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-4/A 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.
**Lead Asset:** CNM-Au8 for Neuro Repair

- Nanocatalyst of Intracellular Biological Reactions
- Robust Preclinical Remyelination & Neuroprotection Data Across Multiple Animal Models in: MS, ALS, and Parkinson’s Disease
- NOAEL Findings From All Toxicity Studies
- Acceptable Phase 1 Safety Profile
- Up to 48-weeks Exposure in Clinical Trials

**Unmet Medical Need & Market Opportunity**

- No Effective Disease-Modifying Drugs for ALS or PD
- No MS Therapies Clinically Impact Remyelination & Neurorepair
- Remyelination and Neurorepair Sales Could Exceed $10B per annum\(^1\)
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\(^1\) Data on file, Clene Nanomedicine, Inc.
Novel electro-chemistry platform produces catalytic Clean Surface Nanocrystal drugs designed to avoid toxicities associated with synthetic chemistry.

### Clean Surface Nanocrystal Therapeutics (CSN®)

**CSN® PLATFORM**

100+ Granted Patents

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**CLENE Platform & Pipeline**

<table>
<thead>
<tr>
<th>CSN® THERAPEUTIC</th>
<th>INDICATION</th>
<th>RESEARCH</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 (CSN® gold)</td>
<td>Bioenergetic Nanocatalyst</td>
<td>Healey ALS Platform Trial</td>
<td>Harvard MGH (Registration Trial)</td>
<td>1H 2022</td>
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<td></td>
<td></td>
<td>RESCUEALS</td>
<td>Phase 2 (Australia)</td>
<td>2H 2021</td>
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<tr>
<td></td>
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<td>MGHALS Expanded Access</td>
<td></td>
<td>Ongoing</td>
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</tr>
<tr>
<td>CNM-ZnAg (CSN® zinc-silver)</td>
<td>Anti-viral Anti-bacterial</td>
<td>@VISIONARY-MS Phase 2</td>
<td>Harvard (MGH) Expanded Access Program</td>
<td>1H 2022*</td>
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<tr>
<td>CNM-AgZn17 (CSN® silver-zinc gel)</td>
<td>Wound Healing, Burn Treatment</td>
<td>RepairMS Phase 2</td>
<td>Brain Imaging Biomarker Study</td>
<td>2H 2021*</td>
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<tr>
<td>CNM-PtAu7 (CSN® platinum-gold)</td>
<td>Ontology</td>
<td>RepairPD Phase 2</td>
<td>Brain Imaging Biomarker Study</td>
<td>1H 2021</td>
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<td>RESCUEPD Phase 2</td>
<td>(Anticipated Launch in 2021)</td>
<td>1H 2024</td>
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</tbody>
</table>

*Subject to ongoing COVID-19 related site research restrictions generally implemented to protect MS patients taking standard-of-care immunosuppressive therapies.
Evolution of Gold as a Therapeutic Modality

2500–1000 BC
Chinese & Ayurvedic Gold Preparations (China, Arabia, India)

1930–1980s
Monoatomic Gold Salts for Rheumatoid Arthritis
(IM Sodium Aurothiomalate; IM Aurothioglucose; Oral Auranofin)
gold 3,4,5-triacetoxyl-6-(acetyloxymethyl) oxane-2-thiolate; triethylphosphanium

1950s–2000s
Surface Modified and Functionalized Colloidal Gold Particles
Drug Carriers; Photothermal Therapy

2020+
Catalytic Clean Surfaced Faceted Gold Nanocrystals
Pioneering Bioenergetic Nanocatalysis
Clene’s Patented Breakthrough
CNM-Au8 | Bioenergetic Nanocatalyst

Lead Asset

- Clean Surfaced Faceted Gold Nanocrystal
- 13 nm Median Diameter (Ribosome = 20-30 nm)
- >1 Quadrillion Nanocrystals per 60 mL Dose (At 30 mg)
- Oral Suspension; Once Daily

Novel mechanism of action to address a range of CNS diseases

CNM-Au8

Improved Cellular Bioenergetics

- Remyelination Failure In MS
- Parkinson’s Disease
- Amyotrophic Lateral Sclerosis
CNM-Au8 Integrating Physics With Biology
Nanocatalytic Electron Transfer

Surface Based Catalytic Activity

Electrons (e-) Move Freely Across Nanocrystal Surface

Vertices, Edges, & Faces Key to Catalytic Activity

Clean-Surfaced Nanocrystals

Up to 4,600 e⁻ per second per nanocystal

AuNP Catalyzed Oxidation of Ascorbic Acid

a. Rayleigh scattering measured by dark field microscopy of surface plasmon resonance of scattering spectra of the AuNP decahedron before and at 1, 2, 3 and 60 min after electron injection by ascorbate ions.

b. Spectral shift as a function of time for the catalysis reaction and for the control experiment.

Treating Bioenergetic Failure | Common Pathological Mechanism In Neurodegenerative Disorders (MS, ALS, PD)

ALS Neuronal Metabolic Failure
- Cognitive Impairment
- Dysphagia/Dysarthria
- Respiratory Insufficiency
- Muscle Weakness/Atrophy
- Neuromuscular Junction Impairment

MS Oligodendrocyte Remyelination Failure and Neuronal Die-Off
- Cognitive Impairment
- Visual Impairment
- Spinal Cord (Movement)
- Dexterity & Coordination

CNM-Au8 MOA → Therapeutic Effects

**Catalytic Gold Nanocrystals**

**Bioenergetic Mechanism**

- Increased NAD \(^a\)
- Increased ATP
- Decreased reactive oxygen species
- Increased proteostasis

**Enhanced Disease Response**

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

**Remyelination**

- Damaged Neuron
- Healthy Neuron

**Neuro Repair**

\(^a\) Nicotinamide Adenine Dinucleotide
MOTOR NEURON DISEASE (ALS, Other Orphan Disorders)

ALS sales >$1B globally by 2029. Current drugs are largely ineffective, mostly generic.

Est. Diagnosed MND Patients by Region

MND includes amyotrophic lateral sclerosis, spinal muscular atrophy, hereditary spastic paraplegia, primary lateral sclerosis, progressive muscular atrophy, and pseudobulbar palsy.

MOTOR NEURON DISEASE

MULTIPLE SCLEROSIS -2.5M pts globally; $23B market

Only approved treatments are immunomodulators.

Est. Diagnosed MS Patients by Region


CNM-Au8 | Evidence for Bioenergetic Improvement
Therapeutic Activity Across Remyelination + Neuroprotection Models

<table>
<thead>
<tr>
<th>REMYELINATION</th>
<th>NEUROPROTECTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic Global CNS Demyelination</td>
<td>Neuroprotection: Dopaminergic</td>
</tr>
<tr>
<td>Chronic Cuprizone (CPZ) Pilot</td>
<td>PD Neurotoxin MPP In Vitro</td>
</tr>
<tr>
<td>Chronic CPZ Repeat Validation</td>
<td>MN Neuroprotection In Vitro, Astrocyte</td>
</tr>
<tr>
<td>Prevent CPZ Damage</td>
<td>MN Glutamate Excitotoxicity In Vitro</td>
</tr>
<tr>
<td>Post-Chronic CPZ Myelin Recovery</td>
<td>MN Amyloid beta In Vitro</td>
</tr>
<tr>
<td>Chronic CPZ Functional Outcome</td>
<td>MN Neuroprotection ALS SOD1, In Vivo</td>
</tr>
</tbody>
</table>

- Lysolecithin Focal Remyelination (I)
- Cerebral Palsy Remyelination Ex Vivo
- Neuroprotection: Motor Neuron

Nanocatalytic activity of clean-surfaced, faceted nanocrystalline gold enhances remyelination in animal models of multiple sclerosis

Andrew P. Robinson¹, Joanne Zhongyan Zhang²,³, Haley E. Titus¹, Molly Karl¹, Mikhail Merzliakov², Adam R. Dorfman², Stephen Karlik⁴, Michael G. Stewart⁵, Richard K. Watt⁶, Benjin D. Facer⁷, Jon D. Facer⁷, Noah D. Christian⁷, Karen S. Ho²,³, Michael T. Hotchkin²,³, Mark G. Mortenson²,³, Robert H. Miller²,³,⁹ & Stephen D. Miller¹,³
Successful Phase 1 First-In Humans Safety Trial + Chronic Animal Toxicity Studies

Phase 2 Brain Biomarker (Proof of Target Effect) $^{31}P$-Magnetic Resonance

Phase 2 & 3 ALS Clinical Neurorepair

Phase 2 MS Clinical Remyelination & Neurorepair

CNM-Au8 Clinical Program Overview
CNM-Au8 | Clean Toxicology Findings
All Studies Resulted in No Adverse Effect Level (NOAEL)\textsuperscript{a}

Standard ICH M3(R2) Toxicology Program

- **Genotoxicity**
  - *In Vitro & In Vivo* (Rodent)

- **Single Dose Toxicokinetics**
  - Canine

- **Max Feasible Toxicokinetics**
  - Rodent (1-Wk, SQ)

- **Chronic Toxicity Rodent**
  - Rodent (6-Month)

- **Safety Pharmacology**
  - CNS, CV, Renal

- **Multi-Dose Toxicokinetics**
  - Canine (7-Day)

- **Max Feasible Toxicokinetics**
  - Canine (3-Wk)

- **Chronic Toxicity Canine**
  - Canine (9-Month)

- **Dose Range Finding**
  - Rodent, Minipig

- **MTD Toxicokinetics**
  - Canine (4-Wk)

- **High Dose Toxicokinetics**
  - Rodent (3-Wk)

\textsuperscript{a} NOAEL = No Dose Limiting Toxicities Observed
CNM-Au8 | Well Tolerated With No Known Safety Issues

No Related SAEs or Related Study Discontinuations In Any Study

Phase 1 First In Human Study Completed (n=80)

- **Single-ascending dose**
  - 4 cohorts of 8 subjects plus one repeat (n=40)
  - 15, 30, 60, 90 mg
  - 3:1 randomized (active:control)
  - 1 dose; 17-day follow-up

- **Multi-ascending dose**
  - 4 cohorts of -12 subjects (n=46)
  - 15, 30, 60, 90 mg
  - 3:1 randomized (active:control)
  - 21 days daily dosing + follow-up (Up to 50 days)

- **Most frequent TEAEs by System Organ Class: Nervous/GI**
  - Nearly all of the TEAEs were Grade 1 severity (mild)

- **No serious TEAEs, TEAEs leading to discontinuation of treatment, or TEAEs considered severe, life-threatening, or resulting in death**

- **No dose responsive TEAEs observed in SAD or MAD**

Phase 2 & 3 Clinical (>75 Years Exposure)

- **VISIONARY-MS** + Long-Term Extension
- **RESCUEALS** + Long-Term Extension
- **HEALEY ALS Platform Trial**
- **RepairPD**
- **RepairMS**

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**CNM-Au8 Effects on Brain Bioenergetic Metabolites**

A Phase 2, Open Label, Sequential Group, Investigator Blinded Study of Magnetic Resonance Spectroscopy ($^3$P-MRS) to Assess the Effects of CNM-Au8 for the Bioenergetic Improvement of Impaired Neuronal Redox State

**Change in Brain Bioenergetic Potential (NAD+/NADH) vs. Baseline**

- Difference in bioenergetic metabolites (e.g., ATP, PCr, NAD) concentration at Week 12 – 16
- Difference in brain membrane markers (PE, PC, etc.) at Week 12 – 16

N = Up to 15 per dosing cohort
(7.5, 15, 30, or 60 mg)

**Anticipated Top-Line Results**
(Cohort 1):
Repair-PD: 1H 2021
Repair-MS: 2H 2021*

*Subject to ongoing COVID-19 related site research restrictions generally implemented to protect MS patients taking standard-of-care immunosuppressive therapies
CNM-Au8 Improved Brain Metabolic Markers
Elevated NAD+/NADH & Normalized \(\beta\)-ATP Levels in MS & PD

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

Exploratory Endpoints
• ALSFRS-R
• Combined Joint-Rank (Survival + ALSFRS-R)
• FVC
• Change in Rate of ALSFRS-R progression
• QOL

Anticipated full unblinded data readout: 2H 2021
Measuring ALS Disease Progression

Electromyography Predicts Clinical Progression

Predictive Endpoints of Disease Progression

- Loss of Motor Units
  Motor Unit Index (MUNIX)

Clinical Endpoints

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


MUNIX(4) Decline Precedes ALSFRS-R Progression
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)

Exploratory Endpoints
- Combined Joint Rank (Survival + ALSFRS-R)
- Voice pathology
- PRO (ALSAQ)
- Pharmacodynamic markers

Slow Vital Capacity
- Hand Held Dynamometry

1°  Change in ALSFRS-R

2°  Anticipated full unblinded data readout: 1H 2022
Treatment of Visual Pathway Deficits In Chronic Optic Neuropathy for Assessment of Remyelination in Non-Active Relapsing MS

**Phase 2**

**VISIONARY-MS STUDY**

**Exploratory Endpoints**
- Optical Coherence Tomography (OCT)
- Multi-focal VEP Amplitude & Latency
- Full field-VEP Amplitude & Latency
- MRI Endpoints
- Visual Function (High Contrast)
- QOL / EDSS

**Change in Low Contrast Letter Acuity (LCLA)** At Week 24

**Change Composite Clinical Response**
- 9HPT / SDMT / T25FW / LCLA / EDSS

**Up to 48-Week Placebo-Control**
- 2:1 Randomization (Active: Placebo)
  - 15mg, 30mg, Placebo (n=150)

**24-Week Blinded Fixed Treatment Period**

**Up to 24-Week Blinded Extension Period** (Until LPLV 24Wk Visit)

**Change Composite Clinical Response**

**1°**

**2°**

**1H 2022**

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

The Visual System is a Window into the Brain

LCLA
Phase 2 Primary: Functional Visual Improvement
LCLA Correlates with clinically meaningful deficits in QOL, EDSS and MSFC, MRI, and OCT

MS Functional Endpoints
Phase 2 Exploratory: Neuroprotection/Remyelination Endpoints

9-Hole Peg Test

Symbol Digit Modalities

KEY

Timed 25-Ft Walk

25 Feet
Emerging Evidence of Clinical Improvement

**LCLA (Best-Corrected)**

Blinded Data LCLA (All Eyes) % Change vs. BL
15-July-2020 Data Cut; All Participants By Completed Visits
(Median + IQR)

**SDMT**

Blinded Data SDMT % Change vs. BL
15-July-2020 Data Cut; All Participants By Completed Visits
(Median + IQR)

**T25FW**

Blinded Data T25FW (Time, Sec) % Change vs. BL
15-July-2020 Data Cut; All Participants By Completed Visits
(Median + IQR)

All Available Data By Completed Study Visit
(Study Ongoing; 1 drop-out to date)

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**Strong Intellectual Property**

Extensive Patent Portfolio With Protection Through 2035\(^a\) & Proprietary Trade Secrets; Plus 7-year Orphan Drug Designation

- **Patent Status**
  - Issued & Allowed Patents: 100+
  - Pending Applications: >30
  - Total Patents/Applications: >130

- **Patent Description**
  - Process And Method/Device (Clean Surface; Gold CSN)
  - State of Matter (CNM-Au8)
  - Method of Use (Prevent Demyelination & MoA)
  - Method of Use (Bi-Metallic Au/Pt; Antimicrobial)

- **Trade Secrets**
  - Plasma Conditioning
  - Electrode Design & Cycling
  - Trough Flow, Temp, Pressure
  - Concentration & Filtration

---

\(^a\) With Patent Restoration Term (assuming 5-year extension).
Clene | Proprietary Nanocrystal Manufacturing
In-House ISO8 Clean Room Clinical Production in North East, MD

Designed to be Scalable to Commercialization

- Patented Hydro-electro-Crystallization
- Proprietary Trade Secrets
- Validated CMC Processes
Anticipated Timeline & Investor Catalysts
2020 - 2023

Amyotrophic Lateral Sclerosis (ALS)
- RESCUEALS Phase 2
- DATA

Parkinsons Disease (PD)
- RepairPD Phase 2 target engagement
- DATA
- RESCUEPD Phase 2

Multiple Sclerosis (MS)
- VisionaryMS Phase 2
- DATA
- RepairMS Phase 2 target engagement
- DATA

Anti-Viral Anti-Bacterial
- ZnAgSTUDY
- DATA
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