Clene Demonstrates Strengthened ALS Survival Benefit with CNM-Au8® Treatment

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New Cross-Regimen Analysis of HEALEY ALS Platform Trial Shows Significant Survival Advantage

SALT LAKE CITY, March 12, 2025 (GLOBE NEWSWIRE) -- Clene, Inc. (Nasdaq: CLNN) and its subsidiary, Clene Nanomedicine, Inc., a clinical-stage biopharmaceutical company focused on revolutionizing the treatment of neurodegenerative diseases, including amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS), today announced new evidence from a cross-regimen, *post hoc* analysis of long-term survival in HEALEY ALS Platform Trial participants. The analyses further substantiate that treatment with CNM-Au8® 30 mg delivers a significant survival benefit for people living with ALS.

New Survival Analyses
The analyses compared survival in participants who received CNM-Au8 30 mg (Regimen C) to those of Regimen A in the HEALEY ALS Platform Trial. Regimen A provided a large concurrent control group vs. CNM-Au8 treatment using the same randomization criteria established within the HEALEY master protocol. Long-term survival status, determined through public records and site reporting, was evaluated over a follow-up period of up to 48 months. 78% of participants across both groups received standard ALS background therapy (riluzole, edaravone, or both) at baseline.

- **Overall Survival Improvement (All-Cause Mortality) Across the Full Analysis Set:**
  - Median Survival: CNM-Au8 30 mg group (Regimen C, n=59) achieved 951 days versus 753 days in the Regimen A comparator group (n=162) – a gain of 198 days (**6.5 months**)
  - Restricted Mean Survival Time (RMST) Benefit: covariate-adjusted RMST improvement of 124 days (**4.1 months**) was observed (95% CI: 3 to 245 days, p=0.045). RMST is a metric that estimates the average time a group survives relative to a comparator. The estimate incorporated the prespecified covariates for survival analyses from the HEALEY ALS Platform Trial (i.e., months from symptom onset, pre-treatment ALSFRS-R slope, age, background riluzole treatment, background edaravone treatment)
  - Sensitivity analyses, which included additional covariate models such as baseline serum neurofilament light (NfL) levels, use of ALS background therapy, and the TRICALS risk score, confirmed the robustness and statistical significance of the findings

- **Enhanced Benefit in Moderate to Severe ALS:**
  - In participants with baseline serum NfL ≥ 33 pg/mL and TRICALS risk score range between –6.5 and –2.5 (i.e., filtering slow progressors where there was an imbalance between groups), median survival improved from 589 days (Regimen A, n=120) to 951 days (CNM-Au8 30 mg, n=51), representing an **11.9 month gain**
  - **Mortality risk in this group decreased by 44%** (Cox HR: 0.556, 95% CI: 0.367–0.842, p=0.006) with an **RMST improvement of 197 days (6.5 month gain**; 95% CI: 65 to 329 days, p=0.004), when using the prespecified covariates for survival analyses from the HEALEY ALS Platform Trial

- **Strongest Survival Benefit Observed in Subset Who Met Planned Phase 3 RESTORE-ALS Trial Enrollment Criteria:**
  - **Among participants who met the core RESTORE-ALS Trial criteria** (e.g., baseline serum NfL ≥ 33 pg/mL, TRICALS risk score range between –6.5 and –2.5, baseline slow vital capacity ≥ 60%, and symptom onset ≤ 36 months), **median survival** improved from 628 days (Regimen A, n=94) to 1079 days (CNM-Au8 30 mg, n=40), an **increase of 451 days (14.8 months)**
  - This subset experienced a **49% reduction in mortality risk** (Cox HR: 0.514, 95% CI: 0.319–0.830, p=0.006) and an **RMST improvement of 215 days** (**7.1 months;** 95% CI: 70 to 360 days, p=0.004), when using the planned covariates for the RESTORE-ALS trial

These results are consistent with previous survival benefits observed in the HEALEY ALS Platform Trial's 24-week double-blind period, the open-label extension of the Phase 2 RESCUE-ALS trial, and analyses of Expanded Access Programs compared to ALS natural history controls.

"We are highly encouraged by these results, as the significant survival advantage demonstrated by CNM-Au8 not only reinforces its potential to extend life for people living with ALS but also validates our strategic direction as we prepare for the launch of our confirmatory Phase 3 RESTORE-ALS study in mid-2025," stated Rob Etherington, President and CEO of Clene. "We look forward to discussing these findings with the FDA as we advance toward commercialization."

Merit Cudkowicz, M.D., M.S.c., Principal Investigator and sponsor of the HEALEY ALS Platform Trial, director of the Sean M. Healey & AMG Center for ALS, and executive director of the Mass General Brigham Neuroscience Institute, said, "The innovative design of the HEALEY ALS Platform Trial has enabled us to extract clear and meaningful survival data that helps make decisions about CNM-Au8 drug development."

About Regimen A

Regimen A was one of the first three regimens investigated in the HEALEY ALS Platform Trial. Eligible participants were randomized in a 3:1 ratio to receive active treatment or matching placebo for a planned duration of 24 weeks. Participants assigned to Regimen A had to receive both quadrivalent and serotype B meningococcal vaccinations at least 14 days prior to the first dose of study drug, and participants were excluded from Regimen A if they had a history of meningococcal disease or prior treatment with a complement inhibitor. Regimen A was stopped prematurely for futility after all participants had been randomized, and approximately 70% had completed the Week 24 visit. Participants were instructed to discontinue study dosing, and a final early termination study visit was conducted. Long-term survival status of Regimen A participants was tracked from public records and site reporting independently of the early termination. There was no difference in long-term survival in participants randomized to Regimen A active compared to Regimen A placebo, supporting the combined analyses of the entire Regimen A population for comparisons of long-term survival to CNM-Au8 30 mg (Regimen C) participants.

About Clene

Clene Inc., (Nasdaq: CLNN) (along with its subsidiaries, "Clene" and its wholly owned subsidiary Clene Nanomedicine, Inc.), is a late clinical-stage biopharmaceutical company focused on improving mitochondrial health and protecting neuronal function to treat neurodegenerative diseases, including amyotrophic lateral sclerosis, Parkinson's disease, and multiple sclerosis. CNM-Au8 ® is an investigational first-in-class therapy that improves central nervous system cells' survival and function via a mechanism that targets mitochondrial function and the NAD pathway while reducing oxidative stress. CNM-Au8® is a federally registered trademark of Clene Nanomedicine, Inc. The company is based in Salt Lake City, Utah, with R&D and manufacturing operations in Maryland. For more information, please visit www.clene.com or follow us on X (formerly Twitter) and LinkedIn.

About CNM-Au8®

CNM-Au8 is an oral suspension of gold nanocrystals developed to restore neuronal health and function by increasing energy production and utilization. The catalytically active nanocrystals of CNM-Au8 drive critical cellular energy producing reactions that enable neuroprotection and remyelination by increasing neuronal and glial resilience to disease-relevant stressors. CNM-Au8® is a federally registered trademark of Clene Nanomedicine, Inc.

About RESTORE-ALS

RESTORE-ALS is a Phase 3 confirmatory global, multi-center, randomized, double-blind, parallel group, placebo-controlled study to evaluate the efficacy, safety, pharmacodynamics, and pharmacokinetics of CNM-Au8 in participants diagnosed with ALS on stable background therapy. The study is designed to investigate the effects of CNM-Au8 on improved survival (primary endpoint) and delayed time to ALS clinical worsening events (secondary efficacy endpoint). Participants will be randomized in a 2:1 ratio to receive either active treatment with CNM-Au8 30 mg or matched placebo daily during the 108-week double-blind treatment period.

The Phase 3 RESTORE-ALS clinical trial, due to launch in mid-2025, is planned to serve as the confirmatory clinical trial required to meet the FDA's guidance for an "underway" clinical trial when a New Drug Application requesting Accelerated Approval is submitted.

Forward-Looking Statements

This press release contains "forward-looking statements" within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended, which are intended to be covered by the "safe harbor" provisions created by those laws. Clene's forward-looking statements include, but are not limited to, statements regarding our or our management team's expectations, hopes, beliefs, intentions or strategies regarding our future operations. In addition, any statements that refer to projections, forecasts or other characterizations of future events or circumstances, including any underlying assumptions, are forward-looking statements. The words "anticipate," "believe," "contemplate," "continue," "estimate," "expect," "intends," "may," "might," "plan," "possible," "potential," "predict," "project," "should," "will," "would," and similar expressions may identify forward-looking statements, but the absence of these words does not mean that a statement is not forward-looking. These forward-looking statements represent our views as of the date of this press release and involve a number of judgments, risks and uncertainties. We anticipate that subsequent events and developments will cause our views to change. We undertake no obligation to update forward-looking statements to reflect events or circumstances after the date they were made, whether as a result of new information, future events or otherwise, except as may be required under applicable securities laws. Accordingly, forward-looking statements should not be relied upon as representing our views as of any subsequent date. As a result of a number of known and unknown risks and uncertainties, our actual results or performance may be materially different from those expressed or implied by these forward-looking statements. Some factors that could cause actual results to differ include our ability to demonstrate the efficacy and safety of our drug candidates; the clinical results for our 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; our ability to achieve commercial success for our drug candidates, if approved; our limited operating history and our ability to obtain additional funding for operations and to complete the development and commercialization of our drug candidates; and other risks and uncertainties set forth in "Risk Factors" in our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q. In addition, statements that "we believe" and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this press release, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. These statements are inherently uncertain and you are cautioned not to rely unduly upon these statements. All information in this press release is as of the date of this press release. The information contained in any website referenced herein is not, and shall not be deemed to be, part of or incorporated into this press release.

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