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Retina Subspecialty Day
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Topline 24-Month Results from the Phase 3 DRAGON Study of Tinlarebant for Adolescent Stargardt Disease

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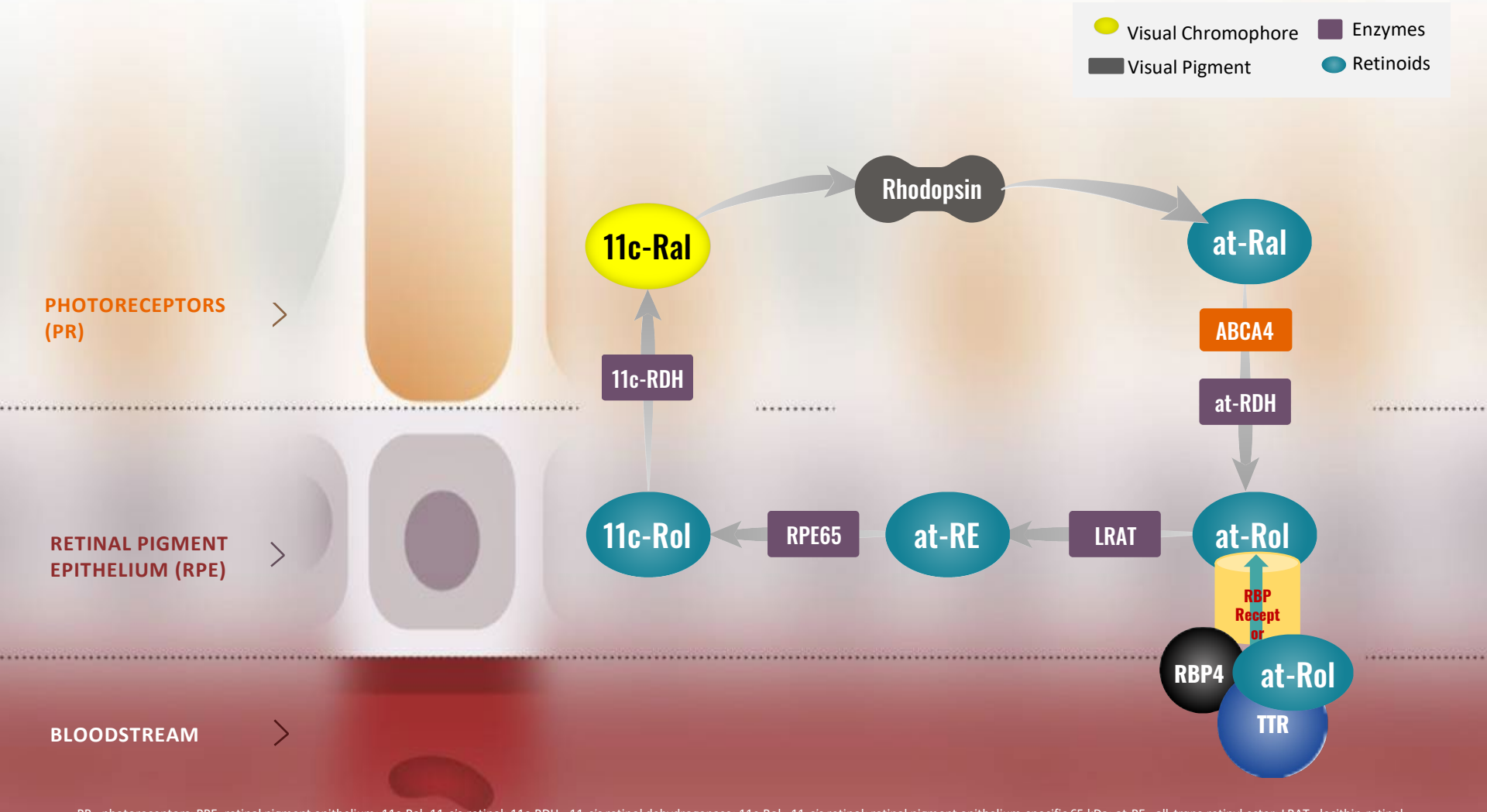
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Financial Disclosures

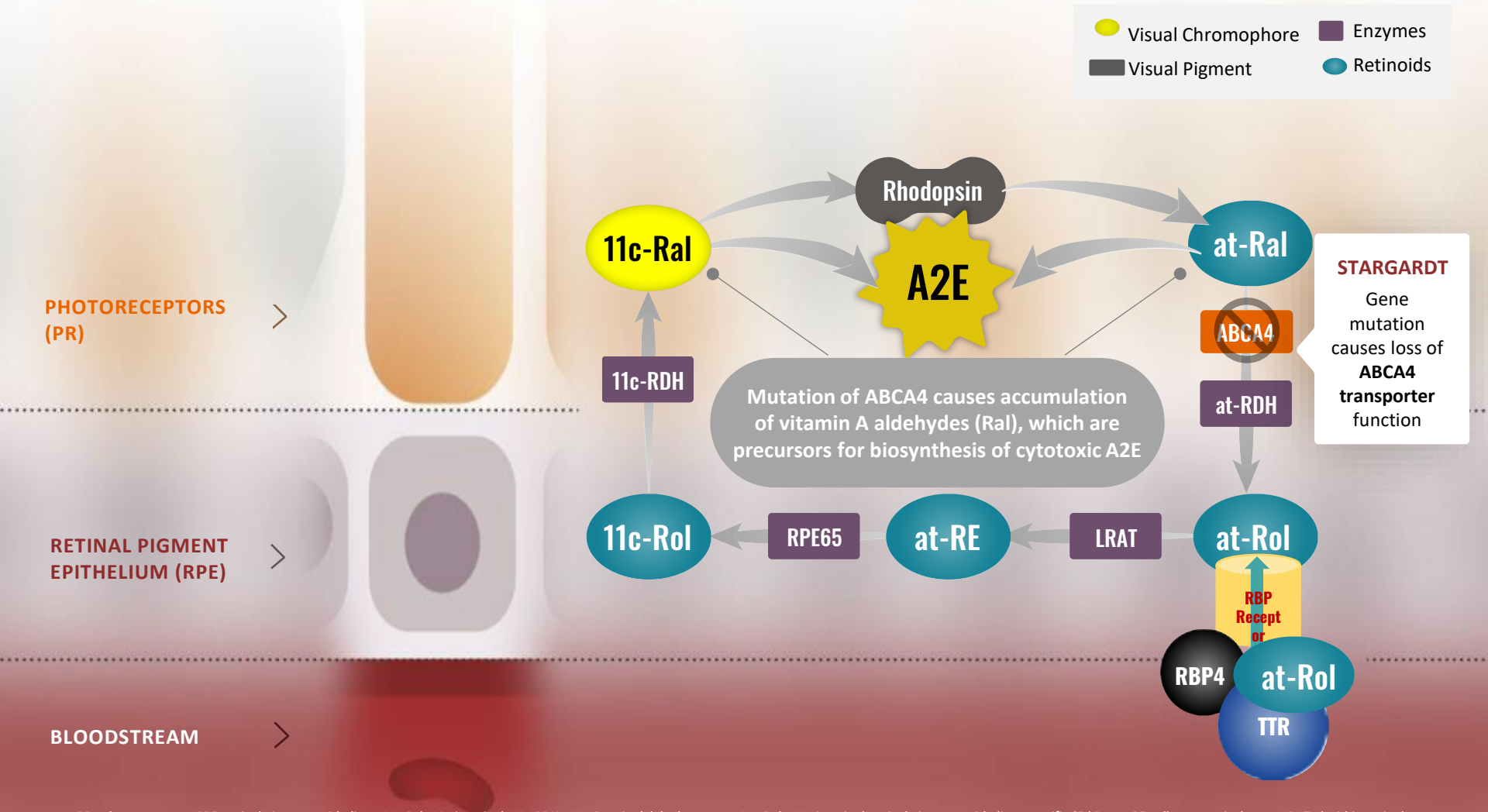
- Stanford University has received research funding from Belite Bio, Boehringer-Ingelheim, Genentech, Priovant, Regeneron, among others
- Dr. Nguyen chairs the Steering Committees for the SAKURA, VISUAL, STOP-Uveitis, and LINNAEA studies, and serves on Scientific Advisory Boards for Belite Bio, Boehringer-Ingelheim, Genentech, Regeneron, Priovant, among others

Normal Processing of Vitamin A in the Visual Cycle



PR= photoreceptors; RPE=retinal pigment epithelium; 11c-Ral=11-*cis*-retinal; 11c-RDH= 11-*cis* retinol dehydrogenase; 11c-Rol= 11-*cis* retinol; retinal pigment epithelium-specific 65 kDa; at-RE= all-*trans*-retinyl ester; LRAT= lecithin-retinol acyltransferase; at-Ral=all-*trans*-retinal; ABCA4=ATP-binding cassette sub-family A member 4; at-RDH=all-*trans*-retinol dehydrogenase; at-Rol=all-*trans*-retinol; RBP=retinal binding protein; RBP4=retinal binding protein 4; TTR=transthyretin; A2E=N-retinyl-N-retinylidene ethanolamine

Formation of Toxic Vitamin A Byproducts in Stargardt Disease 1 (STGD1)



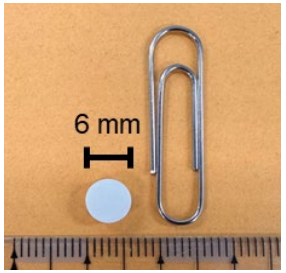
PR= photoreceptors; RPE=retinal pigment epithelium; 11c-Ral=11-*cis*-retinal; 11c-RDH= 11-*cis* retinol dehydrogenase; 11c-Rol= 11-*cis* retinol; retinal pigment epithelium-specific 65 kDa; at-RE= all-*trans*-retinyl ester; LRAT= lecithin-retinol acyltransferase; at-Ral=all-*trans*-retinal; ABCA4=ATP-binding cassette sub-family A member 4; at-RDH=all-*trans*-retinol dehydrogenase; at-Rol=all-*trans*-retinol; RBP=retinal binding protein; RBP4=retinal binding protein 4; TTR=transthyretin; A2E=N-retinyl-N-retinylidene ethanolamine

Tinlarebant
Mechanism of Action

Background

- Patients affected with Stargardt Disease type 1 (STGD1) harbor **genetic mutations in a key protein within the retina which interferes with normal vitamin A processing in the visual cycle,** resulting in significantly increased accumulation of cytotoxic byproducts of vitamin A (**bisretinoids**) and progressive retinal cell death[1]
- Investigational **tinlarebant** aims to **reduce delivery of vitamin A to the eye**. Reduced vitamin A (retinol) levels in the retina **decrease biosynthesis of cytotoxic bisretinoids** which underly disease progression in STGD1

Tinlarebant Tablet



[1] Mata NL, Weng J, Travis GH. Biosynthesis of a major lipofuscin fluorophore in mice and humans with ABCR-mediated retinal and macular degeneration. Proc Natl Acad Sci U S A. 2000, 20;97(13):7154-9.

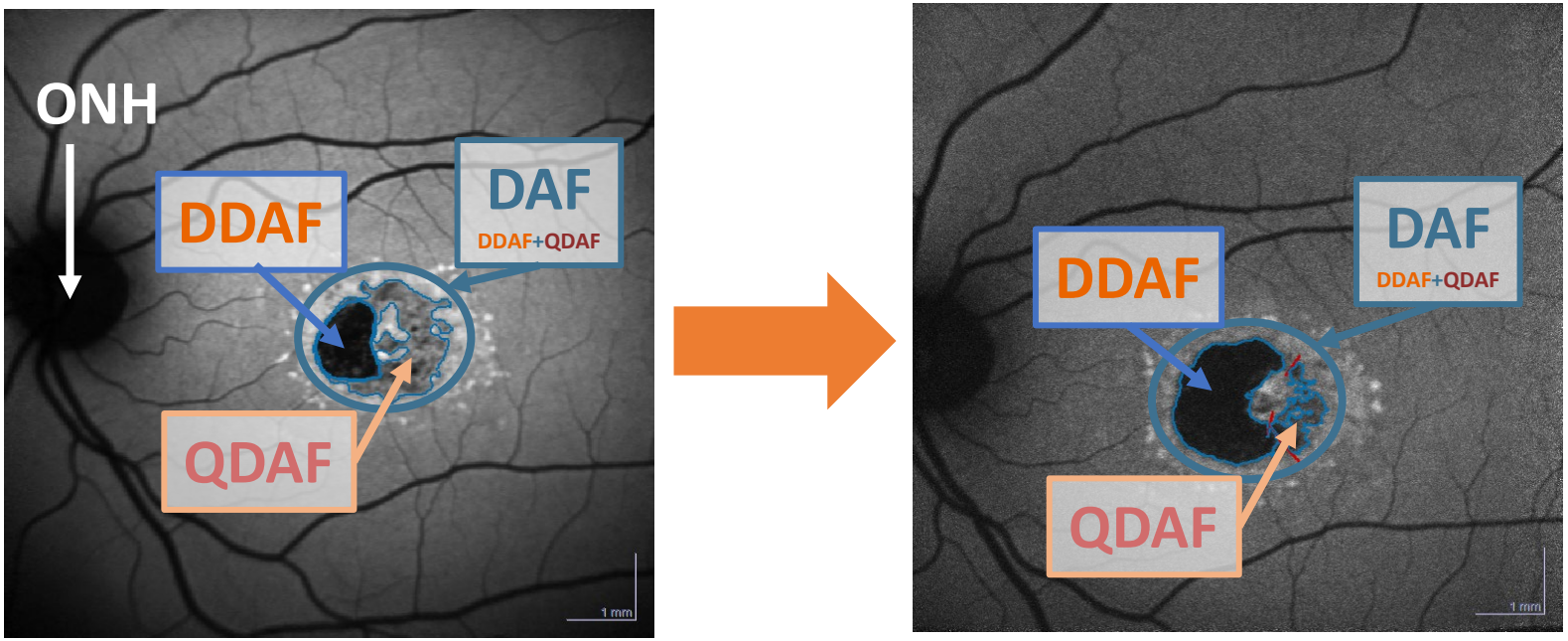
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Phase 3 DRAGON Trial in Stargardt Disease

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DDAF Represents Well-demarcated Areas of Complete RPE Loss and Grows Predictably, Making It an Approvable Primary Endpoint

- **DDAF** (definitely decreased autofluorescence): level of darkness close to 100% (at least 90%) in reference to the ONH
- **QDAF** (questionably decreased autofluorescence): 50% -90% darkness
- **DAF** (decreased autofluorescence): the sum of DDAF and QDAF



Strauss RW, Ho A, Muñoz B, Cideciyan AV, Sahel JA, Sunness JS, Birch DG, Bernstein PS, Michaelides M, Traboulsi EI, Zrenner E, Sadda S, Ervin AM, West S, Scholl HPN; Progression of Stargardt Disease Study Group (2016) The Natural History of the Progression of Atrophy Secondary to Stargardt Disease (ProgStar) Studies: Design and Baseline Characteristics: ProgStar Report No. 1. Ophthalmology. 123: 817-28.

DRAGON Phase 3 Clinical Trial Design

DRAGON Clinical Trial Design	
Enrollment:	N= **104**
Sites:	22 Global sites located in Australia, Belgium, China, France, Germany, Hong Kong, Netherlands, Switzerland, Taiwan, UK, US
Randomization:	**2:1 Tinlarebant : Placebo**
Masking:	Double masked
Treatment duration:	2 years (24 months)
Primary Outcome :	Efficacy as measured through **definitely decreased autofluorescence (DDAF)** lesion growth rate, safety & tolerability
Key Secondary Endpoints:	**Decreased autofluorescence** (**DAF**, calculated as the sum of DDAF and QDAF), BCVA, reduction in RBP4, SD-OCT
Key inclusion criteria:	12-20 years old, clinically diagnosed STGD1 with at least 1 mutation identified in the ABCA4 gene, atrophic lesion size within 3 disc areas (7.62 mm2), BCVA of 20/200 or better, no ocular disease that would complicate assessments and Vitamin A deficiency

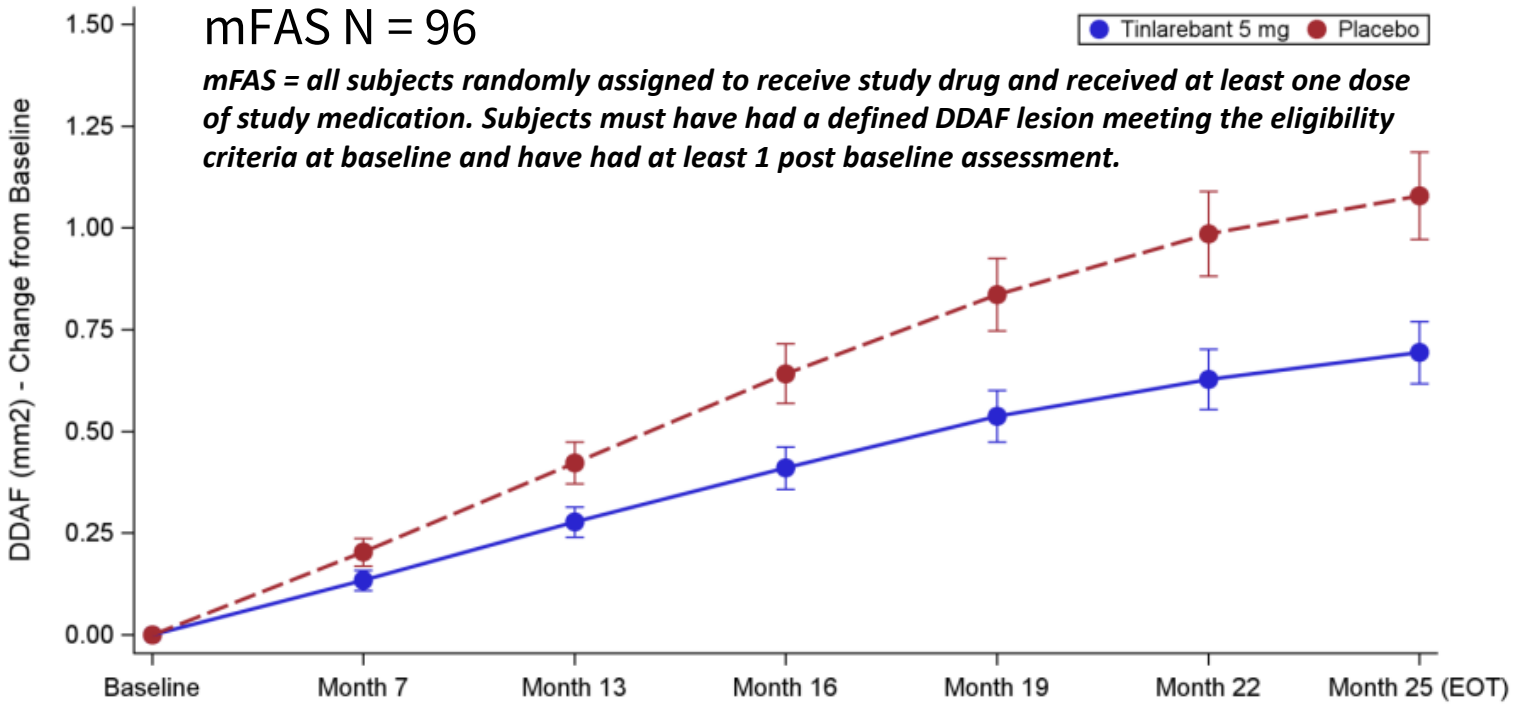
STGD1 = Stargardt disease type 1; DDAF = definitely decreased autofluorescence; DAF = decreased autofluorescence; QDAF = Questionably Decreased Autofluorescence; BCVA = best-corrected visual acuity; RBP4 = retinol binding protein 4;ABCA4 = ATP-binding cassette transporter subfamily A member 4

Phase 3 DRAGON Trial in Stargardt Disease

Data from DRAGON Topline Report

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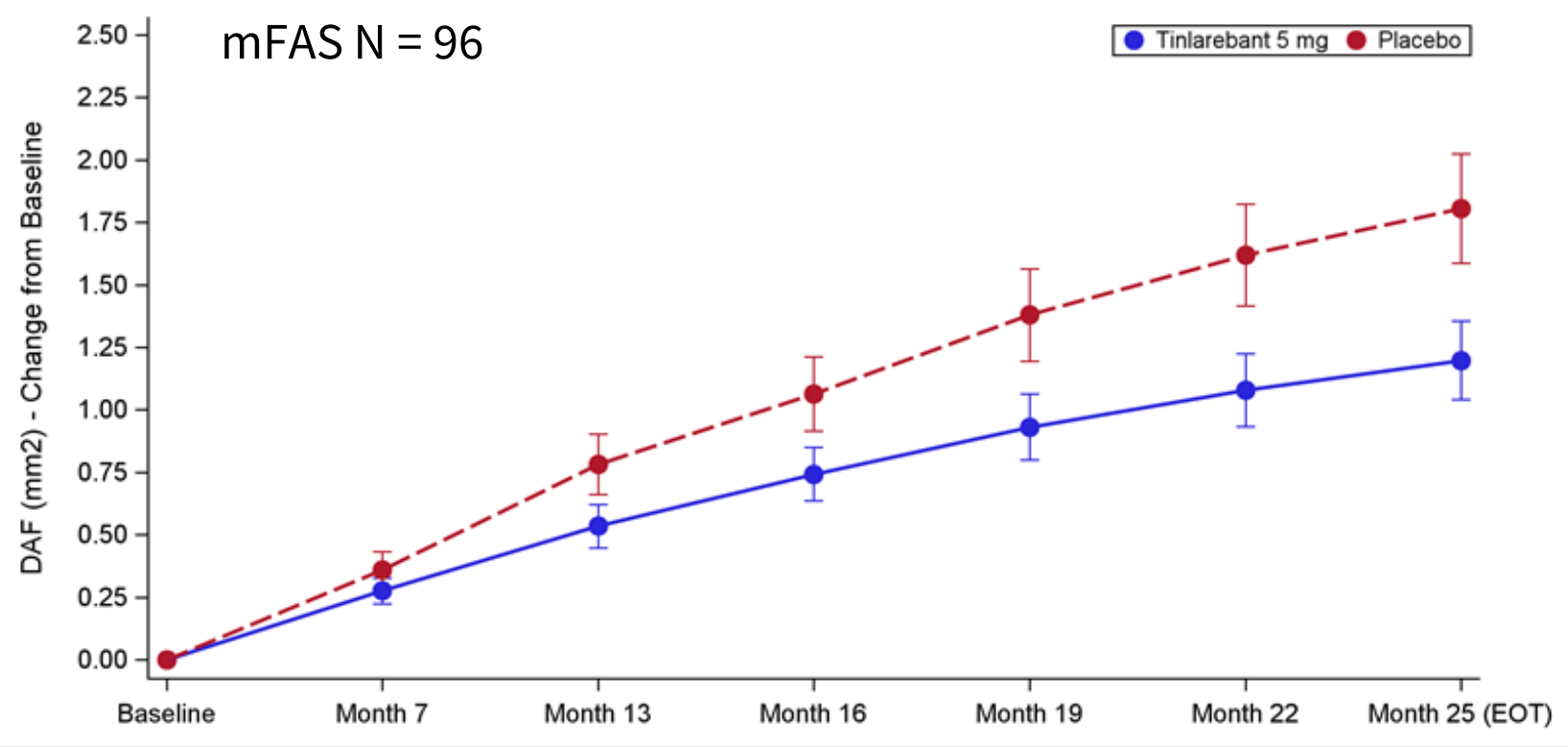
Primary Endpoint: DDAF Change from Baseline (Study Eye)



- Applying an unstructured covariance matrix, the **treatment effect size was 35.7%** compared to placebo and yielded a p-value of **P = 0.0033**
- DDAF lesion growth was **slowed to 0.38 mm^2/year vs. 0.59 mm^2/year for placebo and 0.74 mm^2/year observed in ProgStar**

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Key Secondary Endpoint: DAF Change from Baseline (Study Eye)



- Tinlarebant slowed DAF lesion growth by **33.7%** compared to placebo (**P = 0.027**)

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BCVA (Study Eye)

	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
- 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

BCVA=Best-Corrected Visual Acuity; EOS=end of study; ETDRS=Early Treatment Diabetic Retinopathy Study

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Tinlarebant Safety Profile

Safety Set N = 104; Non-Ocular TEAE

Category	Tinlarebant 5mg (N=69)	Placebo (N=35)
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%)
Study Drug-Related Serious TEAE	0 (0.0%)	0 (0.0%)
TEAE Leading to Study Drug Discontinuation	0 (0.0%)	0 (0.0%)
TEAE Leading to Study Discontinuation	0 (0.0%)	0 (0.0%)
TEAE Leading to Death	0 (0.0%)	0 (0.0%)

- Total of 6 serious adverse events (SAEs) reported in the study – all events were **non-ocular**, with 4 assessed as **unrelated** and 2 assessed as **unlikely related to the study treatment**
- Most reported Non-Ocular adverse events (AEs): Nasopharyngitis (all cases were assessed as unrelated/unlikely related to treatment), Headache, and Acne – most events were mild and resolved during the study period

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Ocular Adverse Events

Safety Set N = 104

Category	Tinlarebant 5mg (N=69)	Placebo (N=35)
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%)
Study Drug-Related Serious TEAE	0 (0.0%)	0 (0.0%)
TEAE Leading to Study Drug Discontinuation	4 (5.8%)	0 (0.0%)
TEAE Leading to Study Discontinuation	2 (2.9%)	0 (0.0%)
TEAE Leading to Death	0 (0.0%)	0 (0.0%)

- Most reported Ocular AEs: Xanthopsia, Delayed dark adaptation, and Night Vision Impairment
- The majority of the events were **mild**, and **most resolved** while on study
- There were **no** serious ocular TEAEs – 4 TEAEs lead to study drug discontinuation and 2 TEAEs lead to study discontinuation

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Phase 3 DRAGON Trial in Stargardt Disease

Structural and Functional Correlation

Analyzed by the Ocular Imaging Research and Reading Center (OIRRC, Sunnyvale, California)



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FAF–MP Mapping and Four-Zone Sensitivity

Spatially Distributed Retinal Sensitivity Loss across Regions

RESULTS

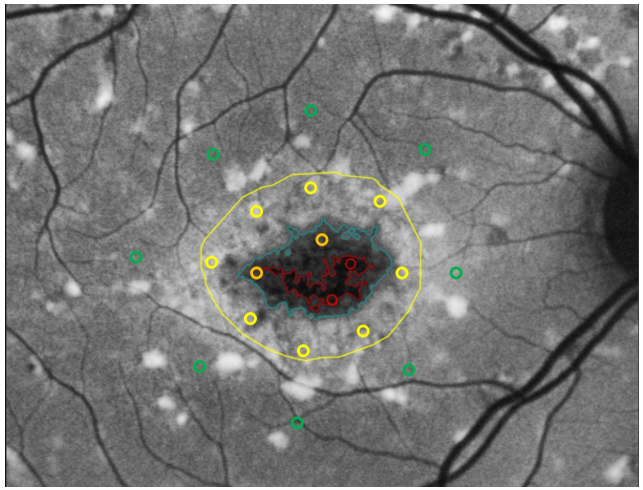


Figure A. FAF image of an eye with STGD1 with annotated segmentation zones: DDAF (red), QDAF (orange), TZ (yellow), and NR (green).

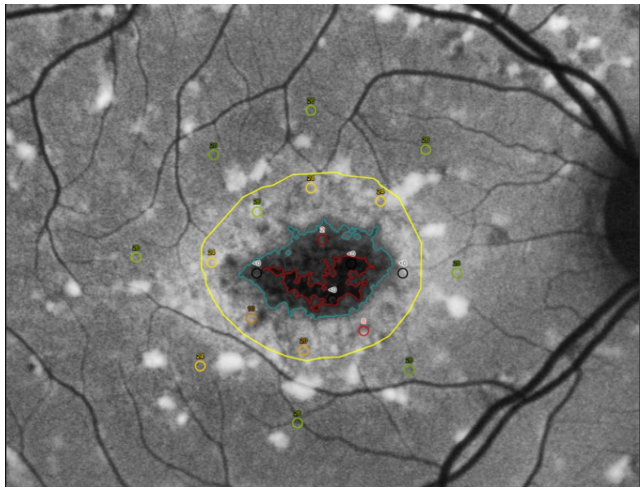


Figure B. MP sensitivity values overlaid on FAF in an eye with STGD1, revealing spatially distributed retinal sensitivity loss across regions.

Table 1. Unadjusted Sensitivity by Zone

n = 2,934 MP points across 89 eyes (47 subjects)

Zone	Mean ± SD (dB)	Median (dB)	% Reduction vs NR
NR	19.0 ± 7.8	22	Reference
TZ	10.4 ± 9.7	8	45.5%
QDAF	3.7 ± 6.9	1	80.4%
DDAF	2.7 ± 5.6	1	85.7%

Descriptive pointwise summaries. Reduction uses distant non-atrophic retina as the reference.

ZONE-WISE SENSITIVITY GRADIENT

19.0 dB
NR Reference mean

10.4 dB
TRANSITION −45.5% vs distant

3.7 dB
QDAF −80.4% · 40.3% ≤0 dB

2.7 dB
DDAF −85.7% · 32.9% ≤0 dB

Shaik et al. Spatially Resolved Structure-Function Correlation in Stargardt Disease: Quantifying Retinal Sensitivity Across Fundus Autofluorescence Zones using FAF guided MP. (ARVO 2026)

DRAGON BASELINE STRUCTURE-FUNCTION

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DRAGON

Baseline Dataset Retains 89 eyes and 2,934 Macular Stimulus Points

ANALYSIS SET

47	89	2,934
subjects	eyes	stimulus points

FAF grading was performed by trained, experienced OIRRC graders

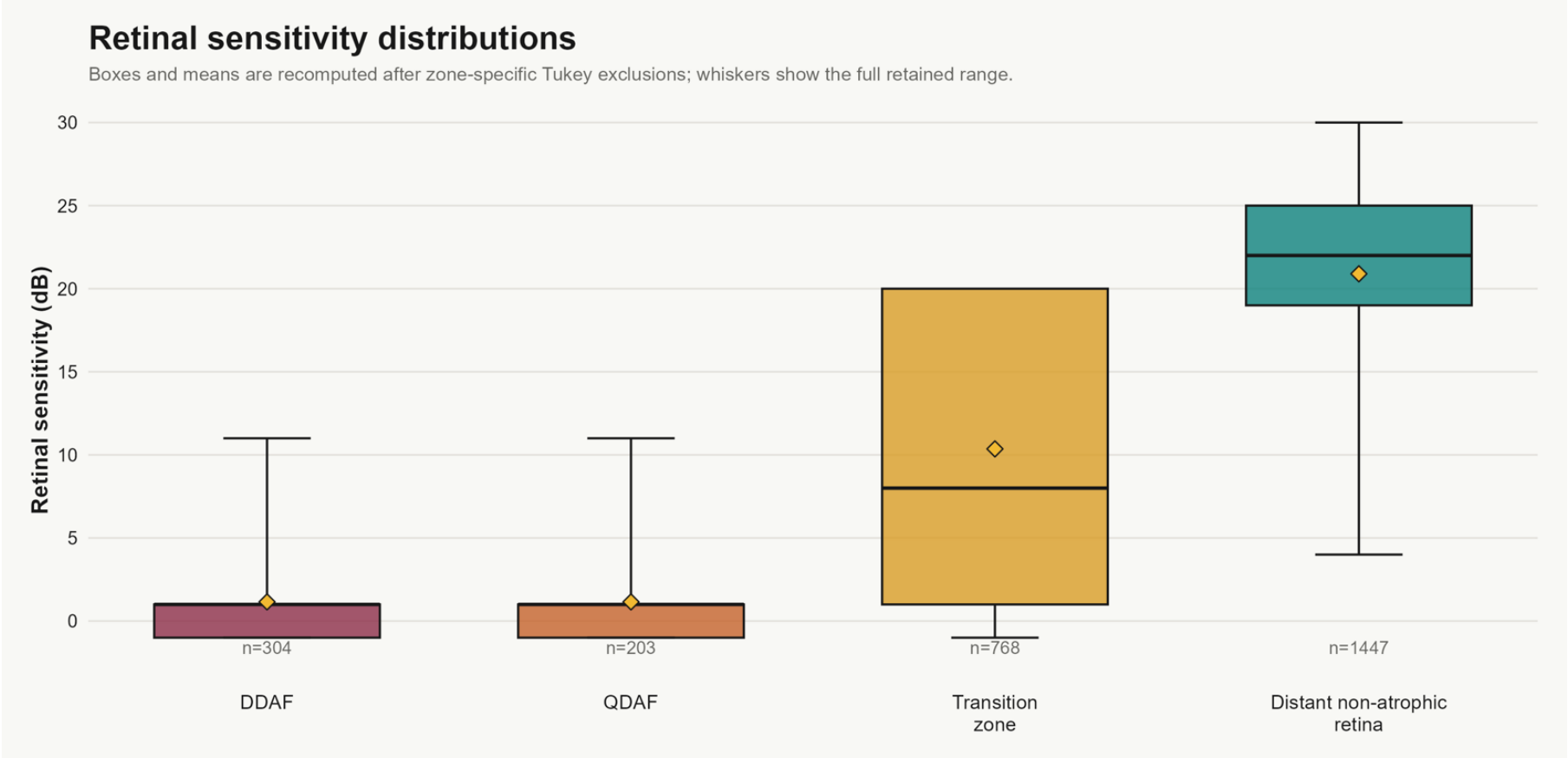
Predefined quality rules

- > 3,700 um from fovea excluded
- Confirmed ungradable images
  - Poor image quality
  - Unreliable MP exams
  - Severely eccentric and poorly positioned test patterns.

All treatment assignments and study/fellow eye labels are pooled at baseline.

Retinal Sensitivity Differs across Four FAF-defined Zones

FOUR-ZONE ANALYSIS · DISTRIBUTION



Summary

- **The DRAGON trial met its primary endpoint with a treatment effect of ~36%**
  - A **statistically significant** slowing in DDAF lesion growth was observed in subjects treated with 5 mg/day oral Tinlarebant as compared to placebo
- 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 po daily)** had a side effect **profile consistent with its mechanism of action** in adolescent and adult STGD1 patients
- **DDAF and QDAF lesions are associated with markedly reduced retinal sensitivity,** including deep scotomas, supporting their clinical relevance as **structural outcome measures** for therapeutic interventions aimed at preserving visual function by slowing lesion progression

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Acknowledgement

- Funding from the National Eye Institute (P30-026877), and Research to Prevent Blindness, Inc.
- **Support for the DRAGON Study is provided by Belite Bio, Inc.**

NIH National Eye Institute

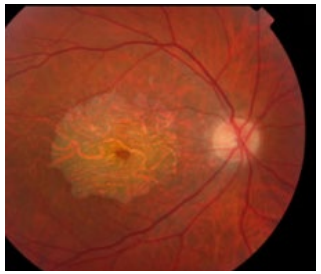
Research to Prevent Blindness

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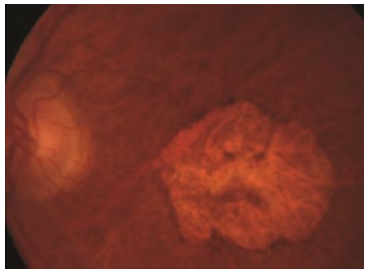
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Tinlarebant Development Plans

- **Phase 3 Study of Tinlarebant in Adolescent Stargardt Disease**
  The DRAGON Study
  (topline results released)



- **Phase 3 Study of Tinlarebant in Geographic Atrophy**
  The PHOENIX Study
  (enrollment completed)



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