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 5, 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 August 5, 2021, Clene Inc. (the "*Company*") issued a press release announcing positive top-line results from its Phase 2 REPAIR clinical trials in Parkinson's disease and multiple sclerosis. 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 press release issued on August 5, 2021, 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 Exhibits 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, 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 5, 2021 announcing positive top-line results from its Phase 2 REPAIR clinical trials in Parkinson's disease and multiple sclerosis
99.2	Corporate Presentation dated August 5, 2021

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 5, 2021

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

Clene Reports Positive Top-line Results from its Phase 2 REPAIR Clinical Trials in Parkinson's Disease and Multiple Sclerosis

Achieved a statistically significant increase in the Phase 2 program's primary endpoint (mean change in brain NAD+/NADH ratio)

CNM-Au8Ò, a gold nanocrystal suspension, significantly improved brain energetic metabolism

Trial results demonstrate consistent brain target engagement in PD and MS patients

Data provide clinical proof-of-mechanism and support the potential of CNM-Au8 to drive meaningful neurological functional improvements in the treatment of neurodegenerative disorders

SALT LAKE CITY, August 5, 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 reported positive top-line results from the Phase 2 REPAIR clinical trials investigating the improvement of brain energetic metabolism in Parkinson's disease (PD) and multiple sclerosis (MS).

The objective of the REPAIR clinical trial program was to demonstrate the effects of Clene's energy-enhancing nanotherapeutic, CNM-Au8Ò, on brain energy metabolites in two sister studies of patients with Parkinson's disease (REPAIR-PD) and multiple sclerosis (REPAIR-MS). Patients were imaged using ^{31}phosphorous magnetic resonance spectroscopy, an innovative non-invasive brain imaging technique, before and after 12 or more weeks of daily oral dosing with CNM-Au8. End of treatment results at week 12 were compared to baseline in 24 patients, 13 patients in REPAIR-PD and 11 patients in REPAIR-MS (all study participants with repeat imaging data).

The results for the primary endpoint, the mean change in the brain NAD^+/NADH ratio (the ratio of the oxidized to reduced form of nicotinamide adenine dinucleotide), demonstrated a statistically significant increase by an average of 0.589 units (10.4%) following 12-weeks of treatment with CNM-Au8 ($p=0.037$, paired t-test), in the pre-specified integrated analysis of the REPAIR-PD and REPAIR-MS studies. Key secondary endpoints, mean change from baseline in the NAD^+ fraction and NADH fraction of the total NAD pool, were concordant with the primary endpoint, demonstrating the NAD^+ fraction increased ($p=0.026$), while the NADH fraction decreased ($p=0.026$). The individual results for these sister studies demonstrated consistent statistical trends toward improvement in the NAD+/NADH ratio with results of $p=0.11$ and $p=0.14$, for REPAIR-PD and REPAIR-MS, respectively.

Analyses of pre-specified exploratory endpoints demonstrated that homeostatic equilibrium was achieved across essential energetic metabolites, including adenosine triphosphate (ATP), intracellular phosphorous ($Pi^{(in)}$), phosphocholine (PC), and phosphorylation potential index (b-ATP/ADP*$Pi^{(in)}$). For these metabolites and indices, the percent change from baseline to the week 12 end-of-treatment was significantly inversely correlated with baseline levels, such that participants with relatively lower baseline levels demonstrated increases, and subjects with relatively higher baseline levels demonstrated a re-balancing effect with levels decreased to the baseline population mean. This relationship was observed both on an integrated basis across the two studies, and independently in both REPAIR-PD and REPAIR-MS, respectively, for: b-ATP ($r^2 = 0.82$, $p < 0.0001$; $r^2 = 0.71$, $p = 0.0011$), phosphorylation potential ($r^2 = 0.72$, $p = 0.0002$; $r^2 = 0.68$, $p = 0.0019$), PC ($r^2 = 0.78$, $p < 0.0001$; $r^2 = 0.54$, $p = 0.0095$), and $Pi^{(in)}$ ($r^2 = 0.42$, $p = 0.017$; $r^2 = 0.48$, $p = 0.018$). In addition, multiple other ^{31}phosphorous energetic metabolites and indices showed consistent homeostatic changes, which will be presented in publications and at forthcoming scientific congresses.

Robert Glanzman, MD FAAN, Clene's Chief Medical Officer, commented on the REPAIR results, "We believe the REPAIR program represents a critical breakthrough for Clene, demonstrating that catalytically active CNM-Au8 improves energy production and utilization in the brains of people with Parkinson's disease and multiple sclerosis. Using a novel, noninvasive brain imaging approach, the study demonstrated that a key driver of cellular ATP energy production, the ratio of NAD+/NADH, was significantly increased in the brains of patients after three months of daily CNM-Au8 oral administration. Remarkably, the data also show a significant rebalancing of brain beta-ATP levels in these patients, a metabolic response to treatment that suggests improved ATP energy efficiency. Our next step will be to demonstrate that these brain energetic changes result in clinically meaningful results in patients with Parkinson's disease and multiple sclerosis."

CNM-Au8 treatment was well tolerated with all treatment emergent adverse events reported as predominantly mild and unrelated to study drug. There were no serious adverse events or treatment discontinuations related to adverse events in either study. As expected, the clinical endpoint of MDS-UPDRS in REPAIR-PD showed no worsening of clinical status across the study population (safety endpoint). The REPAIR-MS clinical endpoints included the modified MS functional composite (m)MSFC (exploratory endpoint), which showed consistent improvements across its four scales of symbol digit modalities test (SDMT), low contrast letter acuity (LCLA), nine-hole peg test (9HPT), and timed 25-foot walk test (T25FW).

Rob Etherington, Clene's Chief Executive Officer, concluded, "Clene is a company driven to pioneer the development of cellular energy-enhancing nanotherapeutics for the treatment of neurodegenerative diseases. We believe the study results also strongly support Clene's ongoing Phase 2 and Phase 3 clinical programs investigating how CNM-Au8's neuro-reparative and neuroprotective properties may impact disease progression in amyotrophic lateral sclerosis, multiple sclerosis, and Parkinson's disease, and may be broadly applicable to the treatment of neurodegenerative diseases."

REPAIR-PD study results will be presented at the upcoming International Parkinson and Movement Disorders Society, MDS Virtual Congress 2021 meeting, September 17-22, 2021. REPAIR-MS results will be presented at the upcoming 37th Congress of the European Committee for Treatment and Research in Multiple Sclerosis, October 13-15, 2021.

The REPAIR program was conducted at the University of Texas Southwestern in collaboration with Dr. Richard Dewey, Jr., Professor in the UT Southwestern Medical Center Department of Neurology and Director of the Clinical Center for Movement Disorders (REPAIR-PD), Dr. Benjamin Greenberg, Professor in the UT Southwestern Medical Center Department of Neurology and Vice Chair of Clinical & Translational Research (REPAIR-MS), and Jimin Ren, PhD, Associate Professor at the UT Southwestern Advanced Research Imaging Center (both studies).

Clene thanks the study participants who directly supported this novel clinical research in the REPAIR program, the research dedication of the UT Southwestern principal investigators, Dr. Richard Dewey Jr. and Dr. Benjamin Greenberg, research colleagues at the Neuro Translational Research Center, and the advanced imaging techniques developed by Jimin Ren, PhD, of the UT Southwestern Advanced Research Imaging Center.

About REPAIR-PD and REPAIR-MS

REPAIR-MS and REPAIR-PD are Phase 2 single-center, active-only, sequential group studies examining the brain metabolic effects, safety, pharmacokinetics and pharmacodynamics of CNM-Au8 in patients who have been diagnosed with MS within 15 years of screening or in patients with PD who have been diagnosed within three years of screening. Investigators and participants are blinded to dose. Participants received orally delivered CNM-Au8 daily each morning for 12 weeks. Participants undergo ^{31}P-MRS brain imaging scans to semi-quantitatively measure central nervous system (CNS) energetic metabolites at baseline, prior to administration of drug, and at the end-of-study following at least 12 weeks of exposure to CNM-Au8. The objective of these studies is to demonstrate target engagement for CNM-Au8 on CNS biomarkers related to energetics and neuronal membrane stability in patients with MS and PD. The studies are taking place 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. For more information see ClinicalTrials.gov Identifiers: NCT03993171 and NCT03815916.

About CNM-Au8^{Ò}

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-Au8^{Ò}, a gold nanocrystal suspension, 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” which are intended to be covered by 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 on Form 10-K, 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.

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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

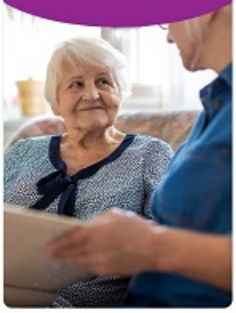
KSV | KENSINGTON-SV GLOBAL

Clene Nanomedicine

CNM-Au8®
in clinical development as the first energetic catalyst to repair & improve neurological function

Topline data from One Registrational Trial[1] by 1H 2022
and
4
Phase 2 Trials[2] by end of 2021

>180
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:
48M
End of Q1
+
PIPE & Venture debt of $24M

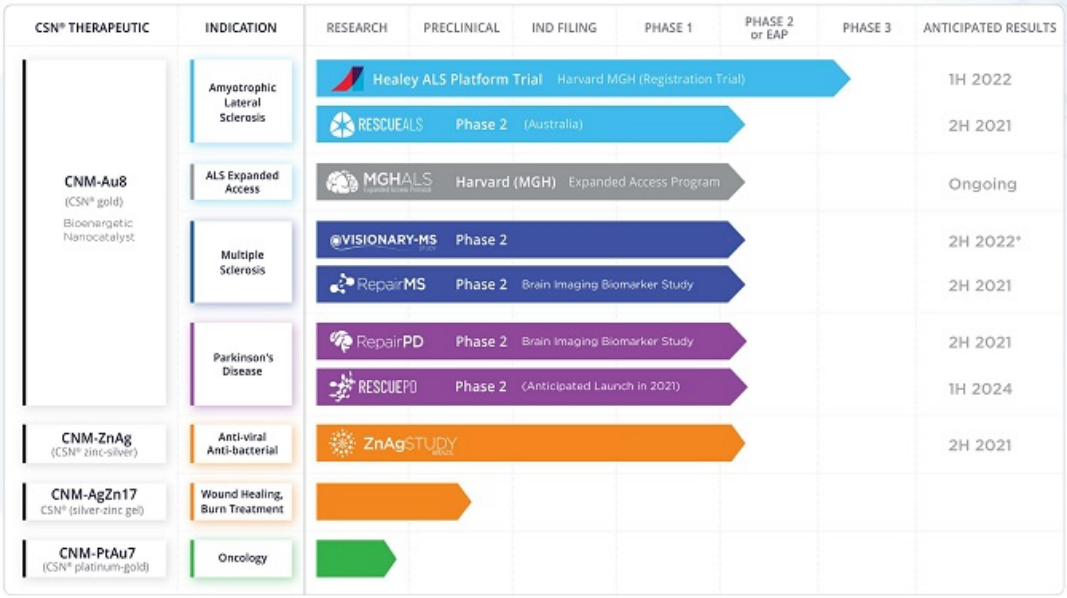
1. HEALEY-ALS: https://clinicaltrials.gov/ct2/show/NCT04414345?term=CNM-Au8&cond=ALS&draw=1&rank=1 2. RESCUE-ALS: https://clinicaltrials.gov/ct2/show/NCT04098406?term=CNM-Au8&cond=ALS&draw=1&rank=3 REPAIR-PD: https://clinicaltrials.gov/ct2/show/NCT03815981?term=cnm-au8&draw=2&rank=1 REPAIR-MS: https://clinicaltrials.gov/ct2/show/NCT03993171?term=cnm-au8&draw=2&rank=3 Anti-viral study: https://clinicaltrials.gov/ct2/show/NCT04160338

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



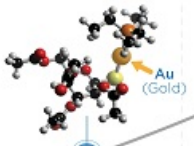
*Subject to ongoing COVID-19 related site research restrictions generally implemented to protect MS patients taking standard-of-care immunosuppressive therapies

clene NANOMEDICINE

Evolution of Gold
as a Therapeutic Modality

Chinese & Ayurvedic Gold Preparations
(China, Arabia, India)

2500–1000 BC

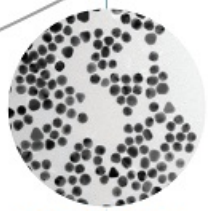


1930–1980s

Monoatomic Gold Salts for Rheumatoid Arthritis
(IM Sodium Aurothiomalate;
IM Aurothioglucose;
Oral Auranofin)

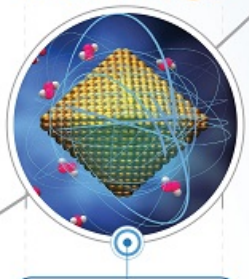
gold 3,4,5-triacetyloxy-6-(acetyloxymethyl oxane-2-thiolate; triethylphosphanium

1950s–2000s



Surface Modified and Functionalized Colloidal Gold Particles
Drug Carriers;
Photothermal Therapy

Clene's Patented Breakthrough



2020+

Catalytic Clean Surfaced Faceted Gold Nanocrystals

Pioneering Bioenergetic Nanocatalysis

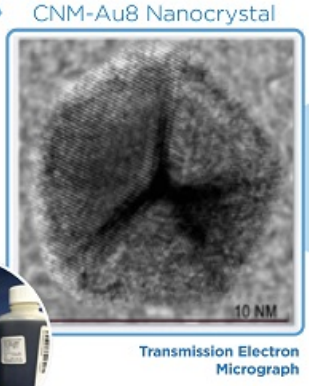
clene NANOMEDICINE

CNM-Au8® | Energy Enhancing Nanotherapeutic

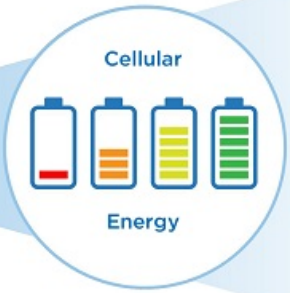
Improved Cellular Energy Production & Utilization

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**



Transmission Electron Micrograph



Remyelination Failure In MS

Parkinson's Disease

Amyotrophic Lateral Sclerosis

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CNM-Au8 | Integrating Physics With Biology

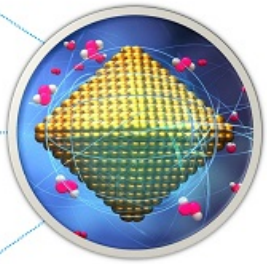
Electron Transfer Is Fundamental to Energy Production

Surface Based Catalytic Activity

Electrons (e-) Move Freely Across Nanocrystal Surface

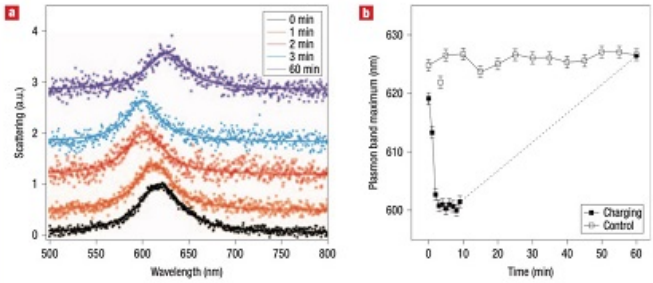
Vertices, Edges, & Faces Key to Catalytic Activity

Clean-Surfaced Nanocrystals



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

AuNP Catalyzed Oxidation of Ascorbic Acid[1]



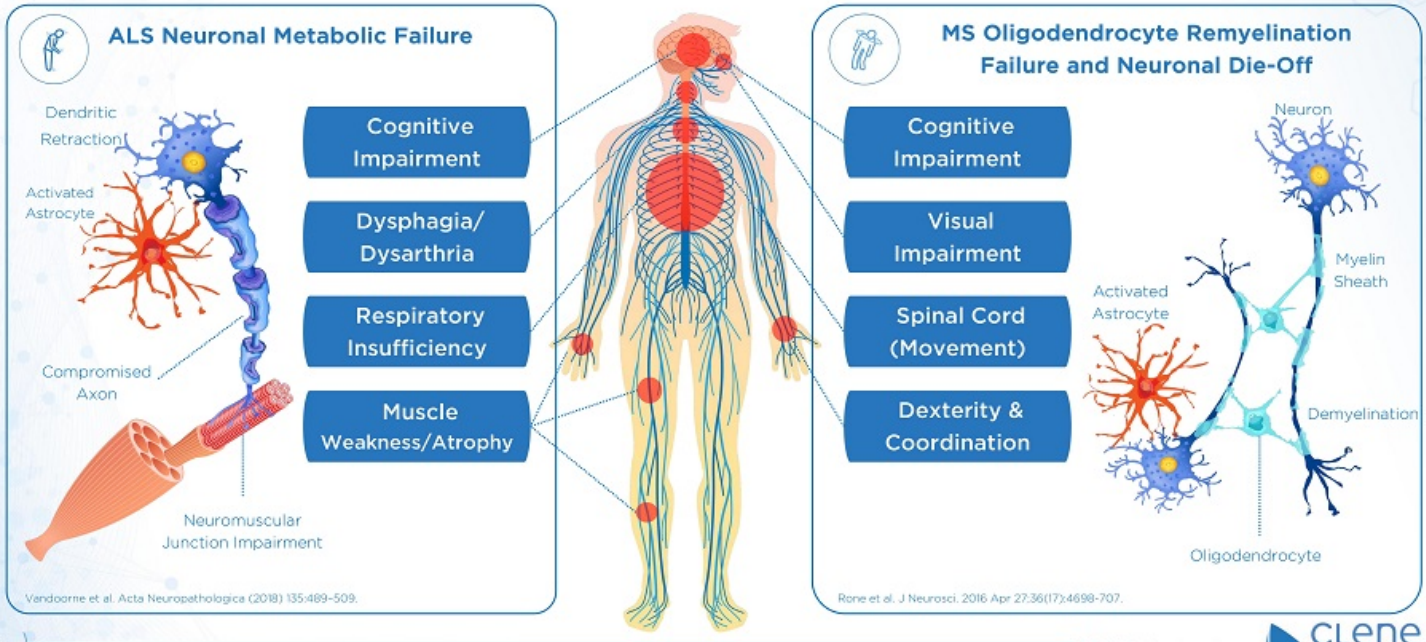
a. Rayleigh scattering measured by dark field microscopy of surface plasmon resonance of scattering spectra of the AuNP decahedron before and at 1, 2, 3 and 60 min after electron injection by ascorbate ions.

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

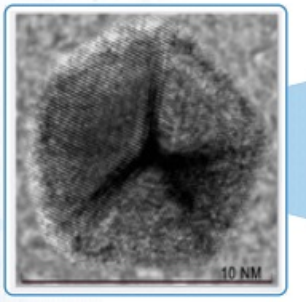
Treating Energetic Failure | Common Pathological Mechanism In Neurodegenerative Disorders (MS, ALS, PD)



CLENE NANOMEDICINE

CNM-Au8 | MOA → Therapeutic Effects

Catalytic Gold Nanocrystals



Bioenergetic Mechanism

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

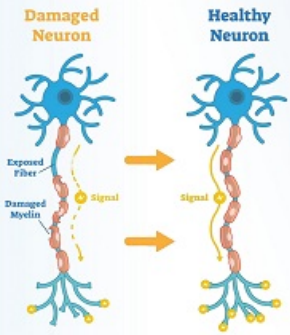
[a] Nicotinamide Adenine Dinucleotide

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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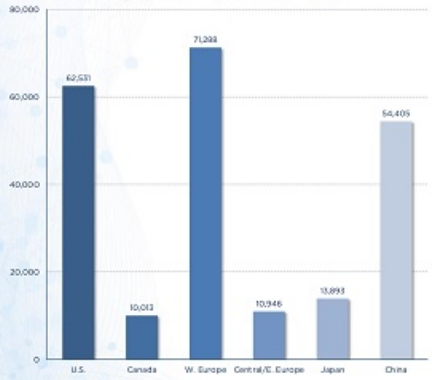
CNM-Au8 | Significant Global Opportunity

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

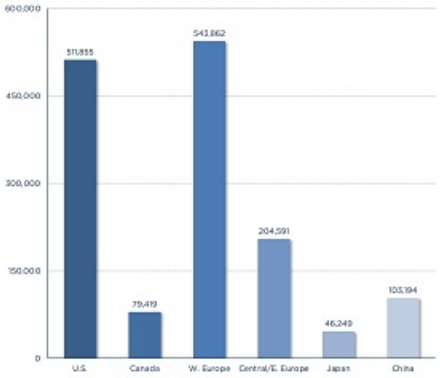


Source: Lancet Neurol. 2018 Dec;17(12):1083-1097.
MND includes amyotrophic lateral sclerosis, spinal muscular atrophy, hereditary spastic paraplegia, primary lateral sclerosis, progressive muscular atrophy, and pseudobulbar palsy

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

Only approved treatments are immunomodulators

Est. Diagnosed MS Patients by Region

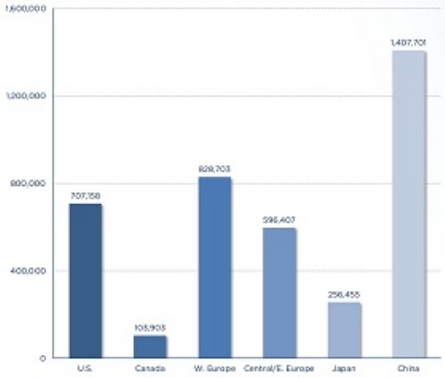


Source: Lancet Neurol. 2019 Mar;18(3):269-285

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



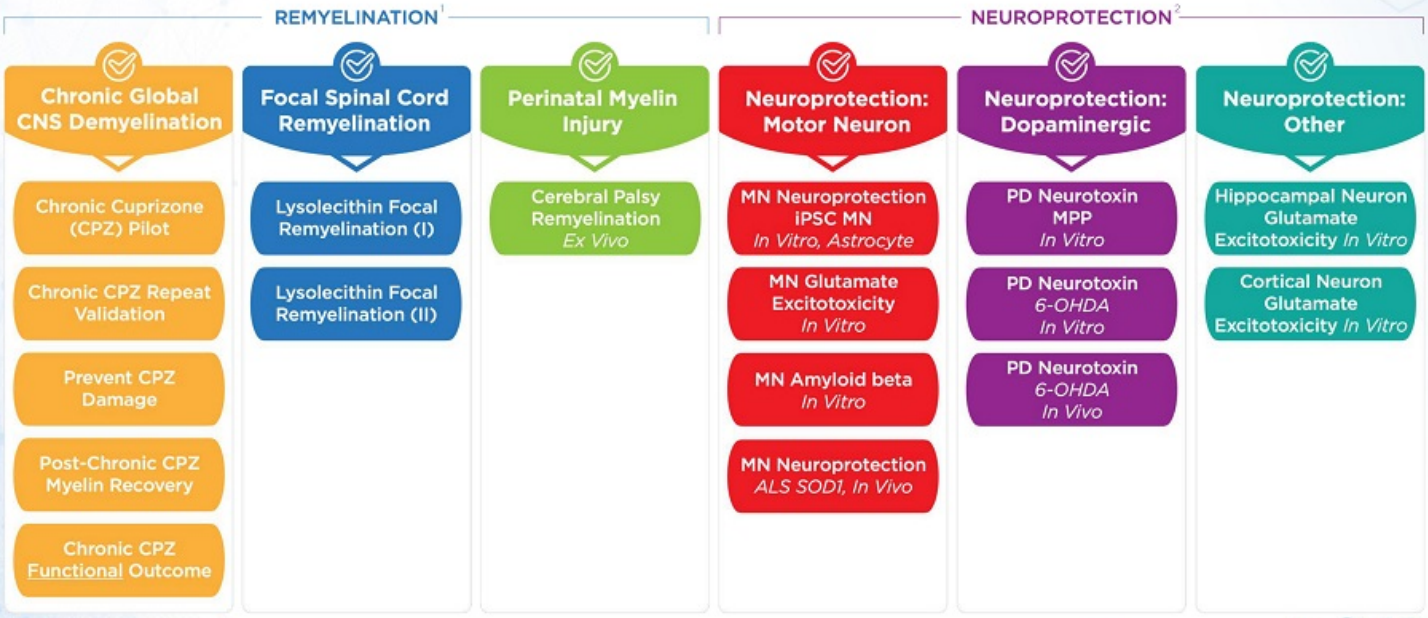
Source: Lancet Neurol. 2018 Nov;17(11):939-953.

[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.

CLENE NANOMEDICINE

CNM-Au8 | MOA & Remyelination Data Published

www.nature.com/scientificreports

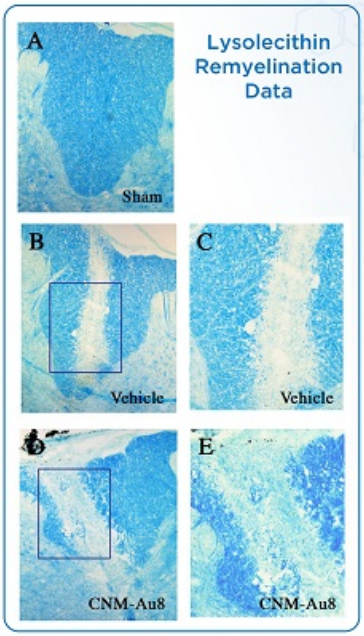
SCIENTIFIC REPORTS
nature research

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



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CNM-Au8 | Clinical Program Overview

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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] NOAEL = No Dose Limiting Toxicities Observed

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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**

Phase 2 & 3 Clinical (>180 Years Exposure)

Up to 89 Weeks Exposure in Clinical Trials;
Up to 96 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

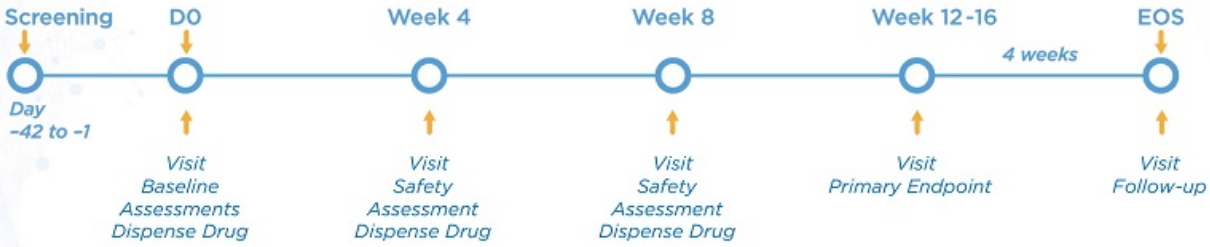
RepairMS

CLENE NANOMEDICINE

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

Top-Line Results
Repair-PD: 2H 2021
Repair-MS: 2H 2021

*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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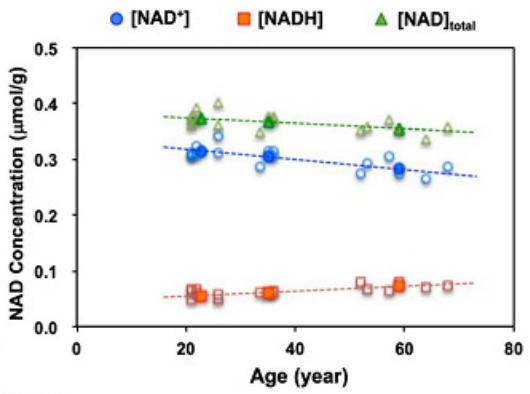
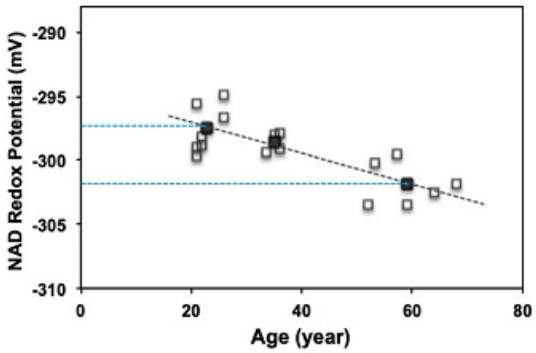
NAD⁺/NADH | Age Related Decline
By ^{31}P-MRS Imaging

NAD⁺ Decline &. NADH Increase
(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.

CLene NANOMEDICINE

Phase 2
RepairPD
RepairMS

CNM-Au8 Improved Brain Energetic Metabolism

Increased NAD+/NADH Ratio (Primary Endpoint)

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Clene Reports Positive Top-line Results from its Phase 2 REPAIR Clinical Trials in Parkinson's Disease and Multiple Sclerosis

Achieved a statistically significant increase in the Phase 2 program's primary endpoint (mean change in brain NAD+/NADH ratio)

CNM-Au8® significantly improved brain energetic metabolism

Trial results demonstrate consistent brain target engagement in PD and MS patients

Data provide clinical proof-of-mechanism and support the potential of CNM-Au8 to drive meaningful neurological functional improvements in the treatment of neurodegenerative disorders

SALT LAKE CITY, August 5, 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 reported positive top-line results from the Phase 2 REPAIR clinical trials investigating the improvement of brain energetic metabolism in Parkinson's disease (PD) and multiple sclerosis (MS).

The objective of the REPAIR clinical trial program was to demonstrate the effects of Clene's energy-enhancing nanotherapeutic, CNM-Au8® on brain energy metabolites in two sister studies of patients with Parkinson's disease (REPAIR-PD) and multiple sclerosis (REPAIR-MS). Patients were imaged using ^{31}phosphorous magnetic resonance spectroscopy, an innovative non-invasive brain imaging technique, before and after 12 or more weeks of daily oral dosing with CNM-Au8. End of treatment results at week 12 were compared to baseline in 24 patients, 13 patients in REPAIR-PD and 11 patients in REPAIR-MS (all study participants with repeat imaging data).

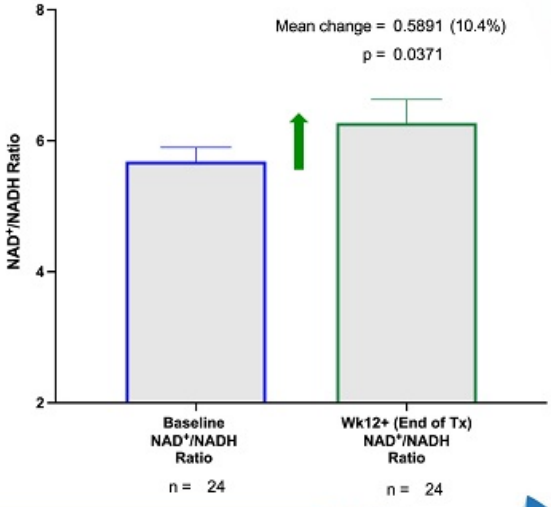
The results for the primary endpoint, the mean change in the brain NAD^+/NADH ratio (the ratio of the oxidized to reduced form of nicotinamide adenine dinucleotide), demonstrated a statistically significant increase by an average of 0.589 units (10.4%) following 12-weeks of treatment with CNM-Au8 ($p=0.037$, paired t-test), in the pre-specified integrated analysis of the REPAIR-PD and REPAIR-MS studies. Key secondary endpoints, mean change from baseline in the NAD^+ fraction and NADH fraction of the total NAD pool, were concordant with the primary endpoint, demonstrating the NAD^+ fraction increased ($p=0.026$), while the NADH fraction decreased ($p=0.026$). The individual results for these sister studies demonstrated consistent statistical trends toward improvement in the NAD+/NADH ratio with results of $p=0.11$ and $p=0.14$, for REPAIR-PD and REPAIR-MS, respectively.

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)



Data on File, Clene Nanomedicine, Inc.

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Phase 2
RepairPD
RepairMS

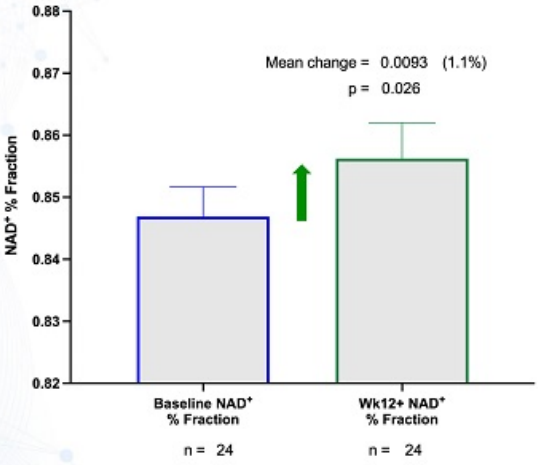
CNM-Au8 Increased NAD⁺ & Decreased NADH
(Secondary Endpoints)

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)

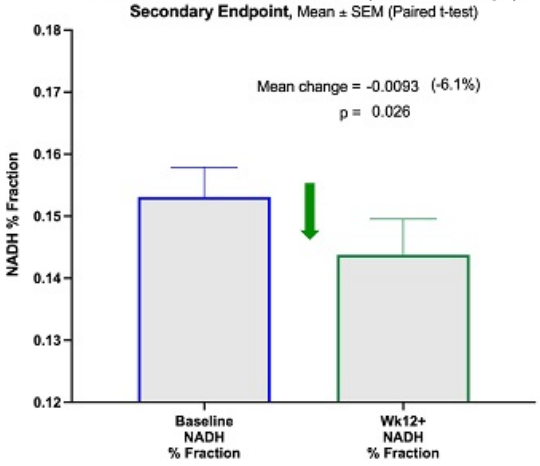


REPAIR Integrated Analysis

^{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)



Data on File, Clene Nanomedicine, Inc.

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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)

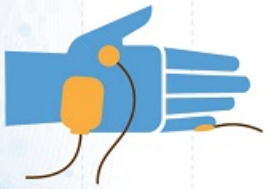
Day -28 to -1 | Week 6 | Week 12 | Week 18 | Week 24 | Week 30 | Week 36 | Week 42 | Week 48 | Week 54 | Week 60 | Week 66 | Week 72 | Week 76

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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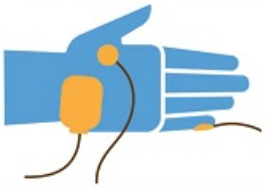
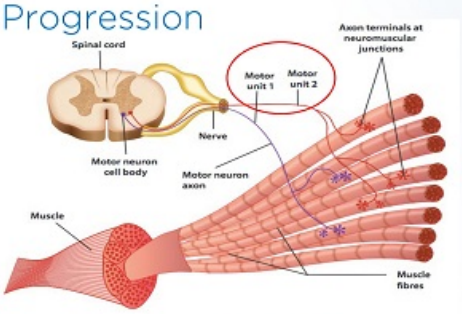
Measuring ALS Disease Progression

Electromyography: Predictive Biomarker of Clinical Progression

Predictive Endpoints of Disease Progression

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

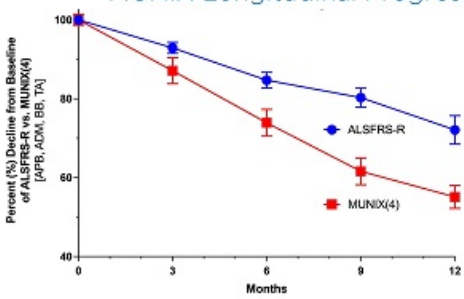




Clinical Endpoints

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

MUNIX Longitudinal Progression



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

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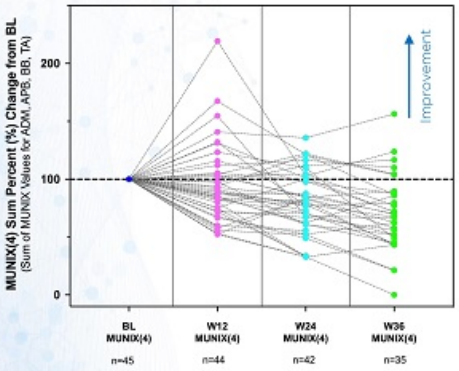
Phase 2 RESCUEALS

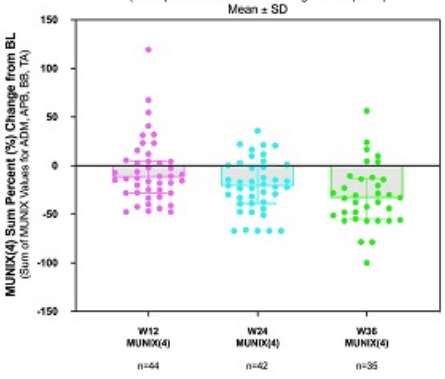
Primary Endpoint: Emerging Evidence of MUNIX Benefit

Blinded Data: MUNIX(4) Sum Percent (%) Change from BL
15-March-2021 Data Cut; Imputed Values; Preliminary Blinded Data
(All Reported Values With Missing Data Imputed)



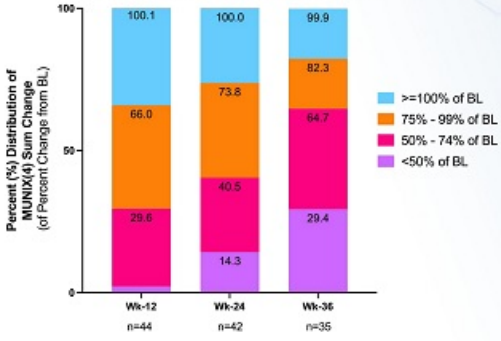
All Subjects With Evaluable Data By Completed Study Visit
(Missing Data Imputed by Linear Regression per Subject; Mortality Imputed with Worst % Change from BL)

Blinded Data: MUNIX(4) Sum Percent (%) Change from BL
15-March-2021 Data Cut; Imputed Values; Preliminary Blinded Data
(All Reported Values With Missing Data Imputed)
Mean ± SD



All Subjects With Evaluable Data By Completed Study Visit
(Missing Data Imputed by Linear Regression per Subject; Mortality Imputed with Worst % Change from BL)

Distribution of MUNIX(4) Sum Percent (%) Change from BL
15-March-2021 Data Cut; Preliminary Blinded Data
(All Reported Values With Missing Data Imputed)



All Subjects With Evaluable Data By Completed Study Visit
(Missing Data Imputed by Linear Regression per Subject; Mortality Imputed with Worst % Change from BL)

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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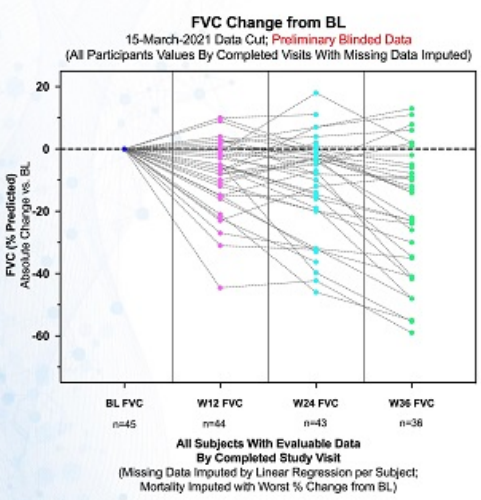
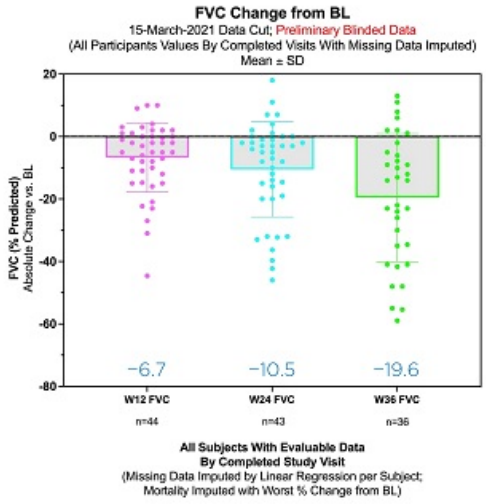
Phase 2 RESCUEALS

Secondary Endpoint: Emerging Evidence of Clinical Benefit | Forced Vital Capacity





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: 1H 2022

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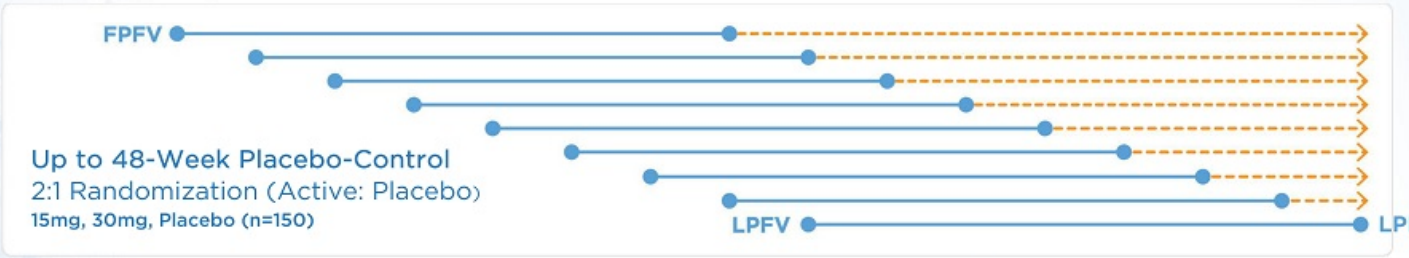
Phase 2

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:
2H 2022*

*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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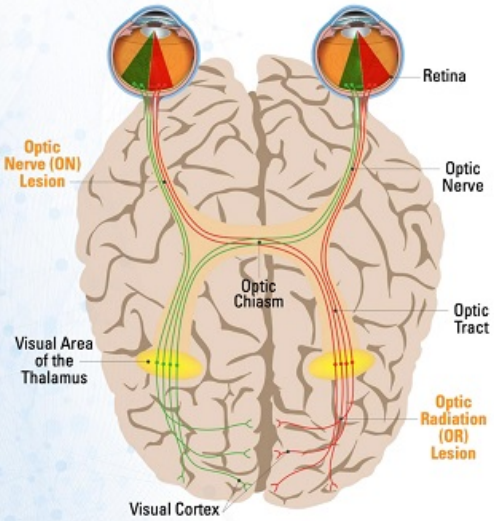
Measuring MS Functional Improvement

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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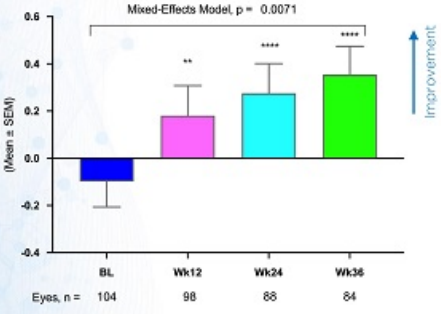
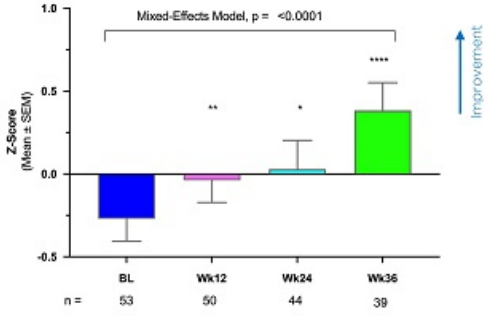
Phase 2 VISIONARY-MS STUDY

Emerging Evidence of Clinical Improvement

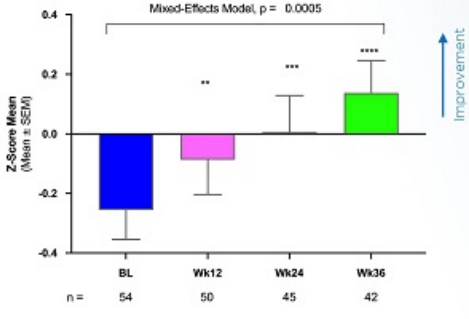
LCLA (Best-Corrected)



SDMT



6-Component Integrated (m)MSFC



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

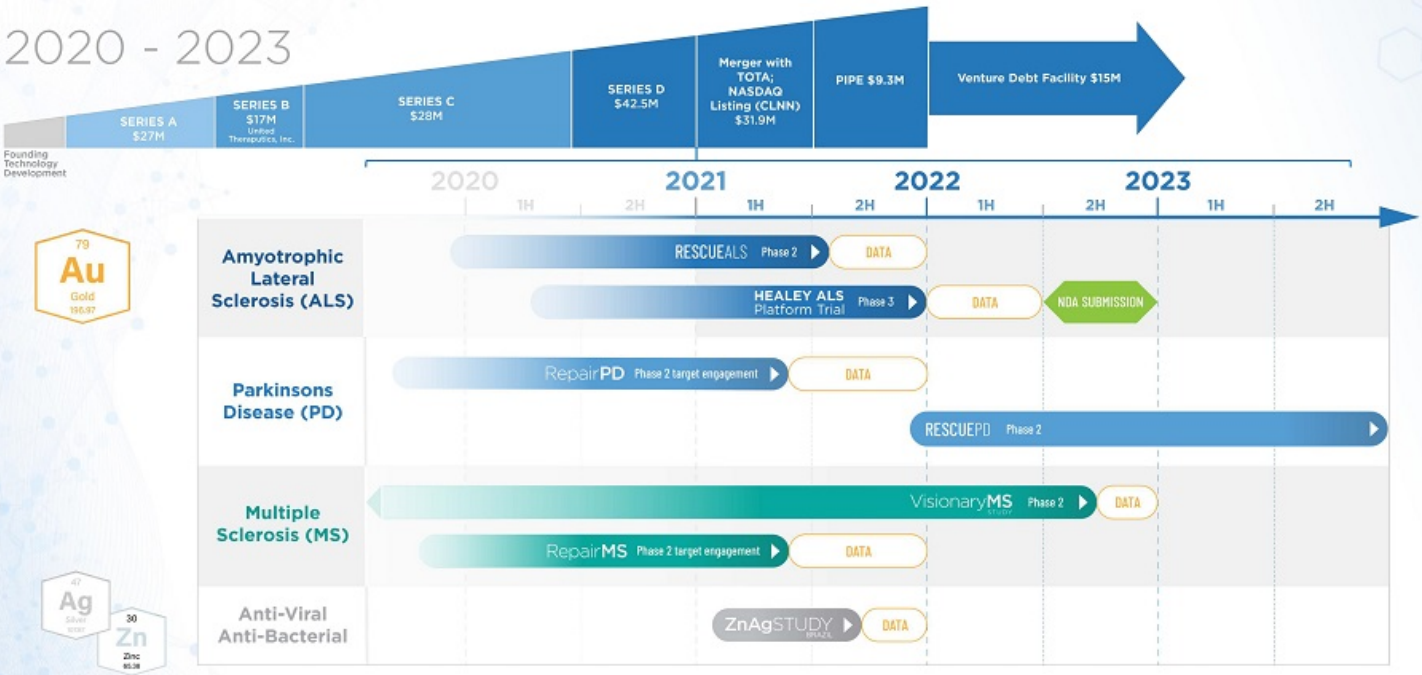
In-House ISO8 Clean Room Clinical Production in North East, MD

Designed to be Scalable to Commercialization

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

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
- Up to 89 Weeks Exposure in Clinical Trials; Up to 97 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 1H 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 2H 2021

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 Q1 2021 of $48.0M (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

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

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