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A Blinded Interim Update on RESCUE-ALS: A Randomized, Placebo-Controlled, Phase 2 Study to Determine the Effects of CNM-Au8 to Slow Disease Progression in Amyotrophic Lateral Sclerosis

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[1]Clene Nanomedicine, Salt Lake City, UT and North East, MD; [2]Westmead Hospital, Sydney Australia; [3]Brain and Mind Centre, Sydney, Australia

Preliminary Blinded Efficacy Data Support a Disease Modifying Potential For CNM-Au8 in the Treatment of ALS

CNM-Au8 (bioenergetic nanocatalyst)

- Proprietary Au nanocrystal suspension
- Daily oral dosing (30mg in 60 mL)
- Mechanism of action:
  1. Neuronal metabolic support (increased ATP)
  2. Decreased ROS
  3. Enhanced proteostasis (↓TDP43)

Rescue-ALS Overview

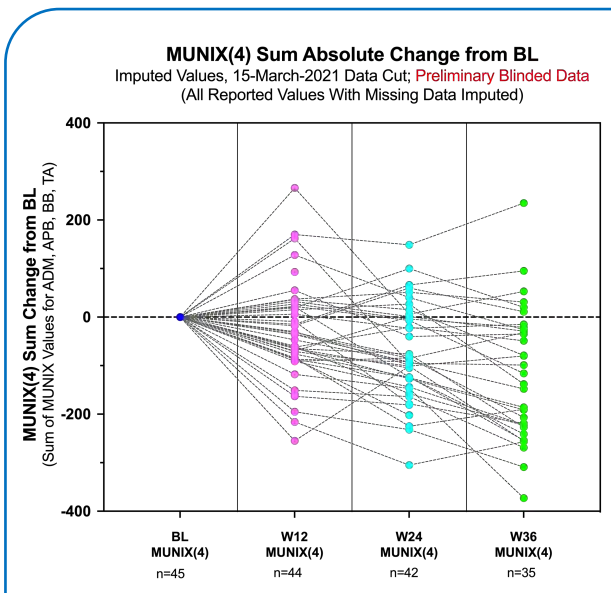
Early symptomatic ALS patients on stable background riluzole therapy

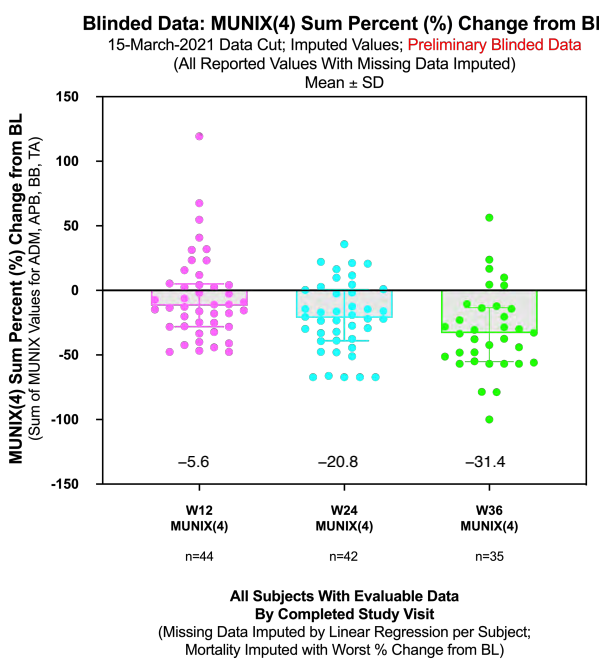
- Randomized (1:1, active (CNM-Au8): placebo; n=45); 36-week treatment period with open-label extension
- Primary endpoint MUNIX(4)sum change from Baseline (BL) for: abductor digiti minimi (ADM) abductor pollicis brevis (APB) tibialis anterior (TA), biceps brachii (BB)

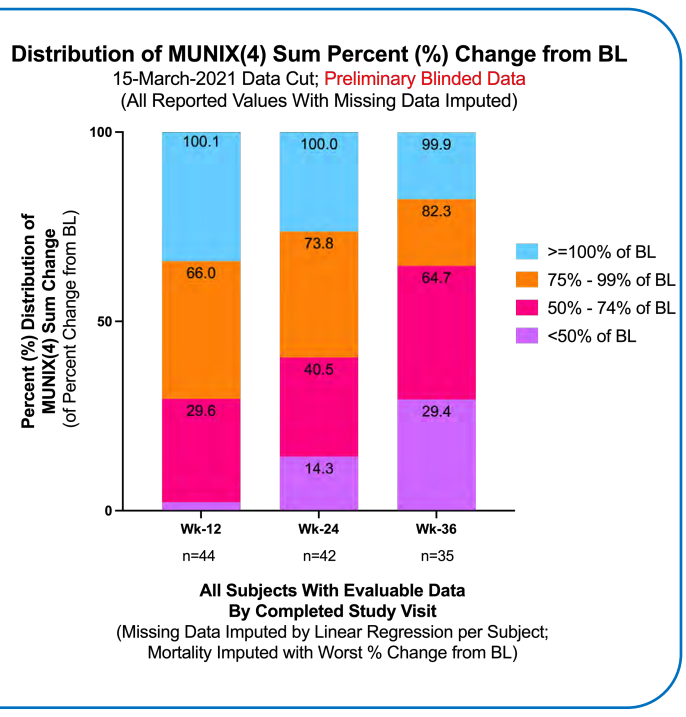
Baseline (BL) Demographics

Subjects n (%)	Age [yrs.] mean (SD)	Months from ALS Diagnosis mean (SD)	Months from ALS Onset mean (SD)	Riluzole Treatment (%)	ALSFRS-R mean (SD)	FVC % mean (SD)
45 (100%) (M: 26 | F: 19)	59.1 (12.2)	4.9 (4.8)	16.7 (9.7)	89%	38.7 (6.0)	81.5 (16.7)

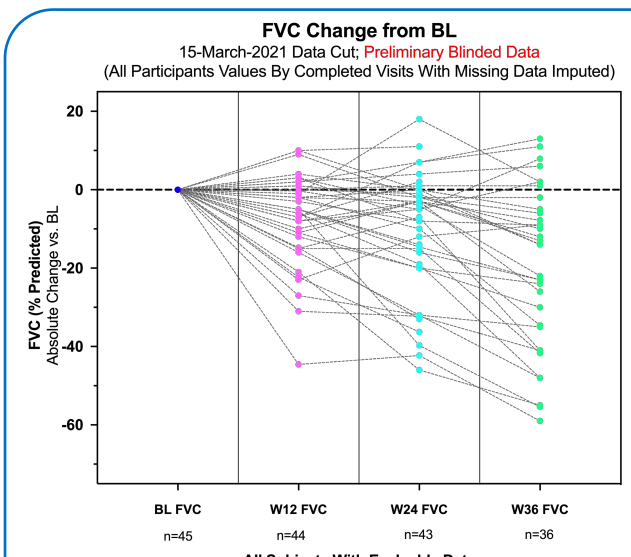
Primary Endpoint Improvement in MUNIX(4) Sum

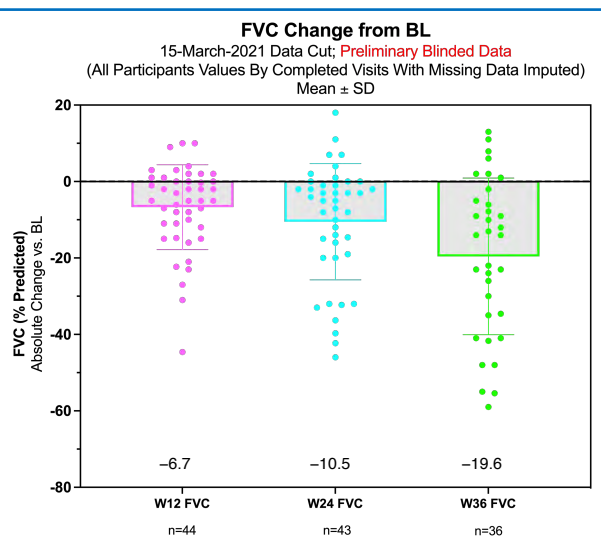






Change in Forced Vital Capacity (FVC)

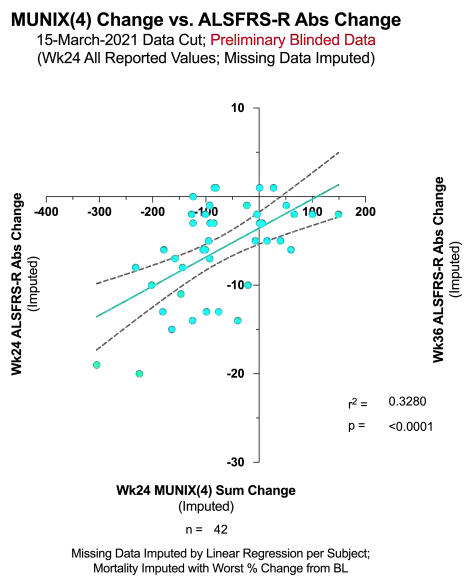


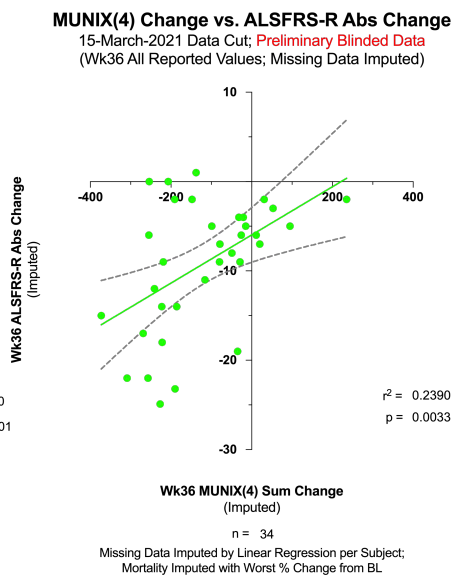


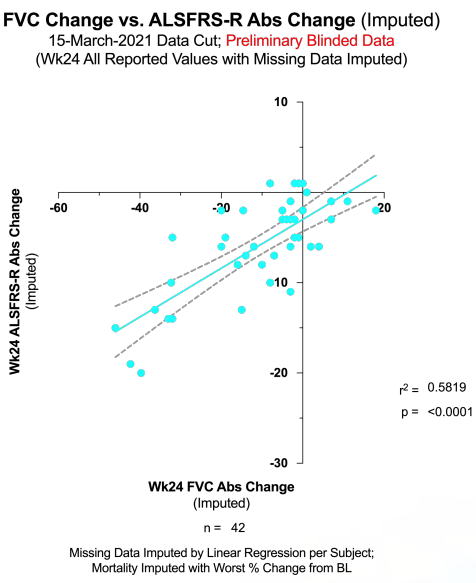
SVC Slope Decline (% points/month)	Avg. Slope Est. (9-months)
Empower (−2.73%)	-24.6%
Benefit (−2.74%)	-24.7%
PRO-ACT (-2.90%)	-26.1%

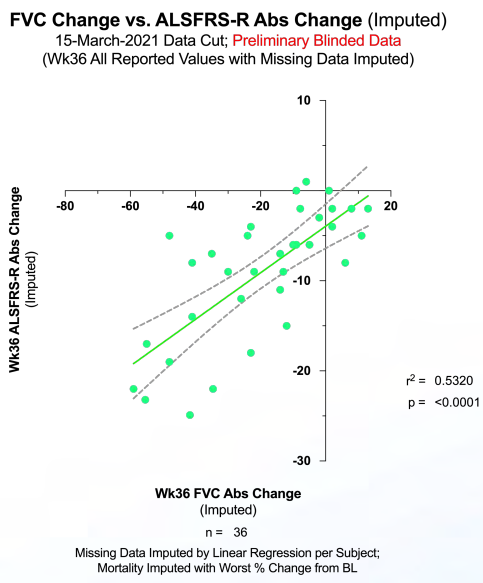
Andrews et al. JAMA Neurol. 2018;75(1):58-64.

MUNIX(4) Sum, FVC, & ALSFRS-R Data Consistency









Acknowledgements

We thank the study 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.

Study Design & Supplemental Information

SCAN ME

ENCALS

European Network to Cure ALS

May 12th, 2021 – May 14th, 2021

RESCUEALS

A Blinded Interim Update on RESCUE-ALS: A Randomized, Placebo-Controlled, Phase 2 Study to Determine the Effects of CNM-Au8 to Slow Disease Progression in Amyotrophic Lateral Sclerosis

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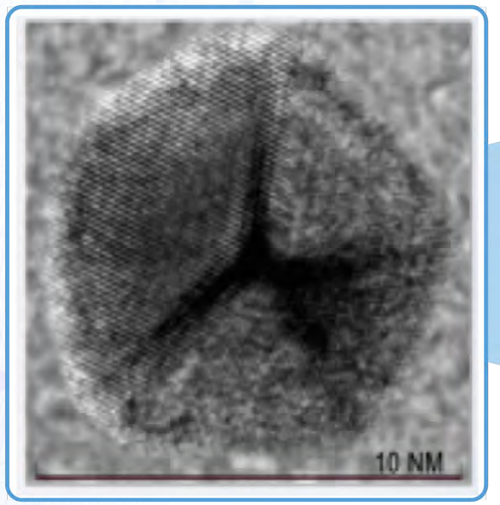
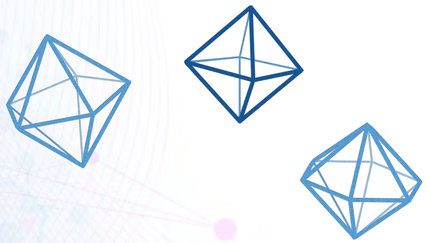
CNM-Au8 | MOA → Therapeutic Effects

Catalytic Gold Nanocrystals





Bioenergetic Mechanism

- Increased NAD [a]
- Increased ATP
- Decreased reactive oxygen species
- Increased proteostasis

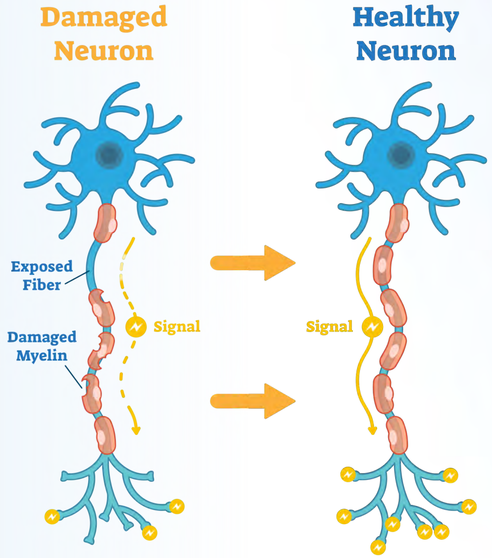
[a] Nicotinamide Adenine Dinucleotide

Enhanced Disease Response

- Increased energetic capacity

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

Remyelination



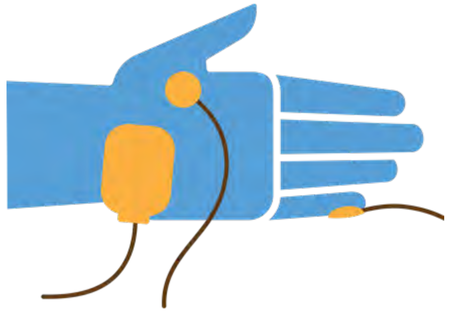
Neuro Repair

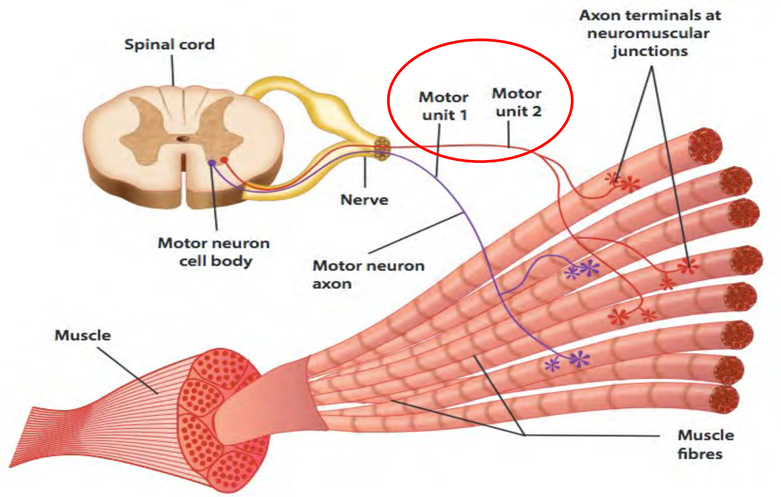
Measuring ALS Disease Progression

Electromyography Predicts Clinical Progression

Predictive Endpoint of Disease Progression

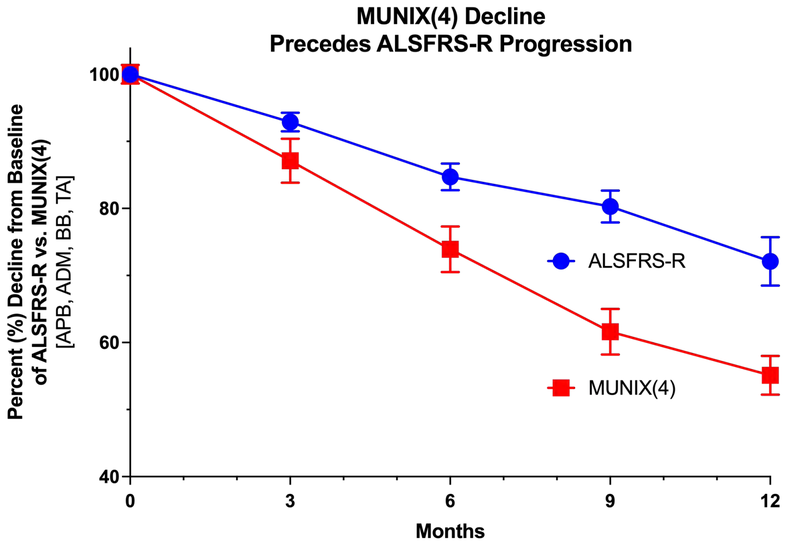
- **Loss of Motor Units**
  Motor Unit Index (MUNIX)





Clinical Endpoints

- **ALSFRS-R**
- **Pulmonary Function** (Vital Capacity)
- **Mortality**



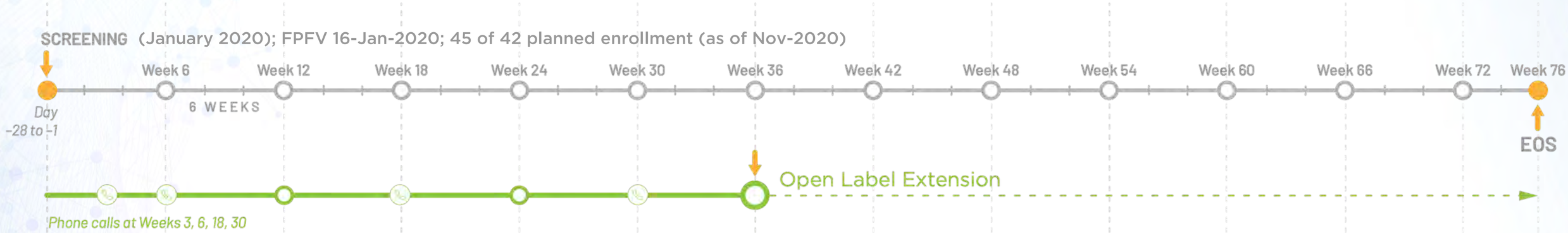
Neuwirth et al. JNNP 2015 Nov;86(11):1172-9.

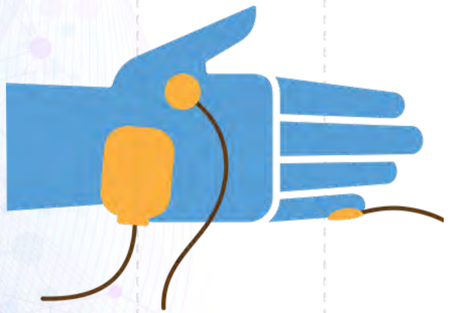
Study Design

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





1° **Change in Sum of Motor Unit Index**
For the Abductor Digiti Minimi (ADM), Abductor Pollicis Brevis (APB), Biceps Brachii (BB), Tibialis Anterior (TA)

2° **Key Secondary: FVC**

Exploratory Endpoints

- Other Electromyography (Split Hand$_{index,}$ Neurophysiology$_{index,}$ MUSIX, MScan MUNE)
- Change in Rate of ALSFRS-R progression
- QOL
- Combined Joint-Rank (Survival + ALSFRS-R)

Phase 2 RESCUE-ALS

Blinded Demographics

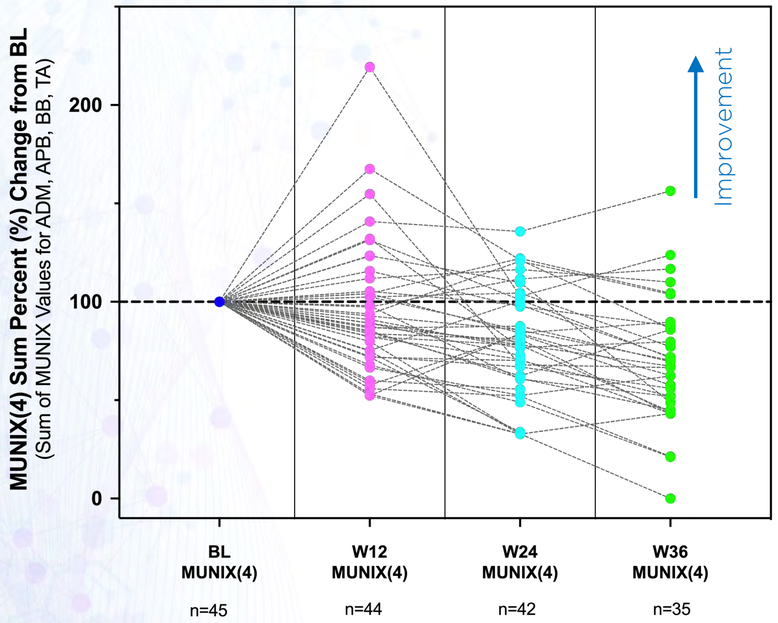
Demographics at Baseline

Baseline Values	Subjects n (%)	Age [yrs.] mean (SD)	Time from ALS Diagnosis [Months] mean (SD)	Time from ALS Onset [Months] mean (SD)	Riluzole Therapy (%)	ALSFRS-R mean (SD)	FVC % mean (SD)
All	45 (100%)	59.1 (12.2)	4.9 (4.8)	16.7 (9.7)	89%	38.7 (6.0)	81.5 (16.7)
Female	19 (42%)	59.8 (13.6)	5.2 (6.2)	19.3 (7.9)	84%	38.6 (5.5)	81.6 (18.1)
Male	26 (58%)	58.5 (11.4)	4.7 (3.6)	14.8 (10.5)	92%	38.7 (6.5)	81.3 (15.9)

Primary Endpoint | MUNIX(4) Sum

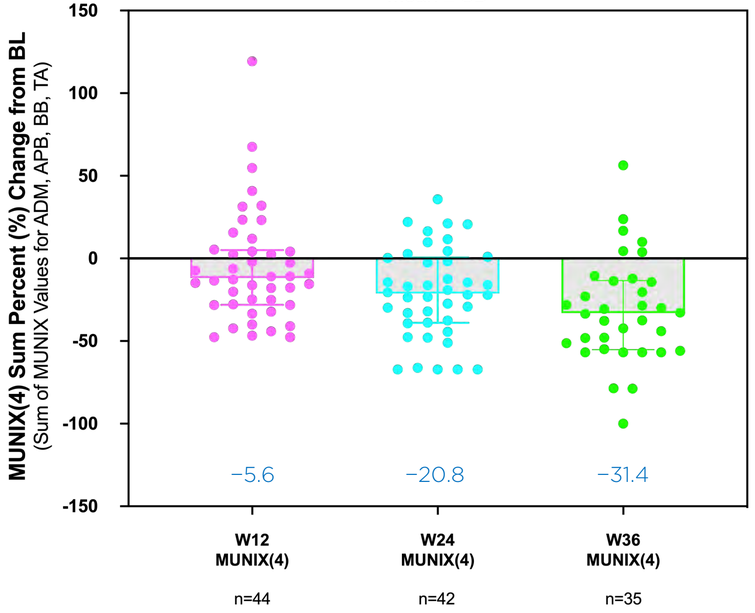
Preliminary Blinded Efficacy Data Support a Disease Modifying Potential For CNM-Au8 in the Treatment of ALS

Blinded Data: MUNIX(4) Sum Percent (%) Change from BL
15-March-2021 Data Cut; Imputed Values; Preliminary Blinded Data
(All Reported Values With Missing Data Imputed)



All Subjects With Evaluable Data
By Completed Study Visit
(Missing Data Imputed by Linear Regression per Subject;
Mortality Imputed with Worst % Change from BL)

Blinded Data: MUNIX(4) Sum Percent (%) Change from BL
15-March-2021 Data Cut; Imputed Values; Preliminary Blinded Data
(All Reported Values With Missing Data Imputed)
Mean ± SD



All Subjects With Evaluable Data
By Completed Study Visit
(Missing Data Imputed by Linear Regression per Subject;
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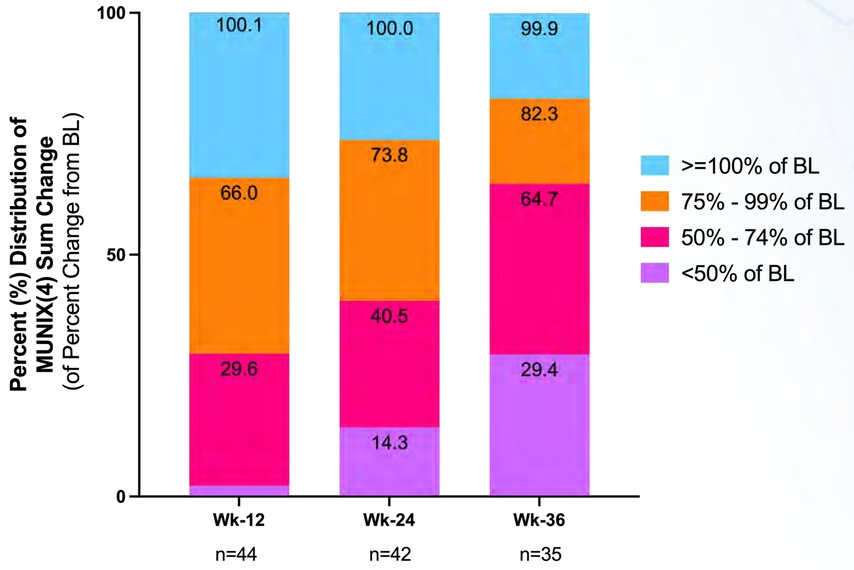
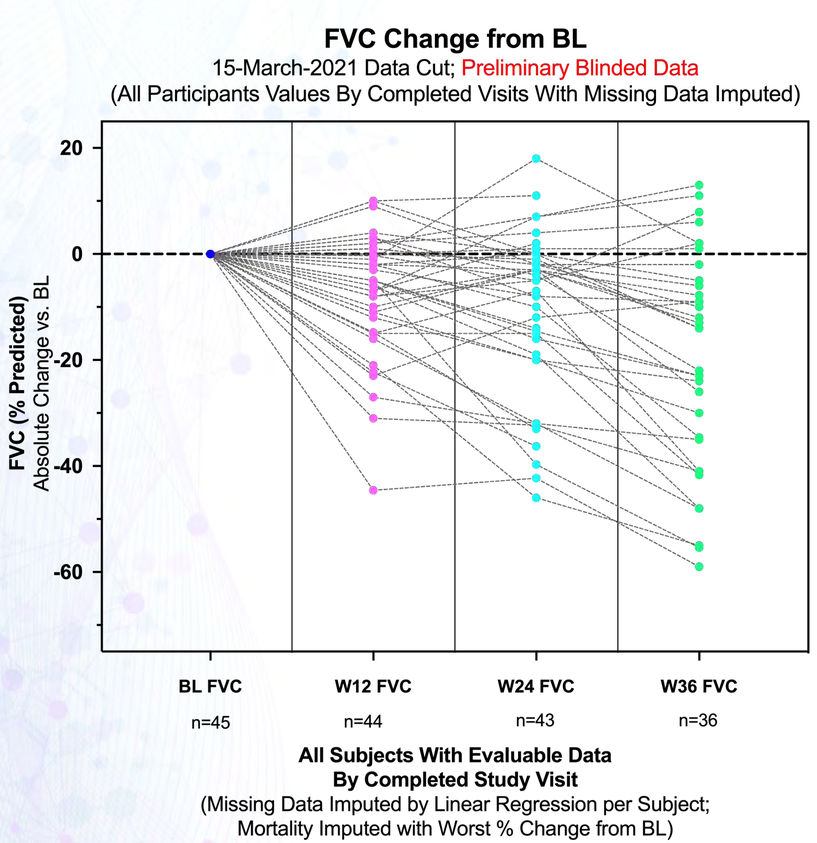
Distribution of MUNIX(4) Sum Percent (%) Change from BL
15-March-2021 Data Cut; Preliminary Blinded Data
(All Reported Values With Missing Data Imputed)

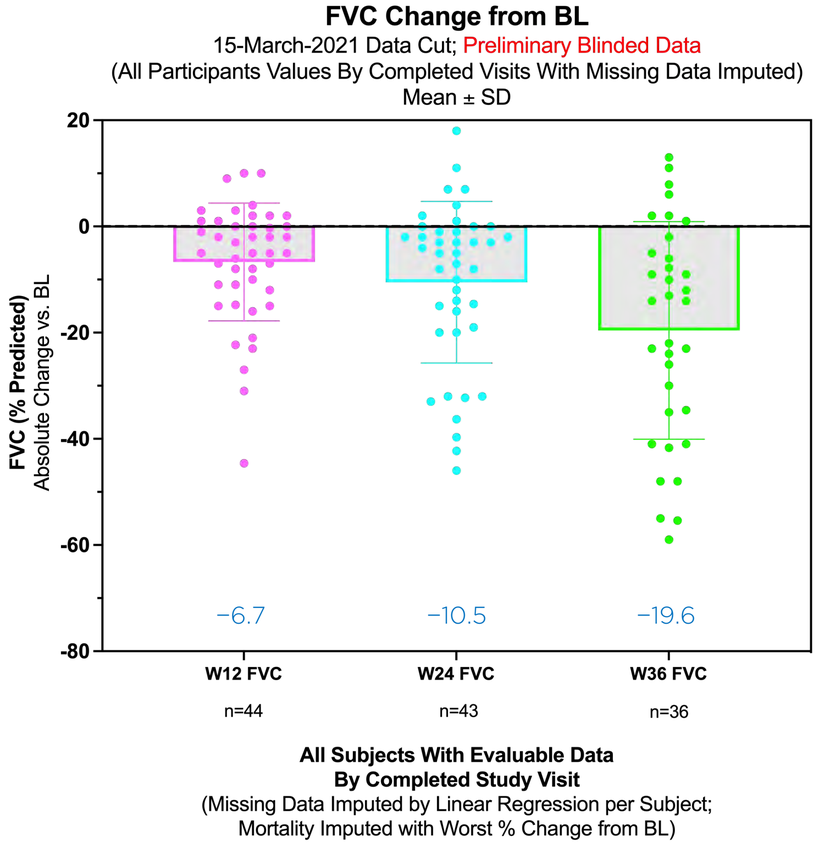


All Subjects With Evaluable Data
By Completed Study Visit
(Missing Data Imputed by Linear Regression per Subject;
Mortality Imputed with Worst % Change from BL)

Forced Vital Capacity | Change

Less Mean Decline Than Expected From Prior Clinical Trials





SVC Avg. Slope Decline (% points/month)	Slope Est. (9-months)
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PRO-ACT (-2.90%)	-26.1%

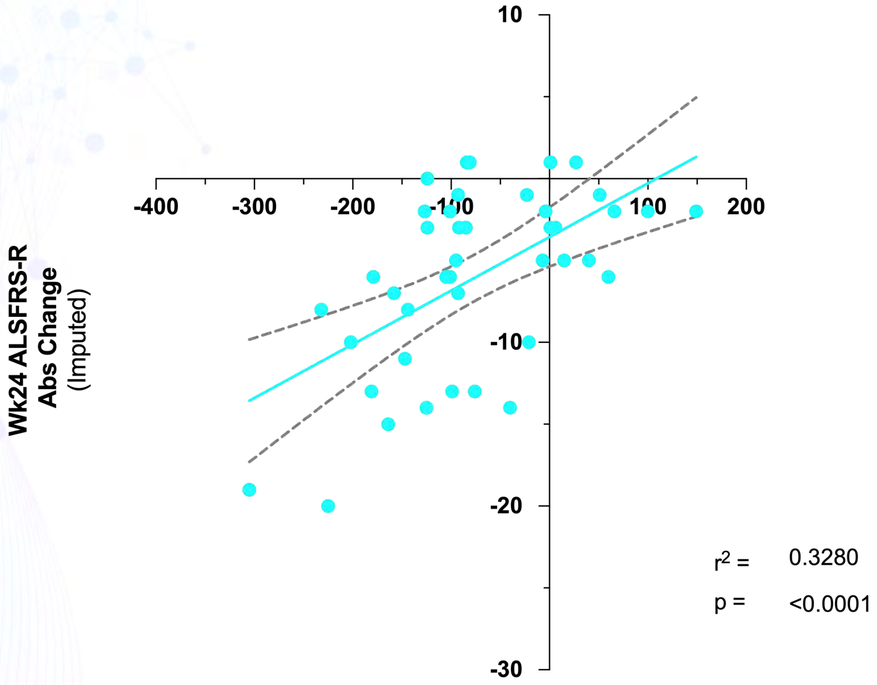
Andrews et al. JAMA Neurol. 2018;75(1):58-64.

RESCUEALS

MUNIX(4) vs. ALSFRS-R Change

Correlations Demonstrate Internal Data Consistency

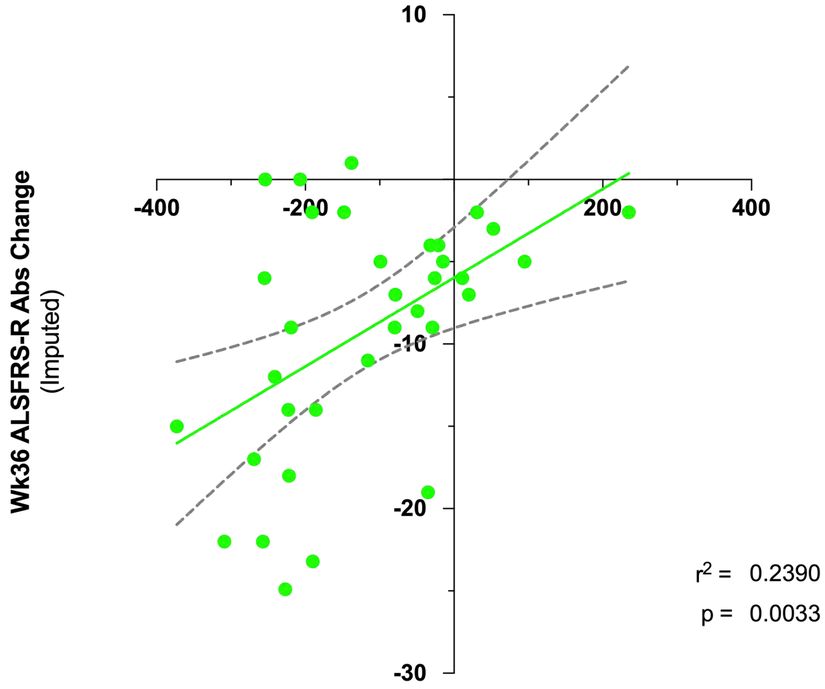
MUNIX(4) Change vs. ALSFRS-R Abs Change
15-March-2021 Data Cut; Preliminary Blinded Data
(Wk24 All Reported Values; Missing Data Imputed)



n = 42

Missing Data Imputed by Linear Regression per Subject;
Mortality Imputed with Worst % Change from BL

MUNIX(4) Change vs. ALSFRS-R Abs Change
15-March-2021 Data Cut; Preliminary Blinded Data
(Wk36 All Reported Values; Missing Data Imputed)



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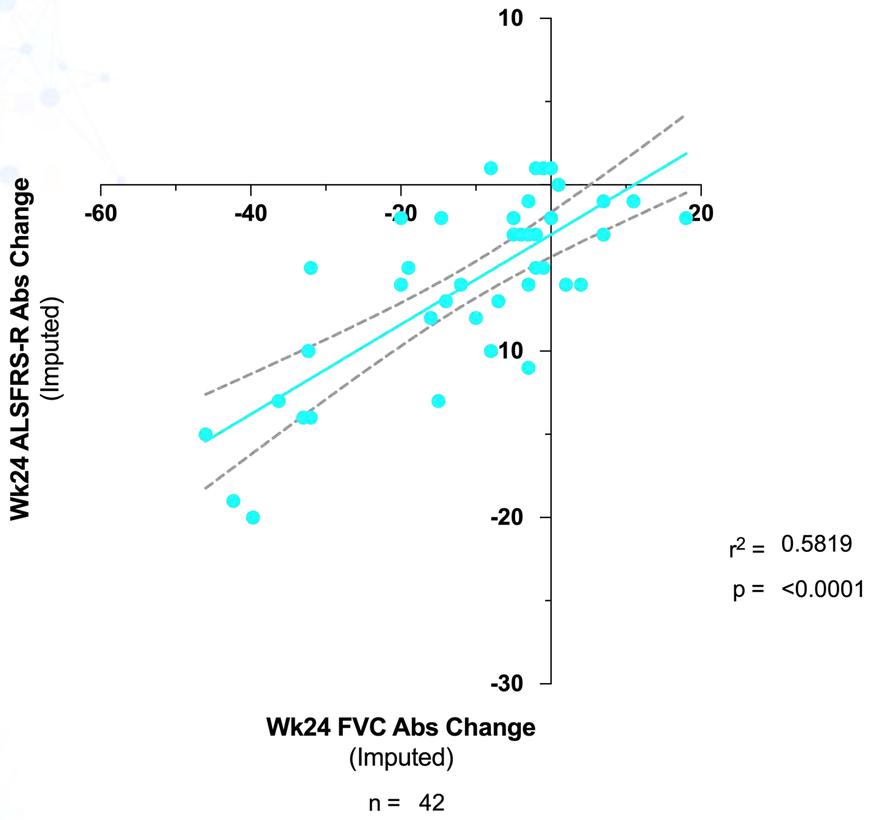
Missing Data Imputed by Linear Regression per Subject;
Mortality Imputed with Worst % Change from BL

FVC vs. ALSFRS-R Change

Correlations Demonstrate Internal Data Consistency

FVC Change vs. ALSFRS-R Abs Change (Imputed)
15-March-2021 Data Cut; Preliminary Blinded Data
(Wk24 All Reported Values with Missing Data Imputed)



r^2 = 0.5819
p = <0.0001

n = 42

Missing Data Imputed by Linear Regression per Subject;
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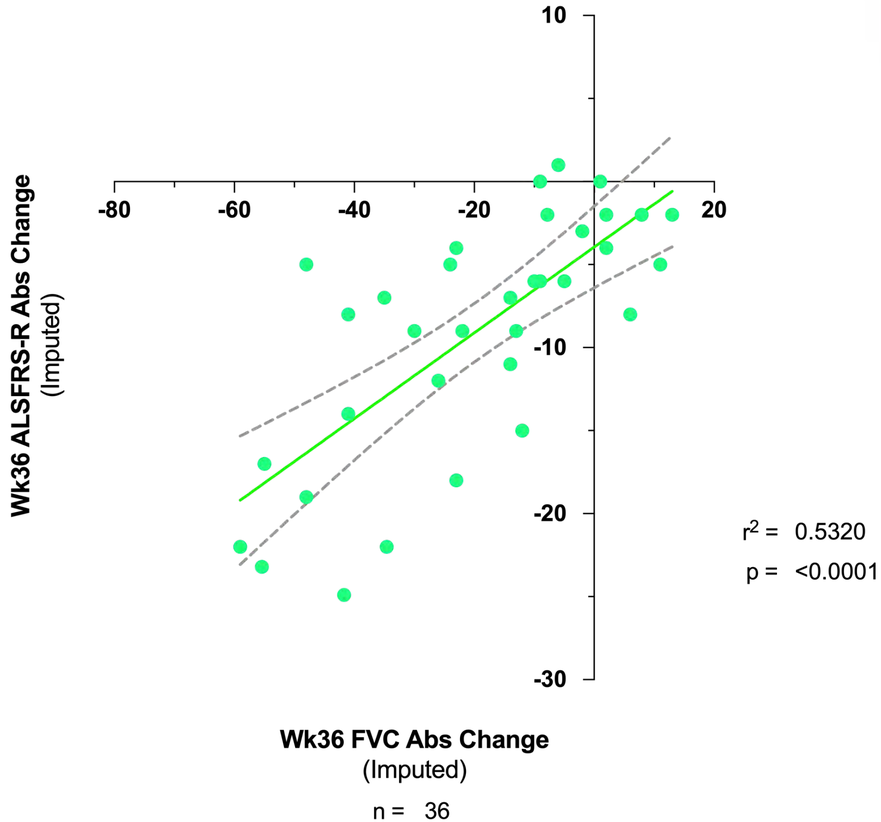
FVC Change vs. ALSFRS-R Abs Change (Imputed)
15-March-2021 Data Cut; Preliminary Blinded Data
(Wk36 All Reported Values with Missing Data Imputed)



r^2 = 0.5320
p = <0.0001

n = 36

Missing Data Imputed by Linear Regression per Subject;
Mortality Imputed with Worst % Change from BL

Acknowledgements

We thank the study 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.

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