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- This study was funded by Neurotech Pharmaceuticals
- This study includes research conducted on human subjects; institutional review board approval was obtained prior to study initiation

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Pooled Functionality Data of Revakinagene Taroretcel-lwey in Patients With Macular Telangiectasia Type 2

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*At the time of study analysis.

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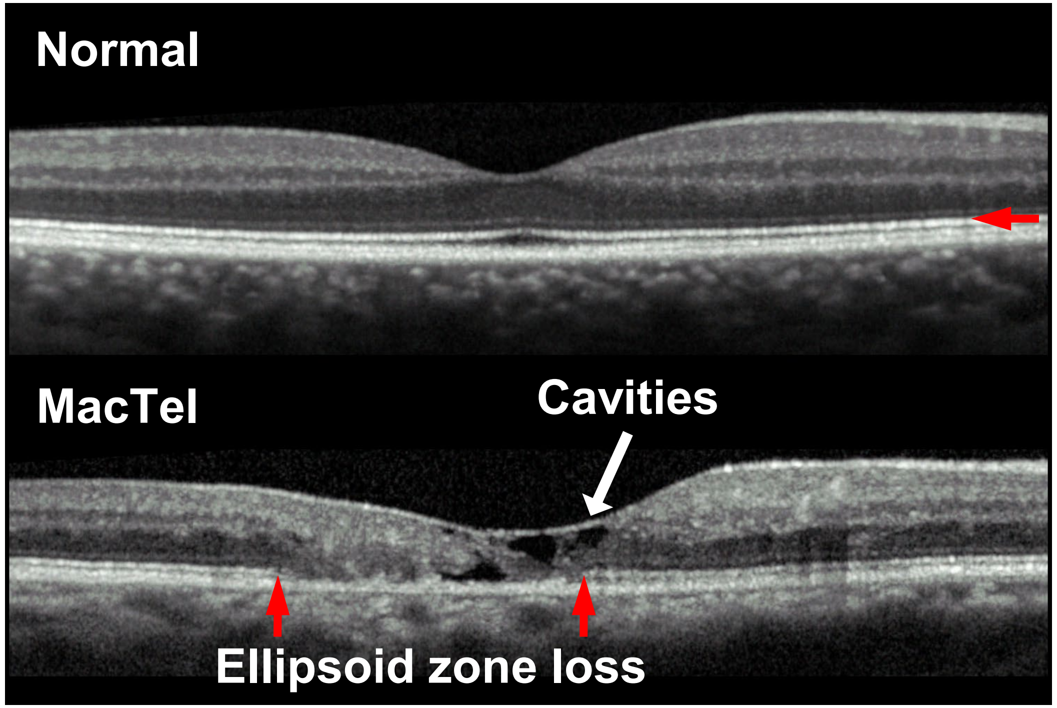
MacTel Is a Neurodegenerative Disease That Leads to Vision Loss[1,2]

- MacTel is a bilateral, progressive retinal neurodegenerative disease[1,2]
  - Leads to vision loss and functional impairment[1,2]
  - Associated with abnormalities in Müller glia, retinal pigment epithelium, and photoreceptors in the central retina[3,4]
  - Characterized by progressive loss of the ellipsoid zone on SD-OCT[3]

SD-OCT



MacTel, macular telangiectasia type 2; SD-OCT, spectral-domain optical coherence tomography.

1. Charbel Issa P, et al. *Prog Retin Eye Res*. 2013;34:49-77. **2.** Heeren TFC, et al. *Ophthalmology*. 2020;127:1539-1548. **3.** Heeren TFC, et al. *Retina*. 2018;38(suppl 1):S20-S26. **4.** Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309.

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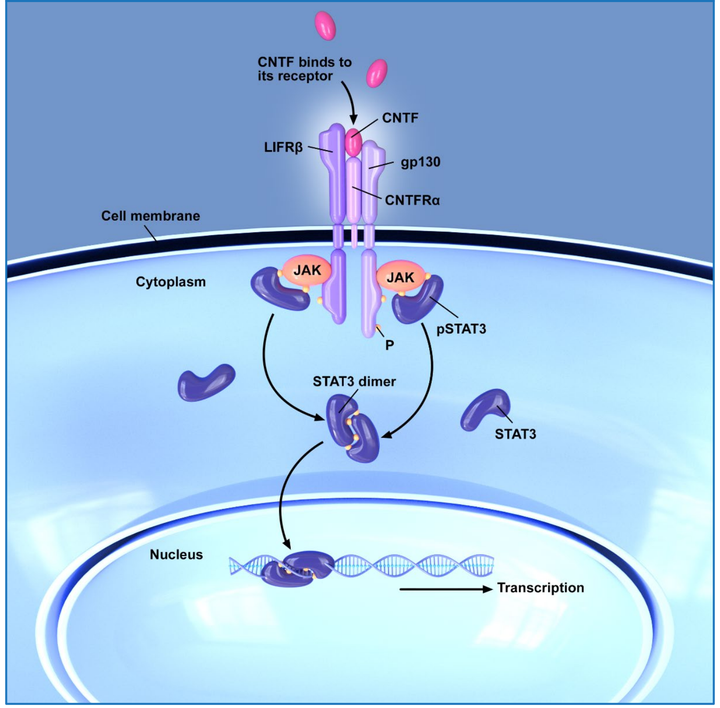
Ciliary Neurotrophic Factor Is a Potent Neuroprotectant[1-3]

- In response to injury, Müller glial cells release the neuroprotective factor CNTF[1]
- **CNTF protects and preserves photoreceptors[2-4]**
- In preclinical models of retinal degeneration, photoreceptors can be rescued with intravitreal injection of CNTF[2,4]

CNTF works through the JAK/STAT3 pro-survival pathway



CNTF, ciliary neurotrophic factor; CNTFRα, ciliary neurotrophic factor receptor α; gp130, glycoprotein 130; JAK/STAT, Janus kinase/signal transducer and activator of transcription; LIFRβ, leukemia inhibitory factor β; P, phosphorous; pSTAT3, phosphorylated signal transducer and activator of transcription 3; STAT3, signal transducer and activator of transcription 3.

1. Bringmann A, et al. *Prog Retin Eye Res*. 2009;28:423-445. **2.** Shen W, et al. *J Neurosci*. 2012;32(45):15715-15727. **3.** Sleeman MW, et al. *Pharm Acta Helv*. 2000;74:265-272. **4.** Tao W, et al. *Invest Ophthalmol Vis Sci*. 2002;43:3292-3298.

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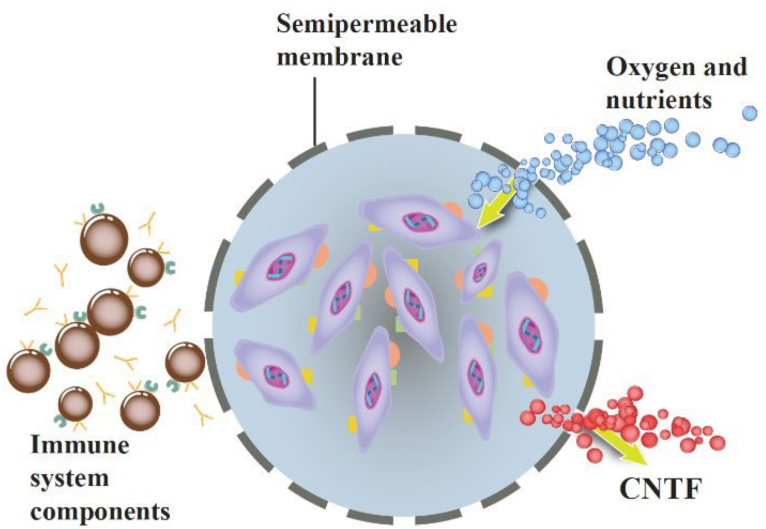
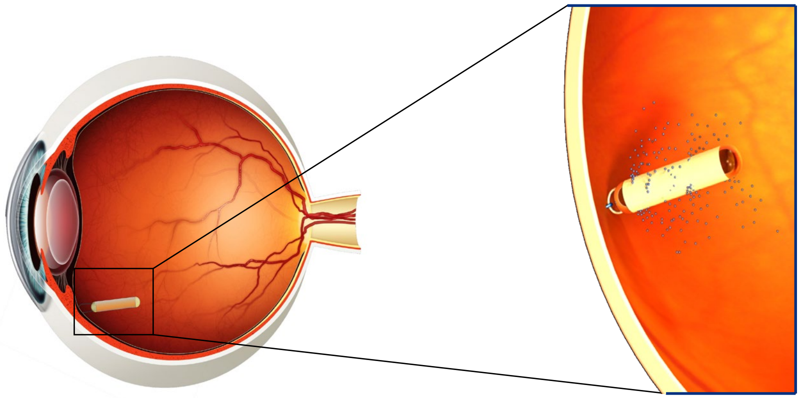
Encapsulated Cell Therapy Is Designed to Deliver Sustained Levels of CNTF

- Revakinagene taroretcel-lwey (formerly known as NT-501) is a first-in-class encapsulated cell therapy[1-3]
  - Contains NTC-201-6A cells[3]
    - Allogeneic retinal pigment epithelial cells expressing recombinant human CNTF[1]
  - Surgically inserted into the vitreous cavity and stably anchored to the sclera[1,3]
  - Developed to release consistent levels of CNTF for long-term durations[3]
- **Revakinagene taroretcel-lwey was approved by the FDA for the treatment of adults with MacTel on March 5, 2025**





CNTF, ciliary neurotrophic factor; FDA, Food and Drug Administration; MacTel, macular telangiectasia type 2.

1. ENCELTO [package insert]. Cumberland, RI: Neurotech Pharmaceuticals, Inc; March 2025. **2.** Chew EY, et al. *NEJM Evid*. 2025;4:EVIDoa2400481. **3.** Kauper K, et al. *Invest Ophthalmol Vis Sci*. 2025;66:3.

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Revakinagene Taroretcel-lwey Has Been Studied Across 3 Randomized, Sham-Controlled Clinical Trials

	NTMT-02[a]	NTMT-03A[b]	NTMT-03B[c]
	67 participants 99 eyes[d] All-treated population	115 participants 115 eyes All-treated population	113 participants 113 eyes All-treated population
Key inclusion criteria	Aged >21 to <80 years; diagnosis of MacTel		
	• **EZ break between 0.16 mm^2 and 4.00 mm^2** • **BCVA of ≥64** ETDRS letters	• **EZ break between 0.16 mm^2 and 2.00 mm^2** • **BCVA of ≥54** ETDRS letters	
Randomization	Treatment: 6 participants[d] Sham: 19 participants Treatment + sham: 32 participants	Treatment: 58 participants Sham: 57 participants	Treatment: 59 participants Sham: 54 participants
Primary endpoint	**Change from baseline** in EZ area loss at Month 24	**Rate of change from baseline** in EZ area loss through Month 24	
Secondary endpoints	Reading speed, aggregate retinal sensitivity (microperimetry), BCVA (safety)		

Each study lasted 24 months

BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; EZ, ellipsoid zone; MacTel, macular telangiectasia type 2.
[a]NCT01949324. [b]NCT03316300. [c]NCT03319849. [d]Participants with one eligible eye (35 participants) received revakinagene taroretcel-lwey (16 eyes) or sham (19 eyes). In participants with two eligible eyes (32 participants), one eye received revakinagene taroretcel-lwey (32 eyes) and one eye received sham procedure (32 eyes). If both eyes were eligible, the right eye was randomized 1:1 to sham or revakinagene taroretcel-lwey and the left eye received other surgery.

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Rationale for a Pooled Functionality Analysis

- Rare disease
- Inherent variability of outcome measures[1-3]
- Similar populations and study designs
- Increase the sample size

1. Alibhai AY, et al. *Int J Retina Vitreous*. 2020;6:16. 2. Patel PJ, et al. *Invest Ophthalmol Vis Sci*. 2011;52:3854-3859. 3. Zhao Y, et al. Poster presented at: Association for Research in Vision and Ophthalmology; May 5-9, 2024. Seattle, WA.

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Changes From Baseline in EZ Area Loss, Reading Speed, Retinal Sensitivity, and BCVA Were Assessed

Assessments

- Change from baseline assessments in the all-treated population in the Phase 2 and Phase 3 studies:
  - Anatomical:
    - Area of photoreceptor (ie, EZ area) loss (primary endpoint)
  - Functional:
    - Monocular reading speed
    - Aggregate retinal sensitivity (microperimetry)
  - Safety:
    - BCVA

BCVA, best corrected visual acuity; EZ, ellipsoid zone.

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Baseline Demographics Were Well Balanced Across Studies and Treatment Arms

By Participant[a]	Phase 2			Phase 3 (Study A)		Phase 3 (Study B)	
	Revakinagene Taroretcel-Iwey (n=16)	Sham (n=19)	Revakinagene Taroretcel-Iwey + Sham (n=32)	Revakinagene Taroretcel-Iwey (n=58)	Sham (n=57)	Revakinagene Taroretcel-Iwey (n=59)	Sham (n=54)
Female, n (%)	9 (56)	11 (58)	21 (66)	39 (67)	40 (70)	46 (78)	36 (67)
Mean age, years (SD)	60.1 (10.7)	59.4 (7.6)	63.4 (8.4)	61.1 (8.0)	60.2 (8.4)	58.5 (7.6)	58.7 (8.9)
Race, n (%)							
White	12 (75)	16 (84)	30 (94)	50 (86)	48 (84)	55 (93)	47 (87)
Asian	0	1 (5)	0	2 (3)	3 (5)	3 (5)	1 (2)
Black or African American	0	0	1 (3)	1 (2)	2 (4)	0	0
American Indian or Alaska Native	0	0	0	0	1 (2)	0	0
Other	4 (25)	2 (11)	1 (3)	5 (9)	3 (5)	1 (2)	6 (11)
Ethnicity, n (%)							
Hispanic or Latino	1 (6)	0	1 (3)	1 (2)	5 (9)	4 (7)	4 (7)

SD, standard deviation.
[a]Results reported for the all-treated population.

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Participants in the Phase 2 Trial had Greater Baseline EZ Area Loss Compared With the Phase 3 Studies

By Eye[a]	Phase 2		Phase 3 (Study A)		Phase 3 (Study B)	
	Revakinagene Taroretcel-lwey (n=48)	Sham (n=51)	Revakinagene Taroretcel-lwey (n=58)	Sham (n=57)	Revakinagene Taroretcel-lwey (n=59)	Sham (n=54)
EZ area loss (mm^2), mean (SD)	0.70 (0.42)	0.77 (0.55)	0.51 (0.48)	0.49 (0.36)	0.52 (0.31)	0.48 (0.29)
EZ area category, n (%)						
<0.5 mm^2	18 (37.5)	20 (39.2)	41 (70.7)	40 (70.2)	31 (52.5)	33 (61.1)
≥0.5 mm^2	30 (62.5)	31 (60.8)	17 (29.3)	17 (29.8)	28 (47.5)	21 (38.9)
Mean BCVA, ETDRS letter (SD)	77.0 (5.6)	76.2 (6.9)	70.8 (9.11)	73.3 (8.64)	74.4 (7.76)	73.6 (9.23)
Snellen equivalent	20/32	20/32	20/40	20/40	20/32	20/32
Reading speed (wpm), n	47	49	57	56	59	53
Mean (SD)	94.29 (46.13)	107.26 (43.17)	92.09 (43.72)	96.01 (54.01)	96.49 (47.31)	94.09 (42.81)
Retinal sensitivity[b], n	40	45	53	54	52	49
Mean (SD)	89.15 (76.15)	107.96 (106.77)	62.14 (77.58)	59.02 (62.63)	57.92 (56.94)	50.48 (58.36)

Patients with MacTel already experience substantial impairment in reading speed

BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; EZ, ellipsoid zone; SD, standard deviation; wpm, words per minute.
[a]Results reported for the all-treated population, unless otherwise noted. Not available in full pool. [b]Results reported for the per-protocol population.

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Baseline Characteristics in the Pooled Population Were Balanced Between Treatment Arms

	Phase 2 and Phase 3 Pool[b]	
	Revakinagene Taroretcel-lwey (n=165)	Sham (n=162)
Demographics, by participant[a]		
Female, n (%)	115 (69.7)	108 (66.7)
Mean age, years (SD)	60.5 (8.4)	60.3 (8.6)
Race, n (%)		
White	147 (89)	141 (87)
Asian	5 (3)	5 (3)
Black or African American	2 (1)	3 (2)
American Indian or Alaska Native	0	1 (1)
Other	11 (7)	12 (7)
Ethnicity, n (%)		
Hispanic or Latino	7 (4)	10 (6)
Ocular characteristics, by eye[a]		
EZ area loss (mm^2), n	165	162
Mean (SD)	0.57 (0.41)	0.57 (0.43)
EZ area category, n (%)		
<0.5 mm^2	90 (54.5)	93 (57.4)
≥ 0.5 mm^2	75 (45.5)	69 (42.6)
Mean BCVA, ETDRS letter (SD)	73.8 (8.2)	74.2 (8.5)
Snellen equivalent	20/40	20/32
Reading speed (wpm), n	163	158
Mean (SD)	94.32 (45.50)	98.86 (47.24)
Retinal sensitivity[c], n		
Mean (SD)	-	-

BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; EZ, ellipsoid zone; SD, standard deviation; wpm, words per minute.
[a]Results reported for the all-treated population, unless otherwise noted. Not available in full pool. [b]Per the NTMT-02 study design, participants with two eligible study eyes received revakinagene taroretcel-lwey in one eye and sham in the other eye. These 32 participants are included in both columns for the pooled summary. [c]Results reported for the per-protocol population.

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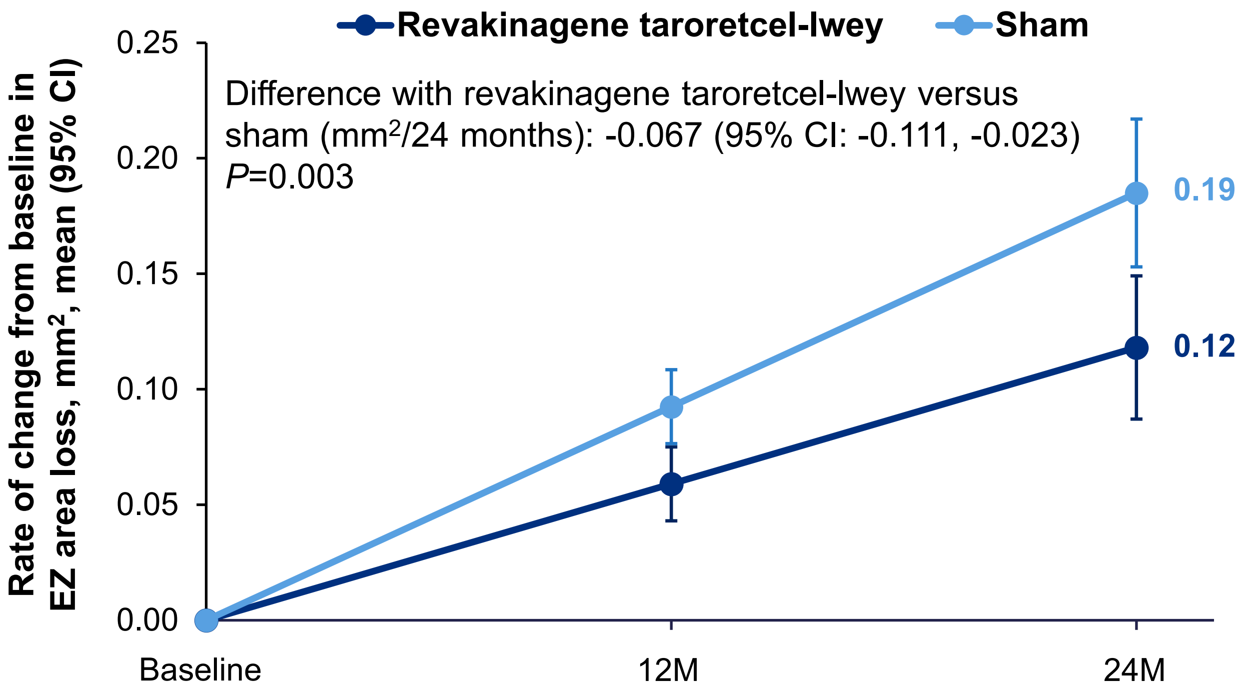
Revakinagene Taroretcel-lwey Demonstrated Greater Preservation of EZ Area Over 2 Years Compared With Sham in All-Treated Participants[a]

- A **7.7%** reduction in photoreceptor loss with revakinagene taroretcel-lwey compared with sham in **Phase 2**
- A **54.6%** reduction in photoreceptor loss with revakinagene taroretcel-lwey compared with sham in **Phase 3, Study A**
- A **30.4%** reduction in photoreceptor loss with revakinagene taroretcel-lwey compared with sham in **Phase 3, Study B**

Rate of Change in EZ Area Loss[b], mm^2



	Baseline	12M	24M
Revakinagene taroretcel-lwey , n	165	153	158
Sham, n	162	157	156

36.2% reduction in photoreceptor loss

CI, confidence interval; EZ, ellipsoid zone; M, month.

[a]Per the NTMT-02 study design, participants with two eligible study eyes received revakinagene taroretcel-lwey in one eye and sham in the other eye. These 32 participants are included in both groups for the pooled analysis, by study eye. [b]Rate of EZ change, difference, and CIs from a repeated measures model. The outcome variable is EZ area assessed longitudinally at baseline, Months 12, 16 (Phase 3 only), 18 (Phase 2 only), 20 (Phase 3 only), and 24. At baseline, EZ area is calculated as the mean area across two independent readers. The model includes treatment group, time (continuous), treatment × time interaction, and participant-specific random intercepts. The difference between treatment groups in rate of EZ change is estimated at Month 12 and Month 24 based on the treatment × time interaction term.

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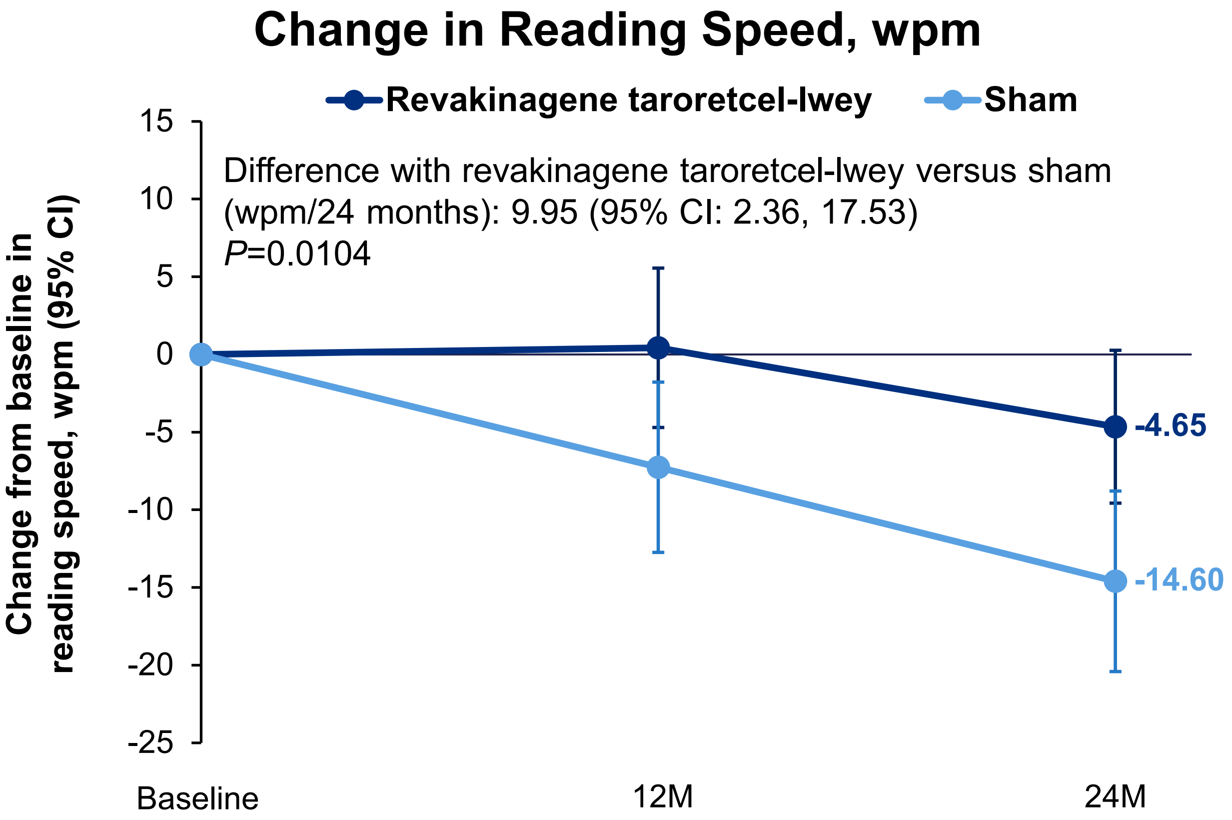
Revakinagene Taroretcel-lwey Preserved Reading Speed Over 2 Years Compared With Sham in All-Treated Participants[a]

- An **86.1%** reduction in reading speed loss with revakinagene taroretcel-lwey compared with sham in **Phase 2**
- A **49.3%** reduction in reading speed loss with revakinagene taroretcel-lwey compared with sham in **Phase 3, Study A**
- A **71.0%** reduction in reading speed loss with revakinagene taroretcel-lwey compared with sham in **Phase 3, Study B**



	Baseline	12M	24M
Revakinagene taroretcel-lwey, n	163	148	155
Sham, n	158	150	151

68.2% reduction in reading speed loss

CI, confidence interval; M, month; wpm, words per minute.
[a]Per the NTMT-02 study design, participants with two eligible study eyes received revakinagene taroretcel-lwey in one eye and sham in the other eye. These 32 participants are included in both groups for the pooled analysis, by study eye.

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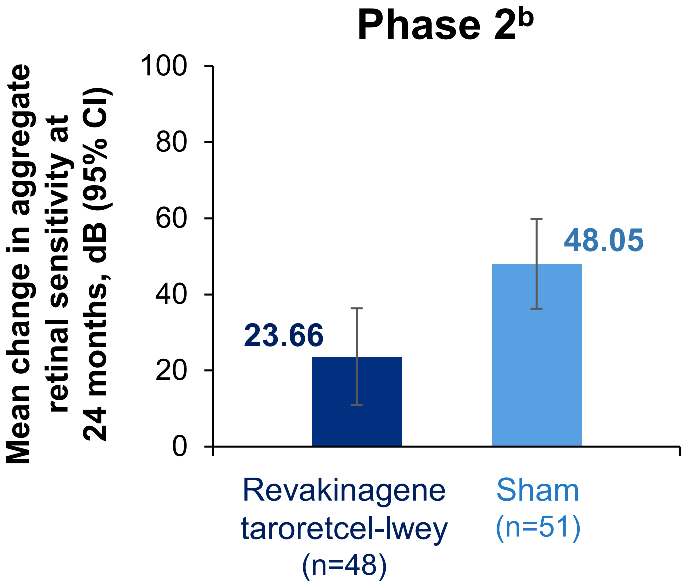
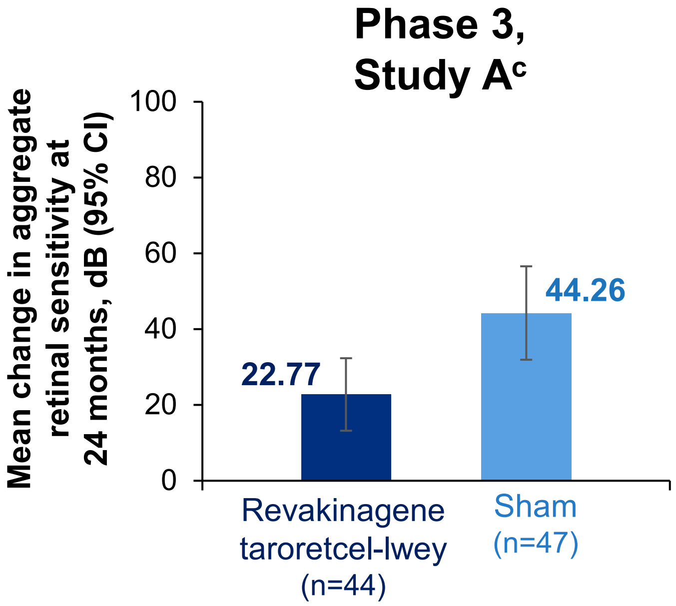
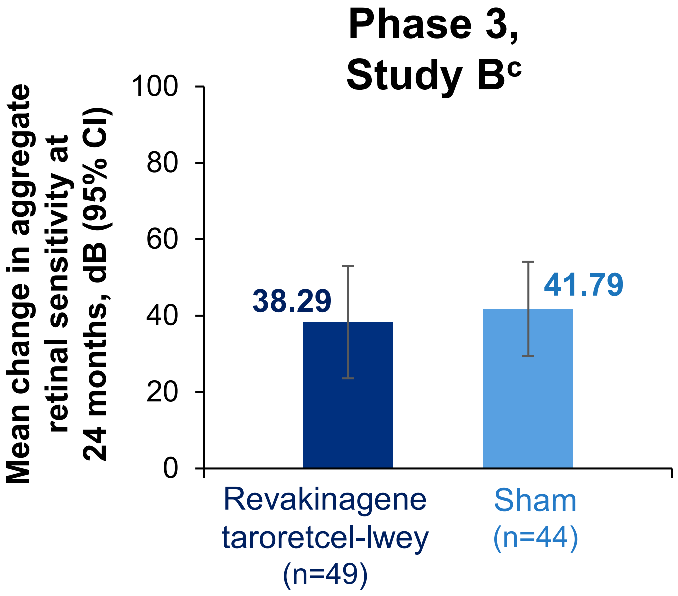
Revakinagene Taroretcel-lwey Preserved Aggregate Retinal Sensitivity (Microperimetry) Over 2 Years Compared With Sham[a]



A **50.7%** reduction in aggregate retinal sensitivity loss with revakinagene taroretcel-lwey compared with sham in NTMT-02



A **48.6%** reduction in aggregate retinal sensitivity loss with revakinagene taroretcel-lwey compared with sham in NTMT-03-A



An **8.4%** reduction in aggregate retinal sensitivity loss with revakinagene taroretcel-lwey compared with sham in NTMT-03-B

36.6% reduction in aggregate retinal sensitivity loss across the three studies[d]

CI, confidence interval; dB, decibel; MAIA, Macular Integrity Assessment.
[a]Retinal sensitivity was measured via MAIA microperimetry. [b]In the Phase 2 study, retinal sensitivity is reported for the per-protocol population, which included all treated participants who had no major protocol infractions (defined prior to unmasking of the study). Per the NTMT-02 study design, participants with two eligible study eyes received revakinagene taroretcel-lwey in one eye and sham in the other eye. These 32 participants are included in both groups for the pooled analysis by study eye. [c]In the Phase 3 studies, the retinal sensitivity per-protocol population is reported, including all treated participants who had a baseline and Month 24 microperimetry collected according to study protocol. [d]Results per study in the respective per-protocol populations were weighted by the proportion of treated eyes with non-missing data in each study and combined descriptively.

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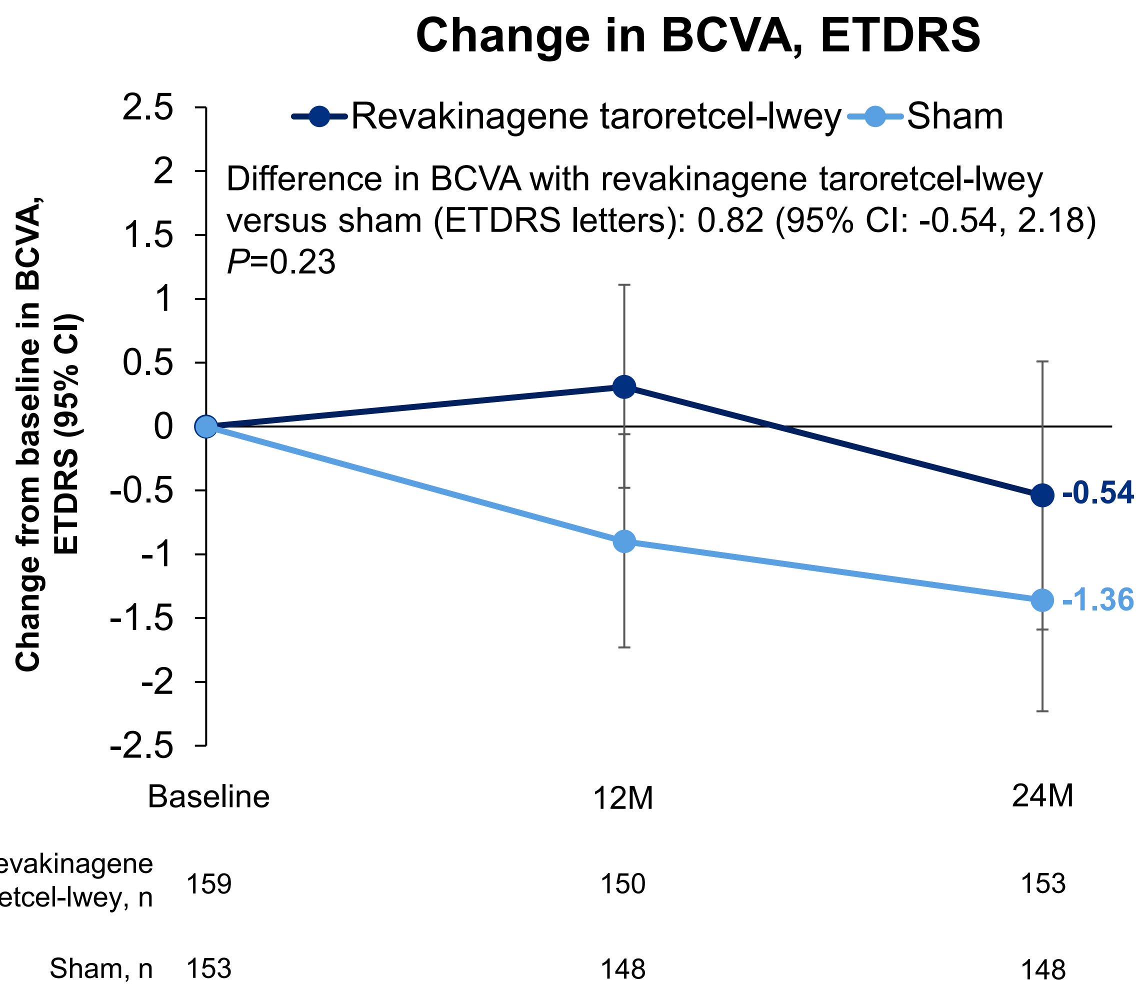
BCVA Remained Stable for Both Treatment Arms Over 2 Years[a]

Mean change in BCVA from baseline to Month 24 (95% CI), ETDRS		
Study	**Revakinagene Taroretcel-lwey**	**Sham**
Phase 2	-1.93 (-3.80, -0.05)	-2.00 (-3.35, -0.65)
Phase 3, Study A	0.19 (-1.81, 2.20)	-0.57 (-2.26, 1.11)
Phase 3, Study B	-0.29 (-1.87, 1.30)	-1.71 (-3.11, -0.30)



60.3% reduction in BCVA loss

BCVA, best corrected visual acuity; CI, confidence interval; ETDRS, Early Treatment Diabetic Retinopathy Study; M, month.

[a]Per the NTMT-02 study design, participants with two eligible study eyes received revakinagene taroretcel-lwey in one eye and sham in the other eye. These 32 participants are included in both groups by study eye.

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Conclusions

- Revakinagene taroretcel-lwey conferred both **anatomic and visual function benefits** across three randomized, sham-controlled studies
- Relative to sham, revakinagene taroretcel-lwey demonstrated a:
  - Preservation of anatomy
    - 36.2% reduction in photoreceptor loss
  - Preservation of function
    - 68.2% reduction in reading speed loss
    - 36.6% reduction in retinal sensitivity loss[a]

[a]Results per study in the respective per-protocol populations were weighted by the proportion of treated eyes with non-missing data in each study and combined descriptively.

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- Study participants with MacTel
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- These data were presented at American Academy of Ophthalmology Retina Subspecialty Day 2024; Chicago, IL; October 18–19, 2024
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