MEIRAGTx

AAO 2019 Data Review

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President and CEO, MeiraGTx

MeiraGTx Forward-Looking Statements

Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. All statements contained in this presentation that do not relate to matters of historical fact should be considered forward-looking statements, including, without limitation, statements regarding expectations relating to meetings with global regulatory authorities and the FDA, product pipeline, anticipated product benefits, goals and strategic priorities, product candidate development and status and expectations relating to clinical trials, growth expectations or targets and pre-clinical and clinical data expectations in respect of collaborations, as well as statements that include the words “expect,” “intend,” “plan,” “believe,” “project,” “forecast,” “estimate,” “may,” “should,” “anticipate” and similar statements of a future or forward-looking nature. These forward-looking statements are based on management’s current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements, including, but not limited to, our incurrence of significant losses; any inability to achieve or maintain profitability, acquire additional capital, identify additional and develop existing product candidates, successfully execute strategic priorities, bring product candidates to market, build-out the manufacturing facility and processes, successfully enroll patients in and complete clinical trials, accurately predict growth assumptions, recognize benefits of any orphan drug designations, retain key personnel or attract qualified employees, or incur expected levels of operating expenses; failure of early data to predict eventual outcomes; failure to obtain FDA or other regulatory approval for product candidates within expected time frames or at all; the novel nature and impact of negative public opinion of gene therapy; failure to comply with ongoing regulatory obligations; contamination or shortage of raw materials; changes in healthcare laws; risks associated with our international operations; significant competition in the pharmaceutical and biotechnology industries; dependence on third parties; risks related to intellectual property; litigation risks; and the other important factors discussed under the caption “Risk Factors” in our most recent quarterly report on Form 10-Q or annual report on Form 10-K or subsequent 8-K reports, as filed with the Securities and Exchange Commission. These and other important factors could cause actual results to differ materially from those indicated by the forward-looking statements made in this presentation. Any such forward-looking statements represent management’s estimates as of the date of this presentation. While we may elect to update such forward-looking statements at some point in the future, unless required by law, we disclaim any obligation to do so, even if subsequent events cause our views to change. Thus, one should not assume that our silence over time means that actual events are bearing out as expressed or implied in such forward-looking statements. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this presentation. Unless otherwise stated or the context otherwise requires, the information herein is as of October 10, 2019.

MeiraGTx AAO 2019 Data Review Agenda

- **Introduction** l Alexandria Forbes, Ph.D.
  - Welcome
  - MeiraGTx overview
  - Introduction to AAV2/5-OPTIRPE65

- **MGT003: A Phase 1/2 Study of AAV2/5-OPTIRPE65** l Michel Michaelides, MD, FRCOphth
  - Disease overview
  - Safety
  - Efficacy and Assessment Validation
    - Vision-Guided Mobility
    - Retinal Sensitivity
    - Central Visual Function
  - Conclusion

- **Q&A** l Michel Michaelides; Alexandria Forbes; Stuart Naylor; Richard Giroux

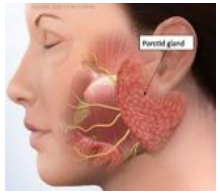
A Vertically Integrated, Clinical Stage Gene Therapy Company

Developing a new pharmaceutical modality designed for the cost-effective treatment of a broad range of serious disorders

Diversified Pipeline of Gene Therapy Candidates

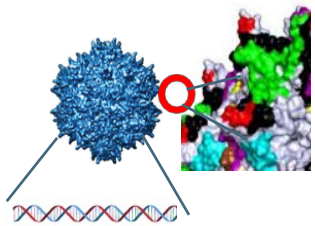
6 ongoing clinical programs:

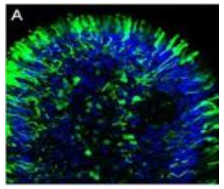
- Inherited retinal diseases
- Salivary gland
- Parkinson's Disease



Platform of Core Viral Vector Engineering Capabilities

Viral vector design, promoters, capsid, transgene optimization, **process development** expertise



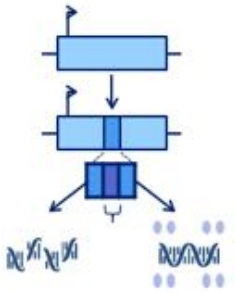


Manufacturing Capacity & Know-How

Flexible and **scalable cGMP manufacturing facility** with capacity for commercial supply for all our programs

Next Generation Gene Therapy Riboswitch-Based Gene Regulation

Proprietary technology that may allow for innovative gene therapy treatments whose **expression can be turned on and off** with an easily administered small molecule



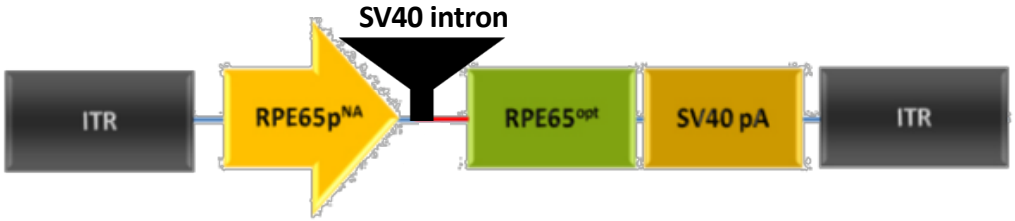
Broad Clinical Pipeline

Product	Indication	Preclinical	Phase 1/2	Details
Ocular				
AAV-RPE65	***RPE65*-associated retinal dystrophy**	**RPDD, Orphan Drug**		
AAV-CNGB3*	Achromatopsia (CNGB3)	RPDD, PRIME, Fast Track, Orphan Drug		janssen
AAV-RPGR*	X-linked RP (RPGR)	Fast Track, Orphan Drug		janssen
AAV-CNGA3*	Achromatopsia (CNGA3)	RPDD, Orphan Drug		janssen
AAV-AIPL1	LCA4 (AIPL1)	Orphan U.S. & EU		EU Compassionate Use under Specials License
A006	Wet AMD (anti-VEGFR2)			
Neurodegenerative Disease				
AAV-GAD	Parkinson's Disease (GAD)			45 patient Phase 2 trial complete, regulatory path intended to be discussed with FDA in 2019
Salivary Gland				
AAV-AQP1	Xerostomia (hAQP1)	Orphan Drug		Phase 1 study at NIH ongoing; multi-site Phase 1/2 trial ongoing
AAV-AQP1	Sjögren's Syndrome (hAQP1)			

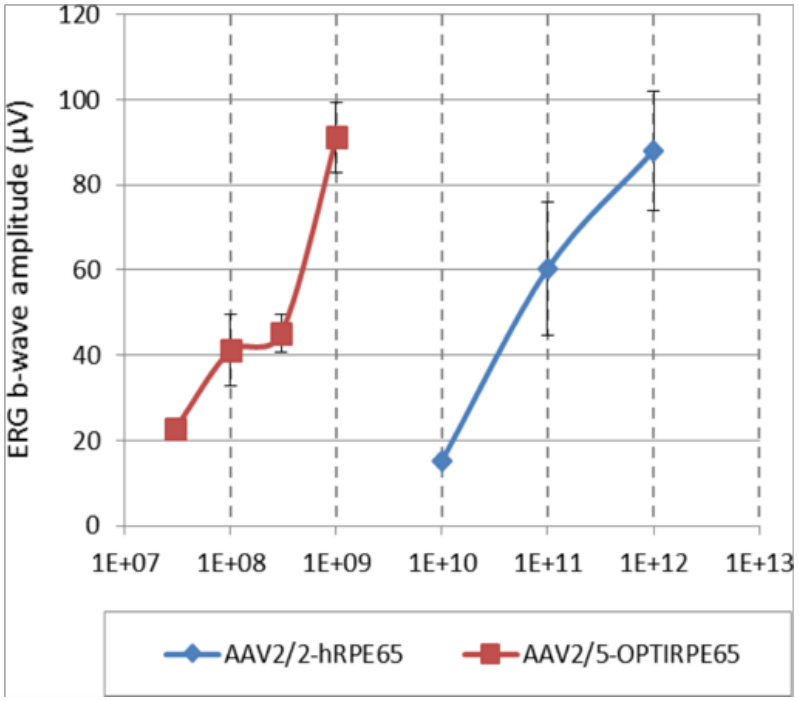
*Co-development program with Janssen Pharmaceuticals pursuant to a collaboration agreement.

MeiraGTx Vector Development Expertise:
AAV2/5-OPTIRPE65 Vector Optimization

Vector optimized to increase efficiency of transduction, transcription and translation



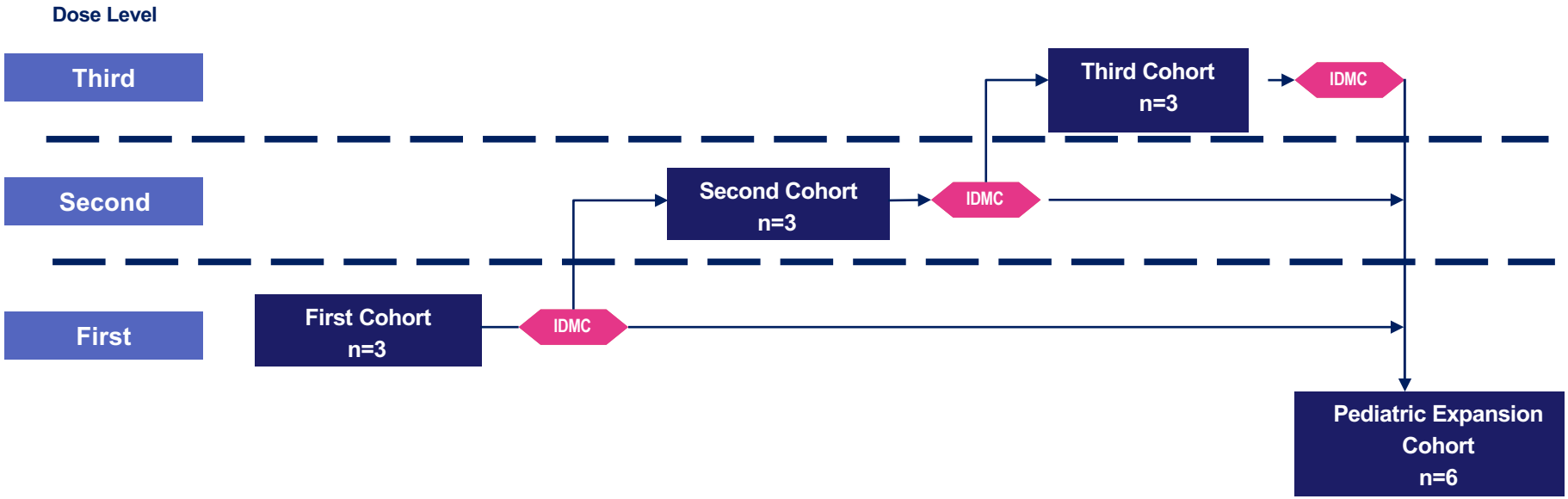
- **AAV5 capsid selected over AAV2 capsid** → 4x transfection efficiency of human RPE cells
- **RPE cell-specific promoter** → 20x protein expression in the RPE cells
- **Optimized transgene sequence** → 7x protein expression in human cells through codon-optimization and an optimized Kozak sequence; added SV40 intron sequences regulatory sequences to improve RNA processing resulting in 2.5x increased mRNA stability



In RPE65-deficient mice, AAV2/5-OPTIRPE65 restores retinal function at 300-1,000-fold lower doses than first generation AAV2/2-RPE65 vector

Georgiadis et al 2016 *Gene Therapy*

MGT003: Phase 1/2 Trial of AAV2/5-OPTIRPE65
Study Design



Key inclusion criteria:
- Aged 3 years or older
- Confirmed biallelic *RPE65*-associated retinal dystrophy
- Structural evidence of photoreceptor preservation on SD-OCT

Primary endpoint:
- Safety and tolerability

Select secondary endpoints to assess activity:
- Vision-guided mobility
- Full-field static perimetry
- BCVA
- Contrast sensitivity
- Reading speed
- Quality of life

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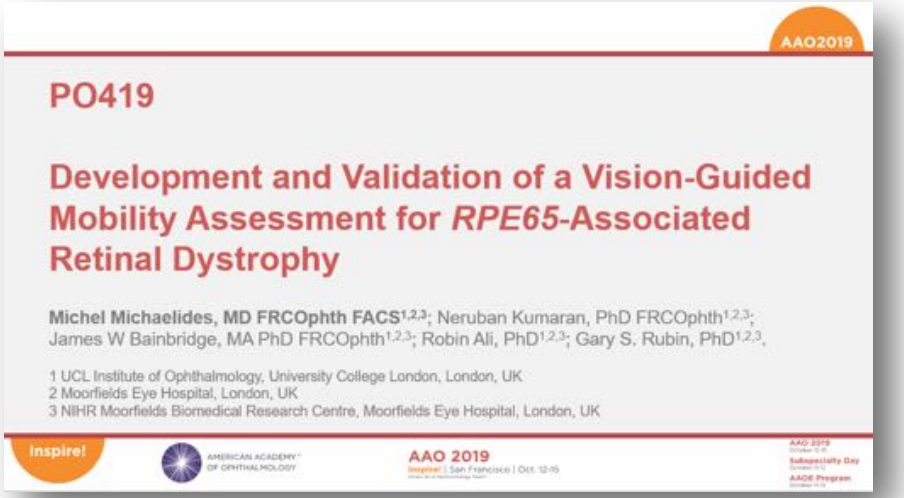
Retina Subspecialty Day
Section XI: Late Breaking Developments, Part II
October 12, 2019



AAO Annual Meeting
Poster Discussion Session: PD38 Retina
October 14, 2019

Michel Michaelides, MD, FRCOphth

- **Professor Michel Michaelides, Consultant Ophthalmic Surgeon, Moorfields Eye Hospital (MEH)**
  - Areas of expertise: Inherited Retinal Disorders, Pediatric Ophthalmology, Genetic Eye Disease
  - 300+ peer-reviewed publications, 25+ book chapters
  - Career Development Award from Foundation Fighting Blindness USA – Award rarely given to a non-US applicant
  - Established a world-class, deep structural and functional phenotyping program at UCL/MEH
    - **20+** new adult and pediatric patients per week
    - **70+** follow up visits per week, including 20-40 pediatric patients

- **Moorfields Eye Hospital**
  - The world's largest catchment of patients with inherited retinal diseases, well characterized patients and prospective Natural History studies
    - **500,000+** total outpatient visits per year
    - **15,000+** affected IRD patients currently being treated
    - **35+** new adult and pediatric IRD patients per week plus 150+ follow-up adult and pediatric IRD patient visits
    - In-house dedicated imaging and functional assessments
  - Moorfields Alumni currently leading centers of excellence around the world

Moorfields Eye Hospital NHS
NHS Foundation Trust

Michel Michaelides, MD, FRCOphth

Consultant Ophthalmic Surgeon, Moorfields Eye Hospital

Professor of Ophthalmology, UCL Institute of Ophthalmology

RPE65 – Associated Retinal Dystrophy

- **Ultra-rare, severe genetic disease that manifests in infancy/early childhood**
- **Caused by mutations in the *RPE65* gene**
- **RPE65 expressed in retinal pigment epithelium (RPE), supporting cells of photoreceptors (rods and cones)**
- **RPE65 required for recycling of the visual pigments allowing photoreceptors to sense light**
- **RPE65-deficiency causes rod-cone retinal dystrophy**
  - Complete lack of rod function from birth
  - Reduced cone function early in life
  - In addition to diminished photoreceptor function, both rods and cones degenerate progressively
  - Complete retinal degeneration in early adulthood

Patient Experience

- Complete lack of rod function
- Night blindness from birth
- Impaired cone function
- Reduced central vision

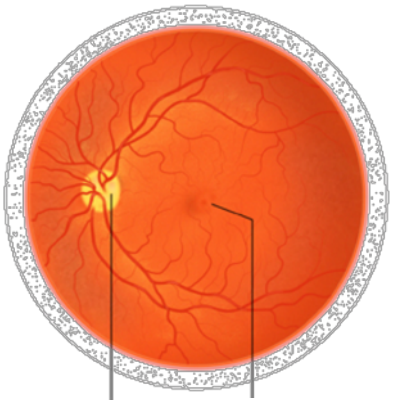
- Cone function impairment progresses over time, impacting central vision
- Rod and cone death through childhood, retinal degeneration with progressive loss of vision

- Complete blindness generally occurs during the third or fourth decade of life

Significant Unmet Need for a Therapy that Safely Treats the Central Region & Fovea

Central visual function is required for many of the most critical aspects of sight:

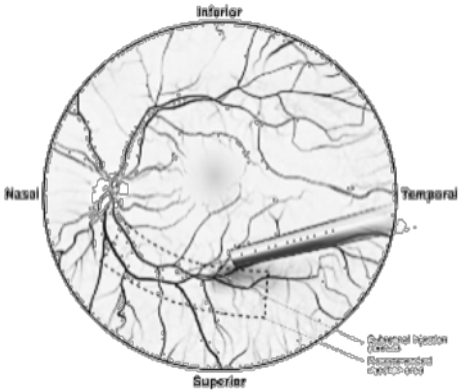
- **Daylight vision, color vision, visual acuity, reading speed, contrast sensitivity**
- **Loss of central visual function most profoundly limits a patient's ability to undertake activities of daily living, including school and work, e.g. reading and recognizing faces**
- **Rod-cone dystrophy – treatment of the central region of the retina required to:**
  - — Improve the function of the central retinal
  - — Improve central vision
  - — Protect central retinal structure from degeneration
  - — Prevent complete blindness



American Academy of Ophthalmology

Therapies not treating the central retina do not address these important patient needs

Luxturna package insert, recommended site of injection



- — Luxturna (AAV2-hRPE65) approved by FDA in 2017
- — Improvement in vision-guided mobility and light sensitivity (FST), both assessments can be driven by peripheral photoreceptors
- — Pivotal study treatment avoided foveal involvement
- — Significant benefit not demonstrated in central visual function (e.g. BCVA, contrast sensitivity, reading speed, central retinal sensitivity)

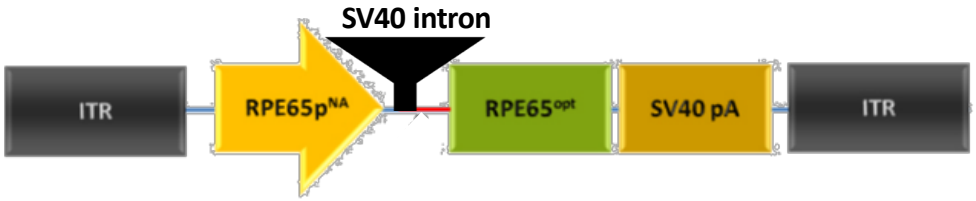
den Hollander *et al*, 2008; Kumaran *et al*, 2017; Weleber et al, 2013; Perrault *et al*, 1999

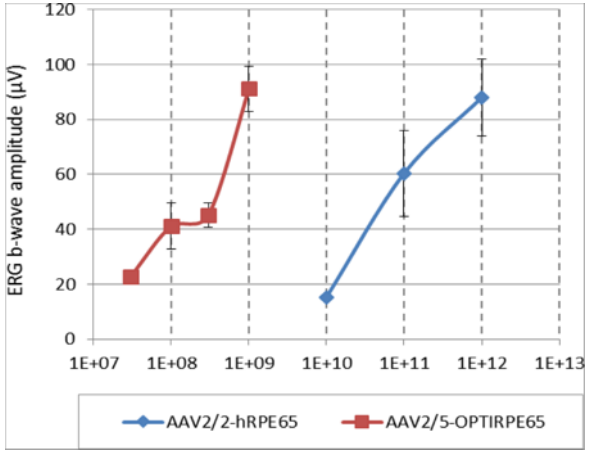
MGT003: Subretinal Administration of Optimized, Potent AAV2/5-OPTIRPE65 Vector to Central Retina, Including the Fovea

Optimized highly potent and cell-specific vector

- **Increased efficiency of transduction, transcription and translation**
  - — RPE strong cell-specific promoter
  - — Optimized transgene sequence
  - — AAV5 capsid selected over AAV2 capsid

AAV2/5-OPTIRPE65

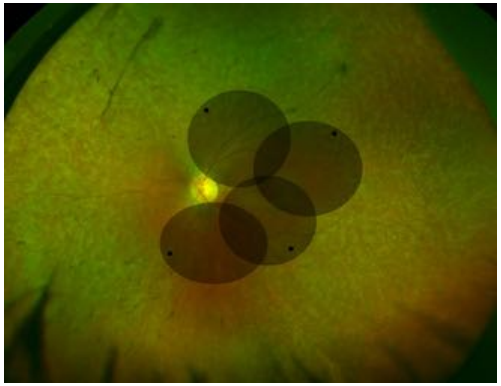




In RPE65-deficient mice, AAV2/5-OPTIRPE65 restores retinal function at 300-1,000-fold lower doses than unoptimized AAV2/2-RPE65 vector

Optimized surgical procedure

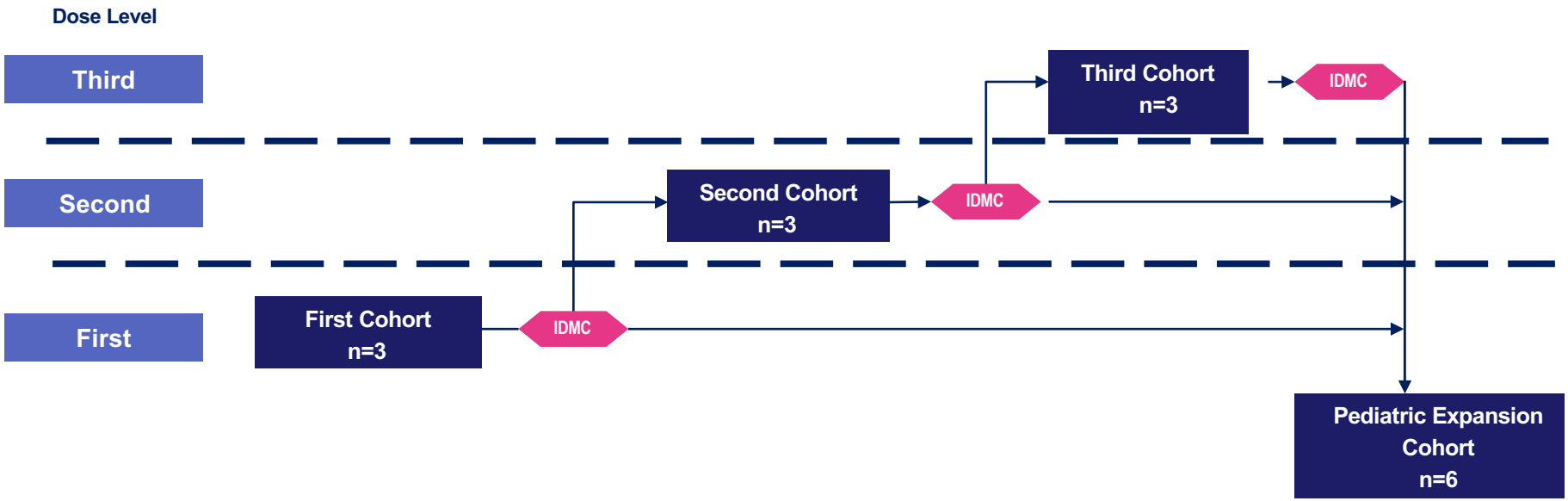
- **Safe and effective coverage of the largest possible area of retina including the fovea**
  - — Subretinal injection
  - — Multiple retinotomies
  - — Volume of up to 1mL



4 subretinal blebs, achieved via 4 retinotomies, targeting the entire central retina and involving a foveal detachment

Georgiadis et al 2016 *Gene Therapy*

MGT003: Phase 1/2 Trial of AAV2/5-OPTIRPE65
Study Design



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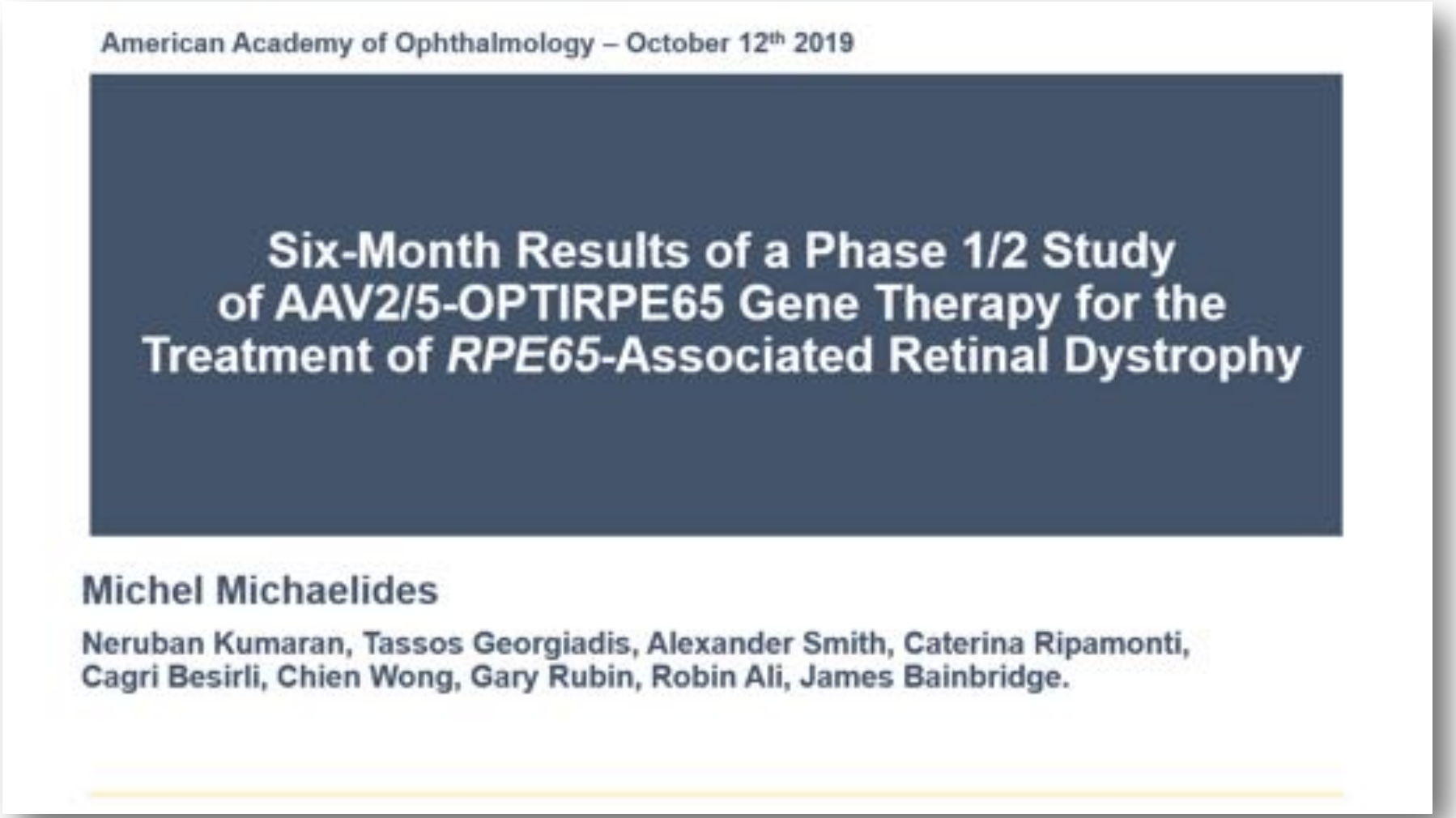
AAO 2019 Retina Subspecialty Day



MGT003: Study Population

	Dose Escalation Phase			Expansion Phase	
	Cohort 1 (1.0×10^{11} vg/mL) (n=3)	**Cohort 2 (3.0×10^{11} vg/mL) (n=3)**	**Cohort 3 (1.0×10^{12} vg/mL) (n=3)**	**Pediatric Cohort (1.0×10^{11} vg/mL) (n=6)**	**Overall (n=15)**
Age at informed consent	19.7	19.0	21.0	9.3	15.7
Age, (range), years	(19-20)	(16-21)	(18-24)	(5-12)	(5-24)
Sex, n (%)					
Male	1 (33.3)	1 (33.3)	3 (100.0)	1 (16.7)	6 (40.0)
Female	2 (66.7)	2 (66.7)	0 (0.0)	5 (83.3)	9 (60.0)
Country					
United States	0	0	0	2 (33.3)	2 (13.3)
United Kingdom	3 (100.0)	3 (100.0)	3 (100.0)	4 (66.7)	13 (86.7)
Adult or pediatric, n (%)					
Adult	3 (100.0)	3 (100.0)	3 (100.0)	0	9 (60.0)
Pediatric	0	0	0	6 (100.0)	6 (40.0)

- **Subjects treated across two clinical sites:**
  - Moorfields Eye Hospital
  - University of Michigan Kellogg Eye Center
- **Three vitreoretinal surgeons administered AAV2/5-OPTIRPE65**

Moorfields Eye Hospital NHS
NHS Foundation Trust

KELLOGG EYE CENTER

MGT003: Dosing and Administration

Differential safety and activity observed in three adult dose escalation cohorts:

Cohort 1: (n=3) 1.0×10^{11} vg/mL – targeted central retina and fovea

- Activity observed, no SAEs or severe treatment-emergent AEs

Cohort 2: (n=3) 3.0×10^{11} vg/mL – peripheral administration

- Reduced activity observed; 2 cases of inflammation (steroid-responsive)

Cohort 3: (n=3) 1.0×10^{12} vg/mL – targeted central retina including fovea

- 1 case of inflammation (steroid-responsive)

Central delivery of 1.0×10^{11} vg/mL determined the optimal treatment:

Pediatric Cohort: (n=6) 1.0×10^{11} vg/mL – targeted central retina and fovea

- Activity observed, no treatment-related SAEs, no inflammation requiring extended steroids

Total population treated at the optimal dose of 1.0×10^{11} vg/mL (n=9; 3 adults, 6 children)

- Central retina including the fovea targeted in all subjects at optimal dose
- In all but 2 cases involved foveal detachment during surgery

Single eye treated in each patient, and the contralateral eye served as control:

Treated eye = worse eye at baseline determined by subject

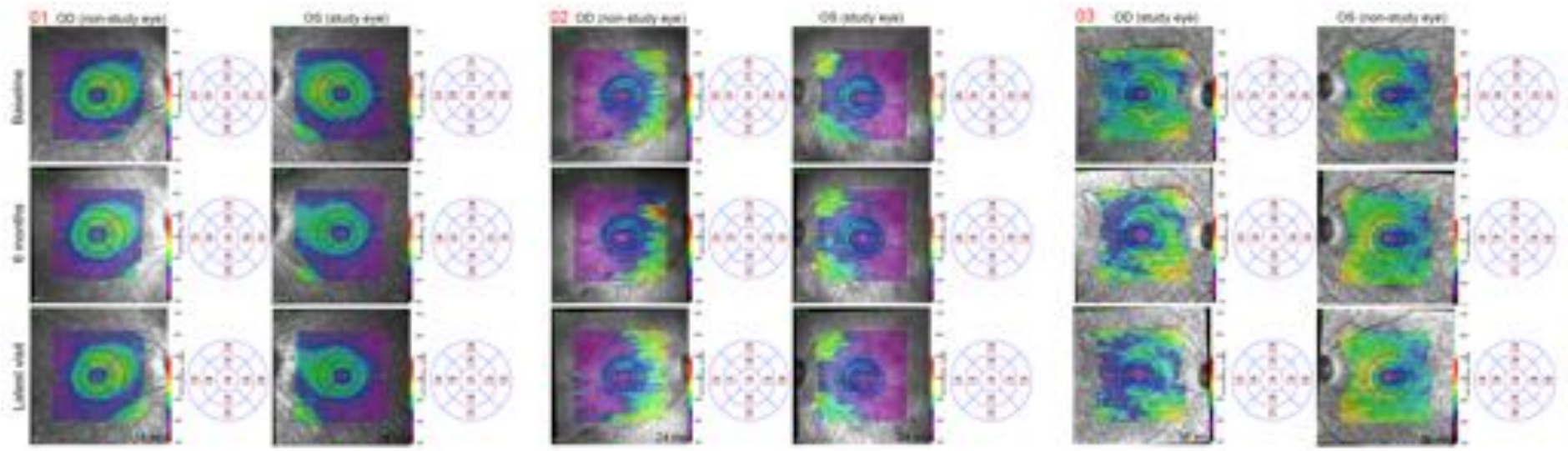
Control eye = eye determined by patient to be the better eye at baseline

For all safety and efficacy statistical analyses, the change in Treated eye from baseline was compared to the change in the Control eye from baseline

MGT003: Safety – Structural

Retinal structure assessed throughout study by OCT and read on a blinded basis by the Belfast Ophthalmic Reading Centre at Queens University

- **No instances of acute retinal thinning in the post-operative period**
- **After up to 36 months, no significant difference in retinal thickness or macular volume**
- **Demonstration of safe treatment of the central region of the retina, including foveal detachment, in RPE65-associated retinal dystrophy**



Baseline (top row), 6-month follow-up (middle row) and latest follow-up (bottom row) of Treated and Control eyes of the adult 1.0×10^{11} vg/mL cohort.

MGT003: AAV2/5-OPTIRPE65 Generally Safe and Well-Tolerated

- Generally well tolerated with an expected safety profile
- Most AEs transient and mild/moderate in severity
- Inflammation observed in 3/6 patients in dose escalation cohorts 2 and 3 - effectively treated with steroid extension
- Inflammation may have mitigated efficacy in these cohorts

MGT003: Selecting Relevant Endpoints in RPE65

Assessment	Screening	Baseline	AAV2/5-OPTIRPE65 Administration	D1	D3	W1	W2	W4	W6	W9	W12	W24
Ocular examination	x	x		x	x	x	x	x	x	x	x	x
Visual mobility		x										x
Octopus static perimetry		x									x	x
Microperimetry		x							x		x	x
Visual acuity (BCVA)	x	x		x	x	x	x	x	x	x	x	x
Contrast sensitivity	x	x									x	x
Reading speed		x									x	x
Color vision		x									x	x
Optical coherence tomography	x	x		x	x	x	x	x	x	x	x	x
Fundus photography		x		x	x	x	x	x	x	x	x	x
Fundus autofluorescence		x									x	x
Adaptive optics imaging		x										x
Flash electroretinography	x	x							x		x	x
Pattern electroretinography	x	x							x		x	x
Multifocal electroretinography	x	x							x		x	x
QOL questionnaires		x										x

- **Blinded independent reading centers used where possible**

UCL INSTITUTE OF OPHTHALMOLOGY

KELLOGG EYE CENTER

BELFAST OPHTHALMIC READING CENTRE

OHSU CASEY EYE Institute

MEDICAL COLLEGE OF WISCONSIN

Moorfields Eye Hospital NHS Foundation Trust NHS

MGT003: Visual Function Efficacy Summary – 6 Months

In population of all subjects treated at $1x10^{11}$ (n=9), statistically significant improvement demonstrated in multiple assessment of visual function and functional vision:

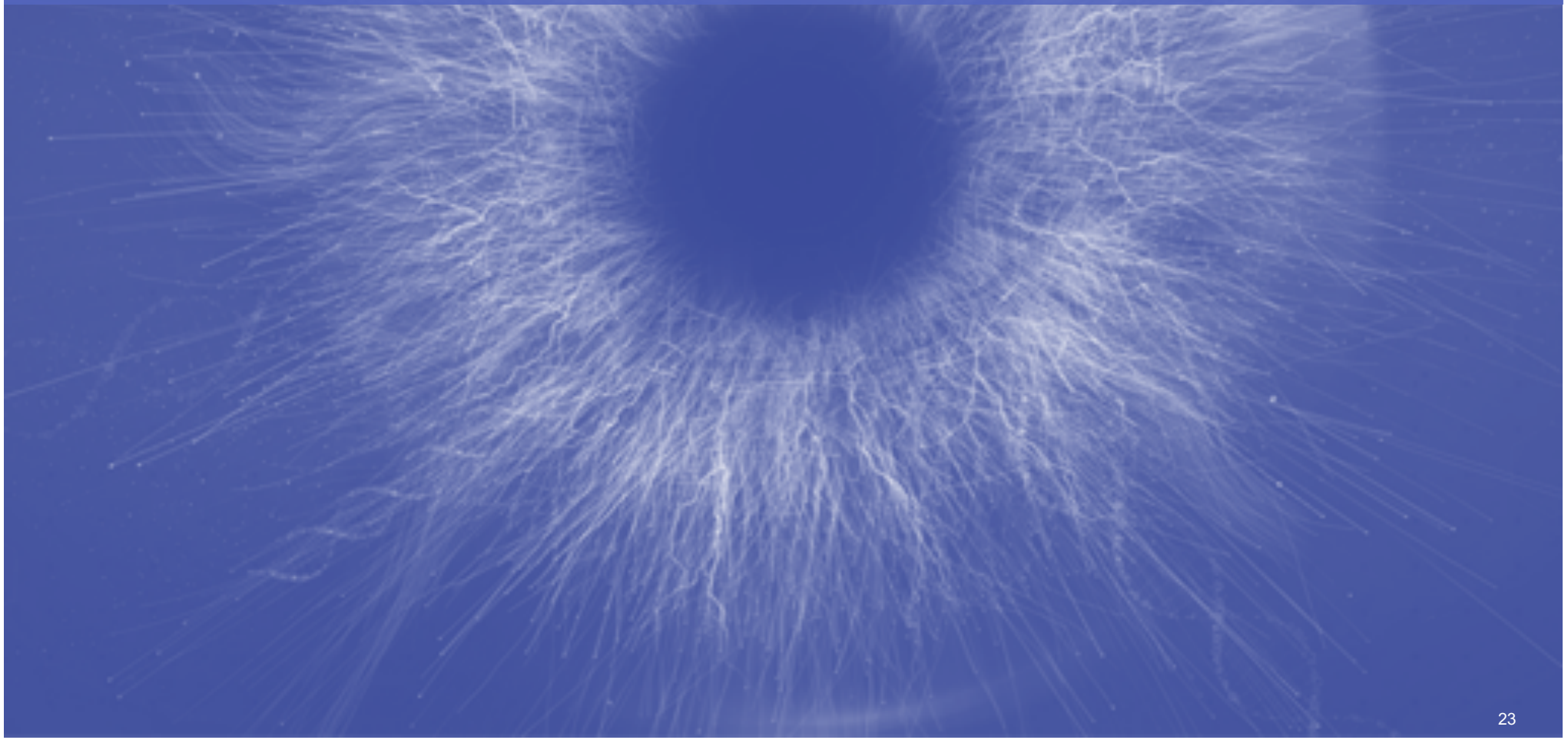
- Vision-guided mobility
- Retinal sensitivity
- Key measures of foveal function

Summary of visual function change from baseline: Treated eye vs baseline compared to Control eye vs baseline ($1x10^{11}$ vg/mL dose)

	Vision-Guided Mobility Maze (seconds)	Retinal Sensitivity, Total* (dB-sr)	Retinal Sensitivity, Central 30° * (dB-sr)	Visual Acuity (ETDRS letters read)	Contrast Sensitivity* (LogCS)	Reading Speed* (words/min)
Mean (SD)	-107.7 (101.5)	9.4 (8.9)	1.87 (1.62)	3.9 (3.4)	0.18 (0.129)	13.2 (14.99)
Median (Min: Max)	-80.3 (-307.5: -26.1)	8.3 (0.2: 22.7)	1.21 (0.2: 5.5)	4.3 (-1: 8)	0.18 (0.0: 0.42)	16.7 (-13: 27)
Signed Rank test P-value	**0.004**	**0.008**	**0.008**	**0.016**	**0.016**	**0.078**

*n=8: one young child unable to complete static perimetry, contrast sensitivity or reading assessments

Vision-Guided Mobility Maze



Vision-Guided Mobility Maze

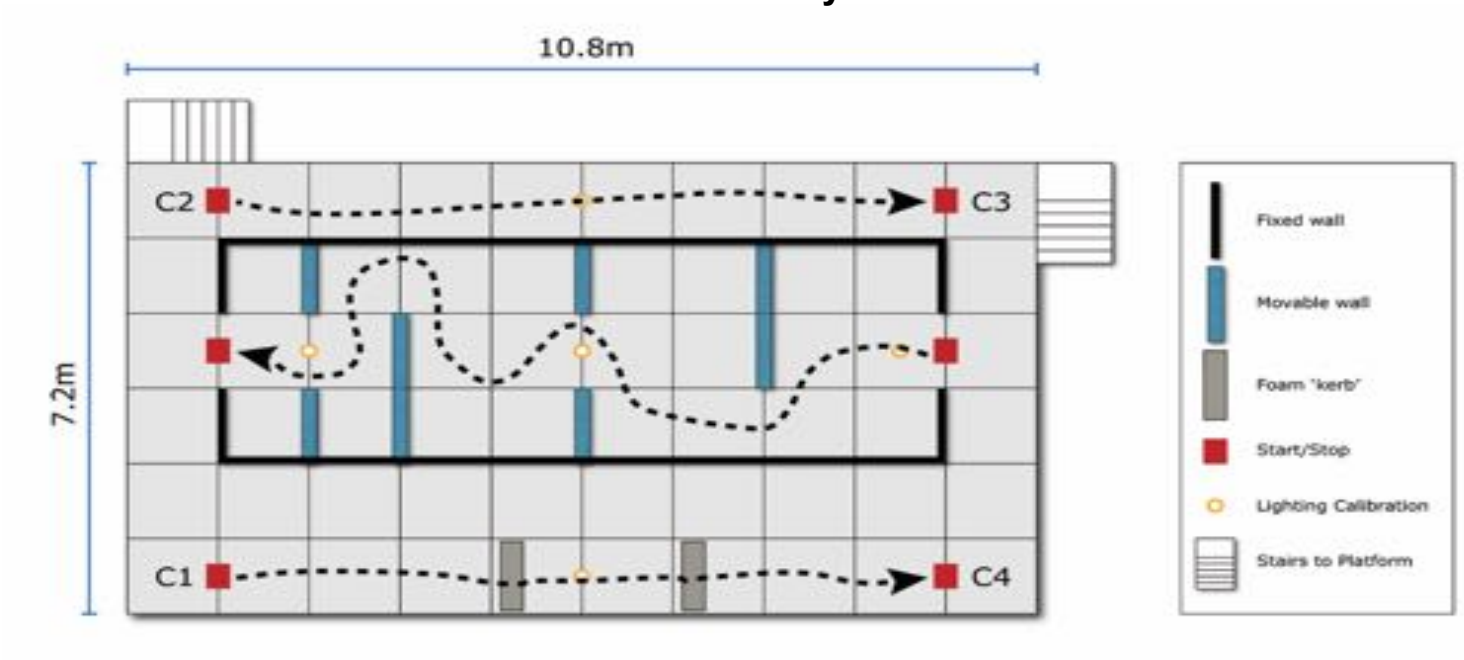
Vision-guided mobility: the ability to use sight to move through the environment in an orderly, safe and efficient manner

- **Vision-guided mobility assessment validated for *RPE65*-associated retinal dystrophy**
- **Life-size simulated sidewalk environment**
  - 13m maze with moveable barriers (8 different configurations)
- **Subjects walk through assessments at 5 computer-controlled light levels**
- **Subjects tested monocularly, with the contralateral eye patched, and performed tests in decreasing order of light level**

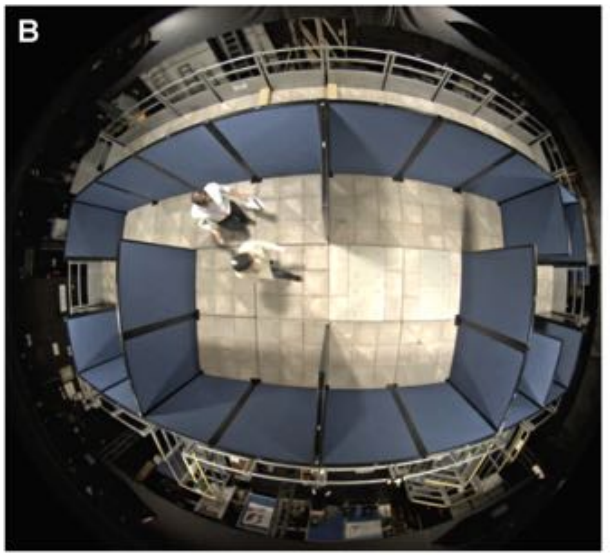
Illumination level (lux)	Equivalent real-world environment
1	Deep twilight
4	Residential street lighting
16	Twilight
64	Car park
256	Office work

Vision-Guided Mobility Maze

Schematic of Vision-Guided Mobility Maze



(A) Raised platform. (B) 'Fisheye' view from overhead camera showing the maze being completed by a participant and followed by a grader.



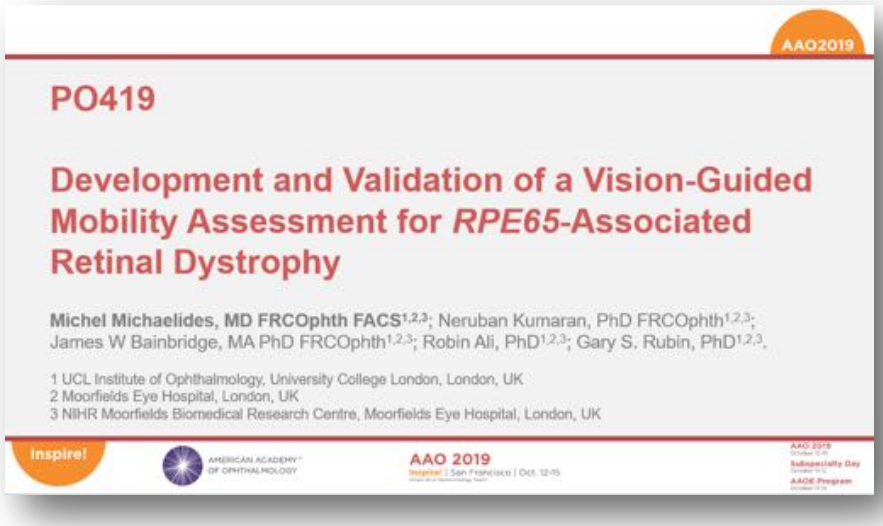
RPE65 Vision-Guided Mobility Maze: Validation Study

Unaffected

- **Ten unaffected individuals: five adults (aged 29-58) and five children (aged 7-10) undertook the assessment following the standard operating procedure**
- **Travel time and mobility errors *did not increase* significantly with decreasing illumination**

RPE65-Associated Retinal Dystrophy Subjects

- **32 *RPE65*-associated retinal dystrophy natural history study participants: aged 9-25**
- **Travel time and mobility errors *increase* rapidly with decreasing illumination**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Development and Validation of a Vision-Guided Mobility Assessment for *RPE65*-Associated Retinal Dystrophy

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Inspire!

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Maze is sensitive to the specific visual impairment of individuals with *RPE65*-associated retinal dystrophy, with course time discriminating between *RPE65*-associated retinal dystrophy and unaffected subjects

Treatment with AAV2/5-OPTIRPE65 Resulted in Significant Improvement in Vision-Guided Mobility

Summary of vision-guided mobility (functional vision) change from baseline: Treated eye vs baseline compared to Control eye vs baseline ($1x10^{11}$ vg/mL dose)

n=9	Vision-Guided Mobility Maze, All Lux Levels (seconds)	Vision-Guided Mobility Maze, 1 Lux (seconds)	Vision-Guided Mobility Maze, 4 Lux (seconds)	Straight-Line Path, All Lux Levels (seconds)	Path with Curbs, All Lux Levels (seconds)
Mean (SD)	-107.7 (101.5)	-23.63 (23.56)	-34.19 (21.5)	-14.03 (10.07)	-32.1 (43.32)
Median (Min: Max)	-80.3 (-307.5: -26.1)	-14.8 (-44.5: -10.8)	-25.7 (-67.8: -14.1)	-14.1 (-28.1: 3.7)	-27.7 (-122.3: 30.7)
Signed Rank test P-value	**0.004**	**0.023**	**0.004**	**0.008**	**0.043**

- Statistically significant improvement in visual mobility demonstrated across all the light levels
- Treatment effect most apparent at the lowest lighting levels (1 and 4 lux)
- Statistically significant benefit at 1 lux and 4 lux
- Treatment effect is further supported by statistically significant improvement across all lux levels in the straight-line path and path with curbs assessments

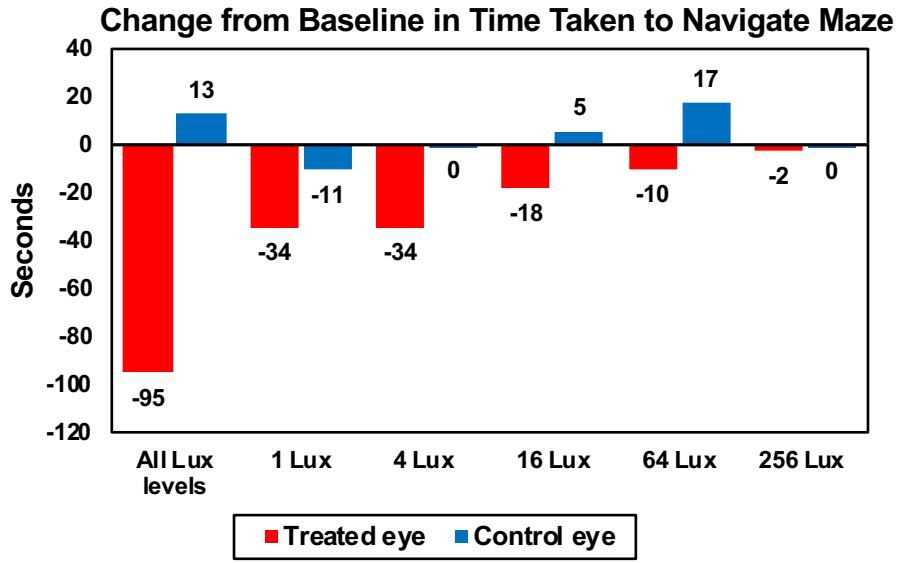
Significantly reduced times through the mobility assessments provides functional measure of meaningful improvement in patients' ability to navigate their surroundings in low-light conditions

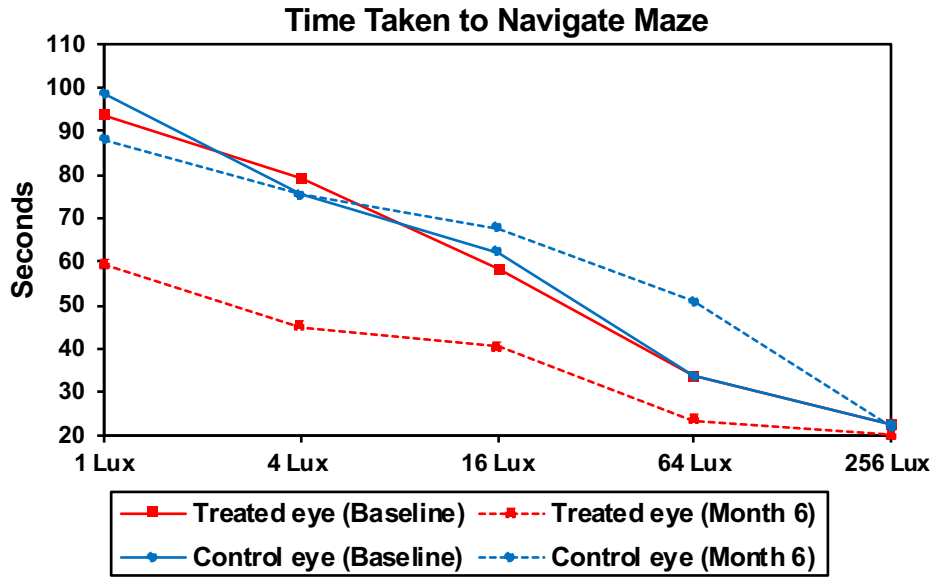
MGT003: Significant Improvement in Vision-Guided Mobility
All $1x10^{11}$ Subjects

Significant reduction in time taken to navigate maze in Treated eye vs baseline compared to Control eye vs baseline:

- **All Lux levels: -107.7 seconds; p=0.004**
- **1 Lux: -23.63 seconds; p=0.023**
- **4 Lux: -34.19 seconds; p=0.004**
- **Most meaningful improvement demonstrated at low light levels**

Lux level	Equivalent real-world environment
1	Deep twilight
4	Residential street lighting
16	Twilight
64	Car park
256	Office work



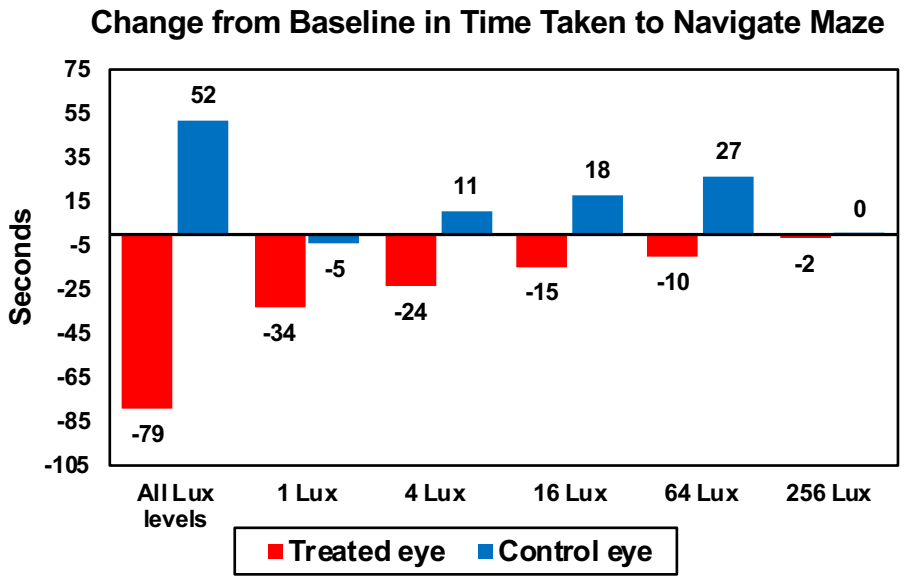


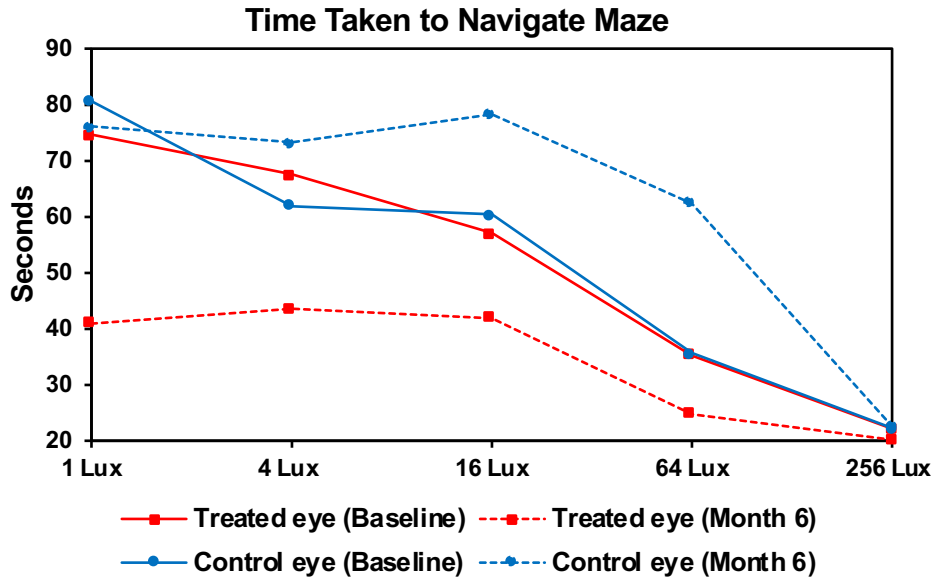
MGT003: Significant Improvement in Vision-Guided Mobility
All Children

Significant reduction in time taken to navigate maze in Treated eye vs baseline compared to Control eye vs baseline:

- **All Lux levels: -131.52 seconds; p=0.031**
- **1 Lux: -29.06 seconds; p=0.063**
- **4 Lux: -34.88 seconds; p=0.031**
- **Most meaningful improvement demonstrated at low light levels**

Lux level	Equivalent real-world environment
1	Deep twilight
4	Residential street lighting
16	Twilight
64	Car park
256	Office work

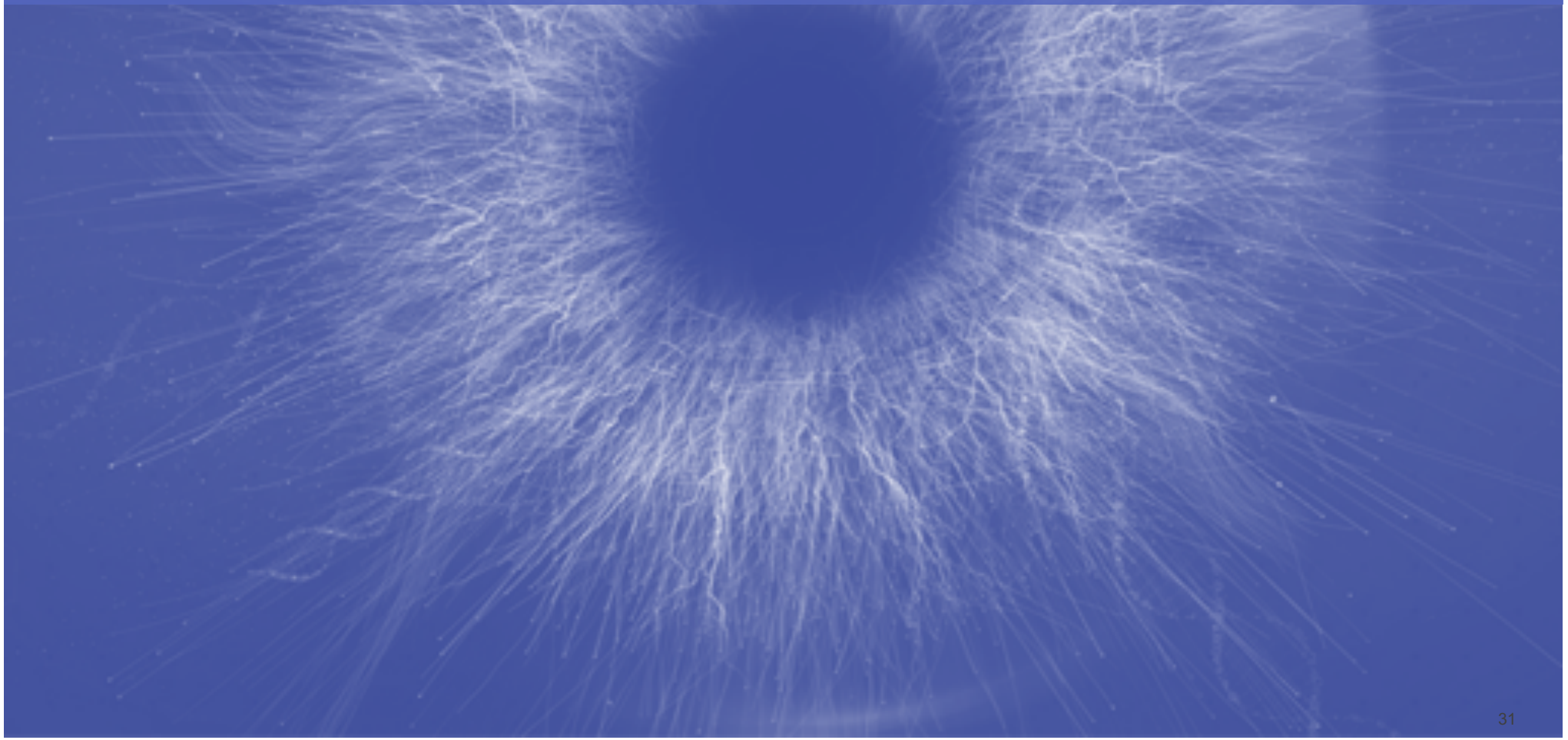




Mobility Maze – Baseline and 6 Months, Treated Eye

Adult Patient treated with $1x10^{11}$ vg/mL

Retinal Sensitivity



Standard of Care Assessment of Retinal Sensitivity – Static Perimetry

Patients experience progressive loss of visual field as the retina degenerates

- **Static perimetry reliably assesses and quantifies retinal sensitivity**

- **Retinal sensitivities can be converted into volumetric measures using visual field modeling and analysis (VFMA) which provides a comprehensive standardized mechanism to assess visual function**
  - VFMA creates a hill of vision (HoV)
  - HoV can be assessed for the entire visual field (VTotal), or for a specific region of interest, e.g. central 30 degrees (V30) targeted by gene therapy

- **Because this volumetric analysis utilizes all 164 test locations on the customized RPE65 static perimetry grid, rather than simply an average value (mean sensitivity), it is a more sensitive and clinically meaningful indicator of gain or loss of visual function**

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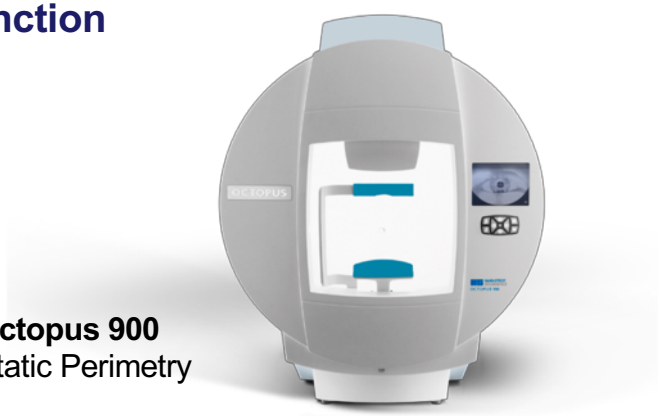
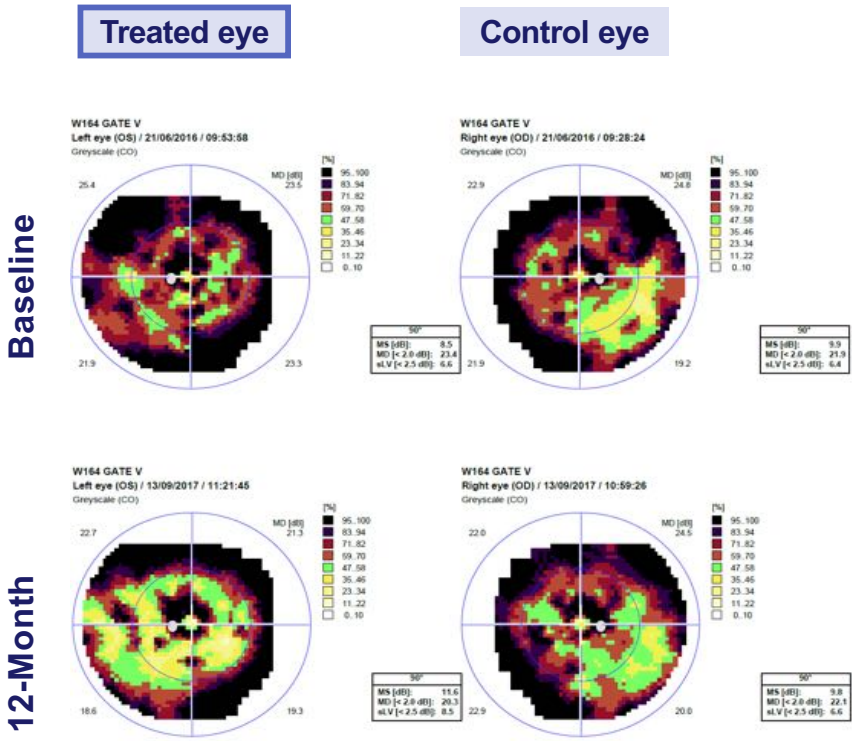
Kumaran *et al*, 2018; Weleber *et al*, 2015; Csaky *et al*, 2017.



Octopus 900
Static Perimetry

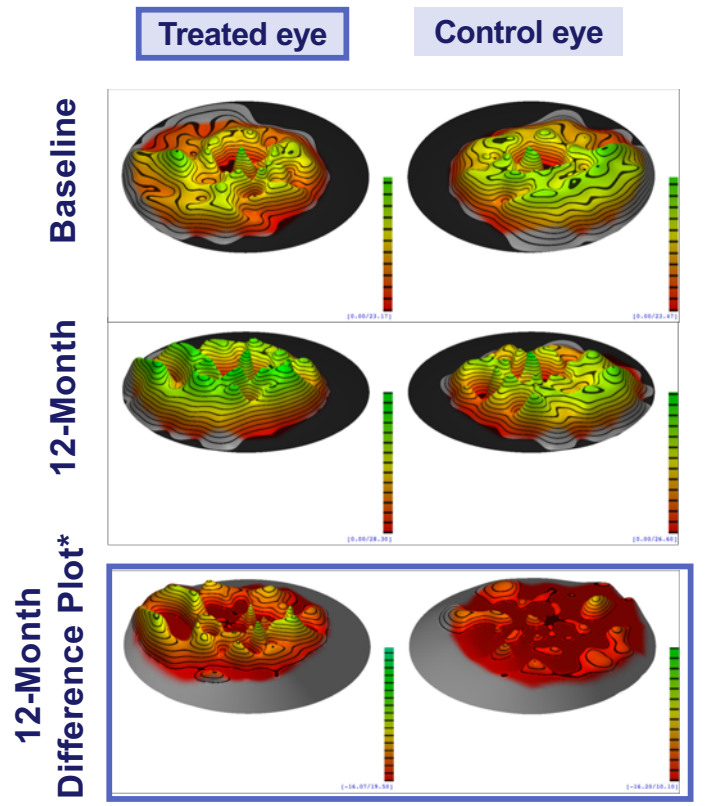
Conventional and Volumetric Static Perimetry at Baseline and 12 Months (Adult Subject)

Mean Retinal Sensitivity (Conventional)



	Octopus900 Derved Mean Sensitivity (dB)	
	Treated eye	Control eye
Baseline	**9.0**	**11.2**
Test / Retest Variability	*0.6*	*0.8*
12 Months	**11.6**	**9.8**

Hill of Vision (VFMA-Derived, Volumetric)

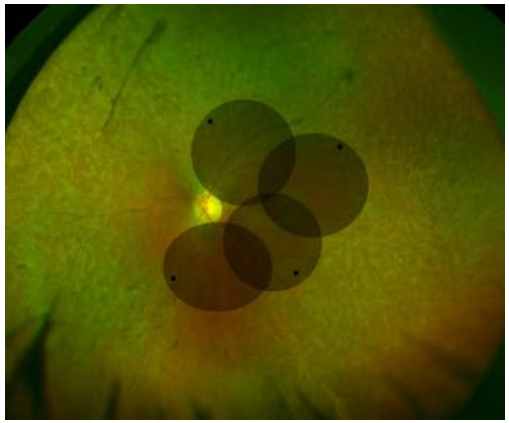


	VFMA-Derived Total HoV (dB-sr)	
	Treated eye	Control eye
Baseline	**32.6**	**41.9**
Test / Retest Variability	*2.1*	*3.1*
12 Months	**44.8**	**36.9**

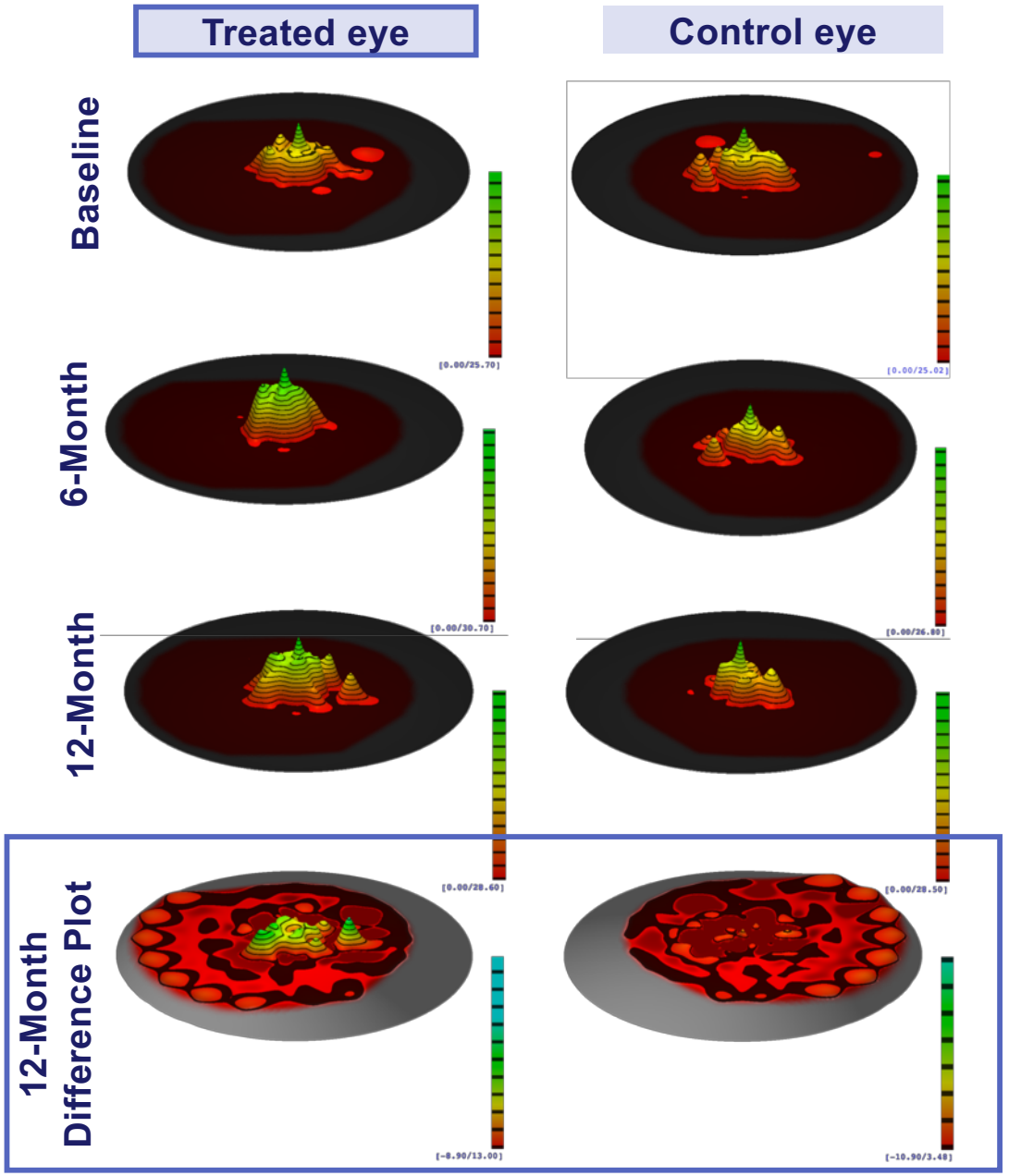
***Improvement is represented by raised areas (hills) and worsening by depressed dark red areas (valleys)**

MGT003: Adult Retinal Sensitivity Improvement (Total Hill of Vision)

- Young adult (age 20) in $1x10^{11}$ cohort
- Advanced retinal degeneration
- Small island of residual central macular structure
- Improvement in retinal function was associated with improvement in visual mobility
- AAV2/5-OPTIRPE65 administered to central retina, included foveal detachment

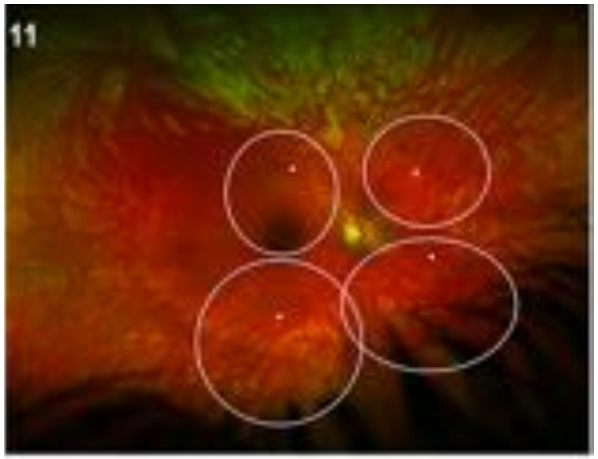


AAV2/5-OPTIRPE65 administered to central retina, included foveal detachment

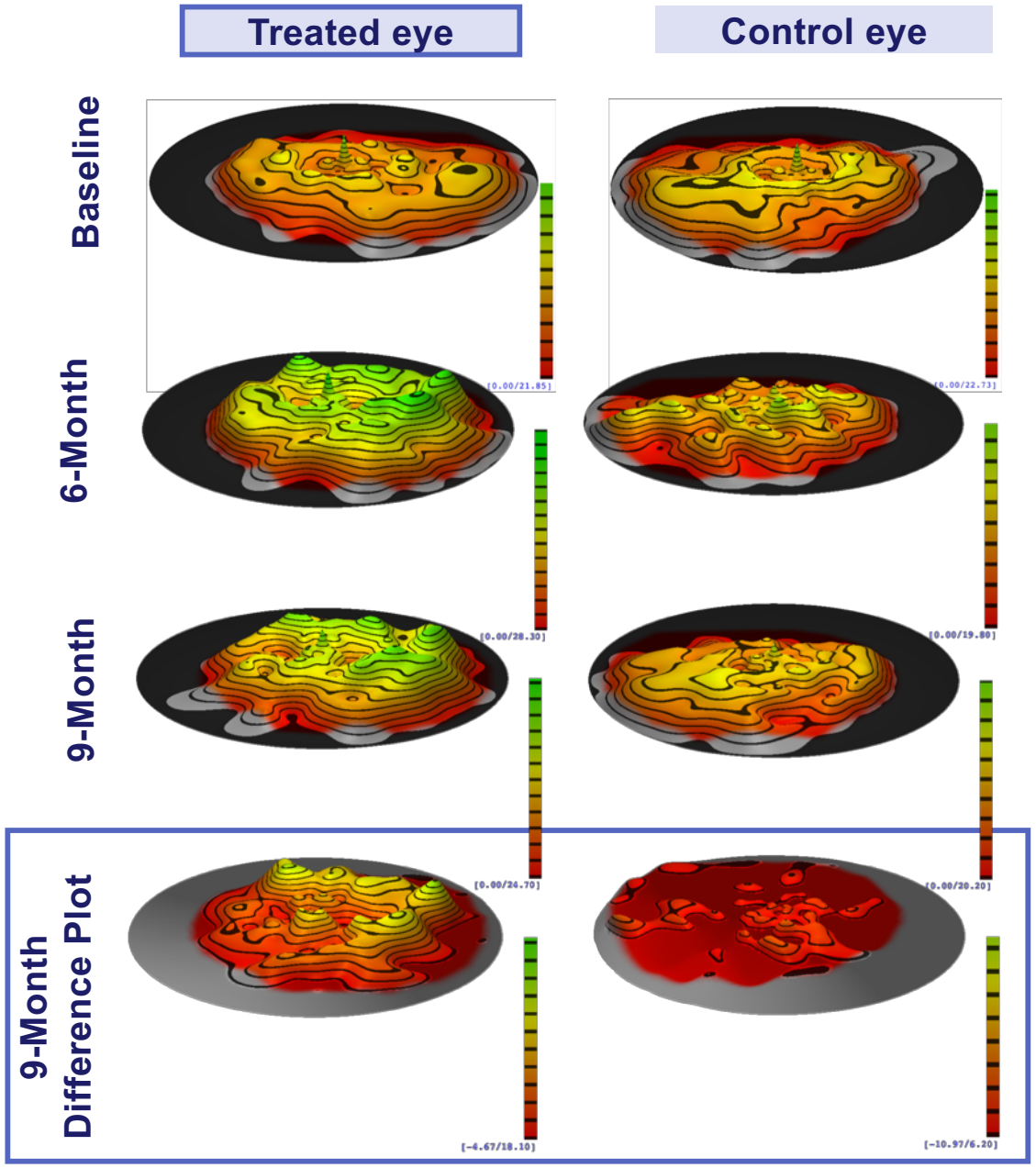


MGT003: Pediatric Retinal Sensitivity Improvement (Total Hill of Vision)

- Child (age 11) in pediatric expansion cohort
- Improvement in retinal function was associated with improvement in visual mobility



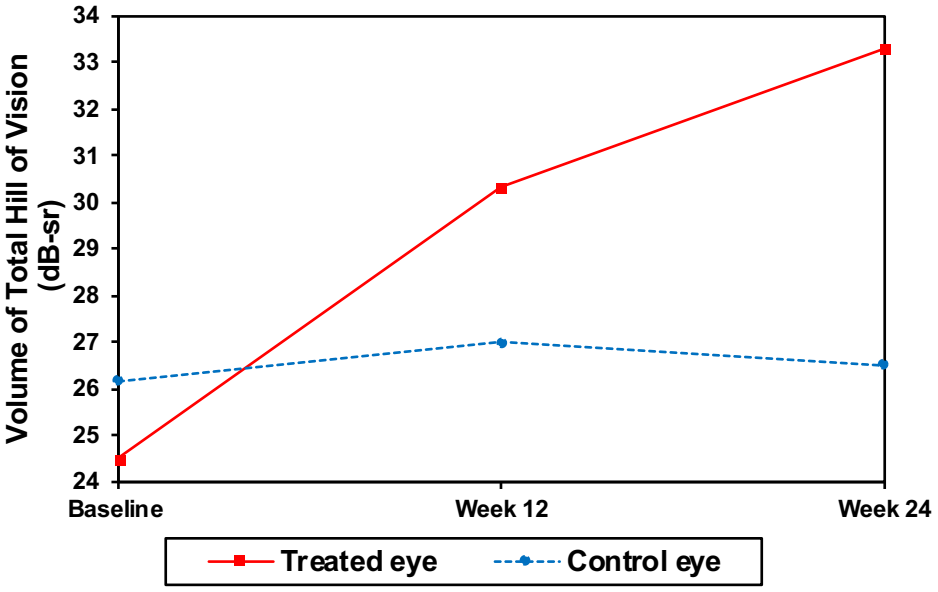
AAV2/5-OPTIRPE65 administered to central retina, included foveal detachment



MGT003: Retinal Sensitivity Significantly Increased Across Retina and in Central Macula – Volumetric Analysis

Total Hill of Vision (dB-sr)

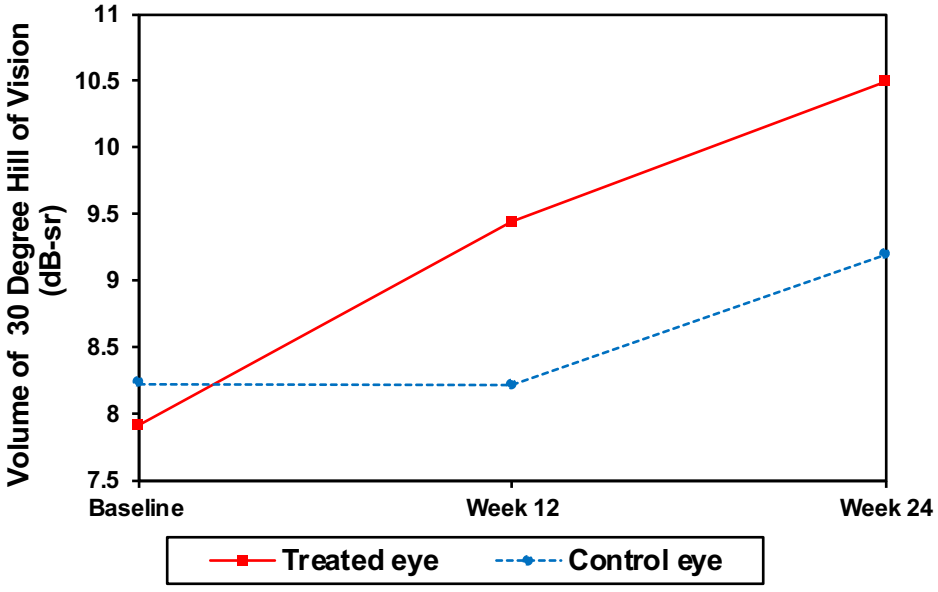
All 1x10^{11} Subjects (n=8*)



Mean 24-week change from baseline, Treated eye vs. Control eye: **+9.39 dB-sr; p=0.0078**

Central 30° Hill of Vision (dB-sr)

All 1x10^{11} Subjects (n=8*)

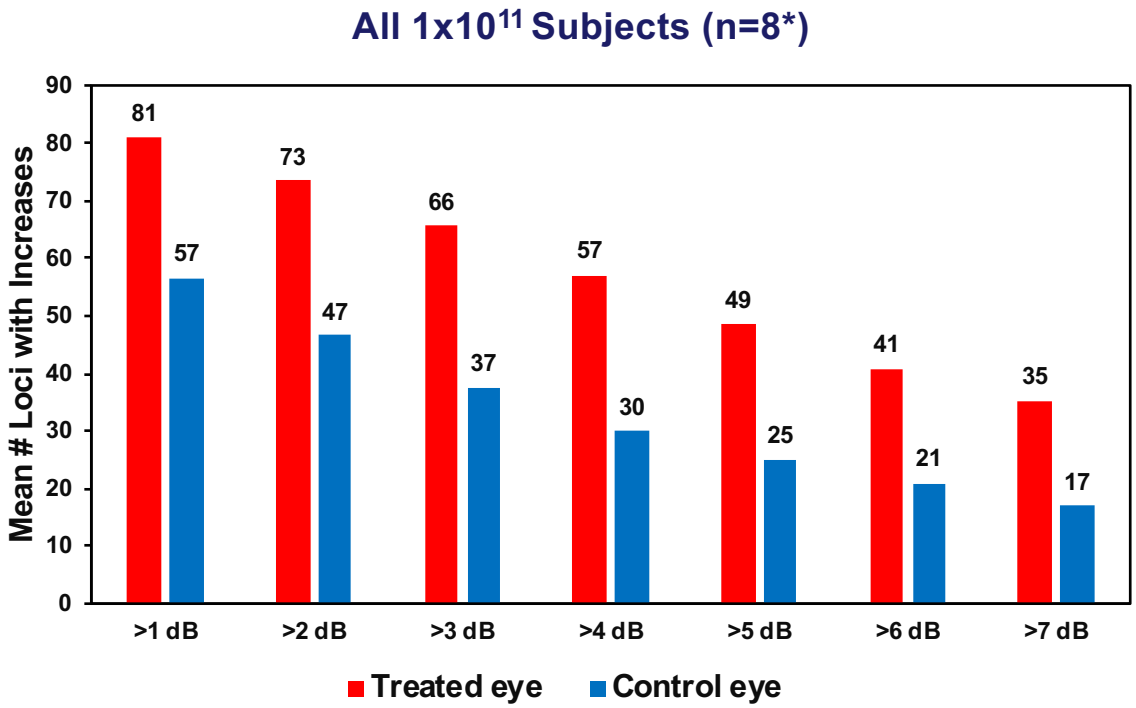


Mean 24-week change from baseline, Treated eye vs. Control eye: **+1.9 dB-sr; p=0.0078**

*One young child did not complete perimetry assessments

MGT003: Significant Improvement in Retinal Sensitivity – Pointwise Analysis

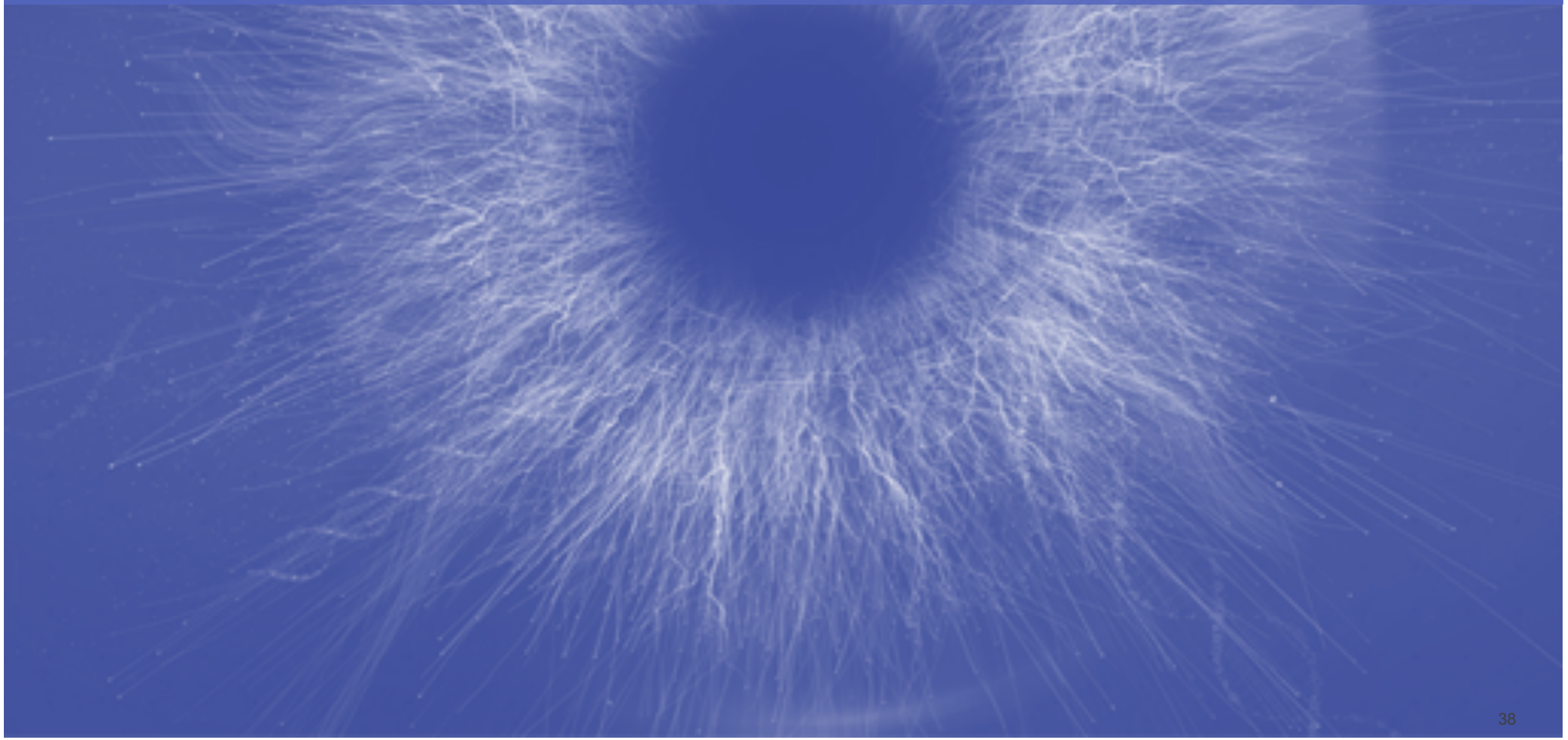
Mean Number of Loci with Increased Retinal Sensitivity from Baseline



Significantly greater improvement in mean number of loci w/ increases > 7dB demonstrated in Treated eye compared to Control eye at 24 weeks (p=0.047)

*One young child did not complete perimetry assessments

Central Visual Function



MGT003: Significant Improvements in Foveal-Driven Visual Function

- **Central retina targeted in all subjects treated at $1x10^{11}$ vg/mL**
- **Foveal detachment during surgery in most subjects (7/9)**
- **Increased foveal function demonstrated in the Treated eye vs baseline compared to Control Eye vs baseline**
- **Statistically significant improvements in foveal-driven visual function tests in population treated at the 1×10^{11} dose:**
  - Retinal sensitivity Central 30˚
  - Best Corrected Visual Acuity (BCVA)
  - Contrast Sensitivity
  - Reading speed (trend)

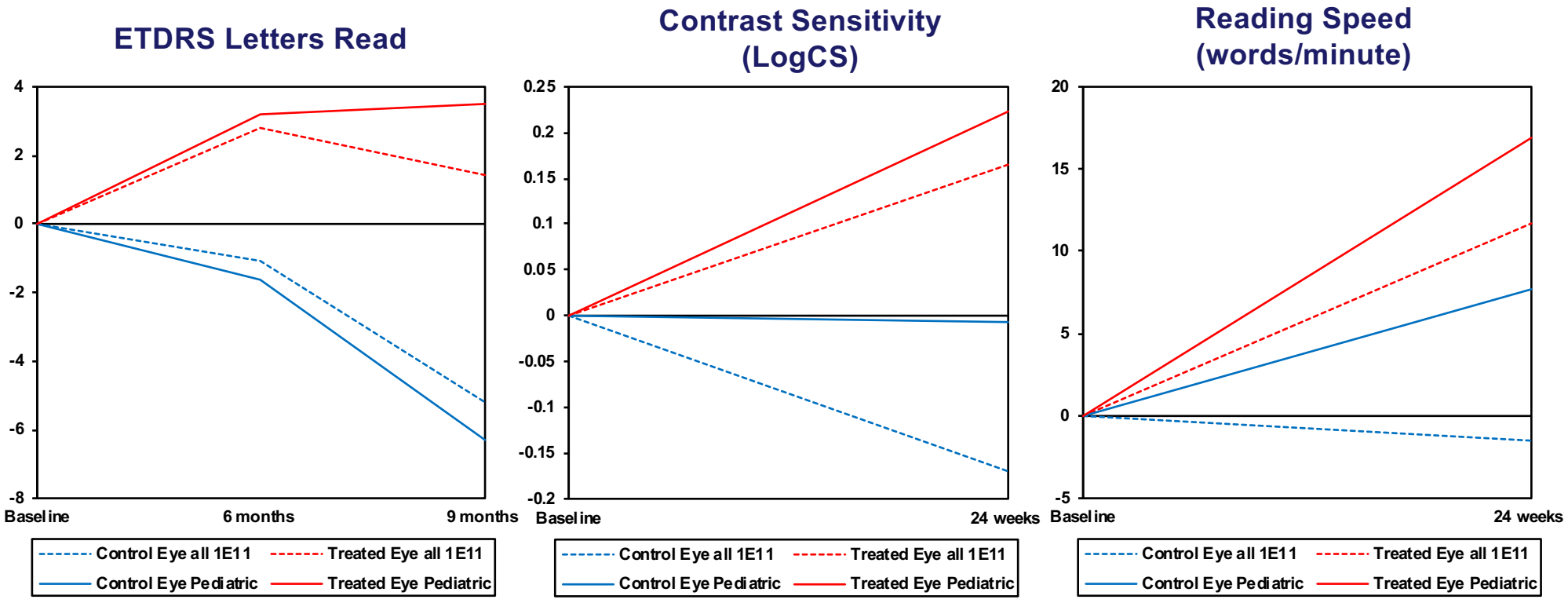
Summary of central visual function change from baseline: Treated eye vs. Control eye ($1x10^{11}$ vg/mL population)

	Retinal Sensitivity, Central 30° * (dB-sr)	Visual Acuity (ETDRS letters read)	Contrast Sensitivity* (LogCS)	Reading Speed* (words/min)
Mean (SD)	1.87 (1.62)	3.9 (3.4)	0.18 (0.129)	13.2 (14.99)
Median (Min: Max)	1.21 (0.2: 5.5)	4.3 (-1: 8)	0.18 (0.0: 0.42)	16.7 (-13: 27)
Signed Rank test P-value	0.008	0.016	0.016	0.078

*n=8: one young child unable to complete static perimetry, contrast sensitivity or reading assessments

MGT003: Significant Improvements in Foveal-Driven Visual Function

Statistically significant improvements vs baseline:
Treated eye compared to Control eye (1x10^{11} vg/mL population)



Conclusions

- **Subretinal delivery of AAV2/5-OPTIRPE65 well tolerated**
- **Safe targeting of the central retina including foveal detachment with AAV2/5-OPTIRPE65**
- **$1x10^{11}$ vg/mL optimal dose for continued clinical development**
- **Improvement in multiple assessments of functional vision, retinal function, and central vision demonstrated**
- **Demonstration of structural preservation following foveal targeting and statistically significant improvement in central visual function**

Visual Function						Structural
Mobility Maze (time to navigate)	**BCVA** (ETDRS letters)	**Reading Speed** (words per minute)	**Contrast Sensitivity** (LogCS)	**Retinal Sensitivity** (full field of vision)	**Retinal Sensitivity** (central 30°)	**OCT**
↓	↑	↑	↑	↑	↑	↔

Acknowledgements

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- Referring clinicians and collaborators: Thiran Jayasundera, Kari Branham, Naheed Khan, Mette Bertelsen, Michael Larsen, Fiona Blanco-Kelly, Carmen Ayuso, Hoai Viet Tran, Francis L Munier
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Q&A