Cyclerion Announces CY6463 Clinical Pipeline Progress and First Quarter 2022 Financial Results

May 4, 2022

Characterizing the novel neuropharmacology of CY6463's NO-sGC-cGMP signal modulation in an integrated clinical strategy currently involving three ongoing, exploratory, biomarker-rich, signal seeking studies:

- *Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like episodes (MELAS) study enrollment closed; topline data expected in Q2 2022*
- *Cognitive Impairment Associated with Schizophrenia (CIAS) study enrollment closed; topline data expected in Q3 2022*
- *Alzheimer's Disease with vascular pathology (ADv) study enrollment ongoing*

CAMBRIDGE, Mass., May 04, 2022 (GLOBE NEWSWIRE) -- Cyclerion Therapeutics, Inc. (Nasdaq: CYCN), a clinical-stage biopharmaceutical company on a mission to develop treatments that restore cognitive function, announced today clinical development progress for CY6463, its lead program, and first quarter 2022 financial results.

"We are building on three previously reported clinical studies that demonstrated a favorable safety and tolerability profile for CY6463 with exposure in the brain that led to neurophysiology changes associated with cognition, by continuing to characterize the novel neuropharmacology of NO-sGC-cGMP signal modulation and advancing CY6463 toward data readouts in three exploratory clinical studies in CNS diseases associated with cognitive impairment." said Peter Hecht, Ph.D., Chief Executive Officer of Cyclerion Therapeutics. "We have recently closed enrollment on our CY6463 studies in MELAS and CIAS and look forward to obtaining topline clinical data from these exploratory studies in Q2 and Q3 2022, respectively. We expect that these pending data may provide further evidence supporting the optimal clinical utility for our most advanced CNS penetrant sGC stimulator and refine our plans for further development efforts, including dose and patient selection, and study endpoints. We have also continued to enroll our CY6463 study in Alzheimer's Disease with vascular pathology, while efficiently driving Cyclerion's earlier stage research programs forward."

Clinical Pipeline Updates

Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like episodes (MELAS)

The MELAS trial (NCT04475549) is an open-label, single-arm study of oral, once-daily CY6463 in adults aged 18 or older with MELAS. The study includes measures of safety, tolerability, pharmacokinetics, and exploratory pharmacodynamic effects, including MRI and various disease-relevant biomarkers. Study enrollment has closed, and topline data are expected in Q2 2022.

Cognitive Impairment Associated with Schizophrenia (CIAS)

The CIAS trial (NCT04972227) is a randomized, placebo-controlled, multiple-ascending-dose study of oral, once-daily CY6463 in adults aged 18-50 diagnosed with schizophrenia. The study includes measures of safety, tolerability, pharmacokinetics, and pharmacodynamics, including a broad battery of EEG-based assessments and a computerized battery of cognitive performance tests. Study enrollment has closed, and topline data are expected in Q3 2022.

Alzheimer's disease with vascular pathology (ADv)

The ADv trial (NCT04798989) is 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. The ADv study is active, and enrollment is ongoing.

First Quarter 2021 Financial Results

- Cash Position: Cash, cash equivalents, and restricted cash balance on Mar. 31, 2022 was approximately $41 million, as compared to approximately $54 million on Dec. 31, 2021.
- Research & Development Expenses: R&D expenses were approximately $9.7 million for the first quarter of 2022, as compared to approximately $8.0 million for the first quarter of 2021. The increase of approximately $1.7 million was driven by increases in external research costs, partially offset by decreases in employee-related expenses and facilities and operating costs.
- General and Administrative Expenses: G&A expenses were approximately $4 million for the first quarter of 2022, as compared to approximately $5.4 million for the first quarter of 2021. The decrease of $1.4 million was driven by decreases

in employee-related expenses and facilities and operating costs.

- Net Loss: Net loss was approximately $13.0 million for the first quarter of 2022, as compared to $13.4 million for the first 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 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, 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 2021 Form 10-K filed on February 24, 2022, and our subsequent SEC filings. 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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