Cyclerion Therapeutics Reports Third Quarter 2021 Financial Results and Corporate Update

November 9, 2021

First patients enrolled in study in Cognitive Impairment Associated with Schizophrenia (CIAS)

Patient screening underway in study in Alzheimer's disease with vascular pathology (ADv)

Enrollment ongoing in study in Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like episodes (MELAS); Topline clinical results expected in H1 2022

CAMBRIDGE, Mass., Nov. 09, 2021 (GLOBE NEWSWIRE) -- Cyclerion Therapeutics, Inc. (Nasdaq: CYCN), a clinical-stage biopharmaceutical company on a mission to develop treatments that restore cognitive function, reported today results for the third quarter 2021 and provided general corporate and pipeline updates.

"Cyclerion has made pipeline progress with three ongoing clinical studies related to CY6463, our lead investigational candidate. CY6463 development program is supported by completed clinical studies including a translational pharmacology study that demonstrated efficient entry into the brain and positive effects on multiple measures of brain neurophysiology associated with cognition. Our strategy is to pursue small concurrent signal-seeking studies to evaluate CY6463 in multiple CNS diseases where effective treatment options are lacking today. We plan to review the clinical data from our ongoing exploratory studies to determine how to optimally advance to later stages of development," said Peter Hecht, Ph.D., Chief Executive Officer of Cyclerion.

"We are pleased to have recently initiated enrollment in our CY6463 clinical study in patients with Cognitive Impairment Associated with Schizophrenia (CIAS), a debilitating aspect of schizophrenia that affects over two million patients in the U.S. alone. There is a tremendous societal need for new treatment options for schizophrenia, especially for its cognitive aspects. In addition, we've continued to make progress with our clinical studies in Alzheimer's disease with vascular pathology (ADv) and Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like episodes (MELAS). We believe that CY6463 has the potential to provide a much-needed new treatment option for each of these serious diseases that affect cognition, and we intend to aggressively advance each of our ongoing development studies and evaluate the data" said Cheryl Gault, Chief Operating Officer of Cyclerion.

Recent Program and Business Updates

Cyclerion continues to develop CY6463 with signal-seeking studies in CIAS, ADv, and MELAS:

- The CIAS trial (NCT04972227) is a randomized, placebo-controlled, multiple-ascending dose study of oral once-daily CY6463 in up to 60 adults aged 18-50 with schizophrenia. The study will evaluate safety, tolerability, pharmacokinetics, and pharmacodynamics over 14 days of dosing and includes a broad battery of EEG-based tests and computerized battery of cognitive tests. Clinical sites are actively recruiting, and the first participants have been enrolled into the study.

- The ADv trial (NCT04798989) is a randomized placebo-controlled study of oral CY6463 in approximately 30 adults older than 65 years of age to evaluate safety, tolerability, and pharmacodynamic effects (EEG, MRI, CSF biomarkers, cognition). CY6463 will be administered once-daily for 12 weeks. Participants must have confirmed AD pathology as assessed by PET and/or CSF biomarkers, cardiovascular risk factors, as well as mild-moderate subcortical small-vessel disease as assessed by MRI. The study is active and patient screening is underway.

- The MELAS trial (NCT04475549) is an open-label, single-arm study in up to 20 participants aged 18 or older to evaluate safety, tolerability, pharmacokinetics, and pharmacodynamics of oral CY6463 in MELAS. CY6463 will be administered once-daily for up to 29 days. Enrollment in the MELAS study has been slowed by several factors, including COVID-19 and disease-specific operational challenges. Cyclerion has implemented measures to improve enrollment and will continue to work with the participating centers of excellence to enroll participants through the end of 2021. Clinical data are expected in H1 2022.

In September, Cyclerion announced a publication in the Journal of Neuroinflammation 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.

Investor Conferences

In September, Cyclerion presented at two investor conferences: H.C. Wainwright 23rd Annual Global Investment Conference and Cantor Fitzgerald Virtual Global Healthcare Conference.

Cyclerion will participate in the upcoming Jefferies London Healthcare Conference. The corporate presentation will be available on-demand beginning

on Thursday, November 18 and will remain available for 30 days in the investor section of the Cyclerion website.

Third Quarter 2021 Financial Results

- Cash Position: Cash, cash equivalents, and restricted cash balance on September 30, 2021 was approximately $63 million, as compared to approximately $70 million on June 30, 2021. The Company's operating discipline, including workforce and leased space reductions, decreased cash burn rate in 2021 compared to 2020.

- Research & Development Expenses: R&D expenses were approximately $7.0 million for the third quarter of 2021, as compared to approximately $13.7 million for the third quarter of 2020. The decrease of approximately $6.7 million was driven by a decrease of approximately $3.9 million in salaries and other employee-related expenses, a decrease of approximately $2.8 million of facilities and operating costs and a decrease of $2.0 million related to completion of the STRONG-SCD study in October 2020, a decrease of $0.5 million in discovery, offset by increases of $1.5 million associated with CY6463 clinical trials (MELAS, CIAS, and Adv) and $1.0 million for CY3018 preclinical development costs.

- General and Administrative Expenses: G&A expenses were approximately $4.6 million for the third quarter of 2021, as compared to approximately $8.0 million for the third quarter of 2020. The decrease of $3.4 million was driven by a decrease of approximately $1.4 million in salaries and other employee-related expenses, a decrease of approximately $1.5 million in fees associated with 2020 company financing, and a decrease of approximately $0.5 million in facilities and operating costs.

- Net Loss: Net loss was approximately $11.3 million for the third quarter of 2021, as compared to $18.8 million for the third quarter of 2020.

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 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, our Form 10-Q filed on November 9, 2021, and our other reports filed with the SEC. 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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