Clene Reports New Data from the VISIONARY-MS Phase 2 Study in Multiple Sclerosis Demonstrating CNM-Au8® Treatment Improved Brain Neuronal Structural Integrity

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- ***MRI results reinforce the clinical neurological improvements previously reported***
- ***MRI results showed improved brain neuronal structural integrity, independent of an immunomodulatory effect***
- ***MRI results consistently favor CNM-Au8 improvement of neuronal integrity and myelin improvement, showing decreased brain deterioration***
- ***The brain improvements in stable MS patients on background therapy are unprecedented***

SALT LAKE CITY, Feb. 13, 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 announced updated MRI results from the Phase 2 double-blinded, 48-week treatment period of the VISIONARY-MS trial in multiple sclerosis (MS) patients. These exploratory MRI results support the previously reported statistically significant clinical improvements in low contrast vision and global neurological function in stable relapsing MS patients reported in the mITT population.

VISIONARY-MS investigated the efficacy and safety of CNM-Au8® (15 mg or 30 mg daily) versus placebo over 48 weeks in stable relapsing remitting MS participants with chronic optic neuropathy. Nearly all participants (92%) were treated with highly effective disease modifying therapies (DMT) as background standard of care. Due to limited enrollment (73 of 150) because of the COVID pandemic, the threshold for significance was pre-specified at p=0.10 prior to database lock and submitted to the FDA in the statistical analysis plan. The study was designed to investigate the hypothesis that supporting neuronal energy metabolism protects neurologic function in patients with MS. Prior to the initiation of VISIONARY-MS, preclinical data characterized CNM-Au8's mechanism of action as improving energy metabolism in neurons. Exploratory endpoints, including advanced MRI imaging, within this study were designed to evaluate mechanistic and biological effects of CNM-Au8 treatment.

The MRI findings provide evidence of brain neuronal structural integrity assessed by diffusion tensor imaging (DTI) that demonstrated statistically significant results for key metrics of axonal integrity and white matter integrity, independent of an immunomodulatory effect. Results include all participants with advanced MRI data collection (n=68).

- Fractional Anisotropy change within the whole brain (Cerebrum) – Week 48 Least-Squares (LS) Mean Difference: 0.0029, 95% CI: 0.0048 to 0.0054, p = 0.0199
- Fractional Anisotropy change within total Cerebral White Matter – Week 48 LS Mean Difference: 0.0026, 95% CI: -0.0003 to 0.0055, p = 0.0805
- Fractional Anisotropy change within total Cerebral Normal Appearing White Matter – Week 48 LS Mean Difference: 0.0025, 95% CI: -0.00025 to 0.0053, p = 0.0737

"Fractional anisotropy is most often used to quantify white matter integrity, with values that range from highly isotropic—with poor white matter integrity—to highly anisotropic associated with improved white matter integrity," explained Professor Michael Barnett, one of the trial's key clinical advisors. "These MRI data show clear overall improvements in measures of brain white matter integrity. Placebo treated patients had deterioration during the 48-week treatment period, while patients treated with CNM-Au8 had preserved white matter integrity. Importantly, these results were robust and consistent across all prespecified brain regions. White matter integrity is important because its loss is associated with cognitive and functional decline in MS patients. These results are unprecedented over and above background disease modifying therapy."

The DTI results independently demonstrated improvements across the domains of fractional anisotropy, radial diffusivity, and mean diffusivity, each favoring CNM-Au8 treated participants across all nine prespecified brain regions and brain white matter tracts for each metric. Similarly, MRI measures of improved myelin integrity, including magnetization transfer ratio and myelin water fraction, also consistently favored CNM-Au8 treated participants across all brain regions and white matter tracts investigated. Additional lesion MRI analyses are underway.

Robert Glanzman, MD, FAAN, Clene's Chief Medical Officer, said, "Importantly, these data further reinforce our hypothesis that improving brain energetic metabolism results in improved neurological structure and function when CNM-Au8 is administered as adjunct to standard immunomodulatory disease-modifying MS therapies. Clene plans to initiate a fully powered Phase 3 study to demonstrate improved global neurological function in patients with progression independent of relapse activity (PIRA), the most urgent unmet need in MS today, in collaboration with a development partner. We look forward to presenting these MRI data at the upcoming forum for Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) taking place February 22-25, 2023."

MS expert and clinical investigator Benjamin Greenberg, MD, MHS, added, "The totality of the clinical and paraclinical data from the VISIONARY-MS trial are robust. These latest MRI results strongly reinforce the previously reported findings of global clinical neurological improvement. There is a critical unmet need in multiple sclerosis therapeutics for interventions that protect neuronal function and myelin health independent of immunomodulation or suppression. Years have been spent seeking a truly neuroprotective therapy for multiple sclerosis and other neurodegenerative diseases. These data argue in favor of pursuing CNM-Au8 in further Phase 3 studies."

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 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.

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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