



HEALEY ALS Platform Trial



Investigational Products Tested in the Trial



CNM-Au8
February 4, 2021



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THE ARTHUR M. BLANK
FAMILY FOUNDATION



Accelerating ALS Therapy Development

Traditional



	Intervention
Disease	Treatment A



Platform

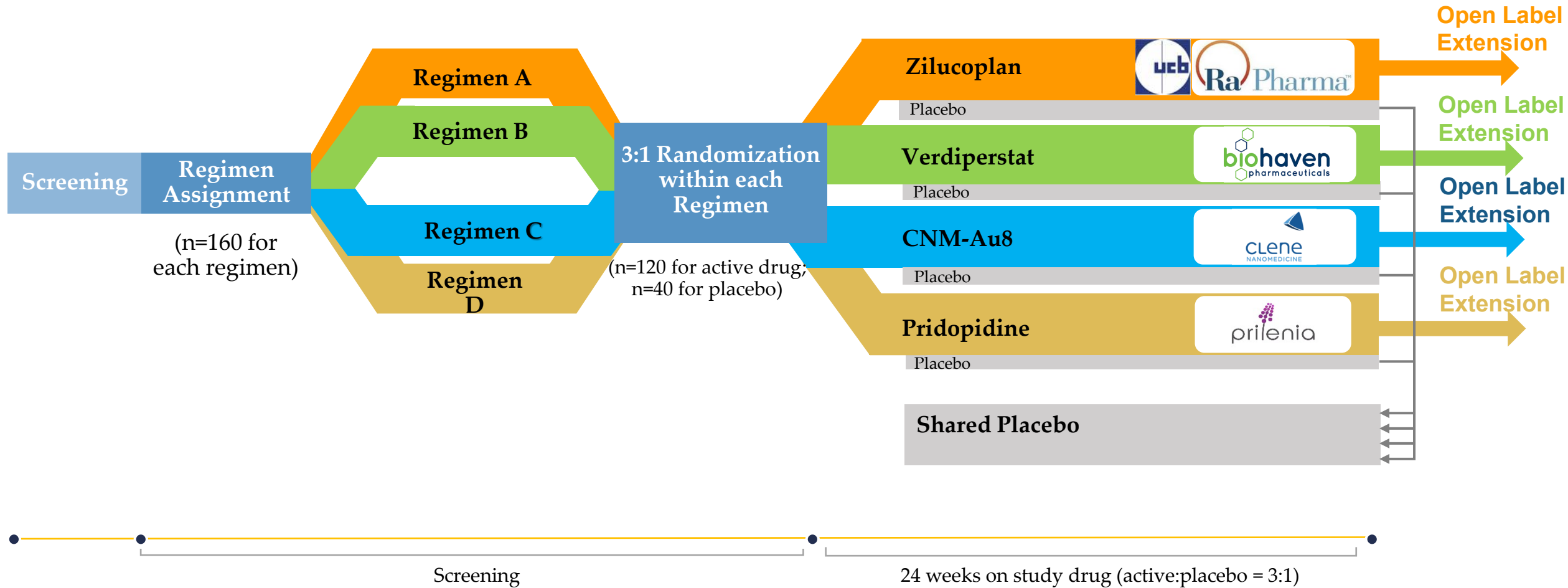


	Intervention			
Disease	Treatment A	Treatment B	Treatment C	Treatment D

Perpetual Adaptive Trial

Randomization Ratio 3:1; Shared Placebo

Open Label Extension offered



Regimen Leads

James Berry, MD, MPH
MGH, Boston, MA
Regimen co-Lead

Nicholas Maragakis, MD
Johns Hopkins, Baltimore, MD
Regimen co-Lead





CLene
NANOMEDICINE

Overview | CNM-Au8 (Regimen C)

1. What It Is

2. How It Works

3. Evidence Supporting Treatment of ALS

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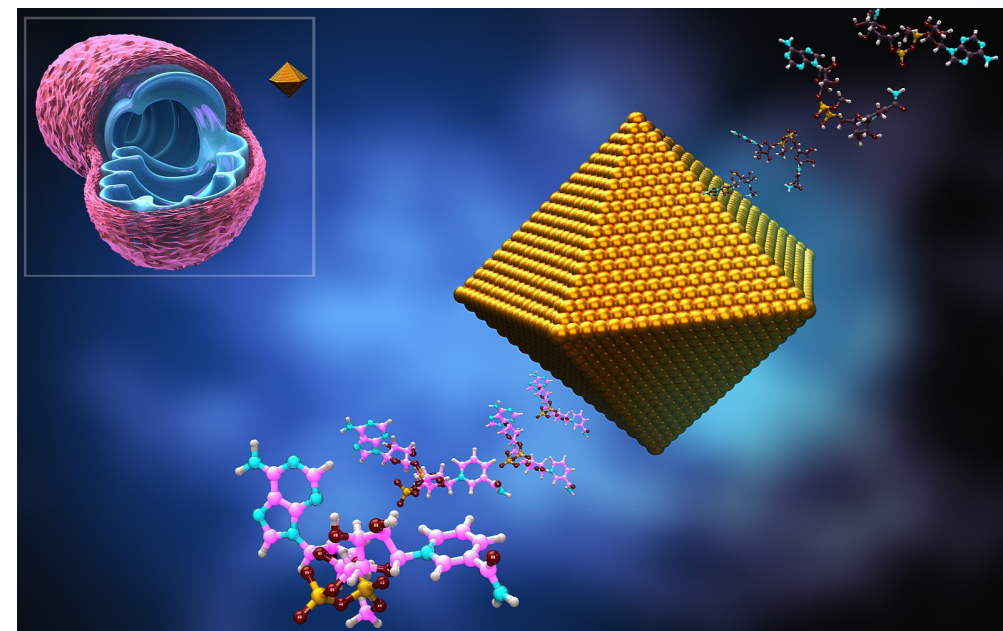
CLENE | Going for the Gold

Bulk Gold



In bulk form, gold is inert and unreactive. It resists corrosion and doesn't rust

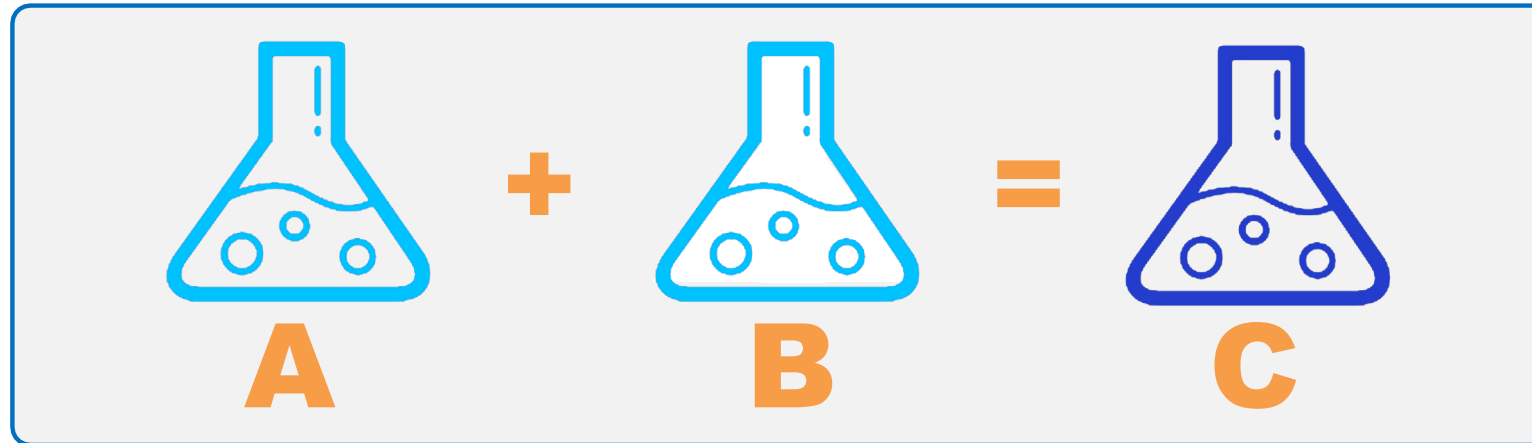
Molecular Nanocrystalline Gold



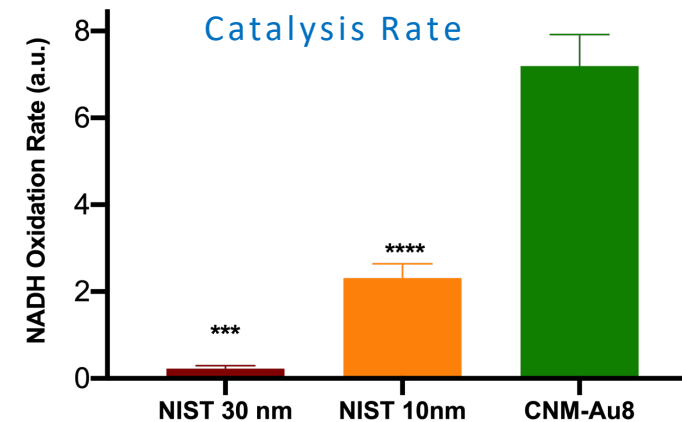
When gold is made into tiny nanocrystals, gold becomes highly active as a **Nanocatalyst**

CNM-Au8 | What is a Nanocatalyst?

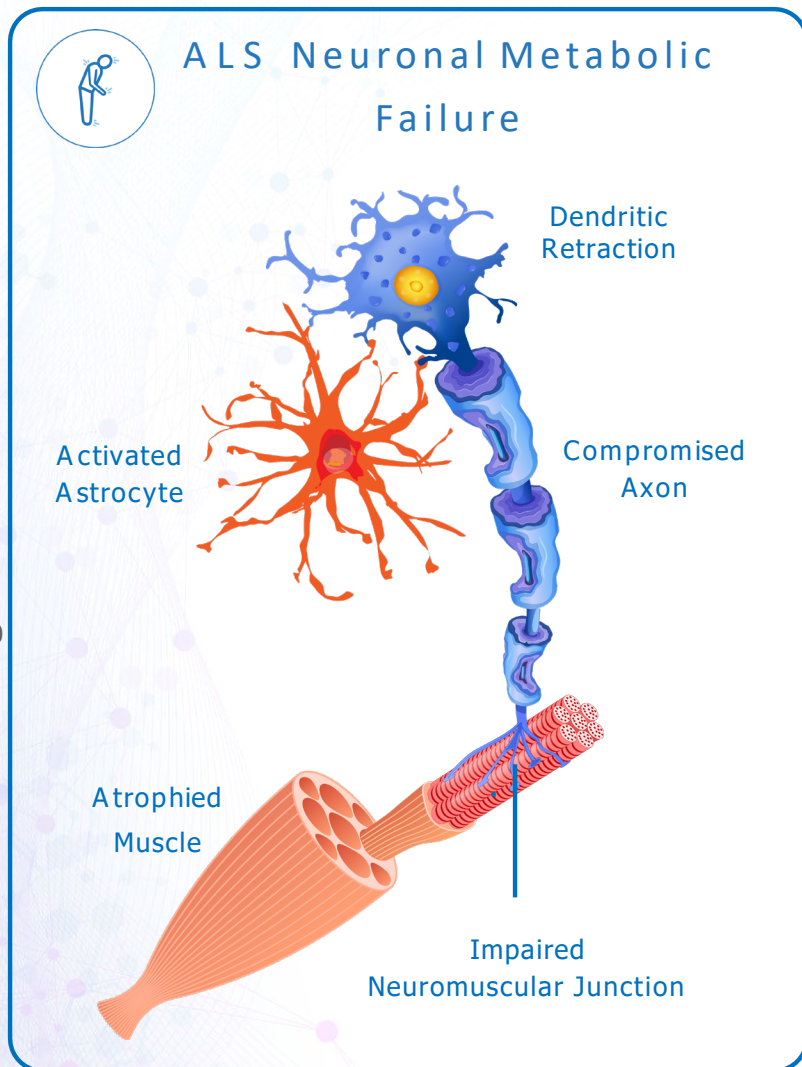
In a biological or chemical **reaction**,
Reactant A and Reactant B combine to make a totally new Product C



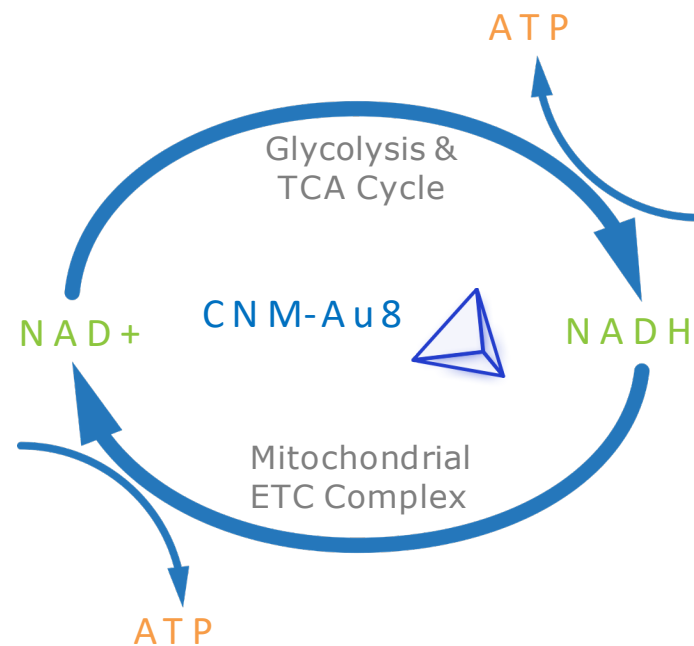
A **nanocatalyst** is a very, very small catalyst that makes specific biological **reactions** go **faster**, so that more of Product C is produced rapidly



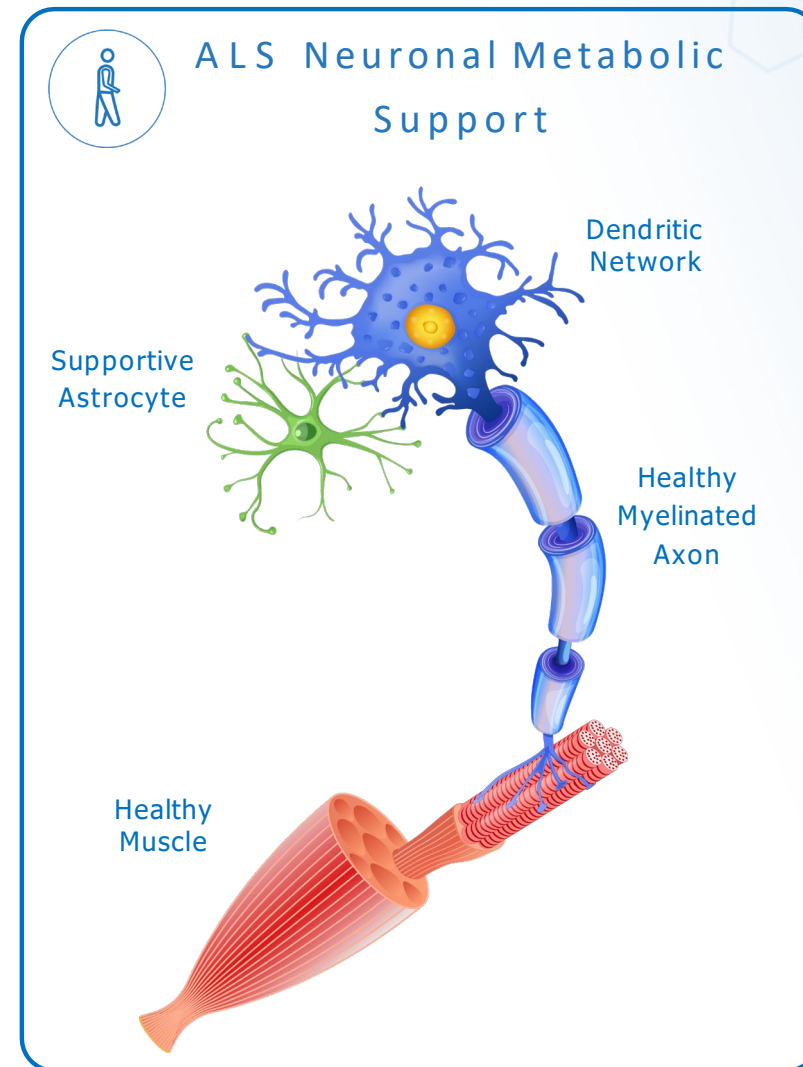
ALS | Restoring Neuronal Energetic Loss Is Essential



CNM-Au8 catalysis supports cellular energy in neurons ...



... providing the brain, spinal cord, and motor neurons with more access to key energy metabolites, improving motor neuron health and survival

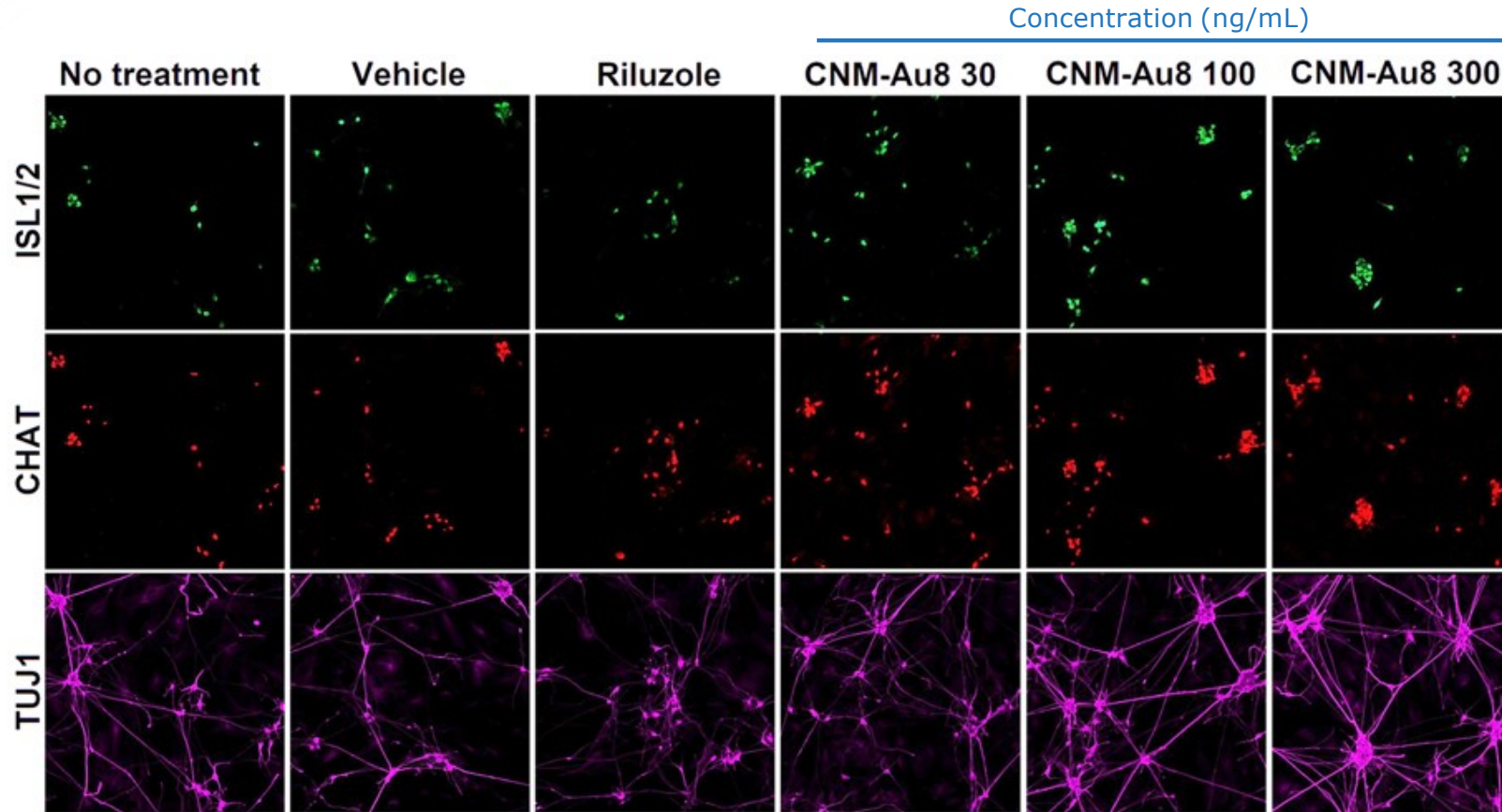
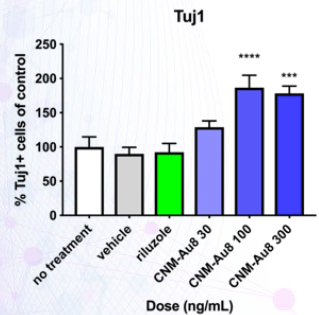
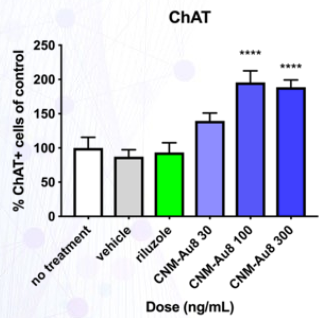
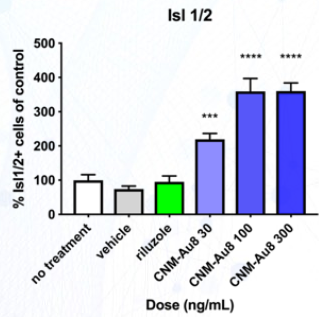


Vandoorne et al. Acta Neuropathologica (2018) 135:489–509.

Data on File, CleneNanomedicine.

CNM-Au8 | ALS Neuroprotection in Human Neurons

Induced Pluripotent Stem Cell *In Vitro* Results – Motor Neuron Markers



CNM-Au8
Improves
ALS Motor
Neuron
Survival &
Neuron
Connections

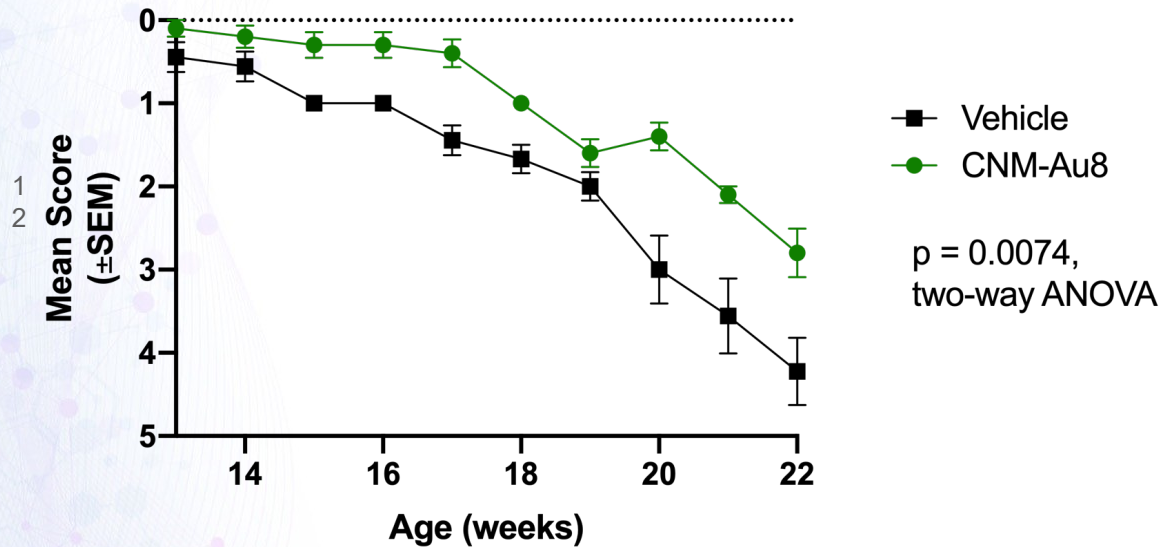
Karen S. Ho et al. "Redox-enhancing nanocatalysis improves motor neuron survival in vitro and SOD1 mouse motor function and survival in vivo." Presented at 30th International Symposium on ALS/MND 2019. December 4-6, 2019.

CNM-Au8 | Treatment Results in ALS Neuroprotection

In Vivo SOD1 Congenic Mouse

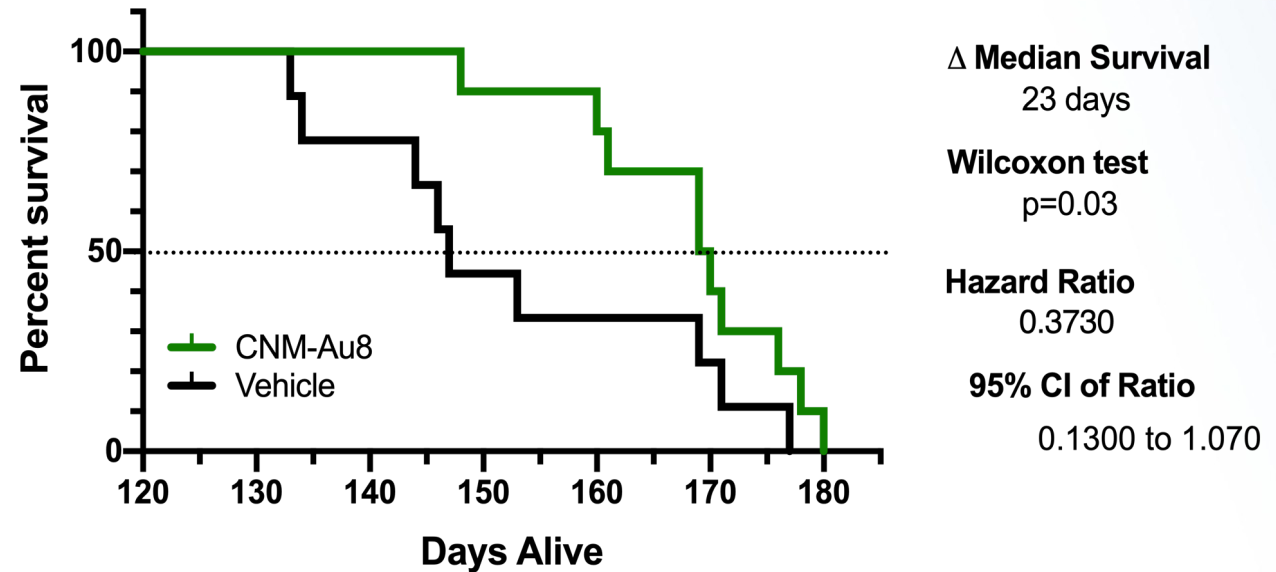
CNM-Au8 Improves Healthspan

Neurological Score
(TDI Rodent Scale)
(Mean \pm SEM)



CNM-Au8 Improves Lifespan

Kaplan-Meier Survival Curve
SOD1^{G93A} Mice



Karen S. Ho et al. "Redox-enhancing nanocatalysis improves motor neuron survival in vitro and SOD1 mouse motor function and survival in vivo."
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CNM-Au8 | Clean Animal Toxicology Findings

All Studies Resulted in No Adverse Effect Level (NOAEL)^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)

^a NOAEL = No Dose Limiting Toxicities Observed

CNM-Au8 | Well Tolerated Safety Profile

No Related SAEs or Related Study Discontinuations Across >75 Yrs. Cumulative Exposure

Phase 1 First In Human Study

- Most frequent Adverse Events by System Organ Class: Nervous/GI – Nearly all 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 MS & Parkinson's

 VISIONARY-MS
STUDY

Up to 48-weeks exposure

 RepairPD

Up to 21-weeks exposure

 RepairMS

Up to 18-weeks exposure

Phase 2 & 3 ALS

 HEALEY ALS
Platform Trial

Up to 16-weeks exposure

 RESCUEALS

Up to 36-weeks exposure

 MGHALS
Expanded Access Protocol

Up to 50-weeks exposure

THANK YOU | From All of Us at Clene

Your trial participation means the world to us ...



... together we will discover treatments for neurodegenerative diseases that help people with ALS, and empower them to **thrive**



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For More Updates

- **Weekly webinars**

The idea of came from our Patient Advisory Committee: we are excited to be talking with you on a weekly basis and take any questions you might have

- **Find the schedule and registration links on our website**

<https://www.massgeneral.org/neurology/als/research/platform-trial-news/>