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Rethinking Ophthalmology

R&D Day

April 15, 2025

Safe Harbor Statements

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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 clinical studies, 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; 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 forward-looking statement, whether as a result of new information, future events or otherwise, except as required by law.

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Oculis Management

Riad Sherif, MD
Chief Executive Officer

Sylvia Cheung
Chief Financial Officer

Snehal Shah, PharmD
President of R&D

Sharon Klier, MD
Chief Development Officer

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World Renowned Ophthalmology and Neuro-Ophthalmology Experts

Retina

Arshad M. Khanani, MD
Clinical Professor, University of Nevada, and **Director of Clinical** Research, Sierra Eye Associates

Baruch D. Kuppermann, MD, PhD
Prof. and Chair, Dept of Ophthalmology
Director, Gavin Herbert Eye Institute
University of California, Irvine

David S. Boyer, MD
Adjunct Clinical Prof. of Ophthalmology
USC/Keck School of Medicine,
Partner Retina Vitreous Associates

Sebastian Wolf, MD, PhD
Professor of Ophthalmology
Universitätsspital Bern**, Managing Director**
Bern Photographic Reading Center

Inflammation & Precision Medicine

Anat Galor, MD, MSPH
Professor of Ophthalmology
Bascom Palmer Eye Institute,
Miller School of Medicine,
University of Miami

Neuro-ophthalmology

Leonard Levin, MD, PhD
Professor of Ophthalmology & Visual Sciences and Neurology & Neurosurgery, McGill University

Mark Kupersmith, MD
Clinical Prof. of Ophthalmology,
Icahn School of Medicine Mount Sinai and New York Eye and Ear Infirmary

Pablo Villoslada, MD, PhD
Chair of the Department of Neurology
Hospital del Mar, Pompeu Fabra University

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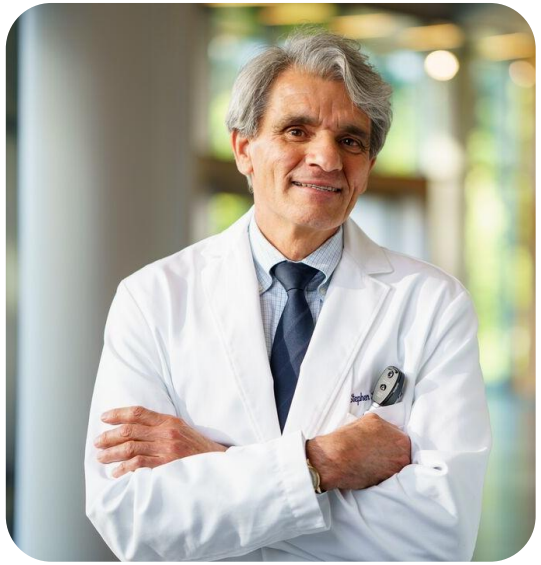
Stephen Hauser, MD, PhD Professor, Neurology Director, UCSF Weill Institute for Neuroscience



A neuroimmunologist, Dr. Hauser's research has advanced our understanding of the genetic basis, immune mechanisms, and treatment of multiple sclerosis (MS).

Dr. Hauser has received numerous awards and honors for his work, including the Jacob Javits Neuroscience Investigator Award, the John Dystel Prize for Multiple Sclerosis Research (2008), the Charcot Award (2013), the Taubman Prize for Excellence in Translational Medical Research (2017), the Scientific Breakthrough Award from the American Brain Foundation (2022), and the Breakthrough Prize in Life Sciences (2025).

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Agenda & Speakers

1	**Opening Remarks: 5 mins.**	**Sylvia Cheung,** Chief Financial Officer
2	**Oculis Corporate Update: 5 mins.**	**Riad Sherif, MD,** Chief Executive Officer
3	**OCS-01 in DME: 30 mins.** • DIAMOND Phase 3 trials update • Q&A	**Sharon Klier, MD,** Chief Development Officer **Prof. Arshad Khanani, MD**, Chair of the DIAMOND Steering Committee **Prof. Baruch D. Kuppermann, MD, PhD** , Chair of the DCRC (DME Central Review Committee) **Prof David Boyer, MD** , DIAMOND Principal Investigator
4	**Licaminlimab (OCS-02) in DED: 20 mins.** • Rethinking DED treatment with precision medicine approach • Q&A	**Snehal Shah, PharmD,** President of R&D **Prof. Anat Galor, MD**

Agenda & Speakers

5	**Privosegtor (OCS-05) – New Frontier in Neuroprotection: 55 mins.** • Phase 2 ACUITY expanded data analysis • Next steps in acute optic neuritis • Neuroprotection beyond acute optic neuritis • Q&A	**Riad Sherif, MD,** CEO **Prof. Stephen Hauser, MD, PhD** **Prof. Mark Kupersmith, MD** **Prof. Leonard Levin, MD, PhD** **Prof. Pablo Villoslada, MD, PhD** **Prof. Sebastian Wolf, MD, PhD**
6	**Closing Remarks: 5 mins.**	**Riad Sherif, MD,** CEO

Corporate Update

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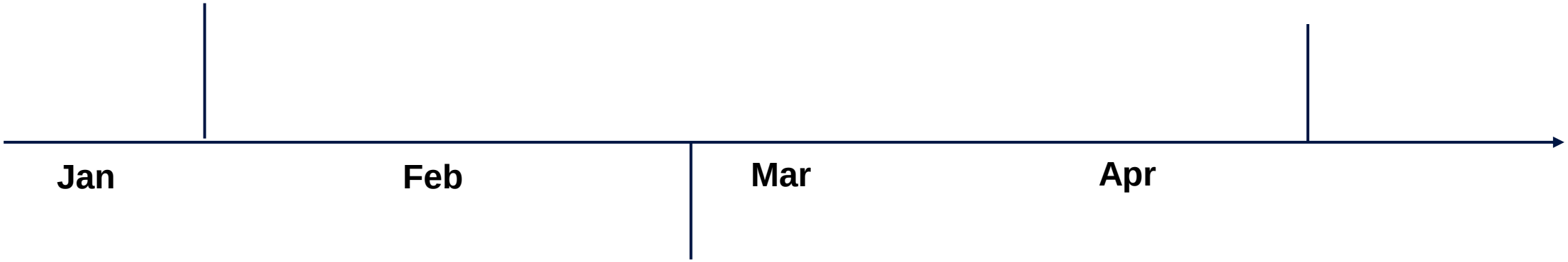
Strong Momentum in 2025

Privosegtor: Positive Phase 2 ACUITY results in Acute Optic Neuritis

OCS-01: Completed enrollment in Phase 3 DIAMOND program in DME with >800 patients



Licaminlimab: Confirmed precision medicine approach in DED with FDA

$100 million raised in an over-subscribed equity financing

Focus on the highest unmet medical needs / market opportunities following successful advancement of all 3 assets

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3 Major Innovations Addressing Substantial Unmet Medical Needs

Highly differentiated late-stage pipeline focused on multi-billion-dollar market opportunities

OCS-01 OPTIREACH® Eye Drops in DME

Topical treatment* for DME** enabling ***early intervention and for patients with ***inadequate response to current SoC***

Licaminlimab (OCS-02) Genotype-Based Dev. in DED

Personalized medicine treatment to address highly unsatisfied patient population

Privosegtor (OCS-05) Breakthrough in Neuroprotection

Novel neuroprotective candidate with broad potential in neuro-ophthalmology and neurology

SoC: Standard of Care.

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Oculis Pipeline Development Strategic Evolution

Advance

OCS-01 would be the first ever topical treatment in DME, if approved

Licaminlimab personalized medicine in DED

Privosegtor neuroprotection in Acute Optic Neuritis

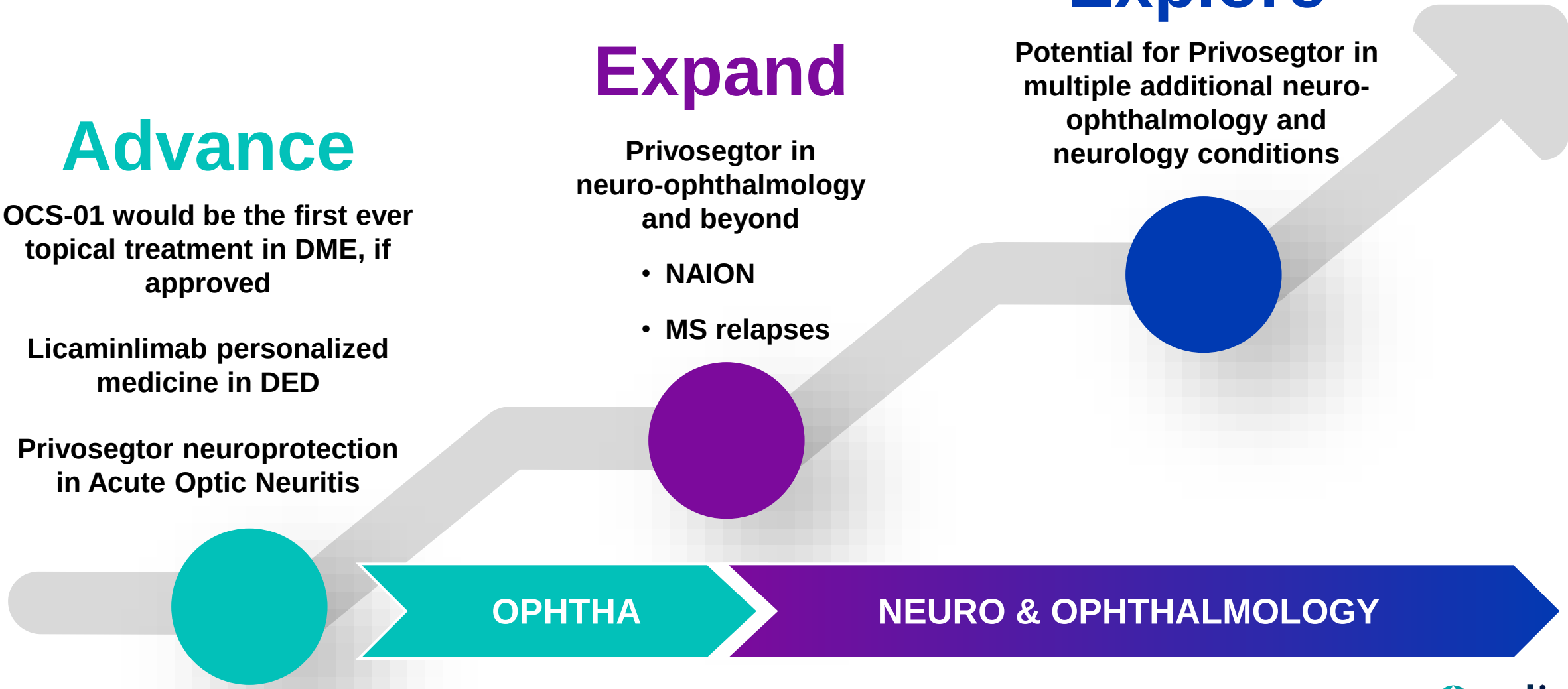
Expand

Privosegtor in neuro-ophthalmology and beyond

- **NAION**
- **MS relapses**

Explore

Potential for Privosegtor in multiple additional neuro-ophthalmology and neurology conditions



DME diabetic macular edema, DED: dry eye disease, NAION: Non-arteritic Anterior Ischemic Optic Neuropathy MS: Multiple Sclerosis.

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OCS-01 in DME

DIAMOND Phase 3 trials update

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Positive and Consistent Results Across 4 Previously Completed Studies

Four (4) clinical trials successfully completed showing positive outcomes

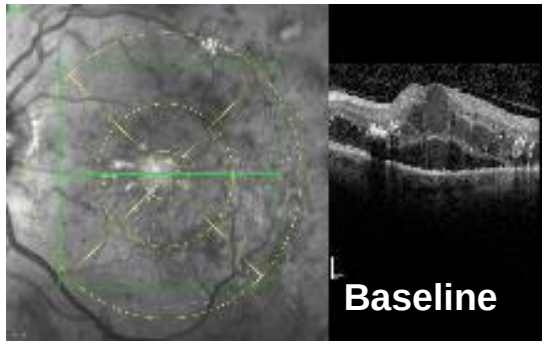
DME Exploratory 1 & 2
19 pts Tanito & **22 pts** Ohira studies[1,2]

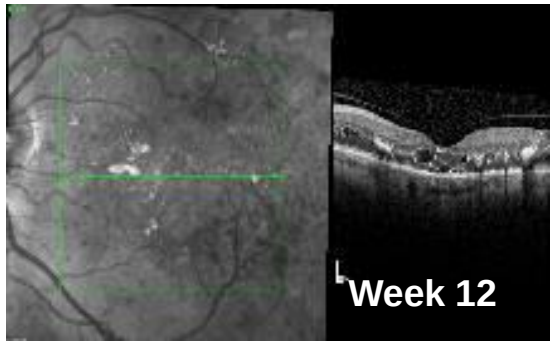
DME Phase 2
144 pts
Randomized & double-masked[3]

DME Phase 3 Stage 1
148 pts
Randomized & double-masked[4]

Patient Case (Phase 2 DX211)
OCS-01 showed consistent biological effect in CMT reduction and BCVA improvement[3]

Age	55
Treatment Group	OCS-01
DME Duration	4 m
Prior DME Tx	No
Baseline CMT	765
Week 12 CMT	328
Baseline BCVA	40
W12 BCVA	56





1. Exploratory 1: Investigator-initiated, open-label, single-center study. Tanito M, et al. Invest Ophthalmology Vis Sci. 2011;52:7944-7948
2. Exploratory 2: Ohira A, et al. Acta Ophthalmologica. 2015;93:610-615.Ohira A, et al. Acta Ophthalmologica. 2015;93:610-615.
3. DME Phase 2 (DX-211): Presented by R. Tadayoni at EURETINA 2020, Late-breaking session on October 3rd, 2020
4. 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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5 Key Takeaways From OCS-01 DIAMOND Phase 3 Stage 1

Consistent with previous trials with robust statistically significant improvement in vision and reduction in retinal edema vs. vehicle

1. 7.2 letter gain in BCVA vs. baseline at Week 6, increasing to 7.6 at Week 12
2. 25.3% of patients gained ≥15 letters at Week 6, increasing to 27.4% at Week 12
3. Rapid and sustained reduction in retinal edema already at Week 2
4. Positive results in both populations: naïve and previously treated with SoC
5. Well-tolerated with no unexpected AEs

AE: adverse event; BCVA: best corrected visual acuity, SoC: Standard of Care.

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, Data on file.

Diamond | Oculis

OCS-01 | Phase 3 DIAMOND Program in DME

Completed enrollment in both Diamond 1 & 2 Phase 3 Studies

Study Design

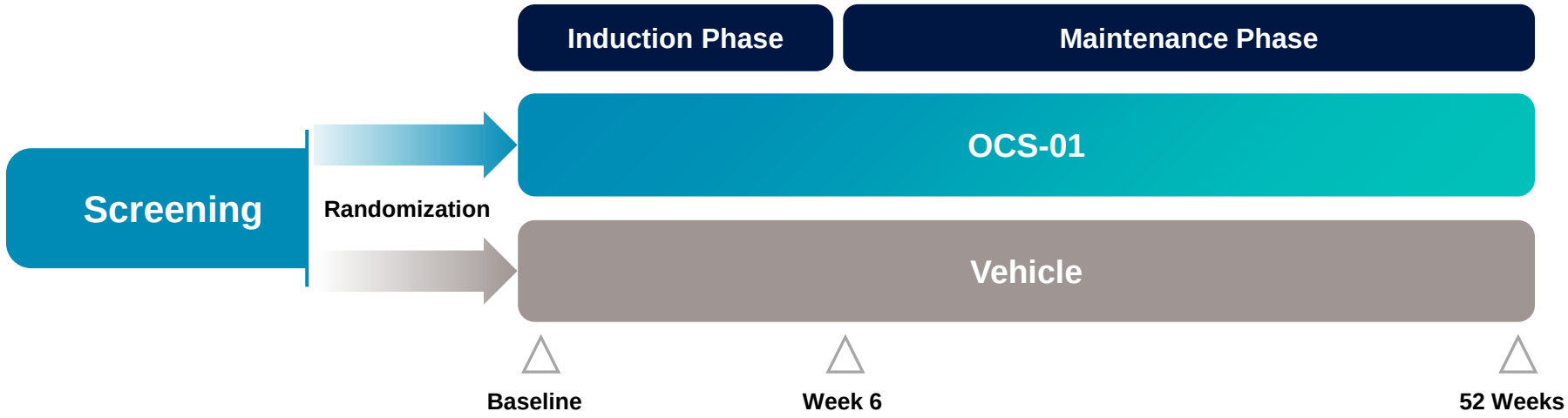
- Randomized, double-blind, placebo-controlled study (registrational trials)
- Multi-center, 12-month trial with >800 subjects randomized
- Induction phase: 1 drop, 6 times a day for first 6 weeks, maintenance phase: 1 drop 3 times a day for 46 weeks

Key Endpoints

- Primary endpoint: Change in BCVA ETDRS letter score at Week 52
- Key secondary endpoint: % with a ≥ 15 ETDRS letter gain in BCVA at Week 52

Study Population

- Age 18-85 years
- Confirmed diagnosis of DME
- Diabetes mellitus 1 and 2
- ETDRS BCVA letter score: 24 - 65
- Retinal thickness (CST) ≥ 310 µm
- Anti-VEGF and corticosteroid naïve or agree to washout



BCVA: best corrected visual acuity; DME: diabetic macular edema; ETDRS: early treatment diabetic retinopathy study, CST: central subfield thickness.

Multicenter Study on the Efficacy and Safety of OCS-01 in Subjects With Diabetic Macular Edema. ClinicalTrials.gov identifier: NCT05066997
Study of the Efficacy and Safety of OCS-01 Eye Drops in Subjects With Diabetic Macular Edema (DIAMOND-2). ClinicalTrials.gov identifier: NCT06172257

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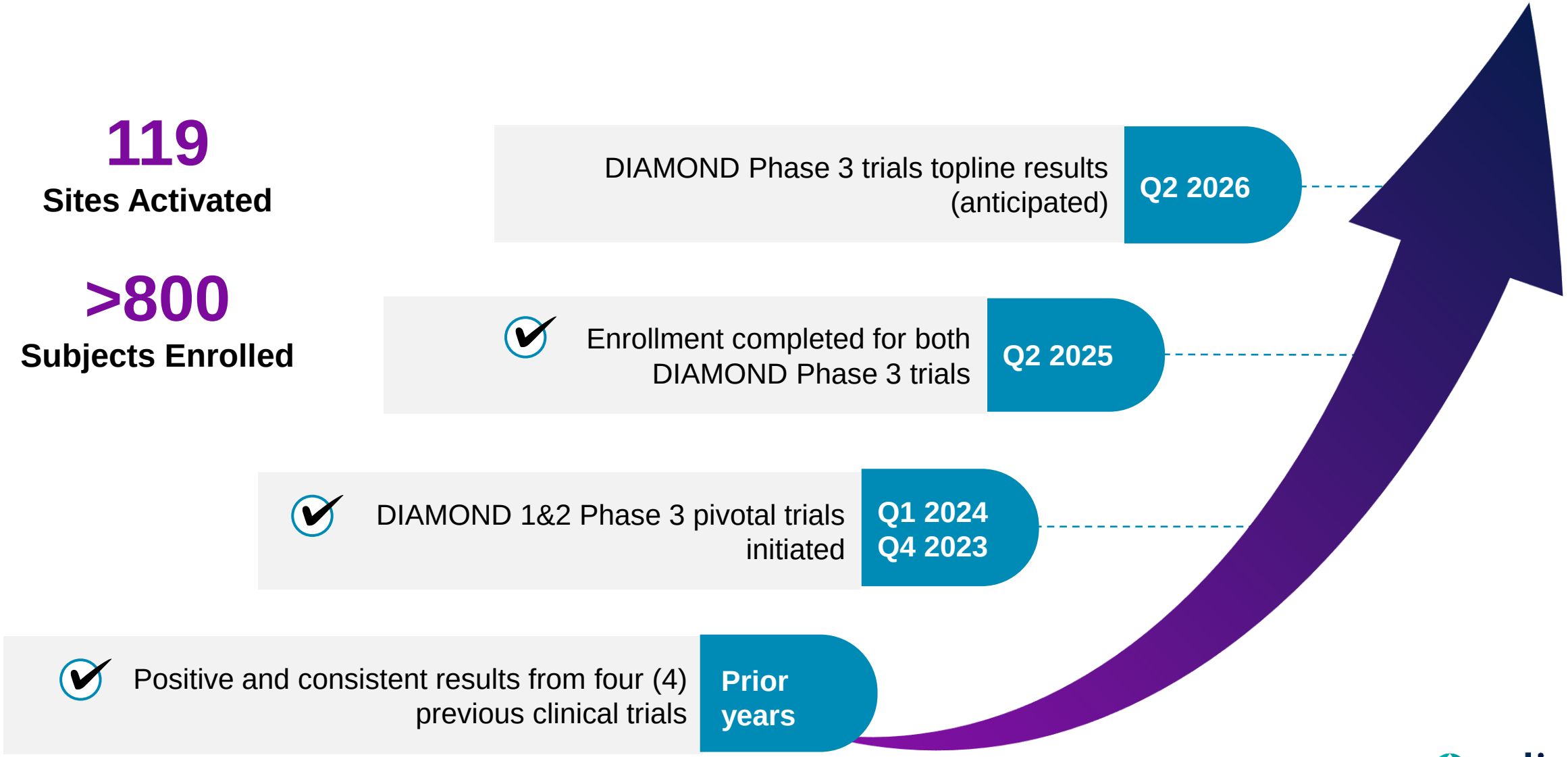
Rapid Enrollment Completed for Both DIAMOND Phase 3 Trials

Strong execution supported by DIAMOND Committees with world-renowned experts

119
Sites Activated

>800
Subjects Enrolled



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2025 DIAMOND Team Focused on Execution and Oversight

01 **Driving strong adherence to the protocol**

02 **Ensuring patient compliance and retention**

03 **Collaborating closely with highly experienced investigators and committees**

Investigator’s perspective: Dr. David Boyer

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DIAMOND Experts Committees

Worldwide renowned retina specialists

Steering Committee


Arshad M. Khanani, MD


David Almeida, MD, PhD


David S. Boyer, MD


Margaret Chang, MD


Saradha Chexal, MD


Sabri Markabi, MD


Carl Danzig, MD


Dilsher Dhoot, MD


Diana Do, MD


Frank Holz, MD


Anat Loewenstein, MD


Kirk Bateman, M.Sc.
Biostatistics expert


Patricio Schlottmann, MD


Ashish Sharma, MD


Veeral Sheth, MD


Michael Singer, MD


Sobha Sivaprasad, MD

DME Central Review Committee (DCRC)


Baruch D. Kuppermann, MD, PhD


Mark Barakat, MD


Timothy Lai, MD


Thomas Wolfensberger, MD


Sebastian Wolf, MD, PhD

Experts' perspective: Dr. Khanani & Dr. Kuppermann

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Licaminlimab in DED

Rethinking DED Treatment with a Genotype-Base Development for Personalized Medicine

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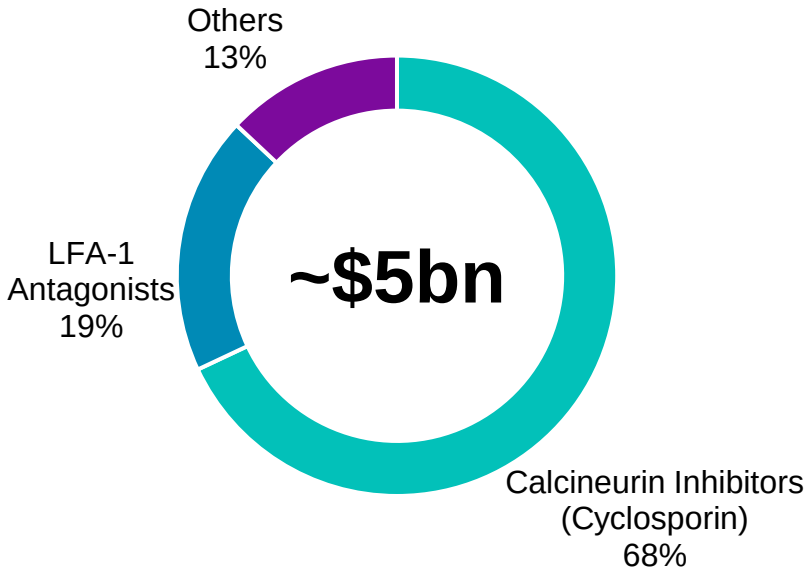
Large Unsatisfied Market Creates Significant Opportunity for Personalized Medicine

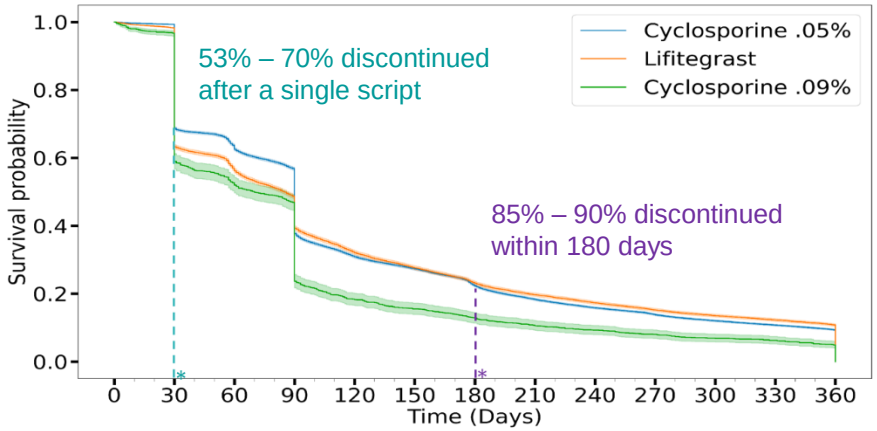
Only 13% experiencing lasting relief after 12 months with current treatments[1]

2024 Dry Eye Rx drug market in G7 countries[2] and U.S. Rx split[3]



Driven by trial and error with significant unmet needs

Discontinuation & switching is commonplace in DED[4]



DED expert's perspective: Dr. Anat Galor

1. 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.
2. DRG Dry Eye Disease Landscape and Forecast 2020 (market value in 2024)
3. IQVIA DED report, data on file. Prescriptions volume in DED March 2024 for split per drug class
4. Mbagwu M, et al. Characterization of Discontinuation and Switching Patterns of Dry Eye Disease Medications Using Linked EHR Registry and Claims Data. Presented at: ASCRS Annual Meeting 2024 https://ophthalmology360.com/study-finds-high-discontinuation-rate-of-dry-eye-medications/

Licaminlimab: Three Positive DED Phase 2 Trials Completed

Consistent positive results in signs and symptoms with potential for a genotype-based development to drive precision medicine

Phase 2 Randomized Controlled Studies in DED

- **DED#1 Symptoms**
  85 patients Phase 2 PoC
- **DED#2 Symptoms**
  134 patients Phase 2 PoC
- **DED#3 (RELIEF) Signs**
  122 patients Phase 2b

Consistent positive results across studies and unique precision medicine strategy

01 Meaningful and rapid treatment effect in signs and symptoms

02 More pronounced treatment effect in TNFR1 genotype positive (5X in signs and 7X in symptoms)

03 Well-tolerated, drop comfort like artificial tears

DED expert's perspective: Dr. Anat Galor

DED#1 and DED#3: Data on file
DED #2: Sheetle L, et al. *Clin. Ophthalmol.* 2022; 16:2167-2177

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First Genotype-Based Development in DED Fully Aligned with FDA Guidance – Meeting Completed in Q1 25

Achieved clarity on:

1. Precision medicine strategy
2. Registrational path forward
3. Study design

- First genotype-based development in DED to drive precision medicine
- Primary endpoint in TNFR1 genotype positive patients; secondary endpoint in total population
- Symptoms and signs endpoints consistent with DED guidance (e.g. global ocular discomfort, inferior corneal staining, etc.)

First-time precision medicine applied to DED, significantly de-risking Phase 3 clinical program and offering a potentially transformative product profile

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Licaminlimab First Genotype-based Development to Drive Precision Medicine in DED

Registration Program to Start in 2H 2025

Phase 2/3 Study Design

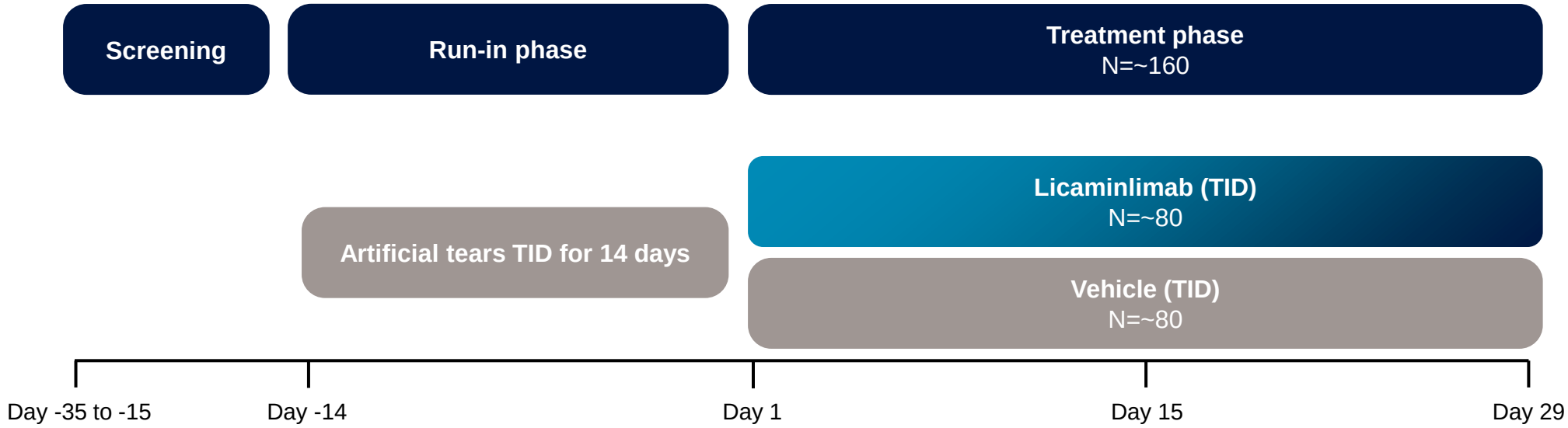
- Randomized, multicenter, double-masked, vehicle-controlled, 4-week study
- N= ~160 patients, 1:1 randomization

Key endpoints

- Primary endpoint: Global ocular discomfort score* at Day 29 in patients with TNFR1 genotype positive
- Key secondary endpoint: Global ocular discomfort score at Day 29 in all patients

Study Population

- TNFR1 genotype: ~2/3 positive
- Diagnosis of DED of at least 6 months
- Global ocular discomfort score of ≥ 50



*Global discomfort score is a composite of discomfort frequency and severity as assessed by a visual analog scale.
DED: dry eye disease. FDA: Food and Drug Administration. TID: Three times a day. TNFR1: Tumor necrosis factor receptor 1

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Privosegtor – Neuroprotection

Phase 2 ACUITY expanded data analysis
Next steps in Acute Optic Neuritis
Neuroprotection beyond Acute Optic Neuritis

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Privosegtor (OCS-05) Key Takeaways

New class of drug potentially unlocking neuroprotection therapy era

01 Privosegtor is a small molecule peptoid that penetrates Blood Brain and Retinal Barrier

02 Pre-clinical data in various in vivo models validated preservation of neurons and axons

03 Acute optic neuritis was chosen as a predictive clinical neuroprotection model

04 Positive ACUITY Phase 2 data showed neuroprotection benefits anatomically and biologically with clinically meaningful visual function improvement

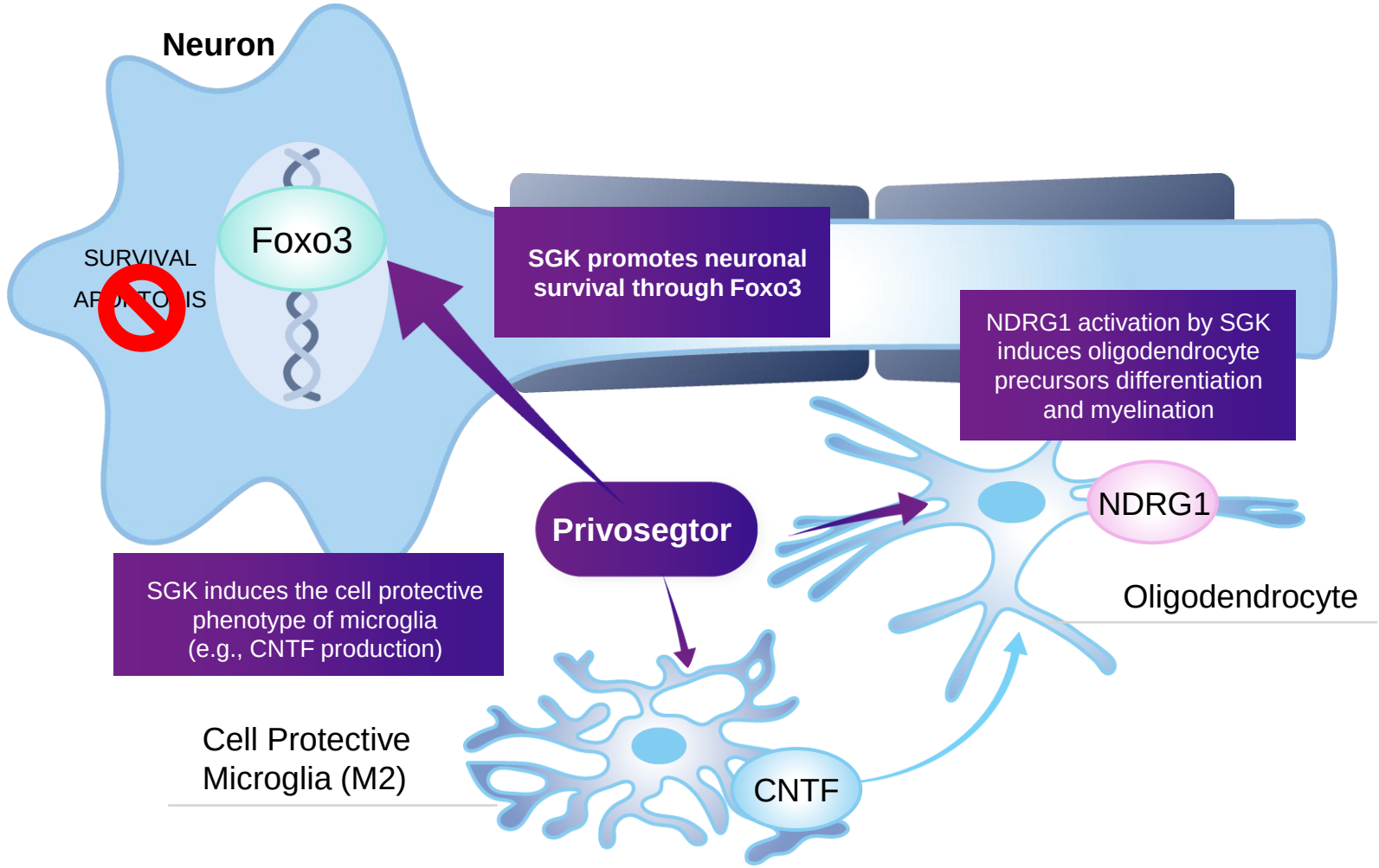
05 Advancing acute optic neuritis program while initiating new programs in NAION and MS relapses

NAION: Non-arteritic Anterior Ischemic Optic Neuropathy, MS: Multiple Sclerosis.

Neuroprotection the New Frontier in Neuro-Ophthalmology and Beyond

Privosegtor is a neuroprotective candidate activating neurotrophic signaling pathways supporting neuronal and axonal survival and preservation

- Privosegtor is a small molecule peptoid that penetrates Blood Brain and Retinal Barrier
- Selected by high-throughput screening (HTS) for neurotrophic and neuroprotective properties, confirmed in vivo in Glaucoma, MS, and acute optic neuritis models
- It activates SGK, thereby activating FOXO3 pathway, which is known to be related to the neuronal survival response. It triggers multiple beneficial effects on apoptosis, oxidation, and inflammation



CNTF: ciliary neurotrophic factor; GSK3b: glycogen synthase kinase-3 beta; MoA: mechanism of action; NDRG1: N-myc downstream regulated 1. BBB: blood brain barrier, MS: multiple sclerosis, SGK: serum glucocorticoid kinase

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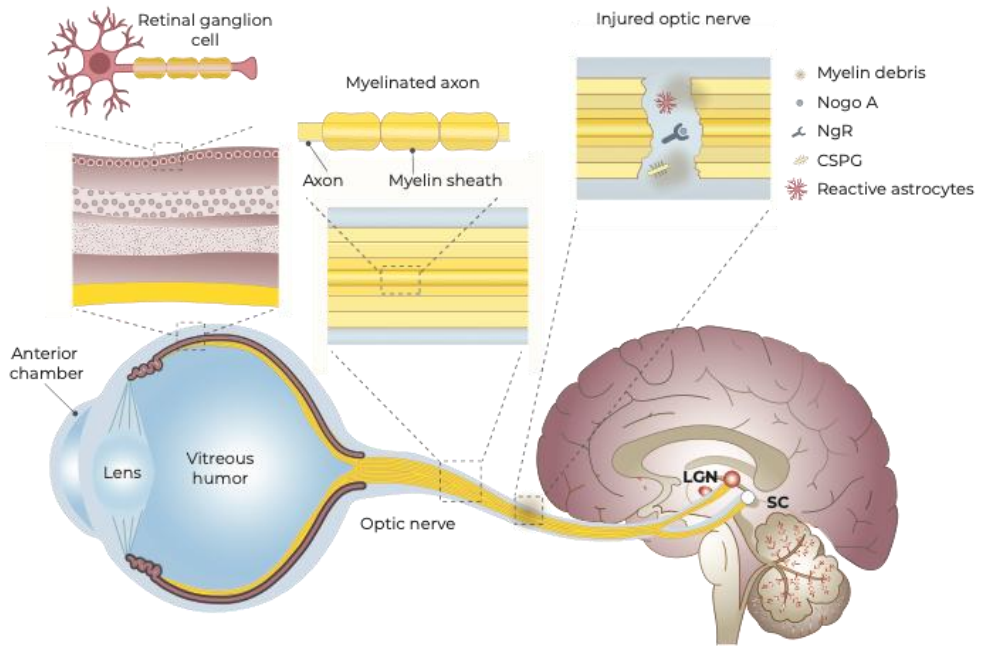
Acute Optic Neuritis a Predictive Model for Neuroprotection

Shares a similar pathophysiology triggered by acute RGC/Axon injuries



Similar pathophysiological mechanisms across AON, MS relapses, and acute RGC & Axons insults

- MS relapses: regardless of their anatomical location, they share fundamental mechanisms of neuroinflammation, demyelination, and axonal injury[1]
- RGC axon insults: other types of injury (e.g., axonal ischemia, elevated intraocular pressure) involve similar mechanisms

Privosegtor tested in Glaucoma, MS and acute optic neuritis in vivo models:

- All show the same benefits of preservation of RGC and axons

1. Reich DS, Lucchinetti CF, Calabresi PA. Multiple Sclerosis. N Engl J Med 2018;378:169-180.

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Acute Optic Neuritis

An acute inflammation of the optic nerve that can lead to permanent visual impairment

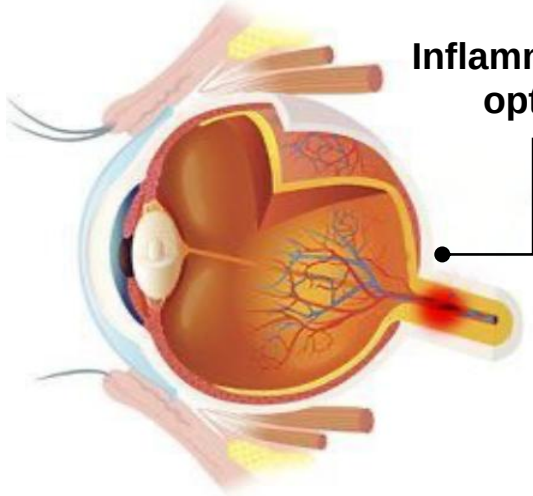
Orphan indication with ~ 65k patients a year (US/EU)[1]

Acute inflammation of the optic nerve impacting retinal ganglion cells

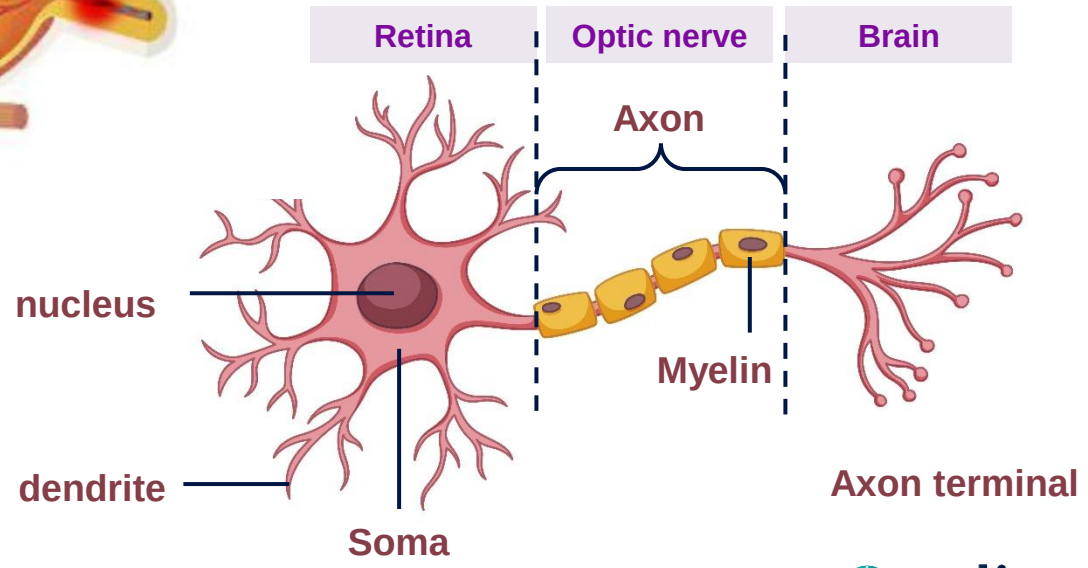
- Type of neuropathy causing **vision loss particularly affecting color and contrast**

- **Inflammation** affects the signals through the **optic nerve**, which connects the eyes and the brain
- Fibers (RGC axons) in the optic nerve are protected by the **myelin sheath** which is damaged in optic neuritis
- Timely treatment may help prevent more severe long-term effects

Direct link with chronic conditions like **multiple sclerosis (MS)** and other autoimmune diseases



Anatomy of a retinal ganglion cell



1. Martínez-Lapiscina EH, et al. (2014): Is the incidence of optic neuritis rising? Evidence from an epidemiological study in Barcelona (Spain) 2008-2012. *J Neurol*. 2014 Apr; 261(4): 759-767.

Acute Optic Neuritis: Orphan Indication With No Approved Neuroprotective Therapy

Current treatment landscape

Current Treatment

High-dose corticosteroids
to resolve acute inflammation

Unmet Needs

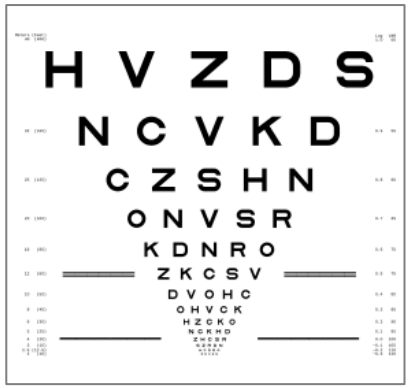
- **Neuroprotective treatment effect on retinal ganglion cells and optic nerve atrophy**
- **Reduce degree of vision deficits / loss**

Visual Sequelae

- **Decreased contrast**
- Decreased visual acuity
- Decreased visual fields
- Uhthoff phenomenon



HCVA



LCVA

HCVA: high contrast visual acuity; LCVA: low-contrast visual acuity

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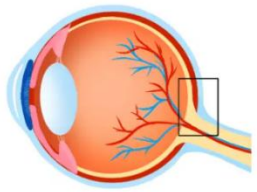
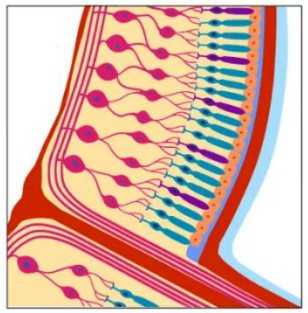
Acute Optic Neuritis: OCT Imaging Biomarker Predicts Outcome

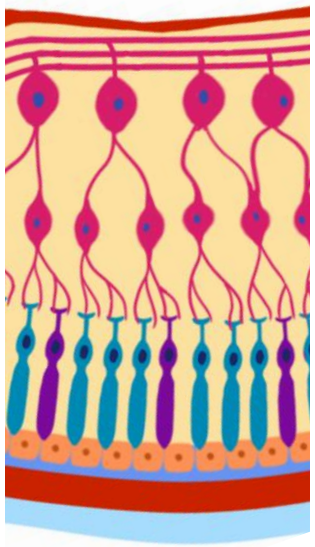
Change in GCIPL thickness in the first month predicts visual impairment by month 6[1]





GCIPL and RNFL are measured using OCT imaging technique

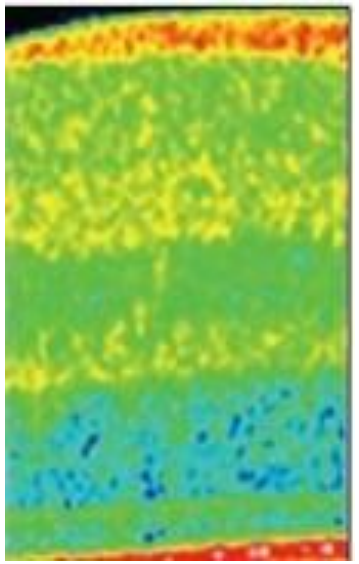
Decrease of ≥ 4.5 µm in GCIPL predicts poor LCVA and ≥ 7 µm predicts poor VF and CVA



→ Axons → RNFL →

→ Retinal Ganglion Cells (RGC) → GCL →

IPL →



RNFL thickness

GCIPL thickness

LCVA

7 letters (1.5 lines) change in LCVA has clinical relevance[2]

OCT: optical coherence tomography, LCVA: low-contrast visual acuity, CVA: color vision, VF: visual fields; RNFL: retinal nerve fiber layer; GCIPL: ganglion cell (GCL) and inner plexiform (IPL) layers

1. Gabilondo et al. Ann Neurol. 2015 Mar;77(3):517-28.
2. https://pubmed.ncbi.nlm.nih.gov/28206829/

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Phase 2 ACUITY Trial in Acute Optic Neuritis

Proof-of-concept for neuroprotection

Study Design

- Randomized, double-masked, placebo-controlled study
- Multi-center, 6-month trial with 36 patients randomized (mITT: 33)
- Once-daily IV infusion of OCS-05 + steroid vs. placebo + steroid for 5 consecutive days

Key endpoints

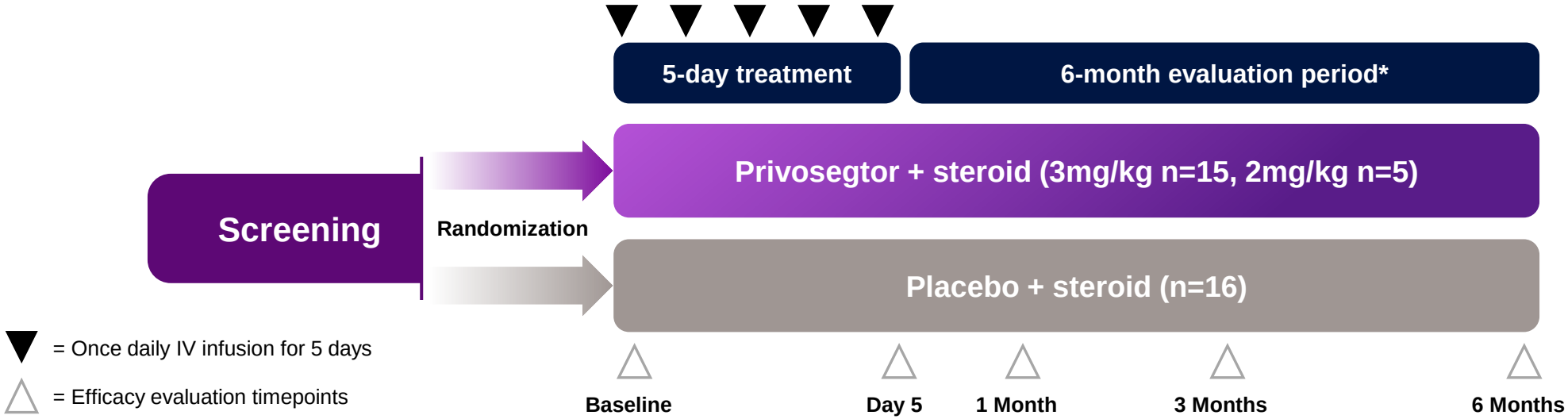
Primary endpoint: Cardiac safety

Secondary endpoints:

- Change in Ganglion Cell and Inner Plexiform Layer (GCIPL) thickness as assessed by OCT
- Change in Retinal Nerve Fiber Layer (RNFL) thickness as assessed by OCT
- Change in visual function (LCVA)

Study Population

- Patients diagnosed with a unilateral acute optic neuritis with a demyelinating origin
- Onset of visual loss symptoms in the last 12 days before randomization



mITT: Modified Intent to Treat
https://clinicaltrials.gov/study/NCT04762017
* D1 is when treatment starts and D180 is at Month 6

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Patient Demographics and Baseline Characteristics

	Privosegtor + steroid 3 mg/kg/day (N = 15)	Placebo + steroid (N = 14)
Age, mean (SD), years	33.7 (9.8)	32.7 (10.3)
Female, n (%)	9 (60.0)	10 (71.4)
GCIPL thickness, mean (SD), µm	89.3 (8.3)	84.3 (13.8)
RNFL thickness, mean (SD), µm	104.6 (13.1)	115.5 (54.1)
HCVA, mean (SD), ETDRS	54.1 (34.5)	42.6 (34.5)
LCVA, mean (SD), ETDRS	19.4 (22.3)	17.8 (24.3)
Visual Field Mean Deviation, mean (SD), dB	-14.1 (11.9)	-14.5 (12.5)
Time since first visual loss symptoms at date of first dose, mean (SD), days	9.5 (2.7)	9.6 (2.5)
Multiple sclerosis at baseline, n (%)	10 (66.7)	9 (64.3)
Disease Modifying Therapies n (%)	10 (66.7)	9 (64.3)

GCIPL, ganglion cell plus inner plexiform layer; HCVA, high contrast visual acuity; LCVA, low contrast visual acuity; RNFL, retinal nerve fiber layer;
Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

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Primary Endpoint of Cardiac Safety Showed No difference in % of Patients that had a change in ECG Outside of Normal

Percentage of subjects with shift from normal (baseline) to outside of normal value in any ECG parameters* from Visit 3 (after treatment) through Visit 4

Events observed in the Privosegtor arms were mild and transient and qualified as not clinically significant by the central review reading center

Primary Analysis

Subjects with any change in ECG outside of normal value at baseline excluded

	Privosegtor + steroid (2mg and 3mg/kg/day) (N = 16)	Placebo + steroid (N = 8)
Overall	2 (12.5%)	1 (12.5%)
Risk Difference (90% CI)	0.0% (−34.4%; 25.1%)	

Patients with any abnormal ECG at baseline were excluded from analysis

Sensitivity Analysis

All mITT subjects included

	Privosegtor + steroid (2mg and 3mg/kg/day) (N = 19)	Placebo + steroid (N = 14)
Overall	2 (10.5%)	4 (28.6%)
Risk Difference (90% CI)	-18.1% (-43.3%; 6.1%)	

*ECG parameters measured: Heart rate, PR interval, QRS duration, QTcB interval, QTcF interval * Oculis is focused on fully reviewing clinical safety as this is a new molecular entity with a *very limited number of patients exposed. Oculis will continue to work with the FDA to monitor safety, the typical number of patients requested by the FDA to be exposed before NDA is aprox 300 patients exposed*

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Safety Summary

- **No AEs leading to drug withdrawal or study discontinuation**
- **No drug-related serious adverse events (SAEs)**
- **2 Unrelated SAEs:**
  - **Hospitalization due to MS relapse (Privosegtor (OCS-05 + steroid) and due to myelitis (placebo + steroid)**

Event, n (%)	Privosegtor + steroid			Placebo + steroid
	2 mg/kg/day (N = 4)	3 mg/kg/day (N = 15)	Pooled (N = 19)	(N = 14)
At least one TEAE *Related to study treatment*	4 (100.0%) *4 (100.0%)*	12 (80.0%) *6 (40.0%)*	16 (84.2%) *10 (52.6%)*	14 (100.0%) *6 (42.9%)*
At least one grade ≥2 TEAE *Related to study drug*	2 (50.0%) *0*	9 (60.0%) *2 (13.3%)*	11 (57.9%) *2 (10.5%)*	6 (42.9%) *0*
At least one serious TEAE *Related to study drug*	0 *0*	1 (6.7%) *0*	1 (5.3%) *0*	1 (7.1%) *0*
At least one SAE leading to death	0	0	0	0
At least one TEAE leading to a dose reduction	0	0	0	0
At least one TEAE leading to a dose interruption	0	0	0	0
At least one TEAE leading to a drug withdrawn	0	0	0	0
At least one TEAE leading to premature discontinuation of the study	0	0	0	0

SAE, serious adverse event; TEAE, treatment emergent adverse event.
Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

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Relapses or Worsening of CNS Inflammatory Disorders

Adverse events related to new relapses or worsening of CNS inflammatory disorders

Event, n (%)	Privosegtor + steroid			Placebo + steroid 1g per day (N = 14)
	2 mg/kg/day (N = 4)	3 mg/kg/day (N = 15)	Pooled (N = 19)	
At least one new relapse of CNS inflammatory disorder	0	2 (13.3%)	2 (10.5%)	4 (28.6%)
At least one event related to worsening of CNS inflammatory disorder	0	0	0	2 (14.3%)
Overall	0	2 (13.3%)	2 (10.5%)	5 (35.7%)*

*One “placebo + steroid” patient had 1 TEAE related to new relapse and worsening

- Lower incidence of AEs related to new relapses or worsening of CNS inflammatory disorders : 10.5% in the Privosegtor (2 or 3 mg/kg/day) + steroid, and 35.7%* in the placebo + steroid treatment groups.
- In patients with MS at baseline: 9% (1/11)** in the Privosegtor (2 or 3 mg/kg/day) + steroid, and 44% (4/9)** in the placebo + steroid treatment groups.

** All patients had MS except 1 OCS-05+ steroid patient with idiopathic optic neuritis and 1 Placebo+ steroid patient with seronegative neuromyelitis optica spectrum disorder

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

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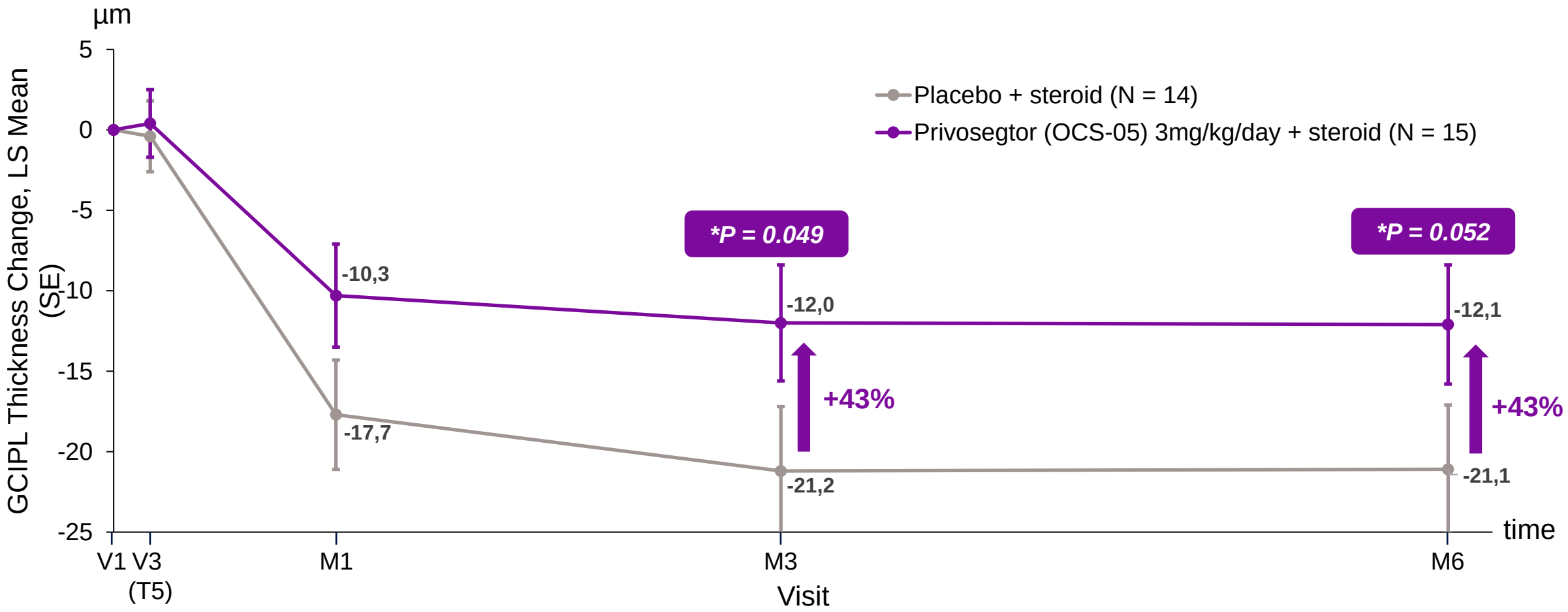
Patients in the Privosegtor 3mg/kg/day Arm Achieved Less GCIPL Thickness Decrease

GCIPL Thickness in the Affected Eye: MMRM, LS Mean Change From Baseline, mITT



*Mixed Model for Repeated Measures (MMRM); Least-Squares Mean Change from Baseline: (1-sided directional nominal p-value), mITT population (affected eye)
GCIPL; ganglion cell plus inner plexiform layer.
Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

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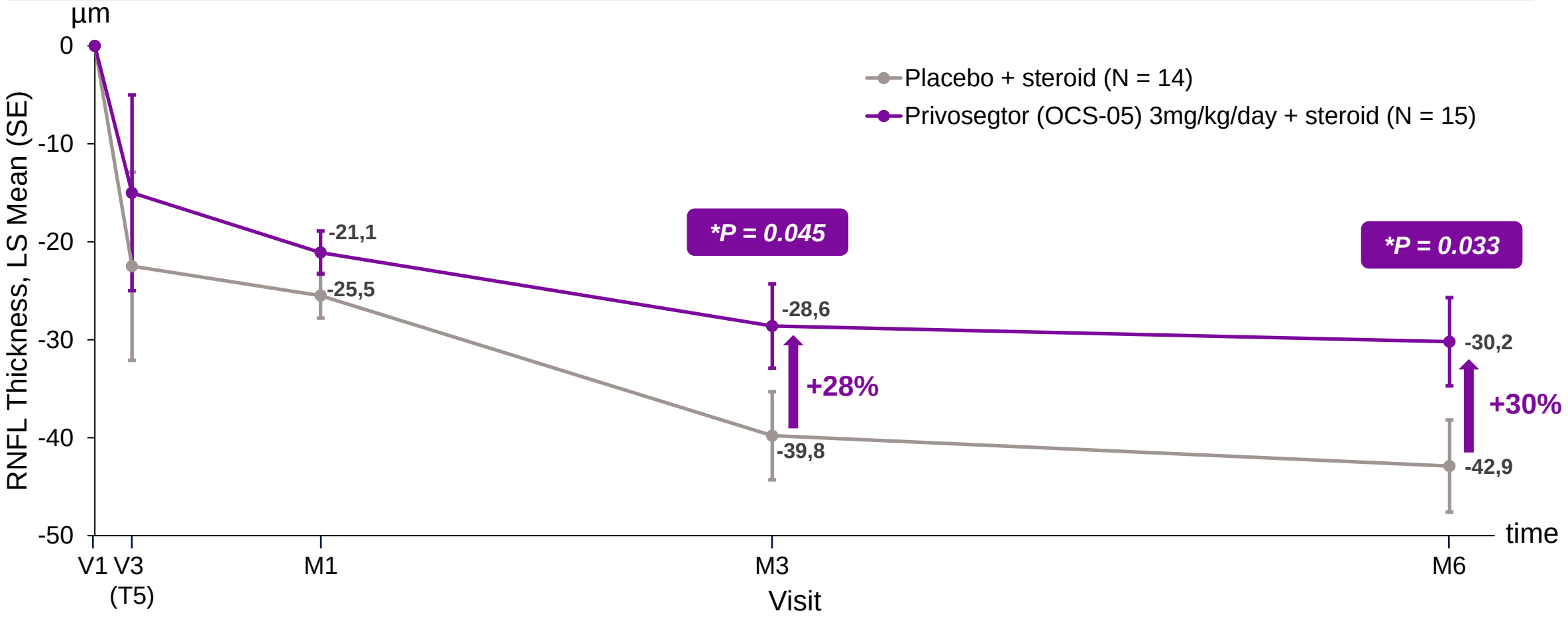
Patients in the Privosegtor 3mg/kg/day Arm Achieved Less RNFL Thickness Decrease

RNFL Thickness in the Affected Eye: MMRM, LS Mean Change from Baseline, mITT



*Mixed Model for Repeated Measures (MMRM); Least-Squares Mean Change from Baseline: (1-sided directional nominal p-value), mITT population (affected eye)
RNFL; retinal nerve fiber layer..
Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

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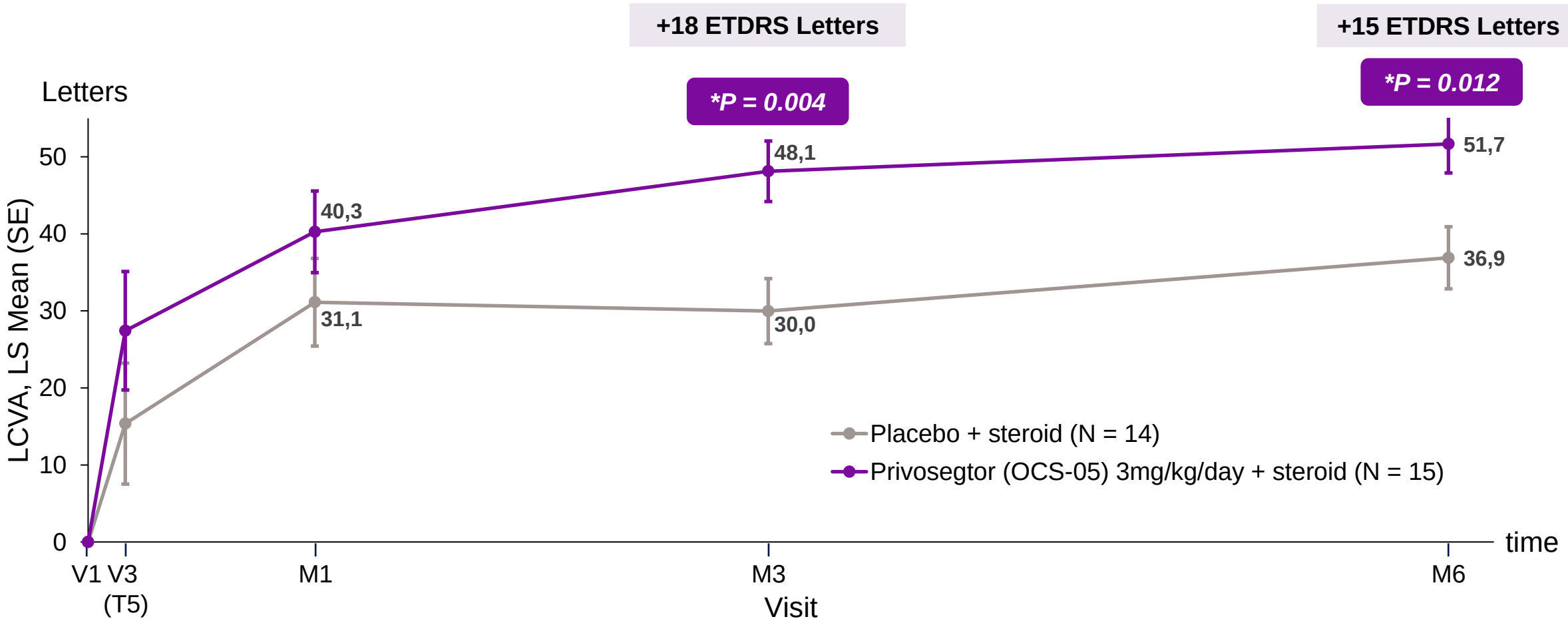
Patients in the Privosegtor 3mg/kg/day Arm Achieved Clinically Meaningful Improvement in Visual Function

2.5% ETDRS LCVA in the Affected Eye: MMRM, LS Mean Change From Baseline, mITT



*Mixed Model for Repeated Measures (MMRM); Least-Squares Mean Change from Baseline: (2-sided nominal p-value), mITT population (affected eye)
LCVA; low contrast visual acuity.
Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

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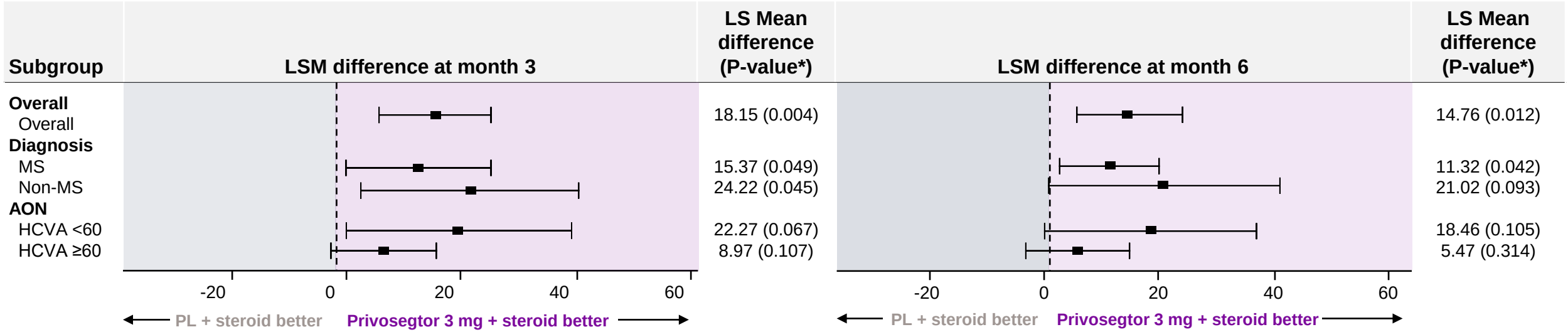
Privosegtor Arm Showed a Robust LCVA Improvement Across all Subgroups and Maintained through Month 6

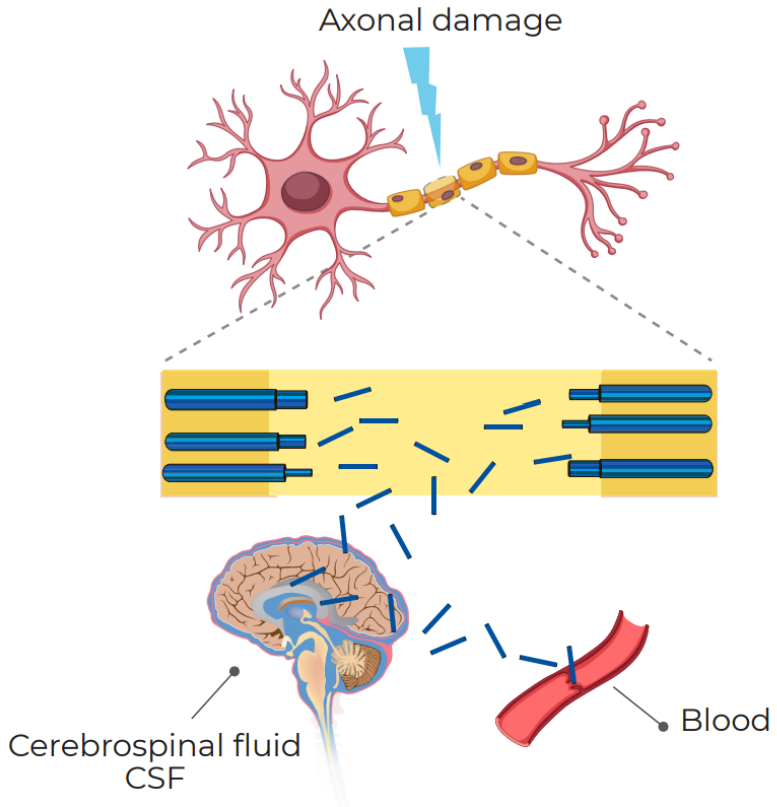
LCVA letters subgroup analyses of Privosegtor 3mg + steroid vs placebo + steroid



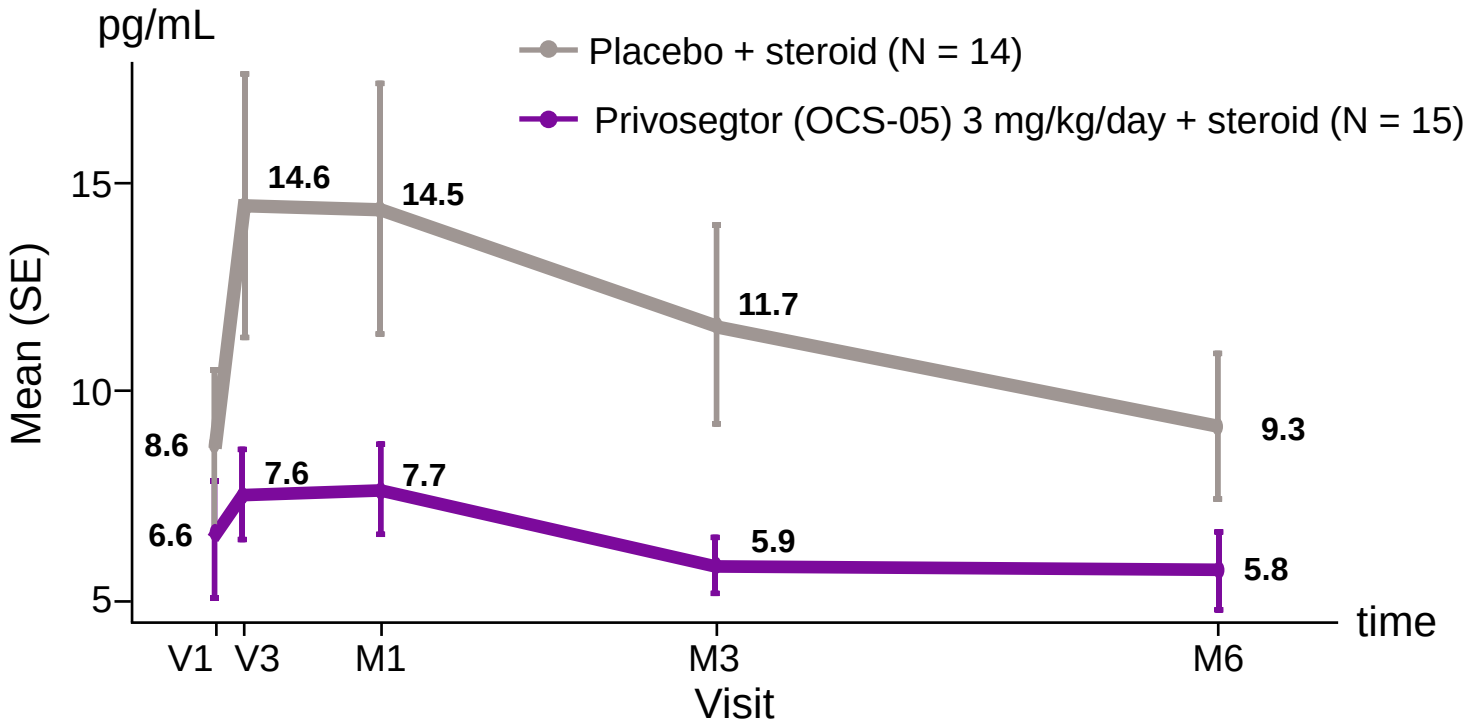
*2-sided nominal p-value based on LSM difference.
AON, acute optic neuritis; HCVA, high-contrast visual activity; LCVA, low-contrast visual acuity; LSM, least square mean; MS, multiple sclerosis; PL, placebo

Patients in the Privosegtor Arm Achieved Lower Neurofilament Release, a Biological Sign of Less Neuronal and Axonal Death

Neurofilaments are released into the CSF and blood as a result of axonal injury or neuronal death[2]



Mean Neurofilaments Over Time, mITT



CSF: cerebrospinal fluid

1. https://pmc.ncbi.nlm.nih.gov/articles/PMC7363489/
2. Yuan A, Rao MV, Veeranna, Nixon RA. Neurofilaments and neurofilament proteins in health and disease. *Cold Spring Harb Perspect Biol*. 2017;9:a018309.

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ACUITY Phase 2 Topline Results Summary

Privosegtor (OCS-05) achieved primary safety endpoint and key secondary endpoints showing functional vision improvement and neuroprotective anatomical & biological benefits

1. **Vision: Improvement in LCVA with 18 letters difference at month 3**
2. **Anatomy: GCIPL and RNFL with less thickness decrease preserving axons and RGC**
3. **Biology: Achieved lower neurofilament release in the blood showing less neuronal and axonal death**

Safety:

- No difference in % of patients shifted post-baseline electrocardiogram (ECG)
- No drug-related serious adverse events (SAEs) or AEs leading to drug withdrawal or study discontinuation
- Lower incidence of AEs related to new relapses or worsening of CNS inflammatory disorders

AE: Adverse Events, RGC: Retinal ganglion cells, CNS: Central Nervous System * Oculis is focused on fully reviewing clinical safety as this is a new molecular entity with a *very limited number of patients exposed. Oculis will continue to work with the FDA to monitor safety, he typical number of patients requested by the FDA to be exposed before NDA is aprox 300*
Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing. Statistical significance achieved based on prespecified statistical analysis plan.

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Acute Optic Neuritis – Next Steps

FDA interaction planned in Q3 2025 following successful Phase 2 ACUITY trial

1. **Meet with FDA to review ACUITY results and discuss full development program to support Acute Optic Neuritis registrational plan**

   The current plan for a registrational trials:
   Primary endpoint: LCVA at 3 months
   Similar regimen and trial design to ACUITY
   Study duration 12 months

2. **Start global registrational study in 1H 2026, pending FDA feedback**

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Privosegtor

Addressing unmet needs in MS: Neuroprotection for MS patients

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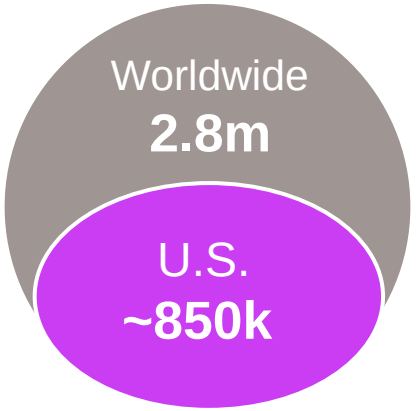
Multiple Sclerosis

Most common CNS condition affecting young adults

High prevalence of multiple sclerosis worldwide[1-3]

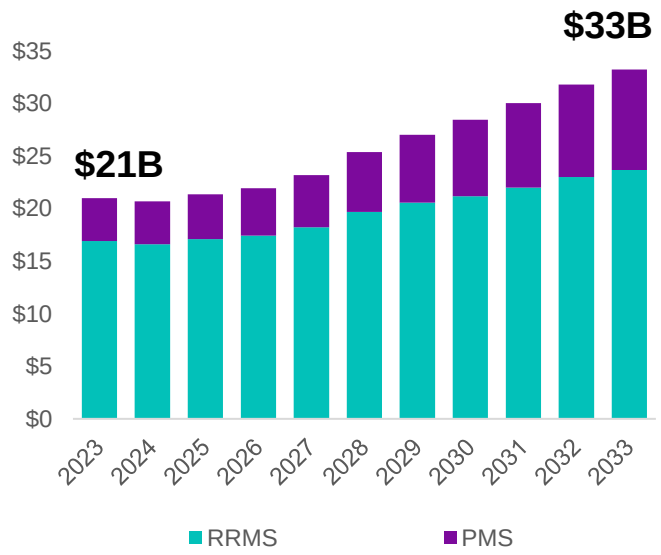


Characterized by relapses or attacks on the central nervous system (CNS), leading to inflammation, demyelination, and neurodegeneration

Main phenotypes:
Relapsing-Remitting and Progressive Multiple Sclerosis (RRMS or PMS)

Large and growing market driven by immuno-modulators

Multiple Sclerosis Market Size in G7 countries in billions (US, EU5 and JP)[4]



Existing therapies only slow disease progression while relapses continue to cause disability

Affects function in cognitive, emotional, motor, sensory, or visual areas

Driven by a person's immune system attacking their brain, spinal cord and optic nerves

1. MS National Society, used for WW prevalence of 2.8m, and combined with references 2 and 3 to calculate an avg prevalence in US Prevalence of Multiple Sclerosis | National MS Society
2. Wallin et al., 2019, The prevalence of MS in the United States: A population-based estimate using health claims data - PubMed
3. McGinley et al., 2021, Diagnosis and Treatment of Multiple Sclerosis: A Review - PubMed
4. Ms Disease Landscape and Forecast Report 2024

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Relapsing-Remitting Multiple Sclerosis (RRMS)

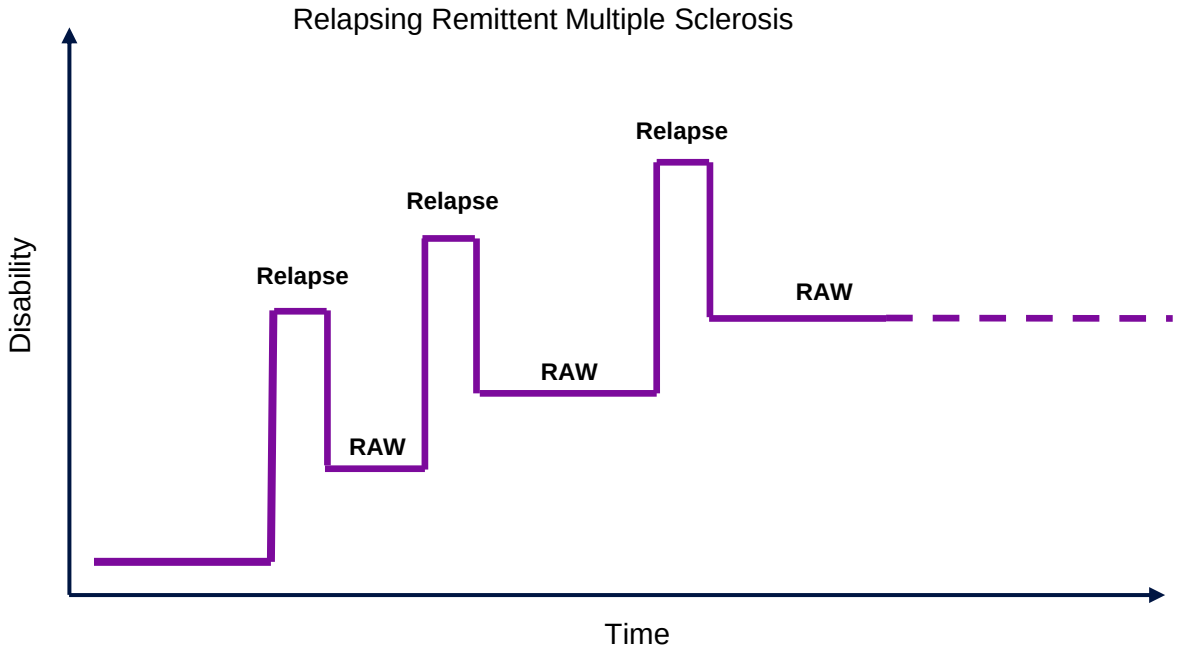
Characterized by acute attacks (relapses) that may cause permanent disability

Estimated number of relapses in U.S. per year
~170K*

CNS damage due to relapses increases the risk of future disability and progression[4]

- RRMS represents ~85% of patients at initial diagnosis[1]
- Symptoms include loss of vision[2], severe weakness or poor balance interfering with mobility, safety or overall ability to function[3]
- Current SoC is steroid IV with incomplete recovery leading to neurodegeneration and can cause permanent disability[3]

RAW: Relapse-Associated Worsening



1. Relapsing-remitting MS | Symptoms, diagnosis, and treatment | Multiple Sclerosis News Today
2. MS international Foundation https://www.msif.org/about-ms/symptoms-of-ms/vision-issues/
3. Mobility and Gait Issues With MS
4. Scott, Thomas F. et al. Journal of the Neurological Sciences, Volume 413, 116773

* US estimated prevalence of relapsing MS: 850K, with annual relapse rate (ARR) estimate of 0.2 based on multiple sources including: Ocrelizumab versus fingolimod after natalizumab cessation in multiple sclerosis: an observational study - PubMed

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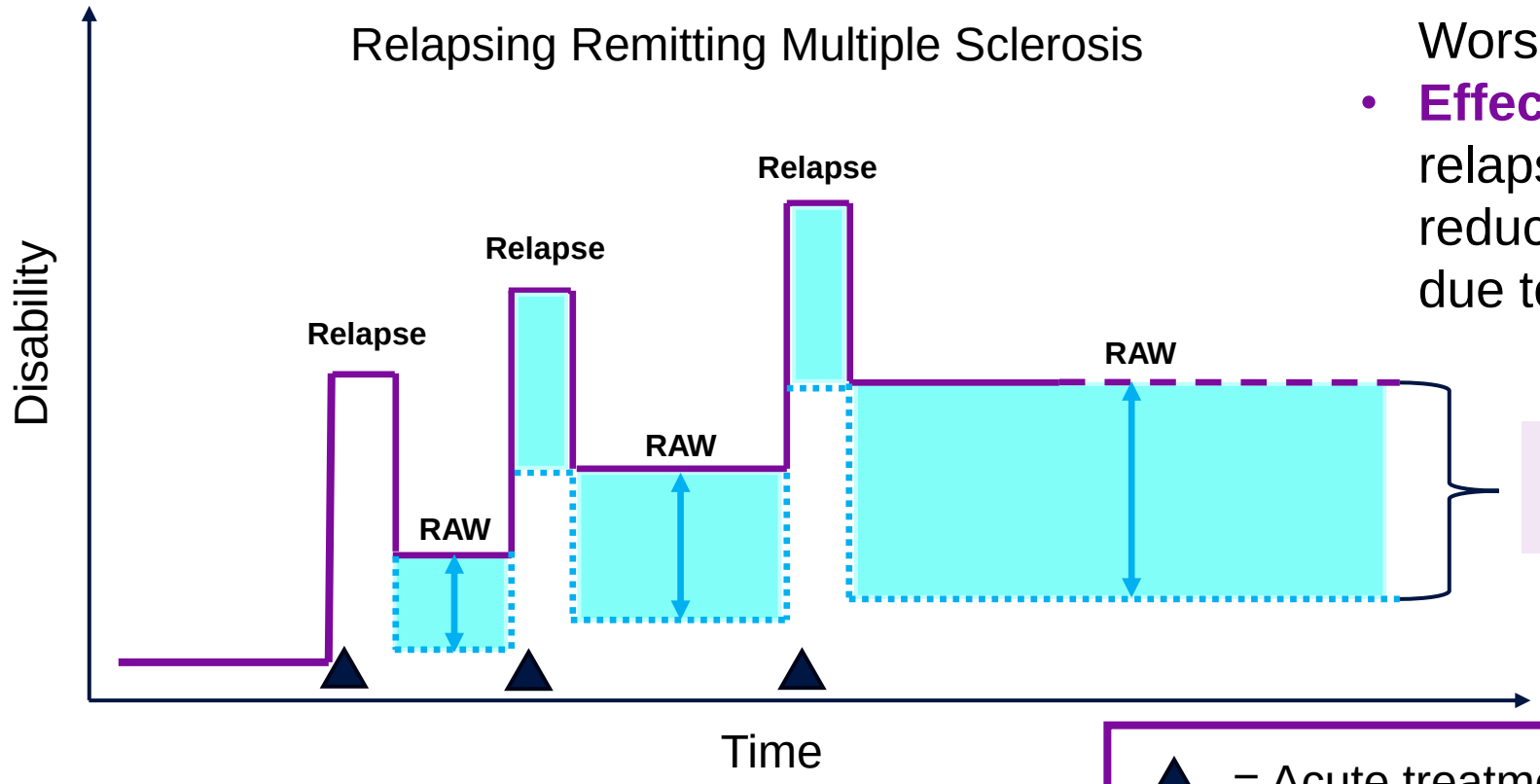
Privosegtor Neuroprotective Effect Observed in Acute Optic Neuritis Could Be Translated into a Reduction of Relapse Associated Worsening



- **RAW:** Relapse-Associated Worsening
- **Effective neuroprotection** in relapses could translate to reduced accumulation of disability due to relapses over time [1-4]

Neuroprotection potential benefits

▲ = Acute treatment of relapses with Privosegtor

1. Susin-Calle S, Martinez-Rodriguez JE, Munteis E, Villoslada P. Ongoing phase 2 agents for multiple sclerosis: could we break the phase 3 trial deadlock? Expert Opinion Investig Drugs 2025;34:217-229.
2. Lublin FD, Haring DA, Ganjgahi H, et al. How patients with multiple sclerosis acquire disability. Brain 2022;145:3147-3161.
3. Montobbio N, Cordioli C, Signori A, Bovis F, Capra R, Sormani MP. Relapse-Associated and Relapse-Independent Contribution to Overall Expanded Disability Status Scale Progression in Multiple Sclerosis Patients Diagnosed in Different Eras. Ann Neurol 2024;97:95-103.
4. Zanghi A, Galgani S, Bellantonio P, et al. Relapse-associated worsening in a real-life multiple sclerosis cohort: the role of age and pyramidal phenotype. Eur J Neurol 2023;30:2736-2744

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Privosegtor

Addressing unmet needs in NAION:
Neuroprotection for patients to improve visual outcomes

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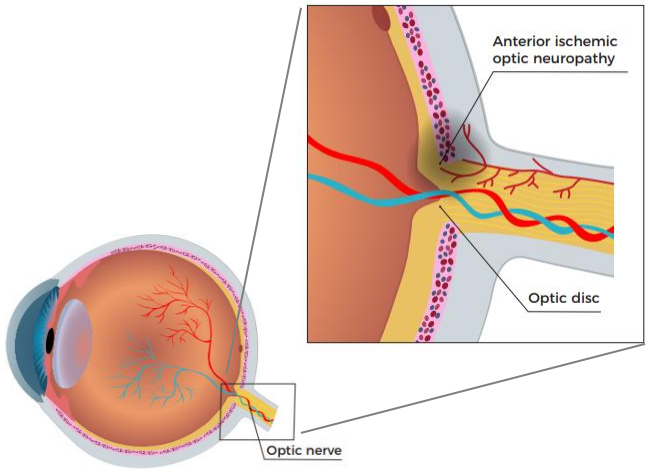
Another Acute Optic Nerve Disorder Non-arteritic Anterior Ischemic Optic Neuropathy

No treatment approved, with severe vision loss in > 60% patients

Orphan indication with US incidence of ~ 20k-30k[1]

- Optic neuropathy mainly affecting patients > 50 years old[2]
- Affects both sexes equally[2]
- Risk factors includes small cup-to-disk ratio, diabetes, hypertension, sleep apnea and use of certain medications[2]

RGC, axons and optic nerve atrophy caused by hypoperfusion[3]



- Decreased blood flow to the front part of the optic nerve (optic disc)[4]
- Causing optic nerve swelling[4]
- Painless rapid monocular vision loss, including visual field defect[1]

Permanent vision loss in many patients

>60%

of patients have significant visual impairment in the affected eye[5]

- No approved treatment for NAION[1]
- Significant unmet need for neuroprotective treatments to improve visual outcomes[6]

NAION: non-arteritic anterior ischemic optic neuropathy, RGC: retinal ganglion cells. Incidence of nonarteritic anterior ischemic optic neuropathy – PubMed and Incidence of nonarteritic anterior ischemic optic neuropathy: increased risk among diabetic patients – PMC and discussions with experts 23/ https://www.aao.org/eyenet/article/naion-diagnosis-and-management 3/ https://pmc.ncbi.nlm.nih.gov/articles/PMC10519420/ 4/ Non-Arteritic Anterior Ischemic Optic Neuropathy | North American Neuro-Ophthalmology Society 5/ https://pubmed.ncbi.nlm.nih.gov/17698200/ 6/ Axonal loss and neuroprotection in optic neuropathies – PubMed

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NAION: Orphan Indication With No Approved Therapy

No medical or surgical treatment shown to improve prognosis of acute NAION other than risk factor modification[1]

Current Treatments

There is no effective treatment for treating the disease or preventing it

Unmet Needs

- Neuroprotective treatment effect on retinal ganglion cells, axons and optic nerve atrophy
- Reduce degree of vision deficits / loss

As showed in the ACUITY trial, Privosegtor (OCS-05) could have neuroprotective benefits in protecting RGC and axons to preserve vision

1. https://www.aao.org/eyenet/article/naion-diagnosis-and-management
2. https://www.retina-specialist.com/article/the-challenge-of-managing-naion

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Privosegtor: Opening a New Era in Neuroprotection with Acute treatments for AON, Relapses of MS and NAION

Next steps to advance efficient development and reduce risk

1. Meet with FDA in 2H 2025 and Advance AON into registrational trials in 1H 2026

2. Expand into NAION and MS Relapse with Pre-IND interactions with FDA to support applications relying on existing Privosegtor data 2H 2025

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Conclusion

Oculis Pipeline Development Strategic Evolution

Advance

OCS-01 could be the first ever topical treatment in DME, if approved

Licaminlimab precision medicine in DED

Privosegtor neuroprotection in Acute Optic Neuritis

Expand

OCS-05 in neuro-ophthalmology and beyond

- **NAION**
- **MS relapses**

Explore

Potential for OCS-05 in multiple additional neuro-ophthalmology and neurology conditions

+$25B[4,5]

+$15B[3]

Estimated G7 Market Size

~$10B[1,2]

OPHTHA

NEURO-OPHTHALMOLOGY

1. DR and DME Disease and Landscape report Nov. 2020 – 2024 market value estimate for G7, 2. DED Disease and Landscape report 2020 - 2024 market value estimate for G7, 3. MS Disease and Landscape report October 2024 – 2024 market value estimate for G7, 4. Optic nerve disorders, Transparency Market Research, 5. Global Market Insights, March 2024 https://www.gminsights.com/industry-analysis/neuroprotection-market

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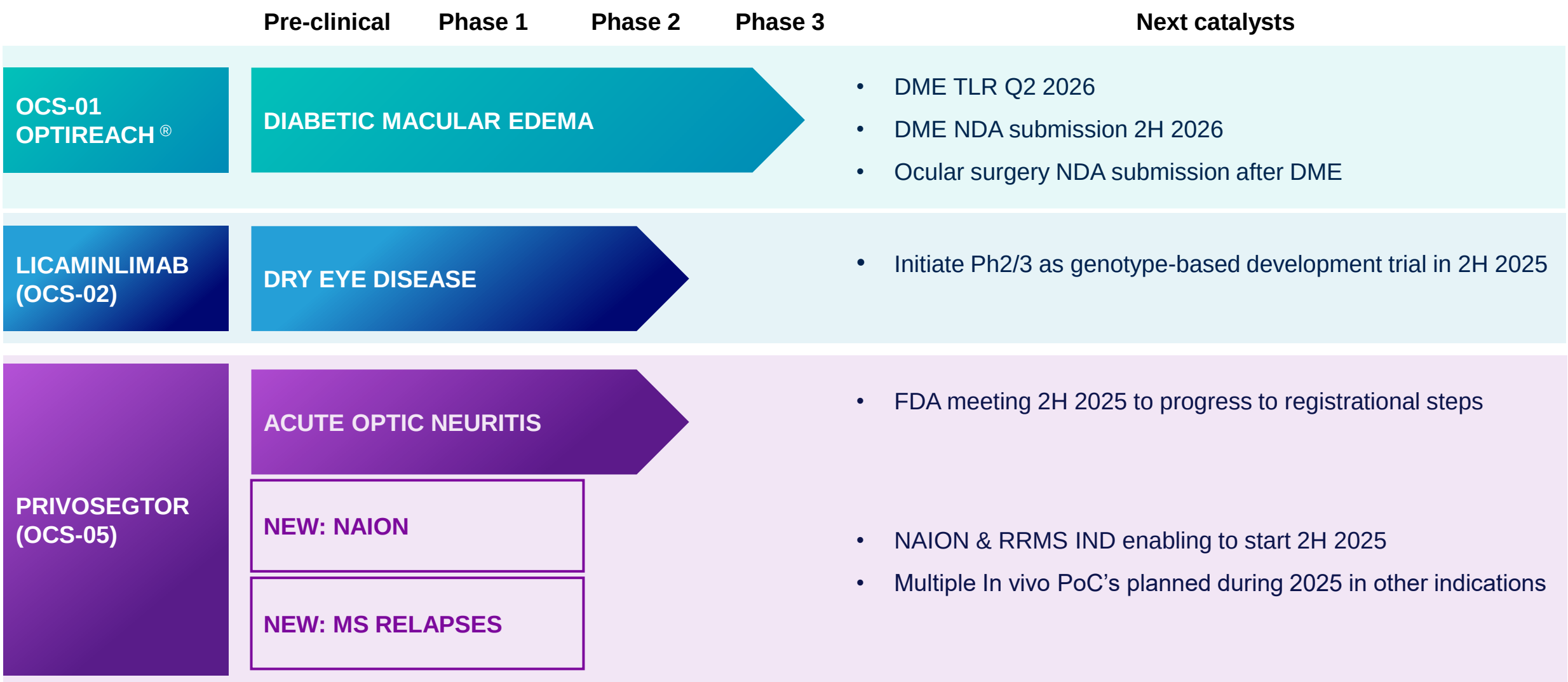
Advanced and Innovative Pipeline



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

Thank you

Oculis | Rethinking Ophthalmology