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): **July 9, 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 Item 7.01 below, on July 9, 2020, Cyclerion Therapeutics, Inc. (the "Company") released a corporate slide presentation. The presentation included preliminary information that, as of June 30, 2020, the Company's unaudited cash, cash equivalents and restricted cash balance was approximately $61 million and that the Company anticipates that this amount will be sufficient to fund planned operating expenses and capital expenditure requirements into the second half of 2021.

The foregoing information constitutes unaudited and preliminary estimates that (i) represent the most current information available to management as of the date of the 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 June 30, 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.

On July 9, 2020, the Company released a corporate slide presentation that included the following updates:

- **Central Nervous System: IW-6463**
  - Dosing has been completed in the ongoing IW-6463 translational pharmacology clinical study. Topline study data are expected in late summer 2020.
  - The Company anticipates initiating two parallel exploratory Phase 2 studies of IW-6463 to evaluate safety and a variety of efficacy measures, including engagement of CNS biomarkers using novel trial designs in Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like Episodes (MELAS) and Alzheimer's disease with vascular features (ADv). These studies are designed to de-risk and direct future development in CNS diseases.
- **Sickle cell disease: olinciguat**
  - The seventy subjects enrolled in the olinciguat Phase 2 STRONG SCD study in patients with sickle cell disease have completed their dosing period.
  - Topline study results are expected in late Q3 2020.
- **Praliciguat out-licensing**
  - The Company remains in ongoing discussions to out-license global rights to praliciguat, its oral once-daily systemic sGC stimulator.
  - In those discussions, the Company has expanded beyond cardiometabolic disorders to additional indications in which sGC stimulators have shown efficacy.
  - Cyclerion can offer no assurances on the prospects or timing of any partnership or licensing transactions generally, or specifically on praliciguat.

A copy of the corporate slide presentation is attached hereto as Exhibit 99.1 and is incorporated by reference into this Current Report on Form 8-K. 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.

In addition, the Company hosted a webcast investor event on July 9, 2020 from 8:15 a.m. to 9:30 a.m. Eastern Time focused on IW-6463, the Company's investigational, orally administered, once-daily CNS-penetrant sGC stimulator designed for the treatment of serious CNS diseases. A copy of the webinar presentation materials is attached hereto as Exhibit 99.2 and is incorporated by reference to this Current Report on Form 8-K. The presentation is also posted to the Company's website, www.cyclerion.com.

The information set forth in and incorporated by reference into 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 and incorporated by reference into this Item 7.01, the Company makes no admission as to the materiality of Item 7.01 in this report or the presentations available on the Company's website. The information contained in the presentations 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 9.01 Financial Statements and Exhibits

(d)

Exhibit No.	Description
99.1	Corporate Update Presentation dated July 9, 2020.
99.2	CNS Update Presentation dated July 9, 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: July 9, 2020

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

Exhibit 99.1


cyclerion
SCD and CNS:
creating breakthrough treatments
harnessing the power of soluble guanylate cyclase (sGC)
Corporate Overview
July 9, 2020

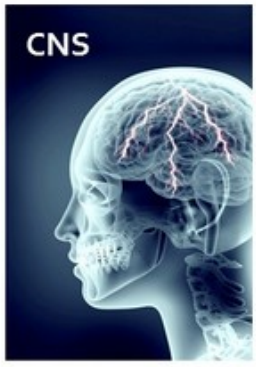
Safe Harbor Statement

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, and in our subsequent SEC filings, including our Quarterly Report on Form 10-Q filed with the SEC on May 4, 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.

Creating value from pioneering approaches to SCD and CNS



Building a company:
our sGC science, pipeline and our team

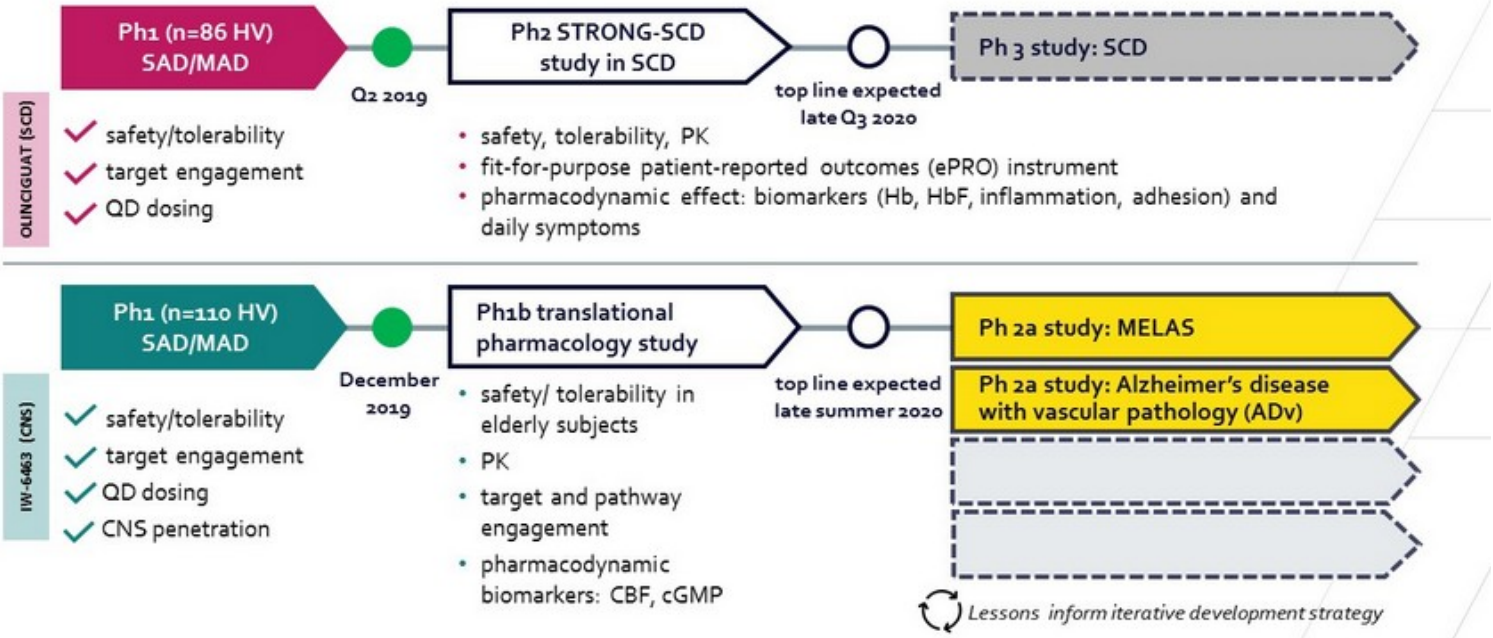
Two priority disease areas creating multiple potential ways to win in sickle cell and CNS

- genetically and phenotypically defined populations with high unmet need
- harness power, signaling precision of sGC
- biomarker-guided fast-to-POC trials underway
- supported by discovery platform
- attractive to investors and partners

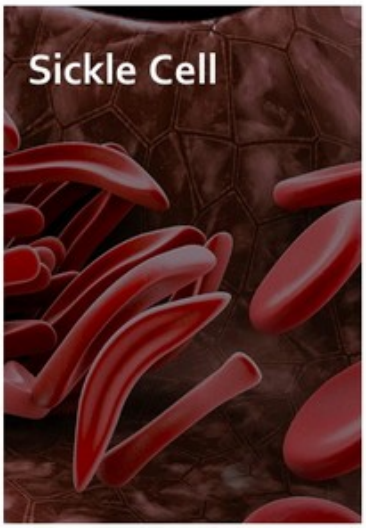
Innovative sGC platform for the NO-sGC-cGMP pathway

- multi-dimensional pharmacology well-suited to disease biology
- molecules tailored to the tissues relevant to the disease
- wholly owned IP
- validated class

Clinical program snapshot



Olinciguat: potential to raise the standard of care for sickle cell disease patients



- potential for broad clinical utility in SCD
- multi-dimensional mechanism that offers both upstream and downstream pharmacology
- 70 patients enrolled; dosing completed
- TL expected late Q3 2020
- Ph3 long-lead items underway: CMC, protocols, global ad board, regulatory plans
- plan to develop and commercialize ourselves, but partnerships will be considered

Potential for broad clinical utility

- 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

Olinciguat: potential upstream and downstream interventions

Increased hemolysis leads to reduced nitric oxide state

sGC stimulation may restore deficient nitric oxide signaling

Upstream

- increased HbF may lead to reduced proportion of sickled RBCs[1]

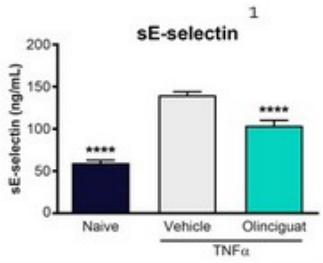
Downstream

- 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.

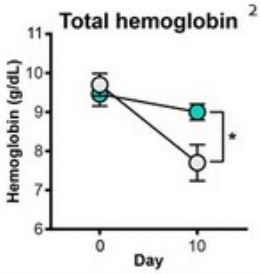
Preclinical data support clinical investigation

INFLAMMATION



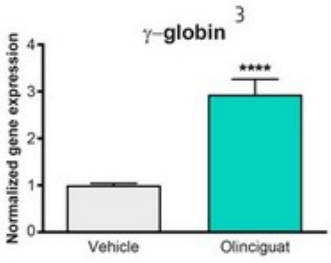
Lower levels of vascular inflammatory markers and improved vascular function in mouse models of inflammation†

ANEMIA



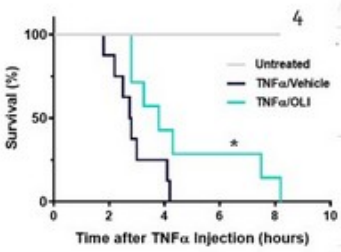
Decrease in progression of hemolytic anemia in Townes SCD mouse model

FETAL HEMOGLOBIN



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

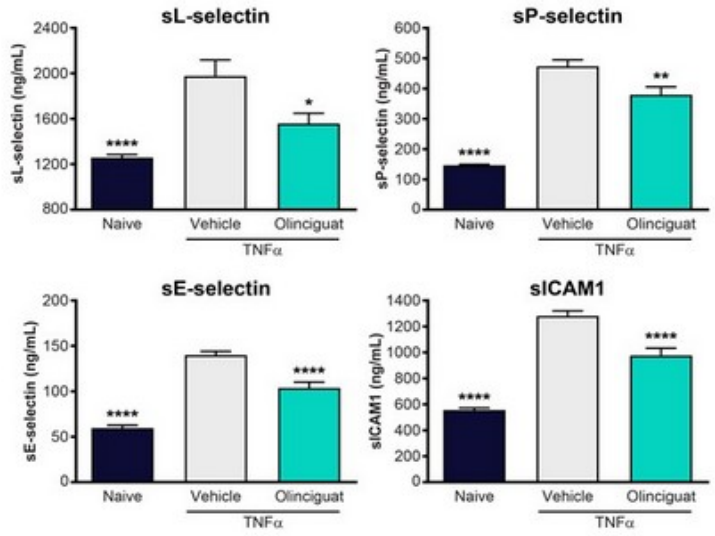
SURVIVAL



Olinciguat extended survival in TNFα challenge Berkeley SCD mouse model

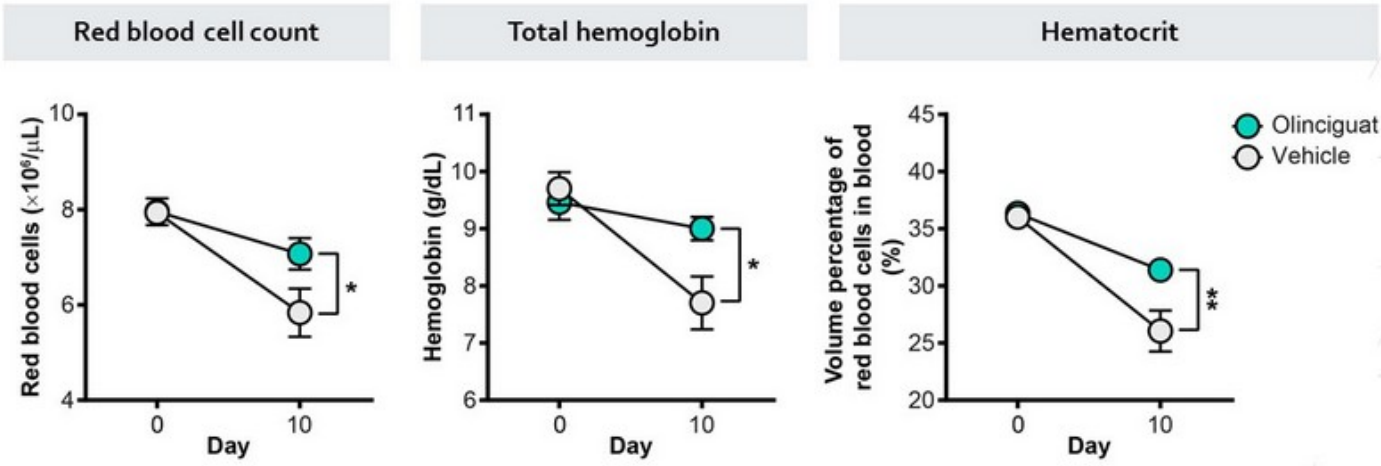
*† Adhesion can occlude microcirculation and lead to painful VOC and other serious complications; 1. **** p<0.0001 vs TNFα-vehicle, 1h predose olinciguat followed by treatment with TNFα in normal mice; 2. *p<0.05; 3. **** p<0.0001 vs vehicle Treatment of K562 cells with vehicle or olinciguat for 7 days 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*

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



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

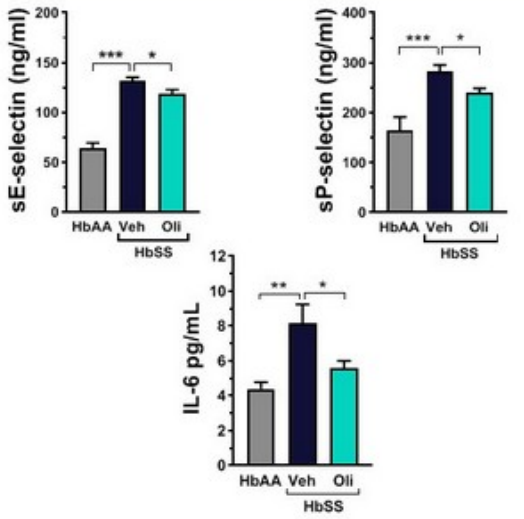
In a preclinical model of SCD, progression of hemolytic anemia was ameliorated in olinciguat treated Townes mice



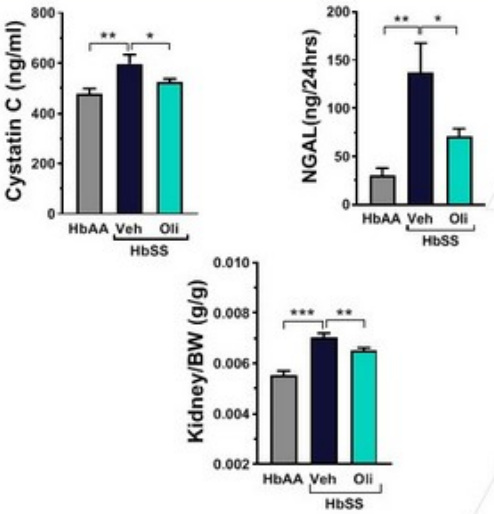
*p<0.05; ** p<0.01 Olinciguat vs Vehicle at Day 10

Olinciguat decreased biomarkers of inflammation, endothelial activation and renal injury in Townes SCD mice after 8 weeks of treatment

Endothelial Activation and Inflammation



Renal Injury



*p<0.05, **p<0.01, ***p<0.001

Olinciguat Phase 1: target engagement, PK, safety, QD dosing

PHASE 1 *(completed)*

Phase 1 design

- 5 Ph1 studies including:
  - SAD
  - MAD
  - clinical pharmacology
- 125 healthy volunteers
- age range 18-57
- standard safety
- PK
- 8 dose levels tested

GOALS ACHIEVED

Results

- linear, predictable PK; consistent with QD dosing
- determined well tolerated dose range
- evidence of target engagement and proof of pharmacology (cGMP elevation, blood pressure)
- well tolerated at all dose levels, no safety signals or discontinuations due to drug-related adverse events (AE)
- balanced tissue: plasma distribution

*Based on positive CNS pharmacology in multiple preclinical models

STRONG SCD

Olinciguat phase 2 trial designed to support rapid advancement

Topline results expected late Q3 2020

Structure

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

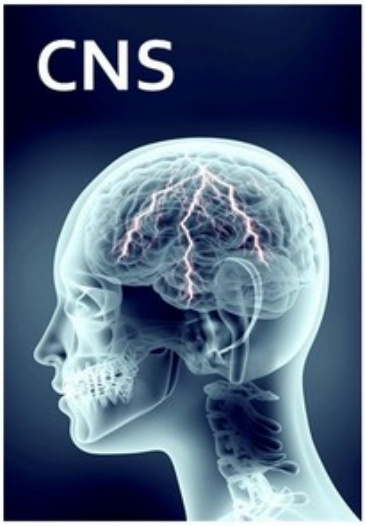
Objectives

- 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, adheion) and daily symptom effects

Insights for Phase 3 design

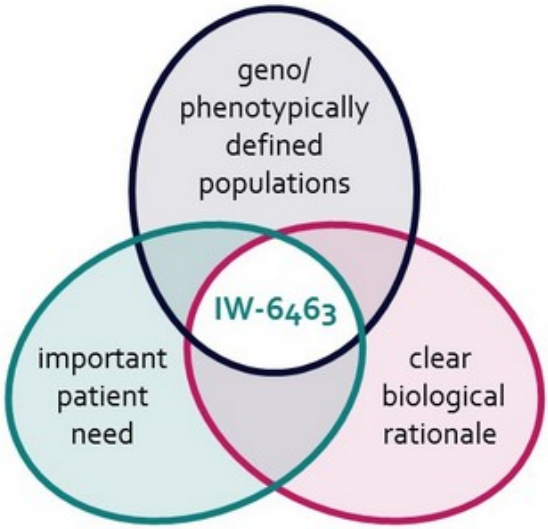
- endpoint selection based on results (biomarkers and ePRO)
- determine study sample size and dose(s)

Our strategy: target identifiable populations with important unmet needs



- targeting the untapped NO neurotransmitter pathway by sGC stimulation
- initial two indications are characterized by strong biological rationale, targeted patient populations, enormous unmet patient need, lack of approved therapies, and biomarker-based development
- MELAS
  - genetically defined rare disease
  - most common mitochondrial disease, >90% have neurological symptoms (stroke-like episodes, dementia, epilepsy, vision loss)
  - identifiable patients with no approved treatment
- Alzheimer's disease with vascular pathology (ADv)
  - intersection of Alzheimer's and vascular dementias
  - well-defined subset of patients, ~2M patients in the US
  - no approved therapies to treat vascular pathology of Alzheimer's disease
- discovery research engine focused on expanding CNS platform
- exploring R&D collaboration to support pursuit of the best opportunities

Our approach: intersection of patients and biology



Raising the odds of success:

- pursue multiple indications in parallel
- leverage biomarkers to drive development
- implement nimble trials with leading edge investigators and imaging analytics
- investigate a strategic R&D partnership to explore full potential of sGC in the CNS

sGC stimulators: potential to be next druggable neurotransmitter system

Nitric oxide
- IW-6463

Successfully drugged neurotransmitter systems

GABAergic
- Valium® (1963)
- Ambien® (1992)

Dopaminergic
- Levodopa (1970)
- Risperdal® (1993)

Adrenergic/Serotonergic
- Amitriptyline (1961)
- Prozac® (1987)
- Paxil® (1992)

Cholinergic
- Scopolamine (1979)
- Aricept® (1996)

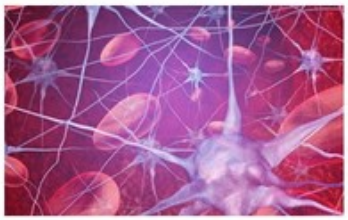
Glutamatergic
- Ketamine (1970)
- Namenda® (2003)

IW-6463 demonstrates in preclinical studies beneficial effects in four important domains of neurodegenerative diseases

IMPROVE

Cerebral Blood Flow

Increased blood flow in areas associated with memory and arousal by fMRI BOLD imaging



ENHANCE

Cellular Bioenergetics

Increased ATP and restored gene expression in cells from patients with mitochondrial diseases

REDUCE

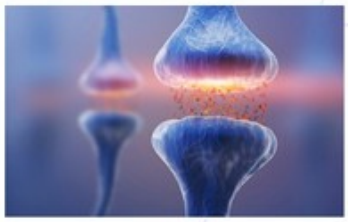
Neuro-inflammation

Decreased markers of LPS-induced neuroinflammation (ICAM1, VCAM1, IL6) *in vitro*

IMPROVE

Neuronal Function

Enhanced memory performance & spine density in aged animals; increased LTP in neurodegenerative disease models



IW-6463 preclinical results support potential broad use in CNS treatment

IMPROVE

Cerebral Blood Flow

ENHANCE

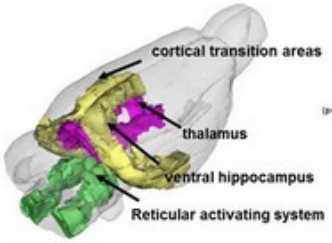
Cellular Bioenergetics

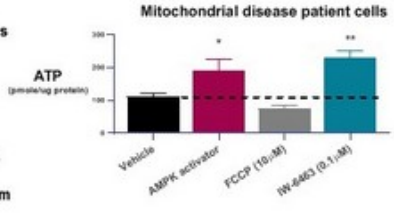
REDUCE

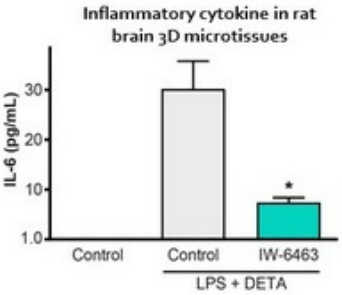
Neuro-inflammation

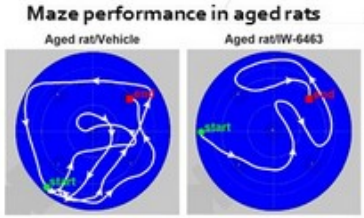
IMPROVE

Neuronal Function









Translational approach from discovery to approval and beyond

Establish PD biomarkers preclinically

Effects across four domains of neurodegenerative disease

Validate PD biomarkers in the clinic

Translational pharmacology study in elderly

top line data late summer 2020

Refine clinical strategy

- *indication selection*
- *patient selection*
- *biomarker enrichment*
- *endpoint selection*
- *trial design*
- *regulatory approach*

Smaller/shorter studies

Evaluate IW-6463 in focused patient populations

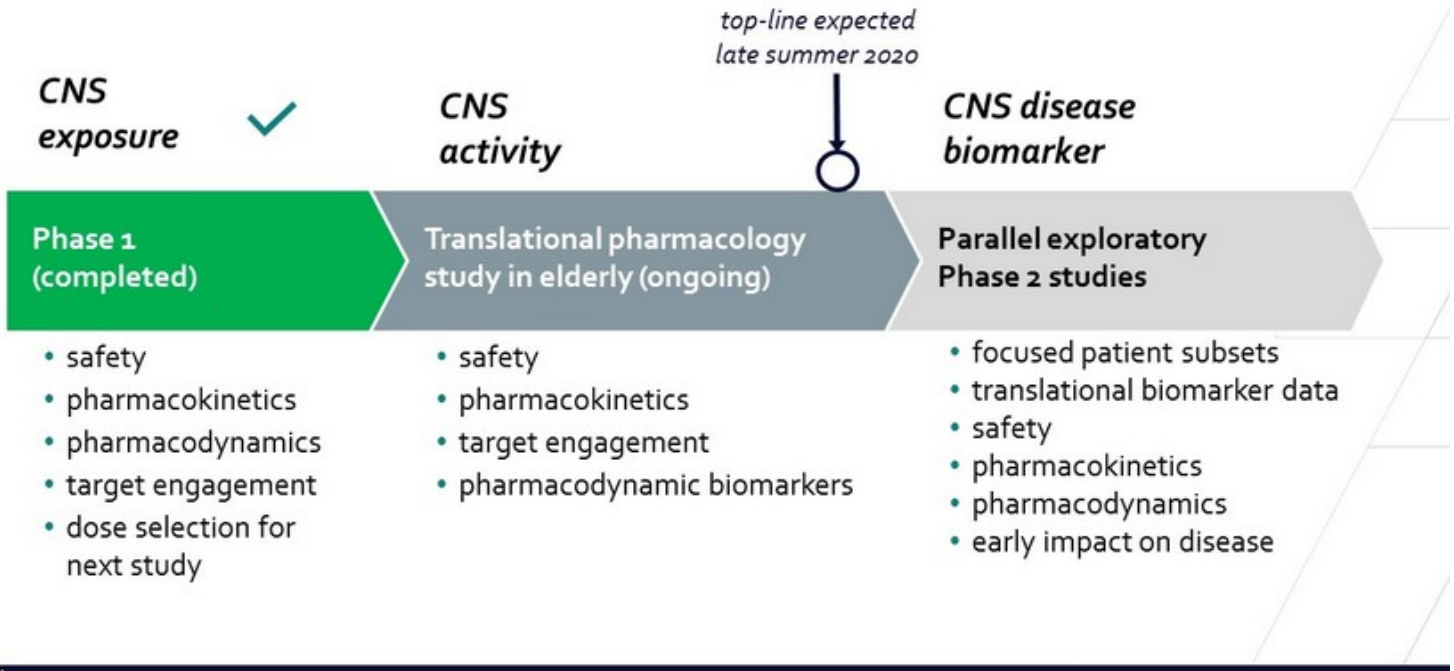
Initial approvals based on predictive surrogate and/or symptomatic and functional endpoints

Larger/longer studies

Evaluate IW-6463's full potential

Potential to expand label to broader populations and to demonstrate disease modification

Biomarker-driven IW-6463 early clinical development strategy



IW-6463 Phase 1: CNS exposure, target engagement, PK, and safety

PHASE 1 *(completed)*

Study design

- three stages:
  - SAD
  - MAD
  - food interaction
- 110 healthy volunteers
- age range 18-63
- standard safety
- PK (blood & CSF)
- wide dose range tested

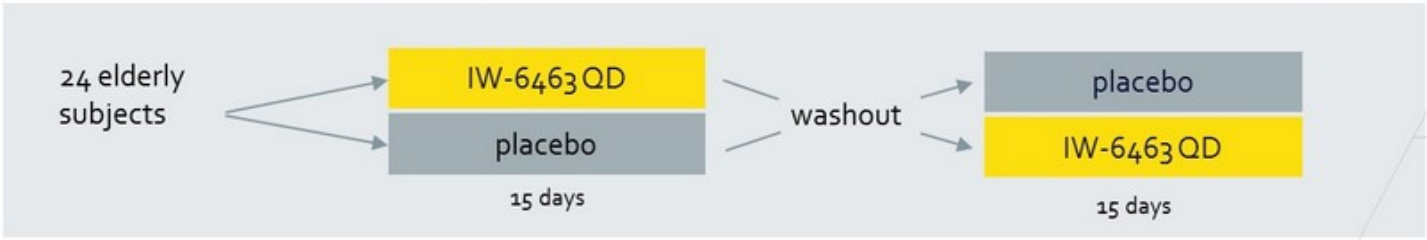
GOALS ACHIEVED

Results

- identified safe and well-tolerated dose levels with steady-state CNS exposure in therapeutic target range*
- linear, predictable PK; consistent with QD dosing
- CNS exposure confirmed
- evidence of target engagement (blood pressure)
- well tolerated at all dose levels, no safety signals
- may be taken with or without food

*Based on positive CNS pharmacology in multiple preclinical models

Translational study design: pharmacodynamic biomarkers and safety



Assessing safety, PK and target engagement in CNS (cGMP)

Top line data expected late summer 2020

IMPROVE

Cerebral Blood Flow

- MRI arterial spin labeling (ASL)

ENHANCE

Cellular Bioenergetics

- brain metabolism via magnetic resonance spectroscopy (MRS)

REDUCE

Neuro-inflammation

- cytokines, adhesion molecules

IMPROVE

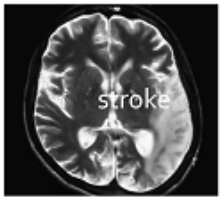
Neuronal Function

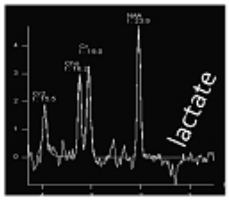
- qEEG
- measures of cognition and behavior (NeuroCart®)

Mitochondrial Encephalomyopathy, Lactic Acidosis,& Stroke-like Episodes (MELAS)

genetically defined orphan disease, serious CNS & multi-system problems, no approved treatments

SYMPTOM OVERVIEW



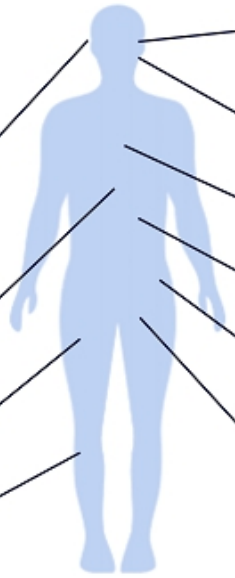


Central Nervous system
Strokes, Stroke-like Episodes (SLEs), Ataxia (Imbalance), Epilepsy (Seizures), Migraine, Headaches, Cognitive Impairment, Learning Disability, Dementia, Mood disorders

Autonomic Nervous System
Dysautonomia, Temperature Intolerance, Heart Rate Instability (POTS)

Peripheral Nervous System
Peripheral Neuropathy

Skeletal muscle
Muscle weakness, myopathy, exercise intolerance



Vision
Vision Loss, Cortical Blindness, Ptosis, Ophthalmoplegia, Retinal-Optic Nerve Disease

Hearing
Sensorineural Hearing Loss, Tinnitus

Cardiac
Sudden Death, Arrhythmias, Cardiomyopathy

Gastrointestinal
Vomiting, Pseudoobstruction

Endocrine/Metabolic
Diabetes Mellitus, Short Stature, Underweight, Fatigue, Lactic Acidosis

Renal
Nephropathy

MELAS: Strong supportive data for NO-sGC-cGMP pathway involvement

SCIENTIFIC RATIONALE FOR INDICATION AND PATIENT SELECTION

Clinical precedence for NO-sGC-cGMP pathway

- L-Arginine (NO precursor) recommended for acute and chronic treatment

Pathophysiology

- CNS metabolic dysfunction, elevated lactate, decreased NO
- CNS vascular pathology - impaired blood flow, inflammation, endothelial dysfunction, small vessel disease

IW-6463 pharmacology

- CYCN preclinical data suggest IW-6463 improves mitochondrial function and cerebral blood flow

Ph 2a: open-label study of IW-6463 in patients with MELAS

STUDY START Q3 2020

Enrichment strategy
- genetically defined MELAS with neurological features and elevated plasma lactate (disease biomarker)

Treatment
- once-daily IW-6463
- 29 days
- up to 20 patients (targeting 12 completers)

Sites
- centers of excellence for mitochondrial diseases: CHOP, MGH, Children's National, Columbia, Hopkins

Objectives
- evaluate safety, tolerability, and pharmacodynamics
- assess near-term impact on disease-specific biomarkers
- de-risk and accelerate future development

DISEASE DOMAIN	ASSESSMENT
Mitochondrial dysfunction	Lactate
Dysregulated brain perfusion	Cerebral Blood Flow (MRI ASL)
Neurodegeneration	NF-L
Cognitive impairment	Cognitive and behavior tests

Improved lactate and CBF would indicate an impact on the underlying disease mechanism and suggest potential for broad benefit for these patients.

AD with vascular pathology (ADv) – focused mixed dementia subset

Defined population well suited for treatment with IW-6463

DISEASE RATIONALE FOR PATIENT SELECTION

Pathophysiology

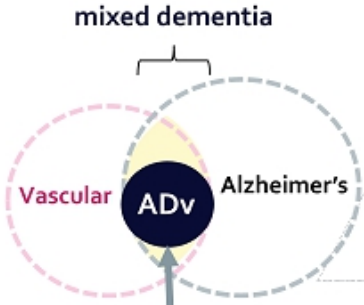
NO dysregulation, endothelial cell loss, impaired blood flow, vascular leakage, inflammation, neuronal dysfunction, and neuronal loss are major contributing factors to rapid disease progression

Standard of care

No approved therapies to treat vascular dementia.
AD therapies offer limited benefits; not disease modifying

Pharmacology

Our preclinical data suggests IW-6463 has potential to improve cerebral blood flow, endothelial health, neuroinflammation, and cellular energetics as well as prevent neurodegeneration



Target population

ADv: an identifiable subset of mixed dementia patients with:

- AD pathology **AND**
- sub-cortical vascular disease **AND**
- CV risk factors

Ph 2a study of IW-6463 in ADv: emerging design

STUDY START 1H 2021

Treatment
- once-daily IW-6463

Enrichment strategy
- confirmed AD pathology (PET, CSF)
- 3+ cardiovascular risk factors
- mild-moderate subcortical small-vessel disease on MRI
- mini Mental State Exam score (16-26)

Objectives
- establish safety and pharmacodynamic effects of IW-6463 in a short-term study
- de-risk progression to larger, longer symptomatic and disease modification trials

DISEASE DOMAIN	ASSESSMENT
Vascular dysfunction	ASL (CBF)
Neurodegeneration	neurofilament light chain
Neuroinflammation	vascular cell adhesion molecule
Mitochondrial dysfunction	N-acetyl aspartate (MRS)
Cognitive impairment	cognitive and behavior tests

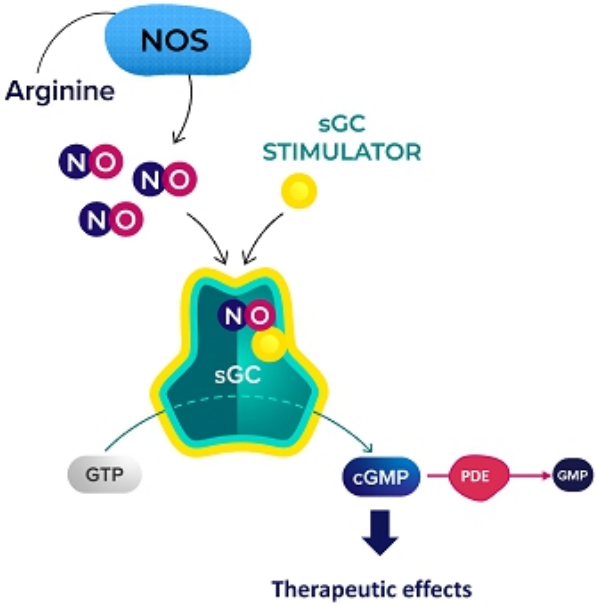
Improved CBF, particularly in the context of memory improvements, would indicate an impact on the underlying disease mechanism and enable a targeted design for the next development stage.

Building our company: the science, the pipeline and the team

- sGC stimulators: powerful intervention in a genetically and clinically validated pathway
- a wholly owned pipeline of differentiated molecules
- exploring partnerships across programs; praliciguat out-licensing scope expanded
- experienced leadership team with a distinctive track record of innovative drug discovery and development
- starting Q3 2020 with ~$61M cash*; supports our priorities into second half of 2021
- limited disruption from Covid-19

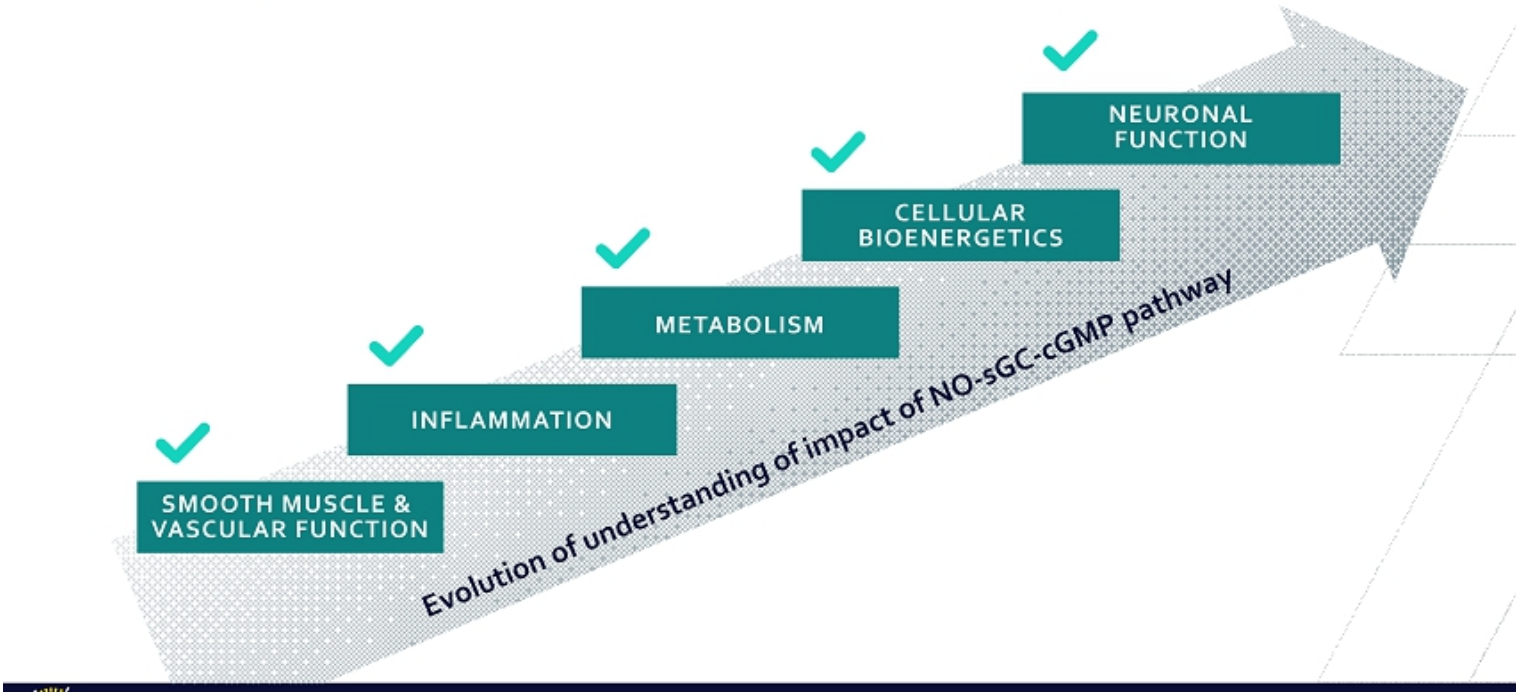
* *Preliminary, unaudited unrestricted cash, cash equivalents and restricted cash balance as of June 30, 2020*

sGC stimulators: ideal intervention in a genetically and clinically validated pathway

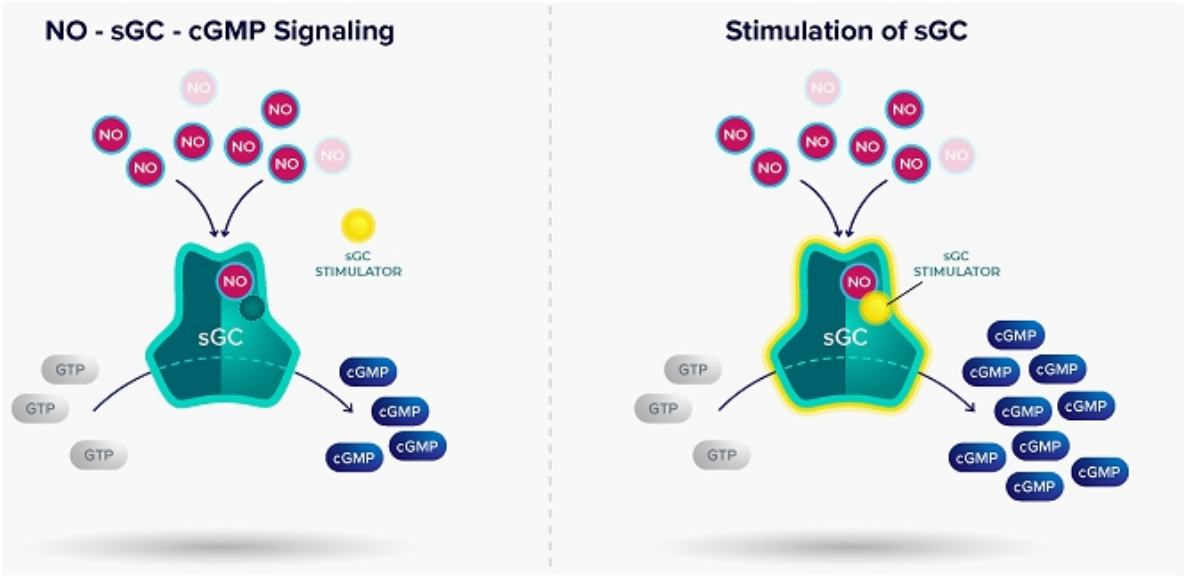


- **multiple successful drugs target the NO-sGC-cGMP pathway for the treatment of CV diseases**
  NO donors, PDE5 inhibitors, sGC stimulators
- **NO-sGC-cGMP pathway plays central role in CNS diseases**
  Network analysis delivers z-scores for CNS diseases similar to validated CV diseases
- **sGC: optimal target for pathway intervention**
  Broadly expressed in CNS, amplifies endogenous signaling, increases cGMP levels at the source with no attenuation of response

Broad impact in the NO-sGC-cGMP pathway



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



A wholly owned pipeline of differentiated molecules

Completed Clinical POC	Ongoing Clinical Programs		Preclinical
Praliciguat  Results support out-license for further development	**Olinciguat**  Phase 2 proof-of-concept study in sickle cell disease ongoing (SCD) Topline data expected late Q3 2020	**IW-6463**  Phase 1 completed, with good CNS exposure, once-daily oral PK, and good safety/tolerability. Translational pharmacology study dosing completed; top line data expected late summer 2020 Anticipate launching two exploratory Phase 2 studies	**Liver-targeted**  **Lung-targeted** 

Praliciguat out-licensing discussions ongoing with expanded scope

Data support further development

- 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 cardio metabolic therapeutic

Out-licensing discussions ongoing

- continuing discussions to out-license global rights to praliciguat
- expanded the scope of its out-licensing discussions beyond cardiometabolic disorders to include additional indications where sGC stimulators have shown efficacy
- no assurances on the prospects or timing of any partnership or licensing transactions--generally or specifically on praliciguat

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

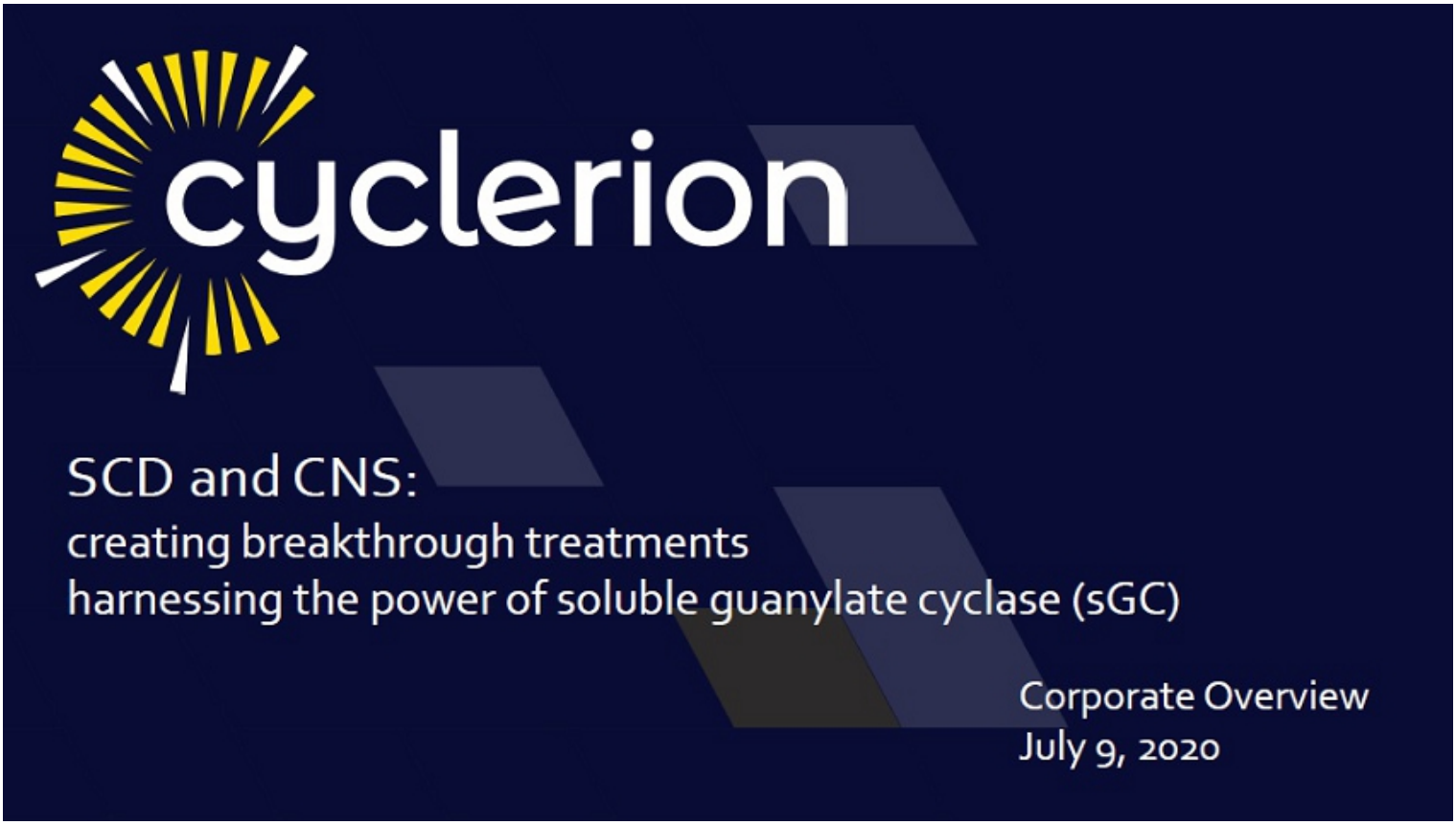

cyclerion
SCD and CNS:
creating breakthrough treatments
harnessing the power of soluble guanylate cyclase (sGC)
Corporate Overview
July 9, 2020

Exhibit 99.2


cyclerion
Delivering impact in CNS diseases
Investor webinar
July 9, 2020

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, and in our subsequent SEC filings, including our Quarterly Report on Form 10-Q filed with the SEC on May 4, 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.

Welcome to Cyclerion's CNS discussion

INDEPENDENT EXPERTS

Marni J. Falk, M.D.

University of Pennsylvania
Professor of Human Genetics; The Children's Hospital of Philadelphia (CHOP), Director of the Mitochondrial Medicine Frontier Program

Eric E. Smith, MD, MPH, FRCPC, FAHA

University of Calgary
Professor of Neurology
Katthy Taylor Chair in Vascular Dementia,
Cumming School of Medicine

CYCLERION LEADERS

Andy Busch, PhD
Chief Innovation Officer

Mark Currie, PhD
President and Chief Scientific Officer

Cheryl Gault
Head of Strategy & Corporate Development

Peter Hecht, PhD
Chief Executive Officer

Christopher Winrow, PhD
Senior Director, Clinical Development – Neuroscience Program Lead

Christopher Wright, MD, PhD
Chief Medical Officer

Pioneering therapeutics in SCD and CNS

Sickle Cell Disease (SCD)

- upstream + downstream pharmacology
- 70 patients enrolled; dosing completed
- top line expected end Q3 2020

Central Nervous System (CNS)

- potential to be next druggable neurotransmitter system
- IW-6463: oral, QD drug
- first CNS-penetrant sGC stimulator in development
- top line expected end of summer 2020

Cyclerion: delivering impact in CNS

1	Now is the time: value in CNS
2	sGC and CNS: scientific and clinical basis for CNS therapies
3	Translational pharmacology study: demonstrating CNS activity
4	Clinical direction in CNS: important indications that yield early answers

Objectives for today

1	Now is the time: value in CNS		**How Cyclerion can create value in CNS**
2	sGC and CNS: scientific and clinical basis for CNS therapies		**Discuss the broad therapeutic potential of sGC stimulators in CNS**
3	Translational pharmacology study: demonstrating CNS activity		**Describe the rich yield of data and its implications (data due late summer)**
4	Clinical direction in CNS: important indications that yield early answers		**Discuss our first indications: focused patient populations, biomarker-based development**

Cyclerion: delivering impact in CNS

1 **Now is the time: value in CNS**

2 sGC and CNS: scientific and clinical basis for CNS therapies

3 Translational pharmacology study: demonstrating CNS activity

4 Clinical direction in CNS: important indications that yield early answers

- growing patient populations and evolving science creates opportunity
- we believe our approach can raise the odds of success
- translational pharmacology data (due late summer) are expected to demonstrate CNS activity

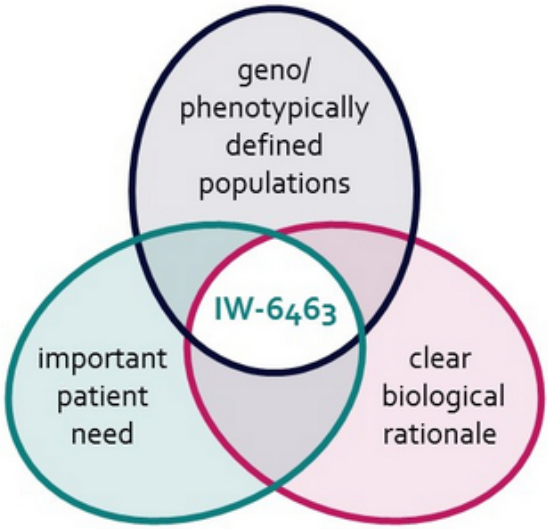
Capturing potential in a high reward therapeutic area

- rapidly growing patient population, lack of approved therapies, important unmet need
- quickly evolving science: genetic insights and technologies
- valued by investors and industry partners
- Cyclerion is the innovator of sGC in the CNS

We've learned from industry history

- understanding disease biology is critically important
- adequate CNS exposure is essential
- identifying translational CNS biomarkers is key

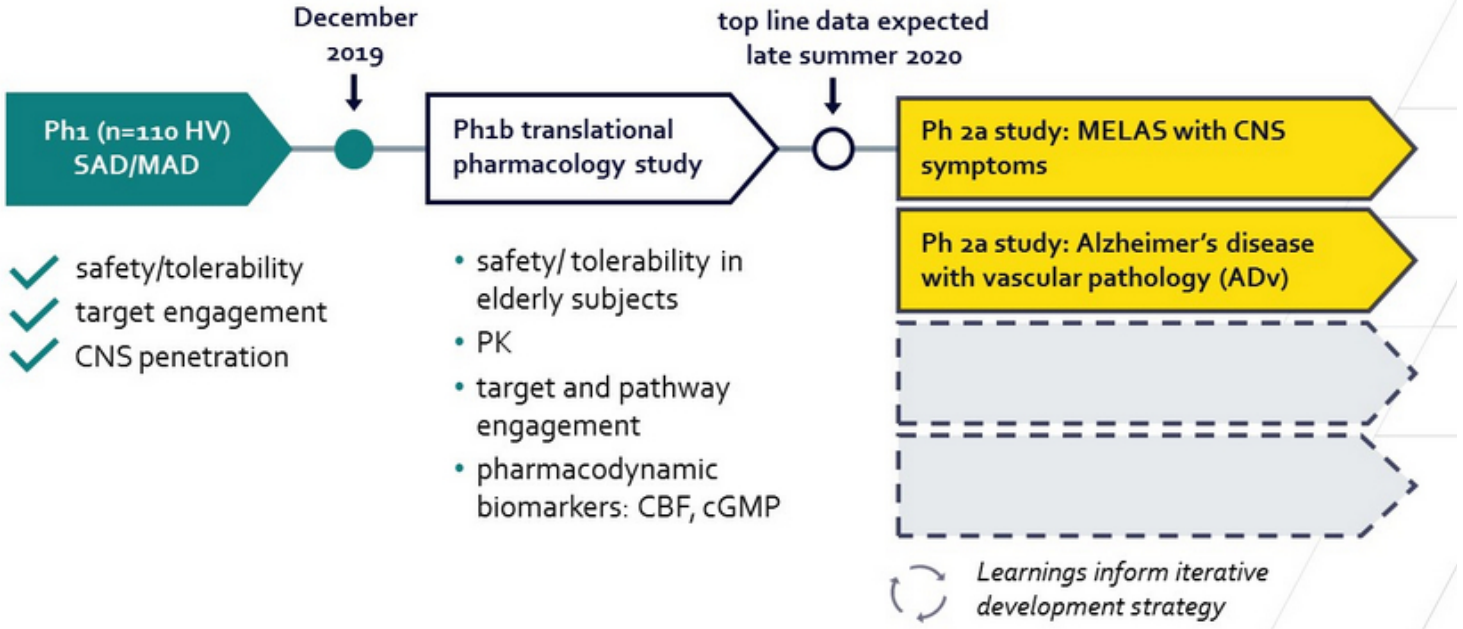
Our approach: intersection of patients and biology



Raising the odds of success:

- pursue multiple indications in parallel
- leverage biomarkers to drive development
- implement nimble trials with leading edge investigators and imaging analytics
- investigate a strategic R&D partnership to explore full potential of sGC in the CNS

IW-6463 biomarker-guided development in focused patient populations



sGC and CNS: scientific and clinical basis for CNS therapies

1 Now is the time: value in CNS

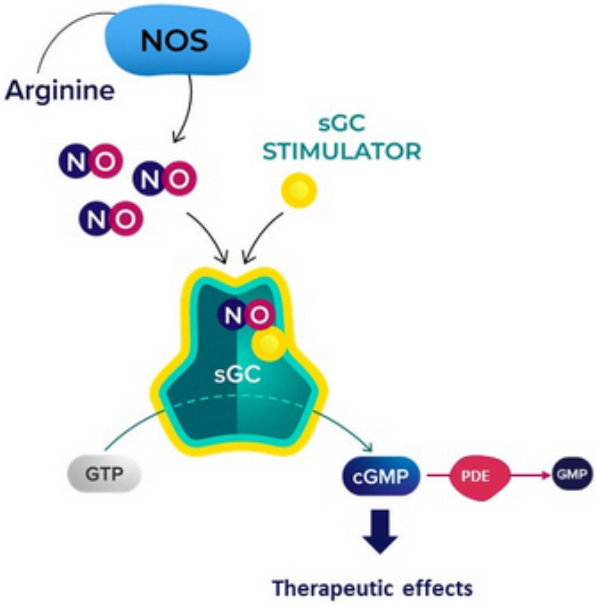
2 **sGC and CNS: scientific and clinical basis for CNS therapies**

3 Translational pharmacology study: demonstrating CNS activity

4 Clinical direction in CNS: important indications that yield early answers

- sGC stimulators are clinically validated in several diseases
- sGC/NO pathway identified as drug target for CNS diseases using systems biology approach
- IW-6463 active in four domains: cerebral blood flow, cellular bioenergetics, neuro-inflammation, neuronal function

sGC stimulators: ideal intervention in a genetically and clinically validated pathway



Multiple successful drugs target the NO-sGC-cGMP pathway for the treatment of CV diseases

NO donors, PDE5 inhibitors, sGC stimulators

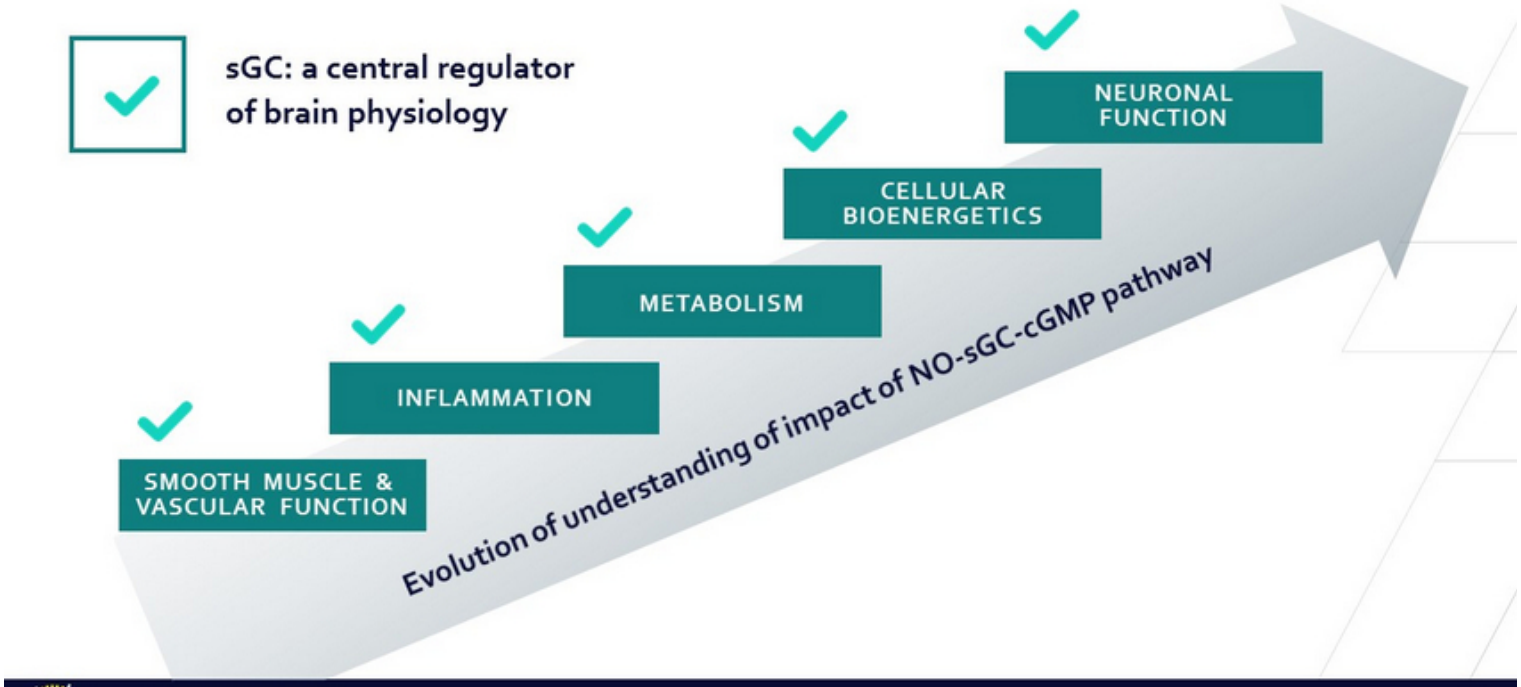
NO-sGC-cGMP pathway plays central role in CNS diseases

Network analysis delivers z-scores for CNS diseases similar to validated CV diseases

sGC: optimal target for pathway intervention

Broadly expressed in CNS, amplifies endogenous signaling, increases cGMP levels at the source with no attenuation of response

Growing appreciation of the role of NO-sGC-cGMP pathway in CNS disease



sGC stimulators: potential to be next druggable neurotransmitter system

Nitric oxide

- IW-6463

Successfully drugged neurotransmitter systems

GABAergic
- Valium® (1963)
- Ambien® (1992)

Dopaminergic
- Levodopa (1970)
- Risperdal® (1993)

Adrenergic/Serotonergic
- Amitriptyline (1961)
- Prozac® (1987)
- Paxil® (1992)

Cholinergic
- Scopolamine (1979)
- Aricept® (1996)

Glutamatergic
- Ketamine (1970)
- Namenda® (2003)

NO-sGC-cGMP pathway:
From validated cardiometabolic diseases to CNS disease validation

Disease genetics network

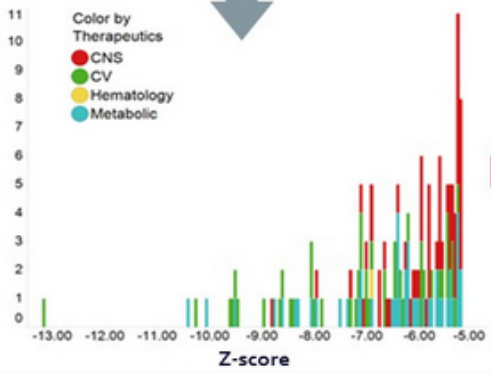
Human interactome

NO-sGC-cGMP pathway

Network analysis reveals disease linkage

Cardiometabolic Diseases

- hypertension*
- diabetic nephropathy*
- heart failure*
- arteriosclerosis
- diabetes*
- PAH*
- sickle cell anemia



CNS Diseases

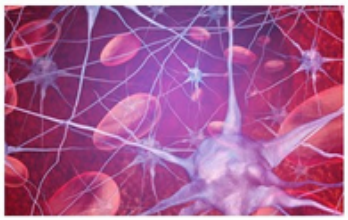
- Alzheimer's disease
- cognitive impairment
- stroke
- bipolar disorder
- schizophrenia
- depression
- Huntington's disease

IW-6463 demonstrates in preclinical studies beneficial effects in four important domains of neurodegenerative diseases

IMPROVE

Cerebral Blood Flow

Increased blood flow in areas associated with memory and arousal by fMRI BOLD imaging



ENHANCE

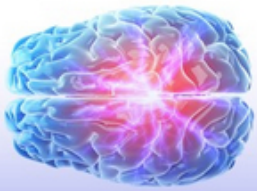
Cellular Bioenergetics

Increased ATP and restored gene expression in cells from patients with mitochondrial diseases

REDUCE

Neuro-inflammation

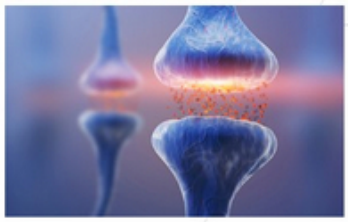
Decreased markers of LPS-induced neuroinflammation (ICAM1, VCAM1, IL6) *in vitro*



IMPROVE

Neuronal Function

Enhanced memory performance & spine density in aged animals; increased LTP in neurodegenerative disease models



Attractive nonclinical profile supports clinical development

- IW-6463 demonstrates pharmacological activity across four distinct domains in multiple preclinical models
- preclinical results support straightforward translation into the clinic
- CNS exposure and target engagement demonstrated in multiple species
- no evidence of CYP enzyme inhibition and IW-6463 not a P-gp substrate
- nonclinical toxicology profile consistent with other sGC stimulators in development

Translational pharmacology study: confirming CNS activity

1 Now is the time: value in CNS

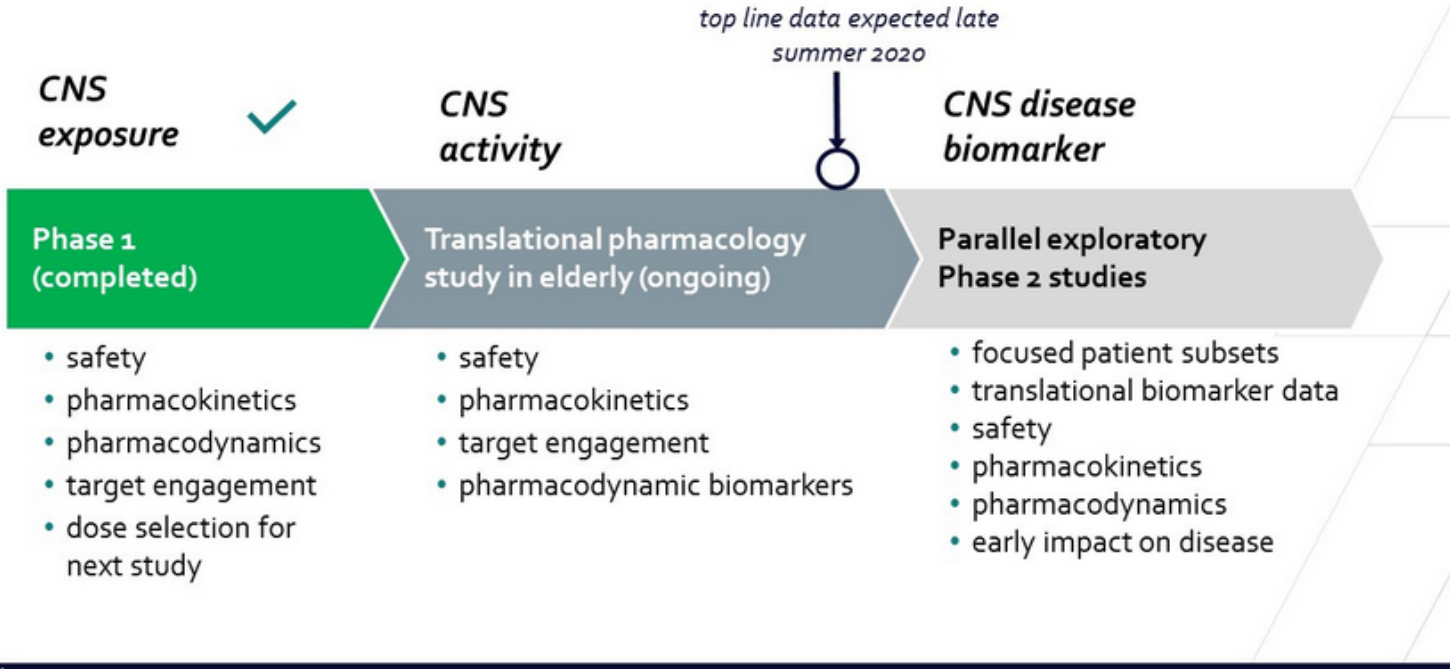
2 sGC and CNS: scientific and clinical basis for CNS therapies

3 Translational pharmacology study: demonstrating CNS activity

4 Clinical direction in CNS: important indications that yield early answers

- rational indication selection approach for CNS diseases
- phase 1 GO – identified well-tolerated doses achieving the desired CNS exposure
- elderly translational pharmacology study focused on CNS target engagement (late summer)

Biomarker-driven IW-6463 early clinical development strategy



IW-6463 Phase 1: CNS exposure, target engagement, PK, and safety

PHASE 1 *(completed)*

Study design

- three stages:
  - SAD
  - MAD
  - food interaction
- 110 healthy volunteers
- age range 18-63
- standard safety
- PK (blood & CSF)
- wide dose range tested

GOALS ACHIEVED

Results

- identified safe and well-tolerated dose levels with steady-state CNS exposure in therapeutic target range*
- linear, predictable PK; consistent with QD dosing
- CNS exposure confirmed
- evidence of target engagement (blood pressure)
- well tolerated at all dose levels, no safety signals
- may be taken with or without food

*Based on positive CNS pharmacology in multiple preclinical models

Translational study design: pharmacodynamic biomarkers and safety

Assessing safety, PK and target engagement in CNS (cGMP)

Top line data expected late summer 2020

IMPROVE

Cerebral Blood Flow

- MRI arterial spin labeling (ASL)

ENHANCE

Cellular Bioenergetics

- brain metabolism via magnetic resonance spectroscopy (MRS)

REDUCE

Neuro-inflammation

- cytokines, adhesion molecules

IMPROVE

Neuronal Function

- qEEG
- measures of cognition and behavior (NeuroCart®)

Translational approach from discovery to approval and beyond

Establish PD biomarkers preclinically

Effects across four domains of neurodegenerative disease

Validate PD biomarkers in the clinic

Translational pharmacology study in elderly

Top line data late summer 2020

Refine clinical strategy

- *indication selection*
- *patient selection*
- *biomarker enrichment*
- *endpoint selection*
- *trial design*
- *regulatory approach*

Smaller/shorter studies

Evaluate IW-6463 in focused patient populations

Initial approvals based on predictive surrogate and/or symptomatic and functional endpoints

Larger/longer studies

Evaluate IW-6463's full potential

Potential to expand label to broader populations and to demonstrate disease modification

Clinical direction in CNS: important indications that yield early answers

1 Now is the time: value in CNS

2 sGC and CNS: scientific and clinical basis for CNS therapies

3 Translational pharmacology study: demonstrating CNS activity

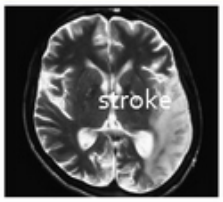
4 **Clinical direction in CNS: important indications that yield early answers**

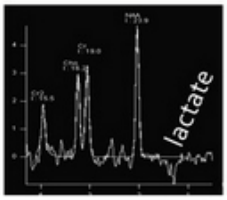
- MELAS and ADv trials designed to uncover meaningful CNS biomarker engagement
- approach efficiently de-risks & allows quick progression to the next development stages

Mitochondrial Encephalomyopathy, Lactic Acidosis,& Stroke-like Episodes (MELAS)

genetically defined orphan disease, serious CNS & multi-system problems, no approved treatments

SYMPTOM OVERVIEW



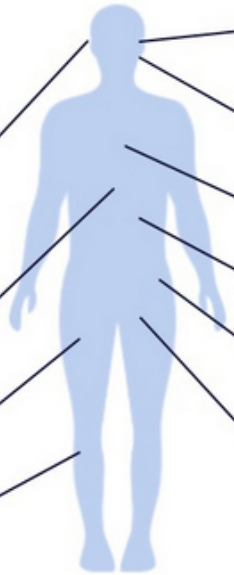


Central Nervous system
Strokes, Stroke-like Episodes (SLEs), Ataxia (Imbalance), Epilepsy (Seizures), Migraine, Headaches, Cognitive Impairment, Learning Disability, Dementia, Mood disorders

Autonomic Nervous System
Dysautonomia, Temperature Intolerance, Heart Rate Instability (POTS)

Peripheral Nervous System
Peripheral Neuropathy

Skeletal muscle
Muscle weakness, myopathy, exercise intolerance



Vision
Vision Loss, Cortical Blindness, Ptosis, Ophthalmoplegia, Retinal-Optic Nerve Disease

Hearing
Sensorineural Hearing Loss, Tinnitus

Cardiac
Sudden Death, Arrhythmias, Cardiomyopathy

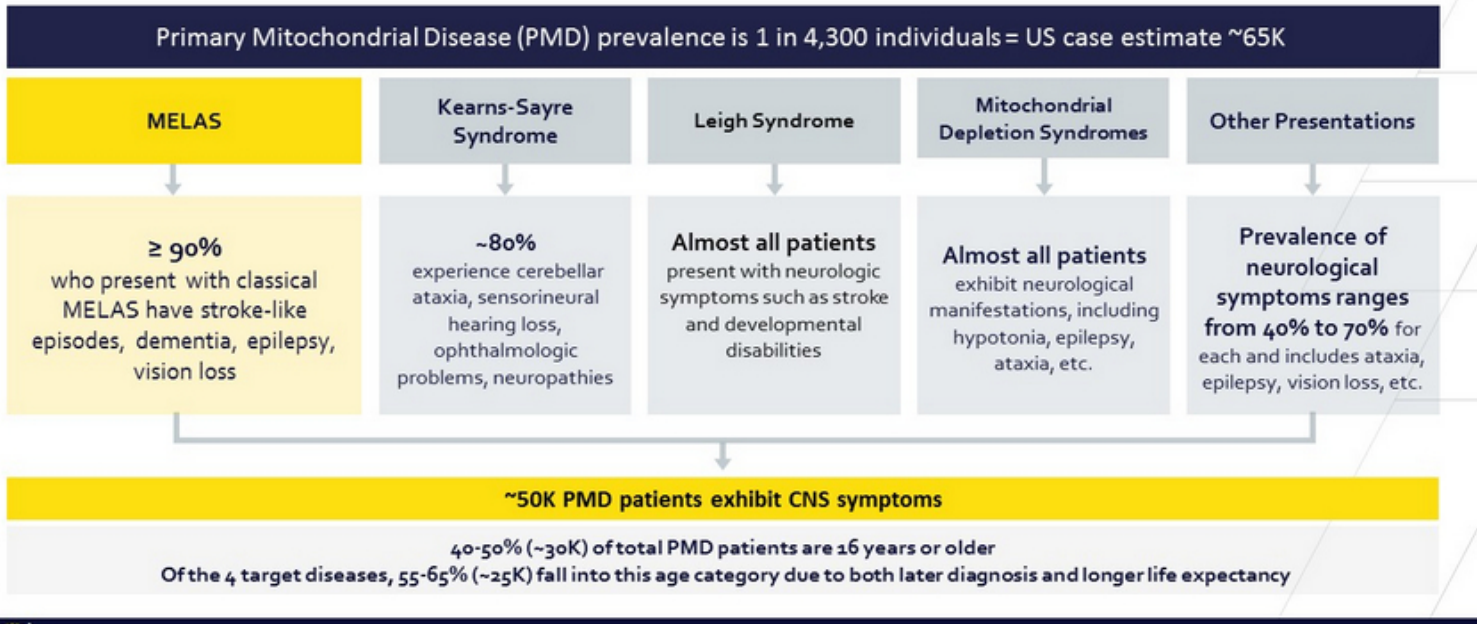
Gastrointestinal
Vomiting, Pseudoobstruction

Endocrine/Metabolic
Diabetes Mellitus, Short Stature, Underweight, Fatigue, Lactic Acidosis

Renal
Nephropathy

Focused MELAS trial population for trials; potential for broader use

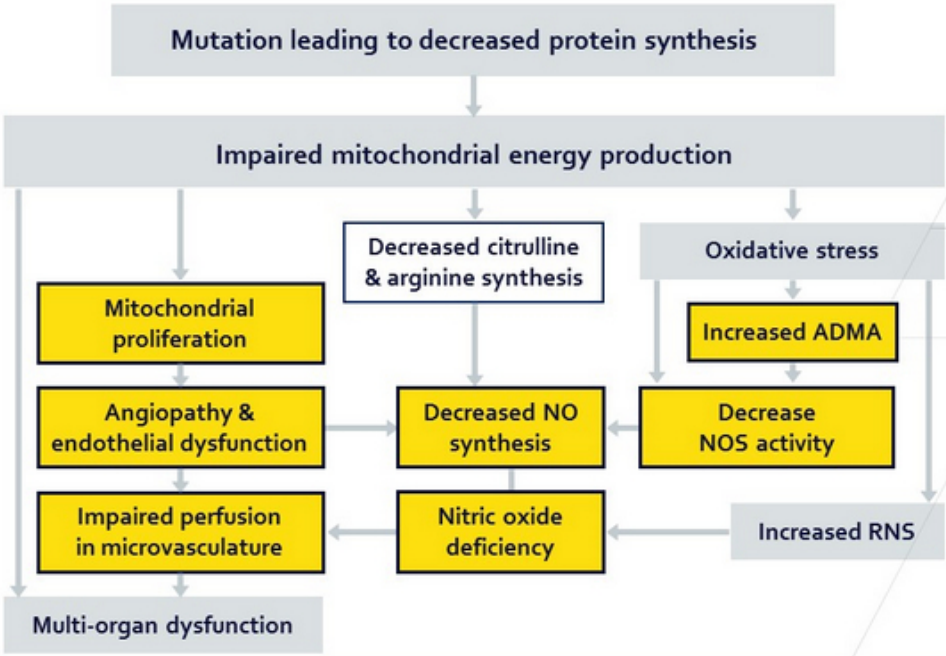
US prevalence of mitochondrial disease and CNS symptoms



IW-6463: potentially impacts MELAS pathophysiology at multiple points

Impact of L-Arginine/citrulline treatment

Potential therapeutic benefit of IW-6463



MELAS: strong supportive data for NO-sGC-cGMP pathway involvement

SCIENTIFIC RATIONALE FOR INDICATION AND PATIENT SELECTION

Clinical precedence for NO-sGC-cGMP pathway

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Mitochondrial dysfunction	Lactate
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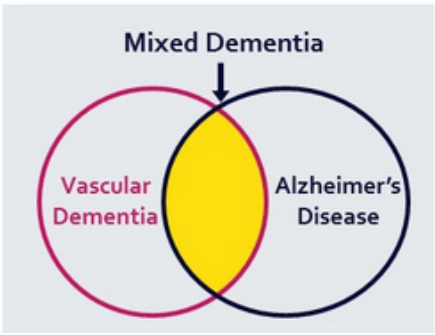
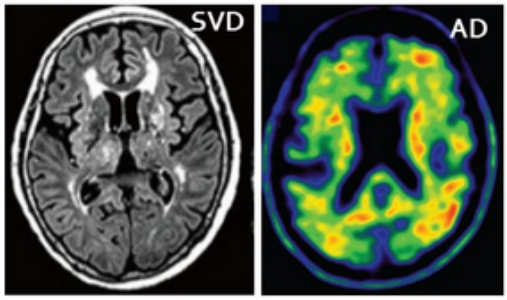
Neurodegeneration	NF-L
Cognitive impairment	Cognitive and behavior tests

Improved lactate and CBF would indicate an impact on the underlying disease mechanism and suggest potential for broad benefit for these patients.

Vascular pathology in dementia – clinical perspective





PATIENT PRESENTATION & CHARACTERISTICS

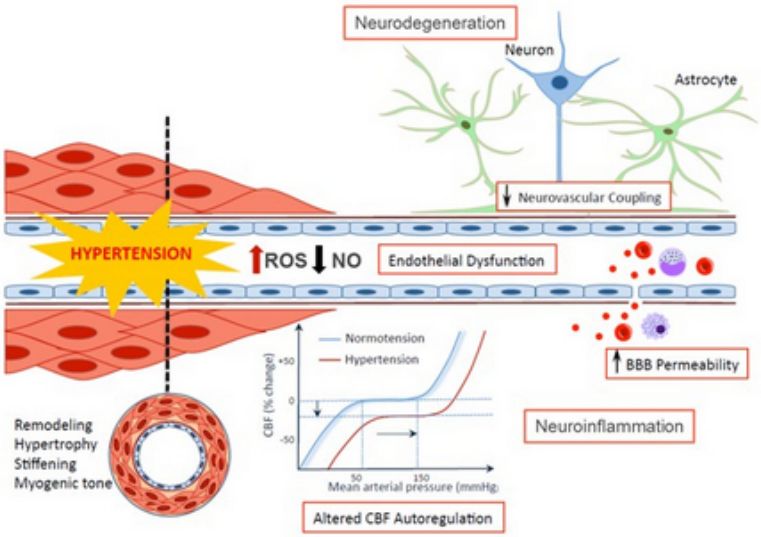
- AD & vascular dementia - two most common dementias
- pure forms exist, but vascular pathology widely prevalent in AD
- mixed dementia = broad area of overlap
- subcortical small vessel disease (SVD) in a significant portion
- mixed dementia patients more rapidly progressive disease, higher symptom severity

UNMET NEED

- ~2M US patients; incidence increasing with aging
- symptomatic treatment for AD – modest, brief benefit
- no disease-modifying therapies, none targeting the vasculature

Dementia type	Pathophysiology
Alzheimer's	• neurofibrillary tangles • amyloid plaques
Vascular	• impaired brain blood flow
Mixed Dementia	• combination of the above

Vascular pathology: a key contributor to dementia



SUPPORTIVE EVIDENCE

- risk factors and common comorbidities: DM, HTN, HL, Smoking, CAD
- ApoE risk partly mediated by endothelial dysfunction and BBB breakdown
- brain ischemic changes present in dementia, including AD; possibly independent disease progression risk factor
- vasculature implicated in a-beta brain clearance, a process that fails in AD

AD with vascular pathology (ADv) – focused mixed dementia subset

Defined population well suited for treatment with IW-6463

DISEASE RATIONALE FOR PATIENT SELECTION

Pathophysiology

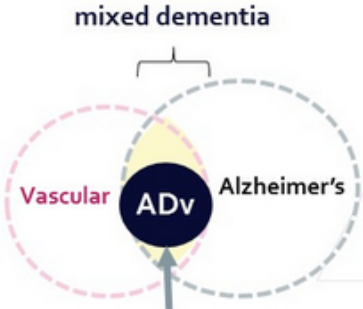
NO dysregulation, endothelial cell loss, impaired blood flow, vascular leakage, inflammation, neuronal dysfunction, and neuronal loss are major contributing factors to rapid disease progression

Standard of care

No approved therapies to treat vascular dementia.
AD therapies offer limited benefits; not disease modifying

Pharmacology

Our preclinical data suggest IW-6463 has potential to improve cerebral blood flow, endothelial health, neuroinflammation, and cellular energetics as well as prevent neurodegeneration



Target population

ADv: an identifiable subset of mixed dementia patients with:

- AD pathology **AND**
- sub-cortical vascular disease **AND**
- CV risk factors

Ph 2a study of IW-6463 in ADv: emerging design

STUDY START 1H 2021

Treatment
- once-daily IW-6463

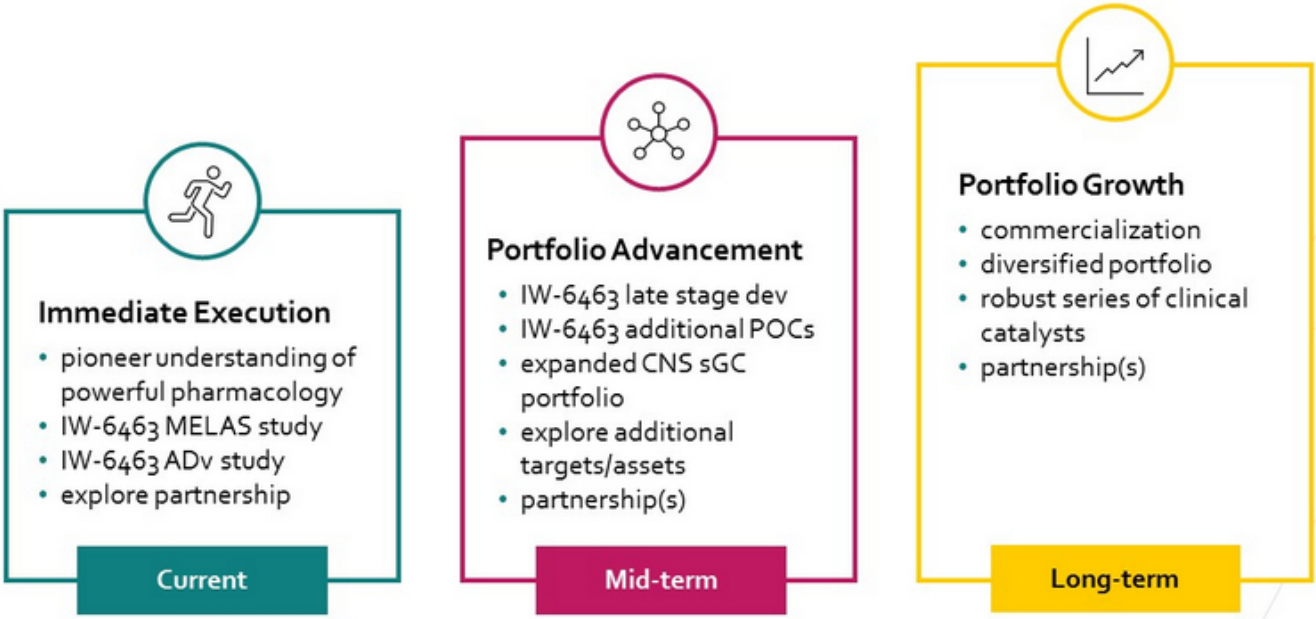
Enrichment strategy
- confirmed AD pathology (PET, CSF)
- 3+ cardiovascular risk factors
- mild-moderate subcortical small-vessel disease on MRI
- mini Mental State Exam score (16-26)

Objectives
- establish safety and pharmacodynamic effects of IW-6463 in a short-term study
- de-risk progression to larger, longer symptomatic and disease modification trials

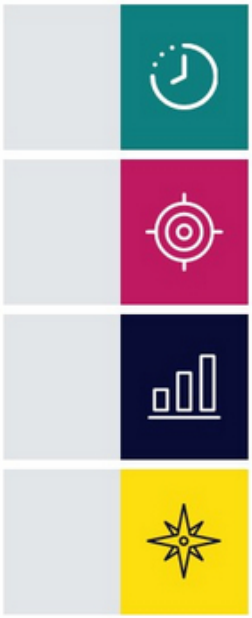
DISEASE DOMAIN	ASSESSMENT
Vascular dysfunction	ASL (CBF)
Neurodegeneration	neurofilament light chain
Neuroinflammation	vascular cell adhesion molecule
Mitochondrial dysfunction	N-acetyl aspartate (MRS)
Cognitive impairment	cognitive and behavior tests

Improved CBF, particularly in the context of memory improvements, would indicate an impact on the underlying disease mechanism and enable a targeted design for the next development stage.

Committed to building CNS as a core therapeutic area



Thank you for joining



- powerful platform for potential CNS therapies
- adaptive, risk-reducing, development approach
- seasoned drug development leaders with specialized scientific advisors
- multiple ways to win: SCD and CNS
- ownership base of long-term investors and employees

Questions

Delivering impact in CNS diseases

Investor webinar
July 9, 2020

Citations

Page	Topic	Citation
25	MELAS epidemiolgy	Sources: 1. J Neurol. 2016; 263: 179–191; US population estimated at 327.2 million; 2. Brain. 2003; 126(5): 1231–1240; 3. NIH Genetics Home Reference; 4. NCBI GeneReviews; 5. Neurotherapeutics. 2013 Apr; 10(2): 186–198
26	MELAS MOA	El-Hattab, AW et al, 2016
30	Vascular pathology	• Smith and Markus. New Treatment Approaches to Modify the Course of Cerebral Small Vessel Diseases (Stroke. 2020;51). • Bakker, Erik NTP et al. Lymphatic clearance of the brain; perivascular, paravascular and significance for neurodegenerative diseases. Cell Molec Neurobiol 36.2 (2016): 181-194. • Venturelli, Ben Aisa et al, (Cur Med Chem, 2016, 23, 2770-2788. Targeting NO/cGMP Signaling in the CNS for Neurodegeneration and Alzheimer's Disease). • Montagne et al, (Nature, 581, 7 May 2020. APOE4 leads to blood-brain barrier dysfunction predicting cognitive decline). • Iadecola C et al. (Vascular Cognitive Impairment and Dementia: JACC Scientific Expert Panel. J Am Coll Cardiol. 2019;73(25):3326-44.). • Coutu JP, et al. (Two distinct classes of degenerative change are independently linked to clinical progression in mild cognitive impairment. Neurobiol Aging. 2017; 54:1-9.).