UNITED STATES
SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 8-K

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

Date of Report (Date of earliest event reported): **October 14, 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:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ 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 8.01 Other Events.

On October 14, 2020, the Company issued two press releases announcing the topline data from the Company's IW-6463 Translational Pharmacology Study and its olinciguat Phase 2 STRONG-SCD study in patients with SCD. Copies of the press releases regarding IW-6463 and olinciguat are attached hereto as Exhibit 99.1 and Exhibit 99.2, respectively, and each is incorporated by reference to this Current Report on Form 8-K.

The Company will host a conference call to discuss the topline results from the IW-6463 translational pharmacology study on October 14, 2020 at 8:30 a.m. Eastern Time. A copy of the conference call presentation materials is attached hereto as Exhibit 99.3 and is incorporated by reference to this Current Report on Form 8-K. The presentation materials are also available on the "Investors & Media" page of the Company's website at https://ir.cyclerion.com/news-events/news-releases.

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

Item 9.01 Financial Statements and Exhibits.

(d)

Exhibit No.	Description
99.1	Press Release of Cyclerion Therapeutics, Inc. dated October 14, 2020
99.2	Press Release of Cyclerion Therapeutics, Inc. dated October 14, 2020
99.3	Investor Presentation of Cyclerion Therapeutics, Inc. dated October 14, 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: October 14, 2020

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

Exhibit 99.1

FOR IMMEDIATE RELEASE

Cyclerion Announces Positive Data from IW-6463 CNS Translational Pharmacology Study in Healthy Elderly Subjects

Showed significant improvements in neurophysiological and objective performance measures associated with age-related cognitive decline and neurodegenerative diseases

Confirmed blood-brain-barrier penetration, desired CNS exposure levels, target engagement and a favorable safety and tolerability profile

Proceeding with its upcoming Phase 2 clinical trials in Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like episodes (MELAS) and Alzheimer's disease with vascular pathology (ADv)

Company to focus on developing treatments for serious diseases of the central nervous system

Webcast at 8:30 a.m. ET today

CAMBRIDGE, Mass., October 14, 2020 — Cyclerion Therapeutics, Inc. (Nasdaq: CYCN), a clinical-stage biopharmaceutical company developing innovative medicines for people with serious diseases of the central nervous system (CNS), today announced results from its Phase 1 translational pharmacology study of IW-6463, the first soluble guanylate cyclase (sGC) stimulator in clinical development for CNS disorders.

Treatment with IW-6463 in this 15-day 24-subject crossover study confirmed and extended results seen in earlier Phase 1 studies: once daily oral treatment demonstrated blood-brain-barrier penetration, desired CNS exposure levels and target engagement. In this study, IW-6463 was shown to be safe and generally well-tolerated. Subjects receiving IW-6463 showed meaningful improvements in certain neurophysiological and objective performance measures that are associated with age-related cognitive decline and neurodegenerative diseases. Effects on cerebral blood flow and markers of bioenergetics were not observed in this study.

These results support the ongoing development of IW-6463 in serious CNS diseases. Cyclerion will soon begin enrolling its Phase 2 clinical trial in Mitochondrial Encephalomyopathy, Lactic Acidosis, and Stroke-like episodes (MELAS). Over the coming months the company will use the findings of the translational pharmacology study, in addition to observations from the previous Phase 1 study of 110 healthy subjects, to inform further clinical development activities, including the initiation of a planned Phase 2 clinical trial in Alzheimer's disease with vascular pathology (ADv) in 2021, as well as to explore other potential indications.

"These data show that IW-6463 has a positive effect on brain neurophysiology that has been associated with age-related cognitive decline and neurodegenerative diseases. Furthermore, these data support the role of nitric oxide as an important neurotransmitter whose potential therapeutic benefits remain underexplored," said Chris Wright, M.D., Ph.D., Cyclerion's Chief Medical Officer. "We expect to initiate enrollment of the MELAS study later this year and are excited to incorporate the learnings from our translational pharmacology study into the design of our planned Phase 2 ADv study. Looking beyond these studies, we will evaluate the potential of IW-6463 to provide clinical benefit for people suffering from a range of serious CNS diseases. Seeing such robust, consistent and rapidly occurring changes in this study gives us confidence that IW-6463 targets a relevant mechanism in cognition and neurodegeneration."

IW-6463 Phase 1 Translational Pharmacology Study Design

The exploratory Phase 1 study conducted in 24 healthy elderly volunteers age 65 and older evaluated safety and tolerability, pharmacokinetics, measures of CNS pharmacodynamic activity, including cerebral blood flow, and a range of measures associated with age-related cognitive decline and neurodegenerative diseases. Participants received study drug once daily across two 15-day dosing periods (Period 1 and Period 2). The dosing periods were separated by a 27-day washout. Participants were randomized to a sequence of receiving IW-6463 for Period 1 and then placebo for Period 2, or vice versa. All 24 subjects completed the first period, and 12 completed the entire crossover due to operational challenges associated with COVID-19.

IW-6463 Phase 1 Translational Pharmacology Study Results

IW-6463 demonstrated blood-brain-barrier penetration, desired CNS exposure levels and engagement of the targeted nitric oxide (NO)-signaling pathway. Mean concentrations of IW-6463 in cerebrospinal fluid (CSF) achieved levels projected to be pharmacologically active based on preclinical studies. Consistent with this, pathway target engagement was confirmed through monitoring blood pressure and CSF cyclic guanosine monophosphate (cGMP) levels. This study reproduced the brain exposure and safety and tolerability data set of the prior Phase 1 study in young healthy volunteers (n=110).

Key results in this healthy elderly population demonstrate an impact on certain neurophysiological and objective performance measures known to be affected by aging and neurodegenerative disease with cognitive impairment. Specifically, Cyclerion observed:

- positive impact on posterior alpha power, a measure that may reflect attentional processing capabilities, with a significant increase from baseline to day 15 in the IW-6463 treatment group, compared to the placebo group ($p<0.02$). Directional improvements in gamma power, a measure associated with memory and attention processing, as well as in other spectral power rhythms, buttress this finding.

- improvements in the N200 auditory event-related potential, a measure associated with stimulus identification and distinction. Latency was significantly shorter with IW-6463 at day 14 compared to untreated subjects (p=0.02).
- positive effects of IW-6463 on an objective saccadic eye movement task that is related to attention and cognitive processing. Saccadic reaction times were significantly shorter (p=0.02) and there was a trend increase in saccadic velocity (p=0.07).

Cyclerion will continue to analyze the data to more fully understand the relationship between IW-6463 and the biomarker effects observed. All p-values are unadjusted for multiplicity. The company intends to present further results of this exploratory study, which represents a novel area of CNS science, in peer-reviewed journals and medical conferences.

“These results bring into focus the exciting opportunity to deliver innovative medicines, with the possibility to improve brain function, for an area in desperate need of new treatment options,” said Andy Busch, Ph.D., Chief Innovation Officer. “We are working at the forefront of CNS drug development and we are learning a great deal about this novel mechanism of action. IW-6463 is a promising molecule with potential in a variety of serious CNS diseases, and we look forward to building on the insights from this study to drive the path forward for the company, the compound, and patients in need beyond our planned clinical trials and current target indications.”

“These exciting and unique results demonstrate that stimulating sGC can positively modulate alpha rhythm and N200 in the elderly, potentially improving age-related deficits in these neurophysiologic measures,” said Brandon Westover, M.D., Ph.D., McCance Center for Brain Health, Associate Professor, Neurology, Massachusetts General Hospital and Harvard Medical School, and Co-Founder of Beacon Biosignals. “Given the relationships between alpha rhythm, N200, brain aging, and cognitive impairment, further study is warranted in patients with debilitating age-associated neurodegenerative diseases.”

The company’s planned Phase 2 trial of IW-6463 in ADv will be supported partially by a grant from the Alzheimer's Association’s Part the Cloud-Gates Partnership Grant Program, which is expected to provide Cyclerion with $2 million of funding over the next two years.

About IW-6463

IW-6463, a CNS-penetrant sGC stimulator, is being developed as a symptomatic and potentially disease modifying therapy for serious CNS diseases. Nitric oxide (NO) is one of several fundamental neurotransmitters, but it has yet to be leveraged for its full CNS therapeutic potential. IW-6463 stimulates sGC, a signaling enzyme that responds to the presence of NO, to enhance the body’s natural ability to produce cyclic guanosine monophosphate (cGMP), an important signaling molecule, naturally. An impaired NO-sGC-cGMP signaling pathway is believed to play an important role in the pathogenesis of neurodegenerative diseases and is critical to basic neuronal functions. Agents that stimulate sGC to produce cGMP may compensate for deficient NO signaling.

About Cyclerion Therapeutics

Cyclerion Therapeutics is a clinical-stage biopharmaceutical company focused on discovering, developing and commercializing innovative medicines for people with serious diseases of the central nervous system (CNS). Cyclerion's lead program is IW-6463, a pioneering CNS-penetrant sGC stimulator in clinical development for Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like episodes (MELAS) and Alzheimer's disease with vascular pathology (ADv).

For more information about Cyclerion, please visit https://www.cyclerion.com/ and follow us on Twitter (@Cyclerion) and LinkedIn (www.linkedin.com/company/cyclerion).

Webcast and Conference Call Details

Cyclerion will host a webcast, with accompanying slide presentation, on Wednesday, October 14, 2020 at 8:30 a.m. EDT to discuss the study results and plans for further development of IW-6463. To access the webcast, please visit https://edge.media-server.com/mmc/p/2zzfo75c. To access the call, please dial (800) 360-8162 (toll-free) or (409) 937-8760 (international) and provide the conference ID 2554703. The archived webcast will remain available online for 30 days. For more information, please visit the investor section of Cyclerion's website at www.cyclerion.com

Forward Looking Statement

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Our forward-looking statements are based on current beliefs and expectations of our management team that involve risks, potential changes in circumstances, assumptions, and uncertainties, including statements about the results and conduct of our Phase 1 translational pharmacology clinical trial of IW-6463; our interpretation of the data from the clinical trial; the potential of further evaluation of IW-6463; the clinical potential of IW-6463; our future business focus; the anticipated timing of our planned clinical trials; and the receipt of cash from the Alzheimer's Association's Part the Cloud-Gates Partnership Grant Program, which is subject to final documentation. We may, in some cases use terms such as "predicts," "believes," "potential," "continue," "anticipates," "estimates," "expects," "plans," "intends," "may," "could," "might," "likely," "will," "should" or other words that convey uncertainty of the future events or outcomes to identify these forward-looking statements. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement. Applicable risks and uncertainties include the risks listed under the heading "Risk Factors" and elsewhere in our 2019 Form 10-K filed on March 12, 2020, and in Cyclerion's subsequent SEC filings, including the Form 10-Q filed on May 4, 2020 and the Form 10-Q filed on August 3, 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.

Investors
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Exhibit 99.2

FOR IMMEDIATE RELEASE

Cyclerion Announces Phase 2 STRONG-SCD Study Results in Patients with Sickle Cell Disease

Study results do not support further internal development

CAMBRIDGE, Mass., October 14, 2020 — Cyclerion Therapeutics, Inc. (Nasdaq: CYCN), a clinical-stage biopharmaceutical company, today announced top-line results from its STRONG-SCD study of olinciguat, an investigational, orally-administered, once daily, vascular sGC stimulator for the potential treatment of sickle cell disease (SCD). Olinciguat was generally well tolerated across all dose ranges. Results did not demonstrate adequate activity to support further internal clinical development. Cyclerion intends to complete its analysis of the study results and present or publish them in a future forum.

"We would like to thank all of the sickle cell patients who participated in the STRONG-SCD study, the SCD advocacy community, and the investigators and study staff who focused their time and efforts on helping us better understand the potential of olinciguat in sickle cell disease," said Peter Hecht, Ph.D., Chief Executive Officer of Cyclerion. "While we are disappointed that we won't be contributing a much-needed new treatment option for SCD, we are continuing to analyze the data to understand several potential biomarker signals, including inflammation, as we explore partnership options for this program."

As described in the Company's IW-6463 press release also issued today, Cyclerion expects to be focused on the development of treatments for serious diseases of the central nervous system (CNS).

About STRONG-SCD Study

The STRONG-SCD study is a randomized, placebo-controlled, dose-ranging Phase 2 study of 70 participants designed to evaluate safety, tolerability, and pharmacokinetics of olinciguat, compared to placebo, as well as to explore effects on daily symptoms and biomarkers of disease activity when dosed over a 12-week treatment period.

About Cyclerion Therapeutics

Cyclerion Therapeutics is a clinical-stage biopharmaceutical company focused on discovering, developing and commercializing innovative medicines for people with serious diseases of the central nervous system (CNS). Cyclerion's lead program is IW-6463, a pioneering CNS-penetrant sGC stimulator in clinical development for Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like episodes (MELAS) and Alzheimer's Disease with Vascular pathology (ADv).

For more information about Cyclerion, please visit https://www.cyclerion.com/ and follow us on Twitter (@Cyclerion) and LinkedIn (www.linkedin.com/company/cyclerion).

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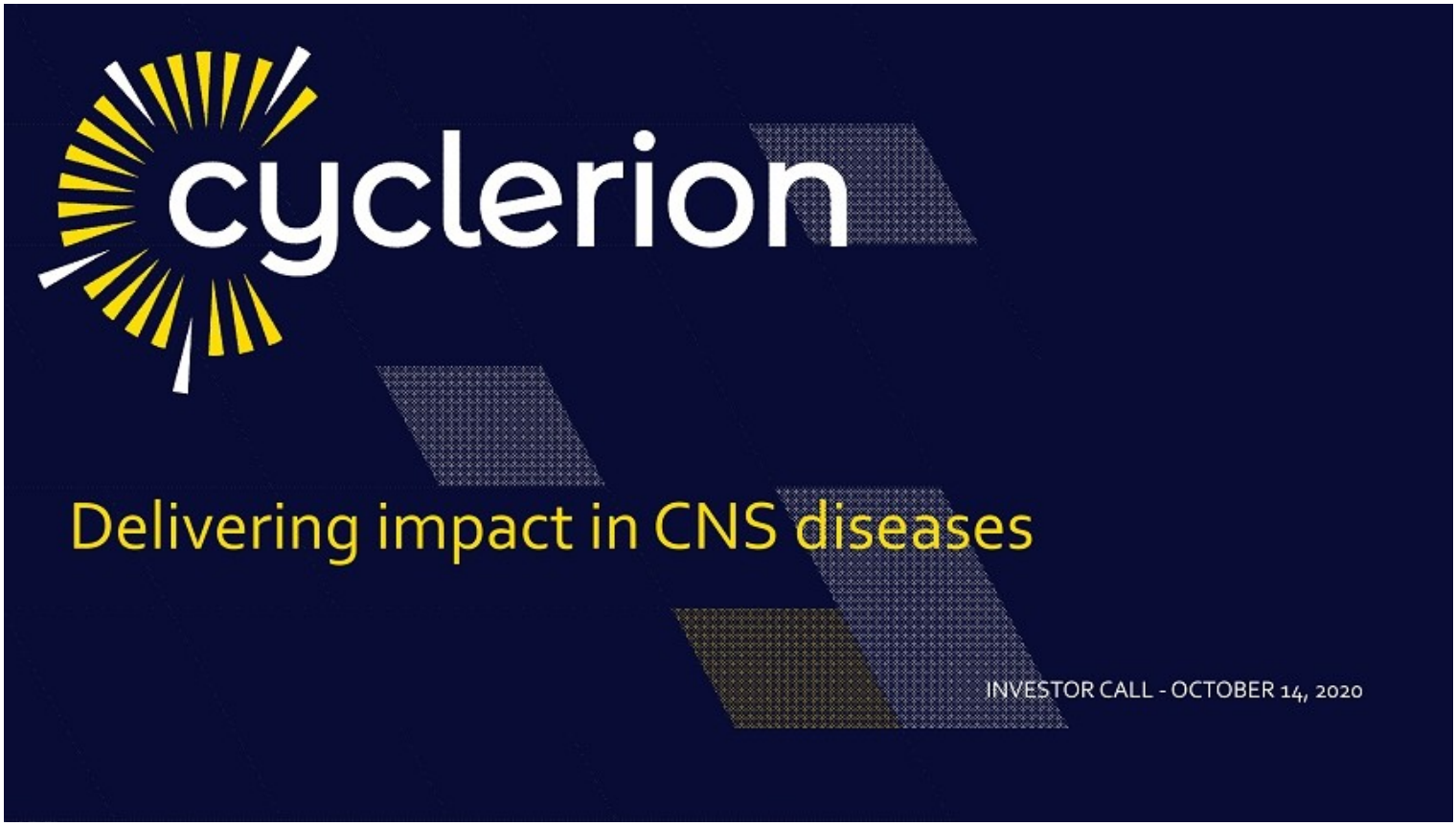
Exhibit 99.3


cyclerion
Delivering impact in CNS diseases
INVESTOR CALL - OCTOBER 14, 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; including statements about the results and conduct of our Phase 1 translational pharmacology clinical trial of IW-6463; our interpretation of the data from the clinical trial; the potential of further evaluation of IW-6463; the clinical potential of IW-6463; our future business focus; the anticipated timing of our planned clinical trials; business strategies, research and development plans, collaborations, partnerships, out-licensing, 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 2019 Form 10-K filed on March 12, 2020, and in Cyclerion’s subsequent SEC filings, including the Form 10-Q filed on May 4, 2020 and the Form 10-Q filed on August 3, 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, except as required by law.

INTRODUCTION

Peter Hecht, Chief Executive Officer

Results in healthy elderly subjects

- ✓ *favorable safety and tolerability*
- ✓ *crossed the blood brain barrier (BBB)*
- ✓ *pathway target engagement confirmed*
- ✓ *delivered rapid, robust, and selective neurophysiological changes*

Independent expert joining us today

Andrew E. Budson, MD
Chief of Cognitive & Behavioral Neurology,
Associate Chief of Staff for Education, and
Director of the Center for Translational Cognitive Neuroscience,
Veterans Affairs (VA) Boston Healthcare System

AFFILIATIONS: Associate Director for Research, Boston University Alzheimer's Disease Center;
Professor of Neurology, Boston University School of Medicine;
Lecturer in Neurology, Harvard Medical School; and
Medical Director, Boston Center for Memory (Newton, MA)

Agenda

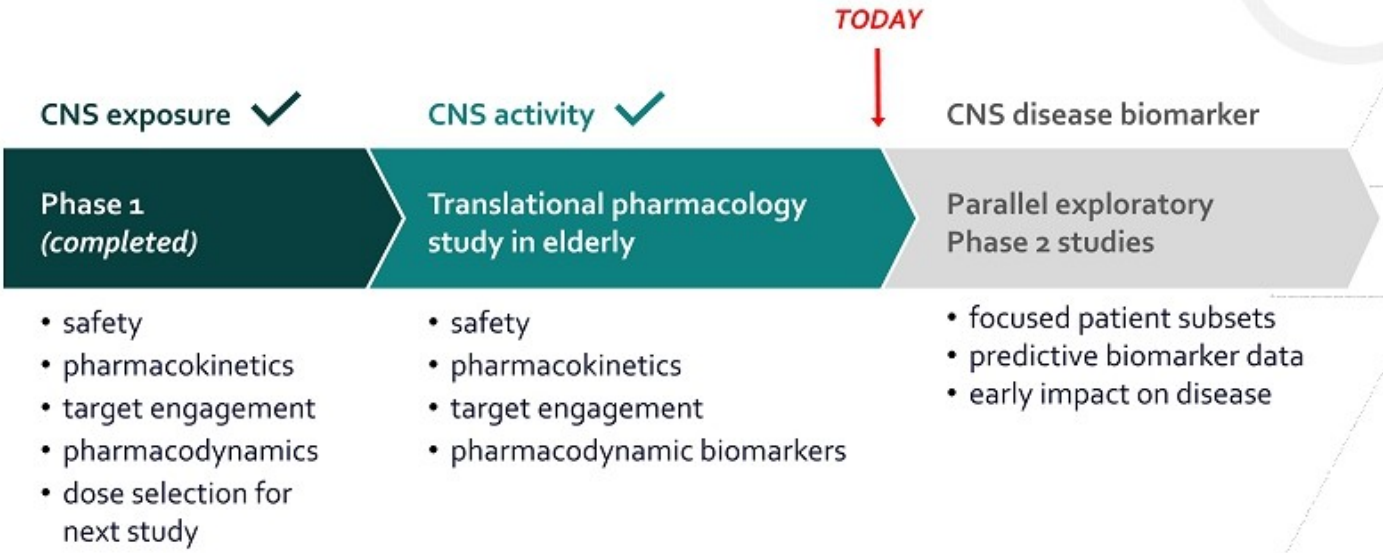
1 Introduction and overview

2 Translational pharmacology results

3 Strategic focus

4 Q&A

Biomarker-driven IW-6463 early clinical development strategy



IW-6463 translational pharmacology study results support advancement

In 24 healthy elderly subjects

- safe and well tolerated
- crosses the blood brain barrier (BBB) at 2-3X concentrations needed for pharmacodynamic effect[1]
- confirmed target engagement: blood pressure, cGMP in CSF
- no effects observed on blood flow or metabolism
- clear improvements--in a short 15-day study---in brain neurophysiology and quantitative performance measures

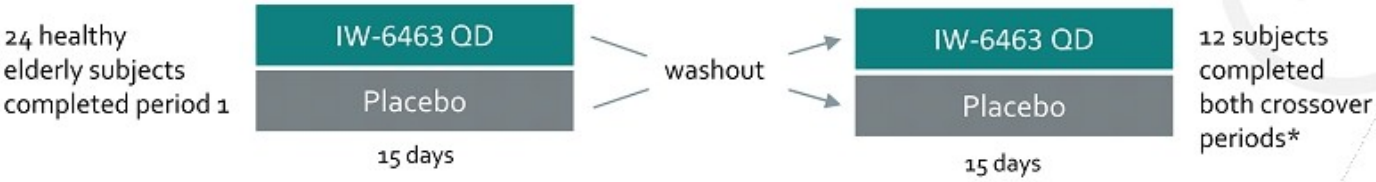
Cyclerion focus on serious CNS diseases

- continue with Phase 2 MELAS* trial activities
- refine and initiate Alzheimer's disease with vascular pathology (ADv) trial in 2021
- focused research and translational science efforts

* Mitochondrial Encephalomyopathy, Lactic acidosis, and Stroke-like episodes

1. Based on pharmacologically active exposures in preclinical studies

C6463-102 study design and objectives



OBJECTIVES TO ASSESS:

✓ *Safety* ✓ *PK* ✓ *Target engagement (cGMP)*

✓ *Activity in the CNS as measured in one or more of the following:*

Neuronal Function
- qEEG, ERP
- cognition and behavior measures

Cerebral Blood Flow
- MRI arterial spin labeling (ASL)

Cellular Bioenergetics
- brain metabolism via magnetic resonance spectroscopy (MRS)

Neuro- inflammation
- cytokines, adhesion molecules

*Period 2 participation was reduced due to Covid-19 related restrictions in the Netherlands

Activity in CNS: neuronal function

Neuronal Function	Encouraging impact on measures associated with aging/cognitive decline • significant increase in alpha power and increase in gamma • improvements in N200 ERP latencies (greater effects at older age) • Significantly shorter saccadic reaction times, trend increase in saccadic velocity
Cerebral Blood Flow	No significant effects observed in this healthy elderly study
Cellular Bioenergetics	No significant effects observed in this healthy elderly study. MELAS study to assess effects of IW-6463 on dysregulated metabolism in mitochondrial disease
Neuro Inflammation	Data analysis ongoing

Positive findings on three relevant CNS biomarkers

- qEEG: Alpha Power
- Event-Related Potential (ERP): N200
- Saccadic eye movement: reaction time and peak velocity

qEEG and basic frequencies

- resting state EEGs: subjects sit facing a featureless wall without moving and are recorded with eyes open and closed for 5 minutes each

EEG-power spectra- analyzing EEG signals in distinct frequency bands

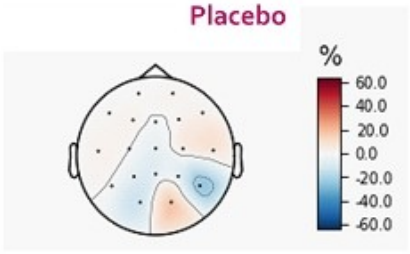
- delta- 0-4 Hz, associated with deep sleep
- theta- 4-8 Hz, waking/falling asleep, some association with cognition
- alpha- 8-14 Hz, passive wakefulness, associated with attention and cognitive processing, declines with aging and in neurodegenerative diseases
- beta- 14-30 Hz, alert, concentration
- gamma- 30-80 Hz, associated with higher cognitive function, declines with aging and in neurodegenerative diseases

BEACON BIOSIGNALS

IW-6463 significantly increases posterior alpha power

Day 15: % Change From Baseline

Placebo

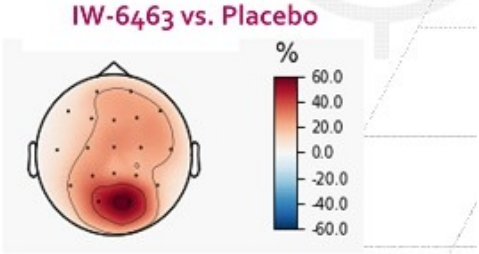


No effect of placebo on EEG alpha power

IW-6463

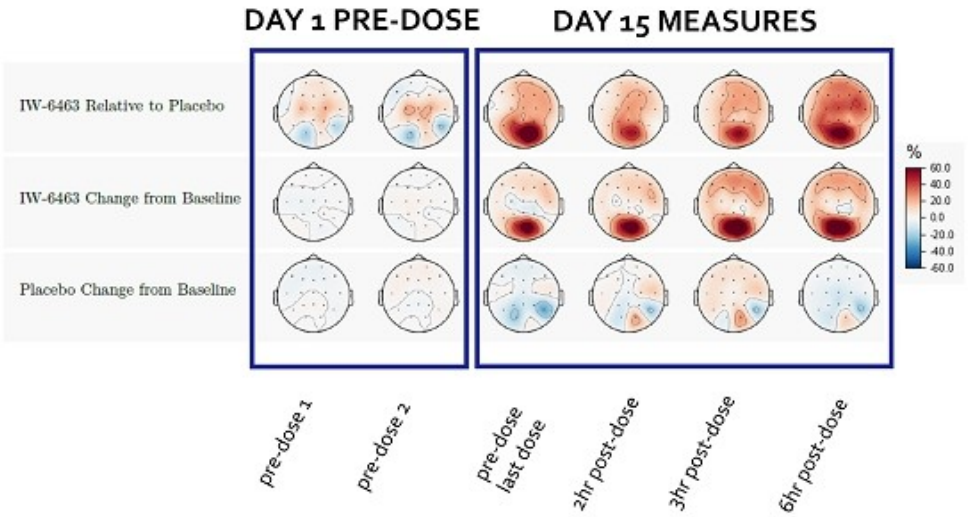
Significant increase in EEG alpha power with IW-6463

IW-6463 vs. Placebo



Significant increase in EEG alpha power with IW-6463 compared to placebo

IW-6463's consistent alpha power effects across repeat sessions indicate a stable and robust signal

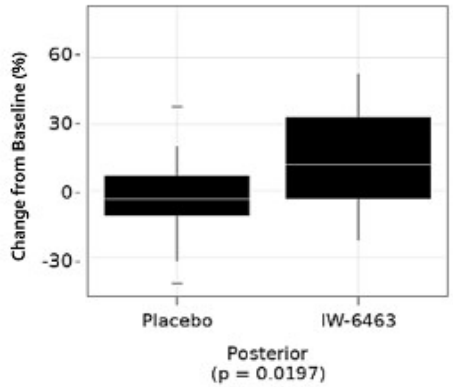


Effect represents up to a 2-year reversal of alpha power aging after 2 weeks of treatment

IW-6463 increases alpha power with consistent treatment responses

Statistically significant alpha power increases

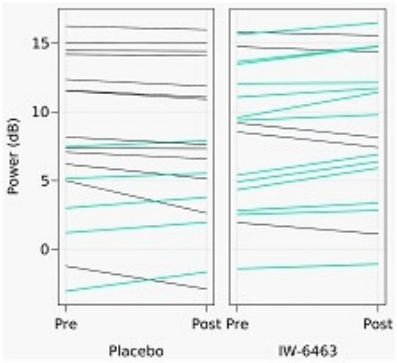
Change in Closed-Eye Alpha (8-12 Hz) Power



- substantial 17% treatment effect
- similar trends in anterior

Persistent, consistent treatment responses

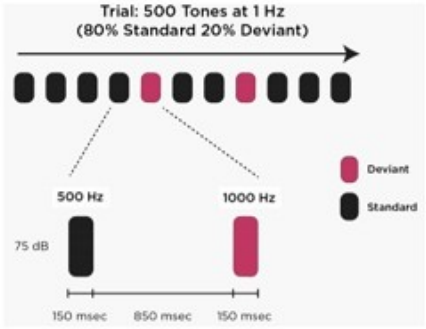
Posterior Closed-Eye Alpha (8-12 Hz) Power

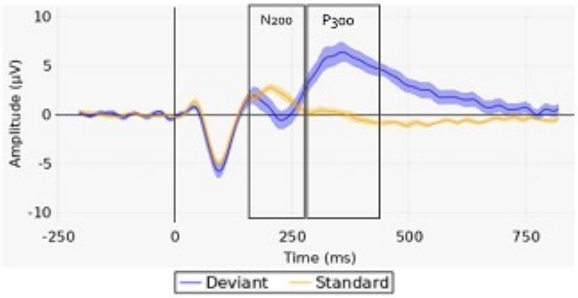


- 13/18 participants exhibit increasing alpha power with IW-6463, vs 5/18 with placebo[1]
- not driven by outliers

1. Includes all subjects. For IW-6463 and pbo each: n=12 for period 1, n=6 for period 2

Event related potential (ERP)

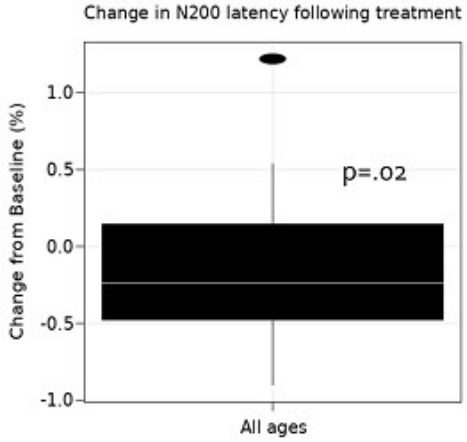


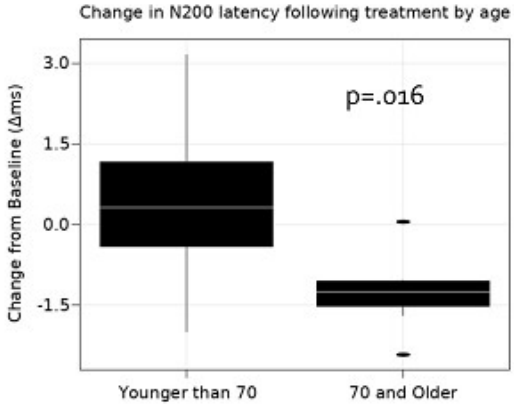


- latency and amplitude of waveforms impacted in aging and neurodegenerative diseases with cognitive impairment (and other CNS diseases)
- participants wear EEG cap and headphones, auditory tones presented with instruction to press a response-button when they hear infrequent/deviant tones
- key ERP waveforms
  - **N200**: associated with stimulus identification and distinction
  - **P300**: associated with cognitive processing capacity
- key parameters
  - **latency**: time after the stimulus to peak signal
  - **amplitude**: size of peak signal

BEACON BIOSIGNALS

IW-6463 improves N200 latency with a greater age-associated effect

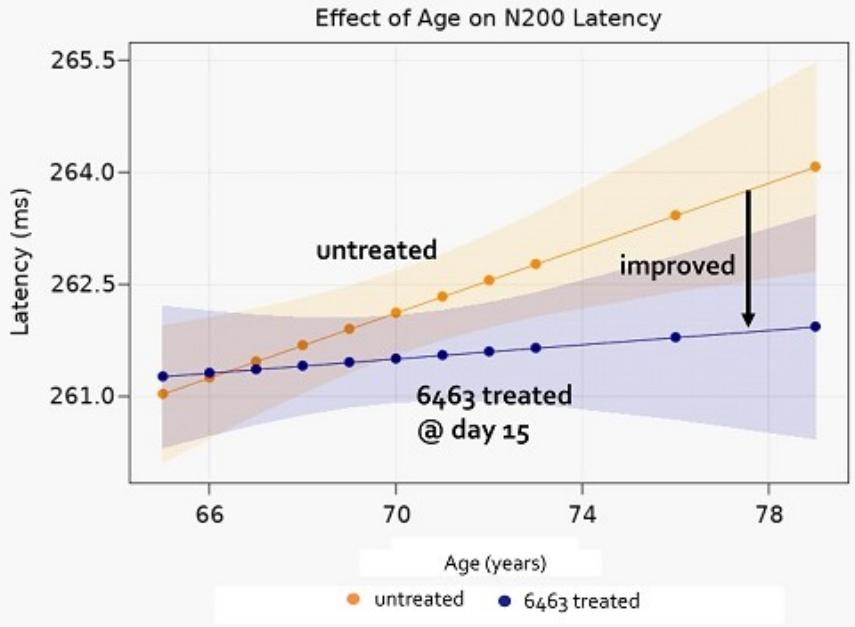




- significant latency reduction of N200 response to IW-6463 in participants treated for 15 days compared to those untreated.

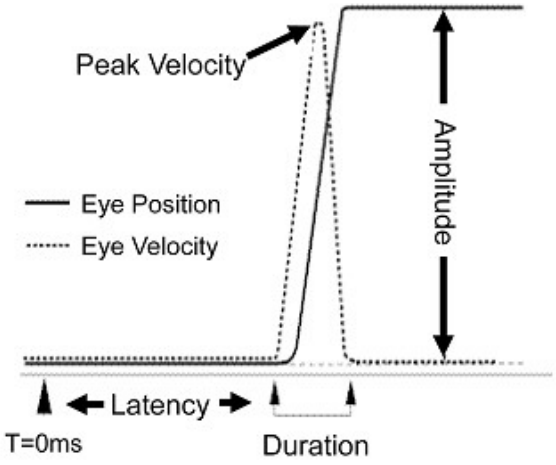
- N200 response to IW-6463 in participants older and younger than 70.
- latency response is significantly stronger with older age.
- narrowing of the variance in 70+ supports a drug effect.

IW-6463 improves N200 latency and effect increases with age



- overall significant decrease in N200 latencies observed on day 15 of IW-6463 treated participants compared to untreated participants (p<.02)
- the effects increased with age and were more pronounced in older subjects (p=.016)
- at the older ages this represents an approximately 10 years reversal of N200 latency aging after 2 weeks of treatment

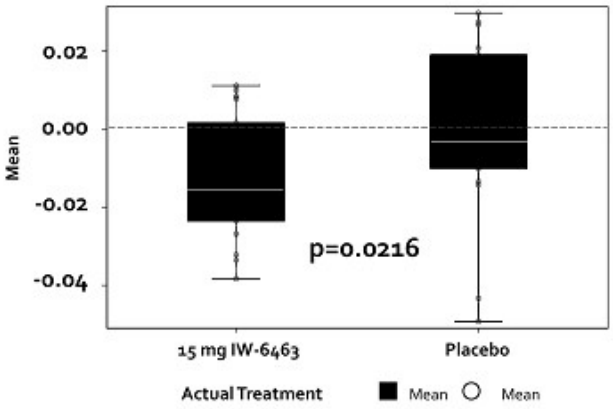
Saccadic eye movement, an objective measure of attention



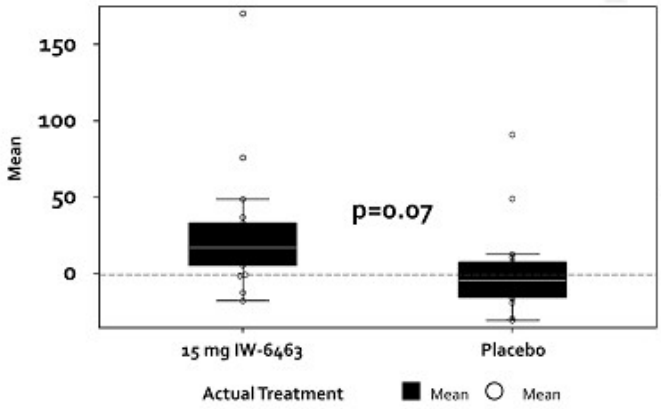
- short, fast, simultaneous tracking of both eyes in the same direction
- related brain areas include the frontal cortex, superior colliculus, substantia nigra, and amygdala
- may be reflective of attention/arousal and influenced by factors such as motivation, time on task, and task difficulty
- sensitive to sedation, fatigue, and CNS depressants/cognitive enhancers and is affected by aging

IW-6463 improves eye movement, an objective functional measure

Mean Change From Baseline in Saccadic Reaction Time (sec) on Day 15 Post-Dose (p=0.0216)



Mean Change From Baseline in Saccadic Peak Velocity (deg/sec) on Day 15 Post-Dose (p=0.07)



Saccadic Peak Velocity is the average of the post dose values on Day 15

- shorter saccadic reaction times along with increased saccadic velocities indicates that IW-6463 is also improving CNS functional performance in addition to CNS neurophysiology
- cognitive enhancers (e.g., modafinil) are also known to positively impact measures of saccadic function

Advancing IW-6463 in Phase 2 clinical trials

MELAS
Initiating Q4 2020
TL data mid 2021

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

Treatment (open label)
- once-daily IW-6463
- up to 20 adults (targeting 12 completers)

Enrichment strategy
- genetically confirmed, with MELAS neurological features
- elevated plasma lactate (disease biomarker)

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

ADv
Initiating 2021*

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

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)

Design to be refined based on TP data and ongoing analyses

* Supported partially by a grant from the Alzheimer's Association's Part the Cloud-Gates Partnership Grant Program, which provides Cyclerion with $2 million of funding over the next two years

Our commitment to CNS

Immediate Execution

- deepen understanding of biology and powerful pharmacology
- MELAS study
- ADv study
- strategic partnership

Current

Portfolio Advancement

Mid-term

Portfolio Growth

Long-term

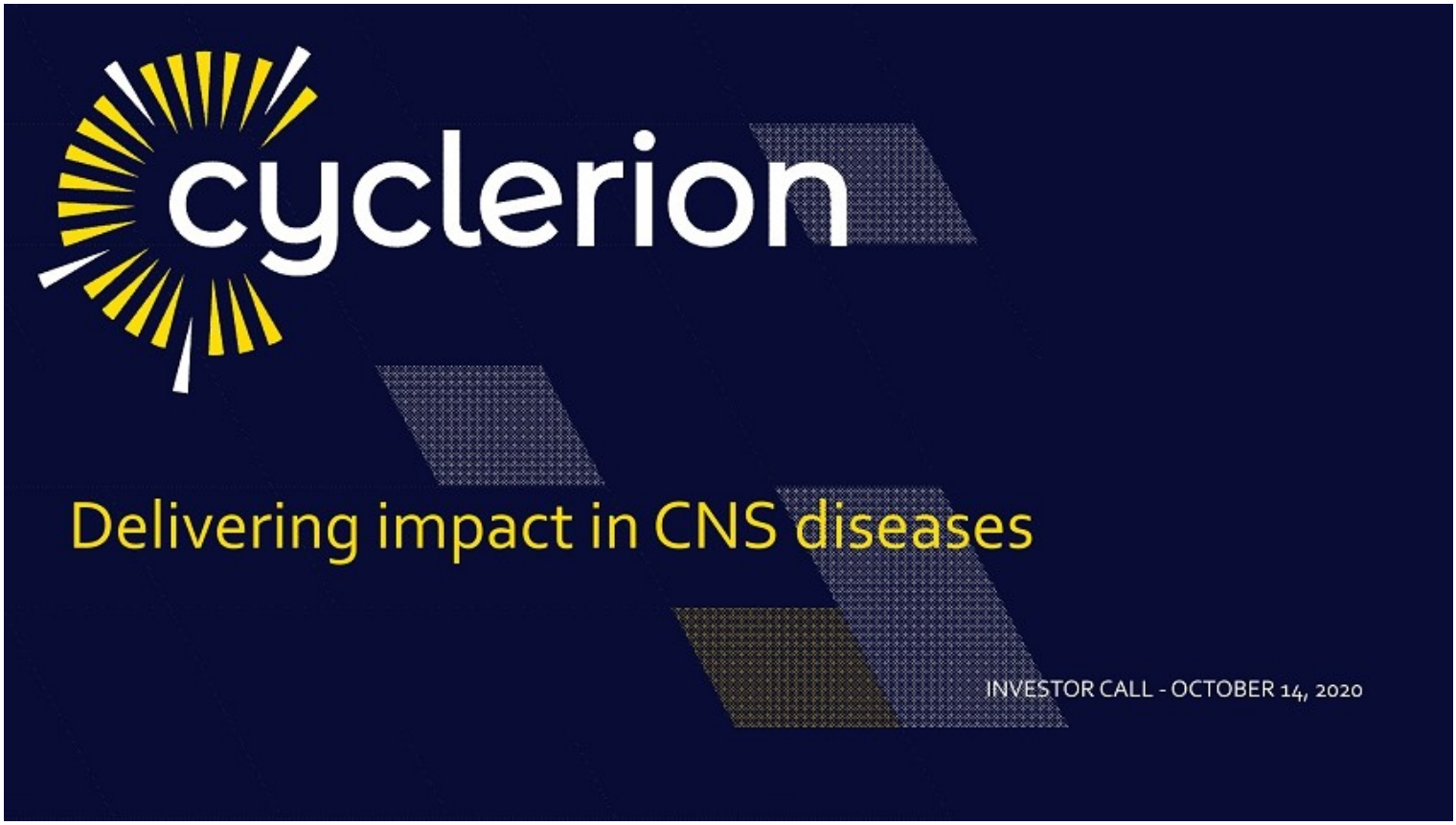
Now

Focused CNS company foundation

- capital allocation to CNS development and pipeline building
- pursuing a risk-reduced development approach
- organization size and capabilities for CNS distinctiveness

Thank you for joining

- ✓ *significant improvements observed in neurophysiological and objective performance measures*
- ✓ *moving forward in MELAS and ADv, informed by these data*
- ✓ *Phase 2 data in 2021*
- ✓ *CNS focus as a company*


cyclerion
Delivering impact in CNS diseases
INVESTOR CALL - OCTOBER 14, 2020