Ultevursen

For individuals with retinitis pigmentosa due to alterations in exon 13 of the *USH2A* gene

Disclosures

Talk Overview

- **The Ultevursen Story**
  Background of the molecule
- **LUNA Study**
  - **What is the science behind the study?**
  - **What is the trial about, and why is it being conducted?**
  - **Who can potentially participate and why?**
  - **What would participation in the trial involve?**
  - **How can you potentially get involved if you’re interested?**
- **Question and Answers**

Normal eyes

Pre- mRNA

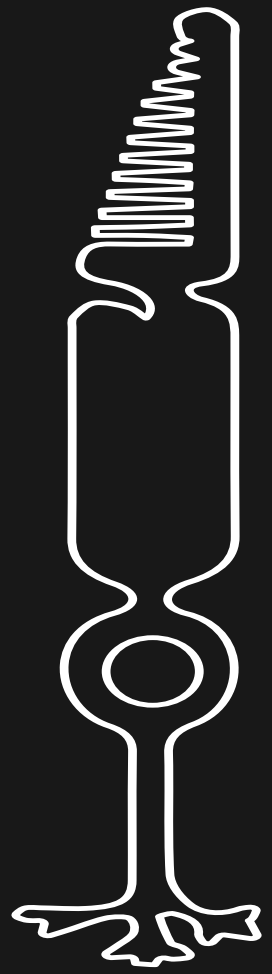
Exon 12 — Exon 13 — Exon 14

mRNA

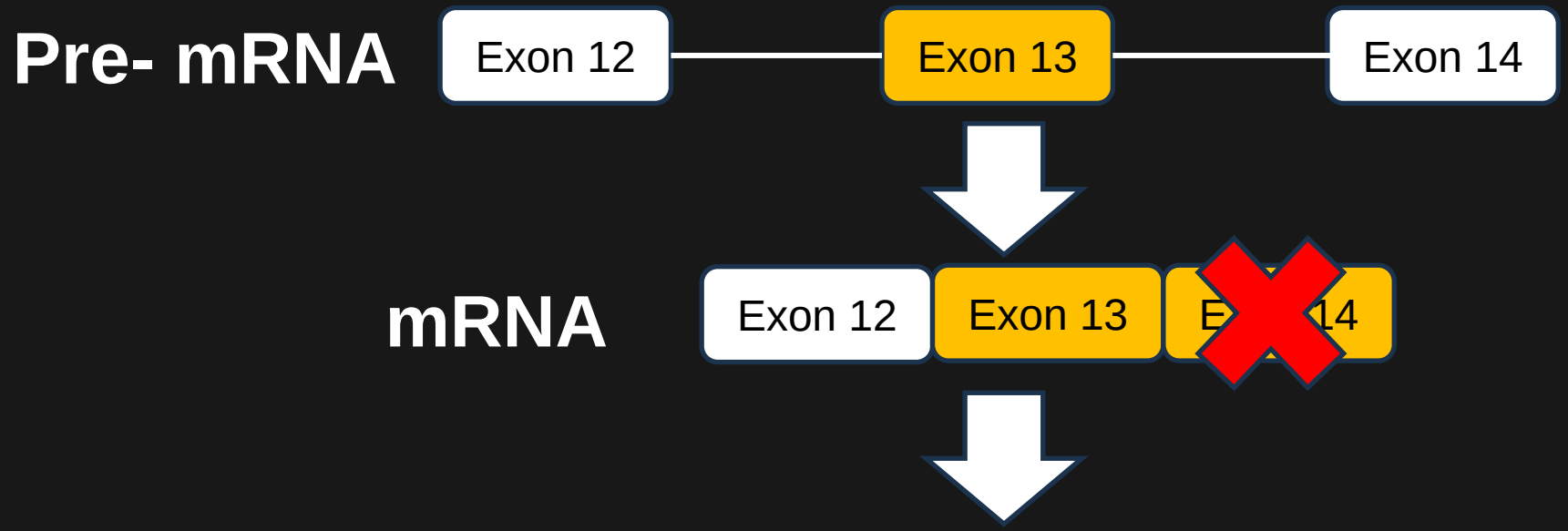
Exon 12 | Exon 13 | Exon 14

Usherin production

Healthy photoreceptors

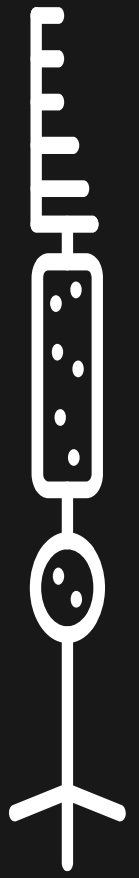


Alteration in exon 13

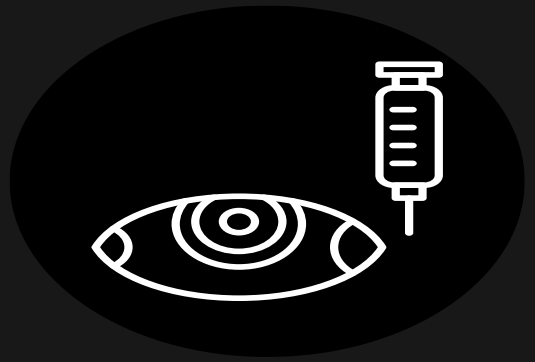


Impaired Usherin production

Damaged photoreceptors



Treatment with Ultevursen



Pre- mRNA

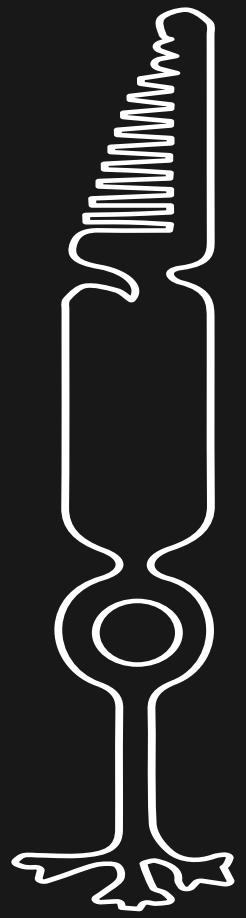
Exon 12 | Exon 13 | Exon 14

mRNA

Exon 12 | Exon 14

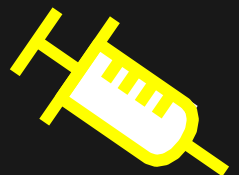
Usherin production
(shortened but functional protein)

Less damaged
photoreceptors



Ultevursen is a first-in-class RNA therapy for *USH2A*-associated RP

Ultevursen aims to **stop or reverse vision loss in RP** due to biallelic mutations in **exon 13 of the *USH2A* gene**



Ultevursen is administered via **intravitreal injection**, and can be used early in the disease course with the aim of preventing early visual decline

The investigational dose of ultevursen is a 180 ug loading dose, followed by 60 ug maintenance doses **every 6 months** (180/60 µg)

Ultevursen was granted **orphan drug designation** in the US and the EU, and has received **fast-track** and **rare pediatric disease designations** from the Food and Drug Administration

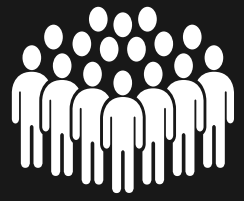
LUNA

LUNA Study

For individuals with retinitis pigmentosa due to mutations in exon 13 of the *USH2A* gene

Study Details

- What is the science behind the study?
- What is the trial about, and why is it being conducted?



- Who can potentially participate and why?

- What would participation in the trial involve?
- How can you potentially get involved if you’re interested?

Collaborative study design with inputs from

Regulators

Experts

IRD/ Usher community

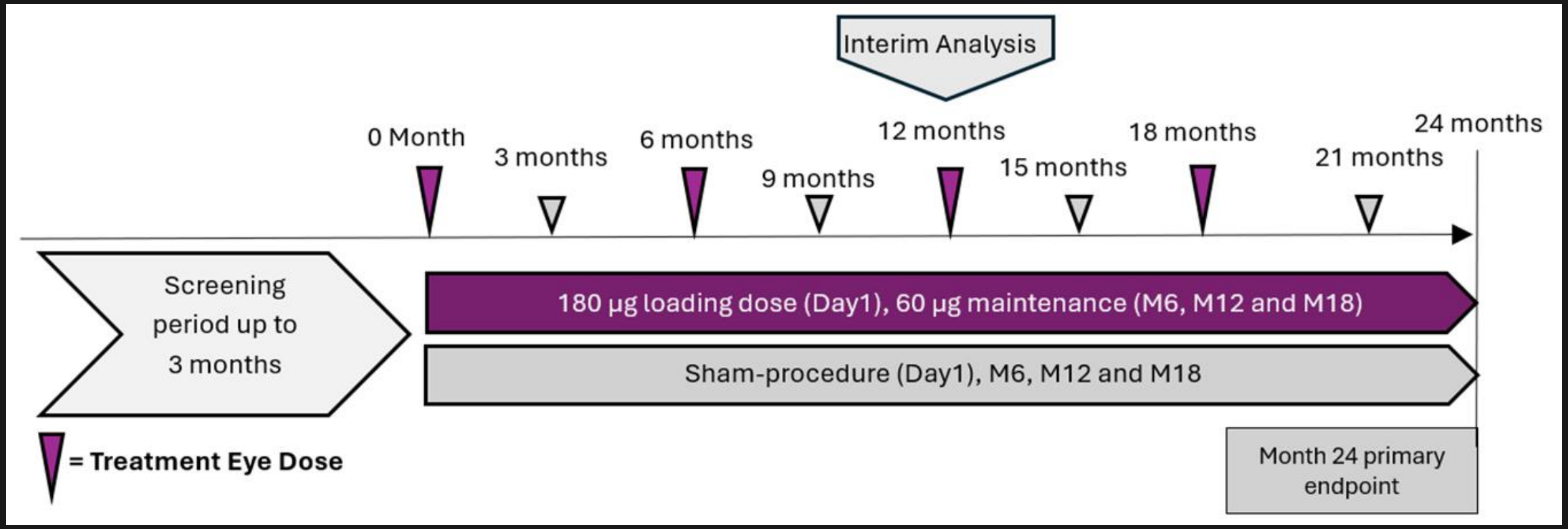
Natural history studies like RUSH2A

What is the study purpose? To understand the efficacy and safety of Ultevursen in individuals with mutations in exon 13 of the *USH2A* gene

Efficacy

Safety

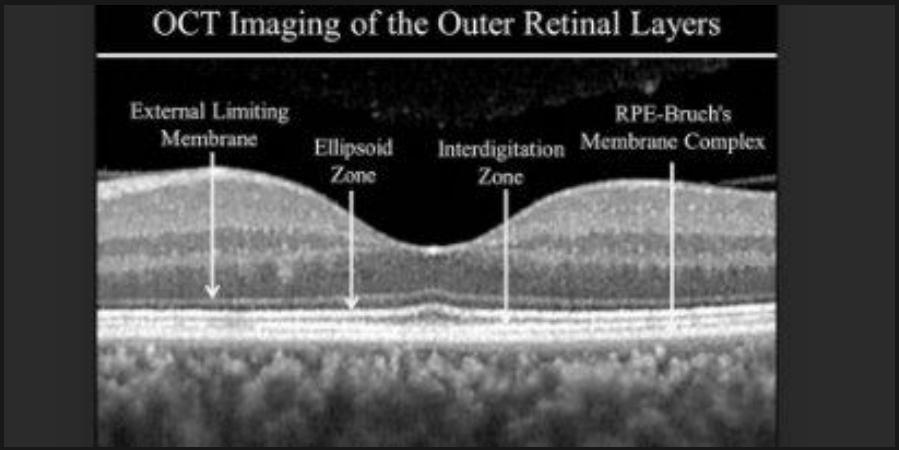
Study design



What is the main goal of the study?

- **Main goal** – assess **width of the ellipsoid zone (EZ) over two years**, using retinal scans.
- Depending **how the EZ changes in people who receive the treatment will inform if** the treatment stops or slows down the disease.
- The **EZ is important** because its directly relates to how well people with Usher's can see and how it may worsen over time

Width in healthy retina



EZ Width in Usher Syndrome

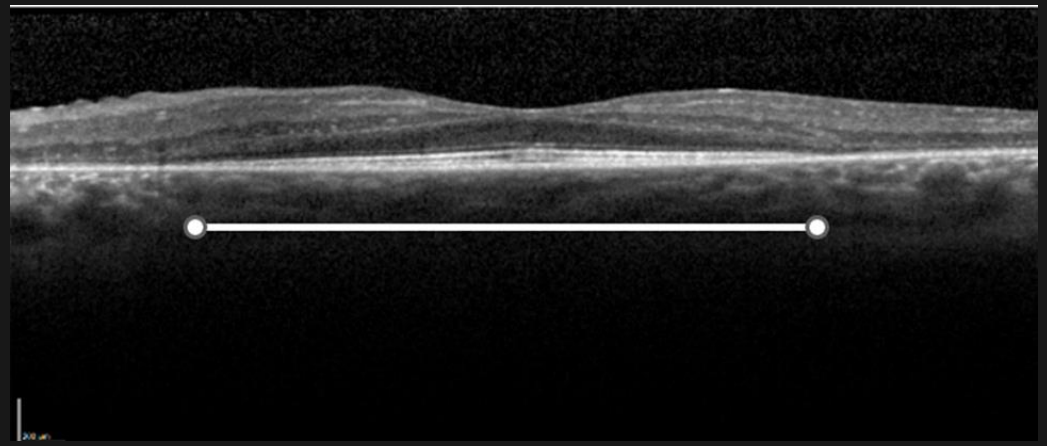


Image courtesy : Duke reading center

Who can potentially participate?

Individuals with retinitis pigmentosa (RP) due to alterations in exon 13 of the *USH2A* gene

Age 8 years and up
12 years and up in EU

Who can potentially participate?

Ellipsoid zone width greater than 2.2mm

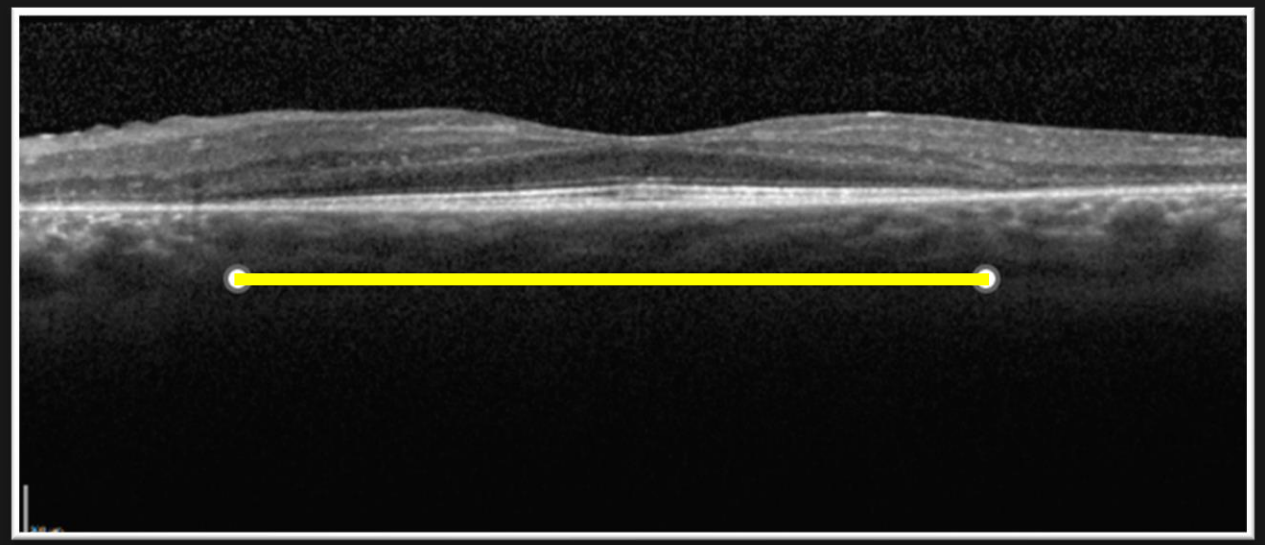


Image courtesy : Duke reading center

What will happen if you participate?

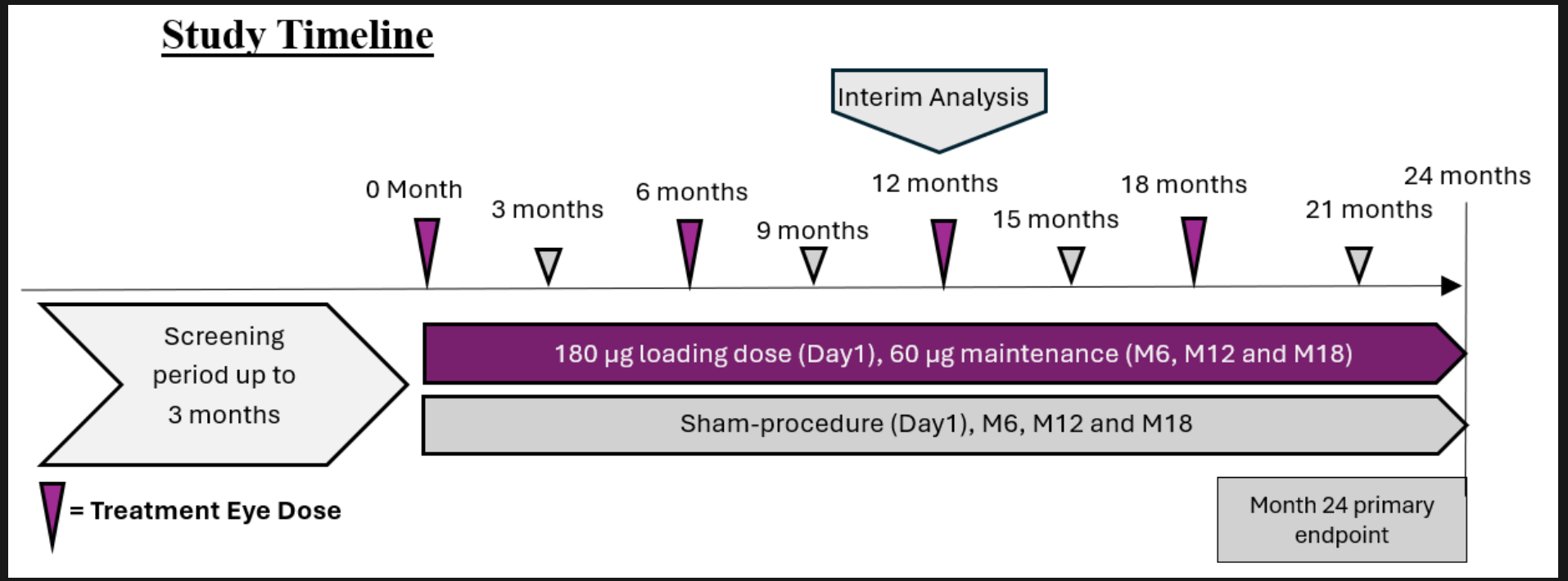
Ultevursen
2/3rd chance

OR

Sham
1/3rd chance

What will happen if you participate?

- **Visits every 3 months** = 10 visits over 27 months
- Injection visits every 6 months = 4 in total



What to expect when you participate?

Screening period

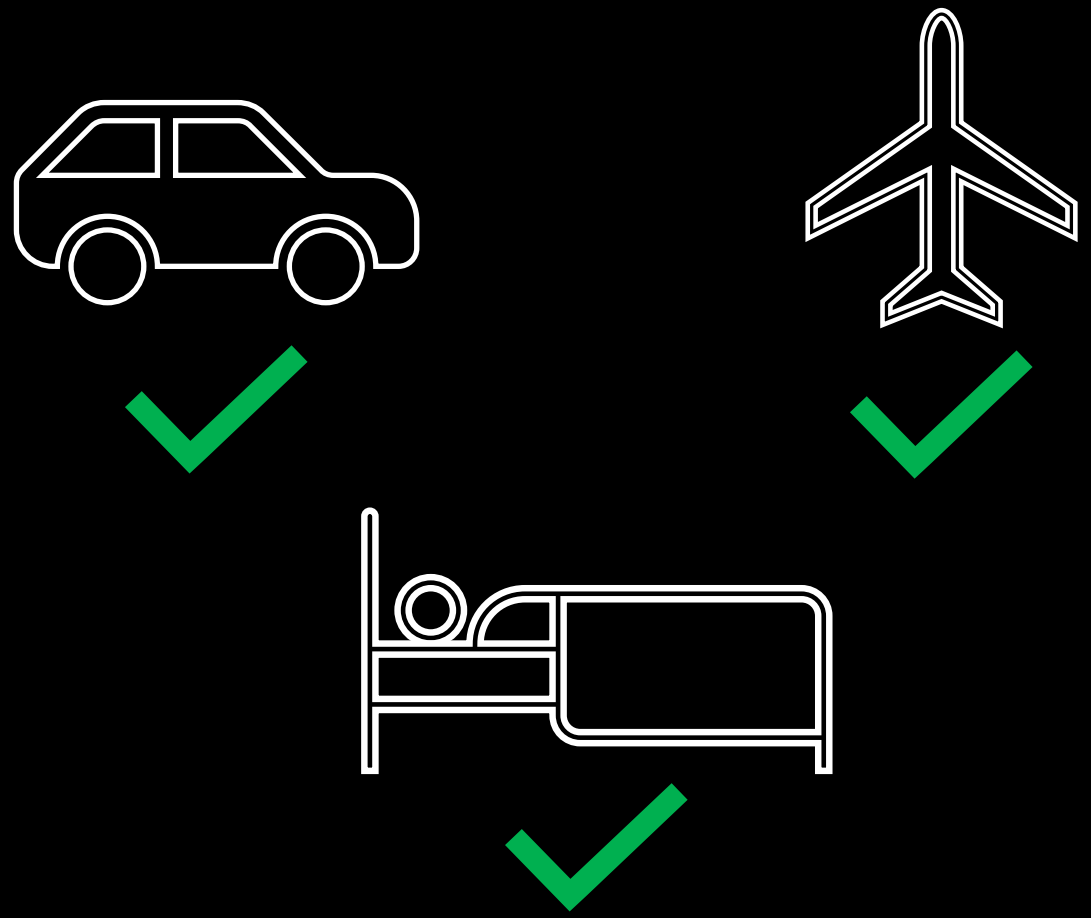
- Genetic analysis
- Optical Coherence Tomography (OCT)
- Ophthalmic examinations and tests
- Virtual reality maze test
- Visual field tests
- Blood samples and urine samples

Treatment period

- Questionnaires
- Interviews
- Blood samples and urine samples,
- Eye tests
- Virtual reality maze test
- Optical Coherence Tomography (OCT)
- Ultevursen or Sham injection
- Safety phone calls

What to expect when you participate?

Visits may last 1-3 days



What are potential benefits of participating?

- **Early Access**: Possible access to a new therapy before it's widely available
- **Contribute to Science**: Help advance medical knowledge for future individuals
- **Close Monitoring**: Receive dedicated care from a specialized medical team
- **Important Note**: No guaranteed benefit — this is an experimental treatment in a clinical trial

What are potential risks and discomforts of participating?

- **Possible side effects** — temporary, permanent, or unexpected
- **Discomfort** from blood draws and tiring tests
- **Time commitment** — multi-day visits and travel required
- **Treatment may not work** as expected

Costs and reimbursement

All the services, procedures, and care directly related to what the study protocol requires will be paid for by the sponsor!

Global multicentre study with 25 participating centres

North and South America

Europe

UK

Summary

LUNA study, focused on individuals with retinitis pigmentosa caused by a specific alteration in ***USH2A* exon 13**. LUNA is a randomized controlled trial comparing **ultevursen to a sham** procedure

Ultevursen, the study medication, is a therapy designed to restore a vital protein in the eye and **potentially slow or stop the disease progression**. Ultevursen is administered via **common intravitreal injections every 6 months**

Eligibility criteria, particularly the requirement for the specific *USH2A* **exon 13** alteration, and the **EZ layer being above 2.2mm**

Outlined what participation involves, including the visit schedule and procedures. Potential benefits and risks. Study-related costs and travel will be reimbursed

Contact for More Information

Email
contact@sepulbio.com

Clinical Trials website

Study Details | Study to Evaluate Ultevursen in Subjects With Retinitis Pigmentosa (RP) Due to Mutations in Exon 13 of the USH2A Gene | ClinicalTrials.gov