Clene's CNM-Au8® Shows Statistically Significant Difference in Plasma Neurofilament Light (NfL) levels in the HEALEY ALS Platform Trial

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- CNM-Au8® treatment demonstrated significantly reduced plasma neurofilament light chain (NfL) levels compared to placebo at 24 weeks (p=0.04)
- Clene plans to discuss the totality of the survival and time-to-event results from the full CNM-Au8 clinical data set, including the plasma NfL biomarker data, at an upcoming FDA meeting to accelerate the path toward approval

SALT LAKE CITY, June 15, 2023 (GLOBE NEWSWIRE) -- Clene Inc. (NASDAQ: CLNN) (along with its subsidiaries, "Clene") and its wholly owned subsidiary, Clene Nanomedicine, Inc., a clinical-stage biopharmaceutical company focused on revolutionizing the treatment of neurodegenerative diseases, today reported new data demonstrating a statistically significant reduction of plasma neurofilament light chain (NfL) levels for CNM-Au8® treated participants compared to placebo after 24 weeks of treatment in the double-blind, placebo-controlled period of the HEALEY ALS Platform Trial.

NfL is a key biomarker of neurodegeneration. NfL is released from neurons following axonal injury, especially in people living with ALS, where higher levels of NfL have been found to predict more rapid decline in clinical function and increased mortality risk. Surrogate biomarkers such as NfL have recently been used to support an FDA approval for the treatment of ALS.

Six-Month Plasma NfL Biomarker Findings from the Regimen C (CNM-Au8) Arm in the HEALEY ALS Platform Trial

The results are based on an analysis of the plasma NfL biomarker across all Regimen C participants (CNM-Au8 or placebo, n=161), representing a broad ALS population, as the least-square mean (LS mean) change of the natural logarithm (Ln) of the plasma NfL values with the standard error (SE):

- CNM-Au8 treatment reduced plasma NfL levels compared to placebo; LS Means on a Ln Scale for the 24-week difference of plasma NfL: CNM-Au8 = -0.024 (SE: 0.024); placebo = +0.076 (SE: 0.042); CNM-Au8 vs. placebo difference of LS Means on a Ln Scale = -0.100 (SE: 0.048), p=0.040.

ALS Participants at the Greatest Risk of Disease Progression Showed Consistent Benefit

In addition to the full analysis across all Regimen C participants, sensitivity analyses showed consistent significant reduction in plasma NfL levels versus placebo observed in specific populations generally considered at greater risk of ALS disease progression, including:

- **Faster progressors** (baseline pre-treatment ALSFRS-R slope $\geq$0.45 points/month (*post hoc*, n=107); Difference of LS Means on a Ln Scale (SE) = -0.144 (0.058); p=0.014.
- **Definite or probable ALS diagnosis** per El Escorial criteria (*post hoc*, n=125); Difference of LS Means on a Ln Scale (SE) = -0.124 (0.054); p=0.023.
- **Higher mortality risk** (baseline plasma NfL $\geq$ median, *post hoc*, n=79); Difference of LS Means on a Ln Scale (SE) = -0.150 (0.068); p=0.031.

Analyses of NfL from serum samples specified as the primary blood matrix for analysis are underway. Additional biomarker and long-term survival data from the HEALEY ALS Platform Trial double-blind and open-label extension periods have been collected and are undergoing testing preparatory for analysis to be reported later this year.

"The totality of survival and time-to event data supports my belief that CNM-Au8 should move forward expeditiously into the next phase of clinical development," said Merit Cudkowicz, M.D., Chair Neurology Department, Director, Sean M Healey & AMG Center for ALS, and the Principal Investigator of the HEALEY ALS Platform Trial. "These clinical and biomarker evidence from the Phase 2 HEALEY ALS Platform Trial will also help advance the design of a Phase 3 trial to increase our confidence in how CNM-Au8 can delay the clinical course of this devastating neurodegenerative disease."

Benjamin Greenberg, M.D., Head of Medical at Clene, commented, "The statistically significant difference in plasma neurofilament levels, a key marker of neurodegeneration, is another independent indicator of slowed disease progression associated with CNM-Au8 treatment. Results with CNM-Au8 treatment in multiple Phase 2 trials in ALS previously showed two independent indicators of slowed disease progression—CNM-Au8 decreased time to clinical worsening and improved survival at the 30 mg dose. These independent pieces of evidence strongly support CNM-Au8 as a potential treatment for ALS."

Rob Etherington, Clene's CEO, added, "For the first time, the FDA has recently granted accelerated approval of another ALS therapy based upon plasma NfL as a biomarker predictive of clinical efficacy. Clene is exploring the possibility for a NDA filing. In addition to planning the global Phase 3 ALS trial, we are preparing the complete CNM-Au8 clinical data package including our strong safety evidence, biomarker, survival, and time-to-event analyses for FDA regulatory discussion in the third quarter. We believe the benefit-risk framework for CNM-Au8 strongly favors a path to approval."

About Clene
Clene is a clinical-stage biopharmaceutical company focused on revolutionizing the treatment of neurodegenerative disease by targeting energetic

failure, an underlying cause of many neurological diseases. 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 Twitter, LinkedIn, and Facebook.

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 Healey ALS Platform Trial

The HEALEY ALS Platform Trial is a perpetual multi-center, randomized, double-blind, placebo-controlled Phase 2program designed to evaluate the efficacy and safety of multiple investigational products in people living with ALS. This landmark platform trial tests multiple treatments utilizing a shared placebo group. 161 participants were randomized to 30 mg CNM-Au8, 60 mg CNM-Au8, or placebo as adjunct to standard of care for a 24-week treatment period. Active drug was offered to all participants who were eligible and elected to continue into the Open Label Extension. The primary outcome of the trial was the change in disease severity over time as measured by ALSFRS-R through 24 weeks accounting for mortality (analyzed using a Bayesian shared parameter model). Prespecified secondary efficacy endpoints included the Combined Assessment of Function and Survival joint rank test (CAFS), change in respiratory function as measured by slow vital capacity (SVC), and overall survival. For more information, please see ClinicalTrials.gov Identifier: NCT04297683.

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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