Cyclerion Therapeutics Reports Second Quarter 2020 Financial Results and Recent Corporate Highlights

August 3, 2020

- IW-6463 and olinciguat top line clinical study results remain on track for late summer and late Q3 2020, respectively -

- Completed $24 million equity private placement to accelerate clinical development of IW-6463 for the CNS diseases MELAS (Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like episodes) and ADv (Alzheimer's Disease with Vascular pathology) and of olinciguat for sickle cell disease -

- CNS focused webcast event held to highlight IW-6463 development plan and opportunity to address serious CNS diseases

CAMBRIDGE, Mass., Aug. 03, 2020 (GLOBE NEWSWIRE) -- Cyclerion Therapeutics, Inc. (Nasdaq: CYCN), a clinical-stage biopharmaceutical company developing treatments for serious and orphan diseases, reported financial results for the second quarter ended June 30, 2020 and provided general corporate and pipeline updates.

"We are looking forward to upcoming top line results from both our translational pharmacology study for IW-6463, the first brain-penetrant sGC stimulator to enter clinical development, and our STRONG olinciguat Phase 2 study for sickle cell disease. Both programs have the potential to provide a fundamentally new approach for patients with limited therapeutic options today", said Peter Hecht, Ph.D., Chief Executive Officer of Cyclerion.

Recent Program and Business Updates

- **IW-6463 Program Update:** Top line data from the translational pharmacology study of IW-6463, the company's investigational, orally administered, once-daily CNS-penetrant sGC stimulator designed for the treatment of two serious CNS diseases are expected in late summer 2020. Each of these indications harness the multi-dimensional pharmacology of the as-yet untapped nitric oxide neurotransmitter system.

  On July 9th, Cyclerion hosted a webcast focused on IW-6463, during which Cyclerion clinical and scientific leaders and external subject matter experts discussed IW-6463 preclinical and Phase 1 clinical study data, design of the ongoing IW-6463 translational pharmacology clinical study, and anticipated development directions into Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like episodes (MELAS) and Alzheimer's Disease with Vascular pathology (ADv). In the session, the company described the potential impact on MELAS, a genetically defined disease for which there is no approved treatment, by addressing multiple aspects of disease including bioenergetic deficits. The company expects to begin an open label study in H2 2020. The company also described the potential impact of IW-6463 in its second indication, Alzheimer's Disease with Vascular pathology (ADv)**.** A study to assess the impact of IW-6463's multi-dimensional pharmacology, including improved cerebral blood flow, reduced neuroinflammation and improved neuronal function on patients with ADv expects to begin in early 2021. A replay of the CNS webinar is available under the Investors and Media section of the Cyclerion website.

- **Olinciguat Program Update:** Cyclerion has completed the treatment period in its STRONG-SCD study of olinciguat, an investigational, orally-administered, once-daily, vascular sGC stimulator, in Sickle Cell Disease (SCD) with a total of 70 patients randomized. STRONG-SCD is a randomized, placebo-controlled, dose-ranging study designed to evaluate safety, tolerability, and pharmacokinetics, as well as to explore effects on daily symptoms and biomarkers of disease activity when dosed over a 12-week treatment period. Top-line study results are expected in late Q3 2020.

- **Praliciguat Update:** The Company is working to out-license rights to praliciguat, its orally administered, once-daily systemic sGC stimulator, and have expanded to discussions beyond treatment of cardiometabolic disorders to include additional indications where sGC stimulators have demonstrated efficacy.

- **On July 30, Cyclerion announced a private equity investment of $24 million:** The capital will accelerate clinical development of IW-6463 in two CNS indications, MELAS and ADv, and further development of olinciguat in sickle cell disease, should the upcoming Phase 2 data support that investment.

- **In June, Cyclerion presented on "Evaluating the Use of IW-6463, a Brain-penetrant sGC Stimulator in Individuals with MELAS"** at the United Mitochondrial Disease Foundation (UMDF) Power Surge 2020 conference. The presentation, held virtually on June 26, 2020, detailed the rationale for the use of sGC stimulators and described the study design.

- **In July, Cyclerion presented on "Leveraging Biomarker Data & Preclinical Models to Guide the Design of Clinical Studies"** at the Annual Biomarkers in Alzheimer's Disease Summit, held virtually on July 15, 2020. The presentation detailed the application of translational biomarkers to guide clinical activities for IW-6463.

Second Quarter 2020 Financial Results

Cash Position: Cash, cash equivalents, and restricted cash balance on June 30, 2020 was approximately $61 million, as compared to approximately $72 million on March 31, 2020. Subsequent to the end of the second quarter, on July 29, the Company raised $24 million in an equity private placement.

Revenue: Revenue, primarily from development services provided to Ironwood, was $0.7 million for the second quarter of 2020, as compared to $1.6 million for the second quarter of 2019.

Research & Development Expenses: Research and development expenses were approximately $14 million for the second quarter of 2020, as compared to approximately $26 million for the second quarter of 2019. The decrease of approximately $12.0 million was driven by a decrease of approximately $3.5 million in stock-based compensation, salaries and other employee-related expenses primarily due to lower average headcount, a decrease of approximately $2.2 million of facilities and operating costs allocated to research and development primarily from reductions the Company's lease footprint and an decrease of approximately $6.2 million in external research costs associated with praliciguat and olinciguat trials.

General and Administrative Expenses: General and administrative expenses were approximately $7 million for the second quarter of 2020, as compared to approximately $9 million for the second quarter of 2019. The decrease was primarily due to a decrease of approximately $1.4 million in stock-based compensation and a decrease of approximately $0.9 million in salaries, bonus and other employee-related expenses.

Net Loss: Net loss was approximately $20 million for the second quarter of 2020, as compared to $32 million for the second quarter of 2019.

About Olinciguat

Olinciguat is an investigational, orally-administered, once-daily, vascular sGC stimulator for the potential treatment of sickle cell disease (SCD). SCD is an inherited red blood cell disorder that causes red blood cells to deform into a sickle shape, impacting blood flow to organs and tissues. These sickled red blood cells are more susceptible to hemolysis (rupturing). Upon red blood cell rupturing, nitric oxide is depleted due to arginase release and hemoglobin scavenging. Nitric oxide is an important regulator of blood flow, and the resulting deficiency of nitric oxide is believed to contribute to symptoms of SCD.

As sGC is a key node in the nitric oxide signaling pathway, olinciguat has the potential to address key symptoms and complications of SCD by addressing the disease's underlying nitric oxide deficiency. The distribution of olinciguat to the vasculature as well as to organs with high blood flow, such as the kidney and lungs, may make it well suited for the potential treatment of SCD.

Olinciguat has been granted Orphan Drug Designation for SCD by the U.S. Food and Drug Administration and is currently in a Phase 2 study in patients with SCD, the STRONG-SCD study.

About IW-6463

IW-6463, a CNS-penetrant sGC stimulator, is being developed as a symptomatic and potentially disease modifying therapy for neurodegenerative diseases. In preclinical studies, IW-6463 has been associated with increased cerebral blood flow, reduced markers of neuroinflammation, enhanced cognition, neuroprotection and enhanced cellular bioenergetics. Nitric oxide is one of several fundamental neurotransmitters, but it has yet to be leveraged for its full CNS therapeutic potential. sGC stimulators work synergistically with the nitric oxide naturally produced in the body to boost the positive effects of nitric oxide, even when the body is not producing enough. Extensive human genetic and preclinical data implicate nitric oxide signaling defects in neurodegenerative diseases. Evidence indicates that nitric oxide dysregulation leads to vascular contributions to neurodegenerative disease (e.g. endothelial cell damage, decreased blood flow and impaired vascular reactivity) and may also directly increase inflammation, neuronal dysfunction/loss and cognitive impairment. sGC is expressed widely throughout the CNS and CNS vasculature.

About Cyclerion Therapeutics

Cyclerion Therapeutics is a clinical-stage biopharmaceutical company harnessing the power of sGC pharmacology to discover, develop and commercialize breakthrough treatments for serious and orphan diseases. Lead programs include its vascular-targeted olinciguat in Phase 2 development for sickle cell disease and IW-6463, a pioneering CNS-penetrant sGC stimulator in clinical development for Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like episodes (MELAS) and Alzheimer's Disease with Vascular pathology (ADv)

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 discovery programs into clinical development; and the business and operations of Cyclerion. 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 those related to the possibility that we may not achieve the expected benefits of the separation, and that a separation could harm the business, results of operations and financial condition of Cyclerion; the risk that we may be unable to make, on a timely or cost-effective basis, the changes necessary to operate as an independent company; risks relating to the design and outcome of our clinical trials; our lack of independent operating history and the risk that our accounting and other

management systems may not be prepared to meet the financial reporting and other requirements of operating as an independent public company; the risk that the separation may adversely impact our ability to attract or retain key personnel; the risks listed under the heading “Risk Factors” and elsewhere in our 2019 Form 10-K filed on March 12, 2020, and in Cyclerion’s subsequent SEC filings, including the Form 10-Q filed on August 3, 2020. 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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