Financial Disclosures

- Dr. Bakri has consulted for AbbVie, Adverum, Allergan, Amgen, Annexon, Apellis, Aviceda, Cholgene, EyePoint, i-Lumen, Iveric Bio, Kala, Genentech, La Science, Neurotech, Novartis, Ocular Therapeutix, Opthea, Outlook Therapeutics, Regenxbio, Regeneron, Rejuvitas, Re-Vana, Roche, and VoxelCloud, and has received research funding from Lowy Medical Foundation and Regenxbio
- This study was funded by Neurotech Pharmaceuticals, Inc.
- This study includes research conducted on human subjects; institutional review board approval was obtained prior to study initiation

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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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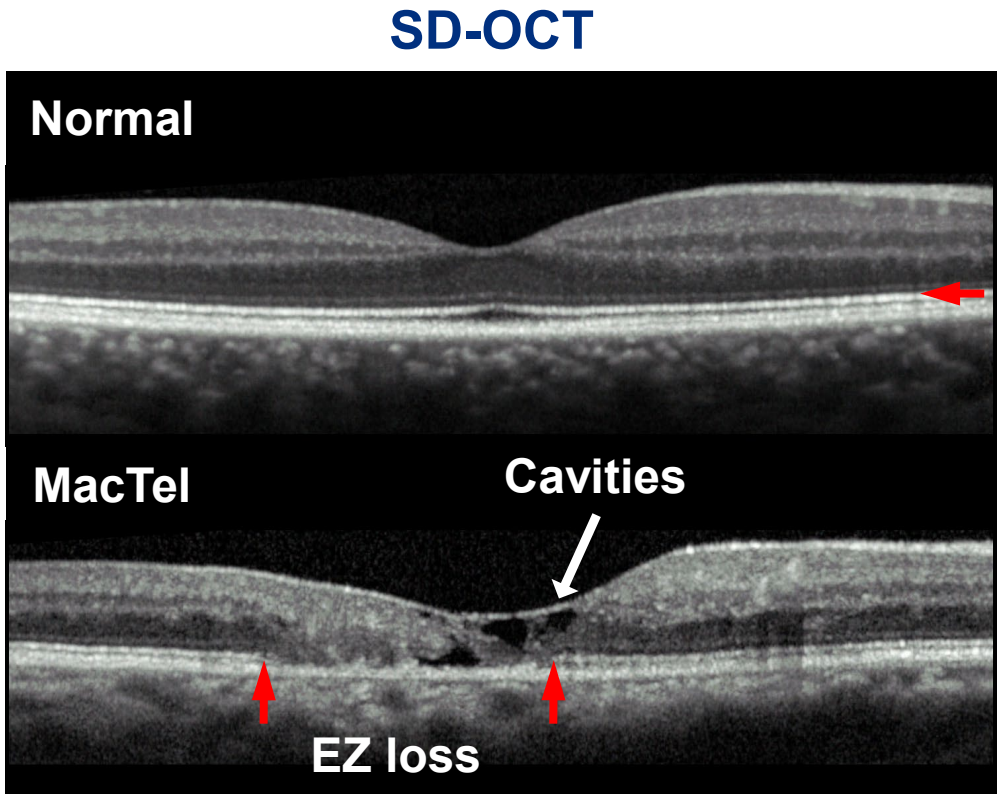
Macular Telangiectasia Type 2

- Bilateral, progressive, retinal neurodegenerative disease that leads to **central vision loss** and **functional impairment**[1,2]
  - **Progressive loss of the EZ**: ~0.08 mm^2/year[3]
  - Healthy macula: mean area of FAZ is 0.258 ± 0.0035 mm^2 for SVC[4]
- Associated with **abnormalities in Müller glia**, retinal pigment epithelia, and photoreceptors in the central retina corresponding with degenerative hyporeflective cavities[5]

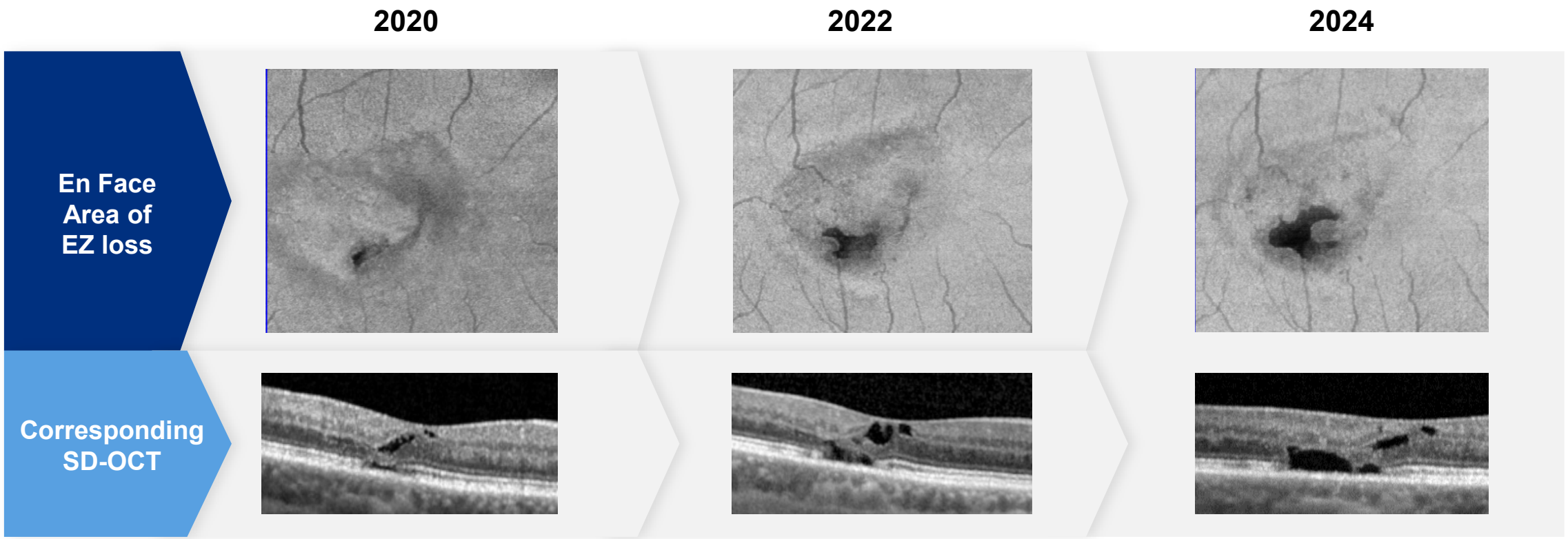


EZ, ellipsoid zone; FAZ, foveal avascular zone; MacTel, macular telangiectasia type 2; SD-OCT, spectral domain-optical coherence tomography; SVC, superficial vascular complex.

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.** Heeren TFC, et al. *Retina*. 2018;38(suppl 1):S20-S26. **4.** Morales D, et al. *Int Ophthalmol*. 2021;41:2187-2196. **5.** Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309.

Image provided by Dr. Thomas Aaberg.

In MacTel, BCVA Does Not Always Reflect Disease Burden[1]



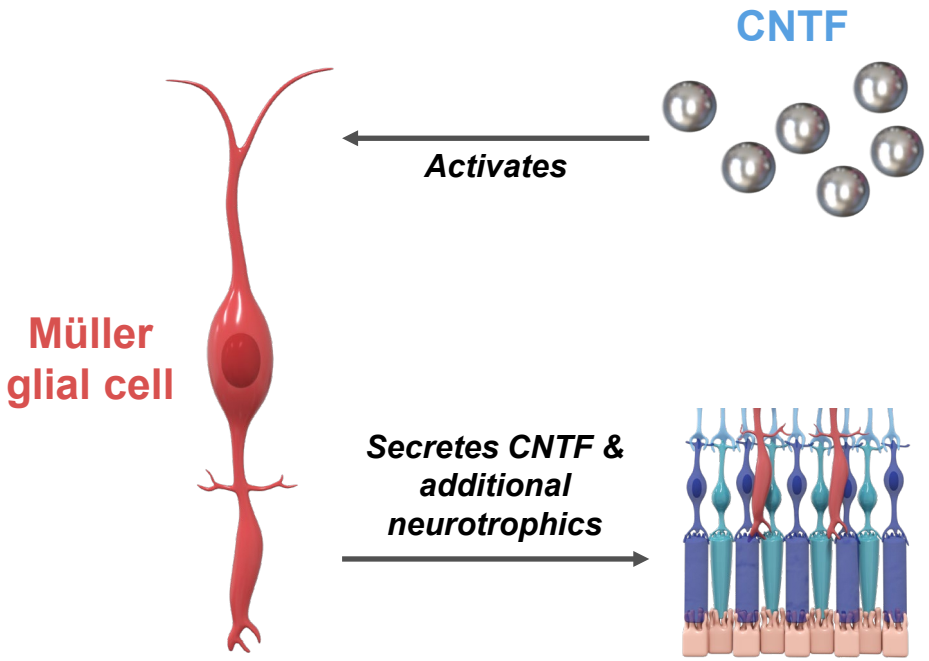
BCVA, best corrected visual acuity; EZ, ellipsoid zone; SD-OCT, spectral domain optical coherence tomography.

1. Pauleikhoff D, et al. *Acta Ophthalmol*. 2019;97:e998-e1005.

Images provided by Dr. Thomas Aaberg.

CNTF Protects and Preserves Photoreceptors

- Under pathological conditions, Müller glial cells can protect photoreceptors from cell death through the production of neurotrophic factors, including CNTF[1]
- Neuroprotective factors, including CNTF, provide structural and neuroprotective support by activating cell survival pathways[1-3]
- ECT enables continual release of CNTF to the retina over long periods of time, without triggering an immune response[4-6]



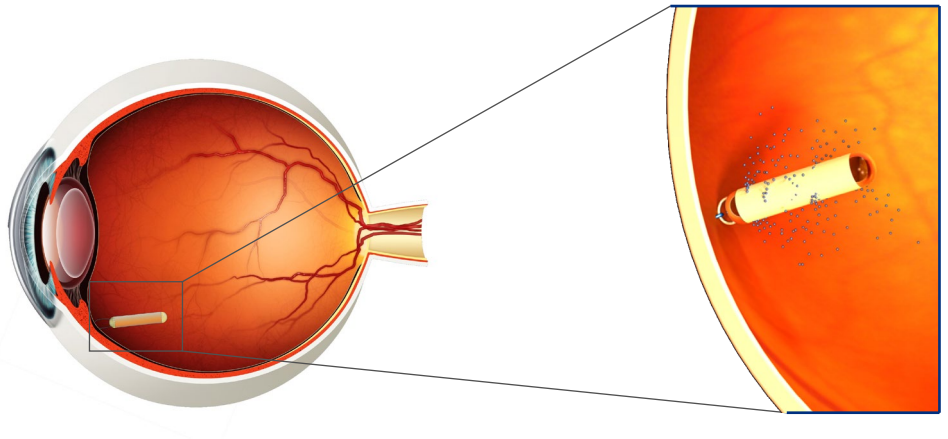
Cell survival pathway activation and macular photoreceptor protection

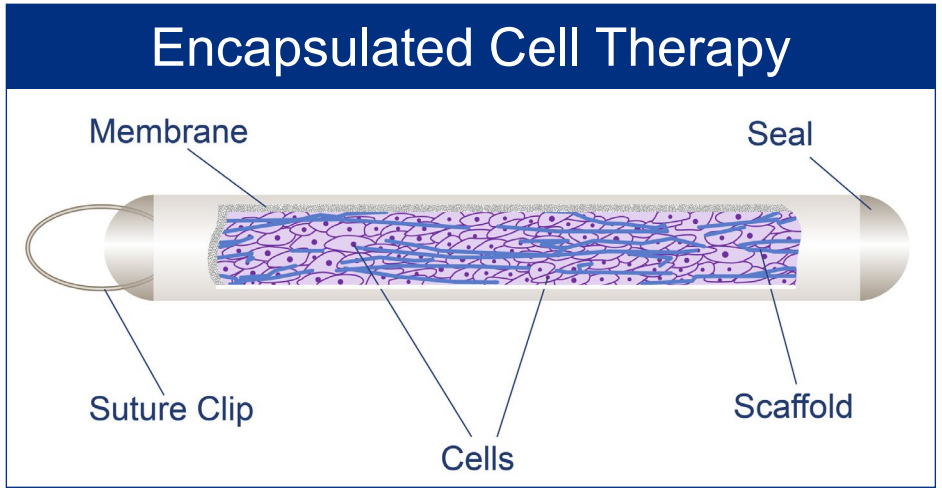
CNTF, ciliary neurotrophic factor; ECT, encapsulated cell therapy.

1. Bringmann A, et al. *Prog Retin Eye Res*. 2006;25:397-424. **2.** Rhee KD, et al. *Proc Natl Acad Sci U S A*. 2013;110:E4520-E4529. **3.** Cayouette M, et al. *J Neurosci*. 1998;18:9282-9293. **4.** Wen R, et al. *Prog Retin Eye Res*. 2012;31:136-151. **5.** Tao W. *Expert Opin Biol Ther*. 2006;6:717-726. **6.** Kauper K, et al. *Invest Ophthalmol Vis Sci*. 2023;64:3680.

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 NTC-201-6A allogenic RPE cells[1] that:
    - Have an expression vector for CNTF release[3,4]
    - Remain alive and productive for many years[5]
    - Obtain oxygen and nutrients from vitreous[5]
    - Are sequestered from the immune system[5]
  - Surgically inserted into the vitreous cavity[1] and attached to the sclera for stability[3]
  - Releases consistent levels of CNTF for long-term durations[1]
- **Revakinagene taroretcel-lwey was approved by the FDA for the treatment of adults with MacTel on March 5, 2025**





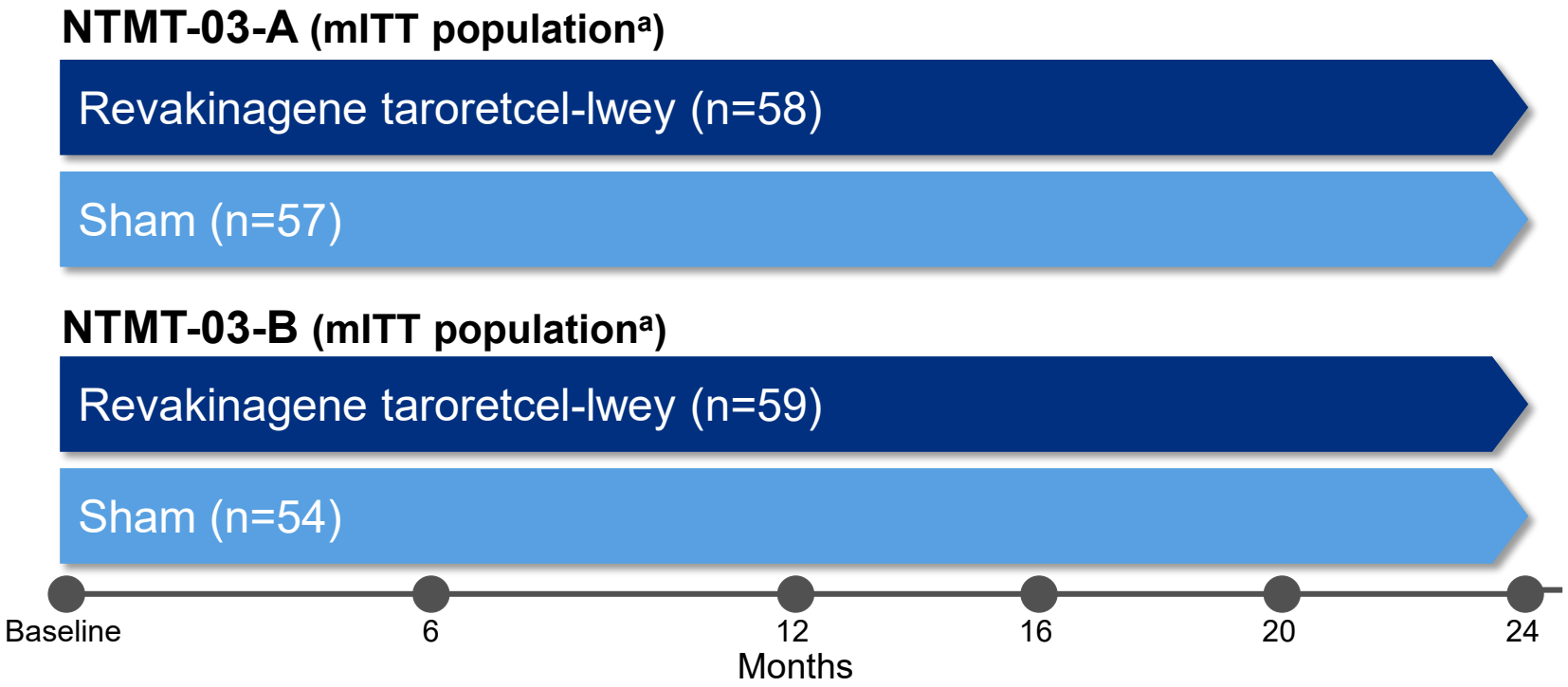
CNTF, ciliary neurotrophic factor; FDA, US Food and Drug Administration; MacTel, macular telangiectasia type 2; RPE, retinal pigment epithelium.

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.

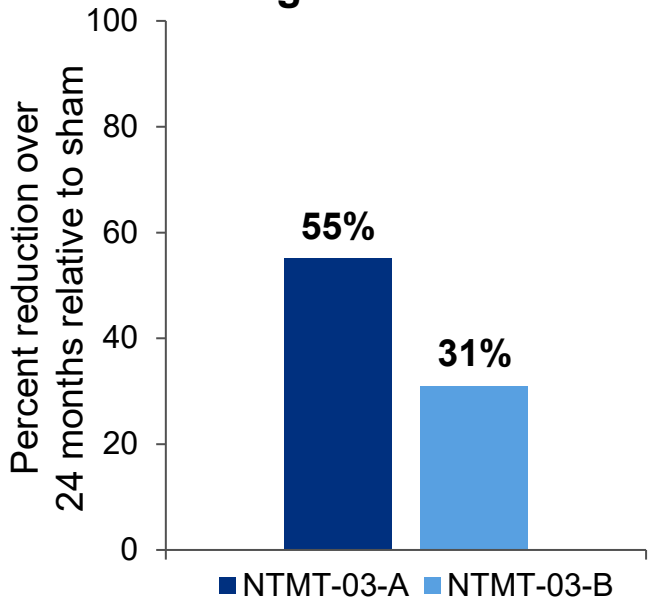
Baseline Characteristics Were Well Balanced Across Treatment Arms Within Each Study

Characteristic in mITT population	NTMT-03-A		NTMT-03-B		Pooled	
	Revakinagene taroretcel-lwey (n=58)	Sham (n=57)	Revakinagene taroretcel-lwey (n=59)	Sham (n=54)	Revakinagene taroretcel-lwey (n=117)	Sham (n=111)
Female, n (%)	39 (67)	40 (70)	46 (78)	36 (67)	85 (73)	76 (68)
Mean (SD) age, years	61.1 (8.0)	60.2 (8.4)	58.5 (7.6)	58.7 (8.9)	59.8 (7.9)	59.5 (8.6)
Age category, n (%)						
<65 years	37 (64)	37 (65)	42 (71)	36 (67)	79 (68)	73 (66)
≥65 years	21 (36)	20 (35)	17 (29)	18 (33)	38 (32)	38 (34)
Race, n (%)						
White	50 (86)	48 (84)	55 (93)	47 (87)	105 (90)	95 (86)
Asian	2 (3)	3 (5)	3 (5)	1 (2)	5 (4)	4 (4)
Black or African American	1 (2)	2 (4)	0	0	1 (1)	2 (2)
American Indian or Alaska Native	0	1 (2)	0	0	0	1 (1)
Other	5 (9)	3 (5)	1 (2)	6 (11)	6 (5)	9 (8)
EZ area loss, mm^2						
Mean (SD)	0.51 (0.48)	0.49 (0.36)	0.52 (0.31)	0.48 (0.29)	0.52 (0.40)	0.48 (0.33)
Median (minimum, maximum)	0.35 (0.15, 1.99)	0.36 (0.16, 1.70)	0.48 (0.16, 1.63)	0.40 (0.16, 1.38)	0.42 (0.15, 1.99)	0.37 (0.16, 1.70)
Mean (SD) BCVA, ETDRS letters	70.8 (9.1)	73.3 (8.6)	74.4 (7.8)	73.6 (9.2)	72.6 (8.6)	73.4 (8.9)
Snellen equivalent	20/40	20/40	20/32	20/32	20/40	20/40
Foveal involvement, n (%)						
No	17 (29)	15 (26)	15 (25)	22 (41)	32 (27)	37 (33)
Yes	40 (69)	42 (74)	44 (75)	32 (59)	84 (72)	74 (67)
Unknown	1 (2)	0	0	0	1 (1)	0
History of diabetes, n (%)						
Yes	27 (47)	19 (33)	22 (37)	16 (30)	49 (42)	35 (32)
No	31 (53)	38 (67)	37 (63)	38 (70)	68 (58)	76 (68)

BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; EZ, ellipsoid zone; mITT, modified intent-to-treat; SD, standard deviation.

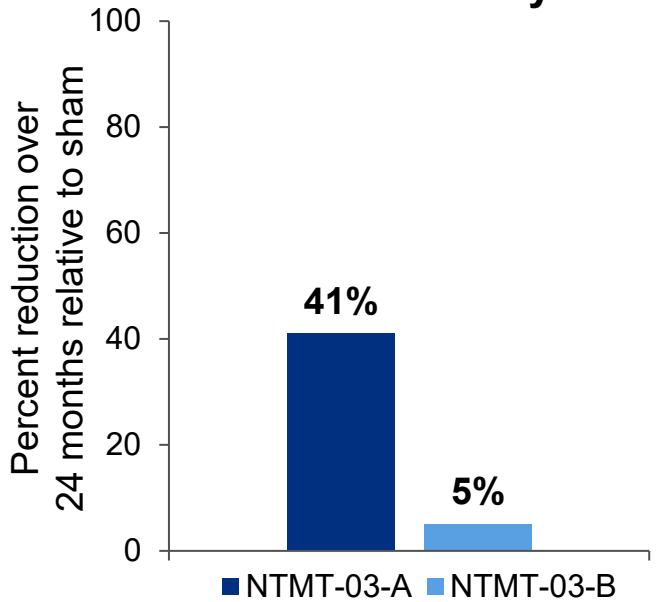
Key Efficacy Outcomes at 2 Years: Revakinagene Taroretcel-lwey Led to Reductions in Loss of EZ Area, Retinal Sensitivity, and Reading Speed When Compared With Sham

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



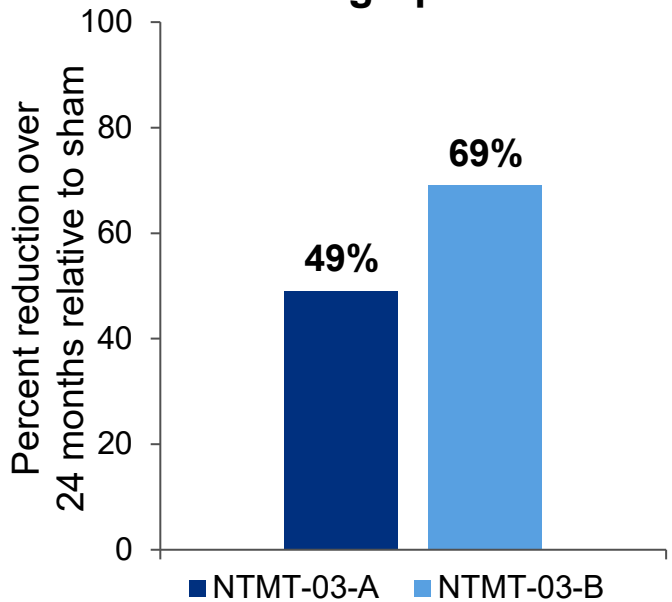
Revakinagene taroretcel-lwey reduced the rate of change in **EZ area loss** by **55%** in NTMT-03-A (*P*<0.001[b,c]) and **31%** in NTMT-03-B (*P*=0.0186[b,c]), relative to sham treatment

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.

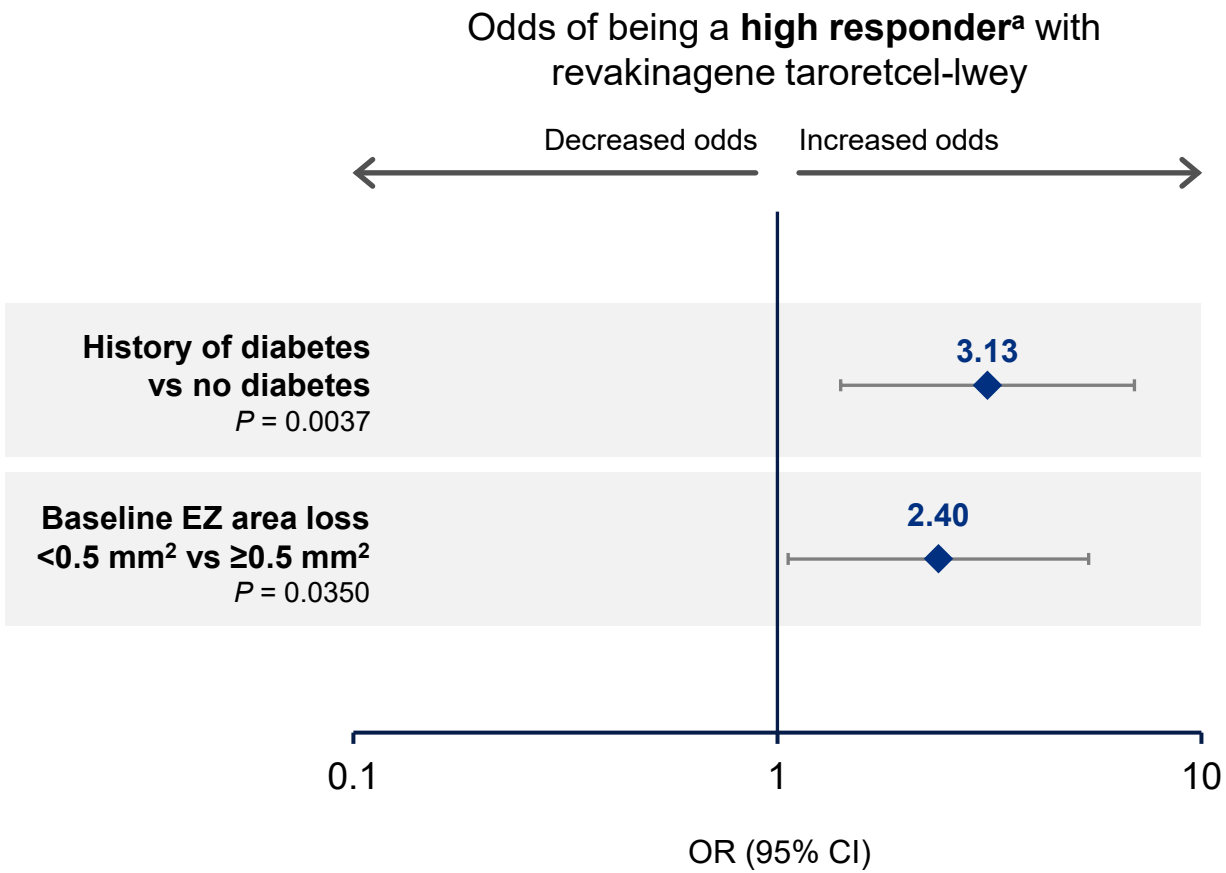
Post Hoc Analysis to Explore Differences in Trials A and B

- The impact of baseline characteristics on treatment responses was evaluated to better understand these observed differences in the efficacy outcomes
- Treatment response was examined as *responder status*
  - Participants were considered high responders if they had a ≥50% reduction in disease progression (based on EZ area loss) compared with the sham treatment
- Nine baseline variables were assessed using a **univariate approach**; the following two were found to be associated with response:
  - **EZ area loss** (<0.5 mm^2 or ≥0.5 mm^2 based on the mean baseline loss in both studies [0.5 mm^2])
  - History of diabetes (yes or no based on medical history)

EZ, ellipsoid zone.

Both Smaller 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
- In a multivariate analysis, **smaller baseline EZ area loss** and a **history of diabetes** were both associated with greater odds of achieving high responder status[a]

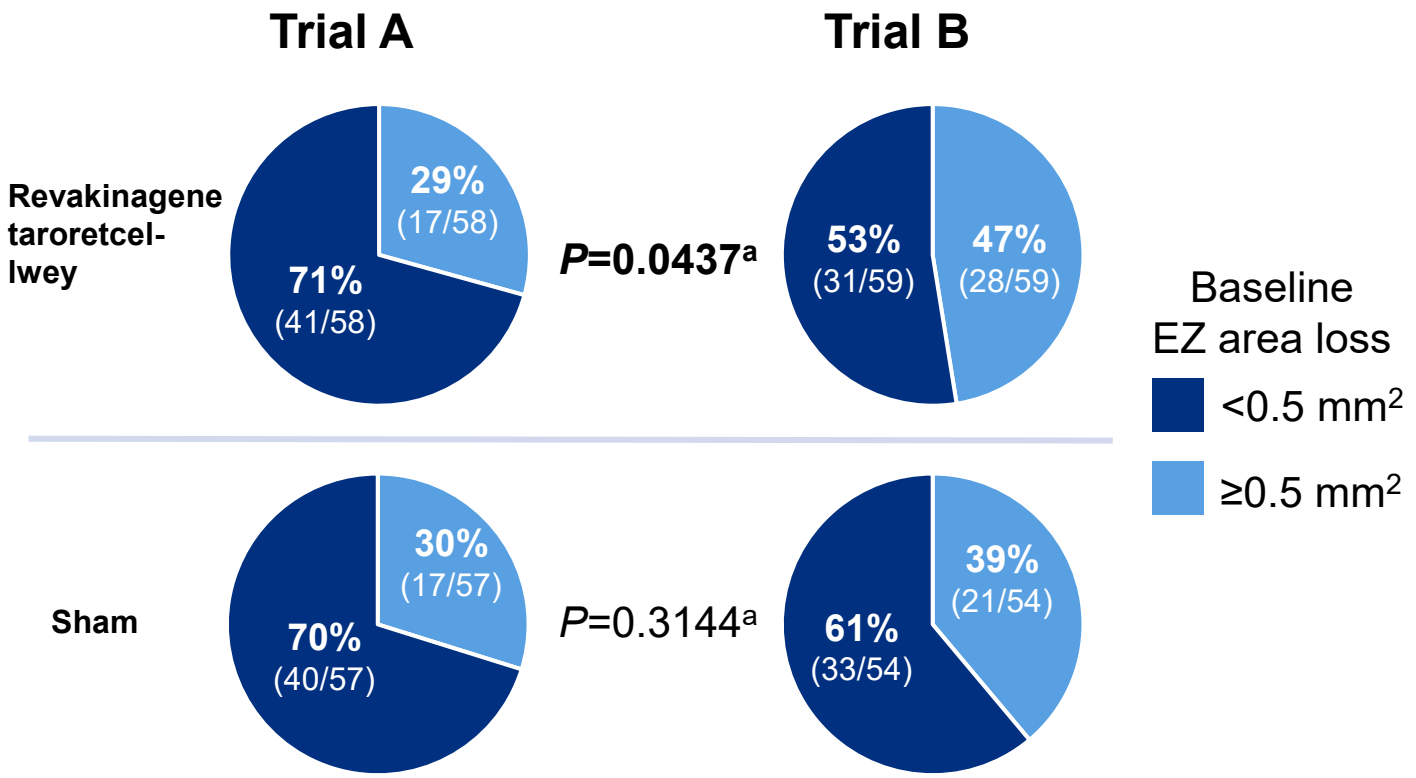


CI, confidence interval; EZ, ellipsoid zone; mITT, modified intent-to-treat; OR, odds ratio.
Results are pooled data from both Phase 3 clinical studies of patients in the mITT population treated with revakinagene taroretcel-lwey. [a]Defined as mean rate of change in EZ area <50% relative to mean rate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

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

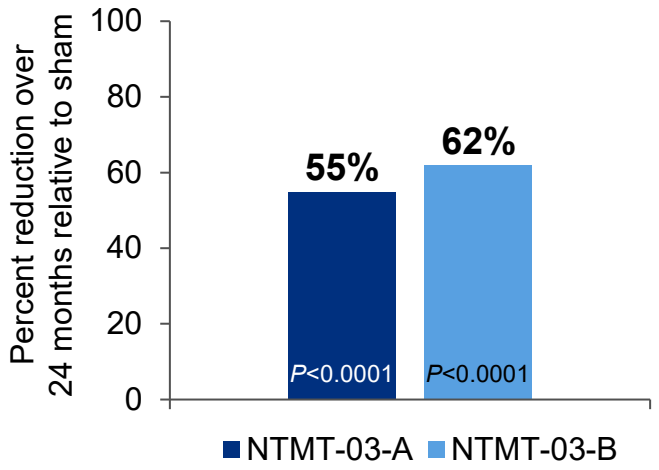
Baseline Lesion Size Between the Phase 3 Clinical Studies



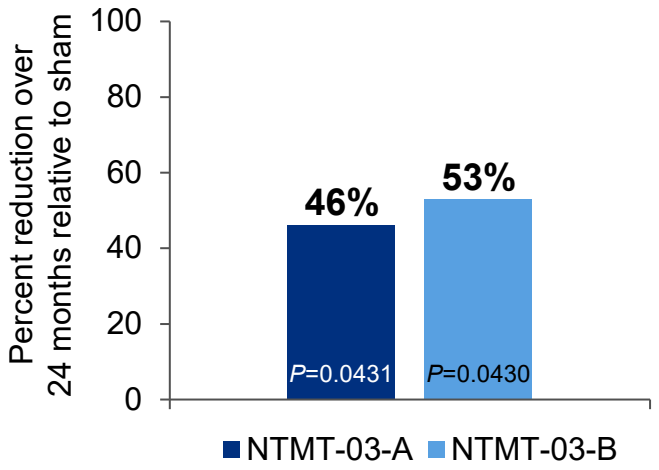
EZ, ellipsoid zone.
[a]Nominal chi-square *P* value; bolded value is statistically significant.

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

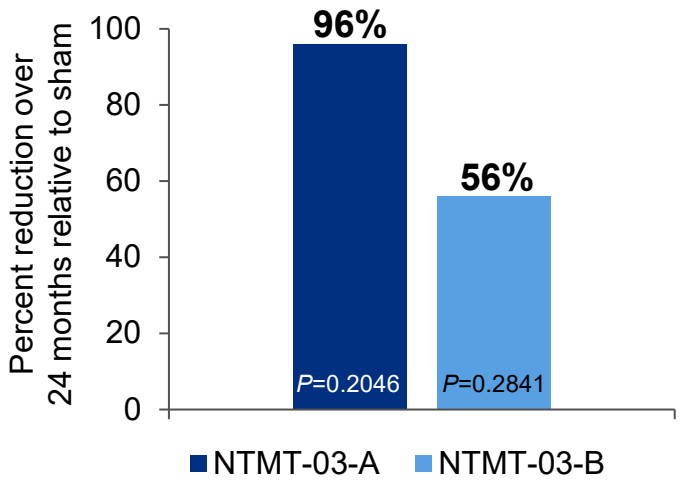
Reduction in Rate of Change in EZ Area Loss[b]



Reduction in Retinal Sensitivity Loss[b]



Reduction in Reading Speed 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

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

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 Trial A and Trial 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
- These studies were funded by Neurotech Pharmaceuticals, Inc
- These data were presented in part at the Macula Society 2025 Annual Meeting; February 12–15, 2025; Charlotte Harbor, Florida
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MacTel, macular telangiectasia type 2.