Cyclerion Therapeutics Reports Full Year 2020 Financial Results and Corporate Update

February 25, 2021

Novel mechanism of CY6463 demonstrated desired blood brain barrier penetration, target engagement, favorable safety and tolerability profile as well as evidence in multiple independent biomarkers associated with cognitive impairment, including neuroinflammatory biomarkers;

MELAS Phase 2a study underway with top-line data anticipated in mid-2021; Phase 2a study Alzheimer's disease with vascular pathology expected to initiate in mid-2021;

Transformation to a nimble and efficient CNS organization with leading clinical and scientific advisory boards to accelerate novel approaches to restore cognitive function for patients

CAMBRIDGE, Mass., Feb. 25, 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 full year 2020 and provided general corporate and pipeline updates.

"The highly encouraging clinical data from our lead asset, CY6463, is guiding our clinical strategy and we expect 2021 to be an exciting year as we begin to explore the impact of modulating a key node in a fundamental CNS signaling network in patients," said Peter Hecht, Ph.D., Chief Executive Officer of Cyclerion. "This positive momentum in the clinic includes the initiation of clinical studies in patients with Alzheimer's disease with vascular pathology (ADv) and Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-like episodes (MELAS). Given the broad potential associated with this novel mechanism in the CNS for a range of patients, we will continue to assess additional indication opportunities for CY6463 and differentiated molecules to deliver the full potential of our pipeline."

Recent Program and Business Updates

- CY6463 Program Updates: Cyclerion announced promising results from its Phase 1 translational pharmacology study of CY6463, the first soluble guanylate cyclase (sGC) stimulator in clinical development for CNS disorders.

  Treatment with CY6463 in the 15-day, 24-subject crossover study confirmed and extended results seen in the earlier Phase 1 study: once daily oral treatment demonstrated blood-brain-barrier penetration, desired CNS exposure levels, target engagement, and showed CY6463 to be safe and generally well-tolerated. In this study, several neurophysiological and objective performance measures associated with age-related cognitive decline and neurodegenerative diseases improved in subjects receiving CY6463 including increased alpha and gamma power, improved mismatch negativity (MMN) latency, faster saccadic eye movement (SEM) reaction time.

  CY6463 administration resulted in improvement in the levels of various neuroinflammatory biomarkers, including alpha-2-macroglobulin (A2M) and Complement C3 (C3). A2M and C3 have been associated with CNS pathology, cognitive decline, and the development of Alzheimer's disease.

- ADv Clinical Trial Initiation: The Company anticipates initiating a 12-week Phase 2a clinical trial in patients with ADv midyear. This exploratory trial is designed to evaluate safety, tolerability, and pharmacodynamic effects including impact on disease-specific biomarkers.

- MELAS Clinical Trial Advancement: Cyclerion has initiated clinical activities for a 29-day open label Phase 2a pilot study in patients with MELAS and anticipates beginning enrollment imminently. A collaboration with a leading MELAS academic center of excellence has also been initiated to further characterize the effects of sGC stimulation in preclinical models of mitochondrial disease and will include assessments of brain health, neuromuscular function, and biochemical markers of mitochondrial dysfunction.

- Clinical and Scientific Advisory Boards: The Company expanded its expert networks and announced advisory boards comprised of an accomplished and diverse group of academic leaders with expertise that spans neurology clinical development and translational science, as well as CNS disease biology. The advisors' expertise will support the continued development of the company's clinical programs and the pipeline.

- Leadership Transitions: Effective January 1, 2021, the Company announced the promotions of Cheryl Gault to Chief Operating Officer and Anjeza Gjino to Chief Financial Officer. Bill Huyett, the Company's prior CFO, continues to work part-time as a Strategic Advisor providing strategic, operational, and organizational development support. Dr. Mark Currie, Cyclerion's prior President and Chief Scientific Officer (CSO), also transitioned to become a Senior Advisor and Chair the

Scientific Advisory Board. Dr. Andreas Busch has assumed the Chief Scientific Officer responsibilities.

- Praliciguat Update: The Company is working to out-license rights to praliciguat, its investigational orally administered, once-daily systemic sGC stimulator.

- Organization Revamping and Strategic Alignment: The Company has made substantial progress revamping its organization and aligning its capabilities with its CNS focus. With a leaner more externally networked organization, Cyclerion expects significantly reduced operating cash use in 2021, including exiting its current laboratory and office facilities in early 2021, from which it expects annual cash savings of about $10 million.

Full Year 2020 Financial Results

- Cash Position: Cash, cash equivalents, and restricted cash balance on December 31, 2020 was approximately $58 million, as compared to approximately $71 million on September 30, 2020.

- Research & Development Expenses: Research and development expenses were approximately $56.4 million for the full year 2020, as compared to approximately $95.1 million for the full year 2019. The decrease of approximately $38.7 million was driven by a decrease of approximately $18.0 million in external research costs, primarily related to the completion of praliciguat trials in the prior year, a net decrease of approximately $12.5 million in personnel and related costs due to lower headcount, and a decrease of approximately $8.2 million of facilities and operating costs primarily from our reduced lease footprint.

- General and Administrative Expenses: General and administrative expenses were approximately $28.8 million for the full year 2020, as compared to approximately $34.4 million for the full year 2019. The decrease of approximately $5.6 million was primarily driven by a decrease in personnel and related cost primarily due to lower average headcount.

- Net Loss: Net loss was approximately $77.8 million for the full year 2020, as compared to $123.0 million for the full year 2019.

- Headcount: The Company had 34 employees as of December 31, 2020, not including employees who were impacted by our recent workforce reduction and who are transitioning out by the end of Q1 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. 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. An impaired NO-sGC-cGMP signaling pathway is believed to play an important role in the pathogenesis of neurodegenerative diseases and is critical to basic neuronal functions. 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's lead program is CY6463, a novel, first-in-class, CNS-penetrant, sGC stimulator that modulates a key node in a fundamental CNS signaling network. The multidimensional pharmacology elicited by the stimulation of sGC has the potential to impact a broad range of CNS diseases. CY6463 has shown rapid improvement in biomarkers associated with cognitive impairment and is currently in clinical development for Alzheimer's Disease with Vascular pathology (ADv) and Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like episodes (MELAS).

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. 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.