### **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); Employment (Annexon Biosciences)
- 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

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

W. Lloyd Clark, MD,<sup>1</sup> Rishi P. Singh, MD,<sup>2</sup> Roger A. Goldberg, MD, MBA,<sup>3</sup> Muna Bitar, PharmD,<sup>4</sup> Debora C. Manning, MPH,<sup>5,\*</sup> Jon Yankey, MS,<sup>5</sup> Thomas Aaberg, Jr, MD,<sup>4,6</sup> and the MacTel Study Investigators

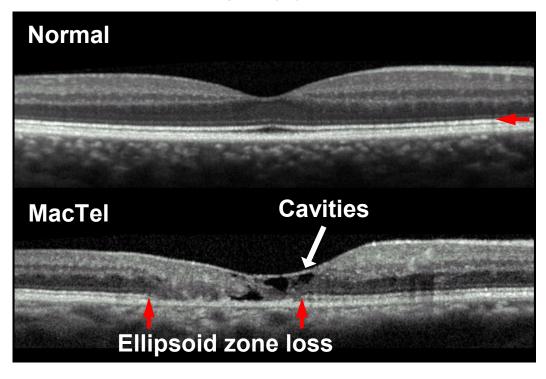
<sup>1</sup>University of South Carolina School of Medicine, Palmetto Retina Center, Retina Consultants of America, Columbia, SC; <sup>2</sup>Cleveland Clinic Martin Health, Stuart, FL; <sup>3</sup>Bay Area Retina Associates, Walnut Creek, CA; <sup>4</sup>Neurotech Pharmaceuticals, Cumberland, RI; <sup>5</sup>Veristat, Southborough, MA; <sup>6</sup>Foundation for Vision Research, Grand Rapids, MI

\*At the time of study analysis.

## MacTel Is a Neurodegenerative Disease That Leads to Vision Loss<sup>1,2</sup>

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

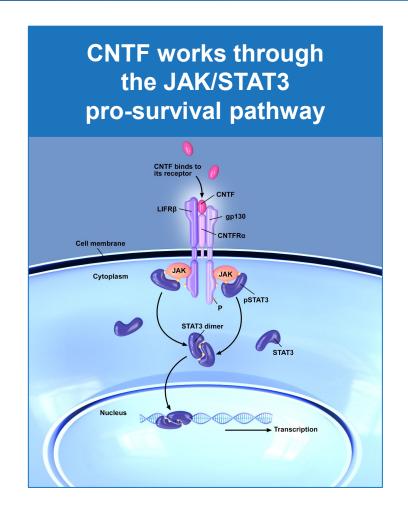
#### **SD-OCT**



US-EO-SC-25090011

### Ciliary Neurotrophic Factor Is a Potent Neuroprotectant 1-3

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

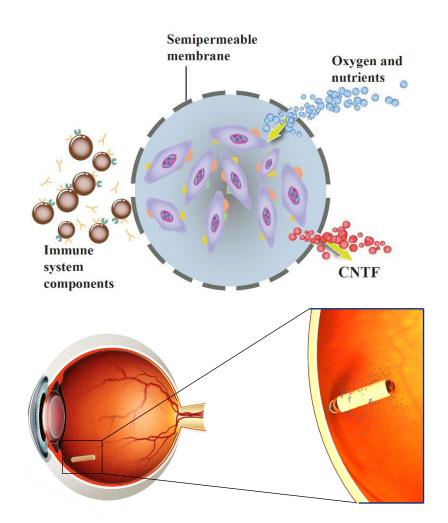


CNTF, ciliary neurotrophic factor; CNTFRα, ciliary neurotrophic factor receptor α; gp130, glycoprotein 130; JAK/STAT, Janus kinase/signal transducer and activator of transcription; LIFRβ, leukemia inhibitory factor β; P, phosphorous; pSTAT3, phosphorylated signal transducer and activator of transcription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

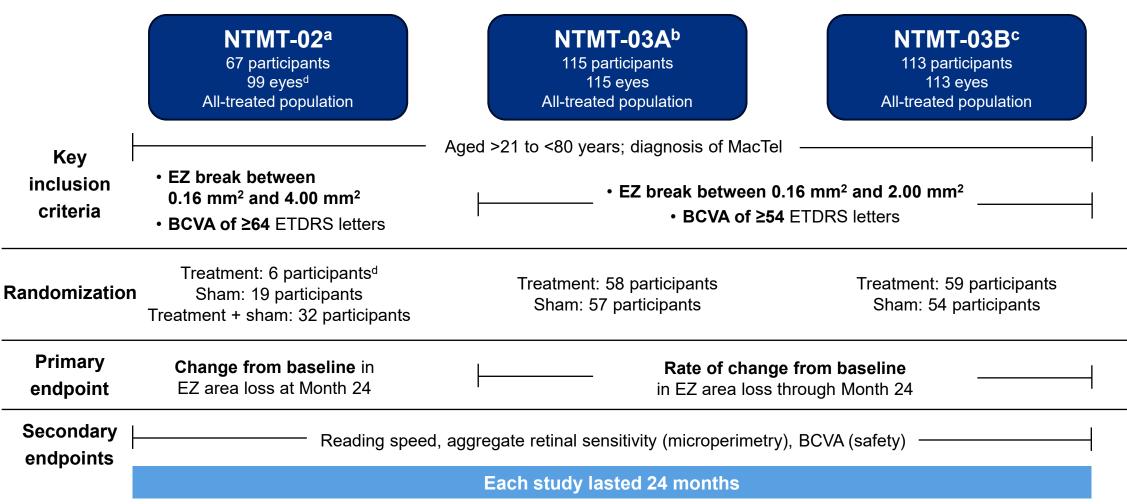
1. Bringmann A, et al. *Prog Retin Eye Res.* 2009;28:423-445. **2.** Shen W, et al. *J Neurosci.* 2012;32(45):15715-15727. **3.** Sleeman MW, et al. *Pharm Acta Helv.* 2000;74:265-272. **4.** Tao W, et al. *Invest Ophthalmol Vis* Sci. 2002;43:3292-3298

## **Encapsulated Cell Therapy Is Designed to Deliver Sustained Levels of CNTF**

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



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

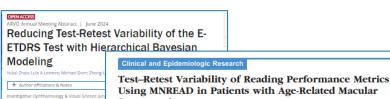


BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; EZ, ellipsoid zone; MacTel, macular telangiectasia type 2.

aNCT01949324. bNCT03316300. cNCT03319849. dParticipants 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.

### Rationale for a Pooled Functionality Analysis

- Rare disease
- Inherent variability of outcome measures<sup>1-3</sup>
- Similar populations and study designs
- Increase the sample size



#### Abstract

ophthalmic trials. However, the high t indicates a lack of precision and redu reduce variability of E-ETDRS testing ( gold standard ETDRS chart.

the generative model of trial-by-trial p rapidly VA behavior changes with incr testing:(1) A Bayesian Inference Proc parameters and hypernarameters fro both E-ETDRS and qVA (Lesmes & Dor each of 4 Bangerter foil conditions w We assessed TRV(1.96×test-retest diff derived from the repeated E-ETDRS ter

Results: Figure 2 displays the Bland-/ from the original E-ETDRS procedure 0.17 for F-FTDRS 0.19 for BIP 0.14 for TRV for BIP is comparable to that of E-

the E-ETDRS tests. Integrating inform tests, the HBIM exhibited the greatest post-hoc procedures can be employ

Degeneration Praveen J. Patel, 1 Fred K. Chen, 1,2 Lyndon D.

PURPOSE. To determine the test-retest variability of readi bility using the MNREAD charts in patients with stable ag related macular degeneration (AMD).

Methods. In this prospective study, reading ability was me sured at two visits in 124 nontreated eyes of 124 patients wit AMD, who were enrolled in an ongoing clinical trial using standardized MNREAD protocol. Only patients with stabl AMD who could perform the reading test at 40 cm at both visit were included in the analysis. Different scoring rules we applied to calculate critical print size and maximum readir

(7.6) years who met the study criteria were analyzed at a me (SD) interval of 43 (6) days between measurements. The 9 coefficient of repeatability (CR) was 0.30 logMAR for readi acuity. The CR for critical print size and maximum readir speed varied depending on the analysis method applied.

CONCLUSIONS. This is a report of estimates of the interse test-retest variability of reading performance metrics in t ients with stable AMD. The results are helpful both in definir end points in clinical trials for AMD and in distinguishi clinical change from measurement variability in clinics practice. (Invest Ophthalmol Vis Sci. 2011;52:3854-3859) DO

Visual acuity is the most widely used measure of macul function in clinical trials and clinical practice. How reading ability is an important component of vision function Reading difficulty diminishes quality of life. 1,2 and improve ment in reading performance is one of the main objectives for elderly low-vision patients.3 The MNREAD charts, developed esota Laboratory for Low-Vision Research, are a cor monly used test in clinical trials and clinical practice to asse

From the <sup>1</sup>National Institutes of Health Research (NIHR) Biomes ical Research Centre for Ophthalmology (Moorfields Eye Hospital an UCI. Institute of Ophthalmology), London, United Kingdom; and th Centre for Ophthalmology and Vision Science, University of Weste

Australia, Perth, Australia. Supported by The Special Trustees of Moorfields Eye Hospita This research has received a proportion of its funding from the D partment of Health's NHR Blomedical Research Centre for Ophth mology at Moorfields Eye Hospital and UCL Institute of Ophthalmo ogy. The views expressed in the publication are those of the authorand not necessarily those of the Department of Health.

Submitted for publication September 19, 2010; revised January and February 21, 2011; accepted February 25, 2011. Disclosure: P.J. Patel, None; F.K. Chen, None; L. Da Cruz, Non G.S. Rubin, None; A. Tufail, None

No reprints will be available. Corresponding author: Praveen J. Patel, Medical Retina Serv Moorfields Eve Hospital, 162 City Road, London ECIV 2PD, U

bhai et al. Int J Retin Vitr (2020) 6:16

International lournal of Retina and Vitreous

#### Test-retest variability of microperimetry in geographic atrophy

A. Yasin Alibhai<sup>1†</sup>, Nihaal Mehta<sup>1†</sup>, Sheila Hickson-Curran<sup>2</sup>, Carlos Moreira-Neto<sup>1</sup>, Emily S. Levine<sup>1</sup>, Elias Reichel<sup>1</sup> Jay S. Duker<sup>1</sup> and Nadia K. Waheed<sup>3</sup>

Purpose: Microperimetry (MP) allows for measurement of retinal sensitivity at precise locations and is now commonly employed as a clinical trial endpoint. Test-retest reliability is important when evaluating treatment effects in patients with geographic atrophy (GA). This study aimed to determine the test-retest variability of MP in patients with noderate to severe GA using the MAIA MP device.

Methods: In this prospective study, patients with a confirmed diagnosis of foveal-involving GA were enrolled. Participants performed three MP assessments of a selected eye over two visits with the Macular Integrity Assessment (MAIA) 2 instrument (Centervue, Padova, Italy) utilizing a wide 30° grid, consisting of 93 stimuli (Goldmann III) using a 4-2 representation strategy, encompassing the entire area of GA and beyond. Mean retinal sensitivity (MS) was expressed as an average threshold value (dB) for the entire field tested. Coefficients of Repeatability at a 95% level (CoR<sub>0c</sub>) were calculated for Point Wise Sensitivity (PWS). Fixation stability (FS) was assessed by evaluating the area of an elliptical epresentation encompassing 95% of the cloud of fixation points (CFP) dataset generated by the MAIA MP, known as the bivariate contour ellipse area (BCEA).

Results: A total of 8 subjects were enrolled (21 tests), with six subjects completing 3 MP assessments. BCVA in these patients ranged from 20/100 to 20/800. The mean area of GA was  $18.7 \pm 12.3$  mm $^2$ . The average time to complete one MP assessment was 13 min 9 s and mean RCFA@95% was 38 5 ± 19 3°2. The MS was 14 3 ± 4.5 dR. No significant increase in MS was noted between testing pairs 1&2 and 2&3. The preferred retinal locus was maintained in the same quadrant on successive tests. The mean CoR95 for PWS were similar for testing pairs 1&2 (±3.50 dB) and 2&3 (±3.40).

Conclusion: Microperimetry using a wide grid can be reliably performed in a reasonable amount of time in patients with moderate and severe vision loss secondary to GA. There was no learning effect seen between sequential assessments when analyzing MS or PWS. A change of approximately 4 dB in PWS provides a threshold for considering a true

the macula. First developed in the 1980s, MP was initially deployed as part of a scanning laser ophthalmoscope

Microperimetry (MP) is a several-decades old technology ficult to use. In the last two decades, however, there has designed to test retinal sensitivity at different points in been a resurgence in development of new microperimetry systems, beginning with the Nidek MP-1 and con tinuing more recently with the Nidek MP-3 and Macular Integrity Assessment (MAIA) 2 systems, which are more user friendly with the addition of features such as eye

evetem. In its early forms, MP evetems were relatively dif-

With newer improvements, microperimetry (MP) has gained more widespread adoption as a means of



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 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

### **Baseline Demographics Were Well Balanced Across Studies** and Treatment Arms

	Phase 2			Phase 3 (Study A)		Phase 3 (Study B)	
By Participant <sup>a</sup>	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)

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

	Phase 2		Phase 3 (	(Study A)	Phase 3 (Study B)	
By Eye <sup>a</sup>	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 (mm²), 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)
<b>EZ area category</b> , n (%) <0.5 mm <sup>2</sup> ≥0.5 mm <sup>2</sup>	18 (37.5)	20 (39.2)	41 (70.7)	40 (70.2)	31 (52.5)	33 (61.1)
	30 (62.5)	31 (60.8)	17 (29.3)	17 (29.8)	28 (47.5)	21 (38.9)
<b>Mean BCVA</b> , 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 <sup>b</sup> , 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

## Baseline Characteristics in the Pooled Population Were Balanced Between Treatment Arms

	Phase 2 and Phase	Phase 2 and Phase 3 Pool <sup>b</sup>		
	Revakinagene Taroretcel-lwey (n=165)	Sham (n=162)		
Demographics, by participant <sup>a</sup>				
Female, n (%)	115 (69.7)	108 (66.7)		
Mean age, years (SD)	60.5 (8.4)	60.3 (8.6)		
Race, n (%) White Asian Black or African American American Indian or Alaska Native Other	147 (89) 5 (3) 2 (1) 0 11 (7)	141 (87) 5 (3) 3 (2) 1 (1) 12 (7)		
Ethnicity, n (%) Hispanic or Latino  Ocular characteristics, by eyea	7 (4)	10 (6)		
<b>EZ area loss</b> (mm²), n Mean (SD)	165 0.57 (0.41)	162 0.57 (0.43)		
<b>EZ area category</b> , n (%) <0.5 mm <sup>2</sup> ≥0.5 mm <sup>2</sup>	90 (54.5) 75 (45.5)	93 (57.4) 69 (42.6)		
Mean BCVA, ETDRS letter (SD) Snellen equivalent	73.8 (8.2) 20/40	74.2 (8.5) 20/32		
Reading speed (wpm), n Mean (SD)	163 94.32 (45.50)	158 98.86 (47.24)		
<b>Retinal sensitivity</b> <sup>c</sup> , n Mean (SD)	-	-		

BCVA, best corrected visual acuity; ETDRS, Early Treatment Diabetic Retinopathy Study; EZ, ellipsoid zone; SD, standard deviation; wpm, words per minute.

aResults reported for the all-treated population, unless otherwise noted. Not available in full pool. bPer 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. aResults reported for the per-protocol population.

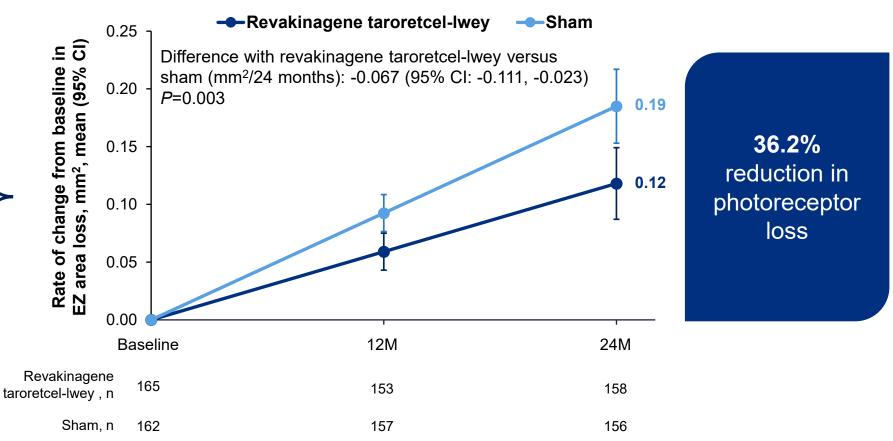
US-EO-SC-25090011

## Revakinagene Taroretcel-Iwey Demonstrated Greater Preservation of EZ Area Over 2 Years Compared With Sham in All-Treated Participants<sup>a</sup>

- 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<sup>b</sup>, mm<sup>2</sup>



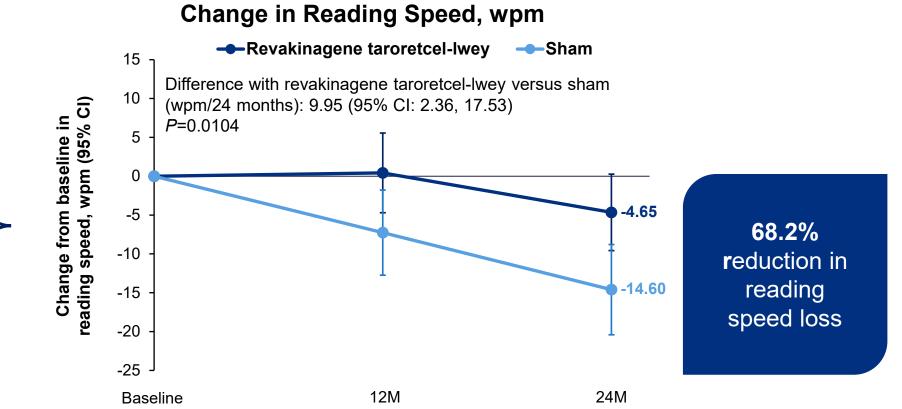
CI, confidence interval; EZ, ellipsoid zone; M, month.

<sup>a</sup>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. <sup>b</sup>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.

# Revakinagene Taroretcel-Iwey Preserved Reading Speed Over 2 Years Compared With Sham in All-Treated Participants<sup>a</sup>

- 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



148

150

Revakinagene

Sham, n

taroretcel-lwey, n

163

158

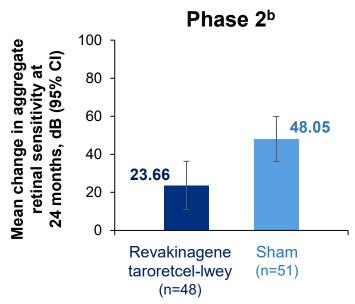
155

151

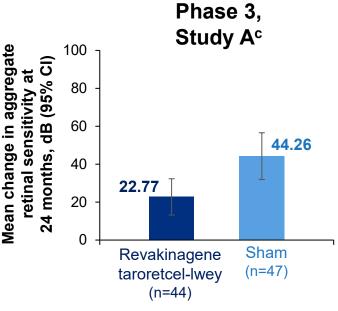
CI, confidence interval; M, month; wpm, words per minute.

<sup>&</sup>lt;sup>a</sup>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.

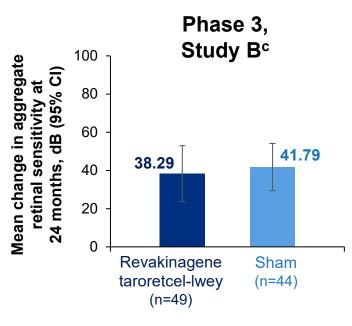
## Revakinagene Taroretcel-Iwey Preserved Aggregate Retinal Sensitivity (Microperimetry) Over 2 Years Compared With Sham<sup>a</sup>



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



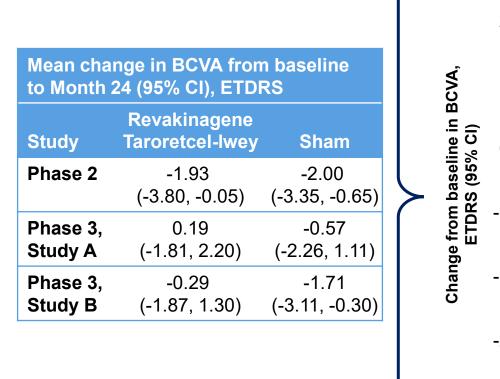
An **8.4%** reduction in aggregate retinal sensitivity loss with revakinagene taroretcel-lwey compared with sham in NTMT-03-B

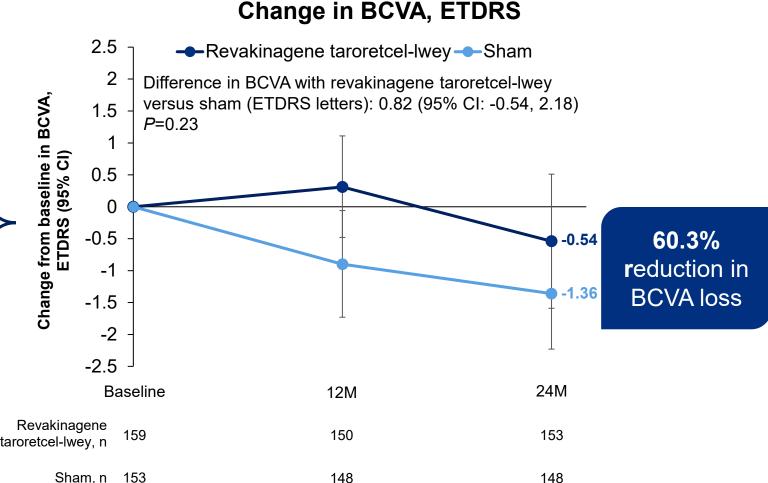
### 36.6% reduction in aggregate retinal sensitivity loss across the three studiesd

CI, confidence interval; dB, decibel; MAIA, Macular Integrity Assessment.

<sup>a</sup>Retinal sensitivity was measured via MAIA microperimetry. <sup>b</sup>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. <sup>c</sup>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. <sup>d</sup>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 Both Treatment Arms Over 2 Years<sup>a</sup>





### 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<sup>a</sup>

### **Acknowledgments**

- 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 with MacTel
- These trials were funded by Neurotech Pharmaceuticals, Inc
- These data were presented at American Academy of Ophthalmology Retina Subspecialty Day 2024; Chicago, IL; October 18–19, 2024
- 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