# Clene Announces Peer-Reviewed Publication Characterizing the Protein Corona of the Investigational Neurodegenerative Disease Drug, CNM-Au8®

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- Proprietary catalytic gold nanocrystals comprising Clene's investigational drug CNM-Au8 ® develop a protein corona upon exposure to human blood plasma comprised of proteins that promote blood-brain barrier penetration, an important feature of the drug's neuroprotective mechanism of action

- The protein corona attracted by CNM-Au8 nanocrystals prevents aggregation upon entering the bloodstream, enabling the drug's longevity in circulation without provoking an inflammatory response

SALT LAKE CITY, March 15, 2024 (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 improving mitochondrial health and protecting neuronal function to treat neurodegenerative diseases, including (ALS) and multiple sclerosis (MS), today reported the publication of "Protein Corona Composition of Gold Nanocatalysts" in the journal *ACS Pharmacology & Translational Science*, a journal of the American Chemical Society that publishes innovative and impactful research with translational relevance across a broad spectrum of biological sciences.

The publication, led by Morteza Mahmoudi, associate professor in the Precision Health program and Department of Radiology at the Michigan State University College of Human Medicine, and members of his laboratory, fully characterized the proteins from human blood plasma that form the protein corona of the gold nanocrystals of CNM-Au8, an investigational drug in development for the treatment of neurodegenerative diseases. CNM-Au8 is comprised of a suspension of clean-surfaced, faceted gold nanocrystals that, once swallowed, pass through the gastrointestinal tract, and enter the body's circulatory system, where they interact with, and become coated by, blood proteins and other biomolecules, forming the 'protein/biomolecular corona.' Using multiple state-of-the-art techniques that have been refined and optimized by the Mahmoudi lab, the group characterized the CNM-Au8 nanocrystals' protein corona and made several important observations:

• Protein corona-coated CNM-Au8 nanocrystals are less likely to aggregate than the non-coated nanocrystals.

• The specific apolipoproteins that are enriched on the surfaces of CNM-Au8 nanocrystals (apolipoproteins A-I, A-II, C-II, C-III, and E) are known to bind to specific receptors on the blood-brain barrier (BBB) and promote the transport of substances across the BBB.

• The protein corona did not show a significant increase in complement proteins and fibrinogens compared to these proteins' relative amounts in human plasma; coupled with the enrichment of apolipoproteins in these coronas, this corona composition is likely to increase colloidal stability and decrease inflammatory reactions from immune cells, consequently extending their circulation time in the blood.

The full publication can be accessed here: https://pubs.acs.org/doi/10.1021/acsptsci.4c00028

"The protein corona of CNM-Au8 gold nanocrystals, tailored for brain delivery applications, exhibits a unique composition, notably enriched with critical apolipoproteins such as apolipoprotein E. This composition enhances the nanocrystals' ability to traverse the blood-brain barrier. Simultaneously, the depletion of opsonin-based proteins in the corona extends their circulation time in the blood, as observed clinically. Our research underlines that these engineered gold nanocrystals, designed with specific structures and without surfactants, can form a distinct protein corona that facilitates access to brain tissue," explained Prof. Mahmoudi.

"When we invented the electro-crystal-chemical method to grow clean-surfaced, highly faceted gold nanocrystals, we certainly had catalytic optimization in mind. However, we also understood that the protein corona can control the location of our nanocrystals *in vivo*. These new data show that the corona composition of the CNM-Au8 nanocrystals contribute further favorable drug properties to our neuroprotective agent, consistent with what we are seeing in our preclinical and clinical studies," said Mark Mortenson, CSO of Clene.

"These results are notably consistent with the activity of CNM-Au8 demonstrated in our completed Phase 2 clinical trials. Our REPAIR-MS and REPAIR-PD biomarker trials showed that orally dosed CNM-Au8 treatment favorably affects levels of brain metabolites in people with multiple sclerosis and Parkinson's disease. Our extensive nonclinical toxicity and clinical pharmacokinetics studies have demonstrated that CNM-Au8 reaches steady state levels in blood without any serious adverse effects, such as inflammatory or immunomodulatory issues, identified as related to CNM-Au8 treatment. Across 500+ years of patient exposure in multiple Phase 2 clinical trials and expanded access programs, CNM-Au8 treatment has been shown to be safe and well-tolerated. These prior clinical results are further enriched by the findings from this work explaining how the protein corona forms around CNM-Au8 once in the bloodstream, and how this corona preferentially aids access through the blood-brain barrier to support CNM-Au8's activity in the brain," said Michael Hotchkin, Chief Development Officer for Clene.

A Phase 3 registrational clinical trial of CNM-Au8 for the treatment of the progressive neurodegenerative disease, amyotrophic lateral sclerosis, is presently planned to launch in 2024.

**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.

**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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