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): November 2, 2021

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

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

6550 South Millrock Drive, Suite G50 Salt Lake City, Utah	84121
(Address of principal executive offices)	(Zip Code)

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

N/A
(Former name or former address, if changed since last report.)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

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

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

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

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

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

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

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

Emerging growth company ☒

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

Item 7.01 Regulation FD Disclosure.

On November 2, 2021, Clene Inc. (the "Company") issued a press release announcing top-line results from its Phase 2 RESCUE-ALS clinical trial in amyotrophic lateral sclerosis ("ALS"). A copy of the press release is furnished as Exhibit 99.1 to this Current Report on Form 8-K (the "Current Report") and is incorporated herein by reference.

In connection with the press release issued on November 2, 2021, the Company hosted a conference call to discuss the Phase 2 RESCUE-ALS topline clinical trial results. A copy of the webinar presentation is furnished as Exhibit 99.2 to this Current Report 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, 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 November 2, 2021 announcing top-line results from the Phase 2 RESCUE-ALS clinical trial
99.2	RESCUE-ALS presentation dated November 2, 2021
104	Cover Page Interactive Data File (formatted as Inline XBRL).

SIGNATURES

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

Clene Inc.

Date: November 2, 2021

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

Exhibit 99.1

Clene Nanomedicine Announces Top-Line Results from Phase 2 RESCUE-ALS Clinical Trial

- ***RESCUE-ALS Phase 2 Trial did not meet primary MUNIX biomarker endpoint or secondary FVC endpoint at week 36; MUNIX efficacy signal was observed at week 12 (p=0.057)***
- ***MUNIX trial results demonstrated protection of lower motor neurons in the pre-specified subset of limb onset ALS subjects (Wk12, p=0.0385; Wk36, p=0.0741), which represents approximately 70% of the ALS population***
- ***Statistically significant reductions in clinically relevant outcomes including ALS disease progression (p=0.0125), ALSFRS-R responder analysis (p=0.035), and improved ALS specific quality of life (p=0.018)***
- ***Evidence for potential long-term survival benefit***
- ***Results for Healey ALS Platform Trial Expected in the Second Half of 2022***

SALT LAKE CITY, Nov. 2, 2021 -- 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 with its potential first-in-class catalytically active nanocrystal suspension, today announced top-line data from RESCUE-ALS, a Phase 2 clinical trial evaluating CNM-Au8 as a disease modifying treatment for people with early amyotrophic lateral sclerosis (ALS).

The trial did not meet the primary or secondary endpoints – Motor Unit Number Index (MUNIX) and forced vital capacity (FVC) – at week 36. However, an efficacy signal was observed for the MUNIX endpoint at week 12 (p=0.057). Furthermore, in a pre-specified analysis in the subset of limb onset ALS, CNM-Au8 demonstrated a significant treatment effect in MUNIX at week 12 (p=0.0385) and a trend for improvement at week 36 (p=0.0741). Limb onset ALS accounts for approximately 70% of the ALS population. MUNIX is a neurophysiological biomarker that estimates the number of functioning lower motor neurons serving selected muscles.

Clinically relevant exploratory endpoints through trial week 36 demonstrated significant benefits with CNM-Au8 treatment, including slowing ALS disease progression (p=0.0125), decreasing the proportion of participants with an ALS Functional Rating Scale Revised (ALSFRS-R) 6-point decline (p=0.035), and improving quality of life as measured by the ALS Specific Quality of Life (ALSSQOL-SF) (p=0.018). In addition, RESCUE-ALS showed evidence for a potential long-term survival benefit when comparing the survival of the trial population to the validated ENCALS predictive model[1].

"These data are very encouraging to us in the ALS research and treatment community as they demonstrate clinical benefits with CNM-Au8 treatment in outcomes that matter to patients and provide evidence for improved long-term survival," said Professor Matthew Kiernan, AM MBBS(Hons), PhD, DSc, FRACP, FAHMS, Bushell Chair of Neurology, University of Sydney and one of the trial's clinical advisors. "RESCUE-ALS was a proof-of-concept trial intended to establish that treatment of neuronal energetic failure can provide disease-modifying effects in ALS. I am pleased to see the potential effectiveness of CNM-Au8 demonstrated in this trial, and it is important to confirm these results in a larger clinical trial."

1 Westeneng et al. Lancet Neurol. 2018 May;17(5):423-433.

Rob Etherington, Clene's Chief Executive Officer, stated, "We believe these results show the potential of CNM-Au8 to bring meaningful benefit to people living with ALS. Befitting of Lou Gehrig, whose legacy is intertwined with the disease, we swung for the fences and ended with a stand-up triple. In the second half of next year, we expect to report results from the HEALEY ALS Platform Trial with the objective of confirming CNM-Au8 as an effective disease-modifying therapy for people with ALS."

RESCUE-ALS was a 36-week randomized, placebo-controlled Phase 2 clinical trial that enrolled 45 patients with early ALS, randomized 1:1 to treatment with CNM-Au8 at 30 mg daily or matching placebo on top of standard of care. The primary endpoint of the trial was the percent change of the sum of MUNIX from baseline to week 36. Secondary endpoints were the change in FVC and the absolute change in MUNIX values to week 36. Exploratory endpoints included multiple clinically relevant measures of ALS: disease progression, ALSFRS-R decline, and ALSSQOL-SF.

CNM-Au8 was found to be well-tolerated through 36 weeks of oral daily dosing. There were no reported serious adverse events (SAEs) related to CNM-Au8 treatment. Treatment-emergent adverse events were predominantly mild-to-moderate in severity. The most frequently reported adverse events associated with CNM-Au8 treatment included aspiration pneumonia (n=3) and transient gastrointestinal distress (n=2). Topline results from RESCUE-ALS are expected to be presented at the upcoming International Symposium on ALS/MND, which will take place Dec. 8-10, 2021.

Robert Glanzman, MD, FAAN, Clene's Chief Medical Officer, concluded, "The results of RESCUE-ALS add to our expanding body of evidence that cellular energetic failure is an important pathophysiological mechanism in ALS. We thank the trial participants and their families for their willingness to engage in clinical research, the site investigators for their research excellence and dedication to patients, and FightMND of Australia for substantially funding the trial."

Bec Sheean, Research Director of FightMND commented, "FightMND is committed to finding new treatment options for motor neurone disease. We awarded Clene a grant in 2019 to support the conduct of this Phase 2 clinical trial with CNM-Au8 in Australia. These clinical trial results are encouraging for people with ALS. By achieving clinically relevant endpoints, this trial demonstrates the potential for CNM-Au8 to support neuronal health. We are excited to see CNM-Au8 continue its advancement into the clinic so that we can bring this potentially transformative treatment to patients."

Conference Call and Webcast Details

Clene will host a conference call and live audio webcast today at 8:00 a.m. ET to discuss the Phase 2 RESCUE-ALS topline clinical trial results. The live webcast may be accessed from the Investors section of the Company's website at www.clene.com. Please connect to the website prior to the start of the conference call to ensure adequate time for any software downloads that may be necessary. Individuals may participate in the conference call by dialing +1 800 309 3488 in the U.S., or +1 929 517 9012 outside the U.S., and using conference ID: 5894034.

An archived version of the webcast will be available for at least one week in the Investors section of the Company's website at www.clene.com.

About CNM-Au8®, a gold nanocrystal suspension

Clene's lead drug candidate, CNM-Au8, a catalytically active gold nanotherapeutic, is the result of a patented manufacturing breakthrough. The catalytically active nanocrystals of CNM-Au8 drive critical cellular energy producing reactions in the brain that enable neuroprotection and remyelination by increasing neuronal and glial resilience to disease-relevant stressors. CNM-Au8 crosses the blood-brain barrier and is not associated with the toxicities related to synthetic gold compounds or nanoparticles manufactured via alternative methods. CNM-Au8 is being evaluated in a Phase 3 registration trial for the treatment of amyotrophic lateral sclerosis (ALS). In the REPAIR Program Phase 2 open-label biomarker clinical trials, CNM-Au8 demonstrated target engagement in the treatment of Parkinson's disease (PD) and multiple sclerosis (MS). REPAIR-PD has concluded, and REPAIR-MS will continue with the initiation of a second MS dosing cohort. Preclinical data, both published in peer-reviewed journals and presented at scientific congresses, demonstrate that treatment of neuronal cultures with CNM-Au8 improves survival of neurons, protects neurite networks, decreases intracellular levels of reactive oxygen species and improves mitochondrial capacity in response to cellular stresses induced by numerous disease-relevant neurotoxins. Oral treatment with CNM-Au8 improved functional behaviors in rodent models of ALS, MS and PD versus vehicle (placebo). CNM-Au8® is a federally registered trademark of Clene Nanomedicine, Inc.

About RESCUE-ALS

RESCUE-ALS is a Phase 2 multi-center, randomized, double-blind, parallel-group, placebo-controlled trial examining the efficacy, safety, pharmacokinetics and pharmacodynamics of CNM-Au8 in patients with early amyotrophic lateral sclerosis (ALS). The trial completed enrollment in the second half of 2020. In the trial, 45 subjects were randomized 1:1 to receive either active treatment with CNM-Au8 (30 mg) or placebo in addition to their current standard of care over a 36-week treatment period. The objective of the trial is to assess the impact of CNM-Au8 on disease progression in patients with early-stage ALS through changes in motor unit index MUNIX. MUNIX values were evaluated for four muscles in the hand, arm, and leg: the abductor digiti minimi, abductor pollicis brevis, tibialis anterior and biceps brachii from baseline through 36 weeks of treatment. CNM-Au8 was selected by FightMND of Australia, and Clene was provided a substantial grant to investigate efficacy in ALS utilizing novel neurophysiological endpoints at two clinical sites in Australia. For more information, please see ClinicalTrials.gov Identifier: NCT04098406.

About FightMND

FightMND is a not-for-profit registered charity, founded in 2014. It was established to raise the awareness of Motor Neurone Disease (MND) in Australia, to increase funding for research to find an effective treatment and cure and to provide care equipment for MND patients. FightMND has a clear objective – to have a world free from MND.

FightMND is Australia's largest independent MND foundation focused on funding large-scale, collaborative research and clinical trials. The generous donations contributed by everyday Australians, right across the country, has enabled FightMND to raise and commit millions to cure and care initiatives.

About Clene

Clene is a clinical-stage biopharmaceutical company focused on revolutionizing the treatment of neurodegenerative disease with potential first-in-class nanotherapeutics to treat energetic failure, an underlying cause of many neurological diseases. Our lead drug candidate, CNM-Au8, is an oral suspension of gold nanocrystals that drive critical cellular energetic metabolism in the central nervous system (CNS). CNM-Au8 increases energy production and utilization to accelerate neurorepair and improve neuroprotection. CNM-Au8 is currently being evaluated in a Phase 3 registration trial in amyotrophic lateral sclerosis (ALS) and a Phase 2 trial for the treatment of chronic optic neuropathy in patients with stable relapsing multiple sclerosis (MS). Clene has also advanced into the clinic an aqueous solution of ionic zinc and silver for anti-viral and anti-microbial uses. The company is based in Salt Lake City, Utah, with R&D and manufacturing operations in Maryland. For more information, please visit www.clene.com or follow us on Twitter, LinkedIn and Facebook.

Forward-Looking Statements

This press release contains “forward-looking statements” which are intended to be covered by the “safe harbor” provisions of the Private Securities Litigation Reform Act of 1995. Clene’s actual results may differ from its expectations, estimates and projections and consequently, you should not rely on these forward-looking statements as predictions of future events. Words such as “expect,” “estimate,” “project,” “budget,” “forecast,” “anticipate,” “intend,” “plan,” “may,” “will,” “could,” “should,” “believes,” “predicts,” “potential,” “might” and “continues,” and similar expressions are intended to identify such forward-looking statements. These forward-looking statements involve significant known and unknown risks and uncertainties, many of which are beyond Clene’s control and could cause actual results to differ materially and adversely from expected results. Factors that may cause such differences include Clene’s ability to demonstrate the efficacy and safety of its drug candidates; the clinical results for its drug candidates, which may not support further development or marketing approval; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials and marketing approval; Clene’s ability to achieve commercial success for its marketed products and drug candidates, if approved; Clene’s ability to obtain and maintain protection of intellectual property for its technology and drugs; Clene’s reliance on third parties to conduct drug development, manufacturing and other services; Clene’s limited operating history and its ability to obtain additional funding for operations and to complete the licensing or development and commercialization of its drug candidates; the impact of the COVID-19 pandemic on Clene’s clinical development, commercial and other operations, as well as those risks more fully discussed in the section entitled “Risk Factors” in Clene’s Annual Report on Form 10-K, as well as discussions of potential risks, uncertainties, and other important factors in Clene’s subsequent filings with the U.S. Securities and Exchange Commission. Clene undertakes no obligation to release publicly any updates or revisions to any forward-looking statements to reflect any change in its expectations or any change in events, conditions or circumstances on which any such statement is based, subject to applicable law. All information in this press release is as of the date of this press release. The information contained in any website referenced herein is not, and shall not be deemed to be, part of or incorporated into this press release.

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Source: Clene Inc.

Exhibit 99.2

Forward Looking Statements

This presentation contains "forward-looking statements" within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Clene's actual results may differ from its expectations, estimates, and projections and consequently, you should not rely on these forward-looking statements as predictions of future events. Words such as "expect," "estimate," "project," "budget," "forecast," "anticipate," "intend," "plan," "may," "will," "could," "should," "believes," "predicts," "potential," "might" and "continues," and similar expressions are intended to identify such forward-looking statements. These forward-looking statements involve significant known and unknown risks and uncertainties, many of which are beyond Clene's control and could cause actual results to differ materially and adversely from expected results. Factors that may cause such differences include Clene's ability to demonstrate the efficacy and safety of its drug candidates; the clinical results for its drug candidates, which may not support further development or marketing approval; actions of regulatory agencies, which may affect the initiation, timing and progress of clinical trials and marketing approval; Clene's ability to achieve commercial success for its marketed products and drug candidates, if approved; Clene's ability to obtain and maintain protection of intellectual property for its technology and drugs; Clene's reliance on third parties to conduct drug development, manufacturing and other services; Clene's limited operating history and its ability to obtain additional funding for operations and to complete the licensing or development and commercialization of its drug candidates; the impact of the COVID-19 pandemic on Clene's clinical development, commercial and other operations, as well as those risks more fully discussed in the section entitled "Risk Factors" in Clene's recently filed registration statement on Form S-1 (filed July 22, 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.

Rob Etherington

Clene Nanomedicine, Inc

President & CEO

CLENE | Webinar Agenda

1	CNM-Au8 overview & upcoming milestones	**Rob Etherington, President and Chief Executive Officer** I Clene Inc.
2	ALS unmet need & current treatment limitations	**Steve Vucic, MBBS (Hons I), PhD, DSc, FRACP, FAHMS, Northcott Chair of Neurology** I The University of Sydney
3	RESCUE-ALS Intro & Results	**Robert Glanzman** (Clene CMO), **Matthew Kiernan, AM, PhD, DSc, FRACP, FAHMS, Bushell Chair of Neurology** I The University of Sydney
4	Questions & Answers	**Dr. Robert Glanzman** (Clene CMO), **Dr. Kiernan, Dr. Vucic**, and **Rob Etherington** (Clene CEO)

clene NANOMEDICINE

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 increases cellular energy production and utilization to promote neuroprotection and remyelination
- Phase 2 ALS proof-of-concept evidence of efficacy across clinical endpoints
- Phase 3 Healey ALS platform trial results expected in 2H 2022
- Phase 2 VISIONARY-MS in multiple sclerosis underway

Strong Execution Capabilities

- Proprietary electrochemical manufacturing process produces nanotherapeutics, scalable to commercialization
- Strong IP, including 130+ granted patents, and trade secrets

CLENE | Pipeline

Creating elemental solutions for human health™

*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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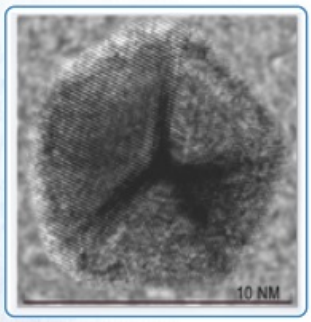
CNM-Au8 | Mechanism of Action

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

CNM-Au8® Nanocrystal



Clean Surfaced, Highly Faceted Shape Enhances Catalytic Activity

- Electrons (e-) Move Freely Across Nanocrystal Surface
- Vertices, Edges, & Facets Key to Catalytic Activity

Mechanistic Effects

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

Increased Energy Production & Utilization

- ↑ Increased energetic potential

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

CLene NANOMEDICINE

Steve Vucic, MD

Northcott Chair of Neurology

The University of Sydney

THE UNIVERSITY OF SYDNEY

Amyotrophic Lateral Sclerosis: Unmet need

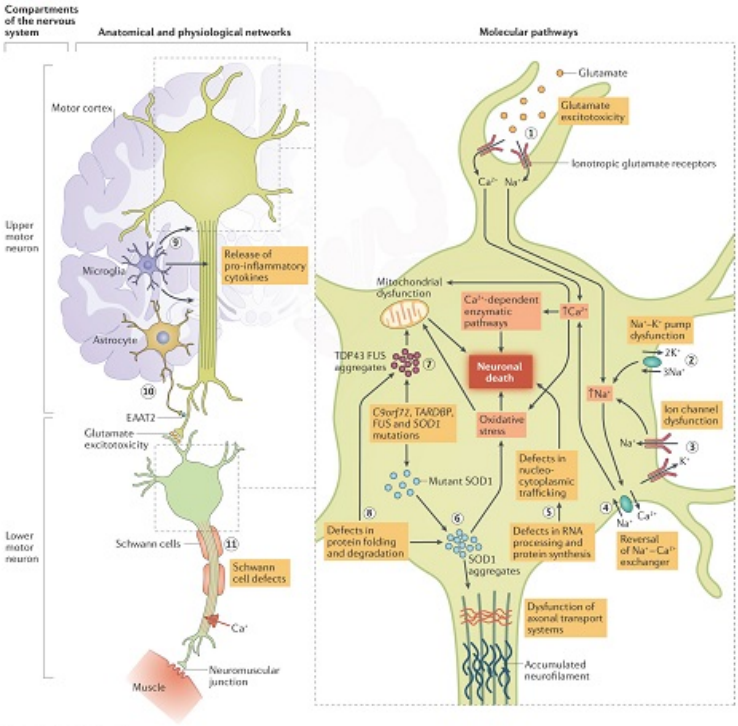
Professor Steve Vucic
Northcott Chair of Neurology
Brain and Nerve Research Centre
Concord Clinical School
University of Sydney

MND/ALS

- Rapidly progressive neurodegenerative disorder
  - Motor neurons
  - Weakness & wasting voluntary muscles
- Prevalence
  - 5.2 – 6.2 per 100,000
  - Mean age onset 50 – 60 years
- Median survival
  - 100% fatal
  - 2 – 3 years
  - 20% survive > 5 – 10 years

Kiernan et al. Lancet. 2011 Mar 12;377(9769):942-55. Brown et al. Neuroepidemiology. 2021;55(5):342-353. Kiernan et al. Nat Rev Neurol 2021 Feb;17(2):104-118. Winhammar et al. Lancet Neurol. 2005 Apr;4(4):229-38.

Improving Clinical Trial Outcomes in ALS



Kiernan et al. Nat Rev Neurol 2021 Feb;17(2):104-118.

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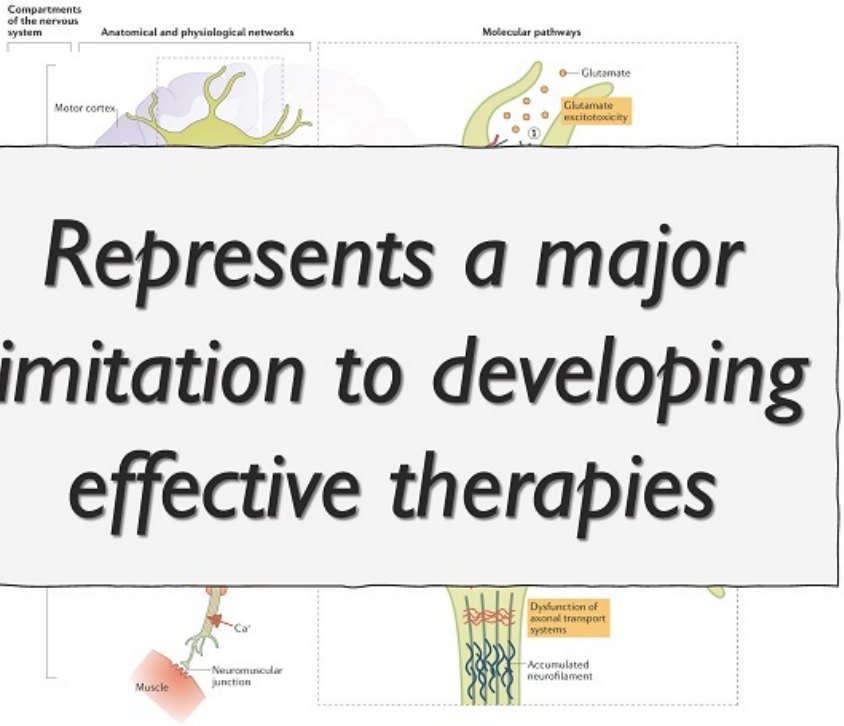
Improving Clinical Trial Outcomes in ALS



Represents a major limitation to developing effective therapies

Kiernan et al. Nat Rev Neurol 2021 Feb;17(2):104-118.

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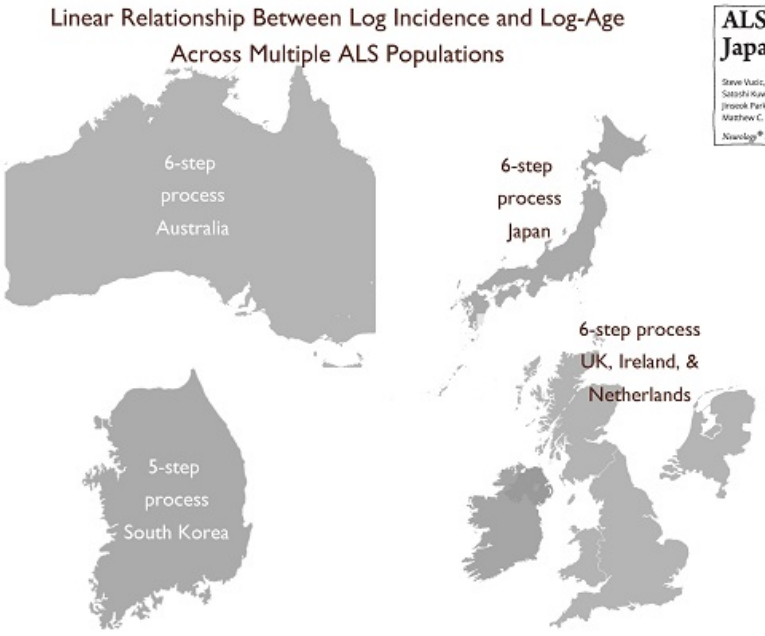
ALS Is a Multistep Disease Process



ALS is a multistep process in South Korean, Japanese, and Australian patients

Steve Vucic, DSc, Mana Higashihara, PhD, Gen Sobue, MD, Naoki Atsuta, MD, Yuriko Doi, MD, Satoshi Kuwabara, PhD, Seung Hyun Kim, MD, PhD, Insh Kim, MD, MPH, PhD, Ki-Wook Oh, MD, PhD, Jinsook Park, MD, PhD, Eun Mi Kim, MPH, Paul Talman, PhD, Parvathi Menon, PhD, and Matthew C. Kiernan, DSc, the PACTALS Consortium

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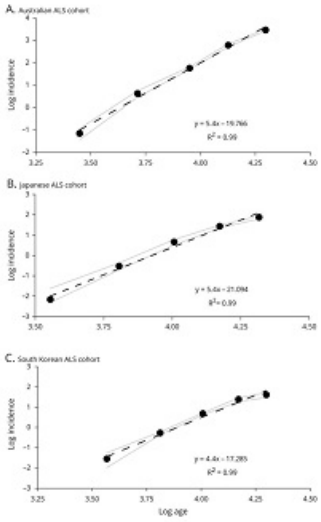
steve.vucic@sydney.edu.au

Neurology® 2020;94:e1657-1663. doi:10.1212/WNL.0000000000009015



Vucic et al. Neurology Apr 2020, 94 (15) e1657-e1663. Al Chalabi et al. Lancet Neurol. 2014 Nov;13(11):1108-1113. https://freevectormaps.com

mproving clinical trial outcomes n amyotrophic lateral sclerosis

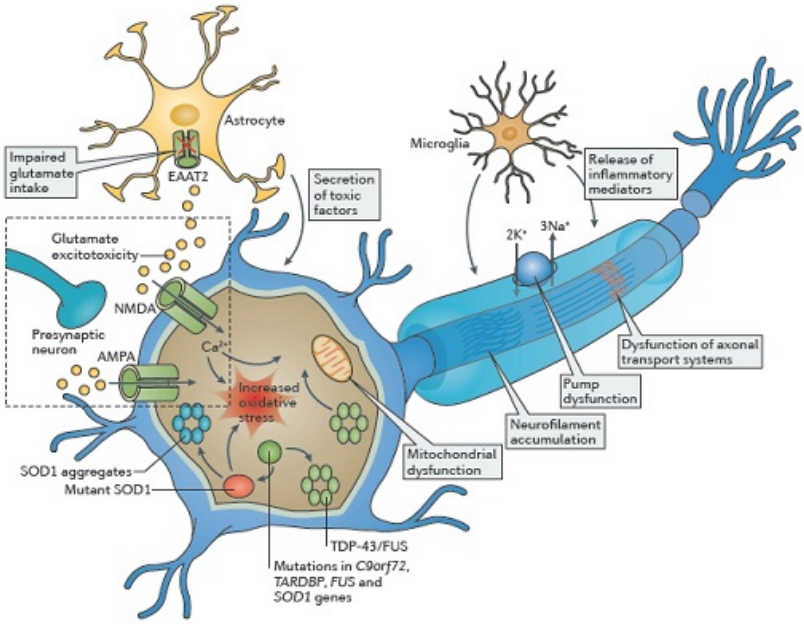
nature reviews neurology

latthew C. Kiernan[1,2]✉, Steve Vucic[3], Kevin Talbot[4], Christopher J. McDermott[5,6], rla Hardiman[7,8], Jeremy M. Shefner[9], Ammar Al-Chalabi[10], William Huynh[1,2], lerit Cudkowicz[11,12], Paul Talman[13], Leonard H. Van den Berg[14], Thanuja Dharmadasa[4], aul Wicks[15], Claire Reilly[16] and Martin R. Turner[4]

Repurposed drugs	Existing use	Targeted pathogenic mechanism	ALS trial identifier	Primary outcome measures	Outcome
Tauroursodeoxy cholic acid	Familial amyloid polyneuropathy (transthyretin)	Endoplasmic reticulum stress, mitochondrial dysfunction	NCT03488524	ALSFRS-R	Reduction in functional decline
			NCT03127514	Survival	Prolonged
Mexiletine	Cardiac arrhythmia	Neuronal hyperexcitability	NCT01811355	Daily cramp frequency	Significant reduction in cramp frequency and severity
			NCT02781454	Change in resting motor threshold	Pending
			NCT01849770	Safety	Safe
Ezogabine	Epilepsy	Neuronal hyperexcitability	NCT02450552	Change in short-interval intracortical inhibition as measured by transcranial magnetic stimulation	Pending
Dimethyl fumarate	Relapsing–remitting multiple sclerosis	Neuroinflammation, upregulation of T_{reg} cells	ACTRN12618000534280	ALSFRS-R	Pending
IL-2	Metastatic melanoma, metastatic renal cancer	Neuroinflammation, cytokine signalling, upregulation of T_{reg} cells	NCT02059759	Change in number of T_{reg} cells	Pending
			NCT03039673	Survival	Pending
Edaravone	Acute stroke	Oxidative stress	NCT01492686	ALSFRS-R	Significant slowing of disease progression vs placebo
Dolutegravir, abacavir and lamivudine (Triumeq)	HIV infection	HERVK expression	NCT02868580	Safety	Safe
Ibudilast (MN-166)	Chronic obstructive pulmonary disease	Neuroinflammation and microglial activation	NCT02238626	Safety and tolerability	Pending
			NCT02714036	Safety and tolerability	Pending
Tamoxifen	Breast cancer	Neuroinflammation, proteostasis	NCT02166944	ALSFRS-R	Not significant
			NCT00214110	Muscle strength	Pending
			NCT01257581	ALSFRS-R	No significant effect
Memantine	Advanced stages of Alzheimer disease	Glutamate excitotoxicity	NCT01020331	ALSFRS-R	No significant effect
			NCT02118727	ALSFRS-R	Pending
			NCT00409721	ALSFRS-R, FVC, muscle strength, cognitive function	Pending
			NCT00353665	ALSFRS-R	No significant effect
Perampanel	Partial-onset seizures	Glutamate excitotoxicity (AMPA-receptor mediated)	NCT03019419	ALSFRS-R	Pending
			NCT03377309	Safety	Pending
			NCT03793868	Motor threshold	Pending
			NCT03020797	Safety	Pending
Rasagiline	Parkinson disease	Oxidative stress and apoptosis	NCT01786603	ALSFRS-R	No significant effect
Masitinib	Mastocytosis, severe asthma	Neuroinflammation (microglia)	NCT02588677	ALSFRS-R	Significant slowing in functional decline
			NCT03127267	ALSFRS-R	Pending
Methyl-cobalamin	Vitamin B12 deficiency	Glutamate excitotoxicity	NCT03548311	ALSFRS-R	No significant effect
Cu(II)ATSM	PET ligand	Copper deficiency	NCT02870634	Safety	Pending
Arimoclomol	Insulin resistance, complications of diabetes mellitus	Impaired proteostasis	NCT00244244	Safety	Safe
			NCT00706147	Time to death, tracheostomy or permanent assisted ventilation	Safe, no significant effect on outcomes
			NCT03491462	Combined assessment of function and survival	Pending
			NCT03836716	Safety	Pending

Kiernan et al. Nat Rev Neurol 2021 Feb;17(2):104-118.

Whole System Approach
Normalise Cellular Function – Energy Dependent Processes



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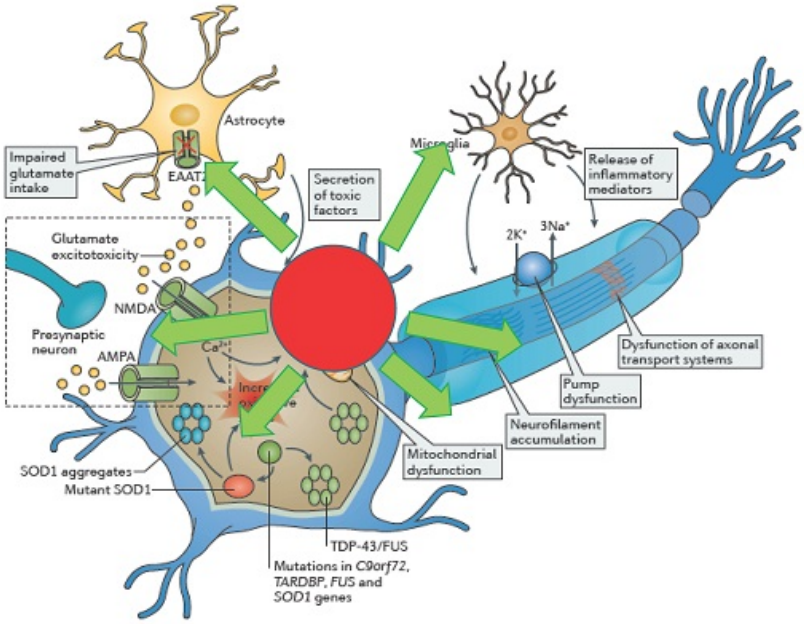
Whole System Approach
Normalise Cellular Function – Energy Dependent Processes



THE UNIVERSITY OF SYDNEY

Robert Glanzman, MD FAAN

Chief Medical Officer

Clene Nanomedicine, Inc

Phase 2

RESCUEALS

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

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

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

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

6 WEEKS

EOS

Open Label Extension

Phone calls at Weeks 3, 6, 18, 30

MUNIX

1° **% Change in Sum of Motor Unit Index (MUNIX)**

For the Abductor Digiti Minimi (ADM), Abductor Pollicis Brevis (APB), Biceps Brachii (BB), Tibialis Anterior (TA)

2° **Key Secondary**

Absolute MUNIX(4) change

Forced Vital Capacity (FVC)

Exploratory Endpoints

- ALS disease progression
- ALSFRS-R 6-point decline
- Quality of life (ALSSQOL-SF)
- ALSFRS-R change
- Other Electromyography (SH_i, NP_i, MUSIX, MScan)
- Combined Joint-Rank (Survival + ALSFRS-R)

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RESCUEALS

We thank FightMND for its philanthropic support of the RESCUE-ALS study

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RESCUE-ALS

Phase 2 Trial

Topline Results

"Befitting of Lou Gehrig, whose legacy is intertwined with ALS, we swung for the fences and ended with a stand-up triple..."

Lou Gehrig
(1903 – 1941)

RESCUEALS | Baseline Demographics

ITT Population

Baseline Value mean (sd)	Age (yrs)	Sex n, (%) Male | Female	Onset Site n, (%) Limb | Bulbar	Months from Diagnosis	Months from Onset	FVC (% pred.)	ALSFRS-R Score	ENCALS Risk Profile[1]
All (n=45)	59.1 (12.3)	M: 26 (58%) F: 19 (42%)	L: 33 (73%) B: 12 (27%)	3.1 (3.0)	15.9 (9.3)	81.5 (16.7)	38.7 (5.95)	-4.4 (1.8)
CNM-Au8 30mg (n=23)	57.0 (13.3)	M: 13 (57%) F: 10 (43%)	L: 16 (70%) B: 7 (30%)	3.0 (2.9)	15.5 (7.6)	84.5 (18.3)	38.6 (6.6)	-4.6 (1.7)
Placebo (n=22)	61.3 (10.9)	M: 13 (59%) F: 9 (41%)	L: 17 (77%) B: 5 (23%)	3.3 (3.2)	16.1 (10.9)	78.2 (14.5)	38.8 (5.4)	-4.2 (1.8)

89% of participants treated with riluzole as background standard of care

ITT Population; Data on File, Clene Nanomedicine, Inc. [1] Van Eijk et al. Neurology 2021;97:528-536.

RESCUEALS | Overview

ITT Population

1. **Neurophysiology**
   MUNIX[1]
2. **Pulmonary Function**
   (Forced Vital Capacity)
3. **Functional Status & QOL**
   (ALSFRS-R,
   ALS Specific QOL)
4. **Disease Progression & Survival**

[1] Study was only powered for MUNIX(4) primary endpoint (Box 1)

ITT Population; Data on File, Clene Nanomedicine, Inc.

RESCUEALS | Results Support Phase 3 Development

- **Proof of Concept Established in ALS**
  - MUNIX Wk36 non-significant; Wk12 efficacy signal ($p<0.06$)
  - MUNIX results demonstrate lower motor neuron protection in limb onset ALS (Wk12, $p<0.04$; Wk36 $p<0.08$)
- **De-risked Phase 3 Development** (Statistically Significant Results)
  - Protection from significant ALS disease progression ($p<0.02$)
  - Consistent evidence of treatment effect in clinically relevant endpoints: ALSFRS-R decline ($p<0.04$), ALSSQOL ($p<0.02$)
  - Evidence of survival benefit using ENCALS model
- **Well-tolerated with no safety concerns**

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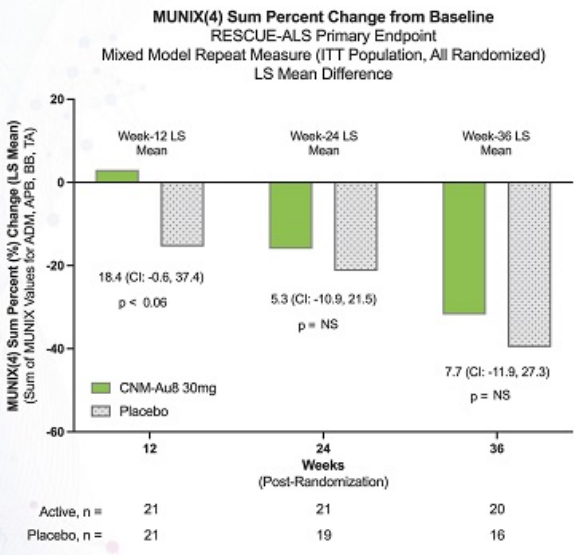
Matthew Kiernan, MD
Bushell Chair of Neurology
The University of Sydney

RESCUEALS | Evidence for Motor Neuron Protection

Primary Endpoint (MUNIX(4) %, LS Mean Change)

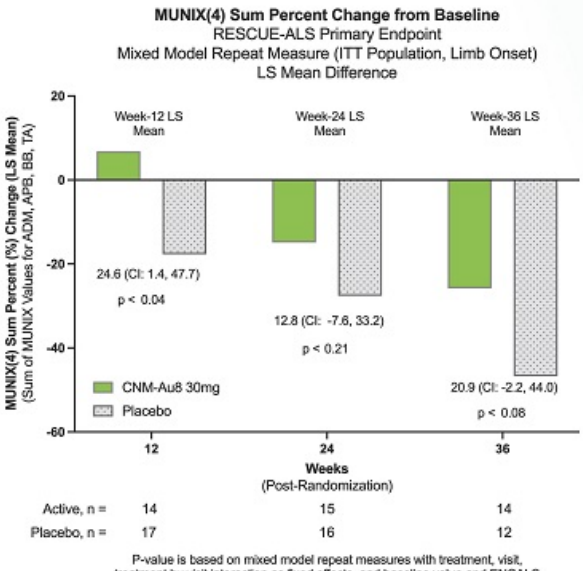
All Randomized



Active, n =	21	21	20
Placebo, n =	21	19	16

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.

Limb Onset (Pre-specified)



Active, n =	14	15	14
Placebo, n =	17	16	12

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.

ITT Population; Data on File, Clene Nanomedicine, Inc.

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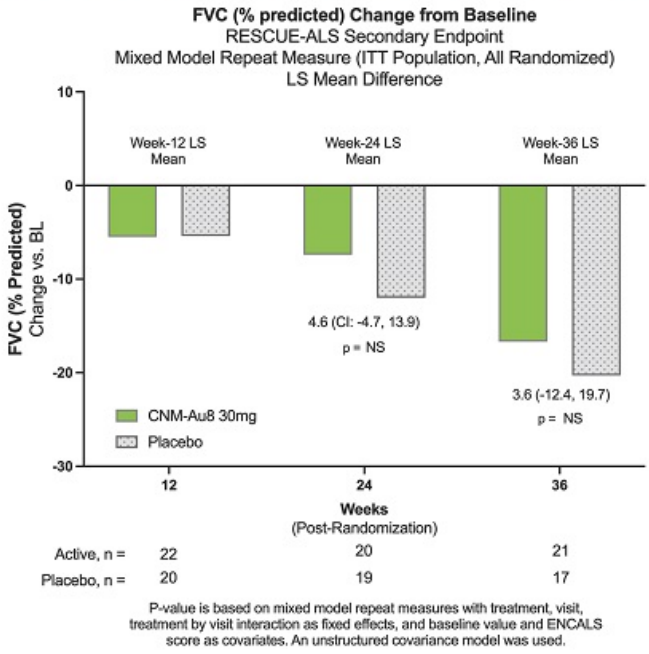
Pulmonary Function

Forced Vital Capacity (FVC)

RESCUEALS | Directional FVC Benefit

Secondary Endpoint[1] (FVC % predicted, LS Mean Change, All Randomized)



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.

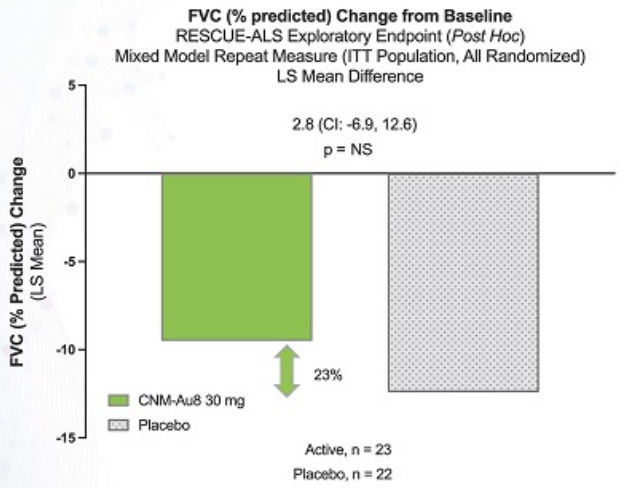
[1]Study Not Powered for FVC change

ITT Population; Data on File, Clene Nanomedicine, Inc.

RESCUEALS | Directional FVC Benefit

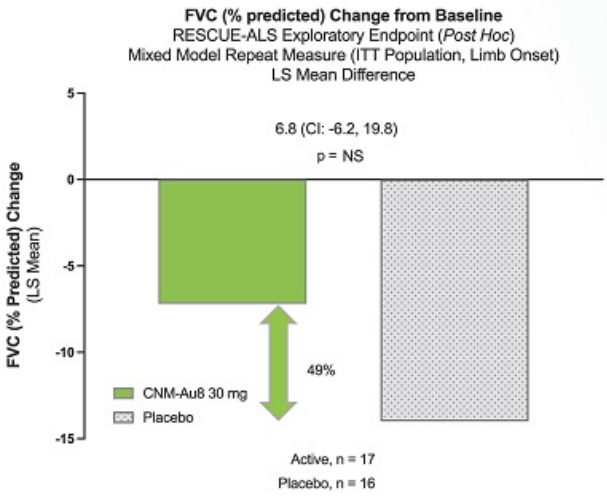
Secondary Endpoint[1] (FVC % predicted, LS Mean Change, Continuous Slope, *Post Hoc*)

All Randomized



P-value is based on a mixed model with treatment, time from first symptom onset, treatment by time from first symptom onset interaction, baseline value, treatment by baseline value interaction and ENCALS score as factors. Time is treated as a random effect.

Limb Onset (pre-specified)



P-value is based on a mixed model with treatment, time from first symptom onset, treatment by time from first symptom onset interaction, baseline value, treatment by baseline value interaction and ENCALS score as factors. Time is treated as a random effect.

[1]Study Not Powered for FVC change

ITT Population; Data on File, Clene Nanomedicine, Inc.

Functional Status and QOL

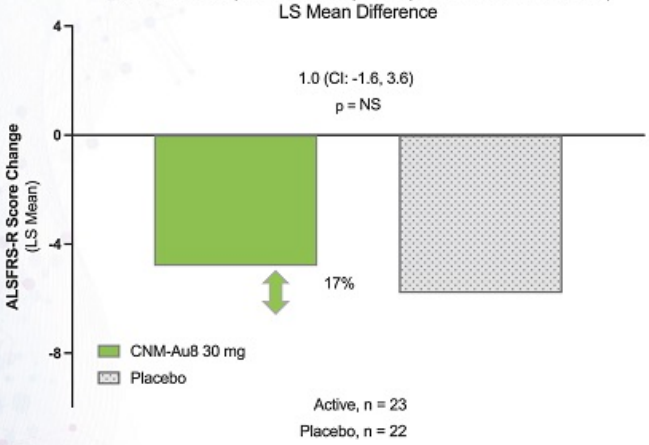
(ALSFRS-R, ALSSQOL-SF)

RESCUEALS | Directional ALSFRS-R Benefit

Exploratory (ALSFRS-R, Continuous Slope, LS Mean Change)

All Randomized

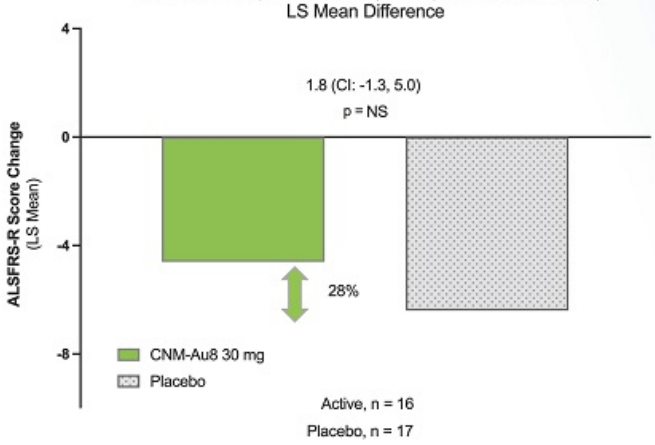
ALSFRS-R Change from Baseline
RESCUE-ALS Exploratory Endpoint
Mixed Model Repeat Measure (ITT Population, All Randomized)
LS Mean Difference



P-value is based on a mixed model with treatment, time from first symptom onset, treatment by time from first symptom onset interaction, baseline value, treatment by baseline value interaction and ENCALS score as factors. Time is treated as a random effect.

Limb Onset (Pre-specified)

ALSFRS-R Change from Baseline
RESCUE-ALS Exploratory Endpoint
Mixed Model Repeat Measure (ITT Population, Limb Onset)
LS Mean Difference



P-value is based on a mixed model with treatment, time from first symptom onset, treatment by time from first symptom onset interaction, baseline value, treatment by baseline value interaction and ENCALS score as factors. Time is treated as a random effect.

ITT Population; Data on File, Clene Nanomedicine, Inc.

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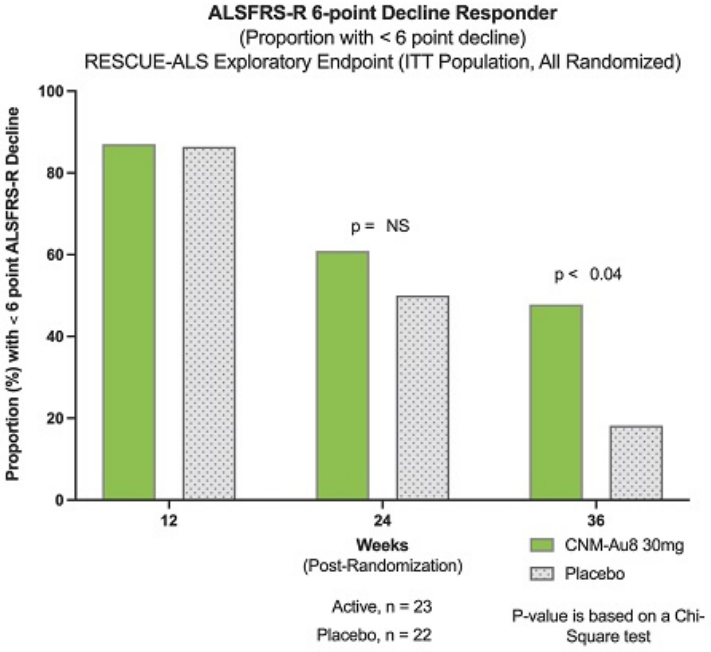
RESCUEALS | Significant Impact on ALSFRS-R Decline

Exploratory (ALSFRS-R Responder Analysis, All Randomized)

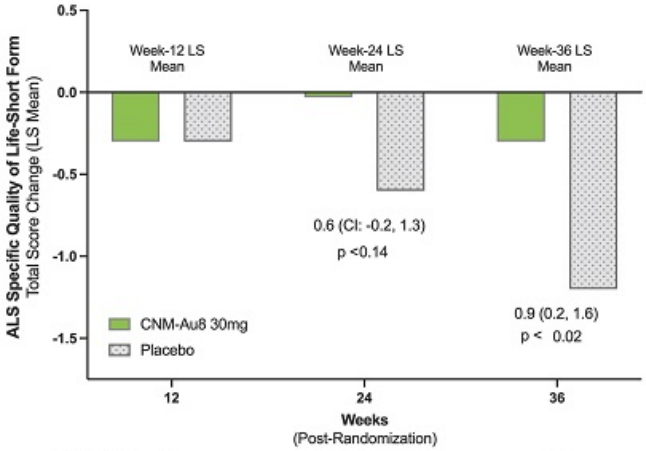


ITT Population; Data on File, Clene Nanomedicine, Inc.

RESCUEALS | Significantly Improves Quality of Life

Exploratory (ALSSQOL-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.

ITT Population; Data on File, Clene Nanomedicine, Inc.

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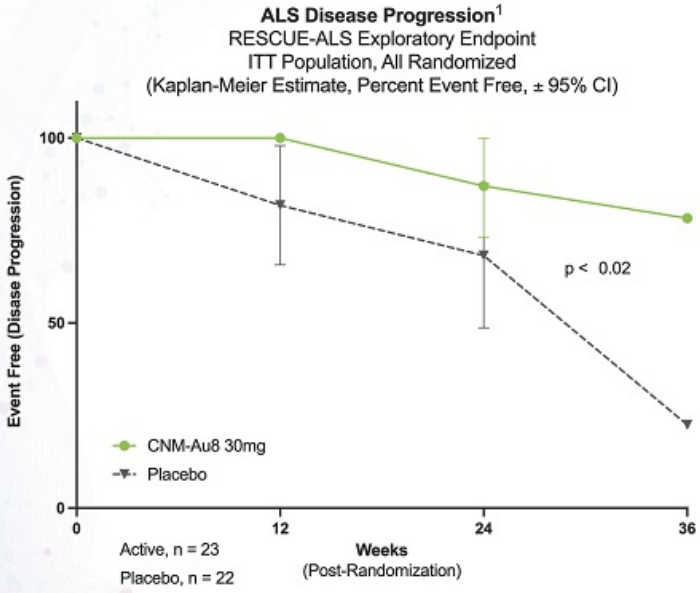
Disease Progression & Survival

RESCUEALS | Significant Impact on ALS Disease Progression

Exploratory Endpoint (All Randomized)



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

ALS Disease Progression defined as:

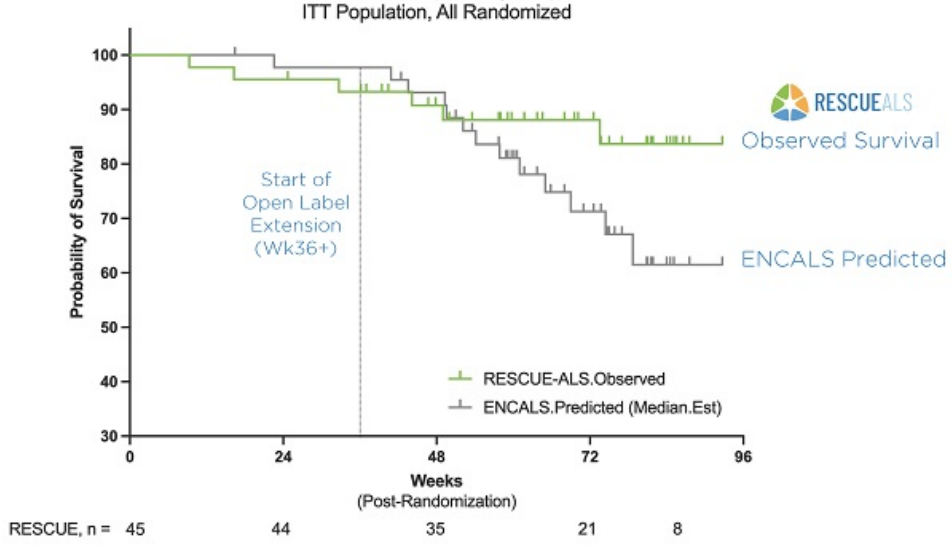
- Death, or
- Tracheostomy, or
- Non-invasive ventilation, or
- Gastrostomy tube

ITT Population; Data on File, Clene Nanomedicine, Inc.

RESCUEALS | Potential Survival Signal

Exploratory Endpoint (Observed Survival vs. Predicted)

Observed Survival vs. ENCALS Predicted Median Survival
RESCUE-ALS Exploratory Endpoint
ITT Population, All Randomized



RESCUE, n =	45	44	35	21	8

All observations censored as of 27-October-2021; Rescue participants who did not transition into the long-term open label extension censored at end of double-blind period

Data on File, Clene Nanomedicine, Inc.

RESCUEALS | Well Tolerated & No Safety Signals

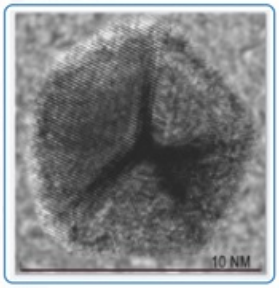
Safety Summary

- No CNM-Au8 related serious adverse events (SAEs)
- No CNM-Au8 related drug discontinuations
- No imbalances in treatment emergent adverse event (TEAEs)
- 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

CNM-Au8



Catalytically Active Nanocrystal

These Results Support Cellular Energetic Impairment as a Therapeutic Target in ALS

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Rob Etherington

Clene Nanomedicine, Inc

President & CEO

RESCUEALS | Results Support Phase 3 Development

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  - MUNIX Wk36 non-significant; Wk12 efficacy signal ($p<0.06$)
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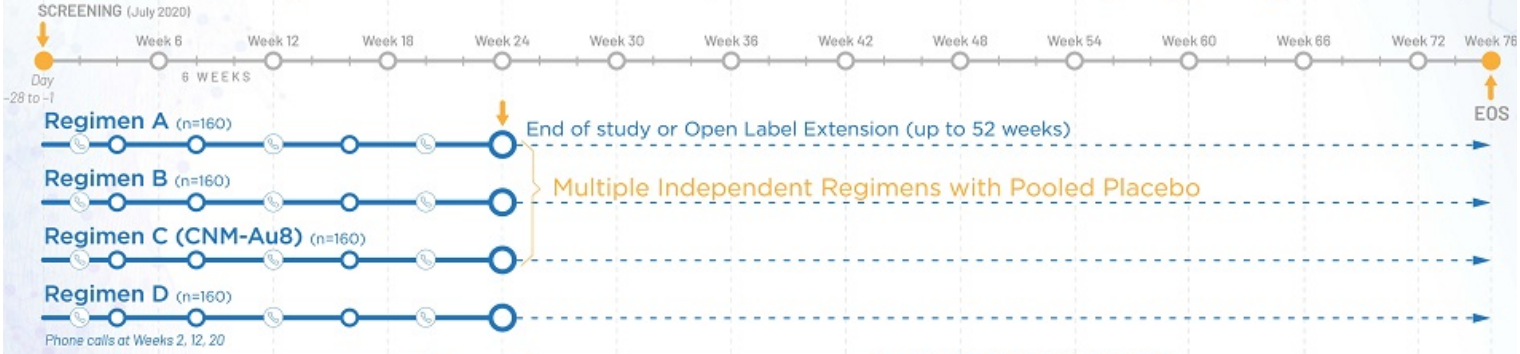
Phase 3
HEALEY ALS Platform Trial

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

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



1° **Change in ALSFRS-R**

2° **Slow Vital Capacity**
Hand-Held Dynamometry
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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Anticipated Timeline & Upcoming Milestones

2020 - 2023

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Questions & Answers

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