Cyclerion Therapeutics Provides a Corporate and Pipeline Overview as a Newly Launched Public Biopharmaceutical Company

May 13, 2019

– Completed enrollment in Phase 2 studies of praliciguat in diabetic nephropathy and heart failure with preserved ejection fraction (HFpEF) –

– Based on encouraging tolerability data, company intends to add a higher olinciguat dose level to the Phase 2 sickle cell disease study (STRONG SCD) –

–Company's first webcast conference call to be held at 8:30 a.m. EDT today –

CAMBRIDGE, Mass., May 13, 2019 (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 provided a general corporate and pipeline overview, as well as financial results for the first quarter of 2019.

"Cyclerion launched with the mission of developing life changing medicines for patients suffering from serious and orphan diseases through the modulation of soluble guanylate cyclase," said Peter Hecht, Ph.D., chief executive officer of Cyclerion. "Our team is advancing a pipeline of differentiated and wholly owned sGC stimulator therapeutic candidates with compelling preclinical and clinical data. Each program targets a devastating disease with limited, if any, treatment options. We look forward to an eventful and data-rich year ahead with anticipated clinical readouts, as well as continued progress on our preclinical programs."

Cyclerion is focused on unlocking the full therapeutic potential of the nitric oxide signaling pathway, a clinically validated pathway with potential for diverse therapeutic applications. 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 sGC pipeline includes three ongoing Phase 2 clinical studies, one ongoing Phase 1 clinical study, and two late-stage discovery programs.

Recent Business and Program Highlights

- **Cyclerion launched as an independent, publicly traded company on April 1, 2019.** Cyclerion spun out of Ironwood Pharmaceuticals with a focus on rapidly advancing its pipeline of sGC stimulators for the treatment of serious and orphan diseases, including sickle cell disease, diabetic nephropathy, and HFpEF. On April 2, 2019, Cyclerion closed a private placement financing with net proceeds of $165 million and participation from leading biotechnology focused investors and certain members of Cyclerion management.

- **Andreas (Andy) Busch, Ph.D. appointed as chief innovation officer (CIO).** As head of Cyclerion's Innovation Center, Dr. Busch is responsible for providing strategic leadership of the company's mission to identify, advance, and optimize value-creating medicines from its sGC portfolio. Dr. Busch brings extensive R&D and portfolio leadership experience across a broad range of therapeutic categories, including significant expertise in rare and orphan diseases and in the discovery and development of sGC stimulators. Dr. Busch was previously executive vice president, head of R&D, chief scientific officer and a member of the executive committee at Shire Plc and executive vice president at Bayer Pharmaceuticals.

- **Praliciguat, a once-daily, orally available systemic sGC stimulator in development for treatment of cardiometabolic diseases:** completed enrollment in Phase 2 studies for diabetic nephropathy and HFpEF. Data are expected for both studies in the fourth quarter of 2019.

    - The ongoing Phase 2 study of praliciguat in patients with diabetic nephropathy is a randomized, placebo-controlled, dose-ranging study in 156 patients to evaluate safety and efficacy following 12 weeks of praliciguat treatment. The primary measure of efficacy is the change in urine albumin to creatinine ratio (UACR). Effects on metabolic parameters will also be assessed as secondary endpoints.

    - The ongoing Phase 2 study of praliciguat in patients with HFpEF (the CAPACITY study) is a randomized, placebo-controlled study in 196 patients to evaluate safety and efficacy following 12 weeks of praliciguat treatment. The primary measure of efficacy is change in exercise tolerance, as assessed by cardiopulmonary exercise testing.

  The development of praliciguat for treatment of diabetic nephropathy and HFpEF is supported by a body of preclinical data, as well as completed Phase 1 healthy volunteer studies and a Phase 2a study in patients with diabetes and hypertension, which collectively

demonstrated tolerability, target engagement, and positive cardiometabolic effects.

- **Olinciguat, a once-daily, orally available vascular sGC stimulator in development for sickle cell disease (SCD):** ongoing enrollment in the Phase 2 STRONG SCD study, and adding an additional (higher) dose. Topline data are expected in mid-2020.

    - Olinciguat is being studied in a randomized, placebo-controlled, dose-ranging Phase 2 study in patients with sickle cell disease (STRONG SCD study) that is expected to enroll up to 88 patients. STRONG SCD is designed to evaluate safety, tolerability, and pharmacokinetics of olinciguat, as well as to explore effects on daily symptoms and biomarkers of disease activity when dosed over a 12-week treatment period.

    - Based on favorable tolerability data from a separate and recently completed ascending dose clinical pharmacology study conducted in healthy volunteers, as well as blinded safety data from the ongoing STRONG SCD study, the company is expanding the dose range being evaluated in the Phase 2 study. Cyclerion expects to add a fourth, higher dose level to the STRONG SCD study design, providing the opportunity to explore a broad range of tolerated doses and optimize the company's understanding of the therapeutic potential of olinciguat in sickle cell disease. With the addition of a higher dose level, topline data from this study are expected in mid-2020.

  The development of olinciguat for treatment of sickle cell disease is supported by a body of preclinical data, as well as completed Phase 1 healthy volunteer studies, that demonstrated tolerability and target engagement.

- **IW-6463: a central nervous system (CNS) penetrant sGC stimulator in development for serious CNS diseases:** Phase 1 study ongoing, with data expected in the fourth quarter of 2019.

    - IW-6463 is being studied in a single and multiple ascending dose level Phase 1 trial to evaluate safety, pharmacokinetics, as well as other CNS functional measures to assess translation of preclinical effects to humans.

  The development of IW-6463 is supported by a body of preclinical data demonstrating the association of IW-6463 administration with beneficial effects on neural function, neuroinflammation, neuroprotection, and brain blood flow.

- **Preclinical stage work:** Cyclerion is also advancing several earlier stage therapeutic programs, including those targeting the lung and liver.

First Quarter 2019 Financial Results

- **Basis of presentation:** For the first quarter of 2019, Cyclerion was a wholly owned subsidiary of Ironwood Pharmaceuticals, Inc. Accordingly, Cyclerion's first quarter 2019 financial statements have been prepared on a stand-alone basis and are derived from Ironwood's financial statements and accounting records. These unaudited condensed combined financial statements reflect the assets, liabilities, and expenses directly attributable to Cyclerion, as well as allocations of certain corporate level assets, liabilities, and expenses, deemed necessary to fairly present the financial position, results of operations, and cash flows of Cyclerion. As such, these allocations may not be indicative of the actual amounts that would have been recorded had Cyclerion operated as an independent, publicly traded company for the periods presented.
- **Research and Development Expense:** Research and development expenses were $26.4 million for the three months ended March 31, 2019, compared to $21.5 million for the three months ended March 31, 2018. The increase of approximately $4.9 million was primarily related to external research costs associated with clinical development of Cyclerion's product candidates, including costs associated with initiation of STRONG SCD, a Phase 2 clinical trial for olinciguat.
- **General and Administrative Expense:** General and administrative expenses were $11.0 million for the three months ended March 31, 2019, compared to $3.8 million for the three months ended March 31, 2018. The increase of approximately $7.2 million was primarily due to an increase of approximately $4.1 million related to non-recurring costs associated with Cyclerion's separation from Ironwood, and an increase of approximately $3.1 million resulting from a higher allocation from Ironwood of employee-related expenses, professional service costs, and facilities and information technology infrastructure costs.
- **Net Loss:** Net loss was $37.4 million for the three months ended March 31, 2019, compared to $25.3 million for the three months ended March 31, 2018.
- **Cash Position:** There were no cash amounts specifically attributable to Cyclerion as of March 31, 2019; therefore, there is no cash reflected in the unaudited condensed combined financial statements. On April 2, 2019, approximately $165 million net proceeds were received from a private placement financing that are expected to fund operations through at least the first quarter of 2021.

Conference Call Information

Cyclerion will host a conference call and live audio webcast on Monday, May 13, 2019 at 8:30 a.m. Eastern Time. For its first webcast conference call as a public company, Cyclerion intends to provide a general corporate overview and discuss its clinical and preclinical development pipeline.

To access the conference call, please dial (800) 360-8162 (U.S. and Canada) or (409) 937-8760 (international) and reference the conference ID number 1979155. To join the live webcast, please visit the “Investors and Media” section of the Cyclerion website at www.cyclerion.com at least 15 minutes prior to the start of the call.

The call will be available for replay via telephone starting May 13, 2019 at approximately 11:30 a.m. Eastern Time, running through 11:30 a.m. Eastern Time on May 20, 2019. To listen to the replay, dial (855) 859-2056 (U.S. and Canada) or (404) 537-3406 (international) and reference the conference ID number 1979155. A webcast replay will be available on the Cyclerion website beginning approximately two hours after the event and will be archived for 21 days.

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 anticipated timing of release of data from our clinical trials; the progression of our discovery programs into clinical development; the business and operations of Cyclerion; hiring of new executives and employees; and our future financial performance and expense levels. 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 Registration Statement on Form S-1 filed on April 18, 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.

Cyclerion Therapeutics, Inc. (as a wholly owned subsidiary of Ironwood Pharmaceuticals, Inc.)

Condensed Combined Statements of Operations

(In thousands)

(Unaudited)

	Three Months Ended March 31,	
	2019	**2018**
Cost and expenses:		
Research and development	$ 26,404	$ 21,514
General and administrative	10,977	3,769
Total cost and expenses	37,381	25,283
Loss from operations	(37,381)	(25,283)
Net loss	$ (37,381)	$ (25,283)

Cyclerion Therapeutics, Inc. (as a wholly owned subsidiary of Ironwood Pharmaceuticals, Inc.)

Condensed Combined Balance Sheets

(In thousands)

(Unaudited)

	March 31,	**December 31,**

	2019	2018
ASSETS		
Current assets:		
Prepaid expenses	$ 927	$ 867
Other current assets	12	12
Total current assets	939	879
Property and equipment, net	8,815	6,497
Other assets	19	25
Total assets	$ 9,773	$ 7,401
LIABILITIES AND NET PARENT INVESTMENT		
Current liabilities:		
Accounts payable	$ 5,671	$ 2,781
Accrued research and development costs	6,243	5,261
Accrued expenses and other current liabilities	5,559	9,804
Total current liabilities	17,473	17,846
Other liabilities	52	-
Net parent investment:		
Net parent investment	(7,752)	(10,445)
Total liabilities and net parent investment	$ 9,773	$ 7,401

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