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
<table>
<thead>
<tr>
<th></th>
<th>CLENE</th>
<th>Webinar Agenda</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>**CLENE</td>
<td>Webinar Agenda**</td>
</tr>
<tr>
<td>1</td>
<td><strong>CNM-Au8 overview &amp; upcoming milestones</strong></td>
<td>Rob Etherington, President and Chief Executive Officer</td>
</tr>
<tr>
<td>2</td>
<td><strong>ALS unmet need &amp; current treatment limitations</strong></td>
<td>Steve Vucic, MBBS (Hons I), PhD, DSc, FRACP, FAHMS, Northcott Chair of Neurology</td>
</tr>
<tr>
<td>3</td>
<td><strong>RESCUE-ALS Intro &amp; Results</strong></td>
<td>Robert Glanzman (Clene CMO), Matthew Kiernan, AM, PhD, DSc, FRACP, FAHMS, Bushell Chair of Neurology</td>
</tr>
<tr>
<td>4</td>
<td><strong>Questions &amp; Answers</strong></td>
<td>Dr. Robert Glanzman (Clene CMO), Dr. Kiernan, Dr. Vucic, and Rob Etherington (Clene CEO)</td>
</tr>
</tbody>
</table>
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™**

<table>
<thead>
<tr>
<th>NANOTherapeutic</th>
<th>Indication</th>
<th>Research Description</th>
<th>Preclinical</th>
<th>Ind Filing</th>
<th>Phase 1</th>
<th>Phase 2 or EAP</th>
<th>Phase 3</th>
<th>Anticipated Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>CNM-Au8® Gold Nanocrystal Suspension</td>
<td>Amyotrophic Lateral Sclerosis</td>
<td>Healey ALS Platform Trial Harvard MGH (Registration Trial)</td>
<td></td>
<td></td>
<td></td>
<td>2H 2022</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RESCUE-ALS Phased 2 (Australia)</td>
<td></td>
<td></td>
<td></td>
<td>COMPLETED</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>ALS Expanded Access</td>
<td>MGH ALS Harvard (MGH) Expanded Access Programs</td>
<td></td>
<td></td>
<td></td>
<td>ONGOING</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Multiple Sclerosis</td>
<td>VISIONARY-MS Phase 2</td>
<td></td>
<td></td>
<td></td>
<td>1H 2023*</td>
<td></td>
<td>COHORT 1 COMPLETED</td>
</tr>
<tr>
<td></td>
<td>Parkinson's Disease</td>
<td>RepairMS Phase 2 Brain Imaging Biomarker Study</td>
<td></td>
<td></td>
<td></td>
<td>COMPLETED</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>RepairPD Phase 2 (Anticipated Launch in 2021)</td>
<td></td>
<td></td>
<td></td>
<td>1H 2024</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNM-ZnAg (zinc-silver)</td>
<td>Anti-viral Anti-bacterial</td>
<td>ZnAgSTUDY Phase 2</td>
<td></td>
<td></td>
<td></td>
<td>1H 2022</td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNM-AgZn17 (silver-zinc gel)</td>
<td>Wound Healing, Burn Treatment</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CNM-PtAu7 (platinum-gold)</td>
<td>Oncology</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

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

Improving Clinical Trial Outcomes in ALS

Improving Clinical Trial Outcomes in ALS

Represents a major limitation to developing effective therapies
ALS Is a Multistep Disease Process

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

6-step process
Australia

6-step process
Japan

5-step process
South Korea

6-step process
UK, Ireland, & Netherlands

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

Steve Vucic, DSC,Mana Higashihara, PhD,Gen Sobue, MD,Naoki Aota, MD,Yuriko Doi, MD,Satoshi Kikunaga, PhD,Seong Hyun Kim, MD, PhD,Yooh Kim, MD, MPH, PhD,Ki-Young Oh, MD, PhD,Jinwook Park, MD, PhD,Sun Ho Kim, MPH,Faye Talman, PhD,Panarat Murnon, PhD, and
Matthew C. Kienan, DSC, the PACT/ALS Consortium

Improving clinical trial outcomes in amyotrophic lateral sclerosis

Matthew C. Kiernan1,2,8, Steve Vucic5, Kevin Talbot6, Christopher J. McDermott2,5,6, ria Hardiman7,8, Jeremy M. Shefner9, Ammar Al-Chalabi10, William Huynh1,2, Hert Cudkovic11,12, Paul Talman11,12, Leonard H. Van den Berg14, Thanuja Dharmadasa4, Paul Wicks11,15, Claire Reilly11,16 and Martin R. Turner11,4

<table>
<thead>
<tr>
<th>Repurposed drugs</th>
<th>Existing use</th>
<th>Targeted pathogenic mechanism</th>
<th>ALS trial identifier</th>
<th>Primary outcome measures</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tauroursodeoxycholic acid</td>
<td>Familial amyloid polyneuropathy (transthyretin)</td>
<td>Endoplasmic reticulum stress, mitochondrial dysfunction</td>
<td>NCT03488524</td>
<td>ALSFRS-R</td>
<td>Reduction in functional decline</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NCT03127514</td>
<td>Survival</td>
<td>Prolonged</td>
</tr>
<tr>
<td>Mexiletine</td>
<td>Cardiac arrhythmia</td>
<td>Neuronal hyperexcitability</td>
<td>NCT01811355</td>
<td>Daily cramp frequency</td>
<td>Significant reduction in cramp frequency and severity</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NCT02781454</td>
<td>Change in resting motor threshold</td>
<td>Pending</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NCT010849770</td>
<td>Safety</td>
<td>Safe</td>
</tr>
<tr>
<td>Ezogabine</td>
<td>Epilepsy</td>
<td>Neuronal hyperexcitability</td>
<td>NCT02450552</td>
<td>Change in short-interval intracortical inhibition as measured by transcranial magnetic stimulation</td>
<td>Pending</td>
</tr>
<tr>
<td>Dimethyl fumarate</td>
<td>Relapsing–remitting multiple sclerosis</td>
<td>Neuroinflammation, upregulation of Treg cells</td>
<td>ACTRN12618000534280</td>
<td>ALSFRS-R</td>
<td>Pending</td>
</tr>
<tr>
<td>IL-2</td>
<td>Metastatic melanoma, metastatic renal cancer</td>
<td>Neuroinflammation, cytokine signalling, upregulation of Treg cells</td>
<td>NCT02059759</td>
<td>Change in number of Treg cells</td>
<td>Pending</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NCT03039673</td>
<td>Survival</td>
<td>Pending</td>
</tr>
<tr>
<td>Edaravone</td>
<td>Acute stroke</td>
<td>Oxidative stress</td>
<td>NCT01492686</td>
<td>ALSFRS-R</td>
<td>Significant slowing of disease progression vs placebo</td>
</tr>
<tr>
<td>Dolasetrindip, abacavir and lamivudine (Triumeq)</td>
<td>HIV infection</td>
<td>HERVK expression</td>
<td>NCT02868580</td>
<td>Safety</td>
<td>Safe</td>
</tr>
<tr>
<td>Ibudilast (MN-166)</td>
<td>Chronic obstructive pulmonary disease</td>
<td>Neuroinflammation and microglial activation</td>
<td>NCT02238626</td>
<td>ALSFRS-R</td>
<td>Safety and tolerability</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NCT02714036</td>
<td></td>
<td>Pending</td>
</tr>
<tr>
<td>Tamoxifen</td>
<td>Breast cancer</td>
<td>Neuroinflammation, proteostasis</td>
<td>NCT02166944</td>
<td>ALSFRS-R</td>
<td>Not significant</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NCT00214110</td>
<td>Muscle strength</td>
<td>Pending</td>
</tr>
<tr>
<td>Memantine</td>
<td>Advanced stages of Alzheimer disease</td>
<td>Glutamate excitotoxicity</td>
<td>NCT01020331</td>
<td>ALSFRS-R</td>
<td>No significant effect</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NCT02118727</td>
<td>ALSFRS-R</td>
<td>Pending</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NCT00409721</td>
<td>ALSFRS-R, FVC, muscle strength, cognitive function</td>
<td>Pending</td>
</tr>
<tr>
<td>Perampanel</td>
<td>Partial-onset seizures</td>
<td>Glutamate excitotoxicity (AMPA-receptor mediated)</td>
<td>NCT03019419</td>
<td>ALSFRS-R</td>
<td>Pending</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NCT03377309</td>
<td>Safety</td>
<td>Pending</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NCT03793868</td>
<td>Motor threshold</td>
<td>Pending</td>
</tr>
<tr>
<td>Rasagiline</td>
<td>Parkinson disease</td>
<td>Oxidative stress and apoptosis</td>
<td>NCT0178603</td>
<td>ALSFRS-R</td>
<td>Pending</td>
</tr>
<tr>
<td>Mastinib</td>
<td>Mastocytosis, severe asthma</td>
<td>Neuroinflammation (microglia)</td>
<td>NCT02586877</td>
<td>ALSFRS-R</td>
<td>Significant slowing in functional decline</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NCT0317267</td>
<td>ALSFRS-R</td>
<td>Pending</td>
</tr>
<tr>
<td>Methylcobalamin</td>
<td>Vitamin B12 deficiency</td>
<td>Glutamate excitotoxicity</td>
<td>NCT03548311</td>
<td>ALSFRS-R</td>
<td>No significant effect</td>
</tr>
<tr>
<td>Cull(II)ATSM</td>
<td>PET ligand</td>
<td>Copper deficiency</td>
<td>NCT02870634</td>
<td>Safety</td>
<td>Pending</td>
</tr>
<tr>
<td>Arimoclomol</td>
<td>Insulin resistance, complications of diabetes mellitus</td>
<td>Impaired proteostasis</td>
<td>NCT00244244</td>
<td>Safety</td>
<td>Safe</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NCT00706147</td>
<td>Time to death, tracheostomy or permanent assisted ventilation</td>
<td>Safe, no significant effect on outcomes</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NCT03249146</td>
<td>Combined assessment of function and survival</td>
<td>Pending</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>NCT03836716</td>
<td>Safety</td>
<td>Pending</td>
</tr>
</tbody>
</table>
Whole System Approach
Normalise Cellular Function – Energy Dependent Processes

- Impaired glutamate intake
- Glutamate excitotoxicity
- Increased oxidative stress
- Mitochondrial dysfunction
- Neurofilament accumulation
- Pump dysfunction
- Dysfunction of exonal transport systems
- Release of inflammatory mediators
- Secretion of toxic factors
- TDP-43/FUS
  Mutations in C9orf72, TARDBP, FUS and SOD1 genes

Astrocyte
Microglia
Presynaptic neuron
NMDA
AMPA
SOD1 aggregates
Mutant SOD1
EAAT
Whole System Approach
Normalise Cellular Function – Energy Dependent Processes
Robert Glanzman, MD FAAN
Chief Medical Officer
Clene Nanomedicine, Inc
36-Week Treatment Period (n=42) 30mg, Placebo

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

Key Secondary
- Absolute MUNIX(4) change
- Forced Vital Capacity (FVC)

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

Phase 2 RESCUE ALS
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
We thank FightMND for its philanthropic support of the RESCUE-ALS study
“Befitting of Lou Gehrig, whose legacy is intertwined with ALS, we swung for the fences and ended with a stand-up triple...”
**Baseline Demographics**

<table>
<thead>
<tr>
<th>Baseline Value</th>
<th>Age (yrs)</th>
<th>Sex n, (%)</th>
<th>Onset Site n, (%)</th>
<th>Months from Diagnosis</th>
<th>Months from Onset</th>
<th>FVC (% pred.)</th>
<th>ALSFRS-R Score</th>
<th>ENCALS Risk Profile¹</th>
</tr>
</thead>
<tbody>
<tr>
<td>All (n=45)</td>
<td>59.1 (12.3)</td>
<td>M: 26 (58%)</td>
<td>L: 33 (73%)</td>
<td>3.1 (3.0)</td>
<td>15.9 (9.3)</td>
<td>81.5 (16.7)</td>
<td>38.7 (5.95)</td>
<td>-4.4 (1.8)</td>
</tr>
<tr>
<td>CNM-Au8 30mg (n=23)</td>
<td>57.0 (13.3)</td>
<td>M: 13 (57%)</td>
<td>L: 16 (70%)</td>
<td>3.0 (2.9)</td>
<td>15.5 (7.6)</td>
<td>84.5 (18.3)</td>
<td>38.6 (6.6)</td>
<td>-4.6 (1.7)</td>
</tr>
<tr>
<td>Placebo (n=22)</td>
<td>61.3 (10.9)</td>
<td>M: 13 (59%)</td>
<td>L: 17 (77%)</td>
<td>3.3 (3.2)</td>
<td>16.1 (10.9)</td>
<td>78.2 (14.5)</td>
<td>38.8 (5.4)</td>
<td>-4.2 (1.8)</td>
</tr>
</tbody>
</table>

89% of participants treated with riluzole as background standard of care
Neurophysiology
MUNIX¹

Pulmonary Function
(Forced Vital Capacity)

Functional Status & QOL
(ALSFRS-R,
ALS Specific QOL)

Disease Progression & Survival

¹ Study was only powered for MUNIX(4) primary endpoint (Box 1)
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
Evidence for Motor Neuron Protection

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

All Randomized

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

<table>
<thead>
<tr>
<th>Weeks (Post-Randomization)</th>
<th>MUNIX(4) Sum Percent (%) Change (LS Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>&lt; 0.06</td>
</tr>
<tr>
<td>24</td>
<td>NS</td>
</tr>
<tr>
<td>36</td>
<td>NS</td>
</tr>
</tbody>
</table>

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

Limb Onset (Pre-specified)

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

<table>
<thead>
<tr>
<th>Weeks (Post-Randomization)</th>
<th>MUNIX(4) Sum Percent (%) Change (LS Mean)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>&gt; 0.04</td>
</tr>
<tr>
<td>24</td>
<td>&gt; 0.04</td>
</tr>
<tr>
<td>36</td>
<td>&gt; 0.04</td>
</tr>
</tbody>
</table>

P-value is based on mixed model repeat measures with treatment, visit, treatment by visit interaction as fixed effects, and baseline value and ENCS score as covariates. An unstructured covariance model was used.
Pulmonary Function
Forced Vital Capacity (FVC)
Directional FVC Benefit
Secondary Endpoint\(^1\) (FVC % predicted, LS Mean Change, All Randomized)

\(^1\)Study Not Powered for FVC change
Secondary Endpoint\(^1\) (FVC % predicted, LS Mean Change, Continuous Slope, Post Hoc)

**Directional FVC Benefit**

All Randomized

FVC (% predicted) Change from Baseline
RESCE-ALS Exploratory Endpoint (Post Hoc)
Mixed Model Repeat Measure (ITT Population, All Randomized)
LS Mean Difference

2.8 (CI: -6.9, 12.6)
\(p = \text{NS}\)

23%

Active, \(n = 23\)
Placebo, \(n = 22\)

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 ENCAFS score as factors. Time is treated as a random effect.

Limb Onset (pre-specified)

FVC (% predicted) Change from Baseline
RESCE-ALS Exploratory Endpoint (Post Hoc)
Mixed Model Repeat Measure (ITT Population, Limb Onset)
LS Mean Difference

6.8 (CI: -6.2, 19.8)
\(p = \text{NS}\)

49%

Active, \(n = 17\)
Placebo, \(n = 16\)

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 ENCAFS score as factors. Time is treated as a random effect.

\(^1\)Study Not Powered for FVC change
Functional Status and QOL
(ALSFRS-R, ALSSQOL-SF)
**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**

![Graph showing ALSFRS-R Score Change](image)

- 1.0 (CI: -1.6, 3.6)
- \( p = \text{NS} \)
- 17%

**Active**, \( n = 23 \)
- Placebo, \( n = 22 \)

**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 ENCLAS 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**

![Graph showing ALSFRS-R Score Change](image)

- 1.8 (CI: -1.3, 5.0)
- \( p = \text{NS} \)
- 28%

**Active**, \( n = 16 \)
- Placebo, \( n = 17 \)

**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 ENCLAS score as factors. Time is treated as a random effect.
Significant Impact on ALSFRS-R Decline

Exploratory (ALSFRS-R Responder Analysis, All Randomized)

ALSFRS-R 6-point Decline Responder

Proportion with < 6 point decline

RESCUE-ALS Exploratory Endpoint (ITT Population, All Randomized)

Weeks (Post-Randomization)

Proportion (%) with < 6 point ALSFRS-R Decline

p = NS

p < 0.04

<table>
<thead>
<tr>
<th>Weeks</th>
<th>Proportion (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>80</td>
</tr>
<tr>
<td>24</td>
<td>60</td>
</tr>
<tr>
<td>36</td>
<td>40</td>
</tr>
</tbody>
</table>

Active, n = 23
Placebo, n = 22

P-value is based on a Chi-Square test
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

Week-12 LS Mean

Week-24 LS Mean

Week-36 LS Mean

-0.5

0.0

0.5

ALS Specific Quality of Life-Short Form Total Score Change (LS Mean)

Weeks
(Post-Randomization)

12

24

36

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.

<table>
<thead>
<tr>
<th>Weeks</th>
<th>CNM-Au8 30mg</th>
<th>Placebo</th>
</tr>
</thead>
<tbody>
<tr>
<td>12</td>
<td>active = 23</td>
<td>placebo = 21</td>
</tr>
<tr>
<td>24</td>
<td>active = 23</td>
<td>placebo = 20</td>
</tr>
<tr>
<td>36</td>
<td>active = 22</td>
<td>placebo = 19</td>
</tr>
</tbody>
</table>

ITT Population; Data on File, Clene Nanomedicine, Inc.
Disease Progression & Survival
ALS Disease Progression defined as:

- Death, or
- Tracheostomy, or
- Non-invasive ventilation, or
- Gastrostomy tube
RESCEUALS | Potential Survival Signal
Exploratory Endpoint (Observed Survival vs. Predicted)

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

Start of Open Label Extension (Wk36+)

Observed Survival
ENCAVES Predicted

RESCEUALS.Oberved
ENCAVES.Predicted (Median.Est)

Weeks (Post-Randomization)

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
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)
These Results Support Cellular Energetic Impairment as a Therapeutic Target in ALS
Rob Etherington
Clene Nanomedicine, Inc
President & CEO
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
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
Anticipated Timeline & Upcoming Milestones
2020 - 2023

- **Amyotrophic Lateral Sclerosis (ALS)**
  - 2020: RESCUEALS Phase 2
  - 2021: DATA
  - 2022: HEALEY ALS Platform Trial Phase 3
  - 2023: DATA, NDA SUBMISSION

- **Parkinson's Disease (PD)**
  - 2020: RepairPD Phase 2 target engagement
  - 2021: DATA
  - 2022: RESCUEPD Phase 2

- **Multiple Sclerosis (MS)**
  - 2021: Visionary MS Study Phase 2
  - 2022: DATA
  - 2023: RepairMS Phase 2 target engagement

- **Anti-Viral Anti-Bacterial**
  - 2021: ZnAgSTUDY
  - 2022: DATA

◆ = COMPLETED
Questions & Answers