Clene Announces Additional CNM-Au8 Biomarker Data Supporting Potential NDA Filing for Upcoming In-Person FDA Meeting

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- *The FDA has granted an in-person Type C meeting during the first quarter of 2026*
- *New independent analyses across large observational ALS cohorts demonstrate that modest (~10%) NfL reductions are significantly associated with lower mortality risk, supporting NfL reduction as a candidate surrogate endpoint for accelerated approval*
- *New exploratory findings demonstrate that in responders with IGFBP7 biomarker decline, CNM-Au8 30mg was strongly associated with 78% reduced mortality risk (HR 0.22, p=0.01) in the HEALEY ALS Platform Trial, consistent with emerging genetic evidence linking lower IGFBP7 to ALS reversals*

SALT LAKE CITY, Jan. 12, 2026 (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 that the U.S. Food and Drug Administration (FDA) has granted Clene an in-person Type C Meeting later this quarter.

Evidence Supporting NfL Trajectory as a Candidate Biomarker for Accelerated Approval

Clene has now submitted its pre-meeting briefing package to the FDA, which includes previously announced statistically significant reductions in neurofilament light chain (NfL) and glial fibrillary acidic protein (GFAP) from the HEALEY ALS Platform Trial and NIH-sponsored Expanded Access Program (EAP) with linked survival evidence (announced December 2025), and new analyses demonstrating that the NfL reductions observed with CNM-Au8 treatment may predict clinical benefit in patients with ALS.

These NfL biomarker-survival analyses were conducted according to a prespecified statistical analysis plan and applied across multiple independent ALS datasets. The analyses evaluated whether longitudinal changes in NfL were associated with survival outcomes, independent of baseline disease severity and other prognostic factors.

The briefing package answers the FDA’s prior requests to **(1)** establish the clinical significance of the observed NfL declines, **(2)** confirm the NfL decline observed in the HEALEY ALS Platform Trial was reproducible and **(3)** link the NfL decline to clinical outcomes such as survival.

Alignment with Potential FDA Accelerated Approval Framework for CNM-Au8

1. **NfL trajectory is independently associated with increased mortality risk in ALS**
   Analyses across two large, independent ALS cohorts (APST, Answer ALS) demonstrated that longitudinal NfL increases were robustly and consistently associated with increased mortality risk ($p<0.001$), independent of baseline NfL and clinical covariates.
   Participants in the highest NfL slope categories experienced a significant 2.3-2.6-fold increased risk of death compared to patients with lower NfL slopes ($p<0.001$), with a clear NfL slope-dose response relationship observed across tertiles.
2. **CNM-Au8 treatment consistently reduces NfL levels, a critical biomarker in ALS**
   Concordant evidence from the HEALEY ALS Platform Trial 24-week double-blind period and the externally controlled NIH-sponsored EAP study at Week 36 demonstrated statistically significant and reproducible NfL reductions following CNM-Au8 treatment (HEALEY Week 24 Plasma NfL GMR 0.905, p=0.0403; NIH EAP Plasma NfL Week 36 full analysis set AUC difference −0.090, p=0.0373).
   These findings demonstrate consistent pharmacodynamic effects of CNM-Au8 on a clinically relevant ALS biomarker across independent study designs.
3. **NfL reduction is quantitatively associated with improved survival**
   Analyses of large ALS patient datasets demonstrate that even modest reductions in NfL are associated with improved survival. Across cohorts, the NfL reduction observed with CNM-Au8 treatment (approximately 9–10%) was associated with an approximately 8–13% lower risk of death, while larger NfL reductions were associated with proportionally greater survival benefit—a clinically meaningful benefit in a rapidly progressive disease with median survival of 2–4 years.

These findings were robust across multiple complementary statistical methods, including parametric survival modeling, joint longitudinal–survival models, and Cox regression approaches designed to address missing biomarker data and survivorship bias. These analyses describe associations observed across ALS patient populations based on statistical models and do not directly represent estimates of treatment effect on survival. For example, from the HEALEY ALS Platform Trial long-term follow-up, CNM-Au8 30 mg treatment resulted in statistically significant survival improvement compared to concurrently randomized controls (HR: 0.272, 95% CI: 0.096 – 0.772, p=0.014) with 93% of participants alive at month 12, a pre-specified analysis timepoint.

Together, these results support the biological and clinical relevance of NfL trajectory as a prognostic biomarker in ALS and provide quantitative context for interpreting NfL changes observed in interventional clinical studies.

New Exploratory Biomarker Findings: CNM-Au8 Induced IGFBP7 Decline was Strongly Associated with Improved Survival

Clene has identified Insulin-like Growth Factor Binding Protein 7 (IGFBP7) as an additional pharmacodynamic biomarker of treatment response to CNM-Au8 30 mg from the double-blind period of the HEALEY ALS Platform Trial. IGFBP7 decline was strongly associated with improved survival with responders, defined as a cumulative AUC IGFBP7 reduction during the 24-week double-blind period, demonstrating 78% mortality risk reduction compared to concurrently randomized controls (n=38 of 56 evaluable; HR: 0.22, 95% CI: 0.07–0.71, p=0.012; 3 events in 38 responders vs 28% mortality in controls).

Notably, the decline in IGFBP7 levels has emerged as a plausible ‘mechanistic hub’ in a coordinated biomarker response. IGFBP7 showed strong, statistically significant correlations with concurrent declines in other disease-relevant biomarkers, including those associated with vascular integrity, synaptic function, protein clearance, and axonal integrity (AUC Week 0-24 change; r = 0.50–0.78; all p<0.001).

This correlation pattern, with IGFBP7 as the central node, supports a hypothesized mechanistic pathway linking CNM-Au8's mode of action to IGFBP7-mediated neuroprotection:

- CNM-Au8 catalyzes NAD+ regeneration → Improved cellular (neuronal) bioenergetics
- Reduced cellular stress → Decreased IGFBP7 secretion → Enhanced free IGF-1 bioavailability
- Downstream neuroprotection → Synaptic stabilization and reduced neuronal stress

These observations align with independent genetic evidence: a variant (rs4242007) associated with decreased IGFBP7 expression was significantly more common in patients with documented ALS reversals compared to typically progressive ALS (Crayle et al. Neurology 2024). Together, these data suggest that lower IGFBP7, whether achieved genetically or pharmacologically, may help protect against ALS progression. These findings are exploratory and hypothesis-generating and require prospective confirmation.

“ALS remains a devastating disease with limited therapeutic options, and the field urgently needs biomarkers that can meaningfully inform drug development,” said Rob Etherington, Chief Executive Officer of Clene. “We appreciate the FDA’s willingness to engage in a detailed discussion of our biomarker and survival data. Our goal in the upcoming Type C meeting is to review the totality of evidence supporting NfL and other emerging biomarkers and to seek FDA guidance on how these data may inform future regulatory pathways for CNM-Au8, including potential accelerated approval.”

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.

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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