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): **April 10, 2020**

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 ☒

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. ☐

Item 2.02 Results of Operations and Financial Condition.

As described in Items 7.01 and 8.01 below, respectively, on April 10, 2020, Cyclerion Therapeutics, Inc. (the "Company") issued a press release and released a corporate slide presentation. The press release and presentation included information that, as of March 31, 2020, the Company's preliminary unaudited cash, cash equivalents and restricted cash balance was approximately $72 million and that the Company anticipates that this cash will fund its operations into the second quarter of 2021, excluding net cash flows from potential business development activities.

The foregoing information constitutes unaudited and preliminary estimates that (i) represent the most current information available to management as of the date of the press release and presentation, (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, March 31, 2020. Accordingly, undue reliance should not be placed on such estimates.

The information set forth in this Item 2.02 is being furnished pursuant to Item 2.02 of Form 8-K and shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section, and it shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended (the "Securities Act"), or under the Exchange Act, whether made before or after the date hereof, except as expressly provided by specific reference in such a filing.

Item 7.01 Regulation FD Disclosure.

In connection with the corporate update described in Item 8.01 of this report, the Company released a corporate slide presentation, which is attached as Exhibit 99.1 to this Current Report on Form 8-K and is incorporated herein by reference. The presentation is also posted to the Company's website, www.cyclerion.com. The Company plans to use its website to disseminate future updates to the presentation and may not necessarily file or furnish a Form 8-K alerting investors if the presentation is updated.

The information set forth in this Item 7.01 is being furnished pursuant to Item 7.01 of Form 8-K and shall not be deemed "filed" for purposes of Section 18 of the Exchange Act or otherwise subject to the liabilities of that section, and it shall not be deemed incorporated by reference in any filing under the Securities Act or under the Exchange Act, whether made before or after the date hereof, except as expressly provided by specific reference in such a filing.

By filing this Current Report on Form 8-K and furnishing the information in this Item 7.01, the Company makes no admission as to the materiality of Item 7.01 in this report or the presentation available on the Company's website. The information contained in the presentation is summary information that is intended to be considered in the context of the Company's filings with the Securities and Exchange Commission (the "SEC") and other public announcements that the Company makes, by press release or otherwise, from time to time. The Company undertakes no duty or obligation to publicly update or revise the information contained in this report, although it may do so from time to time as its management believes is appropriate or as required by applicable law. Any such updating may be made through the filing of other reports or documents with the SEC, through press releases, by updating its website or through other public disclosure.

Item 8.01 Other Events

On April 10, 2020, the Company provided a corporate update. A copy of the Company's press release of the same date summarizing the corporate update is attached hereto as Exhibit 99.2. The information set forth in the press release is incorporated by reference into this Item 8.01 of this report. The press release contains hypertext links to information on our website. The information on our website is not incorporated by reference into this Current Report on Form 8-K and does not constitute a part hereof.

Item 9.01 Financial Statements and Exhibits

(d)

Exhibit No.	Description
99.1	Corporate Update Presentation dated April 10, 2020.
99.2	Press Release dated April 10, 2020.

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: April 14, 2020

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

Exhibit 99.1

April 10, 2020

Creating breakthrough treatments for patients with serious and orphan diseases by harnessing the power of soluble guanylate cyclase (sGC)

Safe Harbor Statement

This presentation contains forward-looking statements. Any statements contained in this presentation that are not historical facts may be deemed to be forward looking statements. Words such as "anticipate," "believe," "potential," "expect," "may," "will," "should," "could," "plan," "estimate," "target," "project," "contemplate," "intend," "future," "will," "predict," "continue," and the negative of these terms and similar expressions are intended to identify these forward-looking statements.

These forward-looking statements are based on Cyclerion's current expectations, projections and trends, are only predictions and involve known and unknown risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statements. Investors are cautioned not to place undue reliance on these forward-looking statements, which include but are not limited to statements about possible or assumed future results of operations; preclinical, clinical and non-clinical studies, the interpretation of data therefrom and the ability to replicate findings from such studies; business strategies, research and development plans, collaborations, partnerships, out-licensing (including without limitation with respect to praliciguat), regulatory activities and any timing thereof; competitive position, potential growth or commercial opportunities; the clinical potential, application, commercialization or potential markets of or for any proposed products; the anticipated timing of release of data from any clinical trials; and the size and design of those clinical trials.

Applicable risks and uncertainties include those listed under the heading "Risk Factors" and elsewhere in our most recent Form 10-K filed with the SEC on March 12, 2020. These forward-looking statements speak only as of the date of this presentation, and we undertake no obligation and do not intend to update these forward-looking statements.

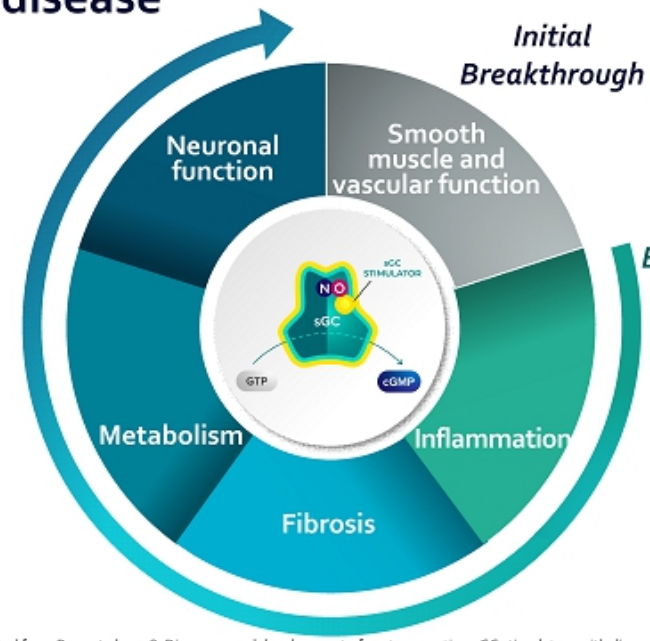
Cyclerion: clinical stage startup developing sGC therapeutics for serious diseases

2020 catalysts across programs → **Patient impact and value creation**

- sGC: a clinically-validated fundamental mechanism
- 2020 priorities
  - out-license praliciguat in cardiometabolic disease
  - clinical trial top-line results in SCD, CNS
- starting Q2 2020 with ~$72M cash[1] ; supports our priorities into Q2 2021
- experienced and successful leadership team

1. Preliminary, unaudited unrestricted cash, cash equivalents and restricted cash balance as of March 31, 2020

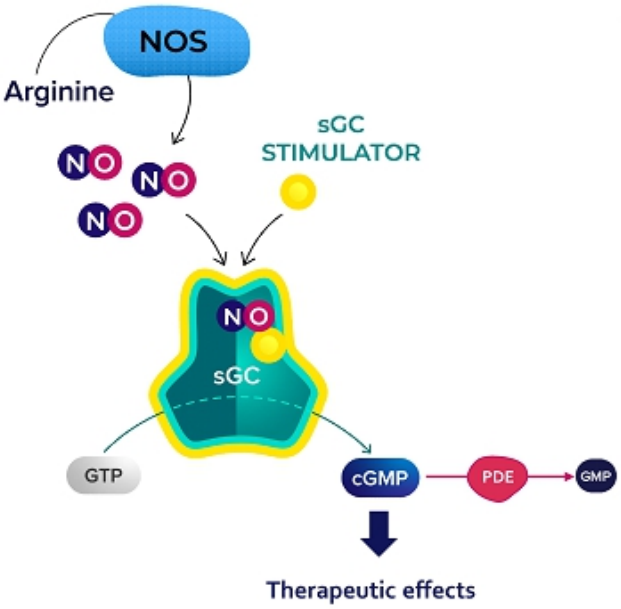
sGC: single target with potential to address multiple aspects of disease



Differentiated sGC stimulators designed to **modulate signaling in tissues most relevant to targeted diseases**

Graphic adapted from Buys et al. 2018. Discovery and development of next generation sGC stimulators with diverse multidimensional pharmacology and broad therapeutic potential. Nitric Oxide 78:72-80

Nitric oxide (NO) signaling: clinically validated pathway



- **Multiple drugs created by targeting different steps in pathway**
  - **NO donors** for angina (e.g., Nitropress®, Imdur®, Corvasal®, Corvaton®)
  - **PDE5 inhibitors** for erectile dysfunction and pulmonary arterial hypertension (e.g., Viagra®, Cialis®, Revatio®, Adcirca®)
  - **sGC stimulator** indicated for multiple forms of pulmonary arterial hypertension: (e.g., Adempas®)
  - **sGC stimulator** demonstrated outcomes benefit in phase 3 for worsening HFrEF (vericiguat)

- **sGC stimulator mechanism has the potential to fully leverage the NO-sGC-cGMP pathway**
  - target is **broadly expressed** in the body (unlike PDEs)
  - **synergizes** with endogenous NO (unlike NO donors)
  - **drives cGMP levels at the source** (unlike PDE inhibitors)
  - has a **durable response** (unlike NO donors)

A wholly owned pipeline of differentiated molecules

Completed Clinical POC

Praliciguat

Results support out-license for further development as a potential best-in-class cardiometabolic therapeutic

Ongoing Clinical Programs

Olinciguat

Phase 2 proof-of-concept study in sickle cell disease ongoing (SCD)

Topline data expected Q3 2020

IW-6463

Phase 1 in young healthy volunteers completed, with good CNS exposure, once-daily oral PK, and good safety/tolerability.

POM study enrolled; TLD expected mid-year 2020

Preclinical

Liver-targeted

Lung-targeted

Experienced team and successful leadership

- distinctive track record of innovative drug discovery/development (e.g.--CELEBREX®, KALYDECO®, LINZESS®, LUNESTA®, OPDIVO®, ORKAMBI®, YERVOY ®)
- successful sGC/cGMP drug hunters; deep knowledge of nitric oxide (NO)-cGMP pathway
- broad experience in creating strong organizations and commercializing products

1 Praliciguat out-licensing discussions ongoing

Data support further development › **Out-licensing discussions ongoing**

- promising DN results:
  - UACR reductions on top of standard of care
  - reductions in blood pressure, HbA1c, total and LDL cholesterol
  - favorable safety profile, consistent with previous studies
  - attractive dosing and PK relative to others in class
- VICTORIA results further validate cardiometabolic potential of the class and suggest potential for praliciguat as a best-in-class cardio metabolic therapeutic

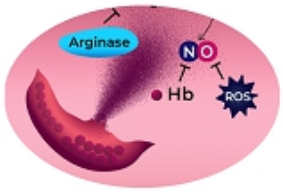
2 Olinciguat in sickle cell disease (SCD): potential for raising standard of care across four therapeutic domains

Dynamic mechanism - alone or complementing approved treatments → **TLD expected Q3 2020**

- upstream + downstream pharmacological intervention
- impact potential in four clinical domains: anemia, daily symptoms, VOC, and organ protection--not fully addressed by approved therapies
- oral, QD drug for use in a broad range of SCD patients
- STRONG SCD trial designed to assess safety and pharmacodynamic effects across full dose range
- mitigating potential impact of COVID-19 on study execution

Olinciguat: potential upstream and downstream interventions in SCD

Increased hemolysis leads to reduced nitric oxide state



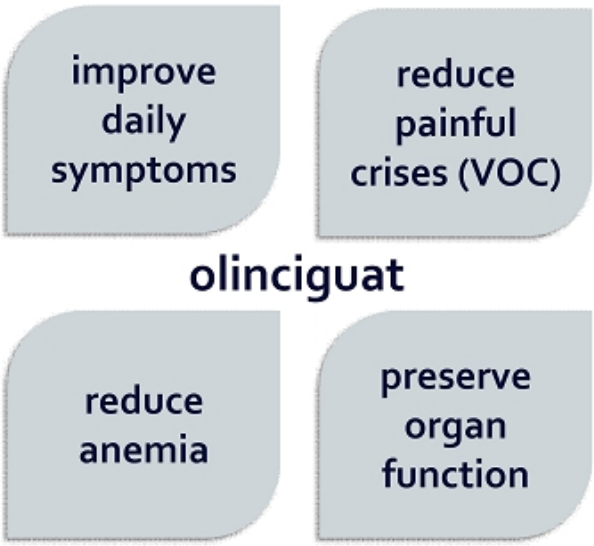
sGC may restore deficient nitric oxide signaling

Upstream
- increased HbF may lead to reduced proportion of sickled RBCs1

Downstream
- improved blood flow
- decreased vascular inflammation & cell adhesion
- improved endothelial integrity

1. Conran, N., & Torres, L. (2019). cGMP modulation therapeutics for sickle cell disease. *Experimental Biology and Medicine*, 244(2), 132–146.

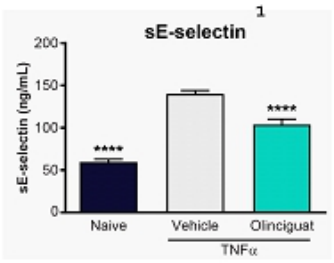
Potential to raise standard of care across four therapeutic domains



- newly approved therapies each target a single clinical domain…
- …olinciguat has the potential to improve four
- daily symptoms and end-organ protection remain unaddressed, decreasing QoL and increasing mortality
- further improvement in anemia and/or VOC possible with olinciguat alone or as add-on therapy serving broad SCD patient population

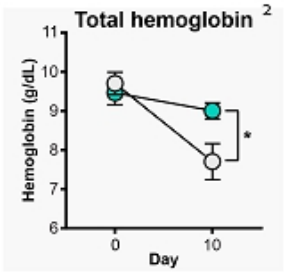
Preclinical data support clinical investigation

Inflammation



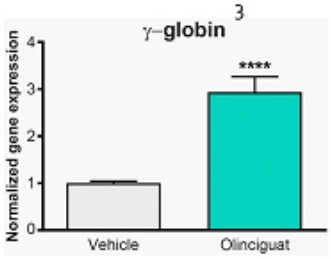
Lower levels of vascular inflammatory markers and improved vascular function in mouse models of inflammation†

Anemia



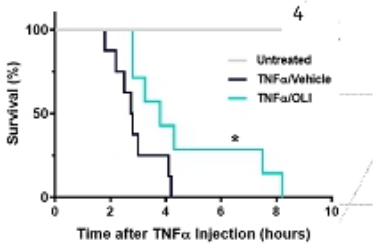
Decrease in progression of hemolytic anemia in Townes SCD mouse model

Fetal Hemoglobin



Higher mRNA expression of the γ-globin subunit of fetal hemoglobin in cultured cells

Survival



Olinciguat extended survival in TNFα challenge Berkeley SCD mouse model

† Adhesion can occlude microcirculation and lead to painful VOC and other serious complications; 1. **** p<0.0001 vs TNFα-vehicle, 1h predose olinciguat followed by treatment with TNFα in normal mice; 2.*p<0.05; 3. **** p<0.0001 vs vehicle Treatment of K562 cells with vehicle or olinciguat for 7 days in cell culture, 4 * p<0.05 vs TNFα-vehicle, work done collaboratively with the laboratory of Paul Frenette (Albert Einstein), HU did not show benefit to survival

STRONG SCD

Olinciguat phase 2 trial designed to support rapid advancement

Topline results expected Q3 2020

STRUCTURE

- 70 patients enrolled in all SCD genotypes, aged 16 – 70
- placebo controlled, double blind
- 4 dose levels
- 12-week treatment

OBJECTIVES

- assess safety and tolerability
- confirm PK profile in SCD patients
- development of the CYCN fit-for-purpose patient-reported outcomes (ePRO) instrument
- signs of pharmacodynamic effect: biomarkers (Hb, HbF, inflammation, adhesion) and daily symptom effects

INSIGHTS FOR PHASE 3 DESIGN

- endpoint selection based on results (biomarkers and ePRO)
- determine study sample size and dose(s)

3 IW-6463 in CNS: advancing development for potential treatment of serious neurodegenerative diseases

Ph 1 showed safety, target engagement, CNS exposure → **TLD data expected mid 2020**

Preclinical evidence: stimulation of nitric oxide-cGMP pathway improves determinants of brain health

Impaired brain function associated with low nitric oxide-cGMP

Enhanced NO-cGMP in the CNS has potential to:

- improve cognition
- increase cerebral blood flow
- increase synaptic density
- decrease neuroinflammation
- improve neuronal bioenergetics

→ Potential for improved brain health

IW-6463 potential to restore nitric oxide-cGMP signaling

Nitric oxide insufficiency leads to

- neuroinflammation and neurodegeneration
- impaired cerebral blood flow

Improved brain health

- decreased neuroinflammation
- increase cerebral blood flow
- neuroprotection and enhanced cognition

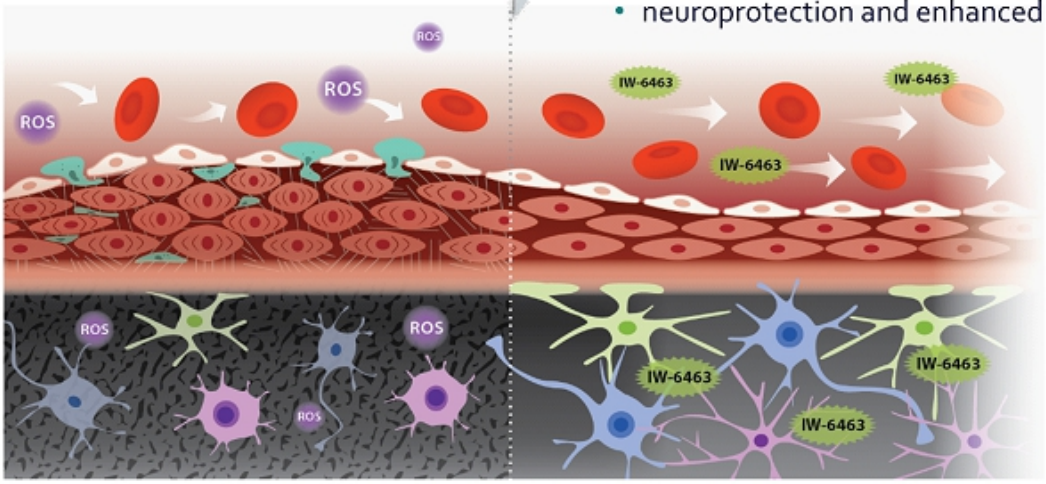
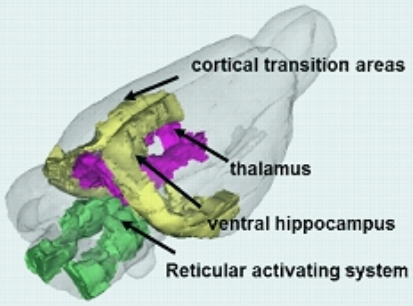


Figure adapted from Tobin, Zimmer et al. J Pharmacol Exp Ther 2018;365:664-675. Copyright © 2018 The Author(s).

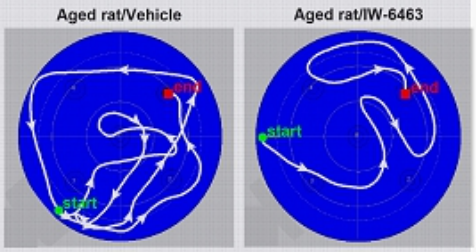
IW-6463 preclinical results support potential broad utility in CNS disease

Cerebral blood flow

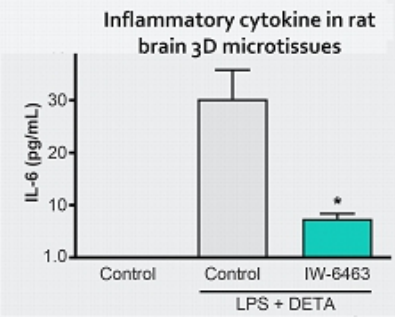


Cognition

Maze performance in aged rats



Neuro-inflammation



Note: data provided in this slide is based on preclinical models, *p<0.05 vs LPS + DETA Control

Positive phase 1 IW-6463 results support further development

Phase 1 study design

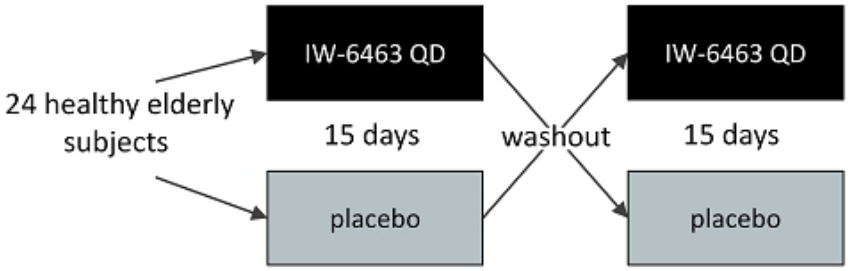
- 3 stage: SAD, MAD and food interaction
- 110 healthy volunteers
- age range 18-63
- assessed safety, PK (blood & CSF)
- wide dose / exposure range tested

Insights

- CNS drug presence at levels expected to be pharmacologically active
- QD dosing, linear and predictable PK
- may be taken with or without food
- evidence of target engagement (blood pressure)
- well-tolerated at all dose levels
- all AEs mild in severity, no SAEs

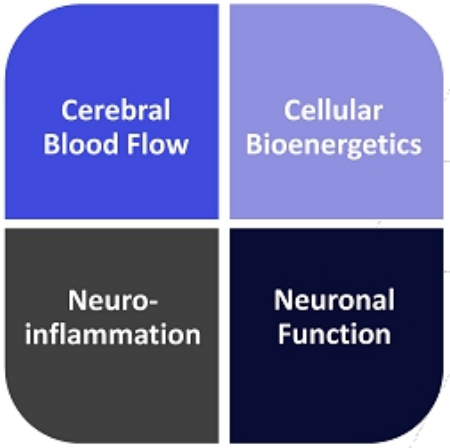
Translational design: IW-6463 pharmacology across 4 domains

Topline data expected mid 2020



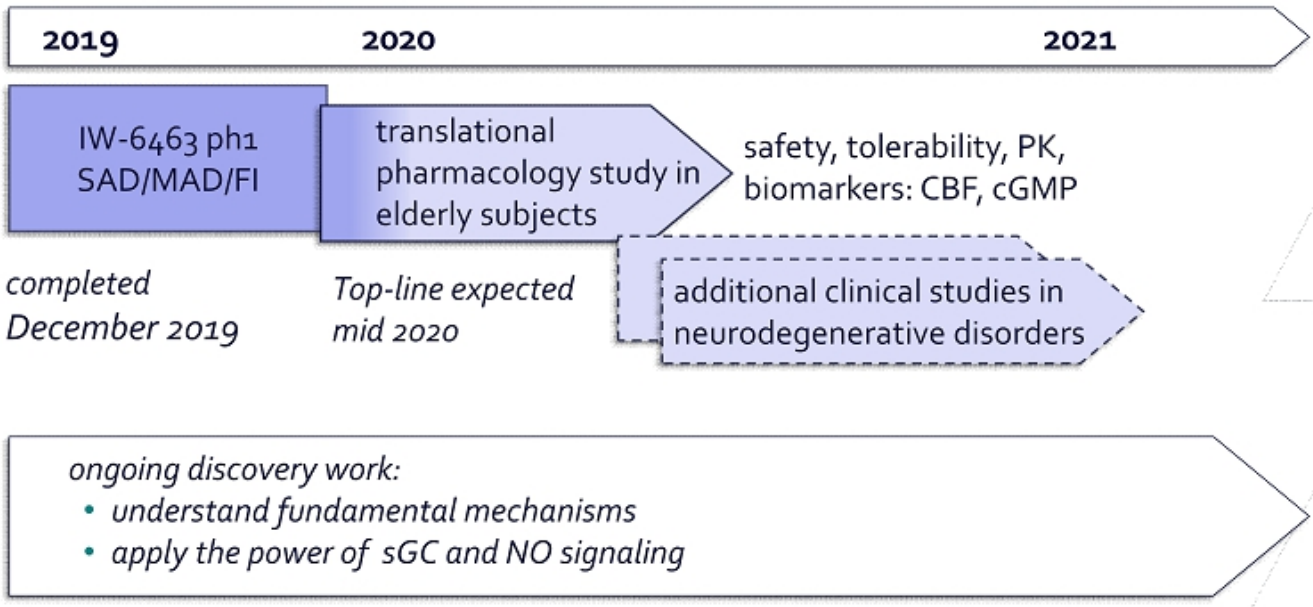
Assessing

- safety
- pharmacokinetics
- target engagement



Note: COVID-19 may reduce the number of participants in the 2nd cross over period or delay its start in some subjects.

Clinical direction: accelerate and de-risk into high value CNS indications



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cyclerion
April 10, 2020
Creating breakthrough treatments for patients with serious and orphan diseases by harnessing the power of soluble guanylate cyclase (sGC)

Appendix

NO-sGC-cGMP signaling

Cyclic Nucleotide Gated Channels

Protein Kinase G

Phosphodiesterases

sGC Stimulation Can Increase

Local vasodilation / blood flow (e.g., vascular and smooth muscle relaxation)

Metabolism (e.g., AMPK activation)

Neuronal health and signaling (e.g., neuroprotection, LTP)

sGC Stimulation Can Decrease

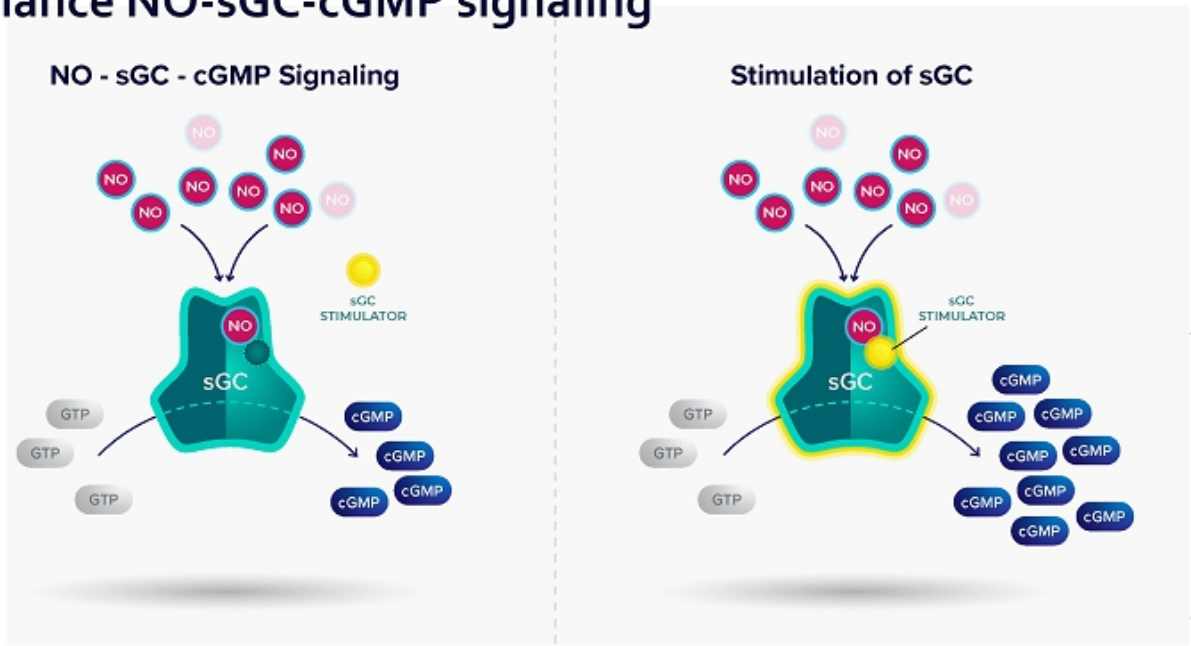
Inflammation (e.g., TNFα signaling, EC activation)

Fibrosis (e.g., TGFβ signaling)

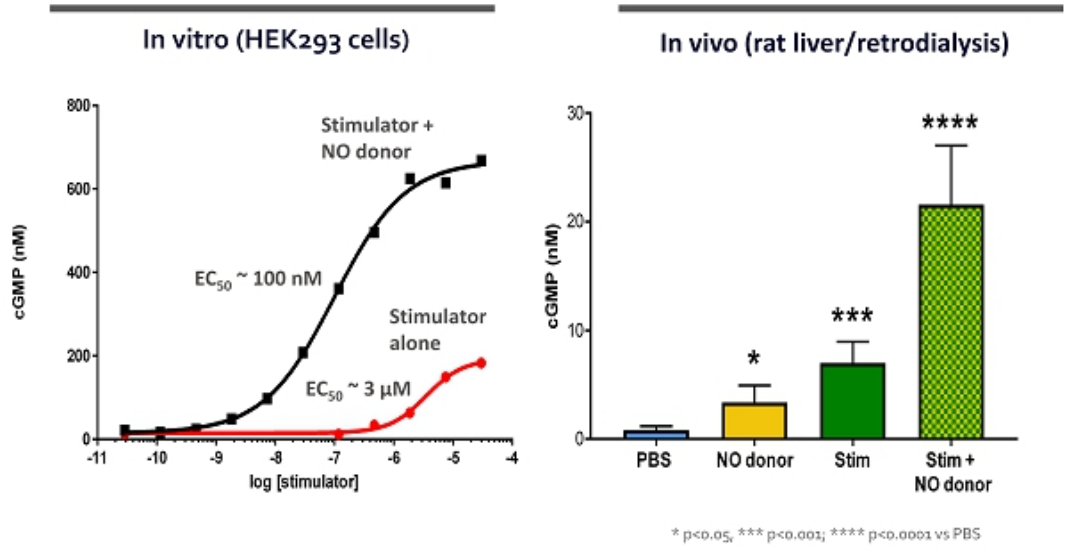
NOS=nitric oxide synthase; cGMP=cyclic guanosine monophosphate; PDE=phosphodiesterase; GTP=guanosine triphosphate; GMP=guanosine monophosphate

Reviewed in: Sandner et al. (2018) Soluble Guanylate Cyclase Stimulators and Activators. In: . Handbook of Experimental Pharmacology. Springer, Berlin, Heidelberg.

sGC stimulators are positive allosteric modulators that enhance NO-sGC-cGMP signaling



sGC stimulators act synergistically with NO



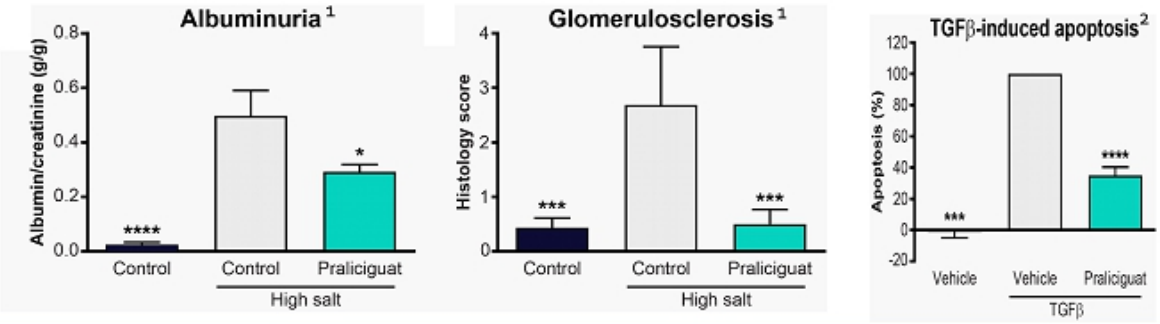
* p<0.05, *** p<0.001; **** p<0.0001 vs PBS

Preclinical data for praliciguat support potential utility in diabetic nephropathy

- preservation of kidney function in multiple animal models†
- corresponding effects on inflammation, fibrosis, and metabolism
- anti-inflammatory and anti-fibrotic effects mechanistically separated from hemodynamic effects
- Positive effects on fasting glucose and lipids in ZSF1 rat model of diabetic nephropathy

Kidney Protection

Anti-Fibrotic



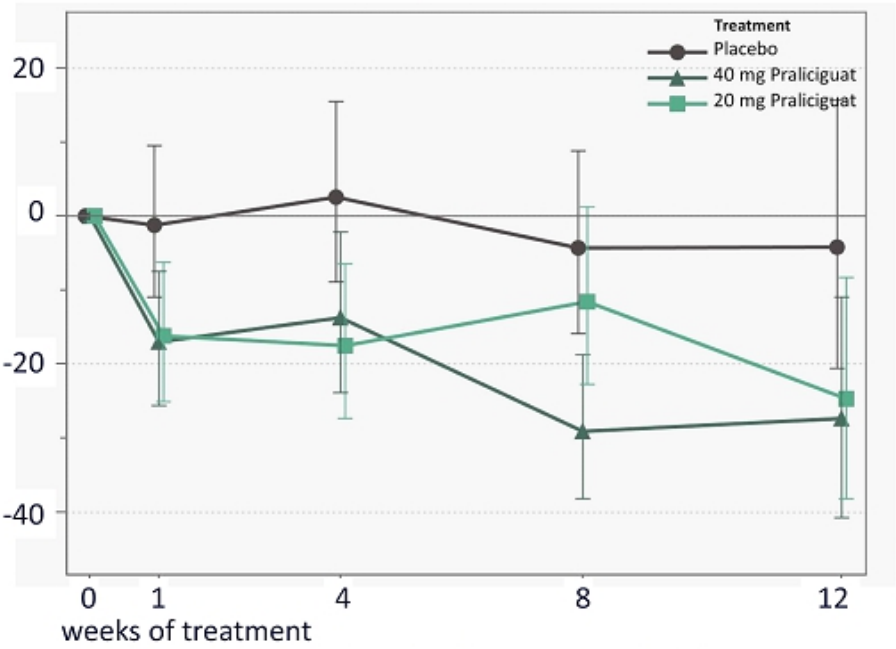
† Dahl salt-sensitive rat model of hypertension and ZSF1 rat model of DN, 1. * p<0.05, *** p<0.001; **** p<0.0001 vs High-salt control in Dahl salt-sensitive rat model; 2.*** p<0.001; **** p<0.0001 vs TGFβ-vehicle in human renal proximal tubule epithelial cells in cell culture

PRALICIGUAT

Phase 2 showed promising improvement in UACR

% UACR change from baseline

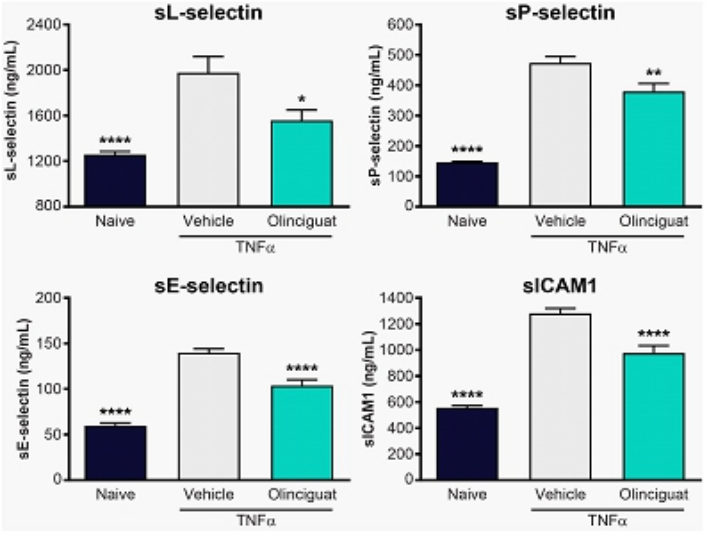
LS mean (90% CI) change UACR in (mg/g) (mITT)[1]



(90 % CIs by dose & timepoint)

1. mITT: modified intent-to-treat population n=133 excludes data from site 00A where data inconsistencies were observed in both the treatment and control groups

Lower expression of cellular adhesion molecules associated with olinciguat treatment in preclinical model†

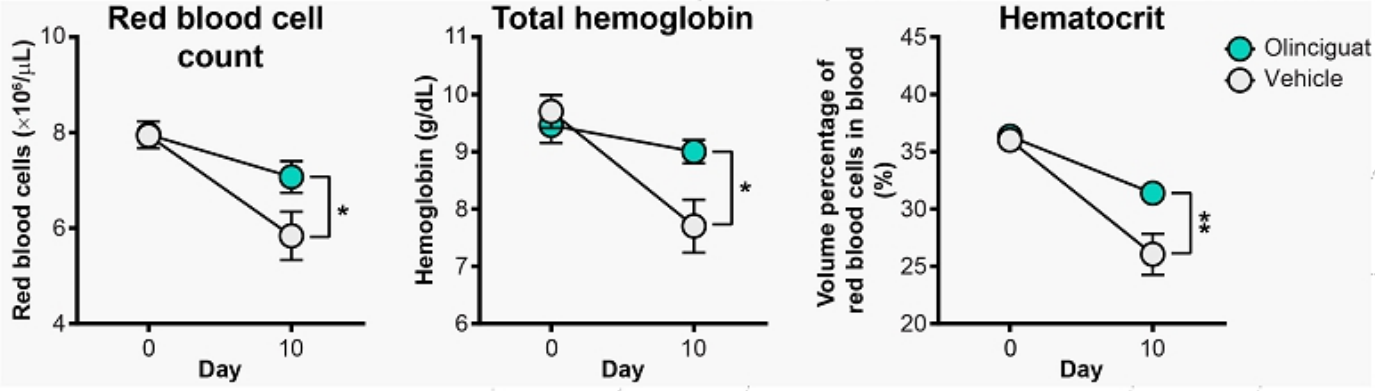


1h predose olinciguat followed by treatment with TNFα in normal mice

Reducing vascular inflammation via blockade of specific adhesion receptors is a clinically validated approach to reducing painful crises (e.g. crizanlizumab)

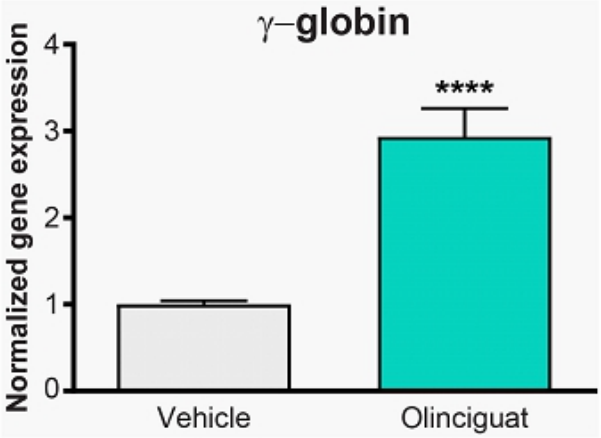
† in models of vascular inflammation, * p<0.05, ** p<0.001; **** p<0.0001 vs TNFα-vehicle

In a preclinical model of SCD, progression of hemolytic anemia was ameliorated in olinciguat treated mice



*p<0.05; ** p<0.01 Olinciguat vs Vehicle at Day 10

Greater normalized expression of the ɣ-globin subunit of fetal hemoglobin in cell culture treated with olinciguat



Treatment of K562 cells with vehicle or olinciguat for 7 days in cell culture

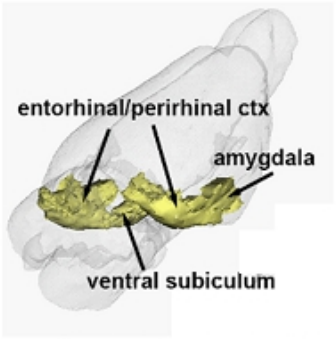
*Increasing fetal hemoglobin is a clinically validated approach to the treatment of sickle cell disease (i.e. hydroxyurea)**

cyclerion

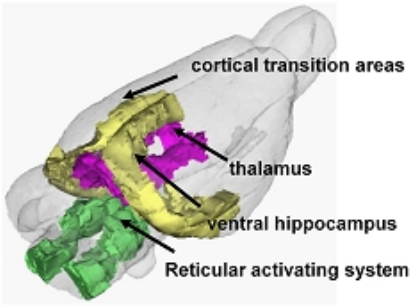
** In patients with SCD, higher HbF levels are associated with reduced rates of VOC, decreased frequency of acute chest syndrome and attenuation of other complications of SCD*
**** p<0.0001 vs vehicle

Increased blood flow to brain areas associated with memory and arousal in rats treated with IW-6463

Cerebral Blood Flow | Neuroinflammation | Neuroprotection | Cognitive Function



sGC stimulator: Peripherally Restricted

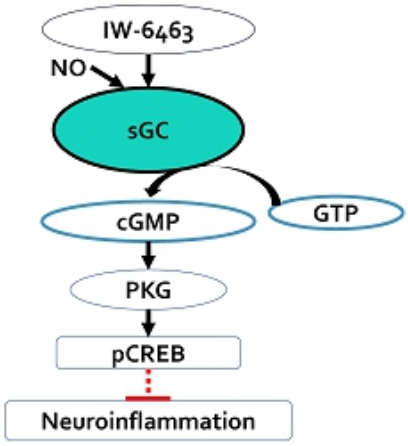


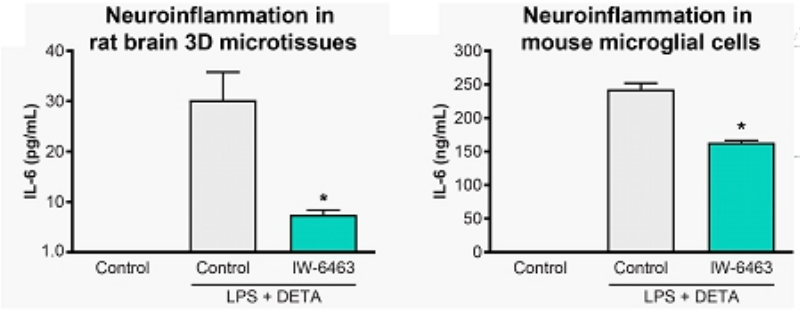
IW-6463: CNS-penetrant

- Increased blood flow to areas associated with memory and arousal in normal rats by fMRI BOLD imaging -

Anti-inflammatory neuroprotective effects in mice treated with IW-6463

Cerebral Blood Flow | **Neuroinflammation** | Neuroprotection | Cognitive Function



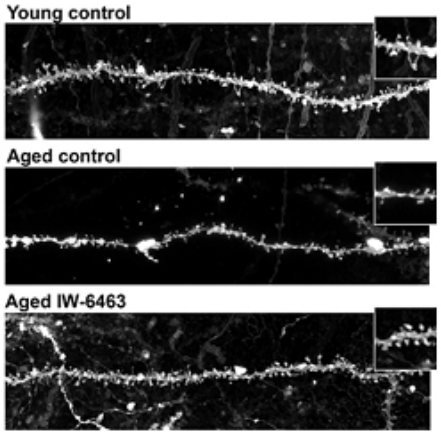


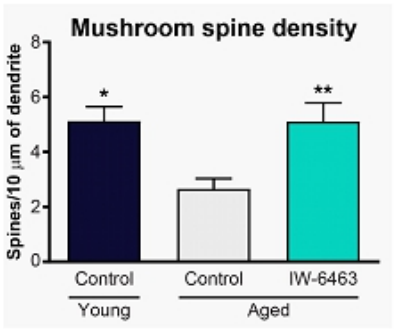
- Increased cGMP and pCREB in rat brain 3D microtissues -
- Decreased inflammatory cytokines in rodent microglial cultures and brain 3D microtissues -

*Note: data based on IW-6463 pretreatment in preclinical models, *p<0.05 vs LPS + DETA Control*

Neuroprotective effects in mice treated with IW-6463

Cerebral Blood Flow | Neuroinflammation | **Neuroprotection** | Cognitive Function





- Synaptic spine density in aged mice at same level observed in young mice -

cyclerion

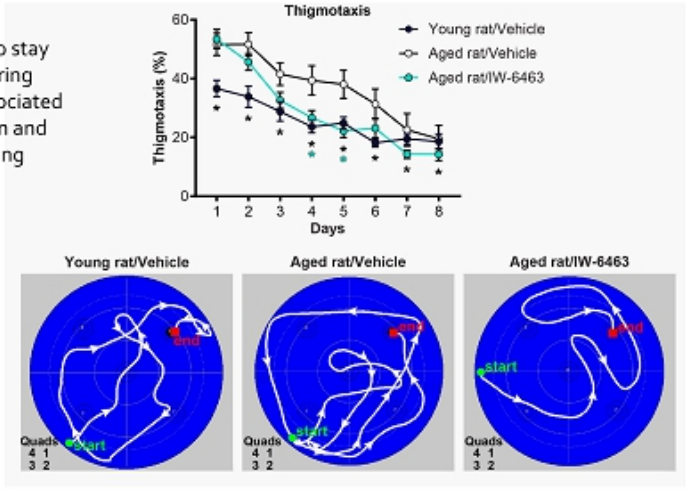
Note: data provided in this slide is based on preclinical models

*p<0.05 vs. control aged mice
**p<0.01 vs. control aged mice

Improved cognitive function in rats treated with IW-6463

Cerebral Blood Flow | Neuroinflammation | Neuroprotection | Cognitive Function

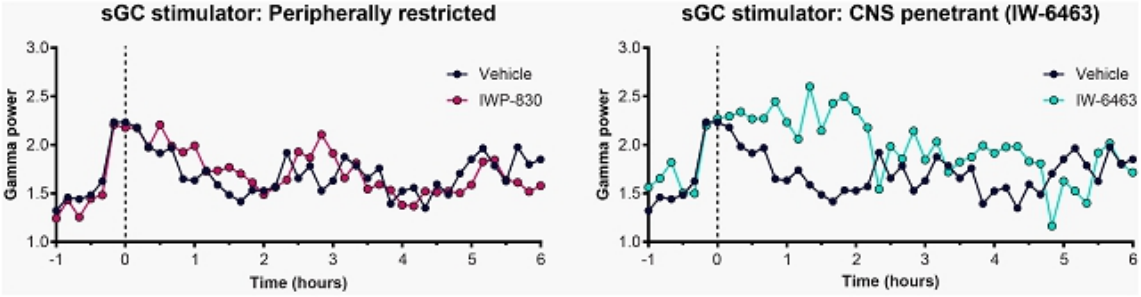
Thigmotaxis: tendency to stay close to walls when exploring open spaces, which is associated with cognitive dysfunction and interferes with maze solving



- Positive effect on cognitive function in multiple animal models, including both aged and pharmacologically impaired rats -

Note: data provided in this slide is based on preclinical models

Cortical brain activity greater in rats treated with IW-6463



- Opportunity for Early Clinical Proof of Pharmacologic Effects –

- Pharmacological effects of IW-6463 can be assessed clinically using translational non-invasive methods including EEG, MRS, ASL, and fMRI BOLD -

Exhibit 99.2

FOR IMMEDIATE RELEASE

Cyclerion Updates Corporate Progress

– Closed enrollment for olinciguat Phase 2 STRONG SCD study for sickle cell disease; topline data readout expected Q3 2020–

– Closed enrollment for IW-6463 translational pharmacology clinical study; topline data readout expected mid-year 2020 –

– Company continues discussions to out-license praliciguat –

CAMBRIDGE, Mass., April 10, 2020 — 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 announced that it recently closed enrollment for both of its ongoing clinical studies. The Company also provided additional corporate updates.

"We are looking forward to a catalyst-rich period in the coming months with top line results from both our translational pharmacology study for IW-6463, our brain-penetrant sGC stimulator designed to treat neurodegenerative diseases, and our olinciguat Phase 2 study for sickle cell disease. We also continue discussions on the out-licensing of praliciguat, a potential best-in-class therapeutic candidate for cardio-metabolic diseases. Recent published outcomes data from other groups provide compelling new support for the use of the sGC stimulator class in treating cardiometabolic diseases", said Peter Hecht, Ph.D., Chief Executive Officer of Cyclerion.

COVID-19

Cyclerion is executing against its previously communicated 2020 corporate priorities, advancing its ongoing olinciguat and IW-6463 clinical programs and out-licensing praliciguat. The company is closely monitoring and adjusting its operations but the pandemic could affect these activities in ways that are difficult to precisely judge at this time. The Company cannot give any assurances as to the potential impact of the pandemic on its operations, clinical trials, corporate development discussions and other activities. Cyclerion is working closely with its clinical trial sites and investigators to deliver its ongoing and planned trials in a manner consistent with the safety of study participants and healthcare professionals. Cyclerion does not anticipate any drug product disruption for its clinical trials and is taking steps to mitigate any disruptions of clinical supply materials to trial participants.

The Company is tightly managing its spending. As of March 31, 2020, Cyclerion's preliminary unaudited cash, cash equivalents and restricted cash balance was approximately $72 million. Cyclerion anticipates that this cash will fund its operations into Q2 2021, excluding net cash flows from potential business development activities.

Program Updates

Sickle Cell Disease (SCD)

Olinciguat is a once-daily oral sGC stimulator that primarily targets the vasculature and highly perfused organs such as the lungs and the kidney. Olinciguat has the potential to address multiple important clinical domains important in SCD by improving local blood flow, decreasing vascular inflammation, reducing anemia, and improving chronic symptoms.

The STRONG-SCD study is a randomized, placebo-controlled, dose-ranging study designed to evaluate safety, tolerability, and pharmacokinetics, as well as to explore effects on daily symptoms and biomarkers of disease activity when dosed over a 12-week treatment period. The study protocol was amended in late 2019 to add a higher-dose arm. Cyclerion recently closed enrollment of the study with a total of 70 participants randomized.

"We are excited to have closed enrollment for our SCD-STRONG study. We look forward to the top line results in Q3 2020 and to making a data-driven decision regarding advancement to the next phases of development," said Chris Wright, M.D., Cyclerion's Chief Medical Officer.

Central Nervous System (CNS)

Cyclerion is developing IW-6463, an oral, once-daily CNS-penetrant sGC stimulator for the treatment of serious neurodegenerative diseases. The nitric oxide pathway and sGC stimulation have long been known as central physiological regulators in the CNS, affecting cerebrovascular blood flow, neuroinflammation, neuronal function and cellular bioenergetics.

In January 2020, the Company reported encouraging Phase 1 healthy volunteer study results for IW-6463. This potential new CNS medicine was well tolerated across the dose range assessed. Pharmacokinetic (PK) data from blood and cerebral spinal fluid (CSF), supported QD dosing and indicated the potential to reach pharmacologically active CNS exposures, based on preclinical data.

An ongoing translational pharmacology clinical study has enrolled 24 elderly subjects. The study will evaluate safety and biomarker measures of CNS activity. Cyclerion expects top-line clinical results in mid-2020.

With supportive study results, the Company plans to direct further development towards serious CNS diseases with high unmet medical need where biological and/or genetic data suggest an important role for nitric oxide and cyclic guanosine monophosphate (cGMP) signaling.

Cardiometabolic

In October 2019, the Company announced encouraging topline results from its Phase 2 proof-of-concept study of praliciguat, a once-daily, orally available systemic sGC stimulator, in diabetic nephropathy. The potential for novel pharmaceutical interventions of the sGC pathway to provide important new tools in the treatment of cardiometabolic disease has been further supported by recent clinical study results published in the New England Journal of Medicine.

Cyclerion continues to engage in discussions to out-license praliciguat for late-stage global development and commercialization as a potentially best-in-class therapeutic for cardiometabolic diseases.

About Olinciguat

Olinciguat is an investigational, orally-administered, once-daily, vascular sGC stimulator for the potential treatment of sickle cell disease (SCD). SCD is an inherited red blood cell disorder that causes red blood cells to deform into a sickle shape, impacting blood flow to organs and tissues. These sickled red blood cells are more susceptible to hemolysis (rupturing). Upon red blood cell rupturing, nitric oxide is depleted due to arginase release and hemoglobin scavenging. Nitric oxide is an important regulator of blood flow, and the resulting deficiency of nitric oxide is believed to contribute to symptoms of SCD.

As sGC is a key node in the nitric oxide signaling pathway, olinciguat has the potential to address key symptoms and complications of SCD by addressing the disease's underlying nitric oxide deficiency. The distribution of olinciguat to the vasculature as well as to organs with high blood flow, such as the kidney and lungs, may make it well suited for the potential treatment of SCD.

Olinciguat has been granted Orphan Drug Designation for SCD by the U.S. Food and Drug Administration and is currently in a Phase 2 study in patients with SCD, the STRONG-SCD study.

About IW-6463

IW-6463, a CNS-penetrant sGC stimulator, is being developed as a symptomatic and potentially disease modifying therapy for neurodegenerative diseases. Nitric oxide is one of several fundamental neurotransmitters, but it has yet to be leveraged for its full CNS therapeutic potential. 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 nitric oxide dysregulation leads to vascular contributions to neurodegenerative disease (e.g. endothelial cell damage decreased blood flow and increased vascular leakage) and may also directly increase inflammation, neuronal dysfunction/loss and cognitive impairment. 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, enhanced cognition, neuroprotection and enhanced cellular bioenergetics.

About Cyclerion Therapeutics

Cyclerion Therapeutics is a clinical-stage biopharmaceutical company harnessing the power of 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 cardiometabolic disease, olinciguat in Phase 2 development for sickle cell disease, IW-6463 in early 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. 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 the risks listed under the heading “Risk Factors” and elsewhere in our 2019 Form 10-K filed on March 12, 2020. 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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