Cyclerion Therapeutics to Present Preclinical Data on its Clinical-Stage sGC Stimulators for Neurodegenerative and Cardiometabolic Diseases at the 9th International Conference on cGMP

June 11, 2019

*– **Series of preclinical studies provide further rationale for study of IW-6463 as a potential treatment for neurodegenerative diseases** –*

*– **Preclinical data provide insights into praliciguat's metabolic effects and mechanism of action** –*

CAMBRIDGE, Mass., June 11, 2019 (GLOBE NEWSWIRE) -- Cyclerion Therapeutics, Inc. (Nasdaq: CYCN), a clinical-stage biopharmaceutical company developing soluble guanylate cyclase (sGC) stimulators for the treatment of serious and orphan diseases, today announced that three upcoming data presentations will be made on two of its clinical-stage pipeline candidates during the 9thInternational Conference on cGMP, held June 14-16 in Mainz, Germany.

One presentation will discuss the results of a series of preclinical studies on IW-6463, Cyclerion's central nervous system (CNS)-penetrant sGC stimulator designed to address serious neurodegenerative diseases, showing an association between treatment with IW-6463 and decreased markers of neuroinflammation, enhanced blood flow in brain regions associated with cognition, improved dendritic spine density and structure and restored cognitive performance. Two presentations will address preclinical studies with praliciguat, Cyclerion's systemic sGC stimulator currently in clinical development as a potential treatment for diabetic nephropathy and for heart failure with preserved ejection fraction (HFpEF). The first preclinical study demonstrated an association between treatment with praliciguat and improved insulin sensitivity, lower triglycerides and increased fat oxidation. The second study provided insights into praliciguat's mechanism of action by characterizing the nature of its high affinity binding to sGC.

"We are excited to present preclinical data supporting the potential of sGC stimulation to treat neurodegenerative and cardiometabolic diseases, both of which are growing medical concerns facing our aging global population," said Mark Currie, Ph.D., president and chief scientific officer at Cyclerion. "These studies contribute to our knowledge of the power of the nitric oxide-cGMP pathway, including its critical role in regulating neuronal, vascular and metabolic function. We remain confident that this pathway represents a largely untapped opportunity to develop a potential new generation of therapeutics. As a company solely focused on this pathway, we are dedicated to advancing our pipeline of differentiated, tissue-targeted sGC stimulators for serious and orphan diseases."

Cyclerion is focused on unlocking the full therapeutic potential of the nitric oxide-cyclic guanosine monophosphate (cGMP) signaling pathway, a clinically validated pathway with potential for therapeutic applications in a wide range of cardiovascular, metabolic, inflammatory, fibrotic and neurological diseases. sGC is a key node in this pathway, and Cyclerion's targeted sGC stimulators are designed to enhance pathway signaling in the tissues of greatest relevance to the diseases each is intended to treat.

Cyclerion's Oral Presentations :

- Cyclerion will present the results of a series of preclinical studies that evaluated the pharmacological effects of IW-6463 and informed the initiation of a Phase 1 clinical study to evaluate the safety, tolerability, pharmacodynamics and pharmacokinetics of IW-6463 in single- and multiple-ascending dose studies in healthy human volunteers.
    - Session 1-02: Evaluating Soluble Guanylate Cyclase Stimulation for Serious Central Nervous System Diseases
    - Presenter: Christopher Winrow, Senior Director, IW-6463 Development Program Lead**,** Cyclerion
    - Friday, June 14, 2:20 p.m. CEST

- Cyclerion will present the results of a preclinical study in which treatment with praliciguat was associated with improved metabolic effects in a diet-induced obesity mouse model.
    - Session 7-01: Praliciguat, a Clinical-Stage sGC Stimulator, Improved Insulin Sensitivity, Lipid Tolerance and Energy Utilization in a Diet-Induced Obesity Mouse Model
    - Presenter: Juli Jones, Director, Head of Pharmacology**,** Cyclerion
    - Sunday, June 16, 10:35 a.m. CEST

Cyclerion's Poster Presentation :

- Cyclerion will present research analyzing the binding of praliciguat to purified human recombinant sGC through a new binding assay.
    - Poster #18: Development of a Soluble Guanylate Cyclase Radioligand Binding Assay Using [^{3}H]-Praliciguat
    - Presenter: Daniel Zimmer, Senior Principal Investigator, Pharmacology, Cyclerion
    - Date/Time:
        - Saturday, June 15, 11:50 a.m.-1:30 p.m. CEST, Poster Session #2
        - Sunday, June 16, 12:25-2:30 p.m. CEST, Poster Session #3

About IW-6463
IW-6463 is a central nervous system (CNS)-penetrant sGC stimulator that Cyclerion believes is the first and only sGC stimulator designed to address neurodegenerative diseases. Nitric oxide is a fundamental neurotransmitter with demonstrated impact on memory and cognition. In serious CNS diseases associated with nitric oxide deficiency, IW-6463 may amplify endogenous nitric oxide signaling to restore neuronal health and function. More broadly, in neurodegenerative diseases of varying etiologies, IW-6463 has the potential to enhance cognition and combat neurodegeneration via the neuroprotective and neurofunctional benefits of nitric oxide signaling.

In preclinical studies, IW-6463 demonstrated significant exposure in the CNS. Treatment with IW-6463 was associated with increases in cerebral blood flow, reductions in markers of neuroinflammation, increased neuroprotection and enhanced cognition across a variety of preclinical models. IW-6463 is currently being evaluated in a Phase 1 clinical study in healthy human volunteers.

About Praliciguat
Praliciguat, a once-daily, orally available systemic sGC stimulator in development for the treatment of cardiometabolic diseases, is being studied in patients with diabetic nephropathy and in patients with heart failure with preserved ejection fraction (HFpEF). Both conditions are growing global epidemics with few or no approved treatment options. Diabetic nephropathy affects an estimated eight million Americans and 20 to 40 percent of all diabetic patients worldwide. It is the leading cause of end-stage renal disease. Currently available products do not treat the underlying pathophysiology of the disease or fully address the needs of this patient population. HFpEF affects an estimated three million Americans and 40 to 70 percent of heart failure patients worldwide. It is a highly symptomatic condition with high rates of morbidity and mortality that can cause insufficient delivery of oxygen to the tissues, fluid in the lungs and edema of the extremities, causing patients to be short of breath and have compromised exercise tolerance. There are no approved therapies to treat HFpEF.

Currently in Phase 2 development for diabetic nephropathy and for HFpEF, praliciguat has the potential to address the underlying causes of these devastating diseases by improving nitric oxide signaling, which may improve vascular and metabolic function and decrease the inflammatory and fibrotic consequences associated with these diseases.

About Cyclerion Therapeutics
Cyclerion Therapeutics is a clinical-stage biopharmaceutical company harnessing the power of soluble guanylate cyclase (sGC) pharmacology to discover, develop and commercialize breakthrough treatments for serious and orphan diseases. Cyclerion is advancing its portfolio of five 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 olinciguat in Phase 2 development for sickle cell disease, praliciguat in Phase 2 trials for heart failure with preserved ejection fraction (HFpEF) and for diabetic nephropathy, IW-6463 in Phase 1 development for serious and orphan central nervous system diseases, and two late-stage discovery 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 therapeutic potential of sGC stimulation and the nitric oxide-cGMP pathway; the ability of preclinical data to predict clinical outcomes; and the progression of our clinical candidates through clinical development. 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 from Ironwood, and that this separation could harm our business, results of operations and financial condition; 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; the risk of cessation or delay of any of the ongoing or planned clinical studies and/or our development of our product candidates; the risk of a delay in the enrollment of patients in our clinical studies; the risk that any one or more of our product candidates will not be successfully developed, approved or commercialized; 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 from Ironwood may adversely impact our ability to attract or retain key personnel; and the other risks and uncertainties listed under the “Risk Factors” section and elsewhere in our Quarterly Statement on Form 10-Q filed on May 13, 2019, with the Securities and Exchange Commission (SEC), and in subsequent reports that we file 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 we undertake no obligation to update these forward-looking statements, except as required by law.

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