RETINA WORLD CONGRESS

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

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[a]At the time of study analysis.

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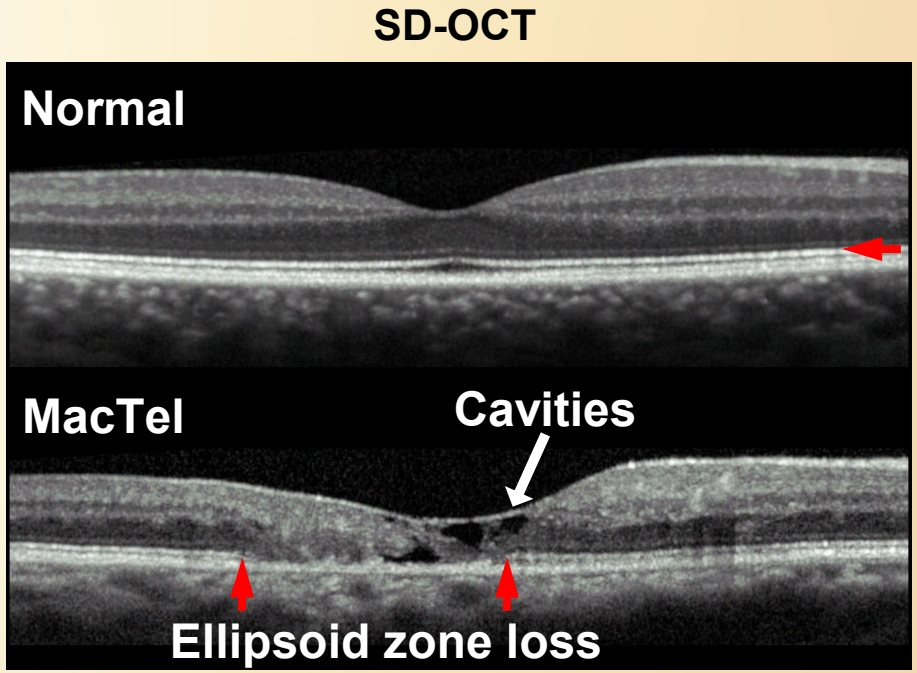
- This study was funded by Neurotech Pharmaceuticals
- This study includes research conducted on human subjects; Institutional Review Board approval was obtained prior to study initiation

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]



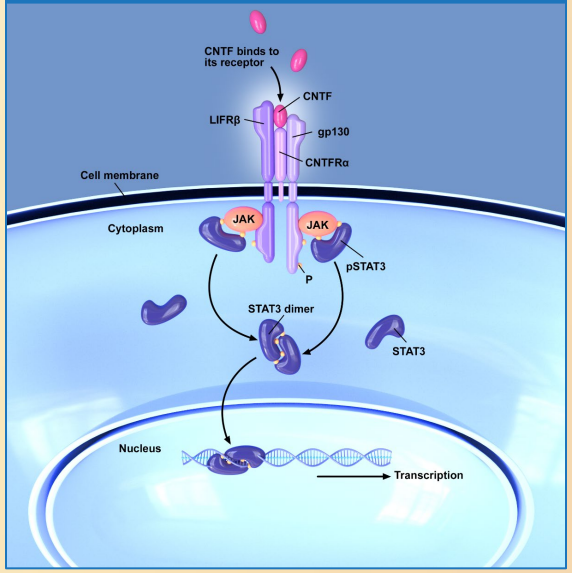
MacTel, macular telangiectasia type 2; SD-OCT, spectral-domain optical coherence tomography.

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;16:3297-309.

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 works through the JAK/STAT3 pro-survival pathway

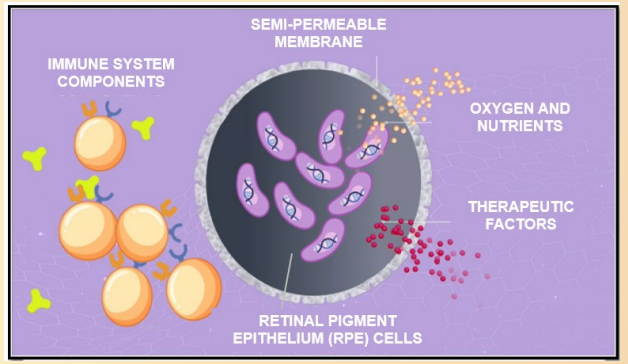


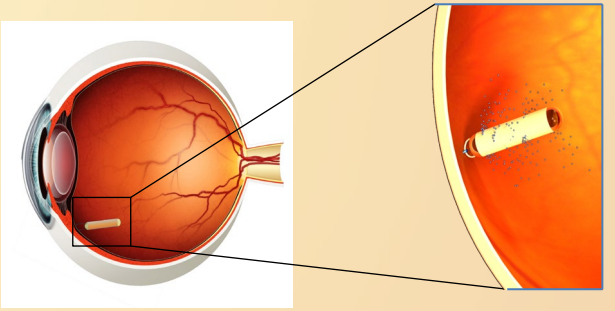
CNTF, ciliary neurotrophic factor; CNTFRα, ciliary neurotrophic factor receptor α; gp130, glycoprotein 130; JAK/STAT, Janus kinase/signal transducer and activator of transcription; LIFRβ, leukemia inhibitory factor β; P, phosphorous; pSTAT3, phosphorylated signal transducer and activator of transcription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

Encapsulated Cell Therapy Is Designed to Deliver Sustained Levels of CNTF

- Revakinagene taroretcel-lwey (NT-501) is a first-in-class encapsulated cell therapy[1,2]
  - Houses NTC-201-6A cells[1]
    - Allogeneic retinal pigment epithelial cells expressing recombinant human CNTF[1]
  - Surgically implanted into the vitreous cavity and stably anchored to the sclera[1]
  - Developed to produce long-term sustained levels of CNTF[3]
  - **NT-501 was approved by the FDA for the treatment of macular telangiectasia type 2 on March 5, 2025**





CNTF, ciliary neurotrophic factor; FDA, Food and Drug Administration.

1. ENCELTO [package insert]. Cumberland, RI: Neurotech Pharmaceuticals, Inc; March 2025. **2.** Lally D, Eliott D. Phase 2 safety study of bilateral ciliary neurotrophic factor-producing revakinagene taroretcel in participants with macular telangiectasia type 2 [abstract]. Presented at: Annual EURETINA; September 19-22, 2024; Barcelona, Spain. **3.** Kauper K, et al. *Invest Ophthalmol Vis Sci.* 2023;64:3680.

NT-501 Has Been Studied Across 3 Randomized, Sham-Controlled Clinical Trials

	NTMT-02[a] 67 participants 99 eyes[d] All-treated population	**NTMT-03A**[b] 115 participants 115 eyes All-treated population	**NTMT-03B**[c] 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	Aged >21 to <80 years; diagnosis of MacTel • **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-lwey.
[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, the right eye was randomized 1:1 to sham or NT-501 and the 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;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.

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 Demographics, by Participant[a]

By Participant	Phase 2			Phase 3 (Study A)		Phase 3 (Study B)	
	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 demographics were well balanced across studies and treatment arms

NT-501, revakinagene taroretcel-lwey; 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-lwey; 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.

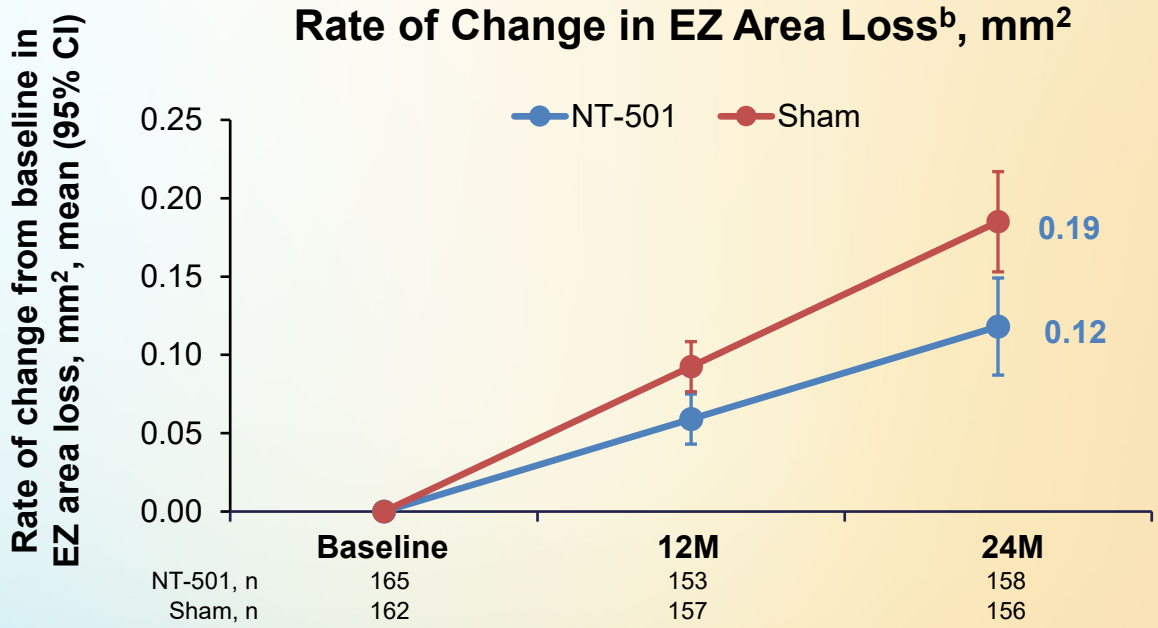
Baseline Demographics, by Participant, and Ocular Characteristics, by Eye, in the Pooled Sample[a]

	Phase 2 and Phase 3 Pool[b]	
	NT-501 (n=165)	Sham (n=162)
Demographics, 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-lwey; 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



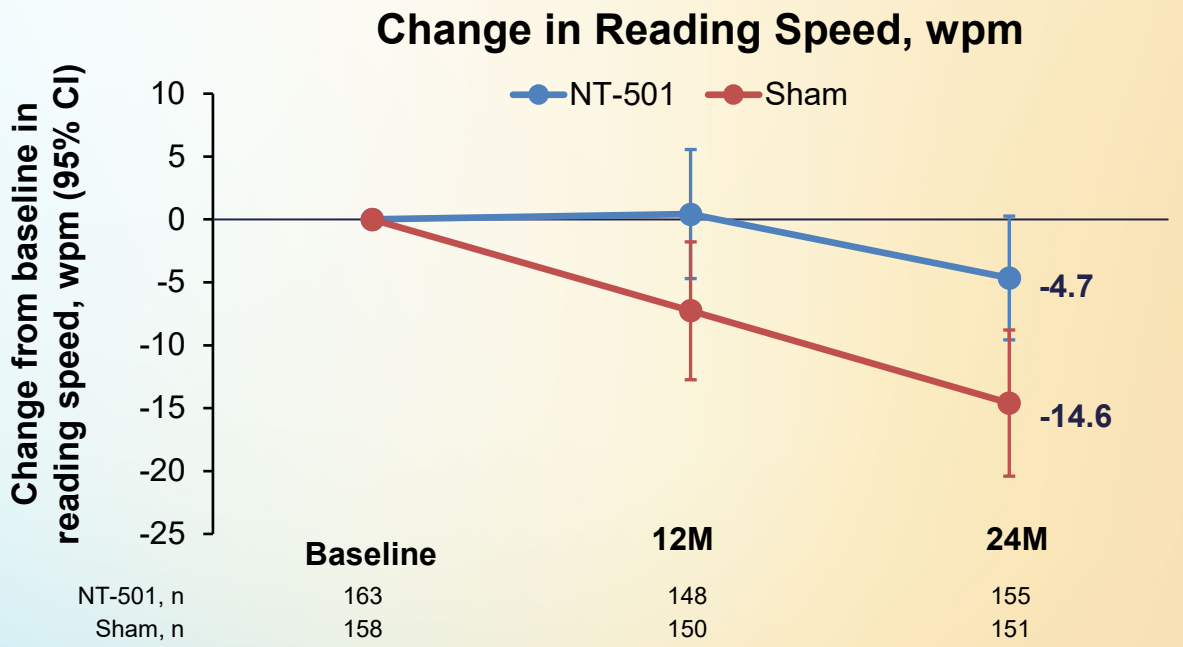
36.2% Reduction in Photoreceptor Loss (p=0.003)

CI, confidence interval; EZ, ellipsoid zone; M, month; NT-501, revakinagene taroretcel-lwey.

[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

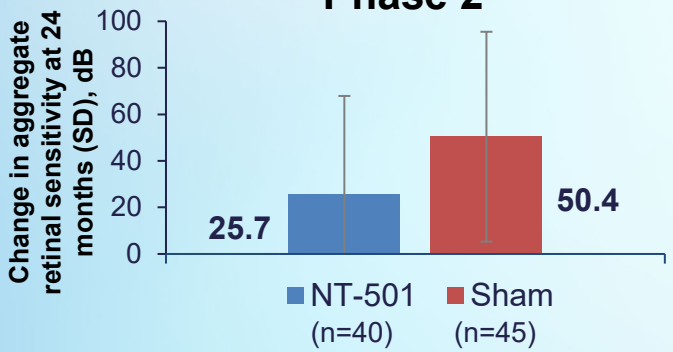


68.1% Reduction in Reading Speed Loss (p=0.0104)

CI, confidence interval; M, month; NT-501, revakinagene taroretcel-lwey; 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.

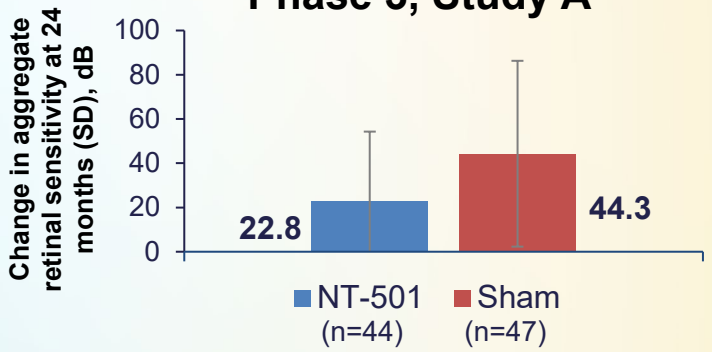
NT-501 Preserved Aggregate Retinal Sensitivity (Microperimetry) Over 2 Years Compared With Sham[a]

Phase 2[b]



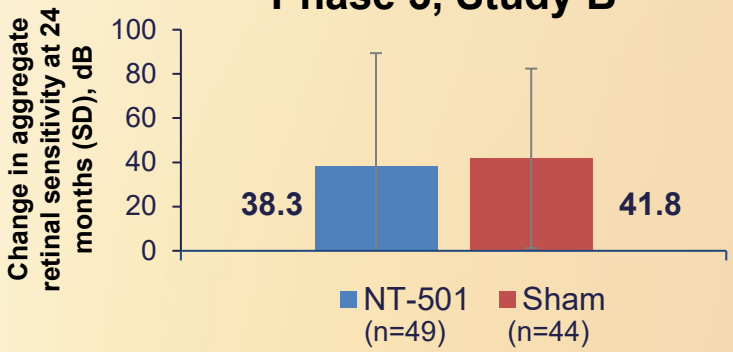
A **49.0%** reduction in aggregate retinal sensitivity loss with NT-501 compared with sham in Phase 2

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 three studies[d]

dB, decibel; MAIA, Macular Integrity Assessment; NT-501, revakinagene taroretcel-lwey; 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 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 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 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.

BCVA Remained Stable for NT-501 and Sham Treatment Arms

Mean Change in BCVA (SD)[a]

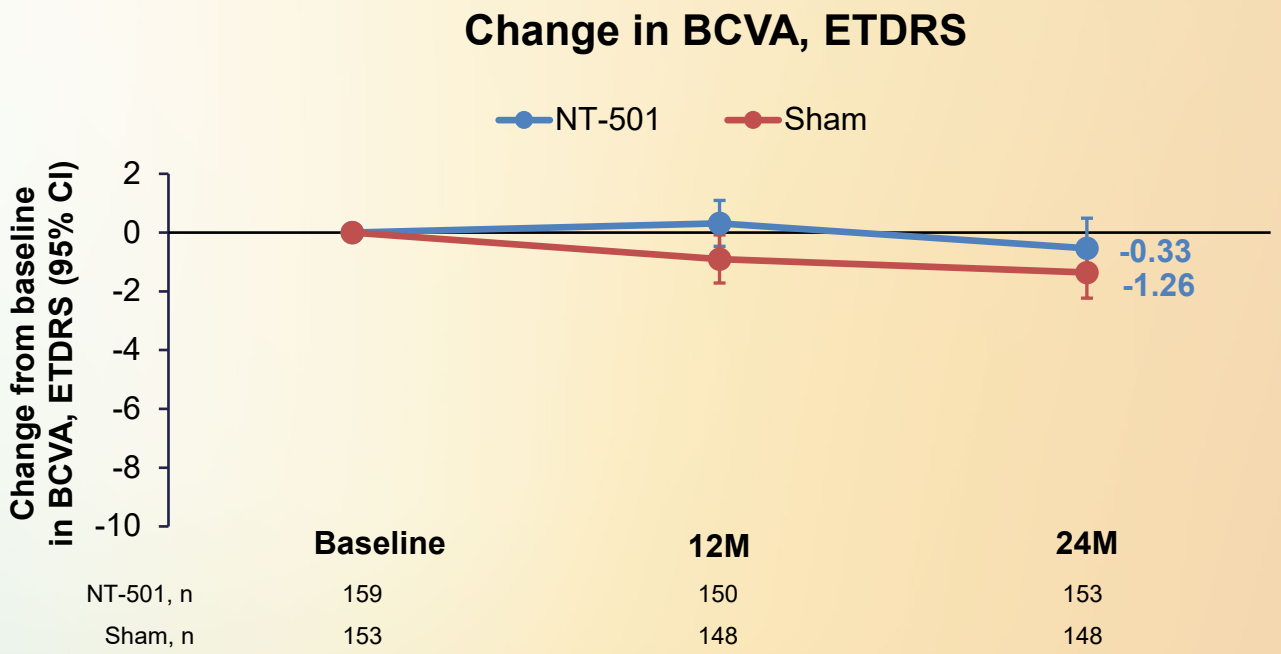
Phase 2	NT-501	Sham
Baseline	77.0 (5.61)	76.2 (6.85)
12M	-0.9 (4.87)	-1.6 (3.81)
24M	-1.9 (5.85)	-2.0 (4.28)

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; M, month; NT-501, revakinagene taroretcel-lwey; SD, standard deviation.
[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.

Conclusions

- 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-lwey.
[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

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