Hawaiian Eye and Retina 2025, Kauai, Hawaii, January 18–24, 2025

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

W. Lloyd Clark, MD,[1] Muna Bitar, PharmD,[2] Debora C. Manning, MPH,[3] Thomas Aaberg, Jr, MD,[2,4] and the MacTel Study Investigators

[1]Assistant Clinical Professor of Ophthalmology, University of South Carolina School of Medicine, Palmetto Retina Center, Retina Consultants of America, Columbia, SC; [2]Neurotech Pharmaceuticals, Inc., Cumberland, RI; [3]Veristat, Southborough, MA; [4]Foundation for Vision Research, Grand Rapids, MI

Financial Disclosures

- W. Lloyd Clark has the following disclosures:
  - Consultant (Amgen, Bayer, Cardinal Health, Genentech/Roche, Neurotech, Ocular Therapeutix, Regeneron); Grant Support (Bayer, Eyepoint, Genentech/Roche, Kodiak, Notal Vision, Ocular Therapeutix, Oculis, Outlook, Regeneron); Speakers Bureau (Genentech/Roche, Regeneron)
- These trials were funded by Neurotech Pharmaceuticals
- This study includes research conducted on human subjects. Institutional Review Board approval was obtained prior to study initiation

Take Home Points

- NT-501 conferred both **anatomic and visual function benefits** across three randomized, sham-controlled studies
- Relative to sham, NT-501 demonstrated a:
  - preservation of anatomy
    - 36% reduction in photoreceptor loss
  - preservation of function
    - 68% reduction in reading speed loss
    - 35% reduction in retinal sensitivity loss[a]

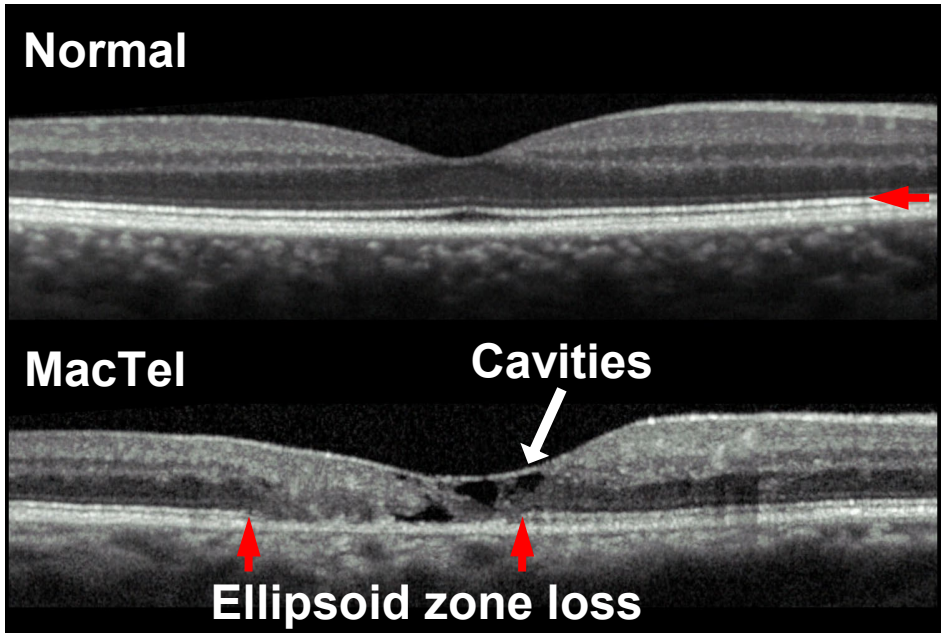
NT-501, revakinagene taroretcel.

[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.

Macular Telangiectasia Type 2 (MacTel) Is a Neurodegenerative Disease That Leads to Vision Loss[1,2]

- MacTel is a bilateral, progressive retinal neurodegenerative disease
  - 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

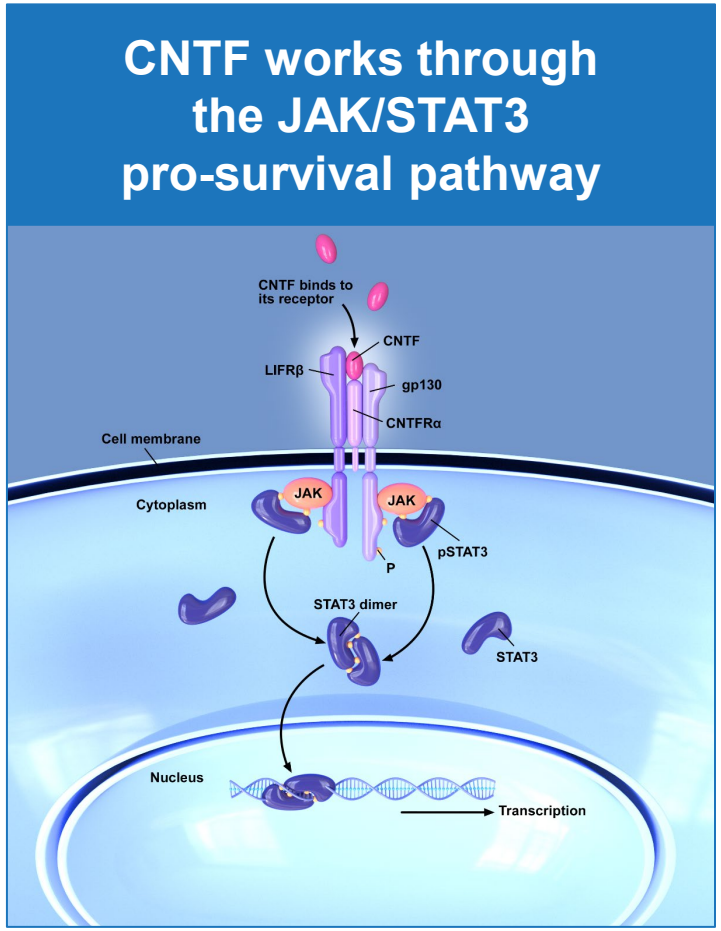


MacTel, macular telangiectasia; SD-OCT, spectral-domain optical coherence tomography.

1. Charbel Issa P, et al. *Prog Retin Eye Res.* 2013;34:49-77. 2. Heeren TFC, et al. *Ophthalmology*. 2020;127:1539-48. 3. Heeren TFC, et al. *Retina*. 2018;38(suppl 1):S20-S26.
4. Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-309.

CNTF 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]

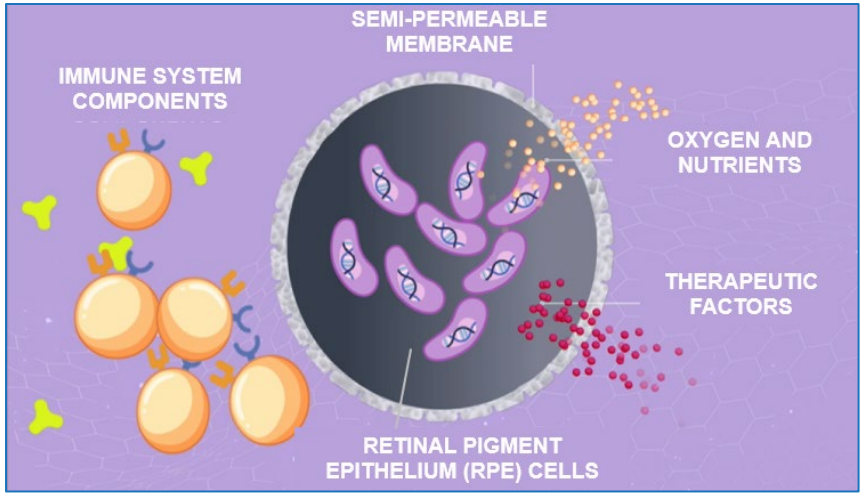


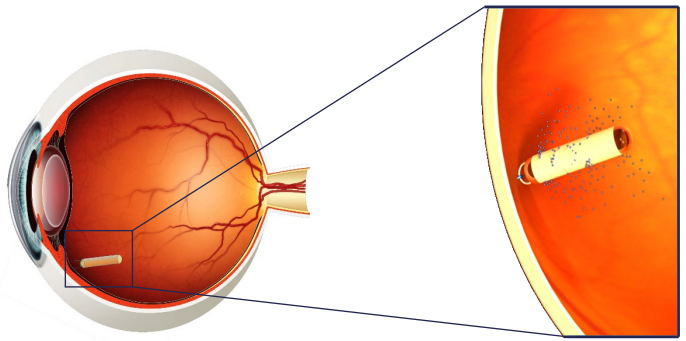
CNTF, ciliary neurotrophic factor; gp130, glycoprotein 130; JAK/STAT, Janus kinase/signal transducer and activator of transcription; LIFRβ, leukemia inhibitory factor ß; P, phosphorous; STAT3, signal transducer and activator of transcription 3.

1. Bringmann A, et al. *Prog Retin Eye Res*. 2009;28:423-45. 2. Shen W, et al. *J Neurosci*. 2012;32(45):15715-27. 3. Sleeman MW, et al. *Pharm Acta Helv*. 2000;74(2-3):265-72. 4. Tao W, et al. *Invest Ophthalmol Vis Sci*. 2002;43(10):3292-8.

Encapsulated Cell Therapy Is Designed to Deliver Sustained Levels of CNTF

- NT-501 is a first-in-class encapsulated cell therapy[1-3]
  - Houses NTC-201-6A cells[1]
  - Allogenic retinal pigment epithelial cells with a unique expression vector for CNTF release[1]
  - Surgically implanted into the vitreous cavity[2] and stably anchored to the sclera[4]
  - Developed to produce long-term sustained levels of CNTF[2]
  - The FDA has set a PDUFA date of March 18, 2025





CNTF, ciliary neurotrophic factor; FDA, Food and Drug Administration; NT-501, revakinagene taroretcel; PDUFA, Prescription Drug User Fee Act

1. Plakkot S, et al. Poster presented at: Association for Research in Vision and Ophthalmology; April 23-27, 2023; New Orleans, LA. 2. Kauper K, et al. Poster presented at: Association for Research in Vision and Ophthalmology; April 23-27, 2023; New Orleans, LA. 3. Kauper K, et al. *Invest Ophthalmol Vis Sci*. 2023;64(8):3680. 4. Chew E, et al. *Ophthalmology*. 2019;126(4):540-9.

NT-501 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 mm² and 4.00 mm²** • **BCVA of ≥64** ETDRS letters	• **EZ break between 0.16 mm² and 2.00 mm²** • **BCVA of ≥54** ETDRS letters	
Randomization	NT-501: 16 participants[d] Sham: 19 participants NT-501 + Sham: 32 participants	NT-501: 58 participants Sham: 57 participants	NT-501: 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; NT-501, revakinagene taroretcel.

[a]NCT01949324. [b]NCT03316300. [c]NCT03319849. [d]Participants with one eligible eye (35 participants) received NT-501 (16 eyes) or sham (19 eyes). In participants with two eligible eyes (32 participants), one eye received NT-501 (32 eyes) and one eye received sham procedure (32 eyes). If both eyes were eligible, right eye was randomized 1:1 to sham or NT-501 and left eye received other surgery.

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 Apr 30;6:16. 2. Patel PJ, et al. *Invest Ophthalmol Vis Sci*. 2011 Jun 1;52(6):3854-9. 3. Zhao Y, et al. Poster presented at: Association for Research in Vision and Ophthalmology; May 5-9, 2024. Seattle, WA.

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 3 and Phase 2 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.

Baseline Demographic Characteristics, by Participant[a]

	Phase 2			Phase 3 (Study A)		Phase 3 (Study B)	
By participant	**NT-501 (n=16)**	**Sham (n=19)**	**NT-501 + Sham (n=32)**	**NT-501 (n=58)**	**Sham (n=57)**	**NT-501 (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)

Baseline demographic characteristics were well balanced across studies and treatment arms

NT-501, revakinagene taroretcel; SD, standard deviation.
[a]Results reported for the all-treated population.

Baseline Ocular Characteristics, by Eye[a]

By eye	Phase 2		Phase 3 (Study A)		Phase 3 (Study B)	
	NT-501 (n=48)	Sham (n=51)	NT-501 (n=58)	Sham (n=57)	NT-501 (n=59)	Sham (n=54)
EZ area loss (mm^2), n Mean (SD)	48 0.70 (0.42)	51 0.77 (0.55)	58 0.51 (0.48)	57 0.49 (0.36)	59 0.52 (0.31)	54 0.48 (0.29)
EZ area category, n (%) <0.5 mm^2 ≥0.5 mm^2	 18 (37.5) 30 (62.5)	 20 (39.2) 31 (60.8)	 41 (70.7) 17 (29.3)	 40 (70.2) 17 (29.8)	 31 (52.5) 28 (47.5)	 33 (61.1) 21 (38.9)
Mean BCVA, ETDRS letter (SD) Snellen equivalent	77.0 (5.6) 20/32	76.2 (6.9) 20/32	70.8 (9.11) 20/40	73.3 (8.64) 20/40	74.4 (7.76) 20/32	73.6 (9.23) 20/32
Reading speed (wpm), n Mean (SD)	47 94.29 (46.13)	49 107.26 (43.17)	57 92.09 (43.72)	56 96.01 (54.01)	59 96.49 (47.31)	53 94.09 (42.81)
Retinal sensitivity[b], n Mean (SD)	40 89.15 (76.15)	45 107.96 (106.77)	53 62.14 (77.58)	54 59.02 (62.63)	52 57.92 (56.94)	49 50.48 (58.36)

Participants in the Phase 2 trial had greater baseline EZ area loss compared with the Phase 3 studies

BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; EZ, ellipsoid zone; NT-501, revakinagene taroretcel; 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.

Baseline Demographic and Ocular Characteristics in Pooled Sample[a]

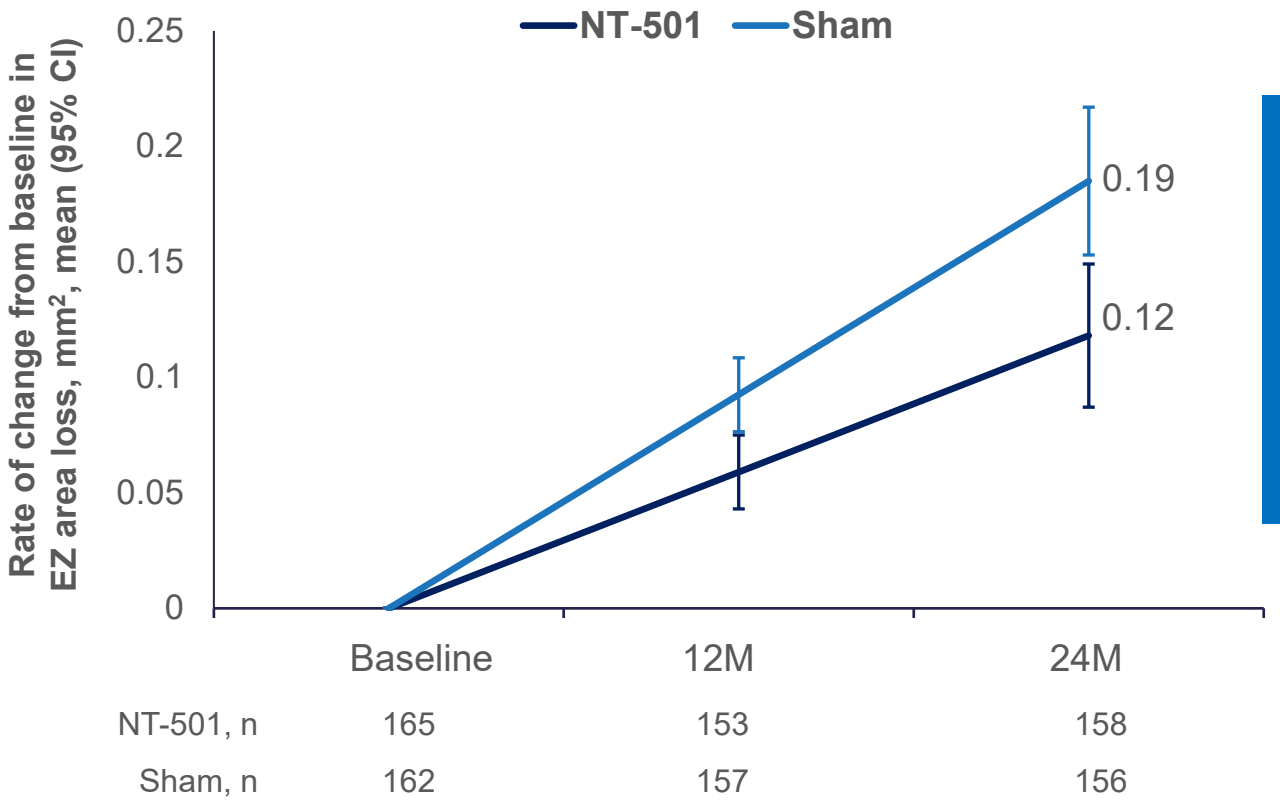
	Phase 2 and Phase 3 Pool[b]	
	NT-501 (n=165)	Sham (n=162)
Demographic characteristics (by participant)		
Female, n (%)	115 (69.7)	108 (66.7)
Mean age, years (SD)	60.5 (8.4)	60.3 (8.6)
Race, n (%)		
White	147 (89)	141 (87)
Asian	5 (3)	5 (3)
Black or African American	2 (1)	3 (2)
American Indian or Alaska Native	0	1 (1)
Other	11 (7)	12 (7)
Ethnicity, n (%)		
Hispanic or Latino	7 (4)	10 (6)
Ocular characteristics (by eye)		
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; NT-501, revakinagene taroretcel; 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 NT-501 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.

NT-501 Demonstrated Greater Preservation of EZ Area Over 2 Years Compared With Sham in All Treated Participants[a]

- A 19.3% reduction in photoreceptor loss with NT-501 compared with sham in Phase 2
- A 54.8% reduction in photoreceptor loss with NT-501 compared with sham in Phase 3, Study A
- A 30.6% reduction in photoreceptor loss with NT-501 compared with sham in Phase 3, Study B

Rate of Change in EZ Area Loss[b], mm²

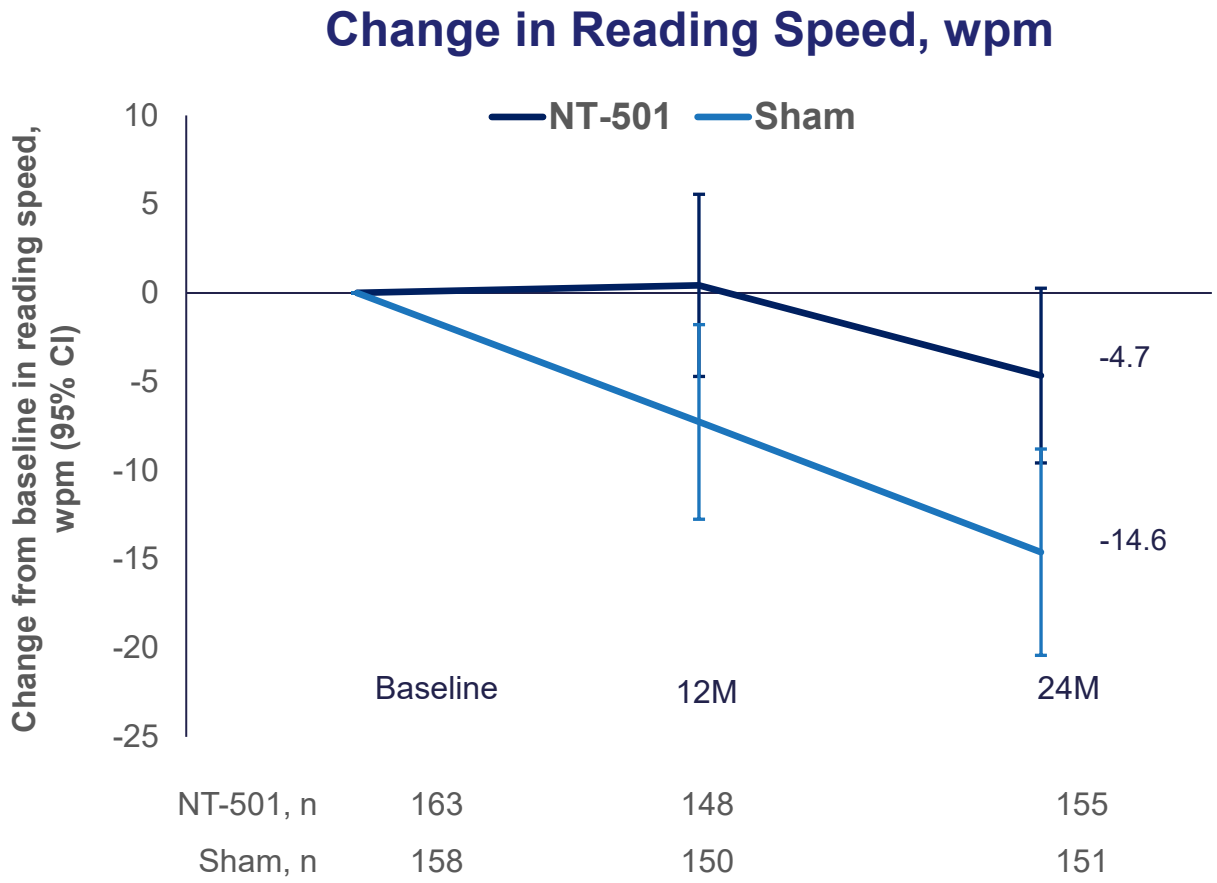


36.2% Reduction in Photoreceptor Loss (p=0.003)

CI, confidence interval; EZ, ellipsoid zone; M, month; NT-501, revakinagene taroretcel.
[a]Per the NTMT-02 study design, participants with two eligible study eyes received NT-501 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.

NT-501 Preserved Reading Speed Over 2 Years Compared With Sham in All Treated Participants[a]

- A 90.7% reduction in reading speed loss with NT-501 compared with sham in Phase 2
- A 49.3% reduction in reading speed loss with NT-501 compared with sham in Phase 3, Study A
- A 69.1% reduction in reading speed loss with NT-501 compared with sham in Phase 3, Study B

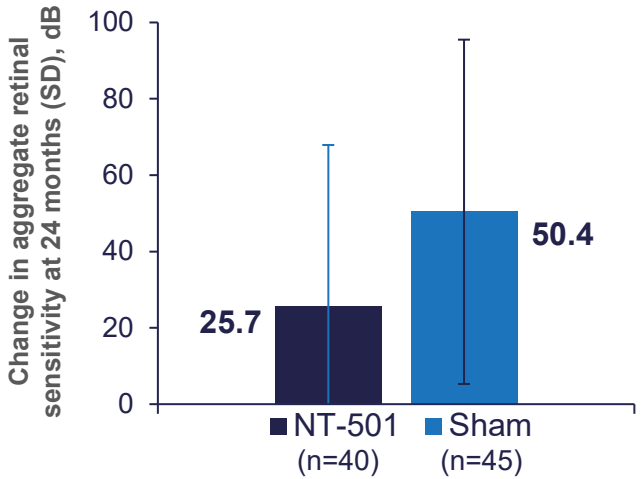


68.1% Reduction in Reading Speed Loss (p=0.0104)

CI, confidence interval; M, month; NT-501, revakinagene taroretcel; SD, standard deviation; wpm, words per minute.
[a]Per the NTMT-02 study design, participants with two eligible study eyes received NT-501 in one eye and sham in the other eye. These 32 participants are included in both groups for the pooled analysis, by study eye.

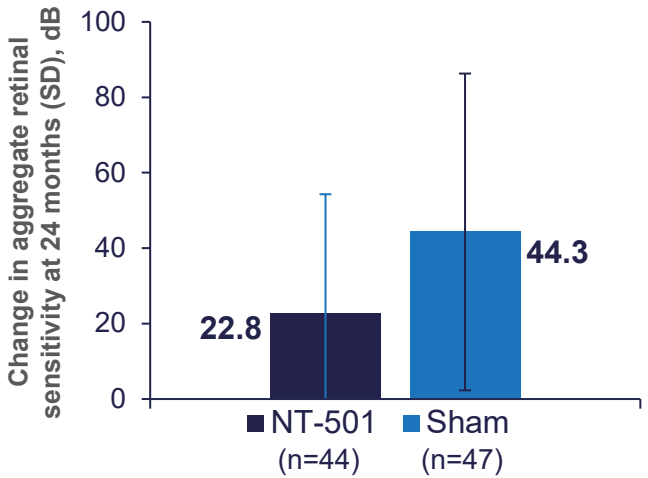
NT-501 Preserved Aggregate Retinal Sensitivity (Microperimetry) Over 2 Years Compared With Sham[a]

Phase 2[b]



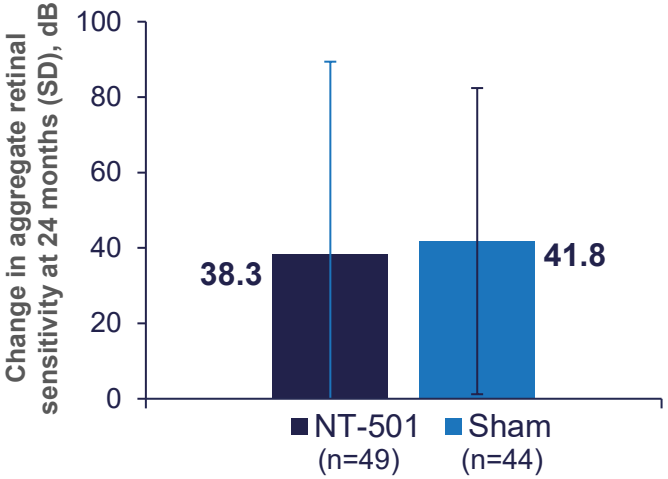
A **49.0%** reduction in aggregate retinal sensitivity loss with NT-501 compared with sham in Phase 2

Phase 3, Study A[c]



A **48.5%** reduction in aggregate retinal sensitivity loss with NT-501 compared with sham in Phase 3, Study A

Phase 3, Study B[c]



An **8.4%** reduction in aggregate retinal sensitivity loss with NT-501 compared with sham in Phase 3, Study B

34.8% Reduction in Aggregate Retinal Sensitivity Loss Across the 3 Studies[d]

dB, decibel; MAIA, Macular Integrity Assessment; NT-501, revakinagene taroretcel; SD, standard deviation.
[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 subjects 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 NT-501 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 subjects 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.

BCVA Remained Stable for NT-501 and Sham Treatment Arms

Mean Change in BCVA, (SD)[a]

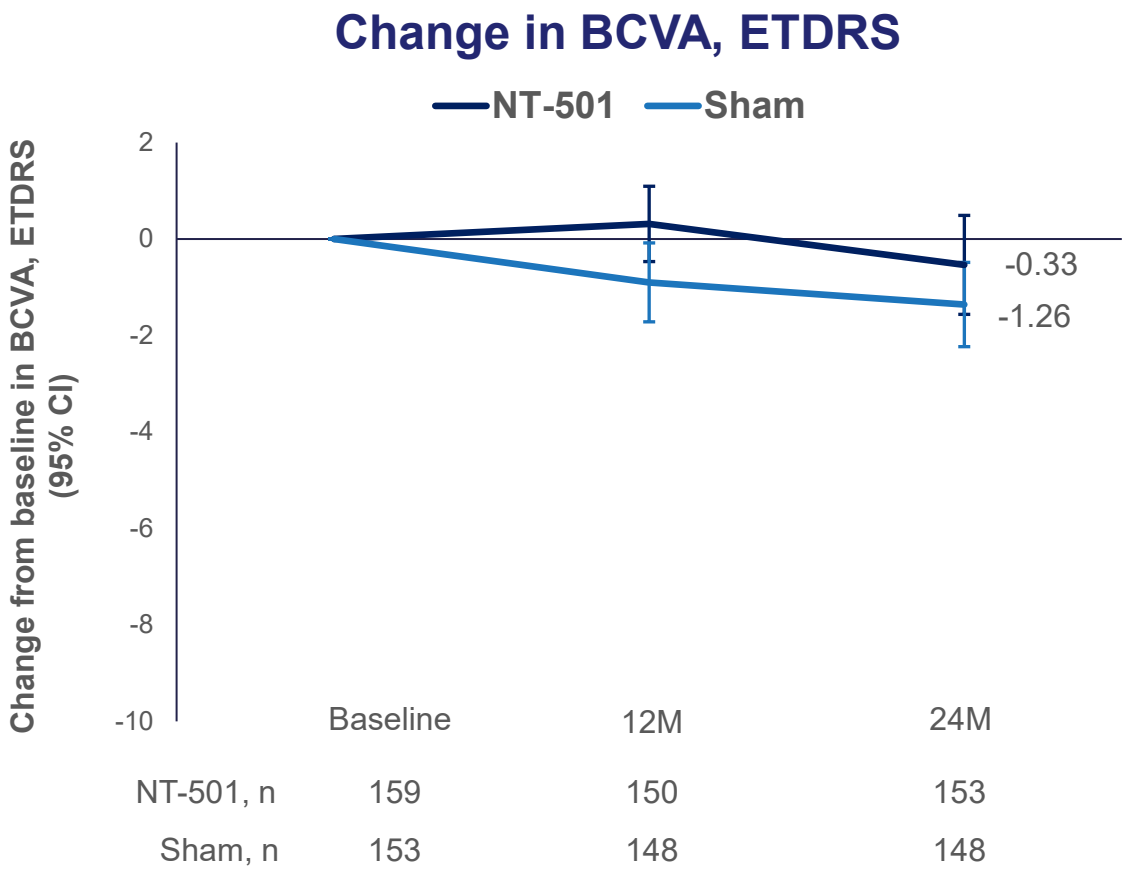
Phase 2	NT-501	Sham
Baseline	77.0 (5.61)	76.2 (6.85)
12M	-0.9 (4.87)	-1.6 (3.81)
24M	-1.9 (5.85)	-2.0 (4.28)

Mean Change in BCVA, (SD)

Phase 3, Study A	NT-501	Sham
Baseline	70.8 (9.11)	73.3 (8.64)
12M	1.0 (4.68)	-0.3 (5.36)
24M	0.2 (7.55)	-0.6 (6.30)

Mean Change in BCVA, (SD)

Phase 3, Study B	NT-501	Sham
Baseline	74.4 (7.76)	73.6 (9.23)
12M	0.6 (5.12)	-0.9 (5.81)
24M	-0.3 (6.01)	-1.7 (4.99)



BCVA, best-corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; NT-501, revakinagene taroretcel.
[a]Per the NTMT-02 study design, participants with two eligible study eyes received NT-501 in one eye and sham in the other eye. These 32 participants are included in both groups by study eye.

Take Home Points

- NT-501 conferred both **anatomic and visual function benefits** across three randomized, sham-controlled studies
- Relative to sham, NT-501 demonstrated a:
  - preservation of anatomy
    - 36% reduction in photoreceptor loss
  - preservation of function
    - 68% reduction in reading speed loss
    - 35% reduction in retinal sensitivity loss[a]

NT-501, revakinagene taroretcel

[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.

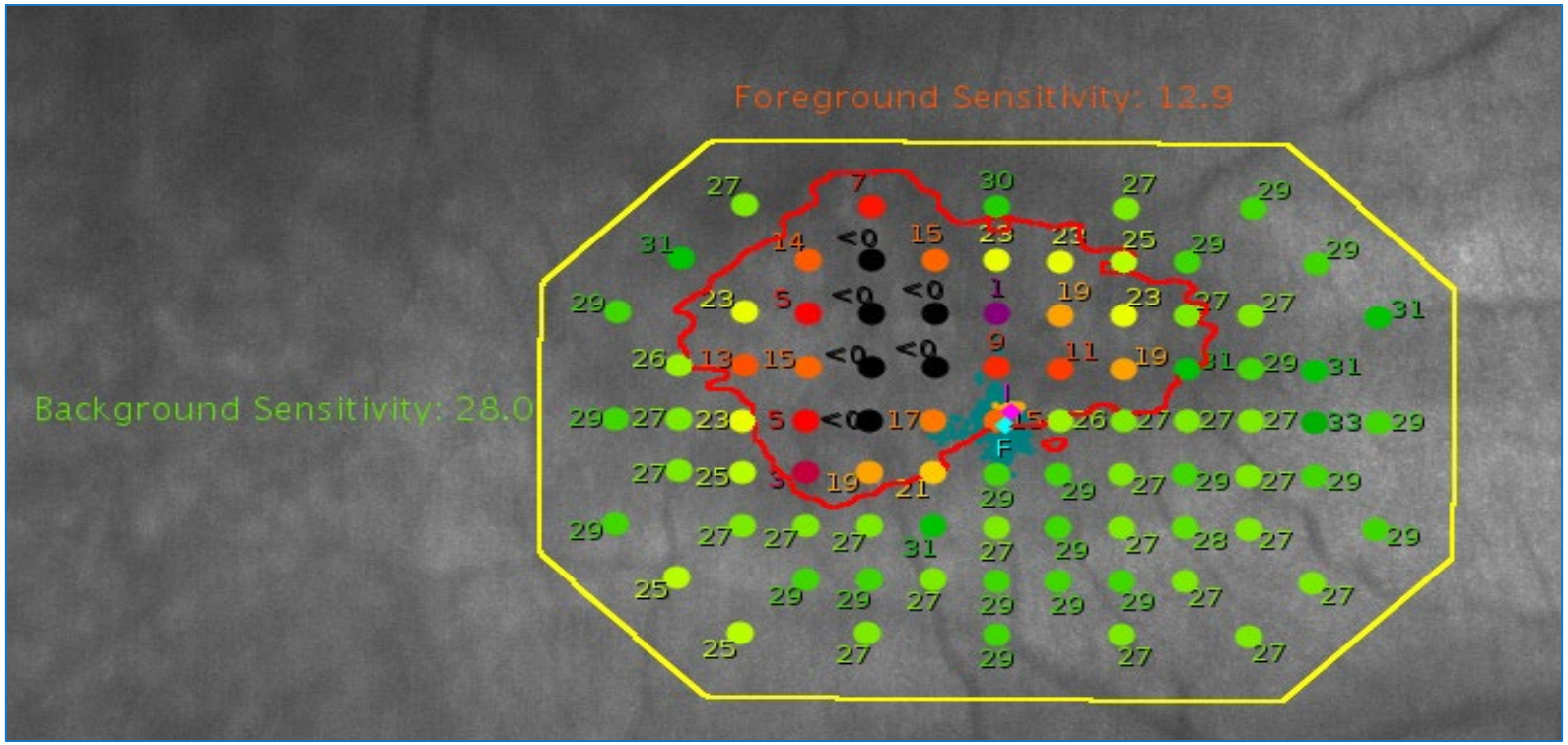
Acknowledgements

- Writing and editorial assistance was provided Elizabeth McSpiritt, MD, MPH, and Kristin Carlin, BS Pharm, RPh, of Peloton Advantage, LLC, an OPEN Health company, and was funded by Neurotech

Appendix

Aggregate Retinal Sensitivity Explained

The boundary in yellow denotes the FOV of the Microperimetry sensitivity map. All calculations are limited to the FOV only, since any extrapolation outside FOV may be subject to error[1]



Calculation Overview[2]

1. Aggregate retinal sensitivity is calculated by summing and averaging test point values on microperimetry outside of the scotoma (considered the background retinal sensitivity)
2. Levels of retinal sensitivity within the scotoma are subtracted from this mean
3. The sum of these differences results in the value known as aggregate sensitivity

FOV, field of view.

Sources: 1. Data on file (includes image). 2. Chew EY, et al. *Ophthalmology*. 2019;126(4):540-549.

MacTel Patient Impact

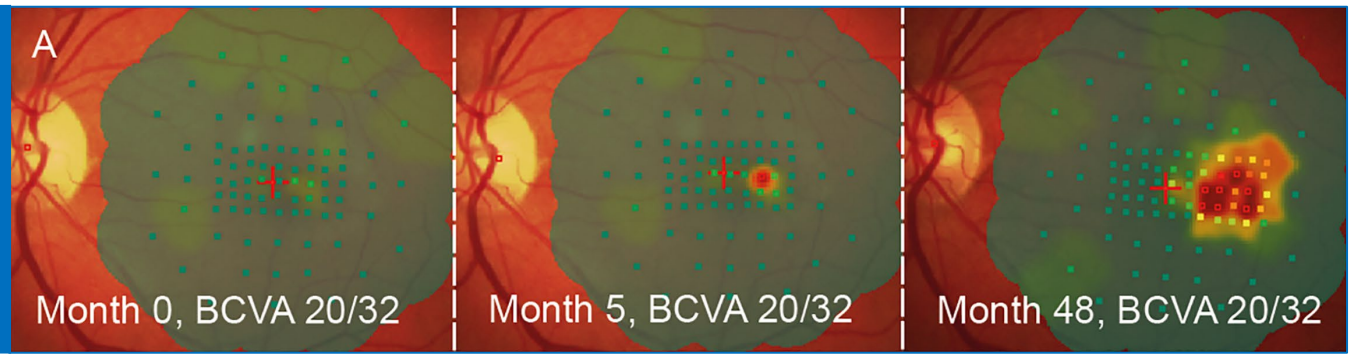
Visual Symptoms[1,2]

- Patients can experience[1]:
  - Blurred vision
  - Distorted vision
  - Expanding Paracentral blind spots
  - Loss of central vision
- Late disease stage defined by a BCVA of 20/200 or worse[3]
- Visual acuity is a suboptimal measure of disease burden

Impact on Activities of Daily Living[2-6]

- Reduced reading capabilities
  - Baseline reading speed for Phase 3 studies was reduced by 50% of normal
- Limitations on driving
- Loss of depth perception impacting mobility

These microperimetry images demonstrate progression of a new scotoma in a MacTel patient over 4 years



1. Finger RP, et al. *Investigative Ophthalmology & Visual Science.* 2009;50(3):1366-70. 2. Neurotech data on file. 3. Bronstad PM, et al. *JAMA Ophthalmol.* 2013;131(3):303-9.
4. Heeren TFC, et al. *Ophthalmology.* 2020;127(11):1539-48. 5. Lee AG, et al. AAO. Driving Restrictions per State. 2023. 6. Issa PC, et al. *Doc Ophthalmol.* 2009;119(2):133-40.

Thank you!

US-EO-SC-25020008