Cyclerion Updates Corporate Progress

April 10, 2020

– Closed enrollment for olinciguat Phase 2 STRONG SCD study for sickle cell disease; topline data readout expected Q3 2020 –

– Closed enrollment for IW-6463 translational pharmacology clinical study; *topline data readout expected mid-year 2020 –*

– Company continues discussions to out-license praliciguat –

CAMBRIDGE, Mass., April 10, 2020 (GLOBE NEWSWIRE) -- Cyclerion Therapeutics, Inc. (Nasdaq: CYCN), a clinical-stage biopharmaceutical company focused on the development of soluble guanylate cyclase (sGC) stimulators for the treatment of serious and orphan diseases, today announced that it recently closed enrollment for both of its ongoing clinical studies. The Company also provided additional corporate updates.

"We are looking forward to a catalyst-rich period in the coming months with top line results from both our translational pharmacology study for IW-6463, our brain-penetrant sGC stimulator designed to treat neurodegenerative diseases, and our olinciguat Phase 2 study for sickle cell disease. We also continue discussions on the out-licensing of praliciguat, a potential best-in-class therapeutic candidate for cardio-metabolic diseases. Recent published outcomes data from other groups provide compelling new support for the use of the sGC stimulator class in treating cardiometabolic diseases", said Peter Hecht, Ph.D., Chief Executive Officer of Cyclerion.

COVID-19

Cyclerion is executing against its previously communicated 2020 corporate priorities, advancing its ongoing olinciguat and IW-6463 clinical programs and out-licensing praliciguat. The company is closely monitoring and adjusting its operations but the pandemic could affect these activities in ways that are difficult to precisely judge at this time. The Company cannot give any assurances as to the potential impact of the pandemic on its operations, clinical trials, corporate development discussions and other activities. Cyclerion is working closely with its clinical trial sites and investigators to deliver its ongoing and planned trials in a manner consistent with the safety of study participants and healthcare professionals. Cyclerion does not anticipate any drug product disruption for its clinical trials and is taking steps to mitigate any disruptions of clinical supply materials to trial participants.

The Company is tightly managing its spending. As of March 31, 2020, Cyclerion's preliminary unaudited cash, cash equivalents and restricted cash balance was approximately $72 million. Cyclerion anticipates that this cash will fund its operations into Q2 2021, excluding net cash flows from potential business development activities.

Program Updates

Sickle Cell Disease (SCD)

Olinciguat is a once-daily oral sGC stimulator that primarily targets the vasculature and highly perfused organs such as the lungs and the kidney. Olinciguat has the potential to address multiple important clinical domains important in SCD by improving local blood flow, decreasing vascular inflammation, reducing anemia, and improving chronic symptoms.

The STRONG-SCD study 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. The study protocol was amended in late 2019 to add a higher-dose arm. Cyclerion recently closed enrollment of the study with a total of 70 participants randomized.

"We are excited to have closed enrollment for our SCD-STRONG study. We look forward to the top line results in Q3 2020 and to making a data-driven decision regarding advancement to the next phases of development," said Chris Wright, M.D., Cyclerion's Chief Medical Officer.

Central Nervous System (CNS)

Cyclerion is developing IW-6463, an oral, once-daily CNS-penetrant sGC stimulator for the treatment of serious neurodegenerative diseases. The nitric oxide pathway and sGC stimulation have long been known as central physiological regulators in the CNS, affecting cerebrovascular blood flow, neuroinflammation, neuronal function and cellular bioenergetics.

In January 2020, the Company reported encouraging Phase 1 healthy volunteer study results for IW-6463. This potential new CNS medicine was well tolerated across the dose range assessed. Pharmacokinetic (PK) data from blood and cerebral spinal fluid (CSF), supported QD dosing and indicated the potential to reach pharmacologically active CNS exposures, based on preclinical data.

An ongoing translational pharmacology clinical study has enrolled 24 elderly subjects. The study will evaluate safety and biomarker measures of CNS activity. Cyclerion expects top-line clinical results in mid-2020.

With supportive study results, the Company plans to direct further development towards serious CNS diseases with high unmet medical need where biological and/or genetic data suggest an important role for nitric oxide and cyclic guanosine monophosphate (cGMP) signaling.

Cardiometabolic

In October 2019, the Company announced encouraging topline results from its Phase 2 proof-of-concept study of praliciguat, a once-daily, orally

available systemic sGC stimulator, in diabetic nephropathy. The potential for novel pharmaceutical interventions of the sGC pathway to provide important new tools in the treatment of cardiometabolic disease has been further supported by recent clinical study results published in the New England Journal of Medicine.

Cyclerion continues to engage in discussions to out-license praliciguat for late-stage global development and commercialization as a potentially best-in-class therapeutic for cardiometabolic diseases.

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. 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. There are clear links between nitric oxide signaling defects and neurodegenerative diseases. Evidence indicates that nitric oxide dysregulation leads to vascular contributions to neurodegenerative disease (e.g. endothelial cell damage decreased blood flow and increased vascular leakage) and may also directly increase inflammation, neuronal dysfunction/loss and cognitive impairment. sGC is expressed widely throughout the CNS and CNS vasculature. In preclinical studies, IW-6463 has been associated with increased cerebral blood flow, reduced markers of neuroinflammation, enhanced cognition, neuroprotection and enhanced cellular bioenergetics.

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. Cyclerion is advancing its portfolio of differentiated sGC stimulator programs with distinct pharmacologic and biodistribution properties that are uniquely designed to target tissues of greatest relevance to the diseases they are intended to treat. These programs include praliciguat which recently completed Phase 2 studies and which the Company intends to out-license for further development in cardiometabolic disease, olinciguat in Phase 2 development for sickle cell disease, IW-6463 in early development for serious CNS diseases, and two preclinical programs targeting serious liver and lung diseases, respectively.

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. 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 2019 Form 10-K filed on March 12, 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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Source: Cyclerion Therapeutics, Inc.