# Cyclerion Therapeutics Announces Praliciguat Topline Phase 2 Results in Diabetic Nephropathy

October 30, 2019

*– **Study did not reach statistical significance on primary endpoint** –*

*– **Positive trends on primary and secondary endpoints indicate profile that merits further investigation** –*

*– **Company intends to pursue out-license of praliciguat for late-stage development** –*

*– **Conference call to be held at 8:30 a.m. ET today** –*

CAMBRIDGE, Mass., Oct. 30, 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 topline results from its Phase 2 proof-of-concept study of praliciguat, a once-daily, orally available systemic sGC stimulator, in diabetic nephropathy.

The study did not meet statistical significance on its primary endpoint of reduction in albuminuria from baseline as compared to placebo, measured by urine albumin creatinine ratio (UACR), but there was a trend toward improvement across the total intention-to-treat (ITT) study population. In addition, improvements were observed in patients treated with praliciguat in several secondary vascular and metabolic measures associated with cardiovascular risk and kidney disease progression, including blood pressure, cholesterol and HbA1c levels, compared to placebo. All patients were on concomitant stable standard of care therapy, including anti-diabetic medications and renin-angiotensin-aldosterone system (RAAS) blockers. As in prior clinical studies, the pharmacokinetic profile of praliciguat was consistent with once-daily dosing. Praliciguat was generally well tolerated, and the safety profile was supportive of continued development.

During statistical validation, data from one clinical trial site were found to be inconsistent with those of the overall study population. At this site, a significantly greater percentage of patients assigned to the praliciguat treatment arms had undetectable or very low praliciguat plasma concentrations than was seen across the broader study population. In a post-hoc sensitivity analysis in which data from this site are excluded, an increased treatment effect and reduced variability are observed; see table below.

“I am encouraged by the estimated reduction in albuminuria of 15% or more, compared with placebo, on top of current standard of care. This molecule modifies pathways that are complementary to those targeted by usual care, and it warrants further investigation as a potential treatment for patients with diabetic kidney disease,” said Ian de Boer, M.D., M.S., Professor, Division of Nephrology, Adjunct Professor, Epidemiology and Associate Director, Kidney Research Institute at University of Washington. “Diabetic kidney disease remains the leading cause of kidney failure requiring dialysis or kidney transplantation. We need more treatment options to address this growing patient population.”

“We believe praliciguat has the potential to be a first-in-category treatment for patients with diabetic nephropathy,” said Mark Currie, Ph.D., president and chief scientific officer at Cyclerion. “We look forward to sharing the data with prospective partners.”

As previously announced, Cyclerion intends to out-license praliciguat for late-stage global development and commercialization.

Cyclerion also announced today the results of its Phase 2 proof-of-concept study of praliciguat in heart failure with preserved ejection fraction (HFpEF). Full results from both studies will be presented at future medical meetings.

“With the praliciguat data in hand, we will focus on partnering praliciguat, advancing our sickle cell disease and central nervous system clinical programs, as well as ongoing innovation,” said Peter Hecht, Ph.D., chief executive officer at Cyclerion. “We are excited about each of these programs and believe they have the potential to help patients with serious diseases and significant unmet medical need.”

The company expects to deliver results from its STRONG SCD Phase 2 study of olinciguat, an sGC stimulator under investigation as a potential treatment for sickle cell disease in mid-2020, its Phase 1 study of IW-6463, a central nervous system-penetrant sGC stimulator, in Q4 2019.

With its praliciguat Phase 2 studies completed, Cyclerion intends to focus its investments on these near-term value-creation opportunities, as well as ongoing innovation, and to reduce its monthly cash expenses by 25%. As of September 30, 2019, Cyclerion had approximately $125 million of cash, cash equivalents and restricted cash. Cyclerion anticipates that this cash will be sufficient to fund its operations through Q1 2021.

**About the Praliciguat Phase 2 Study in Diabetic Nephropathy**
The randomized, placebo-controlled, dose-ranging Phase 2 study evaluated the safety and efficacy of once-daily praliciguat 20 mg, praliciguat 40 mg or placebo in 156 patients with diabetic nephropathy over a 12-week period. Participating patients, who were 43 to 75 years old and had type 2 diabetes and diabetic nephropathy, were on a stable regimen of anti-glycemic medications and renin-angiotensin-aldosterone system (RAAS) inhibitors for the duration of the study period. The primary measure of efficacy was the change in urine albumin to creatinine ratio (UACR), a key indicator of kidney damage.

Topline results were as follows:

| | **ITT Patient Population (n=156)** | **ITT Excluding Site 00A (n=133)** |
|---|---|---|

| ***UACR: Percent change from baseline*** | ***Placebo*** | ***Pooled praliciguat (20 mg and 40 mg)*** | ***Placebo*** | ***Pooled praliciguat (20 mg and 40 mg)*** |
|---|---|---|---|---|
| Average of weeks 8 and 12 | -14.8% | -27.8% | -4.2% | -23.5% |
| Placebo-adjusted, average of weeks 8 and 12 (primary endpoint) | | -15.3% (p=0.1736) | | -20.1% (p=0.0303)* |
| Week 12 | -14.8% | -30.9% | -4.1% | -26.1% |
| Placebo-adjusted, week 12 | | -18.9% (p=0.1956)* | | -22.9% (p=0.0672)* |

**Nominal p-values; not adjusted for multiplicity.*

Praliciguat was generally well tolerated. Most common adverse events (AEs) were dizziness, diarrhea and constipation. Discontinuations due to AEs were 2% in the placebo group, 4% in the 20mg praliciguat group, and 12% in the 40mg group. Serious AEs (SAEs) were observed in 2% of patients in the placebo group, 2% of patients in the 20mg praliciguat arm, 8% of patients in the 40mg arm; all SAEs were judged unrelated to study drug.

**Conference Call Information**
Cyclerion will host a conference call and live audio webcast today at 8:30 a.m. Eastern Time to discuss the topline results from the Phase 2 proof-of-concept studies of praliciguat. 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 5966274. To join the live webcast, please visit the "Investors and Media" section of the Cyclerion website at www.cyclerion.com, or access it directly via the registration link, at least 15 minutes prior to the start of the call.

The call will be available for replay via telephone starting October 30, 2019 at approximately 11:30 a.m. Eastern Time, running through 10:30 a.m. Eastern Time on November 6, 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 5966274. 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 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, IW-6463 in Phase 1 development for serious and orphan central nervous system 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 results and conduct of our Phase 2 proof-of-concept clinical trial of praliciguat; our interpretation of the data from the clinical trial, including regarding the clinical site whose results are inconsistent with the overall study population; the potential of further evaluation of praliciguat for diabetic nephropathy; the potential commercial opportunities of praliciguat, including the potential for a future out-license of praliciguat by us; the clinical potential of praliciguat; our future business focus; the anticipated timing of release of data from our ongoing clinical trials; and our sufficiency of cash. 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. Our statements about the results and conduct of our Phase 2 proof-of-concept clinical trial of praliciguat could be affected by the possibility that there are changes in the data or interpretation of the data ; and our statements about the potential out-licensing commercial opportunity could be affected by the possibility that we are unable to identify a commercial partner to in-license praliciguat; and the risk that our estimates regarding our use of cash may prove inaccurate. In addition, applicable risks and uncertainties regarding our business include those 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, including our Quarterly Report on Form 10-Q filed with the SEC on August 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 we undertake no obligation to update these forward-looking statements, except as required by law.

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