Clene Reports Significant Improvement in Vision and Cognition With CNM-Au8® Treatment in VISIONARY-MS Trial Long-Term Open Label Extension

January 8, 2024

- Long-term CNM-Au8 treatment demonstrated improvement of vision as measured by low contrast visual acuity (LCLA), an assessment of visual function in people living with multiple sclerosis (MS), through 35 months from randomization, p<0.0001
- Long-term CNM-Au8 treatment demonstrated improvement of cognition, measured by the Symbol Digit Modality Test (SDMT), through 35 months from randomization, p<0.0001
- Treatment was well-tolerated, without a single serious adverse event attributed to CNM-Au8 and no significant safety findings reported

SALT LAKE CITY, Jan. 08, 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 new CNM-Au8® results from the long-term open label extension (LTE) of the VISIONARY-MS trial in participants with stable relapsing multiple sclerosis (RMS) totaling nearly three years of follow-up.

After completion of the double-blind period, study participants were offered to continue on CNM-Au8 30mg for up to an additional 96-weeks in the LTE. Analyses are reported for the modified intent to treat (mITT) population that included all study participants with valid clinical data.

- **Progressive Vision Improvement:** The least-square mean difference (SE) at Week 144 for low contrast visual acuity (LCLA) change across both eyes versus the original randomization baseline of participants assigned to CNM-Au8 was: +8.70 letters (1.88), 95% CI: 5.0 to 12.4, p<0.0001.
    - The LCLA least-squared mean difference (SE) vs. the end of the double-blind period was: +4.0 letters (1.67), 95% CI: 0.72 to7.30, p=0.017.

Low contrast vision demonstrated sustained improvement by up to 38 letters across both eyes in individual participants, which represents multiple row gains on a greyed-out MS eye chart.

- **Progressive Cognitive Improvement:** The least-square mean difference (SE) at Week 144 for symbol digit modality test (SDMT) change versus the original randomization baseline of participants assigned to CNM-Au8 was: +8.03 (1.52), 95% CI: 5.01 to 11.0, p<0.0001.
    - The SDMT least-square mean difference (SE) vs. the end of the double-blind period was: +3.11 (1.3), 95% CI: 0.55 to 5.68, p=0.018.

Cognitive improvement, particularly working memory and information processing speed, was improved by up to 35 points in individual participants, where a three-point change in cognitive processing speed has been deemed notable in other MS studies.

Improvements demonstrated during the 48-week double-blind period were maintained in the LTE for timed 25-foot walk test (T25FWT) and nine-hole peg test (9HPT).

Placebo participants who transitioned to CNM-Au8 during the LTE showed significant improvements versus original baseline in LCLA and SDMT that were generally consistent with the increases observed in participants originally randomized to CNM-Au8. Full clinical results for the LTE will be presented at the ninth annual Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Forum taking place February 29 – March 2, 2024 in West Palm Beach, Florida.

VISIONARY-MS, designed to investigate the protection or improvement of neurological function in stable relapsing remitting MS participants with chronic optic neuropathy, was a Phase 2 multicenter, randomized, double-blind, placebo-controlled trial evaluating the efficacy and safety of CNM-Au8 (15 mg or 30 mg daily) versus placebo over 48 weeks of double-blind treatment. The primary outcome was LCLA improvement. Global neurological improvement, measured by the modified Multiple Sclerosis Functional Composite (mMSFC) including vision, cognition, upper extremity function, and walking speed assessment was the secondary outcome. Nearly all participants (92%) were treated with highly effective immunomodulatory disease modifying therapies (DMTs) as background standard of care. In the double-blind portion of the trial, 73 participants were randomized, with 55 of 69 eligible (80%) participants continued in the LTE.

“These observed long-term clinical improvements for participants with stable disease, over and above background immunomodulatory disease modifying therapy, are unprecedented,” commented Professor Michael Barnett, one of the trial’s key clinical advisors. “The data show clear overall improvements in vision and cognition for participants treated for nearly three years from randomization. Importantly, these results were robust and consistent. Positive impacts on disease progression and the potential to at least partially reverse established disability, if confirmed in a larger study, represent a major therapeutic leap for patients with MS.”

“Despite tremendous advances in immunotherapies for MS, there is a significant unmet need for treatments to prevent neurodegeneration and create opportunities for clinical improvement,” added Dr. Benjamin Greenberg, M.D., Head of Medicine at Clene. “Years have been spent investigating

neuroprotective therapies for multiple sclerosis and other neurodegenerative diseases. These data continue to build a strong case in favor of pursuing CNM-Au8 in upcoming Phase 3 studies. Clinically significant improvement is rarely seen in MS patients and this trial provides evidence of CNM-Au8's potential to improve function in this population. Clene is currently reviewing these data with prospective pharmaceutical partners interested in MS."

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.

Media Contact
Ignacio Guerrero-Ros, Ph.D., or David Schull
Russo Partners, LLC
Ignacio.guerrero-ros@russopartnersllc.com
David.schull@russopartnersllc.com
(858) 717-2310

Investor Contact
Kevin Gardner
LifeSci Advisors
kgardner@lifesciadvisors.com
617-283-2856