# Belite Bio® and Focus on Stargardt Disease

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Belite Bio® is a clinical stage biopharmaceutical drug development company focused on advancing novel therapeutics targeting retinal degenerative eye diseases with significant unmet medical needs



# Mission

To preserve vision and pioneer degenerative retinal disease treatments where few or none exist today

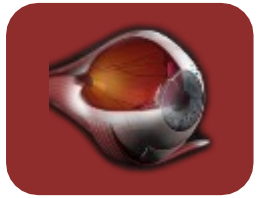


# Vision

To shine light on the shadows of vision loss and degenerative retinal disease by changing how it is recognized and treated

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# Stargardt Disease (STGD1) Overview



**STGD1 and/or *ABCA4*-associated retinal dystrophy is a rare and progressive eye disease leading to legal blindness in almost all cases. There is no approved treatment for STGD1.[1-4]**

## Pathophysiological Changes [1-2,5-7]

- **Autosomal recessive mutations** in the ***ABCA4* gene**, impairing retinoid transport and leading to **toxic bisretinoid buildup** in the **RPE**
- **Bisretinoid accumulation manifests** as yellowish flecks underneath the retina and causes **oxidative stress, toxicity, and eventually RPE cell death**
- RPE damage leads to **secondary degeneration of macular photoreceptors**
- **Progressive macular atrophy** and **retinal degeneration**

## Key Symptoms [3,6,7]

- **Gradual central vision loss** in both eyes, with symptoms often **starting in adolescence/early adulthood**
- Blurry or **distorted** central **vision**
- **Central blind** spots (scotomas)
- **Photophobia** and **delayed dark adaptation**
- **Impaired color vision**
- **Difficulty** with **detailed tasks** like reading or recognizing faces
- **Peripheral vision preserved** in the majority of cases

## Impact on Activities of Daily Living [3]

- Due to **progressive central vision loss**, there are a wide range of challenges:
- Difficulties **reading, using digital screens**, which may affect educational and work activities
- **May limit ability to drive,** impacting mobility and independence
- Reduced participation in **sports, leisure**, and some **everyday tasks**
- Challenges with **social interactions** and relationships; may be due to **inability to recognize faces**
- **Emotional impacts** such as frustration, worry, and depression
- Changes in **career/opportunities** that may affect financial stability and productivity

STGD1=Stargardt disease; ABCA4=TP-binding cassette subfamily A member 4; RPE=retinal pigment epithelium

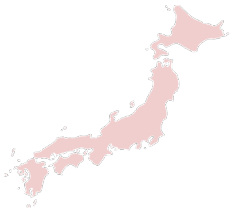
1. Cremers FPM et al. *Prog Retin Eye Res*. 2020;79:100861. 2. Dayma K et al. . *Int J Mol Sci*. 2025;26(14):7006. 3. Roborel de Climens A et al.*Ophthalmic Genet*. 2021;42(2):150-160. 4. Kong X et al. *Ophthalmology*. 2016;123(9):1887-1897. 5. https://medlineplus.gov/ency/article/002052.htm . 6. https://medlineplus.gov/genetics/condition/stargardt-macular-degeneration/. 7. https://www.aao.org/eye-health/diseases/what-is-stargardt-disease

# Estimated Patient Population Sizes of STGD1











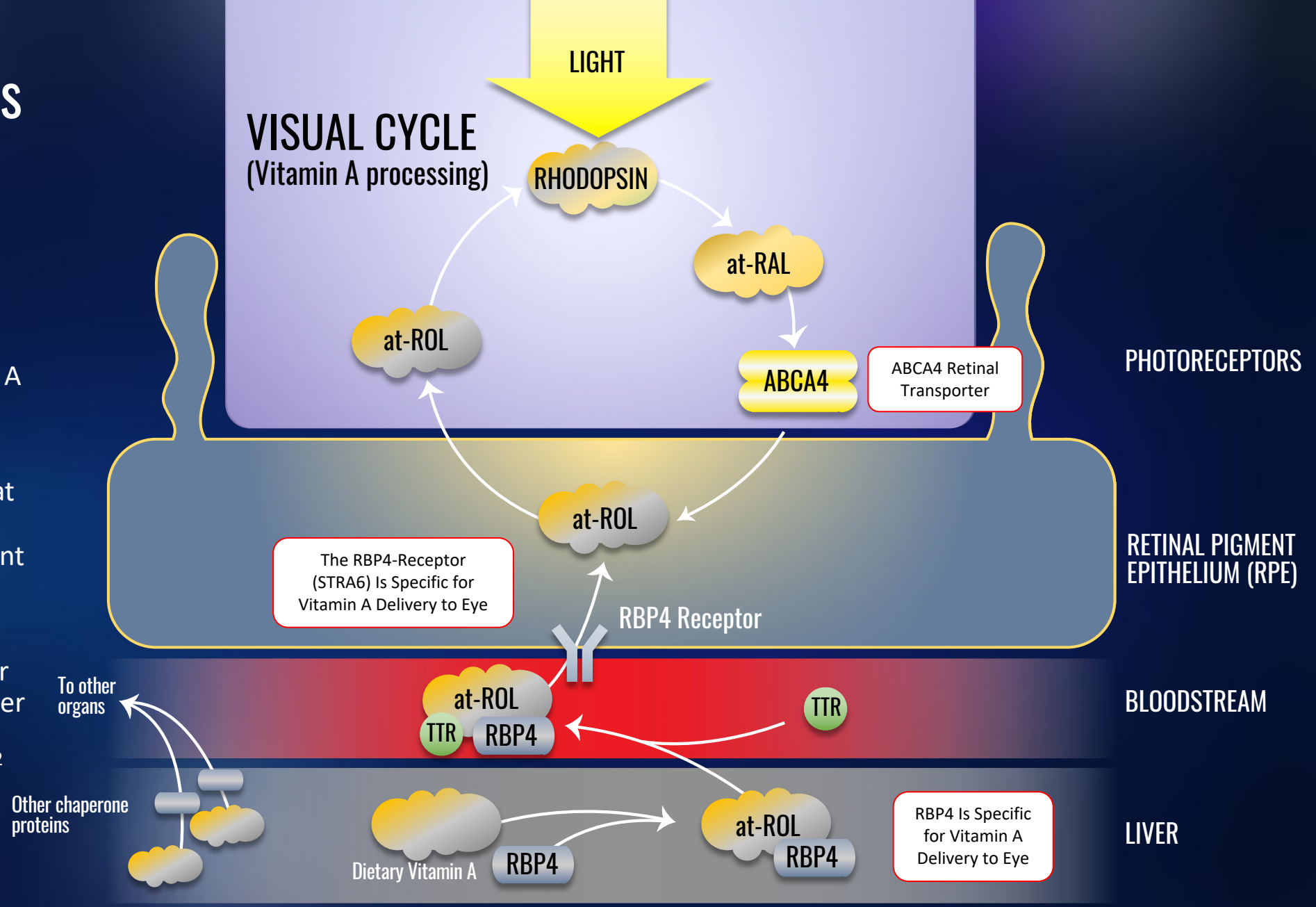
| | Europe | Australia | China | Japan | United States |
|---|---|---|---|---|---|
| **gnomAD Ethnicity** | European | European | East Asian | East Asian | Mixed |
| **Population (N)** | 742,000,000 | 26,640,000 | 1,411,000,000 | 124,500,000 | 334,900,000 |
| **STGD1 Patients (N)** *High Estimate* | **115,345** | **4,141** | **122,135** | **10,777** | **59,235** |
| **STGD1 Patients (N)** *Low Estimate* | **95,517** | **3,429** | **94,940** | **8,377** | **46,767** |

gnomAD = Genome Aggregation Database.

Mata NL, Weng S, Michaelides M, Charbel Issa P, Quinodoz M, Rivolta C, Scholl HPN. Bisretinoids as a Source of Early Photoreceptor Pathology in Stargardt Disease. Ophthalmic Res. 2025;68(1):555-572.

# The Visual Cycle Is Central to STGD1 Pathology

- The visual cycle requires proper processing of vitamin A derivatives, such as retinol[1]
- Retinol Binding Protein 4 (RBP4) is the only protein that facilitates the delivery of retinol into the retinal pigment epithelium (RPE) via an RBP4 receptor[2]
- ABCA4 is a retinal transporter protein in photoreceptor outer segments that appropriately processes retinal derivatives[2]



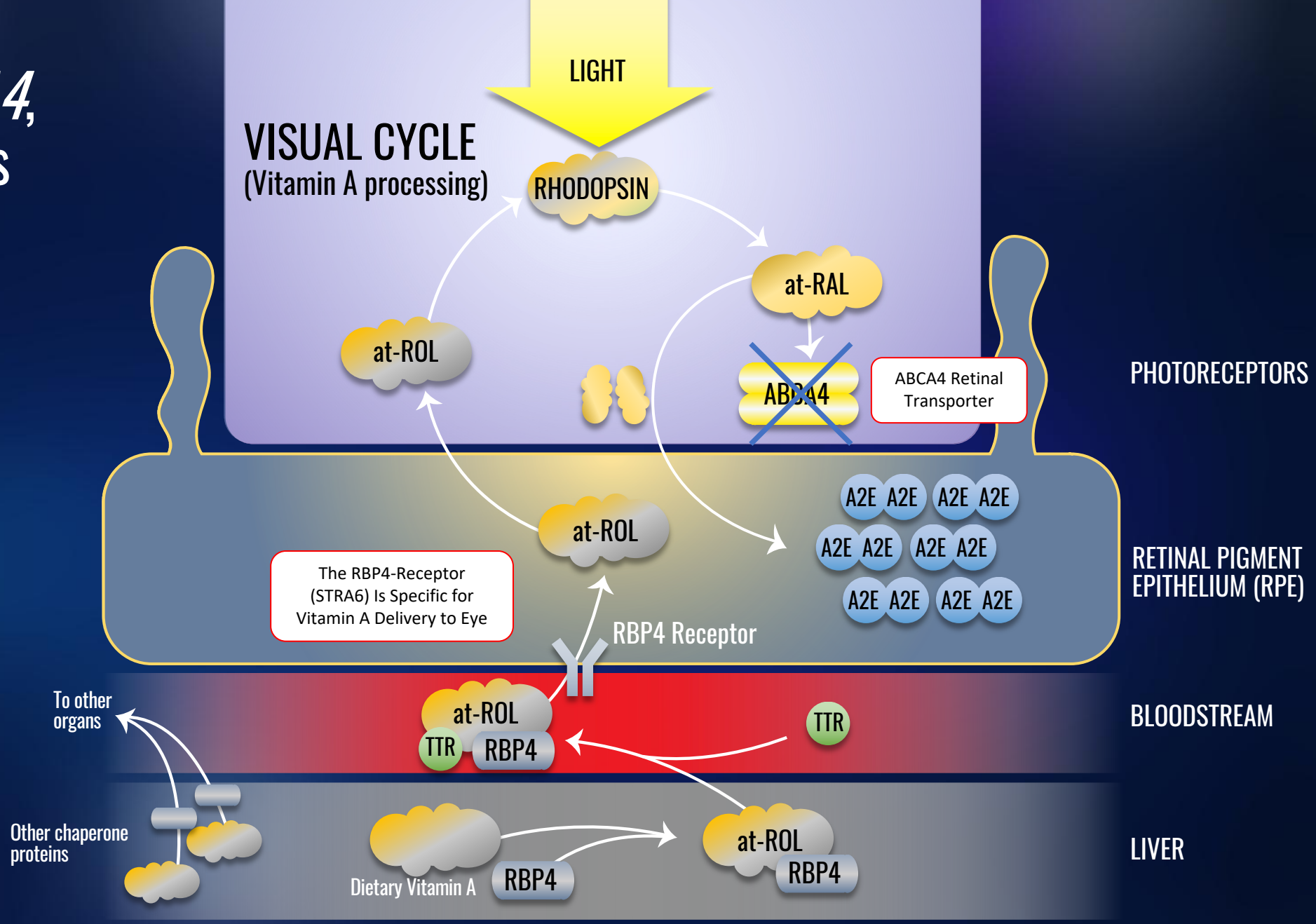

*ABCA4*, ATP-binding cassette transporter subfamily A member 4; at-RAL, all-trans-retinaldehyde; at-ROL, all-trans-retinol (vitamin A); RBP4, retinol binding protein 4; RPE, retinal pigment epithelium; STGD1, Stargardt disease type 1; STRA6; receptor for retinol uptake STRA6; TTR, transthyretin.

**1.** Steinhoff JS, et al. *Front Physiol*. 2021;12:659977. **2.** Zaluski J, et al. *Prog Retin Eye Res*. 2025;106:101360.

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# Mutation of *ABCA4*, in STGD1, Disrupts the Visual Cycle

- Mutation of the ABCA4 gene causes a loss of transporter function, driving bisretinoid formation due to increasing all-*trans*-retinal[1]
- Over time, this causes accumulation of cytotoxic bisretinoid A2E, which drives degeneration of the retinal pigment epithelium and photoreceptors[1]
- This ultimately causes central vision loss that patients with STGD1 experience[1]




A2E, N-retinylidene-N-retinylethanolamine; *ABCA4*, ATP-binding cassette transporter subfamily A member 4; at-RAL, all-trans-retinaldehyde; at-ROL, all-trans-retinol (vitamin A); RBP4, retinol binding protein 4; STGD1, Stargardt disease type 1; TTR, transthyretin.

**1.** Cremers FPM, et al. *Prog Retin Eye Res*. 2020;79:100861.

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# Patients With STGD1 Experience Progressive Central Vision Loss Throughout Life[1]

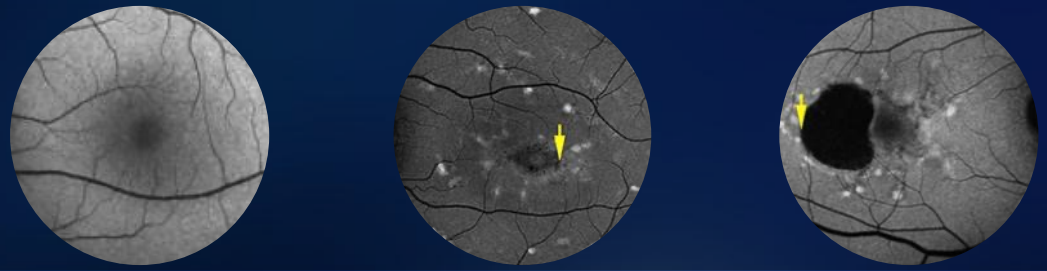
Normal Vision



Severe Visual Impairment

Disease Progression

Healthy Retina[2]



Significant Retinal Degeneration

## Symptoms[1]

- Central vision loss
- Color vision impairment
- Light sensitivity
- Delayed dark adaptation

## Clinical Signs[1]

- Fundus flecks
- Macular/retinal atrophy
- Central scotoma
- Peripapillary sparing

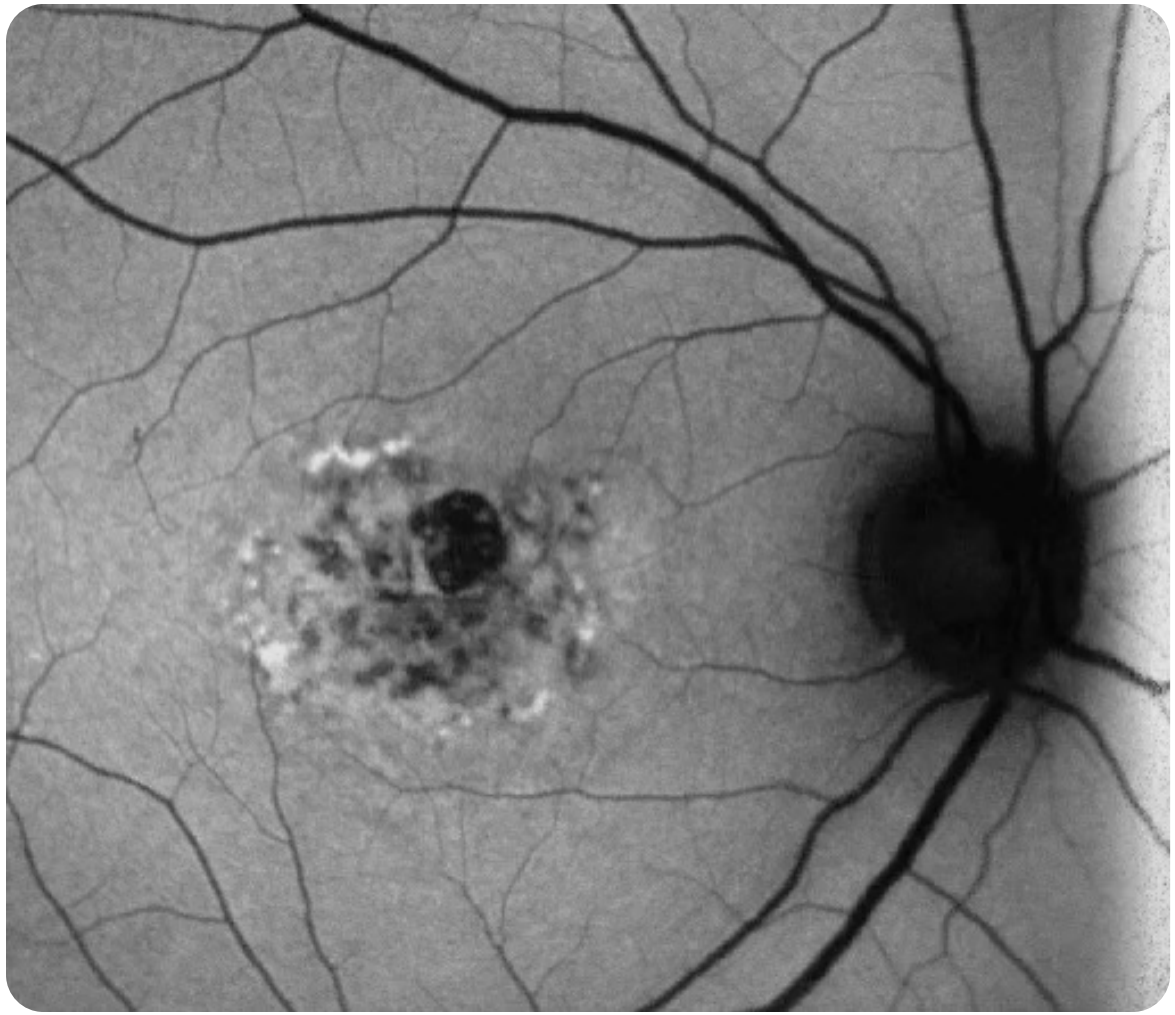
Patients with STGD1 typically progress to legal blindness (BCVA of 20/200 or worse), and significant additional visual decline to “hand motion” or no light perception can occur[1,3-5]

BCVA, best corrected visual acuity; STGD1, Stargardt disease type 1.

**1.** Cremers FPM, et al. *Prog Retin Eye Res*. 2020;79:100861. **2.** Chen L, et al. Sci Rep. 2019;9(1):6436. **3.** Collison FT, et al. *Retina*. 2018;38(12):2387-2394. **4.** Cideciyan AV, et al. *Hum Mol Genet*. 2009;18(5):931-941. **5.** Fujinami K, et al. *Am J Ophthalmol*. 2013;155(6):1075-1088.e13.

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# DDAF Progression and Visual Loss in Stargardt Disease



## Atrophy Progression over 4 Years

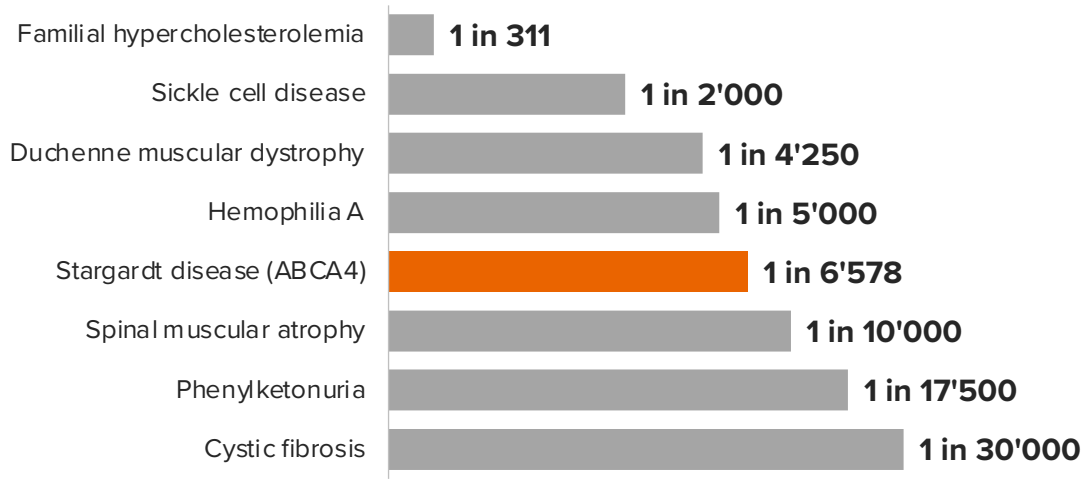
- **37-year-old male patient**
- **Compound heterozygous for mutations in *ABCA4***
  - Visual acuity (baseline): 20/40
  - Visual acuity (at 4Y): 20/80

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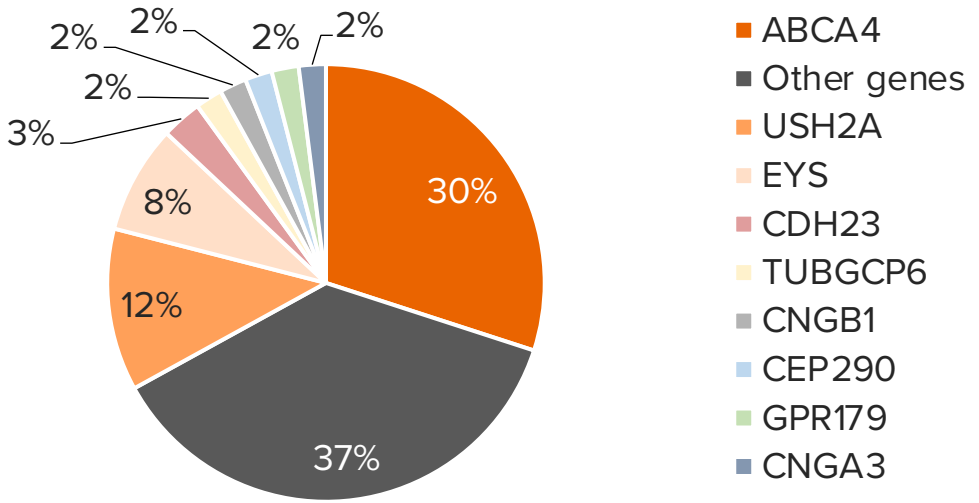
# *ABCA4:* One of the Largest Genetically Defined Rare Disease Opportunities

## Illustrative comparison with selected important monogenic diseases

### Carrier frequency vs. selected monogenic diseases




### Share of inherited retinal disease by gene




- *ABCA4* frequency: ~1 in 6,578 (Hanany M, Rivolta C, Sharon D, PNAS 2020)
- Largest inherited retinal disease gene worldwide (Hanany M, Rivolta C, Sharon D, PNAS 2020)
- Comparable patient population to several successful orphan-drug markets
- Normal life expectancy creates a large prevalent patient pool

Illustrative epidemiologic comparison; estimates represent published incidence/prevalence and are intended for order-of-magnitude benchmarking.

References:
Hanany M, Rivolta C, Sharon D (2020) Worldwide carrier frequency and genetic prevalence of autosomal recessive inherited retinal diseases. Proc Natl Acad Sci U S A. 117: 2710-2716.
Al-Khuzaei S, Broadgate S, Foster CR, et al. Genes (Basel). 2021;12:1241. (ABCA4/Stargardt)
Hu P, Dharmayat KI, Stevens CAT, et al. Circulation. 2020;141:1742-1759. (Familial hypercholesterolemia)
Romitti PA, Zhu Y, Puzhankara S, et al. Prevalence of Duchenne and Becker muscular dystrophies in the United States. Pediatrics. 2015;135(3):513-521. doi:10.1542/peds.2014-2044.

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