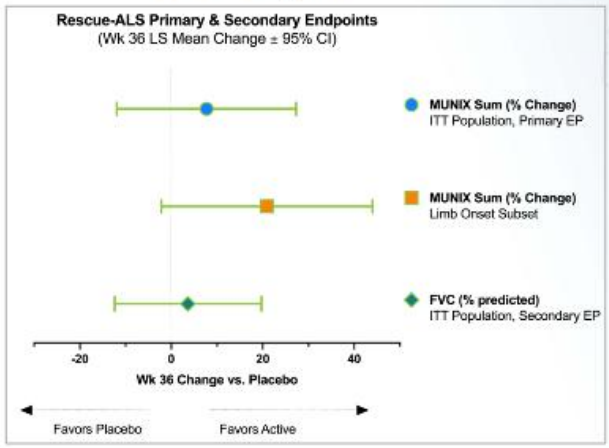
RESCUEALS Encouraging Efficacy Signals in Phase 2 Trial

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

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



1° & 2° Endpoints



Results in favor of CNM-Au8 treatment but study underpowered

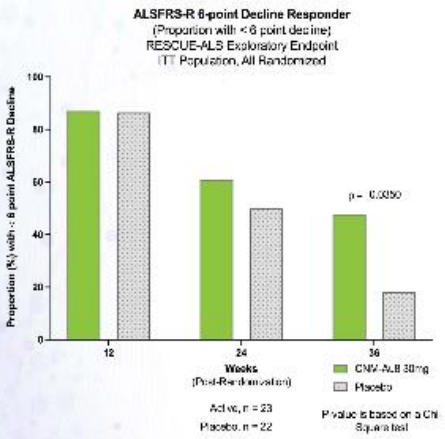
Vucic et al. RESCUE-ALS Trial Results: A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study of CNM-Au8 to Slow Disease Progression in Amyotrophic Lateral Sclerosis; Presented at International Symposium on ALS/MND; 7-10 December 2021.)

CLene NANOMEDICINE

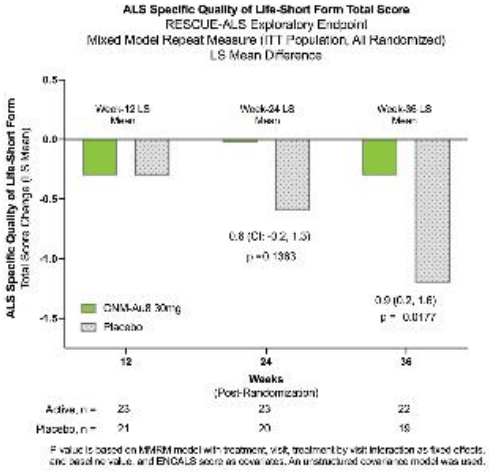
CNM-Au8 Improved Patient Function and QOL, and Slowed ALS Disease Progression

Across Multiple Pre-specified Exploratory Endpoints

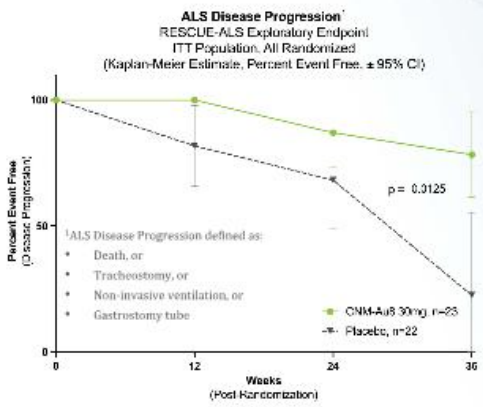
Proportion with <6 point decline



ALS Specific QOL



ALS Disease Progression



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

RESCUEALS CAFS Results: Slowed Disease Progression

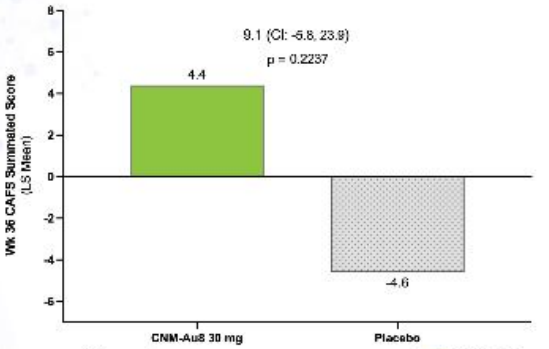
Exploratory Endpoint Pre-specified

CAFS

Survival

ALSFRS-R Decline

CAFS Joint Rank: (i) Survival and (ii) ALSFRS-R Change
RESCUE-ALS Exploratory Endpoint
ANCOVA Model (ITT Population, All Randomized)
Week 36 LS Mean Difference



Active, n = 23
Placebo, n = 22

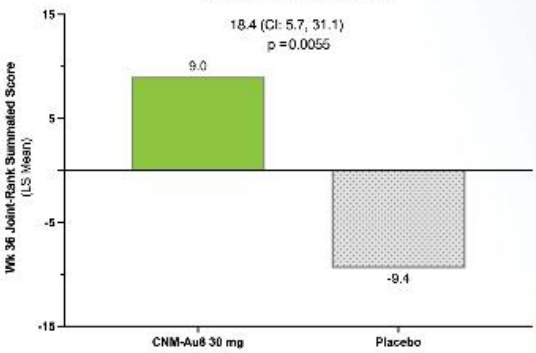
CNM-Au8 30 mg
Placebo

P-value is based on ANCOVA model with baseline ENCALS score as a covariate. Change in ALSFRS-R total score and date of death were combined to determine the CAFS score.

Modified CAFS

King's Clinical Stage 4

Joint-Rank of (I) Survival, (II) King's Clinical Stage 4, and (III) ALSFRS-R Change
RESCUE-ALS *Post Hoc* Endpoint
ANCOVA Model (ITT Population, All Randomized)
Week 36 LS Mean Difference



Active, n = 23
Placebo, n = 22

CNM-Au8 30 mg
Placebo

P-value is based on ANCOVA model with baseline ENCALS score as a covariate. Change in ALSFRS-R total score, date of non-invasive ventilation or gastrostomy, and date of death were combined to determine the joint-rank score.

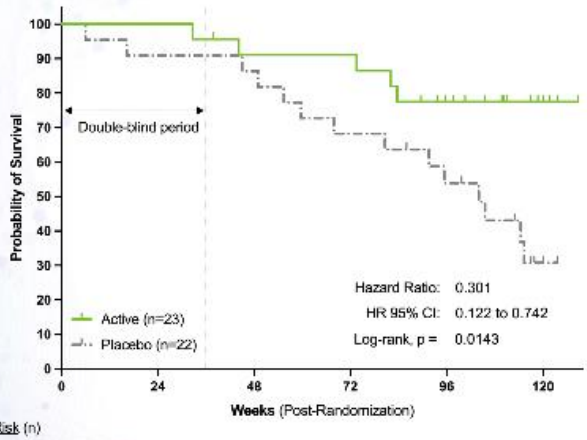
Data on File, Clene Nanomedicine, Inc.

RESCUEALS Demonstrated Significant Impact on Long-Term Survival with 70% Decreased Risk of Death

RESCUE-ALS Active vs. Placebo Randomization

Long-Term Observed Survival (Interim Analysis)

Long-Term Survival: Originally Randomized Active vs. Placebo
Interim Analysis (5-July-2022), ITT Population, All Subjects from Randomization
(Long-term vital status including all study withdrawals)



At Risk (n)

CNM-Au8:	23	23	20	20	14	6
Placebo:	22	20	19	15	11	2

Early CNM-Au8 treatment demonstrated a significant survival benefit:

- Long-term follow-up compared to initial placebo randomization*
- 70% decreased risk of death

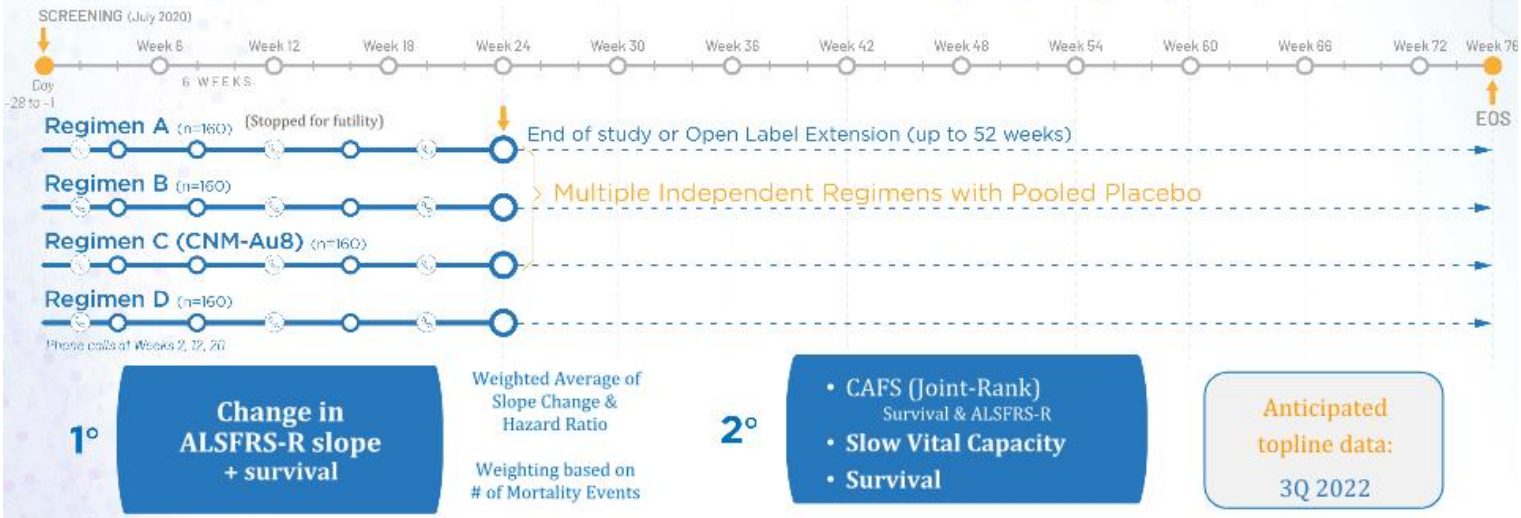
*9-month delayed treatment start or no treatment

Data on File, Clene Nanomedicine, Inc.

Phase 2/3
HEALEY ALS Platform Trial

A Multi-center, Randomized Double-Blind, Placebo-Controlled Clinical Trial Assessing the Efficacy, Safety, Tolerability, Pharmacokinetics, and Pharmacodynamics of CNM-Au8 in Participants with Amyotrophic Lateral Sclerosis

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



1° **Change in ALSFRS-R slope + survival**

Weighted Average of Slope Change & Hazard Ratio

Weighting based on # of Mortality Events

2°
- CAFS (Joint-Rank) Survival & ALSFRS-R
- **Slow Vital Capacity**
- **Survival**

Anticipated topline data: 3Q 2022

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

CLene NANOMEDICINE

VISIONARY-MS STUDY Core Design Elements

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

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

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

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

9HPT SDMT T25FWT LCLA

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

clene NANOMEDICINE

Baseline Demographics Showed Balanced Randomization and Clinical Profile

VISIONARY-MS

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

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

Data on File, Clene Nanomedicine, Inc.

CLENE NANOMEDICINE

Pandemic Significantly Impacted Study Conduct

- Study was ended prematurely due to COVID enrollment challenges (as announced February 2022)
  - Enrolled 73 of 150 planned
  - Underpowered due to limited enrollment
  - Pre-specified statistical threshold set at p=0.10
  - COVID restrictions precluded direct Sponsor monitoring
- Objectives
  - Learn from results
  - Evaluate strength of evidence for further MS development

Data on File, Clene Nanomedicine, Inc.

modified ITT (mITT) Analysis Population

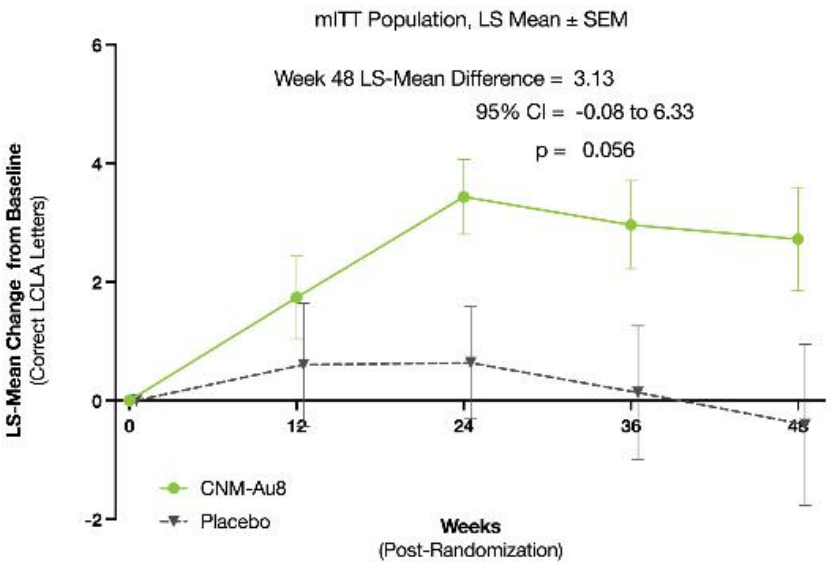
- Censored observations included
  - Change in mobility assist device (cane to walker) for T25FW (n=1)
  - Invalid data from 1 of 11 sites (n=9) with LCLA testing execution errors
    - Multiple testing locations with different light boxes and varying ambient lighting conditions
    - In consultation with study Principal Investigator and external experts, all clinical data from the site were excluded

Data on File, Clene Nanomedicine, Inc.

CNM-Au8 treatment significantly improved vision
Primary outcome - low contrast letter acuity (LCLA)

LCLA

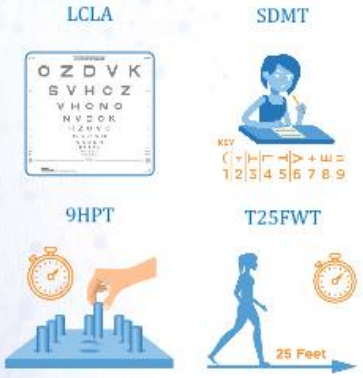
2.5% Contrast

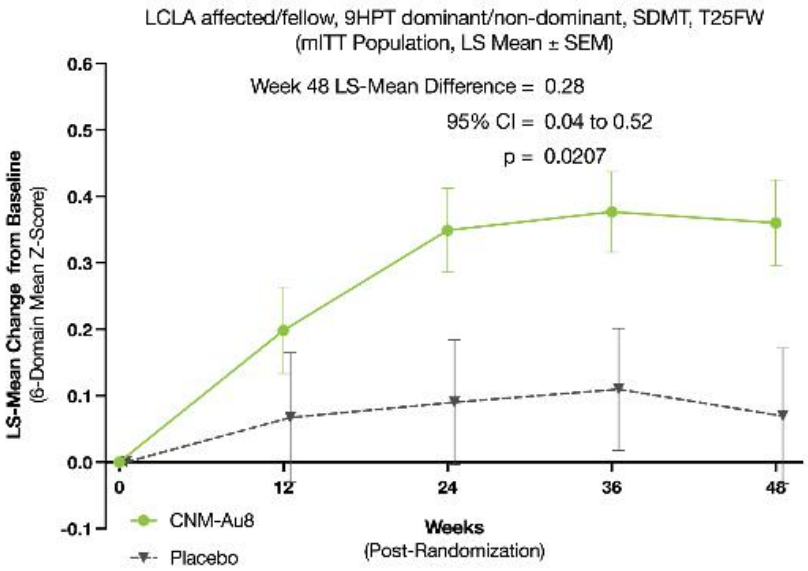


Data on File, Clene Nanomedicine, Inc. mITT excludes one site where data inconsistencies were observed in both active and placebo participants

CNM-Au8 demonstrated global neurological improvement by the modified MS functional composite

Lead 2nd EP | (m)MFSC Composite Mean Standardized Change (6-domain)

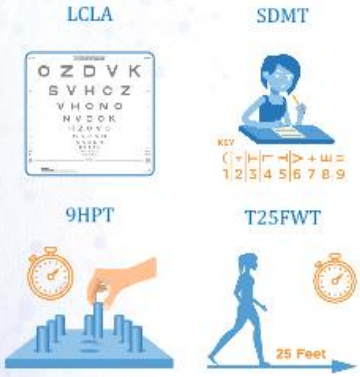




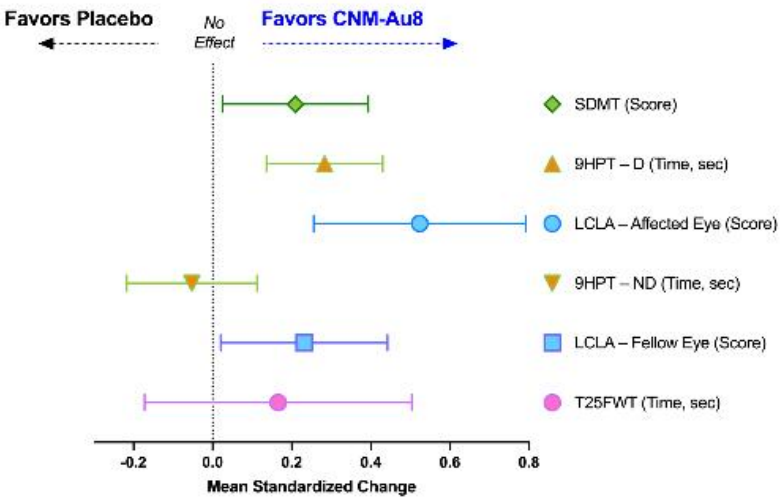
Data on File, Clene Nanomedicine, Inc. mITT excludes one site where data inconsistencies were observed in both active and placebo participants

clene NANOMEDICINE

CNM-Au8 neurological improvement was driven by cognition, manual dexterity, and low contrast vision



Modified MS Functional Composite | Domain Improvements
LCLA affected/fellow, 9HPT dominant/non-dominant, SDMT, T25FW
(mITT Population, LS Mean Difference ± SEM)
CNM-Au8 Less Placebo



Week 48
Mixed Model Repeat Measures

Data on File, Clene Nanomedicine, Inc. mITT excludes one site where data inconsistencies were observed in both active and placebo participants

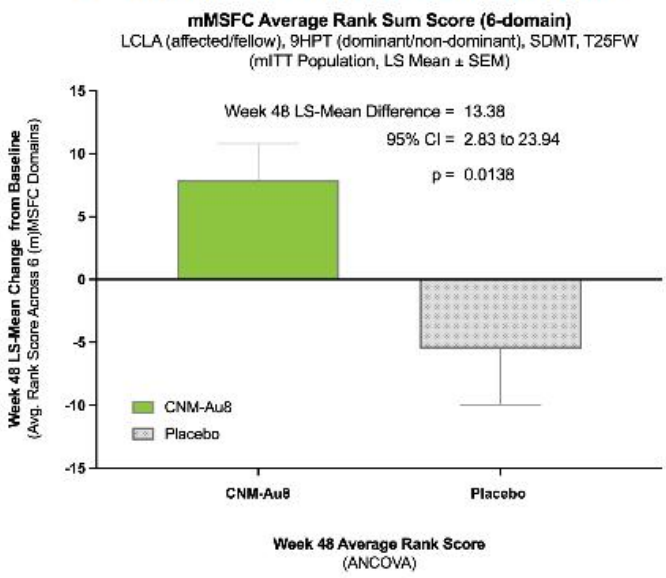
CNM-Au8 treatment improved functional outcomes
Improvement relative to placebo decline

VISIONARY-MS

Score all subjects versus all other subjects by each mMSFC domain

If...	Score
Better function than comparison	+1
Same function as comparison	0
Worse function than comparison	-1

2nd EP | mMFSC Averaged Rank Sum Score



Data on File, Clene Nanomedicine, Inc. mITT excludes one site where data inconsistencies were observed in both active and placebo participants

clene NANOMEDICINE

Safety Summary

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

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

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

Data on File, Clene Nanomedicine, Inc.

CNM-Au8 Efficacy Summary

VISIONARY-MS

Clinical and functional improvements

- LCLA vision improvement
- mMFSC global neurological improvement

Independent quantitative biomarkers of myelin and axonal integrity

- VEP amplitude & latency improvements
- Structural MRI improvements
- Preservation of retinal structure

First therapy to demonstrate global neurological improvement in MS patients on top of background DMT standard of care

Data on File, Clene Nanomedicine, Inc.

clene NANOMEDICINE

Strong IP & Manufacturing Capability

Extensive Patent Portfolio With Protection Through 2035[a] & Proprietary Trade Secrets; Plus 7-year Orphan Drug Designation, and Scalable to Commercialization

Global Patent Status [b]

- Issued & Allowed Patents 150+
- Pending Applications ~20
- Total Patents/ Applications >170

Patent Description

- Process And Method/Device (Clean Surface; Gold CSN)
- State of Matter (CNM-Au8)
- Method of Use (Prevent Demyelination & MoA)
- Method of Use (Bi-Metallic Au/Pt; Antimicrobial)

Trade Secrets

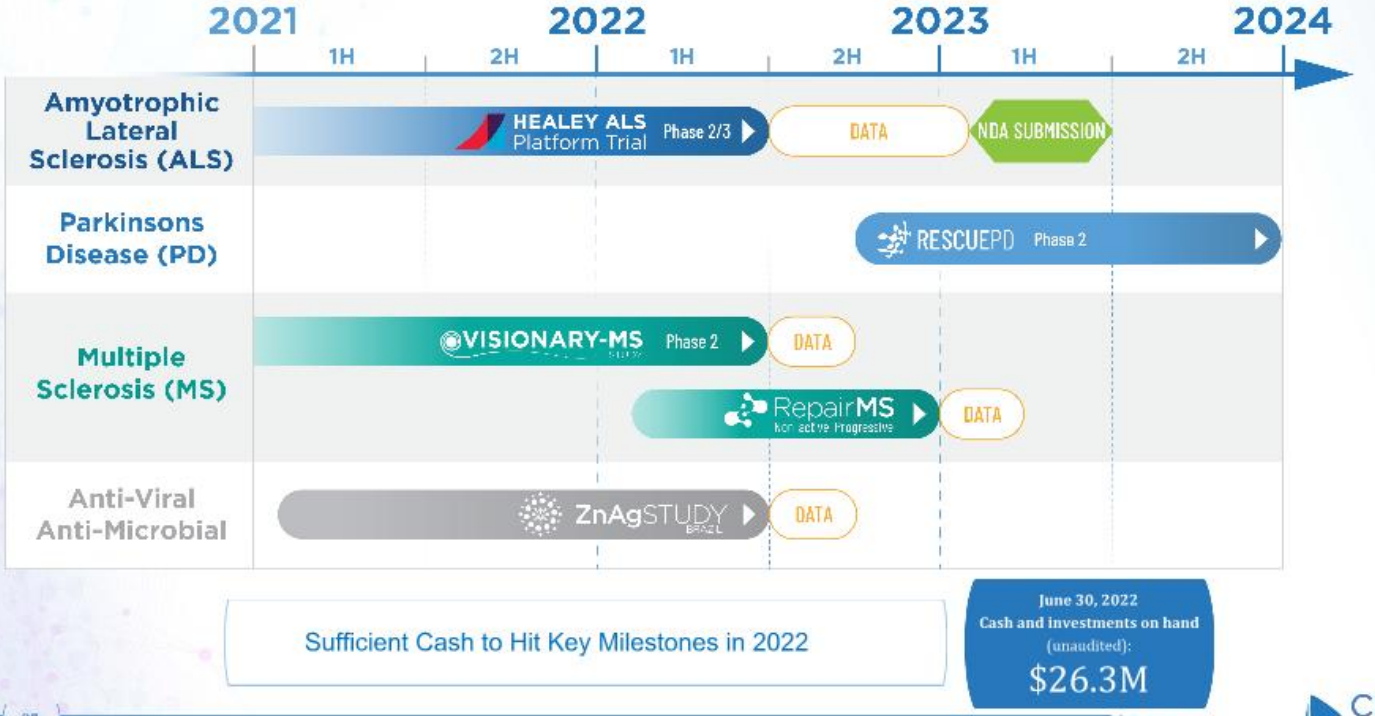
- Plasma Conditioning
- Electrode Design & Cycling
- Trough Flow, Temp, Pressure
- Concentration & Filtration

In-House ISO8 Clean Room Clinical Production in Maryland

[a] With Patent Restoration Term (assuming 5-year extension). [b] As of 31-December-2021.

CLene NANOMEDICINE

Anticipated Timeline & Upcoming Milestones



Sufficient Cash to Hit Key Milestones in 2022

June 30, 2022
Cash and investments on hand
(unaudited):
$26.3M

clene NANOMEDICINE

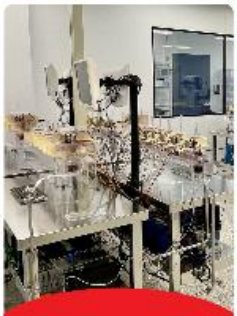
CLENE | Growing Phase 2 Evidence Supports CNM-Au8 Commercial Potential

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

ALS Registration Trial

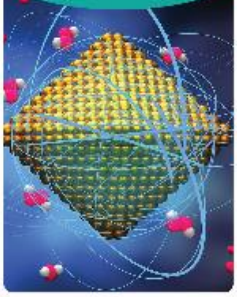
Topline data in 3Q 2022[2]

>350
patient years of CNM-Au8 clinical exposure



Manufacturing expansion in progress, preparing for possible commercialization in
2023

Strong IP:
150+
patents on Clean-Surface-Nanocrystal technology (CSN®) platform



June 30, 2022 Cash and investments on hand (unaudited):
$26.3M

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.

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

Version: 15-Aug-2022

Clene Reports Positive Topline Results for CNM-Au8® in the Phase 2 VISIONARY-MS Trial in Multiple Sclerosis

- ***CNM-Au8 met primary and secondary endpoints of Low Contrast Letter Acuity (LCLA) and modified Multiple Sclerosis Functional Composite (mMSFC) compared to placebo over 48 weeks in the mITT population***
- ***Consistent improvements favoring CNM-Au8 were seen across paraclinical biomarkers, providing physiological evidence for its potential neuroprotective and remyelinating effects***
- ***CNM-Au8 treatment was well-tolerated, and there were no significant safety findings reported***
- ***Results provide support to advance CNM-Au8 into Phase 3 clinical development***
- ***Clene to host a call and webcast at 7:30 am EDT today***

SALT LAKE CITY, August 15, 2022 -- Clene Inc. (Nasdaq: CLNN) (along with its subsidiaries, "Clene") and its wholly owned subsidiary Clene Nanomedicine Inc., a clinical-stage biopharmaceutical company focused on revolutionizing the treatment of neurodegenerative diseases, today announced positive topline results from the Phase 2 VISIONARY-MS trial of CNM-Au8®, an investigational gold nanocrystal suspension, in participants with stable relapsing remitting multiple sclerosis (RRMS).

VISIONARY-MS was a Phase 2 proof-of-concept, multicenter, randomized, double-blind, placebo-controlled trial evaluating the efficacy and safety of CNM-Au8 (15 mg or 30 mg daily) as adjunctive therapy to currently available disease-modifying therapies (DMTs) versus placebo over 48 weeks in stable RRMS participants with chronic optic neuropathy.

As announced in February 2022, the trial was stopped prematurely due to COVID-19 pandemic operational challenges, limiting enrollment to 73 out of the 150 planned participants. Due to the limited enrollment, the threshold for significance was pre-specified at p=0.10 prior to database lock. The primary analysis was conducted in a modified intent to treat (mITT) population, which censored invalid data. The mITT population excluded data from a single site (n=9) with LCLA testing execution errors and the timed 25-foot walk data from one subject with a change in mobility assist device. The ITT results were directionally consistent with the mITT results, although the ITT results were not significant.

"These data are very encouraging to us in the MS research and treatment community as we work to address functional improvement in patients," said Benjamin Greenberg, MD, MHS, FANA, FAAN, CRND Professor of Neurology and one of the trial's clinical advisors. "The MS community has been successful at limiting relapses, but we need therapies to address progression independent of relapse activity (PIRA). This study was designed as a proof-of-concept evaluation to establish that treatment of neuronal and glial energetic failure can support remyelination and neuroprotection in people living with MS. I am pleased to see the potential effectiveness of CNM-Au8 demonstrated in this trial."

Primary and secondary results from Baseline to Week 48 were:

- Primary outcome: LCLA letter change in the clinically affected eye (least squares [LS] mean difference, 3.13; 95% CI: -0.08 to 6.33, p = 0.056)
- Secondary outcomes:
  - mMSFC mean standardized change (LS mean difference, 0.28; 95% CI: 0.04 to 0.52, p = 0.0207)
  - mMSFC average rank score (LS mean difference, 13.38; 95% CI: 2.83 to 23.94, p = 0.0138)
  - Time to first repeated clinical improvement to Week 48 (45% vs. 29%, log-rank p=0.3991)

Consistent improvements favoring CNM-Au8 were observed across multiple paraclinical biomarkers, including multifocal visual evoked potentials (mfVEP) amplitude and latency, optical coherence tomography (OCT), and MRI endpoints, including magnetization transfer ratio and diffusion tensor imaging metrics. Placebo treated patients, in contrast, generally worsened as expected across these

measures during the 48-week period. These data provide independently assessed quantitative physiological evidence that supports the potential neuroprotective and remyelinating effects of CNM-Au8. The full dataset will be reported at an upcoming scientific congress.

CNM-Au8 was well-tolerated, and there were no significant safety findings reported.

Robert Glanzman, MD, FAAN, Clene's Chief Medical Officer, said, "In this study, CNM-Au8 demonstrated neurological improvements in people with stable relapsing MS as adjunctive therapy to immunomodulatory DMTs. I am very impressed by the consistency of structural and functional improvements demonstrated by CNM-Au8 throughout the neuraxis. With these data, Clene looks forward to initiating a Phase 3 clinical program in people with MS who are experiencing progression independent of relapse activity, the most urgent unmet medical need in MS today. We look forward to the next phase of clinical development."

Rob Etherington, Clene's Chief Executive Officer and President, added, "These results further demonstrate the potential of CNM-Au8 to drive neuronal cellular energy production in patients struggling with MS and other neurodegenerative diseases. We also await additional evidence of clinical efficacy from the HEALEY ALS Platform Trial, which is expected to report topline data later in this quarter. Clene will continue to work tirelessly to further CNM-Au8's development to treat neurodegenerative diseases."

Conference Call and Webcast Information
Clene will host a conference call and webcast at 7:30 am EDT to discuss the VISIONARY-MS topline results.

Toll free: 1 (888) 770-7152
Conference ID: 5318408
*Press *1 to ask or withdraw a question, or *0 for operator assistance.*

To access the live webcast, please register online at this link. Participants are requested to register at a minimum 15 minutes before the start of the call. A replay of the call will be available two hours after the call and archived on the same web page for six months. A live audio webcast of the call will be available on the Investors section of the Company's website Presentation page. An archived webcast will be available on the Company's website approximately two hours after the event.

About VISIONARY-MS
VISIONARY-MS was a Phase 2 multi-center, randomized, double-blind, placebo-controlled trial to assess the efficacy and safety of CNM-Au8 in participants with stable relapsing remitting multiple sclerosis (RRMS) with a history of chronic visual impairment who are allowed disease-modifying therapy (DMT). Enrolled subjects were randomized 1:1:1 to CNM-Au8 15 mg/day, 30 mg/day, or placebo. As announced in February 2022, the trial was stopped prematurely due to COVID-19 pandemic operational challenges, enrolling 73 out of the 150 planned participants. Due to limited enrollment, the threshold for significance was pre-specified at p=0.10 prior to database lock. The primary endpoint was the change in best corrected-low contrast letter acuity (BC-LCLA) from baseline to week 48 in the clinically affected eye. Key secondary efficacy outcomes assessed neurological function by the modified MS Functional Composite (mMSFC) including 25-Foot Timed Walk, Symbol Digit Modalities Test, 9-Hole Peg Test (dominant and non-dominant hands), and LCLA (affected and fellow eye) from baseline through Week 48. For more information, see ClinicalTrials.gov. Identifier: NCT03536559. The open label extension of VISIONARY-MS is ongoing.

About CNM-Au8®
CNM-Au8 is an oral suspension of gold nanocrystals developed to restore neuronal health and function by increasing energy production and utilization. The catalytically active nanocrystals of CNM-Au8 drive critical cellular energy producing reactions that enable neuroprotection and remyelination by increasing neuronal and glial resilience to disease-relevant stressors. CNM-Au8® is a federally registered trademark of Clene Nanomedicine, Inc.

About Clene
Clene is a clinical-stage biopharmaceutical company focused on revolutionizing the treatment of neurodegenerative disease by targeting energetic failure, an underlying cause of many neurological diseases. 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

Source: Clene Inc.

Exhibit 99.4


Visionary-MS Webinar
15 August 2022
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.

VISIONARY-MS STUDY

Phase 2 Results

Treatment of Visual Pathway Deficits In Chronic Optic Neuropathy for Assessment of Remyelination in Non-Active Relapsing MS

CLENE NANOMEDICINE

VISIONARY-MS STUDY Core Design Elements

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

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

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

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

9HPT SDMT T25FWT LCLA

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

clene NANOMEDICINE

Baseline Demographics Showed Balanced Randomization and Clinical Profile

VISIONARY-MS

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

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

Data on File, Clene Nanomedicine, Inc.

CLENE NANOMEDICINE

Pandemic Significantly Impacted Study Conduct

VISIONARY-MS

- Study was ended prematurely due to COVID enrollment challenges (as announced February 2022)
  - Enrolled 73 of 150 planned
  - Underpowered due to limited enrollment
  - Pre-specified statistical threshold set at p=0.10
  - COVID restrictions precluded direct Sponsor monitoring
- Objectives
  - Learn from results
  - Evaluate strength of evidence for further MS development

Data on File, Clene Nanomedicine, Inc.

clene NANOMEDICINE

modified ITT (mITT) Analysis Population

- Censored observations included
  - Change in mobility assist device (cane to walker) for T25FW (n=1)
  - Invalid data from 1 of 11 sites (n=9) with LCLA testing execution errors
    - Multiple testing locations with different light boxes and varying ambient lighting conditions
    - In consultation with study Principal Investigator and external experts, all clinical data from the site were excluded

Data on File, Clene Nanomedicine, Inc.

CNM-Au8 treatment significantly improved vision

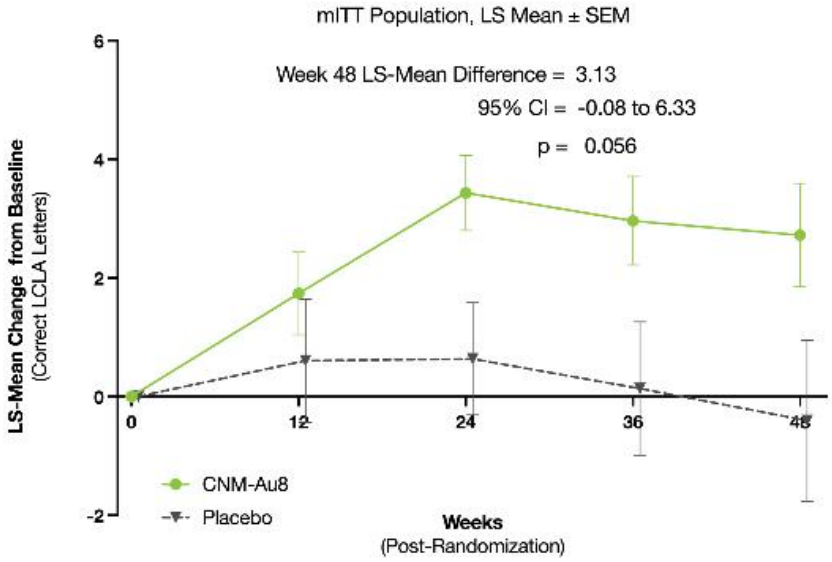
Primary outcome - low contrast letter acuity (LCLA)

VISIONARY-MS

LCLA

2.5% Contrast

LCLA in the Affected Eye

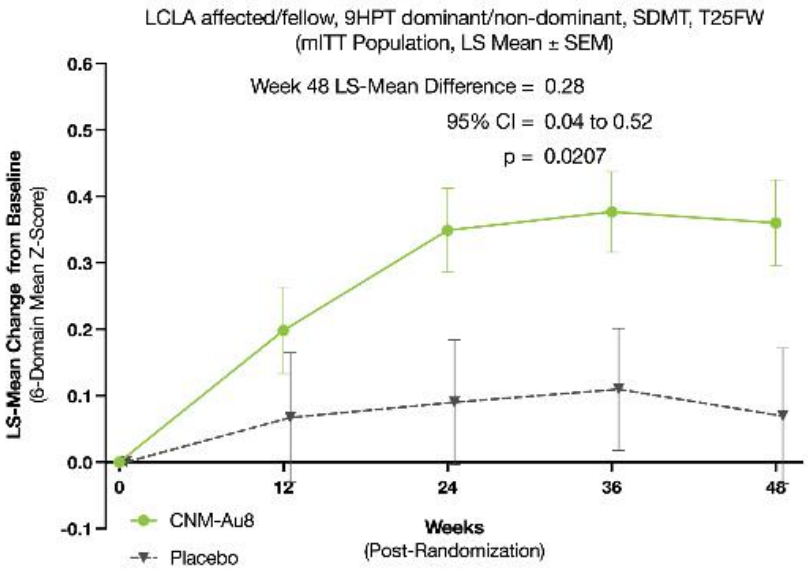


Data on File, Clene Nanomedicine, Inc. mITT excludes one site where data inconsistencies were observed in both active and placebo participants

clene NANOMEDICINE

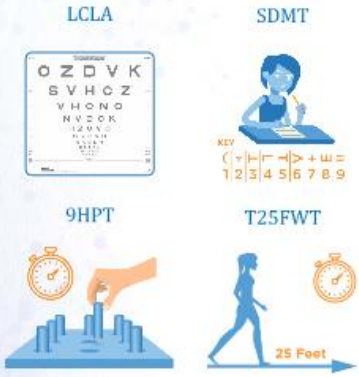
CNM-Au8 demonstrated global neurological improvement by the modified MS functional composite

Lead 2nd EP | (m)MFSC Composite Mean Standardized Change (6-domain)

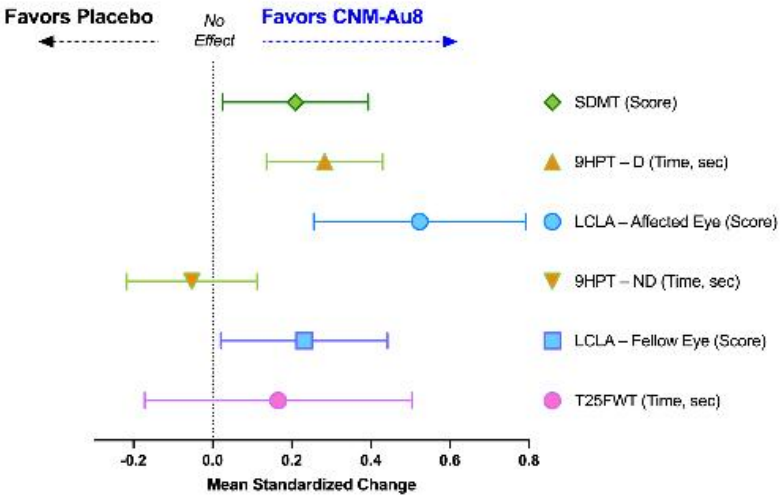


Data on File, Clene Nanomedicine, Inc. mITT excludes one site where data inconsistencies were observed in both active and placebo participants

CNM-Au8 neurological improvement was driven by cognition, manual dexterity, and low contrast vision



Modified MS Functional Composite | Domain Improvements
LCLA affected/fellow, 9HPT dominant/non-dominant, SDMT, T25FW
(mITT Population, LS Mean Difference ± SEM)
CNM-Au8 Less Placebo



Week 48
Mixed Model Repeat Measures

Data on File, Clene Nanomedicine, Inc. mITT excludes one site where data inconsistencies were observed in both active and placebo participants

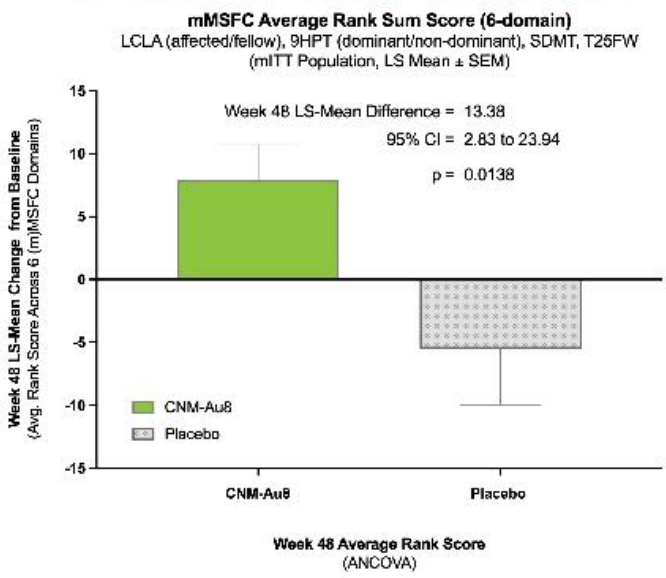
CNM-Au8 treatment improved functional outcomes
Improvement relative to placebo decline

VISIONARY-MS

Score all subjects versus all other subjects by each mMSFC domain

If...	Score
Better function than comparison	+1
Same function as comparison	0
Worse function than comparison	-1

2nd EP | mMFSC Averaged Rank Sum Score

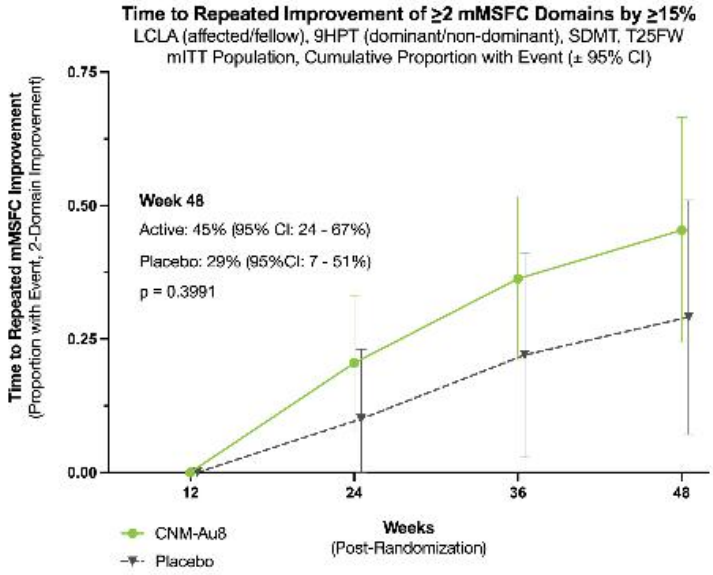


Data on File, Clene Nanomedicine, Inc. mITT excludes one site where data inconsistencies were observed in both active and placebo participants

clene NANOMEDICINE

Time to repeated clinical improvement was not significant

2nd EP | Time to Repeated Clinical Improvement (Last 2nd EP)

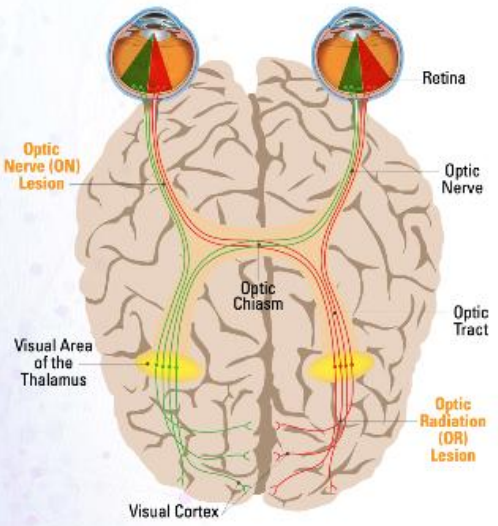


Data on File, Clene Nanomedicine, Inc. mITT excludes one site where data inconsistencies were observed in both active and placebo participants

Quantitative physiological biomarkers of Improved axonal and myelin integrity

VISIONARY-MS

The Visual System is a Window into the MS Brain



1. Visual Evoked Potentials (VEP)
   - multifocal Amplitude
   - multifocal Latency
2. Advanced MRI Techniques
   - Diffusion Tensor Imaging
   - Magnetization Transfer Ratio
3. Optical Coherence Tomography
   - Retinal nerve fiber layer thickness
   - Ganglion cell layer thickness

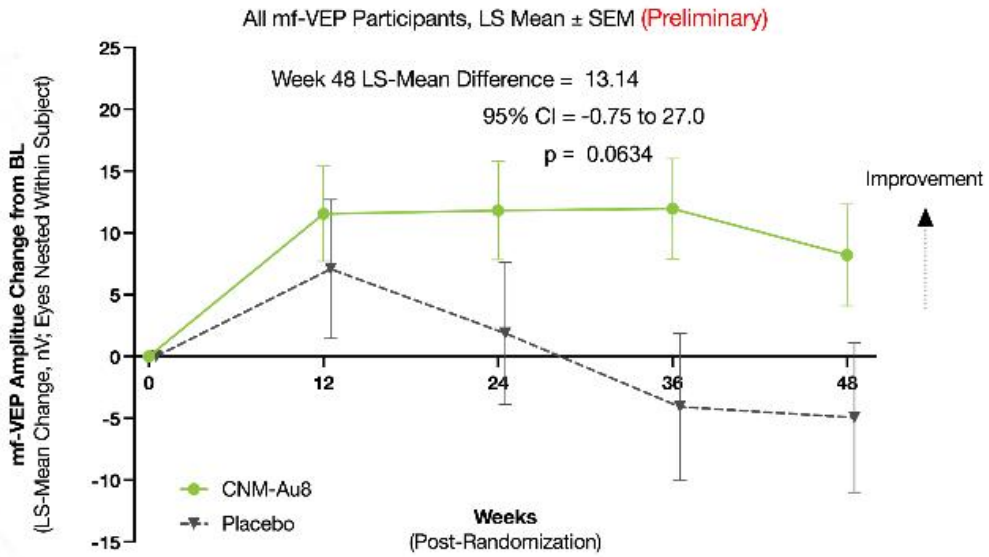
Balcer et la. Mult Scler. 2017 Apr;23(5):734-747.

CLene NANOMEDICINE

CNM-Au8 improved visual information processing
Multi-focal VEP amplitude – marker of axonal integrity

VISIONARY-MS

Increased Amplitude (Signal Strength)



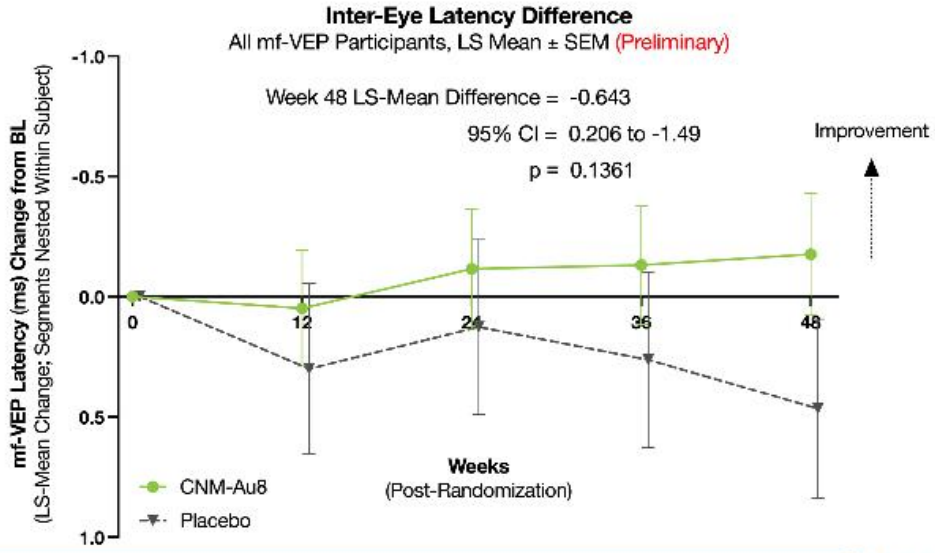
Data on File, Clene Nanomedicine, Inc.

clene NANOMEDICINE

CNM-Au8 improved myelin integrity
Multi-focal VEP latency – marker of remyelination

VISIONARY-MS

Increased Conduction Velocity (Signal Speed)
Supports Remyelination or Enhanced Functional Myelin Integrity



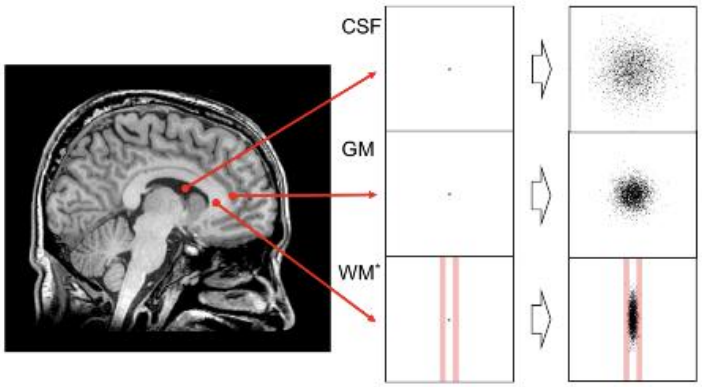
Data on File, Clene Nanomedicine, Inc.

CLENE NANOMEDICINE

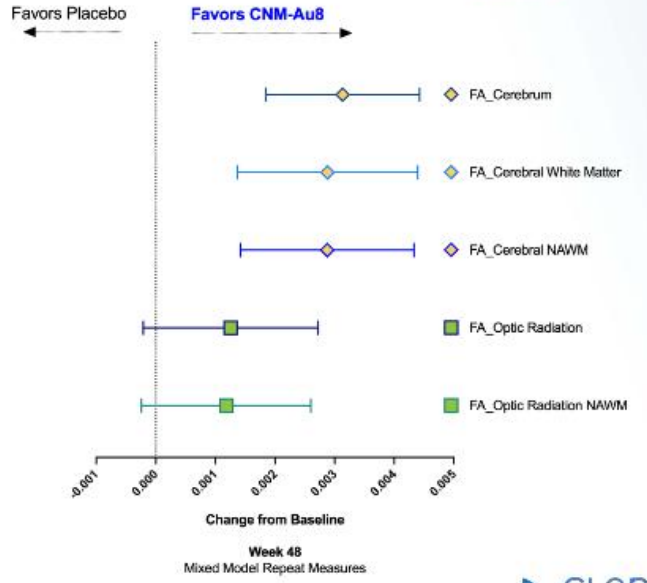
CNM-Au8 improved axonal integrity
Structural MRI marker of fractional anisotropy

VISIONARY-MS

DTI Diffusion Patterns



Diffusion Tensor Imaging | Fractional Anisotropy (FA) Change
All Advanced MRI Imaging Participants, LS Mean Difference ± SEM (Preliminary)



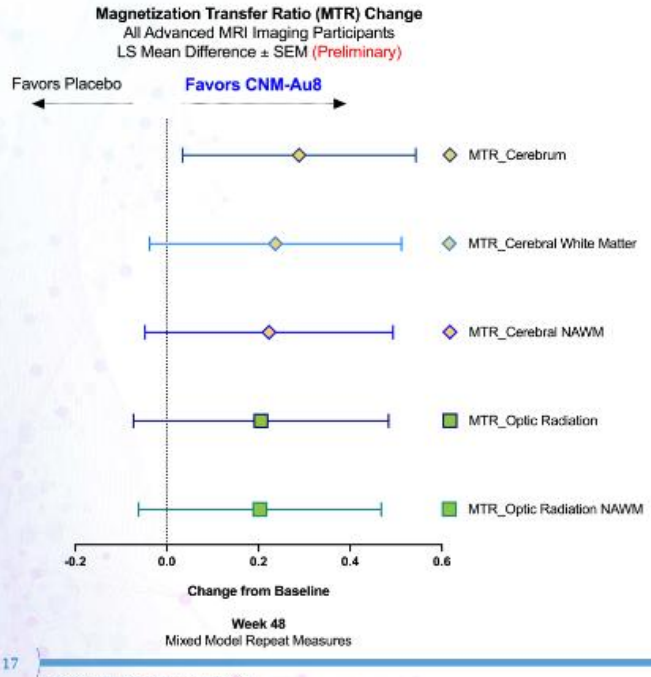
Week 48
Mixed Model Repeat Measures

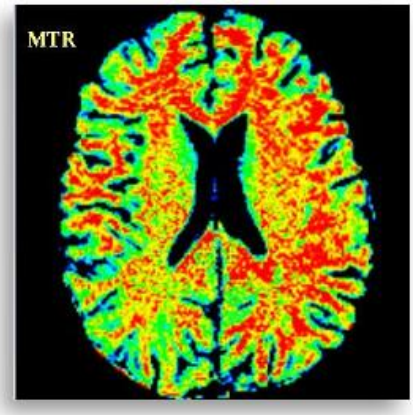
Data on File, Clene Nanomedicine, Inc.

CLENE NANOMEDICINE

CNM-Au8 improved magnetization transfer ratio

Increased myelin integrity throughout the brain





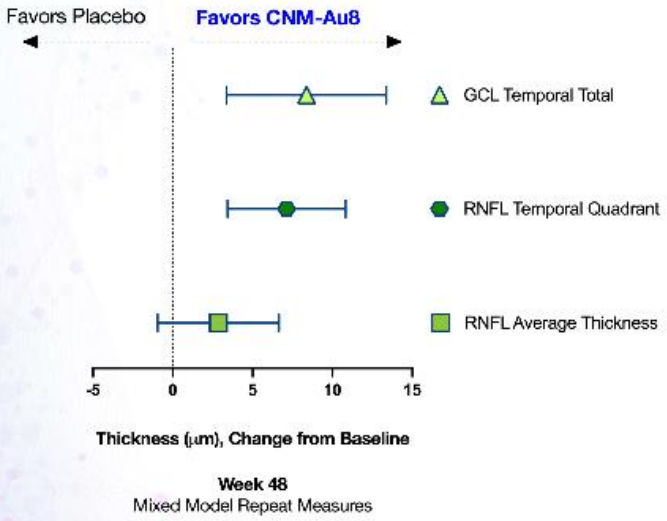
Data on File, Clene Nanomedicine, Inc.

CNM-Au8 preserved retinal structure

Protection of retinal nerve fiber & ganglion cell layers

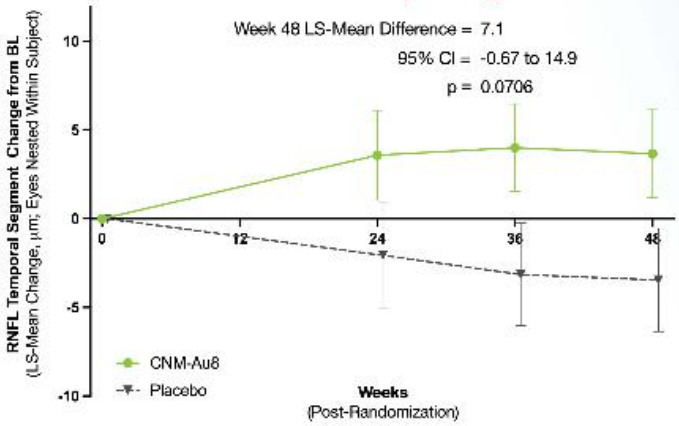
VISIONARY-MS

OCT | RNFL and GCL Temporal Segment Thickness (μm)
All Participants with OCT
LS Mean Difference ± SEM (Preliminary)



Week 48
Mixed Model Repeat Measures

OCT | RNFL Temporal Quadrant Thickness (μm)
All Participants with OCT
LS Mean ± SEM (Preliminary)



Data on File, Clene Nanomedicine, Inc.

CLENE NANOMEDICINE

Safety Summary

VISIONARY-MS

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

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

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

Data on File, Clene Nanomedicine, Inc.

CLENE NANOMEDICINE

CNM-Au8 Efficacy Summary

VISIONARY-MS

Clinical and functional improvements

- LCLA vision improvement
- mMFSC global neurological improvement

Independent quantitative biomarkers of myelin and axonal integrity

- VEP amplitude & latency improvements
- Structural MRI improvements
- Preservation of retinal structure

First therapy to demonstrate global neurological improvement in MS patients on top of background DMT standard of care

Data on File, Clene Nanomedicine, Inc.

clene NANOMEDICINE

Conclusions and Next Steps

VISIONARY-MS

- First proof of neuroprotective and remyelinating treatment for MS
- Multiple signals of clinical and biomarker improvement
  - ✓ Clinical neurological function
  - ✓ Axonal integrity and neuroprotection
  - ✓ Remyelination and myelin integrity
- Results support advancement into Phase 3 MS clinical development

Data on File, Clene Nanomedicine, Inc.

clene NANOMEDICINE

Clene Nanomedicine, Inc.
HQ & Clinical Development
6550 S. Millrock Drive, Suite G50
Salt Lake City, UT 84121

R&D and Manufacturing
500 Principio Parkway, Suite 400
North East, MD 21901