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AAV5-*RPGR* Gene Therapy for *RPGR*-Associated X-Linked Retinitis Pigmentosa Reverses Natural Disease Progression

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**Presenter.*

Financial Disclosures

Michel Michaelides, MD (presenter)

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

Ten Participants From Natural History Study MGT011 With *RPGR*-associated X-linked Retinitis Pigmentosa (*RPGR*-XLRP) Enrolled in MGT009, a Phase 1/2 Trial of an AAV5-*RPGR* Gene Therapy (Botaretigene Sparoparvovec)

MGT011 (NCT03349242):
Natural history study of patients with X-linked retinal dystrophy

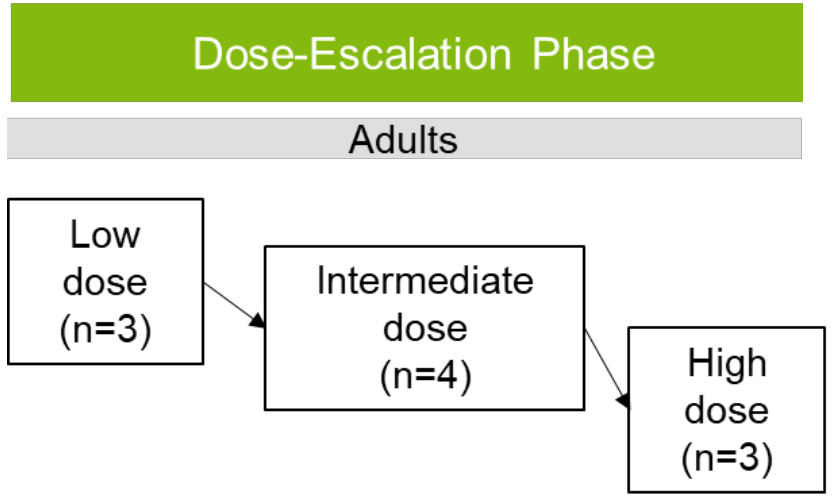
Key inclusion criteria
- Aged 5 years or older
- Have *RPGR*-associated retinal dystrophy
- Able to undertake age-appropriate clinical assessments

Assessments
- Octopus 900 full-field static perimetry
- Mesopic fundus-guided perimetry

Study visits
- At baseline
- Every 6 months for 2 years
- Then annually for up to 5 years

MGT009 (NCT03252847): Multicenter open-label Phase 1/2 trial of AAV5-*RPGR* gene therapy in *RPGR*-XLRP 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



RP, retinitis pigmentosa SD-OCT, spectral domain optical coherence tomography

- **Retinal function was assessed through 12 months post-treatment in MGT009**
- **Changes in mean retinal sensitivity and V30 were examined up to 48 months pre-intervention (MGT011) and 12 months post-intervention (MGT009)**

Baseline Characteristics of MGT011 Participants Enrolling in MGT009 (Dose-escalation Phase)

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

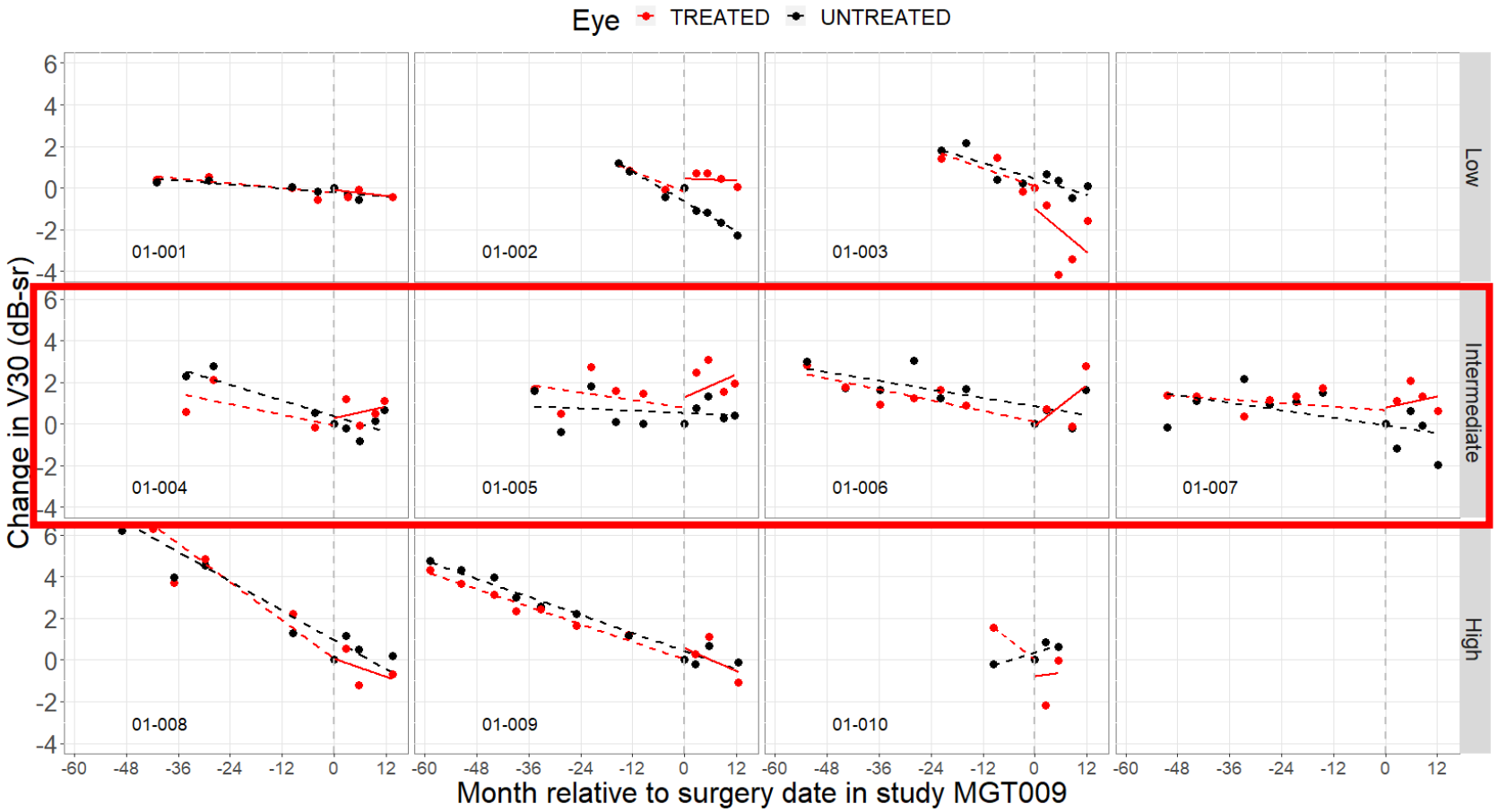
- **At Month 12 post-intervention (MGT009):**
  - The safety profile AAV5-*RPGR* was as expected and has been previously reported
  - In the low (n=3) and intermediate (n=4) dose cohorts, 6 participants demonstrated improvement or stability in treated-eye retinal sensitivity
  - No improvement was observed in the high dose cohort

Mean Retinal Sensitivity in Intermediate Dose Patients Improved Post-intervention, Reversing a Downward Trajectory

dB, decibels.

At Month 12 post-treatment, the treated eye in patients at the intermediate dose demonstrated improvements in mean retinal sensitivity derived from Octopus perimetry, achieving levels observed ≥24 months prior to surgery based on a linear regression model.

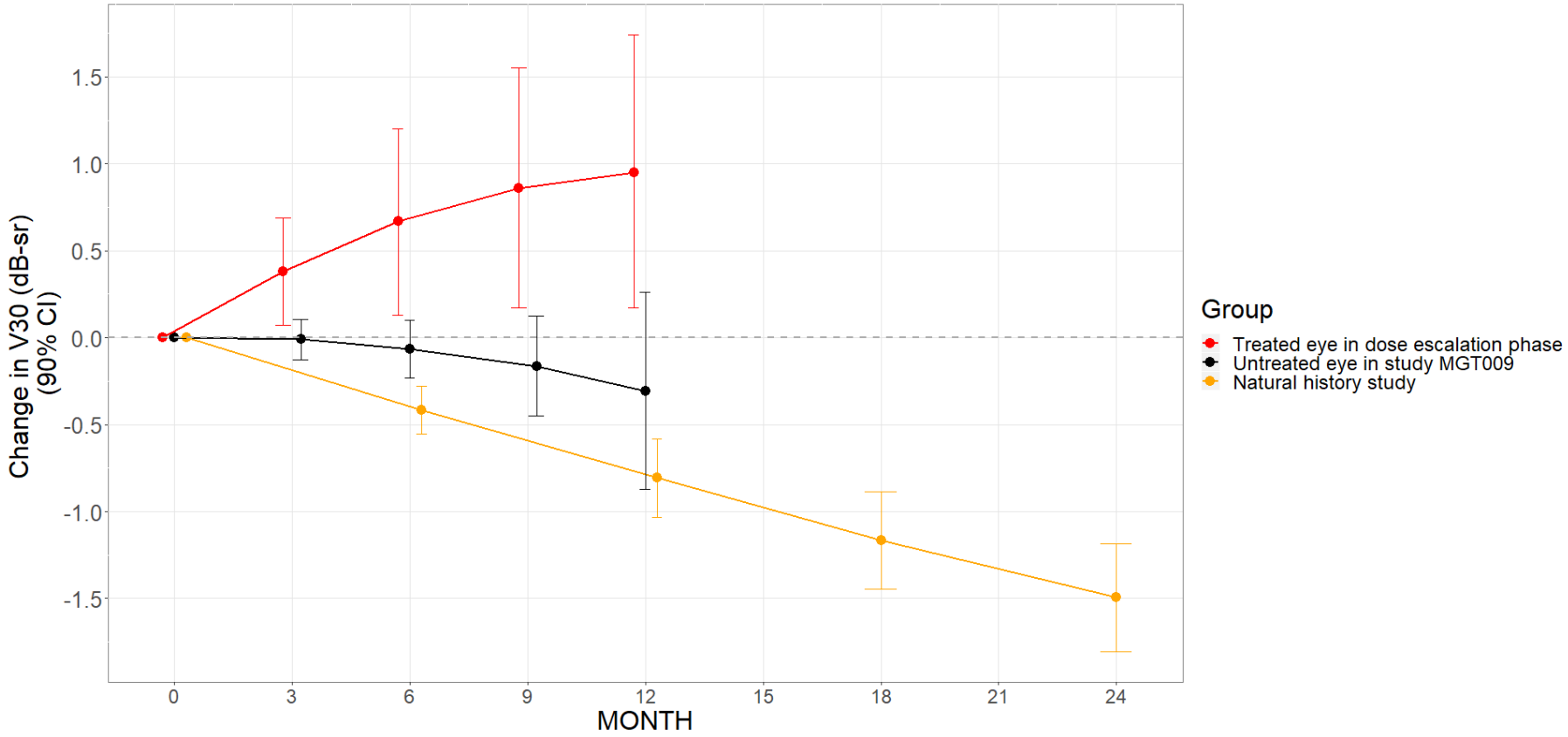
V30 in Intermediate Dose Patients Improved Post-intervention, Reversing a Downward Trajectory



dB-sr, decibel-steradians; V30, 30-degree hill of vision.

At Month 12 post-treatment, the treated eye in patients at the intermediate dose demonstrated improvements in perimetry-derived V30, achieving levels observed ≥24 months prior to surgery based on a linear regression model.

V30 in Untreated Eye in Study MGT009 Decreases at a Similar Rate to Patients in Natural History Study MGT011



Number of participants by treatment and visit

Group	Baseline	Month 3	Month 6	Month 9	Month 12	Month 18	Month 24
Treated eye (low and intermediate doses) in study MGT009	6	6	5	5	6	NA	NA
Untreated eye in study MGT009	34	27	25	5	8	NA	NA
Natural history study MGT011*	99	NA	49	NA	50	28	29

NA, not applicable. *Includes patients enrolled in MGT009.

Conclusions

- **At 12 months post-intervention,** treatment with the low and intermediate doses of AAV5-*RPGR* resulted in **clinically meaningful improvements** in retinal sensitivity across multiple metrics and modalities
- For the intermediate dose cohort, **intervention with AAV5-*RPGR*** therapy in the poorer-seeing eye **altered the course of natural disease progression**
  - At 12 months post-intervention, mean retinal sensitivity and V30 in the treated eye were similar to levels observed 24 months pre-intervention, while the untreated eye showed a continued downward trajectory
- Given the **robust safety and efficacy signals** observed at the low and intermediate doses, these two doses are being further explored in a randomized controlled Phase 3 clinical trial (NCT04671433)

RPGR, Retinitis Pigmentosa GTPase Regulator; V30, 30-degree hill of vision.

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