Surgical-Related Adverse Events With Revakinagene Taroretcel-lwey: A Root Cause Analysis

Roger A. Goldberg, MD, MBA,[1] John S. Pollack, MD,[2*,3] Thomas Aaberg, Jr, MD[2,4]

[1]Bay Area Retina Associates, Walnut Creek, CA; [2]Neurotech Pharmaceuticals, Inc., Cumberland, RI; [3]Illinois Retina Associates, Joliet, IL; [4]Foundation for Vision Research, Grand Rapids, MI

*At the time of analysis.

Hawaiian Eye and Retina, January 17–23, 2026, Waikoloa Village, Hawaii

Financial Disclosures

- Dr. Goldberg has consulted for AbbVie, Alimera, Annexon, Apellis, Boehringer Ingelheim, Clearside, EyePoint, Genentech, Janssen, Neurotech Pharmaceuticals, Ocular Therapeutix, StealthBio, Regeneron, and Zeiss; has received grant support from 4DMT, AbbVie, Affamed, Alexion, Annexon, Apellis, Avirmax, Boehringer Ingelheim, Cognition, EyePoint, Genentech, Janssen, LMRI, Neurotech Pharmaceuticals, NovoNordisk, Ocular Therapeutix, StealthBio, Regeneron, UnityBio, and Zeiss; has received speaker fees from Apellis; and has equity in Emmetrope Ophthalmics
- This analysis was funded by Neurotech Pharmaceuticals
- This analysis includes research conducted on human subjects; institutional review board approval was obtained prior to study initiation

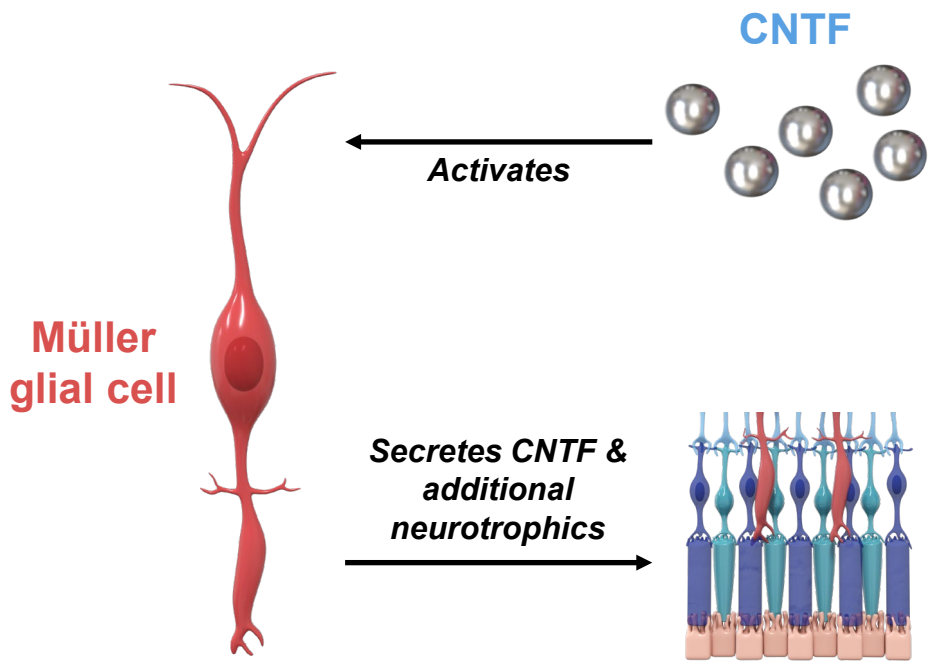
Take-Home Points

- A root cause analysis across six clinical trials of revakinagene taroretcel-lwey for the treatment of MacTel revealed that surgery-related adverse events (AEs) were primarily driven by surgical technique
- Refined surgical protocols and instructions have the potential to significantly reduce AEs and enhance long-term patient outcomes

AE, adverse events; MacTel, macular telangiectasia type 2.

Macular Telangiectasia Type 2 and Ciliary Neurotrophic Factor (CNTF)

- MacTel is a bilateral, progressive, retinal neurodegenerative disease
  - Leads to **central vision loss** and **functional impairment**[1,2]
  - Characterized by abnormalities in macular **Müller glia**, RPE, and photoreceptors,[3] and **progressive loss of ellipsoid zone (EZ)**[4]
- **CNTF**, released from Müller cells under pathologic conditions, **protects and preserves photoreceptors**[5,6]



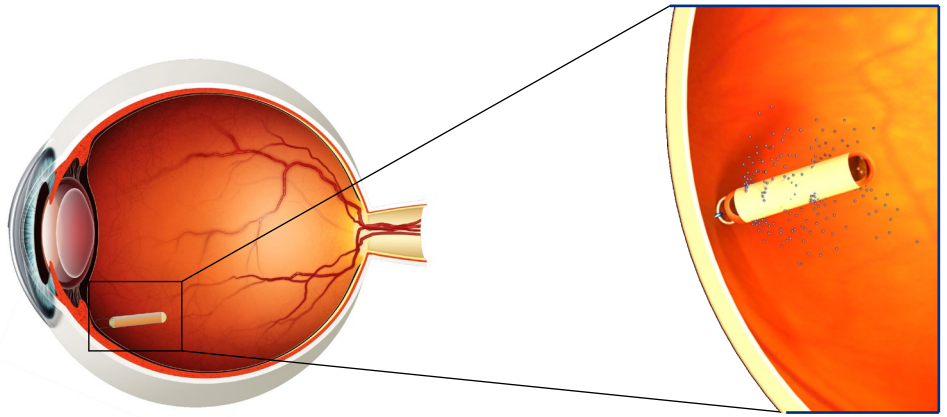
Cell survival pathway activation and macular photoreceptor protection

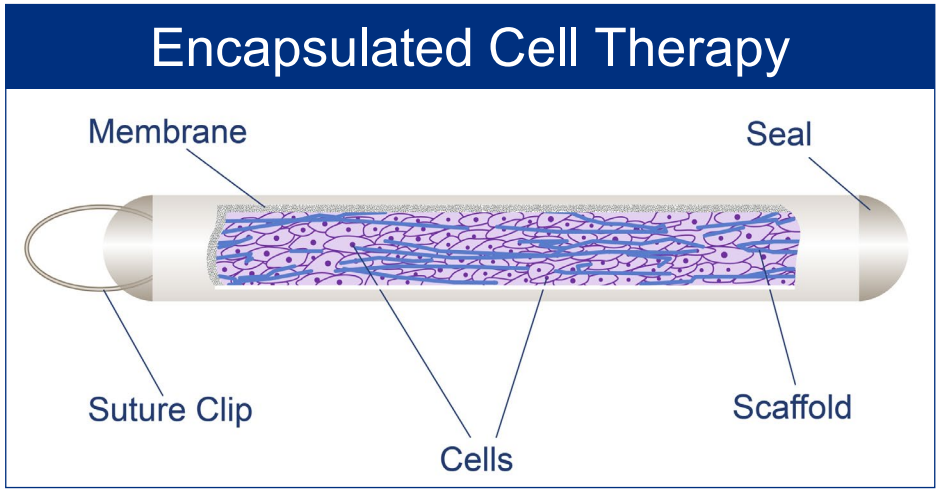
CNTF, ciliary neurotrophic factor; EZ, ellipsoid zone; MacTel, macular telangiectasia type 2; RPE, retinal pigment epithelium.

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.** Kedarisetti KC, et al. *Clin Ophthalmol*. 2022;16:3297-3309. **4.** Heeren TFC, et al. *Retina*. 2018;38(suppl 1):S20-S26. **5.** Bringmann A, et al. *Prog Retin Eye Res*. 2006;25:397-424. **6.** Rhee KD, et al. *Proc Natl Acad Sci U S A*. 2013;110:E4520-E4529.

Encapsulated Cell-Based Gene Therapy: Intravitreal Sustained CNTF Delivery System

- **Revakinagene taroretcel-lwey** (formerly known as NT-501) was **approved by the FDA** on March 5, 2025 for the **treatment of adults with idiopathic macular telangiectasia type 2 (MacTel)**
- This first-in-class encapsulated cell-based gene therapy has been shown to release sustained CNTF for >14 years following a one-time surgical implantation[1,2]
  - Surgical procedure is designed to support ≥10-year retention
- Efficacy and safety of the treatment were demonstrated in two pivotal Phase 3 clinical trials[2]

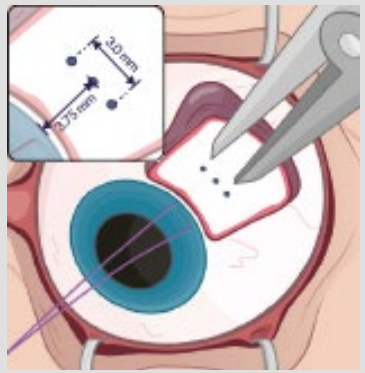




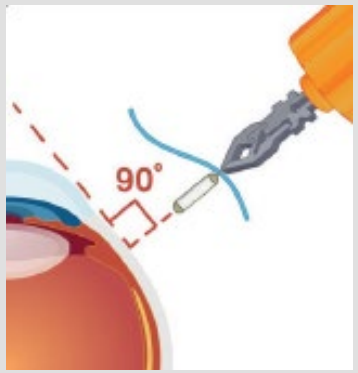
CNTF, ciliary neurotrophic factor; FDA, US Food and Drug Administration; MacTel, macular telangiectasia type 2.

1. Kauper K, et al. *Invest Ophthalmol Vis Sci*. 2025;66:3. **2.** Chew EY, et al. *NEJM Evid*. 2025;4:EVIDoa2400481.

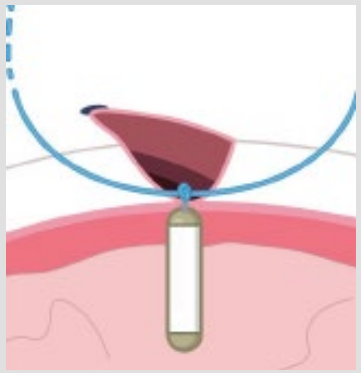
Revakinagene Taroretcel-lwey Is Surgically Implanted Into the Vitreous Cavity[1]



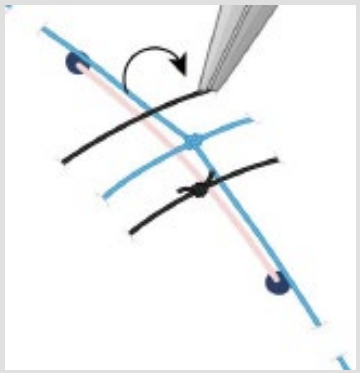
Implanted through 3.0 mm pars plana incision



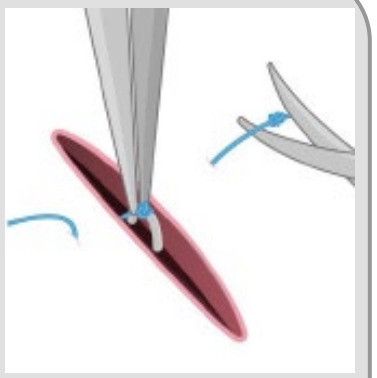
Resides outside of the visual axis



Anchored with a polypropylene knot



Incision is closed with nylon sutures



Explantable if necessary

1. ENCELTO [Instructions for Use]. Cumberland, RI: Neurotech Pharmaceuticals; 2025.

Objective of the Root Cause Analysis

- Identify root causes of surgery-related AEs associated with revakinagene taroretcel-lwey in the treatment of MacTel

AE, adverse event; MacTel, macular telangiectasia type 2.

Root Cause Analysis of Six Revakinagene Taroretcel-lwey Clinical Trials

- Revakinagene taroretcel-lwey has been studied in six clinical trials for MacTel[a]
  - 220 revakinagene taroretcel-lwey–treated eyes
  - 162 eyes underwent sham surgery
- Data analyzed:
  - Integrated summary of safety
  - Ocular AEs and serious AEs (SAEs)
- Ocular AE and SAE data analyzed:
  - AE reporting forms
  - Surgical reports
  - Clinic images and surgical videos (if available)

[a]NCT01327911, NCT01949324, NCT04729972, NCT03071965, NCT03316300, NCT03319849.
AE, adverse event; MacTel, macular telangiectasia type 2; SAE, serious adverse event.

US-EO-SC-26010001

Surgery-Related Ocular AEs Were Identified

Surgery-related ocular AEs that occurred in **≥5% of participants** treated with revakinagene taroretcel-lwey were identified

↓

Among these identified events, AEs occurring in treated participants at an **incidence ≥5% higher** than among those undergoing sham surgery were identified

↓

Identified cases were reviewed by investigators to **identify the root causes**

AE, adverse event.

Surgery-Related Ocular AEs Occurring in ≥5% of Treated Eyes During Six Clinical Trials[a]

Surgery-Related Ocular Adverse Events[a], n (%)	Revakinagene Taroretcel-lwey (n=220)	Sham (n=162)	Difference Between Treatment and Sham (%)
Conjunctival hemorrhage	59 (26.8)	46 (28.4)	−1.6
Eye irritation	52 (23.6)	45 (27.8)	−4.2
Eye pain	46 (20.9)	19 (11.7)	9.2
Vision blurred	45 (20.5)	37 (22.8)	−2.3
Foreign body sensation	25 (11.4)	20 (12.3)	−0.9
Suture-related complication	24 (10.9)	4 (2.5)	8.4
Pruritus	22 (10.0)	11 (6.8)	3.2
Ocular discomfort	21 (9.5)	4 (2.5)	7.0
Conjunctival hyperemia	16 (7.3)	9 (5.6)	1.7
Eye swelling	14 (6.4)	7 (4.3)	2.1
Dry eye	13 (5.9)	6 (3.7)	2.2
Vitreous hemorrhage	13 (5.9)	0	5.9
Conjunctival edema	11 (5.0)	8 (4.9)	0.1
Vitreous floaters	11 (5.0)	1 (0.6)	4.4

[a]Includes surgery-related adverse events that occurred in ≥5% of the treated population.

Late-Onset Vitreous Hemorrhage Was Related to Progressive Revakinagene Taroretcel-lwey Extrusion

19/220 (8.6%) treated eyes developed vitreous hemorrhage (related and unrelated to surgery)

10 cases occurred within 90 days postsurgery

9 cases were late onset, occurring >365 days postsurgery

1 was serious and related to surgery, leading to explantation

Analysis showed that cases of late-onset vitreous hemorrhage were due to progressive implant extrusion

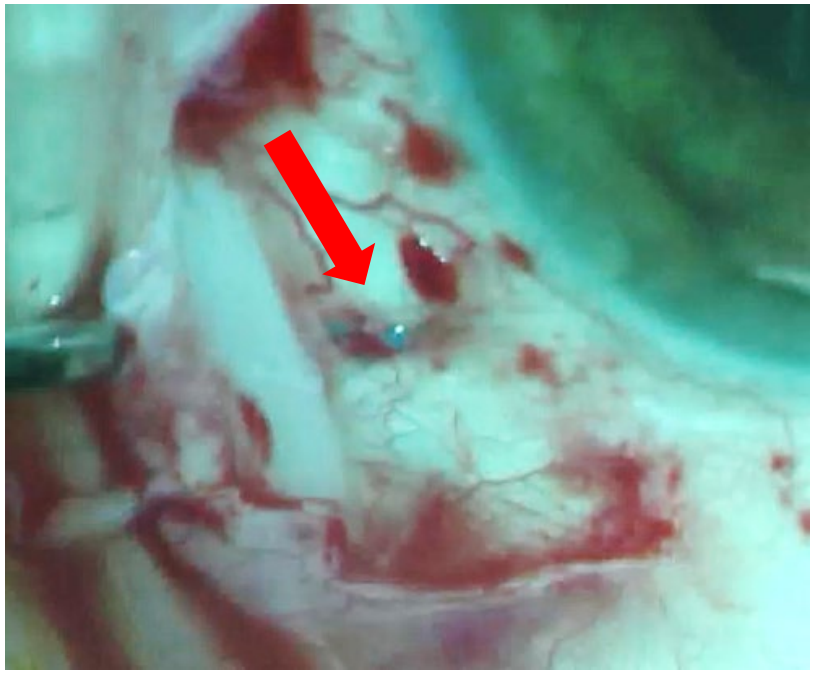


Image provided by Dr. Thomas Aaberg, Jr.

Surgery-Related Ocular SAEs Occurred in 11 Treated Eyes

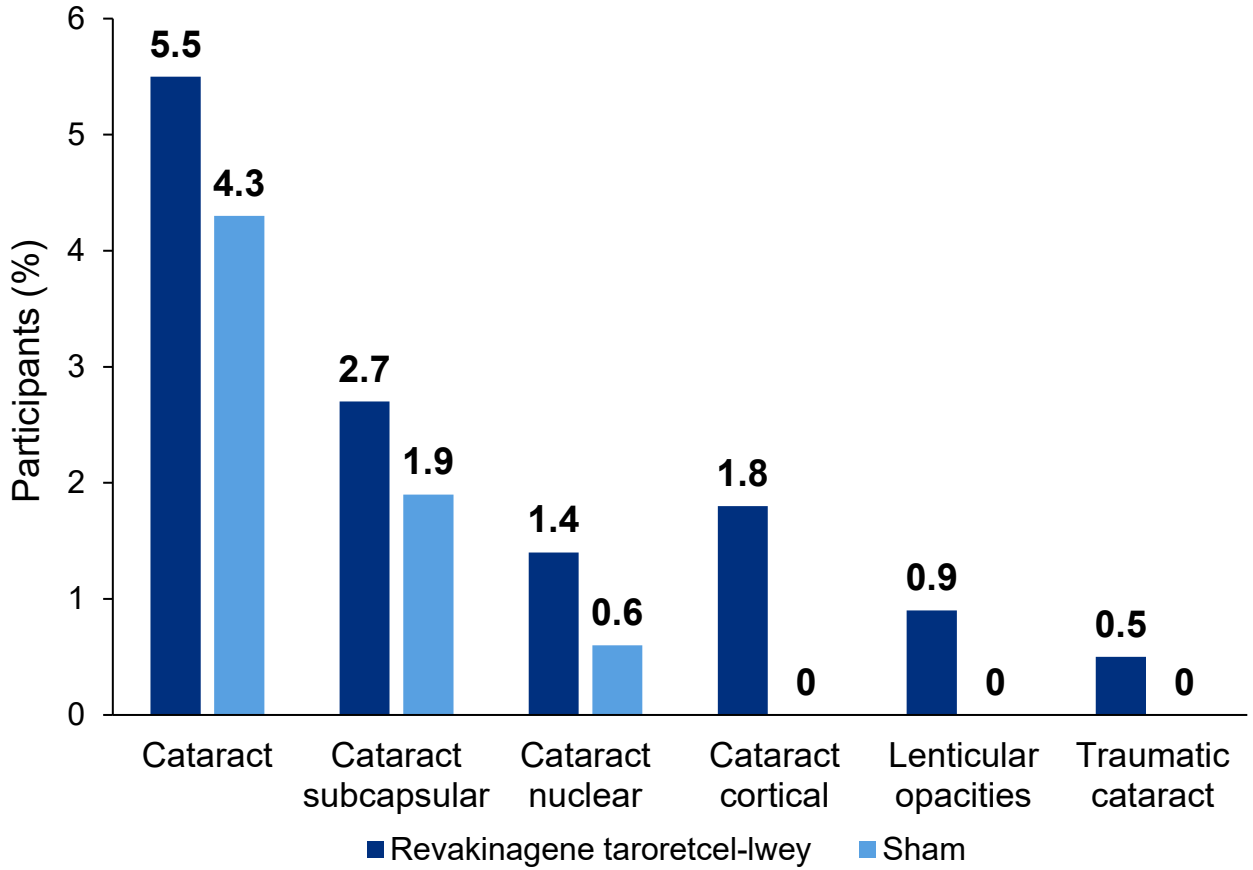
	Revakinagene Taroretcel-lwey (n=220)	Sham (n=162)
All surgery-related ocular SAEs, n (%)	**11 (5.0)**	**2 (1.2)**
Suture-related complication	5 (2.3)	0
Device extrusion	2 (0.9)	0
Vision blurred	2 (0.9)	2 (1.2)
Device expulsion	1 (0.5)	0
Vitreous hemorrhage	1 (0.5)	0

- Rate of explantation across all six MacTel trials was 1.4% (three eyes) with a mean (SD) time to explantation of 75.6 (43.2) months
  - Three cases of explantation due to:
    - Device extrusion related to surgical procedure; reported as serious
    - Vitreous hemorrhage and device expulsion; both reported as serious
    - Suture-related complication; reported as nonserious

MacTel, macular telangiectasia type 2; SAE, serious adverse event; SD, standard deviation.

Cataract Formation Occurred More Commonly in Treated Eyes Vs Sham

- All-cause cataract[a] formation:
  - 28 treated eyes (12.7%)
  - 11 eyes in sham group (6.8%)
- Higher rate may be due to:
  - Surgical trauma
  - Malpositioned capsule placement
  - CNTF



All-cause cataract was created by combining MedDRA preferred terms of cataract, cataract subscapsular, cataract nuclear, cataract cortical, lenticular opacities, and cataract traumatic.
CNTF, ciliary neurotrophic factor; MedDRA, Medical Dictionary for Regulatory Activities.

Root Cause Analysis Conclusions: Surgery-Related Ocular AEs Related to Surgical Technique

Analysis findings and conclusions

Surgical technique

- Scleral fixation
- Scleral wound closure
- Post-op suture removal
- Knot-tying technique and suture tail management

Resulting ocular AEs:

- Suture-related complication
- Implant extrusion/expulsion
- Late-onset vitreous hemorrhage

AE, adverse event.

Surgery-Related Ocular AEs May Be Mitigated With Proper Surgical Technique

- Investigators determined that surgery-related AEs likely to be mitigated through proper:
  - Wound construction
  - Revakinagene taroretcel-lwey insertion
  - Implant fixation
  - Wound closure

AE, adverse event.

Implementation of Surgical Procedure Changes

New anchor knot and suture tail instructions

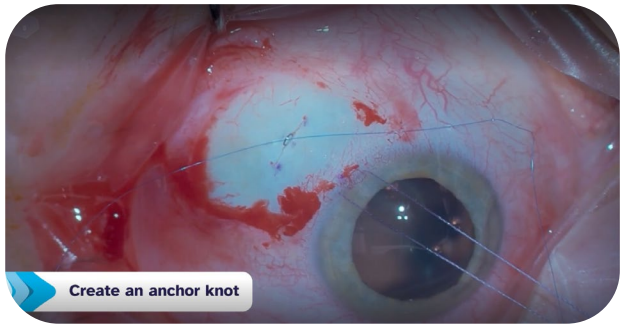
- Use a secure 3-1-1 knot at the apex of the titanium fixation loop and to tie to the sclera
- Bury the prolene suture tails into the sclera to reduce the risk of conjunctival erosion and suture irritation

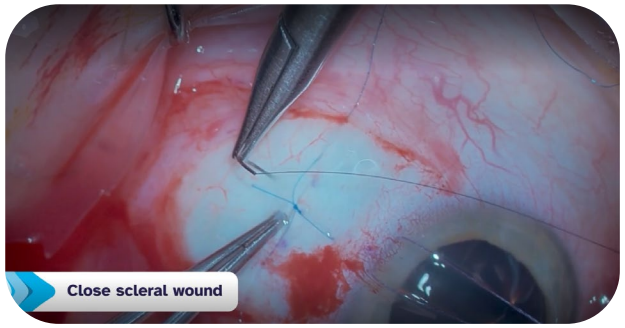
Revised recommendation for location, depth, and order of scleral suture placement

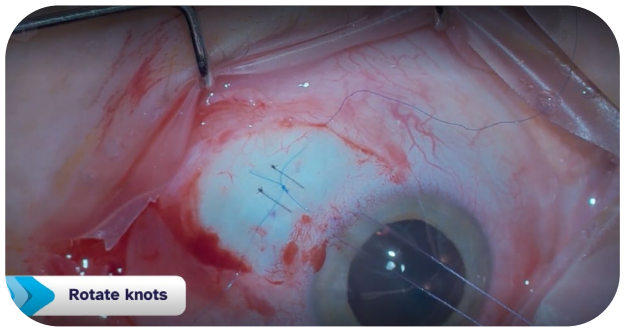
- Prolene suture is NOT a wound closure suture
- Nylon sutures divide the wound into thirds
- Interrupted nylon sutures only

Rotation of nylon suture knots into the sclera is a critical step

- Try 3-1-1 knot first; if it cannot be rotated into the sclera, try replacing that suture and using a 1-1-1 adjustable/locking “Dangel” knot







Take-Home Points

- A root cause analysis across six clinical trials of revakinagene taroretcel-lwey for the treatment of MacTel revealed that surgery-related adverse events (AEs) were primarily driven by surgical technique
- Refined surgical protocols and instructions have the potential to significantly reduce AEs and enhance long-term patient outcomes

AE, adverse event; 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
- Writing and editorial assistance was provided by Elizabeth McSpiritt, MD, MPH, and Christina Mulvihill, PharmD, of Peloton Advantage, LLC, an OPEN Health company, and was funded by Neurotech Pharmaceuticals

MacTel, macular telangiectasia type 2.