Results from the Phase 3 DRAGON Study of Tinlarebant for Adolescent and Adult Stargardt Disease

H. Viet TRAN, MD

SSO-SOG AUG2026

Hôpital ophtalmique Jules-Gonin
Service universitaire d'ophtalmologie
Fondation Asile des aveugles

UNIL | Université de Lausanne
Faculty of Biology and Medicine
CHUV

Financial Disclosures

- Novartis (advisory board, speaker)
- Bayer (advisory board)
- Janssen Pharmaceuticals (consultant)

Stargardt Disease (STGD1) Overview

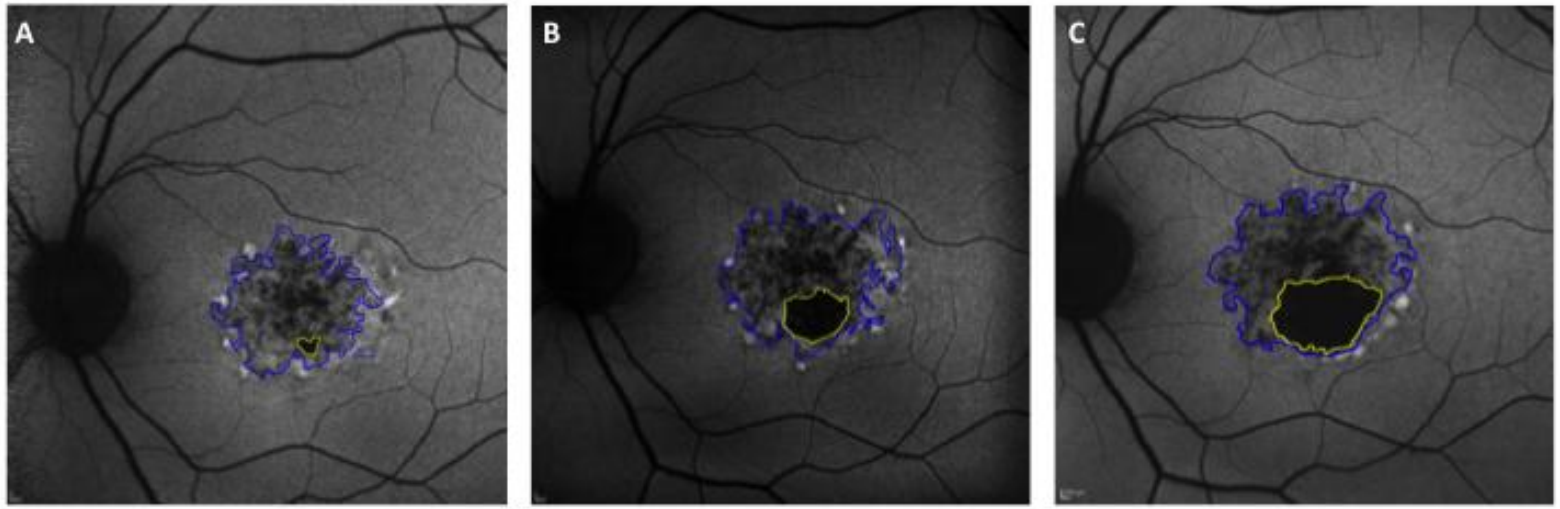
STGD1 and/or *ABCA4*-associated retinal dystrophy is a rare and progressive eye disease leading to severe central visual impairment. There is no approved treatment for STGD1.

Key Symptoms

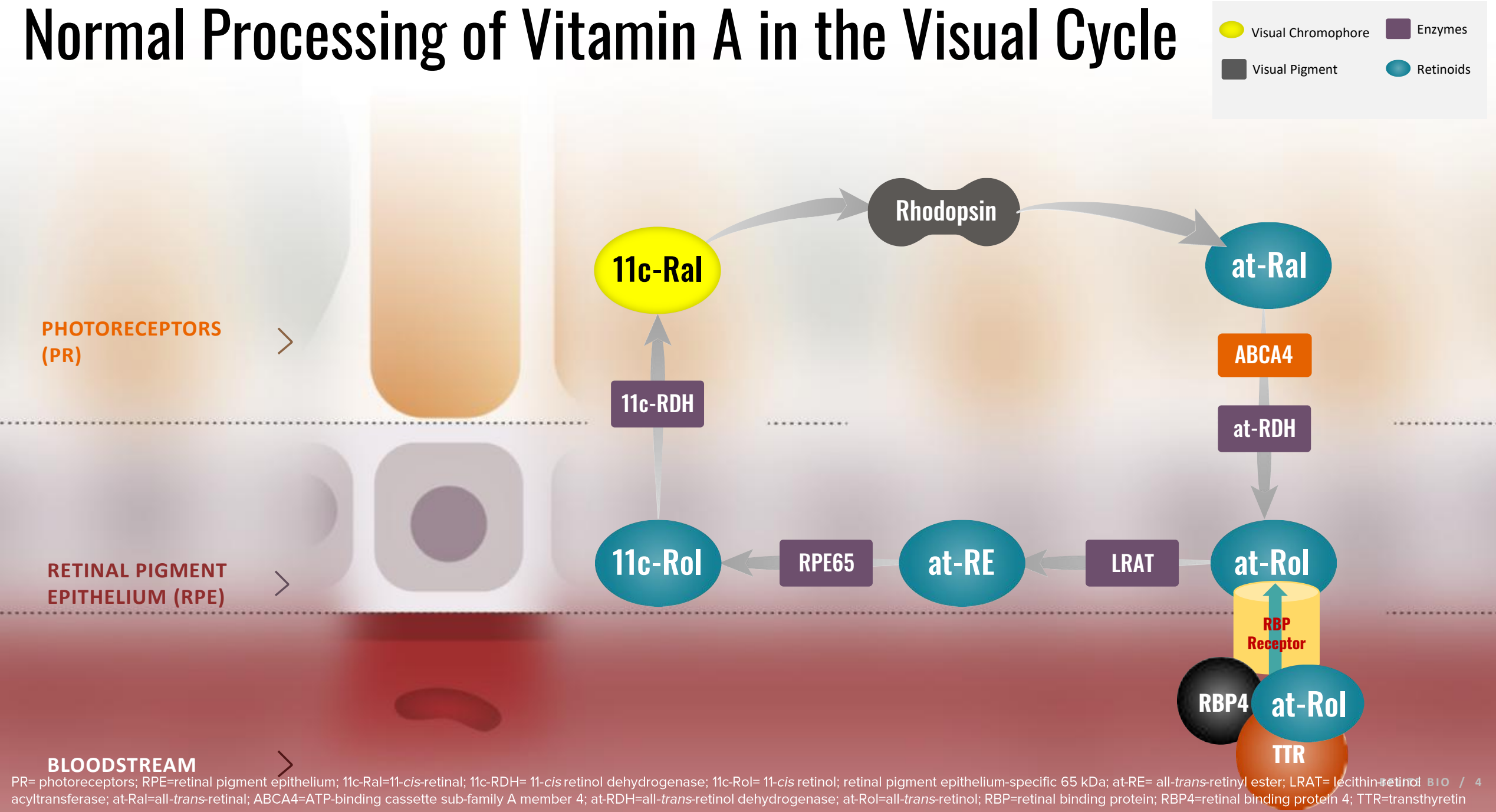
- **Gradual central vision loss** in both eyes, with symptoms often **starting in adolescence/early adulthood**
- **Central blind** spots (scotomas)
- **Photophobia** and **delayed dark adaptation**
- **Impaired color vision**
- **Peripheral vision preserved** in the majority of cases

Overall DDAF growth rate in the ProgStar cohort over 24 months: 0.74 mm²/year

(confidence interval: 0.64 - 0.85 mm²/year)

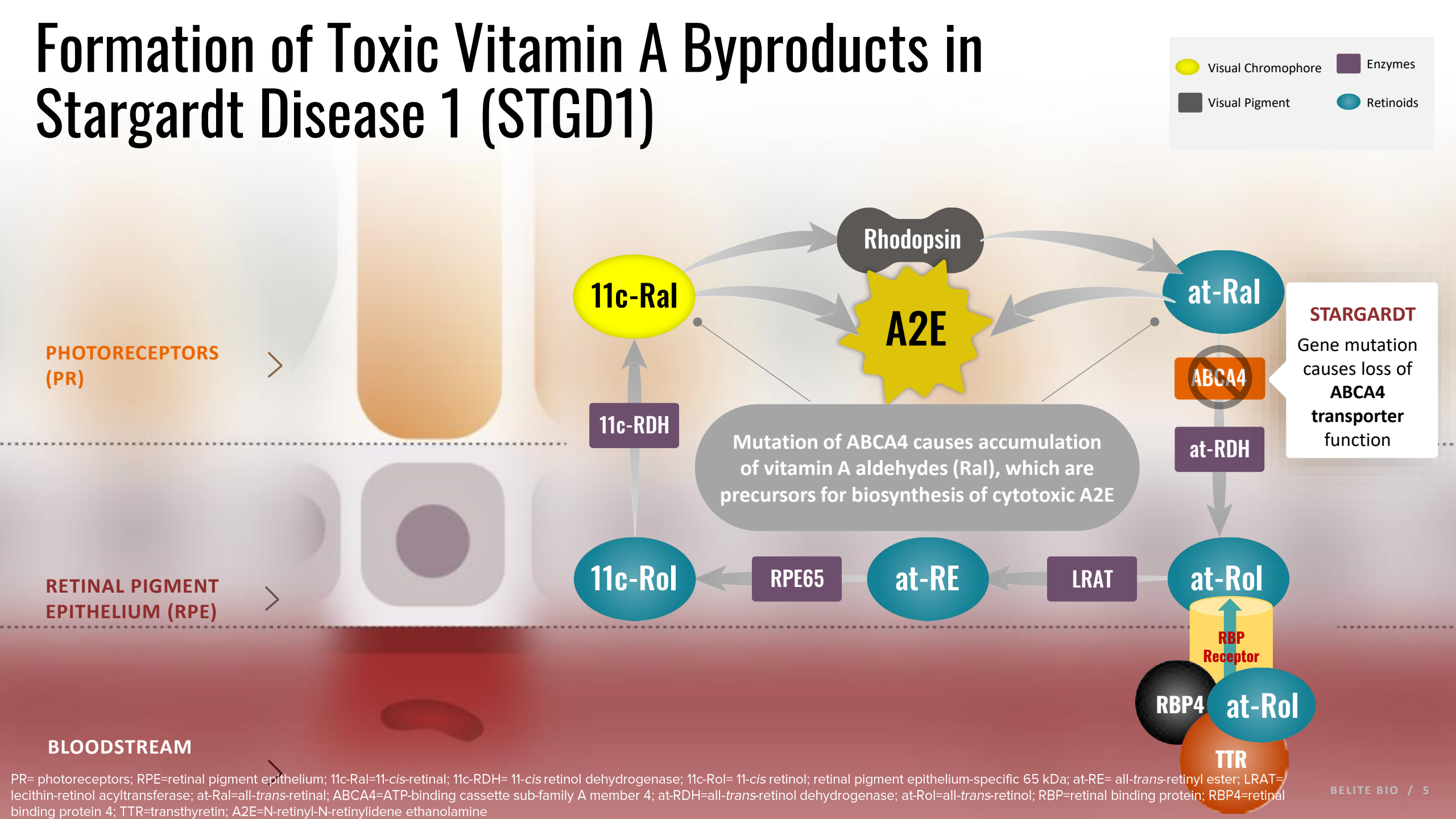


Normal Processing of Vitamin A in the Visual Cycle



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

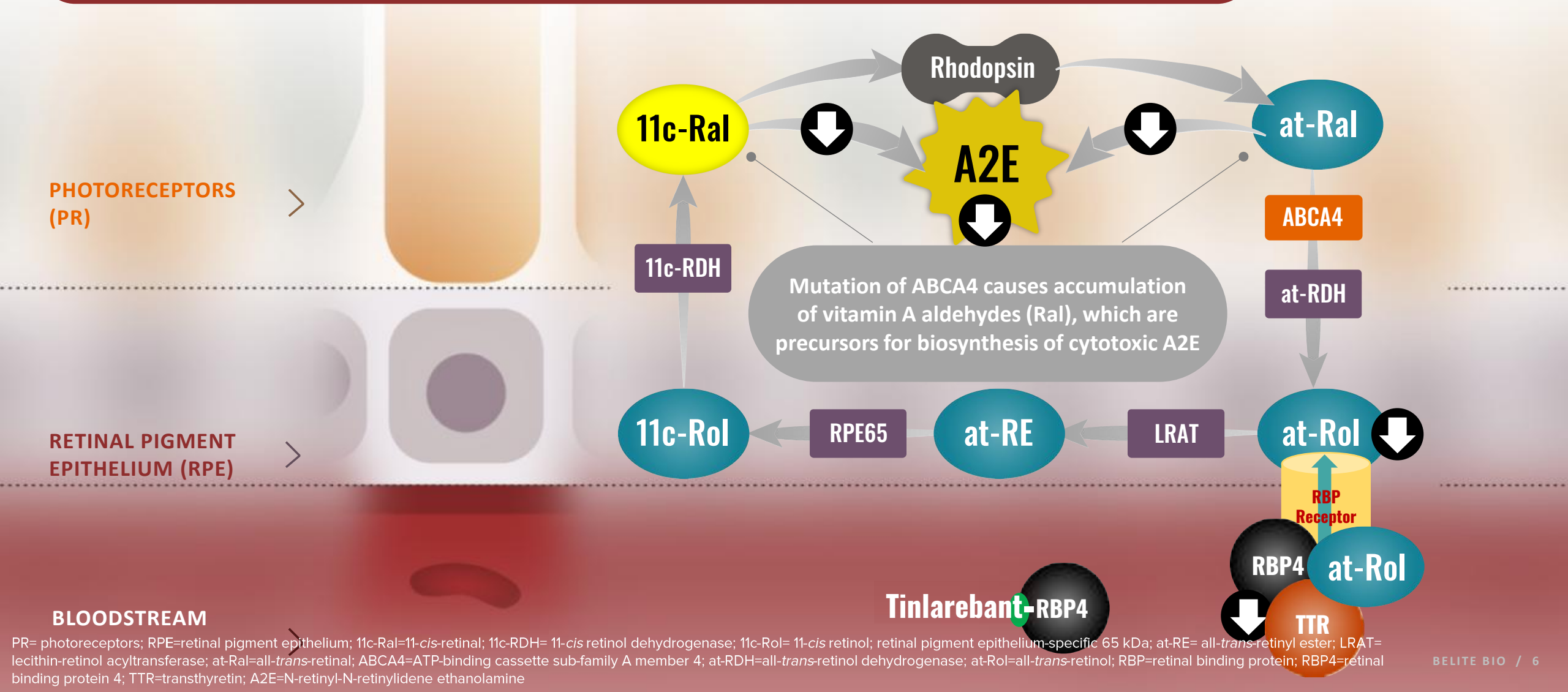
Formation of Toxic Vitamin A Byproducts in Stargardt Disease 1 (STGD1)



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

Mechanism of Tinlarebant Action

Bisretinoids are derived from vitamin A (retinol). Reduced retinol levels in the retina decrease biosynthesis of cytotoxic bisretinoids which underly disease progression in 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

DRAGON Phase 3 Clinical Trial Design

Reduction in atrophic lesion growth rate as measured by fundus autofluorescence imaging is the FDA's accepted primary endpoint in Stargardt disease

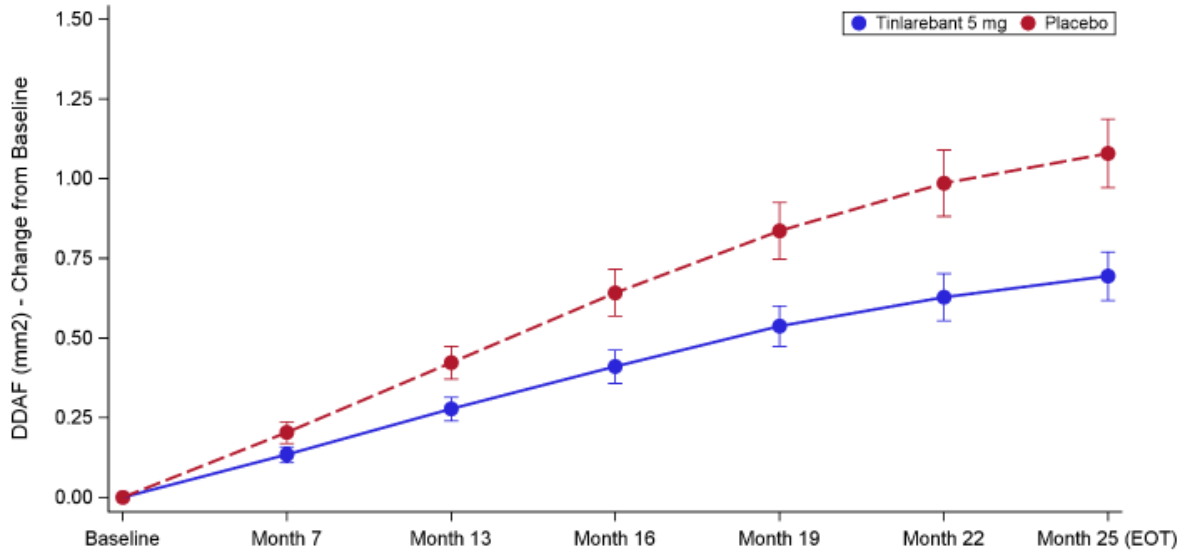
	DRAGON Phase 3 Trial
Key Inclusion Criteria[1]	12-20 years old, clinically diagnosed STGD1 with at least 1 mutation identified in the ABCA4 gene, atrophic lesion size within 7.62 mm^2(appr. 3 disc aera), BCVA of 10% or better, no ocular disease that would complicate assessments and Vitamin A deficiency
Enrollment[1,2]	N=104
Sites[1,3]	22 Global sites located in Australia, Belgium, China, France, Germany, Hong Kong, Netherlands, Switzerland, Taiwan, UK, US
Randomization[1]	2:1 Tinlarebant:Placebo
Masking[1]	Double Blind
Treatment Duration[1]	24 months
Primary Outcome Measures[1]	Efficacy as measured through DDAF lesion growth rate, safety & tolerability
Key Secondary Endpoints[1,3]	DAF (calculated as the sum of DDAF and QDAF), BCVA, reduction in RBP4, SD-OCT

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 Clinical Trial

Primary efficacy results: the DRAGON study met its primary endpoint

- Tinlarebant arm (n=69); placebo arm (n=35)
- Mean age 15,4 yo
- M/F ratio 2/1
- Sustained effect on the rate of atrophy progression



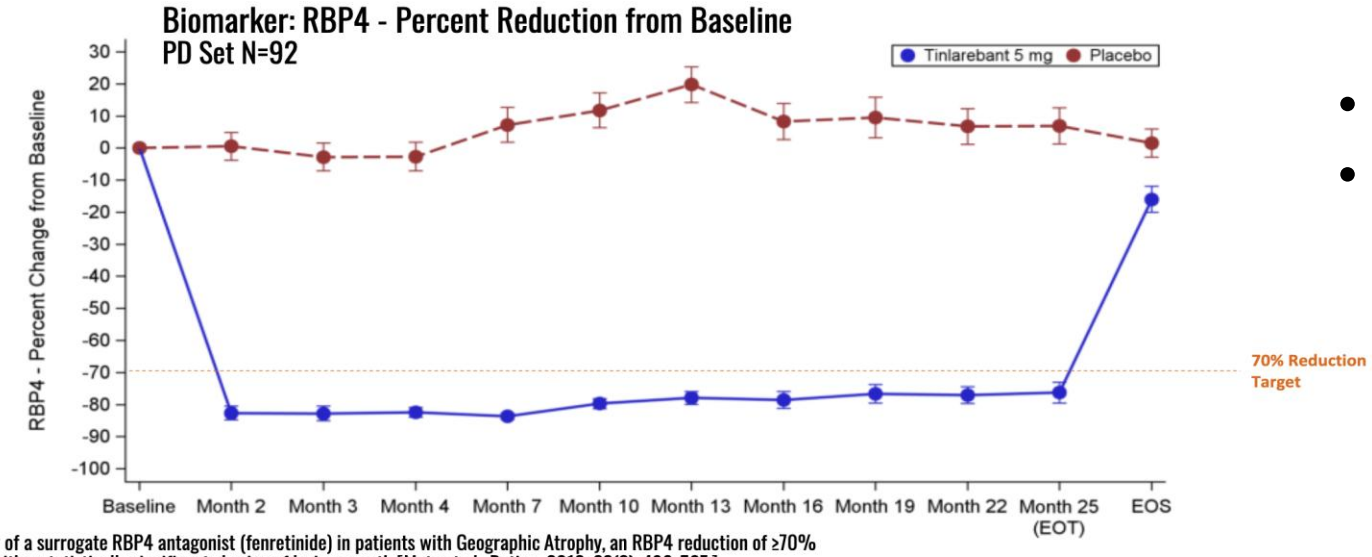
36% reduction in lesion growth (p=0.0033) in study eye

33.6% lesion growth reduction (p = 0.041) in fellow eye

No significant BCVA change from baseline

Phase 3 DRAGON Clinical Trial

Safety Profile



* 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.]

- Sustained 80% reduction of RBP4
- Recovery of RBP4 concentration correlated well with the decreased Tinlarebant exposure

Tinlarebant (5 mg orally, daily) was well tolerated in adolescent STGD1 patients

No drug/trial discontinuations due to non-ocular AE

Most common non-ocular AE: headache

Most common ocular AE: xanthopsia & delayed dark adaptation – mild & self limiting

Ocular Adverse Events

Safety Set N = 104

Subjects Who Experienced at Least One Ocular TEAE, N / (%)

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 led to study drug discontinuation and 2 TEAEs led to study discontinuation**

TEAE=treatment emergent adverse event; AE=adverse event

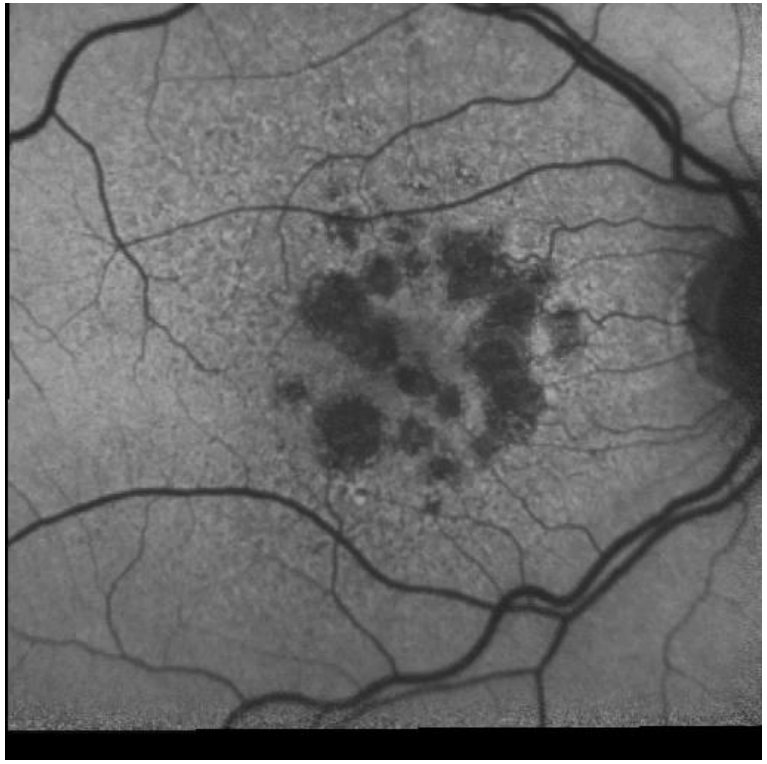
Summary

- **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 p.o., daily)** had a side effect **profile consistent with its mechanism of action** in adolescent and adult STGD1 patients
- NDA accepted by the **FDA with Priority Review**; PDUFA date: **February 12, 2027**

From DRAGON to PHOENIX

Extending RBP4 modulation from Stargardt disease to geographic atrophy

- Shared rationale: Bisretinoid accumulation is also implicated in geographic atrophy (GA), the advanced form of dry AMD.
- PHOENIX: Pivotal global Phase 3 trial of Tinlarebant in GA; 530 participants enrolled. 24-month, randomized 2:1
- Double-masked, placebo-controlled
- Primary endpoint: atrophic lesion growth
- Interim analysis expected early 2027



Can the treatment effect observed in STGD1 translate to geographic atrophy?

Source: Belite Bio Q2 2026 corporate update. Interim analysis expected; results not yet reported.

Thanks

I Audo[2,3]: P Belin[4]: P Bernstein[5]: C Cassiman[6]: Q Chang[7]: TC Chen[8]: T Edwards[9]: N Feltgen[10]: JR Grigg[11]: P Herrmann[12]: C Hoyng[13]: YS Hwang[14]: C Kay[15]: L Kühlewein[16]: BP Leroy[17]: LS Leung[18]: K Ma[19]: M Michaelides[20]: A Sharma[21]: J Self[22]: RF Sui[23]: R Wong[24]: N Mata[25]: HPN Scholl[26-28]:

Centre Hospitalier National d'Ophtalmologie des Quinze-Vingts, Centre de référence maladies rares REFERET, NSERM-DHOS CIC 1423, CHNO des Quinze-Vingts, Paris, France Sorbonne Université, INSERM, CNRS, Institut de la Vision, Paris, France Retina Consultants of Minnesota, Minnesota, United States University of Utah - John Moran Eye Center - PPDS, Utah, United States UZ Leuven, Vlaams Brabant, Belgium EYE & ENT Hospital of Fudan University, Shanghai, China National Taiwan University Hospital, Taiwan Centre For Eye Research Australia Ltd, Victoria, Australia Universitätsspital Basel, Basel, Switzerland Children's Hospital at Westmead, New South Wales, Australia Universitätsklinikum Bonn, Nordrhein-Westfalen, Germany Radboud Universitair Medisch Centrum, Netherlands Chang Gung Memorial Hospital, Taiwan Vitreo Retinal Associates, P.A., Florida, United States Universitätsklinikum Tübingen, Baden-Württemberg, Germany Ghent University Hospital & Ghent University, Ghent, East-Flanders, Belgium Byers Eye Institute at Stanford, California, United States Beijing Tongren Hospital, Capital Medical University, Beijing, China
Moorfields Eye Hospital and UCL Institute of Ophthalmology, London, United Kingdom Queensland Eye Institute, Queensland, Australia Southampton General Hospital, United Kingdom Peking Union Medical College Hospital, Beijing, China Department of Ophthalmology and Visual Sciences, The Chinese University of Hong Kong, Hong Kong Belite Bio Inc, San Diego, California, USA Medical University of Vienna, Department of Clinical Pharmacology, Vienna, Austria Pallas Kliniken AG, Pallas Klinik Zürich, Zürich, Switzerland European Vision Institute, Basel, Switzerland