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# Study drug ELX-02 for patients with Alport syndrome

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| **Submission date**<br>09/03/2022 | **Recruitment status**<br>No longer recruiting | [X] Prospectively registered<br>[X] Protocol<br>[_] Statistical analysis plan<br>[_] Results<br>[_] Individual participant data<br>[X] Record updated in last year |
| **Registration date**<br>05/05/2022 | **Overall study status**<br>Completed | |
| **Last Edited**<br>15/10/2024 | **Condition category**<br>Genetic Diseases | |

## Plain English summary of protocol

Background and study aims
The main aim of this study is to learn how well the study drug, ELX-02, works and how safe it is for patients with Alport syndrome caused by nonsense mutations. Alport syndrome caused by nonsense mutations is a genetic disorder that decreases kidney function and can also affect the ears and decrease hearing. In this form of Alport syndrome, the nonsense mutation prevents the body from producing the full-length Collagen IV protein that forms the filters in the kidney and has an important role in ear function. There is currently no treatment for Alport syndrome caused by nonsense mutations.

Who can participate?
Patients aged between 6 and 30 years with Alport syndrome caused by nonsense mutations

What does the study involve?
Patients will be in the study for about 26 weeks. This includes a screening period of up to 42 days, a treatment period of 60 days and a follow-up period of 90 days. Patients will receive a treatment of ELX-02 injected once a day for 8 weeks. After their last treatment, patients will be followed up for 12 weeks.

What are the possible benefits and risks of participating?
Participating in this research study will allow patients to play an active role in health care, help others by contributing the medical research and learn more about their condition.
Patients may or may not benefit from taking part in this research study. It is possible that their Alport syndrome symptoms will improve while they are receiving the study drug, however, there is no guarantee that patients will receive any benefits.
To date, more than 126 people have been exposed to ELX-02 at different doses. The most commonly reported side effects in studies of ELX-02 were injection site reactions, ear discomfort, ear pain, headaches and dizziness. Common injection site reactions are redness, warmth, pain or itching near the injection site. These reactions occurred in more than 80% of patients receiving ELX-02 and nearly 40% of patients in the placebo (dummy drug) group. Injection site reactions may appear immediately or be delayed by several days after the injection. Most reactions are mild and improve shortly after the injection is administered. Rare injection site reactions may include blistering and scab forming on the injection site several days

later. On very rare occasions, injection site reactions may be slow to improve, continue for an unknown period of time (several months), and may cause a scar on the skin to change colour around the injection site.
Blood sample collection may cause faintness and/or swelling, pain, redness, bruising, bleeding at the collection site, or infection (rarely) at the site where the needle is inserted. Temporary skin irritation may occur during an ECG from the patches or gel that is used. Patients may experience changes in hearing, speech, noise or ringing in the ears, or dizziness. Patients may experience a build-up of waste in their blood due to kidney injury. The most common complication with the kidney biopsy is blood in the urine, which usually stops within a few days, and pain at the biopsy site for a few hours. Rare cases include surgery to control the blood in the urine, kidney hematoma infection that requires antibiotic treatment or high blood pressure. The study may involve risks to the unborn child that are not yet known at this time, so patients and partners of patients should not become pregnant while participating in the study.

Where is the study run from?
Eloxx Pharmaceuticals Inc. (USA)

When is the study starting and how long is it expected to run for?
February 2022 to April 2024

Who is funding the study?
Eloxx Pharmaceuticals Inc. (USA)

Who is the main contact?
Prof. Detlef Bockenhauer
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# Contact information

### Type(s)
Principal Investigator

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Scientific

### Contact name
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# Additional identifiers

### EudraCT/CTIS number
2022-000604-35

### IRAS number
1005163

### ClinicalTrials.gov number
NCT05448755

### Secondary identifying numbers
EL-014, IRAS 1005163, CPMS 52088

# Study information

### Scientific Title
A Phase II open-label pilot study to evaluate the safety and efficacy of subcutaneously administered ELX-02 in patients with Alport syndrome with Col4A5 and Col4A3/4 nonsense mutation

### Study objectives
Primary objective: The safety and tolerability of ELX-02 will be evaluated in this trial.

Secondary objectives: The readthrough effect of ELX-02 in the expression of Col IV will be evaluated in the kidney and ear. The expression of the Col IV in the kidney will be evaluated functionally by the changes in proteinuria and hematuria, two main early hallmarks of kidney disease in AS.

Histologically, the expression of Col IV will be evaluated by the expression of Col IV in the basement membrane. While the focus of the trial is to evaluate the efficacy in the kidney, and as such the patients are not selected based on their auditory phenotype. However, it is expected that most of the participants to have auditory phenotypes. The evaluation of the hearing of the participants is an exploratory endpoint.

### Ethics approval required
Old ethics approval format

### Ethics approval(s)
Approval 04/05/2022, East of England - Cambridge South Research Ethics Committee (Equinox House, City Link, Nottingham, NG2 4LA, UK; +44 (0)20 7104 8284; cambridgesouth.rec@hra.nhs.uk), ref: 22/EE/0064

## Study design
Open-label pilot study

## Primary study design
Interventional

## Secondary study design
Non randomised study

## Study setting(s)
Hospital

## Study type(s)
Treatment, Safety, Efficacy

## Participant information sheet
No participant information sheet available

## Health condition(s) or problem(s) studied
Alport syndrome

## Interventions
Patients will receive a treatment of ELX-02 0.75 mg/kg subcutaneously administered once a day for 8 weeks. After their last treatment, patients will be followed up for 12 weeks.

## Intervention Type
Drug

## Pharmaceutical study type(s)
Pharmacokinetic

## Phase
Phase II

## Drug/device/biological/vaccine name(s)
ELX-02

## Primary outcome measure
1. Incidence and characteristics of adverse events (AEs) collected using Common Terminology Criteria for Adverse Events (CTCAE) Version 5.0 from signing the informed consent form until the day 150/End of Study (EOS) visit
2. Injection site reactions classified and graded as per Division of AIDS (DAIDS) guidelines at the days 1, 15, 30, 45 and 60/End of Treatment (EOT) visits
3. Vital signs and physical examination performed at the initial, baseline, days 1, 15, 30, 45 and 60 /EOT visits
4. Audiometric testing (including high-frequency audiometry) and tinnitus and dizziness status assessed at the initial, baseline, days 30, 60/EOT, 90, 120 and 150/EOS visits
5. 12-lead ECG performed at the initial and day 60/EOT visits
6. Clinical laboratory evaluations (haematology, chemistry, urinalysis) performed at the initial, days 1, 15, 30, 45, 60/EOT, 90, 120 and 150/EOS visits

### Secondary outcome measures
1. Proteinuria measured via the urine protein/creatinine ratio (UPCR) procedure at the initial, baseline, days 1, 15, 30, 60/EOT, 90, 120 and 150/EOS visits
2. Col IV protein expression measured using a renal biopsy collected at the initial and day 60 /EOT visits
3. Hematuria measured microscopically at the initial, baseline, days 1, 15, 30, 60/EOT, 90, 120 and 150/EOS visits

### Overall study start date
28/02/2022

### Completion date
04/04/2024

## Eligibility

### Key inclusion criteria
1. Evidence of signed and dated informed consent/assent document(s) indicating that the participant (and/or their parent/legal guardian) has been informed of all pertinent aspects of the trial
2. Understands, and is willing and able to comply with all scheduled visits, treatment plan, laboratory tests, and other study procedures
3. Male and female participants
4. Aged between 6 and 30 years
5. A confirmed diagnosis of X-linked or autosomal recessive Alport syndrome with a documented nonsense mutation of Col4A5 in a male or nonsense mutation of Col4A3 or Col4A4 (male or female)
6. The nonsense mutation should be UAG or UGA
7. eGFR >60 ml/min/1.73 $m^2$ (based on Chronic Kidney Disease Epidemiology Collaboration [CKD-EPI] for ages ≥18 years and Schwartz formula for participants <18 years)
8. Urinary protein based on two spot urine collections [urine protein/creatinine ratio (UPCR) ≥500 mg/g]
9. Stable regimen of ACEi/ARB for 4 weeks before screening (unless there is a contraindication)
10. Must be willing to abstain from strenuous exercise during the 48 h prior to study visits
11. Females of childbearing potential and males capable of fathering a child must meet the contraception requirements (outlined in protocol section 6.3)
12. Non-lactating females
13. Females on hormone replacement therapy (estrogen or progesterone) or contraceptive therapy must be stabilized on a product and dose for at least 30 days prior to Screening
14. Have not received systemic medications with the potential to impair renal function on a frequent basis (e.g., nonsteroidal anti-inflammatory drugs [NSAIDs]) or with ototoxic potential (e. g., quinine or salicylates), or any injectable aminoglycosides for a period of at least 14 days prior to dosing
15. Negative human immunodeficiency virus (HIV), hepatitis B surface antigen (HBsAg), and hepatitis C virus antigen (HCV Ag) serology tests at Screening
16. No history of alcohol or drug abuse within the 6 months prior to Screening
17. Body Mass Index (BMI) of 19.0 to 30.0 kg/$m^2$ (inclusive). Participants with a lower BMI may be entered into the study at the discretion of the investigator following consultation with the Sponsor

**Participant type(s)**
Patient

**Age group**
Mixed

**Lower age limit**
6 Years

**Upper age limit**
30 Years

**Sex**
Both

**Target number of participants**
4

**Total final enrolment**
3

**Key exclusion criteria**
1. Participants who are investigational site staff members directly involved in the conduct of the study and their family members, site staff members otherwise supervised by the Investigator, or participants who are Eloxx Pharmaceuticals employees directly involved in the conduct of the study
2. Participation in clinical study including administration of any investigational drug or device in the last 30 days or 5 half-lives (whichever is longer) prior to investigational product dosing in the current study
3. Use of prohibited medications as defined in (protocol) section 6.1 within the specified windows
4. History of any comorbidity which in the opinion of the investigator might confound the study or pose an additional risk in administering the study drug to the participant
5. History of any organ transplantation
6. Mutation consistent with autosomal dominant Alport syndrome
7. Liver disease characterized by cirrhosis or portal hypertension. Participants with alanine aminotransferase (ALT), aspartate aminotransferase (AST), and/or a total bilirubin 3.0 times the upper limit of normal (ULN) will be excluded
8. History of congestive heart failure diagnosed clinically or with documented left ventricular ejection fraction (LVEF) ≤40%
9. Evidence or history of clinically relevant psychiatric condition
10. A positive urine drug screen (amphetamines, benzodiazepines, cocaine and opiates) at Screening
11. Screening supine 12-lead electrocardiogram (ECG) demonstrating any clinically significant findings as judged by the Investigator
12. Participants with any abnormalities in clinical laboratory tests at Screening, considered by the study Investigator as clinically relevant
13. Major surgery within 180 days (6 months) of Screening
14. History of dialysis
15. Known allergy to any aminoglycoside
16. Participants with any acute medical situation unresolved within 14 days of first dose that is considered of significance by the Investigator

17. Participants with >10 dB change in threshold between audiometric Initial test to baseline test for the frequencies from 0.5 -12.5 kHz
18. Dizziness Handicap Inventory (DHI) score at screening ≥16 for adults, and active dizziness reported for pediatric participants.

### Date of first enrolment
31/10/2022

### Date of final enrolment
30/03/2023

## Locations

### Countries of recruitment
Australia

England

United Kingdom

### Study participating centre
**Great Ormond Street Hospital for Children**
Great Ormond Street
London
United Kingdom
WC1N 3JH

### Study participating centre
**Royal Free Hospital**
Pond Street
London
United Kingdom
NW3 2QG

### Study participating centre
**Royal Children's Hospital**
Dept of Nephrology
50 Flemington Road
Parkville
Victoria
Australia
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**Study participating centre**
**Monash Medical Center**
246 Clayton Road
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# Sponsor information

**Organisation**
Eloxx Pharmaceuticals (United States)

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**Sponsor type**
Industry

**Website**
https://www.eloxxpharma.com/

**ROR**
https://ror.org/0021myq38

# Funder(s)

**Funder type**
Industry

**Funder Name**
Eloxx Pharmaceuticals Inc.

# Results and Publications

**Publication and dissemination plan**

1. Peer-reviewed scientific journals
2. Internal report
3. Conference presentation
4. Submission to regulatory authorities

## Intention to publish date
03/04/2025

## Individual participant data (IPD) sharing plan
The data-sharing plans for the current study are unknown and will be made available at a later date. All study data collected through the electronic case report form (eCRF) will be anonymized by a unique ID. The paper documents including personal data (Informed consent form and screening log) will be filed in the Investigator's File that will be locked and only the Investigational Team will have access.

## IPD sharing plan summary
Data sharing statement to be made available at a later date

## Study outputs

| Output type | Details | Date created | Date added | Peer reviewed? | Patient-facing? |
|---|---|---|---|---|---|
| Protocol file | version 2.1 | 21/03/2023 | 12/06/2023 | No | No |
| HRA research summary | | | 26/07/2023 | No | No |