EURETINA Virtual Meeting – 3 October 2020

AAV5-*RPGR* Gene Therapy for *RPGR*-Associated X-Linked Retinitis Pigmentosa: 9-month Results From a Phase 1/2 Clinical Trial

Michel Michaelides,[1,2*] Cagri Besirli,[3] Kamron Khan,[4] Yesa Yang,[1,2] Chien Wong,[1,5,6] Jose Sahel,[7] Mahmood Shah,[7] James Tee,[1,2] Neruban Kumaran,[1] Anastasios Georgiadis,[8] Stuart Naylor,[8] Jialin Xu,[9] Peggy Wong,[9] Penny Fleck,[9] Alexander Smith,[1] Caterina Ripamonti,[10] Robin Ali,[1] Alexandria Forbes,[8] James Bainbridge[1,2]

[1]UCL Institute of Ophthalmology, London, UK; [2]Moorfields Eye Hospital, London, UK; [3]Kellogg Eye Center, Ann Arbor, MI, USA; [4]Leeds Centre for Ophthalmology, Leeds, UK; [5]Great Ormond Street Hospital for Children and NIHR Biomedical Research Centre, London, UK; [6]Royal Free Hospital, London, UK; [7]UPMC Eye Center, Pittsburgh, PA, USA; [8]MeiraGTx, New York, NY, USA; [9]Janssen Pharmaceuticals, Raritan, NJ, USA; [10]Cambridge Research Systems Ltd., Rochester, UK

**Presenter.*

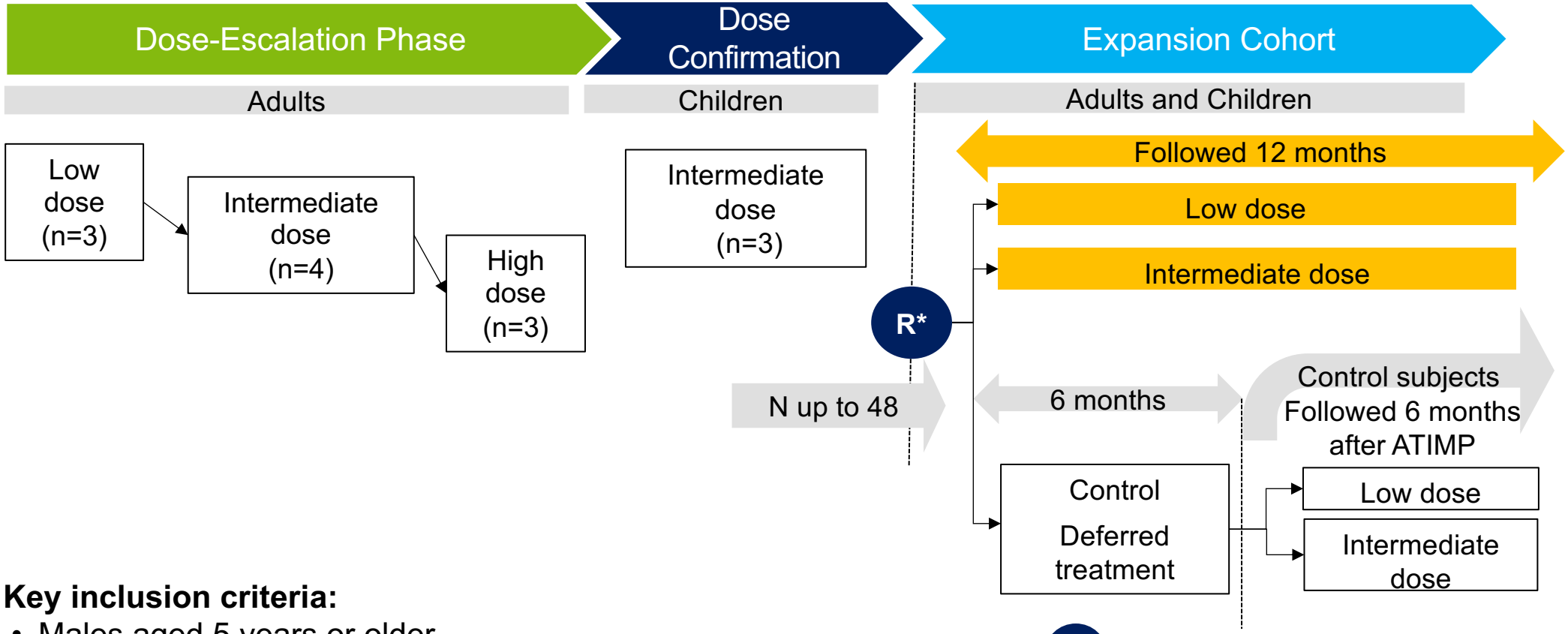
Financial Disclosures

Michel Michaelides, MD (presenter)

- **Consultant:** Acucela, Stargazer Pharmaceuticals, 2C Tech, MeiraGTx, Janssen Pharmaceuticals
- **PI:** Acucela, ProQR, MeiraGTx
- **Equity ownership:** MeiraGTx

MGT009: Phase 1/2 Trial of AAV5-*RPGR*

Multicenter open-label Phase 1/2 trial of an AAV5-*RPGR* gene therapy (NCT03252847) conducted at 5 sites across the **US and UK**



Key inclusion criteria:

- Males aged 5 years or older
- With RP caused by disease-causing variants in *RPGR*
- SD-OCT evidence of relative preservation of retinal structure at the macula
- Able to undertake age-appropriate clinical assessments

R = randomized:
group (immediate or control),
dose (low or intermediate) and
eye (right or left)
*1:1:1 randomization
ATIMP, advanced therapy investigational medicinal product.

Dose-Escalation Population

Cohort	Mean age (range), years	Mean visual acuity (range)	Patients	Ethnic Origin
Total	24 (18, 30)	69 (52, 83)	10	8 White 1 Black 1 Other
Low dose	27 (24, 30)	62 (52,70)	3	3 White
Intermediate dose	25 (19, 29)	72 (60, 77)	4	3 White 1 Other
High dose	21 (18, 24)	73 (59, 83)	3	2 White 1 Black

Clinical Safety in MGT009 Dose-Escalation Phase

- **Safety data obtained to date has ocular and systemic safety profiles that are anticipated and manageable**
- **Half of AEs that occurred were ocular in nature related to the surgical delivery procedure, transient and resolved without intervention**
- **2 SAEs**
  - 1 retinal detachment: related to study procedure and resolved without sequelae
  - 1 panuveitis
- **No dose-limiting events**
- **Inflammatory responses were observed in 2 out of the 3 patients in the high dose cohort, which were effectively treated with extension of steroid cover**

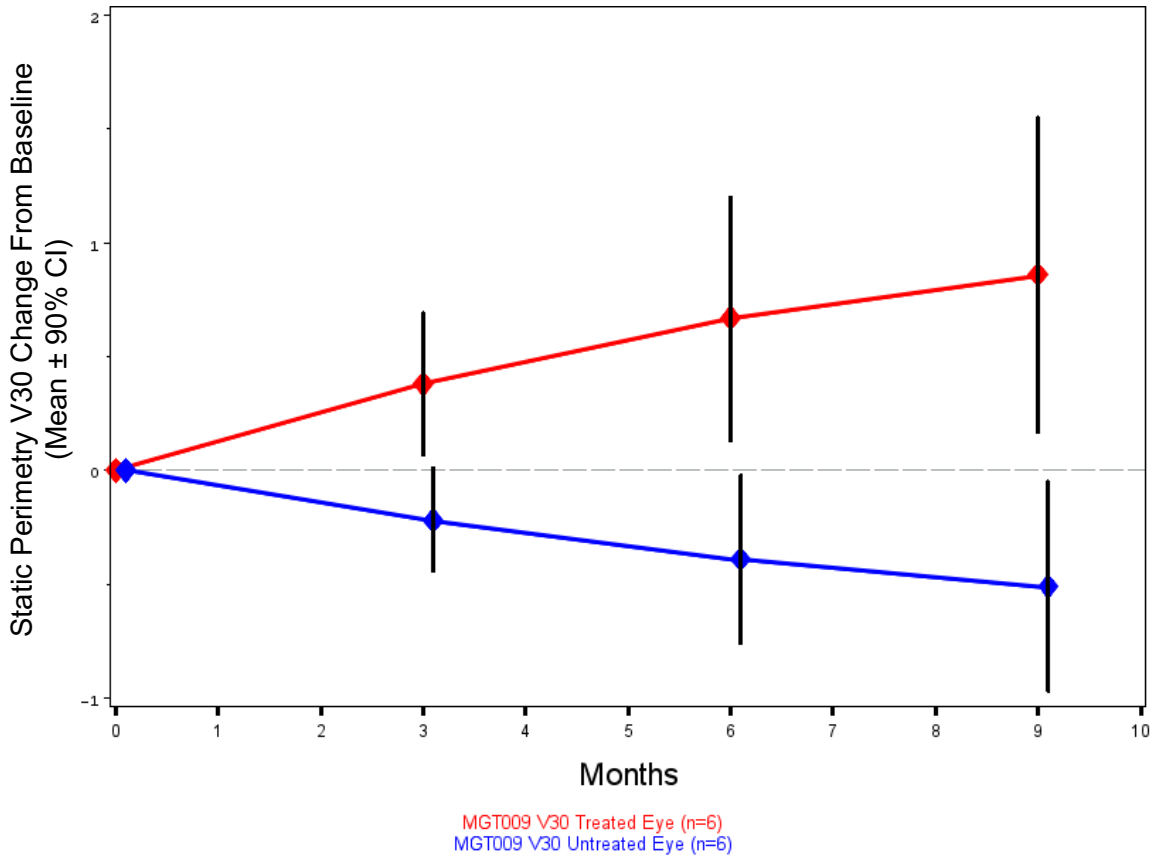
AEs, adverse events; SAEs, serious adverse events.

Statistically Significant Improvement in Retinal Sensitivity in Low and Intermediate Dose Cohorts

Parameter	Treated-Untreated Eye Difference @ 9 months (90% CI adjusted for baseline)
Mean Retinal Sensitivity (dB)	
Low	0.85 (0.05, 1.63)*
Intermediate	1.02 (0.78, 1.25)*
High	N/A
Central 30° Hill-of-Vision (V30, dB-sr/y)†	
Low	1.07 (0.19, 1.94)*
Intermediate	1.10 (0.46, 1.74)*
High	N/A

Response was treated-untreated eye adjusted for baseline (double-delta).
*Statistically significant effects at a one-sided 5% level.
†Currently, at least 9 months of data and up to one year of data.
Excludes one subject with panuveitis in the low dose.
N/A; this assessment was not conducted in the high dose cohort at the 9 month timepoint.

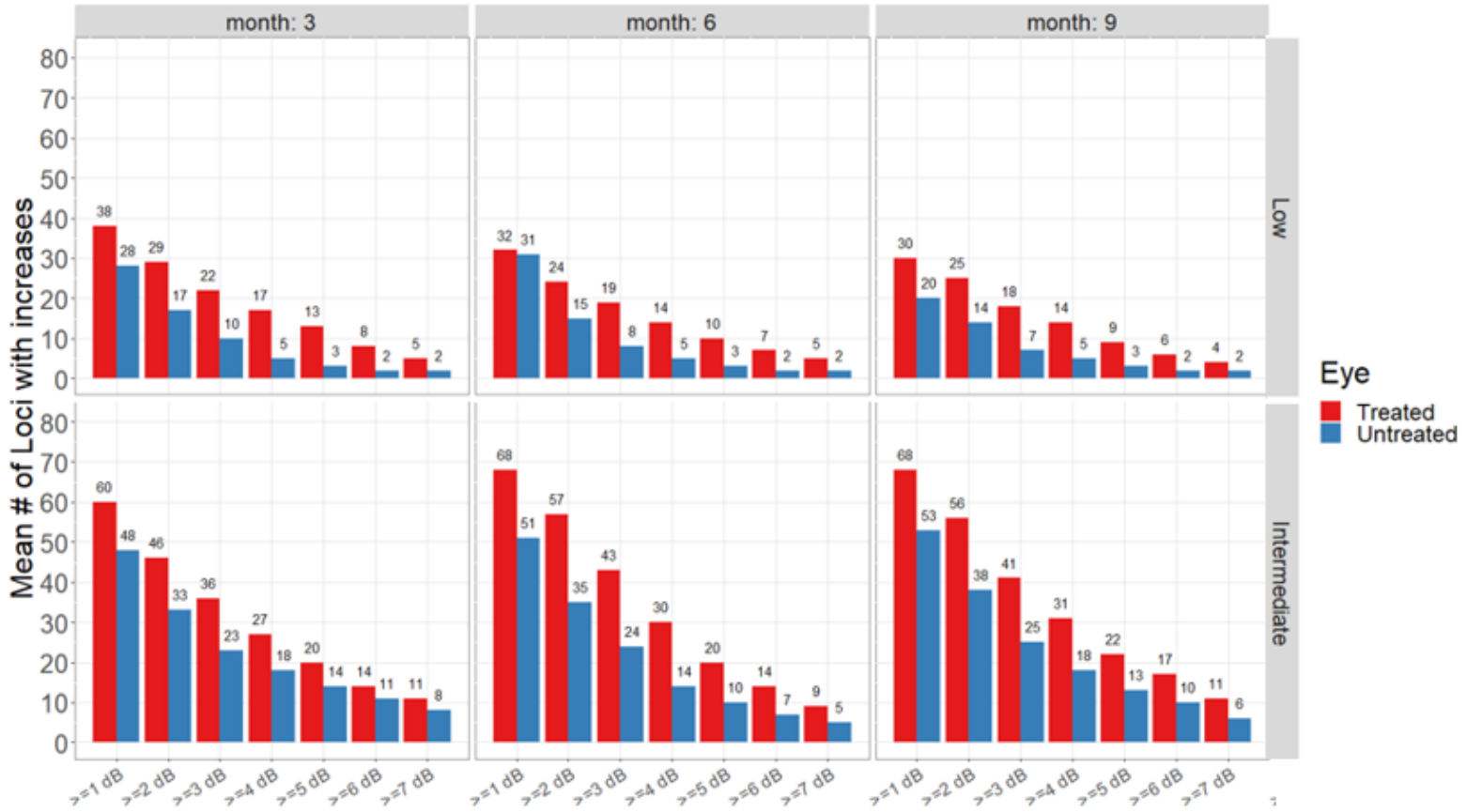
Statistically Significant Improvement in Retinal Sensitivity in Low and Intermediate Dose Cohorts (n=6)*



- **Central retinal sensitivity increased in the treated eye group vs. baseline (0.86 dB-sr [90% CI: 0.17, 1.55]), while it decreased in the untreated eye group (–0.51 dB-sr [–0.97, –0.05]) at 9 months**
- **Statistically significant difference between treated and untreated eyes (1.37 dB-sr)***

*Statistically significant effects at a one-sided 5% level, and based on a small sample size.
Excludes one patient with panuveitis in the low dose cohort.

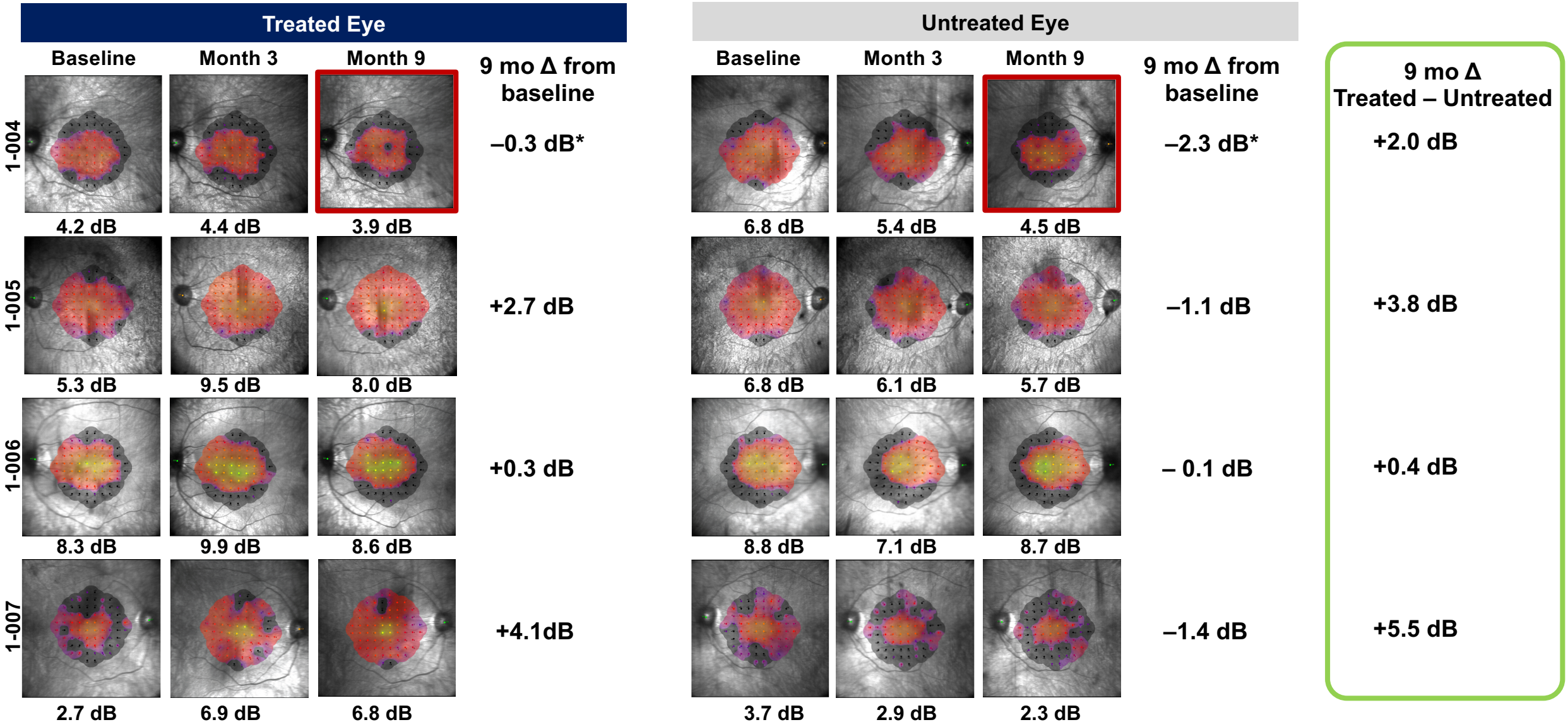
Increased Retinal Sensitivity in Treated Eyes in Low and Intermediate Dose Cohorts



Point by point responder*,†	Eye	Low Dose§	Intermediate Dose
	Treated eye	0/2	3/4
	Untreated eye	0/2	0/4

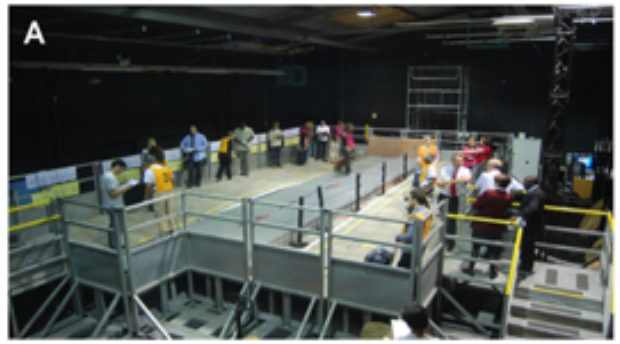
*Responder defined as ≥7dB improvement repeated at month 9 and any other time point for ≥ 5 loci for each eye.
†No high dose measurements taken at 9 months.
§Excludes one patient with panuveitis in the low dose.

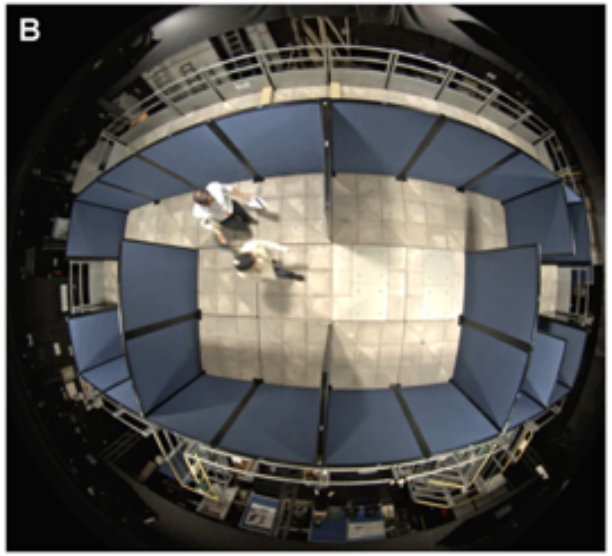
Retinal Sensitivity Improvements on Mesopic Microperimetry: Intermediate Dose Cohort at Month 9

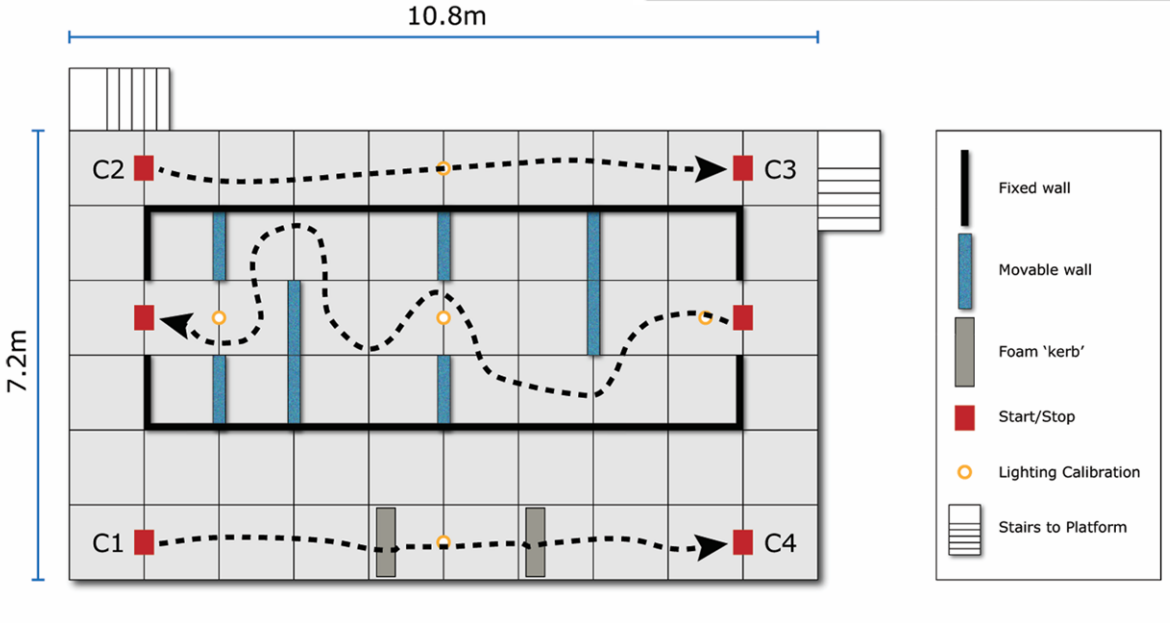


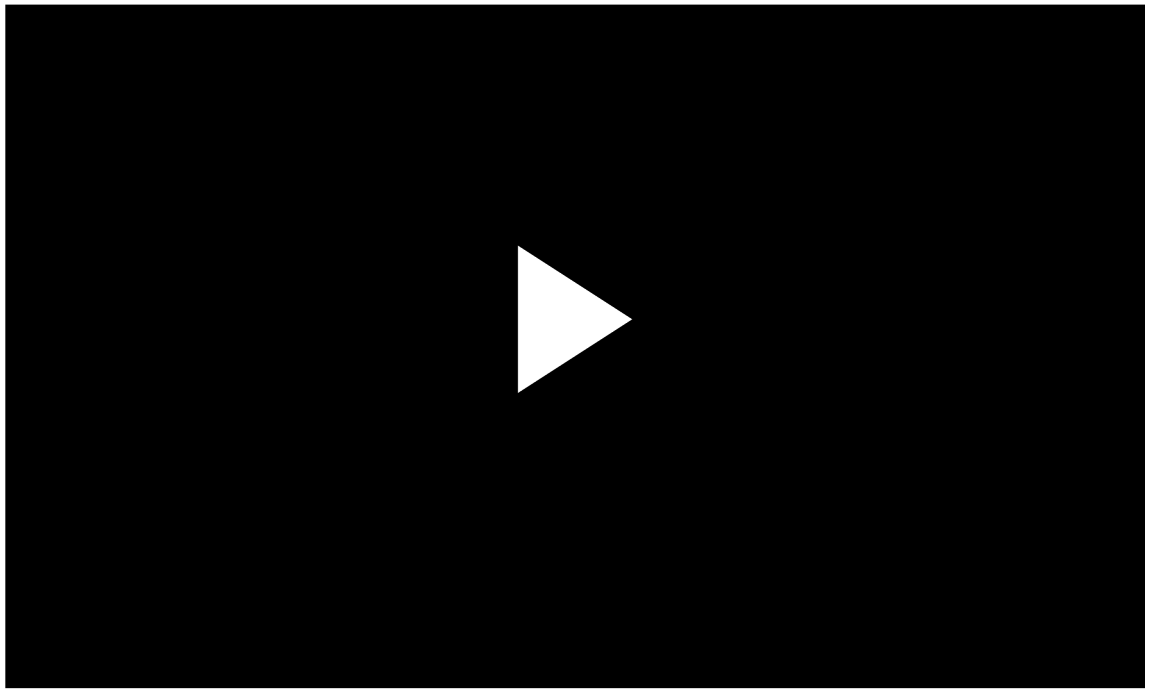
*Subject did not complete 9-month microperimetry assessment; the 6 month change from baseline is displayed.

Functional Vision Assessment: Mobility Maze



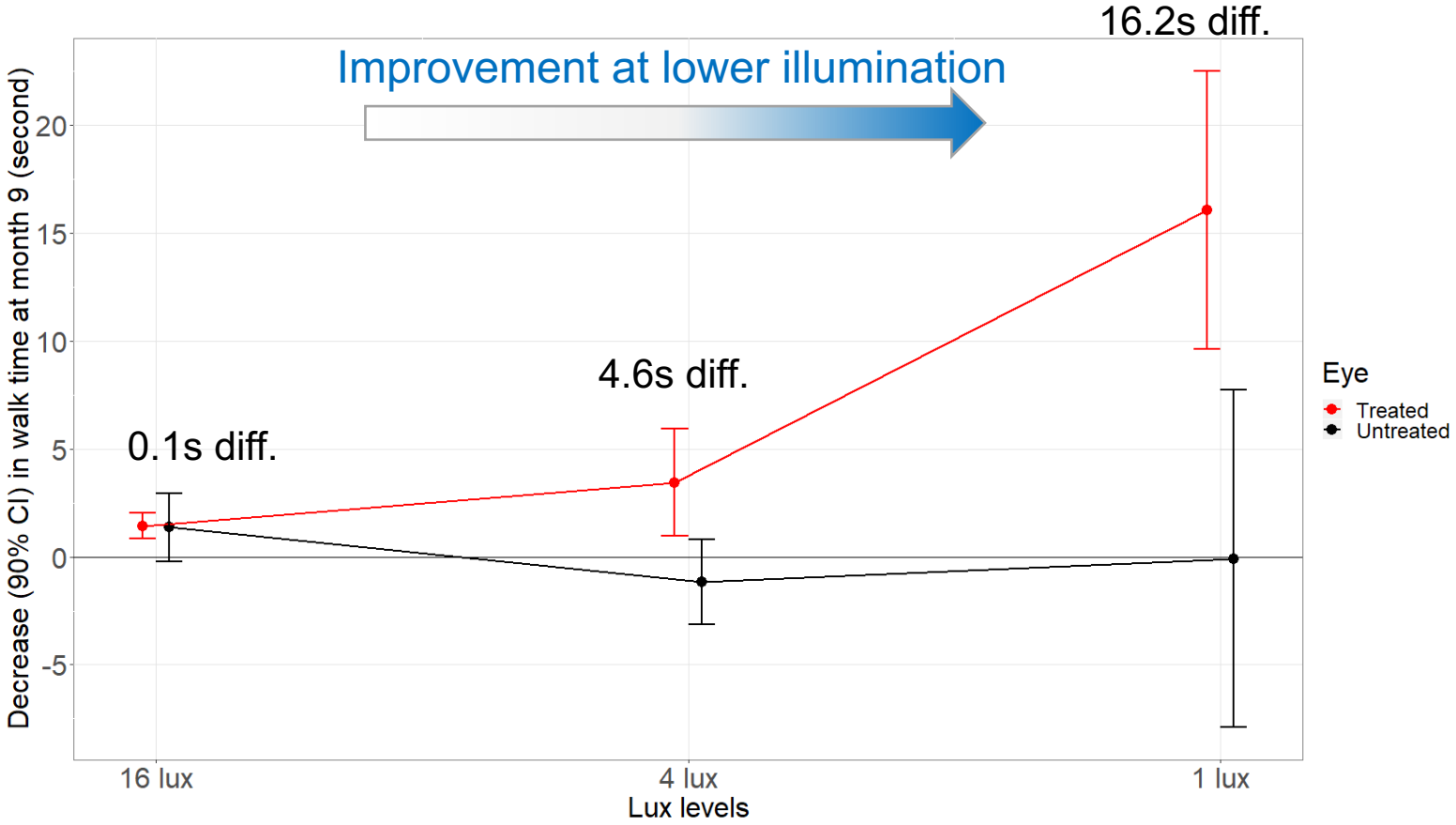






To view the maze assessment please click here

Significant Improvement in Walk Time at Month 9 Compared to Baseline (Low and Intermediate Dose, n=6)



VMA endpoint	Low Dose (n=2)*	Intermediate Dose (n=4)
Number of subjects improving at 1, 4 or 16 lux (treated – untreated < 0 sec)	2/2	3/4

*Excludes one subject with panuveitis in the low dose.
Maze assessments were not conducted in the high dose cohort at the 9 month timepoint.

Conclusions

- **Low and intermediate dose cohorts (n=6) achieved significant improvements in visual mobility at low light levels**
- **Low and intermediate dose cohorts achieved clinically meaningful improvements in retinal sensitivity, evident across multiple metrics (mean sensitivity, volumetric, and pointwise) and modalities (full-field static perimetry and microperimetry)**
  - In low (n=3) and intermediate (n=4) dose cohorts, 6/7 subjects demonstrated improvement or stability in retinal sensitivity in the treated eye
  - Efficacy signals were observed at first post-treatment assessment at 3 months, with improvements sustained or increased at 9 months
- **Safety data obtained to date suggest that AAV5-RPGR is generally safe and well tolerated, the majority of the adverse events were anticipated due to the surgical procedure**
- **Given the robust safety and efficacy signals observed, these doses are being further explored with analyses at additional data time-points in the ongoing randomized, controlled dose-expansion phase of the study**

Acknowledgments

- **Patients and families**
- **Referring clinicians and collaborators**
- **Trial managers, coordinators, and technicians**
- **Reading centers** in Belfast, OHSU, and MCW
- **Trial funding:** MeiraGTx and Janssen

OHSU, Oregon Health and Science University; MCW, Medical College of Wisconsin.