AAO Virtual Meeting – 13 November 2020

AAV5-*RPGR* Gene Therapy for *RPGR*-Associated X-Linked Retinitis Pigmentosa: 12-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,[1,2,5,6] 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.*

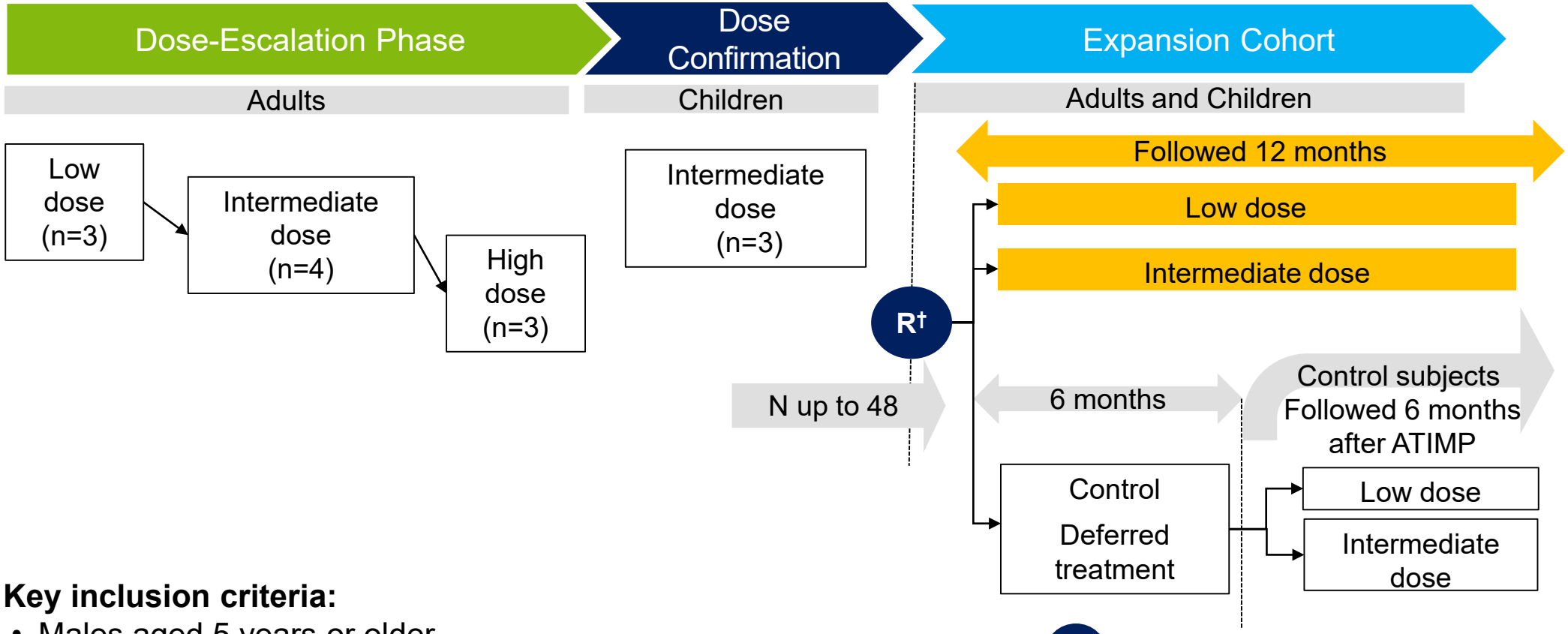
Financial Disclosures

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**

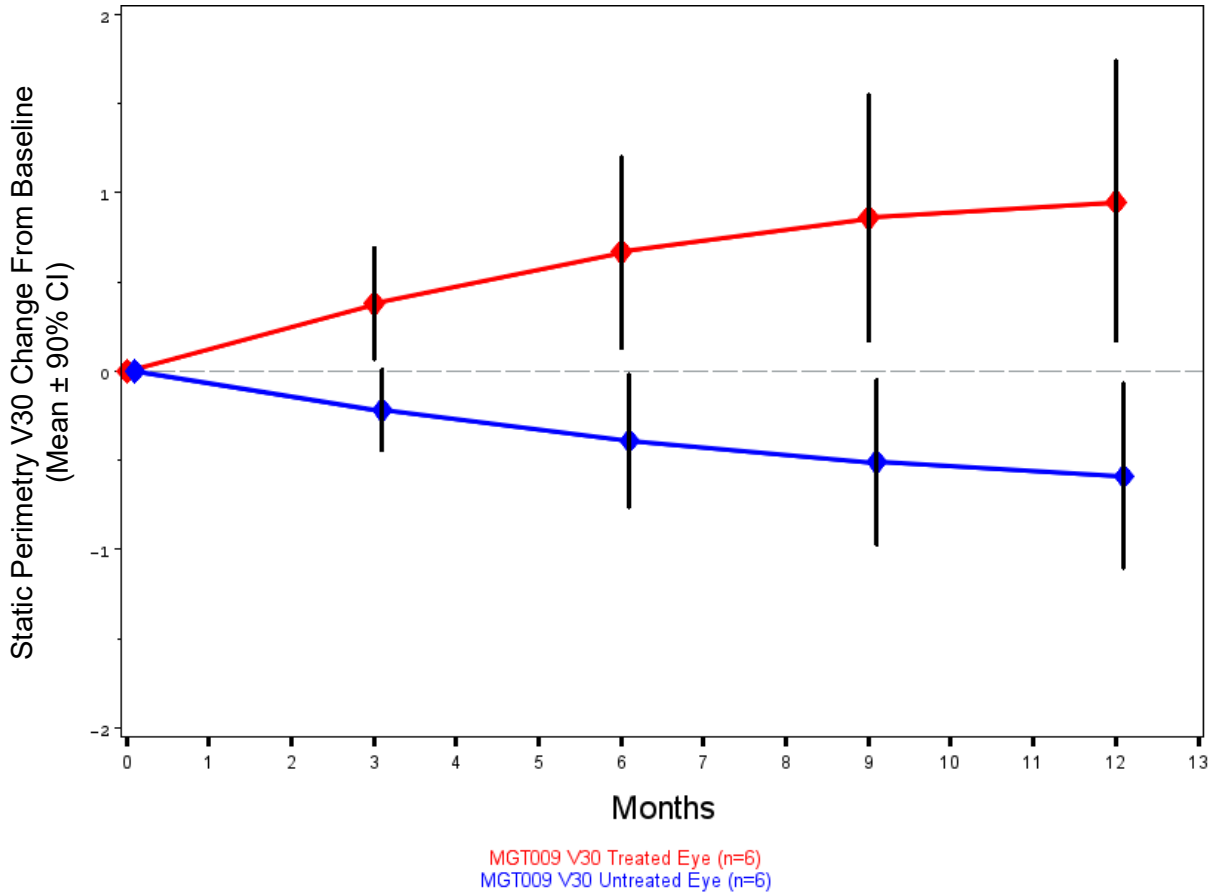
AEs, adverse events; SAEs, serious adverse events.

Statistically Significant Improvement in Retinal Sensitivity in Low- and Intermediate-dose Cohorts

Parameter	Treated-Untreated Eye Difference @ 12 months (90% CI adjusted for baseline)
Mean Retinal Sensitivity (dB)	
Low (n=2)†	0.76 (–0.14, 1.66)
Intermediate (n=4)	1.05 (0.81, 1.29)*
High (n=3)	–1.05 (–1.77, 0.06)
Central 30° Hill-of-Vision (V30, dB-sr)	
Low (n=2)†	1.10 (0.10, 2.10)*
Intermediate (n=4)	1.26 (0.65, 1.86)*
High (n=3)	–0.89 (–1.70, –0.01)

Response was treated-untreated eye adjusted for baseline (double-delta).
*Statistically significant effects at a one-sided 5% level.
†Excludes one patient with panuveitis in the low-dose cohort.

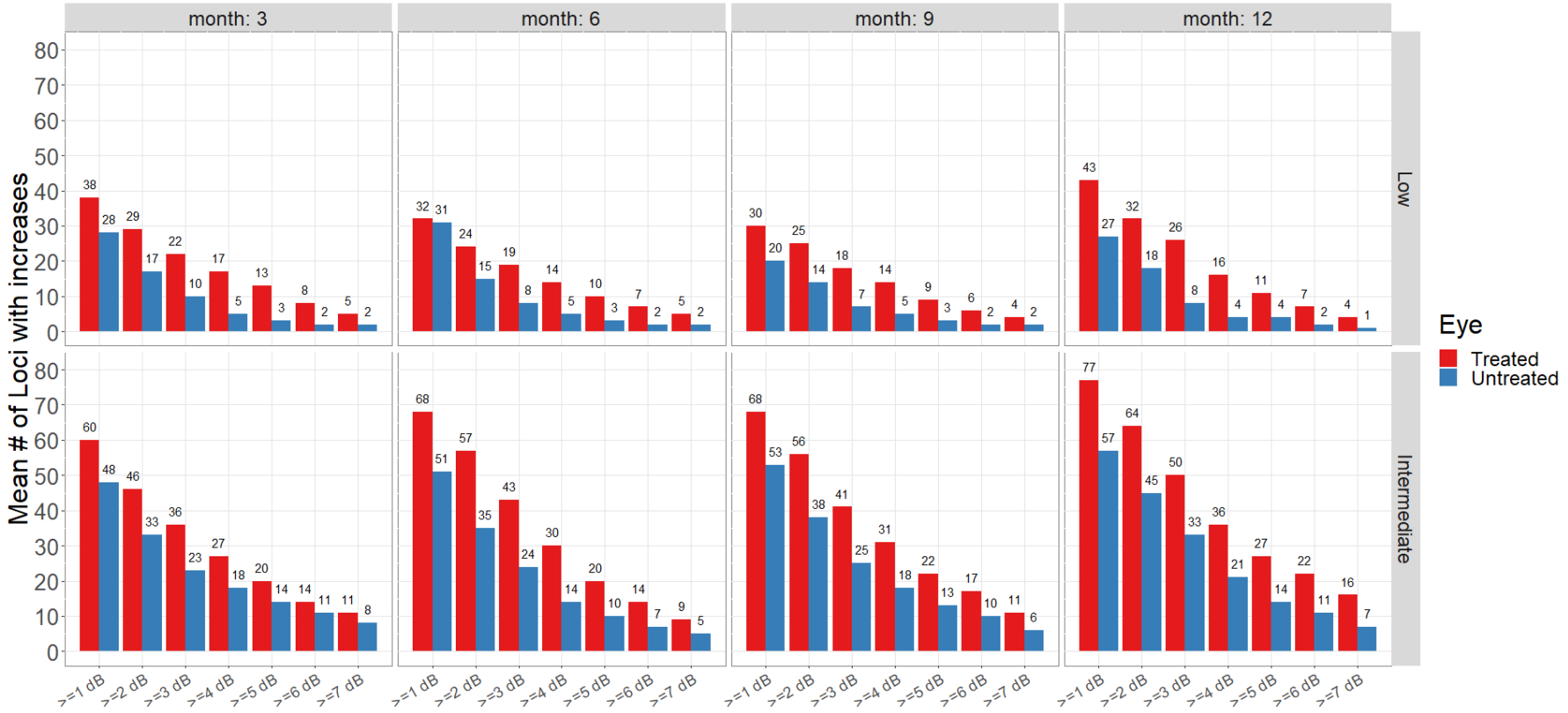
Significant Improvement in Retinal Sensitivity in Low- and Intermediate-dose Treated Subjects (n=6)



Eye	M3	M6	M9	M12
Treated	0.38 (0.07, 0.69)	0.67 (0.13, 1.20)	0.86 (0.17, 1.55)	0.95 (0.17, 1.74)
Untreated	–0.22 (–0.44, 0.01)	–0.39 (–.76, –0.02)	–0.51 (–0.97, –0.05)	–0.59 (–1.10, –0.07)

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	High Dose‡
	Treated eye	0/2	3/4	0/2
	Untreated eye	0/2	0/4	0/2

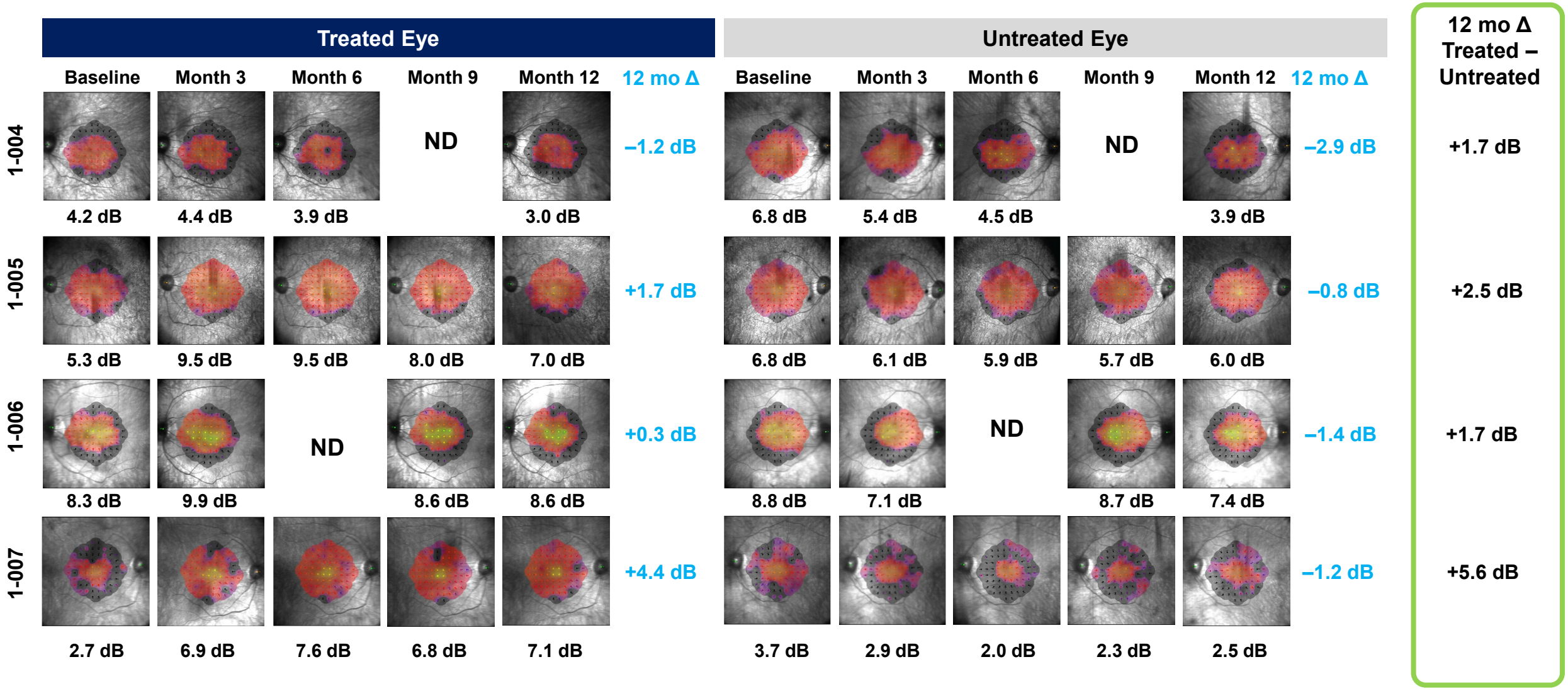
† Excludes one patient with panuveitis in the low dose

¶ Responder defined as ≥7dB improvement repeated at month 12 and any other time point for ≥5 loci for each eye.

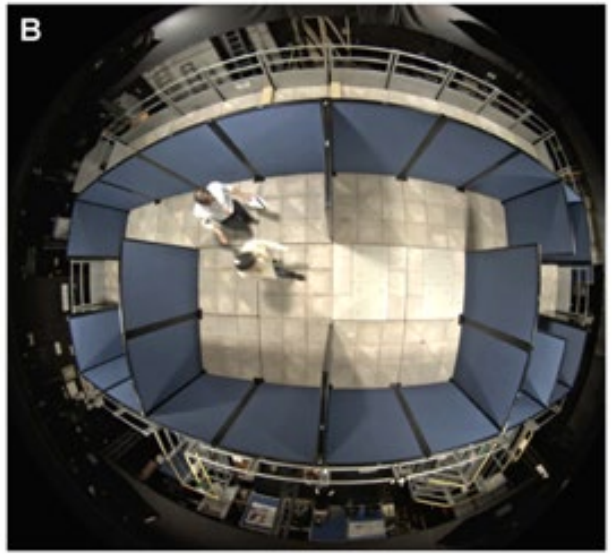
‡ Subject 1-010 did not complete static perimetry at month 9 or 12

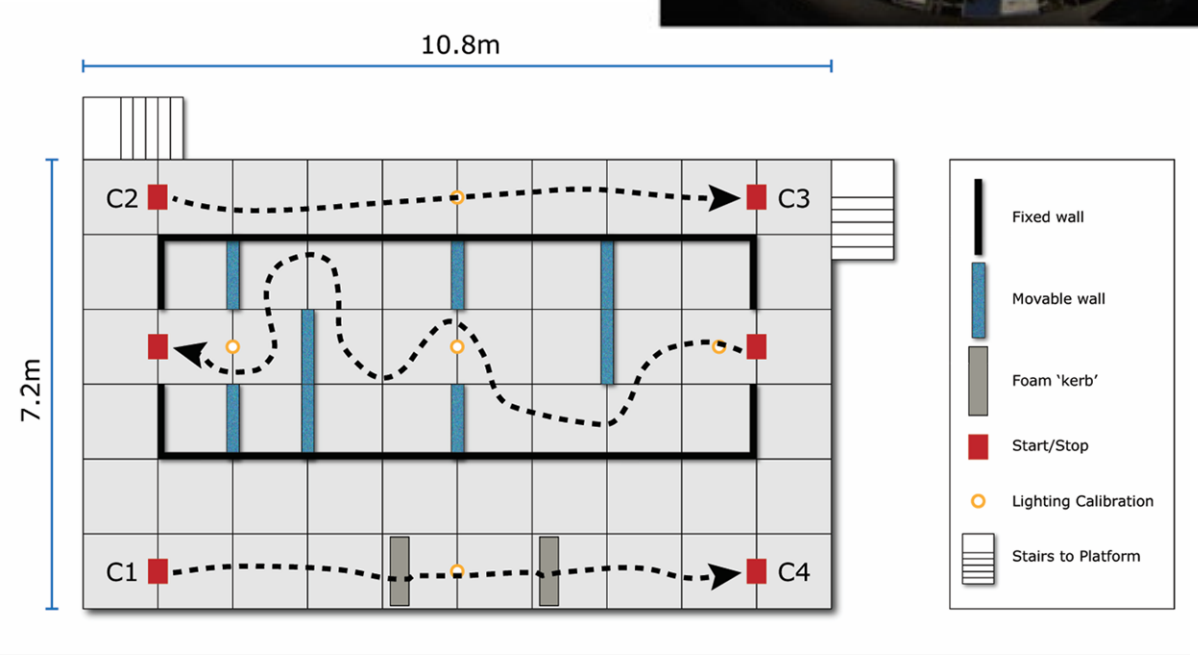
High dose continued to not respond at 12 months, consistent with 6 month data.

Retinal Sensitivity Improvements on Mesopic Microperimetry: Intermediate-dose Cohort at Month 12



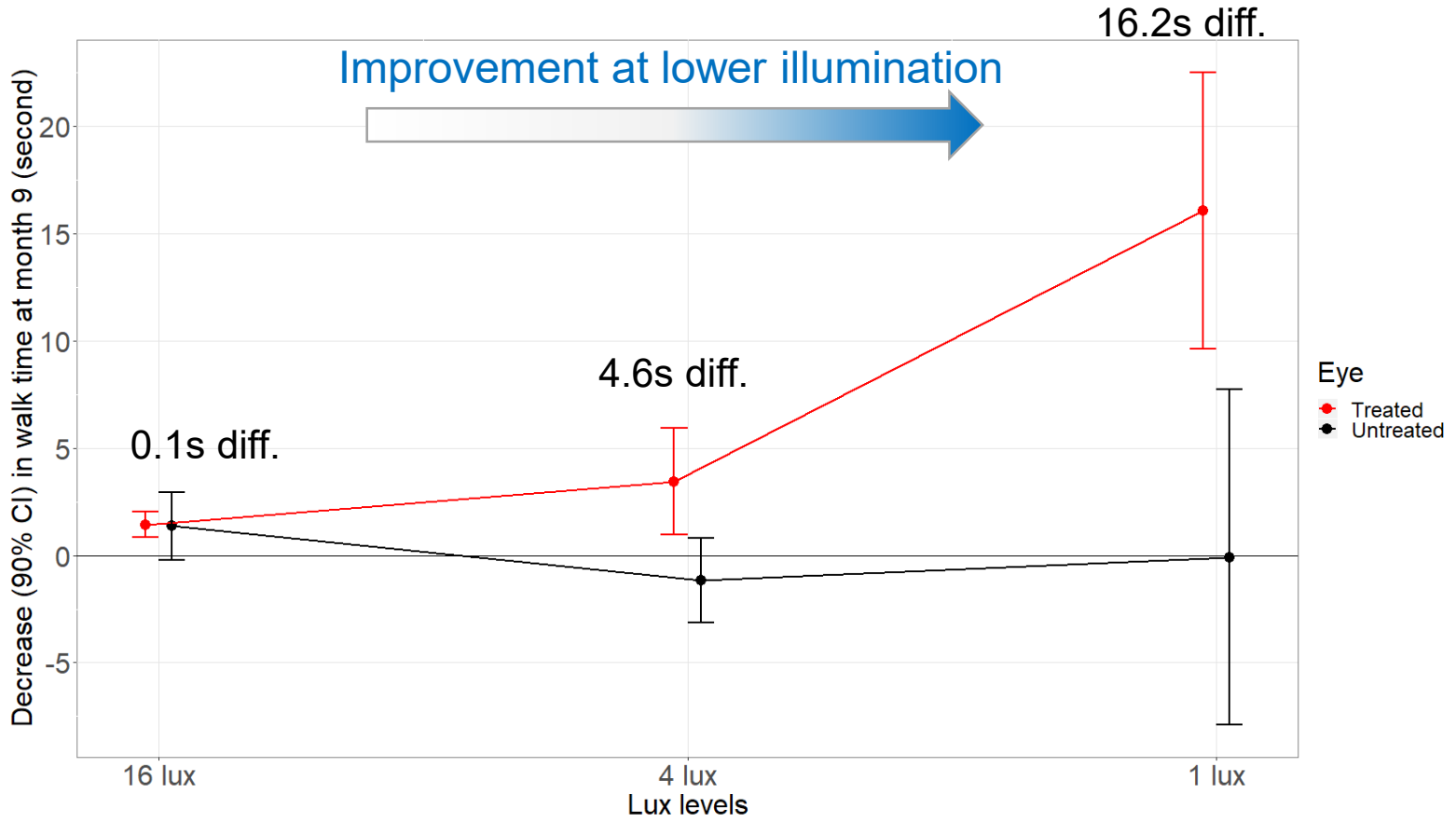
Functional Vision Assessment: Mobility Maze*





*Maze assessment shown at 9-month timepoint; maze assessment not conducted at 12 months.

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 panuvetis in the low dose

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 12 months
- **Safety data obtained to date suggest that AAV5-RPGR is generally safe and well tolerated, the majority of the adverse events were anticipated and due to the surgical procedure**
- **Given the robust safety and efficacy signals observed, these doses are being further explored with analyses at additional data timepoints in the ongoing randomized, controlled dose-expansion phase of the study**

Acknowledgments

- **Participants 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.