An Intravitreal 'Photoswitch' Molecule (KIO-301) for Reanimation in Retinitis Pigmentosa: a first-in-human trial

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* - Disclosures: Employee & Officer of Kiora Pharmaceuticals

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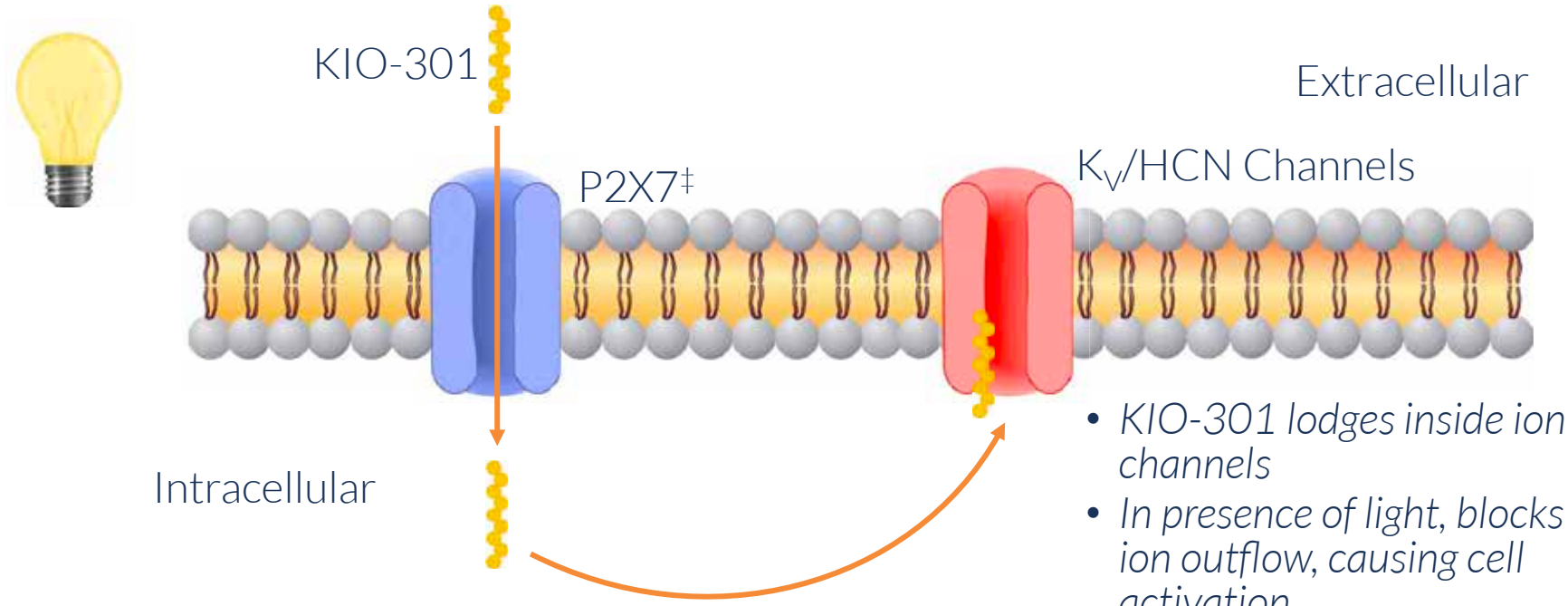
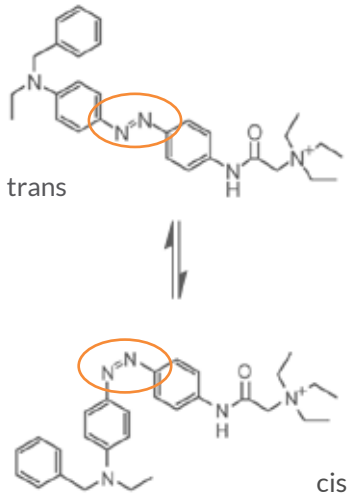
KIO-301 (MOA): Turns RGCs "ON" in the Presence of Light

- In RP, photoreceptors die → downstream neurons (RGCs) are not capable of being activated
- KIO-301 preferentially enters these RGCs and turns them "ON" in the presence of light*



- *KIO-301 lodges inside ion channels*
- *In presence of light, blocks ion outflow, causing cell activation*



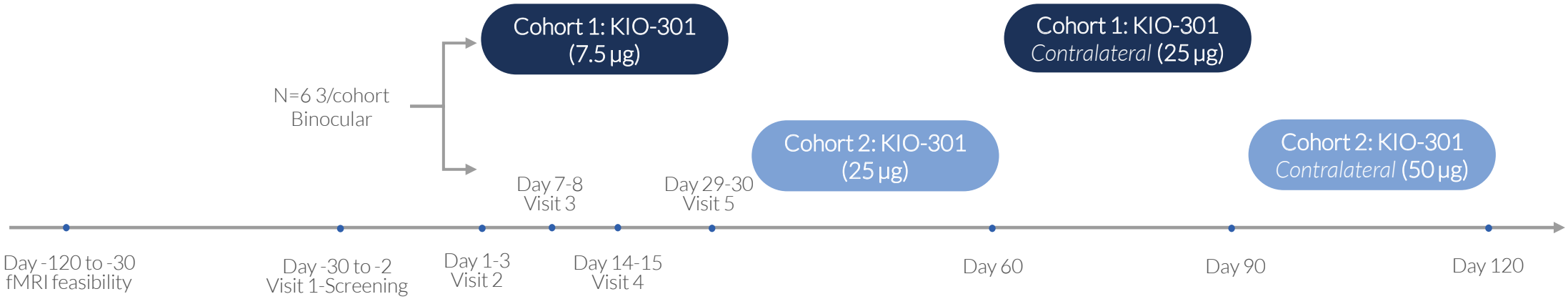
‡ P2X7 is solely expressed on RGCs and amacrine cells in areas of degenerated retina

* Visual light causes reversible isomeric shift, blocking ion efflux through K_V/HCN channels

Neuron. 92, 100-113 (2016)

KIO-301-1101: Phase 1b Study Design (ABACUS)

Open Label, Single Ascending Dose Trial – 2 Sites (Australia)



Study Design

- Two cohorts, non-randomized, open-label, single IVT injection per eye
- Cohort 1- NLP/BLP patients; Cohort 2 – HM/CF patients

Endpoints

- Primary - AEs, PK & labs
- Secondary - Assessment days (shown only for Cohort 1 above) is repeated for each cohort per eye; intensity & contrast assessment, kinetic perimetry, functional MRI, etc.

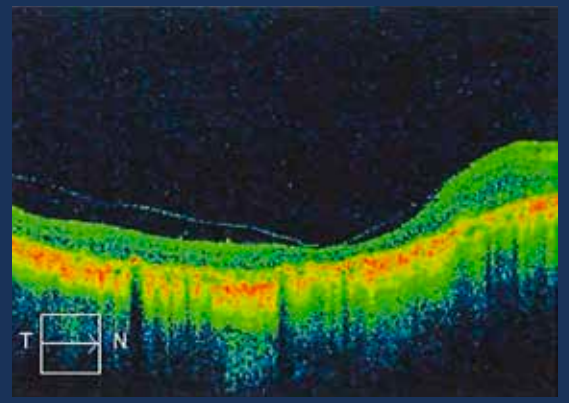
Review

- Safety review conducted after sentinel subject

clinicaltrials.gov: NCT05282953

5th decade of life; male NLP 10+ years
Safety & Tolerability

Systemic & Ocular Safety Assessments



- ✓ Slit-lamp –no changes observed compared to baseline
- ✓ IOP – normal and no change to baseline
- ✓ Dilated Fundus w/ photography* - abnormal at baseline (consistent with RP); no change to baseline
- ✓ OCT - no macular edema, no change in thickness

* Performed within 6 hours of injection & Day 29

Efficacy Assessments

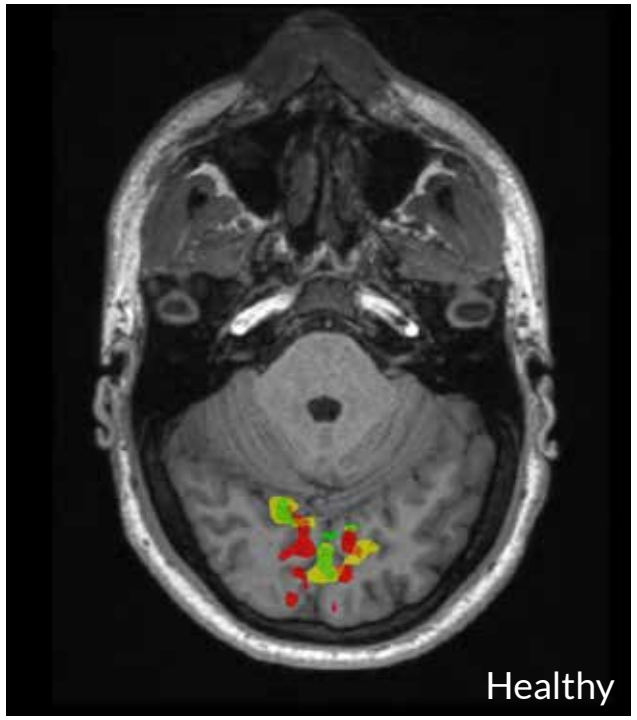
How Do You Measure Success in Ultra-Low Vision Patients?

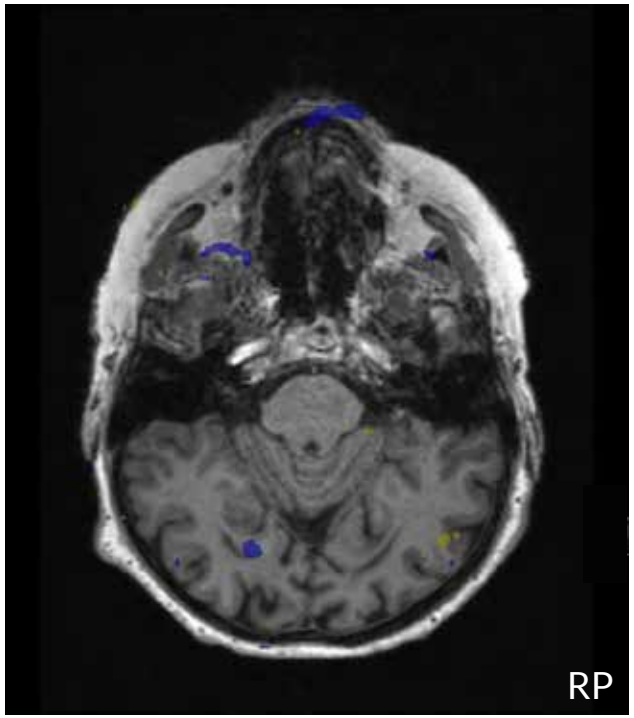
Objective

- Intensity & Contrast Assessment
- Goldmann Kinetic Perimetry
- Functional MRI

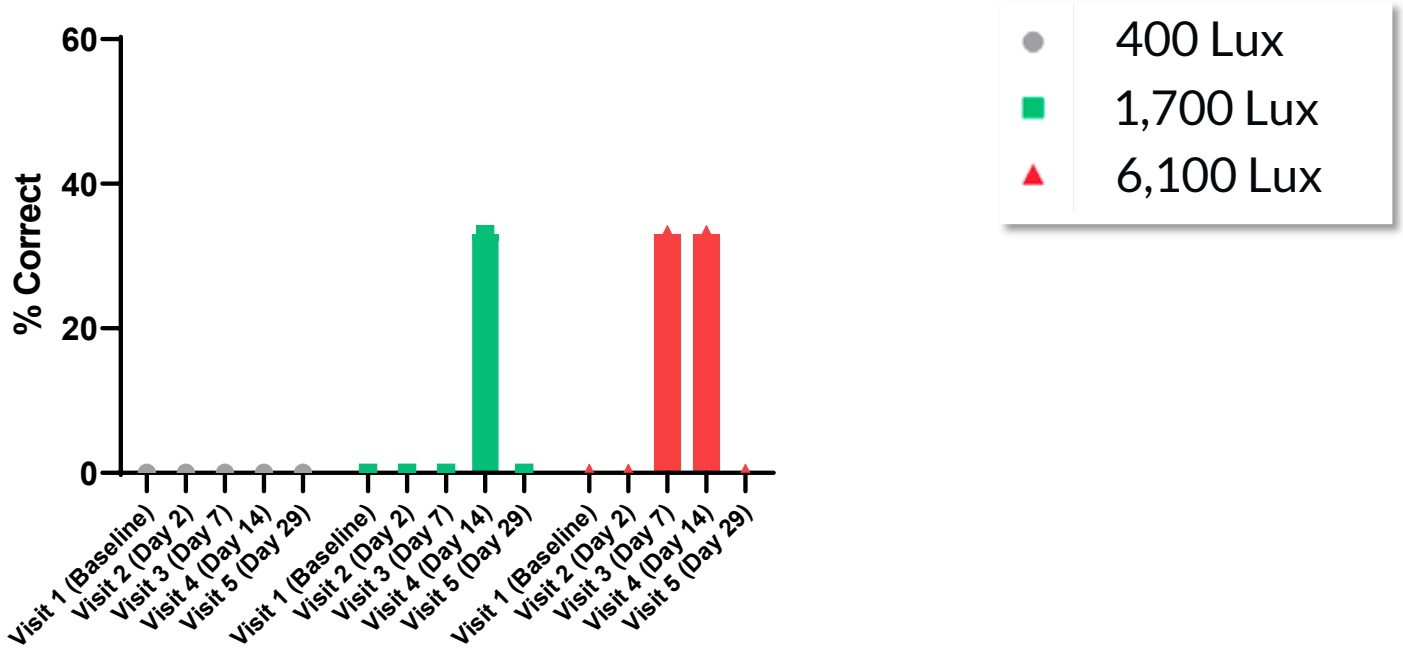
Subjective

- Patient reported feedback
- VFQ-25





Intensity & Contrast Assessment

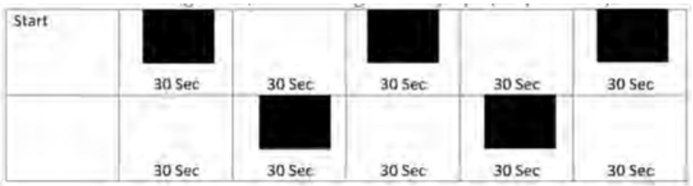


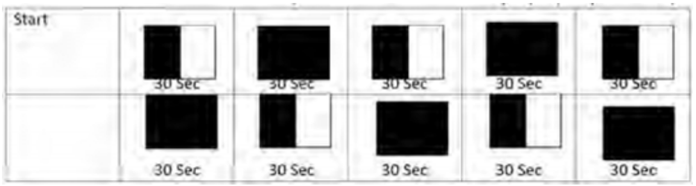
Key Takeaways:

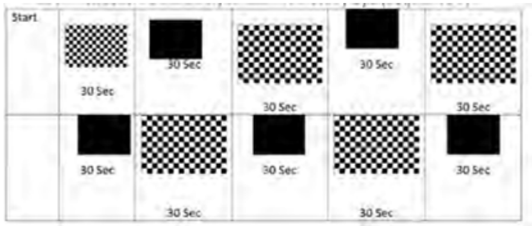
- Light perception increases over first 2 weeks following injection
- Returns to baseline by 4 weeks

Functional MRI – Setup & Analysis

Cohort 1 Paradigm (BLP/NLP)

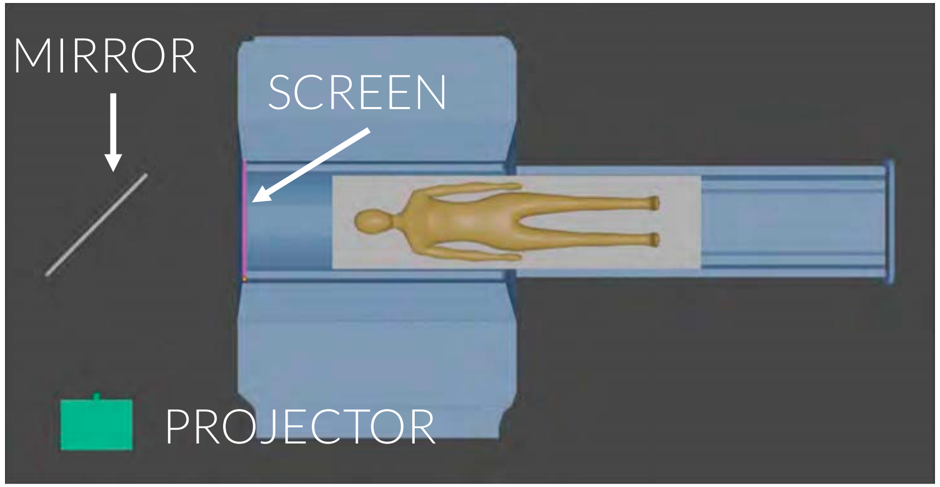






Processing and Analysis

- BOLD signal acquired
- Preprocessing (e.g., spatial normalization)
- Quantitative analysis using FSL (GLM)



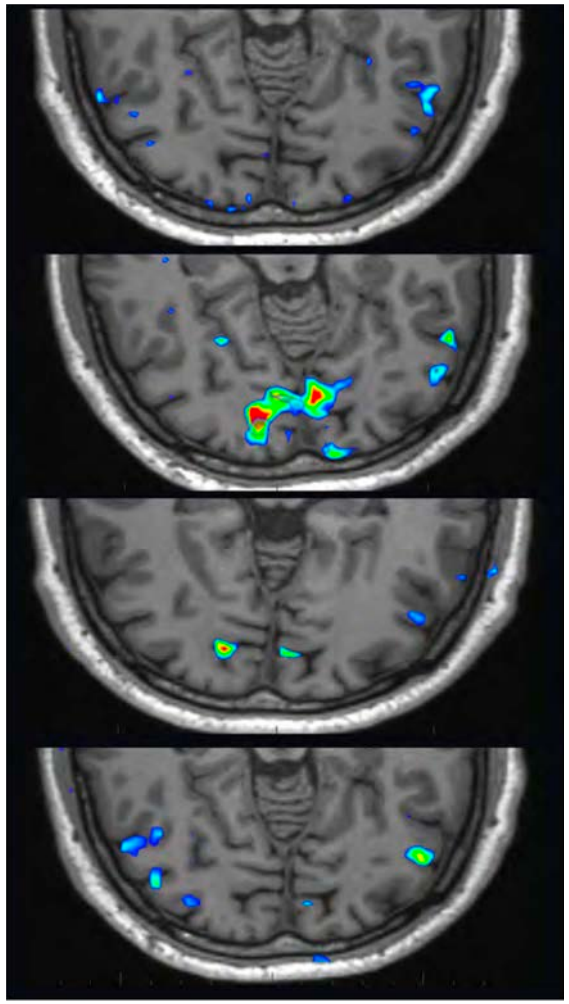
Functional MRI – Qualitative Overlap of 3 Paradigms

Visit 1
(Baseline)

Visit 2
(Day 3)

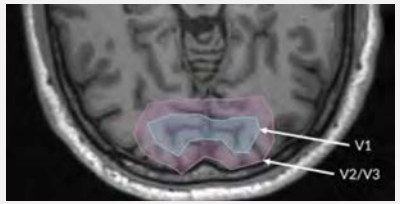
Visit 4
(Day 15)

Visit 5
(Day 30)

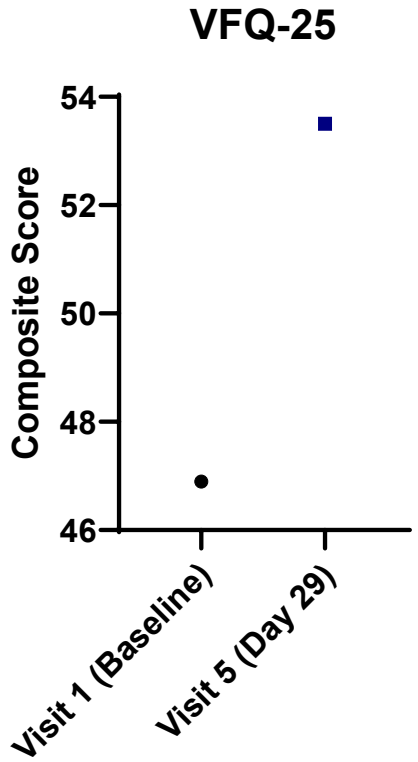


Key Takeaways

- Clear V1 (striate) increase in activity at Visits 2 & 4 compared to Visit 1
- Visit 5 returns to similar activity as baseline



Quality of Life Survey: VFQ-25



NEI-VFQ-25 administered at Visits 1 & 5

2 - 4 point increase is accepted by payers as clinically meaningful*

Overall increase driven by sub-scale increase in Vision Specific Questions (Near Activities, Mental Health & Social Functioning)

* - *HMSA Medical Policy – Luxturna - 2022*

Key Takeaways

- Small molecule capable of retinal reanimation
- Intravitreal KIO-301 safe and tolerable
- Improvements observed in objective and subjective assessments
- Return to baseline effect expected
- Enrollment ahead of schedule with full data expected in Q4 2023

Thank you