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): March 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:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value	CLNN	The Nasdaq Capital Market
Warrants, to acquire one-half of one share of Common Stock for $11.50 per share	CLNNW	The Nasdaq Capital Market

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

Emerging growth company ☒

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

Item 7.01 Regulation FD Disclosure.

On March 14, 2022, Clene Inc. (the "Company") issued a press release announcing four poster presentations, one of which was also selected as an oral presentation, of updated clinical data from the Phase 2 RESCUE-ALS and REPAIR clinical trials and preclinical ALS data at the 2022 MDA Clinical & Scientific Conference, taking place March 13-16, 2022. A copy of the press release, posters, and oral presentation are furnished as Exhibit 99.1, Exhibit 99.2, Exhibit 99.3, Exhibit 99.4, Exhibit 99.5, and Exhibit 99.6 to this Current Report on Form 8-K (the "Current Report") and are incorporated herein by reference.

In connection with the March 14, 2022 press release, the Company released an updated corporate presentation (the "Corporate Presentation") on its website, https://clene.com. A copy of the Corporate Presentation is furnished as Exhibit 99.7 to this Current Report and is incorporated herein by reference. The Company plans to use its website to disseminate future updates to the Corporate Presentation and may not file or furnish a Current Report on Form 8-K alerting investors if the Corporate Presentation is updated.

The information furnished in this Item 7.01, including Exhibit 99.1, Exhibit 99.2, Exhibit 99.3, Exhibit 99.4, Exhibit 99.5, Exhibit 99.6, and Exhibit 99.7, 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 March 14, 2022, announcing the presentation of updated clinical data from the Phase 2 RESCUE-ALS and REPAIR trials and preclinical ALS data at 2022 MDA Clinical & Scientific Conference.
99.2	Poster titled "RESCUE-ALS Trial Results: A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study of CNM-Au8 to Slow Disease Progression in ALS."
99.3	Poster titled "Evidence for a Potential Survival Benefit in ALS with CNM-Au8 Treatment: Results from the RESCUE-ALS Trial Long-Term Open Label Extension."
99.4	Poster titled "Evidence for Brain Energy Metabolic Support with CNM-Au8 Treatment: Results from the REPAIR Phase 2 Clinical Trials."
99.5	Poster titled "CNM-Au8 Gold Nanocrystals Protects Neurons Against Degeneration and Death in Multiple in vitro Models of Amyotrophic Lateral Sclerosis."
99.6	Oral presentation titled "RESCUE-ALS Platform Presentation by Dr. Robert Glanzman, CMO, Clene Nanomedicine."
99.7	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: March 14, 2022

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

Exhibit 99.1

Clene Nanomedicine Presents Updated Clinical Data from Phase 2 RESCUE-ALS and REPAIR trials and Preclinical ALS data at 2022 MDA Clinical & Scientific Conference

- Analyses of long-term open-label extension of RESCUE-ALS trial indicate improved survival compared to predictions derived from validated ENCALS risk model
- Interim results demonstrate approximately 70% decreased risk of death for participants who entered the RESCUE-ALS long-term open label extension

SALT LAKE CITY, March 14, 2022 – Clene Inc. (NASDAQ: CLNN) along with its subsidiaries "Clene" and its wholly owned subsidiary Clene Nanomedicine, Inc., a clinical-stage biopharmaceutical company focused on revolutionizing the treatment of neurodegenerative disease, today announced multiple presentations of updated clinical trial results from the Phase 2 RESCUE-ALS and REPAIR trials in addition to new mechanistic preclinical data in ALS at the 2022 MDA Clinical & Scientific Conference, taking place March 13-16 in Nashville.

The first poster, titled "***RESCUE-ALS Trial Results: A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study of CNM-Au8 to Slow Disease Progression in ALS***," selected as an oral presentation, and the second poster, "***Evidence for a Potential Survival Benefit with CNM-Au8 Treatment from the RESCUE-ALS Trial Long-Term Open Label Extension***," further support Clene's lead drug candidate CNM-Au8®, a catalytically active gold nanocrystal suspension, as a potential disease-modifying therapy for amyotrophic lateral sclerosis (ALS).

RESCUE-ALS, a Phase 2 multi-center, randomized, double-blind, parallel-group, placebo-controlled trial examined the efficacy, safety, pharmacokinetics, and pharmacodynamics of CNM-Au8 in 45 participants with early ALS over a 36-week treatment period. In the 36-week blinded period, there were significant benefits with CNM-Au8 treatment: slowing ALS disease progression (p=0.0125), decreasing the proportion of participants with a 6-point decline in the ALS Functional Rating Scale Revised (ALSFRS-R) (p=0.035), and improving quality of life as measured by the ALS Specific Quality of Life (ALSSQOL-SF) questionnaire (p=0.018).

The second poster presented updated evidence for survival benefit with CNM-Au8 treatment that was reported from the RESCUE-ALS trial long-term open label extension for both the active and placebo groups. Interim analyses of observed survival compared to estimated median survival derived from the validated ENCALS prediction model significantly favored CNM-Au8 treatment with a hazard ratio of 0.3 for participants who entered the open-label extension (HR 0.3; p=0.01, log-rank test). CNM-Au8 was shown to be well-tolerated with no safety signals identified over 96 weeks of treatment.

The third poster, titled "***Evidence for Brain Energy Metabolic Support with CNM-Au8 Treatment: Results from Phase 2 REPAIR Clinical Trial With CNM-Au8***," demonstrated improved brain energy metabolism assessed by high-resolution magnetic resonance spectroscopy (^{31}P-MRS). CNM-Au8 treatment resulted in improved brain NAD^+/NADH ratio (primary endpoint, paired t-test, p=0.0371). This result was driven both by increase in NAD^+ and a decrease in NADH (secondary endpoint, paired t-test, p=0.0264). CNM-Au8 treatment also resulted in homeostatic effects on brain energy-related phosphorous-containing metabolites, including ATP. Study participants with whole-brain ATP levels less than the population's baseline mean saw significantly increased ATP levels, while patients with baseline levels greater than the baseline mean decreased to the population mean (r^2 = 0.711, p<0.0001). These data demonstrate CNS target engagement following treatment with CNM-Au8 and support its candidacy as a disease-modifying therapy for the treatment of neurodegenerative diseases associated with dysregulated neuronal energy metabolism.

The fourth poster accepted for presentation, "***CNM-Au8 Gold Nanocatalysis Protects Neurons Against Degeneration and Death in Multiple* in vitro *models of ALS***," demonstrates CNM-Au8's ability to promote neuronal survival and function in multiple independent in vitro models of ALS: (i) treatment of primary rat spinal motor neurons improved survival, preserves the neurite networks, and reduced cytoplasmic TDP-43 aggregate accumulation after either glutamate excitotoxic injury or exposure to beta-amyloid (Aβ 1-42) oligomers; (ii) treatment of spinal motor neurons from transgenic $SOD1^{G93A}$ rats protected motor neurons from death upon exposure to excitotoxic glutamate in a cAMP-dependent manner, and reduced SOD1 protein accumulation in a manner independent of cAMP; (iii) treatment of human induced pluripotent stem cell (iPSC)-derived neurons from C9ORF72 patients prevented neuronal death in response to stressors; and (iv) survival and neurite outgrowth of human iPSC-derived motor neurons in co-culture with toxic $SOD1^{A4V}$ ALS-patient derived astrocytes were significantly and dose-dependently improved with treatment of CNM-Au8.

“The preclinical and clinical data presented at MDA further support Clene’s lead drug candidate CNM-Au8 as a potential disease-modifying therapy for amyotrophic lateral sclerosis,” said Dr. Robert Glanzman, MD FAAN, Clene’s Chief Medical Officer. “We look forward to the continued advancement of the ALS clinical program with the top-line results from the HEALEY ALS Platform Trial expected in the second half of the year.”

Rob Etherington, Clene’s CEO, added, “This is an exciting time for Clene as we build a bigger body of scientific and clinical evidence in support of our CNM-Au8. Will continue to further the validation of our findings in neurological function and survival as we await results in larger clinical studies underway.”

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 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 https://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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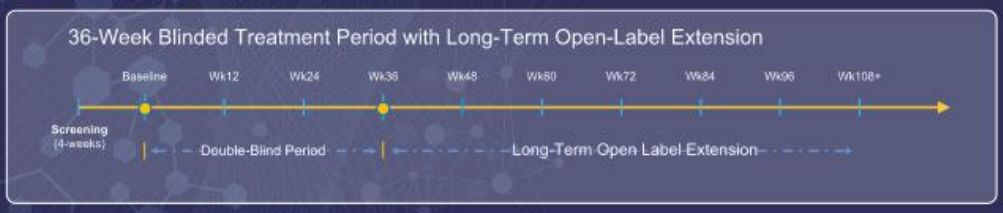
RESCUE-ALS Trial Results: A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study of CNM-Au8 to Slow Disease Progression in ALS

Steve Vucic PhD, DSc, FRACP, FAHMS[1], Parvathi Menon PhD, FRACP[1], William Huynh PhD, FRACP[2], Colin Mahoney, PhD, MB, MRCPI[2], Karen S. Ho, PhD MSc[3], Austin Rynders, RN[3], Jacob Evan[3], Jeremy Evan, PA-C[3], Robert Glanzman, MD FAAN[3], Michael T. Hotchkin[3], Matthew C. Kiernan PhD, DSc, MBBS, FRACP, FAHMS
[1]Concord Repatriation General Hospital, University of Sydney, Australia; [2]Brain and Mind Centre, University of Sydney, Australia; [3]Clene Nanomedicine, Salt Lake City, UT, USA

CONCLUSION: RESCUE-ALS has established safety and suggested efficacy of CNM-Au8, a cellular energetic catalyst, for the treatment of ALS

Design Scheme



Design Summary

- Early symptomatic ALS
- Randomized (1:1, CNM-Au8 30 mg or placebo)
- 36-week treatment period with open label extension
- 1st EP: MUNIX(4) summed %change of ADM, APB, BB, & TA
- 2nd EPs: absolute MUNIX change, % FVC
- Exploratory EPs: disease progression, 6-pt decline in ALSFRS-R, ALSSQOL-SF, & other neurophysiology endpoints

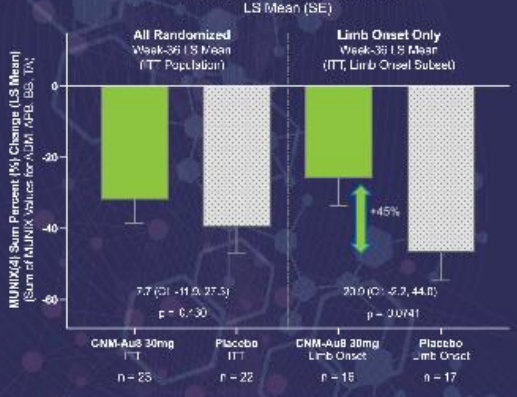
Baseline Demographics

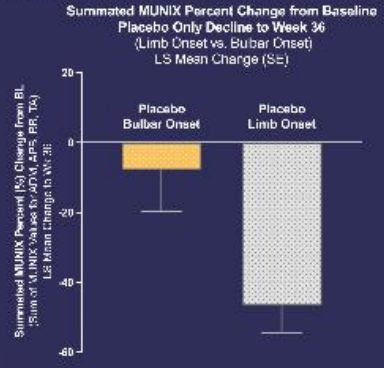
Baseline Value mean (sd)	Age (yrs)	Sex n, (%) Male | Female	Onset Site n, (%) Limb | Bulbar	Months from Onset	FVC (% pred.)	ALSFRS-R Score	ENCALS Risk Profile[1]	MUNIX Sum
All (n=45)	59.1 (12.3)	M: 26 (58%) F: 19 (42%)	L: 33 (73%) B: 12 (27%)	15.8 (9.3)	81.5 (16.7)	38.7 (6.0)	-4.4 (1.8)	378.2 (175.3)
CNM-Au8 30mg (n=23)	57.0 (13.3)	M: 13 (57%) F: 10 (43%)	L: 16 (70%) B: 7 (30%)	15.5 (7.6)	84.5 (18.3)	38.6 (6.6)	-4.6 (1.7)	380.2 (198.0)
Placebo (n=22)	61.3 (10.9)	M: 13 (59%) F: 9 (41%)	L: 17 (77%) B: 5 (23%)	16.1 (10.9)	78.2 (14.5)	38.8 (5.4)	-4.2 (1.8)	376.2 (152.7)

Safety Summary

- No CNM-Au8 related SAEs, drug discontinuations, or adverse event (AE) imbalance by system organ class.
- AEs predominantly mild-to-moderate & transient.
- The AEs most commonly associated with CNM-Au8 included aspiration pneumonia, n=3; nausea, n=2; abdominal discomfort, n=2.

1° Endpoint | Summated MUNIX Change at Week 36

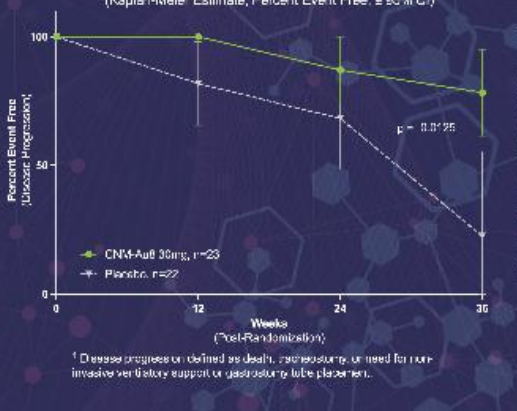




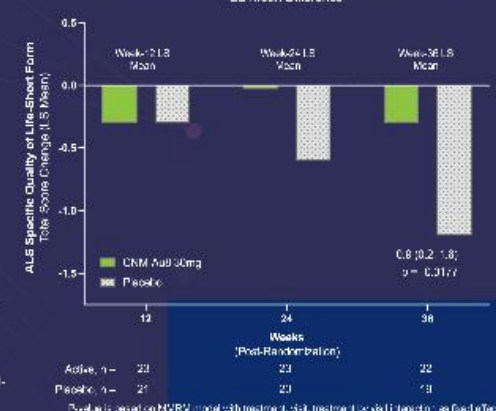
2° EP | FVC Change at Week 36

Primary endpoint p-value is based on mixed model repeat measures with treatment, visit, treatment by visit interaction as fixed effects, and baseline value and ENCALS score as covariates. An unstructured covariance model was used.

Clinical Endpoints | Exploratory



[1] Disease progression defined as death, gastrostomy, or need for non-invasive ventilatory support or gastrostomy tube placement.



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

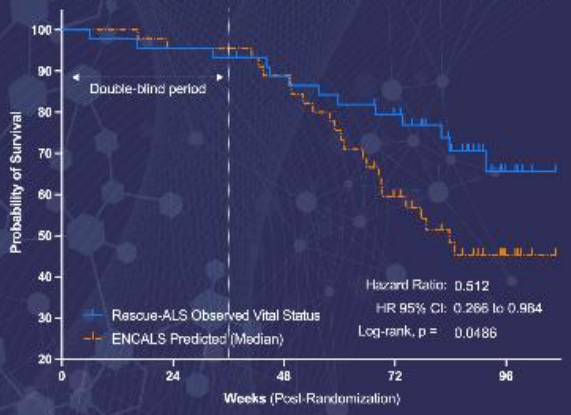
Acknowledgements: We thank the ALS study patients and their families for their support and willingness to engage in clinical research. We thank the site investigators for their research excellence and dedication to patients. We thank FightMND of Australia for substantially funding the RESCUE-ALS trial.

Evidence for an ALS Survival Benefit with CNM-Au8 Treatment: Interim Results from the RESCUE-ALS Trial Long -Term Open Label Extension

Steve Vucic PhD, DSc, FRACP, FAHMS[1], Parvathi Menon PhD, FRACP[1], William Huynh PhD, FRACP[2], Colin Mahoney, PhD, MB, MRCPI[2], Karen S. Ho, PhD MSc[3], Austin Rynders, RN[3], Jacob Evan[3], Jeremy Evan, PA-C[3], Robert Glanzman, MD FAAN[3], Michael T. Hotchkin[3], Matthew C. Kiernan PhD, DSc, MBBS, FRACP, FAHMS
[1]Concord Repatriation General Hospital, University of Sydney, Australia; [2]Brain and Mind Centre, University of Sydney, Australia; [3]Clene Nanomedicine, Salt Lake City, UT, USA

All Randomized

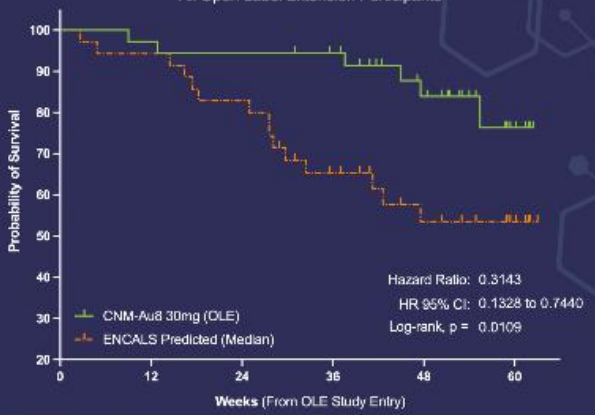
RESCUE-ALS Long-Term Observed Survival (All Randomized) vs. ENCALS Predicted Median Survival
ITT Population, All Subjects from Randomization (Active & Placebo)



At Risk (n): 45 43 39 39 8

All OLE Participants (CNM-Au8 Treated)

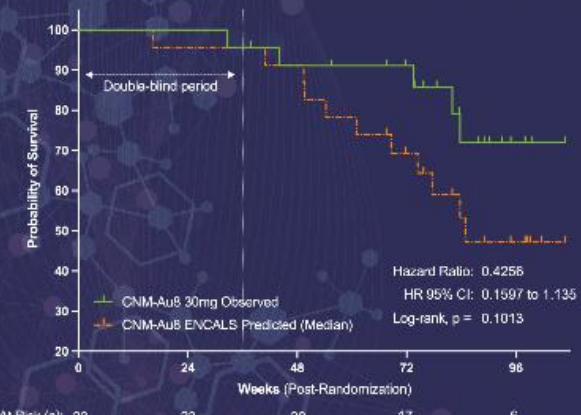
RESCUE-ALS Long-Term Observed Survival (OLE Participants) vs. ENCALS Predicted Median Survival
All Open Label Extension Participants



At Risk (n): 36 35 34 32 21 6

All CNM-Au8 Randomized

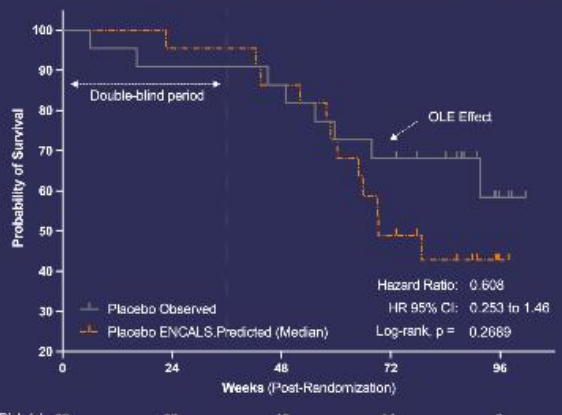
RESCUE-ALS Original CNM-Au8 Randomized Long Term Observed Survival vs. ENCALS Predicted Median Survival
All CNM-Au8 Treated Subjects, Survival from Randomization, ITT Population



At Risk (n): 23 23 20 17 6

All Placebo Randomized

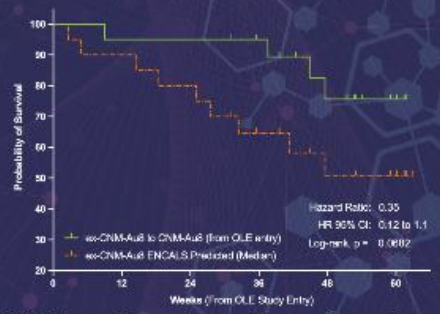
RESCUE-ALS Original Placebo Randomized Long-Term Observed Survival vs. ENCALS Predicted Median Survival
All Placebo Treated Subjects, Survival from Randomization, ITT Population



At Risk (n): 22 20 19 14 2

CNM-Au8 OLE

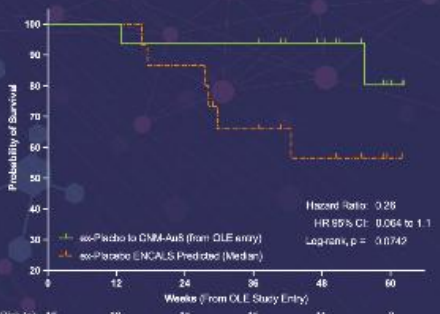
RESCUE-ALS CNM-Au8 to CNM-Au8 OLE Long-Term Observed Survival vs. ENCALS Predicted Median Survival
All CNM-Au8 Subjects Entering OLE, Survival from OLE Entry, ITT Population Subset



At Risk (n): 20 19 19 17 10 3

ex-Placebo to CNM-Au8 OLE

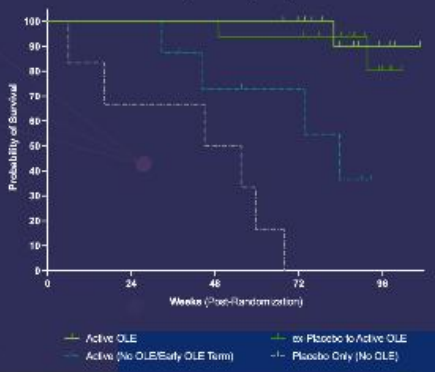
RESCUE-ALS ex-Placebo (to CNM-Au8 OLE) Long-Term Observed Survival vs. ENCALS Predicted Median Survival
All Placebo Subjects Entering OLE, Survival from OLE Entry, ITT Population Subset



At Risk (n): 16 16 15 15 11 3

Survival by OLE Status

Rescue-ALS Study Participants Long-Term Observed Survival
by OLE Entry Group



Notes: All randomized subjects including study withdrawals. Data censored for all subjects of 1-February-2022. Vital status and date of death captured for all subjects withdrawn from the study through Dec 2021. Lost-to-follow-up (n=1) censored as of the last date of last study contact. ENCALS median survival estimate from baseline characteristics.

Acknowledgements: We thank the ALS study patients and their families for their support and willingness to engage in clinical research. We thank the site investigators for their research excellence and dedication to patients. We thank FightMND of Australia for substantially funding the RESCUE-ALS trial.

Evidence for Brain Energy Metabolic Support with CNM-Au8 Treatment: Results from the REPAIR Phase 2 Clinical Trials

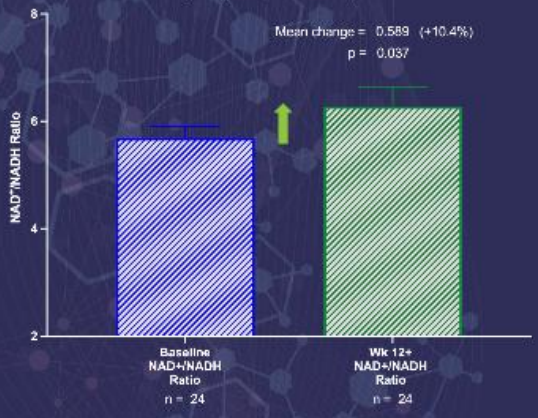
RepairPD
RepairMS

Robert Glanzman[1], MD FAAN, Chief Medical Officer, Jimin Ren[2], PhD, Richard B. Dewey, III MD[2], Austin Rynders[1], RN, Senior Director, Clinical Operations, Karen S. Ho[1] PhD MSc, Head, Translational Medicine Michael T. Hotchkin[1], Chief Development Officer, Richard B. Dewey, Jr.[2] MD, Benjamin Greenberg[2] MD
[1]Clene Nanomedicine, Inc., [2]University of Texas, Southwestern

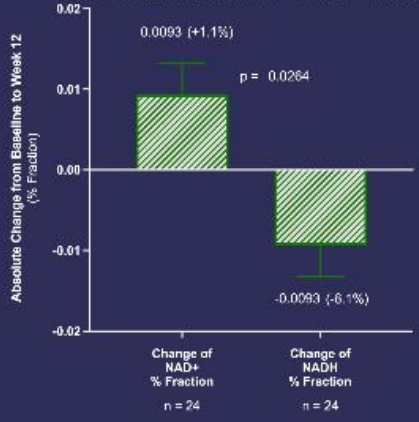
CONCLUSION: The REPAIR clinical trials demonstrate brain target engagement with CNM-Au8 treatment impacting brain energy metabolic support

Design Scheme

1° Endpoint | NAD+/NADH Change at Week 12[1]



2° Endpoint | NAD+ & NADH Fraction



Objective

Demonstration of CNS target engagement with ^{31}P-magnetic resonance spectroscopy (^{31}P-MRS)

Design

Open-label, dose blinded 12-week treatment (Enrolled: REPAIR-PD n=13, REPAIR-MS, n=13)

Endpoints

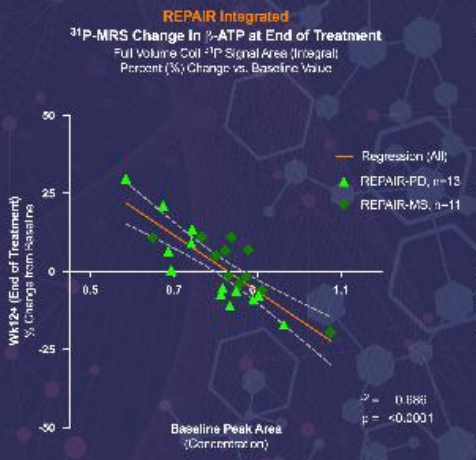
- Primary: change of NAD+/NADH ratio based on pre-specified integrated analyses of PD & MS cohorts
- Secondary: change of NAD+ and NADH fractions of NAD pool

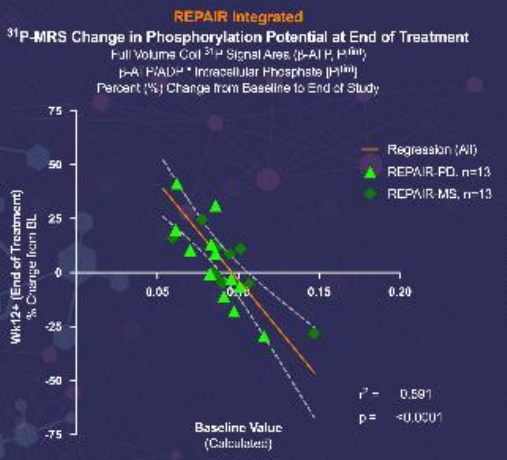
Safety

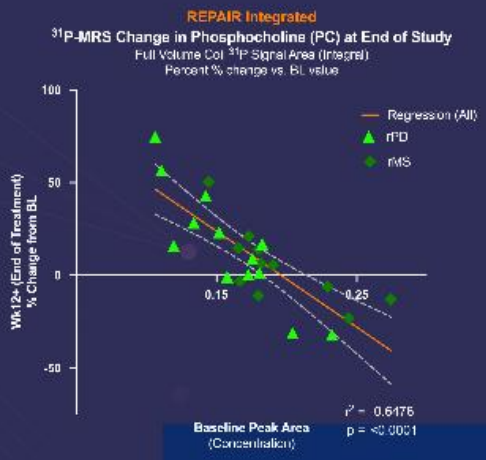
- Well tolerated; 97% treatment compliance
- TEAEs were all mild-to-moderate severity and transient
- No SAEs

[1] NAD+/NADH ratio declines approximately 0.5% per decade in cross-sectional observational studies

Exploratory | Equilibration of Energetic Metabolites







Acknowledgements: We are honored by the PD and MS study patients and their families for their support and willingness to engage in clinical research. We thank the site investigators for their research excellence and dedication to patients. We thank Jimin Ren, PhD and colleagues at the UTSW Advanced Imaging Research Center for development of the ^{31}P-MRS imaging methodology.

clene NANOMEDICINE

CNM-Au8 Gold Nanocatalysis Protects Neurons Against Degeneration and Death in Multiple *in vitro* Models of Amyotrophic Lateral Sclerosis

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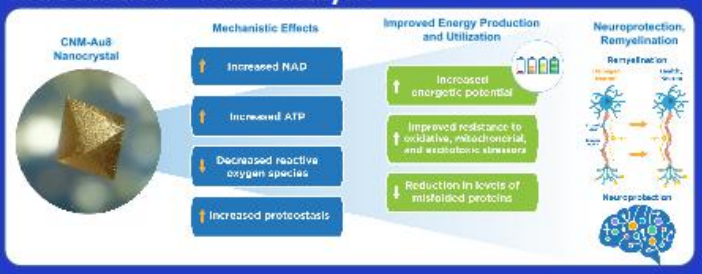
Introduction – Nanocatalysis



CNM-Au8®

- Catalytic mechanism of action enhances redox state in favor of energy production, while simultaneously lowering cellular oxidative stress
- Blood-brain barrier penetrant
- Suspension of 13 nm diameter, catalytically active, clean-surfaced, faceted gold nanocrystals
- Orally administered
- No-adverse effect level (NOAEL) nonclinical toxicology findings
- Well-tolerated; > 300 patient years of clinical exposure
- Results from Phase 2 Clinical trials presented at this meeting: Posters 034, 035, and 036. Oral P-presentation on RESCUE-ALS Clinical Trial results: Wed., Mar. 16, 11:10 AM Tennessee Ballroom.

Objective

To determine whether CNM-Au8, a catalytic suspension of clean-surfaced, faceted gold nanocrystals, promotes neuronal survival and function in multiple independent *in vitro* models of ALS.

Methods/Results

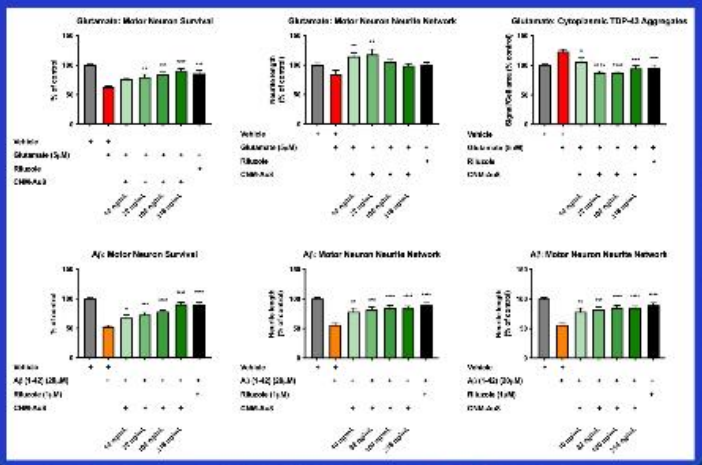
CNM-Au8's ability to promote neuronal survival and function in multiple independent *in vitro* models of ALS: (1) treatment of primary rat spinal motor neurons improves survival, preserves the neurite networks, and reduces cytoplasmic TDP-43 aggregate accumulation after either glutamate excitotoxic injury or exposure to beta-amyloid (Aβ 1-42) oligomers; (2) treatment of spinal motor neurons from transgenic SOD1^{G93A} rats protects motor neurons from death upon exposure to excitotoxic glutamate in a cAMP-dependent manner, and reduces SOD1 protein accumulation in a manner independent of cAMP; (3) treatment of human induced pluripotent stem cell (iPSC)-derived neurons from *C9ORF72* patients prevents their death in response to stress caused by mild neurotrophic factor withdrawal. Finally, we show (4) survival and neurite outgrowth of human iPSC-derived motor neurons in co-culture with toxic, SOD1^{A4V} ALS-patient derived astrocytes are substantially and dose-dependently improved with treatment of CNM-Au8.

Conclusion

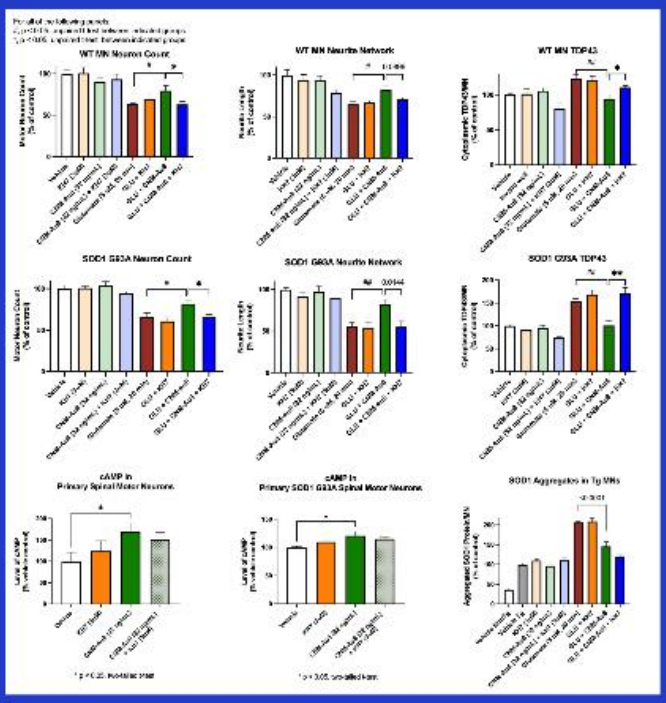
Addressing the deficits of ALS with the energetic catalyst CNM-Au8 appears to be a promising new therapeutic strategy for the treatment and disease-modification of ALS.

Results

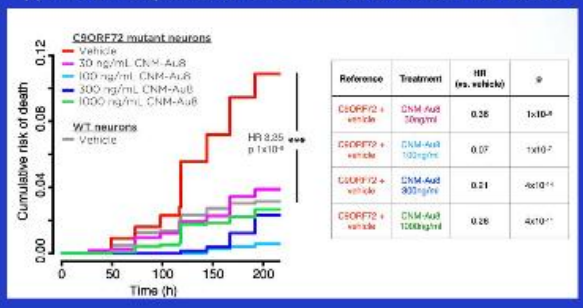
(1) CNM-Au8 Neuroprotection of Rodent Spinal Motor Neurons from Glutamate Excitotoxicity and Amyloid-Beta (1-42) Oligomers



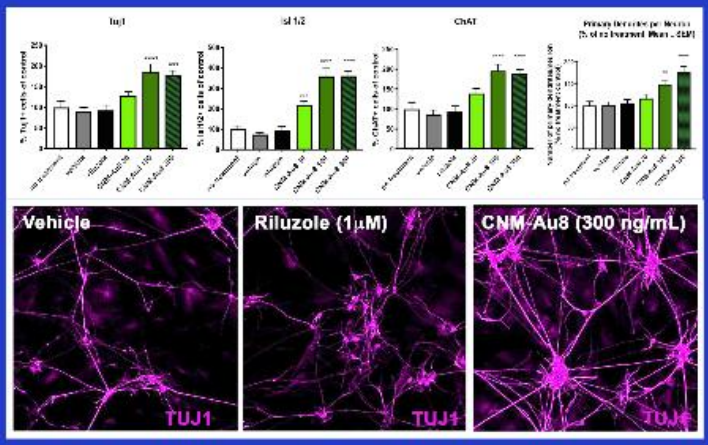
(2) cAMP-Mediated CNM-Au8 Motor Neuron Neuroprotection of Wildtype and SOD1 (G93A) Rodent Motor Neurons



(3) CNM-Au8 Neuroprotection of Human C9ORF72 iPSC-Derived Cortical Neurons



(4) CNM-Au8 Neuroprotection of Human iPSC-derived Motor Neurons Co-Cultured with Toxic Patient iPSC-Derived Astrocytes



Acknowledgments

We are very grateful to the individuals with ALS and healthy volunteers who donated fibroblasts, without whom the iPSC studies would not have been possible. The exceptional professional support of our colleagues at Clene has been invaluable. This study was funded by Clene Nanomedicine, Inc.

Phase 2 Results

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

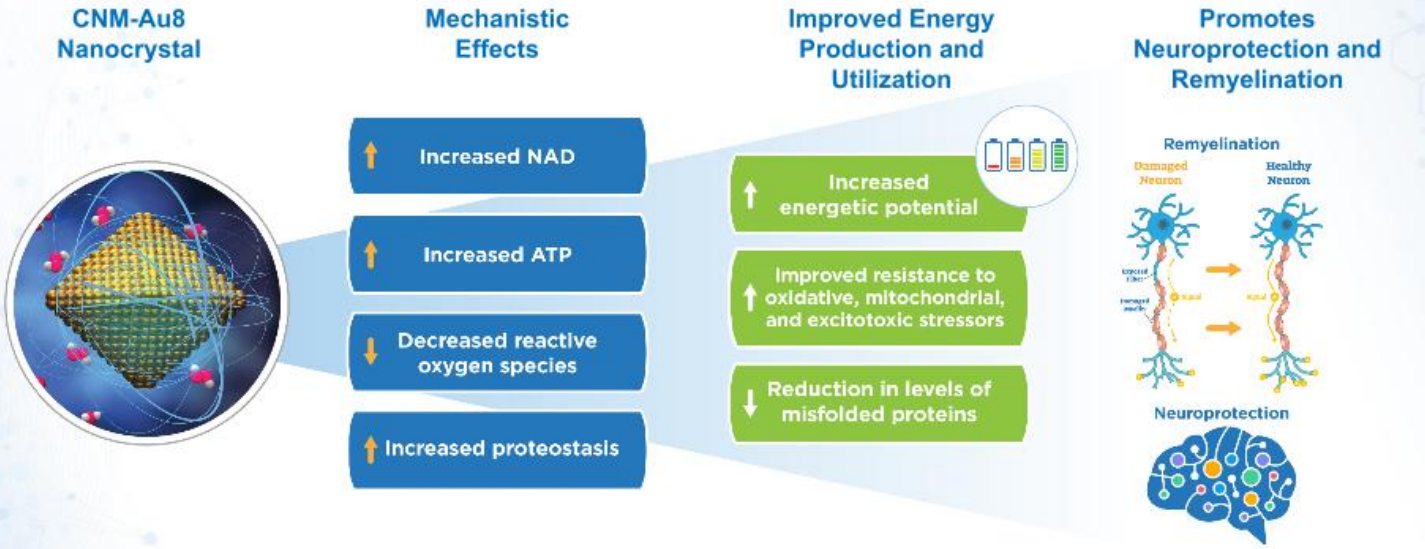
Disclosures & Acknowledgements

- Robert Glanzman, MD FAAN is an employee of Clene Nanomedicine, Inc.
- Funding support from FightMND Australia is gratefully acknowledged
- We thank ALS patients and their caregivers for participating in RESCUE-ALS
- Presenting on behalf of trial investigators

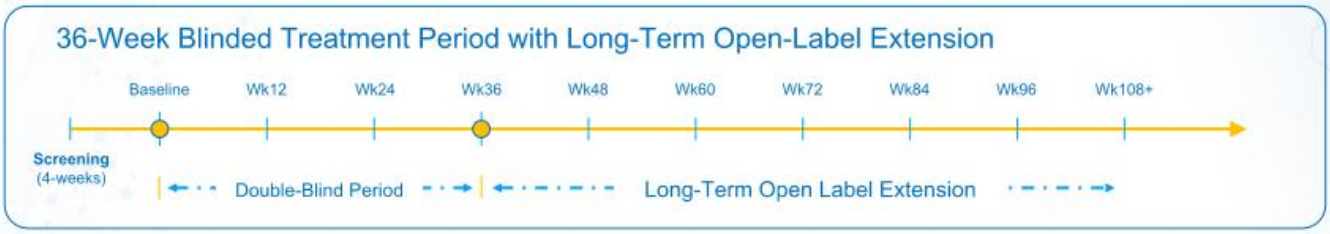
FIGHT MND
IT TAKES PEOPLE

RESCUEALS

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



RESCUE-ALS | Design & Baseline Demographics



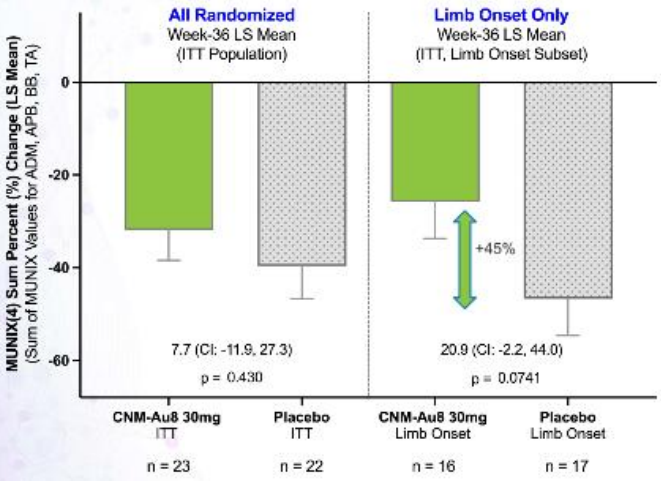
Baseline Value mean (sd)	Age (yrs)	Sex n, (%) Male | Female	Onset Site n, (%) Limb | Bulbar	Months from Onset	FVC (% pred.)	ALSFRS-R Score	ENCALS Risk Profile[1]	MUNIX Sum
All (n=45)	59.1 (12.3)	M: 26 (58%) F: 19 (42%)	L: 33 (73%) B: 12 (27%)	15.8 (9.3)	81.5 (16.7)	38.7 (6.0)	-4.4 (1.8)	378.2 (175.3)
CNM-Au8 30mg (n=23)	57.0 (13.3)	M: 13 (57%) F: 10 (43%)	L: 16 (70%) B: 7 (30%)	15.5 (7.6)	84.5 (18.3)	38.6 (6.6)	-4.6 (1.7)	380.2 (198.0)
Placebo (n=22)	61.3 (10.9)	M: 13 (59%) F: 9 (41%)	L: 17 (77%) B: 5 (23%)	16.1 (10.9)	78.2 (14.5)	38.8 (5.4)	-4.2 (1.8)	376.2 (152.7)

Evidence for Motor Neuron Protection

Primary Endpoint (MUNIX %, LS Mean Change)

All Randomized

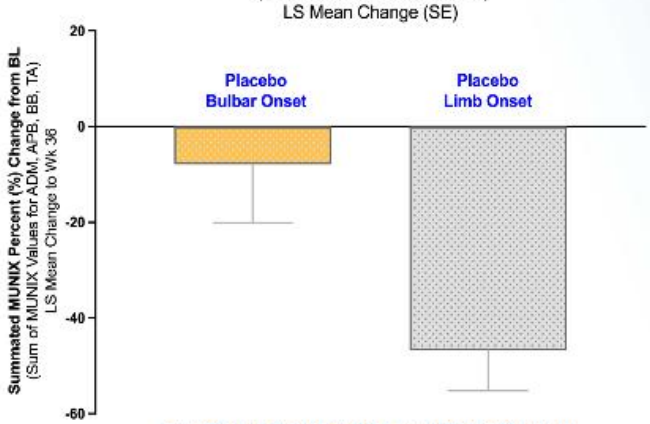
Summated MUNIX Percent Change from Baseline to Week 36
RESCUE-ALS Primary Endpoint
Mixed Model Repeat Measure (ITT Population & Limb Onset Subset)
LS Mean (SE)



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

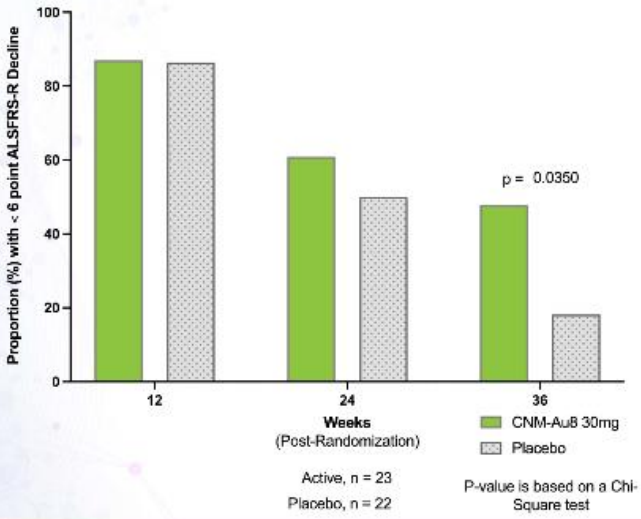
RESCUE-ALS: A Phase 2, randomized, double-blind, placebo-controlled study of CNM-Au8 to slow disease progression in ALS. MNDA Virtual Symposium, 2021 Data on File, Clene Nanomedicine, Inc.

RESCUEALS

Significant Impact on ALSFRS-R Decline

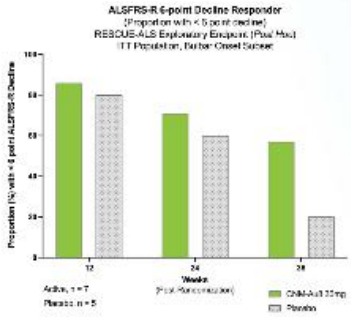
Exploratory (ALSFRS-R Responder Analysis, < 6-point decline)

All Randomized

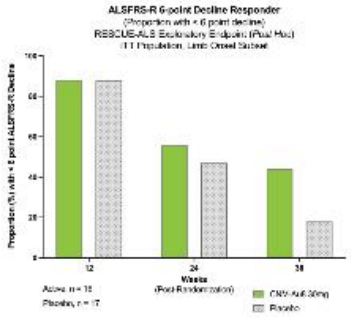


Sensitivity Analysis

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.

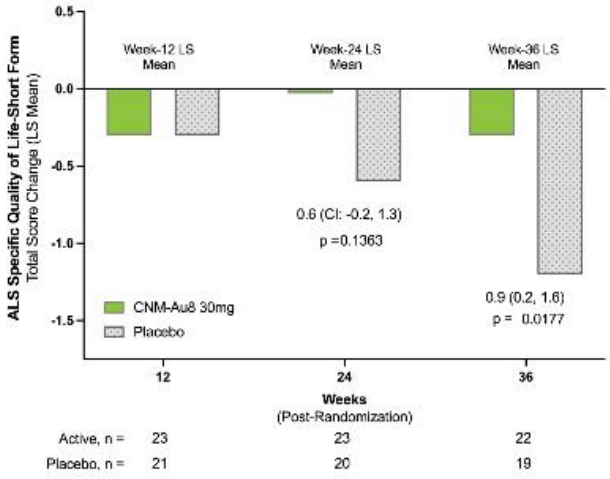
RESCUEALS

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

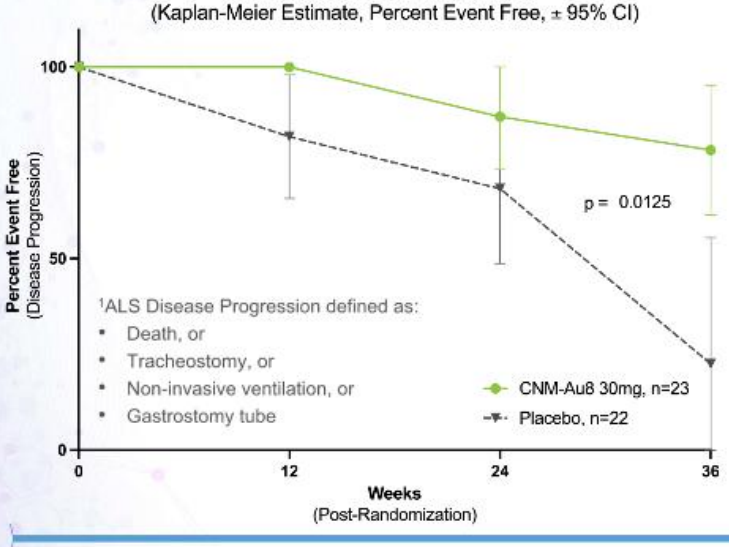
P-value is based on MMRM model with treatment, visit, treatment by visit interaction as fixed effects, and baseline value, and ENCALS score as covariates. An unstructured covariance model was used.

RESCUEALS

Significant Impact on Disease Progression

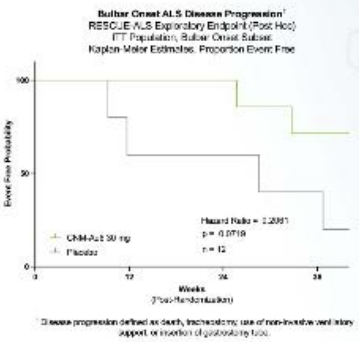
Exploratory Endpoint (Disease Progression)

All Randomized

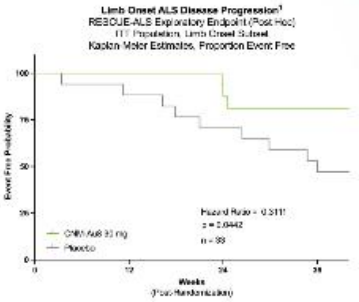


Sensitivity

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.

RESCUEALS

Joint Rank Trend | 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

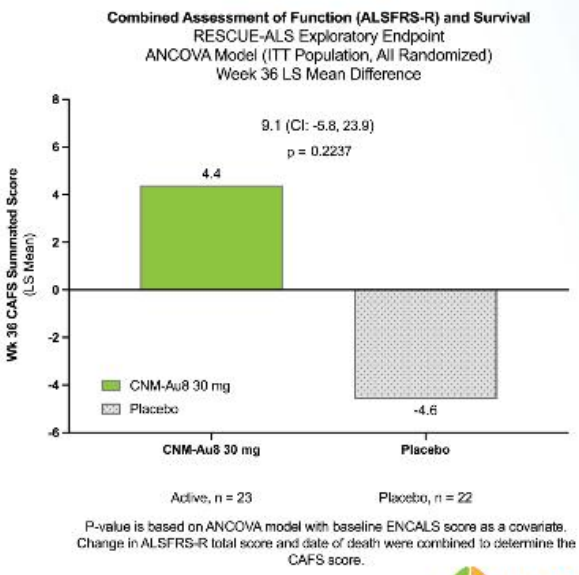
If...	Score
Better function or died later than comparison	+1
Same function or died at the same time as comparison	0
Worse function or died before comparison subject	-1

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.

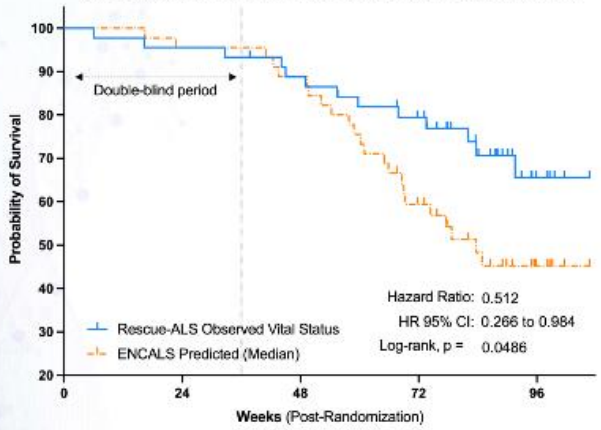
Berry et al. Amyotroph Lateral Scler Frontotemporal Degener. 2013 Apr;14(3):162-8.

RESCUEALS

Impact on Long-Term Survival

All Randomized

RESCUE-ALS Long-Term Observed Survival (All Randomized)
vs. ENCALS Predicted Median Survival
ITT Population, All Subjects from Randomization (Active & Placebo)

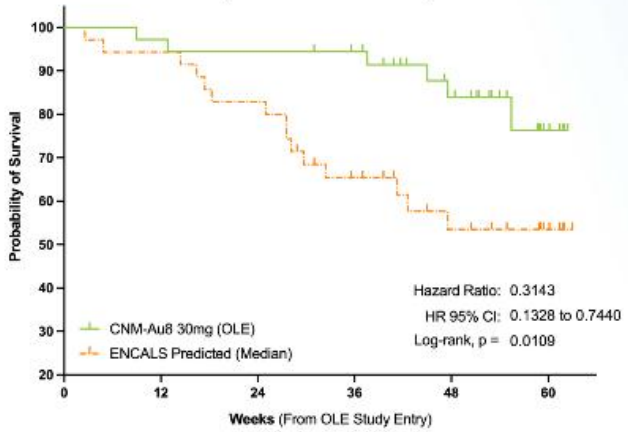


At Risk (n):					
	45	43	39	39	8

All randomized subjects censored as of 1-February-2022. Vital status and date of death captured for all subjects withdrawn from the study through Dec 2021. Lost-to-follow-up (n=1) censored as of the last date of last study contact.

All OLE Participants (CNM-Au8 Treated)

RESCUE-ALS Long-Term Observed Survival (OLE Participants)
vs. ENCALS Predicted Median Survival
All Open Label Extension Participants



At Risk (n):					
	36	35	34	32	21	6

All OLE subjects censored as of 1-February-2022. Vital status and date of death (as applicable) captured for all subjects withdrawn from the study through December 2021.
ENCALS median survival estimate from baseline characteristics.

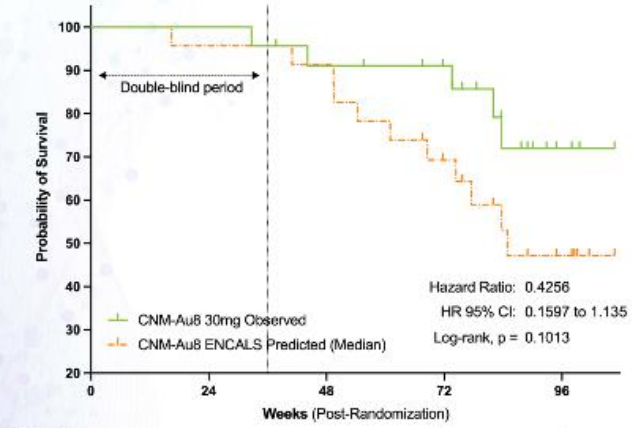
RESCUEALS

Impact on Long-Term Survival | by Randomization Group

All CNM-Au8 Randomized

RESCUE-ALS Original CNM-Au8 Randomized Long Term Observed Survival vs. ENCALS Predicted Median Survival

All CNM-Au8 Treated Subjects, Survival from Randomization, ITT Population



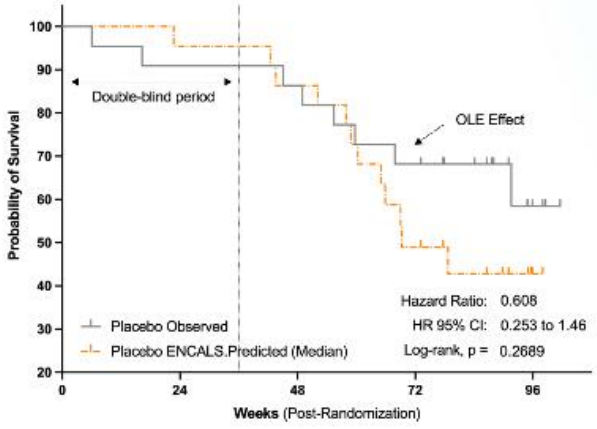
At Risk (n):					
	23	23	20	17	6

All current OLE subjects censored as of 1-February-2022. Vital status and date of death (as applicable) captured for all subjects withdrawn from the study through December 2021. Lost-to-follow-up (n=1) censored as of the last date of last study contact.

All Placebo Randomized

RESCUE-ALS Original Placebo Randomized Long-Term Observed Survival vs. ENCALS Predicted Median Survival

All Placebo Treated Subjects, Survival from Randomization, ITT Population



At Risk (n):					
	22	20	19	14	2

All current OLE subjects censored as of 1-February-2022. Vital status and date of death (as applicable) captured for all subjects withdrawn from the study through December 2021.

RESCUEALS

Safety Summary | Well Tolerated & No Safety Signals

- 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 classification
- 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)

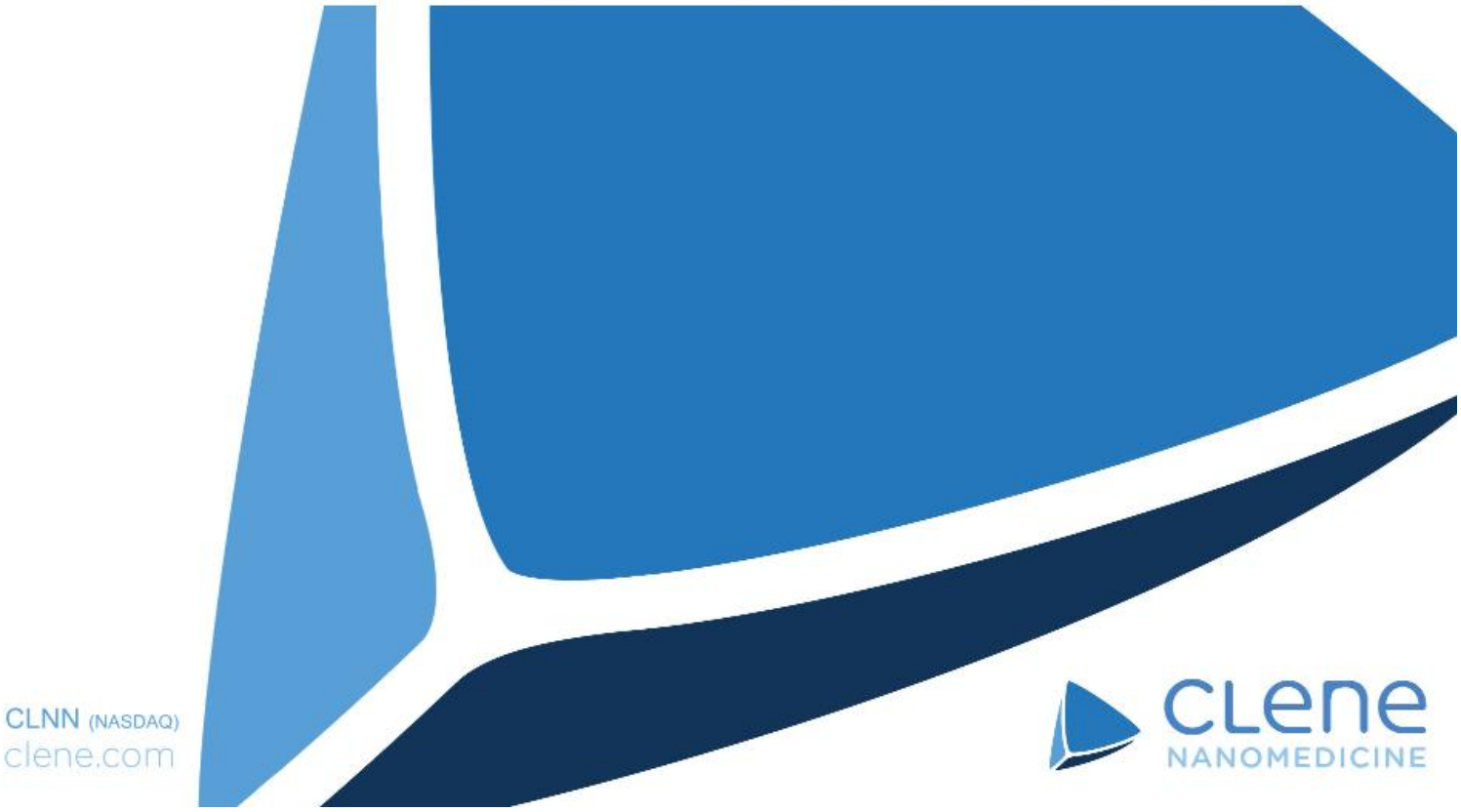
Data on File, Clene Nanomedicine, Inc.

RESCUEALS

Conclusions

- **Evidence of CNM-Au8 therapeutic efficacy**
  - ✓ Improved survival
  - ✓ Significant slowing in disease progression
  - ✓ Significant reduction in functional decline
  - ✓ Significant improvement in quality of life
  - ✓ Preservation of lower motor neurons
- **CNM-Au8, well tolerated and safe in ALS**
- **Larger clinical trial underway**

RESCUEALS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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 Annual Report on Form 10-K (filed March 11, 2022) 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

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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

December 31, 2021 Cash and restricted cash on hand (audited):
$50.3M

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

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CLENE | Pipeline

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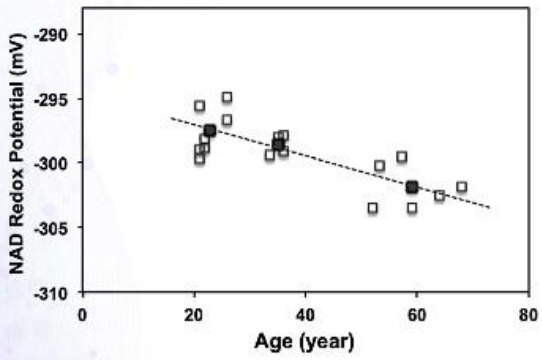
Neurons With High Energetic Demand Are At Increased Risk For Neurodegenerative Disease

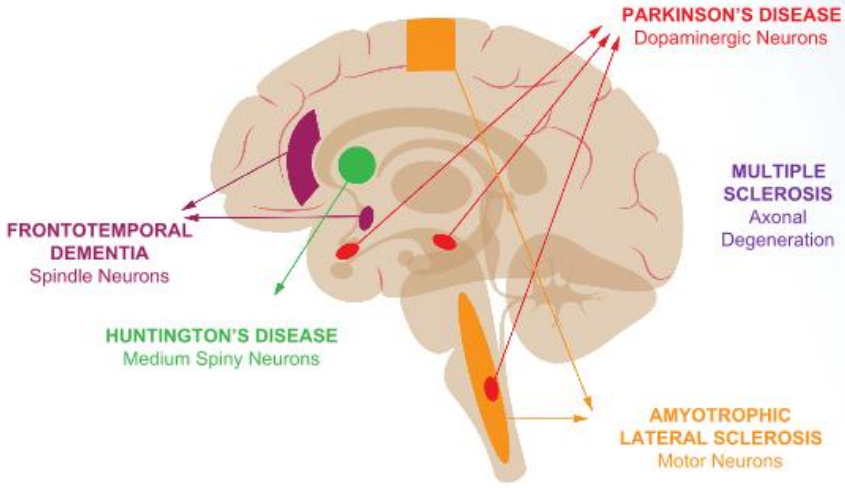
Brain Energy Potential Declines With Normal Aging

~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

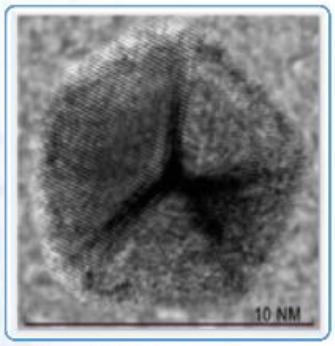


Fu, H., et al; Nature Neuroscience (2018) 21: 1350-1358. Zhu et al. Proc Natl Acad Sci USA . 2015 Mar 3;112(9):2876-81. Rone et al. J Neurosci. 2016 Apr 27;36(17):4698-707.

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

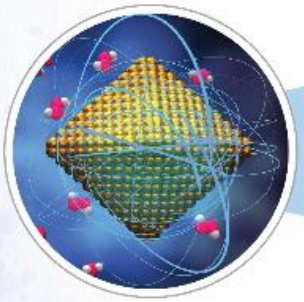
CNM-Au8 Catalytically Active Nanocrystal Suspension

60 mL per bottle (once daily)

CLene NANOMEDICINE

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

CNM-Au8 Nanocrystal



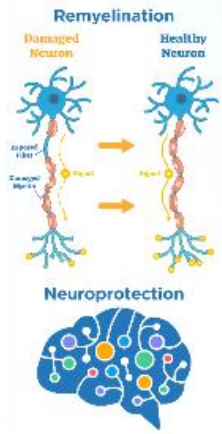
Mechanistic Effects

- ↑ 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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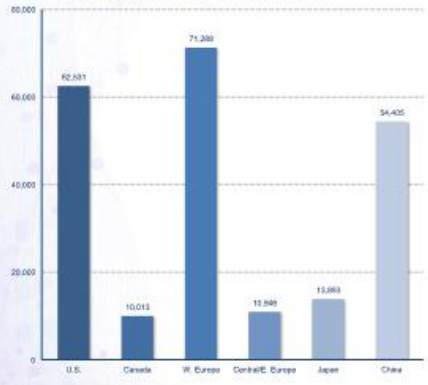
CNM-Au8® | Significant Global Opportunity

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

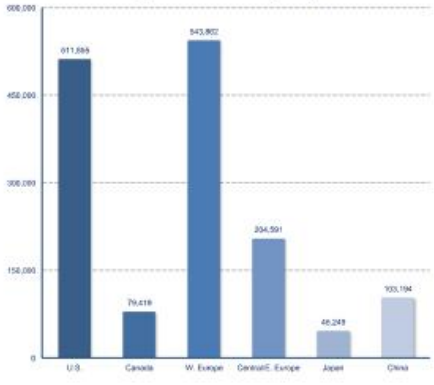


Source: Lancet Neurol. 2018 Dec;17(12):1083-1097.
MND includes amyotrophic lateral sclerosis, spinal muscular atrophy, hereditary spastic paraplegia, primary lateral sclerosis, progressive muscular atrophy, and pseudobulbar palsy

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

Only approved treatments are immunomodulators

Est. Diagnosed MS Patients by Region

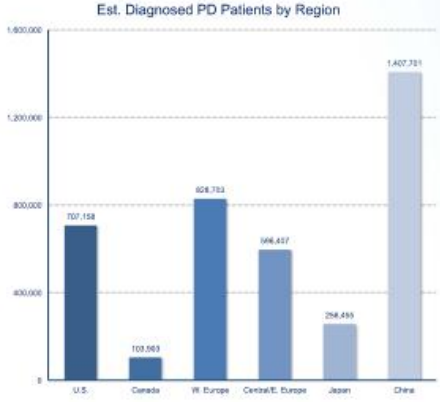


Source: Lancet Neurol. 2019 Mar;18(3):269-285. ~2.2 M patients globally, data as of 2016

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.

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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 Identified 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

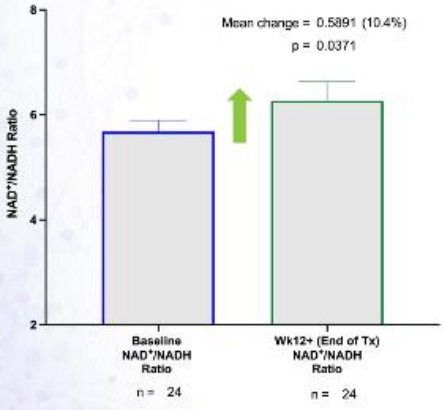
CNM-Au8 Improves Brain Energy Metabolism Increases NAD+/NADH Ratio in MS & PD

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)



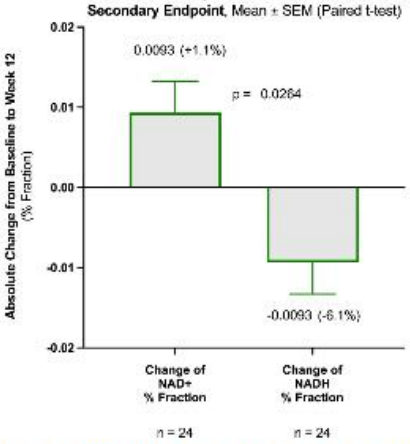
2° Endpoint

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)



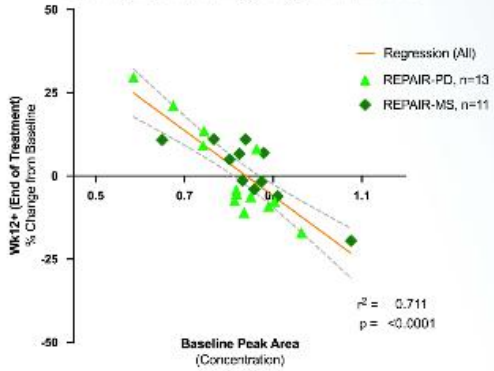
Exploratory (ATP Normalization)

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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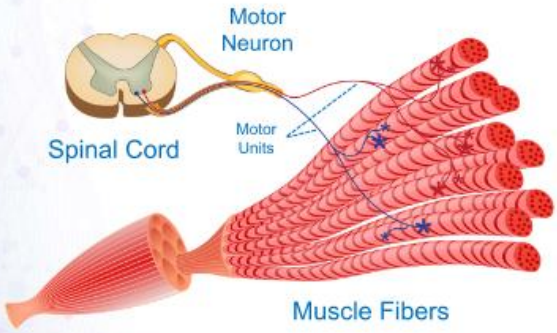
RESCUEALS | Pioneered Use of MUNIX Biomarker

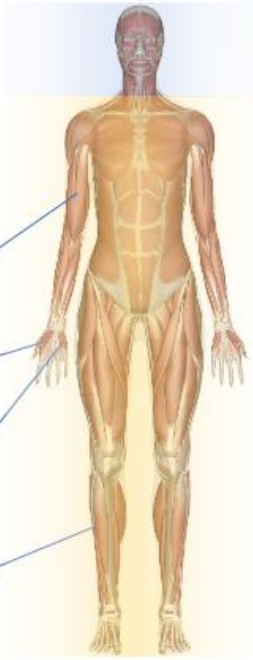
Primary Endpoint: Spinal Cord Lower Motor Neuron Protection

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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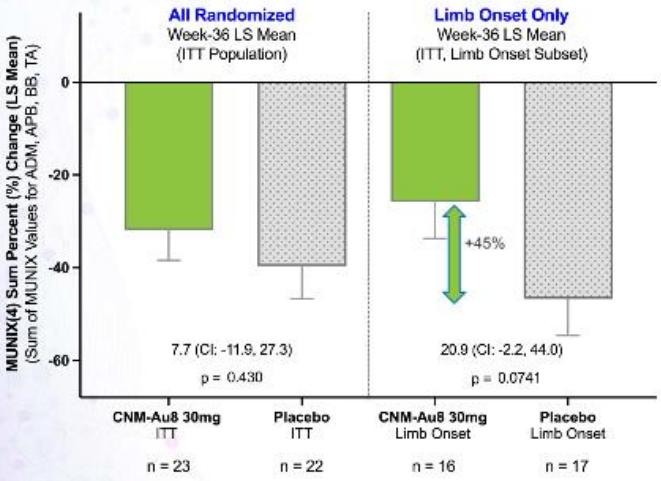
RESCUEALS | Evidence for Motor Neuron Protection

Primary Endpoint (MUNIX %, LS Mean Change)

All Randomized

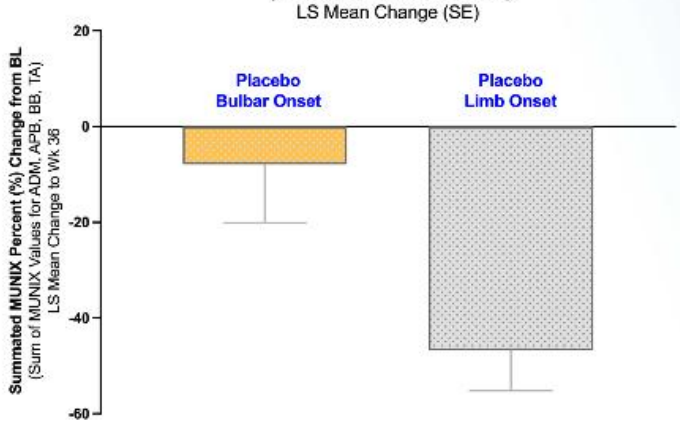
Summated MUNIX Percent Change from Baseline to Week 36
RESCUE-ALS Primary Endpoint
Mixed Model Repeat Measure (ITT Population & Limb Onset Subset)
LS Mean (SE)



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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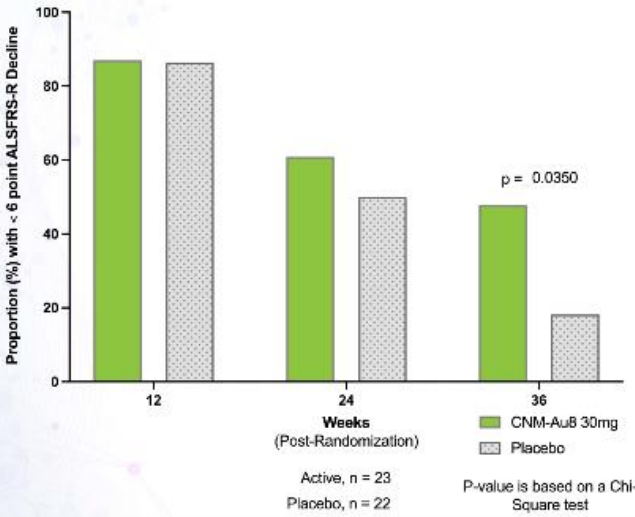
RESCUEALS | Significant Impact on ALSFRS-R Decline

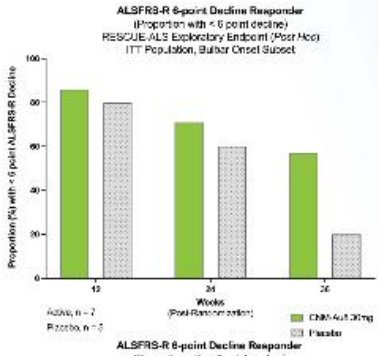
Exploratory (ALSFRS-R Responder Analysis, < 6-point decline)

All Randomized

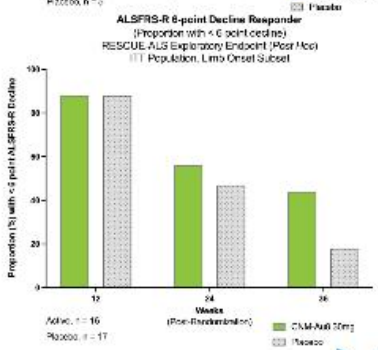


Sensitivity

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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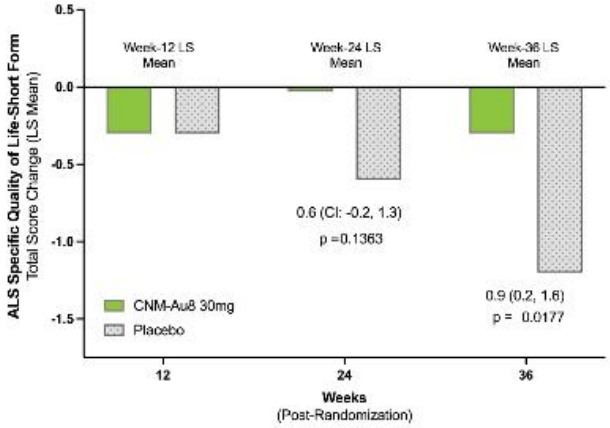
RESCUEALS | Significant Quality of Life Improvement

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.

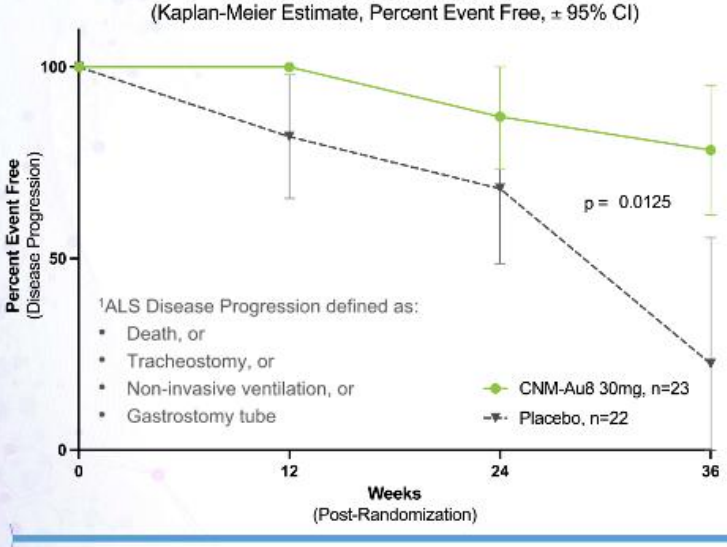
RESCUE-ALS: A Phase 2, randomized, double-blind, placebo-controlled study of CNM-Au8 to slow disease progression in ALS. MNDA Virtual Symposium, 2021 Data on File, Clene Nanomedicine, Inc.

RESCUEALS | Significant Impact on ALS Disease Progression

Exploratory Endpoint (Disease Progression)

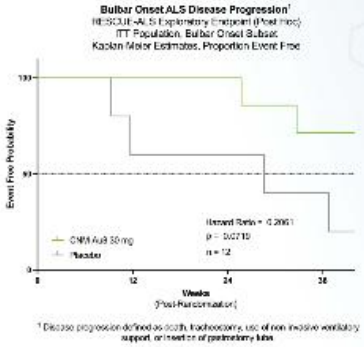
All Randomized

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



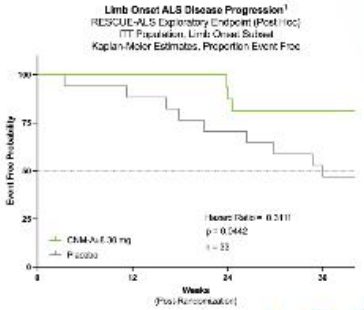
Sensitivity

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

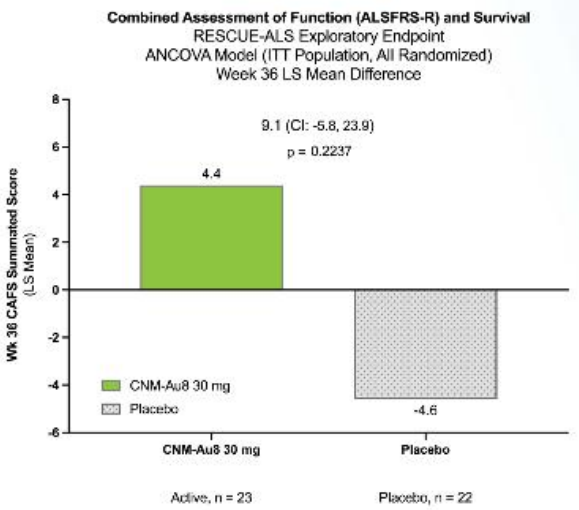
If...	Score
Better function or died later than comparison	+1
Same function or died at the same time as comparison	0
Worse function or died before comparison subject	-1

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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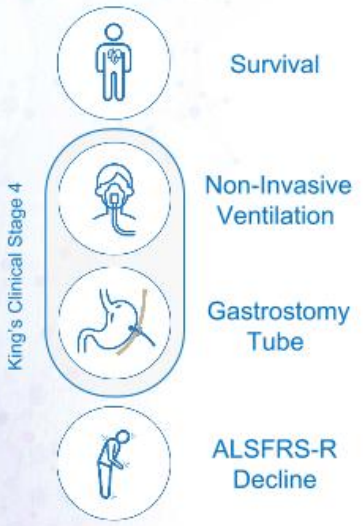
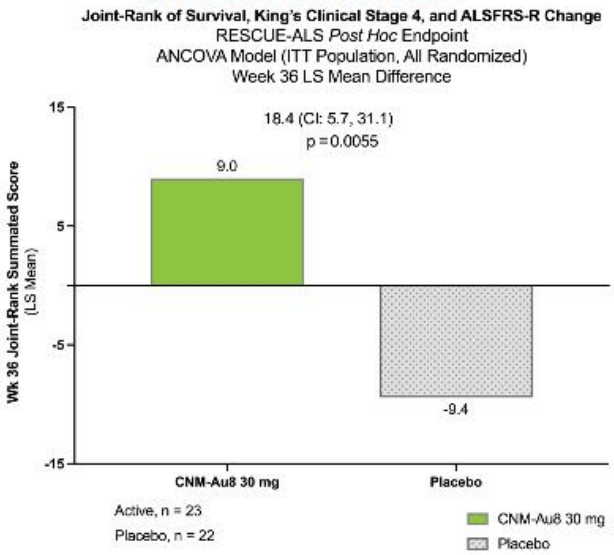
RESCUEALS | Impact on Joint Rank Score to Wk36

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



By Average of Summated Scores



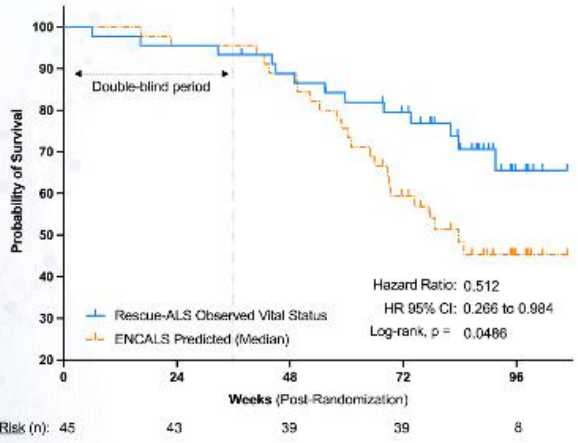
P-value is based on ANCOVA model with baseline ENCALS score as a covariate. Change in ALSFRS-R total score, date of non-invasive ventilation or gastrostomy, and date of death were combined to determine the joint-rank score.

Data on File, Clene Nanomedicine, Inc.

RESCUEALS | Potential Impact on Long-Term Survival

All Randomized

RESCUE-ALS Long-Term Observed Survival
vs. ENCALS Predicted Median Survival
ITT Population, All Subjects from Randomization (Active & Placebo)

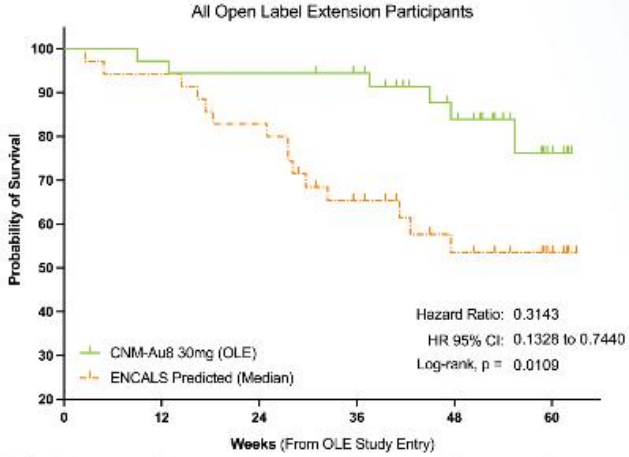


At Risk (n): 45 43 39 39 8

All current OLE subjects censored as of 1-February-2022. Vital status and date of death captured for all subjects withdrawn from the study through Dec 2021. Lost-to-follow-up (n=1) censored as of the last date of last study contact.

All OLE Participants (CNM-Au8 Treated)

RESCUE-ALS Long-Term Observed Survival (OLE Participants)
vs. ENCALS Predicted Median Survival
All Open Label Extension Participants



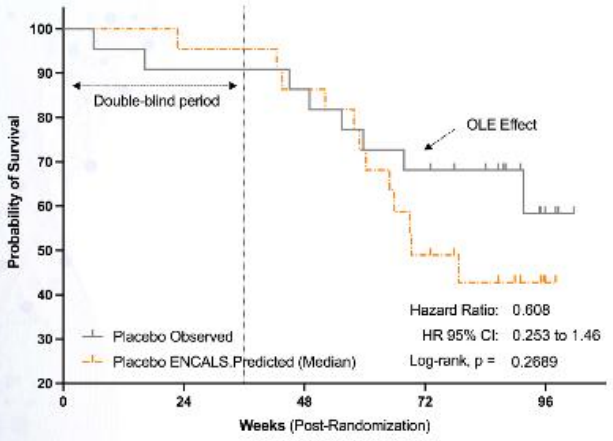
At Risk (n): 36 35 34 32 21 6

All OLE subjects censored as of 1-February-2022. Vital status and date of death (as applicable) captured for all subjects withdrawn from the study through December 2021.
ENCALS median survival estimate from baseline characteristics.

RESCUEALS | Potential Impact on Long-Term Survival

All Placebo Randomized

RESCUE-ALS Original Placebo Randomized Long-Term Observed Survival vs. ENCALS Predicted Median Survival
All Placebo Treated Subjects, Survival from Randomization, ITT Population

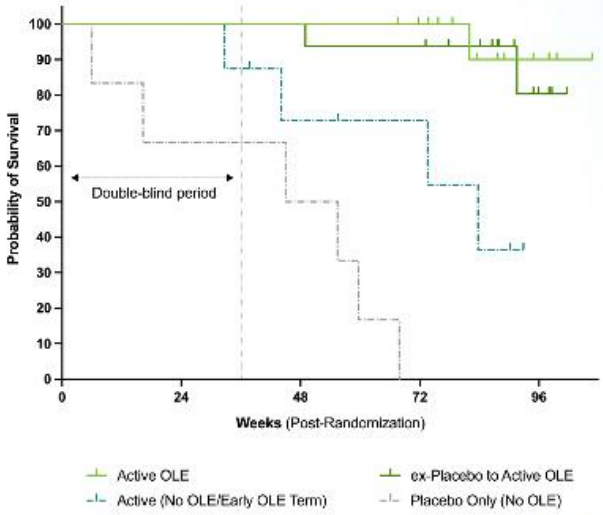


At Risk (n):					
	22	20	19	14	2

All placebo subjects censored as of 1-February-2022. Vital status and date of death (as applicable) captured for all subjects withdrawn from the study through December 2021.

Survival Status by OLE Participation

Rescue-ALS Study Participants Long-Term Observed Survival
by OLE Entry Group



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RESCUEALS | Well Tolerated & No Safety Signals

Safety Summary

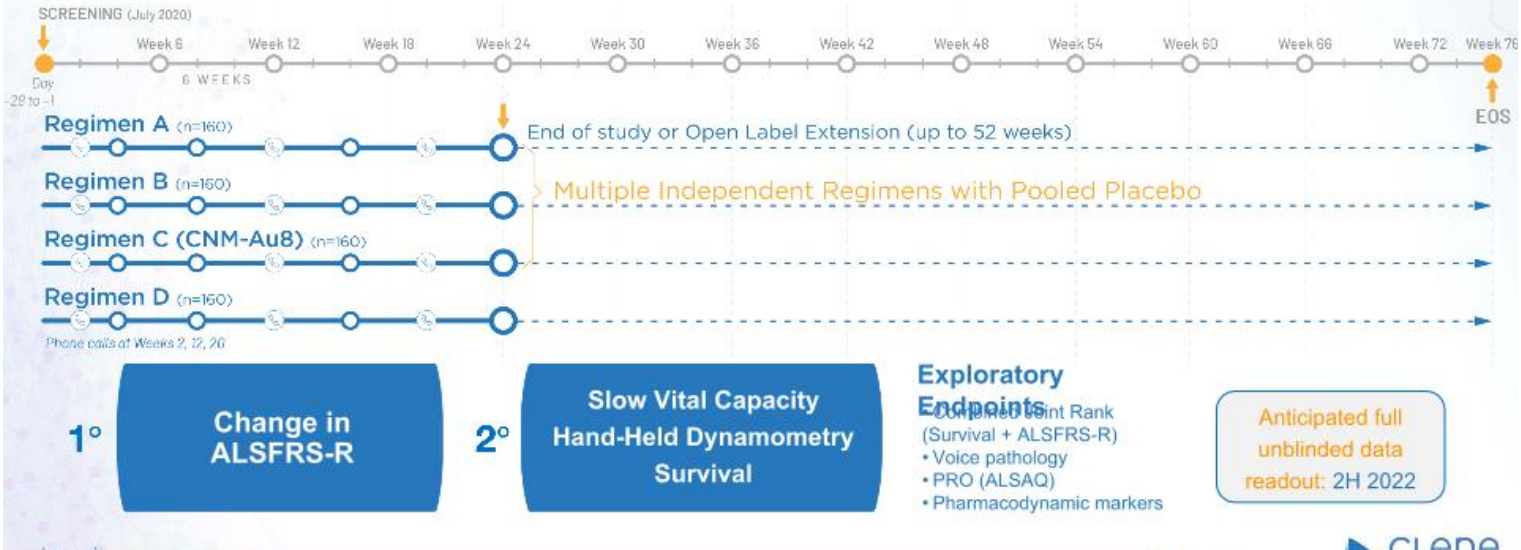
- No CNM-Au8 related serious adverse events (SAEs)
- No CNM-Au8 related drug discontinuations
- No imbalances in treatment emergent adverse event (TEAEs) by system organ class
- TEAEs were predominantly mild-to-moderate and transient
- Most common TEAEs associated with CNM-Au8
  (aspiration pneumonia,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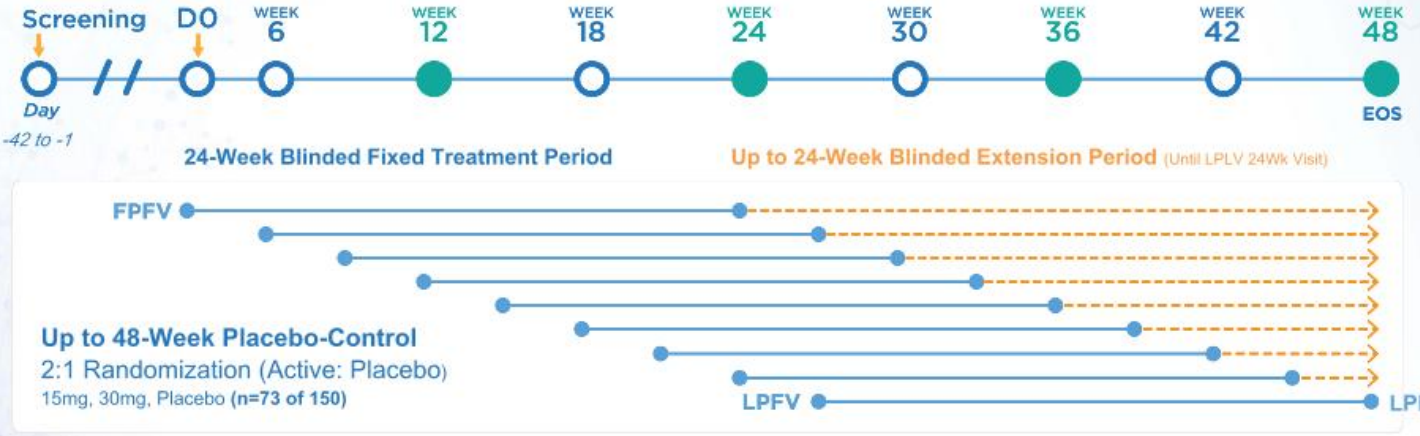
Phase 2

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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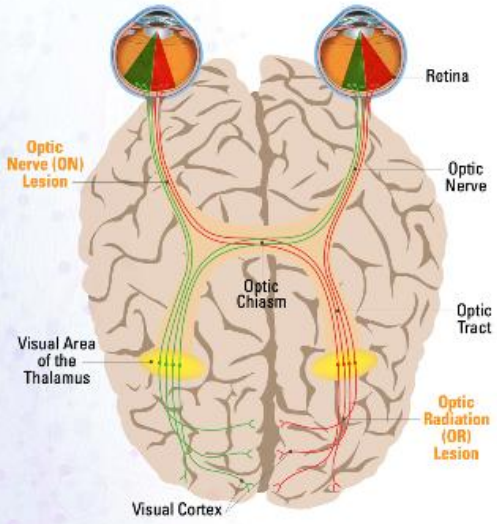
Measuring MS Functional Improvement

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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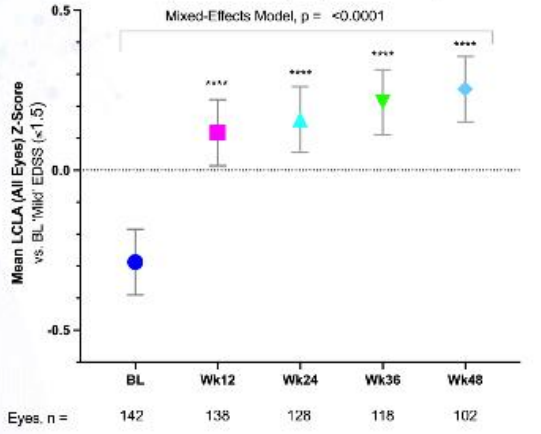
Phase 2 VISIONARY-MS STUDY

Significant Clinical Improvement Across Blinded Study Population

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

1° | LCLA

LCLA (All Eyes) Average Z-Score
14-February-2022 Data Cut, Preliminary Blinded Data
(vs. 'Mild' EDSS [≤1.5]; Mean ± SEM)



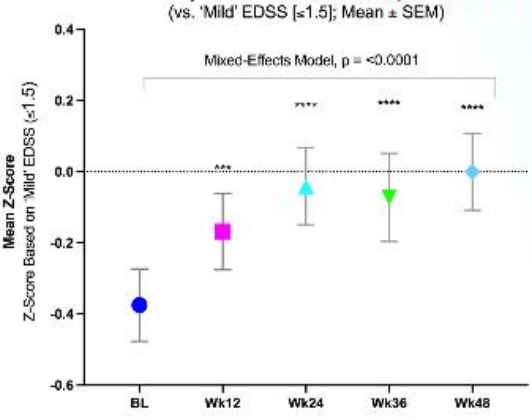
Eyes, n =	142	138	128	118	102

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
14-February-2022 Data Cut, Preliminary Blinded Data
(vs. 'Mild' EDSS [≤1.5]; Mean ± SEM)



n =	73	70	65	60	53

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/OD), 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

Glanzman et al. VISIONARY-MS: Update to a Phase 2 Clinical Trial of CNM-Au8, Catalytically Active Gold Nanocrystals Suspension, for the Treatment of Chronic Optic Neuropathy ACTRIMS, February 2022.

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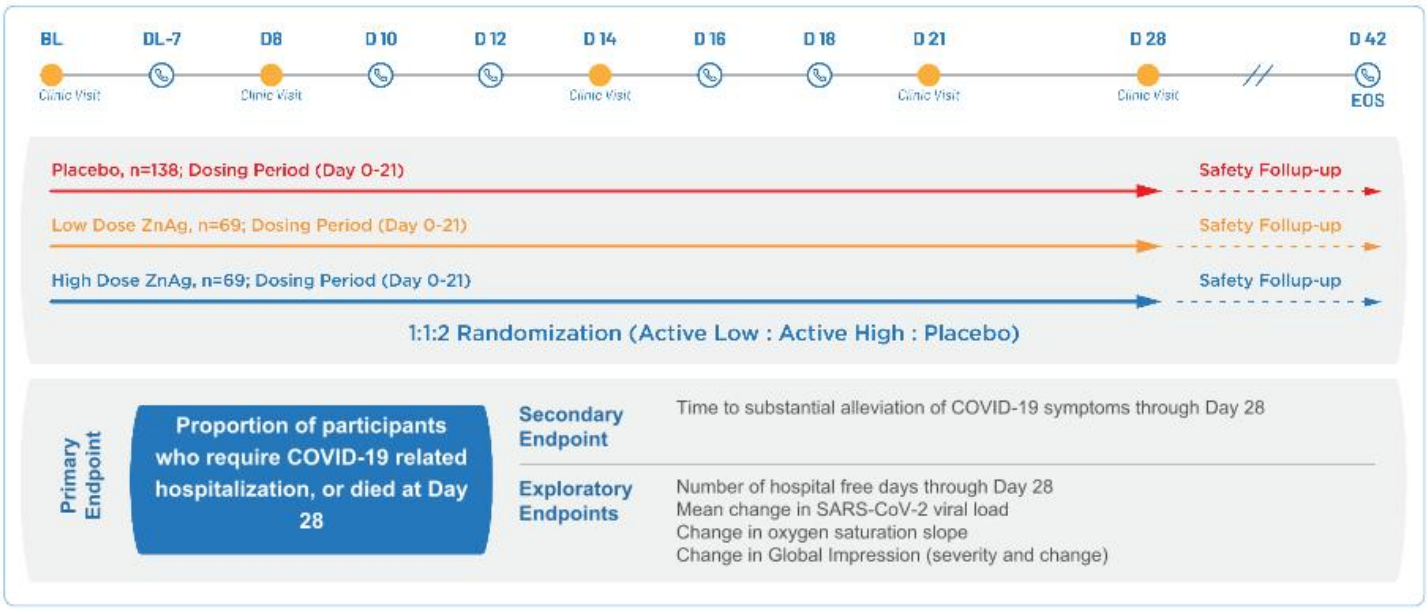
ZnAgSTUDY BRAZIL



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-September-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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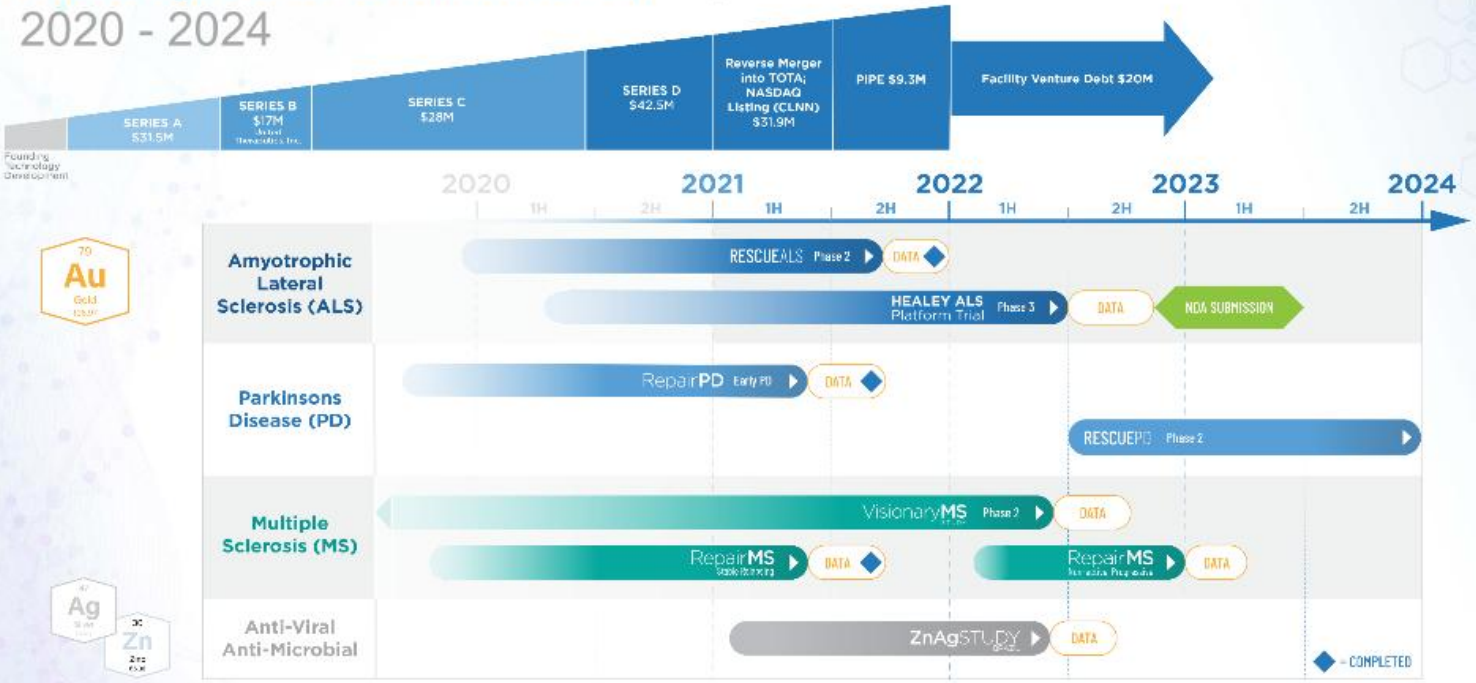
Anticipated Timeline & Upcoming Milestones

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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