Clene Reports Significantly Improved Survival Benefit of 19.3 Months and Significantly Delayed Clinical Worsening in Rescue-Als Open-Label Extension Two Year Follow-Up

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- *19.3 month significant survival difference for CNM-Au8® treated participants versus placebo*
- *52% significant decreased risk of ALS clinical worsening events*
- *Over 475 years of CNM-Au8 treatment exposure without any identified safety signals*

SALT LAKE CITY, Aug. 29, 2023 (GLOBE NEWSWIRE) -- Clene Inc. (Nasdaq: CLNN) through its wholly owned subsidiary Clene Nanomedicine Inc., today announced the 24-month long-term data cut from the Phase 2 RESCUE-ALS ongoing open-label extension (OLE) as of July 2023, which showed a significant median survival benefit of 19.3 months using the rank-preserving structural failure time model (RPSFTM) and a significant 52% decreased risk of ALS clinical worsening events with CNM-Au8® treatment.

RESCUE-ALS was a 36-week double-blind placebo-controlled Phase 2 trial that originally randomized 45 people living with ALS, who were an average of 16 months from symptom onset. Thirty-six participants entered the long-term open-label extension, which included 20 participants originally treated with CNM-Au8 during the blinded period and 16 placebo-treated participants who were subsequently switched to CNM-Au8 during the start of the OLE. Survival status was available for all 45 participants.

Survival Improvement:

- Cross-over adjusted median survival (RPSFTM, all study participants, *post hoc*):
  - 19.3 month median survival benefit (CNM-Au8 median survival of 34.2 months, placebo-adjusted median survival of 14.9 months).
  - 75% decreased risk of long-term all-cause mortality in participants originally randomized to treatment with CNM-Au8 compared to those originally randomized to placebo after adjusting for benefit received by placebo after switching to CNM-Au8 (HR= 0.252, 95% CI: 0.106 to 0.597; bootstrap log-rank p<0.001).

The RPSFTM analysis method estimates the survival gained by receiving active treatment using the data from all study participants and then subtracts the benefit from ex-placebo participants switched to CNM-Au8 during the OLE to provide a comparison of CNM-Au8 versus placebo across the entire study period. This well-recognized method has been used to estimate cross-over treatment effects in a recent ALS trial, and oncology and other rare disease trials.

- Unadjusted median survival (without adjusting for the benefit received in ex-placebo participants; analyses include all study participants):
  - 10.1 month median survival benefit when not accounting for the improvement by ex-placebo treated participants who switched to CNM-Au8 at the start of the OLE (CNM-Au8 median survival of 34.2 months; placebo median survival of 24.1 months).
  - 46% decreased risk of all-cause mortality in participants originally randomized to treatment with CNM-Au8 compared to those originally randomized to placebo (HR: 0.54, 95% CI: 0.25-1.1, log-rank p=0.09).
- Observed survival versus ALS historical placebo controls:
  - 70% decreased risk of long-term mortality in participants originally randomized to treatment with CNM-Au8 compared to matched placebo participants derived from the PRO-ACT database (Cox adjusted HR= 0.300, 95% CI: 0.09 to 0.79; p=0.03).

PRO-ACT contains approximately 12,000 ALS patient records from multiple completed clinical trials.

“This new data include open label participants treated with CNM-Au8—42% of whom remain alive up to 3.5 years from randomization and up to 6.6 years from the onset of ALS symptoms, a profoundly meaningful milestone for people living with this devastating disease," said Benjamin Greenberg, M.D., Head of Medical at Clene. “A median survival improvement of 19.3 months provides people living with ALS, their families, and caregivers more time that is so invaluable, and adds to the totality of data we are seeing in our ALS clinical program.”

Improved Time to Clinical Worsening (defined as the first occurrence of death, tracheostomy, assisted ventilation, or feeding tube placement):

- 52% decreased risk of ALS clinical worsening events (HR: 0.48, 95% CI: 0.23-1.0, log-rank p=0.049) in the participants originally randomized to CNM-Au8 treatment versus original placebo.

Safety:

- Over 475 collective years of exposure across ALS, multiple sclerosis (MS), and Parkinson’s disease participants in

CNM-Au8 clinical trials and Expanded Access Protocol (compassionate use) programs without any observed safety signals.
- No serious adverse events have been assessed as related to CNM-Au8 treatment; adverse events observed with CNM-Au8 have been characterized as transient and predominantly mild-to-moderate in severity.

“The data that continues to be received from the RESCUE-ALS open label extension study is truly impressive, and now shows consistently significant decreased risk of death greater than 70% using two different long-term analysis models,” said Professor Matthew Kiernan, PhD, DSc, Bushell Chair of Neurology, University of Sydney, and one of the trial’s clinical advisors. “The survival benefit across treatment arms is linked to less worsening of disease, as experienced by ALS patients. At the same time, the further safety data confirms that CNM-Au8 is well tolerated in ALS patients.”

About Clene

Clene Inc. (Nasdaq: CLNN) (along with its subsidiaries, “Clene”) and its wholly owned subsidiary Clene Nanomedicine Inc., 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 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 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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