Clene Announces Statistically Significant ALS Biomarker Results Supporting Accelerated Approval Pathway for CNM-Au8®

December 3, 2025

- *FDA recommended biomarker analyses show statistically significant reductions in NfL and GFAP in participants treated with CNM-Au8*
- *Biomarker improvements are strongly associated with longer survival, reinforcing CNM-Au8's potential disease modifying activity*
- *Company has requested a Type C meeting in the first quarter of 2026 to present the newly completed analyses supporting a planned NDA submission under the accelerated approval pathway*
- *Clene is hosting an investor webcast today at 8:30 am ET*

SALT LAKE CITY, Dec. 03, 2025 (GLOBE NEWSWIRE) -- Clene Inc. (Nasdaq: CLNN) (along with its subsidiaries, "Clene" or the "Company") and its wholly owned subsidiary Clene Nanomedicine, Inc., a late clinical-stage biopharmaceutical company focused on revolutionizing the treatment of neurodegenerative diseases, including amyotrophic lateral sclerosis (ALS) and multiple sclerosis (MS), today announced completion of the FDA-recommended biomarker analyses for CNM-Au8® in people living with ALS. The results demonstrate statistically significant reductions in both neurofilament light (NfL) and glial fibrillary acidic protein (GFAP) and provide compelling evidence linking biomarker decline to improved survival.

"We followed the FDA's roadmap — and the data delivered," said Rob Etherington, President and CEO of Clene. "Statistically significant NfL reductions in more advanced real-world ALS patients; a second independent disease-specific biomarker (GFAP) that moves in lock-step with NfL and is itself statistically significant; and clear evidence in placebo switchers (placebo-to-CNM-Au8) showing that CNM-Au8-treated participant's biomarkers follow nearly identical trajectories seen in the original active arm during the double-blind treatment phase of the HEALEY ALS Platform Trial. This is a remarkably consistent dataset that makes a strong case for accelerated approval. We look forward to presenting these analyses to the Division in the requested Type C meeting in the first quarter of 2026 and working with the FDA toward an NDA submission for accelerated approval."

The analyses follow FDA recommendations to support the persuasiveness of the original NfL findings observed in the HEALEY ALS Platform Trial by extending the analyses to the NIH-sponsored EAP (NIH-EAP) for CNM-Au8 in ALS. These biomarker findings build on prior constructive FDA interactions in support of a planned NDA submission under the accelerated approval pathway for the treatment of ALS.

New Biomarker Analyses

In late 2024, the FDA recommended three specific analyses to strengthen the persuasiveness of CNM-Au8's effect on NfL and its relationship to clinical benefit (i.e., effects on survival): (1) NfL change in the NIH-EAP, (2) evaluation of additional disease-relevant biomarkers, and (3) evaluation of NfL trajectory in HEALEY placebo participants who later transitioned to CNM-Au8 in the open-label extension (OLE):

1. Statistically significant decrease in NfL levels compared to matched ALS controls across the full analysis set (all evaluable matched participants) in the NIH-EAP. The Week 36 AUC (area under curve) difference (SEM) of NfL (Ln(pg/mL)*Week) was: –0.0899 (0.0430), p = 0.0373, equivalent to a geometric mean ratio (GMR) difference of 0.914, 95% CI: 0.840 – 0.995. The effect size was similar to the NfL decline observed in the original double-blind phase of the HEALEY ALS Platform Trial: HEALEY W24 AUC GMR of 0.901, 95% CI: 0.845 – 0.959, p=0.0013 compared to the NIH-EAP W24 AUC GMR of 0.911, 95% CI: 0.836 – 0.993, p=0.0339. Multiple pre-specified supportive analyses in the NIH-EAP across the full analysis set at Week 24 and Week 48 confirmed the robustness of the findings (p<0.05). Pre-specified subgroups showed significant effects in participants including those with an age younger than the median, on background riluzole treatment, and in participants with bulbar onset (p<0.05). In the primary analysis population in non-bulbar onset participants (i.e., predominantly limb onset), the Week 36 AUC NfL change was not significant (p=0.2085).
2. Additional disease-relevant biomarker effects on GFAP were identified with statistically significant declines observed during the double-blind period in the HEALEY ALS Platform Trial (p<0.05) and was highly correlated with NfL change. GFAP is a structural protein in astrocytes. GFAP increase in ALS is a marker of harmful reactive astrogliosis, astrocytic injury, and degenerative processes that contribute to motor neuron loss. High GFAP levels are associated with a statistically significant increase in mortality risk in ALS patients. In comparison, placebo participants demonstrated increases across both NfL and GFAP biomarkers during the 24-week double-blind period. Consistent with these findings, in the matched NIH-EAP population, the magnitude and timing of NfL and GFAP reduction were closely correlated (Pearson's r >0.85, p<0.0001) demonstrating concordant effects for NfL and GFAP in the HEALEY ALS Platform Trial and NIH-EAP participants.
3. Among placebo-treated participants who transitioned to CNM-Au8 in the HEALEY ALS Platform Trial OLE, NfL trajectories generally showed decline or stabilization compared to increases observed during the double-blind period. With only relatively few ex-placebo participants (n=31), these analyses had limited power, but the relative decline compared to the

double-blind period showed comparable GMR differences (OLE Week 28 GMR: 0.885, 95% CI: 0.737 – 1.063, p=0.185). These findings are consistent with the NfL effects previously published for CNM-Au8 vs. placebo during the 24-week double-blind period (Week 24 GMR difference: 0.905, 95% CI: 0.822 – 0.996, p=0.040).

4. NfL and GFAP biomarker decline is associated with improved survival. Among participants treated in the HEALEY ALS Platform Trial with CNM-Au8 30 mg, participants with the greatest declines across both NfL and GFAP biomarkers during the double-blind period had the largest long-term overall survival improvement relative to all participants treated with CNM-Au8 30 mg (NfL and GFAP average AUC decline $\leq$ 25th percentile): Cox HR: 0.191, 95% CI: 0.047 – 0.782, p=0.0210, an 80% reduction in the risk of death compared to Regimen A concurrent controls.

CNM-Au8 Strengthens Overall Survival Signal in the HEALEY ALS Platform Trial Open-Label Extension Period

Updated survival analyses (April 2025 data cut) in participants originally randomized to CNM-Au8 30 mg in the HEALEY ALS Platform Trial continue to demonstrate clinically meaningful and statistically significant survival benefit versus concurrent Regimen A controls. Analyses were conducted at intervals of one year (pre-specified OLE timepoint) and beyond using the pre-specified HEALEY ALS Platform Trial covariate model across two populations: the full analysis set (FAS), including all available participant data; and a risk-balanced population, the comparable risk set (CRS) (filtered for disease severity by NfL levels (Ln(NfL) $\geq$ 3.5 and TRICALS risk score)) due to imbalances with significantly more low-progression risk patients present in the Regimen A group.

CNM-Au8 30 mg treatment demonstrated statistically significant improved survival across both the FAS and CRS populations based on a Cox proportional hazard model and restricted mean survival time (RMST) analyses.

In the FAS population:

- 1-year Cox proportional hazard ratio: 0.2723, 95% CI: 0.0961 – 0.7719, p=0.0144 → 73% reduction in risk of death

In the CRS population:

- 1-year Cox proportional hazard ratio: 0.229, 95% CI: 0.07 – 0.752, p = 0.0151 → 77% reduction in risk of death

Even the small cohort of placebo-to-CNM-Au8 switchers (n=31, starting treatment ~6 months later in disease progression) showed a significant RMST benefit of +30.7 days at one year following treatment initiation (95% CI 7.52 – 53.85, p=0.0094).

Strong CNM-Au8 Safety Profile

Across over 1,000 patient years of CNM-Au8 exposure data, treatment with CNM-Au8 continues to demonstrate a safety profile without significant safety concerns or safety trends identified. No serious adverse events (SAEs) have been identified as related to CNM-Au8 treatment by any investigator to date.

ALS Key Opinion Leader Commentary

“We believe these data show the potential enduring effect of CNM-Au8, because this NIH-EAP data includes participants who are generally more advanced than a typical ALS clinical trial population and still show concordant NfL decline,” said Dr. Jinsy Andrews, MD, MSc, Director of the Amyotrophic Lateral Sclerosis Center and Medical Director of Clinical Trials in the Department of Neurology at NYU Grossman School of Medicine and principal investigator of the NIH-sponsored EAP. “The consistency of NfL and GFAP reductions in more advanced patients treated in the Expanded Access Program is particularly compelling and suggests potential disease-modifying activity of CNM-Au8.”

Clene Submitted a Type C Meeting Request to Align on Accelerated Approval NDA Submission

Clene has requested a Type C meeting with the FDA and anticipates the meeting will occur during the first quarter of 2026 to present the full dataset. The Company plans to submit an NDA under the accelerated approval pathway in the same quarter, with the planned Phase 3 RESTORE-ALS trial serving as the post-approval confirmatory study.

The Company will host a conference call and webcast at 8:30 am ET today, on Wednesday, December 3, 2025, to provide an update on its CNM-Au8 program in ALS. Those who would like to participate may access the live webcast here:

Webcast Information:
Title: CNM-Au8 ALS Program Update
Presenters: Rob Etherington, CEO and President; Dr. Ben Greenberg, Head of Medical; Michael Hotchkin, Chief Development Officer, and a KOL
Date: Wednesday, December 3, 2025
Start Time: 8:30 a.m. EST
Webcast link: https://viavid.webcasts.com/starthere.jsp?ei=1744985&tp_key=9fb9583d33
Dial number: 1-877-407-0779 (US) or 1-201-389-0914 (international), Conference ID#13757380

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 the NIH-Sponsored Expanded Access Program (NIH-EAP) for CNM-Au8 in ALS:

This EAP is a collaborative effort between Clene Nanomedicine, NYU, and Synapticure, with a grant awarded by the NIH (NCT06408727). The program enrolled 183 participants at eight sites across the United States. Comparisons of NIH-EAP participants to natural history ALS controls were made using the U.S. ANSWER ALS dataset. A previously considered large European natural-history dataset was determined, upon detailed quality review, not to meet FDA-required quality standards. Clene therefore selected the U.S. ANSWER ALS dataset to ensure the most reliable and defensible external comparator for regulatory purposes.

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.

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 the timing of the Company’s meeting with the FDA, the timing of the Company’s NDA submission, and that the biomarker findings support an NDA submission. 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 general market conditions, whether clinical trials demonstrate the efficacy and safety of our drug candidates to the satisfaction of regulatory authorities, or do not otherwise produce positive results which may cause us to incur additional costs or experience delays in completing, or ultimately be unable to complete the development and commercialization 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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