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Acuity
Acute optiC NeUrITis with a demYelinating origin

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

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Relevant Financial Disclosures

- **Abbvie**
- **Bayer**
- **Oculis**
- **Optic 2000**
- **Roche**

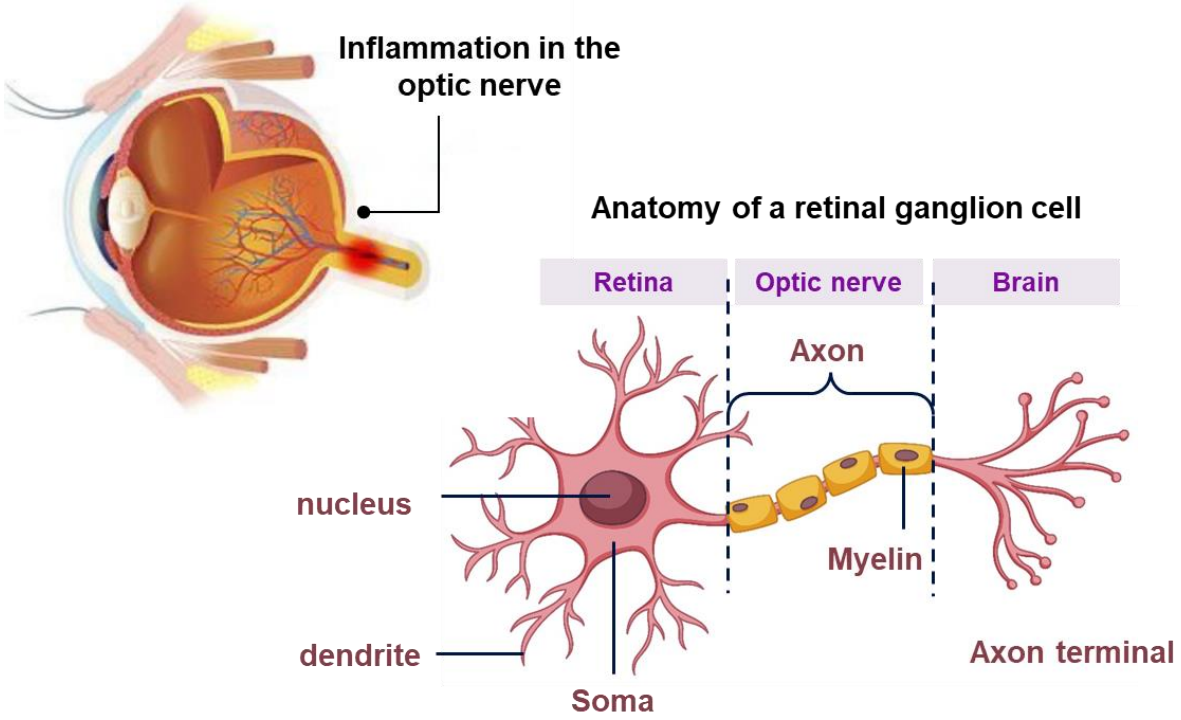
Privosegtor (OCS-05) Overview

New class of drug with neuroprotective benefits

1. Privosegtor is a small molecule peptoid that penetrates the blood brain and retinal barriers

2. Pre-clinical data in various in-vivo models validated **preservation of neurons and axons**[1]

3. Acute optic neuritis was chosen as a **predictive clinical neuroprotection model**



Positive neuroprotective proof of concept:
ACUITY Phase 2 data showed neuroprotective anatomical benefits with clinically meaningful visual function improvement

1. Villoslada P. et al. Neurotherapeutics, published online: 27 February 2019

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

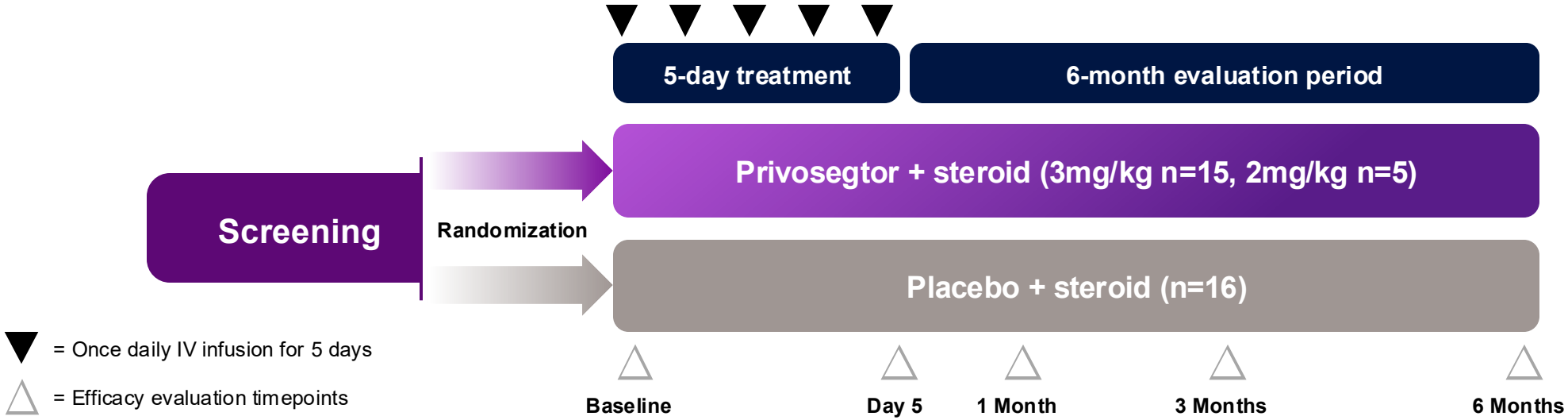
Primary endpoint: Cardiac safety

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



mITT: Modified Intent to Treat

https://clinicaltrials.gov/study/NCT04762017

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;

Safety Summary

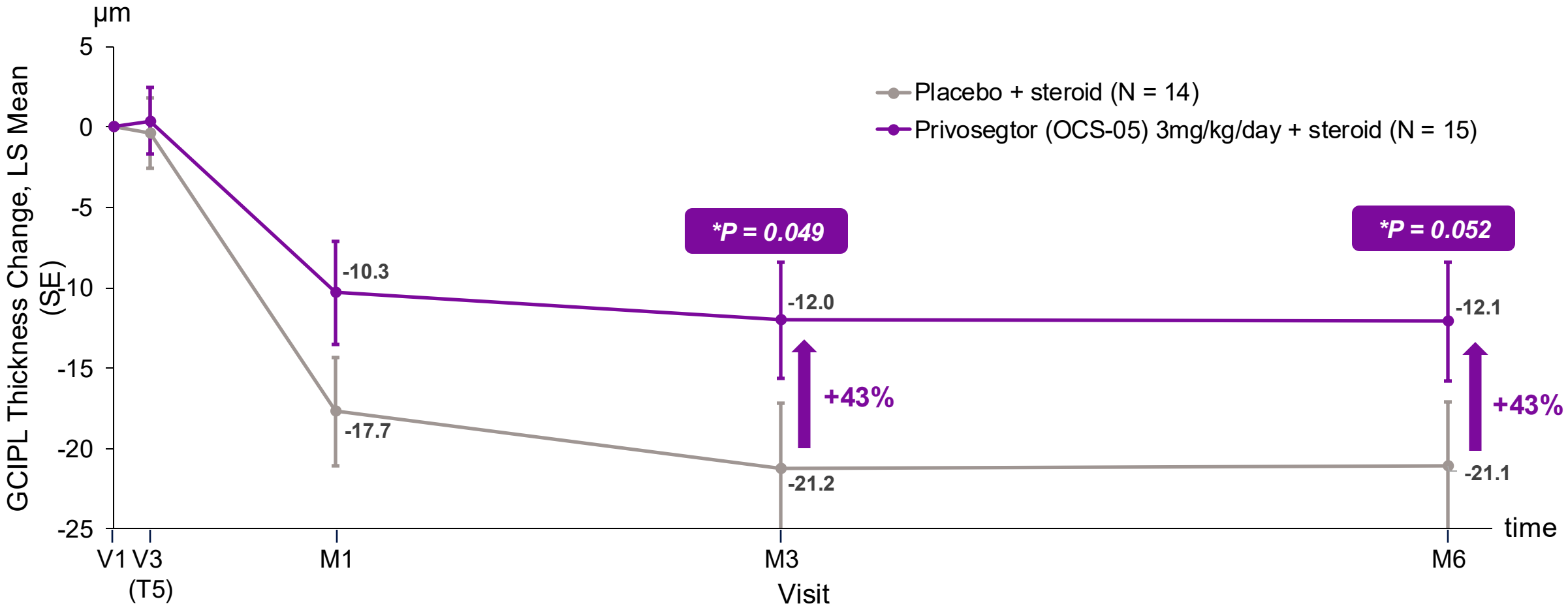
- **Cardiac safety (shifts in ECG parameters) showed no differences between groups**
- **No AEs leading to drug withdrawal or study discontinuation**
- **No drug-related serious adverse events (SAEs)**
- **2 Unrelated SAEs:** Hospitalization due to MS relapse (Privosegtor + steroid) and due to myelitis (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.

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

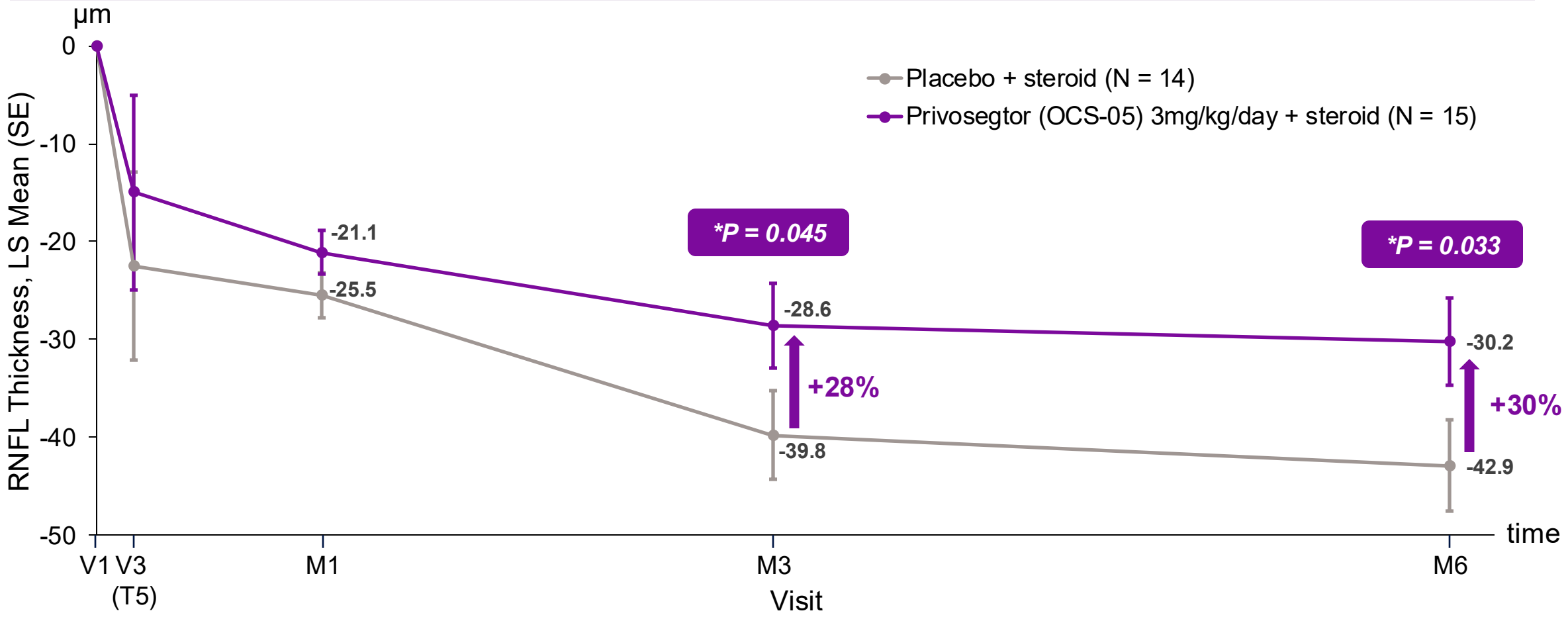
GCIPL Thickness in the Affected Eye: MMRM, LS Mean Change From Baseline, mITT



*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.

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

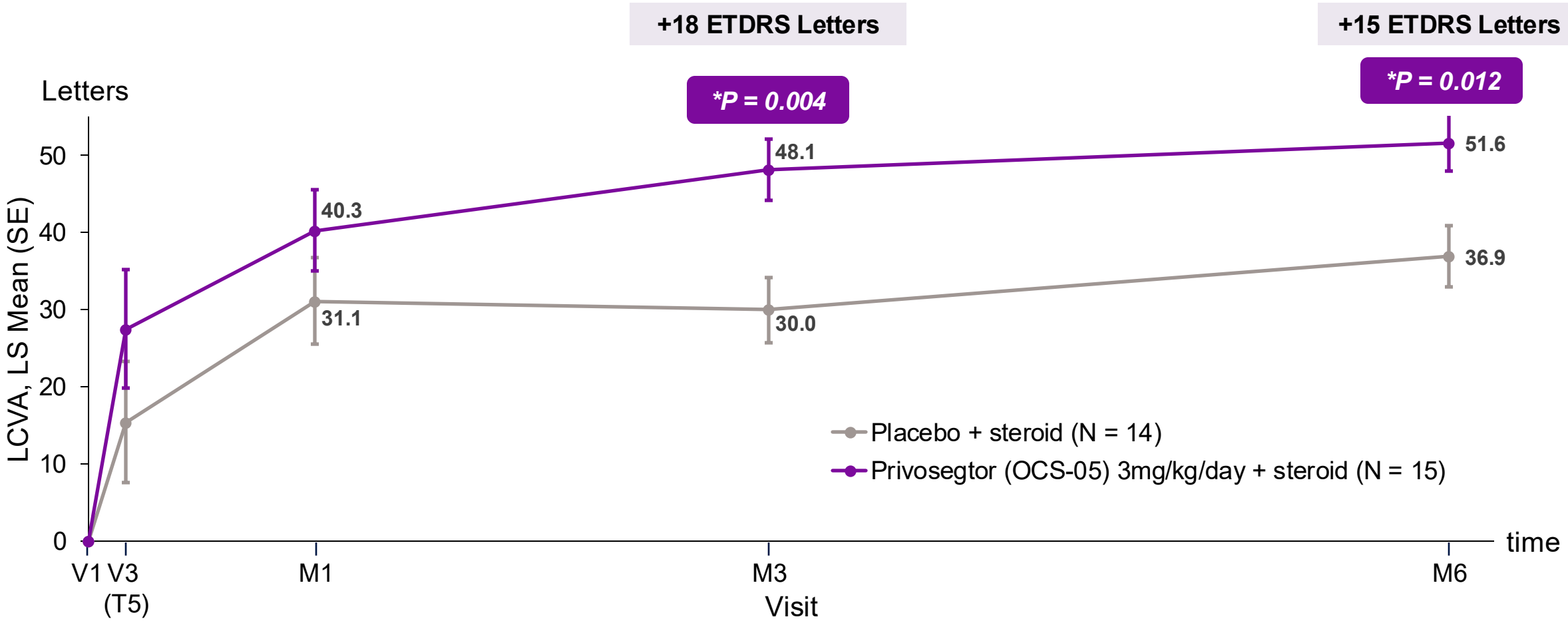
RNFL Thickness in the Affected Eye: MMRM, LS Mean Change from Baseline, mITT



*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..

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.

ACUITY Phase 2 Topline Results Summary

1. **Safety:** **Cardiac safety** showed no differences between groups with no drug-related SAEs

2. **Function:** **Significant improvement in LCVA** with 18 letters difference at month 3

3. **Structure:** **less GCIPL and RNFL thickness decrease** preserving axons and RGCs

Privosegtor showed promising results in protecting vision and structure in AON, which could have benefits in multiple other conditions

RGC: Retinal Ganglion Cell SAE: Serious Adverse Events AE: Adverse Events, CNS: Central Nervous System