Cyclerion Therapeutics Reports Second Quarter 2021 Financial Results and Corporate Update

July 29, 2021

Continuing to progress clinical development of CY6463, a first-in-class, CNS-penetrant soluble guanylate cyclase (sGC) stimulator for the treatment of neurological diseases associated with cognitive impairment

Advancing CY3018, a differentiated, next-generation, CNS-penetrant sGC stimulator, in IND-enabling studies

CAMBRIDGE, Mass., July 29, 2021 (GLOBE NEWSWIRE) -- Cyclerion Therapeutics, Inc. (Nasdaq: CYCN), a clinical-stage biopharmaceutical company on a mission to develop treatments that restore cognitive function, today reported financial results for the second quarter 2021 and provided general corporate and pipeline updates.

"During the first half of the year we have made significant progress advancing our lead program CY6463 into clinical development for multiple neurological indications where we believe we could have a meaningful therapeutic impact. This positive momentum in the clinic includes the advancement of the clinical studies in participants with Alzheimer's disease with vascular pathology (ADv) and Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like episodes (MELAS) and the initiation of start-up activities for a clinical study in participants with Cognitive Impairment Associated with Schizophrenia (CIAS)," said Peter Hecht, Ph.D., Chief Executive Officer of Cyclerion. "We have also conducted additional preclinical work to support the advancement of CY3018, a differentiated, next-generation, CNS-penetrant sGC stimulator, into clinical development for specific serious neurological conditions."

Recent Program and Business Updates

- ADv Clinical Trial Advancement: The U.S. Food and Drug Administration (FDA) reviewed the Investigational New Drug (IND) application for CY6463 in ADv and notified the Company that the study may proceed. Cyclerion has initiated a 12-week Phase 2a clinical trial in patients with ADv.

- CIAS Clinical Trial Start-up: The Company received notification from the FDA that its Ph1b clinical trial in participants with CIAS may proceed and study start-up activities are ongoing.

- MELAS Clinical Trial Advancement: The exploratory 29-day open-label Phase 2a pilot study in patients with MELAS is currently enrolling and data are expected by year end 2021.

- Beacon Partnership: In July, Cyclerion and Beacon Biosignals announced an extended and expanded strategic partnership between the two companies. This collaboration is expected to identify disease-relevant biomarkers to refine patient selection and endpoints to guide the clinical development of Cyclerion's investigational therapeutics for neurological diseases associated with cognitive impairment.

- Equity Raises: In June, Cyclerion closed a direct private sale of approximately $18 million of Cyclerion shares of common stock to EcoR1 Capital, LLC, Slate Path Capital LP, MFN Partners, LP, Invus, Peter Hecht, Ph.D., Lincoln Park Capital Fund, LLC and Polaris Partners. In addition, the Company received net proceeds of approximately $12.5 million in Q2 2021 for shares sold under the ATM Offering.

- Praliciguat Out-license: In June, the Company entered into an exclusive, global license agreement with Akebia Therapeutics, Inc. for the development and commercialization of praliciguat. Under the terms of the agreement, Akebia has obtained an exclusive license to research, develop, and commercialize praliciguat globally and will be solely responsible for these activities going forward. Cyclerion is eligible to receive up to $225M in pre-commercial milestones, including up to $15M in the first 18 months. Total potential future development, regulatory, and commercialization milestone payments could result in up to $585M. Cyclerion is also eligible to receive tiered, sales-based royalties ranging from single-digit to high-teen percentages.

- Scientific Conferences and Publications:

    - In July, Cyclerion presented a poster at the Alzheimer's Association International Conference 2021 (AAIC) highlighting the clinical trial design for a Phase 2a study of CY6463 in participants with Alzheimer's disease with vascular pathology. In addition, Anna Marin, a researcher in the laboratory of Dr. Andrew Budson and Dr. Katherine Turk in the Department of Neurology, Boston University School of Medicine and Center for Translational and Cognitive Neuroscience, VA Boston Healthcare System, presented results from the Cyclerion-sponsored study highlighting alpha peak frequency and N200 latency as predictors of neuropsychological performance in a memory

disorders clinic.

- In May, Cyclerion announced the publication of preclinical data for CY6463 in Frontiers in Pharmacology. The publication includes preclinical pharmacology data with CY6463 and, along with decades of research, highlights the crucial role of the sGC pathway in brain physiology and cognition. Across a range of preclinical models, administration of CY6463 resulted in physiologically relevant drug levels in cerebrospinal fluid and led to improvements in neuronal function, neuroprotection, and cognitive performance.

- In April, Cyclerion hosted a webinar and provided an update on its clinical programs for its first-in-class, CNS-penetrant sGC stimulator, CY6463, in ADv, MELAS and CIAS. The event included neuropsychiatric key opinion leader, Andreas Reif, M.D., Chair, Department of Psychiatry, University Hospital Frankfurt, who discussed the sGC pathway and its role in cognitive function and CIAS. Cyclerion also introduced its latest development candidate, CY3018, a differentiated, next-generation, CNS-penetrant sGC stimulator.

- Board of Directors Transitions: In April, the Company announced that Errol De Souza, Ph.D., was appointed to the Company's board of directors. Dr. De Souza is currently a member of the board of directors of Royalty Pharma and Catalyst Biosciences and executive chairman of Bionomics Limited. Previously, Dr. De Souza founded Neurocrine Biosciences, Inc., served as CEO of numerous publicly traded and private companies, including Biodel, Inc., Synaptic Pharmaceutical Corp., Archemix Corp. and Neuropore Therapies, Inc. In addition, he led CNS R&D at DuPont Merck and US R&D at Aventis. Dr. De Souza received a B.A. in physiology and a Ph.D. in endocrinology from the University of Toronto.

Second Quarter 2021 Financial Results

- Cash Position: Cash, cash equivalents, and restricted cash balance on June 30, 2021 was approximately $70 million, as compared to approximately $45 million on March 31, 2021.

- Research & Development Expenses: Research and development expenses were approximately $12.1 million for the second quarter of 2021, as compared to approximately $13.8 million for the second quarter of 2020. The decrease of approximately $1.7 million was driven by a decrease of approximately $4.2 million in salaries, stock-based compensation, and other employee-related expenses due to lower average headcount, a net increase of approximately $2.3 million of facilities and operating costs allocated to research and development primarily due to $4.2 million of non-cash write-off of leasehold improvements partially offset by $1.9 million reduction in the Company's total leased premises expense, and a net increase of approximately $0.2 million in external research costs, primarily related to the start-up costs for CY6463 in CIAS and ADv, offset by the completion of praliciguat and olinciguat trials in the prior year.

- General and Administrative Expenses: General and administrative expenses were approximately $6.2 million for the second quarter of 2021, as compared to approximately $6.6 million for the second quarter of 2020. The decrease of approximately $0.4 million was primarily driven by a decrease of approximately $1.3 million in salaries, stock-based compensation, and other employee-related expenses due to lower average headcount, and a decrease of approximately $1.2 million in facilities and other operating costs, partially offset by an increase of approximately $2.1 million of non-cash write-off of leasehold improvements.

- Net Loss: Net loss was approximately $16.2 million for the second quarter of 2021, as compared to $19.5 million for the second 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. Nitric oxide (NO) is one of several fundamental neurotransmitters, but it has yet to be leveraged for its full CNS therapeutic potential. CY6463 stimulates sGC, a signaling enzyme that responds to the presence of NO, to enhance the body's natural ability to produce cyclic guanosine monophosphate (cGMP), an important signaling molecule that regulates diverse and critical biological functions in the CNS including neuronal function, neuroinflammation, cellular bioenergetics, and vascular dynamics. Impaired NO-sGC-cGMP signaling is believed to play an important role in the pathogenesis of many neurodegenerative and neuropsychiatric diseases. Agents that stimulate sGC to produce cGMP may compensate for deficient NO signaling.

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 and include, among other things, whether the praliciguat out-license will result in the creation of any therapies for the treatment of patients with kidney disease; the uncertain utility, development, promise, and commercialization of praliciguat; and whether any development, regulatory and commercialization milestones or royalty payments provided for in the agreement with Akebia will be achieved. 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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