



Cyclerion Therapeutics Announces CY6463 Data Demonstrating Improved Cellular Energetics in Preclinical Models of Mitochondrial Disease

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CY6463 alleviated mitochondrial dysfunction and reduced inflammation in preclinical models of mitochondrial complex 1 deficiency

Data provide support for ongoing CY6463 clinical studies in CNS diseases associated with mitochondrial dysfunction

CAMBRIDGE, Mass., June 17, 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 research from preclinical studies demonstrating treatment with its lead soluble guanylate cyclase (sGC) stimulator, CY6463, was associated with improved cellular energetics and reduced inflammation in preclinical models of mitochondrial disease. The data will be presented today at the 10th International Conference on cGMP, taking place June 17-19, 2022, in Augsburg, Germany.

"We're excited to share results highlighting the beneficial impact of sGC stimulation in multiple preclinical models of mitochondrial disease," said Juli Jones, Ph.D, Head of Disease Biology at Cyclerion Therapeutics. "These results are consistent with our recent clinical data in MELAS patients demonstrating that CY6463 was associated with improvements across multiple domains of disease activity, including mitochondrial function and inflammation, and further support the therapeutic potential of CY6463 to address a broad range of diseases characterized by mitochondrial dysfunction."

Data will be presented by Emmanuel Buys, Ph.D., Head of Network Excellence at Cyclerion Therapeutics in a poster titled, "CY6463, a CNS-penetrant sGC stimulator, elicits benefits in preclinical models of mitochondrial complex 1 deficiency" during today's poster session. The poster is made available on the Cyclerion website on the following [link](#).

Presentation highlights:

- CY6463 significantly increased ATP levels in lymphoblasts derived from patients with mitochondrial complex 1 deficiency (Leber hereditary optic neuropathy or Leigh syndrome)
- CY6463 restored mitochondrial gene expression in lymphoblasts derived from patients with mitochondrial complex 1 deficiency (Leber hereditary optic neuropathy or Leigh syndrome)
- CY6463 significantly decreased the astrocytic marker, GFAP, linked to inflammation in a mouse model of mitochondrial complex 1 deficiency

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 is advancing novel, first-in-class, CNS-penetrant, sGC stimulators that modulate a key node in a fundamental CNS signaling pathway. The multidimensional pharmacology elicited by the stimulation of sGC has the potential to impact a broad range of CNS diseases. The most advanced compound, CY6463, has shown rapid improvement in biomarkers associated with cognitive function and is currently in clinical development for Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like episodes (MELAS), Cognitive Impairment Associated with Schizophrenia (CIAS) and Alzheimer's Disease with Vascular pathology (ADv). Cyclerion is also advancing CY3018, a next-generation sGC stimulator.

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 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, the success, timing and cost of our ongoing or future clinical trials and anticipated clinical trials for our current product candidates; our ability to fund additional clinical trials to continue the advancement of our product candidates; the timing of and our ability to 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 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 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.

For more information about Cycleron, please visit cycleron.com and follow us on [Twitter](#) and [LinkedIn](#).

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