November 2, 2021

CLene NANOMEDICINE

CLNN (NASDAQ)
clene.com

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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 | 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

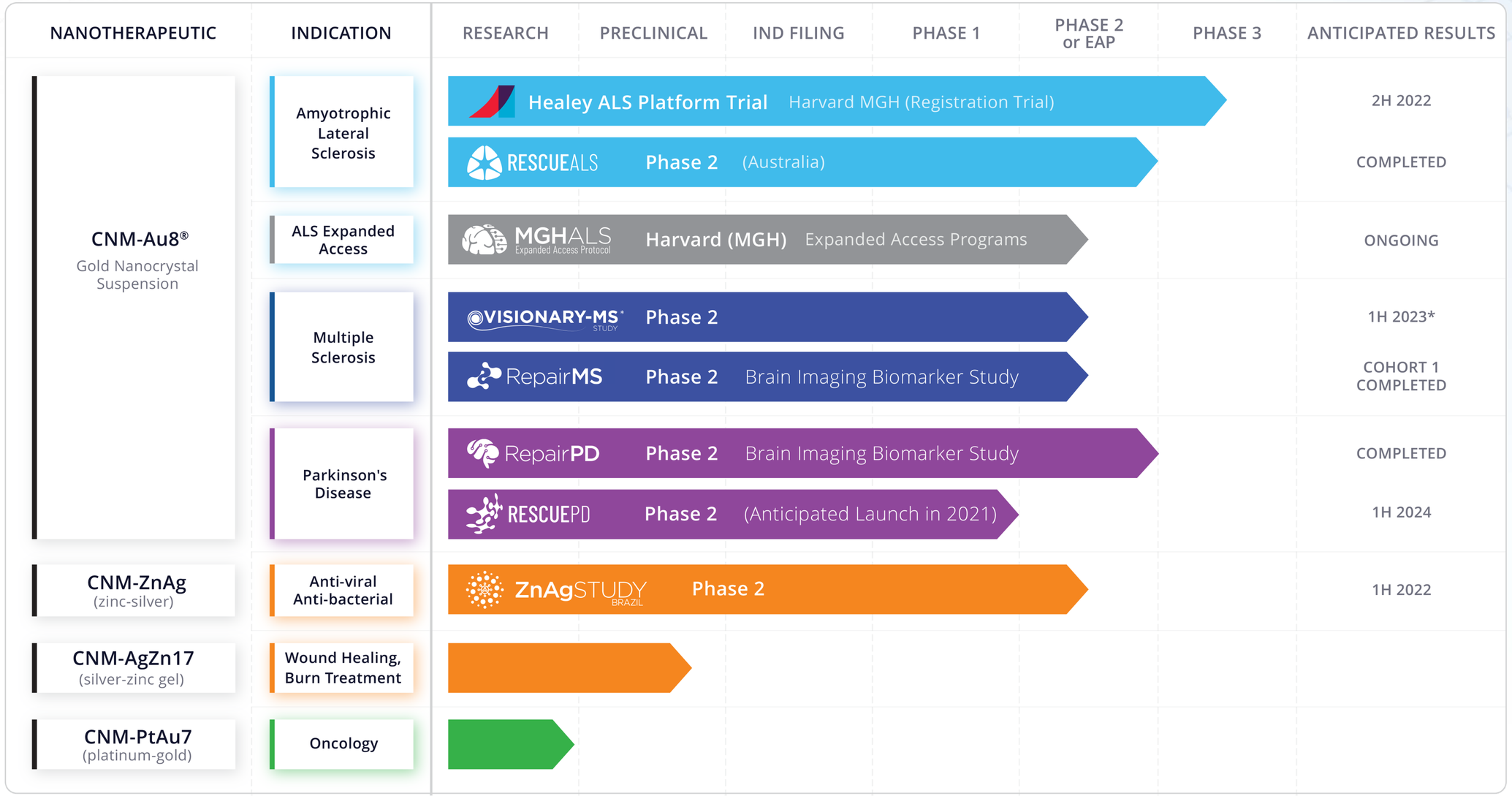
- CNM-Au8 increases cellular energy production and utilization to promote neuroprotection and remyelination
- Phase 2 ALS proof-of-concept evidence of efficacy across clinical endpoints
- Phase 3 Healey ALS platform trial results expected in 2H 2022
- Phase 2 VISIONARY-MS in multiple sclerosis underway

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™



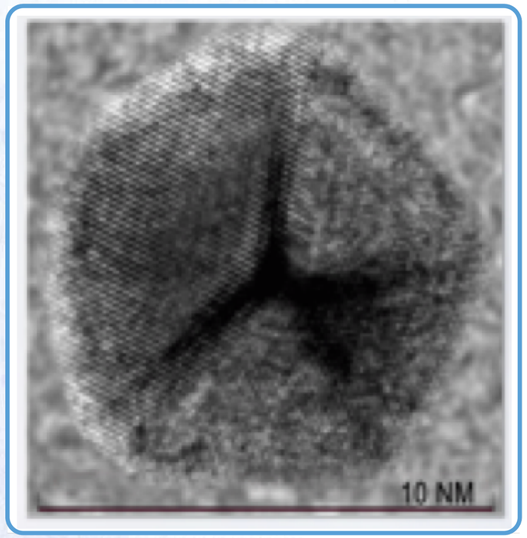
*Subject to ongoing COVID-19 related site research restrictions generally implemented to protect MS patients taking standard-of-care immunosuppressive therapies

CLENE NANOMEDICINE

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

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Steve Vucic, MD

Northcott Chair of Neurology

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

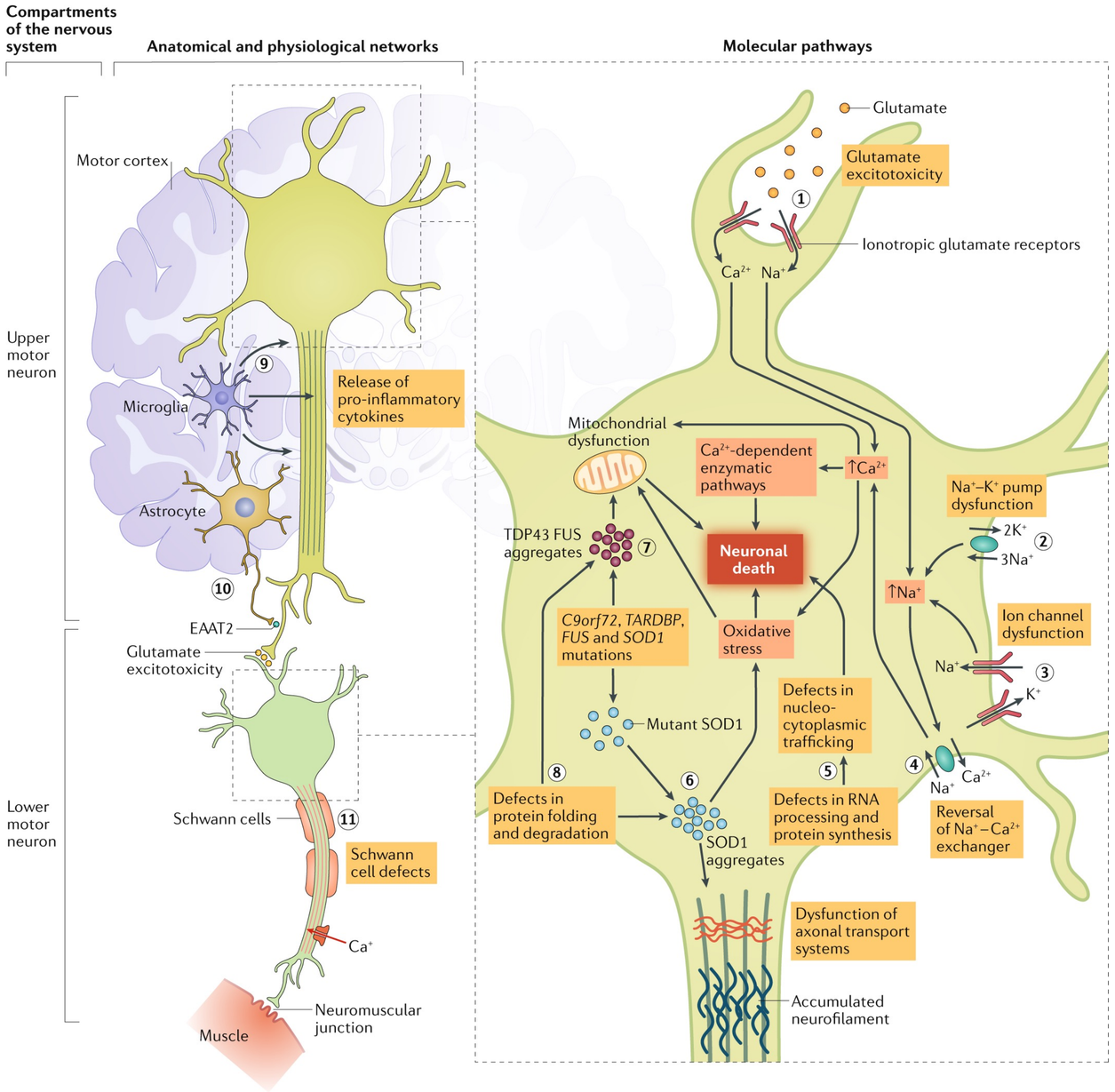
- Prevalence
  - 5.2 – 6.2 per 100,000
  - Mean age onset 50 – 60 years

- 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.

THE UNIVERSITY OF SYDNEY

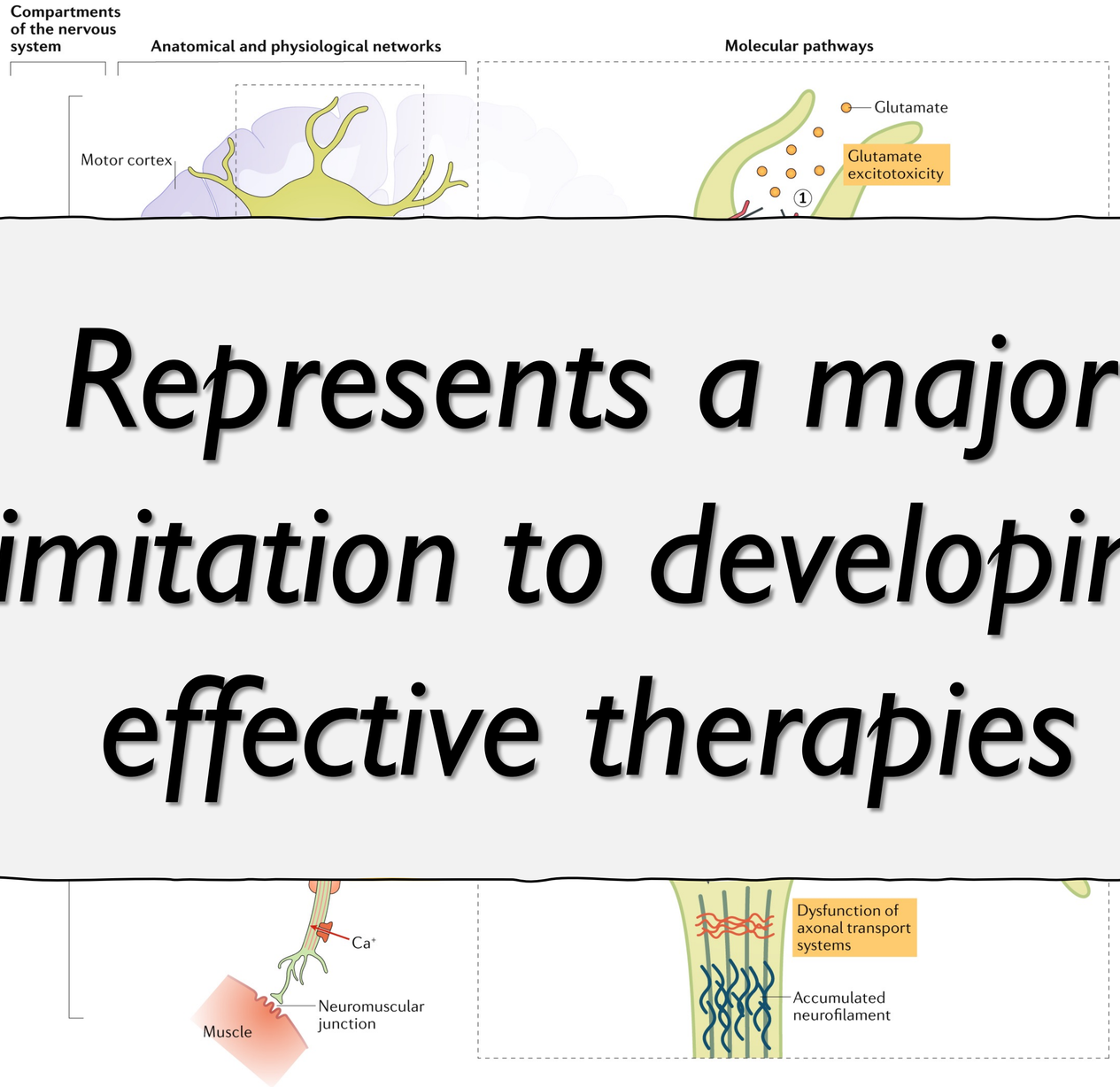
Improving Clinical Trial Outcomes in ALS



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

THE UNIVERSITY OF SYDNEY

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.

THE UNIVERSITY OF SYDNEY

ALS Is a Multistep Disease Process

Linear Relationship Between Log Incidence and Log-Age Across Multiple ALS Populations

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, Inah Kim, MD, MPH, PhD, Ki-Wook Oh, MD, PhD, Jinseok 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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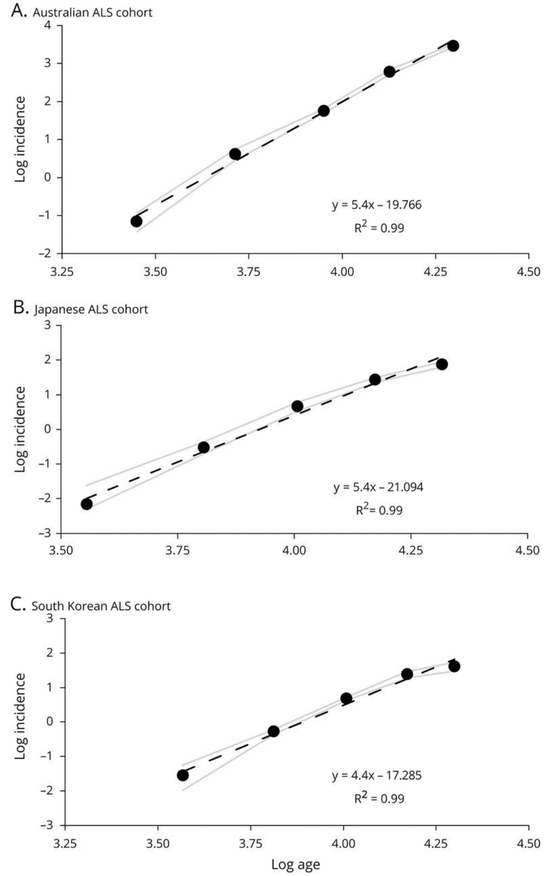
steve.vucic@sydney.edu.au

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

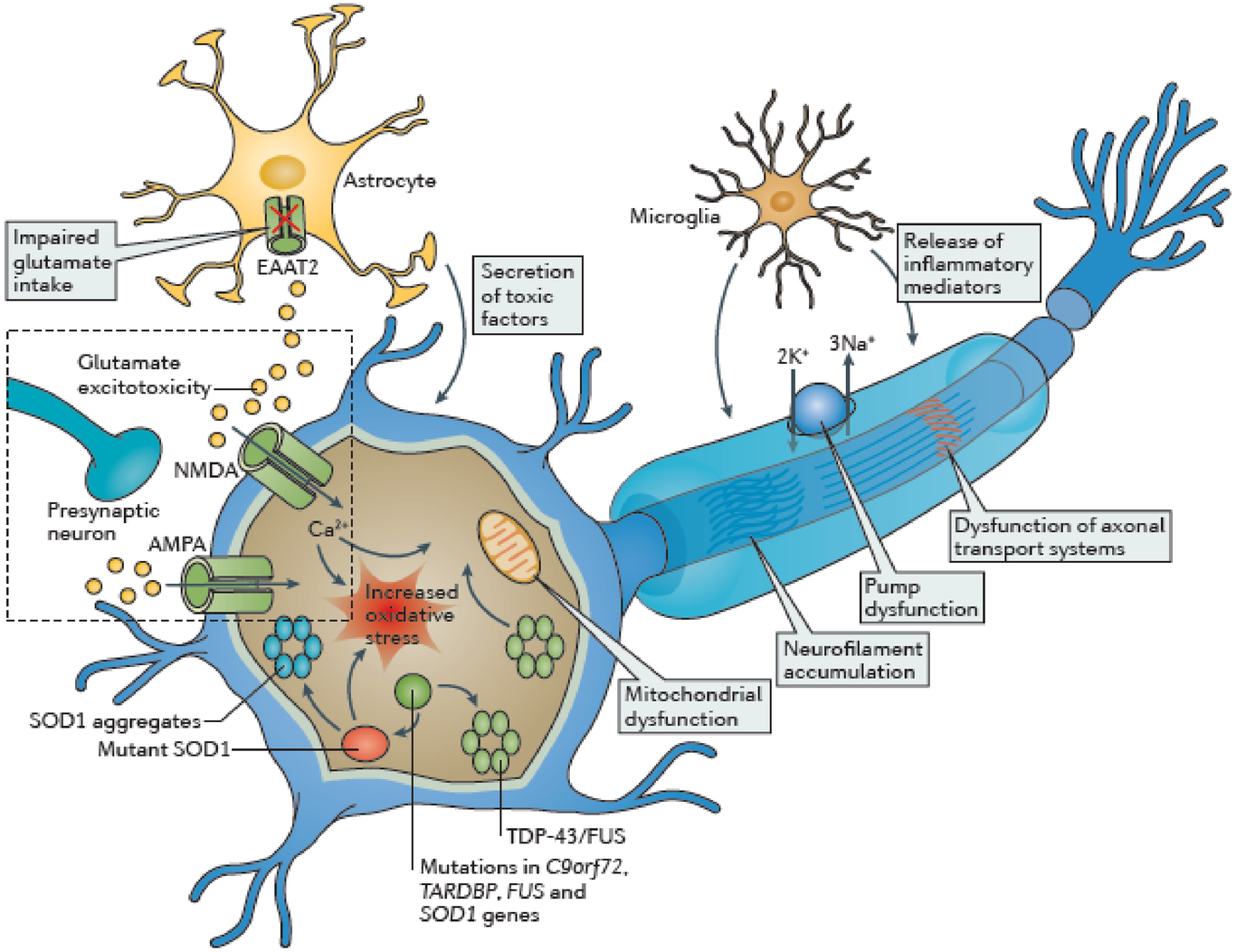
latthew C. Kiernan[1,2]✉, Steve Vucic[3], Kevin Talbot[4], Christopher J. McDermott[5,6], rla Hardiman[7,8], Jeremy M. Shefner[9], Ammar Al-Chalabi[10], William Huynh[1,2], lerit Cudkowicz[11,12], Paul Talman[13], Leonard H. Van den Berg[14], Thanuja Dharmadasa[4], aul Wicks[15], Claire Reilly[16] and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

nature reviews neurology

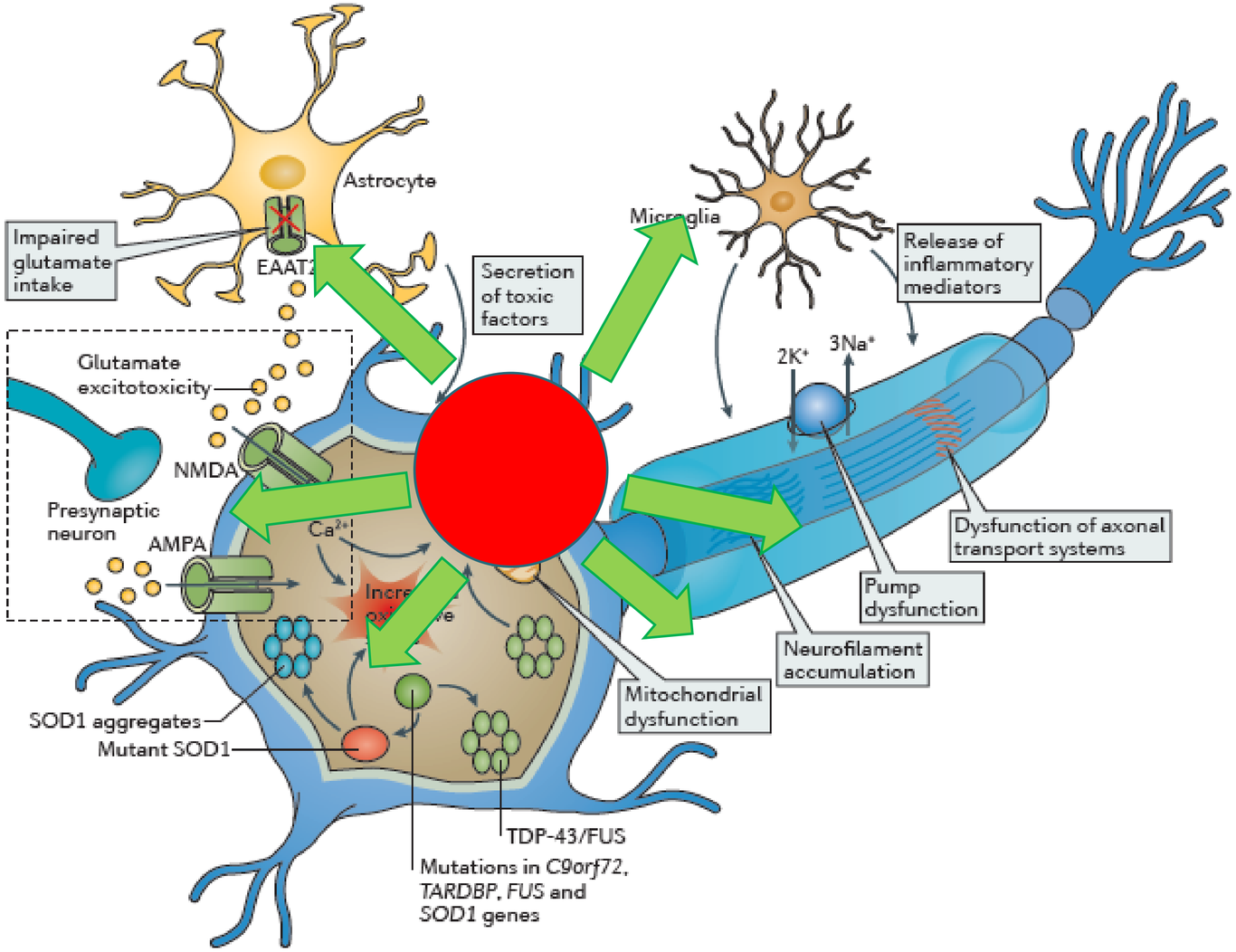
Repurposed drugs	Existing use	Targeted pathogenic mechanism	ALS trial identifier	Primary outcome measures	Outcome
Tauroursodeoxy cholic acid	Familial amyloid polyneuropathy (transthyretin)	Endoplasmic reticulum stress, mitochondrial dysfunction	NCT03488524	ALSFRS-R	Reduction in functional decline
			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



Whole System Approach
Normalise Cellular Function – Energy Dependent Processes



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

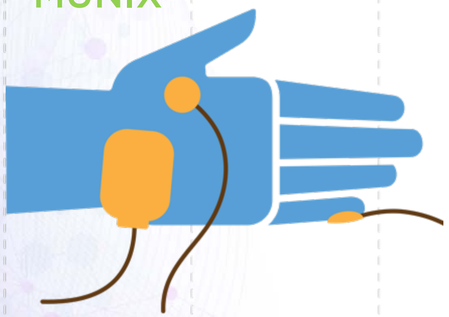
6 WEEKS

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

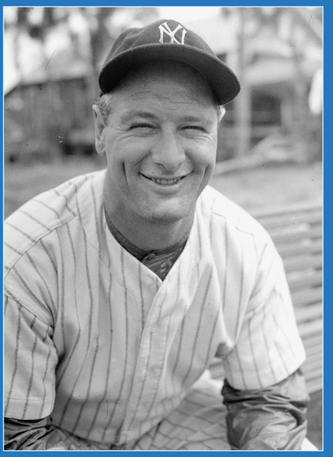
CLene NANOMEDICINE

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**

Matthew Kiernan, MD

Bushell Chair of Neurology

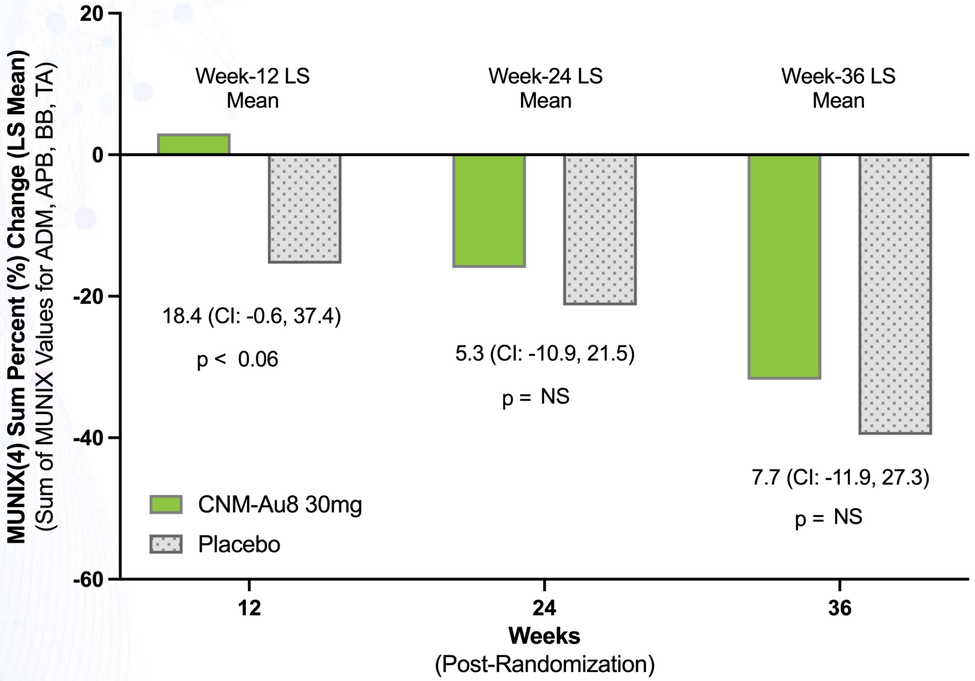
The University of Sydney

RESCUEALS | Evidence for Motor Neuron Protection

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

All Randomized

MUNIX(4) Sum Percent Change from Baseline
RESCUE-ALS Primary Endpoint
Mixed Model Repeat Measure (ITT Population, All Randomized)
LS Mean Difference

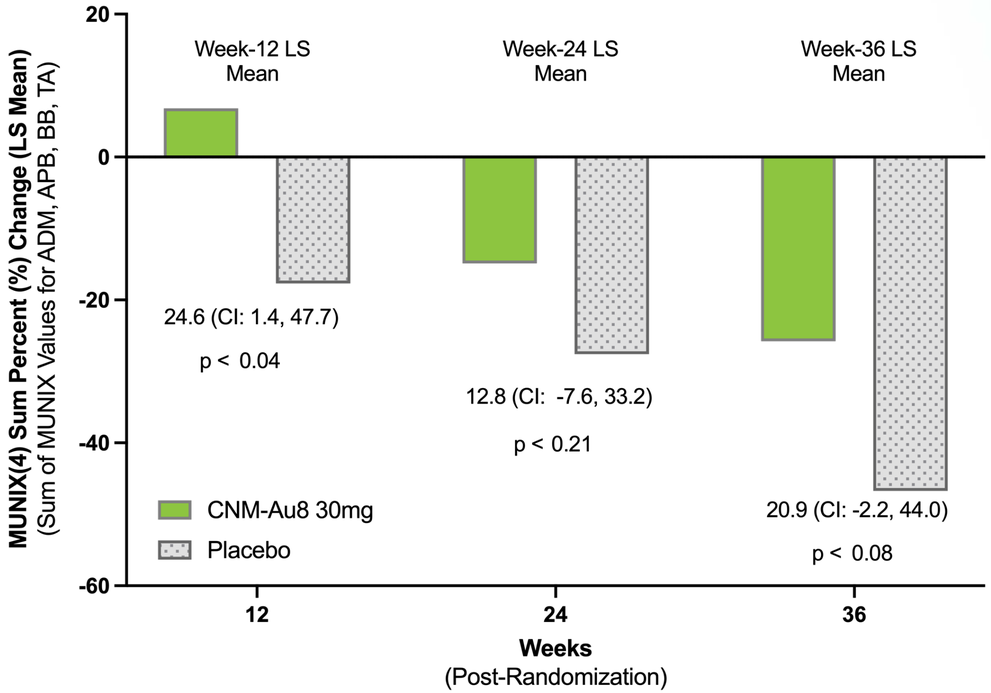


Active, n =	21	21	20
Placebo, n =	21	19	16

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)

MUNIX(4) Sum Percent Change from Baseline
RESCUE-ALS Primary Endpoint
Mixed Model Repeat Measure (ITT Population, Limb Onset)
LS Mean Difference



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.

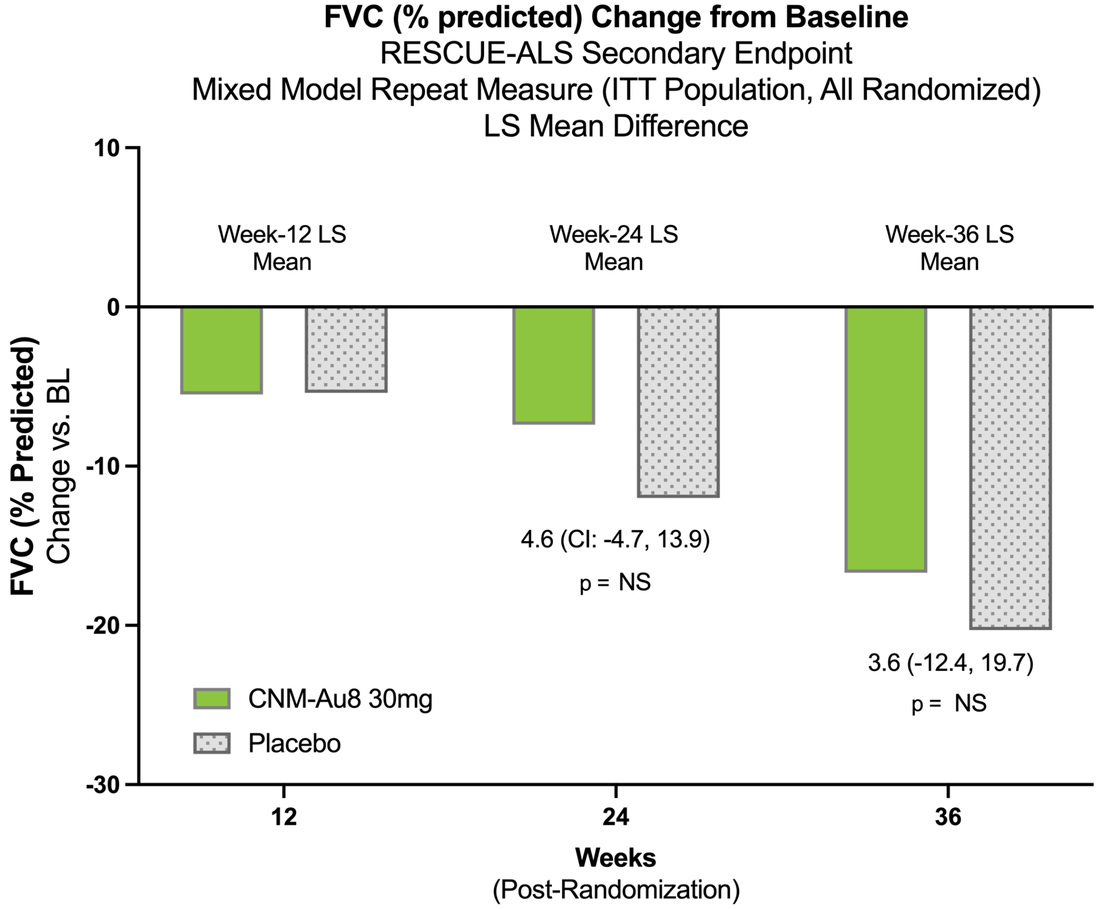
ITT Population; Data on File, Clene Nanomedicine, Inc.

Pulmonary Function

Forced Vital Capacity (FVC)

RESCUEALS | Directional FVC Benefit

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



Active, n =	22	20	21
Placebo, n =	20	19	17

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.

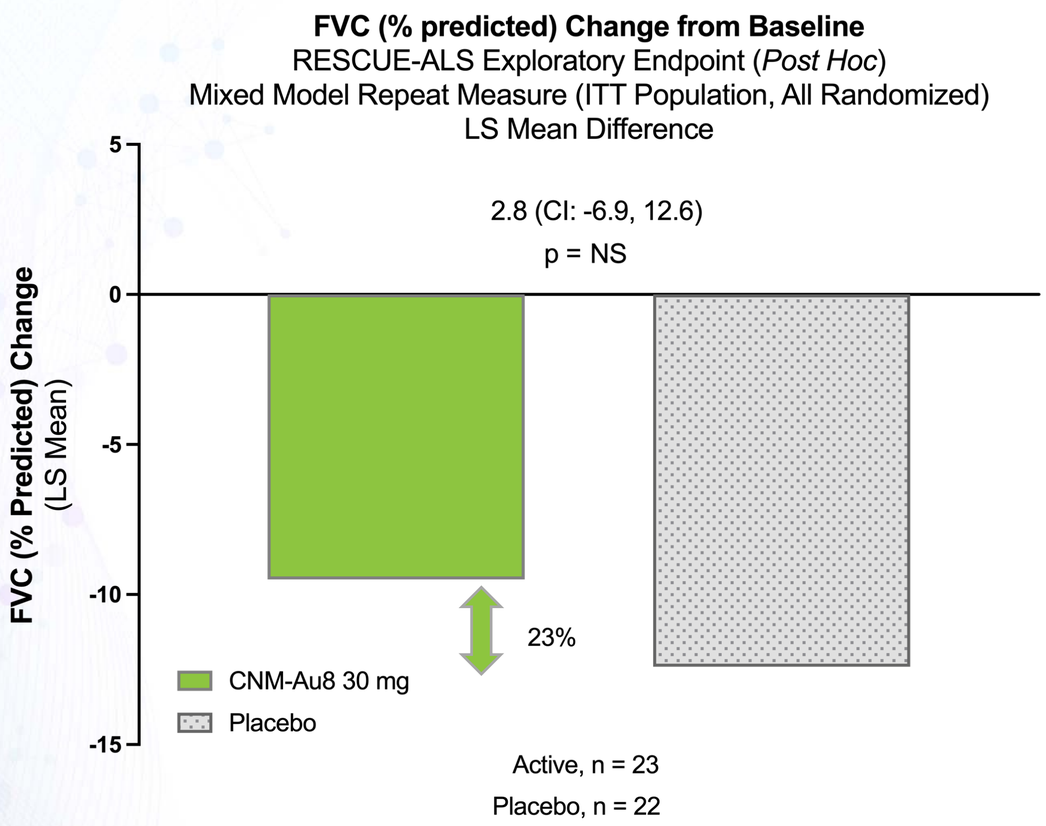
[1]Study Not Powered for FVC change

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

RESCUEALS | Directional FVC Benefit

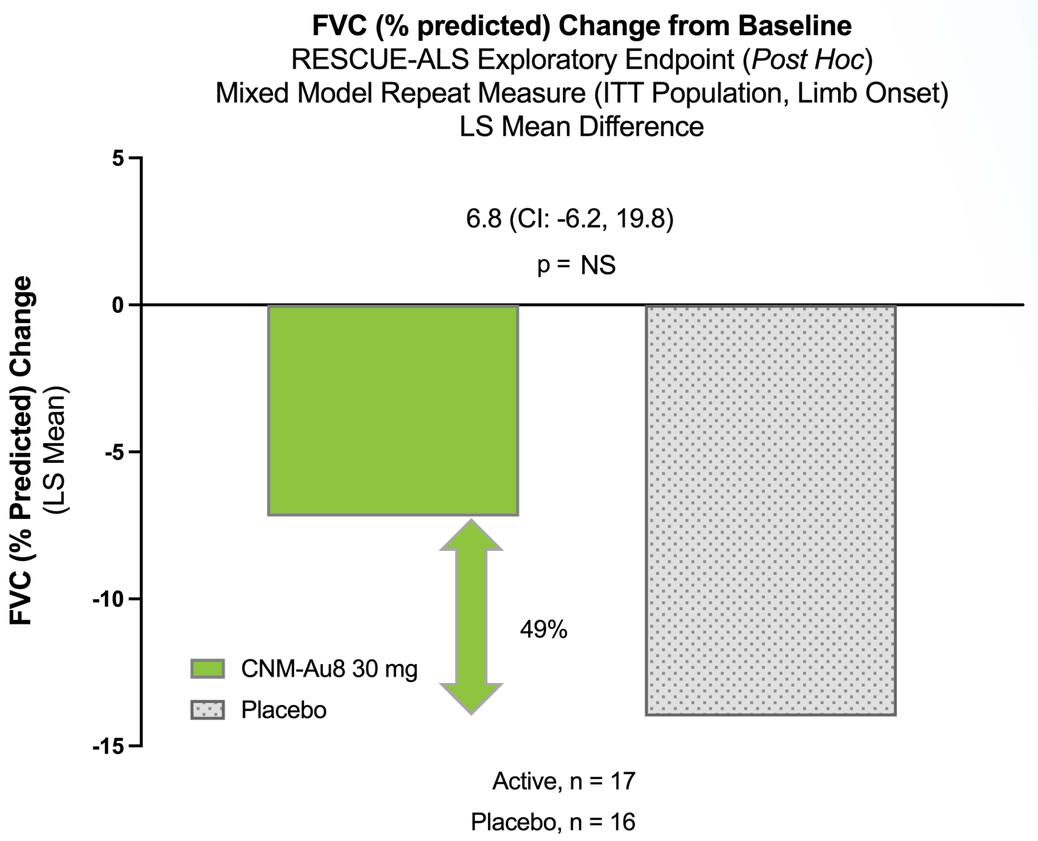
Secondary Endpoint[1] (FVC % predicted, LS Mean Change, Continuous Slope, *Post Hoc*)

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

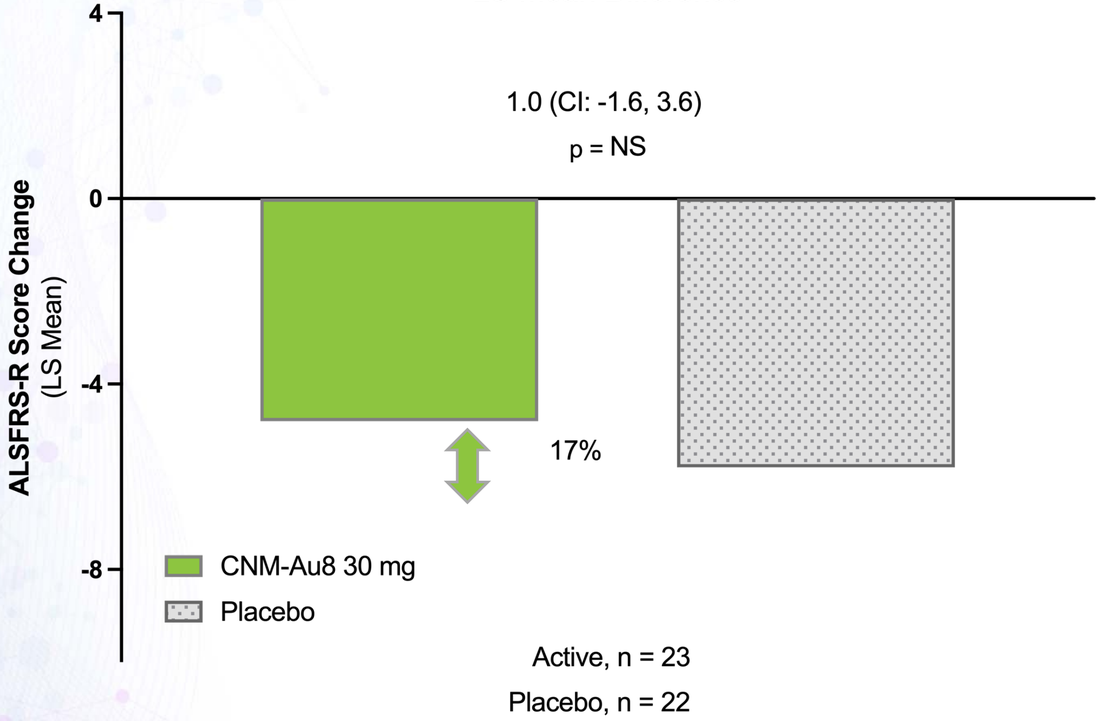
(ALSFRS-R, ALSSQOL-SF)

RESCUEALS | Directional ALSFRS-R Benefit

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

All Randomized

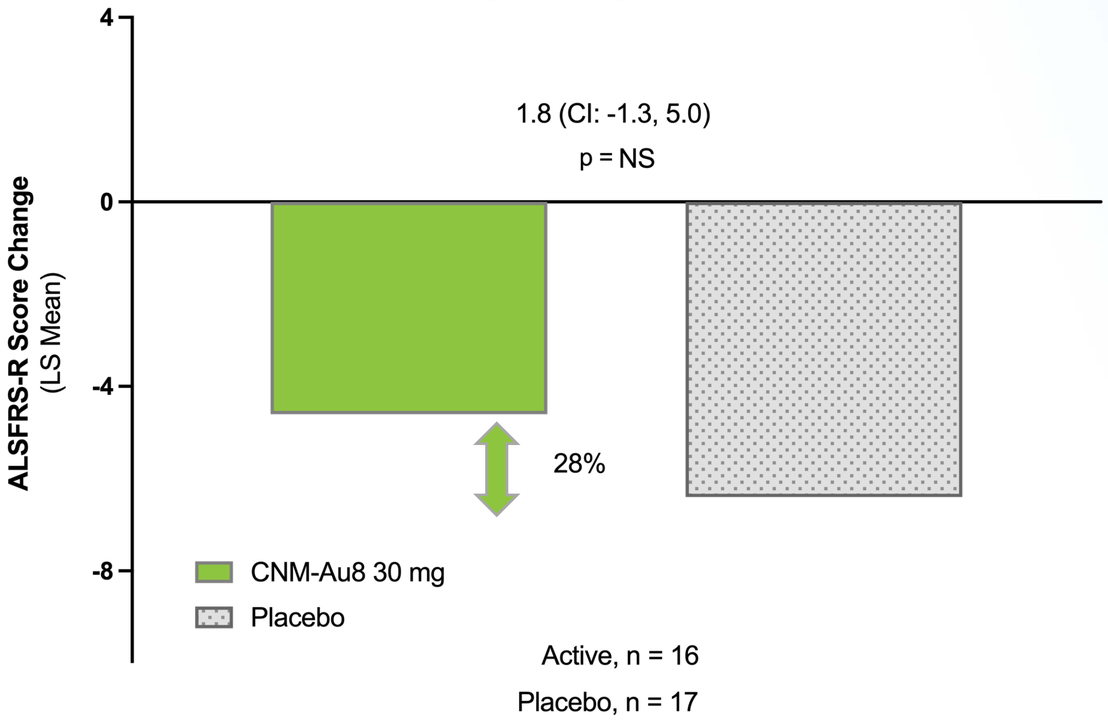
ALSFRS-R Change from Baseline
RESCUE-ALS Exploratory Endpoint
Mixed Model Repeat Measure (ITT Population, All Randomized)
LS Mean Difference



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

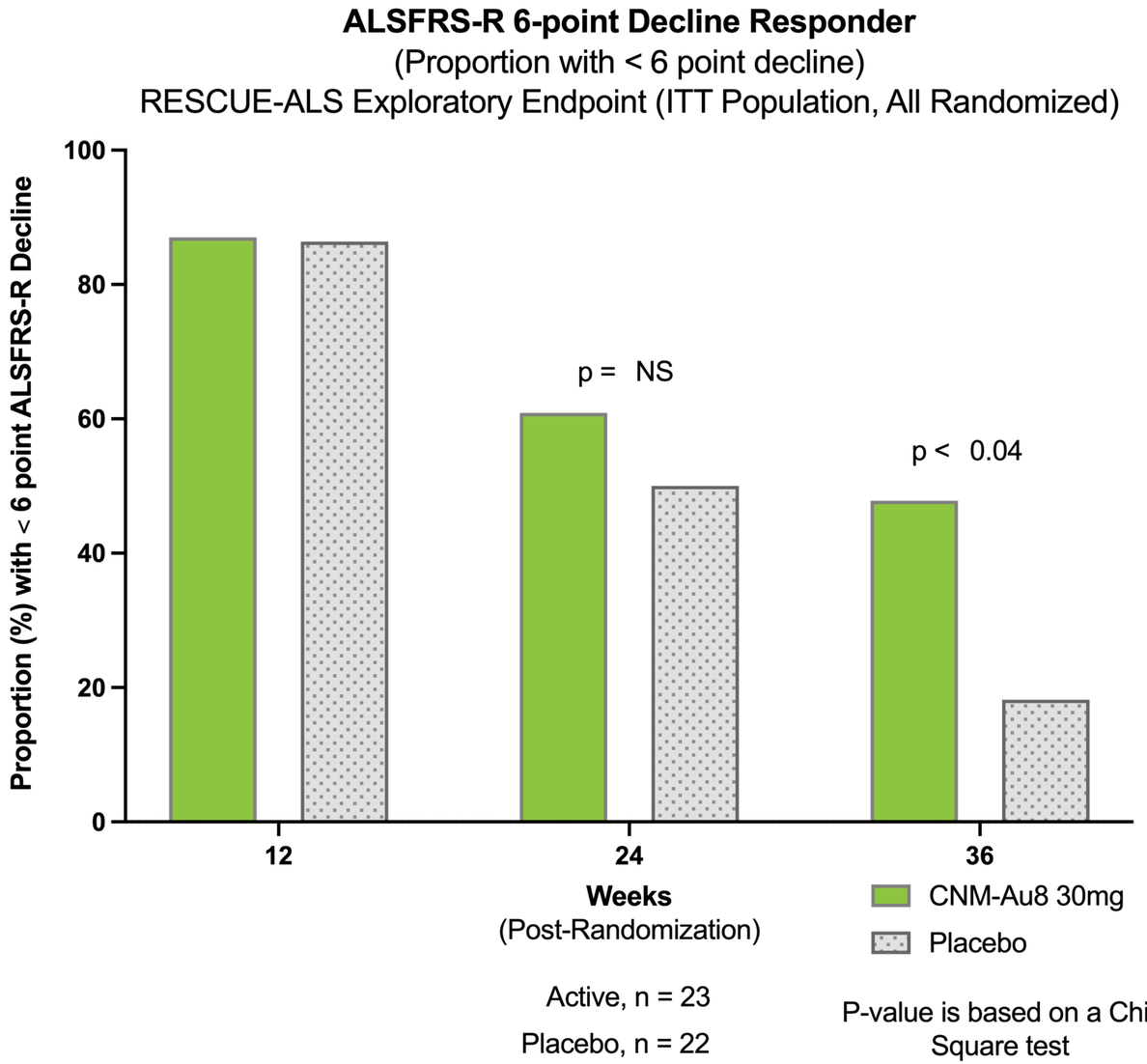


P-value is based on a mixed model with treatment, time from first symptom onset, treatment by time from first symptom onset interaction, baseline value, treatment by baseline value interaction and ENCALS score as factors. Time is treated as a random effect.

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

RESCUEALS | Significant Impact on ALSFRS-R Decline

Exploratory (ALSFRS-R Responder Analysis, All Randomized)

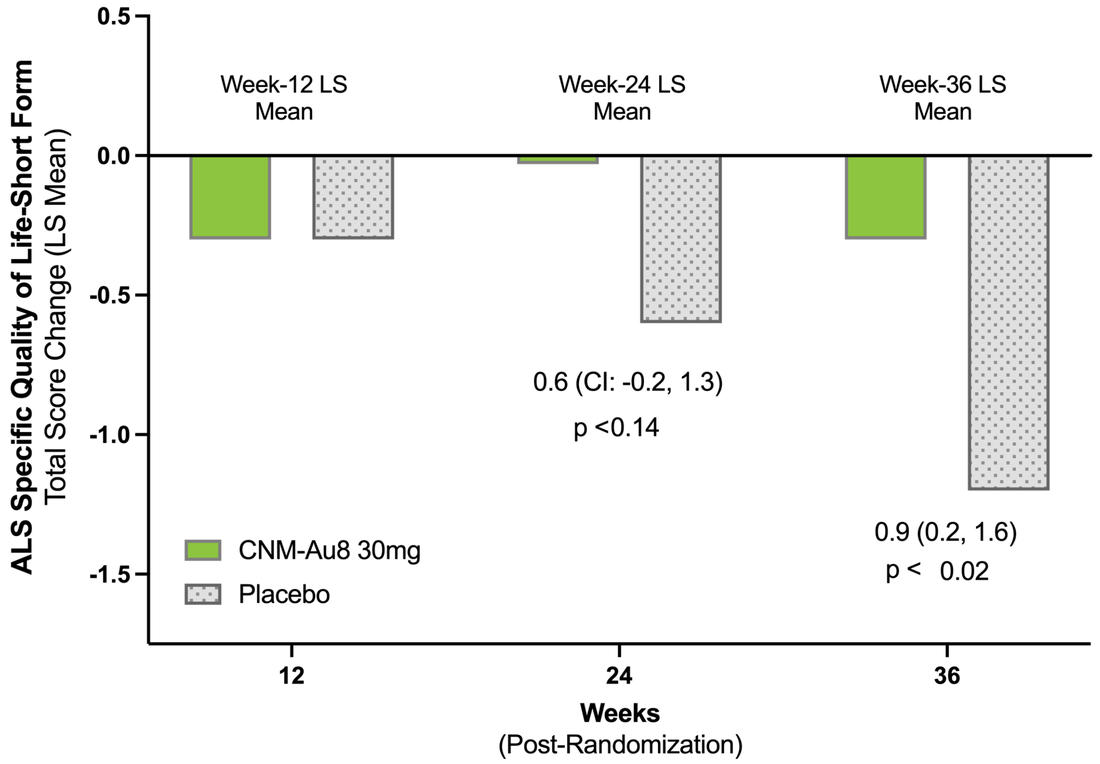


ITT Population; Data on File, Clene Nanomedicine, Inc.

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.

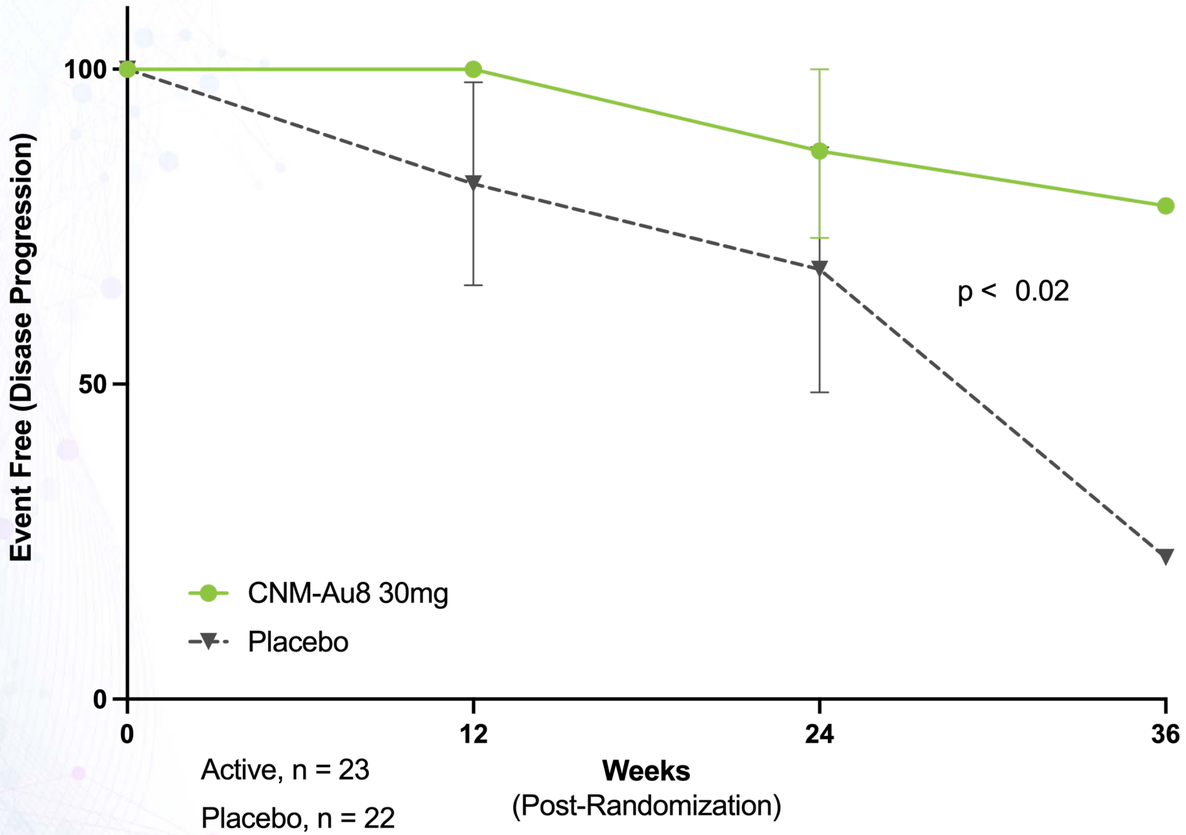
ITT Population; Data on File, Clene Nanomedicine, Inc.

Disease Progression & Survival

RESCUEALS | Significant Impact on ALS Disease Progression

Exploratory Endpoint (All Randomized)

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



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

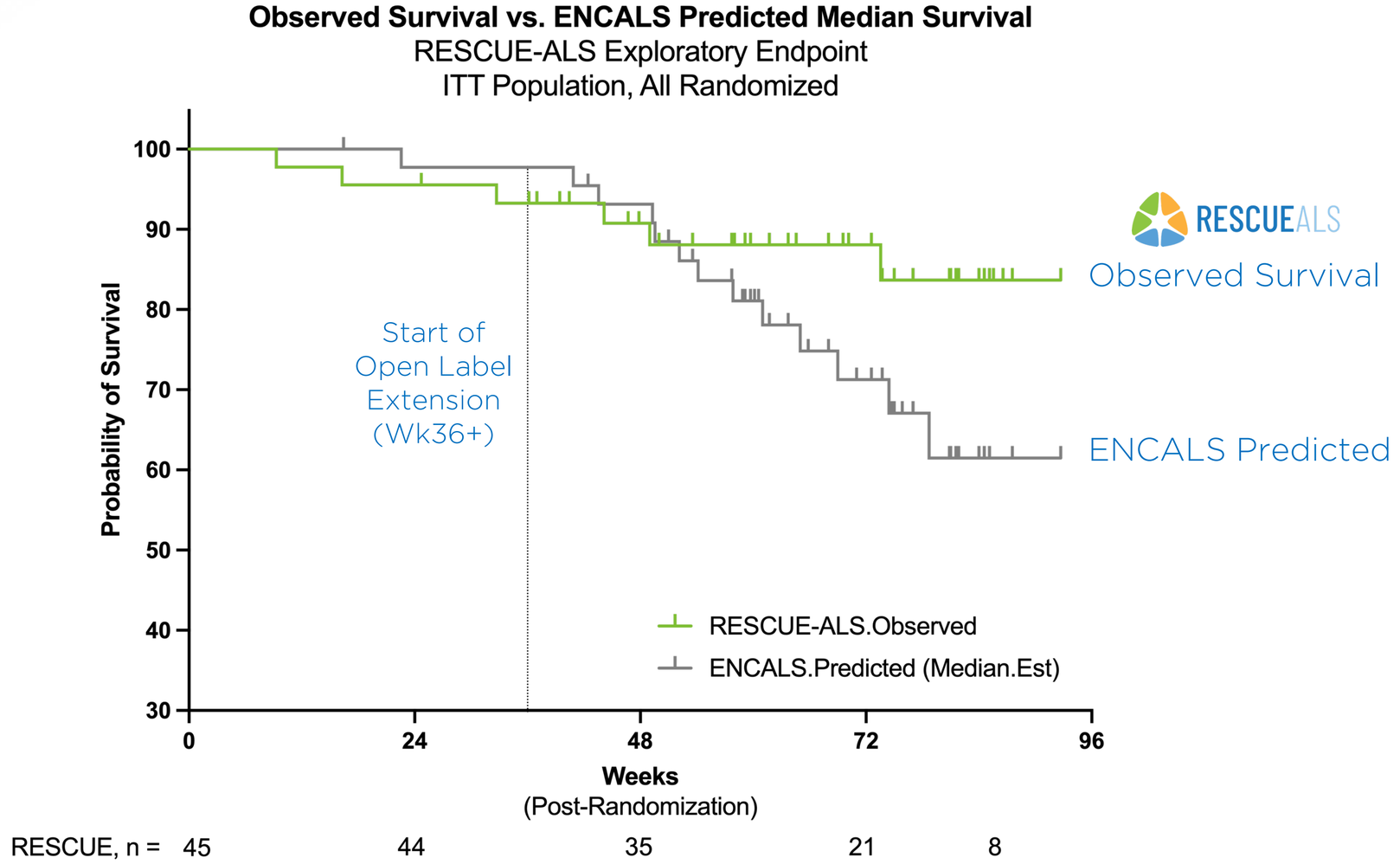
ALS Disease Progression defined as:

- 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)



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

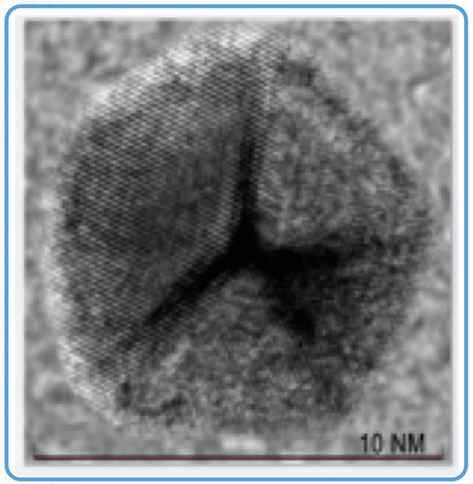
Safety Summary

- 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

CLene NANOMEDICINE

Rob Etherington

Clene Nanomedicine, Inc

President & CEO

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

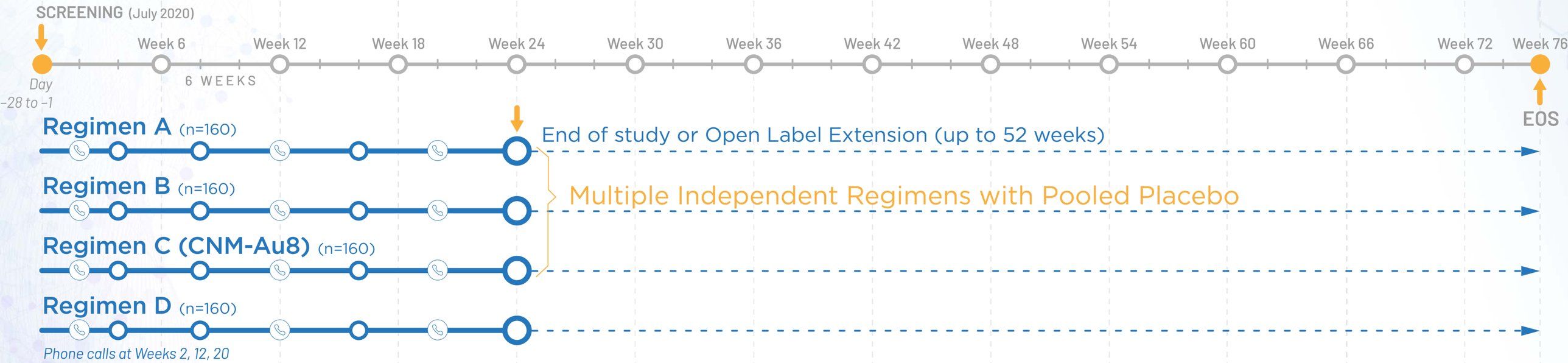
- **Well-tolerated with no safety concerns**

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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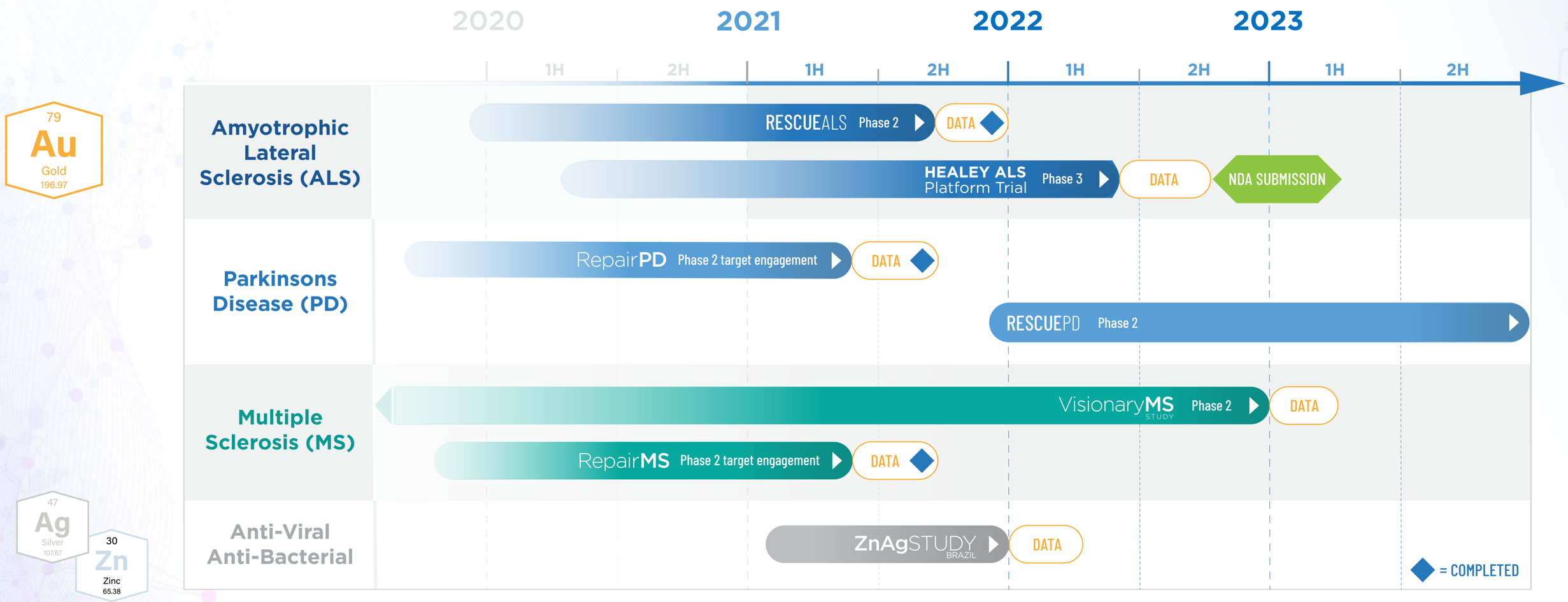
Anticipated Timeline & Upcoming Milestones

2020 - 2023



Questions & Answers

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Version: 2-November-2021