Clene Nanomedicine Presents Blinded Interim Update from VISIONARY-MS and Positive Results from REPAIR-MS Phase 2 Clinical Trials

October 14, 2021

VISIONARY-MS blinded interim data show clinically relevant improvements in the modified MS Functional Composite for the study population through 48 weeks of treatment

REPAIR-MS clinical trial demonstrated improved brain energetic metabolism following treatment with CNM-Au8®, a catalytically active gold nanocrystal suspension

SALT LAKE CITY, Oct. 14, 2021 (GLOBE NEWSWIRE) -- Clene Nanomedicine, Inc., a clinical-stage biopharmaceutical company, presented positive results from the Phase 2 REPAIR-MS target engagement clinical trial and blinded interim data from the Phase 2 VISIONARY-MS clinical trial with CNM-Au8, a catalytically active nanotherapeutic, at the 37th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS), taking place October 13-15, 2021.

VISIONARY-MS is a double-blind, placebo-controlled Phase 2 clinical trial evaluating the efficacy and safety of CNM-Au8 as a remyelinating and neuro-reparative treatment in stable relapsing MS (RMS) patients. Blinded analyses presented compared changes in the overall study population's modified Multiple Sclerosis Functional Composite (mod-MSFC) values over the 48-week treatment period to the baseline values of study participants with mild disease, as defined by pre-treatment Expanded Disability Status Scale (EDSS) scores of 1.5 or less. This mild disease population of patients demonstrated milder neurological impairment at baseline than the overall study population, providing a valid comparator group with which to evaluate changes in neurological function in the overall study population over the 48-week treatment period. Changes in the four mod-MSFC sub-scales (low contrast letter acuity (LCLA), symbol digit modalities test (SDMT), 9-hole peg test (9HPT), and timed 25-foot walk test (T25FWT)) were compared to baseline scores of the mild disease comparator group at each 12-week study time-point (Weeks 12, 24, 36, and 48). At each visit, the overall study population (randomized 2:1, active CNM-Au8 to placebo) showed increasing improvements in mean standardized change for LCLA (primary endpoint, mixed-effects model; $p<0.0001$ vs. baseline), average MSFC scores (secondary endpoint, mixed-effects model; $p<0.0001$ vs. baseline), and other MSFC sub-scales. These data support CNM-Au8's potential to drive meaningful neurological improvements in stable RMS patients. Unblinded topline data are anticipated in the first half of 2023.

The objective of the REPAIR clinical trial program was to demonstrate the effects of treatment with CNM-Au8 on brain energy metabolism across two sister clinical trials. Patients with Parkinson's disease (REPAIR-PD) and multiple sclerosis (REPAIR-MS) were imaged utilizing ^{31}phosphorous magnetic resonance spectroscopy (^{31}P-MRS), an innovative non-invasive brain imaging technique, before and after 12 weeks of daily oral dosing with CNM-Au8. All patients were administered active CNM-Au8 in a dose-blinded fashion. The results for the primary endpoint, the mean change in brain NAD^+/NADH ratio (the ratio of the oxidized to reduced form of nicotinamide adenine dinucleotide), demonstrated a statistically significant increase of 10.4% (0.589 units) following 12-weeks of treatment with CNM-Au8 ($p=0.037$, paired t-test), in the pre-specified integrated analysis across the two clinical trials. The individual results for the REPAIR-MS clinical trial demonstrated a 14.3% (0.8296 units) improvement ($p=0.14$, paired t-test). The REPAIR-MS clinical trial incorporated a third ^{31}P-MRS scan following a 6-week treatment washout, which demonstrated that the mean levels of the NAD^+/NADH ratio returned to baseline following the 6-week withdrawal of CNM-Au8. Exploratory endpoints showed that taking CNM-Au8 resulted in normalization of several critical markers of brain energy production capacity including beta-ATP levels ($r^2 = 0.71$, $p = 0.001$) and phosphorylation potential ($r^2 = 0.68$, $p = 0.002$). Modified Multiple Sclerosis Functional Composite (see above VISIONARY-MS clinical trial for description) data showed directional, exposure-related improvements in the mod-MSFC subscale values from baseline through Week 12. There were no serious adverse events and treatment-emergent adverse events were predominantly mild, transient, and assessed as unrelated to treatment.

"The final REPAIR-MS results and blinded interim data from VISIONARY-MS demonstrated consistent and complementary findings," said Robert Glanzman, MD, FAAN, chief medical officer of Clene. "Results from the REPAIR-MS trial demonstrated CNM-Au8's ability to enter the brain and address energetic failure, a key driver in the pathophysiology of MS and other neurodegenerative diseases. These mechanistic results provide important support for the updated, blinded interim VISIONARY data analysis, which we believe suggests that CNM-Au8 has the potential to drive clinically meaningful improvements in recognized MS functional endpoints when administered in addition to standard of care. We look forward to the continued advancement of the VISIONARY-MS trial."

"We believe these data from REPAIR-MS and VISIONARY-MS clinical trials showed that CNM-Au8 is working mechanistically to address a foundational challenge common to many neurodegenerative diseases, namely that stressed or failing neurons and oligodendroglial progenitor cells need additional energetic support for their survival, repair, and normal function. These data provide evidence that CNM-Au8 is capable of driving cellular energetic capacity within the brain, which we believe is a foundational insight for the further development of Clene's neurorepair clinical programs. Results from these and our other ongoing studies aim to establish Clene as a pioneer in therapeutic neurorepair and neuroprotection," said Rob Etherington, President and CEO of Clene.

About the REPAIR Clinical Trial Program

REPAIR-MS and REPAIR-PD are Phase 2 single-center, active-only, sequential group studies examining the brain metabolic effects, safety, pharmacokinetics, and pharmacodynamics of CNM-Au8 in patients who have been diagnosed with MS within 15 years of screening or in patients with PD who have been diagnosed within three years of screening. Investigators and participants are blinded to dose. Participants received orally delivered CNM-Au8 daily each morning for 12 weeks. Participants undergo ^{31}P-MRS brain imaging scans to semi-quantitatively measure central nervous system (CNS) energetic metabolites at baseline, prior to administration of drug, and at the end-of-study following at least 12 weeks of exposure to CNM-Au8. The objective of these studies is to demonstrate target engagement for CNM-Au8 on CNS biomarkers related to energetics and neuronal membrane stability in patients with MS and PD. The studies are taking place at the University of Texas Southwestern Medical Center with a team of internationally recognized experts in brain imaging and treatment of disorders of the CNS. For more information see ClinicalTrials.gov Identifiers:

NCT03993171 and NCT03815916.

About VISIONARY-MS

VISIONARY-MS is a Phase 2 multi-center, double-blind, randomized, placebo-controlled trial evaluating the efficacy and safety of CNM-Au8 for remyelination and neurorepair in stable relapsing multiple sclerosis (MS) patients with chronic visual impairment. 150 participants are being enrolled at expert MS clinical trial sites within Australia, Canada, and the United States. Subjects are randomized 1:1:1 (high-dose:low-dose:placebo). The primary endpoint is improvement in Low Contrast Letter Acuity (LCLA) from baseline to week-24. Key secondary endpoints include improvements from baseline to week-24 in the remaining modified-Multiple Sclerosis Functional Composite (MSFC) subscales (Symbol Digit Modalities Test, 9-Hole Peg Test, and Timed 25-Foot Walk). Subject to ongoing pandemic-related research restrictions at MS clinical trial sites, unblinded topline data are anticipated in the first half of 2023. For more information, see ClinicalTrials.gov Identifier: NCT03536559.

About Multiple Sclerosis (MS)

MS is an inflammatory, demyelinating disease of the central nervous system and is the most common (non-traumatic) cause of neurological disability in young adults. The most common clinical presentation, relapsing MS (RMS), is characterized by sub-acute attacks of neurological disability, ranging from loss of vision to numbness and tingling, walking difficulty, dizziness, and/or paralysis. Most people with RMS are diagnosed between the ages of 20 and 40, with three times more women being affected than men. A recent study led by the National MS Society estimates that approximately 800,000 people are living with MS in the United States. Despite currently available disease-modifying therapies, approximately 26% of people with MS have developed a non-active, progressive form of the disease, for which there are limited approved, effective therapies, leading to significant loss of quality of life. There remains an urgent need for therapies that promote repair, neuroprotection, and remyelination for all people with MS.

About CNM-Au8®, a gold nanocrystal suspension

Clene's lead drug candidate, CNM-Au8, is an aqueous suspension of catalytically-active, clean-surfaced, faceted gold nanocrystals. Resulting from a patented manufacturing breakthrough, the catalytically active nanocrystals of CNM-Au8 drive critical cellular energy producing reactions in the brain that enable neurorepair and remyelination by increasing neuronal and glial resilience to disease-relevant stressors. CNM-Au8 crosses the blood-brain barrier and is not associated with the toxicities related to synthetic gold compounds or nanoparticles manufactured via alternative methods. CNM-Au8 has demonstrated safety in Phase 1 studies in healthy volunteers and has shown both remyelination and neuroprotective effects in multiple preclinical (animal) models. Preclinical data, both published in peer-reviewed journals and presented at scientific congresses, demonstrate that treatment of neuronal cultures with CNM-Au8 improves survival of neurons, protects neurite networks, decreases intracellular levels of reactive oxygen species, and improves mitochondrial capacity in response to cellular stresses induced by numerous disease-relevant neurotoxins. Oral treatment with CNM-Au8 improved functional behaviors in rodent models of ALS, MS, and PD versus vehicle (placebo). CNM-Au8 is a federally registered trademark of Clene Nanomedicine, Inc.

About Clene

Clene, a clinical-stage biopharmaceutical company focused on neurodegenerative disease treatments, is leading the way by using nanotechnology to treat energetic failure, which underlies many neurological diseases. Clene has innovated a novel nanotherapeutic platform to create a new class of drugs. Clene's lead drug candidate, CNM-Au8, is an aqueous suspension of catalytically-active, clean-surfaced, faceted gold nanocrystals that drive critical cellular energetic metabolism in the central nervous system (CNS). CNM-Au8 increases cellular energy production to accelerate neurorepair and improve neuroprotection. CNM-Au8 is currently being evaluated in a Phase 3 registration trial in amyotrophic lateral sclerosis (ALS), a Phase 2 trial examining disease progression via a novel electromyography technique in patients with early ALS, a Phase 2 trial for the treatment of chronic optic neuropathy in patients with stable relapsing multiple sclerosis (MS), and a Phase 2 brain target engagement study in patients with MS. Clene has also advanced into the clinic an aqueous solution of ionic zinc and silver for anti-viral and anti-microbial uses. 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" 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.

Media Contact
Maggie Beller
Russo Partners, LLC
Maggie.Beller@RussoPartnersLLC.com
+1-646-942-5631

Investor Contact
John Woolford
Managing Director, Westwicke

clene@westwicke.com
+1-443-213-0506

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