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): September 17, 2021

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)

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 (see General Instruction A.2. below):

☐ 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, par value US$0.0001 per share	CLNN	The Nasdaq Stock Market LLC
Warrants, to acquire one-half of one share of Common Stock for $11.50 per share	CLNNW	The Nasdaq Stock Market LLC

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

Emerging growth company ☒

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

Item 7.01 Regulation FD Disclosure.

On September 17, 2021, Clene Inc. (the "Company") issued a press release announcing a poster presentation titled "Homeostatic Improvement of Brain Bioenergetic Metabolism in Parkinson's Disease: Results From A Phase 2 REPAIR-PD Clinical Trial With CNM-Au8" at the International Parkinson and Movement Disorder Society (MDS) Virtual Congress 2021 which takes place September 17 – 22, 2021. A copy of the press release is filed as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

In connection with the September 17, 2021 press release, the Company released an updated corporate presentation (the "Corporate Presentation") on its website, www.clene.com. A copy of the Corporate Presentation is filed as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference. The Company plans to use its website to disseminate future updates to the Corporate Presentation and may not file or furnish a Current Report on Form 8-K alerting investors if the Corporate Presentation is updated.

The information furnished in this Item 7.01, including Exhibit 99.1 and 99.2, 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, 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 September 17, 2021 announcing Clene presents Phase 2 CNM-Au8 data at the International Parkinson and Movement Disorder Society Virtual Congress 2021.
99.2	Corporate Presentation dated September 17, 2021.
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: September 17, 2021

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

Exhibit 99.1

Clene Presents Phase 2 CNM-Au8 CNS Target Engagement Data at the International Parkinson and Movement Disorder Society Virtual Congress 2021

CNM-Au8® , a catalytically active gold nanocrystal suspension, significantly improved brain energetic metabolism in Parkinson's patients

SALT LAKE CITY, September 17, 2021 -- Clene Inc. (NASDAQ: CLNN) along with its subsidiaries "Clene" and its wholly owned subsidiary Clene Nanomedicine, Inc., a clinical-stage biopharmaceutical company dedicated to the treatment of neurodegenerative disease using nanotechnology to treat energetic failure, today announced a poster presentation titled "Homeostatic Improvement of Brain Bioenergetic Metabolism in Parkinson's Disease: Results From A Phase 2 REPAIR-PD Clinical Trial With CNM-Au8" at the International Parkinson and Movement Disorder Society (MDS) Virtual Congress 2021 which takes place September 17 – 22, 2021. The poster presentation is available for view here.

Clene's Phase 2 REPAIR program achieved a statistically significant increase in its primary endpoint, the mean change in brain NAD^+/NADH ratio (p=0.037). NAD is an essential molecule responsible for cellular energy production. While the NAD^+/NADH ratio declines normally during aging by approximately 0.5% per decade, reduced NAD^+/NADH ratios have been reported in multiple neurodegenerative diseases, and the decline in the ratio is implicated in Parkinson's disease. In the REPAIR-PD study, the trend in NAD+/NADH ratio improvement was driven by both increased NAD^+ and decreased NADH. Patients were evaluated using an innovative non-invasive brain imaging technique, phosphorous magnetic resonance spectroscopy, before and after 12 or more weeks of daily oral dosing with CNM-Au8. End of treatment results were compared to baseline. Exploratory endpoints revealed that taking CNM-Au8 resulted in the normalization of several critical markers of brain energy production capacity including beta-ATP levels and phosphorylation potential. There were no serious adverse events and treatment-emergent adverse events were mild and transient.

Robert Glanzman, MD FAAN, Clene's Chief Medical Officer, commented, "We are very pleased to share our results with the Parkinson's treatment community at the MDS Virtual Congress. We see CNM-Au8's impact on brain bioenergetics as a breakthrough in the way Parkinson's will be treated. The 10% increase in the NAD+/NADH ratio seen in our Phase 2 REPAIR Program corresponds to a reversal of approximately 20 decades of normal aging based on an anticipated decline of 0.5% per decade, a significant result."

Rob Etherington, Clene's Chief Executive Officer, added, "In addition to achieving its primary endpoint, the RESCUE-PD study reinforced our lead candidate CNM-Au8's central nervous system target engagement, as well as its ability to significantly rebalance brain metabolites, both of which have implications across most neurodegenerative diseases."

Approximately 7 million people are living with Parkinson's disease, the second most common neurogenerative disorder. Only symptomatic treatments are currently available in a market projected to reach $6 billion by 2025.

The International Parkinson and Movement Disorder Society (MDS) is a professional society of more than 11,000 clinicians, scientists and other healthcare professionals dedicated to improving the care of patients with movement disorders through education and research.

About REPAIR-PD

REPAIR-PD, a Phase 2 single-center, active only, sequential group, investigator blinded study assessed the metabolic effects, safety, pharmacokinetics and pharmacodynamics of CNM-Au8 in patients with Parkinson's disease (PD) diagnosed within 3 years of screening. Investigators and participants were blinded to dose. Participants received orally delivered CNM-Au8 daily each morning for 12 weeks. Participants underwent ^{31}P-MRS brain imaging scans to semi-quantitatively measure energetic metabolites at baseline, prior to and after administration of the drug. The objective of this study was to demonstrate target engagement for CNM-Au8 on central nervous system (CNS) biomarkers related to cellular energy metabolism in patients with PD. The study was conducted at the University of Texas Southwestern Medical Center with a team of internationally recognized experts in brain imaging and treatment of disorders of the CNS. Interim results from REPAIR-PD presented at the MSVirtual2020 Meeting and the ACTRIMS Forum 2021 Meeting showed improvements across key CNS bioenergetic metabolites, including total nicotinamide adenine dinucleotide (NAD) levels, NAD+/NADH ratio (primary endpoint), and adenosine triphosphate (ATP) levels (secondary endpoint), indicating a homeostatic effect of CNM-Au8 on brain energetics. For more information see ClinicalTrials.gov Identifier: NCT03815916.

About CNM-Au8®, a gold nanocrystal suspension

Clene's lead drug candidate, CNM-Au8, is an aqueous suspension of catalytically-active, clean-surfaced, faceted gold nanocrystals. Resulting from a patented manufacturing breakthrough, the catalytically active nanocrystals of CNM-Au8 drive critical cellular energy producing reactions in the brain that enable neurorepair and remyelination by increasing neuronal and glial resilience to disease-relevant stressors. CNM-Au8 crosses the blood-brain barrier and is not associated with the toxicities related to synthetic gold compounds or nanoparticles manufactured via alternative methods. CNM-Au8 has demonstrated safety in Phase 1 studies in healthy volunteers and has shown both remyelination and neuroprotective effects in multiple preclinical (animal) models. Preclinical data, both published in peer-reviewed journals and presented at scientific congresses, demonstrate that treatment of neuronal cultures with CNM-Au8 improves survival of neurons, protects neurite networks, decreases intracellular levels of reactive oxygen species and improves mitochondrial capacity in response to cellular stresses induced by numerous disease-relevant neurotoxins. Oral treatment with CNM-Au8 improved functional behaviors in rodent models of ALS, MS, and PD versus vehicle (placebo). CNM-Au8Ò is a federally registered trademark of Clene Nanomedicine, Inc.

About Clene

Clene, a clinical-stage biopharmaceutical company focused on neurodegenerative disease treatments, is leading the way by using nanotechnology to treat energetic failure, which underlies many neurological diseases. Clene has innovated a novel nanotherapeutic platform to create a new class of drugs. Clene's lead drug candidate, CNM-Au8, is an aqueous suspension of catalytically-active, clean-surfaced, faceted gold nanocrystals that drive critical cellular energetic metabolism in the central nervous system (CNS). CNM-Au8 increases cellular energy production to accelerate neurorepair and improve neuroprotection. CNM-Au8 is currently being evaluated in a Phase 3 registration trial in amyotrophic lateral sclerosis (ALS), a Phase 2 trial examining disease progression via a novel electromyography technique in patients with early ALS, a Phase 2 trial for the treatment of chronic optic neuropathy in patients with stable relapsing multiple sclerosis (MS), and Phase 2 brain target engagement studies in patients with Parkinson's disease (PD) and MS. Clene has also advanced into the clinic an aqueous solution of ionic zinc and silver for anti-viral and anti-microbial uses. 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 the “safe harbor” provisions of the Private Securities Litigation Reform Act of 1995. Clene’s actual results may differ from its expectations, estimates and projections and consequently, you should not rely on these forward-looking statements as predictions of future events. Words such as “expect,” “estimate,” “project,” “budget,” “forecast,” “anticipate,” “intend,” “plan,” “may,” “will,” “could,” “should,” “believes,” “predicts,” “potential,” “might” and “continues,” and similar expressions are intended to identify such forward-looking statements. These forward-looking statements involve significant known and unknown risks and uncertainties, many of which are beyond Clene’s control and could cause actual results to differ materially and adversely from expected results. Factors that may cause such differences include Clene’s ability to demonstrate the efficacy and safety of its drug candidates; the clinical results for its 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; Clene’s ability to achieve commercial success for its marketed products and drug candidates, if approved; Clene’s ability to obtain and maintain protection of intellectual property for its technology and drugs; Clene’s reliance on third parties to conduct drug development, manufacturing and other services; Clene’s limited operating history and its ability to obtain additional funding for operations and to complete the licensing or development and commercialization of its drug candidates; the impact of the COVID-19 pandemic on Clene’s clinical development, commercial and other operations, as well as those risks more fully discussed in the section entitled “Risk Factors” in Clene’s Annual Report filed on Form 10K, as well as discussions of potential risks, uncertainties, and other important factors in Clene’s subsequent filings with the U.S. Securities and Exchange Commission. Clene undertakes no obligation to release publicly any updates or revisions to any forward-looking statements to reflect any change in its expectations or any change in events, conditions or circumstances on which any such statement is based, subject to applicable law. 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
Gwendolyn Schanker
LifeSci Communications
(269) 921-3607
gschanker@lifescicomms.com

Investor Contact
Bruce Mackle
LifeSci Advisors, LLC
(929) 469-3859
bmackle@lifesciadvisors.com

Source: Clene Inc.

Exhibit 99.2

Forward Looking Statements

This presentation contains "forward-looking statements" within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Clene's actual results may differ from its expectations, estimates, and projections and consequently, you should not rely on these forward-looking statements as predictions of future events. Words such as "expect," "estimate," "project," "budget," "forecast," "anticipate," "intend," "plan," "may," "will," "could," "should," "believes," "predicts," "potential," "might" and "continues," and similar expressions are intended to identify such forward-looking statements. These forward-looking statements involve significant known and unknown risks and uncertainties, many of which are beyond Clene's control and could cause actual results to differ materially and adversely from expected results. Factors that may cause such differences include Clene's ability to demonstrate the efficacy and safety of its drug candidates; the clinical results for its 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; Clene's ability to achieve commercial success for its marketed products and drug candidates, if approved; Clene's ability to obtain and maintain protection of intellectual property for its technology and drugs; Clene's reliance on third parties to conduct drug development, manufacturing and other services; Clene's limited operating history and its ability to obtain additional funding for operations and to complete the licensing or development and commercialization of its drug candidates; the impact of the COVID-19 pandemic on Clene's clinical development, commercial and other operations, as well as those risks more fully discussed in the section entitled "Risk Factors" in Clene's recently filed registration statement on Form S-4/A as well as discussions of potential risks, uncertainties, and other important factors in Clene's subsequent filings with the U.S. Securities and Exchange Commission. Clene undertakes no obligation to release publicly any updates or revisions to any forward-looking statements to reflect any change in its expectations or any change in events, conditions or circumstances on which any such statement is based, subject to applicable law. All information in this presentation is as of the date of presented or the date made publicly available. 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 | Management Team

BOARD CHAIR

David J. Matlin

MatlinPatterson

CREDIT SUISSE

CEO

Rob Etherington

ACTELION

Pfizer

PARKE-DAVIS

CMO

Robert Glanzman, MD, FAAN

geneuro

NEKTAR

PURDUE

Roche

NOVARTIS

Pfizer

CSO, FOUNDER

Mark Mortenson

DUPONT

ALCAN

Lanxide Corporation

Dupont Lanxide Composites

Lanxide Armor Company

Lanxide Performance Materials

Lanxide Electronic Components

CDO

Michael Hotchkin

ACTELION

Pfizer

PARKE-DAVIS

AVantureBio

CFO

Ted Jeong, DM

NeuroBo PHARMACEUTICALS

rexahn PHARMACEUTICALS

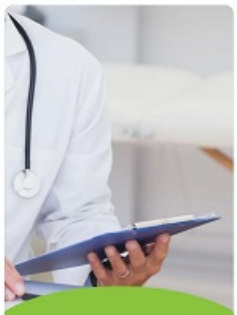
HVIC

KSV KENSINGTON-SV GLOBAL

Clene Nanomedicine

CNM-Au8®

a gold nanocrystal suspension, in development as the first energetic catalyst to repair & improve neurological function



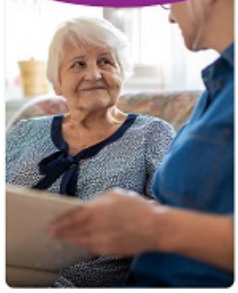
Topline data from One Registrational Trial[1] by mid-2022 and

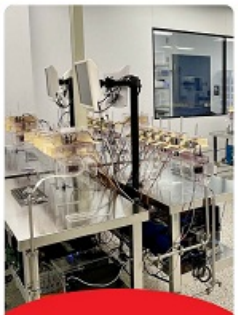
3

Phase 2 Trials[2] by end of 2021

>200

patient years of CNM-Au8 clinical exposure





Manufacturing expansion in progress, preparing for possible commercialization in

2023

Strong IP:

130+

patents on Clean-Surface-Nanocrystal technology (CSN®) platform

Cash on hand:

$63M

End of Q2 including

PIPE & Venture debt of $24M

1. HEALEY-ALS https://clinicaltrials.gov/ct2/show/NCT04414345?term=CNM-Au8&cond=ALS&draw=1&rank=1 2. RESCUE-ALS https://clinicaltrials.gov/ct2/show/NCT04298476?term=CNM-Au8&cond=ALS&draw=1&rank=3 REPAIR-PD https://clinicaltrials.gov/ct2/show/NCT03815591?term=cnm-au8&draw=2&rank=1 REPAIR-MS https://clinicaltrials.gov/ct2/show/NCT03963713?term=cnm-au8&draw=2&rank=1

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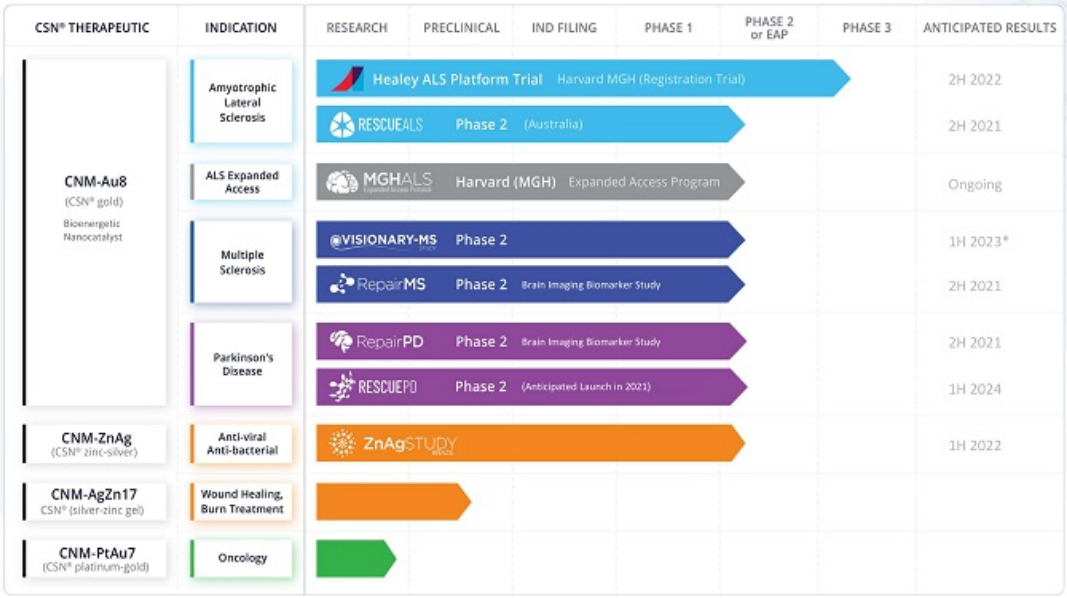
CLENE | Platform & Pipeline

Clean Surface Nanocrystal Therapeutics (CSN®)

CSN® PLATFORM — 130+ Granted Patents

Novel electro-chemistry platform produces catalytic Clean Surface Nanocrystal drugs designed to avoid toxicities associated with synthetic chemistry



*Subject to ongoing COVID-19 related site research restrictions generally implemented to protect MS patients taking standard-of-care immunosuppressive therapies

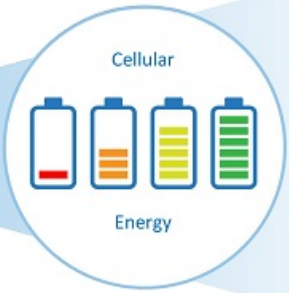
clene NANOMEDICINE

CNM-Au8® | Catalytically-Active Nanotherapeutic

Improved Cellular Energy Production & Utilization

Novel mechanism of action to address a range of CNS diseases

- Clean Surfaced Faceted Nanocrystal
- 13 nm Median Diameter (Ribosome = 20-30 nm)
- > 100 Trillion Nanocrystals per 60 mL Dose (At 30mg)
- Oral Suspension; Once Daily



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CNM-Au8 | Integrating Physics With Biology

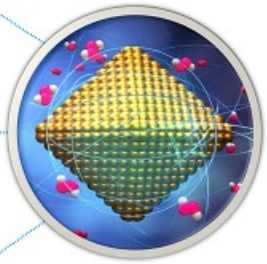
Electron transfer (to-and-from) CNM-Au8 nanocrystals drives catalytic activity and cellular energy production

Surface Based Catalytic Activity

Electrons (e-) **Move Freely Across Nanocrystal Surface**

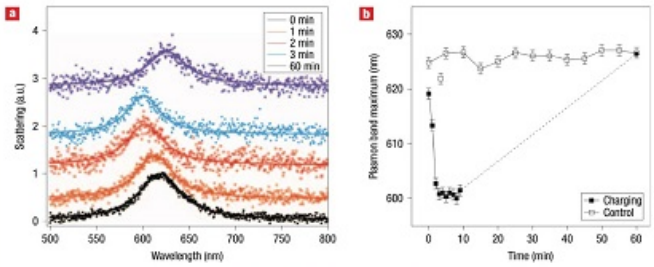
Vertices, Edges, & Faces Key to Catalytic Activity

Clean-Surfaced Nanocrystals



Up to 4,600 e^- per second per nanocrystal[1]

AuNP Catalyzed Oxidation of Ascorbic Acid[1]



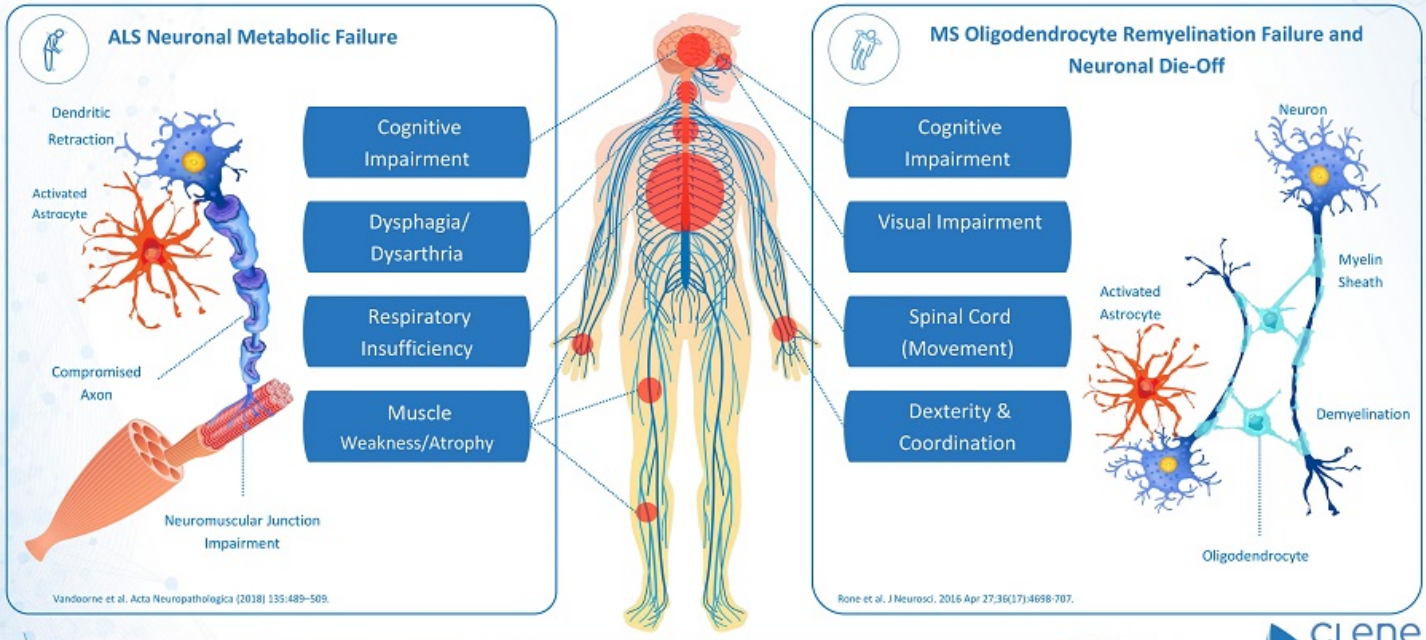
a. Rayleigh scattering measured by dark field microscopy of surface plasmon resonance of scattering spectra of the AuNP decahedron before and at 1, 2, 3 and 60 min after electron injection by ascorbate ions.

b. Spectral shift as a function of time for the catalysis reaction and for the control experiment..

[1] Novo et al. Nature Nanotech 3, 598–602 (2008).

CLENE NANOMEDICINE

Treating Energetic Failure | Common Pathological Mechanism In Neurodegenerative Disorders (MS, ALS, PD)



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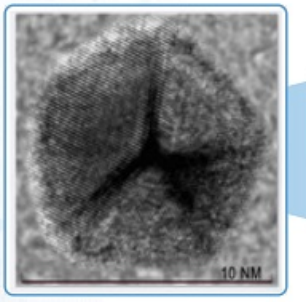
CNM-Au8 | MOA → Therapeutic Effects

Catalytic Gold Nanocrystals



Bioenergetic Mechanism

- ↑ Increased NAD [a]
- ↑ Increased ATP
- ↓ Decreased reactive oxygen species
- ↑ Increased proteostasis

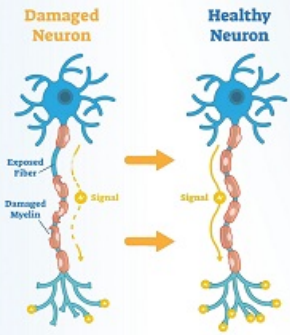
[a] Nicotinamide Adenine Dinucleotide

Enhanced Disease Response

- ↑ Increased energetic capacity

- Improved resistance to oxidative, mitochondrial, and excitotoxic stressors
- ↓ Reduction in levels of misfolded proteins

Remyelination



Neuro Repair

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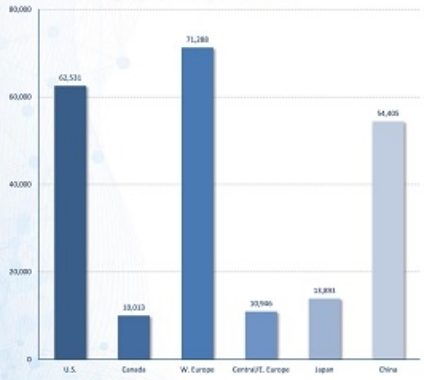
CNM-Au8 | Significant Global Opportunity

MOTOR NEURON DISEASE (ALS, Other Orphan Disorders)

ALS sales >$1B globally by 2029[1]. Current drugs are largely ineffective, mostly generic

Est. Diagnosed MND Patients by Region

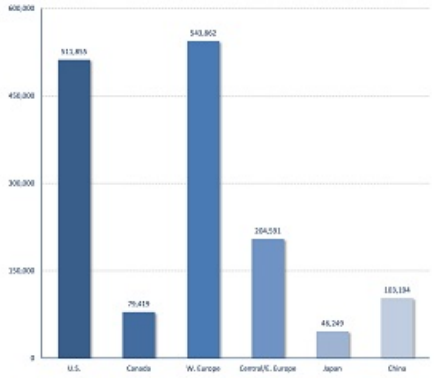


Source: Lancet Neurol. 2018 Dec;17(12):1083-1097.
MND includes amyotrophic lateral sclerosis, spinal muscular atrophy, hereditary spastic paraplegia, primary lateral sclerosis, progressive muscular atrophy, and pseudobulbar palsy

MULTIPLE SCLEROSIS ~2.5M pts globally; $23B market[2]

Only approved treatments are immunomodulators

Est. Diagnosed MS Patients by Region

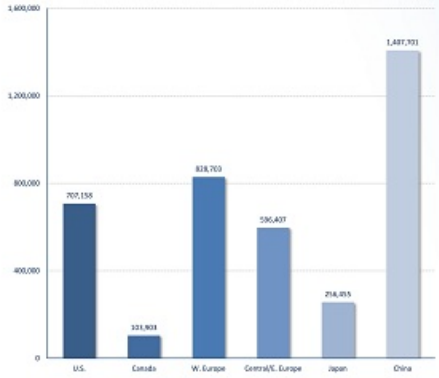


Source: Lancet Neurol. 2019 Mar;18(3):269-285

PARKINSON'S DISEASE ~7M pts globally; $6B projected by 2025[3]

2ND most common neurodegenerative disorder; only symptomatic treatments

Est. Diagnosed PD Patients by Region



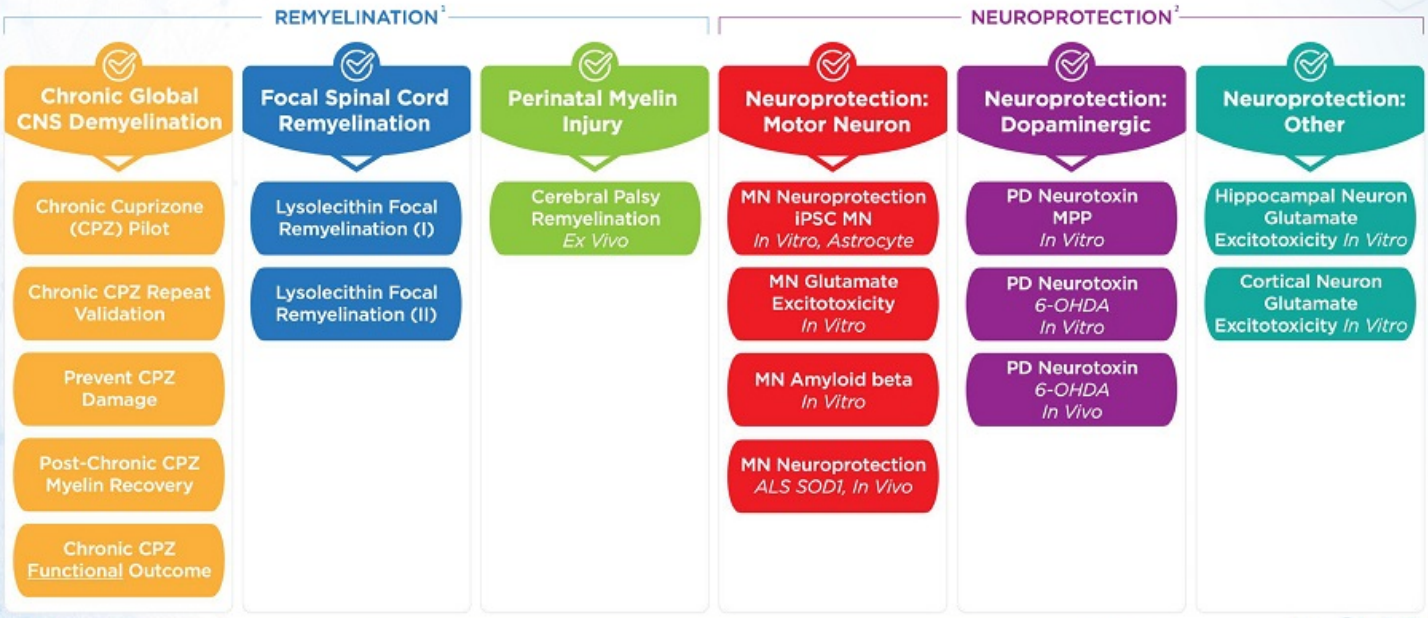
Source: Lancet Neurol. 2018 Nov;17(11):939-953.

[1]Clarivate, DRG, ALS 2020 [2]Westad et al. 2017, doi:10.1038/nrd.2017.107. [3]Parkinson's Market Data Forecast, February 2020.

CLene NANOMEDICINE

CNM-Au8 | Evidence for Energetic Improvement

Therapeutic Activity Across Remyelination + Neuroprotection Models



[1]Robinson et al. Sci Rep. 2020, DOI: 10.1038/s41598-020-58709-w. [2]Ho et al. Society for Neuroscience Meeting, 2019. Ho et al. Motor Neuron Disease Associating Meeting, 2019. Data on File, Clene Nanomedicine, Inc.

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CNM-Au8 | MOA & Remyelination Data Published

www.nature.com/scientificreports

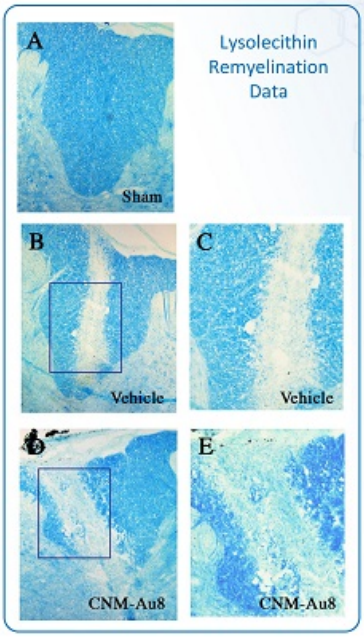
SCIENTIFIC REPORTS
nature research

OPEN

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

Andrew P. Robinson[1,9], Joanne Zhongyan Zhang[2,9], Haley E. Titus[1], Molly Karl[3], Mikhail Merzliakov[2], Adam R. Dorfman[2], Stephen Karlik[4], Michael G. Stewart[5], Richard K. Watt[5], Benjin D. Facer[6], Jon D. Facer[5], Noah D. Christian[7], Karen S. Ho[2,8*], Michael T. Hotchkin[2,9], Mark G. Mortenson[2,9], Robert H. Miller[3,9] & Stephen D. Miller[1,9]

Robinson et al. Sci Rep. 2020 Feb 11;10(1):1936. doi: 10.1038/s41598-020-58709-w



CLene NANOMEDICINE

CNM-Au8 | Clinical Program Overview

CLene NANOMEDICINE

CNM-Au8 | Clean Toxicology Findings

All Studies Resulted in No Adverse Effect Level (NOAEL)[a]

Standard ICH M3(R2) Toxicology Program

Genotoxicity *In Vitro & In Vivo (Rodent)*	**Single Dose Toxicokinetics** *Canine*	**Max Feasible Toxicokinetics** *Rodent (1-Wk, SQ)*	**Chronic Toxicity Rodent** *Rodent (6-Month)*
Safety Pharmacology *CNS, CV, Renal*	**Multi-Dose Toxicokinetics** *Canine (7-Day)*	**Max Feasible Toxicokinetics** *Canine (3-Wk)*	**Chronic Toxicity Canine** *Canine (9-Month)*
Dose Range Finding *Rodent, Minipig*	**MTD Toxicokinetics** *Canine (4-Wk)*	**High Dose Toxicokinetics** *Rodent (3-Wk)*	**Carcinogenicity Dose Range Finding** *rasH2 (1-Month)*

[a] No Adverse Event Level (NOAEL) findings

CLene NANOMEDICINE

CNM-Au8 | Well Tolerated; No Dose-Limiting Safety Issues

Phase 1 First In Human Study Completed (n=86)

- **Single-ascending dose**
  - 4 cohorts of 8 subjects plus one repeat (n=40)
  - 15, 30, 60, 90 mg
  - 3:1 randomized (active:control)
  - 1 dose; 17-day follow-up
- **Multi-ascending dose**
  - 4 cohorts of ~12 subjects (n=46)
  - 15, 30, 60, 90 mg
  - 3:1 randomized (active:control)
  - 21 days daily dosing + follow-up (Up to 50 days)

- **Most frequent TEAEs by System Organ Class: Nervous/GI**
  - Nearly all of the TEAEs were Grade 1 severity (mild)
- **No serious TEAEs, TEAEs leading to discontinuation of treatment, or TEAEs considered severe, life-threatening, or resulting in death**
- **No dose responsive TEAEs observed in SAD or MAD**

>200 Years of Human Exposure

>90 Weeks Exposure in Clinical Trials;
>100 Weeks in ALS Expanded Access

VISIONARY-MS STUDY + Long-Term Extension

RESCUEALS + Long-Term Extension

HEALEY ALS Platform Trial + Long-Term Extension

MGHALS Expanded Access Protocol

RepairPD

RepairMS

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Phase 2
RepairPD
RepairMS

CNM-Au8 Effects on Brain Energetic Metabolites

A Phase 2, Open Label, Sequential Group, Investigator Blinded Study of Magnetic Resonance Spectroscopy (^{31}P-MRS) to Assess the Effects of CNM-Au8 for the Bioenergetic Improvement of Impaired Neuronal Redox State (REPAIR)

1° **Change in Brain Bioenergetic Potential (NAD+/NADH) vs. Baseline**

N = Up to 15 per dosing cohort

(7.5, 15, 30, or 60 mg)

2° Exploratory

- Difference in brain NAD+ and NADH fraction at Week 12-16
- Difference in bioenergetic metabolites (e.g., ATP, PCr, NAD) concentration at Week 12 – 16
- Difference in brain membrane markers (PE, PC, etc.) at Week 12 – 16

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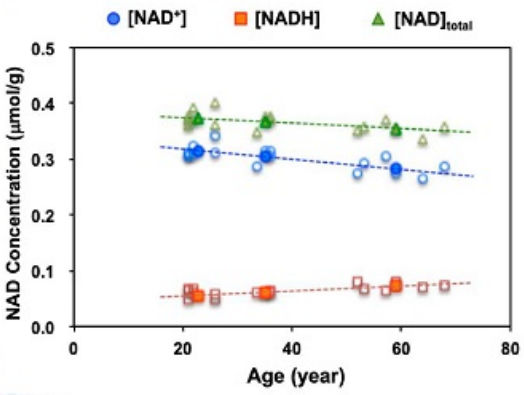
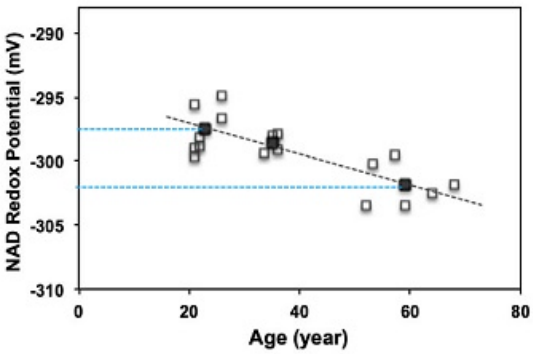
NAD⁺/NADH | Age Related Decline of Brain Energy Metabolism
(By ^{31}P-MRS Imaging)

NAD⁺ Declines / NADH Increases
(Aging Change by Decade)



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



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

Zhu et al. Proc Natl Acad Sci USA . 2015 Mar 3;112(9):2876-81.

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Phase 2 Results

RepairPD

RepairMS

CNM-Au8 | Improved Brain Energy Metabolism

Increased NAD+/NADH Ratio in MS & PD Patients

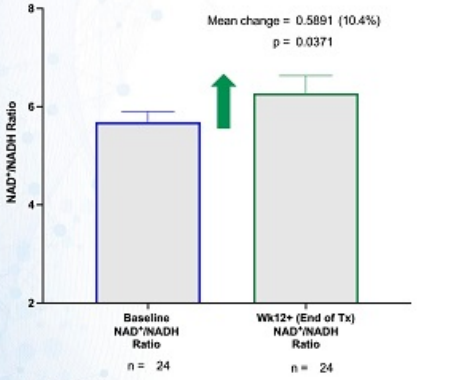
1° Endpoint

REPAIR Integrated Analysis

^{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)



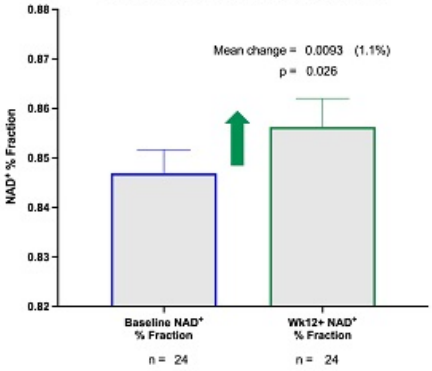
2° Endpoints

REPAIR Integrated Analysis

^{31}P-MRS Change in Brain NAD$^+$ % Fraction at End of Treatment

Partial Volume Coil; % Fraction of NAD$^+$, (NAD$^+$, NADH Couple)

Secondary Endpoint, Mean ± SEM (Paired t-test)

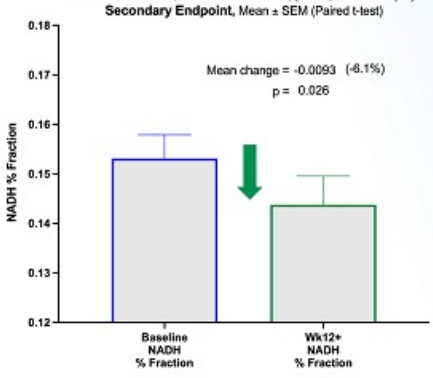


REPAIR Integrated Analysis

^{31}P-MRS Change in Brain NADH % Fraction at End of Treatment

Partial Volume Coil; % Fraction of NADH, (NAD$^+$, NADH Couple)

Secondary Endpoint, Mean ± SEM (Paired t-test)



NAD is an essential molecule responsible for cellular energy production

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Phase 2 Results

RepairPD

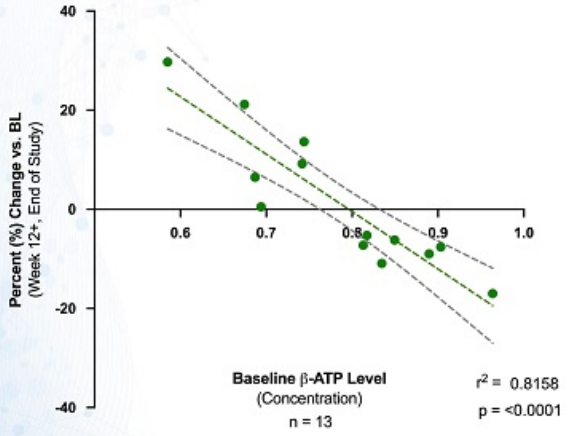
CNM-Au8 | Treatment Normalized Key Markers of Brain Metabolism in PD Patients

Exploratory Endpoint

^{31}P-MRS Change in β-ATP at End of Study

Full Volume Coil ^{31}P Signal Area (Integral)

Percent (%) Change from Baseline at End of Study



β-ATP is used by the cell to maintain cellular metabolism and normal function

Post Hoc Endpoint

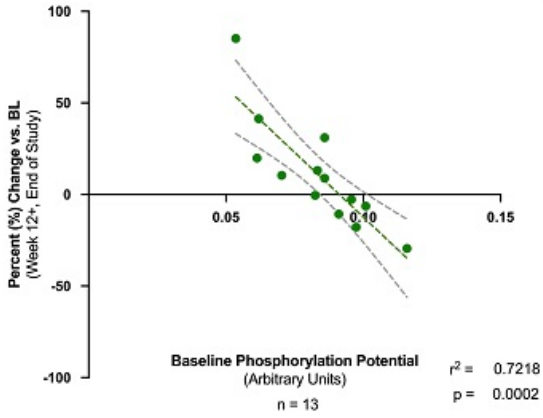
^{31}P-MRS Change in Phosphorylation Potential

Full Volume Coil ^{31}P Signal Area (β-ATP, $P_i^{(in)}$)

β-ATP/ADP * Intracellular Phosphate [$P_i^{(in)}$]

Percent (%) Change from Baseline at End of Study

[Post Hoc]



Phosphorylation potential is the amount of available phosphorous that can be used to make ATP in times of stress or high metabolic activity

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Phase 2

RESCUEALS

Randomized, Double-Blind, Placebo-Controlled Study in Early Symptomatic Amyotrophic Lateral Sclerosis Patients on Stable Background Therapy to Assess Bioenergetic Catalysis with CNM-Au8 to Slow Disease Progression in ALS

36-Week Treatment Period (n=42) 30mg, Placebo

SCREENING (January 2020); FPFV 16-Jan-2020; 45 of 42 enrolled (Nov-2020)

Day -28 to -1

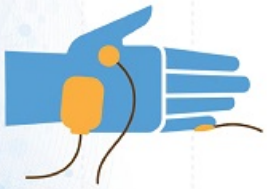
Week 6 | Week 12 | Week 18 | Week 24 | Week 30 | Week 36 | Week 42 | Week 48 | Week 54 | Week 60 | Week 66 | Week 72 | Week 76

6 WEEKS

EOS

Open Label Extension

Phone calls at Weeks 3, 6, 18, 30



1° **Change in Sum of Motor Unit Index**
For the Abductor Digiti Minimi (ADM), Abductor Pollicis Brevis (APB), Biceps Brachii (BB), Tibialis Anterior (TA)

2° **Key Secondary: Forced Vital Capacity**

Exploratory Endpoints

- Other Electromyography (SH_i, NP_i, MUSIX, MScan)
- ALSFRS-R
- Change in Rate of ALSFRS-R progression
- QOL
- Combined Joint-Rank (Survival + ALSFRS-R)

Anticipated full unblinded data readout: 2H 2021

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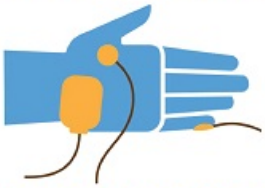
Electromyography | Sensitive Biomarker Predictive of Clinical Progression

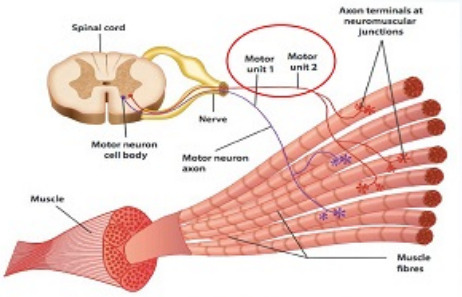
Predictive Endpoints of Disease Progression

- **Loss of Motor Units**
  Motor Unit Index (MUNIX)

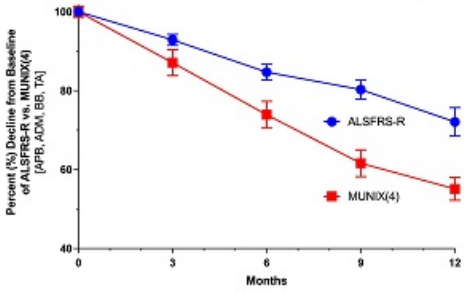


Clinical Endpoints

- **ALSFRS-R**
- **Pulmonary Function** (Vital Capacity)
- **Mortality**



MUNIX Longitudinal Progression



Neuwirth et al. JNNP 2015 Nov;86(11):1172-9.

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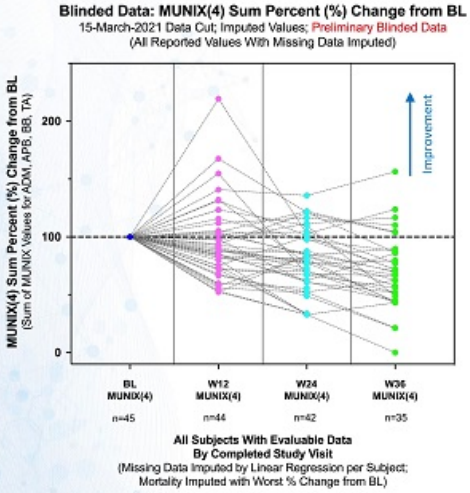
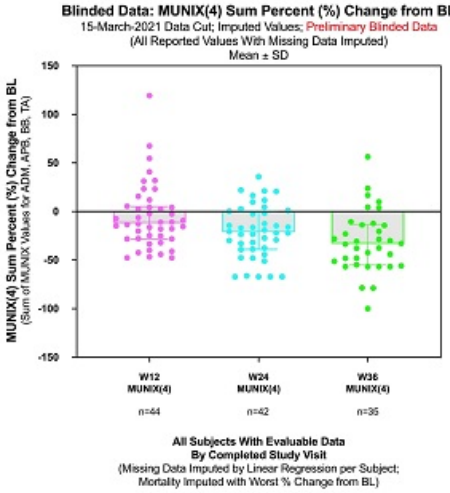
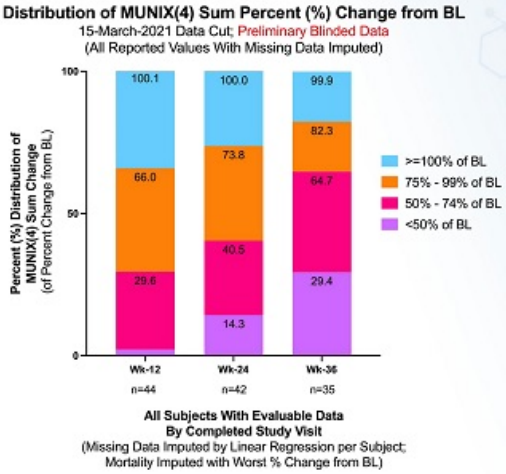
Phase 2 RESCUEALS

Emerging Evidence Predictive of Clinical Efficacy | MUNIX(4) Sum Change







Robert Glanzman MD FAAN, et al. "A Blinded Interim Update on RESCUE-ALS: A Randomized, Placebo-Controlled, Phase 2 Study to Determine the Effects of CNM-Au8 to Slow Disease Progression in Amyotrophic Lateral Sclerosis" Presented at ENCALS 2021 Virtual Meeting, 12-May-2021.

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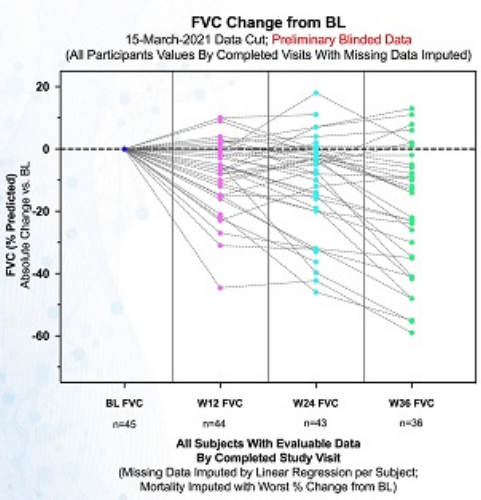
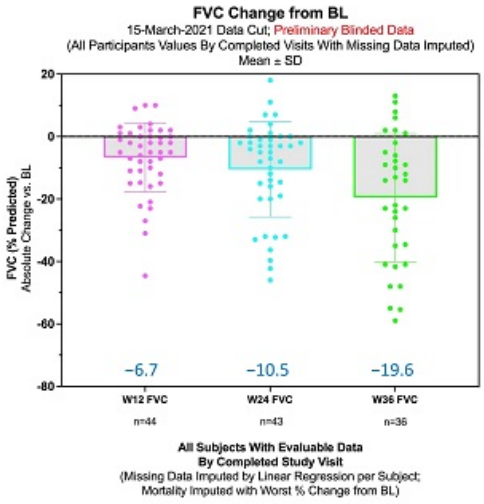
Phase 2 RESCUEALS

Slower Rate of Vital Capacity Loss Than Comparable Clinical Trial Datasets





SVC Avg. Slope Decline (% points/month)	Slope Est. (9-months)
Empower (−2.73%)	-24.6%
Benefit (−2.74%)	-24.7%
PRO-ACT (-2.90%)	-26.1%

Andrews et al. JAMA Neurol. 2018;75(1):58-64.

Robert Glanzman MD FAAN, et al. "A Blinded Interim Update on RESCUE-ALS: A Randomized, Placebo-Controlled, Phase 2 Study to Determine the Effects of CNM-Au8 to Slow Disease Progression in Amyotrophic Lateral Sclerosis" Presented at ENCALS 2021 Virtual Meeting, 12-May-2021.

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Phase 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**

2° **Slow Vital Capacity Hand Held Dynamometry**

Exploratory Endpoints

- Combined Joint Rank (Survival + ALSFRS-R)
- Voice pathology
- PRO (ALSAQ)
- Pharmacodynamic markers

Anticipated full unblinded data readout: 2H 2022

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Phase 2

VISIONARY-MS STUDY

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

24-Week Blinded Fixed Treatment Period

Up to 24-Week Blinded Extension Period (Until LPLV 24Wk Visit)

Up to 48-Week Placebo-Control

2:1 Randomization (Active: Placebo)

15mg, 30mg, Placebo (n=150)

1° **Change in Low Contrast Letter Acuity (LCLA)**
At Week 24

2° **Change Composite Clinical Response**
9HPT / SDMT / T25FW / LCLA / EDSS

Exploratory Endpoints

- Optical Coherence Tomography (OCT)
- Multi-focal VEP Amplitude & Latency
- Full field-VEP Amplitude & Latency
- MRI Endpoints
- Visual Function (High Contrast)
- QOL / EDSS

Anticipated top-line unblinded data:
1H 2023*

*Subject to ongoing COVID-19 related site research restrictions generally implemented to protect MS patients taking standard-of-care immunosuppressive therapies

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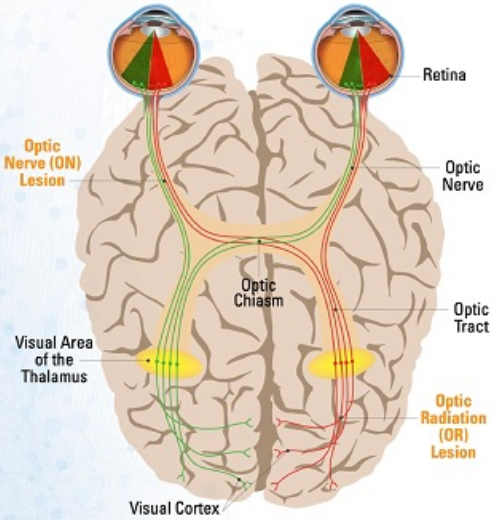
Measuring MS Functional Improvement

The Visual System is a Window into the Brain



LCLA

Phase 2 Primary:
Functional Visual Improvement

LCLA Correlates with clinically meaningful deficits in QOL, EDSS and MSFC, MRI, and OCT

MS Functional Endpoints

Phase 2 Exploratory:
Neuroprotection/Remyelination Endpoints

9-Hole Peg Test

Symbol Digit Modalities

Timed 25-Ft Walk

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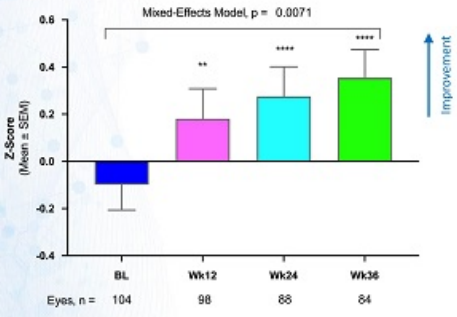
Phase 2 VISIONARY-MS STUDY

Emerging Evidence of Clinical Improvement

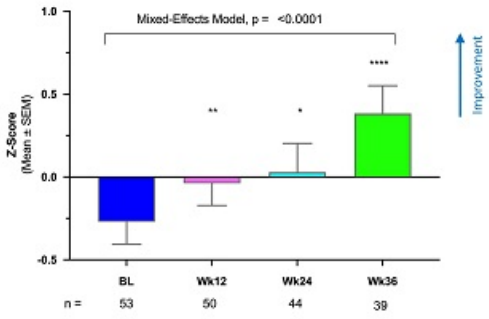
LCLA (Best-Corrected)

LCLA (All Eyes) Z.Score
13-January-2021 Data Cut, Preliminary Blinded Data
(Based on 'Mild' EDSS [≤1.5]; Mean ± SEM)



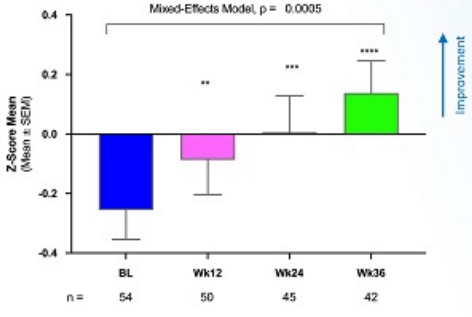
SDMT

SDMT Z.Score
13-January-2021 Data Cut, Preliminary Blinded Data
(Based on 'Mild' EDSS [≤1.5]; Mean ± SEM)



6-Component Integrated (m)MSFC

(m)MSFC 6-component Average Z.Score
13-January-2021 Data Cut, Preliminary Blinded Data
(Based on 'Mild' EDSS [≤1.5]; Mean ± SEM)



Z-Score change compared to the least-affected patients at Baseline (with EDSS <= 1.5)

All Available Values (by Completed Subject Visit)
Mixed Effects Model, Dunnett's test for multiplicity;
* p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001

Glanzman, R., H. Beadnall, M. T. Hotchkin, A. Klistorner, M. Barnett, R. Sergott, A. Rynders, K. S. Ho, and Mark G. Mortenson. "Update to a Phase 2 clinical trial of catalytic gold nanocrystals, CNM-Au8, for the treatment of chronic optic neuropathy." Presented at the ACTRIMS Forum 2021, February 26, 2021.

CLENE NANOMEDICINE

Strong Intellectual Property

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

CSN®
Clean surface nanocrystal (CSN) therapeutics

Patent Status	Patent Description	Trade Secrets
Issued & Allowed Patents 130+	Process And Method/Device (Clean Surface; Gold CSN)	Plasma Conditioning
Pending Applications >30	State of Matter (CNM-Au8)	Electrode Design & Cycling
Total Patents/ Applications >160	Method of Use (Prevent Demyelination & MoA)	Trough Flow, Temp, Pressure
	Method of Use (Bi-Metallic Au/Pt; Antimicrobial)	Concentration & Filtration

[a] With Patent Restoration Term (assuming 5-year extension).

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Clene | Proprietary Nanocrystal Manufacturing

In-House ISO8 Clean Room Clinical Production in North East, MD

Designed to be Scalable to Commercialization

- Patented Hydro-electro-Crystallization
- Proprietary Trade Secrets
- Validated CMC Processes

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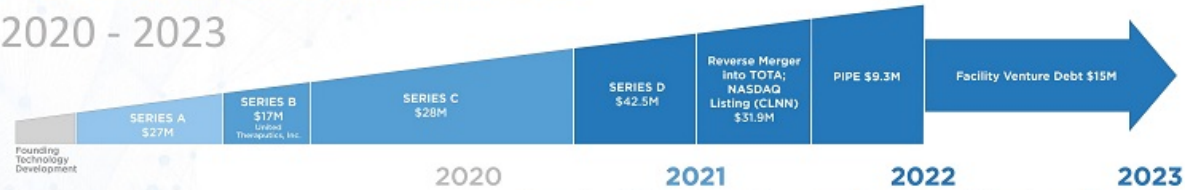
Anticipated Timeline & Investor Catalysts

2020 - 2023



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CLENE | Investment Highlights

Lead Asset: CNM-Au8 for Neuro Repair

- Energy enhancing nanotherapeutic
- Robust Preclinical Remyelination & Neuroprotection Data Across Multiple Animal Models in:
  - MS,
  - ALS, and
  - Parkinson's Disease
- NOAEL Findings From All Toxicity Studies
- Acceptable Phase 1 Safety Profile
- >90 Weeks Exposure in Clinical Trials; >100 Weeks in ALS Expanded Access (EAP)

Unmet Medical Need & Market Opportunity

- No Effective Disease-Modifying Drugs for ALS or PD
- No MS Therapies Clinically Impact Remyelination & Neurorepair
- Remyelination and Neurorepair Sales Could Exceed $10B per annum[1]
  - ALS is a Lethal Motor Neuron Disease With Suboptimal Therapies
  - PD is Highly Prevalent With No Disease Modifying Treatments

Clinical Development Pipeline

- Two Phase 2 Brain Target Engagement Studies in PD and MS with Top Line Results Reported Aug 2021
- Three Phase 2 POC Studies in ALS, MS, and COVID with Results Anticipated in the next 12-18 Months
- Phase 3 ALS Registrational Trial in with Full Results Anticipated in mid- 2022
- Ongoing ALS Early Access Program
- USA FDA Granted ALS Orphan Drug Designation

CNM-ZnAg for COVID-19

- Zinc-Silver Antiviral + Immune Support
- Phase 2 Trial in Brazil To Treat Acutely Symptomatic Non-Hospitalized COVID-19 Patients Underway
  - 1st Endpoint: Prevention of Hospitalization
  - 2nd Endpoint: Time to Symptomatic Improvement (Up to 28 Days)
- Results Anticipated 1H 2022

Strong IP Portfolio

- 130+ Issued Patents Worldwide; 30+ Pending Patent Applications
- State of Matter Claims Cover Myelin Protection Mechanisms, Remyelination, and Neuroprotection to 2035 (with Patent Restoration Term)
- Manufacturing Device and Process Patents to 2030 and Beyond

Financials

- CLNN (NASDAQ)
- $31.9M USD (Gross) Raised via SPAC merger + PIPE (2020)
- Cash on Hand at end of Q2 2021 of $63.0M (Unaudited)
- Anticipated Cash Runway to EOY 2022
- $114M USD Raised Privately (Series A-D)
- +$16.7M in Additional Grant and Indirect Financial Support for ALS and MS Phase 2 & 3 Clinical Programs
- $24.3M USD (Gross) Raised via PIPE + Venture debt for MFG (2021)

[1] Data on file, Clene Nanomedicine, Inc.

Clene NANOMEDICINE

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: 16-September-2021