Topline Results from the Phase 3 DRAGON Study of Tinlarebant for Adolescent Stargardt's Disease

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Disclosures

- **Principal Investigator in clinical trials**
  - Belite Bio
  - Foundation Fighting Blindness
  - Frontera
  - Drug Farm
- **Consultant**
  - Innovec Bio (SAB)

Tinlarebant

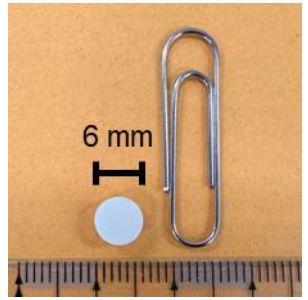
Introduction to Tinlarebant

- Patients affected with Stargardt Disease (STGD1) harbor genetic mutations in a key protein within the retina which interferes with normal vitamin A processing in the visual cycle; this results in the accumulation of cytotoxic byproducts of vitamin A (*bisretinoids*) and progressive retinal cell death. [1]

- Tinlarebant is a novel, **once-a-day oral tablet** designed to bind to serum retinol binding protein 4 (RBP4) as a means to specifically reduce retinol delivery to the eye in order **to slow or halt the accumulation of cytotoxic bisretinoids**.

- Belite Bio believes that **intervention directed at emerging retinal pathology**, which is not primarily mediated by complement activation/inflammation, would be the best approach to potentially slow disease progression in STGD1 & GA.

Tinlarebant Tablet



[1] Mata NL, Weng J, Travis GH (2000) Biosynthesis of a major lipofuscin fluorophore in mice and humans with ABCR-mediated retinal and macular degeneration. Proc Natl Acad Sci U S A. 97: 7154-9.

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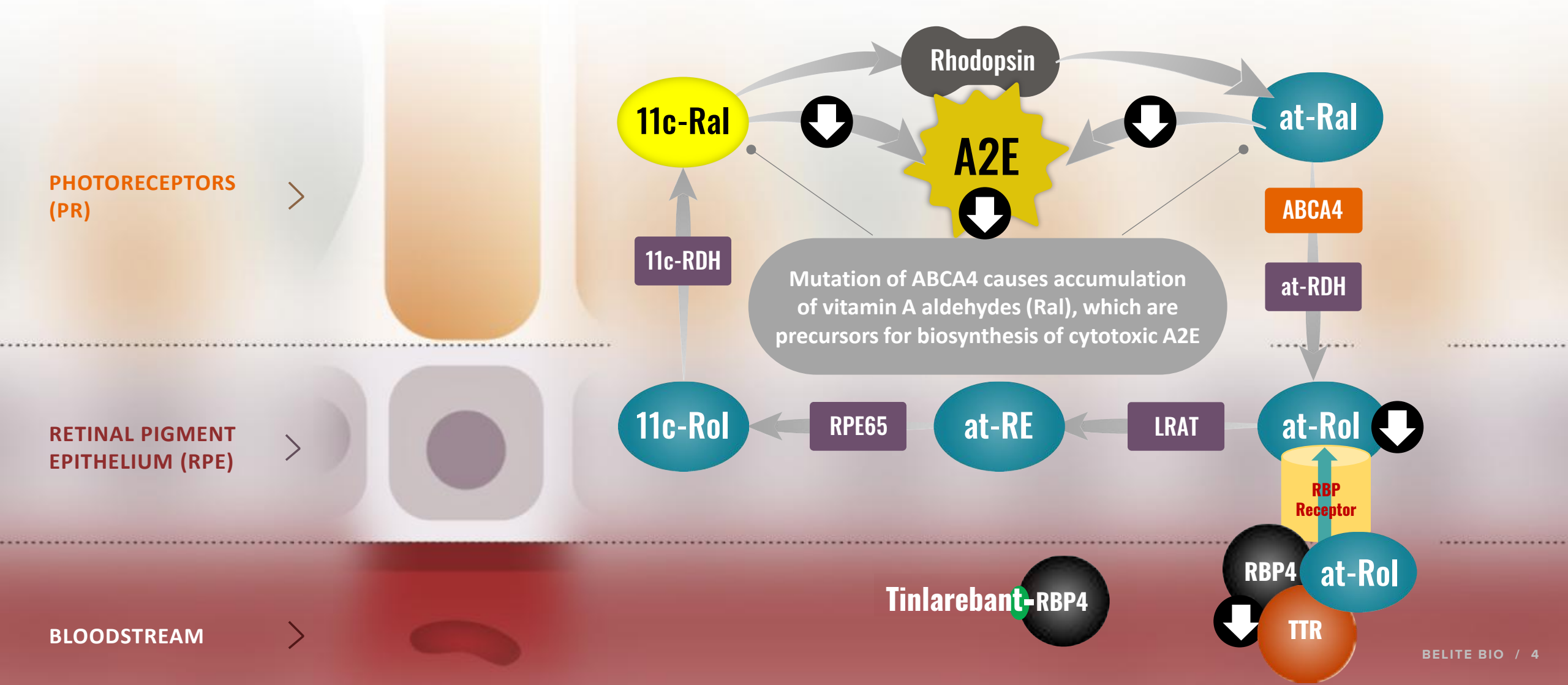
Mechanism of Tinlarebant Action

Bisretinoids are derived from vitamin A (retinol). Therefore, reducing the delivery of retinol to the eye is expected to reduce bisretinoid levels in the eye leading to preservation of the retina



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Phase 3 DRAGON Trial in Stargardt Disease

-Data from DRAGON Topline Report

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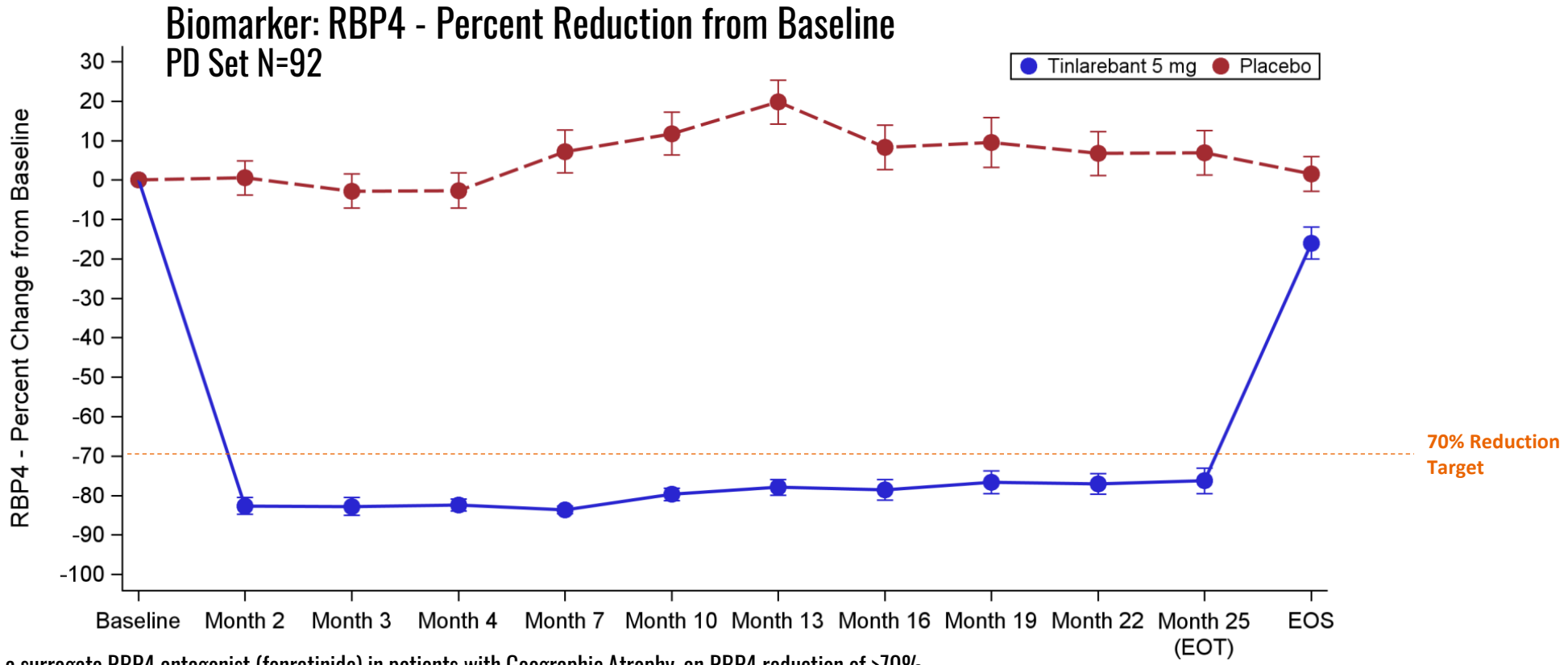
Tinlarebant Treatment Led to 80% Reduction in RPB4, Well Above Goal of 70%*



* In a prior study of a surrogate RBP4 antagonist (fenretinide) in patients with Geographic Atrophy, an RBP4 reduction of ≥70% was associated with a statistically significant slowing of lesion growth [Mata et al., Retina. 2013; 33(3): 498-507.]

Daily dosing of 5 mg/day Tinlarebant led to a sustained 80% reduction of RPB4 and RPB4 levels returned to 84 % of the baseline value at the End of Study (EOS)

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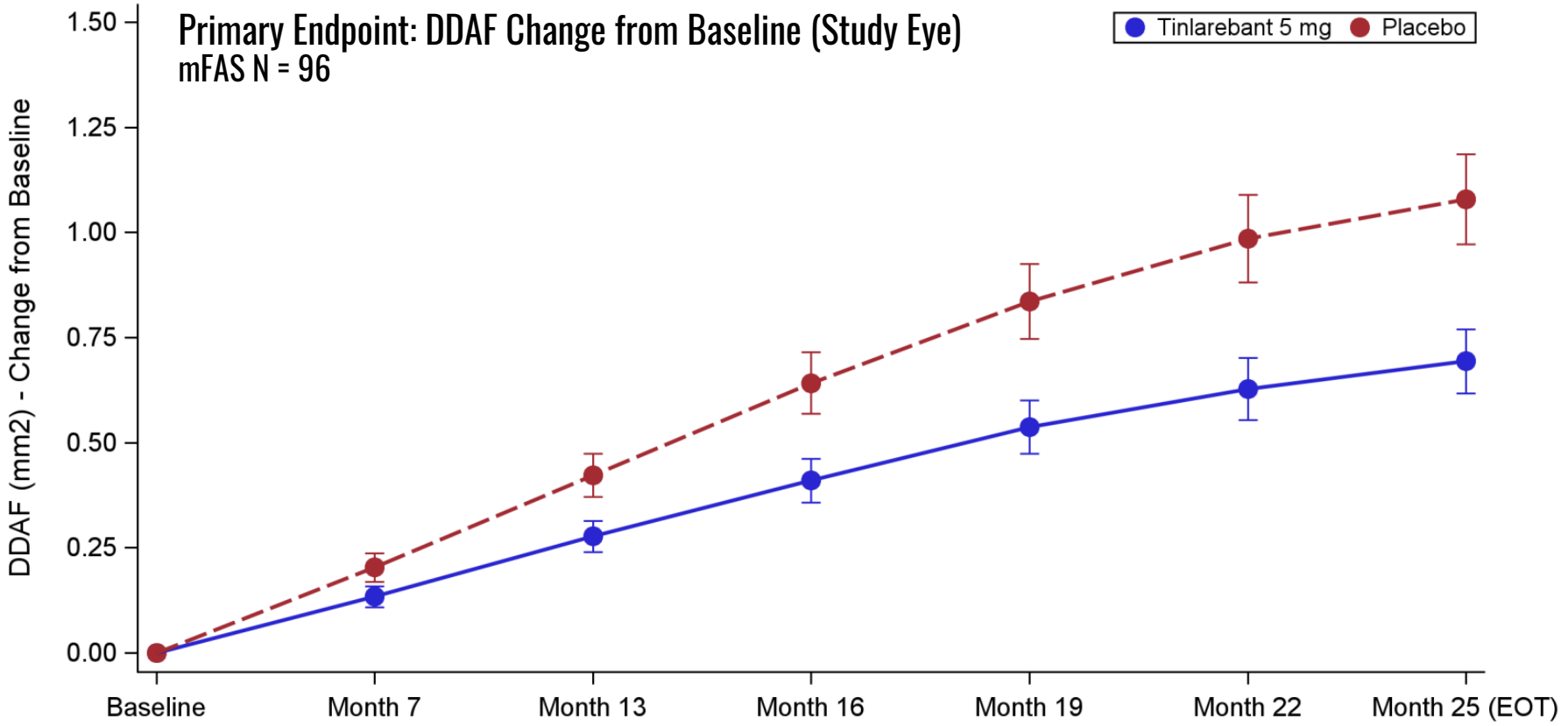
Primary Endpoint Showed a Statistically Significant & Clinically Meaningful Outcome



- Applying an unstructured covariance matrix, the **treatment effect size was 35.7%** compared to placebo and yielded a **p-value of P = 0.0033**
- With a first-order autoregressive covariance matrix, the **treatment effect size remained consistent (35.4%)** with **P <0.0001**
- DDAF lesion growth was **slowed to 0.38 mm²/year vs. 0.59 mm²/year for placebo and 0.74 mm²/year observed in ProgStar**

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As Expected, BCVA in Study Eye Did Not Show Any Significant Change

	Tinlarebant	Placebo
BCVA at Baseline	39.9	39.4
BCVA at EOS	39.7	40.0

- The overall change of visual acuity was minimal over the period of 24 months in both treatment groups
- Test–retest variability for ETDRS change scores in Stargardt disease are known to yield a repeatability coefficient ≈ 8 letters [(1)]
- Such minor changes in average visual acuity over two years are in line with the natural history of Stargardt disease and were observed in the ProgStar Study

(1) Parker MA, Choi D, Erker LR, Pennesi ME, Yang P, Chegarnov EN, Steinkamp PN, Schlechter CL, Dhaenens CM, Mohand-Said S, Audo I, Sahel J, Weleber RG, Wilson DJ. Test-Retest Variability of Functional and Structural Parameters in Patients with Stargardt Disease Participating in the SAR422459 Gene Therapy Trial. Transl Vis Sci Technol. 2016 Oct 1;5(5):10.

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Tinlarebant Demonstrated a Well Tolerated Safety Profile

*TEAE=Treatment-emergent adverse event

Category	Tinlarebant 5mg (N=69)	Placebo (N=35)
Ocular TEAE	**53 (76.8%)**	**8 (22.9%)**
Severe TEAE	2 (2.9%)	0 (0.0%)
Serious TEAE	0 (0.0%)	0 (0.0%)
Study Drug-Related TEAE	49 (71.0%)	8 (22.9%)
Non-Ocular TEAE	**59 (85.5%)**	**27 (77.1%)**
Severe TEAE	2 (2.9%)	1 (2.9%)
Serious TEAE	2 (2.9%)	4 (11.4%)
Study Drug-Related TEAE	14 (20.3%)	4 (11.4%)

- Ocular TEAE: **Xanthopsia, Delayed Dark Adaptation, and Night Vision Impairment** are the most reported
  - The majority of the events were mild, and most resolved while on study.
- Non-ocular TEAE: **Nasopharyngitis (unrelated/unlikely related to treatment), Headache, and Acne** are the most reported
  - Most events were mild and resolved during the study period.
- Total of 6 Serious TEAEs were reported in the study
  - All events were non-ocular, with 4 assessed as unrelated and 2 assessed as unlikely related to the study treatment.
- No serious ocular TEAEs were reported; 4 TEAEs led to study drug discontinuation, and 2 led to study discontinuation.

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Summary

- **The DRAGON trial met its primary endpoint:** A highly statistically significant slowing in DDAF lesion growth was observed in subjects treated with 5 mg/day oral Tinlarebant as compared to placebo
- **The treatment effect was ~36%** and is considered **clinically meaningful**
- The **change in best-corrected visual acuity was minimal** in both the treatment and the placebo group – and is **in-line with natural history data**
- The biomarker of tinlarebant treatment, **RBP4 reduction, showed a sustained 80% reduction with very little variability**
- **Tinlarebant (5 mg p.o., daily) was safe and well tolerated** in adolescent STGD1 patients

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THANK YOU