UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): **October 29, 2019**

CYCLERION THERAPEUTICS, INC.
(Exact name of registrant as specified in its charter)

Massachusetts	**001-38787**	**83-1895370**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification Number)

301 Binney Street
Cambridge, Massachusetts 02142
(Address of principal executive offices, including Zip Code)

Registrant's telephone number, including area code: **(857) 327-8778**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- o Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
- o Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
- o Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
- o Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, no par value	CYCN	The Nasdaq Stock Market LLC (Nasdaq Global Select Market)

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter). Emerging growth company x

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. o

Item 2.02 Results of Operations and Financial Condition.

As described in Item 8.01 below, on October 30, 2019, Cyclerion Therapeutics, Inc. (the "Company") issued press releases announcing the topline data from the Company's Phase 2 clinical trials of praliciguat in patients with diabetic nephropathy and heart failure with preserved ejection fraction ("HFpEF"). These press releases also contained information regarding the Company's preliminary, unaudited unrestricted cash, cash equivalents and restricted cash balance as of September 30, 2019, and the Company's expectations regarding the amount of time such amount will fund the Company's operations.

The financial results included in the press releases are unaudited and preliminary estimates that (i) represent the most current information available to management as of the date of this Current Report on Form 8-K, (ii) are subject to completion of financial closing and procedures that could result in significant changes to the estimated amounts, and (iii) do not present all information necessary for an understanding of the Company's financial condition as of, and its results of operations for the quarter ended, September 30, 2019. Accordingly, undue reliance should not be placed on such preliminary estimates.

The information contained in this Item 2.02 shall not be incorporated by reference into any filing of the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing, unless expressly incorporated by specific reference to such filing. The information in this Item 2.02 shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended.

Item 2.05 Costs Associated with Exit or Disposal Activities.

On October 29, 2019, the Board of Directors of the Company approved the reduction of the Company's current workforce by approximately thirty (30) full-time employees in order to better align its resources with its ongoing clinical and preclinical programs and innovation strategy following the announcement of topline data from the Company's Phase 2 clinical trials of praliciguat. The Company expects that this workforce reduction will take place primarily during the fourth quarter of 2019.

The Company estimates that it will incur aggregate charges in connection with the workforce reduction of approximately $3 million for one-time employee severance and benefit costs primarily in the fourth quarter of 2019, nearly all of which are expected to result in cash expenditures. As a result of the workforce reduction, the Company expects to reduce its cash operating expenses by approximately $7 to $8 million during the fiscal year ending December 31, 2020. The Company may also incur other charges or cash expenditures not currently contemplated due to events that may occur as a result of, or associated with, the workforce reduction.

Item 8.01 Other Events.

On October 30, 2019, the Company issued two press releases announcing topline data from the Company's Phase 2 clinical trials of praliciguat in patients with diabetic nephropathy and HFpEF. Copies of the press releases regarding diabetic nephropathy and HFpEF are attached hereto as Exhibit 99.1 and Exhibit 99.2, respectively, and, other than the information described in Item 2.02 above, each is incorporated by reference to this Current Report on Form 8-K.

The Company will also host a conference call to discuss the topline results from these clinical trials on October 30, 2019 at 8:30 a.m. Eastern Time. A copy of the conference call presentation materials is attached hereto as Exhibit 99.3 and is incorporated by reference to this Current Report on Form 8-K. The presentation materials are also available on the "Investors & Media" page of the Company's website at https://ir.cyclerion.com/news-events/news-releases.

All information included in the press releases and the investor presentation is presented as of the respective dates thereof, and the Company assumes no obligation to correct or update such information in the future.

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	Description
99.1	Press Release of Cyclerion Therapeutics, Inc. dated October 30, 2019
99.2	Press Release of Cyclerion Therapeutics, Inc. dated October 30, 2019
99.3	Investor Presentation of Cyclerion Therapeutics, Inc. dated October 30, 2019

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Cyclerion Therapeutics, Inc.

Dated: October 30, 2019

By: /s/ William Huyett
Name: William Huyett
Title: Chief Financial Officer

FOR IMMEDIATE RELEASE

Cyclerion Therapeutics Announces Praliciguat Topline Phase 2 Results in Diabetic Nephropathy

— 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., October 30, 2019 — 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 4% in the placebo group, 8% 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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FOR IMMEDIATE RELEASE

Cyclerion Therapeutics Announces Topline Phase 2 Results for sGC Stimulator Praliciguat in Heart Failure with Preserved Ejection Fraction (HFpEF)

— Study in HFpEF patients did not meet primary endpoint; company discontinuing development of praliciguat in HFpEF —

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

CAMBRIDGE, Mass., October 30, 2019 — 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 CAPACITY Phase 2 proof-of-concept study of praliciguat, a once-daily, orally available systemic sGC stimulator, in heart failure with preserved ejection fraction (HFpEF).

The study did not meet statistical significance on its primary endpoint of improved exercise capacity from baseline as compared to placebo, measured by cardiopulmonary exercise testing (CPET). There was clear evidence of drug exposure and pharmacological activity as judged by expected reductions in blood pressure. Praliciguat was generally well tolerated, and the safety profile supported investigation of praliciguat in other indications. While there were no trends observed in improving HFpEF symptoms, a positive trend in reducing HbA1c levels was observed in the subset of patients with diabetes. This is consistent with the results observed in the company's Phase 2 study of praliciguat in diabetic nephropathy, which were also reported today.

Cyclerion is discontinuing development of praliciguat in HFpEF. Full results from the study will be presented at a future medical meeting.

"CAPACITY-HFpEF had an innovative design, focused on those patients we believed were more likely to respond to therapy. While we are disappointed with the study results, particularly given the unmet need in HFpEF, we are very grateful to the patients who participated, as well as the physicians, other study staff and our internal teams who ran a high-quality trial that enabled us to arrive at a clear result for this indication," said Chris Wright, M.D., Ph.D., chief medical officer at Cyclerion.

With its praliciguat Phase 2 studies completed, Cyclerion intends to focus its investments on near-term value-creation opportunities — including out-licensing praliciguat for diabetic nephropathy, advancing its STRONG SCD Phase 2 study of olinciguat in sickle cell disease, its Phase 1 study of IW-6463 for central nervous system disorders, 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 Praliciguat Phase 2 Study in HFpEF (CAPACITY)

The CAPACITY study, a randomized, placebo-controlled Phase 2 study, evaluated the safety and efficacy of once-daily praliciguat 40 mg or placebo in 196 patients with HFpEF over a 12-week period. Participating patients were 45 years or older and had HFpEF with an ejection fracture greater than or equal to 40%. The primary measure of efficacy was change in exercise tolerance, as assessed by cardiopulmonary exercise testing (CPET). No statistically significant effects were observed.

Praliciguat was generally well tolerated in this study. The most common adverse events (AEs) reported in patients treated with praliciguat in this study were headache, dizziness, urinary tract infection and hypotension. The frequency of AEs and serious AEs were similar between the treatment and placebo groups. Discontinuations due to AEs were 4.8% of praliciguat-treated patients compared to 3.3% of placebo-treated patients.

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“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; our risk that our estimates regarding our use of cash may prove inaccurate; 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, 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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Exhibit 99.3


cyclerion
Praliciguat Phase 2 Proof of Concept Studies in HFpEF and DN
Topline Results
October 30th, 2019

Safe Harbor Statement

This presentation 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 progression of our discovery programs into clinical development; our business and operations; our sufficiency of cash; our interpretation of the data from the clinical trials, including regarding the clinical site whose results are inconsistent with the overall study population; the potential of further evaluation of praliciguat; the potential commercial opportunities of praliciguat, including the potential for a future out-license of praliciguat by us; and the anticipated timing of release of data from our ongoing clinical trials.

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; 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 our statements about 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 presentation, and we undertake no obligation to update these forward-looking statements, except as required by law.

Praliciguat DN and HFpEF phase 2 study results

- HFpEF: terminated development
  - Missed primary endpoint with no observed improvement on HFpEF symptoms
  - Evidence of pharmacological activity
  - Generally well tolerated
- Diabetic nephropathy: merits further investigation and discussion with potential partners
  - Missed primary endpoint
  - Positive efficacy trends (UACR and cardiometabolic) suggest potential for a large and underserved patient population
  - Generally well-tolerated

Diabetic Nephropathy (DN) Proof of Concept Study: Topline Results

Praliciguat DN proof of concept study overview

Study Design

- RCT designed to assess safety and tolerability of praliciguat and the effect on renal function in patients with DN on RAAS inhibitors
- Primary endpoints: Urine albumin creatinine ratio (ΔUACR) and TEAEs
- Secondary endpoints: BP, HR, and metabolic measures such at HBA1c and lipid levels.
- Key inclusion criteria: DM2 on stable medical regimen, ACE/ARB required, albuminuria (200-5000 mg/g), eGFR 30-75 mL/min/1.73 m2, SBP 110-160 mmHg

Study Population

- n=156 randomized 1:1:1 praliciguat 20mg vs. 40mg vs. placebo
- Demographics were balanced across the treatment arms largely consistent with the known epidemiology of the disease.
- Baseline characteristics also generally well-balanced: UACR in the 1000 mg/g range and, even though on concomitant standard of care treatments, HBA1c and blood pressure were elevated at baseline.

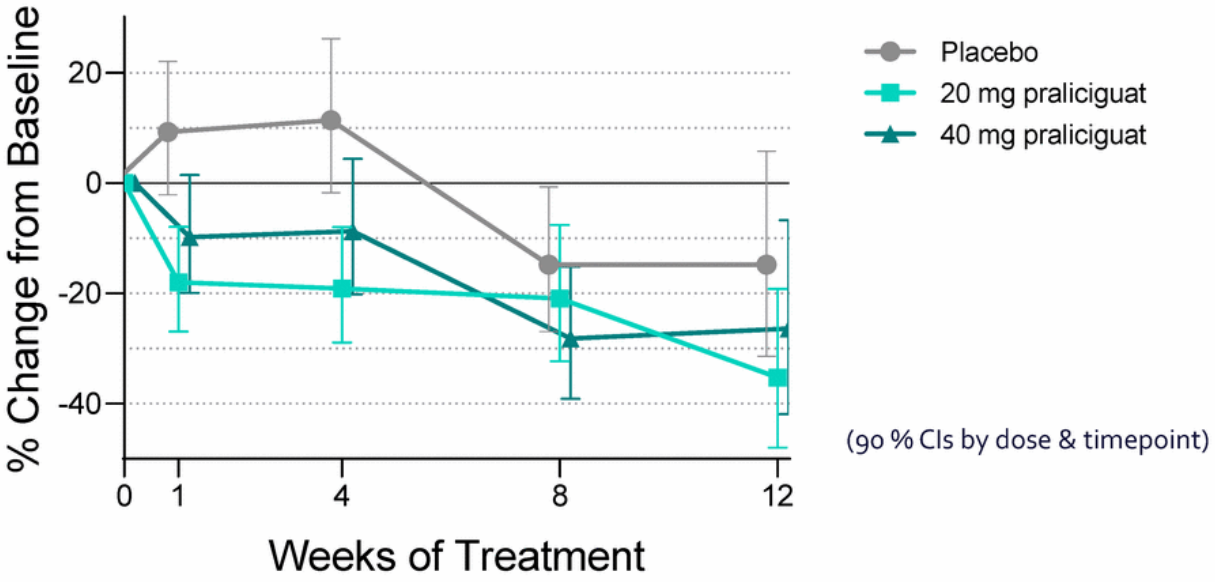
DN study results overview

Outcome Variable: UACR	PBO (n=54)	PRL 20 mg (n=50)	PRL 40 mg (n=52)	PRL Combined (n=102)
Average of Weeks 8 and 12 (primary analysis)				
Geometric Mean % Change (90% CI)	**-14.8%** (-27, +0.4)	**-28.4%** (-39, -15)	**-27.3%** (-39, -13)	**-27.8%** (-36, -18)
Pbo Adj. Geo. Mean % Change (90% CI) P-Value		**-16.0%** (-33, +6)	**-14.6%** (-33, +8)	**-15.3%** (-31, +4) 0.174
Week 12				
Geometric Mean % Change (90% CI)	**-14.8%** (-31.4, 5.8)	**-35.2%** (-48.0, -19.2)	**-26.4%** (-41.9, -6.7)	**-30.9%** (-41.4, -18.6)
Pbo Adj. Geo. Mean % Change (90% CI) P-Value		**-23.9%** (-44.0, 3.3)	**-13.6%** (-37.1, 18.6)	**-18.9%** (-38.0, 5.9) 0.1956*

- Treatment was associated with improvements in several vascular and metabolic parameters including blood pressure, HbA1c and LDL cholesterol levels.
- Praliciguat was generally well tolerated. Most common AEs were dizziness, diarrhea and constipation. Discontinuations due to AEs were 4% in the placebo group, 8% in the 20mg praliciguat group, and 12% in the 40mg praliciguat 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 and; all SAEs were judged unrelated to study drug.

* Nominal p-value; not adjusted for multiplicity

DN study: change in UACR over 12 weeks

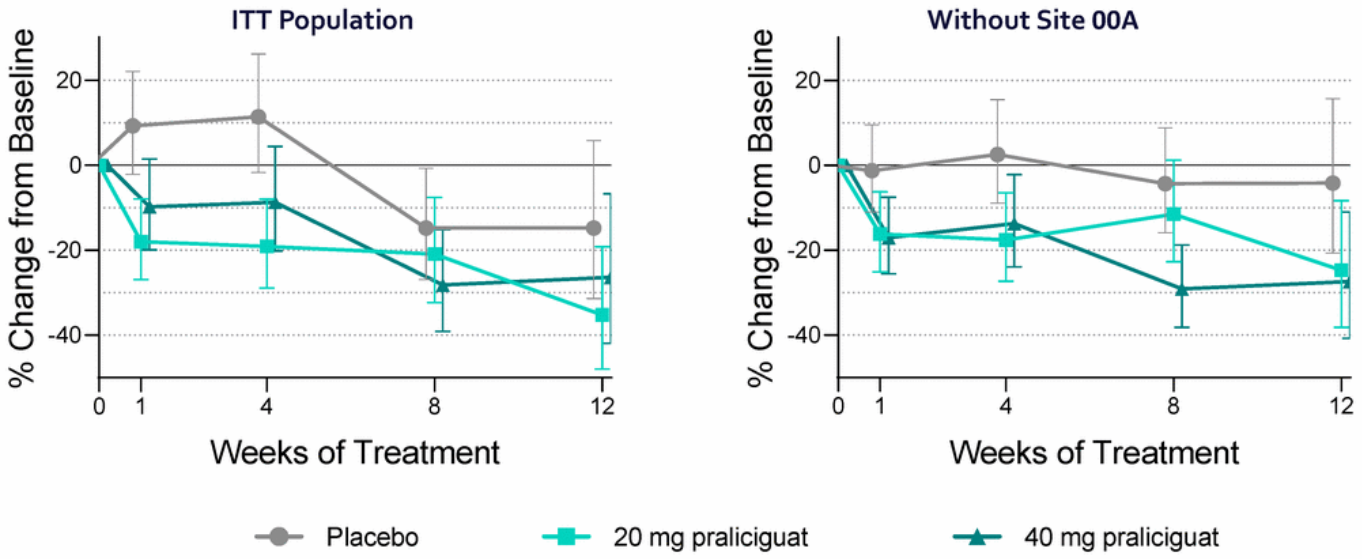


(90 % CIs by dose & timepoint)

DN study: data from one site inconsistent with overall study population

- During statistical validation, data from one clinical trial site (00A) were found to be inconsistent with those of the overall study population
- At site 00A, 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

DN study: comparison of UACR change over time with and without site 00A



DN study: primary analysis and week 12 data with and without site 00A

Outcome Variable: UACR	ITT (n=156)		Without Site 00A (n=133)	
	PBO	**PRL Combined**	**PBO**	**PRL Combined**
Average of Weeks 8 and 12				
Geometric Mean % Change (90% CI)	**-14.8%** (-27, +0.4)	**-27.8%** (-36, -18)	**-4.2%** (-16.7, 10.1)	**-23.5%** (-31.2, -14.8)
Pbo Adj. Geo. Mean % Change (90% CI) P-Value		**-15.3%** (-31, +4) 0.174		**-20.1%** (-32.6, -5.3) 0.0303*
Week 12				
Geometric Mean % Change (90% CI)	**-14.8%** (-31.4, 5.8)	**-30.9%** (-41.4, -18.6)	**-4.1%** (-20.6, 15.7)	**-26.1%** (-36.0, -14.6)
Pbo Adj. Geo. Mean % Change (90% CI) P-Value		**-18.9%** (-38.0, 5.9) 0.1956*		**-22.9%** (-38.9, -2.6) 0.0672*

* Nominal p-value; not adjusted for multiplicity

Praliciguat in diabetic nephropathy: next steps

- Based on these results, we believe praliciguat warrants further investigation as a potential treatment to improve kidney function and cardiometabolic parameters in diabetic nephropathy
- We intend to pursue an out-license of praliciguat for late-stage global development and commercialization to capture its full therapeutic potential

DN is a common and serious complication of diabetes leading to progressive loss of kidney function

Diabetic Nephropathy:

- Affects up to 40% of diabetes patients
- Leads to end-stage renal disease (ESRD) requiring renal replacement therapy (dialysis or kidney transplant)
  - Survival on dialysis is worse than for many types of cancer
- Patients are at higher risk of heart failure, MI, stroke and death[3]
- Shortens life span by 16 years[1]
- Lead to $22B in Medicare expenditures in 2016[2]

1. Wen CP, et al. Kidney Int. 2017;92:388-396 2.United States Renal Data System 2018 Annual Report 3. Foley RN, J Am Soc Nephrol 2005; 16: 489-95

Strategic focus

- Praliciguat diabetic nephropathy out licensing
- IW-6463 CNS (phase 1) topline results expected Q4 2019
- Olinciguat sickle cell disease (phase 2) topline results expected mid-2020
- Preclinical programs
- Reduce our monthly cash expenses by 25%; expect cash on hand to cover operations through Q1 2021

Conclusion: Praliciguat DN and HFpEF phase 2 study results

- HFpEF: terminated development
  - Missed primary endpoint with no observed improvement on HFpEF symptoms
  - Evidence of pharmacological activity
  - Generally well tolerated
- Diabetic nephropathy: merits further investigation and discussion with potential partners
  - Missed primary endpoint
  - Positive efficacy trends (UACR and cardiometabolic) suggest potential for a large and underserved patient population
  - Generally well-tolerated

Appendix

Capacity-HFpEF Proof of Concept Study

Topline Results

CAPACITY HFpEF (C1973-204) Study Design and Topline Results

Study Design

- Designed to assess safety and tolerability of praliciguat and the effects on peak exercise capacity in patients with HFpEF (EF ≥ 40%)
- Primary endpoints: change in peak VO_2 (CPET) and TEAEs at 12 weeks
- n=196 randomized 1:1 praliciguat 40mg vs. placebo

Topline Study Results

- No statistically significant effects on primary efficacy measure
- Clear evidence of drug exposure and pharmacologic activity (modest effects on blood pressure)
- Positive trends in reduction in HbA1c levels in diabetic patients
- Most common AEs reported in praliciguat-treated patients: headache, dizziness, urinary tract infection, and hypotension. The frequency of AEs and SAEs were similar between treatment and placebo groups

Change from Baseline to Week 12 Peak VO2 (mL O2/kg/min)	Placebo (N=78)	Praliciguat 40 mg (N=65)
n'*	72	64
Mean ± SD (90% Confidence Interval)	0.056 (-4.50, 3.95)	-0.282 (-6.50, 3.50)
Between PRL and PBO Group LS mean (95% Confidence Interval) [2]	0.036 (-0.492, 0.565)	-0.261 (-0.830, 0.308)
P Value of Change from PBO		0.3681

CPET-cardiopulmonary exercise test, TEAEs-treatment emergent adverse events , NCT03254485. *n' is the number of patients with measurements at both Baseline and the specific visit. [2] ANCOVA model with treatment group and atrial fibrillation stratification factor as categorical variable terms and baseline peak VO_2 value as a covariate. Week 8 and Week 12 are analyzed in separate models. Patients with missing change from baseline values are excluded. No imputation is performed for missing observations.