Subretinal Gene Therapy Drug AGTC-501 for X-Linked Retinitis Pigmentosa Phase 2 Randomized, Controlled, Multicenter Clinical Trial (Skyline) 3-Month Results

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Disclosures

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Biogen (C)
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X-Linked Retinitis Pigmentosa: Progressive photoreceptor degeneration that leads to blindness; No treatment options

Severe, aggressive, inherited retinal disease characterized by progressive photoreceptor degeneration

Orphan Disease @ 1:40,000 affecting young males

17K patients in U.S./EU5[1]

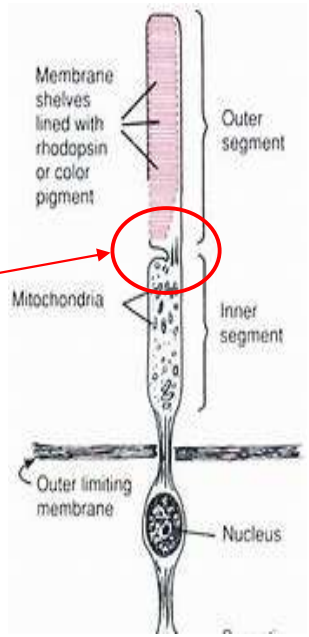
Caused by mutation in $RPGR_{orf15}$ gene, that is responsible for long term maintenance of photoreceptor viability

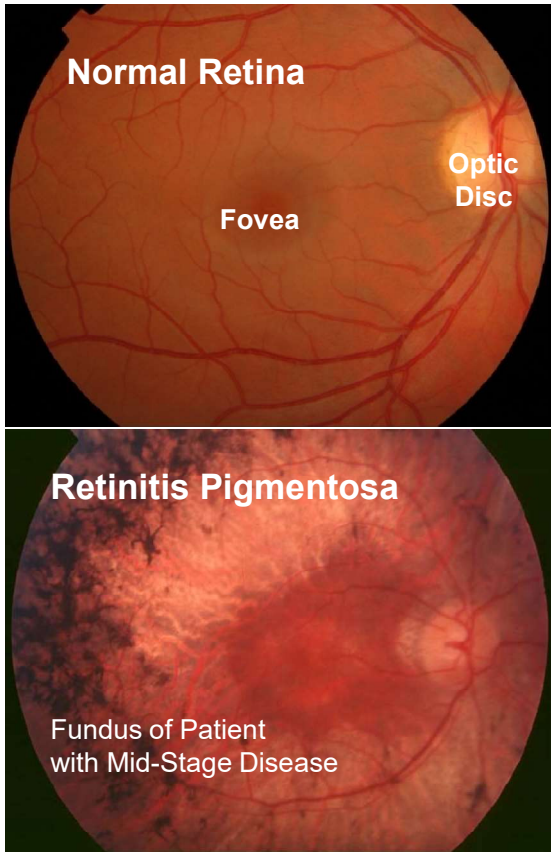
RPGR localized in cilium, the connective body between inner and outer segment of photoreceptors

Disease progression

- Early - Night blindness
- Mid - Peripheral vision loss
- Late - Central vision loss

Legally blind by median age of 45[2]

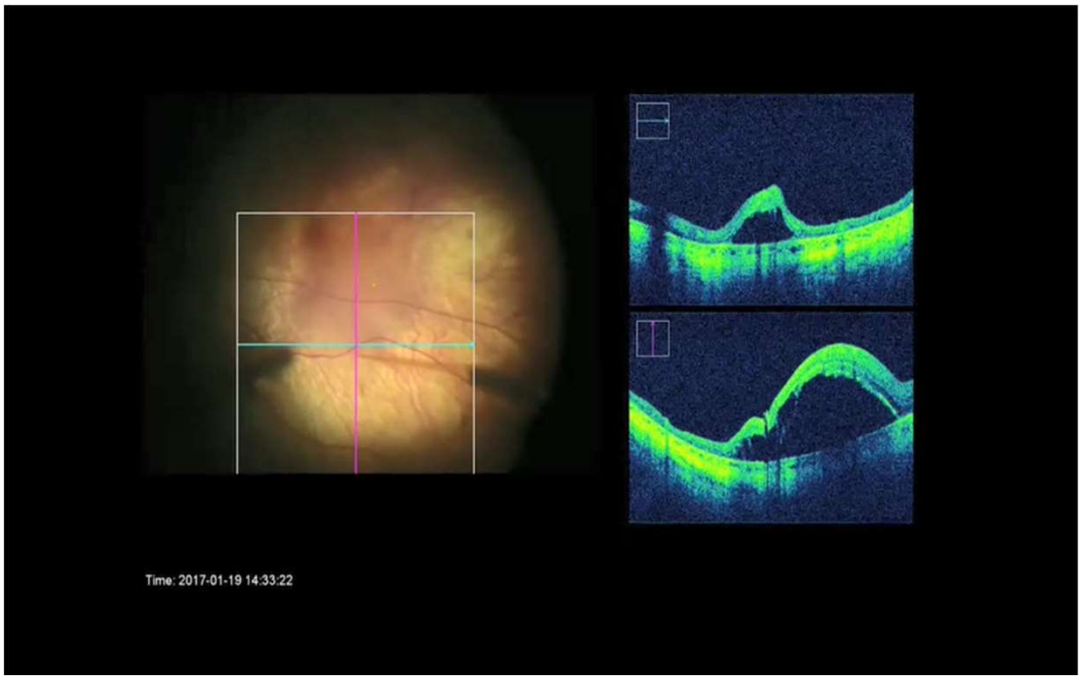




1. Vinikoor-Imler LC, et al. Ophthalmic Genet. 2022 Oct;43(5):581-588 2. Chivers M, et al. Clinicoecon Outcomes Res. 2021;13:565–572

AGTC-501 targets XLRP

- Delivering a correct copy of RPGR gene using AAV vector
- Delivered sub-retinally
- Proprietary capsid AAV2tYF
- Photoreceptor specific GRK1 promoter
- Codon optimised to allow for production of full-length RPGR transgene
- Phase I/II dose open label dose escalation study complete n=29
- Phase II High/Low dose study complete N=14 demonstrating robust improvement in retinal sensitivity



Potential Therapeutic Benefits of Using Full-length RPGR

AGTC-501 is the only late-stage program expected to restore the natural function of photoreceptors

Beacon uses a stable, full-length RPGRORF15 gene therapy vector, overcoming the pitfalls of a truncated RPGR^{ORF15}

As a full-length RPGR gene therapy, AGTC-501 therefore has a higher probability of restoring the natural function of cone photoreceptors, yielding greater visual improvement[1,2]

AGTC-501 and BIIB112 (Biogen) express the same correct full-length RPGR protein and undergo full glutamylation during post-translational modification.

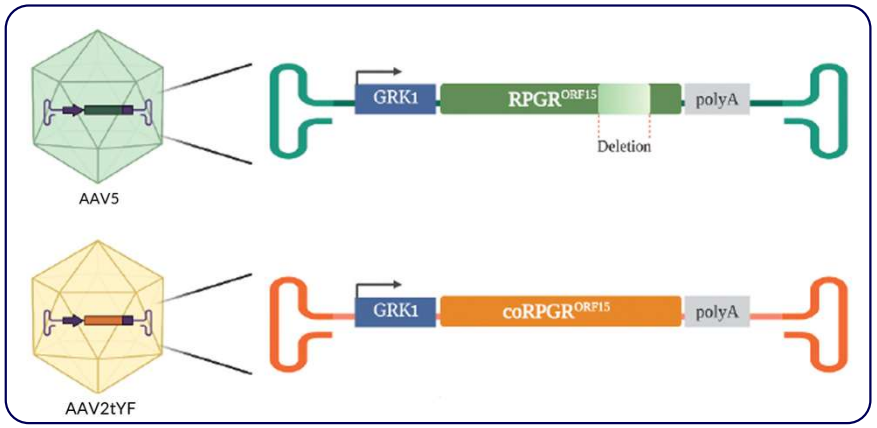
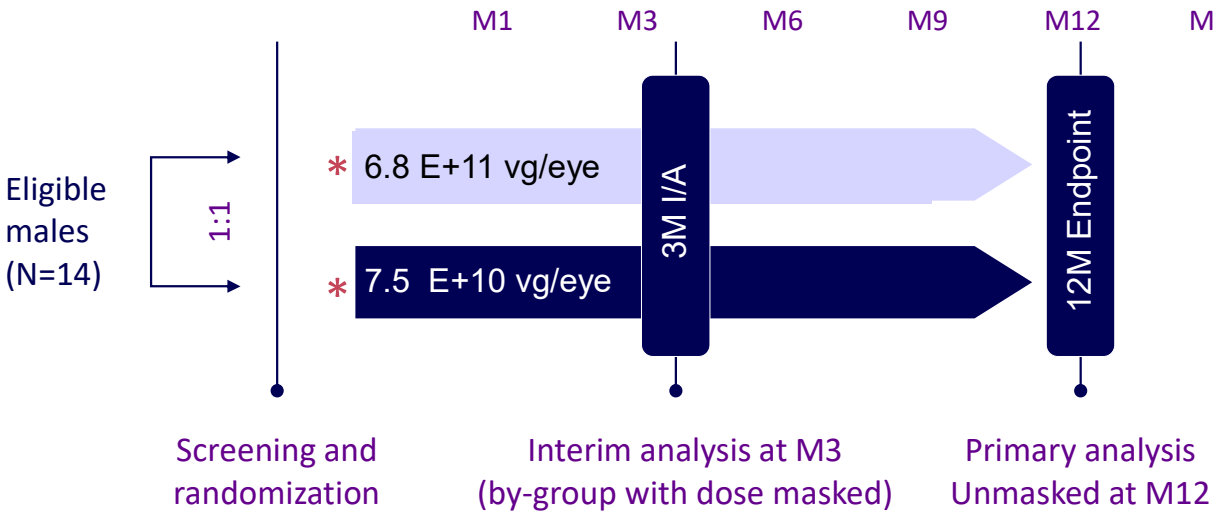


Figure adapted from Pawlyk B, et al. Gene Ther. 2016;23, 196–204 and Sun X, et al. Proceedings of the National Academy of Sciences. 2016;113(21): E2925-E2934

1. Pawlyk B, et al. Gene Ther. 2016;23, 196–204; 2. Sun X, et al. Proceedings of the National Academy of Sciences. 2016;113(21): E2925-E2934

Phase 2 SKYLINE Study Design

Randomized, Controlled, Multicenter Study to Evaluate the Safety and Efficacy of AGTC-501 in Patients with XLRP caused by *RPGR* mutations



FPI: 13 April 2021; 5-year follow-up post treatment

*All patients centrally dosed

Primary Endpoint

Retinal sensitivity, change from baseline:

- ≥ 7 dB improvement in ≥ 5 loci (MAIA)

Key Secondary Endpoints

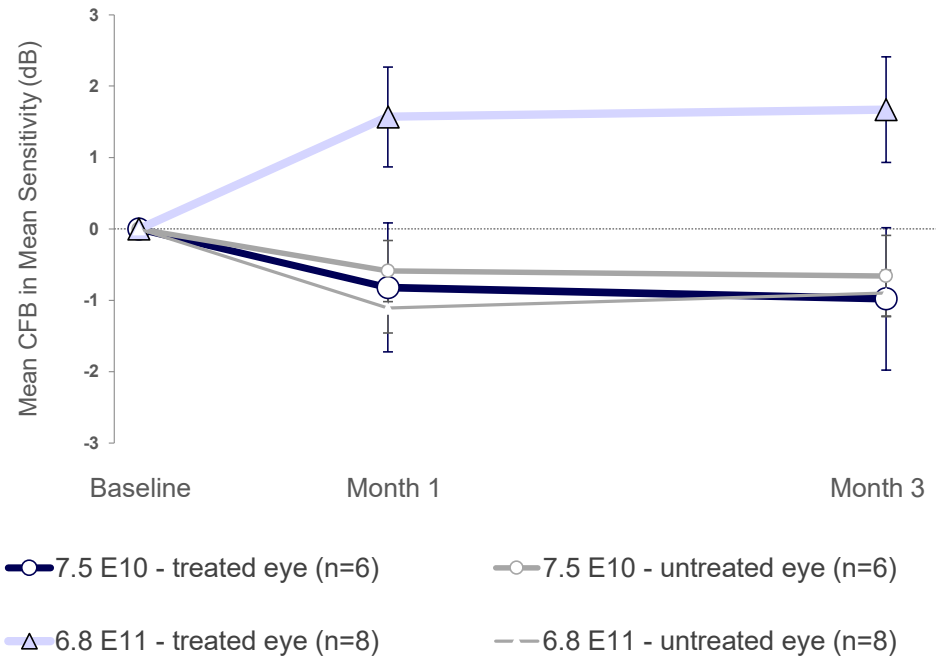
Change from baseline in:

- Mean sensitivity (MAIA)
- BCVA (ETDRS)

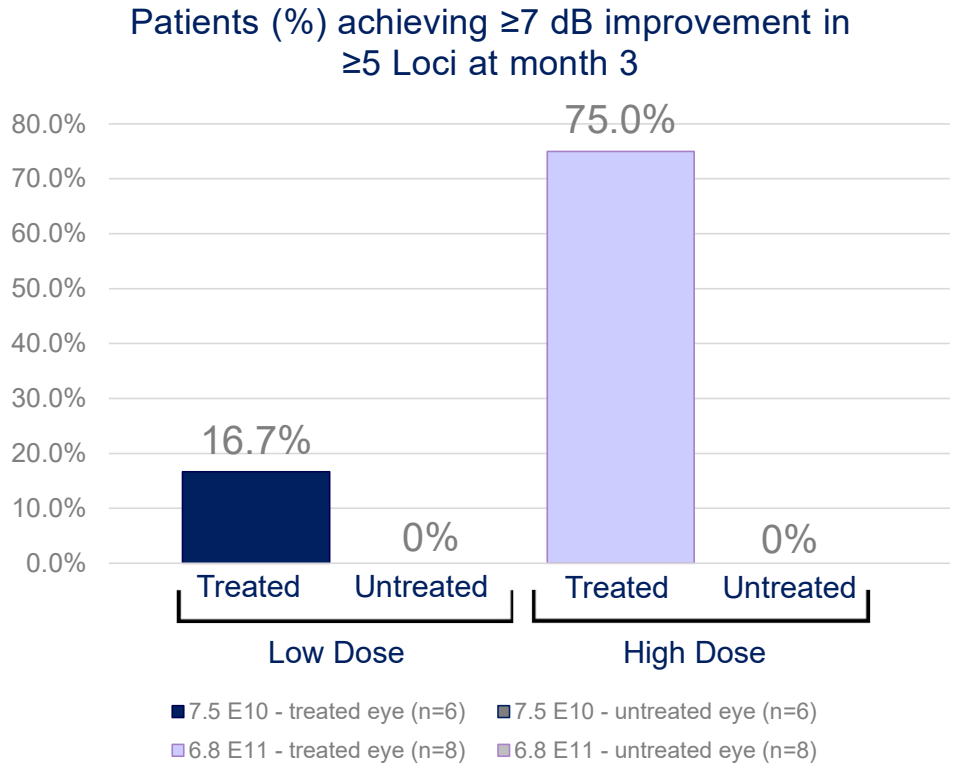
Efficacy Summary for 3-month analysis

Significant improvement in retinal sensitivity demonstrated in the high dose group

Change from Baseline Mean Sensitivity (Whole Grid)



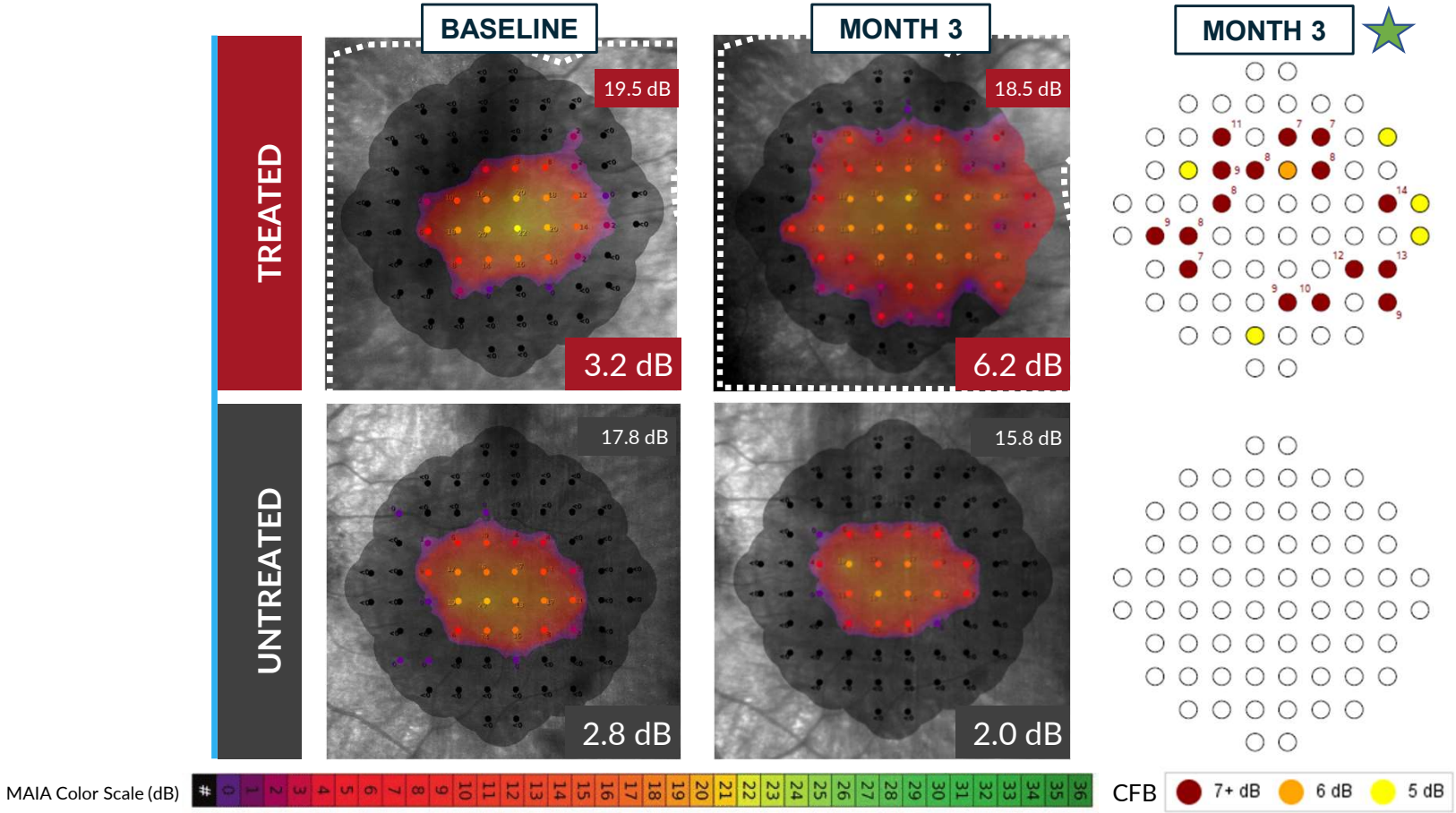
Responder Rate Month 3



Example 1 of a responding eye per microperimetry

★ ≥7 dB in ≥5 loci

Age	Treatment	Study Eye	Type of Mutation
16	6.8 E+11 vg/eye	OD	c.151delA(p.Thr51ProfsTer17) in exon 2

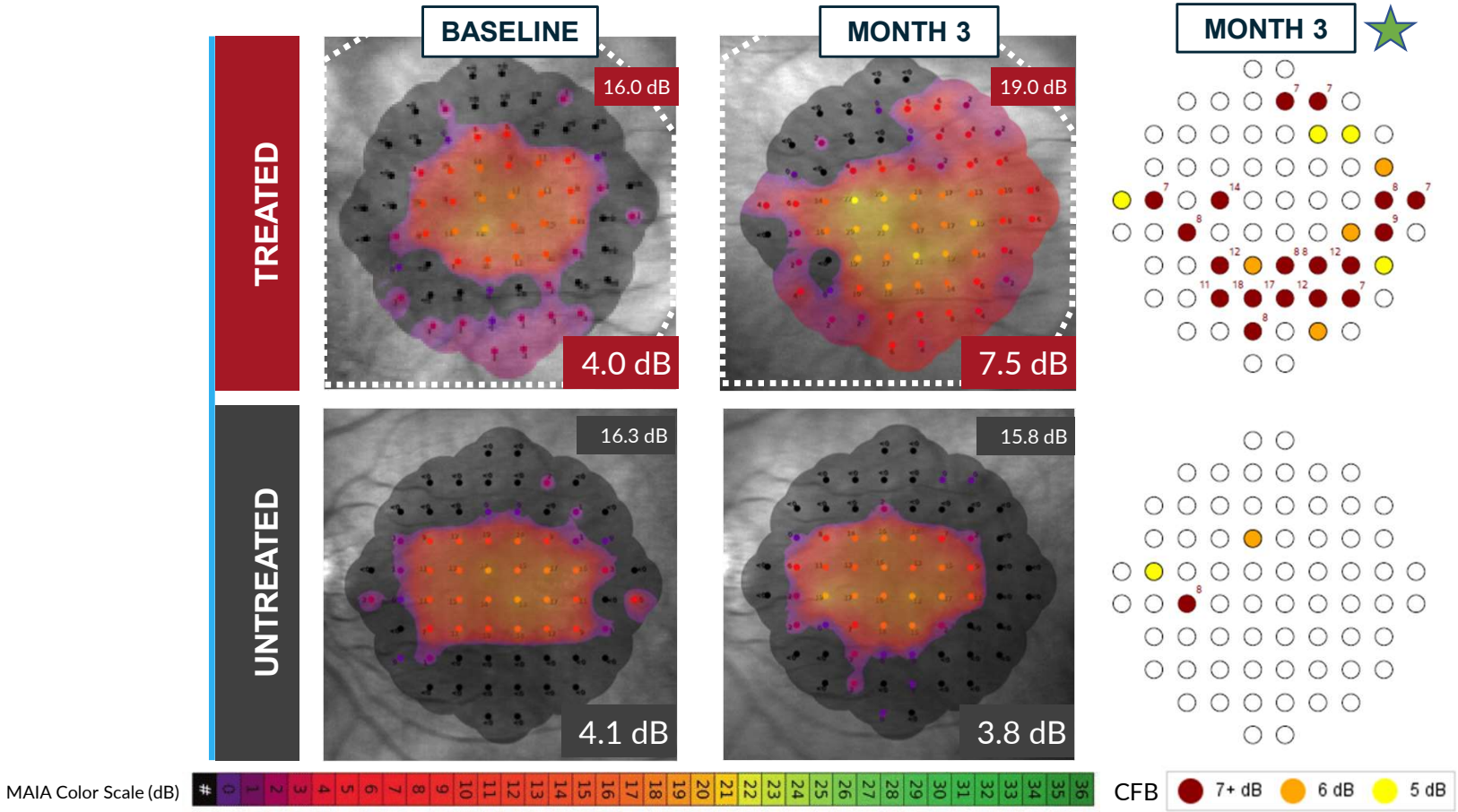


CFB = Change from Baseline; SE = study eye (treated); FE = fellow eye (untreated)

Example 2 of a responding eye per microperimetry

≥7 dB in ≥5 loci

Age	Treatment	Study Eye	Type of Mutation
14	6.8 E+11 vg/eye	OD	hemizygous missense variant (VUS) in the RPGR gene. NM_001034853.2(RPGR):c353A>C(p.Gln118Pro)



CFB = Change from Baseline; SE = study eye (treated); FE = fellow eye (untreated)

Safety Summary for Month 3 Analysis

No clinically significant safety events related to the study agent

- **No Suspected Unexpected Serious Adverse Reactions (SUSARs)**
- **No endophthalmitis reported**
- **Majority of ocular AEs were non-serious**
  - Favorable safety data in both dose groups
  - No difference between groups
- **2 ocular SAEs were reported; neither related to study agent**
  - Persistent decreased vision after surgery, deemed related to study injection
  - Increased IOP, deemed related to corticosteroids (concomitant medication)
- **1 non-ocular SAE**
  - Asthma exacerbation

Ocular SAEs – None study agent-related

MedDRA Preferred Term:	Description:	Related to Study Agent	Related to Study Injection	Related to ConMed
IOP increased	Post-op D48, controlled with medications, resolved	No	No	**Yes** (Corticosteroids)
Visual impairment	Borderline retinal structure at baseline, decrease in BCVA significant, resolving	No	**Yes**	No

Non-Serious Ocular AEs – Related to Study Agent & All Grade 2 and Transient

MedDRA Preferred Term:	7.5E+10 vg/eye (Low Dose) (N=5)	6.8E+11 vg/eye (High Dose) (N=8)	All Subjects (N=13)
Vitritis	1 (20%)	2 (25%)	3 (23%)
Eye pain	1 (20%)	0	1 (8%)

Conclusions: AGTC-501 Phase 2 Skyline XLRP 3 Month Interim Results

- **Robust and statistically significant improvement in retinal sensitivity in the high dose group**
- **Response rate of 75% in the high dose (6.8 E+11 vg/eye) group (6/8) at 3 months**
- **Pattern of response implies therapy rescues photoreceptor sensitivity**
- **Generally safe and well tolerated**
- **No clinically significant safety findings related to study agent**
  - No Suspected Unexpected Serious Adverse Reactions (SUSARs), no endophthalmitis reported
  - 2 ocular SAEs were reported; neither related to study agent
- **12 month confirms 3 month data, will be presented at upcoming meeting**

Acknowledgments

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