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Gene therapy study to assess the safety, tolerability and effectiveness of AXV-101 when injected into the eye in patients with a mutated BBS1 gene to prevent sight loss

Submission date
09/05/2025

Recruitment status
Not yet recruiting

Registration date
15/07/2025

Overall study status
Ongoing

Last Edited
20/11/2025

Condition category
Eye Diseases

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
This is a gene therapy study to assess the safety, tolerability and efficacy of AXV-101 being injected into the eye in participants with BBS1 bi-allelic mutations and retinal degeneration. The treated eye will be compared with the eye not injected with AXV-101.

Who can participate?
Participants between the age of 4 to 17 years with BBS1 bi-allelic mutations and retinal degeneration

What does the study involve?
The study consists of two parts (cohort 1 and cohort 2).
Cohort 1 will include up to three participants. Participants in this cohort will be administered a minimally effective dose of AXV-101 (3 E11 Viral genomes; Vg). The safety data for the first participant will be reviewed by an Independent Data Monitoring Committee (IDMC) before the next participants are enrolled. The IDMC will then review the next two participants' data before opening the next part of the study (Cohort 2).
Cohort 2 will include up to nine participants. Participants in this cohort will be administered a therapeutic dose of AXV-101 (5 E11 Vg). The IDMC will review the safety data after each dose for the first three participants, and if no safety concerns are raised, the remaining six participants in cohort 2 will be dosed sequentially.
As there is a risk of an immune reaction with this type of therapy, all participants will be given a course of steroids (1 mg/kg/day, maximum of 40 mg/day) for a total of 28 days. The steroid course will be started 5 to 7 days before the AXV-101 injection. The dose of the steroid will then be decreased over the next 21 days.
Participants will be followed for 5 years; during this time, participants will undergo regular eye and health assessments. Safety and efficacy monitoring will continue after the first 12 months after the AXV-101 dose. Participants will then be assessed at one and a half years, 2 years, and then for a further 3 years (long-term follow-up) annually. When the participant reaches

adulthood (at the investigator’s discretion) follow-up care in the study will be transferred to an adult facility at a partnered hospital trust.

What are the possible benefits and risks of participating?
Benefits:
Not provided at time of registration
Risks:
An immune reaction following IMP injection. To decrease this, participants will be started on a course of steroid 5 to 7 days prior to IMP injection, and this will be taken up to 21 days after the IMP injection. The level of AAV antibodies will also be monitored via blood tests.
Surgical risks: The surgical procedure to inject the IMP into the eye has a potential infection risk. To prevent this, the treatment solution will be prepared and administered in sterile conditions by trained and qualified personnel. Participants will also be closely monitored for any potential side effects.
Damage to the liver after IMP dosing. This is highly unlikely, participants' liver function will be closely monitored by the study doctor throughout the follow-up period.
Blood withdrawals may be mildly painful and may cause bruising. The site staff will make every effort to minimise this discomfort and the minimal blood volume required for the tests will be taken.

Where is the study run from?
Axovia Therapeutics Ltd (UK)

When is the study starting and how long is it expected to run for?
March 2026 to November 2031

Who is funding the study?
Axovia Therapeutics Ltd (UK)

Who is the main contact?
Steffy George, Steffy.George@axoviatherapeutics.com

Contact information

Type(s)
Public, Scientific, Principal investigator

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
1011952

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CLIN101-AXV-101(SR), CPMS 67544

Study information

Scientific Title
A first-in-human, open label, dose escalation trial to evaluate the safety, tolerability and pharmacodynamics of a single dose of AXV-101 in patients with Bardet-Biedl syndrome 1 (BBS1) bi-allelic mutations and retinal degeneration

Acronym
AXIS

Study objectives

Primary objective:
To evaluate the preliminary safety and tolerability of AXV-101 in participants with BBS1

Secondary objectives:
1. To determine the therapeutic dose of AXV-101 in participants with BBS1
2. To investigate the concentration of AXV-101 in blood, urine and tears (both eyes)

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 10/07/2025, London - Brent Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)2071048128, +44 (0)207 104 8117, +44 (0) 2071048131; brent.rec@hra.nhs.uk), ref: 25/LO/0396

Study design
First-in-human open-label dose-escalation trial

Primary study design
Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Bardet-Biedl syndrome 1 (BBS1) mutation affecting multiple organs, including the eyes and vision

Interventions
Up to 12 children between the ages of 4 to 17 years with BBS1 with deteriorating eyesight will be enrolled on the study.

The study consists of two parts (cohort 1 and cohort 2):
Cohort 1 participants (n = 3) will be given a dose of 3 x 10^11 viral genomes AXV-101
Cohort 2 participants (n = 9) will be given a dose of 5 x 10^11 viral genomes of AXV-101

The children will be followed up for a total of 5 years at set timepoints (up to 19 hospital visits) to check the safety and effectiveness of the study drug.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
AXV-101 [AXV-101 Drug Substance, Viralgen Vector Core No INN Name has been assigned]

Primary outcome(s)

Frequency and severity of all adverse events (AEs) including serious adverse events (SAEs) and their relationship to AXV-101 measured using medical & physical examinations at screening, baseline, days 0, 1, 2, 3, 7, 14, 30, 60, 90, 180, 270, 365 and years 1.5, 2, 3, 4 and 5.

Key secondary outcome(s))
At screening, baseline, days 0, 1, 2, 3, 7, 14, 30, 60, 90, 180, 270, 365 and years 1.5, 2, 3, 4 and 5:
1. Ophthalmology assessment to check function and vision - change from baseline to 1 year in parameters in the treated eye compared to untreated using OCT, visual evoked potential, full-field light sensitivity threshold, Fundus autofluorescence, electroretinography, visual acuity and visual field)
2. Blood, urine and tear tests for safety and PK tests to check the study drug in the system
3. Quality of life (QoL) – completed by both participants and caregiver

Completion date
01/11/2031

Eligibility

Key inclusion criteria
To be eligible to participate in this trial, an individual must meet all the following criteria:
1. Male or female participants aged 4 to 17 years (inclusive).
2. Able to provide written informed consent:
2.1. Parent(s)/guardian(s) prior to the initiation of any study-specific procedures for participants who are under the age of 18
2.2. Participants aged 6-17 years of age may (according to the judgement of the investigator) provide their written assent; consent will also be required from the legal guardian of the participant.
2.3. Participants aged below 6 years of age will not be required to sign an assent form; however, their views should be considered; consent will be required from the legal guardian of the participant.
3. Participant with a confirmed diagnosis of bi-allelic BBS1 mutations. Molecular diagnosis /genetic testing will have been undertaken by an accredited laboratory using an assay that has the relevant mark of conformity and is used as per its intended use. UK diagnostic genetic laboratories must conform to the Association for Clinical Genomic Science (ACGS) and adopt the ACMG guidelines for the determination of pathogenicity. US diagnostic genetic laboratories must be CLIA-approved.
4. Participants with presentation of retinal degeneration (evidence of early Rod-Cone Dystrophy, Cone-Rod Dystrophy or Night vision loss [nyctalopia])
5. Participants with sufficient viable retinal cells as determined by OCT. Participants must have either:
5.1. A measurable area of intact ellipsoid within the posterior pole - minimum 1500 microns horizontal width
5.2. ≥3-disc areas of retina without atrophy or pigmentary degeneration within the posterior pole; or
5.3. Remaining visual field within 30 degrees of fixation as measured by a III4e isopter or equivalent.
6. Post-pubertal male participants and female participants of childbearing potential must be willing to comply with the contraceptive requirements

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
4 years

Upper age limit
17 years

Sex
All

Total final enrolment
0

Key exclusion criteria
An individual who meets any of the following criteria will be excluded from participation in this trial:
1. A fully blind participant.
2. Participant or participant's legal guardian is unable or unwilling to meet the requirements of the study, or unable to provide written informed consent/assent
3. Participant has been administered any investigational medicinal product (IMP) during the last 6 months prior to individual enrolment of the participant and/or within five half-lives of the previous IMP, whichever is longer
4. Other than as required per protocol, the participant has received immune-modulating agents within 90 days before dosing (use of inhaled corticosteroids to manage chronic respiratory conditions is allowed)
5. Glucocorticoid intolerance
6. Use of other concomitant medications to manage chronic conditions must have been stable for at least 30 days before dosing
7. Presence of severe diabetes or uncontrolled blood glucose
8. Presence of active infection or recent severe infection (elevated WBC)
9. Participant with any prior intraocular surgery in either eye within 6 months
10. Participant with any known sensitivity to AXV-101, its excipients and the medications planned for use in the peri-operative period
11. Participant with significant renal, liver or haematological disease as defined by:
12. Laboratory evidence of liver disease (aspartate aminotransferase greater than two times the upper limit of normal [ULN] of the testing laboratory).
13. Laboratory evidence of renal disease (eGFR<30).
14. Laboratory evidence of haematological disease (absolute neutrophil count < 1,500/mm3; haemoglobin < 0.9 times the lower limit of normal [LLN] of the testing laboratory, by sex; or platelet count < 140,000/mm3).
15. Any pre-existing eye conditions or complicating systemic diseases that would preclude the planned surgery or interfere with the interpretation of the study or the safety of the participant. Active uveitis or intraocular inflammation (infectious or non-infectious). Complicating systemic diseases would include those in which the disease itself, or the treatment for the disease, can

alter ocular function. Examples are malignancies whose treatment could affect central nervous system function (for example: radiation treatment of the orbit; leukaemia with central nervous system (CNS)/optic nerve involvement). Participants with diabetes or sickle cell disease will be excluded if they have had any manifestation of advanced retinopathy (e.g., macular oedema or proliferative changes). Also excluded would be participants with immunodeficiency (acquired or congenital), as there could be susceptibility to opportunistic infection (such as cytomegalovirus retinitis).
16. Participants with evidence of chronic or active viral disease, including:
17. Participant has human immunodeficiency virus HIV-1 or HIV-2, including serological or viral load evidence of HIV 1 or HIV-2.
18. Participant has an active viral infection (systemic bacterial or fungal infection) based on clinical observation.
18.1. Active hepatitis B (HBV) or C (HCV), and HBsAg, HBcAb, HBV-DNA positivity or HCV-Ribonucleic acid (RNA) viral load positivity, respectively. A negative viral load assay in two samples, collected at least 6 months apart, will be required to be considered negative. Both natural clearers and those who have cleared HCV on antiviral therapy are eligible.
19. Any other circumstance that would not allow the potential participant to complete follow-up examinations during the course of the study or, in the opinion of the Investigator, makes the potential participant unsuitable for the study.
20. Pregnant and/or breastfeeding participant.

Date of first enrolment
15/03/2026

Date of final enrolment
31/03/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Great Ormond Street Hospital for Children
Great Ormond Street
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Study participating centre
Guys and St Thomas' NHS Foundation Trust
249 Westminster Bridge Road
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Sponsor information

Organisation
Axovia Therapeutics Ltd

Funder(s)

Funder type
Industry

Funder Name
Axovia Therapeutics Ltd

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be published as a supplement to the results publication

IPD sharing plan summary
Published as a supplement to the results publication

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes