NASDAQ: CLNN

Pioneering Therapeutic Nanocatalysts That Improve Cellular Bioenergetics

Clene Inc. (NASDAQ: CLNN) is a clinical stage biopharmaceutical company dedicated to revolutionizing the treatment of neurodegenerative disease using nanocatalysis. Clene has developed a new class of drugs, bioenergetic nanocatalysts, using biologically active nanocrystals designed to catalyze reactions in the body, enhancing cellular repair by increasing bioenergy. These drug candidates are clean-surfaced metallic nanocrystals suspended in highly pure water and are taken orally, daily. Clene's lead drug candidate, CNM-Au8, a suspension of pure gold nanocrystals, has shown promising efficacy in improving neurological function in multiple preclinical studies[1], and has demonstrated effects on key brain energetic metabolites in patients with Parkinson's disease (PD) and multiple sclerosis (MS)[2].

CNM-Au8 is under investigation in multiple clinical trials for disease modification in the treatment of neurodegenerative disease including a Phase 3 registration trial in amyotrophic lateral sclerosis (HEALEY-ALS Platform), a Phase 2 study in ALS (RESCUE-ALS), a Phase 2 study in MS (VISIONARY-MS) for the treatment of stable relapsing multiple sclerosis, and Phase 2 target engagement studies in Parkinson's disease and MS (REPAIR-PD) and (REPAIR-MS). Clene is leading the way by using nanotechnology to treat bioenergetic failure, which underlies many neurological diseases, Clene is delivering the potential for neuroreparative treatment. Clene has over 100 issued patents and multiple pending patents, proprietary in-house manufacturing, and a Phase 3 study which, if successful, could lead to approval and commercialization in 2023.

Bioenergetic Nanotherapeutics Pipeline

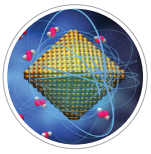
*Subject to ongoing COVID-19 related site research restrictions generally implemented to protect MS patients taking standard-of-care immunosuppressive therapies

New Paradigm, a Bioenergetic Approach in Neurodegenerative Medicine:

Effective treatment of patients with neurodegenerative disorders requires a therapeutic breakthrough. The World Health Organization predicts neurodegenerative diseases will become the second-most prevalent cause of death within 20 years. Bioenergetic failure underlies the pathophysiology of many of these diseases. Clene's breakthrough nanocatalysts sustain cellular bioenergetics.

Platform Technology Integrates Physics with Biology:

Clene's Clean-Surfaced Nanocrystal (CSN®) therapeutics are produced utilizing a patented electro-crystal-chemistry growth process that results in highly faceted clean-surfaced nanocrystals or ions of pure transition elements including gold, silver, platinum, and zinc as well as alloy and composite combinations. These nanocatalysts or ions work in many cell types, for example, to improve multiple bioenergetic processes that may effectively treat many different diseases.



Lead Drug Candidate CNM-Au8 a Bioenergetic Nanocatalyst:

CNM-Au8, a concentrated nanocrystalline gold (Au) suspended in water, enhances critical intracellular bioenergetic reactions necessary for repairing and reversing neuronal damage. Clene's patented breakthrough is the production of biologically active, clean-surfaced gold nanocrystals that cross the blood-brain barrier, and have not exhibited toxicities associated with synthetic gold compounds or synthetic nanoparticle chemistry.

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CNM-Au8 | Significant Global Opportunity

MOTOR NEURON DISEASE
(ALS, Other Orphan Disorders)

ALS sales >$1B globally by 2029.[6] Current drugs are largely ineffective, mostly generic.

MULTIPLE SCLEROSIS
~2.5M pts globally; $23B market[7]

Only approved treatments are immunomodulators

PARKINSON'S DISEASE
~7M pts globally; $6B projected by 2025[8]

2nd most common neurodegenerative disorder; only symptomatic treatment

HEALEY ALS Platform Trial

HEALEY ALS Platform Trial is a Registrational Phase 3, multi-center, multi-regimen, placebo-controlled trial evaluating safety and efficacy of investigational products including CNM-Au8 for the treatment of ALS.

- Funded by philanthropic donors and led by Harvard's Massachusetts General Hospital, Healy is the first-ever ALS platform trial designed to reduce trial time, costs, and increase patient participation in developing novel therapies.
- CNM-Au8 was selected as one of the first drugs to be evaluated.
- 54 expert ALS US clinical trial sites; each regimen will enroll 160 participants with 3:1 randomization (active:placebo).
- Full enrollment is expected by the end of 1H 2021, with top-line data expected 1H 2022.

RESCUEALS

Rescue-ALS is a Phase 2, multi-center, randomized, double-blind, placebo-controlled study designed to evaluate the efficacy, safety, pharmacokinetics and pharmacodynamics of CNM-Au8 in early symptomatic ALS patients.

- CNM-Au8 was selected by FightMND of Australia with a substantial grant to investigate improvement of novel electromyography endpoints at two expert sites in Australia in 42 participants.
- **Preliminary blinded data presented at the 31st International Symposium on ALS/MND** show that more than 40% of enrolled patients with completed 12-week data experienced improvements in motor neuron function as assessed by the mean motor unit number index-4 [MUNIX(4)] score, the study's primary endpoint. Compared to baseline values, the average MUNIX(4) score of the overall trial population showed an absolute increase which exceeded the expectations of the statistical models on which the study was based, which predicted a continuing linear decrease in average MUNIX(4) score from study onset[3].
- Enrollment in the trial completed in 2H 2020 with top-line data anticipated in 2H 2021.

RepairPD RepairMS

REPAIR-PD and REPAIR-MS are Phase 2, single-center, active-only, sequential group, investigator-blinded studies to assess the central nervous system (CNS) metabolic effects, safety, pharmacokinetics and pharmacodynamics of CNM-Au8 in Parkinson's disease (PD) and MS patients.

- Novel 31-Phosphorous magnetic resonance spectroscopy investigation of brain metabolites in cohorts of up to 15 participants.
- **Interim results from the Phase 2 REPAIR-MS presented at the ACTRIMS Forum 2021**[9]**, and from both REPAIR-MS and REPAIR-PD presented at the MSVirtual2020 Meeting**[2] show improvements across key CNS bioenergetic metabolites, including total nicotinamide adenine dinucleotide (NAD) levels, NAD+/NADH ratio, and adenosine triphosphate (ATP) levels, indicating a homeostatic effect of CNM-Au8 on brain bioenergetics.
- Data from REPAIR-PD expected 2H 2021.
- Data from REPAIR-MS expected 2H 2021[4].
- Initiation of an additional Phase 2 PD efficacy trial is planned by the end of 2021.

VISIONARY-MS STUDY

VISIONARY-MS is a Phase 2, multi-center, double-blind, randomized, placebo-controlled trial evaluating the efficacy and safety of CNM-Au8 as a remyelinating and neuro-reparative treatment in stable relapsing MS patients with chronic visual impairment.

- 10 expert MS clinical trial sites in Australia; 150 participants planned with 1:1:1 randomization (high-dose:low-dose:placebo)
- **Interim blinded data from the Phase 2 VISIONARY-MS trial, as presented at the ACTRIMS Forum 2021 Meeting**[9]**,** demonstrated notable, exposure-related median improvements in both low contrast letter acuity (primary endpoint), as well as the core components of the modified MS Functional Composite (MSFC) scale[5].
- Full enrollment in VISIONARY-MS expected by the end of 2021[3].

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