November 30, 2021

CLNN (NASDAQ)

clene.com

Forward Looking Statements

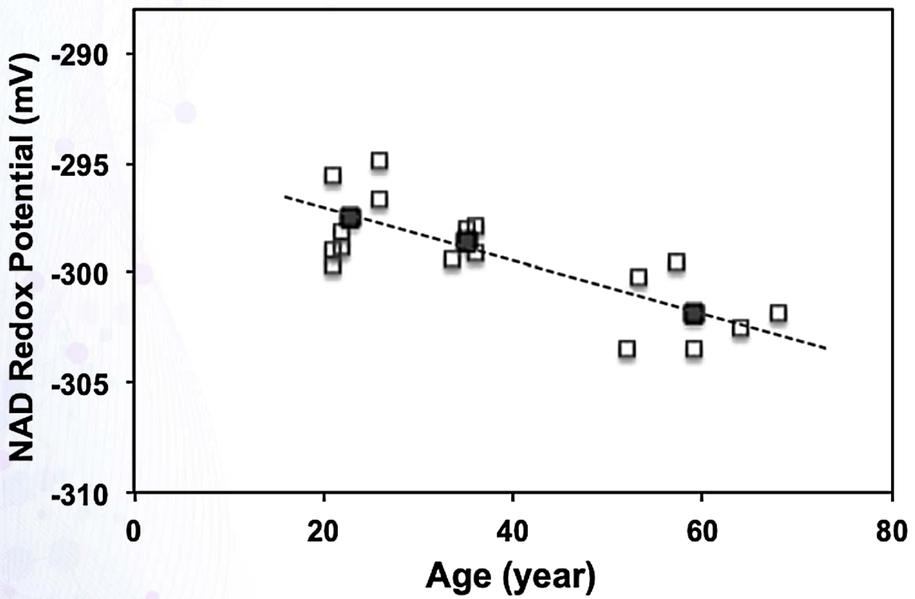
This presentation contains "forward-looking statements" within the meaning of the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Clene's actual results may differ from its expectations, estimates, and projections and consequently, you should not rely on these forward-looking 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.

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

Brain Energy Potential Declines With Normal Aging

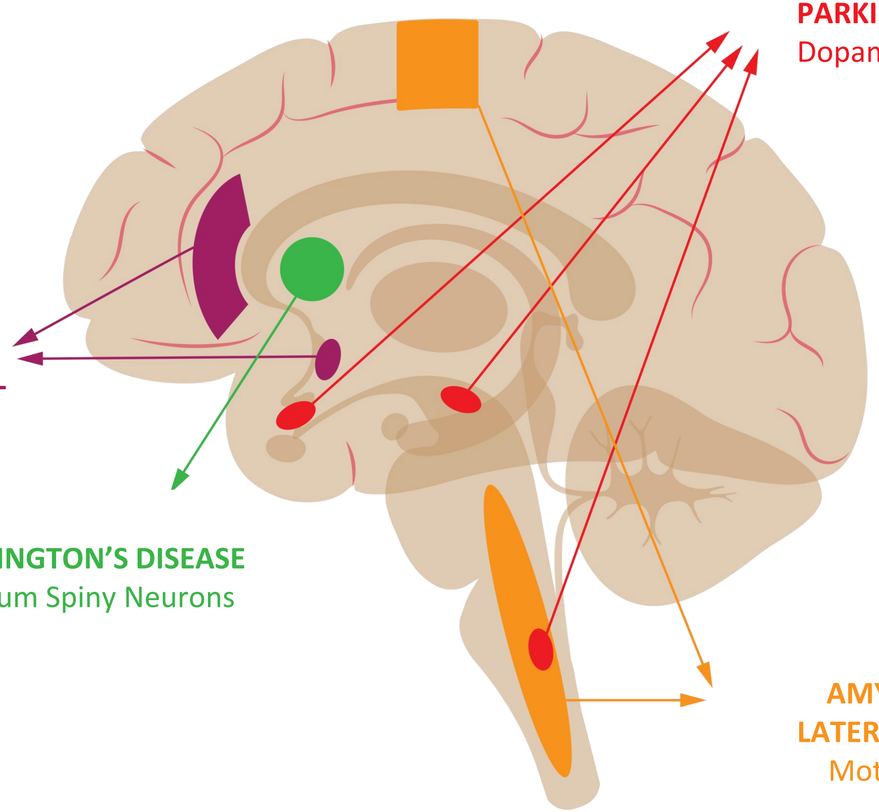
~0.5% NAD^+/NADH unit decline per decade

(~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



PARKINSON'S DISEASE
Dopaminergic Neurons

MULTIPLE SCLEROSIS
Axonal Degeneration

FRONTOTEMPORAL DEMENTIA
Spindle Neurons

HUNTINGTON'S DISEASE
Medium Spiny Neurons

AMYOTROPHIC LATERAL SCLEROSIS
Motor Neurons

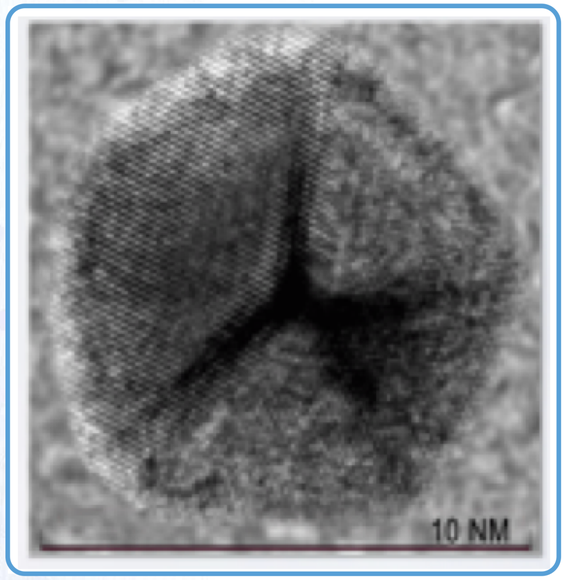
Fu, H., et al; Nature Neuroscience (2018) 21: 1350-1358. Zhu et al. Proc Natl Acad Sci USA . 2015 Mar 3;112(9):2876-81. Rone et al. J Neurosci. 2016 Apr 27;36(17):4698-707.

CLene NANOMEDICINE

CNM-Au8® | Catalytically-Active Nanocrystals

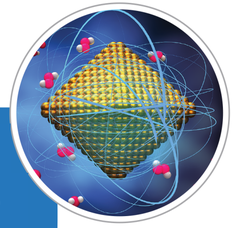
Intersection of Physics and Biology

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

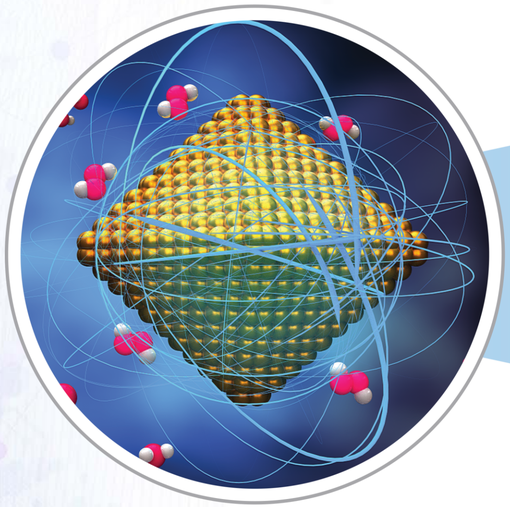
CNM-Au8
Catalytically Active
Nanocrystal Suspension

Once Daily Oral Suspension

CLene NANOMEDICINE

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

CNM-Au8 Nanocrystal



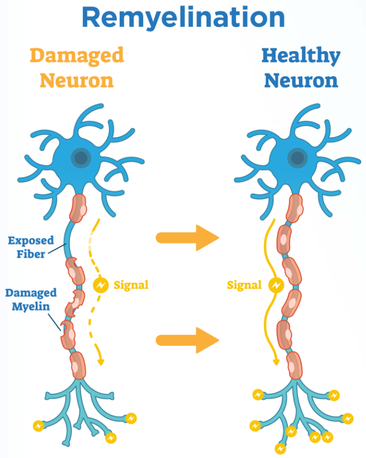
Mechanistic Effects

- ↑ 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

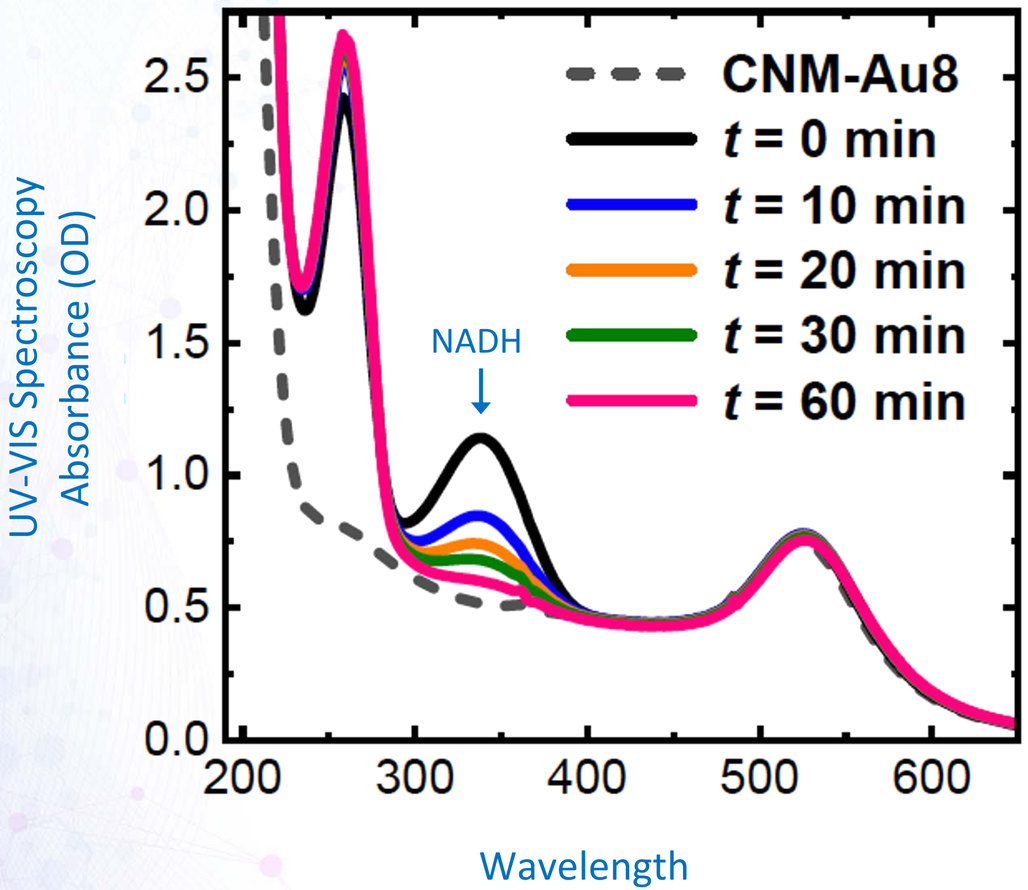


Neuroprotection

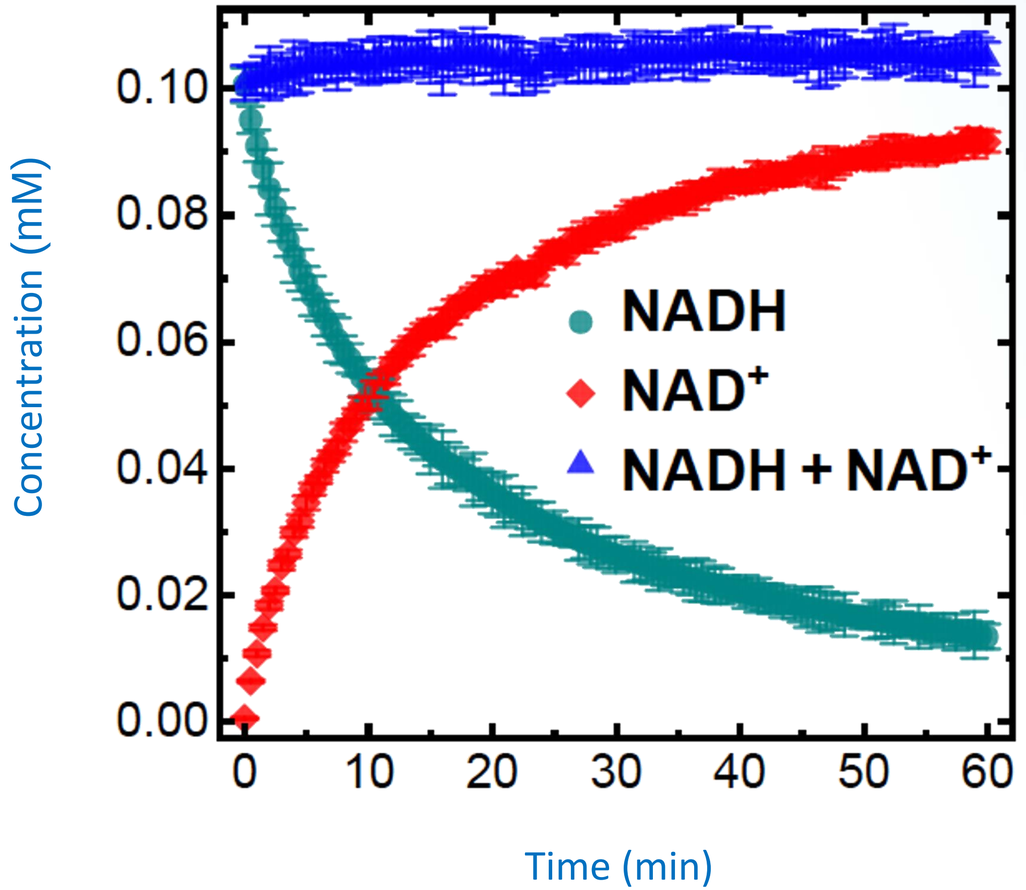
CLene NANOMEDICINE

CNM-Au8 | Catalysis of NADH to NAD$^+$

Catalysis of NADH to NAD$^+$



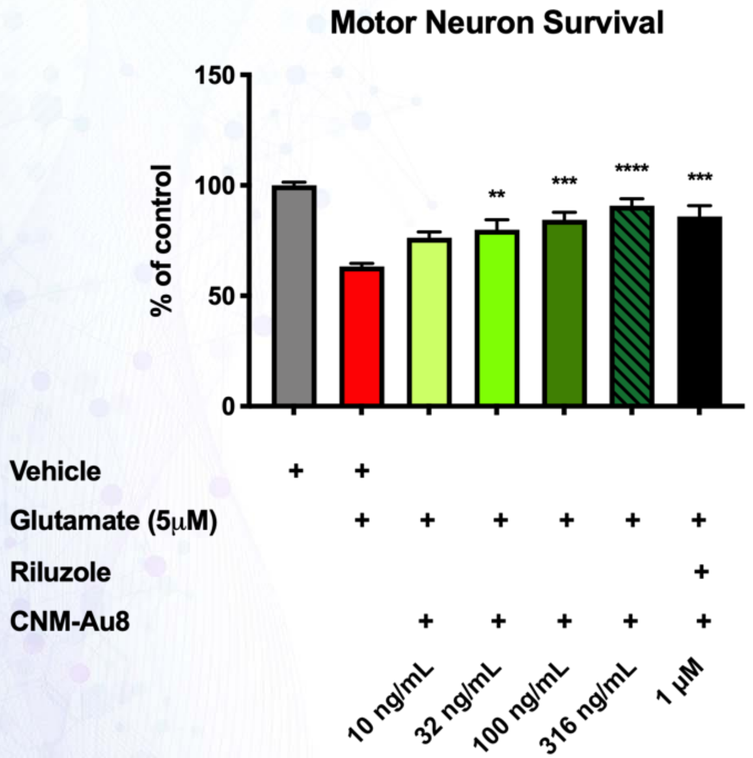
NAD$^+$ & NADH Concentration vs. Time

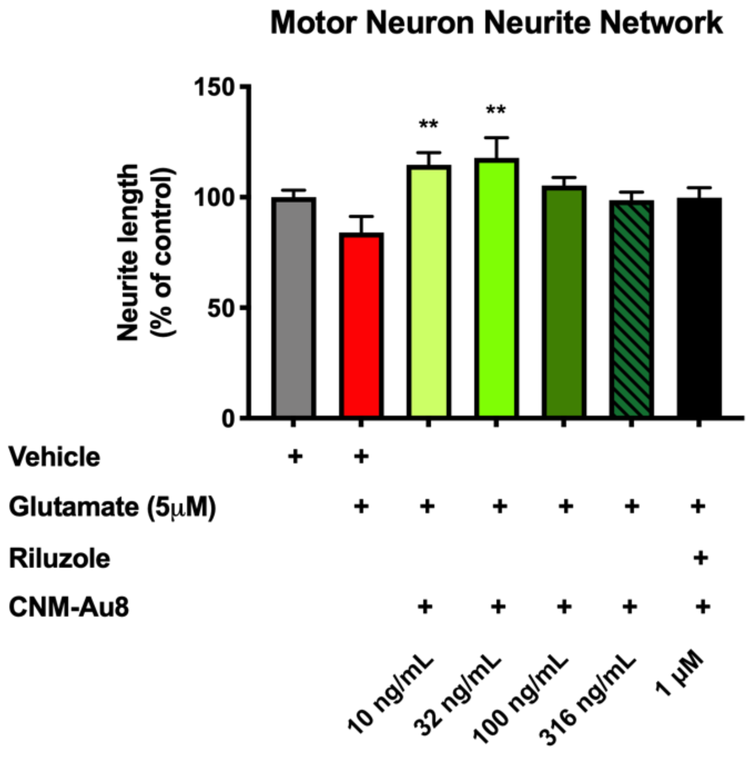


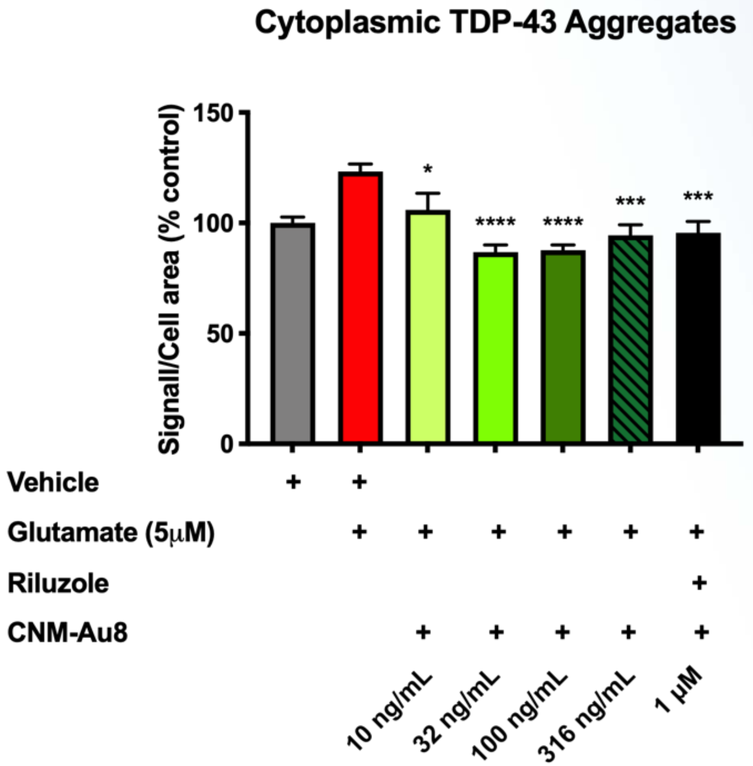
Data on File, Clene Nanomedicine, Inc. Robinson et al. Sci Rep. 2020 Feb 11;10(1):1936.

CNM-Au8 | Neuroprotection from Excitotoxic Glutamate

Rat Primary Motor Neurons *In Vitro* Results

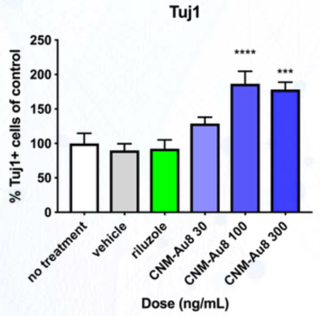


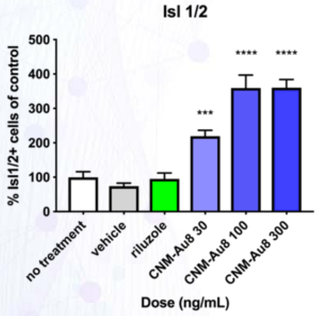


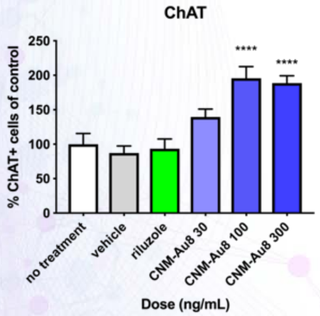


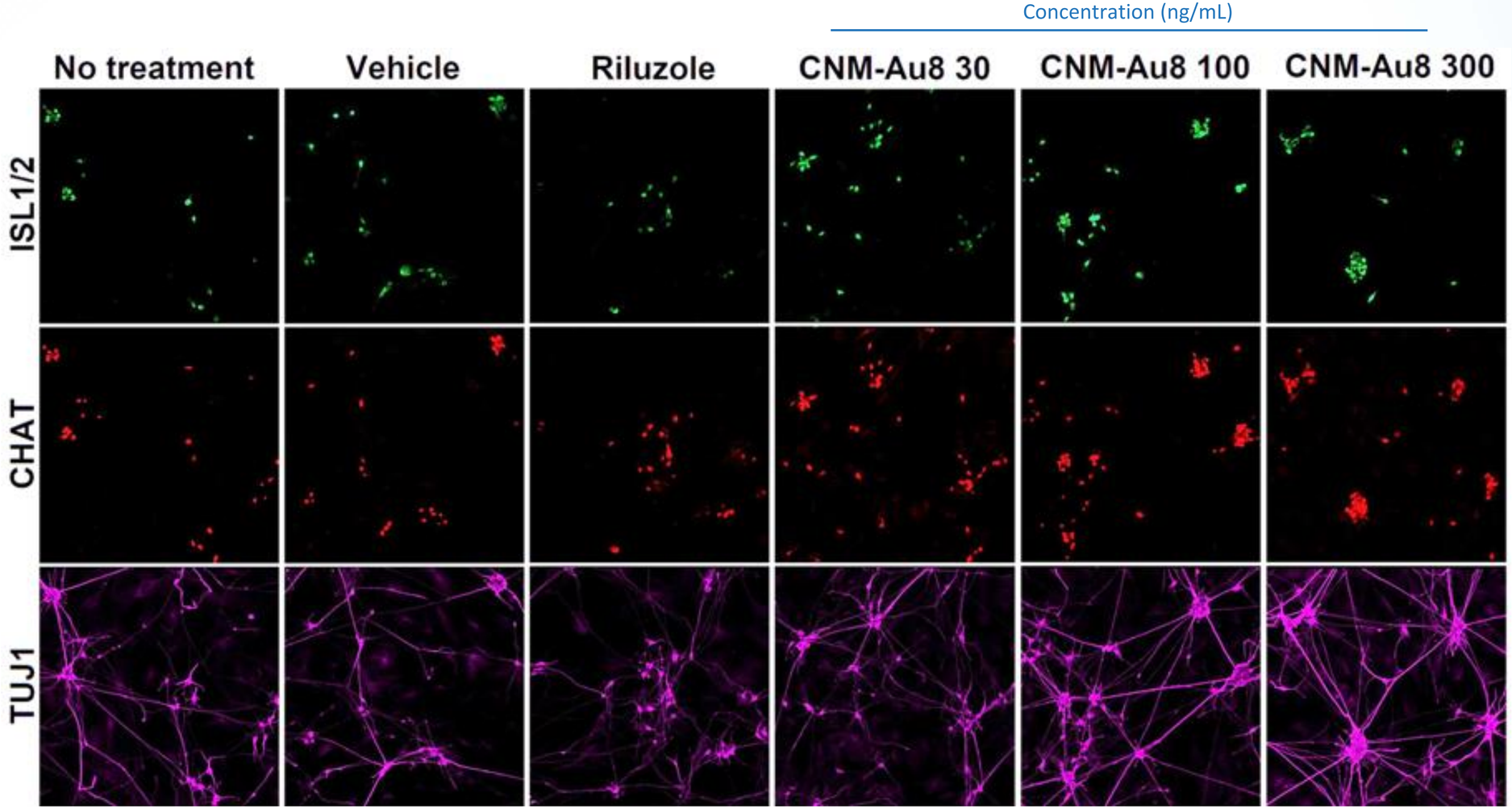
CNM-Au8 | ALS Neuroprotection in Human iPSCs

iPSC *In Vitro* Survival Results – SOD1^{A4V} Astrocytes with Human Motor Neuron





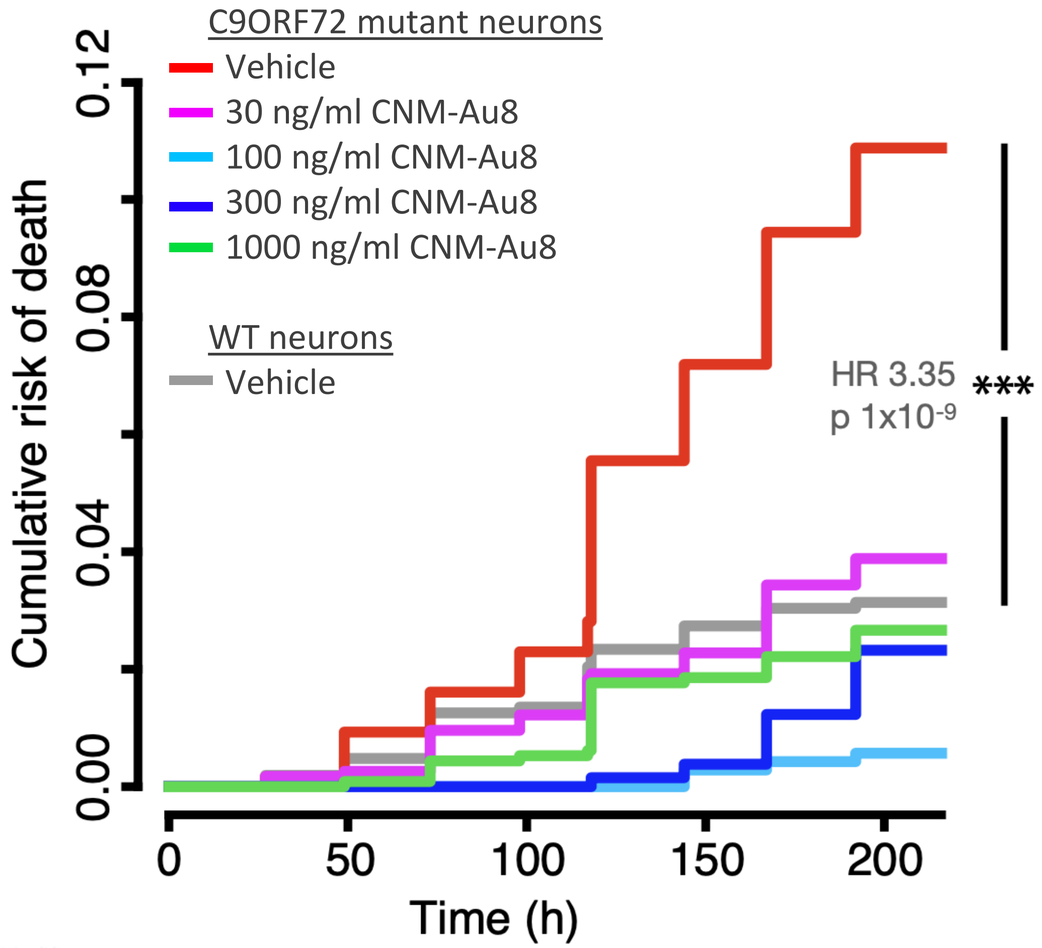




Ho et al.

CNM-Au8 | Survival in Human C9ORF72 iPSC Neurons

iPSC Derived Neurons *In Vitro* Results – Cortical Neurons (Forebrain)



Significant Survival Benefit

Reference	Treatment	HR (vs. vehicle)	p
C9ORF72 + vehicle	CNM-Au8 30ng/ml	0.36	$1x10^{-8}$
C9ORF72 + vehicle	CNM-Au8 100ng/ml	0.07	$1x10^{-7}$
C9ORF72 + vehicle	CNM-Au8 300ng/ml	0.21	$4x10^{-14}$
C9ORF72 + vehicle	CNM-Au8 1000ng/ml	0.26	$4x10^{-11}$

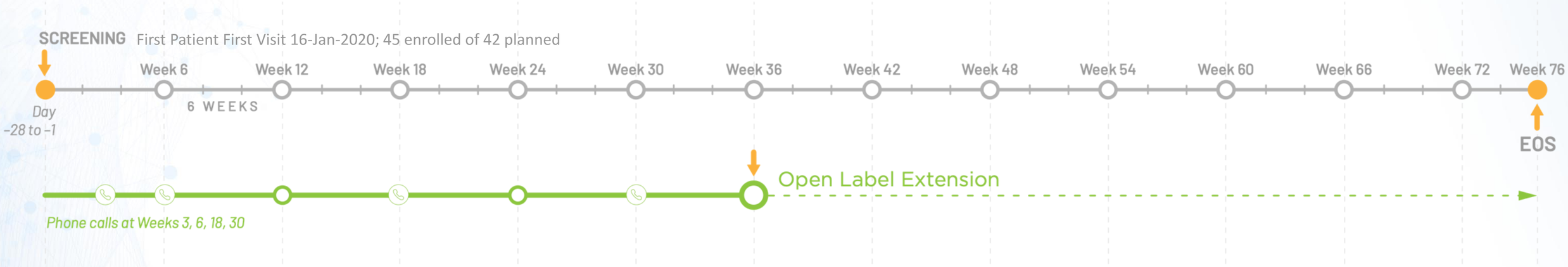
Data on File, Clene Nanomedicine, Inc.

Phase 2

RESCUEALS

Design Overview

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



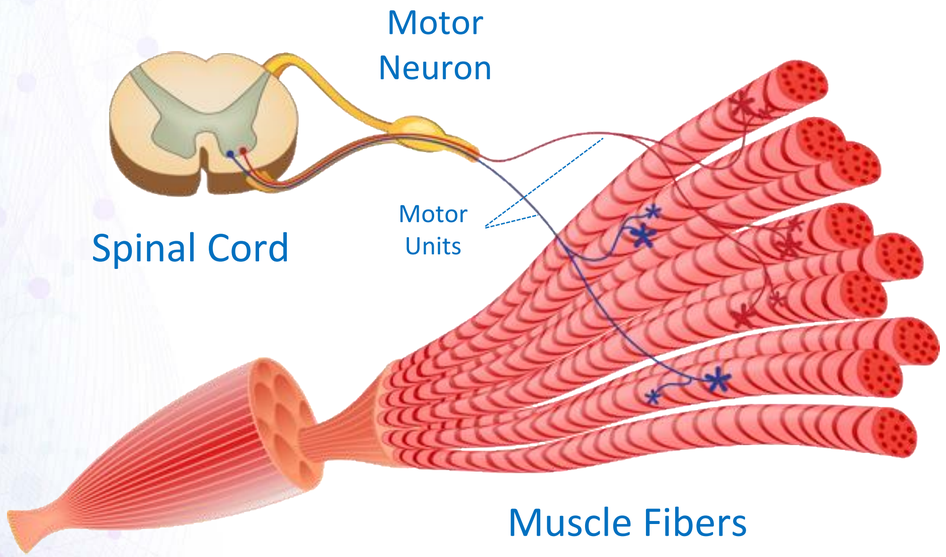
Neurophysiology	Pulmonary Function	Function & QoL	Disease Progression & Survival
MUNIX[1]	Forced Vital Capacity	ALSFRS-R, ALSSQOL-SF	

[1] Study was powered for MUNIX primary endpoint based on 50% relative decrease in rate of MUNIX decline

RESCUEALS | Pioneered Use of MUNIX Biomarker

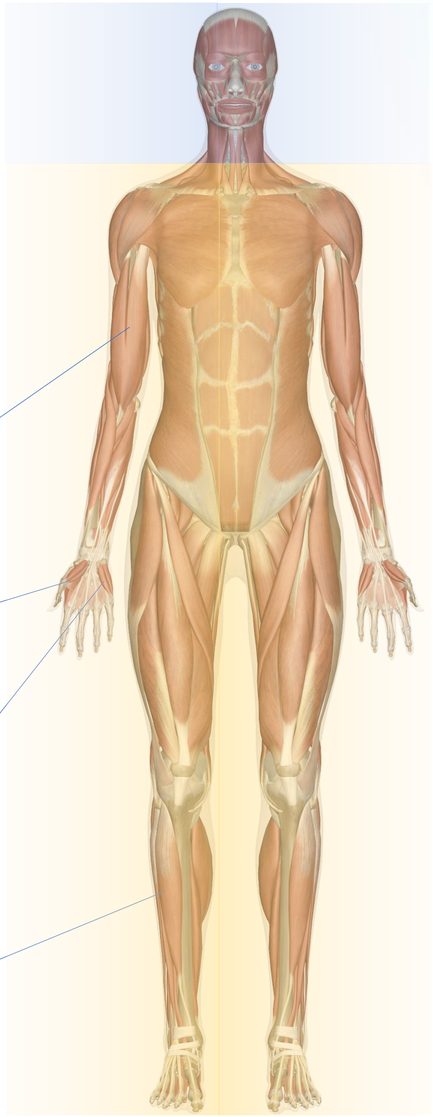
Primary Endpoint: Spinal Cord Lower Motor Neuron Protection

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)

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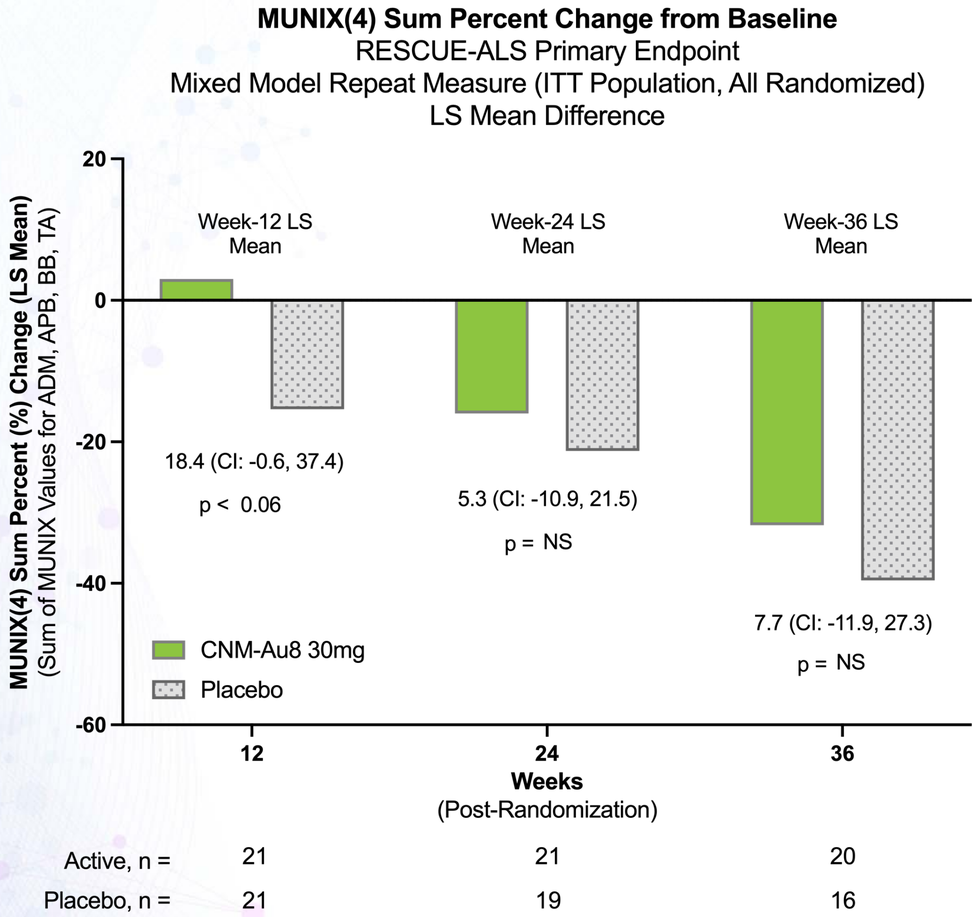
RESCUEALS | Evidence for Motor Neuron Protection

Primary Endpoint (MUNIX %, LS Mean Change)

All Randomized

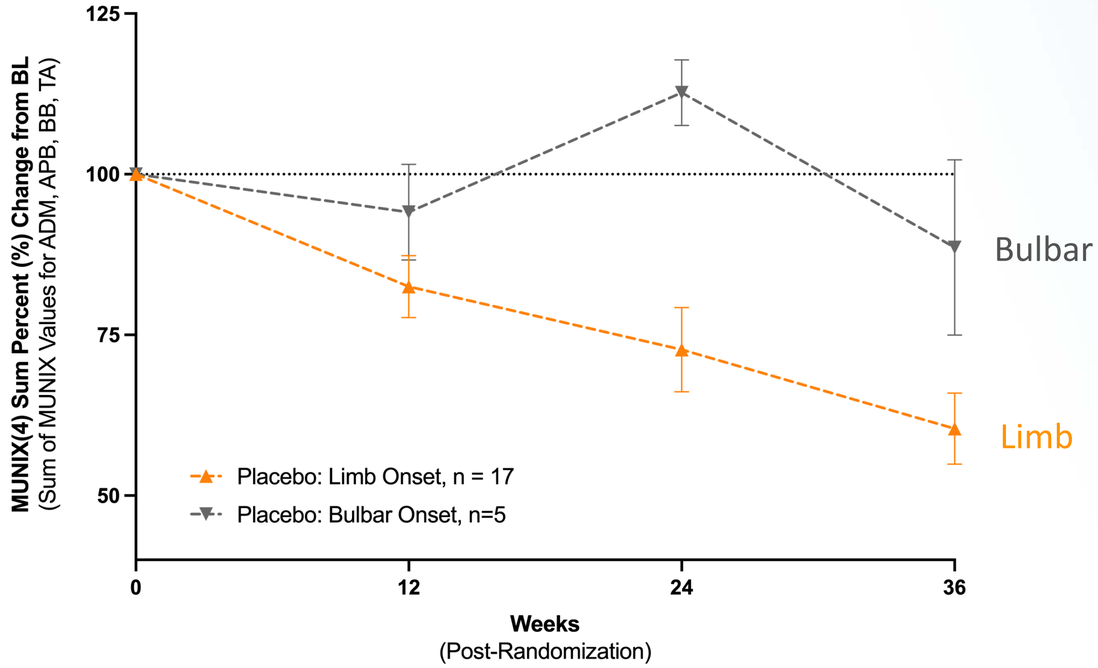


Active, n =	21	21	20
Placebo, n =	21	19	16

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.

All Placebo

Limited Rate of MUNIX Decline in Bulbar Onset



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

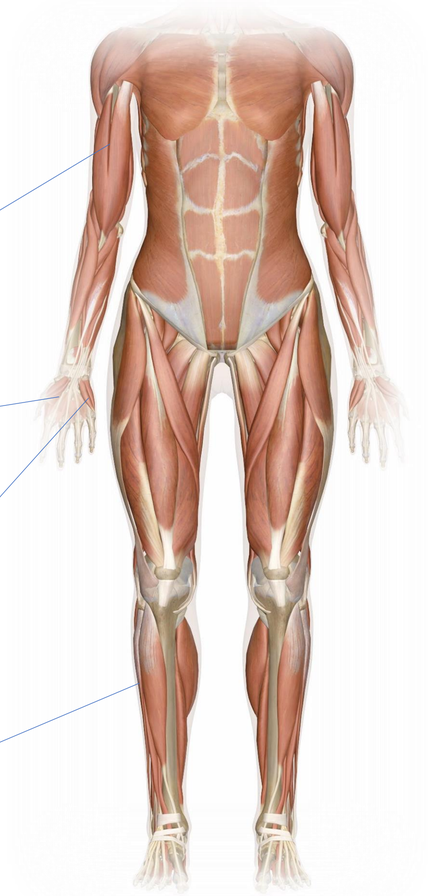
Data on File, Clene Nanomedicine, Inc.

RESCUEALS | MUNIX Biomarker Efficacy in Limb Onset

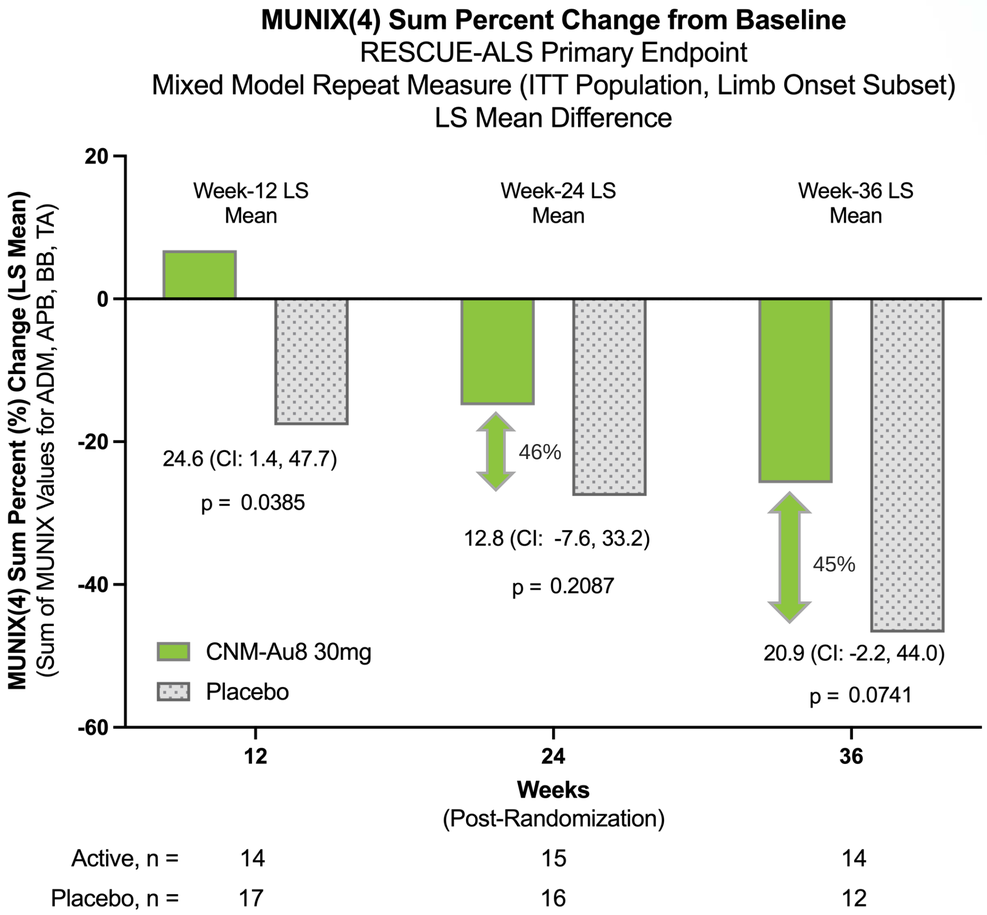
Primary Endpoint (MUNIX %, LS Mean Change, Limb Onset Subset)

Spinal Cord
Lower Motor Neuron
Motor Unit Index
(MUNIX) Sum

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



Pre-specified: Limb Onset



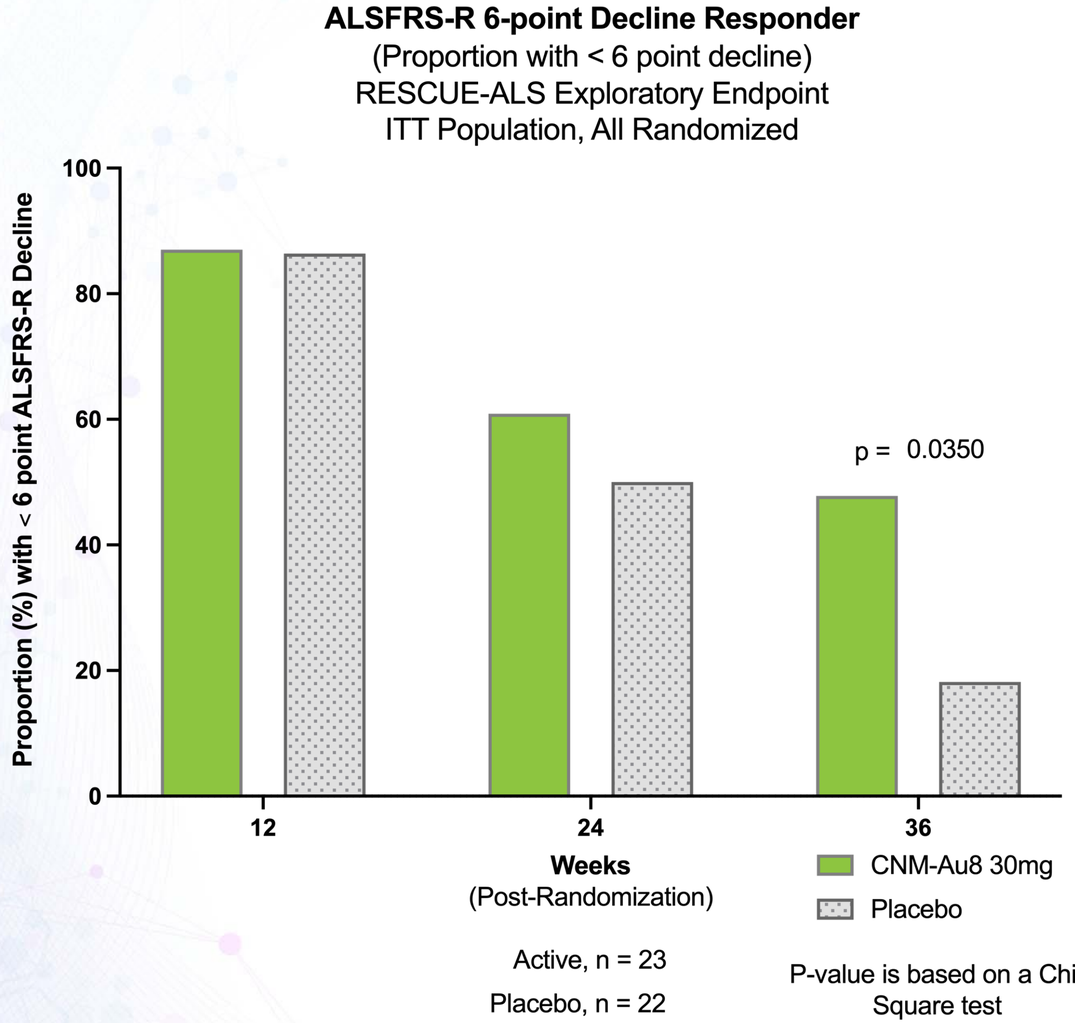
P-value is based on mixed model repeat measures with treatment, visit, treatment by visit interaction as fixed effects, and baseline value and ENCALS score as covariates. An unstructured covariance model was used.

Data on File, Clene Nanomedicine, Inc.

RESCUEALS | Significant Impact on ALSFRS-R Decline

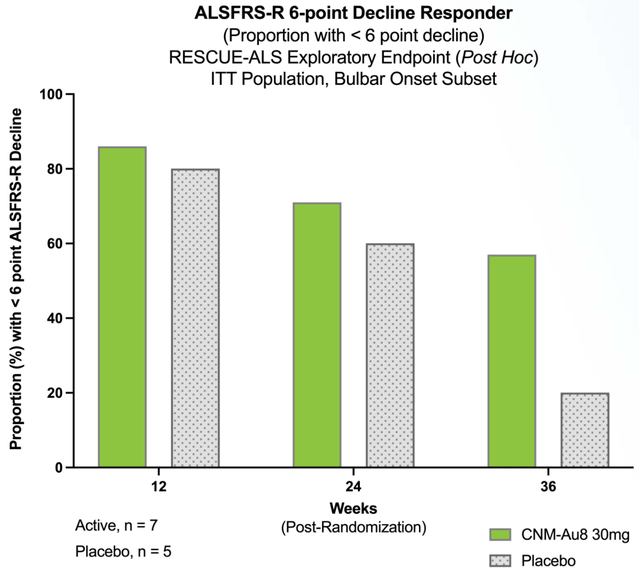
Exploratory (ALSFRS-R Responder Analysis, < 6-point decline)

All Randomized

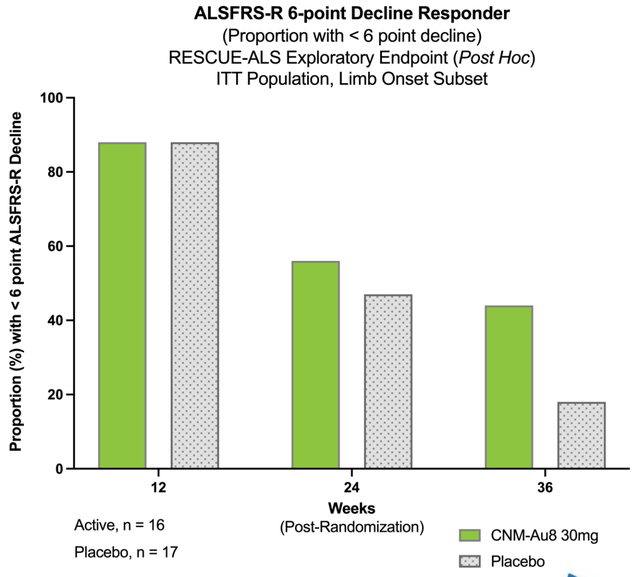


Sensitivity

All Bulbar



All Limb

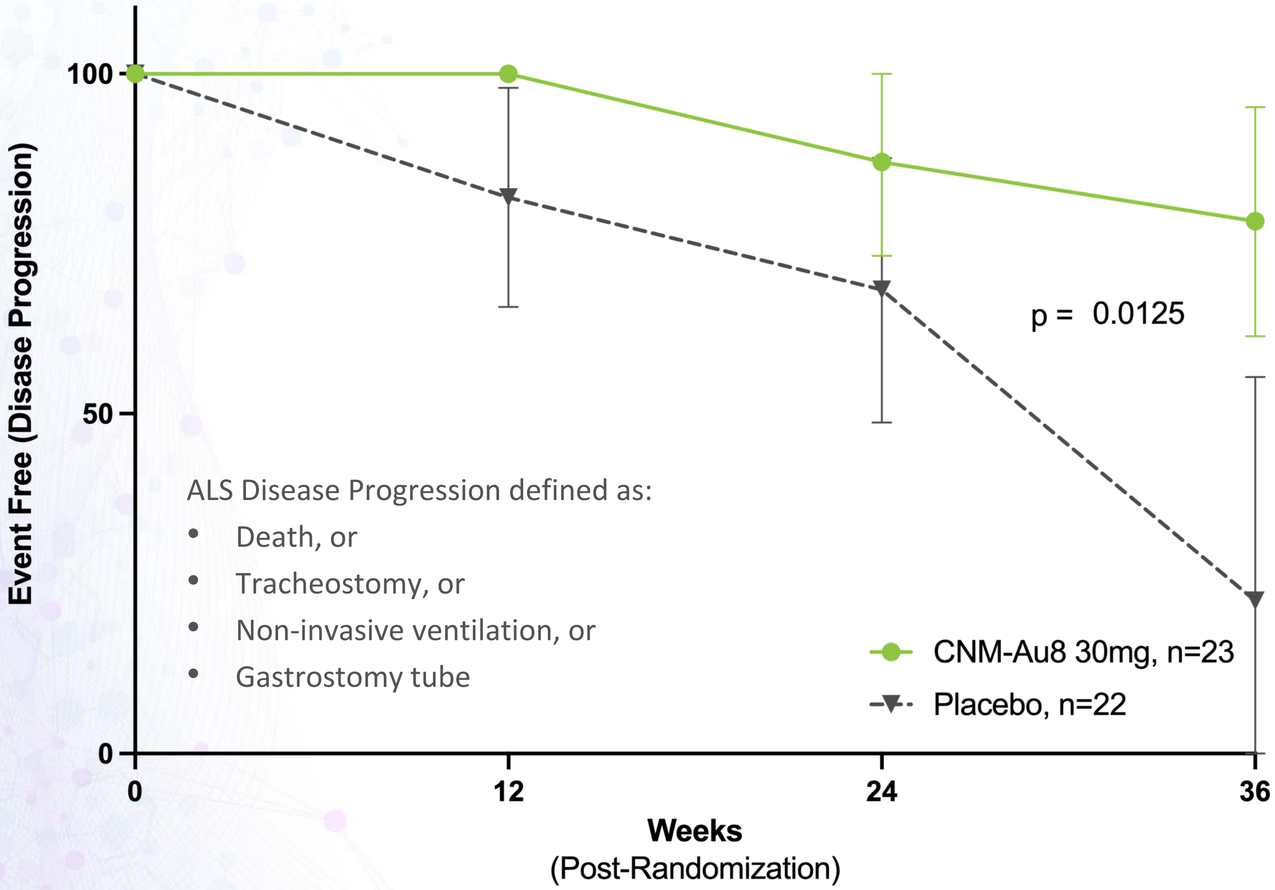


Data on File, Clene Nanomedicine, Inc.

RESCUEALS | Significantly Reduced Disease Progression Risk

Exploratory Endpoint (Disease Progression)

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

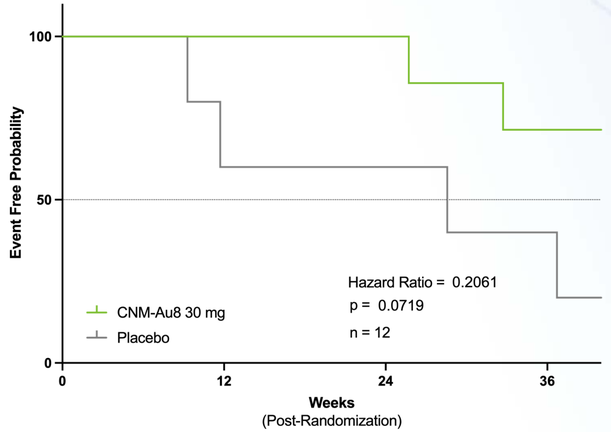


Sensitivity

All Bulbar

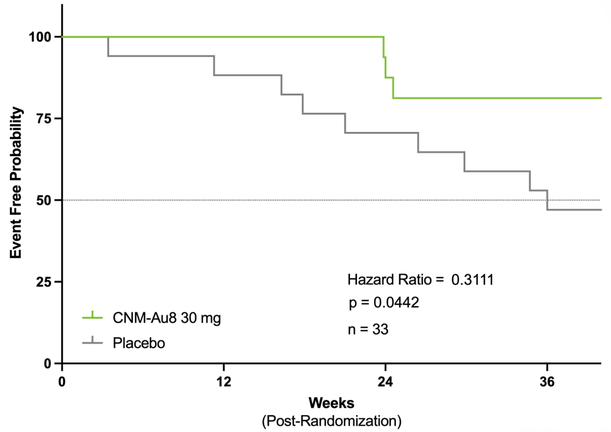
All Limb

Bulbar Onset ALS Disease Progression[1]
RESCUE-ALS Exploratory Endpoint (Post Hoc)
ITT Population, Bulbar Onset Subset
Kaplan-Meier Estimates, Proportion Event Free



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

Limb Onset ALS Disease Progression[1]
RESCUE-ALS Exploratory Endpoint (Post Hoc)
ITT Population, Limb Onset Subset
Kaplan-Meier Estimates, Proportion Event Free



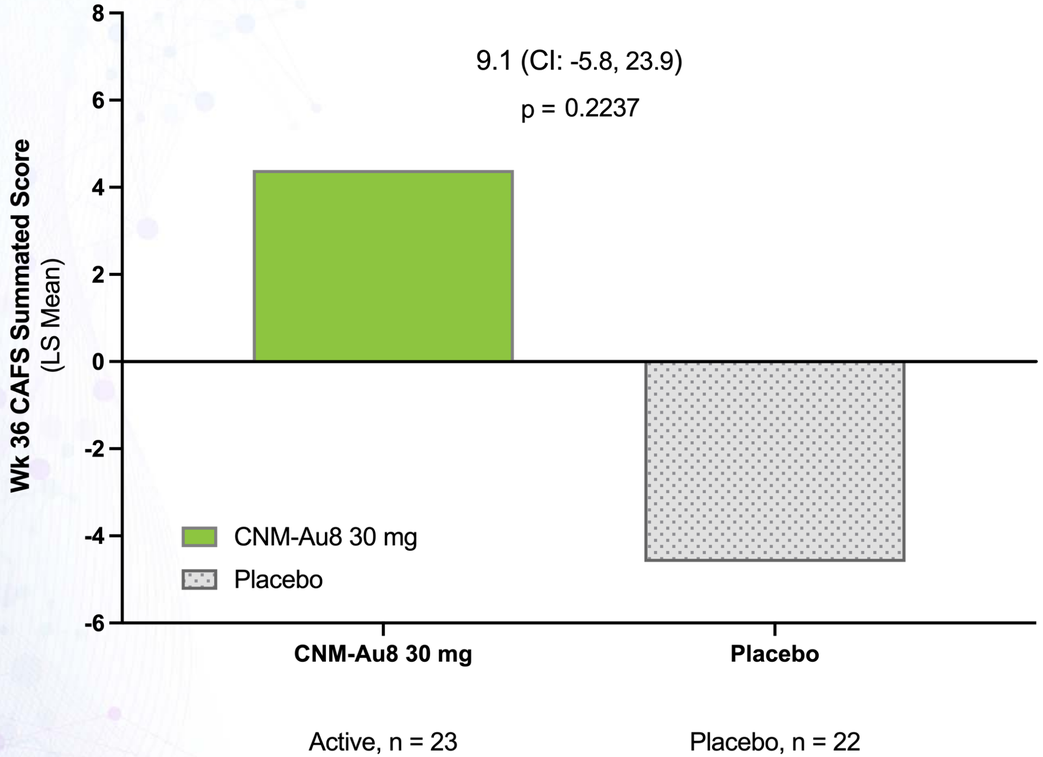
Data on File, Clene Nanomedicine, Inc.

RESCUEALS | Impact on CAFS Progression to Wk36

Exploratory (Combined Assessment of Function & Survival)

By Average of Summated Scores

Combined Assessment of Function (ALSFRS-R) and Survival
RESCUE-ALS Exploratory Endpoint
ANCOVA Model (ITT Population, All Randomized)
Week 36 LS Mean Difference

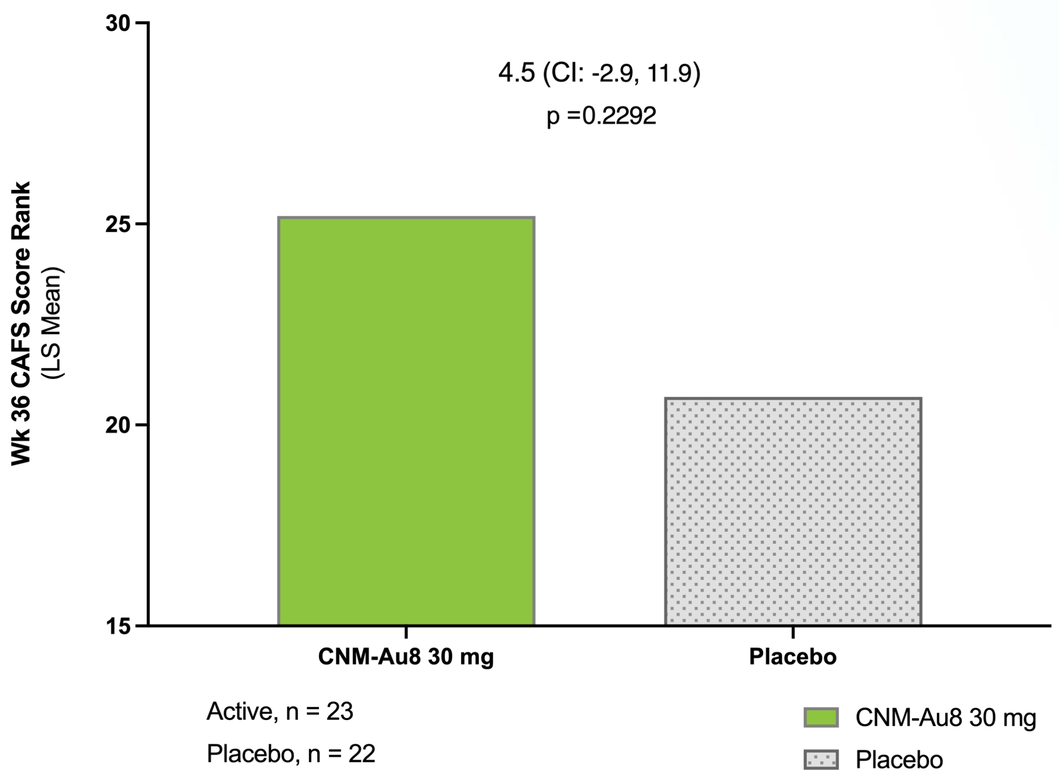


Active, n = 23 Placebo, n = 22

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.

By Average of Ranks

Combined Assessment of Functional (ALSFRS-R) and Survival
RESCUE-ALS *Post Hoc* Endpoint
Ranked Analysis (ITT Population, All Randomized)
Week 36 LS Mean Difference



Active, n = 23
Placebo, n = 22

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.

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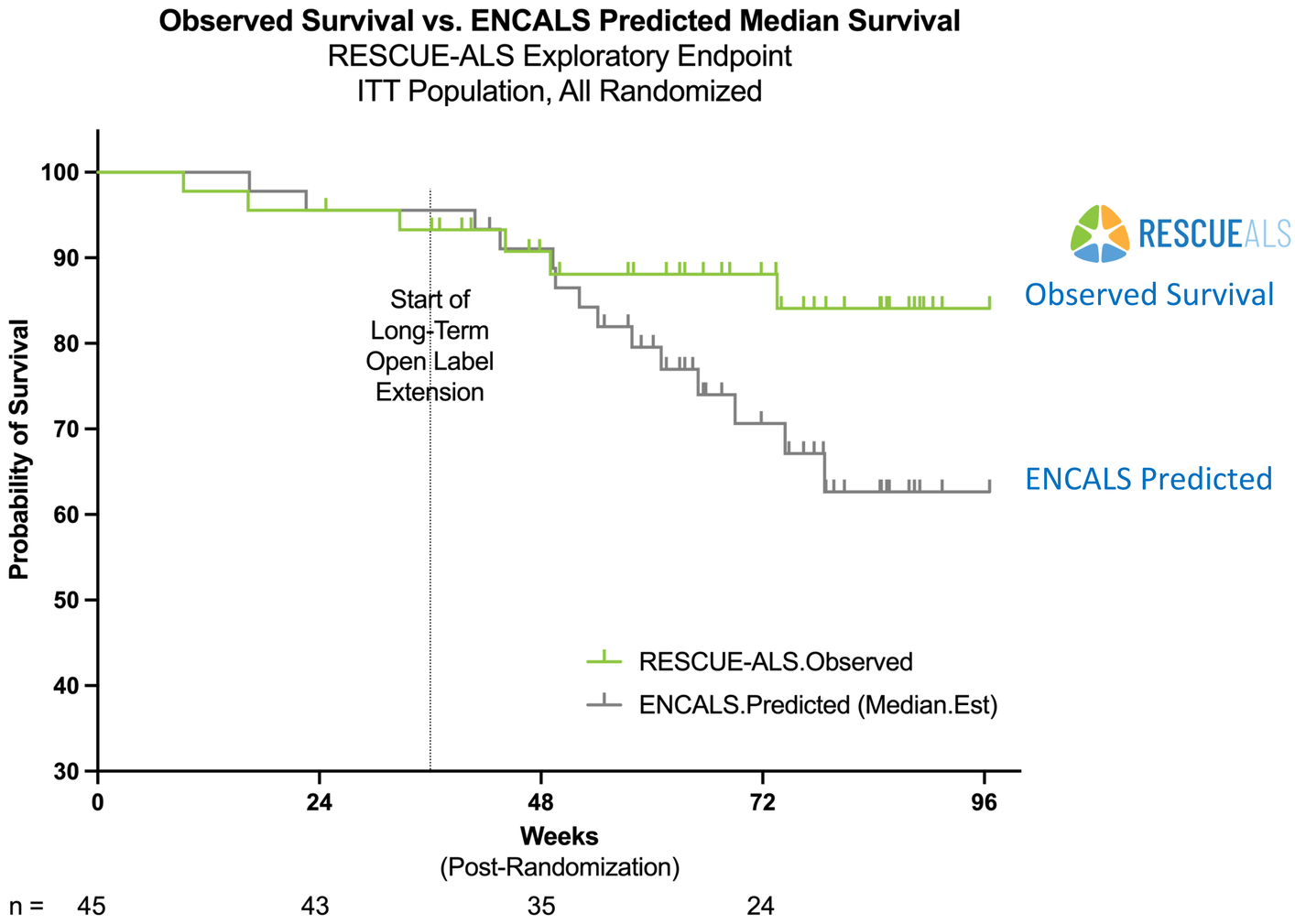
RESCUEALS | Potential Survival Signal

Exploratory Endpoint (Observed Survival vs. Predicted)



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

Data on File, Clene Nanomedicine, Inc.

RESCUEALS | Well Tolerated & No Safety Signals

Safety Summary

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

Clene NANOMEDICINE

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