

A close-up photograph of a human eye. The iris is highly detailed and colorful, showing shades of blue, green, and yellow. The pupil is a bright blue. The eye is surrounded by dark, thick eyelashes. The background is a soft, out-of-focus light green.

Oculis

Rethinking Ophthalmology

OCS-01 | DIAMOND Trial - DME Phase 3 Stage 1 Results

May 22, 2023

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Agenda

01

Opening Remarks

Sylvia Cheung
Chief Financial Officer

02

OCS-01 Phase 3 DIAMOND
Stage 1

Riad Sherif, M.D.
Chief Executive Officer

03

Q&A Session
Moderated by:
Pravin Dugel, M.D., Director

David Boyer, M.D., Keck School of Medicine (USC); Co-PI for DIAMOND Study
Arshad Khanani, M.D., M.A., Sierra Eye Associates, University of Nevada; Co-PI for DIAMOND Study
Riad Sherif, M.D., Chief Executive Officer
Sylvia Cheung, Chief Financial Officer

04

Concluding Remarks

Riad Sherif, M.D.
Chief Executive Officer

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OCS-01 | DIAMOND Trial - DME Phase 3 Stage 1 Results

May 22, 2023

Ph 3 Stage 1: OCS-01 Eye Drops for DME Meets Primary Endpoint

Rapid and sustained improvements in vision and anatomic structure with robust statistical significance

Primary Objective Achieved

- Results validated loading and maintenance regimen to optimize OCS-01 efficacy potential in DME

Met Primary and Secondary Endpoints with Robust Statistical Significance

Primary Endpoint:

- Mean change in BCVA letter score at week 6:
 - **+7.2** with OCS-01 vs. **+3.1** with vehicle (**p = 0.007**)

Secondary Endpoints:

- Percentage with ≥ 3 -line (15 letter) gain in BCVA at week 6:
 - **25.3%** with OCS-01 vs. **9.8%** with vehicle (**p = 0.015**)
- Mean change in CST at week 6:
 - **-63.6 μm** with OCS-01 vs. **+5.5 μm** with vehicle (**p < 0.0001**)

All differences maintained or improved at week 12

No unexpected safety findings

Next Step: Phase 3 Stage 2

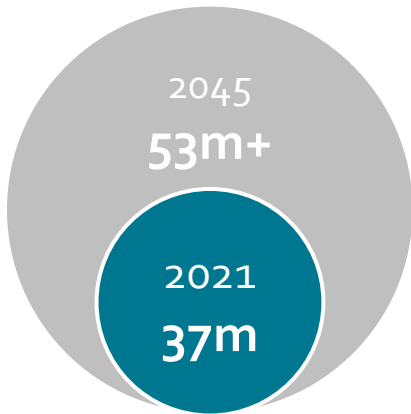
- Two global, 52-week Phase 3 trials commencing in 2H 2023; N = 350-450 for each
- Designed to support NDA for OCS-01 as treatment for DME

DME is a Large and Growing Market with Critical Unmet Needs

OCS-01 Eye Drops: potential to expand pool of treated DME patients & improve outcomes for those currently treated

Growing DME patient population size⁽¹⁾

Global DME Patients
(7% of diabetics⁽²⁾)



A leading cause of new cases of blindness in US adults⁽³⁾

Current therapies sold ~\$3B in 2019 with rapid growth⁽⁴⁾

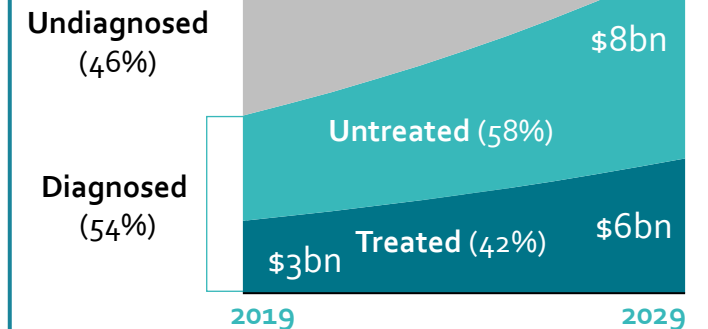
Only invasive treatments approved



High burden of treatment
Low patient compliance⁽⁵⁾

Late start of treatment

DME – Treatment rate and market size in G7 countries (US, EU5 and JP)⁽⁴⁾



(1) International Diabetes Federation – diabetesatlas.org Estimated diabetes around the world in 2021: 537m, reaching 783m in 2045

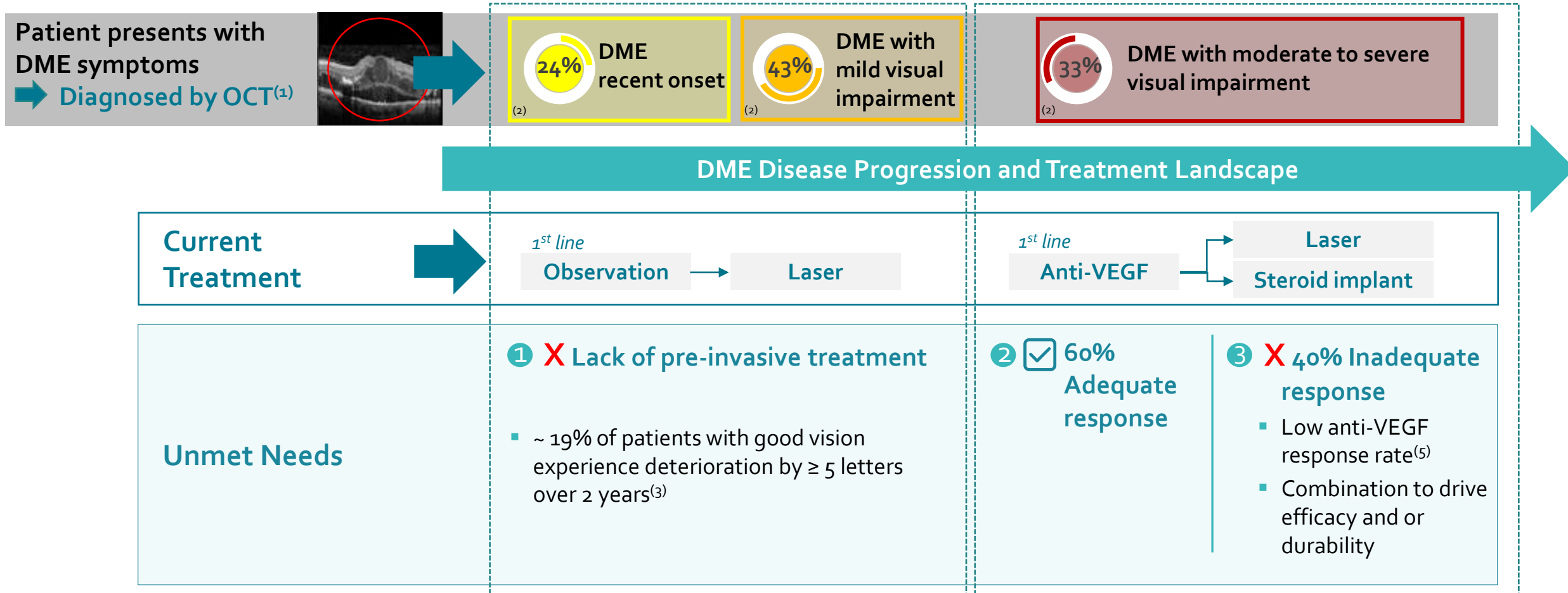
(2) Yau et al. Global Prevalence and Major Risk Factors of Diabetic Retinopathy, Diabetes Care 2012 Mar; 35(3): 556-564.

(3) <https://preventblindness.org/diabetic-macular-edema-dme/>

(4) DRG Diabetic Macular Edema / Diabetic Retinopathy Disease Landscape & Forecast 2020

(5) Berenberg and Kiss: "Real-World Utilization of Anti-VEGF Agents", Review of Ophthalmology, Feb 5, 2016

OCS-01 | Current DME Treatment Paradigm Leaves Two Patient Segments Undertreated and Losing Vision



Addressable US patient population: 1.2 million⁽⁴⁾⁽⁶⁾

(1) Optical coherence tomography (OCT) imaging.

(2) Baseline Demographics and Clinical Characteristics of Treatment-Naïve Patients with Diabetic Macular Edema Listed in the IRIS Registry (Table S1) www.aao.org

(3) Baker, Carl W., et al. "Effect of initial management with aflibercept vs laser photocoagulation vs observation on vision loss among patients with diabetic macular edema involving the center of the macula and good visual acuity: a randomized clinical trial." *Jama* 321.19 (2019): 1880-1894.

(4) Gonzalez 2016 Early and Long-term Responses to VEGF Therapy in DME: Analysis of protocol I data

(5) Kiss 2014 ; Berenger and Kiss, Feb. 2016, Real-world Utilization of VEGF agents (DME section), Review of Ophthalmology <https://www.reviewofophthalmology.com/article/realworld-utilization-of-antivegf-agents>

(6) Decision Resources Group: DME – DR Landscape Forecast – Disease Landscape Forecast 2020

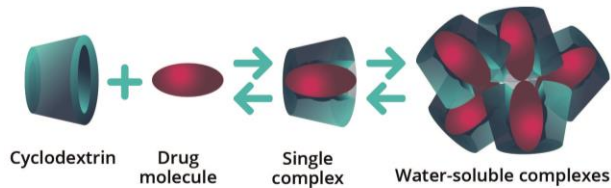
OCS-01 | First Eye Drop for DME – Results Consistent with Previous Trials

OCS-01 shown to be superior to vehicle on BCVA and CST endpoints in Phase 2 trial

Unique product candidate with clinically validated MOA

OCS-01: High-concentration Optireach® formulation of dexamethasone (15mg/ml)

OPTIREACH® Formulation Technology



Ozurdex®, an IVT implant of dexamethasone, is FDA-approved for DME and annualizing at \$460M and 7% growth¹

Positive results in exploratory and Phase 2 studies in DME

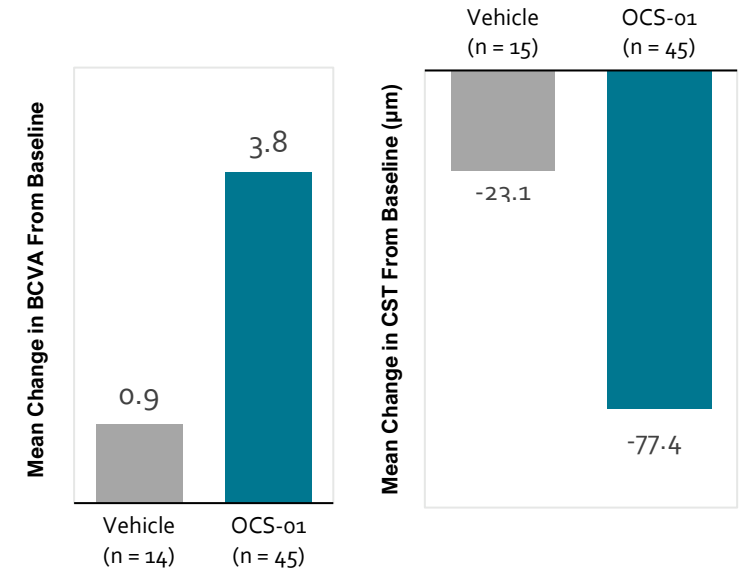
DME Exploratory 1²
19 pts Tanito Study
successfully completed

DME Exploratory 2³
22 pts Ohira Study
successfully completed

DME Phase 2⁴ 144 pts
Randomized & double-
masked successfully
completed

Positive Phase 2 results⁵

Change in BCVA & CST (Same Patient Population as Ph3 Diamond Trial)



Phase 2 results supported successful End of Phase 2 Meeting

1. Abbvie Q1 2023 earnings report
 2. Investigator-initiated, open-label, single-center study. Tanito M, et al. Invest Ophthalmol Vis Sci. 2011;52:7944-7948
 3. Ohira A, et al. Acta Ophthalmologica. 2015;93:610-615. Ohira A, et al. Acta Ophthalmologica. 2015;93:610-615.
 4. DME Phase 2: Note: Data presented at Angiogenesis, Exudation and Degeneration, 2020 by KOL (Dugel P.)
 5. Dugel PU. The Oculis OCS-01 phase 1/2 study: an effective topical therapeutic for DME. Presented at: Angiogenesis, Exudation, and Degeneration 2020; Feb. 8, 2020; Miami
 Central macular thickness (CMT); Best-corrected visual acuity (BCVA)
 visual acuity (BCVA); Dugel PU. The Oculis OCS-01 phase 1/2 study: an effective topical therapeutic for DME. Presented at: Angiogenesis, Exudation, and Degeneration 2020; Feb. 8, 2020; Miami.

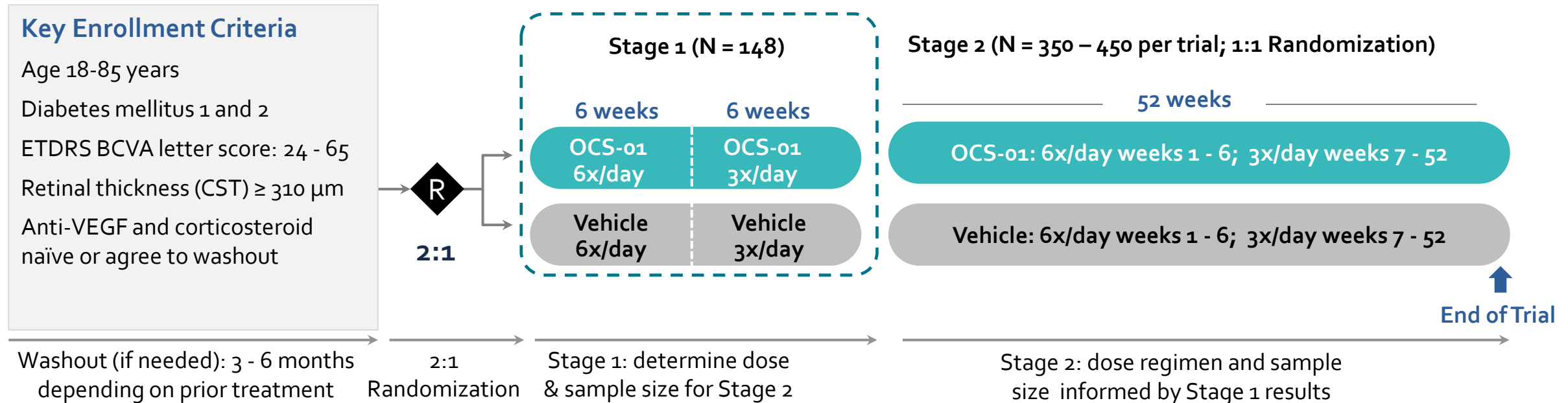
Diamond

DIAbetic Macular edema patients ON a Drop

Stage 1 Trial Results

OCS-01 | Phase 3 Program in DME Patients

Loading dose regimen & enriched population increase probability of success



Stage 1: Assess if loading dose optimizes efficacy

- 1^o endpoint:** Change in BCVA ETDRS letter score at wk 6
- 2^o endpoint:** % with a ≥ 3 -line (15 letters) gain in BCVA at wk 6
- 2^o endpoint:** Change in CST as measured by SD-OCT⁽¹⁾ at wk 6
- 2^o endpoint:** Change in BCVA at wk 12

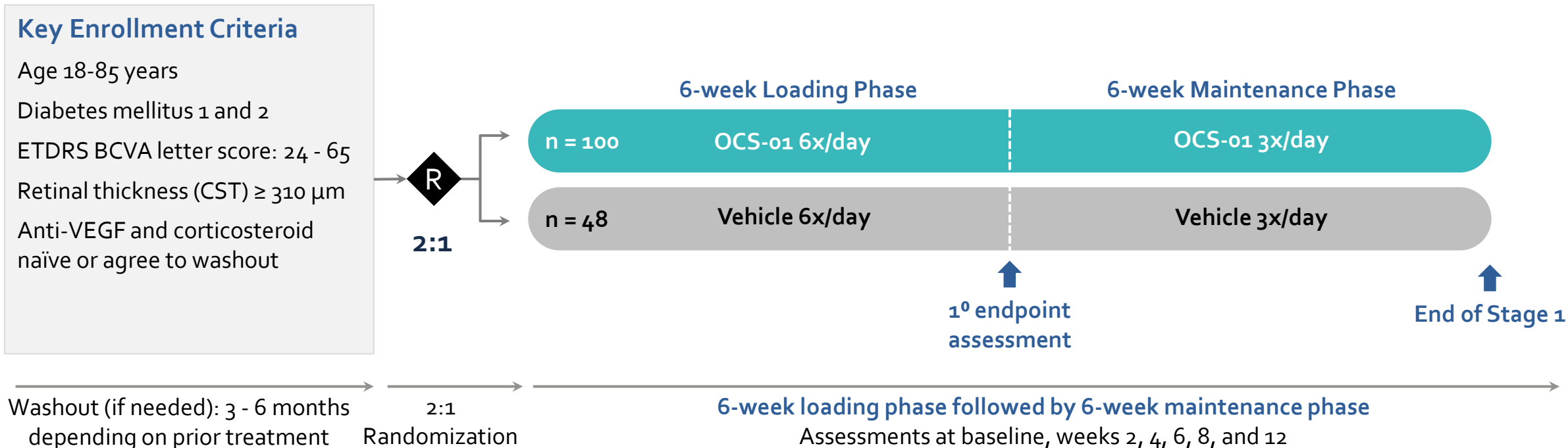
Stage 2: Two Phase 3's to support NDA filing for DME

- 1^o endpoint:** BCVA at wk 52
- Key 2^o endpoint:** ≥ 3 -line (15 letters) at wk 52
- 2^o endpoint:** CST at wk 52

(1) Spectral Domain Optical Coherence Tomography

OCS-01 | Phase 3 in DME Patients – Stage 1

Loading dose regimen & enriched population increase probability of success



Stage 1 : Assess if loading dose optimizes efficacy

1^o endpoint: Change in BCVA ETDRS letter score at wk 6

2^o endpoint: % with a ≥ 3 -line (15 letters) gain in BCVA at wk 6/12

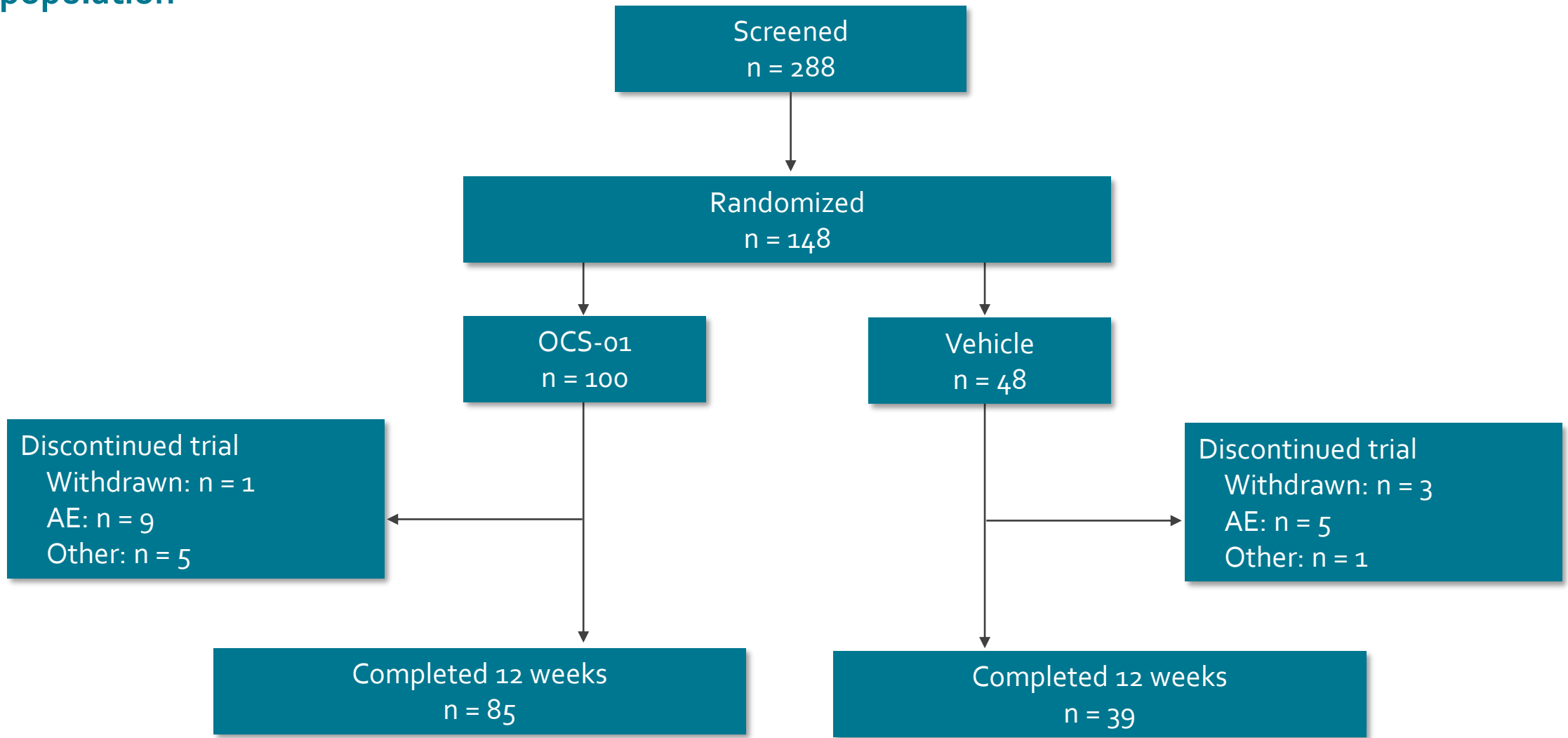
2^o endpoint: Change in CST as measured by SD-OCT⁽¹⁾ at wk 6/12

2^o endpoint: Change in BCVA at wk 12

(1) Spectral Domain Optical Coherence Tomography

Patient Disposition

ITT population



AE, adverse event; ITT, intention-to-treat.
Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

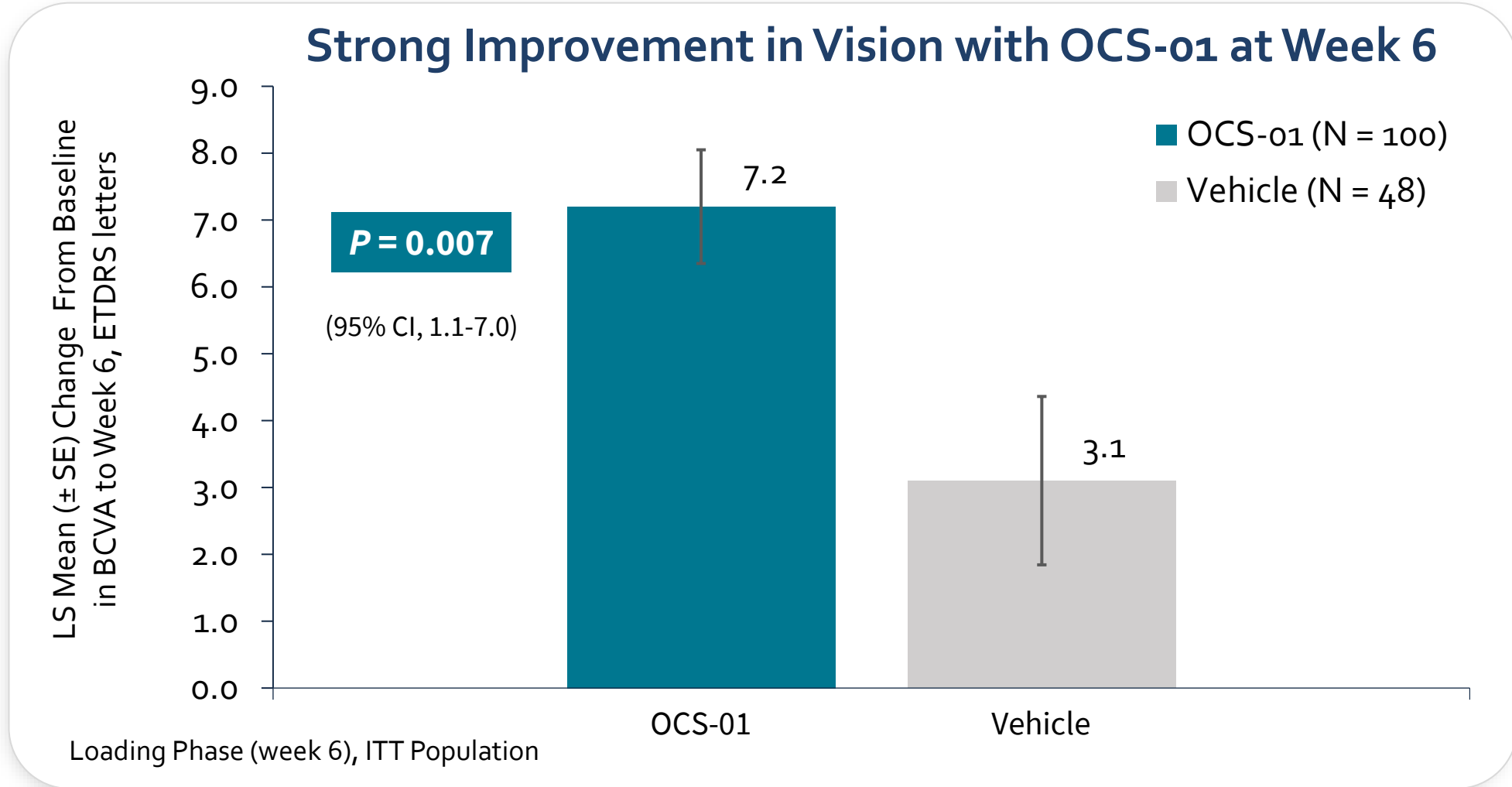
Demographics: Well-balanced Between Arms

Parameter	OCS-01 (n = 100)	Vehicle (n = 48)
Age, mean (SD), years	61.9 (9.0)	63.9 (7.3)
Male, n (%)	53 (53.0)	26 (54.2)
Duration of DME, mean (SD), years	2.0 (2.6)	1.9 (2.7)
BCVA, mean (SD), ETDRS letter score	57.5 (9.3)	58.3 (7.5)
CST, mean (SD), μm	453.0 (131.8)	445.3 (112.5)
IOP ⁽¹⁾ , mean (SD), mmHg	15.3 (3.1)	14.7 (3.0)

(1) Intraocular pressure. Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

Primary Endpoint Achieved with Robust Statistical Significance

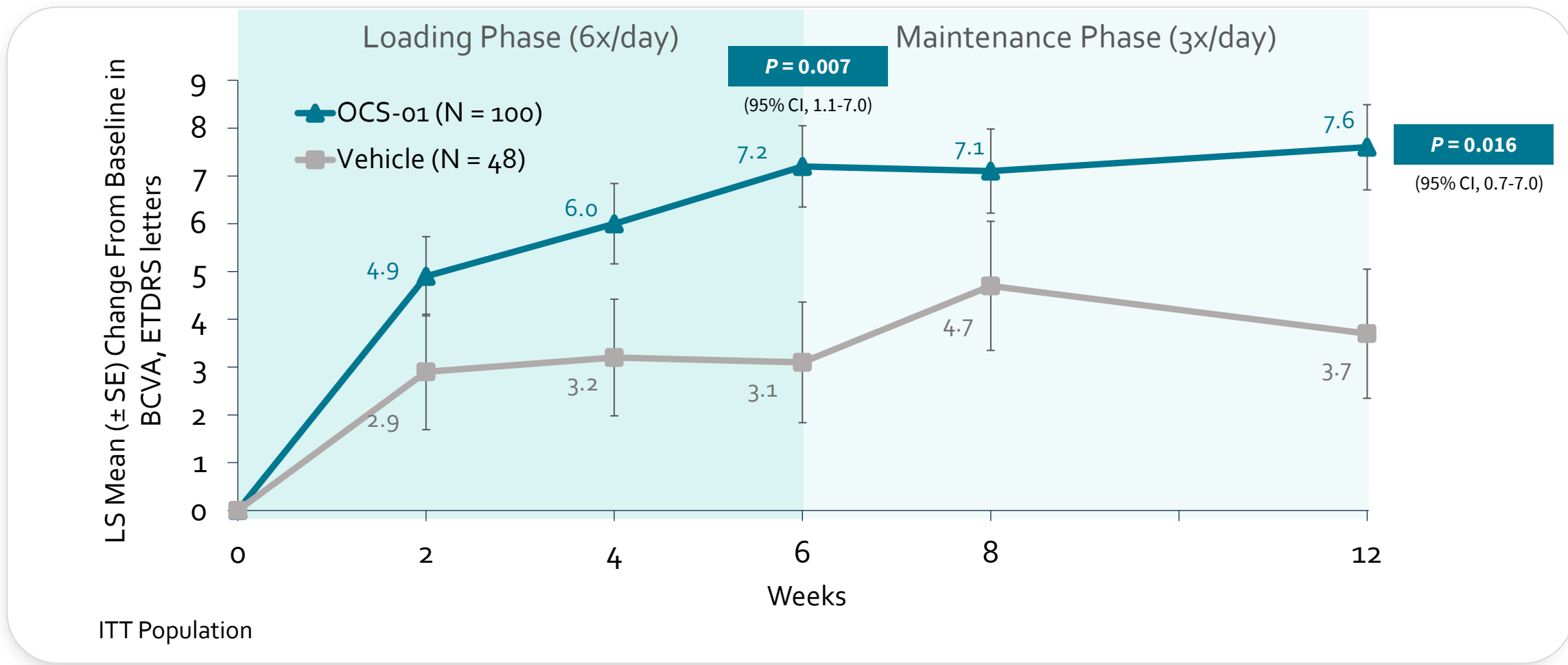
Rapid improvement in vision with OCS-01 treatment, as assessed by BCVA



BCVA, best corrected visual acuity; CI, confidence interval; ETDRS, Early Treatment Diabetic Retinopathy Study; ITT, intention-to-treat; LS, least squares; SE, standard error. Multiple imputations for missing data. Imputation rules are applied based on a pattern-mixed model approach. Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

Improvement in Vision with OCS-01 Sustained to Week 12

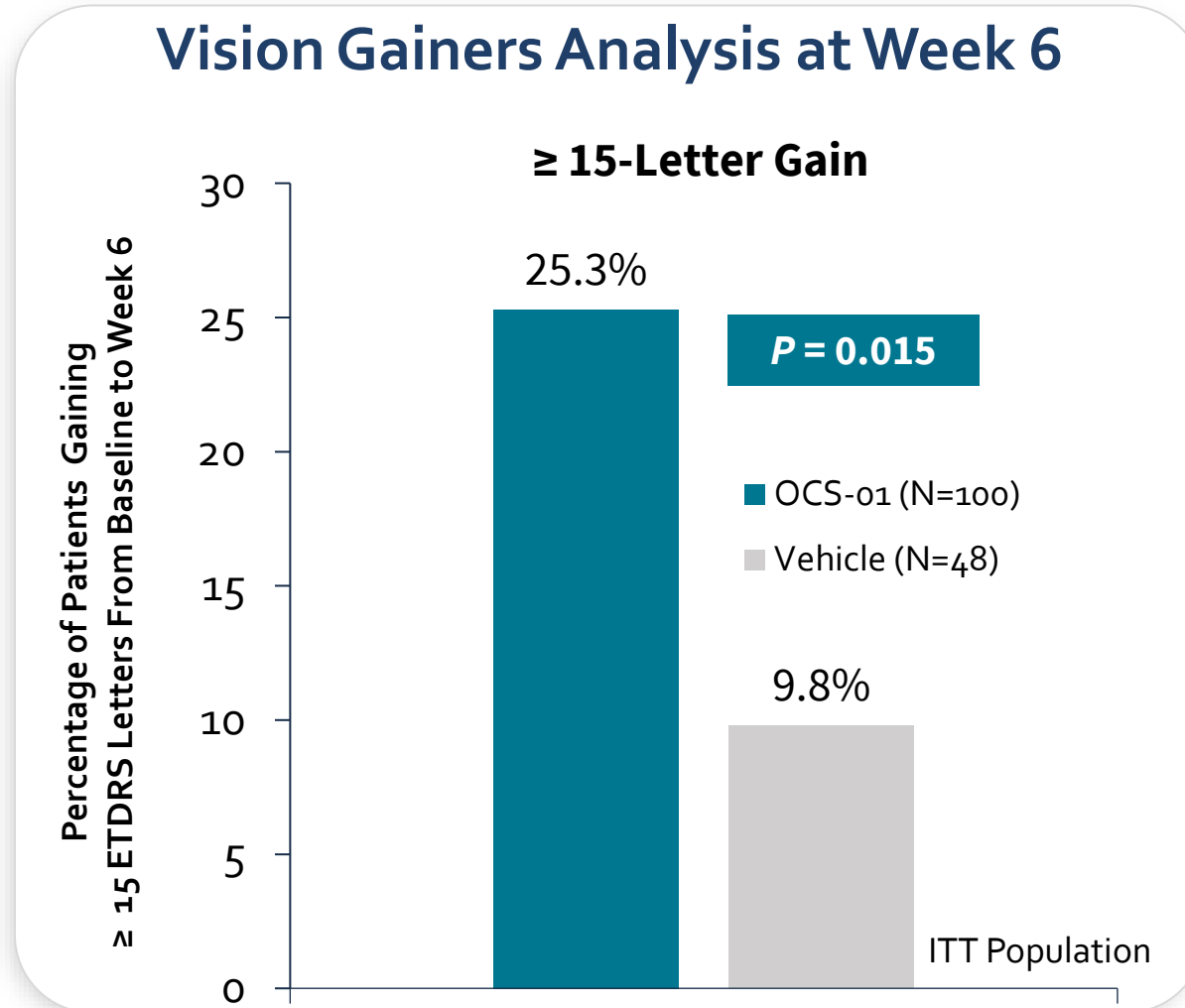
Rapid improvement in BCVA with loading dose regimen sustained with maintenance regimen



BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; ITT, intention-to-treat; SD, standard deviation; SE, standard error. Multiple imputations for missing data. Imputation rules are applied based on a pattern-mixed model approach. Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

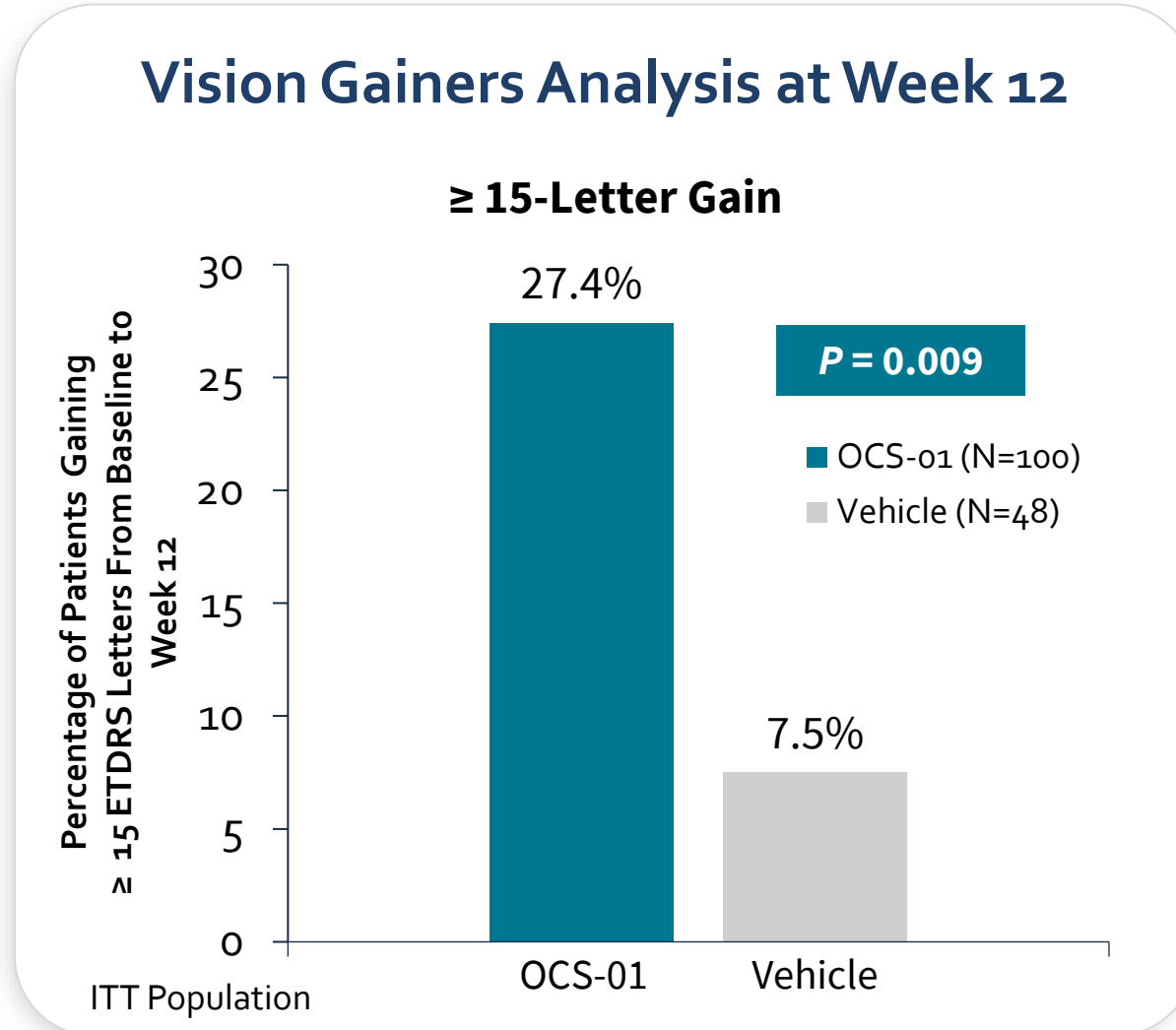
25% of OCS-01 Patients Achieve ≥ 3 Line Improvement in BCVA at Week 6

3-line (15 letter) improvement in BCVA deemed highly clinically relevant



ETDRS, Early Treatment Diabetic Retinopathy Study; ITT, intention-to-treat.
Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

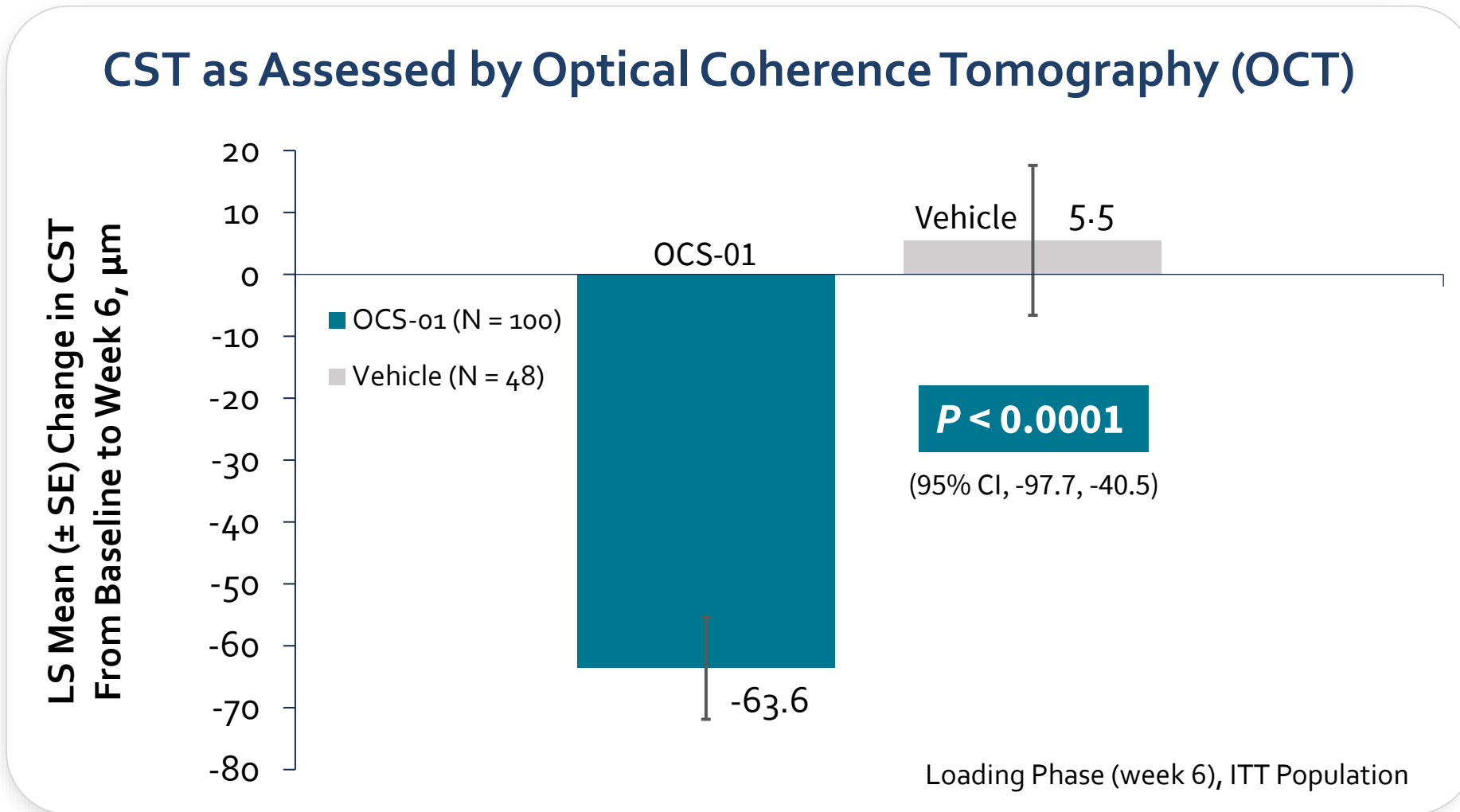
27% of OCS-01 Patients with ≥ 3 -Line Improvement in BCVA at Week 12
3-line (15 letter) improvement in BCVA deemed highly clinically relevant



ETDRS, Early Treatment Diabetic Retinopathy Study; ITT, intention-to-treat.
Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

63.6 μm Reduction in CST Achieved with OCS-01 at Week 6

Central subfield thickness (CST) is a key metric used by physicians to manage DME patients

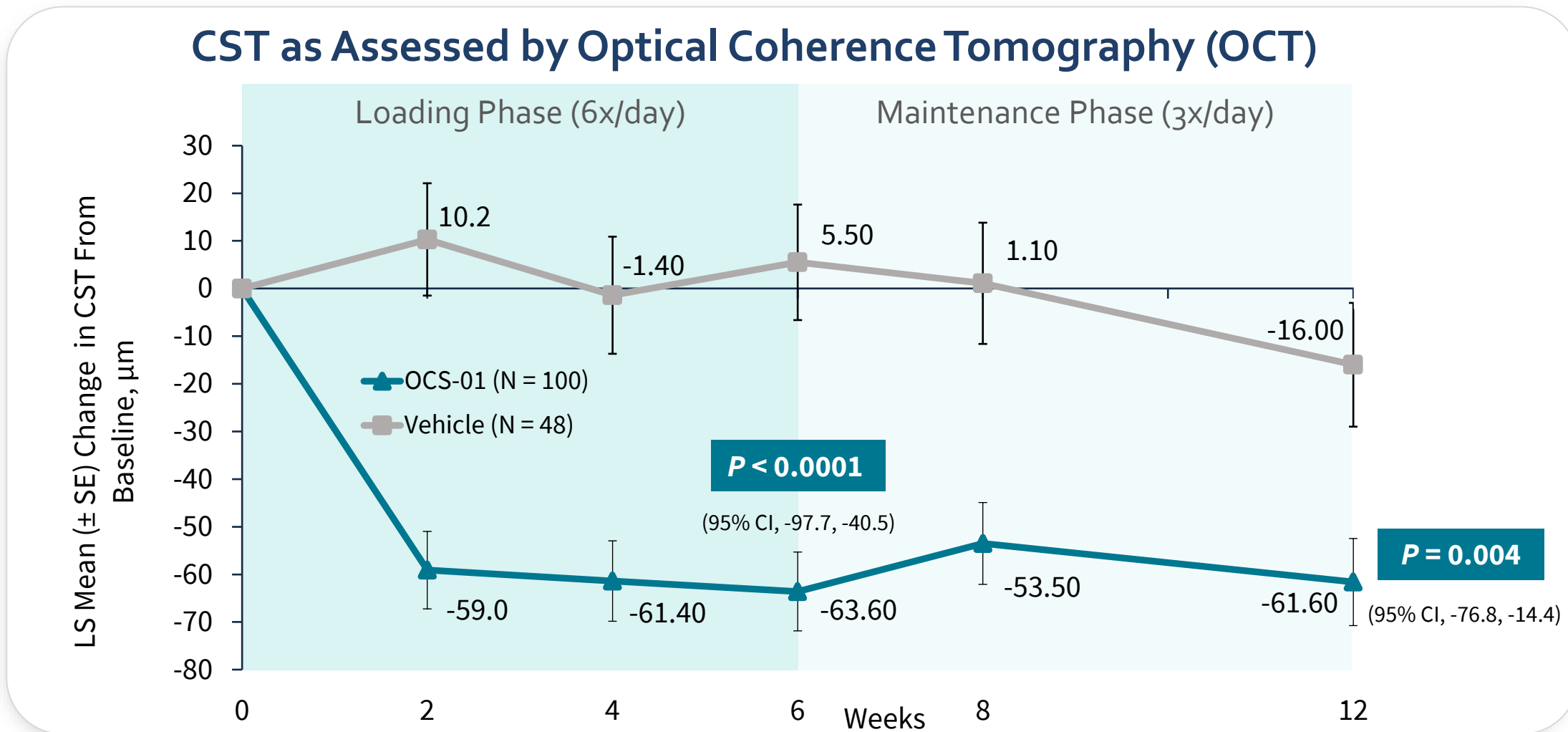


CI, confidence interval; CST, central subfield thickness; ITT, intention-to-treat; LS, least squares; SE, standard error. Multiple imputations for missing data. Imputation rules are applied based on a pattern-mixed model approach.

Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

Reduction in CST Achieved with OCS-01 Sustained to Week 12

Rapid improvements in CST with loading dose regimen sustained with maintenance regimen



BCVA, best corrected visual acuity; CI, confidence interval; ETDRS, Early Treatment Diabetic Retinopathy Study; ITT, intention-to-treat; LS, least squares; SE, standard error. imputations for missing data. Imputation rules are applied based on a pattern-mixed model approach. Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

No Unexpected Safety Findings

Treatment Emergent Adverse Events

	OCS-01 (N = 100) n (%)	Vehicle (N = 48) n (%)
Any TEAE	70 (70.0)	30 (62.5)
Diabetic retinal edema	10 (10.0)	9 (18.8)
Intraocular pressure increased	14 (14.0)	1 (2.1)
Hypertension	10 (10.0)	1 (2.1)
Ocular hypertension	8 (8.0)	0
Macular edema	2 (2.0)	4 (8.3)
COVID-19	2 (2.0)	2 (4.2)
Dry eye	3 (3.0)	1 (2.1)
Diabetes mellitus	3 (3.0)	0
Dizziness	3 (3.0)	0
Dysgeusia	3 (3.0)	0
Nasopharyngitis	2 (2.0)	1 (2.1)
Type 2 diabetes	2 (2.0)	1 (2.1)
Visual acuity reduced	1 (1.0)	2 (4.2)
Vitreous haemorrhage	2 (2.0)	1 (2.1)
Arthralgia	2 (2.0)	0
Blood glucose increased	2 (2.0)	0

Treatment Emergent Serious Adverse Events (SAE)

	OCS-01 (N = 100) n (%)	Vehicle (N = 48) n (%)
Any ocular SAE	1 (1.0)	0
Vitreous haemorrhage	1 (1.0)	0
Any non-ocular SAE	4 (4.0)	3 (6.3)
Death	1 (1.0)	0

- None of the SAEs reported were deemed related to study drug
- No evidence of cataract formation up to 12 weeks

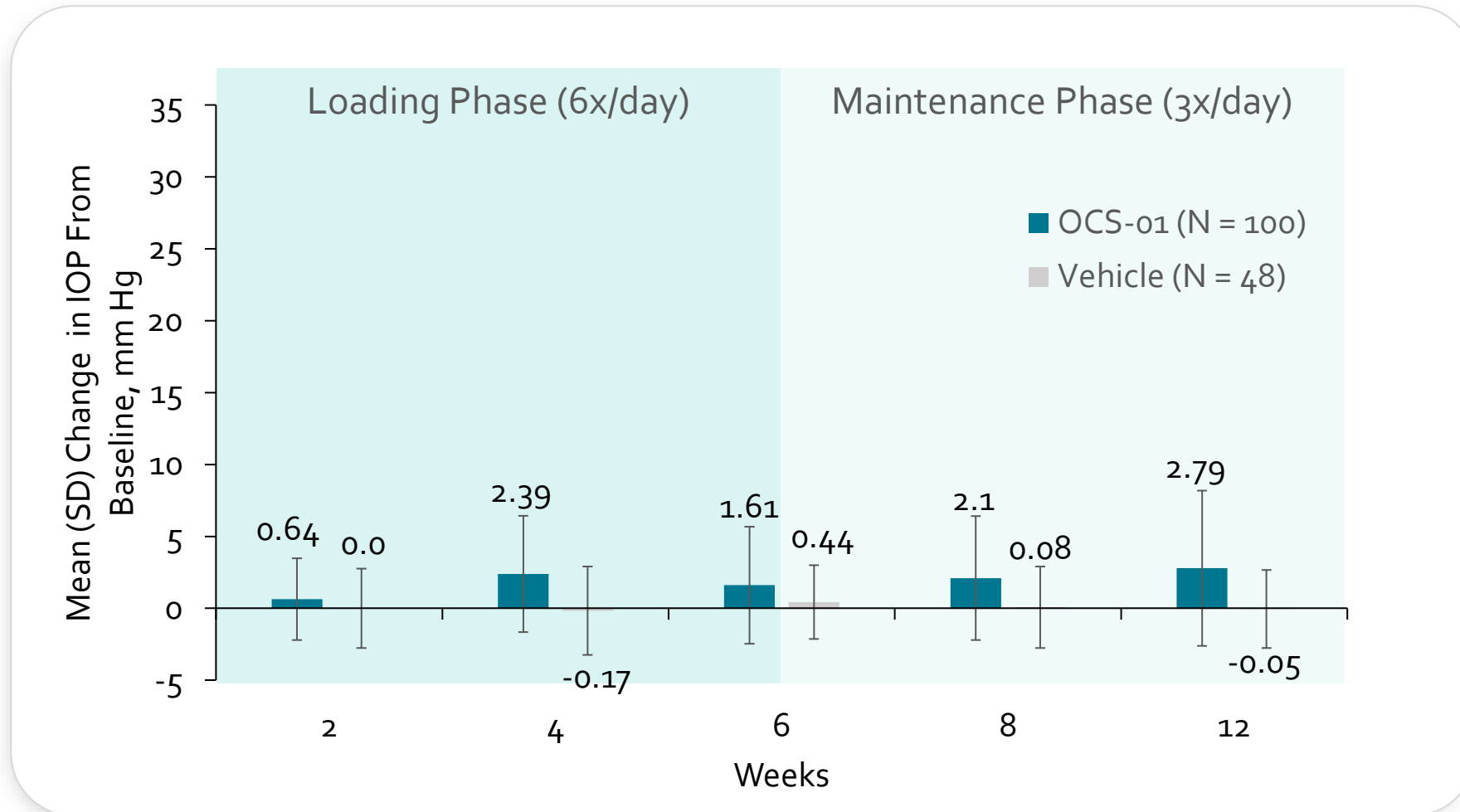
TEAE, treatment-emergent adverse event.

Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

IOP Increase Consistent with Literature

	OCS-01 n=100 n (%)	Vehicle n=48 n (%)
Any IOP related AE	22/100 (22.0)	1/48 (2.1)
10 mmHg IOP change from baseline at any visit	16/97 (16.5)	0/47 (0)
Higher than 25 mmHg IOP at any visit	19/97 (19.6)	1/47 (2.1)
Higher than 35 mmHg IOP at any visit	1/97 (1.0)	0/47 (0)
IOP lowering medications administered for AE	11/22	1/1

Minimal Mean IOP Increase is Similar Across Loading and Maintenance



IOP, intraocular pressure. Mean (SD) baseline IOP: OCS-01, 15.3 (3.1) mm Hg; vehicle, 14.7 (3.0) mm Hg. Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

OCS-01 Met Primary and Secondary Endpoints in Ph 3 Stage 1

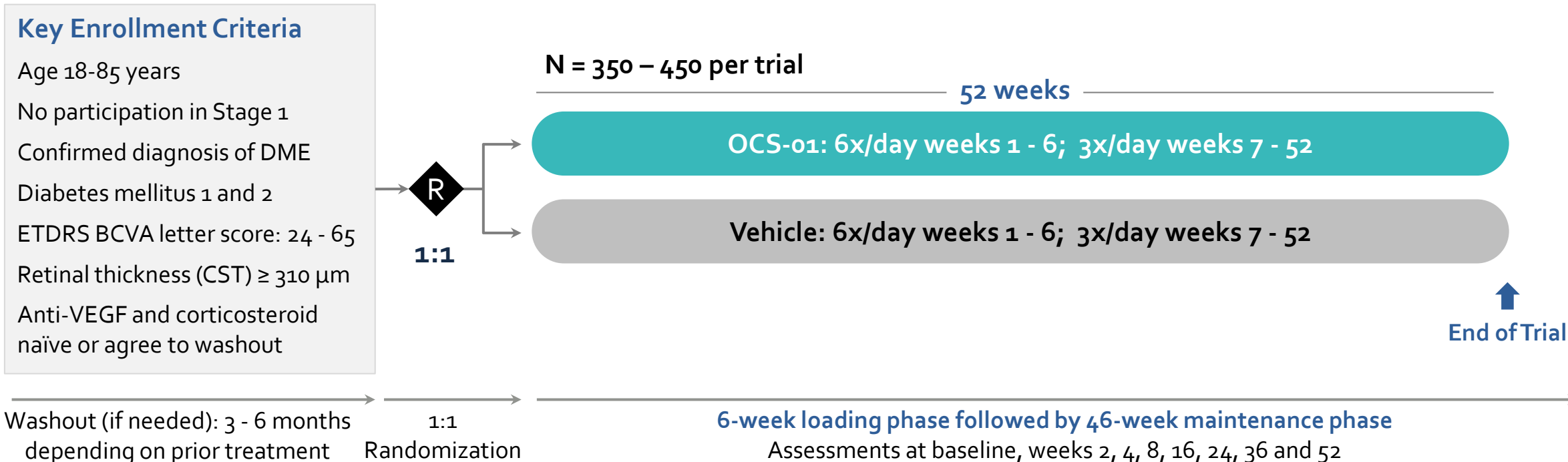
	OCS-01 (n = 100)	Vehicle (n = 48)	Vehicle Adjusted Change	P Value
Mean Change in BCVA at Week 6	+7.2 letters	+3.1 letters	+4.1 letters	0.007
Mean Change in BCVA at Week 12	+7.6 letters	+3.7 letters	+3.9 letters	0.016
% with ≥ 3-line gain in BCVA at Week 6	25.3%	9.8%	15.5%	0.015
% with ≥ 3-line gain in BCVA at Week 12	27.4%	7.5%	19.9%	0.009
Mean Change in CST at Week 6	-63.6 μm	+5.5 μm	-69.1 μm	< 0.0001
Mean Change in CST at Week 12	-61.6 μm	-16.0 μm	-45.6 μm	0.004

No unexpected safety findings observed

Next Step: Continuation of Ph 3 program to support NDA filing for treatment of DME

OCS-01 | Next Step: Phase 3 DME Trial Stage 2

Two global Ph 3 trials (N = 350-450 each) to support NDA filing for treatment of DME



Endpoints

- 1^o endpoint:** Change in BCVA ETDRS letter score at wk 52
- Key 2^o endpoint:** % with ≥ 3 -line gain in BCVA at wk 52
- 2^o endpoint:** Change in CST as measured by SD-OCT⁽¹⁾ at wk 52

Anticipated Timelines

Stage 2 Start: 2H 2023

(1) Spectral Domain Optical Coherence Tomography



Summary

OCS-01 Ph 3 Stage 1 Recap

- **Trial objectives met:** Results validated loading and maintenance regimen to optimize OCS-01 efficacy potential in DME with **robust statistical significance**
- OCS-01 met **all Functional and Clinical benefit endpoints** in a robust, statistically superior manner (in 3-month trial):
 - Improvement of visual acuity (**Functional Endpoint**)
 - Increase in proportion of patients with a 3-line or greater gain (**Clinical Benefit Endpoint**)
 - Reduction in macular edema as measured by OCT imaging (**Pharmacodynamic Endpoint**)
- No unexpected safety findings observed

Next Step: Commence Stage 2 of Ph 3 program to support NDA filing of OCS-01 for DME treatment

Innovative, Diversified and Late-stage Pipeline



Product Candidate(s)	Investigational Indication(s)	Pre-clinical	Phase 1	Phase 2	Phase 3	Next Catalysts	
						2023	2024
OCS-01 Optireach® technology	DIABETIC MACULAR EDEMA					1 ^o endpt. met Stage 1	
	INFLAMMATION AND PAIN FOLLOWING OCULAR SURGERY					Ph3 readout	NDA
	CYSTOID MACULAR EDEMA						PoC readout
OCS-02 Anti TNF	DRY EYE DISEASE						Ph2b readout
	UVEITIS						Ph2b readout
OCS-05 SGK2 Activator	ACUTE OPTIC NEURITIS						PoC readout
	GLAUCOMA						
	GEOGRAPHIC ATROPHY						
	DIABETIC RETINOPATHY						
	NEUROTROPHIC KERATITIS						
OCS-03	CORNEAL NV, PTERYGIUM						
OCS-04	CORNEAL TRANSPLANT						
(Undisclosed)	Wet-AMD ⁽¹⁾ , RVO ⁽²⁾ , DR ⁽³⁾						

OCS-01 is based on the OPTIREACH® technology, OCS-02 is a single chain antibody fragment (ScFv) against TNFα and OCS-05 is a SGK-2 activator peptidomimetic small molecule with novel MoA targeting the activation of the trophic factor pathways.

(1) Age-related macular degeneration (AMD).

(2) Retinal Vein Occlusion (RVO).

(3) Diabetic Retinopathy (DR).

Uniquely Positioned to Build Significant Value

Targeting critical unmet needs in 3 major ophthalmology segments

- **OCS-01: 1st Eye drop for Diabetic Macular Edema (DME) in Ph3**
- **OCS-02: 1st Biologic eye drop for Dry Eye Disease (DED) in Ph2b**
(upside potential from biomarker-driven precision medicine approach)
- **OCS-05: 1st Neuroprotective agent for neuro-retina treatments in PoC**

Near-term value inflection points expected

2023

2024

- ✓ OCS-01 DME Phase 3 (Stage 1) readout
- OCS-01 Ocular Surgery Phase 3 readout
- OCS-01 Ocular Surgery NDA
- OCS-01 CME⁽¹⁾ PoC readout
- OCS-02 DED Phase 2b readout
- OCS-02 Uveitis Phase 2b readout
- OCS-05 AON⁽²⁾ PoC readout

(1) Cystoid Macular Edema (CME).

(2) Acute Optic Neuritis (AON).



Our Purpose

To drive innovation to save sight and improve eye care

Q&A Session

Moderated by:

Dr. Pravin Dugel

Director, Oculis Holding AG

