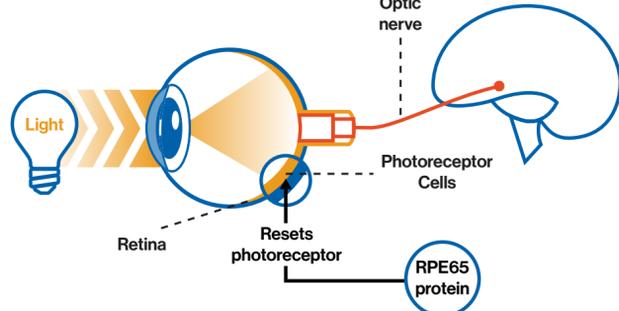


How does Luxturna[®] (voretigene neparvovec) work?

What is the visual cycle?

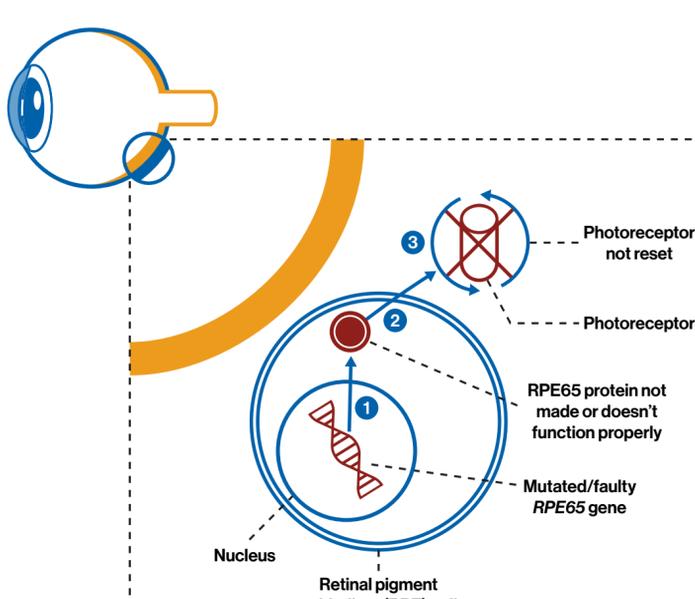
The visual cycle is the process that converts light entering the eye into electrical signals that are transmitted to the brain¹.

A particle of light (photon) hits a photoreceptor in the retina - the light-sensitive tissue that lines the back of the eye - triggering electrical signals along the optic nerve to the brain¹. However the photoreceptor needs to be reset to be ready for the next photon¹. A protein called **RPE65** is involved in this task¹.



Vision loss due to a genetic mutation in both copies of the *RPE65* gene

If the *RPE65* gene carrying the instructions to make the protein is mutated/faulty, the protein won't be made or will not function properly¹. Therefore, the photoreceptors are unable to reset and will start to degenerate over time^{1,2}.



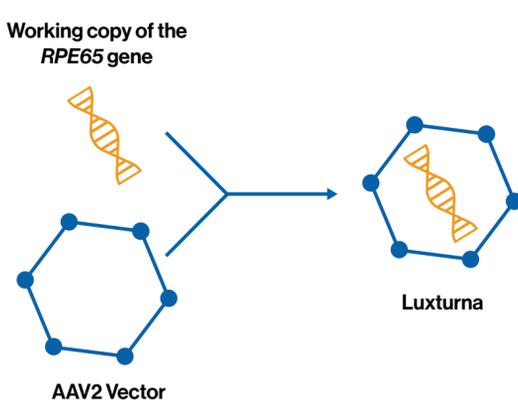
As the photoreceptors degenerate, people lose the ability to detect light, leading to night blindness and vision loss¹.

What is Luxturna?

Each person has two copies of the *RPE65* gene³. Luxturna is a one-time gene therapy for patients with vision loss due to a genetic mutation in both copies of the *RPE65* gene, and who have enough viable retinal cells. This mutation affects approximately **1 in 200,000** people worldwide⁴.

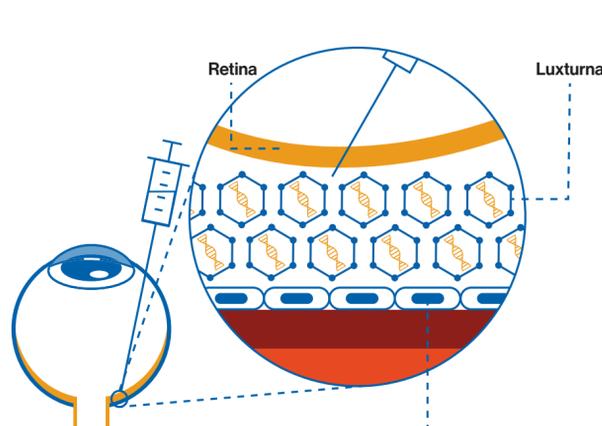
Luxturna provides a working copy of the *RPE65* gene to act in place of the mutated *RPE65* gene². This working gene has the potential to restore vision and improve sight².

Luxturna consists of a piece of DNA – containing a working copy of the *RPE65* gene – that is packaged inside a transporter known as a vector, which is made from a modified, inactivated virus².



How is Luxturna administered?

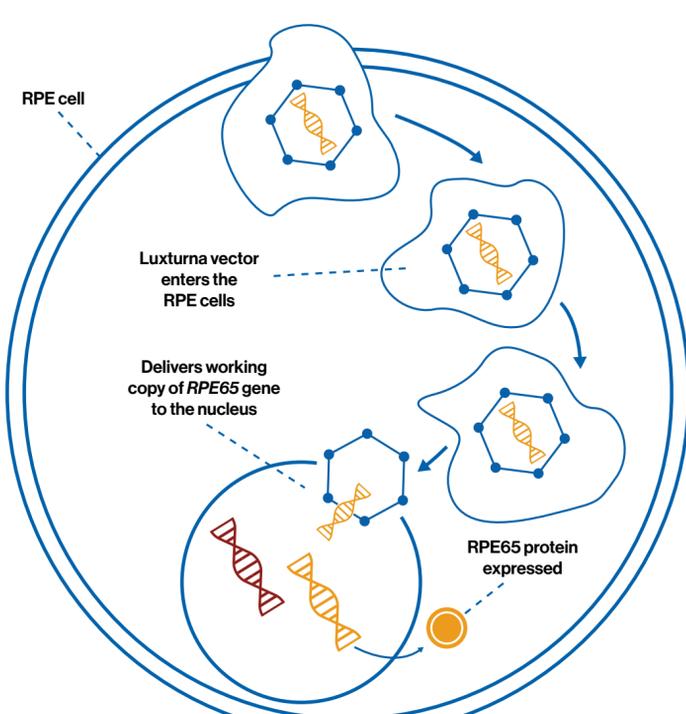
Luxturna is a one-time injection per eye⁵.



A specialized retinal surgeon injects the gene therapy behind the retina, into the subretinal space⁵.

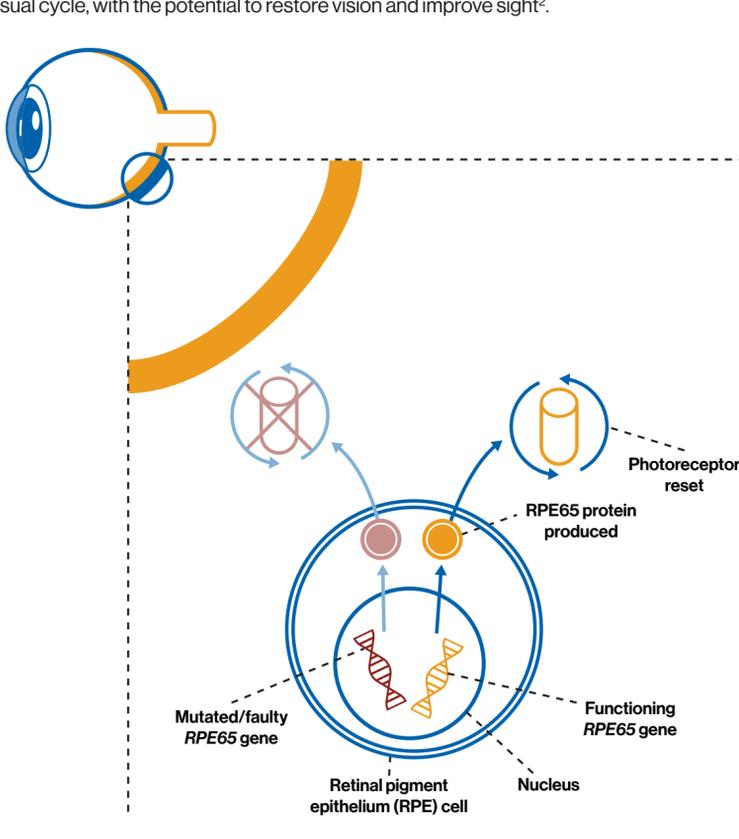
What does Luxturna do in the eye?

The Luxturna vector enters the RPE cells and delivers a working copy of the *RPE65* gene to the cell nucleus⁵. The cells then begin producing the RPE65 protein⁵.



How does Luxturna restore vision and improve sight?

Luxturna provides a working copy of the *RPE65* gene to act in place of the mutated *RPE65* gene². The working *RPE65* gene creates the RPE65 protein⁵, thus restoring the visual cycle, with the potential to restore vision and improve sight².



⁵ Luxturna is a registered trademark of Spark Therapeutics, Inc. used under license by Novartis Pharmaceuticals Canada Inc.

¹ Luxturna is indicated for the treatment of adult and paediatric patients with vision loss due to inherited retinal dystrophy caused by confirmed biallelic RPE65 mutations and who have sufficient viable retinal cells.

Important Safety Information
Some patients who received Luxturna experienced red or painful eyes, sensitivity to light, an eye infection, cataracts, increased pressure in the eye, or temporary visual disturbances, like flashes or floaters, worsening of or blurred vision. Some of these may be related to the medicine itself, or the use of corticosteroids. This information is not complete. For full information please see the complete Product Monograph.

References
1. NIH U.S. National Library of Medicine (2018). Genetics Home Reference. RPE65 gene. Available at: <https://ghr.nlm.nih.gov/gene/RPE65>.
2. Russell S et al. Efficacy and safety of voretigene neparvovec (AAV2-hRPE65v2) in patients with RPE65-mediated inherited retinal dystrophy: a randomised, controlled, open-label, phase 3 trial. The Lancet 2017; 390:849-860. Available at: <https://www.ncbi.nlm.nih.gov/pubmed/28712537>
3. NIH U.S. National Library of Medicine. What is a gene? Available at: <https://ghr.nlm.nih.gov/primer/basics/gene>
4. Novartis. Data on File. 2018
5. Novartis Pharmaceuticals Canada Inc. Luxturna[®] (voretigene neparvovec) Product Monograph. October 13, 2020