Improved Low Contrast Visual Acuity, Reduction in Retinal Ganglion Cell Loss, and Neurofilaments–light with Privosegtor in Acute Optic Neuritis: Results from a Multicenter, Randomized, Placebo–Controlled, Double–Masked Trial

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Disclosures

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Pablo Villoslada holds several patents covering privosegtor composition of matter and its use for the treatment of CNS and ophthalmological diseases. He holds stocks or stock options and has received consultancy fees from Oculis SA, Bionure Therapeutics, and Accure Therapeutics as part of the development of this program.

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Sabri Markabi is consultant to Oculis SA.

Caroline Papeix has been an advisory board member or conference speaker for Roche, Biogen, Novartis, Amgen, and Alexion.

Martin S. Zinkernagel has been a consultant for Bayer, Roche, Alcon, and Oculis, and has received grants from Bayer.

Sebastian Wolf is consultant for Celltrion Healthcare, Novartis Pharma, Oculis SA, and Priothera SAS.

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Optic Neuritis, an Acute Inflammation of the Optic Nerve Which Can Lead to Permanent Visual Impairment

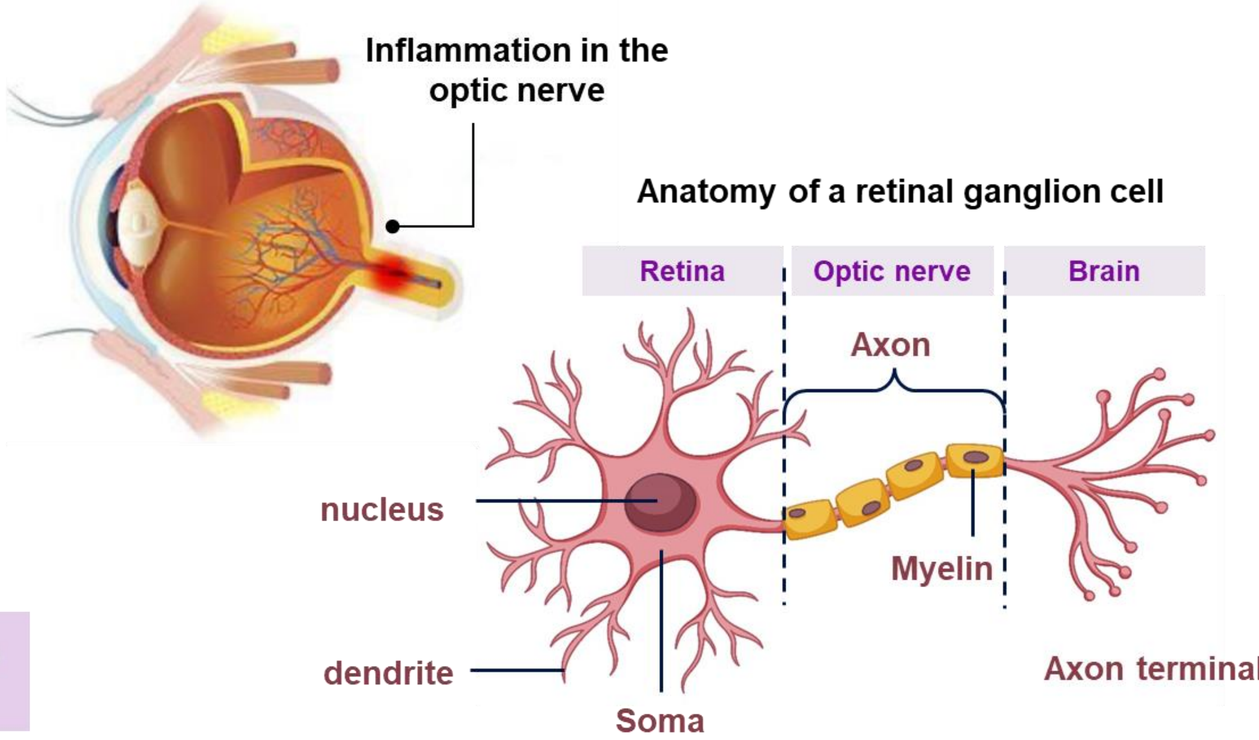
Orphan indication with ~ 65k patients a year (US/EU)[1,2]

Acute inflammation of the optic nerve impacting retinal ganglion cells and leading to vision loss

- Type of neuropathy causing vision loss and pain, and **can lead to permanent visual impairment**

- **Inflammation** affects the signals through the **optic nerve**, which connects the eyes and the brain
- **Mainly affecting young women** with an average onset at age 32[3]

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



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.
2. Weidong Gu et al. (2023) Incidence of Optic Neuritis and the Associated Risk of Multiple Sclerosis for Service Members of U.S. Armed Forces, Military Medicine, vol. 188, March/April 2023
3. Guier CP, Kaur K, Stokkermans TJ. Optic Neuritis. January 2025. StatPearls. https://www.ncbi.nlm.nih.gov/books/NBK557853

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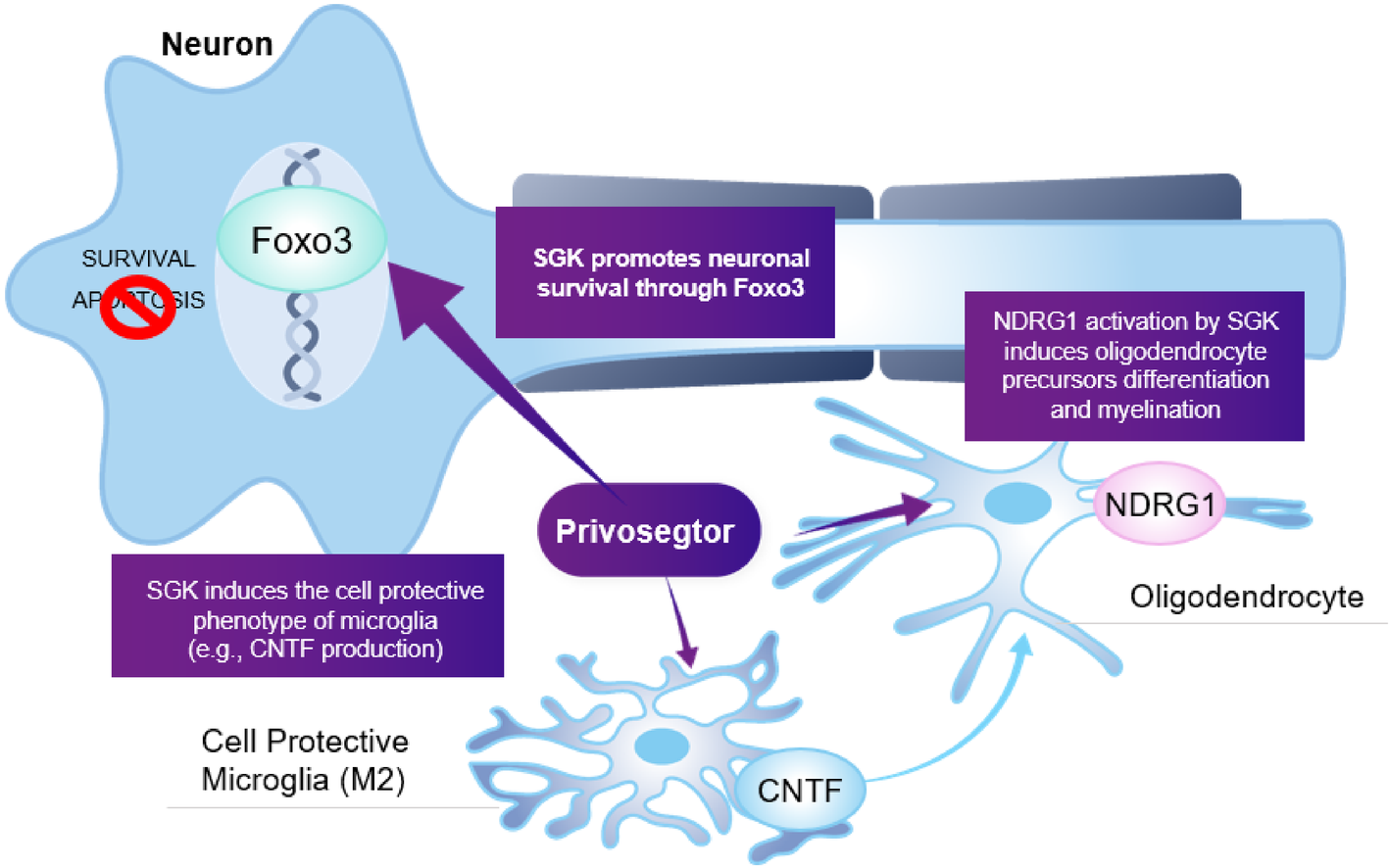
Privosegtor is a Novel Neuroprotective Candidate with Broad Potential for Neuro-axonal Diseases

- Peptoid small molecule that **crosses blood brain and retinal barriers**
- **Selected by high-throughput screening (HTS) for its unique ability to promote neuro-axonal survival,** validated across multiple in vitro injury models: **apoptosis, oxidation, and inflammation**
- It activates SGK which triggers **multiple beneficial neuroprotective effects**, confirmed in vivo in glaucoma, MS, and optic neuritis models
- **Breakthrough Therapy Designation** granted by U.S. FDA for optic neuritis



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

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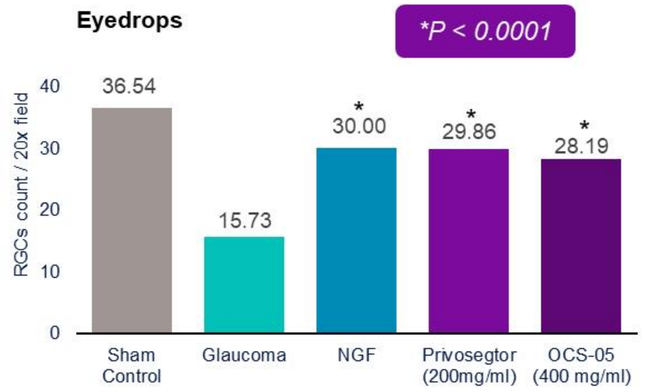
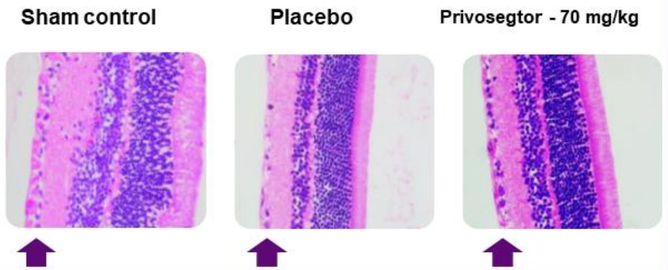
Preclinical Data Showed Neuroprotection Benefits with Neurons and Axons Preservation/Survival

Prevention of RGC Damage[1,2,3]

H&E for RGC density at week 6 in high-pressure glaucoma rat model[1,3]

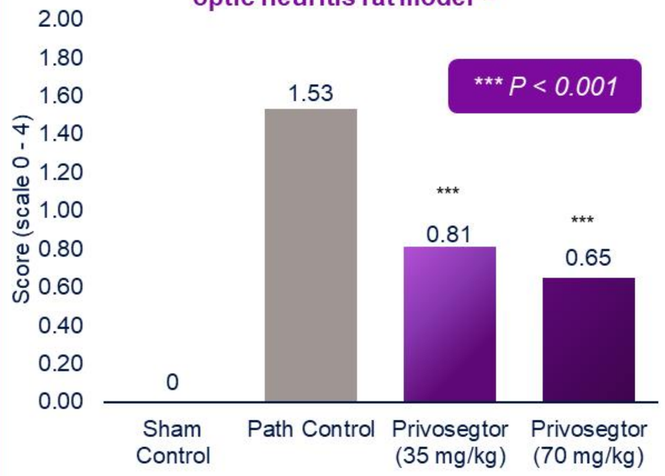


Visual of RGC Protection after 5-days of treatment in optic neuritis rat model[1,2]



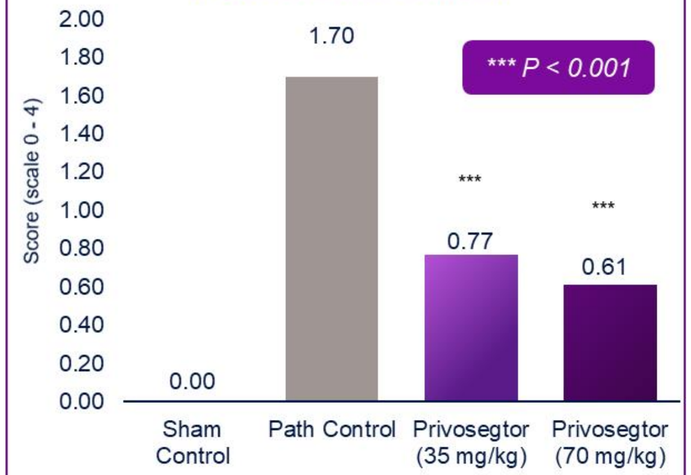
Reduction of Optic Nerve Axonal Loss[1,2]

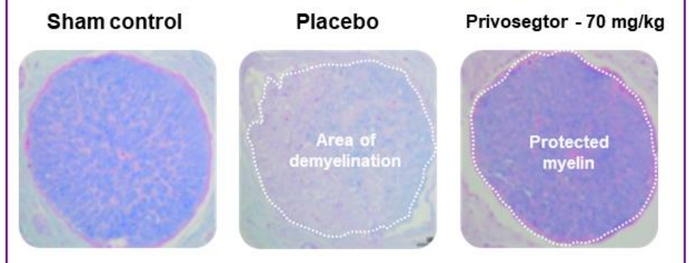
Optic nerve axonal loss after 5-days of treatment in optic neuritis rat model[1,2]



Reduction Optic Nerve Demyelination[1,2]

Optic nerve demyelination after 5-days of treatment in optic neuritis rat model[1,2]





1. H&E: hematoxylin and eosin staining; RGC: retinal ganglion cell.
2. Villoslada P, et al. Neurotherapeutics. 2019;16(3):808–827
3. Lysolecithin induced demyelinating model in rat (model of acute optic neuritis)– Assessment after 5-days of treatment
4. High pressure Glaucoma rat model of neurodegeneration without inflammation

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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 Privosegtor + steroid vs. placebo + steroid for 5 consecutive days

Key endpoints

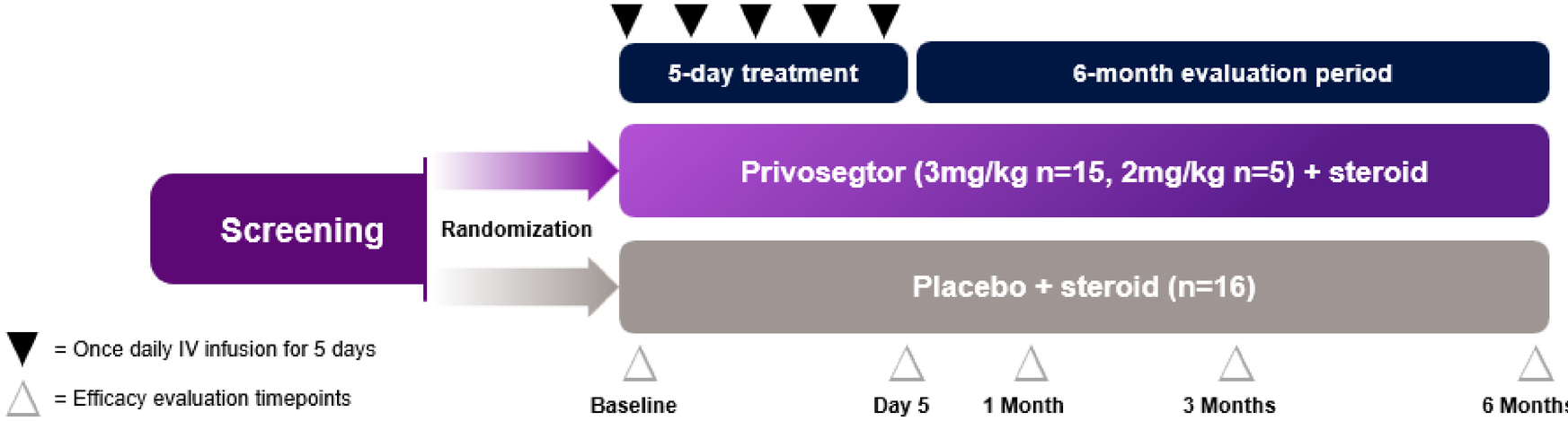
Primary endpoint: Safety

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
- Onset of visual loss symptoms in the last 12 days before randomization



1. mITT: Modified Intent to Treat
   https://clinicaltrials.gov/study/NCT04762017

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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

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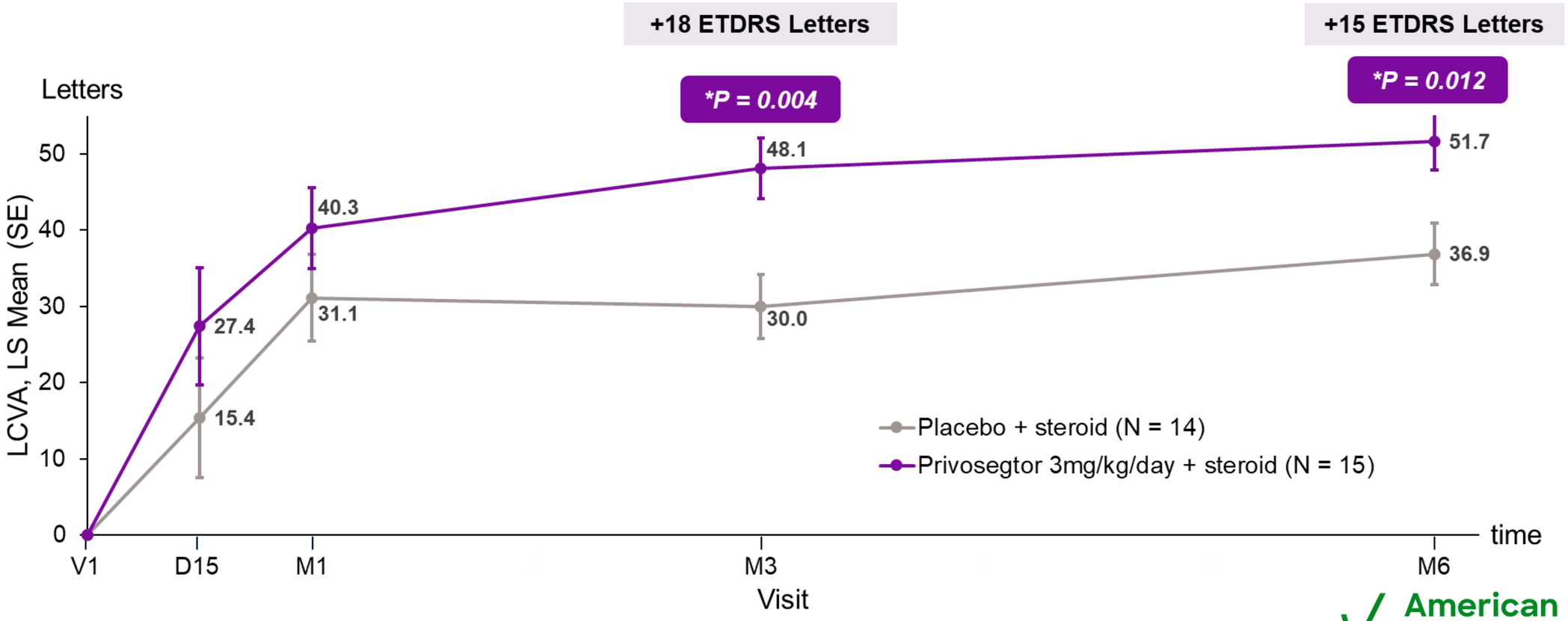
Patients in the Privosegtor 3mg/kg/day Arm Achieved Clinically Meaningful Improvement in Visual Function

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.

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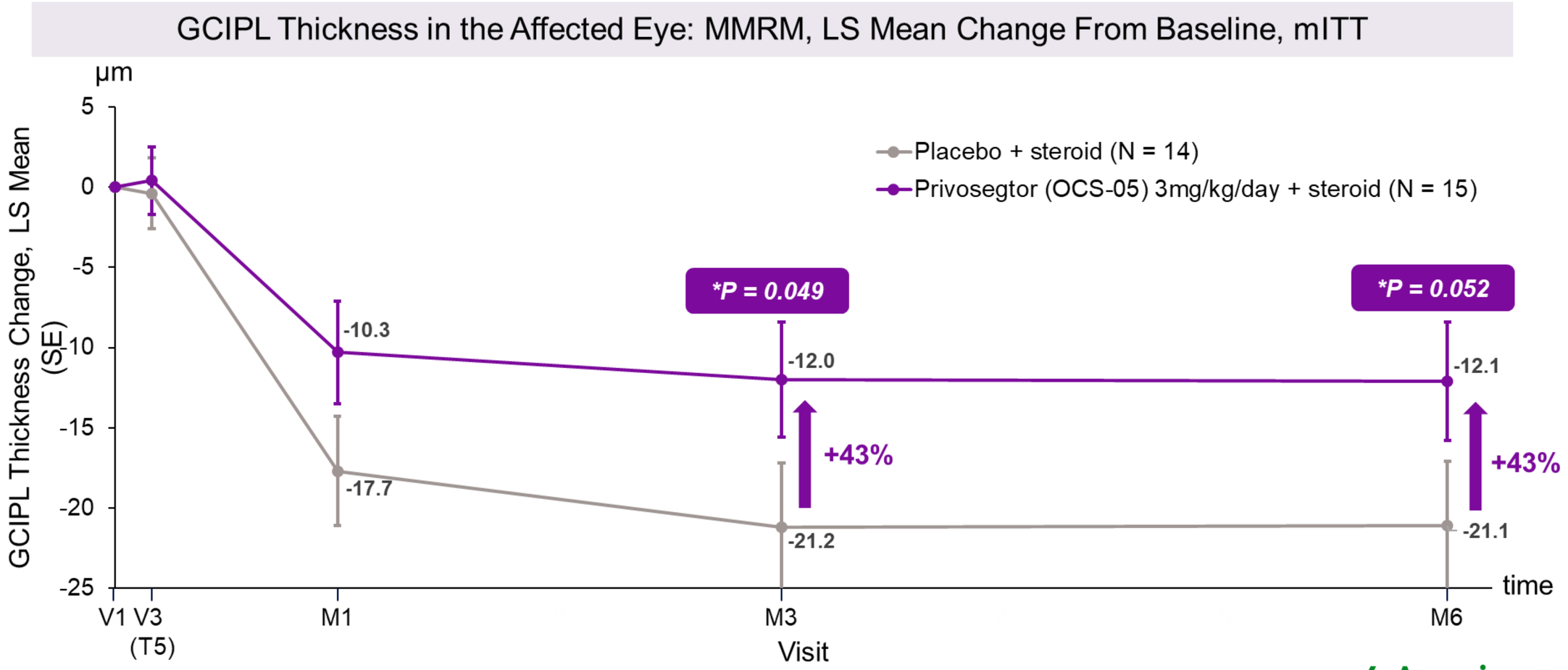
Patients in the Privosegtor 3mg/kg/day Arm Achieved Less GCIPL Thickness Decrease



*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.

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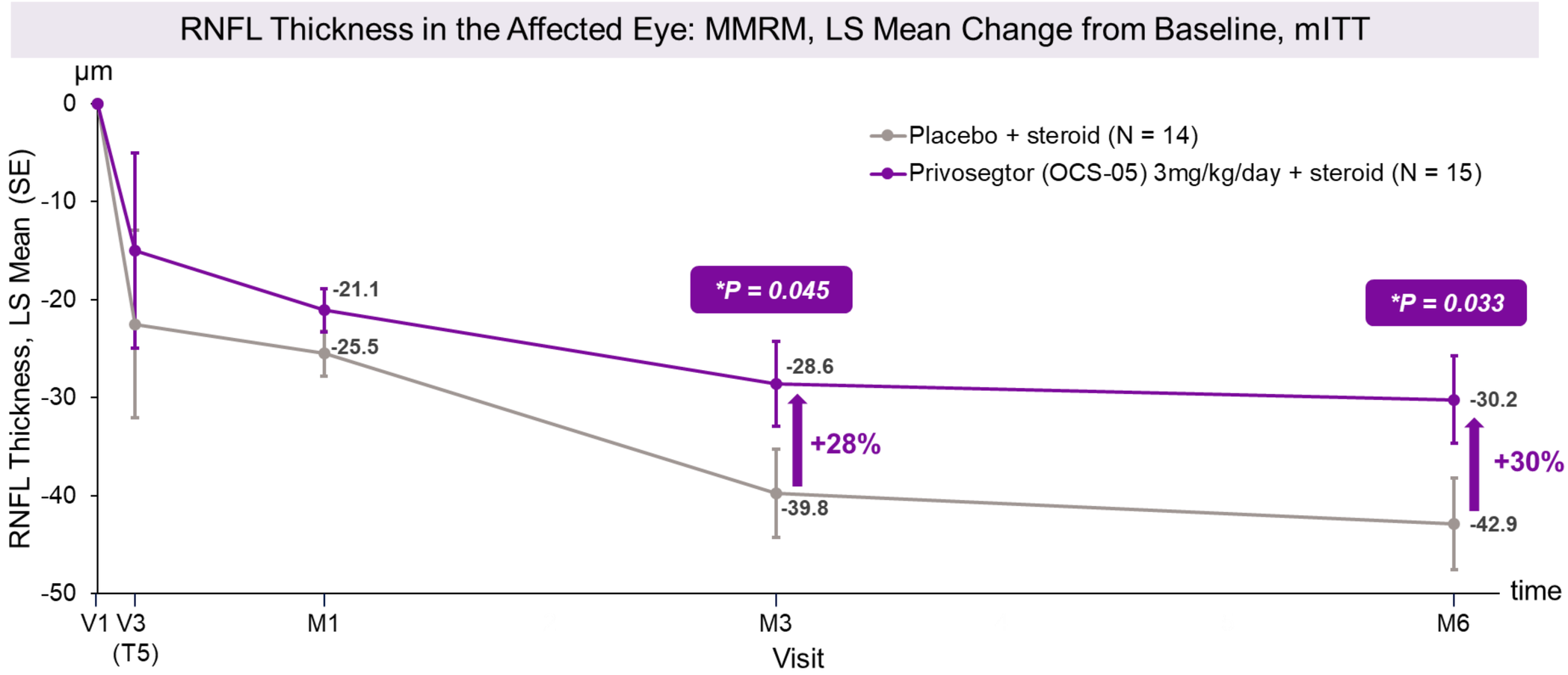
Patients in the Privosegtor 3mg/kg/day Arm Achieved Less RNFL Thickness Decrease



*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..

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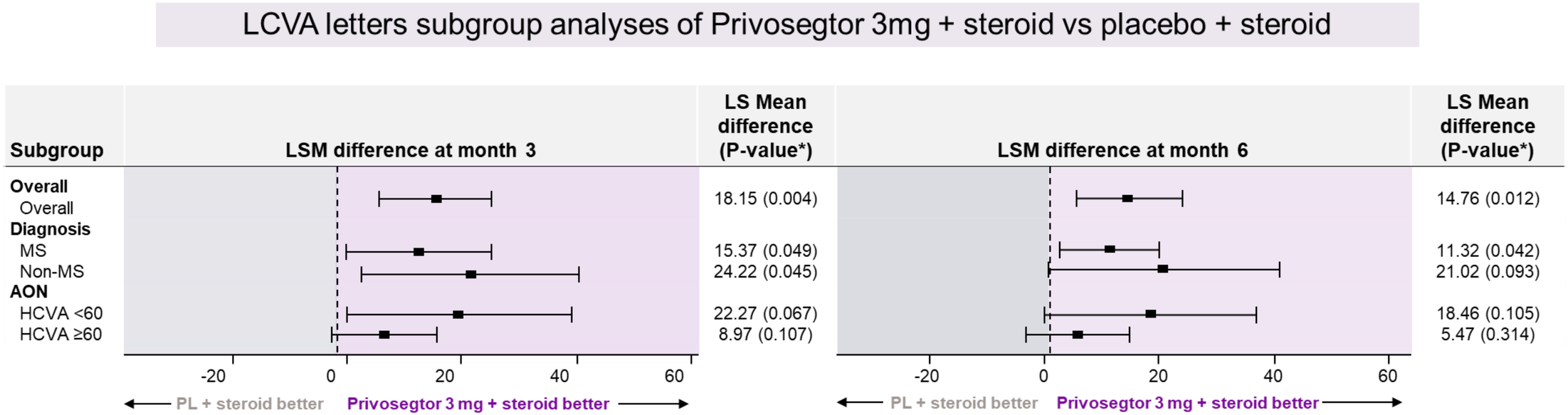
Privosegtor Arm Showed a Robust LCVA Improvement Across all Subgroups and Maintained through Month 6



*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

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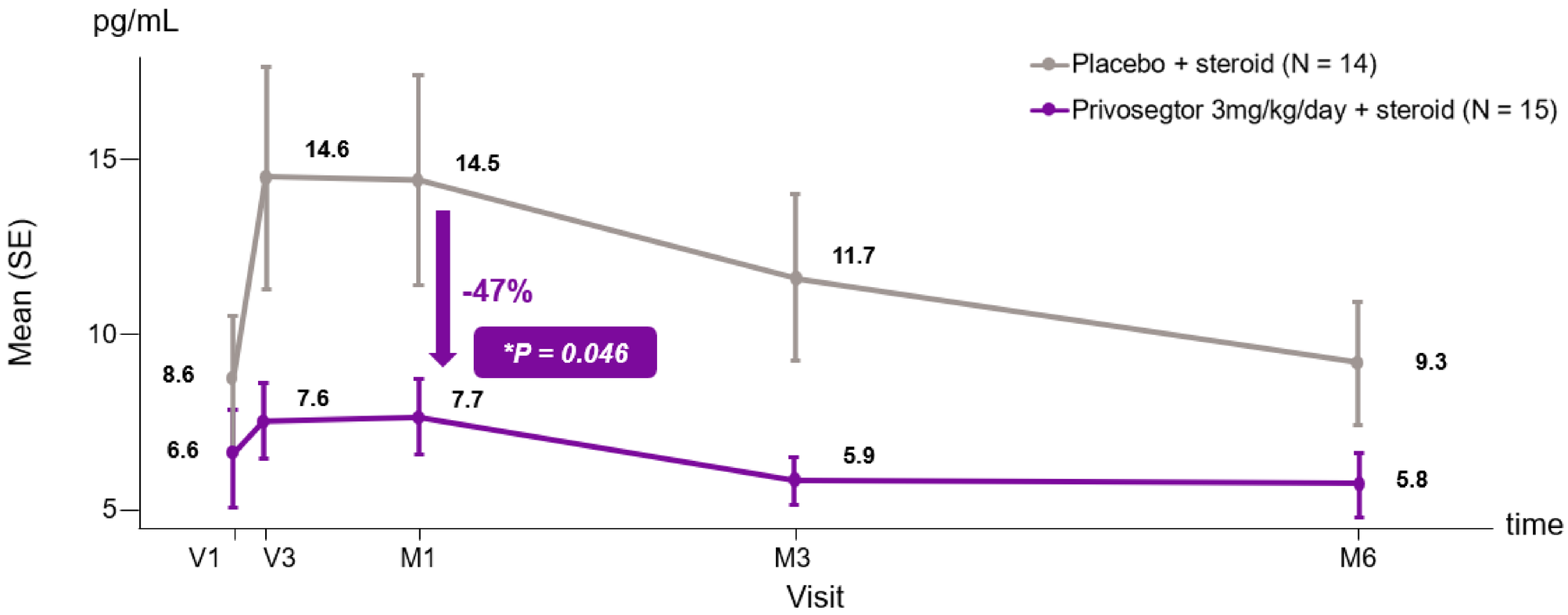
Neuroprotective Benefits with Privosegtor Also Observed in Biological Sign of Neuronal and Axonal Death

Mean Neurofilaments Over Time, mITT



*Mixed Model for Repeated Measures (MMRM); Least-Squares Mean Change from Baseline: (2-sided nominal p-value), mITT population (affected eye).

Gafson AR and al. Neurofilaments: neurobiological foundations for biomarker applications. Brain. 2020 Jul 1;143(7):1975–1998.
Stern S and al. Trends in clinical studies evaluating neurofilament light chain as a biomarker. Biomark Med. 2025 Sep;19(17):813–823.

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Safety Profile Reported in ACUITY Phase 2 Trial Showed No AEs Leading to Drug Withdrawal or Study Discontinuation

- No AEs leading to drug withdrawal or study discontinuation
- No drug-related serious adverse events (SAEs)

Event, n (%)	Privosegtor + steroid			Placebo + steroid (N = 14)
	2 mg/kg/day (N = 4)	3 mg/kg/day (N = 15)	Pooled (N = 19)	
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.
Two (2) unrelated SAEs: Hospitalization due to MS relapse (Privosegtor (OCS-05 + steroid) and due to myelitis (placebo + steroid)

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ACUITY Phase 2 Results Summary

- **Function:** **Significant improvement in LCVA** with 18 letters difference at month 3
- **Structure:** **Less GCIPL and RNFL thickness decrease**, preserving axons and RGCs
- **Biomarker:** **Stable plasma NfL concentration and significantly lower than the placebo group**, suggesting neuroaxonal preservation
- **Safety:** **No AEs leading to drug withdrawal or study discontinuation and no drug related SAEs**

Privosegtor showed promising results in restoring vision and preserving RGCs and the optic nerve, which could benefit multiple neuroaxonal diseases

RGC: Retinal Ganglion Cell SAE: Serious Adverse Events AE: Adverse Events

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Thank you!

Thank you to all the investigators, study teams, and patients who contributed to this work

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