# Cyclerion Announces CY6463 Clinical Pipeline Progress and Second Quarter 2022 Financial Results

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*Positive topline results for CY6463 announced in two clinical studies in patients with Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like episodes (MELAS) and Cognitive Impairment Associated with Schizophrenia (CIAS)*

*Study in Alzheimer's Disease with vascular pathology (ADv) enrollment ongoing*

*Appointed Steven E. Hyman, M.D. to its Board of Directors*

CAMBRIDGE, Mass., Aug. 09, 2022 (GLOBE NEWSWIRE) -- Cyclerion Therapeutics, Inc. (Nasdaq: CYCN), a clinical-stage biopharmaceutical company on a mission to develop treatments that restore cognitive function, today announced second quarter 2022 financial results and a business update.

"The data generated from our recent CY6463 CIAS and MELAS studies demonstrate highly encouraging therapeutic activity and favorable safety and tolerability in two distinct patient populations. The results from these studies provide further evidence of the pro-cognitive and anti-inflammatory effects of CY6463 observed in preclinical studies and prior clinical trials. We also continue to enroll a Phase 2a study in Alzheimer's Disease and look forward to seeing topline results in 2023." said Peter Hecht, Ph.D., Chief Executive Officer of Cyclerion.

Dr. Hecht continued: "The promising clinical results we have seen to date strongly support the advancement of CY6463, a first-in-class, CNS-penetrant sGC stimulator. We are preparing to meet with the FDA to align on the development path for CY6463 in MELAS, including potential opportunities to accelerate development in this rare disease. We are also evaluating potential partnerships that would support our objective to fully explore the broad therapeutic potential of CY6463 as a novel treatment for CNS disorders."

**Clinical Pipeline Updates**

- In June, the Company announced positive topline data in its signal-seeking clinical study of CY6463 for the potential treatment of Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like episodes (MELAS). Results from the study were also presented at the United Mitochondrial Disease Foundation (UMDF) Mitochondrial Medicine 2022 Symposium. In this open-label, single-arm study of the oral, once-daily sGC stimulator in eight adults with MELAS, improvements were seen across a range of assessments, including mitochondrial disease-associated biomarkers such as lactate and GDF-15, a broad panel of inflammatory biomarkers, cerebral blood flow, and functional connectivity between neural networks. CY6463 was well tolerated with no AEs leading to treatment discontinuation, and pharmacokinetics (PK) were consistent with Phase 1 studies in healthy volunteers.
- In July, the Company announced positive topline data from its clinical study of CY6463 for the potential treatment of Cognitive Impairment Associated with Schizophrenia (CIAS) in individuals with stable schizophrenia on a stable, single, atypical antipsychotic regimen. Study data from the 14-day, double-blind, randomized, placebo-controlled, multiple-ascending-dose study demonstrate a strong effect on cognitive performance after two weeks of 15mg once-daily dosing. Positive movement on inflammatory biomarkers was also observed. Data also demonstrate that CY6463 was safe and well tolerated, with no reports of serious adverse events (SAEs), severe adverse events (AEs), or treatment discontinuation due to AEs.
- In July, the Company announced the appointment of Steven E. Hyman, M.D., to its Board of Directors effective July 25. Dr. Hyman is a Distinguished Service Professor and the Harald McPike Professor of Stem Cell and Regenerative Biology at Harvard University and a Core Institute Member of the Broad Institute of MIT and Harvard. Dr. Hyman also serves as Chairman of the Board of Directors of the Charles A. Dana Foundation. He is founder of Emugen Therapeutics, a Director of Voyager Therapeutics and Q-State Biosciences, and serves on the scientific advisory boards of Janssen Pharmaceuticals and F-Prime Capital.
- The Company continues to enroll its ADv study (NCT04798989), a randomized, placebo-controlled study of oral, once-daily CY6463 over a twelve-week dosing period. Study participants must have confirmed Alzheimer's disease pathology as assessed by PET or CSF biomarkers, cardiovascular risk factors, as well as mild-to-moderate subcortical small-vessel disease as assessed by MRI. The study will evaluate safety, tolerability, and pharmacokinetics as well as explore the impact of CY6463 on various disease-relevant pharmacodynamic biomarkers (e.g., EEG, MRI, neuroinflammatory biomarkers) and cognitive performance.

**Second Quarter 2022 Financial Results**

- Cash Position: Cash, cash equivalents, and restricted cash balance on June 30, 2022 was approximately $30.3 million, as compared to approximately $41.1 million on Mar. 31, 2022.
- Research & Development Expenses: R&D expenses were approximately $10.2 million for the second quarter of 2022, as

compared to approximately $12.1 million for the second quarter of 2021. The decrease of approximately $1.9 million was driven by decreases in facilities and operating costs, partially offset by increases in external research costs and employee-related expenses.

- General and Administrative Expenses: G&A expenses were approximately $3.5 million for the second quarter of 2022, as compared to approximately $6.2 million for the second quarter of 2021. The decrease of $2.7 million was driven by decreases in facilities and operating costs and employee-related expenses.
- Net Loss: Net loss was approximately $13.4 million for the second quarter of 2022, as compared to $16.2 million for the second quarter of 2021.

**About CY6463**

CY6463 is the first CNS-penetrant sGC stimulator to be developed as a symptomatic and potentially disease-modifying therapy for serious CNS diseases. The nitric oxide (NO)-soluble guanylate cyclase (sGC)-cyclic guanosine monophosphate (cGMP) signaling pathway is a fundamental mechanism that precisely controls key aspects of physiology throughout the body. In the CNS, the NO-sGC-cGMP pathway regulates diverse and critical biological functions including neuronal function, neuroinflammation, cellular bioenergetics, and vascular dynamics. Although it has been successfully targeted with several drugs in the periphery, this mechanism has yet to be fully leveraged therapeutically in the CNS, where impaired NO-sGC-cGMP signaling is believed to play an important role in the pathogenesis of many neurodegenerative and neuropsychiatric diseases and other disorders associated with cognitive impairment. As an sGC stimulator, CY6463 acts as a positive allosteric modulator to sensitize the sGC enzyme to NO, increase the production of cGMP, and thereby amplify endogenous NO signaling. By compensating for deficient NO-sGC-cGMP signaling, CY6463 and other sGC stimulators may have broad therapeutic potential as a treatment to improve cognition and function in people with serious CNS diseases.

**About Cyclerion Therapeutics**

Cyclerion Therapeutics is a clinical-stage biopharmaceutical company on a mission to develop treatments that restore cognitive function. Cyclerion's lead molecule is CY6463, a novel, first-in-class, CNS-penetrant, sGC stimulator that modulates a key node in a fundamental CNS signaling network. The multidimensional pharmacology elicited by the stimulation of sGC has the potential to impact a broad range of CNS diseases. CY6463 has shown rapid improvement in biomarkers associated with cognitive function and is currently in clinical development for Alzheimer's Disease with Vascular pathology (ADv) and Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like episodes (MELAS) and Cognitive Impairment Associated with Schizophrenia (CIAS). Cyclerion is also advancing CY3018, a next generation sGC stimulator.

For more information about Cyclerion, please visit https://www.cyclerion.com/ and follow us on Twitter (@Cyclerion) and LinkedIn (http://www.linkedin.com/company/cyclerion).

**Forward Looking Statement**

Certain matters discussed in this press release are "forward-looking statements". We may, in some cases, use terms such as "predicts," "believes," "potential," "continue," "estimates," "anticipates," "expects," "plans," "intends," "may," "could," "might," "will," "should", "positive" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. In particular, the Company's statements regarding the potential for CY6463 in the treatment of CNS diseases, including CIAS and MELAS, the potential for any successful development of CY6463, the sufficiency of our resources and other abilities to pursue the development of CNS, and other trends and potential future results are examples of such forward-looking statements. The forward-looking statements include risks and uncertainties, including, but not limited to, our ability to continue with sufficient liquidity and capital resources to pursue our business plan regarding CY6463 or any other product (including without limitation our ability to fund additional clinical trials); our ability to successfully demonstrate the efficacy, safety and therapeutic effectiveness of CY6463; the success, timing and cost of our ongoing or future clinical trials and anticipated clinical trials for our current product candidates, including statements regarding the timing of initiation and completion of the trials, futility analyses and receipt of interim results, which are not necessarily indicative of or supported by the final results of our ongoing or subsequent clinical trials; any results of clinical studies not necessarily being indicative of or supported by the final results of our ongoing or subsequent clinical trials;; the timing of and our ability to pursue, obtain and maintain U.S. Food and Drug Administration ("FDA") or other regulatory authority approval of, or other action with respect to, our product candidates; the potential for the CY6463 clinical trial to provide a basis for approval for treatment of MELAS and CIAS; the Company's ability to successfully defend its intellectual property or obtain necessary licenses at a cost acceptable to the Company, if at all; the successful implementation of the Company's research and development programs and collaborations; the success of the Company's license agreements; the acceptance by the market of the Company's product candidates, if approved; and other factors, including general economic conditions and regulatory developments, not within the Company's control. The factors discussed herein could cause actual results and developments to be materially different from those expressed in or implied by such statements. The forward-looking statements are made only as of the date of this press release and the Company undertakes no obligation to publicly update such forward-looking statements to reflect subsequent events or circumstance.

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