Cyclerion announces IW-6463 phase 1 healthy volunteer study results that support further development for neurodegenerative diseases

January 13, 2020

– Results in 110 subjects demonstrate favorable safety, CNS pharmacokinetics, and evidence of target engagement –

– Study underway in elderly subjects to further assess cerebral blood flow and additional translational measures of CNS target engagement; topline readout anticipated in mid-2020 –

– Company will present, with webcast, at the J.P. Morgan Healthcare Conference on Wednesday, January 15, 2020 at 9AM PST (noon EST) –

CAMBRIDGE, Mass., Jan. 13, 2020 (GLOBE NEWSWIRE) -- Cyclerion Therapeutics, Inc. (Nasdaq: CYCN), today announces positive Phase 1 study results that provide the foundation for continued development of IW-6463, an oral, once-daily central nervous system (CNS)-penetrant soluble guanylate cyclase (sGC) stimulator for the treatment of serious neurodegenerative diseases. The nitric oxide pathway and sGC stimulation have long been known to be a central physiological regulator in the central nervous system, impacting cerebrovascular blood flow, neuroinflammation, neuronal function and metabolism.

“Our Phase 1 healthy volunteer study results indicate that IW-6463 was well tolerated. Pharmacokinetic (PK) data, obtained from both blood and cerebral spinal fluid (CSF), support once-daily dosing with or without food and demonstrate IW-6463 penetration across the blood-brain-barrier at levels expected to be pharmacologically active. We are excited about the therapeutic possibilities for IW-6463 as a first-in-class, brain penetrant sGC stimulator,” said Chris Wright, M.D., Chief Medical Officer of Cyclerion. “These results, together with our preclinical data, provide strong support for continued development of IW-6463 as a potential new medicine for serious neurodegenerative diseases.”

Phase 1 Study Design and Topline Results

The company’s first IW-6463 Phase 1 study was conducted in 110 healthy volunteers aged 18-63 years to evaluate safety and pharmacokinetics in blood and CSF. The three-stage study evaluated: a) single ascending doses, b) multiple ascending doses (over 14 days) and c) food interaction effects. Study results demonstrated that IW-6463 was well tolerated across the tested dose levels. The most common adverse events (AEs) observed in the active treatment group were headache, nausea, dizziness, somnolence and fatigue. All AEs were mild and no serious adverse events (SAEs) were observed. IW-6463 administration resulted in a mild reduction in blood pressure, a known characteristic of sGC stimulators, providing evidence of peripheral pharmacological activity and target engagement. PK data obtained from the CSF demonstrate penetration of IW-6463 into the CNS at levels expected to be pharmacologically active. Food interaction results indicate that IW-6463 may be taken with or without food. These data, together with plasma PK results, support development of IW-6463 as a once-daily orally administered therapeutic.

Ongoing and Planned Development Activities

A translational pharmacology study in approximately 24 elderly subjects is ongoing. This study will evaluate safety, PK, and measures of CNS pharmacological activity, including cerebral blood flow by MRI and additional translational measures. Topline study results are expected in mid-2020. These results are intended to enable Cyclerion to direct further development in high-value CNS indications where biological and genetic data suggest an important role for nitric oxide and cyclic guanosine monophosphate (cGMP) signaling.

Presentation at J.P. Morgan Healthcare Conference

Cyclerion will discuss IW-6463 and its CNS program, along with its diabetic nephropathy and sickle cell disease clinical programs, at the J.P. Morgan Healthcare Conference on Wednesday, January 15, 2020. The presentation will be webcast at 9:00AM PST (12:00PM EST). Note that the webcast presentation EST time was incorrect on the company’s December 23, 2019 webcast press release announcement, and the correct time is 12:00PM EST.

The presentation will be followed by a question and answer session to be held at 9:30AM PT (12:30PM EST). A live webcast of the presentation and the Q&A session can be accessed on the following links:

Presentation link:
https://jpmorgan.metameetings.net/events/hc20/sessions/29869-cyclerion/webcast

Q&A link:
https://jpmorgan.metameetings.net/events/hc20/sessions/30203-cyclerion-q-a/webcast

A replay of the presentation will be posted on the Cyclerion website following the event.

About IW-6463

IW-6463, a CNS-penetrant sGC stimulator, is being developed as a potentially disease modifying therapy for neurodegenerative diseases. Nitric oxide is one of several fundamental neurotransmitters, one that has yet to be leveraged for its therapeutic potential in the CNS. 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 endothelial cell loss and nitric oxide dysregulation are contributors to neurodegenerative diseases and result in reduced blood flow, vascular leakage, inflammation, and neuronal dysfunction/loss. 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, improved neuronal health, neuroprotective effects and enhanced cellular bioenergetics and mitochondrial function.

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 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 diabetic nephropathy, olinciguat in Phase 2 development for sickle cell disease, IW-6463 in Phase 1 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. 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 our ability to obtain necessary approvals from regulatory authorities; our ability to advance product candidates in clinical trials; that regulatory approval processes are lengthy, time-consuming and inherently unpredictable; that significant variability in safety or efficacy may appear in different clinical studies of the same product candidate; that product candidates in later stages of clinical studies often fail to demonstrate adequate safety and efficacy despite promising preclinical testing and earlier clinical studies; the timing, investment and associated activities involved in developing and obtaining regulatory approval for our product candidates; our plans with respect to the development of our product candidates and the associated timing thereof, including the design and results of pre-clinical and clinical studies; the efficacy of our product candidates; and the risks more fully listed under the heading “Risk Factors” and elsewhere in our Registration Statement on Form 10 filed on March 11, 2019, and in Cyclerion’s subsequent SEC filings, including the Form 10-Q filed on November 12, 2019. 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.