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

FORM 6-K

**REPORT OF FOREIGN ISSUER
PURSUANT TO RULE 13a-16 OR 15d-16
OF THE SECURITIES EXCHANGE ACT OF 1934**

For the Month of July 2023

(Commission File No. 001-41636)

Oculus Holding AG
(Translation of registrant's name into English)

Bahnhofstrasse 7
CH-6300
Zug, Switzerland
(Address of registrant's principal executive office)

Indicate by check mark whether the registrant files or will file annual reports under cover of Form 20-F or Form 40-F.

Form 20-F Form 40-F

INFORMATION CONTAINED IN THIS REPORT ON FORM 6-K

On July 11, 2023, Oculis Holding AG (the “Registrant”) held a R&D Day: Retina, and gave a presentation regarding updates on its clinical programs, including with respect to its OCS-01 diabetic macular edema (DME) DIAMOND program: the recent stage 1 read-out of the DIAMOND trial and plans for the upcoming DIAMOND 1 and DIAMOND 2 trials, its OCS-01 LEOPARD trial: an investigator-led study to assess safety and efficacy of OCS-01 in uveitic and post-surgical macular edema, and its OCS-05 ACUTTY trial: a first-in-patient trial in France to assess safety of OCS-05 for treatment of acute optic neuritis. The presentation is attached hereto as Exhibit 99.1 and is incorporated by reference herein.

The information contained in this Form 6-K, including Exhibit 99.1, is intended to be furnished 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, nor shall it be deemed incorporated by reference in any filing under the Securities Act of 1933 or the Exchange Act, except as expressly set forth by specific reference in such filing.

EXHIBIT INDEX

Exhibit	Description
99.1	Presentation dated July 11, 2023

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, thereunto duly authorized.

Date: July 12, 2023

OCULIS HOLDING AG

By: /s/ Sylvia Cheung
Sylvia Cheung
Chief Financial Officer



Oculis

Rethinking Ophthalmology

Oculis R&D Day: Retina

July 11, 2023

Nasdaq: OCS

Cautionary Note on Forward-looking Statements

These slides and the accompanying oral presentation contain forward-looking statements and information. The use of words such as "may," "might," "will," "should," "expect," "plan," "anticipate," "believe," "estimate," "project," "intend," "future," "potential," or "continue," and other similar expressions are intended to identify forward-looking statements. For example, all statements we make regarding the initiation, timing, progress and results of: our expected cash runway; our preclinical studies and our clinical studies; our research and development programs; our regulatory strategy; our future development plans; our ability to advance product candidates into, and successfully complete clinical trials; and the timing or likelihood of regulatory filings and approvals and statements regarding the potential therapeutic benefits of our product candidates, are forward looking. All forward-looking statements are based on estimates and assumptions by our management that, although we believe to be reasonable, are inherently uncertain. All forward-looking statements are subject to risks and uncertainties that may cause actual results to differ materially from those that we expected. Factors that may cause actual results to differ materially from current expectations include, but are not limited to: the possibility that Oculis may be adversely affected by economic, business, and/or competitive factors; Oculis' estimates of expenses and profitability; Oculis' ability to develop, manufacture and commercialize the product candidates in its pipeline; actions of regulatory authorities, which may affect the initiation, timing and progress of clinical studies or future regulatory approvals or marketing authorizations; the ability of Oculis or its partners to enroll and retain patients in clinical studies; the ability of Oculis or its partners to gain approval from regulators for planned clinical studies, study plans or sites; Oculis' ability to obtain and maintain regulatory approval or authorizations of its products, including the timing or likelihood of expansion into additional markets or geographies; the success of Oculis' current and future collaborations, joint ventures, partnerships or licensing arrangements; and other risks and uncertainties set forth in the sections entitled "Risk Factors" and "Cautionary Note Regarding Forward-Looking Statements" in documents that Oculis may from time to time file or furnish with the U.S. Securities and Exchange Commission (the "SEC"). Any forward-looking statement speaks only as of the date on which it was made. We undertake no obligation to update or revise any forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

Copyright of this presentation is owned by Oculis. No part of this presentation may be reproduced in any manner without the permission of Oculis.

Agenda

01	Opening Remarks	Riad Sherif, M.D. Chief Executive Officer	5mn	
02	OCS-01 Phase 3 DIAMOND Program in Diabetic Macular Edema: Stage 1 Recap and Next Steps	Arshad Khanani, M.D., M.A. Sierra Eye Associates, University of Nevada; Co-PI for DIAMOND; Oculis SAB member	15mn	
		David Boyer, M.D. Keck School of Medicine, USC; Co-Principal investigator for DIAMOND; Oculis SAB member	15mn	
03	OCS-01 PoC LEOPARD Trial Cystoid Macular Edema	Quan Dong Nguyen, MD, MSc, FARVO, FASRS Stanford University School of Medicine; Principal Investigator for LEOPARD Trial ; Oculis SAB member	15mn	
04	OCS-05 PoC ACUITY Trial in Acute Optic Neuritis	Sophie Bonnin, M.D. Rothschild Foundation Hospital, Paris	15mn	
05	Q&A Session Moderated by: Riad Sherif, M.D., CEO	David Boyer, M.D. Arshad Khanani, M.D., M.A., Quan Dong Nguyen, MD, MSc, FARVO, FASRS Sophie Bonnin, M.D.	Pravin Dugel, M.D., Oculis Director Sabri Markabi, M.D., Independent R&D Adviser Ramin Tadayoni, M.D., Paris University Pablo Villoslada, M.D., Stanford University Bastian Dehmel, M.D., Oculis Head of Development	50mn
06	Concluding Remarks	Riad Sherif, M.D. Chief Executive Officer	5mn	

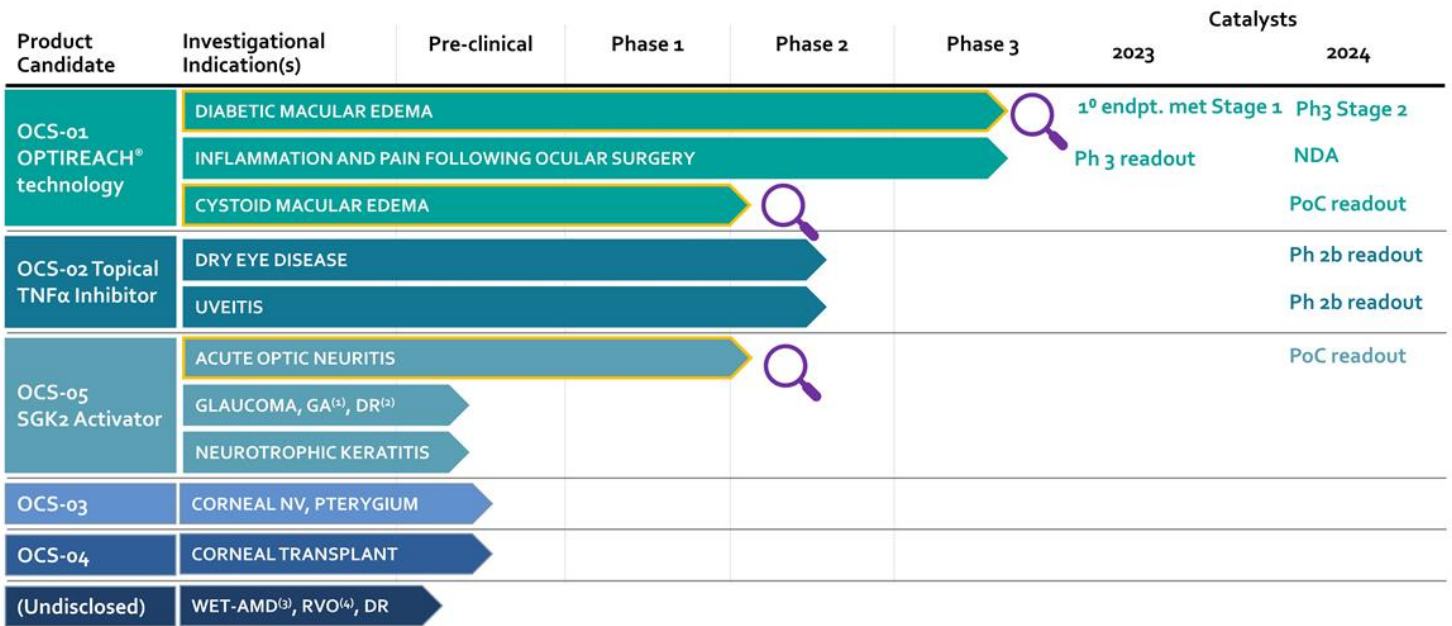


Our Purpose

To drive innovation to save sight and improve eye care

Oculis is Uniquely Positioned to Build Significant Value

With a multi-assets, Late-stage Pipeline and near-term Catalysts

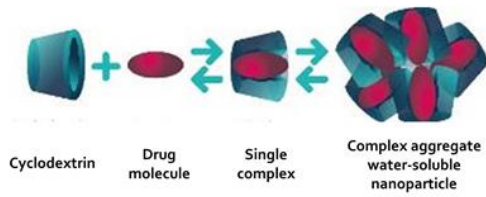


OCS-01 is based on the OPTIREACH® technology, OCS-02 is a single chain antibody fragment (ScFv) against TNFα and OCS-05 is a SGK-2 activator peptidomimetic small molecule with novel MoA targeting the activation of the trophic factor pathways.

- (1) Geographic Atrophy (GA).
- (2) Diabetic Retinopathy (DR).
- (3) Age-related Macular Degeneration (AMD).
- (4) Retinal Vein Occlusion (RVO).

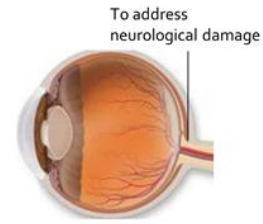
OCS-01

OPTIREACH® enables eye drops treating retinal disease:



OCS-05

Promising neuroprotective agent for neuro-retina diseases



Two Phase 3 programs: DME, Ocular Surgery and PoC in CME

Topical **Diabetic Macular Edema** and **Cystoid Macular Edema** treatment candidate based on **Optireach** technology with **consistent positive & significant clinical readouts**

PoC in Acute Optic Neuritis, with multiple additional applications

SGK-2 activator with neuroprotective potential for **Glaucoma, Geographic Atrophy, Diabetic Retinopathy & Neurotrophic Keratitis**

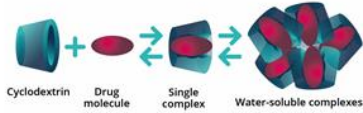
OCS-01 | First Eye Drop for DME

OCS-01 delivered consistent positive results in previous DME trials

Unique product candidate with clinically validated MoA

OCS-01: High-concentration OPTIREACH® formulation of dexamethasone (15 mg/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

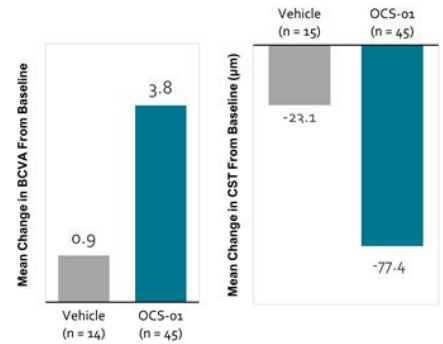
DME Exploratory 1²
19 pts Tanito Study
successfully completed

DME Exploratory 2³
22 pts Ohira Study
successfully completed

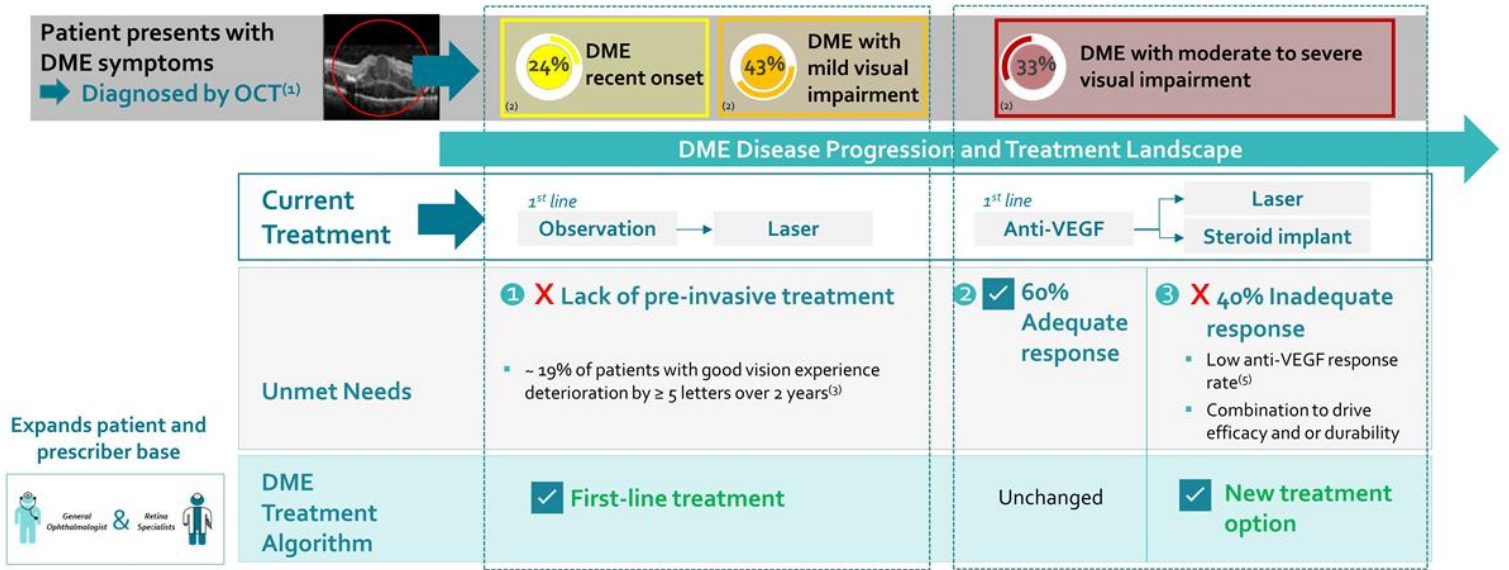
DME Phase 2⁴ 144 pts
Randomized & double-
masked successfully
completed

Phase 3 program initiated after positive Phase 2 results & EoP2 meeting

Change in BCVA & CST in Phase 2 Trial
(Same Patient Population as Ph 3 DIAMOND Trial)



¹ Abbvie Q1 2023 earnings report
² Investigator-initiated, open-label, single-center study. Tanito M, et al. Invest Ophthalmol Vis Sci. 2013;52:7944-7948
³ Ohira A, et al. Acta Ophthalmologica. 2015;93:60-64; Ohira A, et al. Acta Ophthalmologica. 2015;93:60-64.
⁴ DME Phase 2: Note: Data presented at Angiogenesis, Exudation and Degeneration, 2020 by KÖL (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)



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 S5) 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 Disease Landscape Forecast 2020 and Third parties research (Akceso and Clearview)

Diamond

DIAbetic Macular edema patients ON a Drop

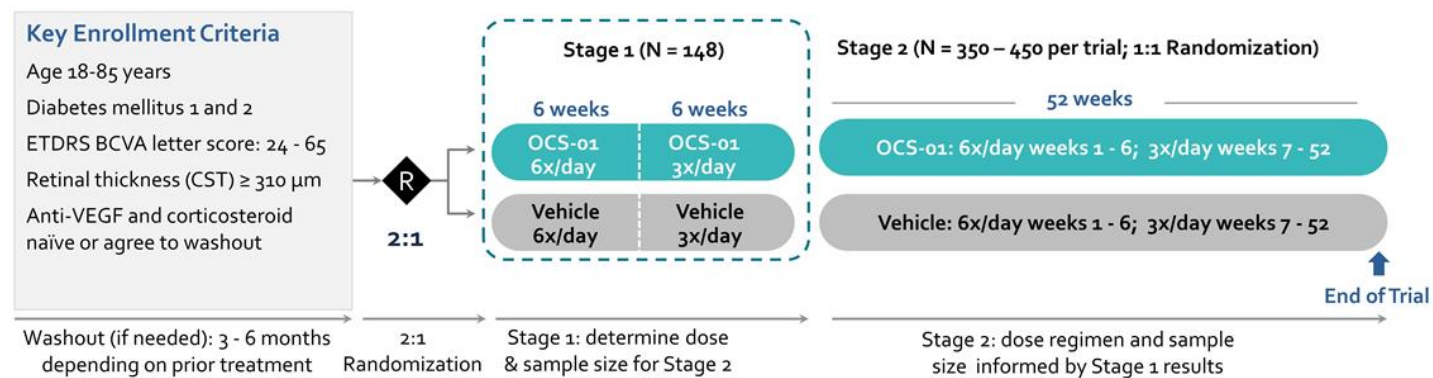
Stage 1 Recap and Next Steps

Arshad M. Khanani, M.D., M.A.

- Consultant: AbbVie, Adverum, Aerie, Applied Genetics Technologies Corporation, Aldebaran, Allergan, Apellis, Arrowhead, Aviceda Therapeutics, Bausch + Lomb, Broadwing Bio, Clearside, 4D Molecular Therapeutics, Exgenesis, EyePoint, Frontera, Genentech, Inc., Gyroscope, iLumen, Iveric Bio, Janssen, Kato, Kartos, Kodiak Sciences, Kriya, Ocular Therapeutix, Oculis, OcuTerra, Olives Bio, Opthea, Oxurion, Nanoscope, Notal, Novartis, Perfuse, PolyPhotonix, Protagonist, Ray Therapeutics, RecensMedical, Regeneron, Regenxbio, Roche, RevOpsis, Stealth, Thea, Unity, Vanotech, Vial; Research Support: Adverum, Annexon, Apellis, 4D Molecular Therapeutics, Genentech, Inc., Gyroscope, Iveric Bio, Kodiak, Neurotech, NGM Bio, Novartis, Ocular Therapeutix, Oculis, OcuTerra, Opthea, Oxurion, Regenxbio, Roche, Unity

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 \geq 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

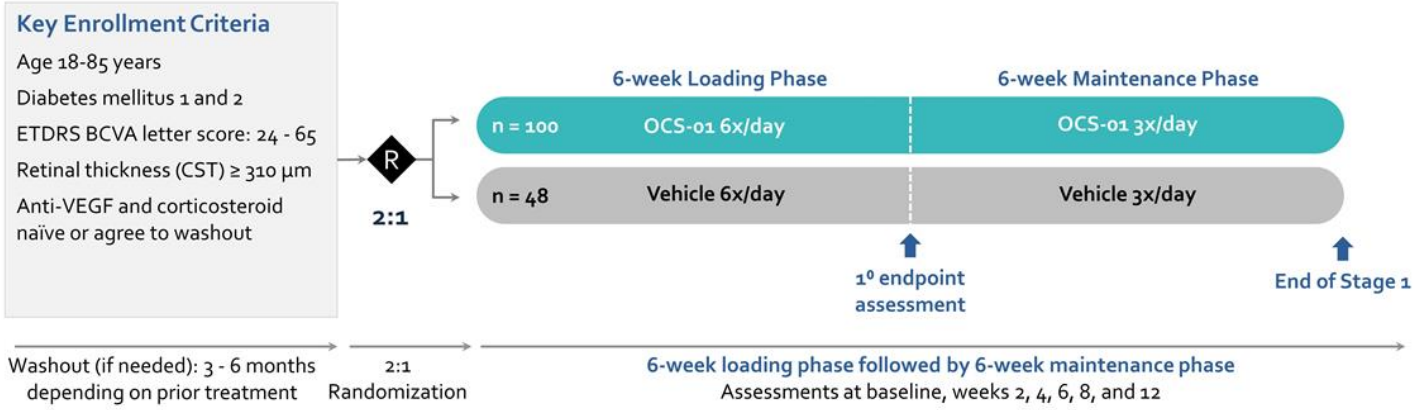
Stage 2: Two Phase 3's to support NDA filing for DME

- 1^o endpoint:** BCVA at wk 52
- Key 2^o endpoint:** \geq 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



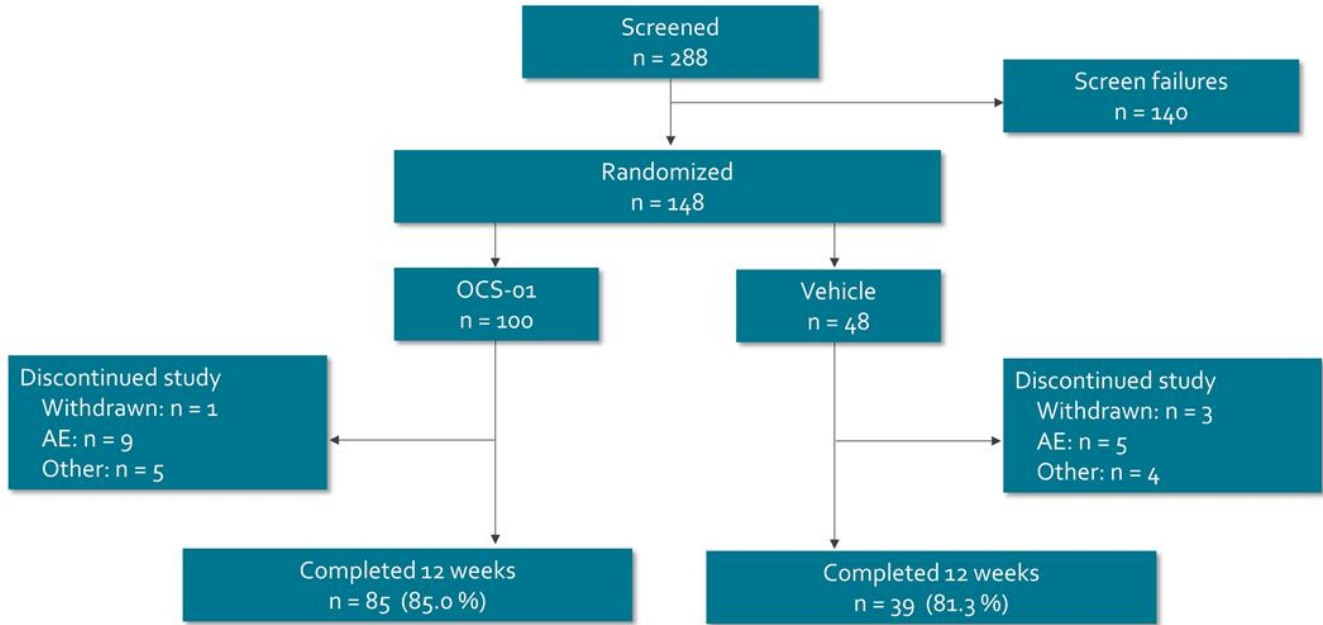
Stage 1 : Assess if loading dose optimizes efficacy

- 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.

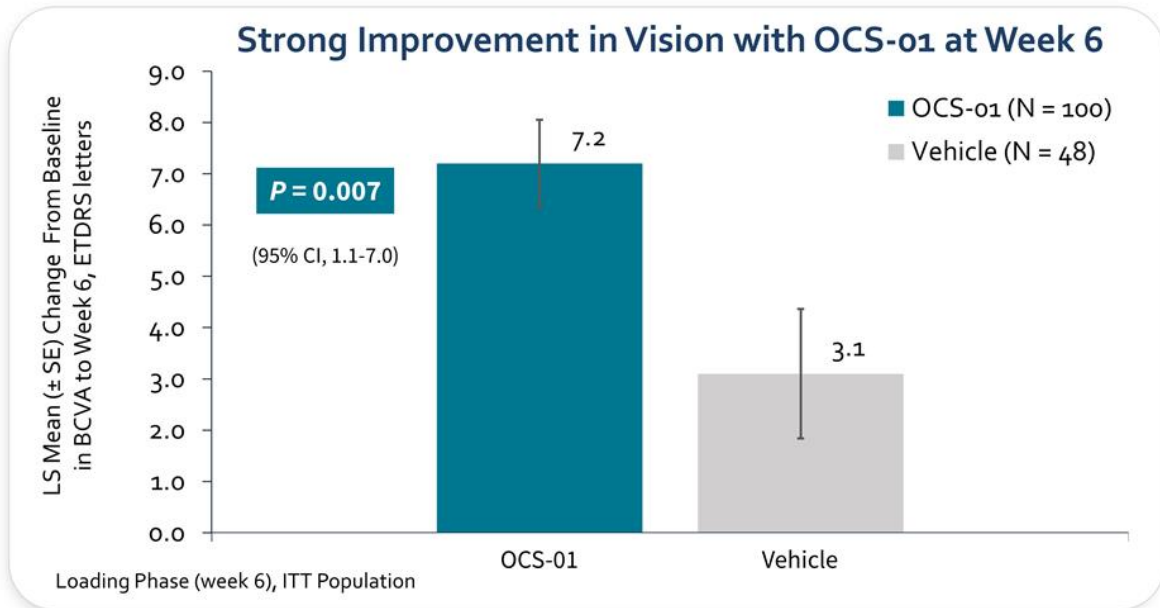
Demographics: Well-balanced Between Arms

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

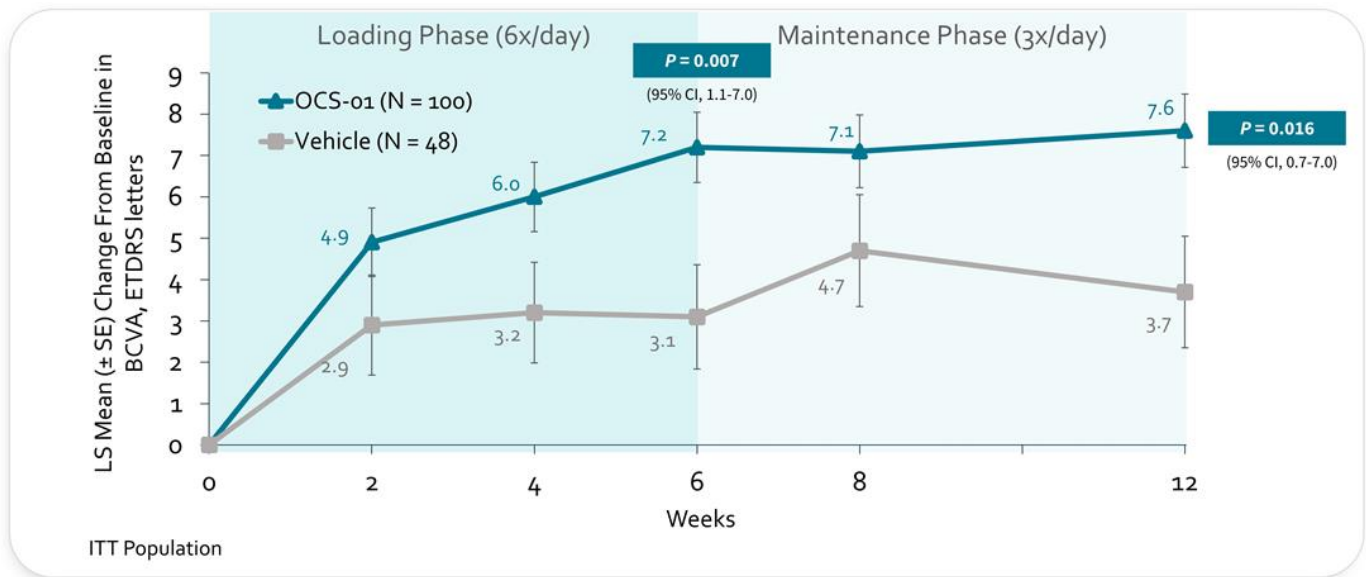
Rapid improvement in vision with OCS-01 treatment, as assessed by BCVA



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

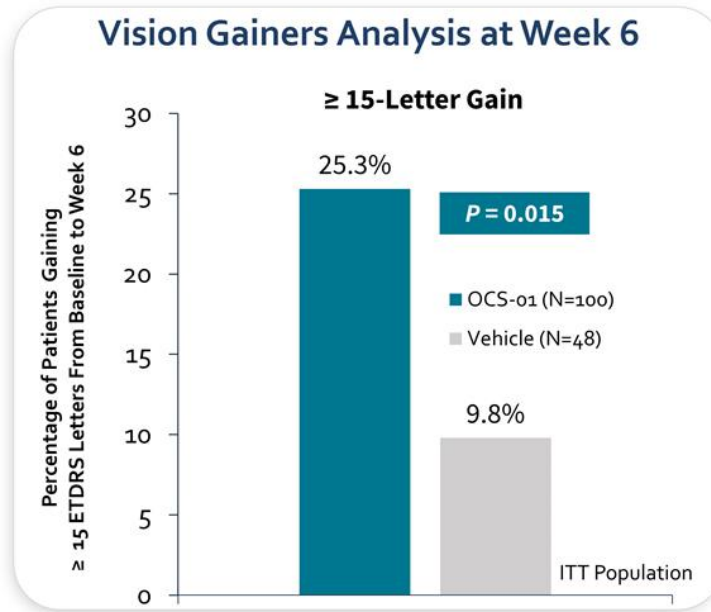
Rapid improvement in BCVA with loading dose regimen sustained with maintenance regimen



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.

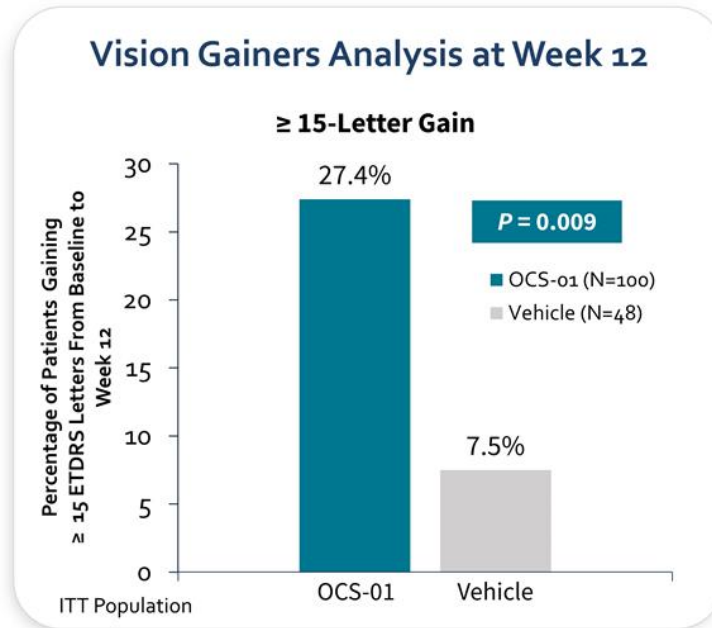
25% of OCS-01 Patients Achieve ≥ 3 Line Improvement in BCVA at Week 6

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.

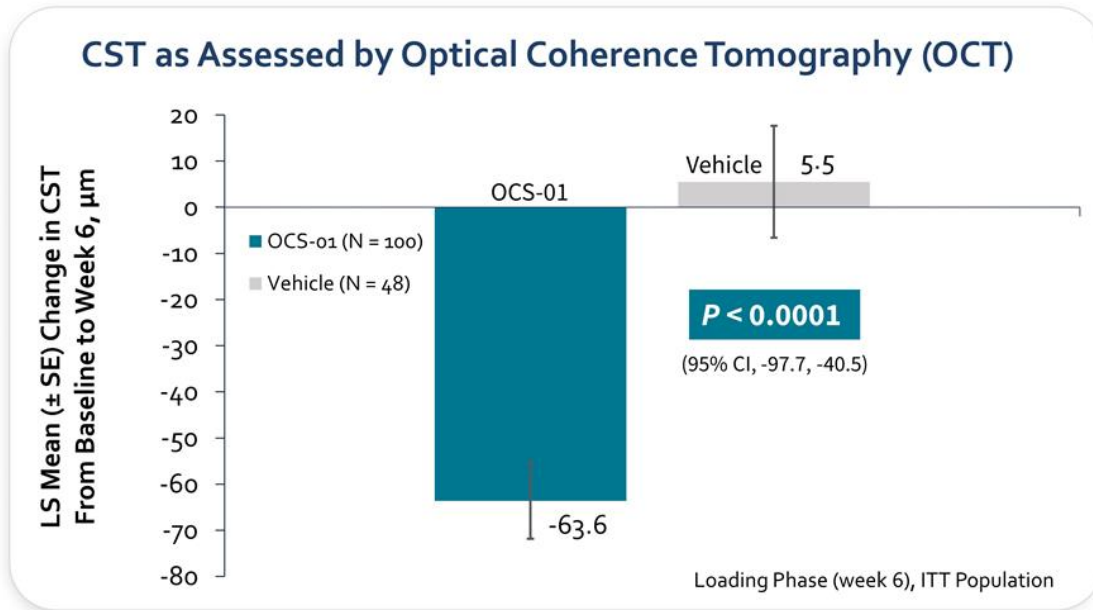
27% of OCS-01 Patients with ≥ 3 -Line Improvement in BCVA at Week 12
3-line (15 letter) improvement in BCVA deemed highly clinically relevant



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

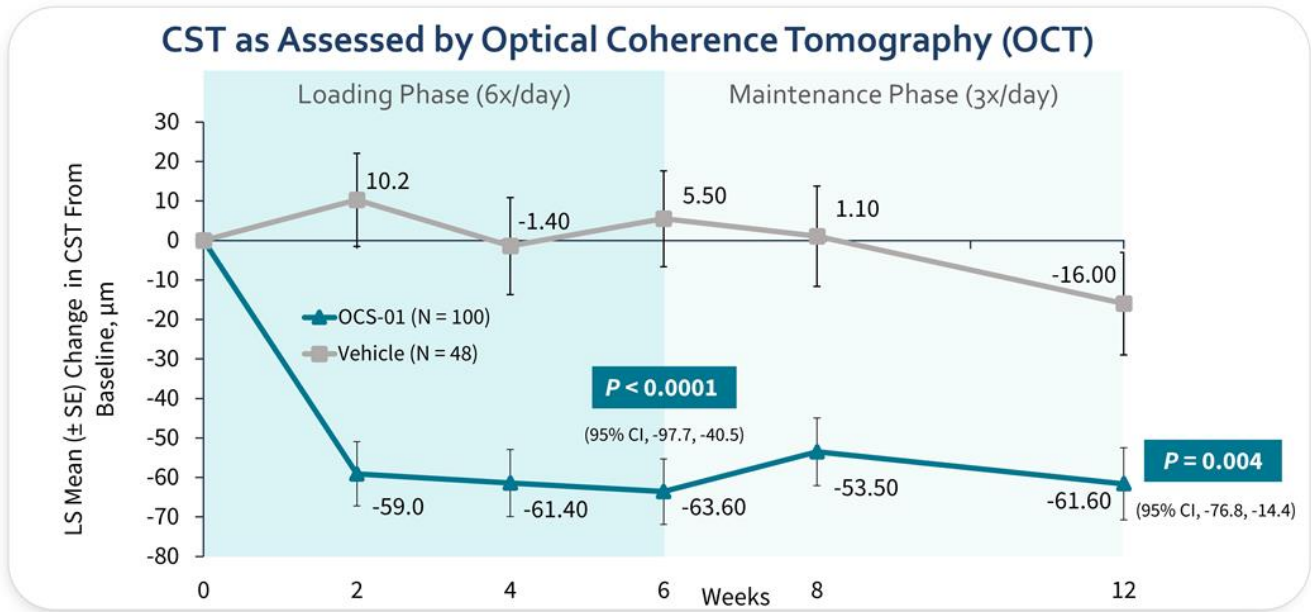
Central subfield thickness (CST) is a key metric used by physicians to manage DME patients



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; ETRDS, 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

TEAE, treatment-emergent adverse event.

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

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

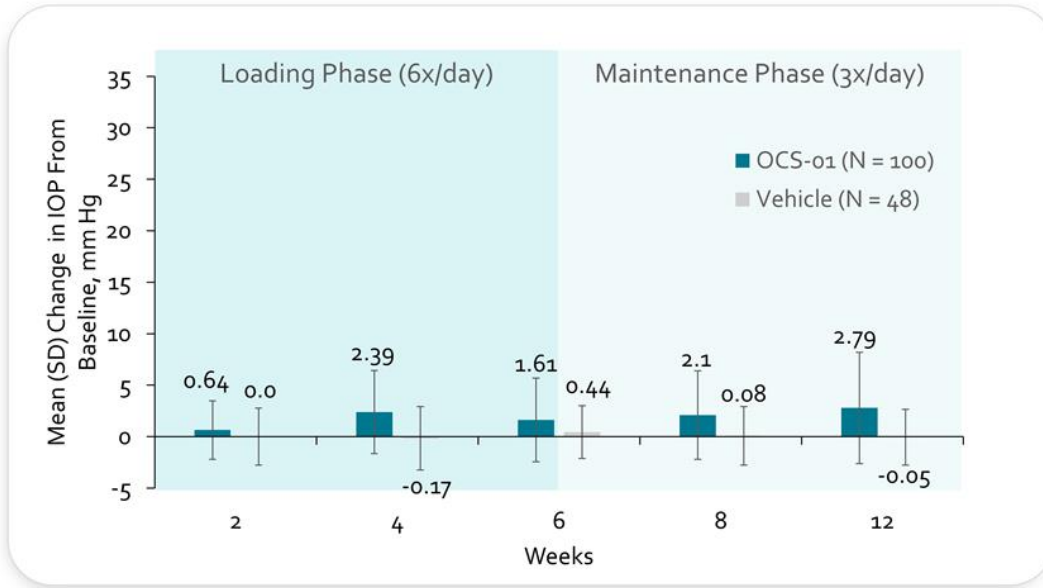
- None of the SAEs reported were deemed related to study drug
- No evidence of cataract formation up to 12 weeks

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)
Greater or equal to 25 mmHg IOP at any visit	19/97 (19.6)	1/47 (2.1)
Greater or equal to 35 mmHg IOP at any visit	1/97 (1.0)	0/47 (0)
IOP lowering medications administered for AE	11/22	1/1

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

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.

Study **met its pre-specified objective** i.e. to enable the selection of a dosing regimen for stage 2



Loading with 6 and Maintenance with 3 drops/day is an effective **dosing regimen** as proven by analysis at Week 12



Six times a day dosing of OCS-01 was observed to be a highly effective **Loading Dose**:

- To improve visual acuity
- To reduce macular edema and
- To increase the % of patients with a clinically relevant 3-line or greater improvement in BCVA



Three times a day dosing of OCS-01 was found to be an effective **Maintenance Dose**

No unexpected safety findings were observed



BCVA, best corrected visual acuity.
Data, analysis, and conclusions are preliminary, and subject to change as full analysis is ongoing.

OCS-01 in DME Phase 3
DIAMOND-1 and DIAMOND-2 Next Steps

David S. Boyer, MD

- Consultant: 4DMT, Achillion Pharma, Acucela, Adverum Biotechnologies, Aerie, AiViva Biopharma, Alcon, Aldeyra Therapeutics, Alimera Sciences, Alkahest, Allegro, Allergan, Allgenesis, Alzheon, Amgen, Amydis, Annexon Biosciences, Apellis, AGTC, AsclepiX, Ashvattha, Aviceda, Bausch & Lomb, Bayer, Biogen, Bionic Vision Technologies, Biovisics Medical, Boehringer Ingelheim, Boxer Capital, Cell Care Therapeutics, Chengdu Kanghong Biotechnology, Ciana, Clearside Biomedical, Curacle Co, Delsitech, DTx, Eloxx, EyePoint, Gemini Therapeutics, Genentech, Glaukos, GrayBug Vision, jCyte, I2vision, Kala, Isarna, Iveric Bio, Kriya, Kyowa Kirin, Lineage Cell, LumiThera, Nanoscope, NGM Biotherapeutics, Novartis Ophthalmics, Ocular Therapeutix, Ocugen, Oculis SA, Ocuphire Pharma, OcuTerra, Ocutrx Vision Technologies, Opthea, Optigo Biotechnology, Oxurion NV, Palatin Technologies, Pfizer, Regeneron, RetinAI Medical AG, Ripple, Roche, Santen, Shenyang XingQi Pharma, Smilebiotek Zhuhai, Stealth BioTherapeutics, Surrozen, Syneos, Thea Laboratories, Unity Biotech, Vanotech Corp, Verseon Corp, Vitranu, Vitro Biopharma, Viva Vision Biotech
- Stock/Shareholder: Allegro, DigiSight (Verana Health)

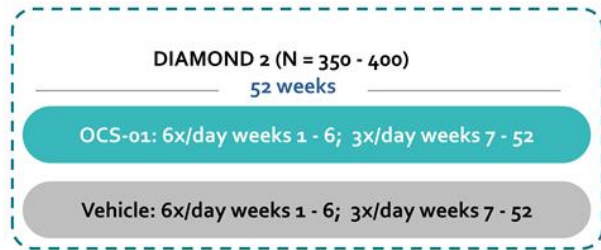
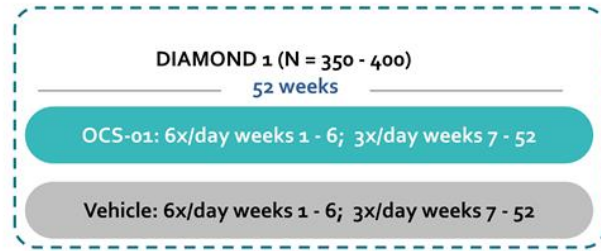
Purpose and Design

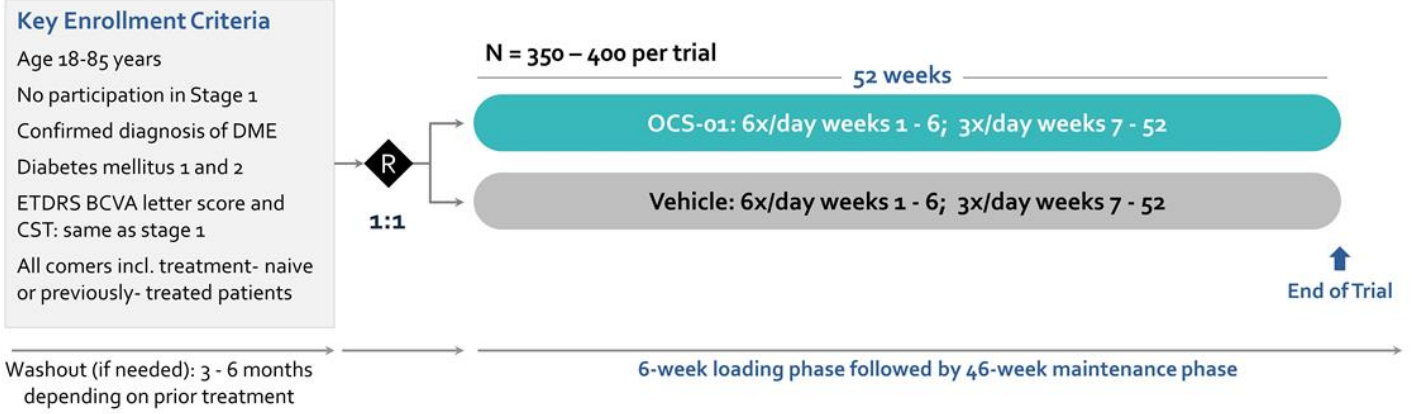
Purpose

To evaluate the efficacy and safety of OCS-01 in the treatment of patients with Diabetic Macular Edema (DME) The studies will provide the required clinical data for a New Drug Application (NDA) to the US FDA

Design

- Two randomized, multi center, masked, vehicle-controlled phase 3 pivotal clinical studies with identical protocols will be conducted.
- The design of the studies was agreed as pivotal by FDA in EoP2 meeting minutes.





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

Timelines

FPFV: 2H 2023

(1) Spectral Domain Optical Coherence Tomography

Population

Eligibility Criteria and Number of Patients

- Approximately 700 - 800 patients with DME (across both studies), aged 18-85 years with best corrected vision (BCVA) of 24-65 letters, and central retinal thickness (CST) ≥ 310 μm will be enrolled.
- Eligibility criteria defining DME were selected to be similar:
 - to criteria used in previous pivotal studies (e.g. Ozurdex) leading to approval
 - to previous studies of OCS-01 where efficacy was demonstrated
- The number of patients to be enrolled accounted for the power needed to test the statistical hypothesis as well as mitigating the risk of missing data and drop-out over the 52 weeks period.

Methods

- Patients will be randomized 1:1 to study treatment with OCS-01 or matching vehicle and will be followed for 52 weeks.
- Study treatment will be administered as an eye drop 6 times a day (loading phase) for 6 weeks followed by 3 times a day (maintenance phase) for the remaining 46 weeks.

Main Outcome Measures

- Pre-defined efficacy endpoints for FDA are:
 - Primary : mean change in BCVA from baseline to week 52 and
 - Key secondary: proportion of patients achieving 15 letters or more gain from baseline.
 - Other secondary: mean change in CST as measured by SD-OCT at wk 52
- Safety outcomes include adverse events, Intraocular pressure (IOP), lens clarity and HbA_{1c}.

Operational Organization

- The studies will be conducted globally in selected sites based on expertise and experience. Centers in the US and ex-US will be included in each study.
- A best-in-class CRO was selected for the global conduct of the study.
- A Steering Committee, composed of experienced industry experts and leading retina specialists was formed to support and oversee the design and conduct of the program.

Timelines

- First Patient First Visit (FPFV) for the DIAMOND program is targeted for 2H 2023.

SC member	Affiliation
David S. Boyer, MD	Retina -Vitreous Associates Medical Group, Los Angeles, CA, USA
Bastian Dehmel, MD	Oculis Head of Development, Lausanne, Switzerland
Arshad M. Khanani, MD	Retina- Sierra Eye Associates, Reno, NV, USA
Sabri Markabi, MD	R&D Adviser, Miami, FL, USA
Steve Snapinn, PhD	Seattle-Quilcene Biostatistics, Seattle, WA, USA
Ramin Tadayoni, MD	Retina- Université Paris Cité, Lariboisiere & St. Louis and Rothschild Foundation Hospitals, Paris, France

OCS-01 PoC LEOPARD Trial in CME

Quan Dong Nguyen,
MD, MSc, FARVO, FASRS

Research and Development Retina Day with Oculis
July 11, 2023 – New York City



Efficacy and Safety Of Dexamethasone Ophthalmic
Suspension Eye Drops In Uveitic and Post Surgical
Macular Edema – The LEOPARD Study

LEOPARD

Study Overview

Quan Dong Nguyen, MD, MSc, FAAO, FARVO, FASRS
Byers Eye Institute
Stanford University School of Medicine
Palo Alto, California



34

DISCLOSURE

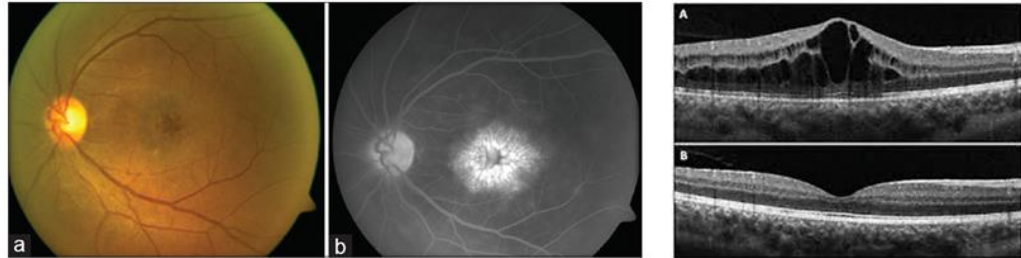
- Stanford University, the employer of Dr. Nguyen, has received research funding from Boehringer-Ingelheim, Genentech, Novartis, Oculis, Regeneron, Santen, and Belite Bio among others
- Dr. Nguyen serves on the Scientific Advisory Boards for Belite Bio, Boehringer-Ingelheim, Genentech, Kriya, Oculis, Regeneron, and Santen, among others
- The LEOPARD Study is an Investigator-Sponsored Trial coordinated by the Global Ophthalmic Research Center (GORC) and the Byers Eye Institute at Stanford University with the study drug provided by Oculis

A collection of four geometric shapes: a teal parallelogram, a green right-angled triangle, and a yellow right-angled triangle, all positioned on the left side of the page.

INTRODUCTION AND STUDY RATIONALE

UVEITIC MACULAR EDEMA

- Uveitic macular edema (UME) is a **common** complication of uveitis ~ 33%⁽¹⁾
- Even after control of active inflammation, uveitic macular edema may persist⁽²⁾
- Intravitreal steroid results in complete resolution of 50-60% of uveitic macular edema⁽³⁾



(1) Lardenoye et al. Impact of Macular Edema on Visual Acuity in Uveitis, *Ophthalmology*, AAO, vol. 113, Issue 8, P1446-1449 August 2006
(2) Koronis et al. Update in treatment of uveitic macular edema, *Drug Des Devel Ther* 2019, v.13; 667-680
(3) Thorne et al. The POINT trial, *Ophthalmology*, Feb. 2019, 126(2): 283-295

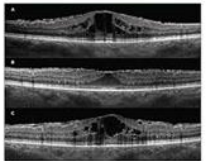
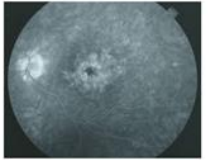
POST-SURGICAL MACULAR EDEMA

- Cataract extraction is the most prevalent surgical procedure of all medical specialties with an estimated 3.7 million cases per year in the USA, 7 million in Europe and 20 million worldwide⁽¹⁾
- Clinically significant CME occurs in up to 5.8% of cataract surgeries⁽²⁾ representing up to:
 - ~ 215,000 cases in the USA, and ~ 400,000 cases in EU and ~1.16M cases worldwide per year
- PSME can also occur after other intraocular surgeries, i.e., vitreoretinal surgery
- Cystoid Macular Edema (CME) is the most significant cause of postoperative vision loss after ocular surgery
- **Approximately 30% of patients⁽³⁾ who undergo ocular surgery have higher risk of CME**, including patients with **diabetes, uveitis** and other risk factors
- Up to **56% of high-risk patients⁽²⁾** may experience clinically significant CME following ocular surgery
- No established guidelines (topical steroids, topical NSAIDs, intravitreal steroids/anti-VEGFs, interferon, tocilizumab)
- Can be refractory

(1) Tommaso Rossi et Al., Cataract surgery practice patterns worldwide: a survey, BMJ 2020, Volume 6, Issue 1.

(2) <https://crstodayeurope.com/articles/2013-julaug/prevention-of-cme-after-cataract-surgery>

(3) ARVO Annual Meeting Abstract, June 2021, Hennings et al. Prognostic determinants of postoperative pseudophakic macular oedema in a tertiary hospital setting



THE UNMET NEEDS TO BE ADDRESSED BY LEOPARD

- There is no optimal treatment for **uveitic and post-surgical macular edema**
- **OCS-01** has demonstrated excellent safety and efficacy profiles in diabetic macular edema in clinical trials to-date
- Previous study (Shulman et al, 2015) has shown that topical dexamethasone-cyclodextrin nanoparticle eye drops was effective for non-infectious uveitic macular edema, and thus ... we believe **OCS-01** would work in UME and PSME

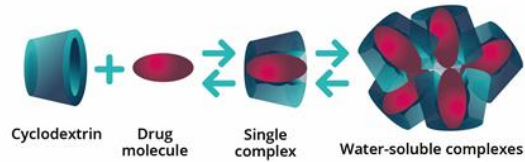
We Need More Effective Therapeutic Options

(1) Shulman, Shiri, et al. Topical dexamethasone-cyclodextrin nanoparticle eye drops for non-infectious Uveitic macular oedema and vitritis—a pilot study. Acta ophthalmologica 93.5 (2015): 411-415.



DEXAMETHASONE OPHTHALMIC SUSPENSION (OCS-01)

- A **high-concentration OPTIREACH formulation of dexamethasone (15 mg/ml)** conjugate forming nano- and microparticles
- Cyclodextrins are hydrophilic carriers that can:
 1. Enhance the permeation of relatively lipophilic molecules (e.g., dexamethasone) through bio-membranes (e.g., cornea)
 2. Maintain high concentrations of molecules in aqueous environments (e.g., aqueous humor)



- Preclinical trials have shown that OCS-01 can reach the retina in significant concentrations

A collection of three geometric shapes: a teal parallelogram, a green right-angled triangle, and a yellow equilateral triangle, all positioned on the left side of the page.

STUDY DESIGN

STUDY OBJECTIVES

1. To evaluate the effects of OCS-01 Ophthalmic Suspension on **visual acuity** and **central subfield thickness (CST)** in subjects with **UME** and **PSME**
2. To monitor the **safety** of OCS-01



STUDY OVERVIEW

- **Prospective, multi-center, single masked, randomized, controlled** study
- Subjects and BCVA examiner will be masked
- 24 eligible subjects
 - 12 with UME
 - 12 with PSME
 - Study Duration: 24 weeks for each subject
- **Four Phases**
 1. **Screening Phase**
 2. **Loading Phase:** All subjects will receive 1 drop of OCS-01 Ophthalmic Suspension 6 times a day (every 4 hours) for 4 weeks.
 3. **Treatment Phase:** At week 4, both UME and PSME subjects will be randomized into 2 groups and receive treatment until **primary end point - Week 12:**
 - a. **High dose** group (6 drops of OCS-01 per day)
 - b. **Low dose** group (3 drops of OCS-01 and 3 placebo per day)
 4. **Follow-up Phase :** Retreatment or Taper

PRIMARY OUTCOMES

1. Mean change in **central subfield thickness (CST)** on optical coherence tomography (OCT) at week 12 compared to baseline
2. Mean change in **ETDRS BCVA letter score** at **Week 12**



SECONDARY OUTCOMES

1. Mean **change in ETDRS BCVA letters** at weeks 2, 4, 6, 8, 16, 20, and 24 compared to baseline
2. The percentage of subjects who **gain ≥ 10 or ≥ 15 ETDRS letters** at week 12 and 24 compared to baseline
3. Mean change in **central subfield thickness (CST)** at weeks 2, 4, 6, 8, 16, 20, and 24 compared to baseline
4. Improvement in **quality of life** as assessed by NEI VFQ-25 at Week 12, and 24 compared to baseline
5. The percentage of subjects showing **reduction of macular leakage** on FA at week 12 and 24 compared to baseline

SAFETY ENDPOINTS



- Adverse Events (AEs) at 8, 12, and 24 weeks
- Slit Lamp Examination Parameters indicating ocular toxicity to the investigational drug at 8, 12, and 24 weeks
- Intraocular Pressure at 8, 12, and 24 weeks
- Percentage of subjects who lose ≥ 15 ETDRS letters or more at weeks 8, 12, and 24 compared to baseline

RETREATMENT CRITERIA

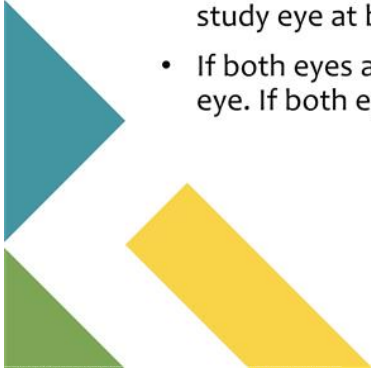
- Subjects who continue to have ME on OCT from week 12 onwards, will be treated according to the following criteria:
 - Subjects randomized to **High-Dose** group (6 drops OCS-01 daily) will **continue to receive 6 drops** OCS-01 daily.
 - Subjects randomized to **Low-Dose** group (receive 3 drops OCS-01 + 3 drops placebo daily) will be **switched to receive 6 drops** OCS-01 daily.



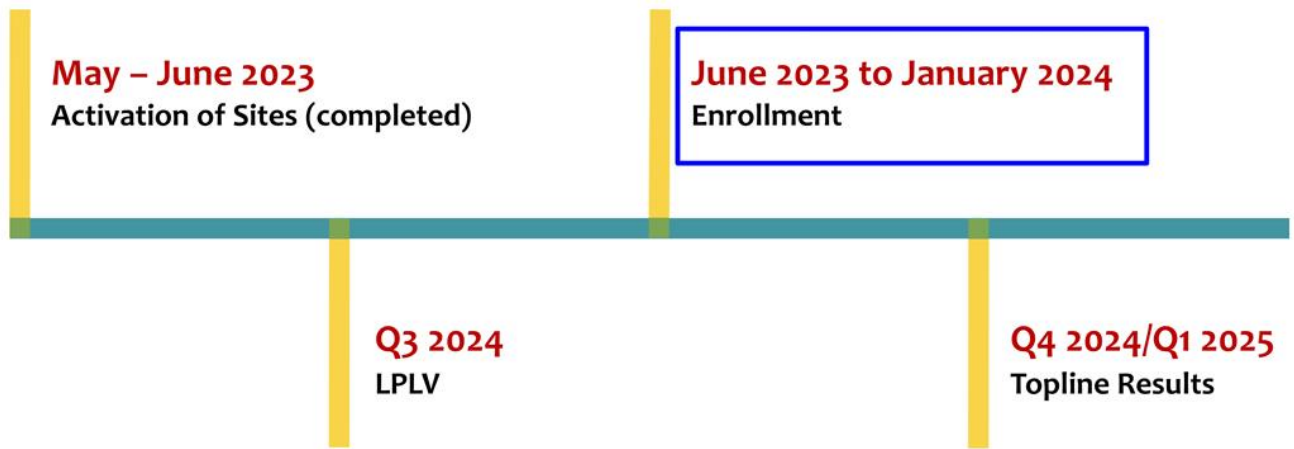
ELIGIBILITY CRITERIA

INCLUSION CRITERIA

- Age 18 years or older
- A diagnosis of UME or PSME
- Can provide written informed consent prior to any study procedure being performed, able and willing to follow all instructions, and attend all study visits
- An ETDRS BCVA letter score ≤ 70 (Snellen 20/40) and ≥ 35 (Snellen 20/200) in the study eye at baseline (Visit 2)
- If both eyes are eligible, the eye with the worse BCVA will be selected as the study eye. If both eyes have the same BCVA, the non-dominant eye will be selected



STUDY TIMELINES



CLINICAL SITES

- Byers Eye Institute at Stanford, Palo Alto, CA
- Texas Retina Associates, Dallas, TX
- Valley Retina Institute, McAllen, TX
- Stein Eye Institute at UCLA, Los Angeles, CA
- Retina Vitreous Associates Medical Group, Beverly Hills, CA



SUMMARY

- OCS-01, a **high-concentration OPTIREACH formulation of dexamethasone (15 mg/ml)**, is being evaluated as therapeutic option for **uveitic macular edema (UME)** and **post-surgical macular edema (PSME)**, aiming to address important unmet needs, in addition to diabetic macular edema (DME)
- Strong safety profile observed with no unexpected adverse events beyond what have been seen in other studies with DME
- The **LEOPARD Study** is ongoing at multiple clinical centers of excellence in the United States

OCS-01 May Become a Potent, Relatively Non-Invasive Therapeutic Option for Retinal Vascular and Uveitic Diseases and First-Line Therapy for Macular Edema in Post-Operative High-Risk Patients and High-Risk Surgeries





LEOPARD
STUDY

THANK YOU



OCS-05 PoC ACUITY Trial in AON

Sophie Bonnin, M.D.

ACUITY study: towards neuroprotection

Sophie Bonnin, MD

Why neuroprotection is an unmet medical need?

Glaucoma:
blurred or no
peripheral vision



Diabetic Retinopathy:
spots or dark strings floating
in vision



Macular Degeneration:
blurred or no vision in the
center of visual field



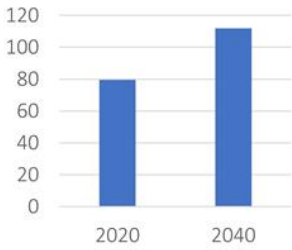
In all these diseases, the loss of neurons, i.e. ganglion cells, is responsible for the loss of vision.

Neuroprotection aims to preserve neurons from damage, delaying disease progression.

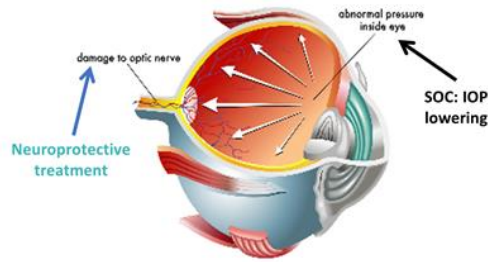
Unmet medical need in glaucoma

~ 80M people have glaucoma WW – reaching 111M by 2040⁽¹⁾

Global number of glaucoma patients in M ⁽¹⁾

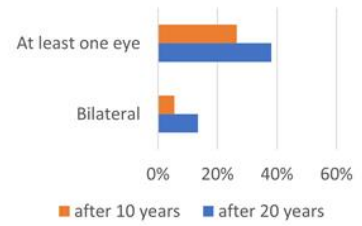


While standard-of-care drugs reduce IOP (a risk factor), there is no treatment to protect against optic nerve damage



About 10% of patients still go blind or suffer from sight impairment⁽²⁾

Cumulative incidences of blindness⁽²⁾



“Currently available therapies for [glaucoma] **only attempt to reduce intraocular pressure**, the major risk factor, without addressing the associated optic neuropathy and retinopathy.

“Development of **glaucoma neuroprotective treatment is therefore a pressing unmet medical need**”⁽³⁾

“...subset of patients with glaucoma may have more aggressive disease and may be particularly susceptible to progression, possibly because of **non-IOP-related factors that contribute to retinal ganglion cell (RGC) death** and vision loss” ⁽⁴⁾

(1) <https://www.brightfocus.org/glaucoma/article/glaucoma-facts-figures>

(2) Peters D, Bengtsson B, Heijl A. Lifetime risk of blindness in open-angle glaucoma. Am J Ophthalmol. 2013;156:724–730

(3) Yang et al 2013;

(4) Forchheimer et al 2011

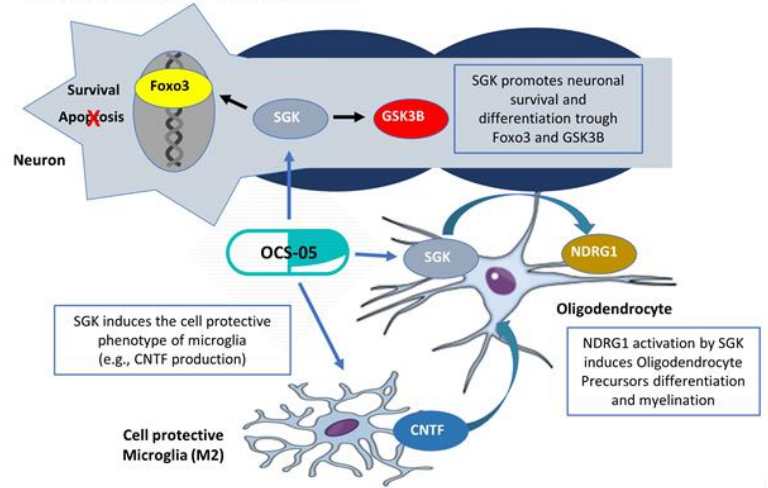
Is OCS-05 effective in neuroprotection?

SGK-2 activator peptidomimetic small molecule with a *unique mode of action* for neuro-ophthalmology

Disease modifying drug to protect and repair neurons

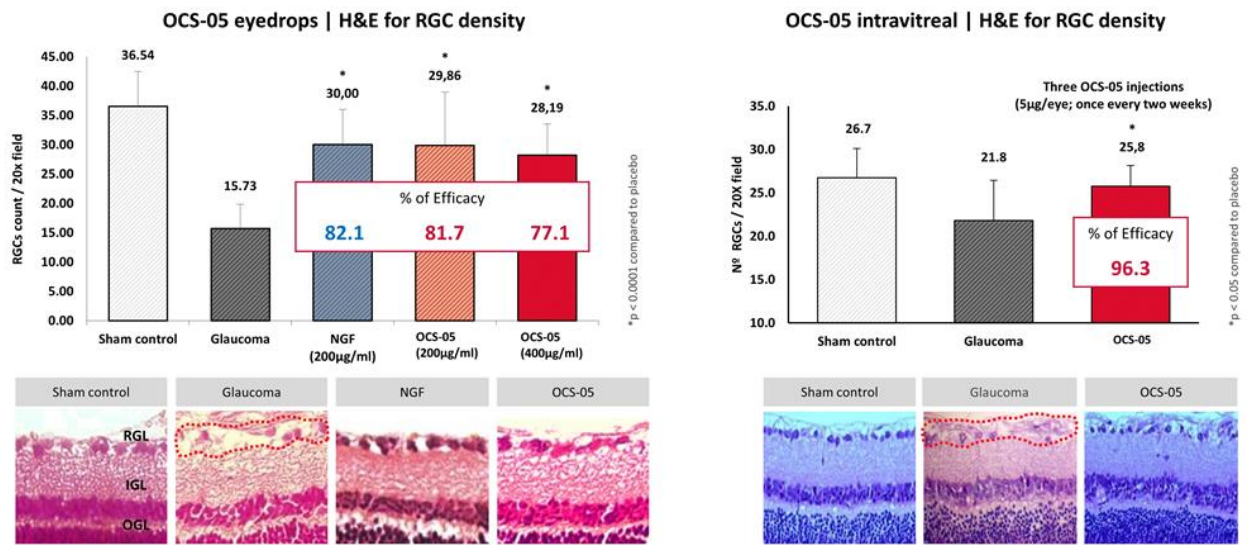
- Activates neurotrophic signalling pathways supporting neuronal survival and repair

OCS-05 targets SGK as part of the neurotrophic factor signalling pathways triggering multiple beneficial effects on apoptosis, anti-oxidation and anti-inflammation



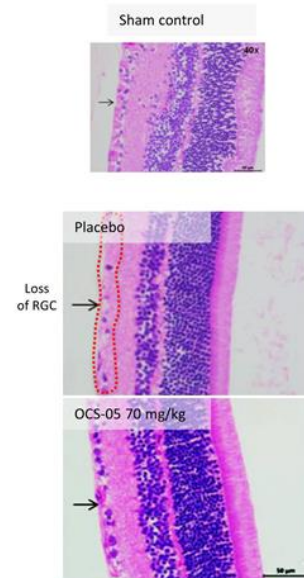
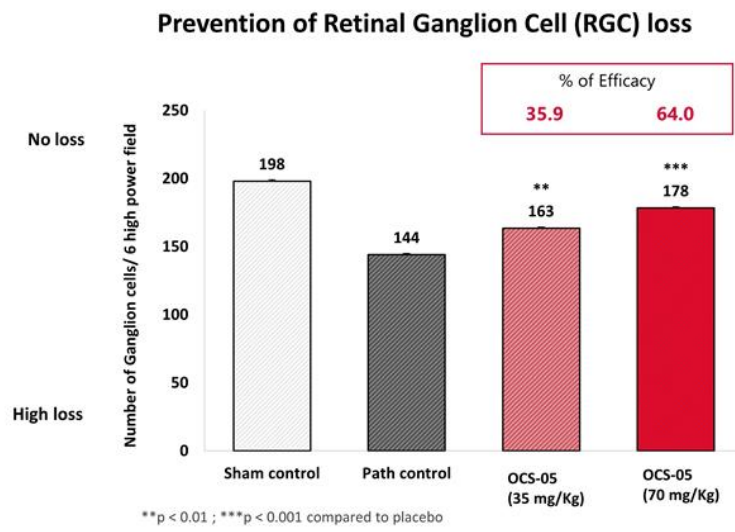
OCS-05: Glaucoma neuroprotection model results

OCS-05 promotes neuroprotection in glaucoma by preventing damage to the retinal ganglion cells



OCS-05 (eyedrops and intravitreal) prevents RGCs damage without reducing intraocular pressure.

OCS-05: Prevention of retinal ganglion cell loss in optic neuritis



Lysolecithin induced demyelinating model in rat (model of acute optic neuritis)

OCS-05: Safety and pharmacokinetic in healthy subjects

Phase I study included 48 healthy subjects: 36 were treated by OCS-05.

No serious adverse events were reported in the OCS-05 group.

	Placebo (N=4)	2.4 mg/kg OCS-05 (N=6)	3.0 mg/kg OCS-05 (N=6)	Overall (N=16)
Number of TEAEs	7	1	1	9
Number (%) of subjects reporting at least one:				
TEAE	3 (75.0)	1 (16.7)	1 (16.7)	5 (31.3)
Serious TEAE	1 (25.0)	0 (0.0)	0 (0.0)	1 (6.3)
TEAE Leading to Withdrawal	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Number (%) of subjects with TEAE by severity:				
Mild	2 (50.0)	0 (0.0)	1 (16.7)	3 (18.8)
Moderate	0 (0.0)	1 (16.7)	0 (0.0)	1 (6.3)
Severe	1 (25.0)	0 (0.0)	0 (0.0)	1 (6.3)
Number (%) of subjects with TEAE by relationship to IMP:				
Almost Definite	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Probable	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Possible	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Unlikely	1 (25.0)	0 (0.0)	1 (16.7)	2 (12.5)
Unrelated	2 (50.0)	1 (16.7)	0 (0.0)	3 (18.8)

Table 3. Overall summary of TEAEs–MAD part.

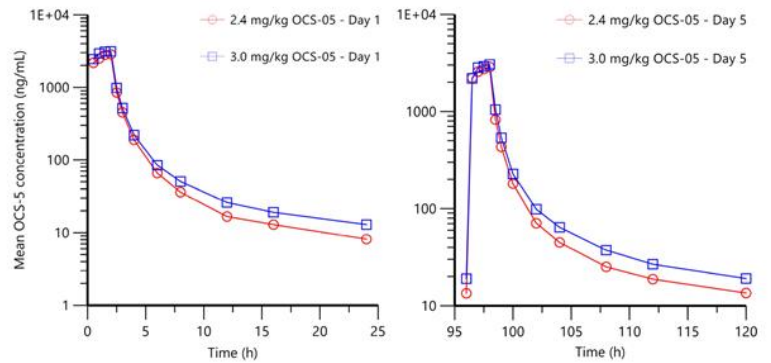


Figure 2. Summary of Derived Pharmacokinetic Parameters Following Multiple Dose Administration of OCS-05 (I.V. infusion) to Healthy Male and female Subjects.

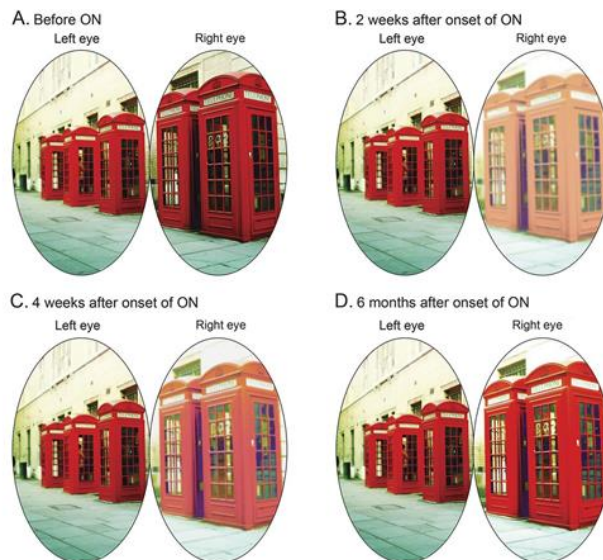
Towards the assessment of the efficacy of OCS-05 in patients: Phase 2 ACUITY Trial in acute optic neuritis

Acute optic neuritis :

Rare disease with acute inflammation and demyelination of the optic nerve, occurring in young patients.

Sub-acute loss of vision and eye pain occurring over several days.

Slow improvement but persistent vision deficits.



Acute optic neuritis and multiple sclerosis

Acute optic neuritis: occurring in adults between the age 20 and 40 years

Aetiology: multiple sclerosis, idiopathic, neuromyelitis optica, ...

Multiple sclerosis is affecting more than 2.8 million persons worldwide⁽¹⁾

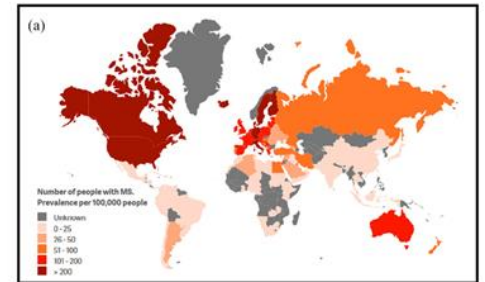
Mean age at diagnosis: 32 years and with heterogeneous prognosis

(1) <https://www.medicalnewstoday.com/articles/newly-discovered-marker-of-multiple-sclerosis-severity-may-lead-to-better-treatments#:~:text=As%20of%202020%2C%20about%202.8,over%20time%2C%20causing%20permanent%20issues.>

Jacobs LD, et al. *N Engl J Med* 2000;343(13):898–904

Scalfari A, et al. *Brain* 2010;133(pt 7):1914–29

Walton C, et al. *Multiple Sclerosis Journal*, 2020; 26(14):1816–1821



Disability
Need for walk after a median of 18 years



Cognitive impairment
in 43% to 65% of cases⁴

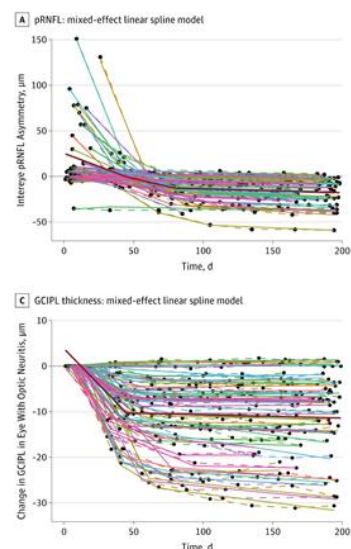
Acute optic neuritis: towards neuroprotection

Ongoing multiple sclerosis treatment : anti-inflammatory drugs

Neuroprotective therapies are required for multiple sclerosis and acute optic neuritis.

The retinal changes can be non-invasively and accurately measured by optical coherence tomography.

“Acute optic neuritis is a suitable condition to test neuroprotective and remyelinating therapies after acute inflammation”



Andorrà, M., Alba-Arbalat, S., Camos-Carreras, A., Gabilondo, I., Fraga-Pumar, E., Torres-Torres, R., Pulido-Valdeolivas, I., Tercero-Urbe, A. I., Guerrero-Zamora, A. M., Ortiz-Perez, S., Zubizarreta, I., Sola-Valls, N., Llufrui, S., Sepulveda, M., Martinez-Hernandez, E., Armangue, T., Blanco, Y., Villoslada, P., Sanchez-Dalmau, B., ... Martinez-Lapiscina, E. H. (2019). Using Acute Optic Neuritis Trials to Assess Neuroprotective and Remyelinating Therapies in Multiple Sclerosis. *JAMA Neurology*.

OCS-05 in acute optic neuritis: Phase 2 ACUITY Trial

ACUITY (Acute optic neURITis with a demYelinating origin)

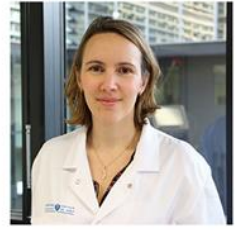
Aim: To assess the safety and to explore the efficacy of OCS-05, compared to placebo, in patients with acute optic neuritis receiving the standard of care

Design: 2 arms randomized double-blind placebo-controlled study (1 OCS-05: 1 placebo)

Drug treatment:

Intra-venous perfusion once-a-day for 5 days, and 6 months follow-up

All patients receive concomitant standard of care therapy (corticosteroid IV)



Dr. Céline Louapre



Dr. Louise-Laure Mariani

Collaborations: Dr Natalia Shor (Neuroradiology)
Ophthalmology PSL: Pr Valérie Touitou, Dr Federico Maestri
CHNO 15-20: Dr Catherine Vignal, Dr Jennifer Aboab

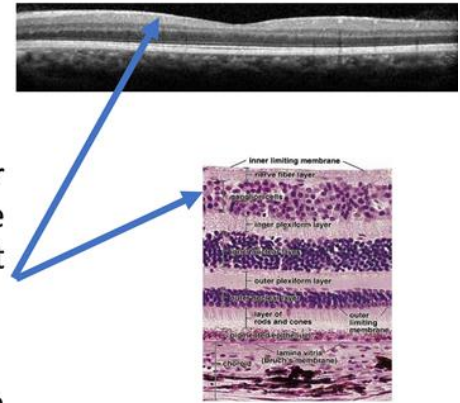
OCS-05 in acute optic neuritis: Phase 2 ACUITY Trial

ACUITY (Acute optiC neURITis with a demYelinating origin)

Primary endpoints: safety & tolerability

Exploratory endpoints: efficacy

Gold Standard vision-related outcome measures consider structure and function of the visual pathway including routine non-invasive optical coherence tomography and low-contrast visual acuity



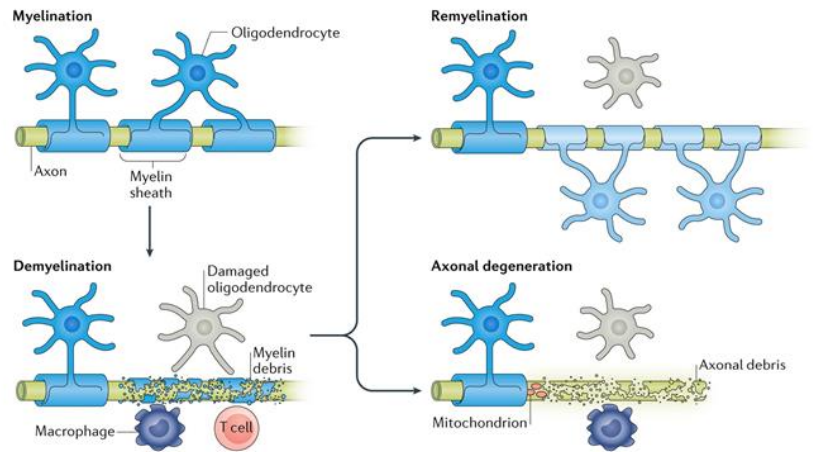
Sites: Hôpital La Pitié Salpêtrière, Paris, Rothschild Foundation Hospital in Paris, Nice and Lyon)



OCS-05: this neuroprotective treatment offers hope for our patients





Multiple sclerosis : several neuroprotective drugs in development but no validated drug.

Optic neuropathies and retinal diseases : the focus is on anti-inflammatory treatment or anti-VEGF treatment but not on neuroprotection even though neurons are crucial for the vision



Franklin et al, 2017, Nat Rev Neuroscience

OCS-05 summary: First SGK neuroprotective candidate in ophthalmology

 <p>First SGK neuroprotective ophthalmic candidate</p>	<ul style="list-style-type: none">▪ Disease modifying drug which protects and repairs neurons▪ Potential paradigm shift in treating major blinding diseases by acting directly on retinal neurons
 <p>Data supporting MoA and safety</p>	<ul style="list-style-type: none">▪ Preclinical data showing neuroprotection by preventing retinal ganglion cell death and improvement of function in Glaucoma, MS and AON models▪ Phase 1 study data demonstrated OCS-05 was well-tolerated in 48 healthy volunteers
 <p>ACUITY First-in-patient study ongoing</p>	<ul style="list-style-type: none">▪ Proof-of-concept data readout in AON expected in 2H 2024
 <p>Potential impact of neuroprotection in ophthalmology</p>	<ul style="list-style-type: none">▪ Potential applications for a neuroprotective agent in ophthalmology include Glaucoma, Geographic Atrophy, Diabetic Retinopathy, and corneal indications such as Neurotrophic Keratitis






Thank you for your
attention



Q&A Session and Closing Remarks

Dr. Riad Sherif
Chief Executive Officer



<p>Trial Objectives Met </p>	<p>Results validated loading and maintenance regimen to optimize OCS-01 efficacy potential in DME with robust statistical significance</p>
<p>Functional & Clinical Benefits </p>	<p>OCS-01 met all functional and clinical benefit endpoints in a robust, statistically superior manner (in 3-month trial):</p> <ul style="list-style-type: none">▪ 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)
<p>Safety </p>	<p>No unexpected safety findings observed</p>

Next Step: Continue DIAMOND program with full 52 weeks trials to support NDA filing of OCS-01 for DME treatment

DME- OCS-01 Offers Significant Potential Value to all Key Stakeholders

Benefits highlighted in third-party market research performed independently with payers & physicians^(1,2)



DME Patients

- + Early intervention treatment
- + Accessible: Eye drops always preferred
- + Benefits for working-age DME patients



Ophthalmologists

- + Expand prescriber pool by offering a pre-invasive solution
- + Provide versatility for retina specialist as standalone or combination with anti-VEGFs



Payors

- + Potential lower total cost with an efficacious and safe alternative
- + Early intervention could result in reducing cost burden for payor system and improving long term patient outcomes

Current addressable US patient population: 1.2 million^(3,4)

(1) Clearview market research 2019 following Phase 2 DX-211 results and associated TPP – In-depth interviews with 40 experts (16 Retina specialists, 16 Ophthalmologists and 8 Payors) – 25 US and 15 EU
(2) Akceso Payer and Clinical Expert Research 2020 based on DX-211 Phase 2 results and associated TPP - In-depth interviews with 24 experts (10 payers, 11 retina experts and 3 general ophthalmologists) – 16 US, 8 EU
(3) Gonzalez 2016 Early and Long-term Responses to VEGF Therapy in DME: Analysis of protocol I data
(4) Decision Resources Group: DME – DR Landscape Forecast – Disease Landscape Forecast 2020

Transformative Eye Drop

- Potential to be the first topical and non-invasive treatment for DME
- Total addressable US patient population for DME ~1.2M⁽¹⁾⁽²⁾

In Phase 3 with a broad reach

- **On-going Phase 3 programs** in DME and Ocular Surgery
- Positive Phase 3 Stage 1 in **DME**
- PoC study in **CME**

DME and CME Next Steps

- Continue DIAMOND program with full 52 weeks trials to start in 2H 2023
- OCS-01 could if approved provide significant value to patients, physicians & payors

(1) ARVO Annual Meeting Abstract, June 2021, Hennings et al. Prognostic determinants of postoperative pseudophakic macular oedema in a tertiary hospital setting.
(2) Data on file, Skyggn phase 2 study.
(3) Cystoid Macular Edema (CME).

First SGK Neuroprotective Ophthalmic Candidate

- Disease modifying drug which protects and repairs neurons
- Potential application in ophthalmology including Glaucoma, Geographic Atrophy, Diabetic Retinopathy, and corneal indications such as Neurotrophic Keratitis

In PoC status and IND enabling in the US

- Preclinical data showing neuroprotection by preventing retinal ganglion cell death and improvement of function in MS⁽¹⁾ models
- Phase 1 study data showed OCS-05 was well-tolerated in 48 healthy volunteers

Next Steps

- To continue ACUITY trial with FPFV 2H 23.
- IND enabling activities on-going in the US to achieve IND status

(1) Multiple Sclerosis.

Targeting critical unmet needs in 3 major ophthalmology segments

- **OCS-01: 1st** Eye drop for Diabetic Macular Edema (DME) in Ph 3
- **OCS-02: 1st** Biologic eye drop for Dry Eye Disease (DED) in Ph 2b
(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⁾ Ph 2 PoC readout
- OCS-02 DED Ph 2b readout
- OCS-02 Uveitis Ph 2b readout
- OCS-05 AON⁽²⁾ Ph 2 PoC readout

(1) Cystoid Macular Edema (CME)
(2) Acute Optic Neuritis (AON)

A photograph of three people—an elderly woman on the left, a young girl in the center, and a younger woman on the right—all smiling and holding their glasses up to their eyes. They are wearing aprons, suggesting a kitchen or workshop setting. The background is a bright, indoor space with a white wall and a wooden railing.

Our Purpose

To drive innovation to save sight and improve eye care