Clene Nanomedicine Presents Updated Clinical Data from Phase 2 RESCUE-ALS and REPAIR trials and Preclinical ALS data at 2022 MDA Clinical & Scientific Conference

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- Analyses of long-term open-label extension of RESCUE-ALS trial indicate improved survival compared to predictions derived from validated ENCALS risk model
- Interim results demonstrate approximately 70% decreased risk of death for participants who entered the RESCUE-ALS long-term open label extension

SALT LAKE CITY, March 14, 2022 (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 disease, today announced multiple presentations of updated clinical trial results from the Phase 2 RESCUE-ALS and REPAIR trials in addition to new mechanistic preclinical data in ALS at the 2022 MDA Clinical & Scientific Conference, taking place March 13-16 in Nashville.

The first poster, titled “***RESCUE-ALS Trial Results: A Phase 2, Randomized, Double-Blind, Placebo-Controlled Study of CNM-Au8 to Slow Disease Progression in ALS***,” selected as an oral presentation, and the second poster, “ ***Evidence for a Potential Survival Benefit with CNM-Au8 Treatment from the RESCUE-ALS Trial Long-Term Open Label Extension,”*** further support Clene’s lead drug candidate CNM-Au8®, a catalytically active gold nanocrystal suspension, as a potential disease-modifying therapy for amyotrophic lateral sclerosis (ALS).

RESCUE-ALS, a Phase 2 multi-center, randomized, double-blind, parallel-group, placebo-controlled trial examined the efficacy, safety, pharmacokinetics, and pharmacodynamics of CNM-Au8 in 45 participants with early ALS over a 36-week treatment period. In the 36-week blinded period, there were significant benefits with CNM-Au8 treatment: slowing ALS disease progression (p=0.0125), decreasing the proportion of participants with a 6-point decline in the ALS Functional Rating Scale Revised (ALSFRS-R) (p=0.035), and improving quality of life as measured by the ALS Specific Quality of Life (ALSSQOL-SF) questionnaire (p=0.018).

The second poster presented updated evidence for survival benefit with CNM-Au8 treatment that was reported from the RESCUE-ALS trial long-term open label extension for both the active and placebo groups. Interim analyses of observed survival compared to estimated median survival derived from the validated ENCALS prediction model significantly favored CNM-Au8 treatment with a hazard ratio of 0.3 for participants who entered the open-label extension (HR 0.3; p=0.01, log-rank test). CNM-Au8 was shown to be well-tolerated with no safety signals identified over 96 weeks of treatment.

The third poster, titled **“*Evidence for Brain Energy Metabolic Support withCNM-Au8 Treatment: Results from Phase 2 REPAIR Clinical Trial With CNM-Au8*,”** demonstrated improved brain energy metabolism assessed by high-resolution magnetic resonance spectroscopy (^{31}P-MRS). CNM-Au8 treatment resulted in improved brain NAD^+/NADH ratio (primary endpoint, paired t-test, p=0.0371). This result was driven both by increase in NAD^+ and a decrease in NADH (secondary endpoint, paired t-test, p=0.0264). CNM-Au8 treatment also resulted in homeostatic effects on brain energy-related phosphorous-containing metabolites, including ATP. Study participants with whole-brain ATP levels less than the population's baseline mean saw significantly increased ATP levels, while patients with baseline levels greater than the baseline mean decreased to the population mean (r^2 = 0.711, p<0.0001). These data demonstrate CNS target engagement following treatment with CNM-Au8 and support its candidacy as a disease-modifying therapy for the treatment of neurodegenerative diseases associated with dysregulated neuronal energy metabolism.

The fourth poster accepted for presentation, “***CNM-Au8 Gold Nanocatalysis Protects Neurons Against Degeneration and Death in Multiple* in vitro *models of ALS*,**” demonstrates CNM-Au8’s ability to promote neuronal survival and function in multiple independent *in vitro* models of ALS: (i) treatment of primary rat spinal motor neurons improved survival, preserves the neurite networks, and reduced cytoplasmic TDP-43 aggregate accumulation after either glutamate excitotoxic injury or exposure to beta-amyloid (Aβ 1-42) oligomers; (ii) treatment of spinal motor neurons from transgenic $SOD1^{G93A}$ rats protected motor neurons from death upon exposure to excitotoxic glutamate in a cAMP-dependent manner, and reduced SOD1 protein accumulation in a manner independent of cAMP; (iii) treatment of human induced pluripotent stem cell (iPSC)-derived neurons from C9ORF72 patients prevented neuronal death in response to stressors; and (iv) survival and neurite outgrowth of human iPSC-derived motor neurons in co-culture with toxic $SOD1^{A4V}$ ALS-patient derived astrocytes were significantly and dose-dependently improved with treatment of CNM-Au8.

“The preclinical and clinical data presented at MDA further support Clene’s lead drug candidate CNM-Au8 as a potential disease-modifying therapy for amyotrophic lateral sclerosis,” said Dr. Robert Glanzman, MD FAAN, Clene’s Chief Medical Officer. “We look forward to the continued advancement of the ALS clinical program with the top-line results from the HEALEY ALS Platform Trial expected in the second half of the year.”

Rob Etherington, Clene’s CEO, added, “This is an exciting time for Clene as we build a bigger body of scientific and clinical evidence in support of our CNM-Au8. Will continue to further the validation of our findings in neurological function and survival as we await results in larger clinical studies underway.”

About CNM-Au8®, a gold nanocrystal suspension
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 https://clene.com or follow us on Twitter, LinkedIn and Facebook.

Forward-Looking Statements

This press release contains "forward-looking statements" which are intended to be covered by the "safe harbor" provisions of the Private Securities Litigation Reform Act of 1995. Clene's actual results may differ from its expectations, estimates and projections and consequently, you should not rely on these forward-looking statements as predictions of future events. Words such as "expect," "estimate," "project," "budget," "forecast," "anticipate," "intend," "plan," "may," "will," "could," "should," "believes," "predicts," "potential," "might" and "continues," and similar expressions are intended to identify such forward-looking statements. These forward-looking statements involve significant known and unknown risks and uncertainties, many of which are beyond Clene's control and could cause actual results to differ materially and adversely from expected results. Factors that may cause such differences include Clene's ability to demonstrate the efficacy and safety of its drug candidates; the clinical results for its 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; Clene's ability to achieve commercial success for its marketed products and drug candidates, if approved; Clene's ability to obtain and maintain protection of intellectual property for its technology and drugs; Clene's reliance on third parties to conduct drug development, manufacturing and other services; Clene's limited operating history and its ability to obtain additional funding for operations and to complete the licensing or development and commercialization of its drug candidates; the impact of the COVID-19 pandemic on Clene's clinical development, commercial and other operations, as well as those risks more fully discussed in the section entitled "Risk Factors" in Clene's Annual Report on Form 10-K, as well as discussions of potential risks, uncertainties, and other important factors in Clene's subsequent filings with the U.S. Securities and Exchange Commission. Clene undertakes no obligation to release publicly any updates or revisions to any forward-looking statements to reflect any change in its expectations or any change in events, conditions or circumstances on which any such statement is based, subject to applicable law. 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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