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): February 14, 2022

Clene Inc.
(Exact name of registrant as specified in its charter)

Delaware	001-39834	85-2828339
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)

6550 South Millrock Drive, Suite G50 Salt Lake City, Utah	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 Capital Market
Warrants, to acquire one-half of one share of Common Stock for $11.50 per share	CLNNW	The Nasdaq Capital Market

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

Emerging growth company ☒

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

Item 7.01 Regulation FD Disclosure.

On February 14, 2022, Clene Inc. (the "Company") issued a press release providing an update on its clinical programs. A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference.

On February 15, 2022, in connection with the press release, the Company released an updated corporate presentation (the "Corporate Presentation") on its website, www.clene.com. 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. A copy of the Corporate Presentation is furnished as Exhibit 99.2 to this Current Report on Form 8-K and is incorporated herein by reference.

The information furnished in this Item 7.01, including Exhibit 99.1 and Exhibit 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, as amended, regardless of any general incorporation language in any such filings, except as shall be expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Exhibit Description
99.1	Press Release, dated February 14, 2022, providing an update on Clene Nanomedicine's clinical programs.
99.2	Corporate Presentation.
104	Cover Page Interactive Data File (formatted as Inline XBRL).

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, hereunto duly authorized.

CLENE INC.

Date: February 15, 2022

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

Exhibit 99.1

Clene Nanomedicine Provides Clinical Program Update

- ***Healey ALS Platform Trial fully enrolled; top-line data expected 2H 2022***
- ***Significant survival benefit from RESCUE-ALS open label extension (OLE) Phase 2 trial to be presented at upcoming Muscular Dystrophy Association (MDA) Clinical & Scientific Conference in Nashville, TN March 13-16, 2022***
- ***VISIONARY-MS to conclude early due to COVID pandemic-related challenges. Unblinded data expected 2H 2022; insights to inform new Phase 2/3 MS trial.***
- ***REPAIR-MS Phase 2 Trial initiates second cohort to confirm target engagement in non-active progressive MS***
- ***COVID-19 Phase 2 trial completes enrollment; top-line results expected mid-year 2022***

SALT LAKE CITY, Feb. 14, 2022 (GLOBE NEWSWIRE) -- Clene Inc. (NASDAQ: CLNN) along with its wholly owned subsidiary Clene Nanomedicine, Inc. (Clene) is a clinical-stage biopharmaceutical company focused on revolutionizing the treatment of neurodegenerative disease. Today, Clene provided clinical program updates for its lead nanotherapeutic platform drug candidate: CNM-Au8®, as well as its antiviral candidate, CNM-ZnAg. CNM-Au8 is a gold nanocrystal suspension, developed to increase cellular energy production and utilization to restore neuronal health. CNM-ZnAg is a proprietary zinc-silver ionic solution that has demonstrated both antiviral and antimicrobial properties.

HEALEY-ALS Phase 2/3 Platform Trial on track to report top-line data in the second half of 2022
Enrollment into the HEALEY ALS Platform Trial, led by the Sean M. Healey & AMG Center for amyotrophic lateral sclerosis (ALS) at Massachusetts General Hospital (MGH), completed in November 2021. This Phase 2/3 trial is evaluating Clene's lead drug candidate, CNM-Au8, for the treatment of ALS. Top-line data are expected in the second half of this year. In anticipation of positive results, Clene is preparing for potential regulatory approval, including development of a new manufacturing facility in Maryland and commercialization planning. The U.S. Food and Drug Administration (FDA) has granted CNM-Au8 Orphan Drug designation in ALS.

Updated survival data from RESCUE-ALS OLE Phase 2 trial to be presented at upcoming MDA Clinical & Scientific Conference
Updated evidence for a long-term survival benefit with CNM-Au8 treatment from the RESCUE-ALS trial open label extension will be presented at the upcoming MDA Clinical & Scientific Conference March 13-16, 2022 in Nashville, TN. Observed survival in study participants was compared to the estimated median survival derived from the validated ENCALS prediction model with results significantly in favor of CNM-Au8 treatment.

Long-Term Expanded Access Program (EAP) treatment continues
Clene continues to support expanded access programs providing CNM-Au8 treatment at four clinical sites in over 50 participants with ALS. CNM-Au8 treatment has been well tolerated in this group of people with ALS who are not eligible for current clinical trials. Long-term use of CNM-Au8 now exceeds 2 years in these programs. Data from these EAPs will support potential regulatory filings with health authorities.

VISIONARY-MS Phase 2 Trial to conclude early due to COVID pandemic-related challenges. Unblinded results expected second half of 2022.
The VISIONARY-MS Phase 2 trial is evaluating the efficacy and safety of CNM-Au8 for remyelination and neurorepair in stable relapsing MS patients. The study has enrolled 73 of the 150 planned participants with chronic visual impairment typically treated with background disease-modifying therapy (DMT). MS patients on current DMTs typically have compromised immune systems. Consequently, MS clinical trials requiring multiple in-person clinic visits have experienced continued enrollment and operational challenges stemming from the ongoing COVID-19 pandemic and repeated viral variant waves.

Unblinded VISIONARY-MS data are targeted for the second half of 2022, with announcement of the next clinical trial in MS planned thereafter. Clene is currently working with the VISIONARY-MS trial investigators and participants to conclude the trial. Clene will utilize the available data collected from up to 48 weeks of clinical visits to better understand the efficacy and safety profile of CNM-Au8 and to inform further clinical development in MS.

“On behalf of Clene, I want to thank the investigators, site staff, and, most importantly, the participants and their families for their contribution to the VISIONARY-MS study. We will leverage the learnings from VISIONARY-MS to inform the design of our next Phase 2/3 clinicial trial in MS,” said Robert Glanzman MD, Clene’s Chief Medical Officer.

REPAIR-MS Phase 2 trial has been Initiated in patients with non-active, progressive MS
Following the robust target engagement results demonstrated in the REPAIR-MS Phase 2 trial in relapsing MS patients, Clene has initiated a second MS Cohort to confirm target engagement in the more severe, non-active progressive MS population. Non-active progressive MS patients currently have limited therapeutic options and high unmet need.

CNM-ZnAg Phase 2 COVID trial in Brazil completes full enrollment; top-line data expected mid-2022
Clene’s Phase 2 trial of its antiviral CNM-ZnAg in acutely symptomatic, non-hospitalized COVID-19 patients has achieved full enrollment. Top-line results are expected by mid-year 2022. Clene plans to advance CNM-ZnAg into a registration trial, contingent upon positive Phase 2 results.

About the HEALEY ALS Platform Trial
The HEALEY ALS Platform Trial is a perpetual multi-center, randomized, double-blind, placebo-controlled Phase 2/3 program designed to evaluate the efficacy and safety of multiple investigational products in people living with ALS. The HEALEY ALS Platform Trial is the first-ever platform trial in ALS and was designed to reduce trial time, costs and increase patient participation in developing novel therapies. This landmark platform trial tests multiple treatments utilizing a shared master protocol and combined placebo group data. CNM-Au8 was selected as one of the first three drugs to be evaluated. Subjects are randomized 3:1 to receive active treatment or placebo for the 24-week double-blind treatment period followed by the option to enroll in the Open Label Extension in which all subjects receive active drug. The primary endpoint is rate of change in disease severity over time as measured by the ALS Functional Rating Scale-Revised (ALSFRS-R). Secondary endpoints include change in respiratory function over time as measured by slow vital capacity and change in isometric muscle strength over time as measured using hand-held dynamometry. Top-line data are expected in 2H 2022. For more information, please see ClinicalTrials.gov Identifier: NCT04297683.

About VISIONARY-MS
VISIONARY-MS is a Phase 2 multi-center, randomized, double-blind, placebo-controlled trial evaluating the efficacy and safety of CNM-Au8 for remyelination and neurorepair in stable relapsing MS patients, with chronic visual impairment, who are allowed disease-modifying therapy. Target enrollment is 150 participants at expert MS clinical trial sites within Australia, Canada and the United States. The primary endpoint is improvement in Low Contrast Letter Acuity (LCLA) from baseline to week-24. Key secondary endpoints include improvements from baseline to week-24 in the remaining modified-Multiple Sclerosis Functional Composite (MSFC) subscales (Symbol Digit Modalities Test, 9-Hole Peg Test, and Timed 25-Foot Walk). Interim blinded data presented at the ACTRIMS Forum 2021 demonstrated exposure-dependent, statistically significant improvements in both LCLA scores and across the averaged components of the modified MSFC scale for the total study population in comparison to baseline values from the mildest sub-population ($p<0.001$). Unblinded top-line data are anticipated in the second half of 2022. For more information, see ClinicalTrials.gov Identifier: NCT03536559.

About CNM-ZnAg Phase 2 COVID Trial
This Phase 2 study, being implemented in Brazil, is a multicenter, randomized, double-blind, placebo-controlled study in acutely symptomatic, non-hospitalized patients, with moderately severe COVID-19 infection. The study randomized patients 1:1:2 to receive either a low or high dose of CNM-ZnAg or placebo in addition to standard supportive care. The primary endpoint of the study is the rate of hospitalizations at day 28, with secondary endpoints assessing time to symptom resolution.

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

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

About Clene
Clene is a clinical-stage biopharmaceutical company focused on revolutionizing the treatment of neurodegenerative disease by targeting energetic failure, an underlying cause of many neurological diseases. The company is based in Salt Lake City, Utah, with R&D and manufacturing operations in Maryland. For more information, please visit www.clene.com or follow us on Twitter, LinkedIn and Facebook.

Forward-Looking Statements
This press release contains “forward-looking statements” 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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clene.com
February 15, 2022
CLene
NANOMEDICINE

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 the section entitled "Risk Factors" in Clene's recently filed Quarterly Report on Form 10-Q (filed November 8, 2021)," 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 | Leadership

BOARD CHAIR	CEO	CMO	CSO, FOUNDER	CDO	CFO	HR
						
David J. Matlin	Rob Etherington	Robert Glanzman	Mark Mortenson	Michael Hotchkin	Morgan Brown	Mary Anne McNeil

MatlinPatterson · Credit Suisse · Actelion · Roche · Novartis · Pfizer · Parke-Davis · NPS Pharma

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CLENE | Overview

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

ALS Registration Trial
Topline data in 2H 2022[2]

>300
patient years of CNM-Au8 clinical exposure

Manufacturing expansion in progress, preparing for possible commercialization in 2023

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

September 30, 2021 Cash and restricted cash on hand (unaudited):
$60.6M

Data on File, Clene Nanomedicine, Inc. [1]Robinson et al. Sci Rep. 2020 Feb 11;10(1):1936.[2]https://clinicaltrials.gov/ct2/show/NCT04414345.

CLENE | Pipeline

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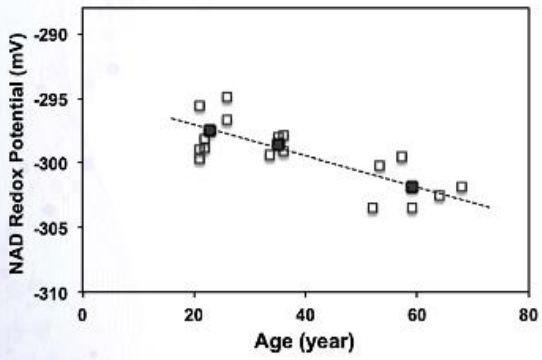
Neurons With High Energetic Demand Are At Increased Risk For Neurodegenerative Disease

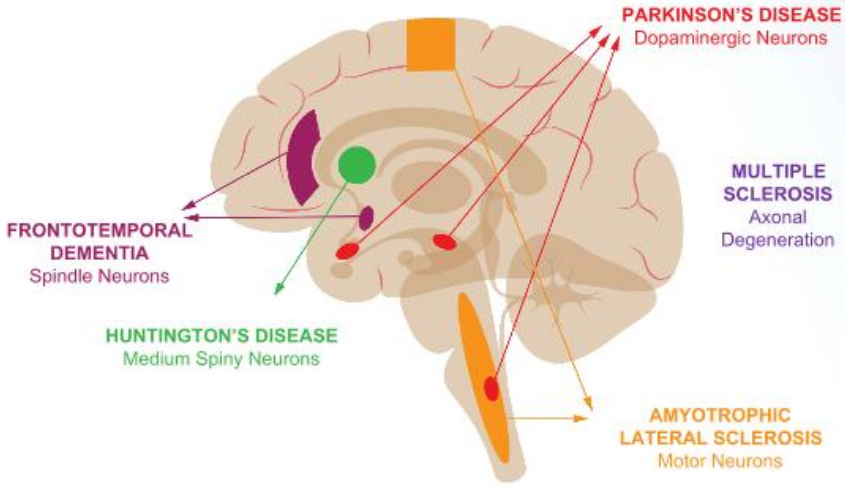
Brain Energy Potential Declines With Normal Aging

~0.5% NAD^+/NADH unit decline per decade
(~0.13 mV units per year by ^{31}P-MRS Imaging)



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

Specific Neuronal Populations Are Vulnerable to Energetic Failure

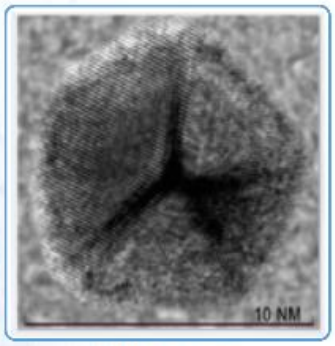


Fu, H., et al; Nature Neuroscience (2018) 21: 1350-1358. Zhu et al. Proc Natl Acad Sci USA . 2015 Mar 3;112(9):2876-81. Rone et al. J Neurosci. 2016 Apr 27;36(17):4698-707.

CNM-Au8® | Catalytically-Active Nanocrystals

Intersection of Physics and Biology

CNM-Au8 Nanocrystal



> 100 Trillion Nanocrystals per 60 mL Dose (At 30mg)

Clean Surfaced, Highly Faceted Shape Enhances Catalytic Activity

Electron Sharing Drives Catalytic Activity

Vertices, Edges, & Facets Key to Catalytic Activity

CNM-Au8 Catalytically Active Nanocrystal Suspension

60 mL per bottle (once daily)

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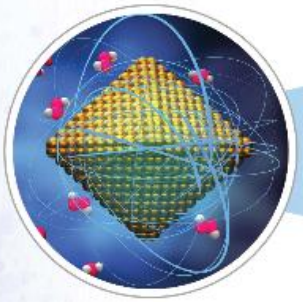
CNM-Au8® | Improves Energy Production to Promote Neuroprotection and Remyelination

CNM-Au8 Nanocrystal



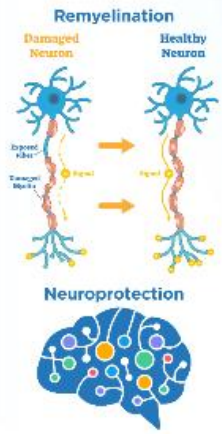
Mechanistic Effects

- ↑ Increased NAD
- ↑ Increased ATP
- ↓ Decreased reactive oxygen species
- ↑ Increased proteostasis

Improved Energy Production and Utilization

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

Promotes Neuroprotection and Remyelination



CLene NANOMEDICINE

CNM-Au8® | Preclinical Evidence for Energetic Improvement

Therapeutic Activity Across Remyelination + Neuroprotection Models

REMYELINATION[1]

Chronic Global CNS Demyelination

- Chronic Cuprizone (CPZ) Pilot
- Chronic CPZ Repeat Validation
- Prevent CPZ Damage
- Post-Chronic CPZ Myelin Recovery
- Chronic CPZ Functional Outcome

Focal Spinal Cord Remyelination

- Lysolecithin Focal Remyelination (I)
- Lysolecithin Focal Remyelination (II)

Perinatal Myelin Injury

- Cerebral Palsy Remyelination *Ex Vivo*

PUBLICATION

Robinson et al.
Sci Rep. 2020
Feb 11

SCIENTIFIC REPORTS

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

NEUROPROTECTION[2]

Neuroprotection: Motor Neuron

- MN Neuroprotection iPSC MN *In Vitro, Astrocyte*
- MN Glutamate Excitotoxicity *In Vitro*
- MN Amyloid beta *In Vitro*
- MN Neuroprotection *ALS SOD1, In Vivo*
- MN Neuroprotection *ALS SOD1, In Vitro*

Neuroprotection: Dopaminergic

- PD Neurotoxin MPP *In Vitro*
- PD Neurotoxin *6-OHDA In Vitro*
- PD Neurotoxin *6-OHDA In Vivo*

Neuroprotection: Other

- Hippocampal Neuron Glutamate Excitotoxicity *In Vitro*
- Cortical Neuron Glutamate Excitotoxicity *In Vitro*
- Forebrain Neuroprotection *C9ORF72 In Vitro*
- Alzheimer's Disease Induced Neurons *In Vitro*

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

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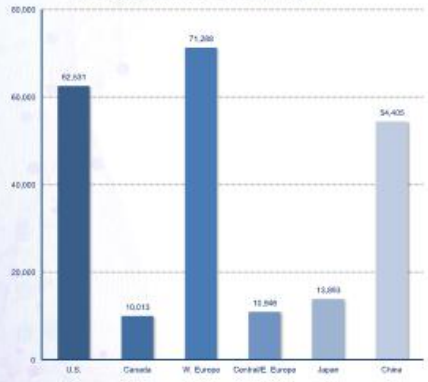
CNM-Au8® | Significant Global Opportunity

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

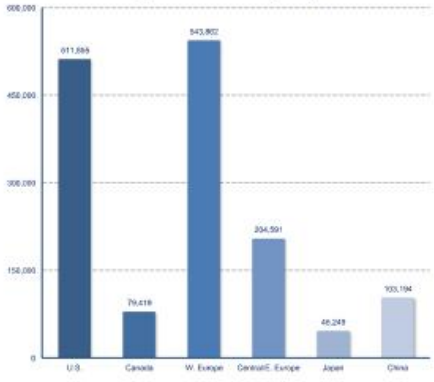


Source: Lancet Neurol. 2018 Dec;17(12):1083-1097.
MND includes amyotrophic lateral sclerosis, spinal muscular atrophy, hereditary spastic paraplegia, primary lateral sclerosis, progressive muscular atrophy, and pseudobulbar palsy

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

Only approved treatments are immunomodulators

Est. Diagnosed MS Patients by Region

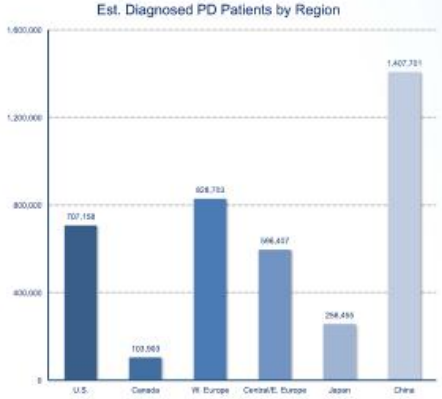


Source: Lancet Neurol. 2019 Mar;18(3):269-285. ~2.2 M patients globally, data as of 2016

PARKINSON'S DISEASE
~6.1M pts globally; $6B projected by 2026[3]

2ND most common neurodegenerative disorder; only symptomatic treatments

Est. Diagnosed PD Patients by Region



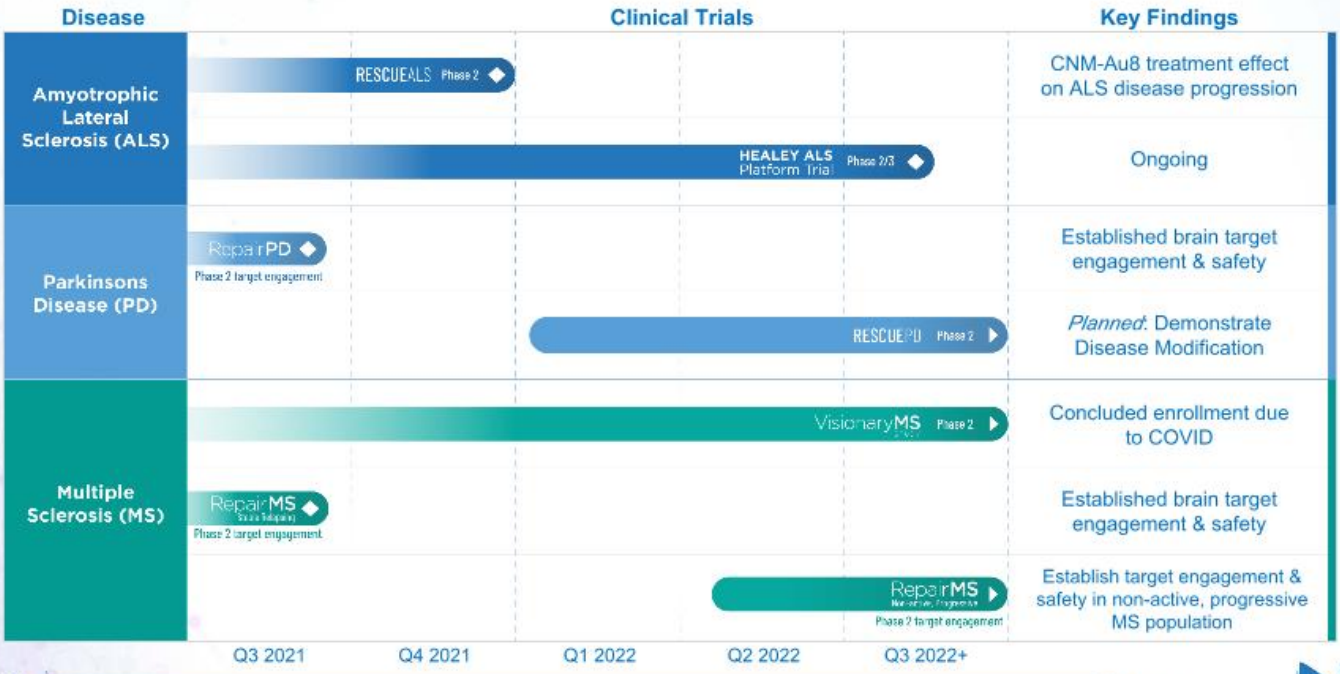
Source: Lancet Neurol. 2018 Nov;17(11):939-953. ~6.1M patients globally, data as of 2016.

[1] Clarivate, DRG, ALS 2020 [2] Westad et al. 2017, doi:10.1038/nrd.2017.107;. [3] Parkinson's Market Data Forecast, April 2021.

CLENE NANOMEDICINE

CNM-Au8® | Neuroprotection & Remyelination

Phase 2 and Phase 3 Clinical Trials



Data on File, Clene Nanomedicine, Inc.

CNM-Au8® | Safety Summary

Clean Toxicology Findings

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

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

Well Tolerated Adverse Event (AE) Profile

Assessed as Predominantly Mild-to-Moderate Severity and Transient

- No related CNM-Au8 AEs leading to discontinuation of treatment
- No SAEs related to CNM-Au8 considered severe, life-threatening, or resulting in death

Patient Exposure Across PD, MS, & ALS

Over 300 Years of Subject Exposure Without Any Safety Signals

- Long-term dosing experience up to 125 weeks

Data on File, Clene Nanomedicine, Inc.

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)

RepairPD

Early Parkinson's Disease

RepairMS

Stable Relapsing MS

RepairMS

Non-Active Progressive MS

(Underway)

Non-active, progressive MS patients is more severe than relapsing MS., and a high unmet need for disease modifying therapeutic options

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 (End of Treatment)
- Difference in bioenergetic metabolites (e.g., ATP, NAD) concentration at Week 12 – 16
- Difference in brain membrane markers (PE, PC, etc.) at Week 12 – 16

Data on File, Clene Nanomedicine, Inc.

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Phase 2 Results

RepairPD

RepairMS

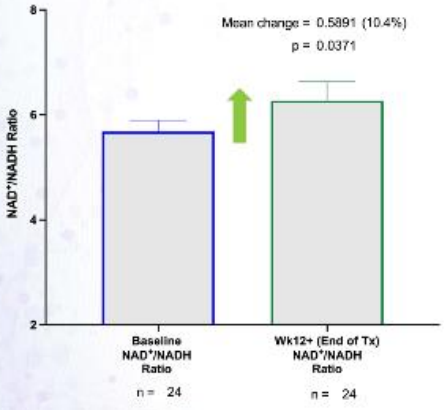
CNM-Au8 Improves Brain Energy Metabolism Increases NAD+/NADH Ratio in MS & PD

1° Endpoint

^{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)



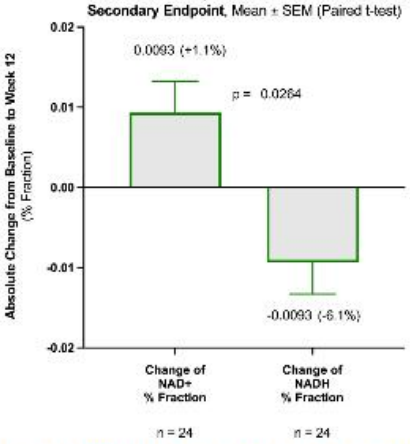
2° Endpoint

REPAIR Integrated Analysis

^{31}P-MRS Average Change in Brain NAD (% Fraction)

Partial Volume Coil; % Fraction of NAD$^+$ and NADH

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



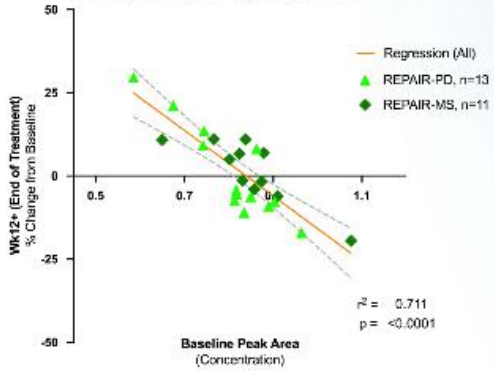
Exploratory (ATP Normalization)

REPAIR Integrated Analysis

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

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

Exploratory Endpoint, Percent (%) Change vs. Baseline Value



NAD is an essential molecule responsible for cellular energy production

Glanzman et al. 2021. International Parkinson and Movement Disorder Society (MDS) Virtual Congress 2021. September 17 – 22, 2021 . 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

Neurophysiology	Pulmonary Function	Function & QoL	Disease Progression & Survival
MUNIX[1]	Forced Vital Capacity	ALSFRS-R, ALSSQOL-SF	

[1] Study was powered for MUNIX primary endpoint

Vucic et al. BMJ Open. 2021 Jan 11;11(1):e041479. Data on File; Clene Nanomedicine, Inc.

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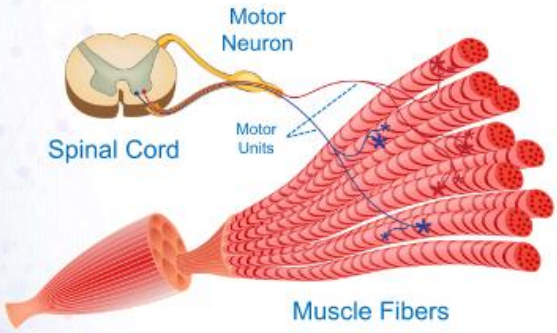
RESCUEALS | Pioneered Use of MUNIX Biomarker

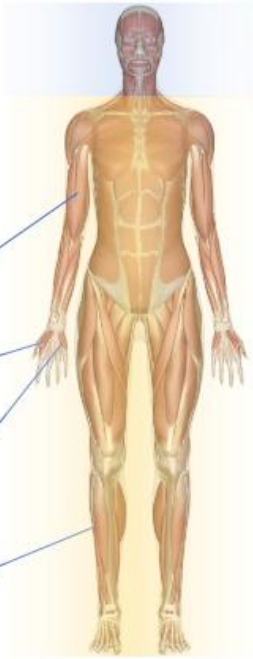
Primary Endpoint: Spinal Cord Lower Motor Neuron Protection

MUNIX biomarker estimates the number of functioning lower motor neurons serving specific muscles



Primary Endpoint: Spinal Cord Lower Motor Neuron Motor Unit Index (MUNIX) Sum

- Biceps brachii
- \+
- Abductor Pollicis Brevis
- \+
- Abductor Digiti Minimi
- \+
- Tibialis Anterior



Bulbar Onset ALS (Brainstem)

Limb Onset ALS (Spinal Cord)

Vucic et al. BMJ Open. 2021 Jan 11;11(1):e041479.

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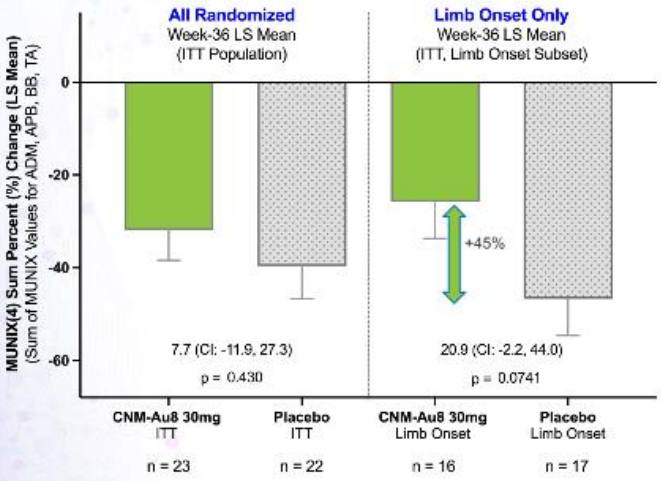
RESCUEALS | Evidence for Motor Neuron Protection

Primary Endpoint (MUNIX %, LS Mean Change)

All Randomized

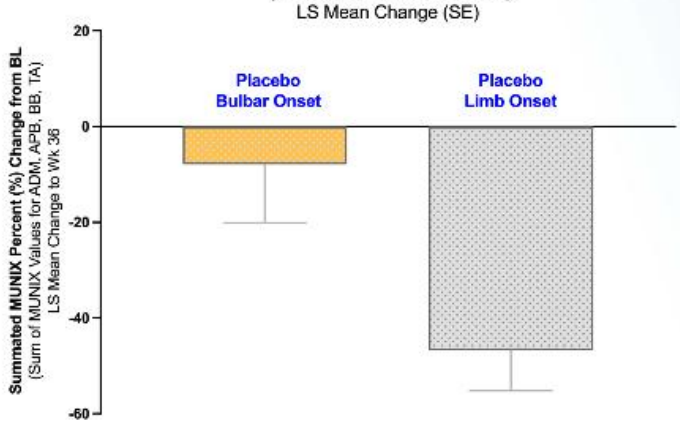
Summated MUNIX Percent Change from Baseline to Week 36
RESCUE-ALS Primary Endpoint
Mixed Model Repeat Measure (ITT Population & Limb Onset Subset)
LS Mean (SE)



All Placebo

Limited Rate of MUNIX Decline in Bulbar Onset

Summated MUNIX Percent Change from Baseline
Placebo Only Decline to Week 36
(Limb Onset vs. Bulbar Onset)
LS Mean Change (SE)



Insufficient Spinal Cord Lower Motor Neuron Progression in Early Bulbar Trial Participants

RESCUE-ALS: A Phase 2, randomized, double-blind, placebo-controlled study of CNM-Au8 to slow disease progression in ALS. MNDA Virtual Symposium, 2021 Data on File, Clene Nanomedicine, Inc.

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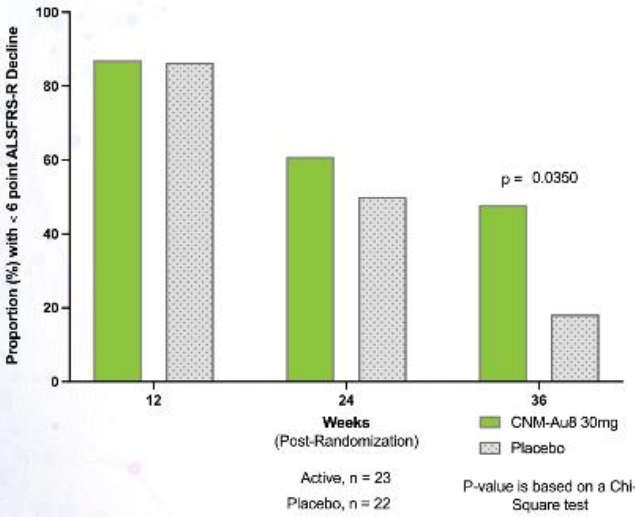
RESCUEALS | Significant Impact on ALSFRS-R Decline

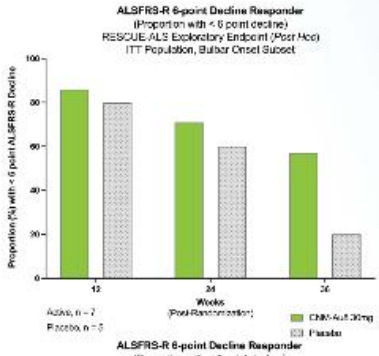
Exploratory (ALSFRS-R Responder Analysis, < 6-point decline)

All Randomized

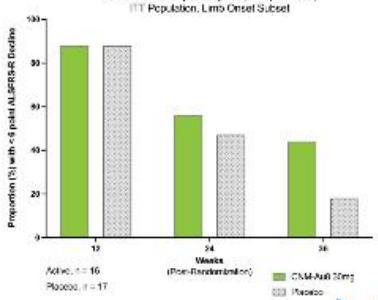


Sensitivity

All Bulbar



All Limb



RESCUE-ALS: A Phase 2, randomized, double-blind, placebo-controlled study of CNM-Au8 to slow disease progression in ALS. MNDA Virtual Symposium, 2021 Data on File, Clene Nanomedicine, Inc.

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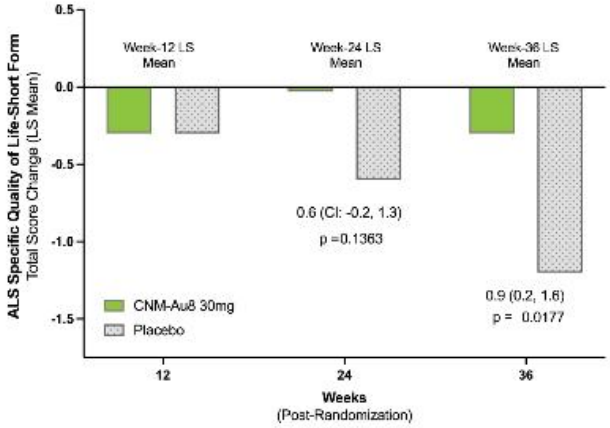
RESCUEALS | Significant Quality of Life Improvement

Exploratory (ALS Specific QOL-SF)

All Randomized

ALS Specific Quality of Life-Short Form Total Score
RESCUE-ALS Exploratory Endpoint
Mixed Model Repeat Measure (ITT Population, All Randomized)
LS Mean Difference



Active, n =	23	23	22
Placebo, n =	21	20	19

P-value is based on MMRM model with treatment, visit, treatment by visit interaction as fixed effects, and baseline value, and ENCALS score as covariates. An unstructured covariance model was used.

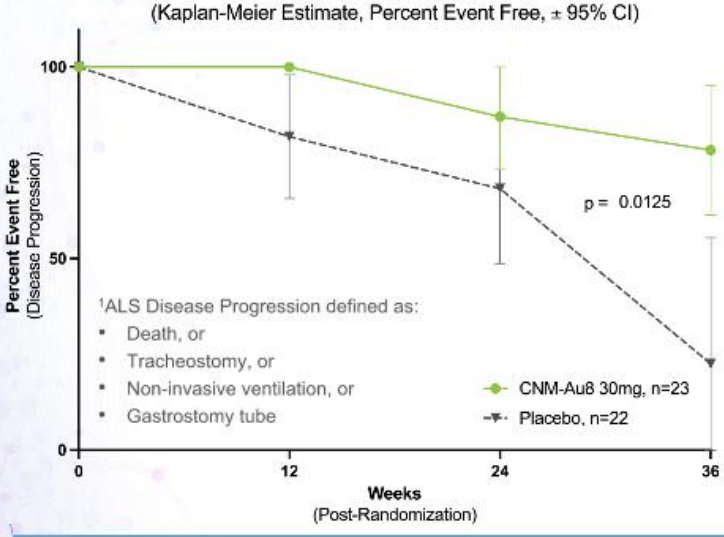
RESCUE-ALS: A Phase 2, randomized, double-blind, placebo-controlled study of CNM-Au8 to slow disease progression in ALS. MNDA Virtual Symposium, 2021 Data on File, Clene Nanomedicine, Inc.

RESCUEALS | Significant Impact on ALS Disease Progression

Exploratory Endpoint (Disease Progression)

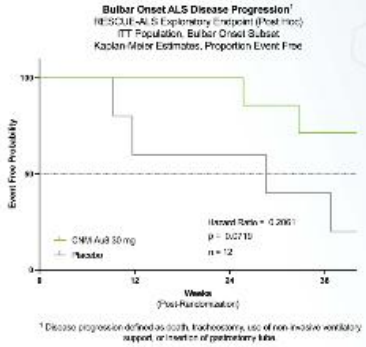
All Randomized

ALS Disease Progression[1]
RESCUE-ALS Exploratory Endpoint
ITT Population, All Randomized
(Kaplan-Meier Estimate, Percent Event Free, ± 95% CI)



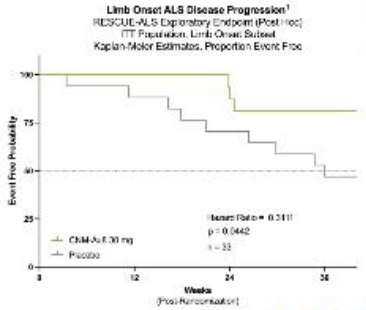
Sensitivity

All Bulbar



[1] Disease progression defined as death, tracheostomy, use of non-invasive ventilatory support, or insertion of gastrostomy tube.

All Limb



RESCUE-ALS: A Phase 2, randomized, double-blind, placebo-controlled study of CNM-Au8 to slow disease progression in ALS. MNDA Virtual Symposium, 2021 Data on File. Clene Nanomedicine, Inc.

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RESCUEALS | Joint Rank: Survival & ALSFRS-R

Exploratory Endpoint Pre-specified (Combined Assessment of Survival and Function [CAFS])

Score participants based on relative function or time of death

Scoring

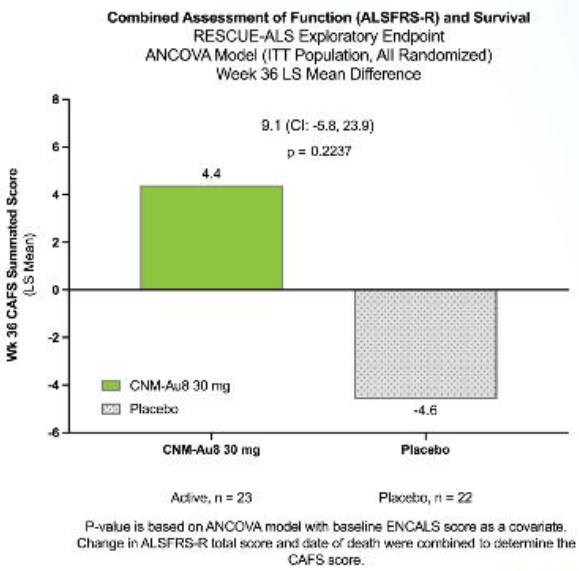
If...	Score
Better function or died later than comparison	+1
Same function or died at the same time as comparison	0
Worse function or died before comparison subject	-1

CAFS

Survival

ALSFRS-R Decline

All Randomized



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

Berry et al. Amyotroph Lateral Scler Frontotemporal Degener. 2013 Apr;14(3):162-8.

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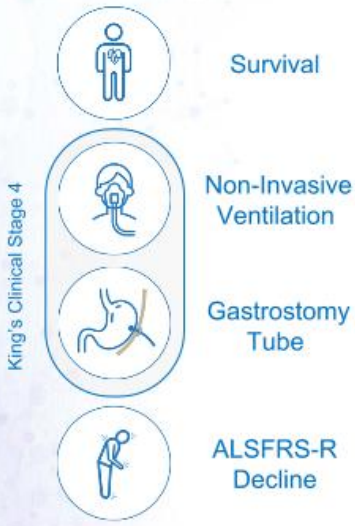
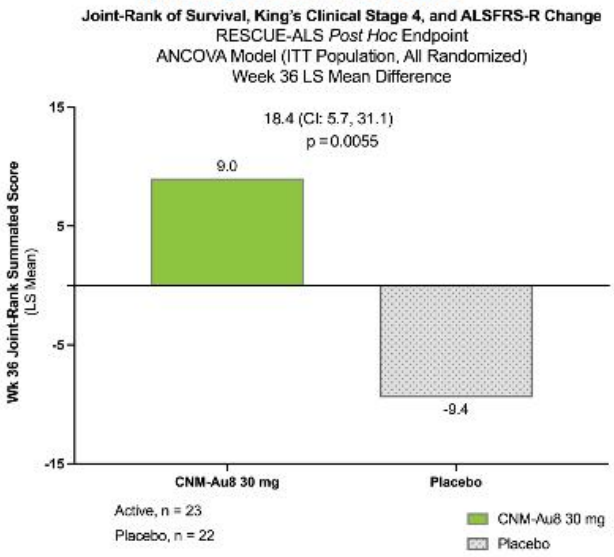
RESCUEALS | Impact on Joint Rank Score to Wk36

Post Hoc (Combined Assessment of (i) Survival, (ii) King's Clinical Stage 4, (iii) ALSFRS-R)



By Average of Summated Scores

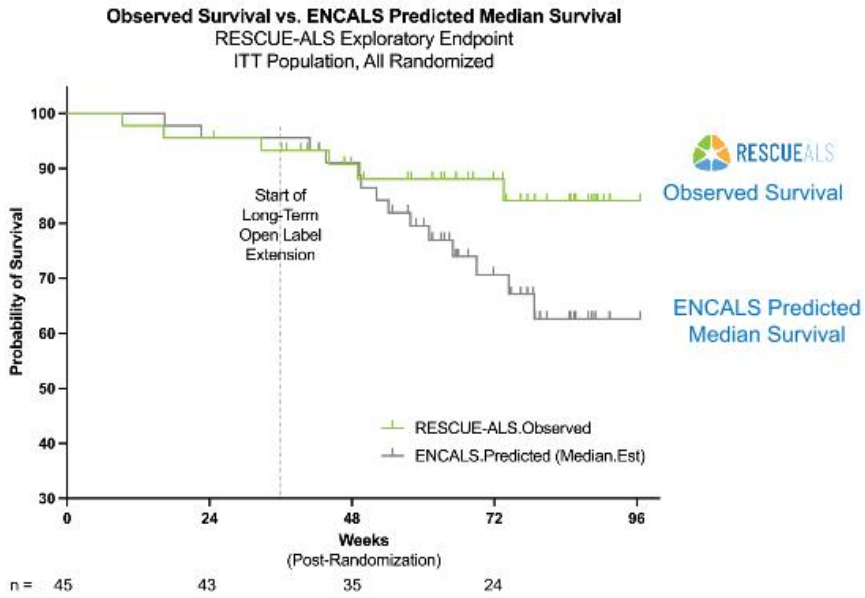


P-value is based on ANCOVA model with baseline ENCALS score as a covariate. Change in ALSFRS-R total score, date of non-invasive ventilation or gastrostomy, and date of death were combined to determine the joint-rank score.

Data on File, Clene Nanomedicine, Inc.

RESCUEALS | Potential Impact on Survival

Exploratory Endpoint (Observed Survival vs. Median Predicted)



All observations censored as of 22-November-2021. Participants who did not transition into the long-term open label extension (n=5) are censored at the safety follow-up visit.

Data on File, Clene Nanomedicine, Inc.

RESCUEALS | Well Tolerated & No Safety Signals

Safety Summary

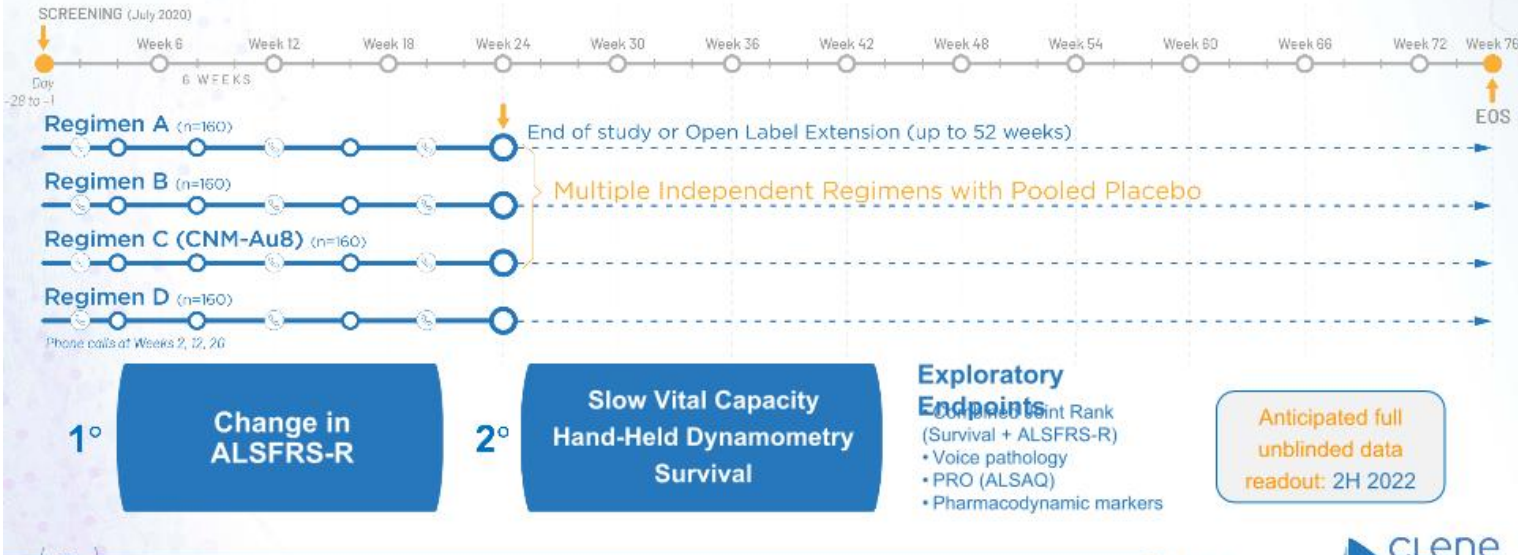
- No CNM-Au8 related serious adverse events (SAEs)
- No CNM-Au8 related drug discontinuations
- No imbalances in treatment emergent adverse event (TEAEs) by system organ class
- TEAEs were predominantly mild-to-moderate and transient
- Most common TEAEs associated with CNM-Au8
  (aspiration pneumonia, n=3; nausea, n=2; abdominal discomfort, n=2)

Data on File, Clene Nanomedicine, Inc.

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; Survival

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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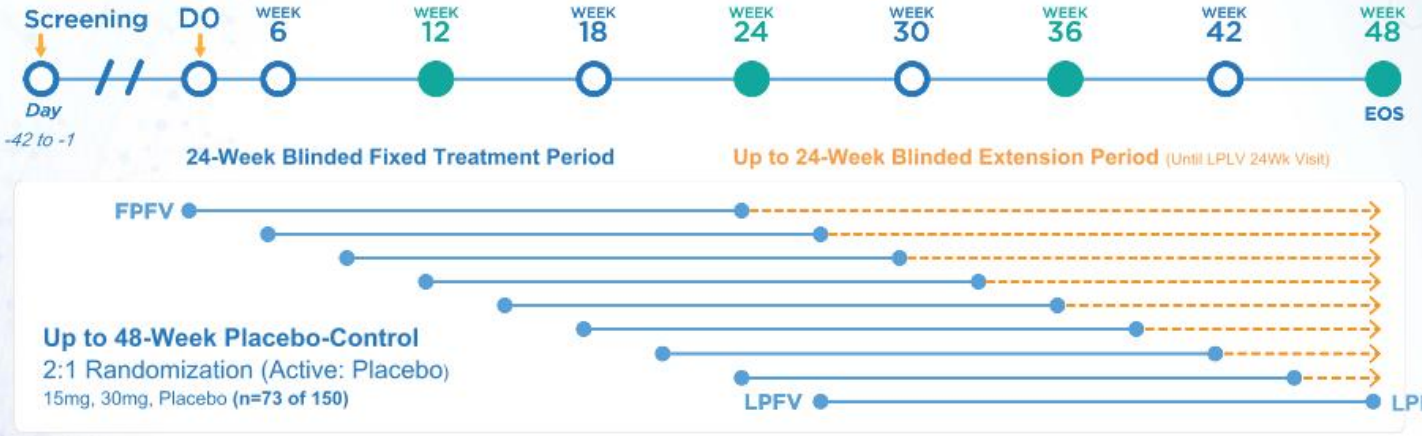
Phase 2

VISIONARY-MS STUDY

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



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

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

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
Insights to inform new Phase 2/3 MS trial

*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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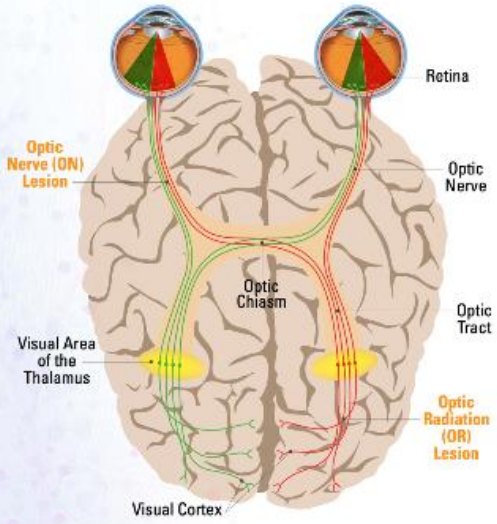
Measuring MS Functional Improvement

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[1]

MS Functional Endpoints

Phase 2 Exploratory: Neuroprotection/Remyelination Endpoints

9-Hole Peg Test

Symbol Digit Modalities

Timed 25-Ft Walk

[1]Balcer et la. Mult Scler. 2017 Apr;23(5):734-747. doi: 10.1177/1352458517690822.

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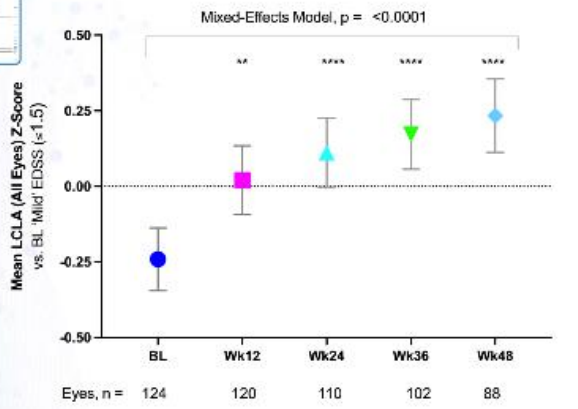
Phase 2 VISIONARY-MS STUDY

Significant Clinical Improvement Across Blinded Study Population

Primary Endpoint: LCLA (Best-Corrected) & Secondary Endpoint: (m)MSFC

1° | LCLA

LCLA (All Eyes) Average Z-Score (vs. Mild EDSS ≤1.5)
23-August-2021 Data Cut, Preliminary Blinded Data
(vs. 'Mild' EDSS [≤1.5]; Mean ± SEM)

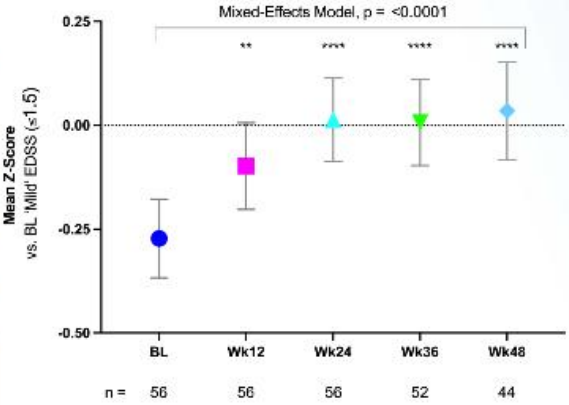


Z-Score Change Based on EDSS 'Mild' Severity (e.g., BL Low EDSS [≤1.5])
All Available Values (by Completed Subject Visit)

Mixed Effects Model, Dunnett's test for multiplicity;
* p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001

2° | (m)MSFC

(m)MSFC 6-Component Average Z-Score
23-August-2021 Data Cut, Preliminary Blinded Data
(vs. 'Mild' EDSS [≤1.5]; Mean ± SEM)



Z-Score Change Based on EDSS 'Mild' Severity (e.g., BL Low EDSS [≤1.5])
All Subjects with at least 4 of 6 (m)MSFC Domains by Completed Subject Visit.
(m)MSFC domains include LCLA (OD/SD), 9HPT (D/ND), T25FW, SDMT.

Mixed Effects Model, Dunnett's test for multiplicity;
* p<0.05, ** p<0.01, *** p<0.001, **** p<0.0001

Gianzman et al. VISIONARY-MS: Update to a Phase 2 clinical trial of catalytic gold nanocrystals, CNM-Au8; ECTRIMS 2021 – Late Breaking News ePoster, October 12, 2021

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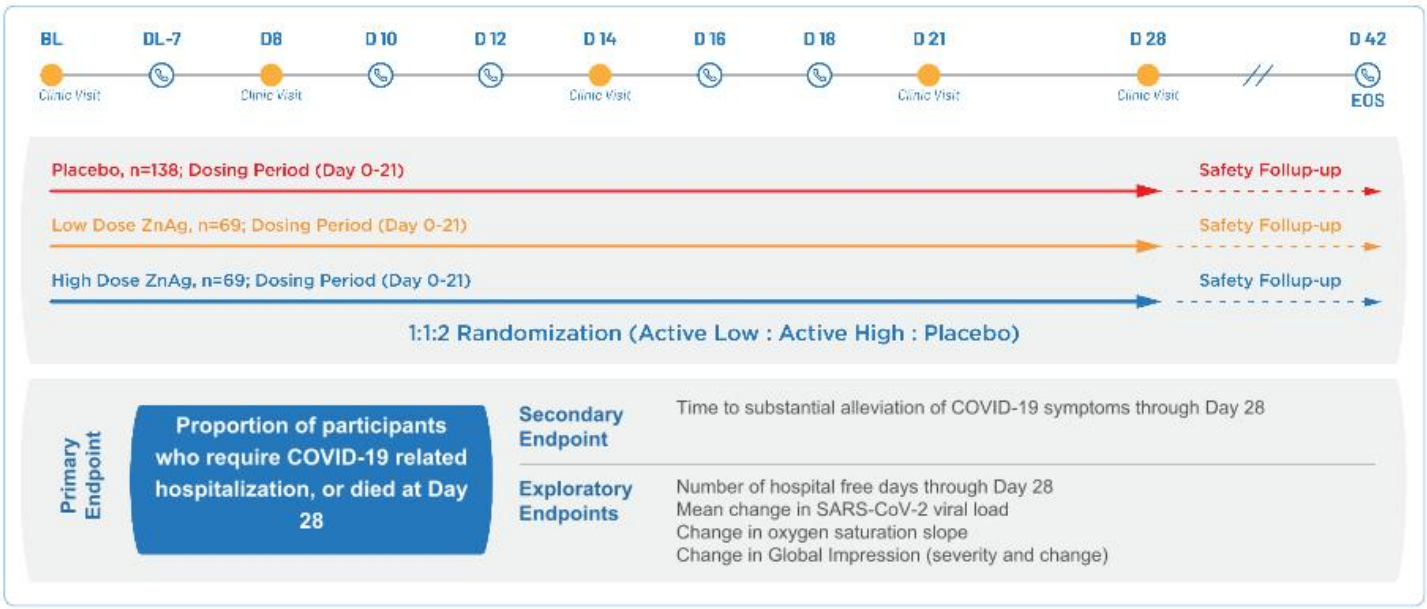
ZnAgSTUDY BRAZIL



Primary Endpoint

Proportion of participants who require COVID-19 related hospitalization, or died at Day 28

Secondary Endpoint

Time to substantial alleviation of COVID-19 symptoms through Day 28

Exploratory Endpoints

Number of hospital free days through Day 28
Mean change in SARS-CoV-2 viral load
Change in oxygen saturation slope
Change in Global Impression (severity and change)

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 [b]	Patent Description	Trade Secrets
Issued & Allowed Patents 150+	Process And Method/Device (Clean Surface; Gold CSN)	Plasma Conditioning
Pending Applications ~20	State of Matter (CNM-Au8)	Electrode Design & Cycling
Total Patents/ Applications >170	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). [b] As of 30-Sepbember-2021.

Clene | Proprietary Nanocrystal Manufacturing

In-House ISO8 Clean Room Clinical Production in Maryland

Designed to be Scalable to Commercialization

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

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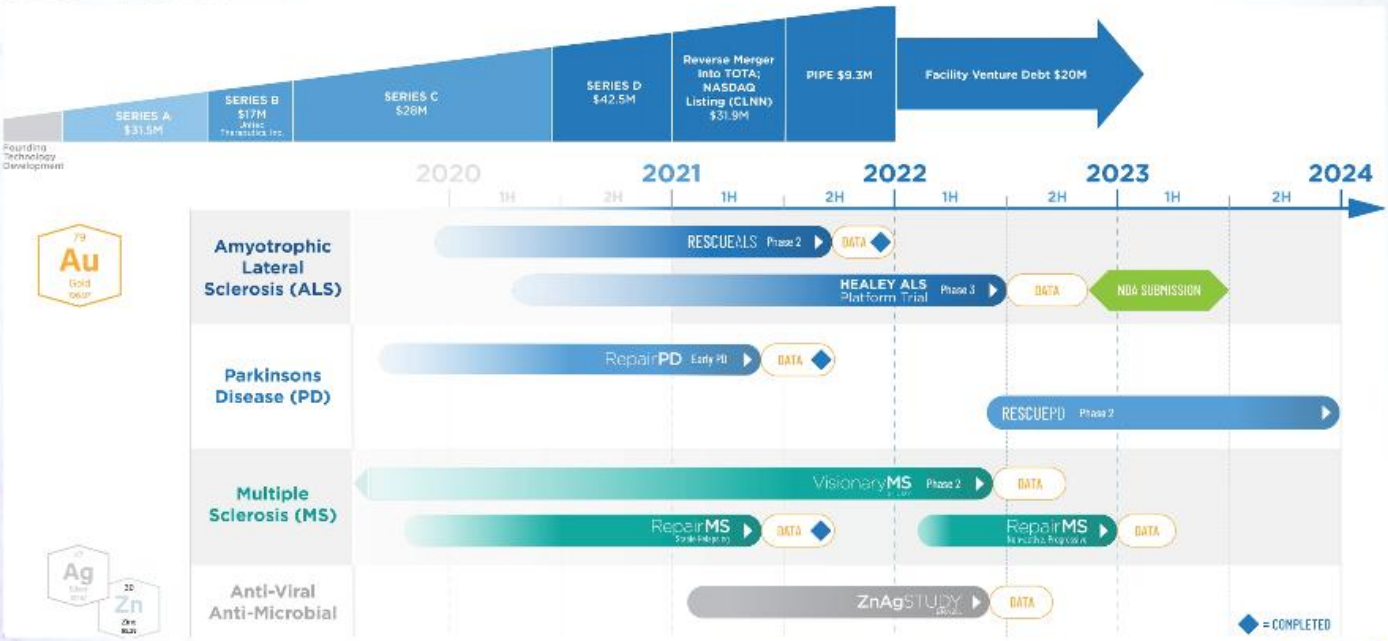
Anticipated Timeline & Upcoming Milestones

2020 - 2024



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CLENE | Company Highlights

Nanotherapeutics Platform	• Potential first-in-class nanotherapeutic with high catalytic activity to drive energy production and utilization in stressed CNS cells • Applications across neurology, infectious disease, and oncology
Lead Asset: CNM-Au8 for Neurorepair	• CNM-Au8 improves cellular energy production and utilization to promote neuroprotection and remyelination • Phase 2 ALS proof-of-concept evidence of clinical meaningful benefit • Phase 3 Healey ALS platform trial results expected in 2H 2022 • Phase 2 VISIONARY-MS trial results expected 2H 2022
Strong Execution Capabilities	• Proprietary electrochemical manufacturing process produces nanotherapeutics, scalable to commercialization • Strong IP, including 150+ granted patents, and trade secrets

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

Version: 15-February-2022