

Oculis

Acuity

Acute optic NeURITis with a demYelinating origin

OCS-05 Phase 2 Topline Results in Acute Optic Neuritis

January 6, 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.

ACUITY Phase 2 Topline Results in Acute Optic Neuritis - Speakers



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Agenda & Speakers

1

Opening Remarks

Sylvia Cheung

Chief Financial Officer

2

ACUITY Trial Results

Riad Sherif, MD

Chief Executive Officer

3

KOL Interpretation

Prof Mark Kupersmith, MD (U.S.)

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Prof Pablo Villoslada, MD, PhD (U.S. & Spain)

Prof Sebastian Wolf, MD, PhD (Switzerland)

4

Q&A

Oculis Management

KOLs

ACUITY Phase 2 Topline Results Summary

OCS-05 achieved primary safety and key secondary endpoints showing neuroprotective anatomical benefit and vision improvement

Primary Endpoint: Safety

- ✓ No difference in % of patients shifted from normal baseline to abnormal post-baseline electrocardiogram (ECG) events

Secondary Endpoints: Efficacy - Preservation of Retinal Ganglion Cells and Optic Nerve Structure and Vision Improvement

- ✓ Statistically significant difference in mean GCIPL thickness (biomarker of RGC preservation) of 43% with OCS-05 (3mg/kg/d) arm at month 3 with treatment effect maintained through month 6
- ✓ Statistically significant difference in mean RNFL thickness (biomarker of axon preservation) of 28% with OCS-05 (3mg/kg/d) arm at month 3 with treatment effect maintained through month 6
- ✓ Statistically significant and clinically meaningful improvement in low contrast visual acuity (LCVA) with 18 letters difference in OCS-05 (3mg/kg/d) arm at month 3 with treatment effect maintained through month 6 vs steroid alone.

Treatment Emergent Adverse Events (AEs):

- 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 with OCS-05

OCS-05

Development status

OCS-05 | Novel Peptidomimetic with Trophic Factors Impacting Neuroprotective Activity

Unique pathway for neuro-ophthalmology indications

Disease modifying drug aimed to protect and repair neurons

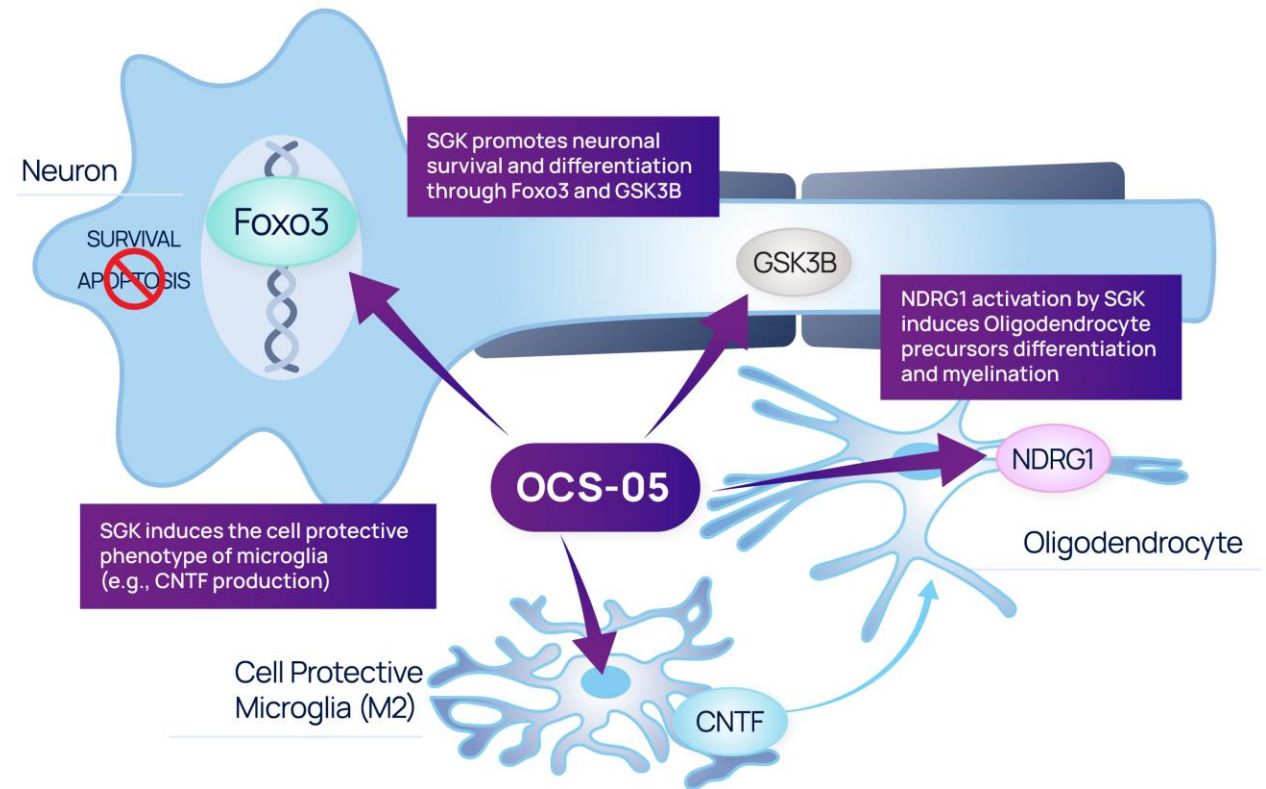
- Activates neurotrophic signalling pathways supporting neuronal survival and repair

Multiple potential clinical applications:

- Acute Optic Neuritis
- Glaucoma
- Ischemic Optic Neuropathy
- Neurotrophic Keratitis
- Diabetic Retinopathy
- CNS disorders (MS)

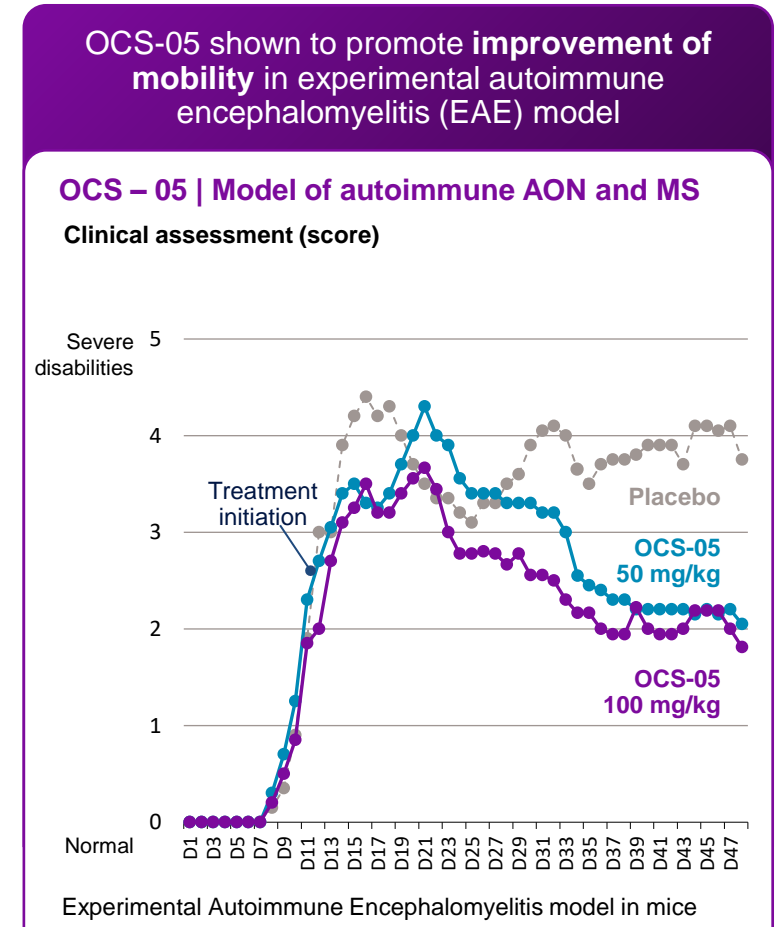
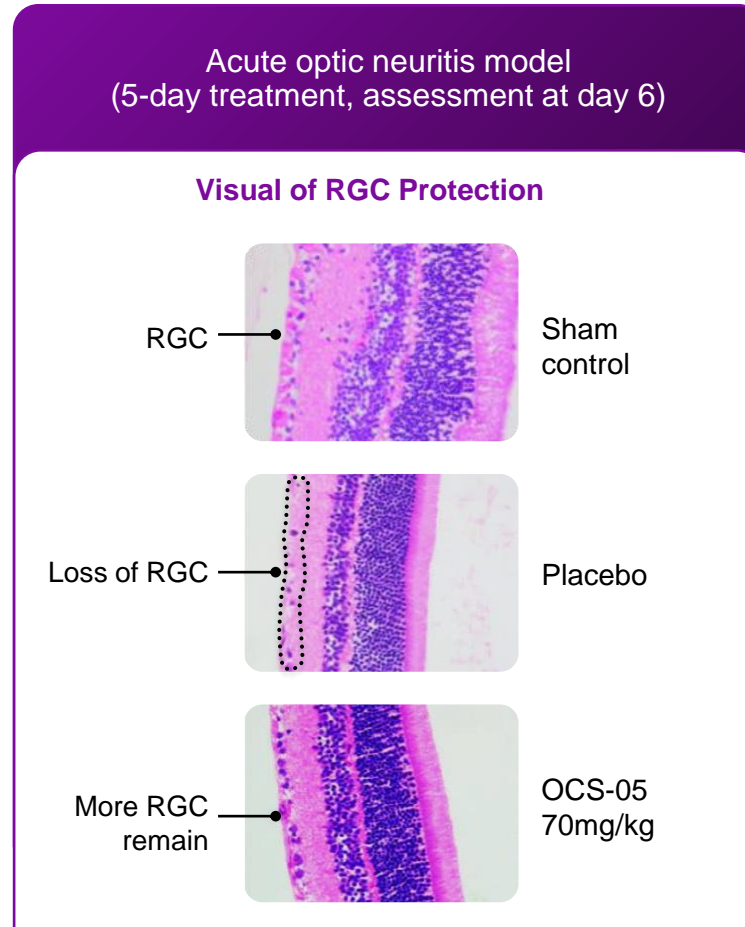
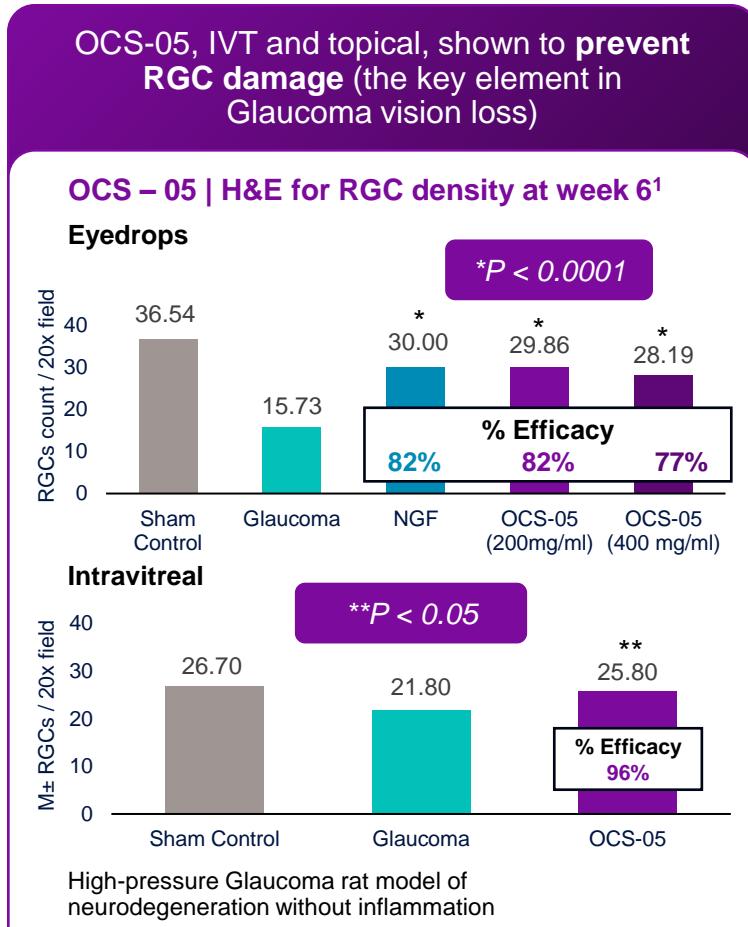
Differentiated Pathway

OCS-05 targets IGF-1 signalling including SGK as part of the neurotrophic factor pathways triggering multiple beneficial effects on apoptosis, oxidation and inflammation



OCS-05 | Pre-clinical Evidence of Neuroprotective Activity (1/2)

Compelling data showing prevention of RGC damage in glaucoma and acute optic neuritis and functional improvement in EAE models



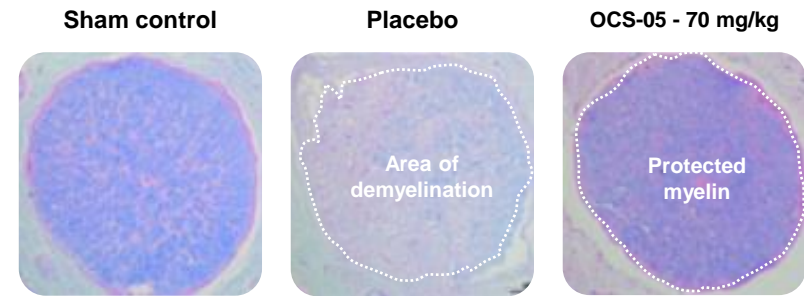
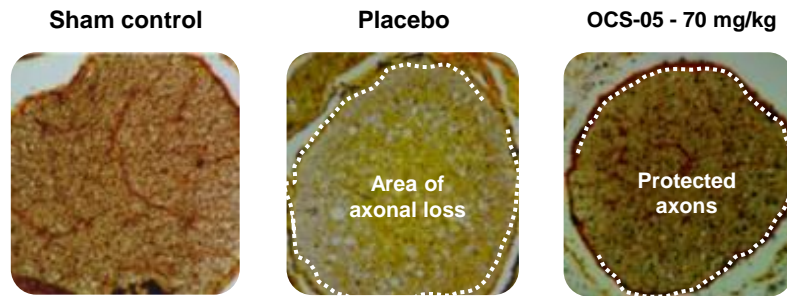
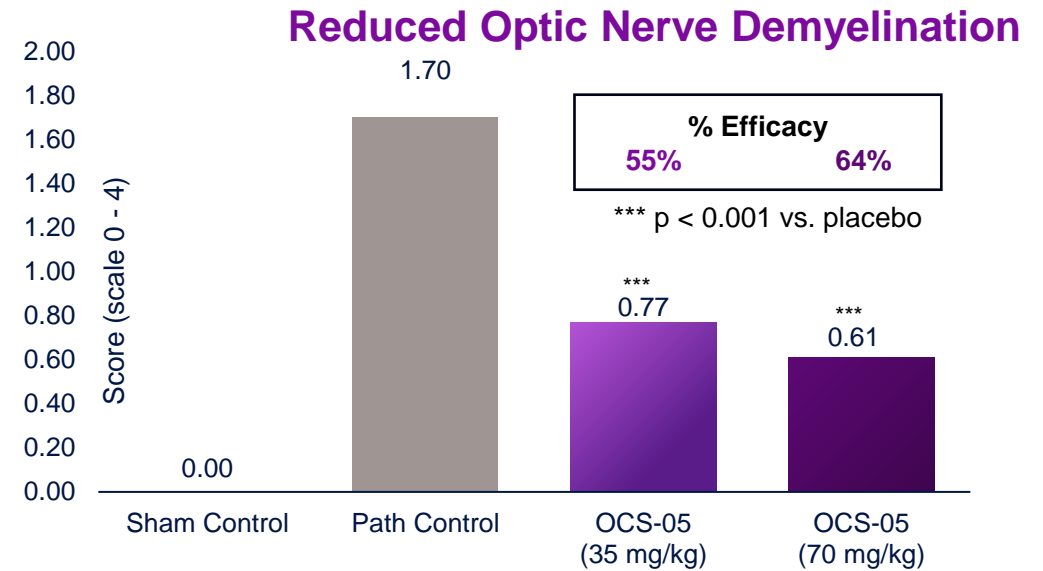
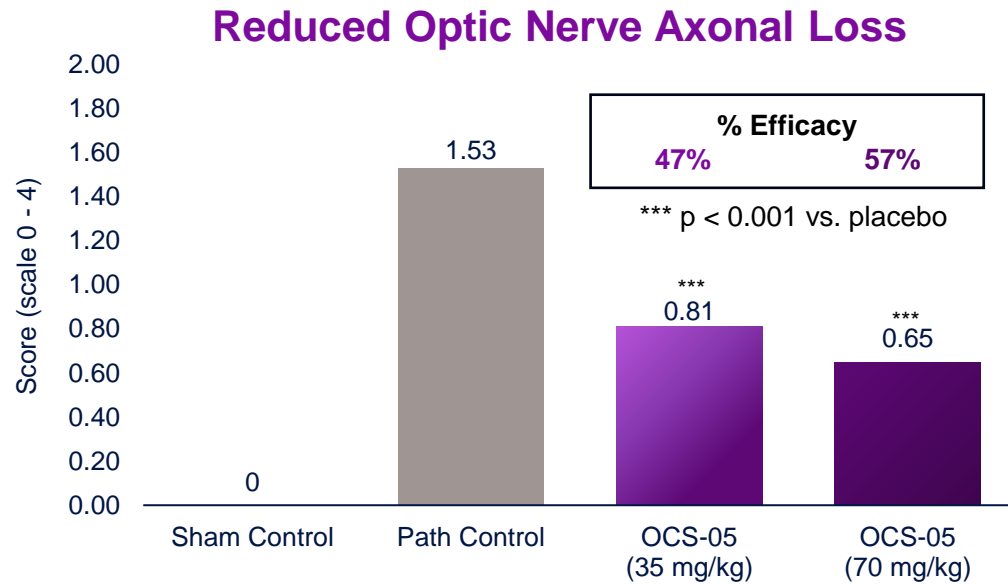
EAE: experimental autoimmune encephalomyelitis; H&E: hematoxylin and eosin staining; MS: multiple sclerosis; RGC: retinal ganglion cell; IVT: intravitreal; NGF; nerve growth factor.

1. Villoslada P. et al. Neurotherapeutics. 2019; 16(3):808-827

OCS-05 | Pre-clinical Evidence of Neuroprotective Activity (2/2)

Promotes axonal sparing and reduces demyelination in model of acute optic neuritis

Assessment after 5-days of treatment¹



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

OCS-05 | Development Status

Compelling pre-clinical data set, IND clearance and positive phase 2 well-positioning OCS-05 development in Acute Optic Neuritis and future potential Neuro Ophthalmology applications

- 1 Preclinical data** showing neuroprotection by preventing retinal ganglion cell death, promoting axonal sparing, reducing demyelination and improving function in MS model.
- 2 Successfully completed Phase 1:**
 - Randomized, double-blind, placebo-controlled, single and multiple ascending dose study of the safety, tolerability and PK (UK, MHRA) in 48 healthy volunteers (36 OCS-05, 12 placebo)
- 3 U.S.* IND cleared with clinical hold lifted for OCS-05 in acute optic neuritis**
- 4 Successfully completed Phase 2 ACUITY trial: **First-in-patient trial in acute optic neuritis****
 - Randomized, double-blind, placebo-controlled, multi-center trial in France to evaluate safety and explore efficacy of OCS-05 + steroid compared to placebo + steroid in 36 patients diagnosed with a first unilateral acute optic neuritis of a demyelinating origin

Acute Optic Neuritis

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

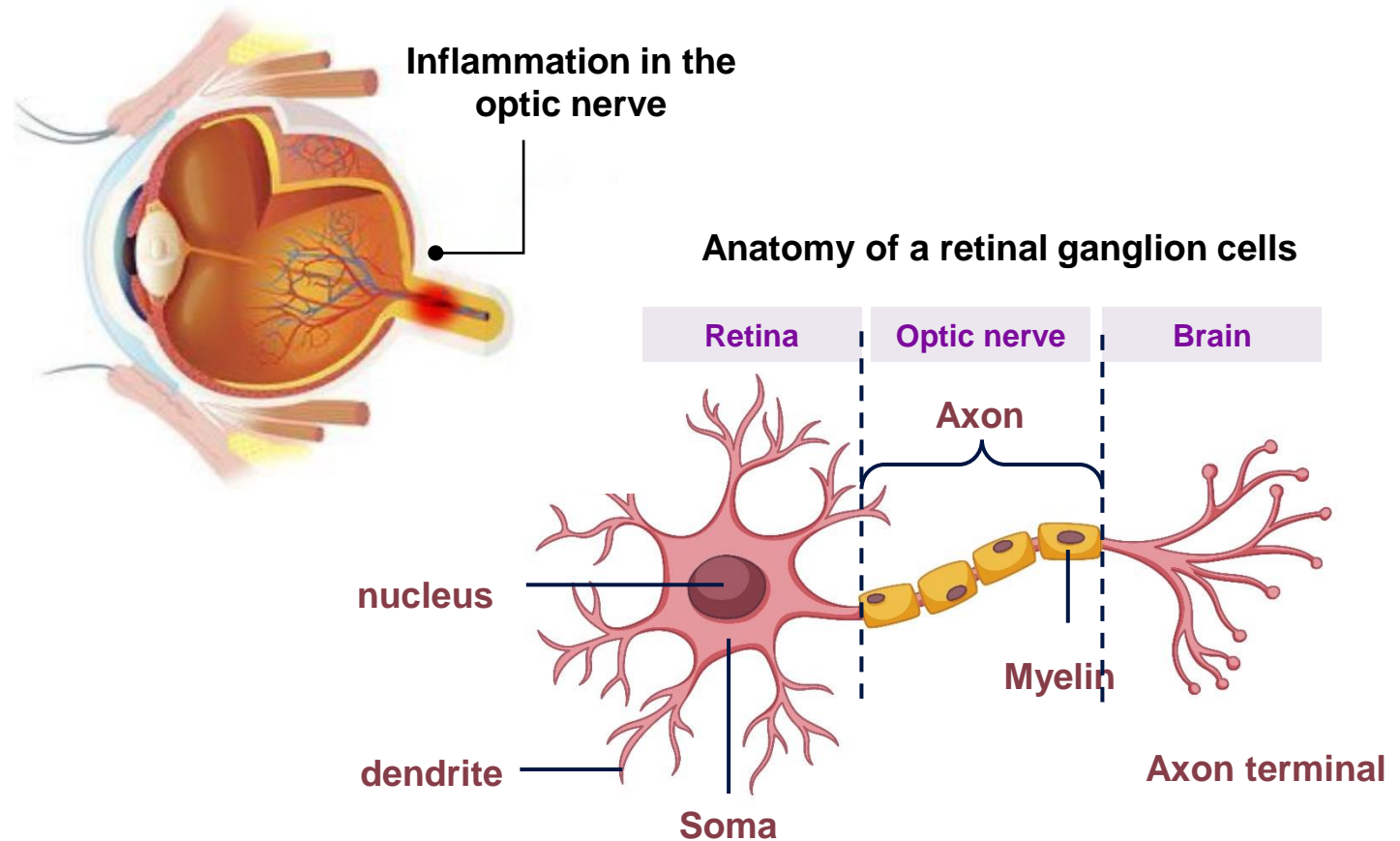
Orphan indication with
~ 65k patients a year (US/EU)¹

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



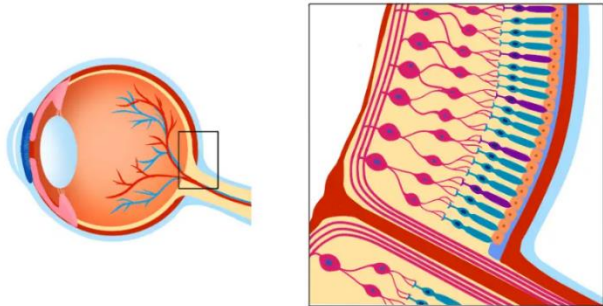
- Inflammation** affects the signals through the **optic nerve**, which connects the eyes and the brain
- Fibers in the optic nerve are protected by the **myelin sheath** which is damaged in optic neuritis
- Strong link with chronic conditions like **multiple sclerosis (MS)** and other autoimmune diseases
- Timely treatment may help prevent more severe long-term effects

Acute inflammation of the optic nerve
impacting retinal ganglion cells



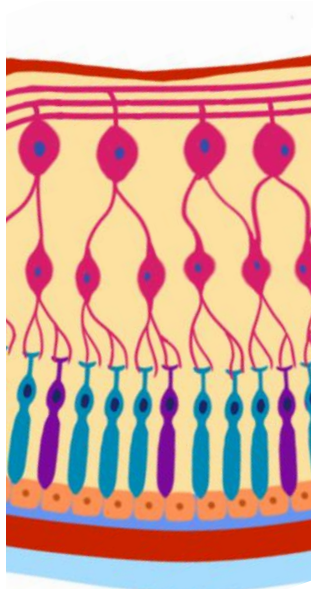
Acute Optic Neuritis

OCT Biomarker Predicts Visual Outcome: Change in GCIPL thickness in the first month predicts visual impairment by month 6¹

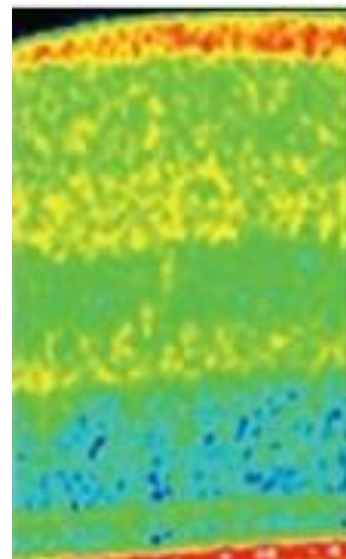


GCIPL and RNFL are measured using OCT imaging technique

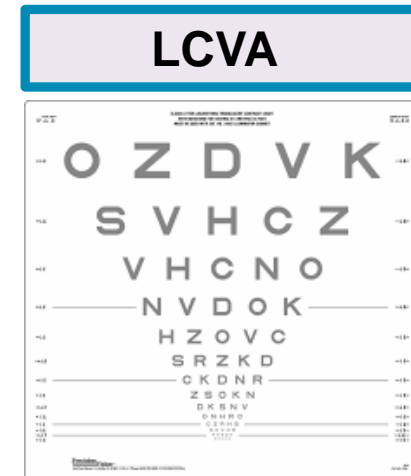
Decrease of $\geq 4.5 \mu\text{m}$ in GCIPL predicts poor LCVA and $\geq 7 \mu\text{m}$ predicts poor VF and CVA



→ Axons → RNFL
→ Retinal Ganglion Cells (RGC) → GCL
→ IPL



RNFL thickness
GCIPL thickness



7 letters (1.5 lines) change in LCVA has clinical relevance²

OCT: optical coherence tomography, LCVA: low-contrast visual acuity, CVA: color visual acuity, VF: visual fields

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

Acute Optic Neuritis: an Orphan indication without an Approved Therapy

Current treatment landscape

Current Treatment

High-dose corticosteroids to resolve acute inflammation

Unmet Needs

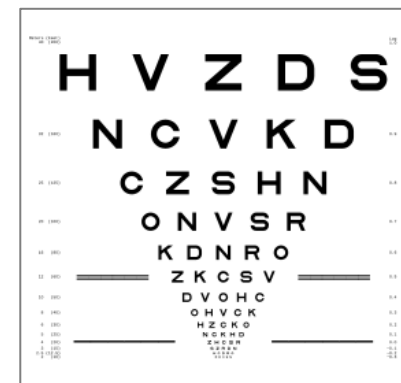
- ✗ Neuroprotective treatment effect on retinal ganglion cells and optic nerve atrophy
- ✗ Reduce degree of vision deficits / loss

Visual Sequelae

- Decreased contrast
- Decreased visual acuity
- Decreased visual fields
- Uhthoff's phenomenon
- Pulfrich phenomenon



HCVA



LCVA



Phase 2 ACUITY Trial

Study Design and Topline Results

OCS-05 ACUITY Trial in Acute Optic Neuritis

ACUITY Phase 2 Trial Objectives

- 1 Evaluate the safety and tolerability of OCS-05 + steroid compared with steroid I.V. alone
- 2 Explore the potential neuroprotective effects of OCS-05 by focusing on retinal structure (GCIPL and RNFL) and visual function (LCVA)

OCS-05 | Phase 2 ACUITY trial in Acute Optic Neuritis

Study Design

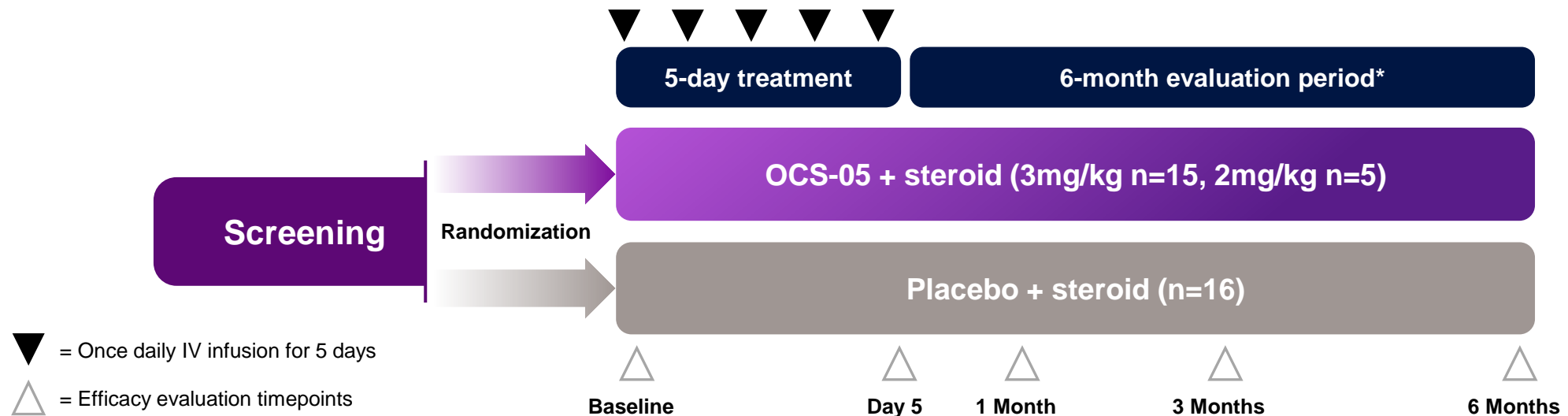
- Randomized, double-blind, placebo-controlled study
- Multi-center, 6-month trial with 36 patients randomized (mITT: 33)
- Once-daily IV infusion of OCS-05 + steroid vs. placebo + steroid for 5 consecutive days

Objectives of the study

- 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

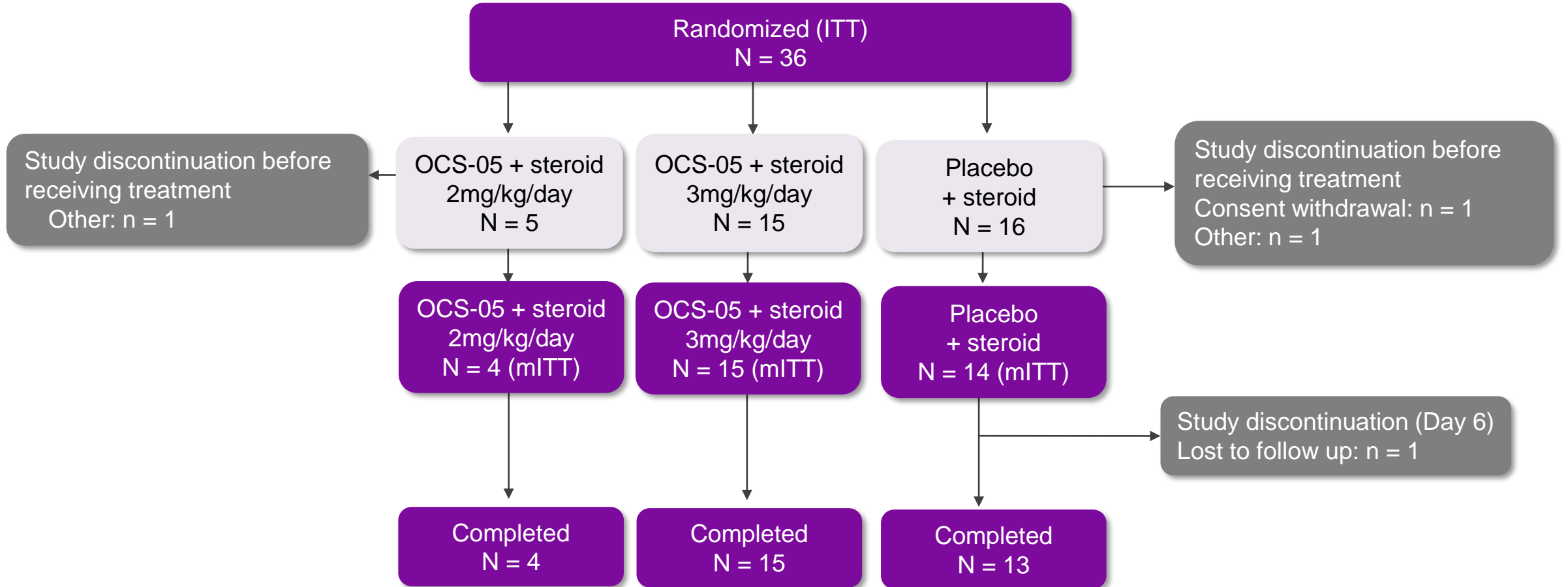


mITT: Modified Intent to Treat

<https://clinicaltrials.gov/study/NCT04762017>

* D1 is when treatment starts and D180 is at Month 6

OCS-05 | Phase 2 ACUITY Trial - Patient Disposition



ITT: Intent to Treat. mITT: Modified Intent to Treat.
Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

OCS-05 | Phase 2 ACUITY Trial: Patient Demographics and Baseline Characteristics

	OCS-05 + steroid			Placebo + steroid
	2 mg/kg/day (N = 4)	3 mg/kg/day (N = 15)	Pooled (N = 19)	1g per day (N = 14)
Age, mean (SD), years	44.0 (9.8)	33.7 (9.8)	35.9 (10.5)	32.7 (10.3)
Female, n (%)	4 (100.0)	9 (60.0)	13 (68.4)	10 (71.4)
GCIPL thickness, mean (SD), μm	85.9 (17.5)	89.3 (8.3)	88.6 (10.3)	84.3 (13.8)
RNFL thickness, mean (SD), μm	174.3 (134.1)	104.6 (13.1)	119.3 (63.1)	115.5 (54.1)
HCVA, mean (SD), ETDRS	28.5 (28.8)	54.1 (34.5)	48.7 (34.4)	42.6 (34.5)
LCVA, mean (SD), ETDRS	1.5 (3.0)	19.4 (22.3)	15.6 (21.1)	17.8 (24.3)
Visual Field Mean Deviation, mean (SD), dB	-18.2 (12.5)	-14.1 (11.9)	-15.0 (11.8)	-14.5 (12.5)
Time since first visual loss symptoms at date of first dose, mean (SD), days	11.3 (1.7)	9.5 (2.7)	9.8 (2.6)	9.6 (2.5)
Multiple sclerosis at baseline, n (%)	1 (25%)	10 (66.7%)	11 (57.9%)	9 (64.3%)

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

Safety: Primary Endpoint of Cardiac ECG Showed No difference in % of Patients that Shifted to Abnormal Electrocardiogram (ECG) Events

Percentage of patients with shift from normal (baseline) to abnormal in any ECG parameter from Visit 3 (after treatment) through Visit 4

ECG parameters measured:

- Heart rate
- PR interval
- QRS duration
- QTcB interval
- QTcF interval

Prespecified Primary Analysis

Patients with any abnormal ECG at baseline were excluded from analysis

	OCS-05 + 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%)	

- **Events observed in the OCS-05 arms were mild and transient and qualified as not clinically significant by the central review reading center**

*Patients with any abnormal ECG at baseline were excluded from analysis
Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

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 (OCS-05 + steroid) and due to Myelitis (Placebo + steroid)

Event, n (%)	OCS-05 + steroid			Placebo + steroid (N = 14)
	2 mg/kg/day (N = 4)	3 mg/kg/day (N = 15)	Pooled (N = 19)	
At least one TEAE <i>Related to study treatment</i>	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 <i>Related to study drug</i>	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 <i>Related to study drug</i>	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

Safety – Most Common Treatment-related TEAEs (Occurring in ≥5% of Patients in Any Single Cohort) (1/2)

Event, n (%)	OCS-05 + steroid Pooled (N = 19)	Placebo + steroid (N = 14)
Skin and subcutaneous tissue disorders		
Acne	2 (10.5%)	-
Rash pruritic	-	1 (7.1%)
Dermatitis acneiform	1 (5.3%)	-
Papule	1 (5.3%)	-
Pruritus	1 (5.3%)	-
Rosacea	-	1 (7.1%)
Gastrointestinal disorders		
Constipation	-	2 (14.3%)
Vomiting	-	1 (7.1%)
Abdominal pain	1 (5.3%)	-
Diarrhoea	1 (5.3%)	-
Nausea	1 (5.3%)	-
Infections and infestations		
Pharyngitis	1 (5.3%)	-
Cardiac disorders		
Tachycardia	1 (5.3%)	-
Respiratory, thoracic and mediastinal disorders		
Oropharyngeal pain	1 (5.3%)	-

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

Safety – Most Common Treatment-related TEAEs (Occurring in ≥5% of Patients in Any Single Cohort) (2/2)

Event, n (%)	OCS-05 + steroid Pooled (N = 19)	Placebo + steroid (N = 14)
Nervous system disorders		
Headache	2 (10.5%)	-
Dizziness	1 (5.3%)	-
Dizziness postural	1 (5.3%)	-
Electric shock sensation	-	1 (7.1%)
General disorders and administration site conditions		
Catheter site pain	1 (5.3%)	-
Fatigue	1 (5.3%)	-
Infusion site phlebitis	1 (5.3%)	-
Investigations		
Electrocardiogram QRS complex prolonged	-	1 (7.1%)
Electrocardiogram QT prolonged	1 (5.3%)	-
Musculoskeletal and connective tissue disorders		
Myalgia	1 (5.3%)	-
Neck pain	-	1 (7.1%)

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

Safety: Relapses or Worsening of CNS inflammatory disorders

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

Event, n (%)	OCS-05 + 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%)*

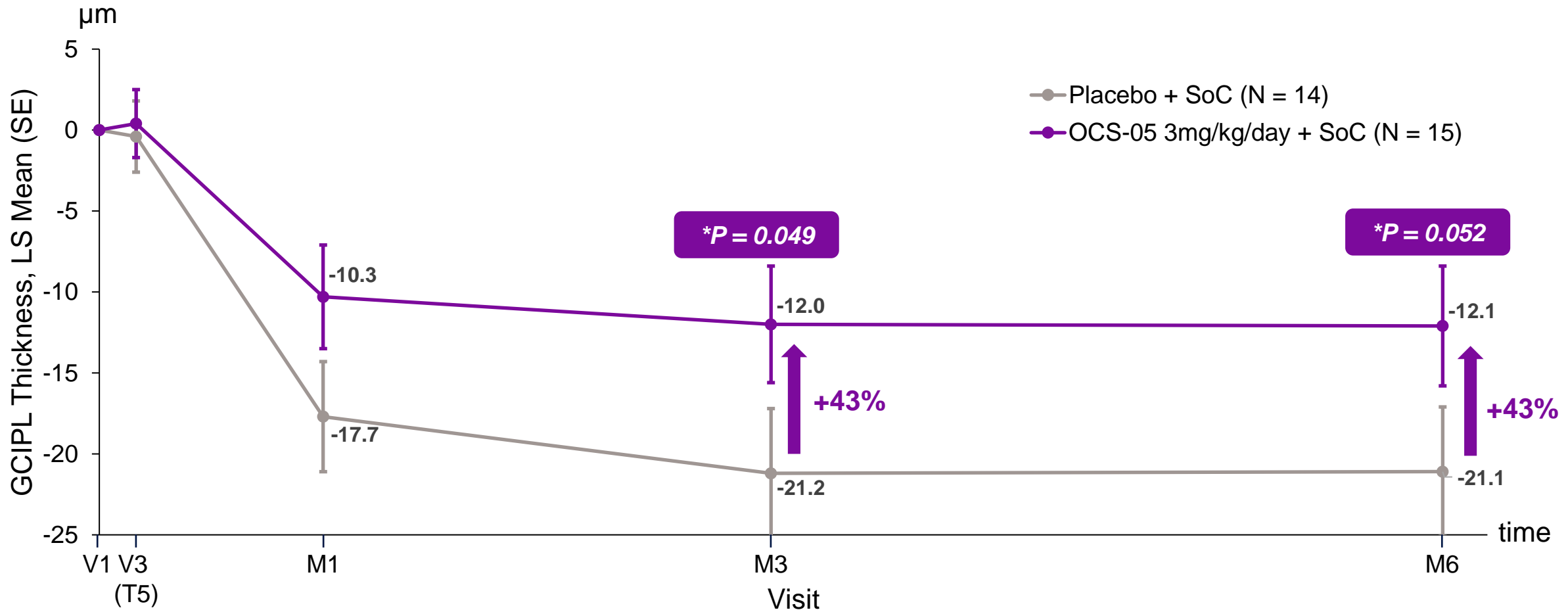
*One “placebo + steroid” patient had 1 TEAE related to new relapse and worsening

- Lower incidence of AEs related to new relapses or worsening of CNS inflammatory disorders in patients receiving OCS-05: 10.5% in the OCS-05 (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 OCS-05 (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

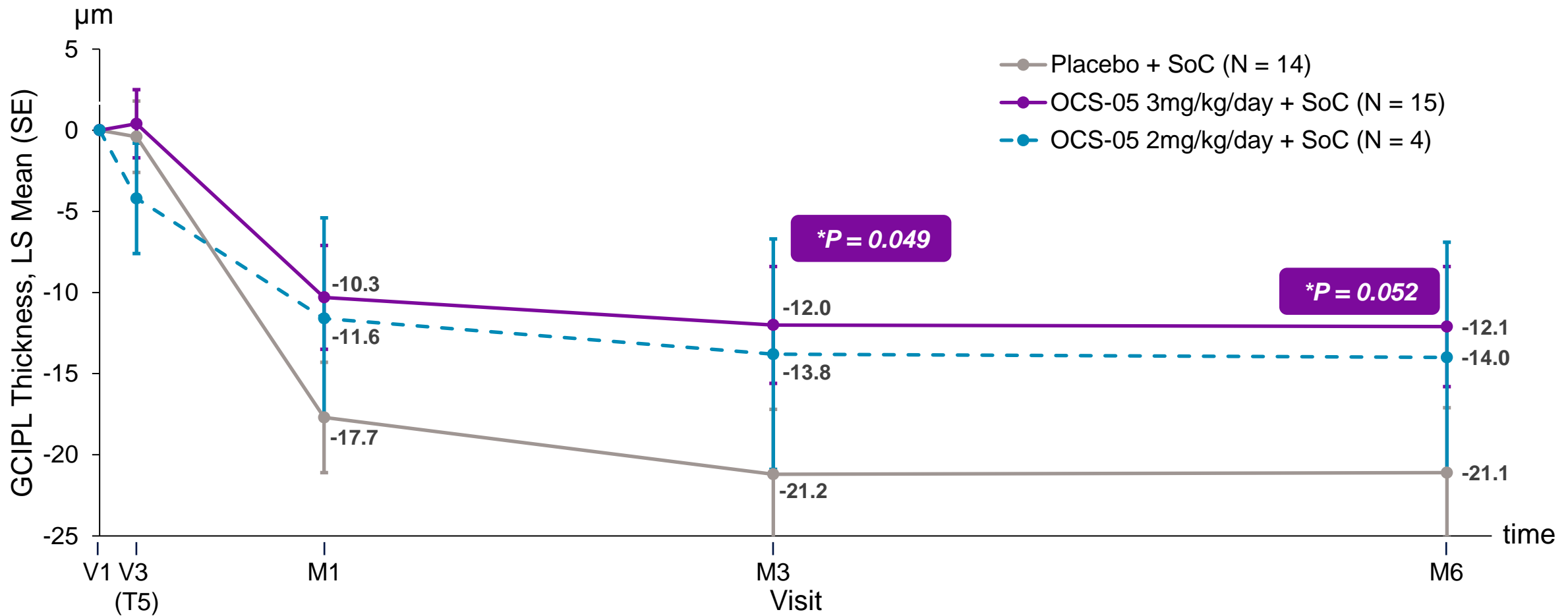
Patients in the OCS-05 3mg/kg/day Arm Achieved Preservation in GCIPL Thickness

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



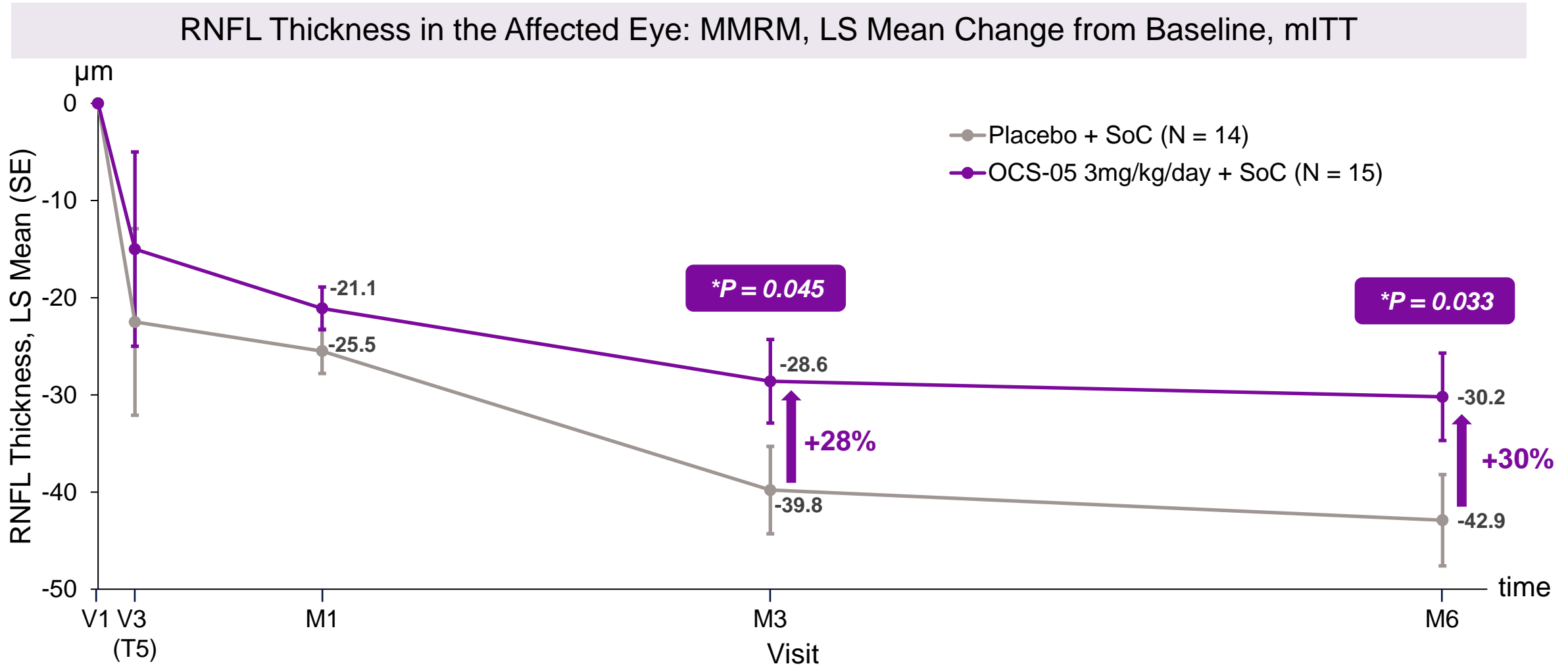
*Mixed Model for Repeated Measures (MMRM); Least-Squares Mean Change from Baseline: (nominal directional p-value), mITT population (affected eye)
 GCIPL; ganglion cell plus inner plexiform layer.
 Data, analysis and conclusions are preliminary, and subject to change as full analysis is ongoing.

Patients in the OCS-05 3mg/kg/day and 2mg/kg/day Arms Achieved Preservation in GCIPL Thickness



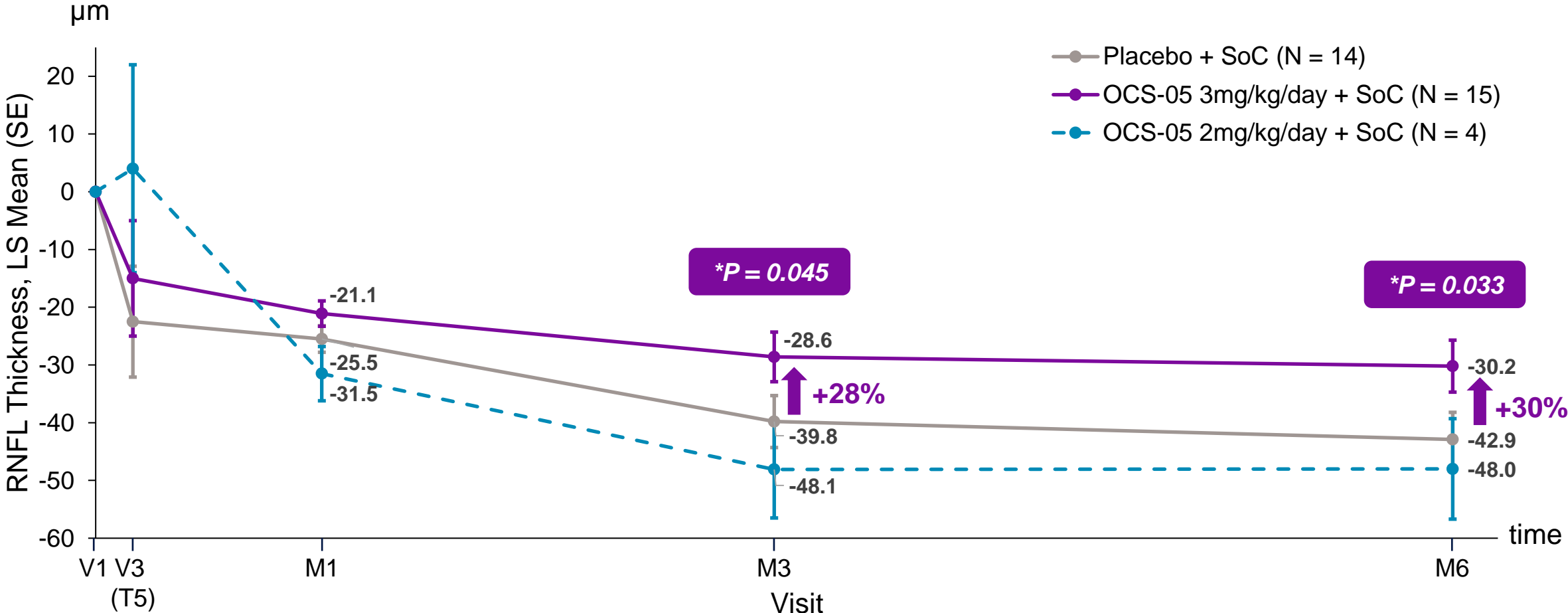
*Mixed Model for Repeated Measures (MMRM); Least-Squares Mean Change from Baseline: (nominal directional p- value), mITT population (affected eye) RNFL; retinal nerve fiber layer.
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Patients in the OCS-05 3mg/kg/day Arm Achieved Preservation in RNFL Thickness



*Mixed Model for Repeated Measures (MMRM); Least-Squares Mean Change from Baseline: (nominal directional p-value), mITT population (affected eye)
 RNFL; retinal nerve fiber layer.
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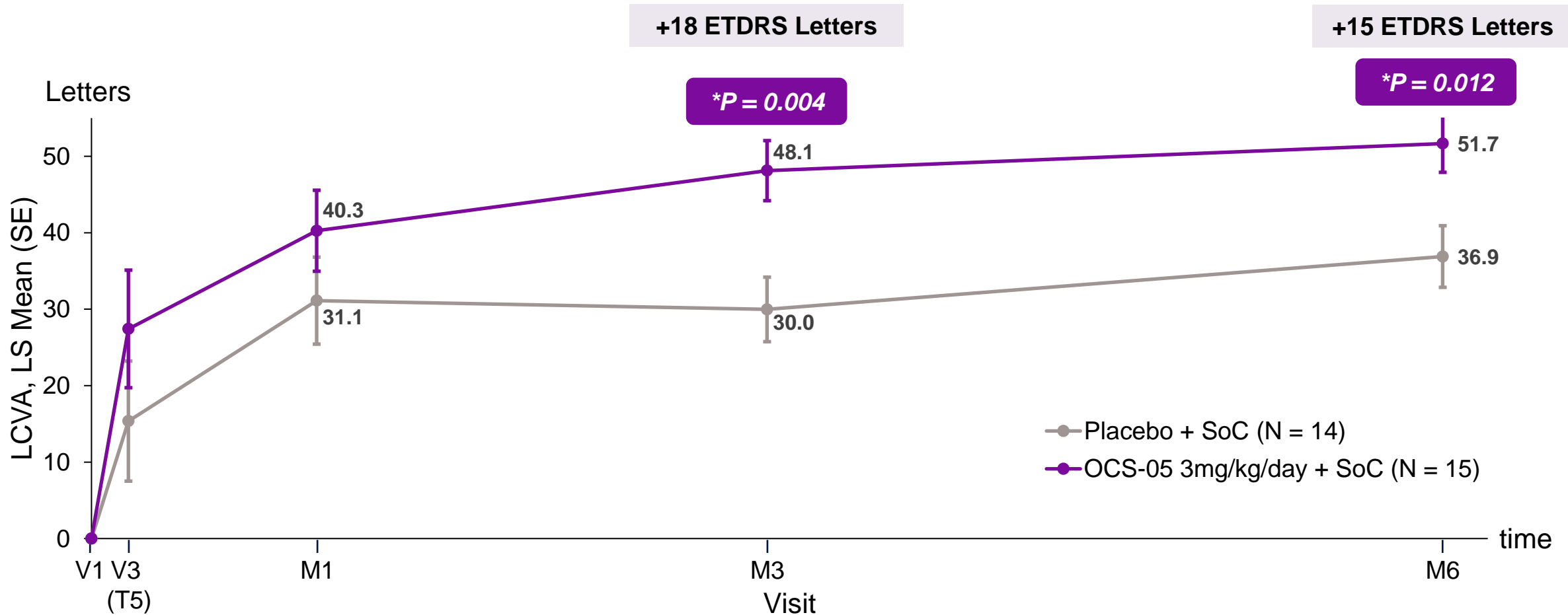
Patients in the OCS-05 3mg/kg/day Arm Achieved Preservation in RNFL Thickness



*Mixed Model for Repeated Measures (MMRM); Least-Squares Mean Change from Baseline: (nominal directional p- value), mITT population (affected eye)
 RNFL; retinal nerve fiber layer.
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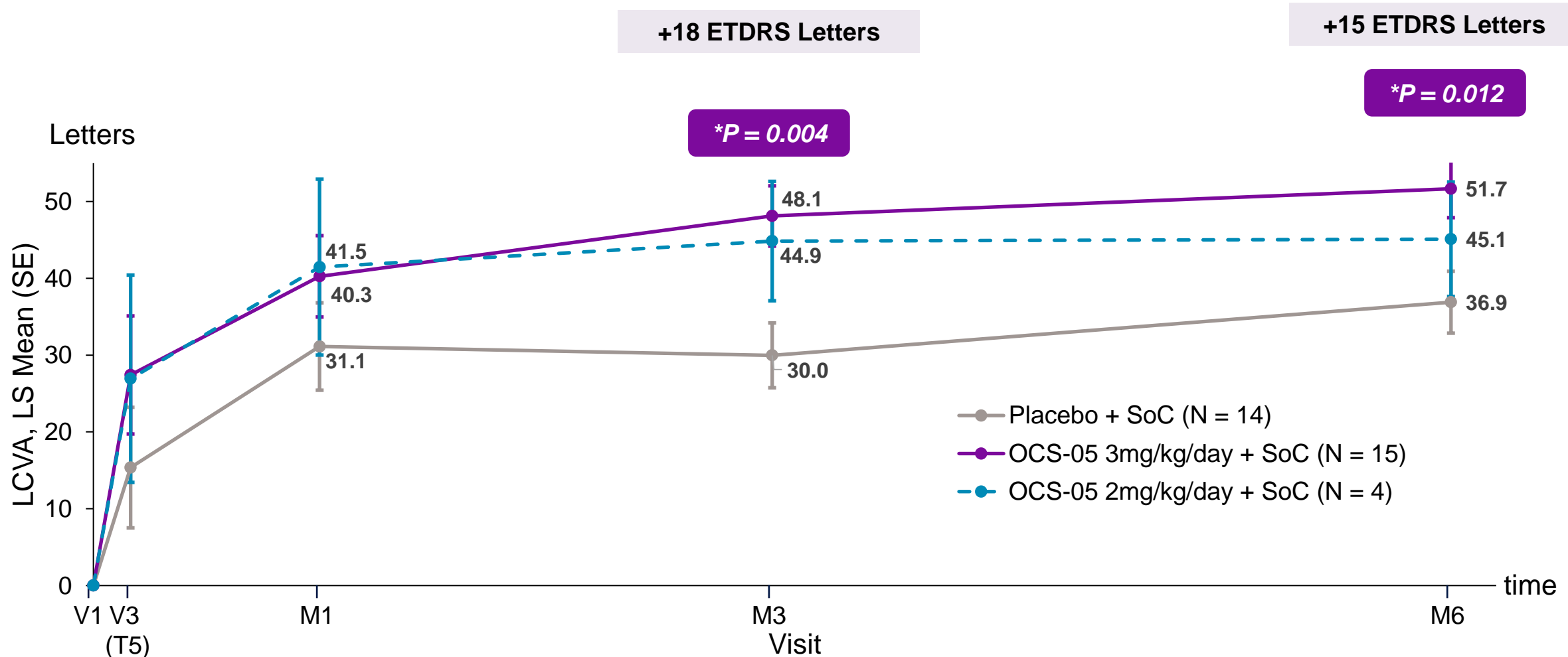
Patients in the OCS-05 3mg/kg/day Arm Achieved Clinically Meaningful Improvement in Visual Function

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: (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.

Patients in the OCS-05 3mg/kg/d Arm Achieved Clinically Meaningful Improvement in Visual Function



*Mixed Model for Repeated Measures (MMRM); Least-Squares Mean Change from Baseline: (nominal p-value), mITT population (affected eye)
 LCVA; low contrast visual acuity.
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Summary

ACUITY Phase 2 Topline Results Summary

OCS-05 achieved primary safety endpoint, and key secondary endpoints showing neuroprotective anatomical benefit and vision improvement

Primary Endpoint: Safety

- ✓ No difference in % of patients shifted from normal baseline to abnormal post-baseline electrocardiogram (ECG) events

Secondary Endpoints: Efficacy - Preservation of Retinal Ganglion Cells and Optic Nerve Structure and Vision Improvement

- ✓ Statistically significant difference in mean GCIPL thickness (biomarker of RGC preservation) of 43% with OCS-05 (3mg/kg/d) arm at month 3 with treatment effect maintained through month 6
- ✓ Statistically significant difference in mean RNFL thickness (biomarker of axon preservation) of 28% with OCS-05 (3mg/kg/d) arm at month 3 with treatment effect maintained through month 6
- ✓ Statistically significant and clinically meaningful improvement in low contrast visual acuity (LCVA) with 18 letters difference in OCS-05 (3mg/kg/d) arm at month 3 with treatment effect maintained through month 6 vs steroid alone.

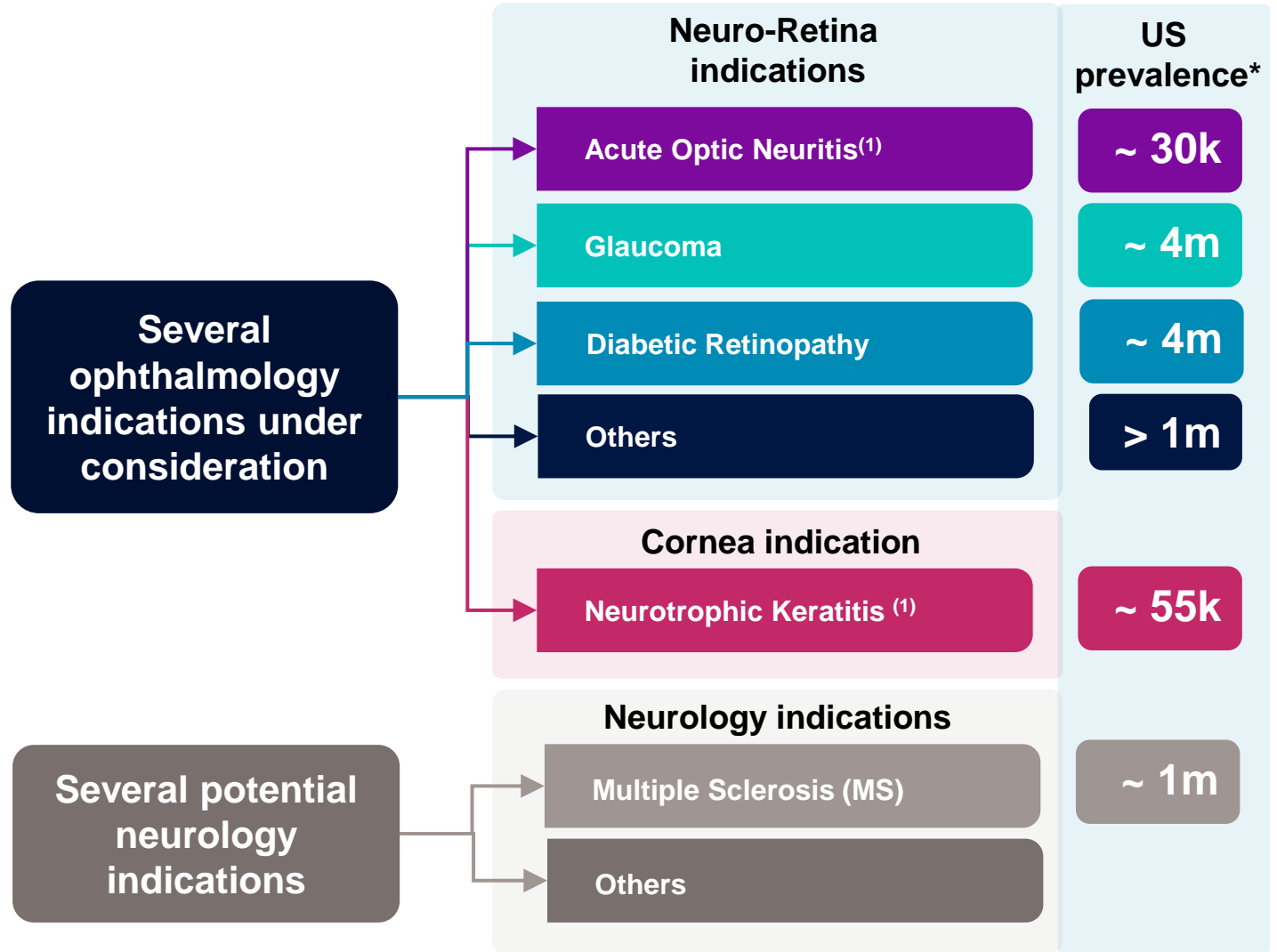
Treatment Emergent Adverse Events (AEs):

- 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 with OCS-05

FDA IND Clearance and Successful Acuity Trial Drive Acute Optic Neuritis Development Program and Maximize OCS-05 in Neuro Ophthalmology

Next steps

1. Interact with FDA to advance OCS-05 development program in acute optic neuritis
2. Explore additional indications to maximize OCS-05 neuroprotective pathway in Neuro-Ophthalmology



⁽¹⁾ Acute optic neuritis & neurotrophic keratitis are both orphan indications

*Prevalence references: Acute optic neuritis: 8 per 100,000 * US and EU population, Glaucoma: Glaucoma Research Foundation, GA: American Macular Degeneration Foundation, DR: Prevent Blindness, JAMA Ophthalmology 2021, NK: Sacchetti, Clinical Ophthalmology, 2014 (from Clearview report), MS: MS International Federation

Thank you



Oculis | Rethinking
Ophthalmology