Oculis

Rethinking Ophthalmology

March 2024

Nasdaq: OCS

Safe Harbor Statements

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 preclinical studies, 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, 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; the ongoing and evolving COVID-19 pandemic on Oculis' business, financial position, strategy and anticipated milestones; 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 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 forwardlooking statement, whether as a result of new information, future events or otherwise, except as required by law.

Oculis



Our Purpose

To drive innovation to save sight and improve eye care

Experienced Leadership Team with Successful Track Record



Committed to build an industry leader in ophthalmic innovation

- ✓ Highly experienced leadership team
- Expertise in drug development leading to approvals and launches of >40 approved drugs globally
- Expertise in public company management and launching new classes of therapeutics



Strong Start to 2024 after a Successful 2023

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Diamond

DIAbetic Macular edema patients ON a Drop Successful Phase 3 Stage 1 completed



Once daily Post ocular surgery Treatment for InflaMmation and paIn to minimiZE drops

Successful Phase 3 completed



3 Major Innovations Addressing Highly Meaningful Unmet Medical Needs

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OCS-01

OPTIREACH® enables eye drops treating retinal disease



Phase 3 in Diabetic Macular Edema and Ocular Surgery

Proprietary technology for front and back of the eye: Topical treatment for **Diabetic Macular Edema** and **inflammation and pain following ocular surgery**

> Investigator-initiated trial for treatment of **Cystoid Macular Edema**

OCS-02 (Licaminlimab)

Antibody fragment technology enables biologic eye drop



Phase 2b in Dry Eye Disease and Uveitis

Topical TNFα inhibitor for **moderate-to-severe Dry Eye Disease** with potential biomarker for precision medicine

OCS-05 Promising neuroprotective agent for neuro-ophtha diseases



Phase 1/2a in Acute Optic Neuritis, with multiple additional applications

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

Innovative, Diversified and Late-stage Pipeline

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Product Candidate(s)	Investigational Indication(s)	Pre-clinical	Phase 1	Phase 2	Phase 3	2023 Accomplishments	Upcoming Key Catalysts
OCS-01	DIABETIC MACULAR EDEMA					Positive DIAMOND Stage 1 Initiated Ph3 Stage 2	
Optireach [®]	INFLAMMATION AND PAIN	FOLLOWING OCULAR S	SURGERY			Positive OPTIMIZE-1 Initiated OPTIMIZE-2	Q4 '24: Ph3 readout
technology	CYSTOID MACULAR EDEMA						Q1 '25: PoC readout
OCS-02	DRY EYE DISEASE					Initiated RELIEF Ph2b trial	Q2 '24: Ph2b readout
AntiTNF	UVEITIS						Q4 '24: Ph2b initiation
	ACUTE OPTIC NEURITIS						Q4 '24: PoC readout
005-05	GLAUCOMA						
OCS-05 SGK2 Activator	GEOGRAPHIC ATROPHY						
	DIABETIC RETINOPATHY						
	NEUROTROPHIC KERATITIS						
OCS-03	CORNEAL NV, PTERYGIUM						
OCS-04	CORNEAL TRANSPLANT						
(Undisclosed)	Wet-AMD, RVO, DR			1	:		

AMD; age-related macular degeneration; DR, diabetic retinopathy; RVO, retinal vein occlusion.

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

OCS-01 in Diabetic Macular Edema





OCS-01 Eye Drops in Diabetic Macular Edema (DME)

















DME is a Large and Growing Market with Critical Unmet Needs Oculis

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



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. Diabetes-Related Macular Edema. Prevent Blindness. Accessed 2023. <u>https://preventblindness.org/diabetic-macular-edema-dme/</u> 4. Berenberg and Kiss: "Real-World Utilization of Anti-VEGF Agents", Review of Ophthalmology, Feb 5, 2016 5. DRG Diabetic Macular Edema / Diabetic Retinopathy Disease Landscape & Forecast 2020

OCS-01 | Would Be Able to Address All Segments while Leading 2 Oculis Segments : Early Intervention and Treatment Customization



Addressable U.S. patient population: 1.3 million^{3,4}

OCT, Optical coherence tomography imaging.

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

OCS-01 | Phase 3 DIAMOND Program in DME

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Evaluating OCS-01 efficacy and safety



BCVA (Best corrected visual acuity); DME (Diabetic macular edema); ETDRS (Early Treatment Diabetic Retinopathy Study).

Multicenter Study on the Efficacy and Safety of OCS-01 in Subjects With Diabetic Macular Edema. Clinical Trials.gov identifier: NCT05066997. Updated January 17, 2023.

Study of the Efficacy and Safety of OCS-01 Eye Drops in Subjects With Diabetic Macular Edema (DIAMOND-2). Clinical Trials.gov identifier: NCT06172257. Updated December 15, 2023.

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Robust statistically significant improvement in vision and reduction in retinal edema vs vehicle

7.2-letter gain in BCVA vs baseline at week 6, increasing to 7.6 at week 12



25.3% of patients gained ≥15 letters at week 6, increasing to 27.4% at week 12



Rapid reduction in retinal edema already at week 2



Well-tolerated with no unexpected AEs



Results supported Stage 2 initiation

Oculis Diamond

7.2-letter gain in BCVA vs baseline at week 6, increasing to 7.6 at week 12



Imputation rules are applied based on a pattern-mixture model approach.

BCVA (Best corrected visual acuity); ETDRS (Early Treatment Diabetic Retinopathy Study); ITT (Intention-to-treat).

Tadayoni R, et al. A 12-week phase 2/3 double-masked, randomized, multicenter study of OCS-01 OPTIREACH® technology topical dexamethasone eye drops in subjects with diabetic macular edema (DME): efficacy and safety findings. Presented at: EURETINA; 2023.

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25.3% of patients gained ≥15 letters at week 6, increasing to 27.4% at week 12



≥15-LETTER GAINERS AT WEEK 12

* There was no loss of \geq_3 lines (>15 ETDRS letters) from baseline to week 6 in either treatment group.

P-value is based on difference in marginal effects. Imputation rules are applied based on a pattern-mixture model approach.

ETDRS (Early Treatment Diabetic Retinopathy Study); ITT (Intention-to-treat).

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3

Rapid reduction in retinal edema already at week 2

CHANGE IN CST AS ASSESSED BY SD-OCT



Mean (±SD) baseline CST: OCS-01, 453.0 (±131.81) μm; vehicle, 445.3 (±112.46) μm. Imputation rules are applied based on a pattern-mixture model approach. Data, analysis, and conclusions are preliminary, and subject to change as full analysis is ongoing. CST (Central subfield thickness); ITT (Intention-to-treat); SD-OCT (Spectral domain optical coherence tomography). Oculis. Data on file.

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Well-tolerated with no unexpected AEs

Treatment-Emergent Adverse Events				
>2.0% in the OCS-01 arm or >4.0% in the vehicle arm	OCS-01 (n=100) n (%)	Vehicle (n=48) n (%)		
AnyTEAE	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

	OCS-01 (n=100) n (%)	Vehicle (n=48) n (%)
Any ocular SAE	1 (1.0)	0 (0.0)
Vitreous hemorrhage	1 (1.0)	0 (0.0)
Any non-ocular SAE	4 (4.0)	3 (6.3)
Death	1(1.0)	0 (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

Minimal mean IOP increase was similar across induction and maintenance phases

Safety population

AE (Adverse event); IOP (Intraocular pressure); SAE (Serious adverse event); TEAE (Treatment-emergent adverse event).

Tadayoni R, et al. A 12-week phase 2/3 double-masked, randomized, multicenter study of OCS-01 OPTIREACH® technology topical dexamethasone eye drops in subjects with diabetic macular edema (DME): efficacy and safety findings. Presented at: EURETINA; 2023.

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(4)

Minimal mean IOP increase similar across induction and maintenance

CHANGE IN IOP ACROSS INDUCTION AND MAINTENANCE



Mean (±SD) baseline IOP: OCS-01, 15.3 (±3.1) mmHg; Vehicle, 14.7 (±3.0) mmHg.

IOP (Intraocular pressure).

Tadayoni R, et al. A 12-week phase 2/3 double-masked, randomized, multicenter study of OCS-01 OPTIREACH® technology topical dexamethasone eye drops in subjects with diabetic macular edema (DME): efficacy and safety findings. Presented at: EURETINA; 2023.

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Positive OCS-01 Phase 3 Stage 1 Results De-risking Stage 2 Trial Oculis



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

OCS-01 | Phase 3 DIAMOND Program in DME

Oculis Diamond



Results supported Stage 2 initiation

STAGE 2

TWO IDENTICAL 52-wk GLOBAL PIVOTAL TRIALS INITIATED

Evaluating OCS-01 efficacy and safety



BCVA (Best corrected visual acuity); DME (Diabetic macular edema); ETDRS (Early Treatment Diabetic Retinopathy Study). Multicenter Study on the Efficacy and Safety of OCS-01 in Subjects With Diabetic Macular Edema. ClinicalTrials.gov identifier: NCT05066997. Updated January 17, 2023. Study of the Efficacy and Safety of OCS-01 Eye Drops in Subjects With Diabetic Macular Edema (DIAMOND-2). ClinicalTrials.gov identifier: NCT06172257. Updated December 15, 2023.

OCS-01 | Would Be Able to Address All Segments while Oculis Diamond Leading : Early Intervention and Treatment Customization



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OCS-01 Total Addressable Market Potential

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Addressable Market Size
USD Bn

~\$10B+ Potential Market

Opportunity



1. DR and DME Disease and Landscape report Nov. 2020 – 2023 market value estimate for G7, \$3.9Bn. **2.** IQVIA 2019 Ex-factory Sales for Ocular Steroids (without Ozurdex & Iluvien sales) for US and EU5, \$0.8Bn. **3.** DR and DME Disease and Landscape report Nov. 2020 – 2023 market value estimate for G7, Diagnosed untreated patient proportion with ratio applied to current sales (43% treated, 57% untreated). \$5.2Bn. **4.** Estimated CME market potential based on 1.5 injections of Ozurdex per patient * 2.3% Clinically significant CME incidence following cataract surgery * 11M Cataract surgery / year for US & EU. \$0.6Bn. **5.** Global RVO Estimated Market Value - https://www.futuremarketinsights.com/reports/retinal-vein-occlusion-treatment-market. \$2.3Bn. **6.** GlobalData – Opportunity Analysis and Forecasts November 2017 – Estimated global sales in G7 in 2023. \$0.8Bn

OCS-02 in Dry Eye Disease



Large and Growing DED Opportunity

Market still underpenetrated and unsatisfied





Significant unmet need and market opportunity

- Large and growing unmet medical need with ~10 million diagnosed moderate to severe DED patients in the U.S.^{1,2} with a G7 market forecasted to reach \$7.3bn in 2029¹
- Untapped market potential: Only 13% of U.S. diagnosed patients receiving prescription treatment¹
- **87% Unsatisfied** patient population with only 13% of patients who feel their chronic DED is well-managed ³

1. DRG Dry Eye Disease Landscape and Forecast 2020. 2. Downs P. 2023. Dry Eye Products Market Report, Global Analysis for 2022 to 2028. Market Scope. 3. Mukamal, R. Why is Dry Eye So Difficult to Treat? 2021 https://www.aao.org/eye-health/tips-prevention/fix-dry-eye-treatment-eyedrops.

Despite New Treatment Options, Patient Satisfaction Remains a Challenge

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DED (Dry eye disease).

Downs P. 2023 Dry Eye Products Market Report, Global Analysis for 2022 to 2028. Market Scope; 2023. 2. Jain H, et al. Dry eye disease landscape and forecast. Decision Resources Group (DRG); 2020.
 Health Union Community Editorial Team. 2021 In America Survey Findings: Living With Chronic Dry Eye. Chronic Dry Eye. 2021. https://chronicdryeye.net/infographic/in-america-findings.

High Unmet Need for Novel Treatments for DED



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Innovations in DED Lag in Comparison to Other Specialties



The rise of TNF- α inhibitors



* Humira indicated as systemic treatment for posterior, pan-, and intermediate uveitis.

DED (Dry eye disease)

1. Yavuz B, et al. Sci World J. 2012;2012:194848. 2. Leone GM, et al. J Clin Med. 2023;12(4)1630. 3. Lindsley CW. ACS Chem Neurosci. 2016;7(7):842-843. 4. Mikulic M. Leading pharmaceutical products by sales worldwide in 2022. Statista. Published August 30, 2023. Accessed February 20, 2024. Available at: https://www.statista.com/statistics/258022/top-10-pharmaceutical-products-by-global-sales-2011/#statisticContainer.

OCS-02 | Novel anti-TNFα Eye Drop for Ocular Inflammation

Clinically proven MoA with potential transformative impact in ocular inflammatory diseases

Topical Biologic Candidate

OCS-02 is an **anti-TNFα antibody fragment** formulation with potential to become the first approved topical biologic for DED



Clinically proven MoA

Anti-inflammation and anti-necrosis MoA approved as systemic treatment for ocular disease and with transformative impact in other areas

Enhanced ocular penetration

Lower molecular weight, enhanced ocular penetration and higher concentration

Proprietary genetic biomarker

Associated with OCS-o2 response highlighting opportunity for a precision treatment in DED

Innovative Antibody Fragment Technology



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OCS-02 (Licaminlimab) Has a Dual MOA and is a Potent Inhibitor of TNF- $\!\alpha$



DUAL MOA: ANTI-INFLAMMATORY & ANTI-APOPTOTIC Inflammation Inhibits release of inflammatory factor (INF-γ, TNF-α, ILs) and MMP Inhibits activation, recruitment, and infiltration of immune cells OCS-02 (primarily T-cells) Apoptosis Inhibits nerve stimulation and cell death in conjunctival epithelium

TNF-α inhibitor potencies			
Compound	IC50		
CS-02 (Licaminlimab)	1.2 ng/mL		
dalimumab	9.2 ng/mL		

15.0 ng/mL

Infliximab

IL (Interleukin); MMP (Matrix metalloproteinase); MOA (Mechanism of action). Oculis. Data on file.

OCS-02 | Positive Phase 2 Results in DED and Uveitis

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De-risked programs advancing into Phase 2b

Positive Phase 2 / PoC studies in DED and Uveitis

DED#1

85 patients Phase 2 PoC Successfully completed

DED#2

131 patients Phase 2 PoC Successfully completed

Uveitis 32 patients Phase 2 PoC Successfully completed

Advancing into Phase 2b for both indications

Phase 2b to evaluate signs in DED (with secondary endpoint in symptoms)

Further validate CC genetic biomarker

Phase 2b as steroid-sparing alternative for chronic and recurring Non-Infectious Anterior Uveitis OCS-02 (Licaminlimab) Phase 2a Trial in Patients with Severe DED



Phase 2a trial evaluating the efficacy, safety and tolerability of OCS-02 in reducing ocular symptoms in patients with severe DED



Randomized, double-masked, vehicle-controlled study

6-week multi-center trial

134 participants

PRIMARY ENDPOINT

Change from baseline in global ocular discomfort score* at Day 29

SECONDARY ENDPOINT

Percentage of high responder[#] patients at Day 29

SAFETY ASSESSMENTS

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Ophthalmic evaluation & adverse events

* Change from baseline in global ocular discomfort score based on the Symptom Assessment iN Dry Eye (SANDE) questionnaire. # High responding patients is defined as patients who improve in global ocular discomfort score* by >20 points. DED (Dry eye disease). Shettle L, et al. *Clin. Ophthalmol.* 2022 ;16:2167-2177. OCS-02 (Licaminlimab) Phase 2a: Significantly Improved DED Symptoms **Oculis** Primary endpoint – Change from baseline in global ocular discomfort score* at Day 29



* Change from baseline in global ocular discomfort score based on the Symptom Assessment iN Dry Eye (SANDE) questionnaire. DED (Dry eye disease). Shettle L, et al. *Clin. Ophthalmol.* 2022;16:2167-2177. **OCS-o2 statistically significantly reduced ocular discomfort** in patients with DED compared to vehicle (*P* = 0.04)

OCS-02 (Licaminlimab) Phase 2a: Treated Group Had Clinically Meaningful Results

Secondary endpoint – Percentage of high responder patients at Day 29



* Change from baseline in global ocular discomfort score based on the Symptom Assessment iN Dry Eye (SANDE) questionnaire. Shettle L, et al. *Clin. Ophthalmol.* 2022;16:2167-2177.

There was a greater percentage of high responder patients treated with OCS-o2 compared to vehicle at Day 29 (*P* = 0.018)

High responding patients is defined as patients who improve in global ocular discomfort score^{*} by >20 points

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OCS-02 (Licaminlimab) Phase 2a: Well Tolerated by Patients



	OCS-02 (n=69)	Vehicle (n=65)
Patients with at least one TEAEs, n (%)	13 (18.8%)	9 (13.8%)
Related to study treatment	2 (2.9%)	2 (3.1%)
Patients with any serious TEAEs, n (%)	0 (0%)	1* (1.5%)
Deaths	0 (0%)	0 (0%)
Nonfatal serious TEAE	0 (0%)	1(1.5%)
Related to study treatment	0 (0%)	0 (0%)
Patients with TEAE leading to study discontinuation, n (%)	1(1.4%)	0 (0%)
Related to study treatment	0 (0%)	0 (0%)
TEAE ≥2%, n (%)		
Dry eye	2 (2.9%)	0 (0%)
Eye pruritus	2 (2.9%)	o (o%)

No burning, blurred vision, and ocular hyperemia were reported in either group

Safety data set population

* Patient reported to have pneumonia.

BCVA (Best-corrected visual acuity); IOP (Intraocular pressure); TEAE (Treatment-emergent adverse event).

Shettle L, et al. Clin. Ophthalmol. 2022;16:2167-2177.

Consistent Results in Ocular Discomfort Improvement with ESBA105* Oculis

Rapid onset with significant change from baseline as of Day 14 (post hoc analysis)



*OCS-o2 predecessor. Novartis. Data on file.

OCS-02 | Biomarker Identified for High Responders – Oculis Potential upside to de-risk Phase 3 and Precision Medicine Approach¹

Genetic Biomarker for OCS-02 Response

Pre-specified exploratory pharmacogenetic analysis focused on the genes relevant to TNF pathway and Sjogren's syndrome



Solid association between gene variants and global ocular discomfort score response at treatment day 29 was tested:

- Among the gene variants tested, one variant out of 8 showed significant effect on the response to OCS-o2
- Patients with this gene variant tended to have larger improvement vs. other p < 0.0001
- Oculis is planning to further validate OCS-02 biomarker in the upcoming Phase 2b study

Successful Phase 2b will support advancement to Phase 3 while evaluating the potential for a precision medicine for DED

Perez. Presented at ARVO 2021 <u>https://iovs.arvojournals.org/article.aspx?articleid=2774294</u>

 $[\]text{2.} \quad \text{https://www.ensembl.org/Homo_sapiens/Variation/Population?db=core; r=12:6330343-6331343; v=rs1800693; vdb=variation; vf=760495013 and variation and variation$

OCS-02 | Phase 2b Trial in Dry Eye Disease



A multi-center, randomized, double-masked, vehicle-controlled study evaluating the efficacy and safety of OCS-02 for the treatment of signs and symptoms of DED

 Phase 2b study design: Randomized, masked, vehicle-controlled study Multi-center, 10-week, approx. 120 subjects Stratification based on genotype (CC SNP) 20% patients Objectives: The objective of this study is to evaluate the efficacy and safety of OCS-02 for the treatment of signs of dry eye disease 	 Key Enrollment Criteria: Subjects with history of DED for 6 months Schirmer's test at baseline < 10 mm Corneal fluorescein stain ≥ 2 in at least 1 region (inferior, superior)
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	2 week run in, all subjects	6 weeks		TBD
		OCS-02 3x/day (TID)	\rightarrow	Follow-up
Screening	Artificial tears TID			
	Patients who respond to artificial tears will not be randomized	Vehicle (TID)	→	Follow-up
	Randomiz	zation		

OCS-02 | Potential to Transform Treatment of Moderate-to-Severe Dry Eye Patients with Novel Anti-TNF-α Eye Drop

20 million diagnosed U.S.	Moderate (35%) ²	Severe (14%) ²					
DED patients ¹	~ 10 million diagnosed moderate-to-severe DED pati	~ 10 million diagnosed moderate-to-severe DED patients in the U.S. ^{1,2}					
Significant unmet needs	87% Unsatisfied patient population with only 13% of patients w chronic DED is well-managed ³	ho feel their					
Patient and Physician Expectations	 Significant efficacy in relieving DED symptoms Rapid onset of action Well-tolerated without burning and redness 						
Opportunity for OCS-02 Novel anti-inflammatory treatment for moderate-to-severe DED patients Potential to deliver significant efficacy and rapid onset with good tolerability Potential upside with precision medicine approach to predict response 		DED patients ood tolerability response					

DED (Dry eye disease).

1. DRG Dry Eye Disease Landscape and Forecast 2020. 2. Downs P. 2023. Dry Eye Products Market Report, Global Analysis for 2022 to 2028. Market Scope. 3. Mukamal, R. Why is Dry Eye So Difficult to Treat? 2021 https://www.aao.org/eye-health/tips-prevention/fix-dry-eye-treatment-eyedrops.

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OCS-05 in Neuro-Ophthalmology: Acute Optic Neuritis (AON)

Normal vision



Early glaucoma



Advanced glaucoma



OCS-05 | Candidate Overview



SGK-2 activator peptidomimetic small molecule with a unique MoA for neuro-ophthalmology

Disease modifying drug to protect and repair neurons

 Activates neurotrophic signalling pathways supporting neuronal survival and repair

Multiple potential applications:

- Glaucoma
- Dry AMD / Geographic Atrophy
- Diabetic Retinopathy
- Acute Optic Neuritis
- Neurotrophic Keratitis

Unique & Differentiated MoA

OCS-o5 targets SGK as part of the neurotrophic factor signalling pathways triggering multiple beneficial effects on apoptosis, anti-oxidation and anti-inflammation



OCS-05 | Neuro-Ophthalmology Candidate

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Compelling preclinical data showing prevention of RGC damage in Glaucoma and AON models

OCS-05, IVT and topical, shown to **prevent RGC damage** (the key element in Glaucoma vision loss)



OCS – 05 | H&E for RGC density at week 6¹

High-pressure Glaucoma rat model of neurodegeneration without inflammation

EAE, experimental autoimmune encephalomyelitis; H&E, hematoxylin and eosin staining; MS, multiple sclerosis; RGC, retinal ganglion cell 1. Villoslada P. et al. *Neurotherapeutics.* 2019; 16(3):808-827 AON model: Short term study (5-day treatment, assessment at day 6)



OCS-05 shown to promote **improvement of clinical function** (disability) in experimental autoimmune encephalomyelitis (EAE) model

OCS – 05 | Model of autoimmune AON and MS



Experimental Autoimmune Encephalomyelitis model in mice

OCS-05 | Short Term Study (5-Day Treatment, Assessment at Day 6)¹

Study AON: Promotes axonal sparing and reduces demyelination



Reduced optic nerve axonal loss



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

1. Villoslada P. et al. Neurotherapeutics, published online: 27 February 2019 ***p < 0.001 compared to placebo

1.70 **High loss** 2.00 % of Efficacy 1.80 1.60 64.0 55.0 1.40 Score (scale 0 - 4) 1.20 ***

1.00

0.80

0.60

0.40

Reduced optic nerve demyelination

0.77

0.61





Acute Optic Neuritis

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Optic neuritis trial allows to validate OCS-05 in neuro-ophthalmology

130k patients a year (US/EU)

AON mean annual prevalence of acute: 8 cases per 100,000 person-year and AON mean annual incidence rate is cases per 100,000 person-years¹



- No approved therapy for AON
- SoC is intravenous methylprednisolone, that is not reducing permanent disability³



Retinal thickness (pRNFL and GCIPL) as surrogate of permanent visual impairment



Martínez-Lapiscina et al. J Neurol. 2014 Apr;261(4):759-67; 2. Gabilondo et al. Ann Neurol. 2015 Mar;77(3):517-28; 3. 3Beck RW, et al. N Engl J Med. 1992 Feb 27;326(9):581-8

LCVA: Low Contrast Visual Acuity. 2.

OCS-05 | Development Status

Paving the way to multiple indications

Oculis became new sponsor in Q3 2022

Previous and ongoing studies in Europe

Completed Phase 1: No drug-related side effects

 Randomized, double-blind, placebo-controlled, single and multiple ascending dose study of the safety, tolerability and PK in adult healthy volunteers (UK, MHRA) in 48 healthy volunteers (36 OCS-05, 12 placebo)

Ongoing Phase 2a: First-in-patient trial in AON

 Randomized, double-blind, placebo-controlled, multi-center trial in France to evaluate safety and explore efficacy of OCS-05 compared to placebo in patients diagnosed with a first unilateral AON of a demyelinating origin

• Oculis is working with FDA on pursuing development in the U.S.*

Several neuroophthalmology indications under consideration Acute Optic Neuritis (AON)

Oculis

Glaucoma

Geographic Atrophy

Diabetic Retinopathy

Cornea: Neurotrophic Keratitis

CNS: Multiple Sclerosis (MS)



Summary

Track Record of Efficient Capital Deployment





- > USD 110 m private funding from leading international life sciences investors
- Successful clinical validation of OPTIREACH® / OCS-01 in DME and post-ocular Surgery

Financial nighlights

- Strong and balanced portfolio: OCS-01, OCS-02 and OCS-05
- Efficient deployment of of capital transforming Oculis into multiple assets with late-stage candidates

- Successful Merger with EBAC and listing on Masdaq: March 3, 2023
- \$146M gross proceeds raised in 2023
- Adequately capitalized with cash runway through late 2025
- Track record of success and well funded to deliver upcoming milestones
 - 4 clinical readouts
 - 1 NDA application

Multiple Near-Term Value Inflection Points for All Three Assets Oculis

2023 ACHIEVEMENTS

Key corporate and clinical milestones:

- NASDAQ listing and \$146M raise
- Positive OCS-01 DME Phase 3 (Stage 1)
- ✓ Positive OCS-01 Ocular Surgery Phase 3

Advanced innovative pipeline development:

- ✓ Initiated OCS-01 Phase 3 DME DIAMOND-1 trial
- ✓ Initiated OCS-01 Phase 3 Ocular Surgery OPTIMIZE-2 trial
- ✓ Initiated OCS-01 PoC CME LEOPARD trial
- ✓ Initiated OCS-o₂ Phase ₂b DED RELIEF trial

2024 CLINICAL MILESTONES

• Q1 '24:

- ✓ Initiated OCS-01 Phase 3 DME DIAMOND-2 trial
- Completed enrollment in OCS-02 Phase 2b DED RELIEF trial
- **Q2 '24:** OCS-02 Phase 2b readout in DED RELIEF trial

- Q3 '24: OCS-05 IND
- Q4 ′24:
 - OCS-01 Phase 3 topline readout in Ocular Surgery
 - OCS-02 Phase 2b initiation in Uveitis
 - OCS-05 PoC Acute Optic Neuritis readout

