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  - For the site in France, the fees have been paid to the Hôpital Lariboisière in Paris
- This study includes research conducted on human subjects; institutional review board approval was obtained prior to study initiation

The Effect of Baseline Ellipsoid Zone Area Loss on Treatment Response of Revakinagene Taroretcel-lwey (NT-501) in Macular Telangiectasia Type 2

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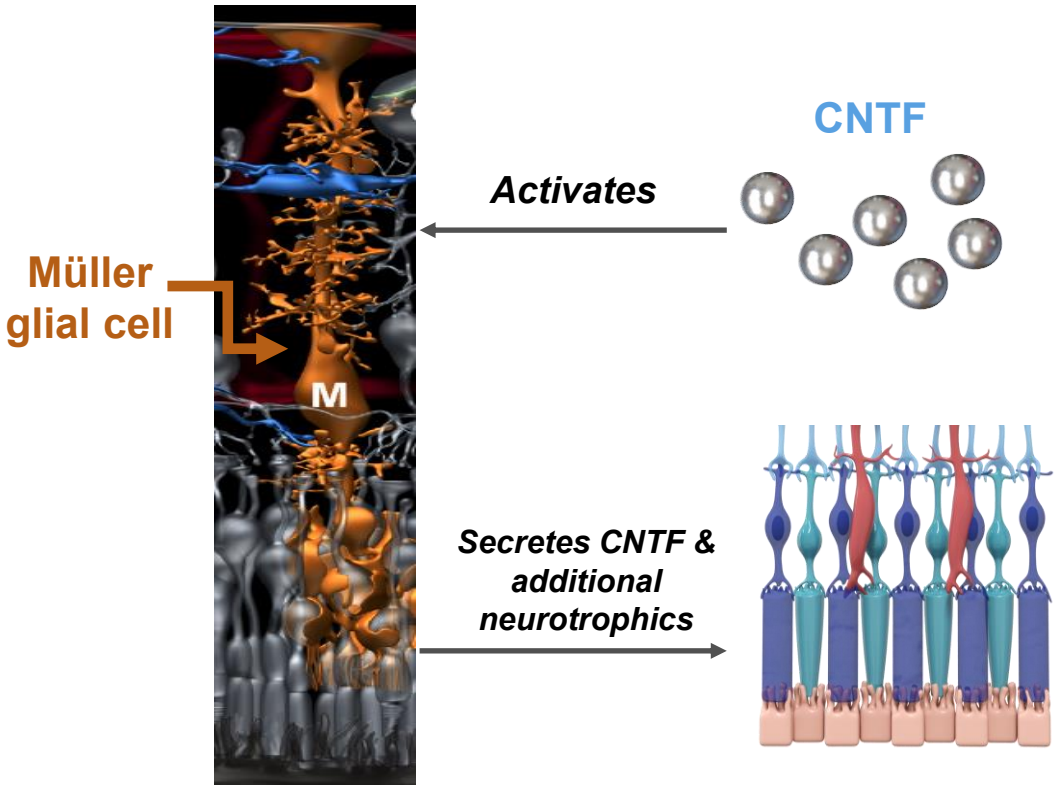
Macular Telangiectasia Type 2 (MacTel) and Ciliary Neurotrophic Factor (CNTF)

- MacTel is a bilateral, progressive, retinal neurodegenerative disease
  - Leads to **central vision loss** and **functional impairment**[1,2]
  - Characterized by abnormalities in **Müller glia**, retinal pigment epithelium, and photoreceptors in the central retina,[3] and **progressive loss of the EZ**[4]
- **CNTF**, released from Müller cells under pathologic conditions, **protects and preserves photoreceptors**[5,6]



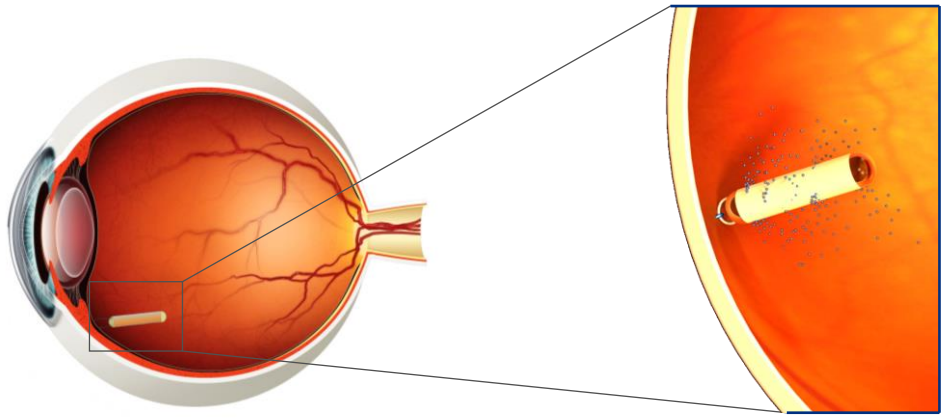
Cell survival pathway activation and macular photoreceptor protection

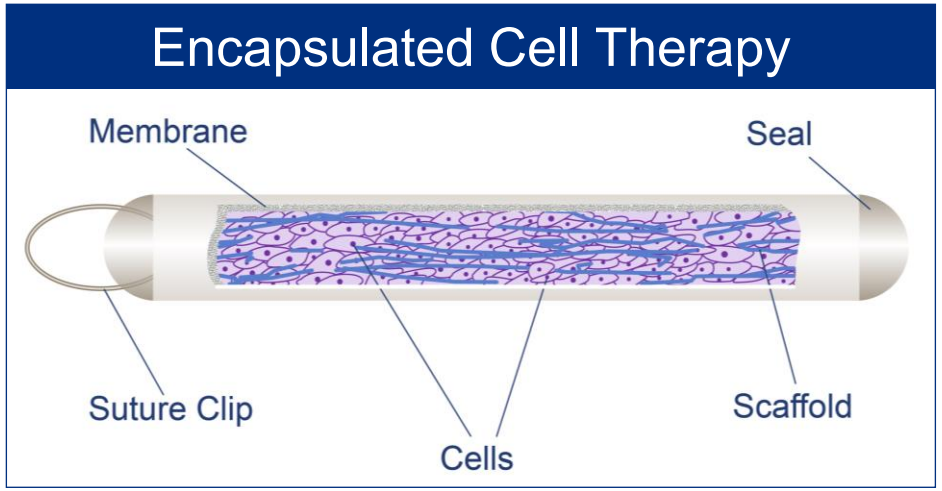
CNTF, ciliary neurotrophic factor; EZ, ellipsoid zone; MacTel, macular telangiectasia type 2.

1. Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **2.** Hereen TFC, et al. *Ophthalmology*. 2020;127:1539-1548. **3.** Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309.
4. Heeren TFC, et al. *Retina*. 2018;38(suppl 1):S20-S26. **5.** Bringmann A, et al. *Prog Retin Eye Res*. 2006;25:397-424. **6.** Rhee KD, et al. *Proc Natl Acad Sci U S A*. 2013;110:E4520-E4529.

Encapsulated Cell Therapy: Intravitreal Sustained CNTF Delivery System

- Revakinagene taroretcel-lwey (formerly known as NT-501) is a first-in-class encapsulated cell therapy[1-3]
  - Houses allogeneic RPE cells with an expression vector for CNTF release (NTC-201-6A cells),[1,3,4] which:
    - Release consistent levels of CNTF for long-term durations[1]
    - Remain alive and productive for many years[5]
    - Obtain oxygen and nutrients from vitreous[5]
    - Are sequestered from the immune system[5]
- **Revakinagene taroretcel-lwey was approved by the FDA for the treatment of adults with MacTel on March 5, 2025**





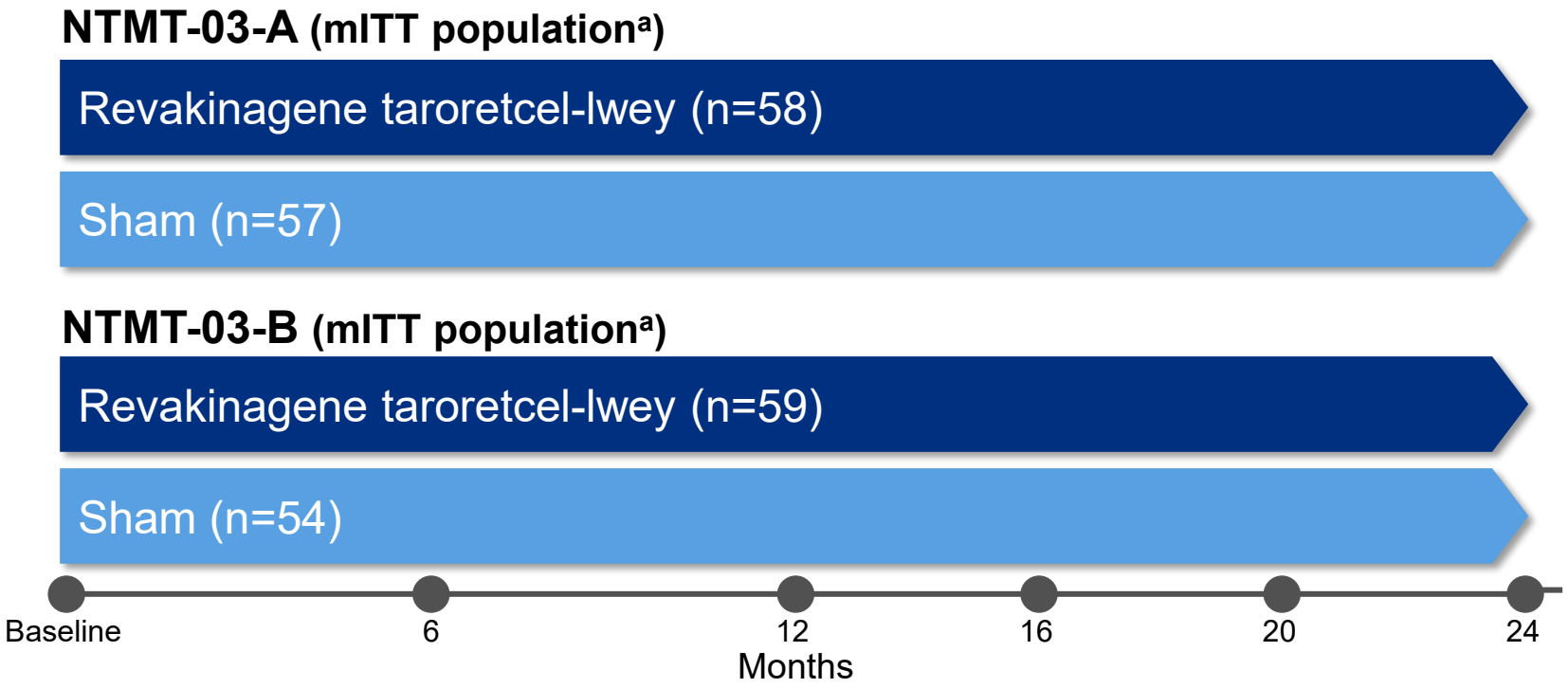
CNTF, ciliary neurotrophic factor; FDA, US Food and Drug Administration; MacTel, macular telangiectasia type 2; RPE, retinal pigment epithelium.

1. Kauper K, et al. *Invest Ophthalmol Vis Sci*. 2025;66(11):3. **2.** Chew EY, et al. *NEJM Evid*. 2025;4(8):EVIDoa2400481. **3.** Encelto [package insert]. Cumberland, RI: Neurotech Pharmaceuticals; 2025. **4.** Plakkot S, et al. Poster presented at: Association for Research in Vision and Ophthalmology; April 23–27, 2023; New Orleans, LA. **5.** Tao W. *Expert Opin Biol Ther*. 2006;6:717-726.

Revakinagene Taroretcel-lwey Was Studied in Two Identical Phase 3 Trials Involving More Than 200 Participants

Key inclusion criteria

- Diagnosis of MacTel
- Aged >21 to <80 years
- EZ break between 0.16 and 2.00 mm^2
- BCVA of ≥54 ETDRS letters (Snellen 20/80 or better)



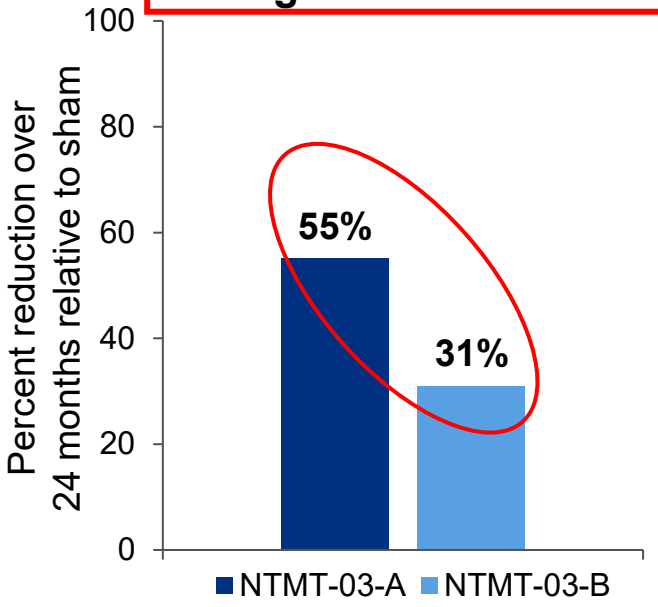
Primary endpoint: Rate of change in EZ area loss from baseline through Month 24

Secondary endpoints: Changes in retinal sensitivity and reading speed at Month 24

BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; EZ, ellipsoid zone; MacTel, macular telangiectasia type 2; mITT, modified intent-to-treat.
[a]The mITT population includes all randomized participants who underwent surgery (revakinagene taroretcel-lwey or sham); this was the primary population for efficacy evaluations.

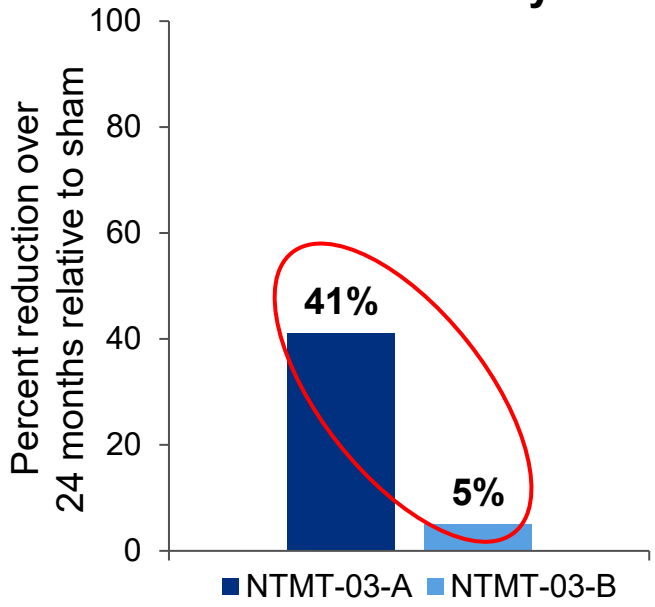
Key Efficacy Outcomes at 2 Years: Revakinagene Taroretcel-lwey Led to Reductions in Loss of EZ Area, Retinal Sensitivity, and Reading Speed When Compared With Sham

Primary Endpoint: Reduction in Rate of Change in EZ Area Loss[a]



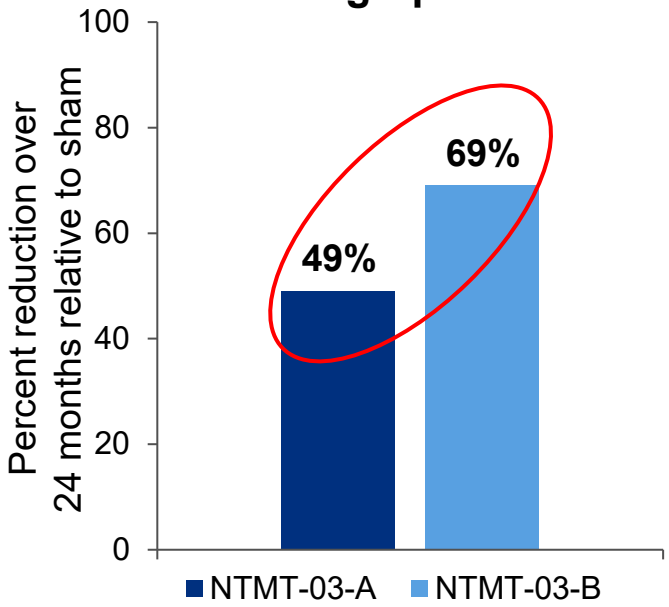
Revakinagene taroretcel-lwey reduced the rate of change in **EZ area loss** by **55%** in NTMT-03-A (*P*<0.001[b,c]) and **31%** in NTMT-03-B (*P*=0.0186[b,c]), relative to sham treatment

Secondary Endpoint: Reduction in Retinal Sensitivity Loss[a]



Revakinagene taroretcel-lwey reduced **retinal sensitivity** loss by **41%** in NTMT-03-A (*P*=0.020[b,d]) and **5%** in NTMT-03-B (*P*=0.835[b,d]), relative to sham treatment

Secondary Endpoint: Reduction in Reading Speed Loss[a]



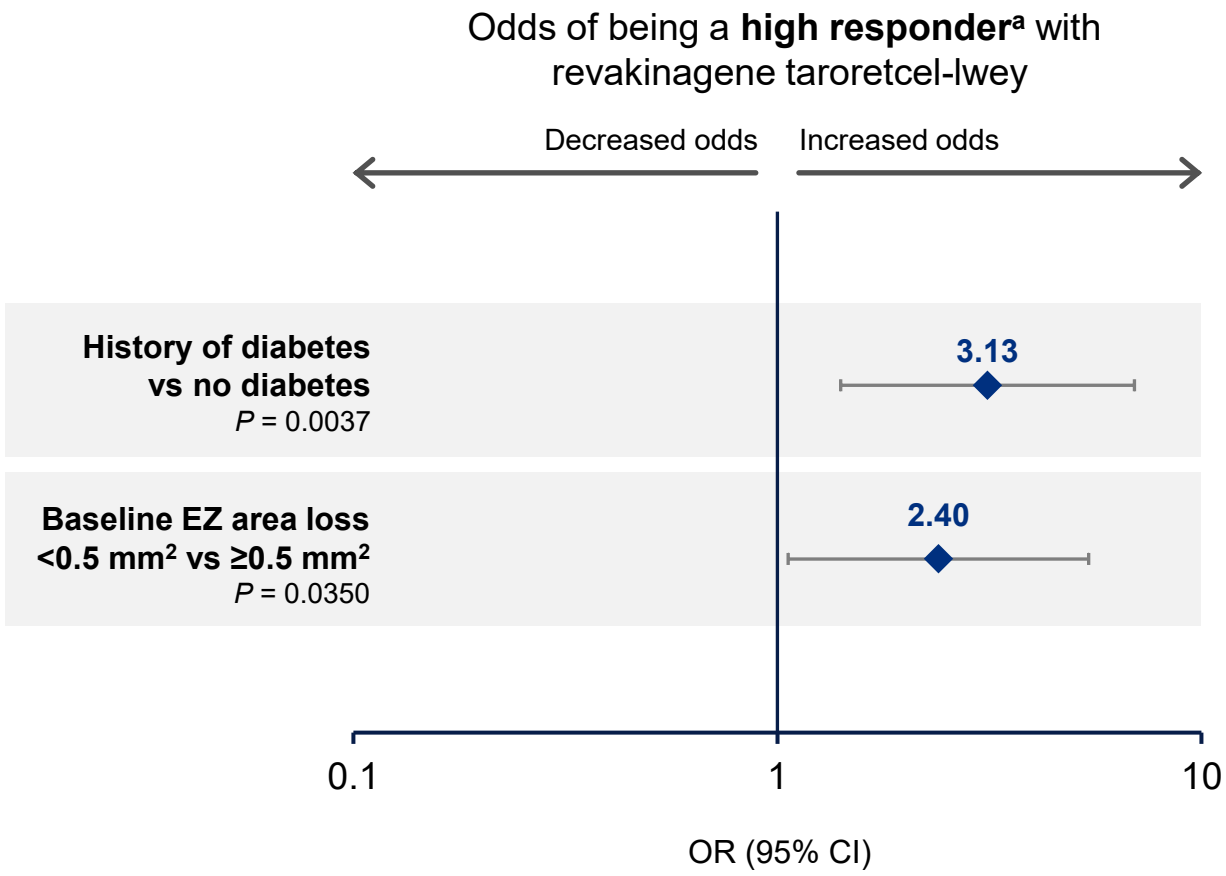
Revakinagene taroretcel-lwey reduced **reading speed** loss by **49%** in NTMT-03-A (*P*=0.385[b,d]) and **69%** in NTMT-03-B (*P*=0.033[b,d,e]), relative to sham treatment

EZ, ellipsoid zone; mITT, modified intent-to-treat.

[a]Analyzed in the mITT population. [b]*P* values based on difference in measures of revakinagene taroretcel-lwey versus sham through 24 months. [c]Based on a repeated-measures model that included baseline and Months 12, 16, 20, and 24, adjusting for study group, time (continuous), treatment × time interaction, and participant-specific random intercepts. The difference in rates of change in EZ area loss over 2 years between study groups was based on the treatment × time interaction term. [d]Two-sample *t* test comparing change from baseline to Month 24 in revakinagene taroretcel-lwey versus sham. [e]Nominal *P* value.

Both Baseline EZ Area Loss and Diabetes Were Associated With Higher Odds of Treatment Response

- Revakinagene taroretcel-lwey demonstrated **consistent efficacy versus sham** across the MacTel population
- Baseline EZ area loss and history of diabetes were variables found to be associated with high responder status
- In a subsequent multivariate analysis, ***smaller baseline EZ area loss*** and ***history of diabetes*** were both associated with greater odds of achieving high responder status[a]

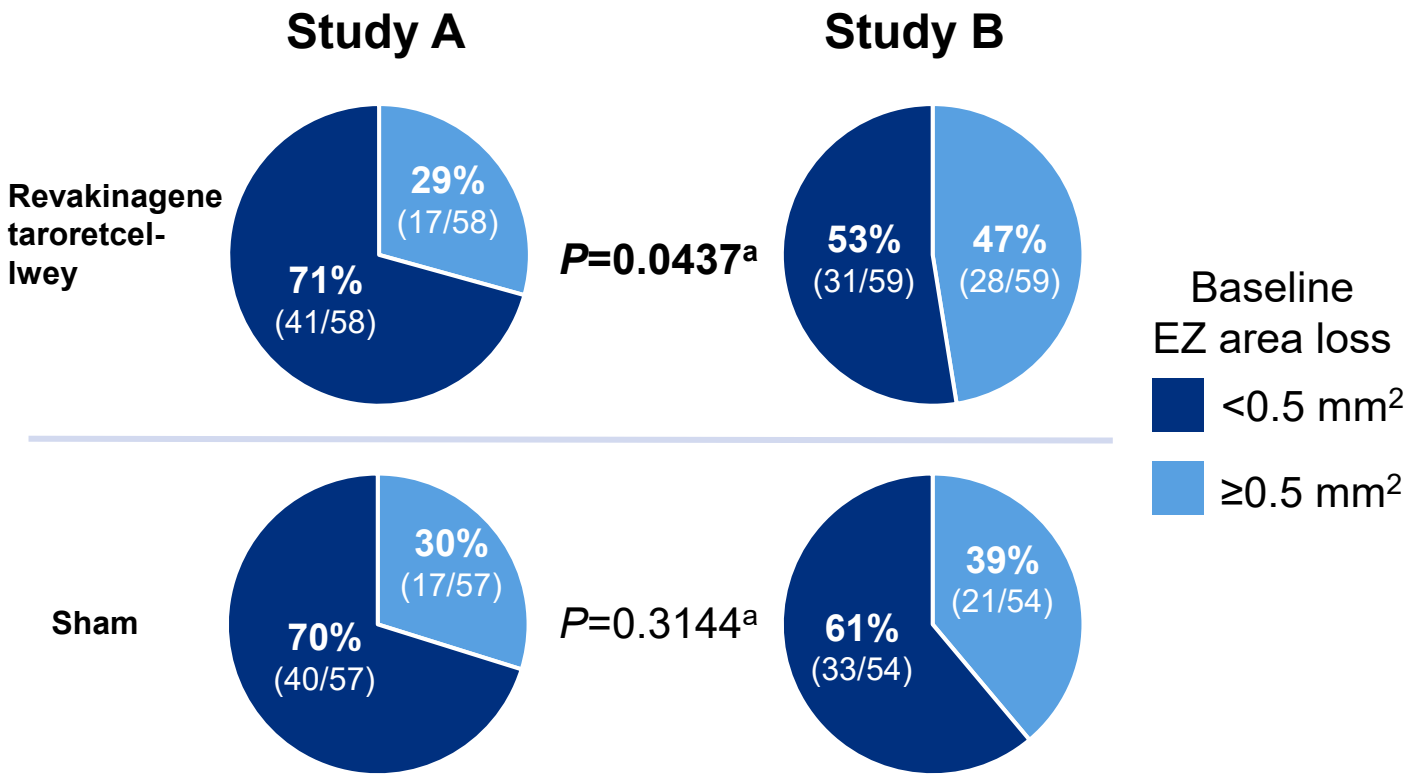


CI, confidence interval; EZ, ellipsoid zone; MacTel, macular telangiectasia type 2; mITT, modified intent-to-treat; OR, odds ratio.
Results are pooled data from both Phase 3 clinical studies of patients in the mITT population treated with revakinagene taroretcel-lwey. [a]Defined as mean rate of change in EZ area <50% relative to mean rate of change in sham-treated group.

Distribution of Baseline Factors in the Phase 3 Trials: More Participants in Study A Had Smaller Baseline Lesions Versus Study B

- **A significant difference** was found in **the distribution of baseline lesion sizes** in the revakinagene taroretcel-lwey groups between studies
- **No significant difference** was found in the **distribution of participants with diabetes** in revakinagene taroretcel-lwey or sham surgery groups between studies

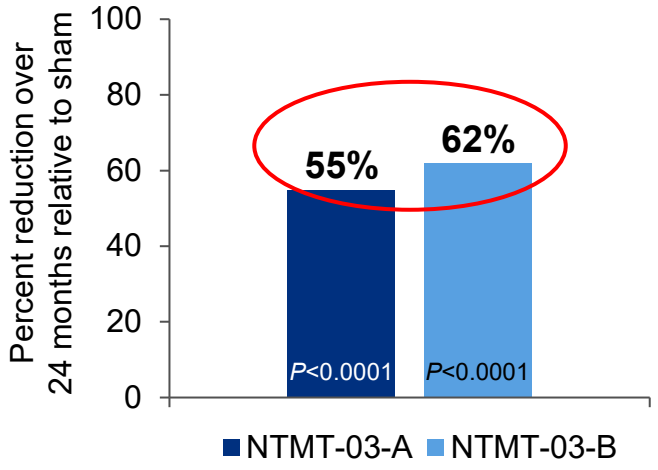
Baseline Lesion Size Between the Phase 3 Clinical Studies



EZ, ellipsoid zone.
[a]Nominal chi-square *P* value; bolded value is statistically significant.

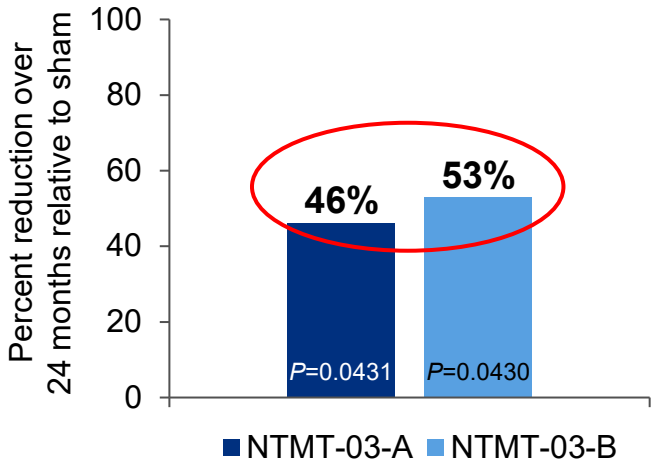
Subgroup of Participants With Smaller Baseline Lesions (<0.5 mm²)[a] in Trials A and B: Efficacy Outcomes

Reduction in Rate of Change in EZ Area Loss[b]



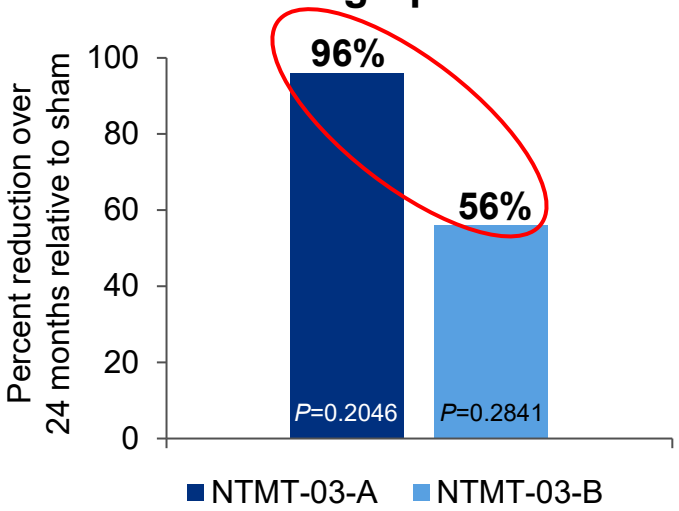
Rate of change in EZ area loss from baseline over 24 months			
	Treatment	0.066 mm²	0.059 mm²
	Sham	0.146 mm²	0.155 mm²

Reduction in Retinal Sensitivity Loss[b]



Mean reduction in aggregate retinal sensitivity from baseline			
	Treatment	17.04 dB	16.73 dB
	Sham	31.59 dB	35.37 dB

Reduction in Reading Speed Loss[b]



Mean reduction in reading speed from baseline			
	Treatment	0.41 wpm	6.68 wpm
	Sham	10.30 wpm	15.24 wpm

Magnitude of reductions in EZ area loss and retinal sensitivity loss was more consistent between the studies with revakinagene taroretcel-lwey treatment

dB, decibel; EZ, ellipsoid zone; mITT, modified intent-to-treat; wpm, words per minute.
All *P* values are nominal. [a]For participants with baseline lesion size <0.5 mm² in NTMT-03-A, 51% (n=41) received revakinagene taroretcel-lwey and 49% (n=40) received sham; in NTMT-03-B: 48% (n=31) received revakinagene taroretcel-lwey and 53% (n=33) received sham. [b]Among participants with baseline lesion size <0.5 mm² in the mITT population.

Take-Home Points

- Revakinagene taroretcel-lwey **led to significant reductions in the rate of EZ area loss** in participants with MacTel, meeting the primary endpoint, and is now FDA approved and available for patients in clinical practice
- **In this post hoc analysis, smaller baseline EZ area loss and diabetes independently conferred greater odds of being a high responder** among participants that received revakinagene taroretcel-lwey
- The treatment response difference between Study A and Study B appears to be **related to baseline lesion size differences**
- Among participants with **smaller baseline lesions, consistent reductions** were found in **EZ area loss and retinal sensitivity**
- Participants throughout the Phase 3 cohort had a treatment benefit; participants treated **earlier in the disease process** had the greatest **anatomic and functional treatment benefit**, with increased likelihood of **reducing further disease progression**

EZ, ellipsoid zone; FDA, US Food and Drug Administration; MacTel, macular telangiectasia type 2.

Thank You

- Lowy Medical Research Institute
- MacTel Project investigators and their research teams (in the Natural History Registry Study and the Phase 1, 2, and 3 clinical trials)
- Study participants in both Phase 3 trials
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- These data were presented in part at the Macula Society 2025 Annual Meeting; February 12–15, 2025; Charlotte Harbor, Florida
- *Writing and editorial assistance was provided by Juhi Buch, PharmD, Elizabeth McSpiritt, MD, MPH, and Christina Mulvihill, PharmD, of Peloton Advantage, LLC, an OPEN Health company, and was funded by Neurotech*

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