



Cyclerion Therapeutics Announces Initiation of Patient Dosing in CY6463 Phase 2a Study in Alzheimer's Disease with Vascular Pathology

January 26, 2022

Study to evaluate safety, tolerability, pharmacokinetics, and potential to improve cognition

CAMBRIDGE, Mass., Jan. 26, 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 that patient dosing has begun in its Phase 2a study in Alzheimer's Disease with Vascular Pathology (ADv).

"The need for effective new treatments for Alzheimer's disease is immense, and, given the aging population demographics and increasing rate of diagnosis, this need will continue to expand. We believe that CY6463 has potential to provide meaningful cognitive benefits and are very pleased to have initiated this important clinical study," said Andreas Busch, Ph.D., Chief Scientific Officer of Cyclerion. "Our CY6463 ADv development efforts are supported by preclinical data which demonstrate beneficial effects on cognition measures and the neuronal and microglia cellular activity thought to have a central role in the pathology and the cognitive dysfunction experienced by individuals living with ADv. Furthermore, a Phase 1 study in elderly subjects demonstrated an impact on biomarkers relevant to neurodegeneration and cognitive impairment. The ongoing Phase 2a study will focus on a segment of the Alzheimer's disease population where we believe our therapeutic candidate has the best opportunity to provide a clinical benefit. We expect this trial to deliver a rich dataset that will deepen our understanding of the therapeutic potential of CY6463 and will enable well-informed decisions regarding further development."

The Phase 2a ADv study (NCT04798989) is a randomized, placebo-controlled study of oral once-daily CY6463 in approximately 30 participants 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 on various disease-relevant pharmacodynamic biomarkers (e.g., EEG, MRI, neuroinflammatory biomarkers) and cognition performance.

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 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](https://twitter.com/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, including statements about the anticipated timing of release of topline results of our clinical trials; the progression of our clinical programs; and the business and operations of the Company. 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, July 29, 2021, and November 9, 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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Source: Cyclerion Therapeutics, Inc.