Clene Announces Updated VISIONARY-MS Phase 2 Trial Data Presented at 2023 ACTRIMS Forum Show CNM-Au8® Demonstrated Significant Improvements in Clinical Outcomes, Brain Structure, and Visual System

February 27, 2023

- ***Positive clinical results demonstrated in stable relapsing multiple sclerosis patients adjunctive to immunomodulatory disease modifying therapy was previously reported***
- ***Updated Visual Evoked Potential (VEP) findings provide evidence of improved information signaling from the eye to the brain's visual cortex***
- ***These significant VEP results alongside the previously reported significant MRI results add to the totality of evidence supporting the clinical benefits of CNM-Au8***
- ***CNM-Au8 treatment was well-tolerated, and no significant safety findings were observed***

SALT LAKE CITY, Feb. 27, 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 results from the VISIONARY-MS Phase 2 trial were presented this weekend at the 8th annual Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS) Forum 2023.

The poster titled, "CNM-Au8 Phase 2 VISIONARY-MS Updated Trial Results," contributes to the growing body of evidence supporting improvements in clinical neurologic function and significant paraclinical MRI and VEP findings. The VEP and MRI analyses presented were prespecified exploratory endpoints.

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 multiple sclerosis (MS) patients with chronic optic neuropathy. The study was designed to investigate the hypothesis that supporting neuronal energy metabolism protects neurologic function in patients with MS. 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, attributed to 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. Clene announced the topline results of the study in August 2022.

Updated VEP Results

The updated multi-focal Visual Evoked Potential (mf-VEP) findings provide evidence of improved information transmission in the visual system (from the eye to the visual cortex) supported by statistically significant increases in amplitude. The VEP *least affected* eye was defined as the eye with the shortest latency delay at baseline. Results included all participants with recorded VEP data (n=64):

- mf-VEP amplitude percent change in the *least affected* eye at baseline – Week 48 least squares [LS] mean difference: 9.7%, 95% CI: 3.1% to 16.3%, p=0.0047
- mf-VEP amplitude percent change in the *most affected* eye at baseline – Week 48 LS mean difference: 6.1%, 95% CI: -0.6% to 12.7%, p=0.0730
- mf-VEP amplitude percent change across both eyes – Week 48 LS mean difference: 7.9%, 95% CI: 1.4% to 14.4%, p=0.0184

The increased amplitude signal suggests previously impaired neurons subsequently increase information transmission following CNM-Au8 treatment, supporting improved axonal integrity.

Previously Reported Clinical and MRI Results

The primary and secondary endpoints demonstrated improved clinical outcomes in the mITT population, independent of an immunomodulatory effect:

- The primary endpoint of LCLA change demonstrated significant improvement – Week 48 LS Mean Difference: 3.13; 95% CI: -0.08 to 6.33, p = 0.056
- The secondary endpoint of global neurological improvement, mMSFC mean standardized change demonstrated significant improvement – Week 48 LS Mean Difference: 0.28; 95% CI: 0.05 to 0.51, p = 0.0197
- CNM-Au8 was well-tolerated, and no significant safety findings were observed.

The exploratory 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. Preservation of white matter integrity is associated with decreased cognitive and functional decline in MS patients. Results included all participants with advanced MRI data collection (n=68):

- Fractional Anisotropy change within the whole brain (Cerebrum): 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

Since many non-relapsing MS patients continue to clinically deteriorate even while receiving immunomodulatory DMTs, a therapy which improves clinical outcomes, brain structure, and visual system remains a significant unmet medical need in MS.

MS expert and clinical investigator Benjamin Greenberg, MD, MHS, noted, “The totality of the clinical and paraclinical data from the VISIONARY-MS trial are robust. Alongside the previously released MRI findings, the newly released mf-VEP data provide further evidence of neuronal preservation. 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 help build a strong case in favor of pursuing CNM-Au8 in further Phase 3 studies.”

About VISIONARY-MS
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 multiple sclerosis (MS) patients with chronic optic neuropathy. The study was designed to investigate the hypothesis that supporting neuronal energy metabolism protects neurologic function in patients with MS. 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) attributed to 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 primary outcome was change in low contrast letter acuity in the most clinically affected eye at baseline. The secondary outcome was global neurological improvement assessed by the modified Multiple Sclerosis Functional Composite (mMSFC), evaluating low contrast vision, cognition, upper extremity function, and walking speed with CNM-Au8 as adjunct to approved background immunomodulatory DMTs in stable MS patients. The mITT population included all study participants with valid clinical data. Censored observations included a subject with a change in mobility assist device (cane to walker) for timed 25-foot walk test (T25FWT, n=1), and invalid data from 1 of 11 sites (n=9) with low contrast letter acuity (LCLA) testing issues.

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.

Media Contact
Ignacio Guerrero-Ros, Ph.D., or David Schull
Russo Partners, LLC
Ignacio.guerrero-ros@russopartnersllc.com

Investor Contact
Kevin Gardner
LifeSci Advisors
kgardner@lifesciadvisors.com

David.schull@russopartnersllc.com 617-283-2856
(858) 717-2310