



Cyclerion Announces Publication of Preclinical Data Demonstrating Reduction in Neuroinflammation by Brain-Penetrant sGC Stimulator

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Company developing lead sGC stimulator, CY6463, in multiple CNS diseases associated with cognitive impairment

CAMBRIDGE, Mass., Sept. 22, 2021 (GLOBE NEWSWIRE) -- Cyclerion Therapeutics, Inc. (Nasdaq: CYCN), a clinical-stage biopharmaceutical company developing treatments that restore cognitive function, today announced a publication demonstrating that administration of a small molecule soluble guanylate cyclase (sGC) stimulator reduced markers associated with neuroinflammation in multiple preclinical models. Neuroinflammation is a hallmark of numerous CNS diseases, including Alzheimer's disease and other neurodegenerative diseases, and targeting this pathology is a promising drug development strategy.

In preclinical research [published](#) in the Journal of Neuroinflammation, a small molecule sGC stimulator was shown to cross the blood-brain barrier and resulted in the stimulation of cGMP levels in cerebral spinal fluid, providing evidence of activation of the nitric oxide – sGC – cGMP pathway. Furthermore, pharmacological sGC stimulation resulted in a statistically significant decrease in the expression of several inflammatory genes, including TNF, CD40, Icam1, Cybb, and GFAP, in rodent models. These data suggest that CNS penetrant sGC stimulators, such as Cyclerion development candidates CY6463 and CY3018, could provide therapeutic benefit to individuals living with CNS diseases associated with neuroinflammation.

"This research extends our understanding of the pharmacology of brain-penetrant sGC stimulation and provides further support for the potential of our investigational therapeutics to treat CNS diseases. These new preclinical data demonstrate that our approach is able to reduce neuroinflammation, which is widely considered to be a core contributor of many serious CNS diseases, including Alzheimer's disease," said Chris Winrow, Ph.D. Study Author and Head of Translational Medicine, Cyclerion Therapeutics. "A body of preclinical and clinical data supports the development of CY6463 and CY3018, our brain-penetrant sGC stimulators, and administration of CY6463 has been shown to result in positive clinical effects on multiple measures of brain neurophysiology. We are eager to advance our ongoing CY6463 clinical studies to meaningful data readouts to more fully understand the potential to provide individuals living with CNS diseases with a meaningful clinical benefit."

About CY6463

CY6463 is the first brain-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 for the treatment of 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 Alzheimer's Disease with Vascular pathology (ADv), 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 (www.linkedin.com/company/cyclerion).

Forward Looking Statement

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Our forward-looking statements are based on current beliefs and expectations of our management team that involve risks, potential changes in circumstances, assumptions, and uncertainties. We may, in some cases use terms such as "predicts," "believes," "potential," "continue," "anticipates," "estimates," "expects," "plans," "intends," "may," "could," "might," "likely," "will," "should" or other words that convey uncertainty of the future events or outcomes to identify these forward-looking statements. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement. Applicable risks and uncertainties include the risks listed under the heading "Risk Factors" and elsewhere in our 2020 Form 10-K filed on February 25, 2021, and our subsequent SEC filings including the Form 10-Qs filed on April 30, 2021 and July 29, 2021. Investors are cautioned not to place undue reliance on these forward-looking statements. These forward-looking statements (except as otherwise noted) speak only as of the date of this press release, and Cyclerion undertakes no obligation to update these forward-looking statements, except as required by law.

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