

A first-in-human single and multiple ascending dose study of AX-202

Submission date 03/12/2022	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input type="checkbox"/> Protocol
Registration date 06/01/2023	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input type="checkbox"/> Results
Last Edited 24/07/2024	Condition category Skin and Connective Tissue Diseases	<input type="checkbox"/> Individual participant data <input type="checkbox"/> Record updated in last year

Plain English summary of protocol

Background and study aims

The Sponsor, Arxx Therapeutics, is developing a new experimental medication called AX-202 for the purpose of treating inflammatory diseases (when the immune system attacks the body's own tissues, resulting in inflammation) and fibrotic diseases (diseases caused by the thickening or scarring of tissue). Psoriasis is a chronic, relapsing inflammatory disease of the skin affecting approximately 1-3% of the world's population. The most common form is plaque psoriasis representing 80-90% of all cases. Plaque psoriasis is defined by well-defined red, scaly plaques or patches which can occur anywhere on the body. The immune system normally defends the body against harmful substances, diseases and infections. However, in people who have an autoimmune disease such as psoriasis, the immune system becomes overactive and attacks its own healthy cells. S100A4 is a protein released in the body which can cause harm, contributing to over-activation of the immune system (inflammation) and tissue damage in diseases like psoriasis. AX-202 is a type of medication called a 'monoclonal antibody', which are antibodies designed to specifically bind to a disease-causing protein. AX-202 binds to and blocks the activity of S100A4, so may reduce inflammation and tissue damage in psoriasis.

Who can participate?

Adult healthy volunteers and patients with mild to moderate chronic plaque psoriasis

What does the study involve?

This is the first study with AX-202 in humans and is designed to determine whether the drug is safe and well tolerated in healthy participants (Part A) and people with plaque psoriasis (Part B). The following will also be investigated:

1. Pharmacokinetic blood analysis (levels of AX-202 in the body)
2. Immunogenicity in the blood (to see if the body is making antibodies against AX-202)
3. Target engagement in blood and urine (interaction of AX-202 with its target protein 'S100A4')
4. Biomarker analysis (which looks at specific biological features of the blood and skin)
5. Disease activity in patients will be assessed using scoring systems (Part B only)

What are the possible benefits and risks of participating?

Participants will be informed about potential side effects and risks of AX-202/study procedures and that they have the right to withdraw at any time, without giving a reason and without their

medical care or legal rights being affected. Participants will be monitored for possible side effects and will be asked to contact their Study Doctor/GP ASAP if they think they are having a medical problem/side effect/change in their condition/health. They will be told to seek immediate medical treatment if they are unable to contact the Study Doctor/GP, or if they feel it's an emergency.

Part A of this study is the first time AX-202 is being administered to humans, therefore, side effects in humans are unknown. There is a chance that an unexpected or serious side effect may happen when taking AX-202 or any other drug. The participant will be asked to report any new symptoms/signs of illness to the study staff.

Potential risks for AX-202:

1. Side effects associated with the development of ADAs: Immunogenicity sampling will take place to monitor this.
2. Infusion-related reactions: Participants will be monitored for 72 hours post-dose for signs of treatment-related toxicity or intolerability of AX-202. Site staff are trained appropriately and will have access to medications/devices needed to manage medical emergencies.

Other drugs that work in a similar way to AX-202 may cause increased susceptibility to infections. This risk has not been identified in AX-202, however, as a precautionary measure, participants will be monitored for signs of infection.

There is a chance the participant may experience an allergic reaction after taking the drug however this is unlikely. If this does occur the drug will be stopped and appropriate treatment will be given.

Drug interaction

AX-202 is a biological which is not metabolised in the liver, therefore the risk of interaction with other medications is low. The importance of keeping to the restrictions and telling the study doctor about medication use while on the study will be highlighted.

Unknown risks:

As with any investigational drug, there may be side effects that are not known, and current knowledge regarding all potential harms and the probability of the occurrence of all harm is limited.

Reproductive risks

It is not known if AX-202 will affect an unborn baby.

Males who are sexually active with women of childbearing potential must use, with their partner, a condom and an approved method of highly effective contraception from consent until 120 days after the last dose.

Females who are pregnant/lactating/breastfeeding are excluded. Females who are sexually active and of childbearing potential must use an approved method of highly effective contraception from consent until 120 days after the last dose. Female participants of non-childbearing potential do not need to use contraception.

There is a risk of drug exposure through ejaculation that might be harmful to the sexual partners. Therefore, a condom should be used by all male participants during the study and for 120 days after the last dose. Males should not donate sperm and females should not donate ova/oocytes during the study and for at least 120 days after the last dose.

Risk assessment:

In the population selected for this study, AX-202 and all study procedures do not pose any significant risks. All staff are competent in the study procedures.

Study procedures:

Blood sampling: On days when several samples are taken a cannula may be used. Placing a cannula and drawing blood via a needle may cause some discomfort/bleeding/bruising. Rarely, fainting, local inflammation or infection may occur.

ECGs: The electrodes used for this test may cause skin irritation. The sites of the body where the pads are placed need to be clean and sometimes hair may have to be shaved to ensure they stick firmly.

Skin Biopsy: Skin biopsies can cause the following;

Scarring: It is impossible to cut the skin without scarring. Some people have an abnormal response to skin healing and may have a larger scar.

Bleeding: The overall risk of bleeding is 2%. The doctor will make sure any bleeding has stopped before the participant is discharged.

Infection: The overall risk of infection is 1%. The participant will be advised to keep the wound clean and dressings will be provided. If the wound becomes infected the participant will be advised to contact the site or a GP.

Allergic reaction: Allergic reactions to dressings, gloves, antiseptics, and anaesthetics are unusual. Participants will be asked about any allergies.

Participants will be advised to report immediately to the study doctor any unusual symptoms or undesirable effects.

In case of emergencies, an experienced physician will be available. Trained medical staff and the necessary equipment/medication are available at the unit, or at a nearby hospital.

Where is the study run from?

Arxx Therapeutics (Norway)

When is the study starting and how long is it expected to run for?

November 2022 to July 2024

Who is funding the study?

Arxx Therapeutics (Norway)

Who is the main contact?

Sylvia Vetrhus, sylvia.vetrhus@arxxtx.com

Contact information

Type(s)

Scientific

Contact name

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Principal Investigator

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Public

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Additional identifiers

EudraCT/CTIS number

2022-002534-13

IRAS number

1006661

ClinicalTrials.gov number

NCT05965089

Secondary identifying numbers

AX-202-01, IRAS 1006661

Study information

Scientific Title

A first-in-human, randomised double-blind, placebo-controlled 2-part study to evaluate the safety, tolerability, immunogenicity and pharmacokinetics of single ascending doses of AX-202 in healthy subjects and multiple ascending doses of AX-202 in patients with mild to moderate chronic plaque psoriasis

Study objectives

Part A - To assess the safety and tolerability of a single ascending intravenous (IV) dose of AX-202 in healthy subjects.

Part B - To assess the safety and tolerability of multiple ascending IV doses of AX-202 in patients with mild to moderate chronic plaque psoriasis.

Part A

To characterise systemic Pharmacokinetics (PK) of AX-202 after a single ascending IV dose in healthy subjects

To evaluate the immunogenicity of AX-202 after a single ascending IV dose in healthy subjects

Part B

To characterise systemic PK of AX-202 after multiple ascending IV doses in patients with mild to moderate chronic plaque psoriasis.

To evaluate the immunogenicity of AX-202 after multiple ascending IV doses in patients with mild to moderate chronic plaque psoriasis.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Approved 02/03/2023, North West - Greater Manchester Central Research Ethics Committee (3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)2071048328, (0) 2071048131; gmcentral.rec@hra.nhs.uk), ref: 22/NW/0333

Study design

Randomized placebo-controlled double-blind study

Primary study design

Interventional

Secondary study design

Randomised controlled trial

Study setting(s)

Pharmaceutical testing facility

Study type(s)

Treatment

Participant information sheet

Not available in web format, please use the contact details to request a participant information sheet

Health condition(s) or problem(s) studied

Healthy volunteers and patients with mild to moderate chronic plaque psoriasis

Interventions

Current intervention as of 20/11/2023:

Part A (Single-ascending-dose): A single dose of the monoclonal antibody AX-202 or a matching placebo (Sodium Chloride; 0.9% NaCl) will be administered by intravenous infusion on Day 1. The starting dose in Cohort 1 is 0.5 mg/kg. Subsequent doses will be determined from the review of safety and Pharmacokinetic (PK) data from the preceding cohorts. The maximum dose will not be higher than 20 mg/kg and each dose escalation will not exceed a 3.3 dose increment.

Part B (Multiple-ascending-dose): Doses of the monoclonal antibody AX-202 or matching placebo (Sodium Chloride; 0.9% NaCl) will be administered by intravenous infusion on Days 1, 22, 43 and 64. The planned starting dose of AX-202 to be administered in Part B Cohort 1 will be confirmed during the interim review of safety and PK data from Part A cohorts. The doses administered in Part B will not exceed the maximum dose administered safely in Part A. Subsequent doses in Part B will be determined from the review of safety and PK data from the preceding cohorts.

All doses will be given as an infusion over approximately 30-60 minutes. The participants will be randomised manually to AX-202 or placebo at a single centre using a paper randomisation schedule for each dosing cohort and study part. All participants that are randomised and receive Investigational Medicinal Product (IMP) will be followed up until 99 days after their last dose of IMP.

Previous intervention:

Part A (Single-ascending-dose): A single dose of the monoclonal antibody AX-202 or a matching placebo (Sodium Chloride; 0.9% NaCl) will be administered by intravenous infusion on Day 1. The starting dose in Cohort 1 is 0.5 mg/kg. Subsequent doses will be determined from the review of safety and Pharmacokinetic (PK) data from the preceding cohorts. The maximum dose will not be higher than 20 mg/kg and each dose escalation will not exceed a 3.3 dose increment.

Part B (Multiple-ascending-dose): Doses of the monoclonal antibody AX-202 or matching placebo (Sodium Chloride; 0.9% NaCl) will be administered by intravenous infusion on Days 1 and 22. The planned starting dose of AX-202 to be administered in Part B Cohort 1 will be confirmed during the interim review of safety and PK data from Part A cohorts. The doses administered in Part B will not exceed the maximum dose administered safely in Part A. Subsequent doses in Part B will be determined from the review of safety and PK data from the preceding cohorts.

All doses will be given as an infusion over approximately 30-60 minutes. The participants will be randomised manually to AX-202 or placebo at a single centre using a paper randomisation schedule for each dosing cohort and study part. All participants that are randomised and receive Investigational Medicinal Product (IMP) will be followed up until 99 days after their last dose of IMP.

Intervention Type

Biological/Vaccine

Phase

Phase I

Drug/device/biological/vaccine name(s)

AX-202

Primary outcome measure

Current primary outcome measures as of 20/11/2023:

Safety and tolerability in Part A/B of the study measured by monitoring AEs, physical examinations, infusion site assessments, changes in vital signs, clinical laboratory parameters and ECG throughout the study to the time points defined below:

Physical Exams:

Part A Screen, Days -1, 4, 100

Part B Screen, Days -1, 4, 22, 25, 43, 64, 67, 163

Vital signs:

Part A Screen, Days -1-4 (pre, 0, 1, 2, 4, 8, 24, 48, 72 hours), 8, 15, 22, 57, 100

Part B Screen, Days -1-4 (pre, 24, 48, 72 hours), 8, 15, 22, 23, 25, 29, 43, 50, 64-67 (pre, 24, 48, 72 hours), 71, 78, 99, 141, 163

Clinical labs

Part A Screen, Days 1-4, 8, 15, 22, 57, 100

Part B Screen, Days 1-4, 8, 15, 22, 23, 25, 29, 43, 50, 64, 65, 67, 71, 78, 99, 141, 163

ECG

Part A Screen, Days -1-2 (pre, 0, 1, 24 hours), 15, 22, 57, 100

Part B Screen, Days -1-2 (pre, 0, 1, 24 hours), 15, 22, 23, 29, 43, 50, 64-65 (pre, 0, 1, 24 hours), 78, 99, 141, 163

Previous primary outcome measures:

Safety and tolerability in Part A/B of the study measured by monitoring AE's, physical examinations, infusion site assessments, changes in vital signs, clinical laboratory parameters and ECG throughout the study to the time points defined below:

Physical Exams:

Part A Screen, Days -1, 4, 100

Part B Screen, Days -1, 4, 22, 25, 121

Vital signs:

Part A Screen, Days -1-4 (pre, 0, 1, 2, 4, 8, 24, 48, 72 hours), 8, 15, 22, 57, 100

Part B Screen, Days -1-4 (pre, 0, 1, 2, 4, 8, 24, 48, 72 hours), 8, 15, 22-25(pre, 0, 1, 2, 4, 8, 24, 48, 72 hours), 29, 36, 57, 85, 121

Clinical labs

Part A Screen, Days 1-4, 8, 15, 22, 57, 100

Part B Screen, Days 1-4, 8, 15, 22, 23, 25, 29, 36, 57, 85, 121

ECG

Part A Screen, Days -1-2 (pre, 0, 1, 24 hours), 15, 22, 57, 100

Part B Screen, Days -1-2 (pre, 0, 1, 24 hours), 15, 22-23 (pre, 0, 1, 24 hours), 36, 57, 85, 121

Secondary outcome measures

Current secondary outcome measures as of 20/11/2023:

1. Quantification of AX-202 in plasma will be performed followed by calculation of pharmacokinetic parameters, including but not limited to; C_{max}, t_{max}, AUC (AUC [0-∞], AUC [0-t]), and t_{1/2}, CL, V_{ss}. Dose and time dependency will be assessed for the pharmacokinetic parameters. In Part A, outcomes assessed on Days 1-4 (pre, 0, 1, 2, 4, 8, 24, 48, 72 hours), 8, 15, 22, 57, 100 and in Part B on Days 1-4 (pre, 0, 4, 8, 24, 48, 72 hours), 8, 15, 22, 43, 64-67 (pre, 0, 4, 8, 24, 48, 72 hours), 71, 78, 85, 99, 113, 141, 163
2. Antibodies to AX-202 in serum will be measured to evaluate immunogenicity in Part A on Days 1 (pre-dose), 22, 57, 100 and in Part B on Days 1 (pre-dose), 22 (pre-dose), 43 (pre-dose), 64 (pre-dose), 78, 141, 163

Previous secondary outcome measures:

1. Quantification of AX-202 in plasma will be performed followed by calculation of pharmacokinetic parameters, including but not limited to; C_{max}, t_{max}, AUC (AUC [0-∞], AUC [0-t]), and t_{1/2}, CL, V_{ss}. Dose and time dependency will be assessed for the pharmacokinetic parameters. In Part A, outcomes assessed on Days 1-4 (pre, 0, 1, 2, 4, 8, 24, 48, 72 hours), 8, 15, 22, 57, 100 and in Part B on Days 1-4 (pre, 0, 1, 2, 4, 8, 24, 48, 72 hours), 8, 15, 22-25 (pre, 0, 1, 2, 4, 8, 24, 48, 72 hours), 29, 36, 57, 85, 121
2. Antibodies to AX-202 in serum will be measured to evaluate immunogenicity in Part A on Days 1 (pre-dose), 22, 57, 100 and in Part B on Days 1 (pre-dose), 22 (pre-dose), 36, 85, 121

Overall study start date

30/11/2022

Completion date

31/07/2024

Eligibility

Key inclusion criteria

Part A

1. Subjects must have written informed consent obtained prior to any study-related procedures.
2. Subjects must be able to understand and comply with the requirements of the study, as judged by the Investigator.
3. Male and female subjects must be between 18-55 years inclusive, at the time of informed consent.
4. Female subjects must either be of non-childbearing potential or if of childbearing potential, must not be pregnant, breastfeeding or lactating and must use, with their partner, a condom with or without spermicide plus a highly effective birth control method from the time of informed consent and for 120 days following last administered dose.
5. Male subjects who are sexually active with a partner of childbearing potential must use, with their partner, a condom with or without spermicide plus an approved method of highly effective contraception from the time of informed consent and for 120 days following their last administered dose of IMP.
6. Subject must agree not to donate semen or ova/oocytes from consent and for 120 days after the last dose of IMP.
7. Subjects must have a Body Mass Index (BMI) ≥ 18 and ≤ 32 kg/m² and weight of at least 45kg at screening.
8. Subjects must be in good health as determined by medical history, physical examination, vital

signs, 12-lead ECG and clinical laboratory assessments at the time of screening, as judged by the Investigator.

Part B

1. Patients must have written informed consent obtained prior to any study-related procedures.
2. Patients must be able to understand and comply with the requirements of the study, as judged by the Investigator.
3. Male and female patients must be between 18-65 years inclusive, at the time of informed consent.
4. Patients must have a documented diagnosis of plaque psoriasis for ≥ 6 months prior to screening.
5. Physicians Global Assessment (PGA) of 2/3 i.e. mild or moderate plaque psoriasis at baseline.
6. Body Surface Area (BSA) $\geq 2\%$ and $\leq 10\%$ at baseline.
7. A minimum of 2 psoriatic lesions of at least 2 cm x 2 cm at baseline, with at least 1 plaque in a site suitable for biopsy and be willing and able to undergo skin biopsies.
8. Female patients must either be of non-childbearing potential or if of childbearing potential, must not be pregnant, breastfeeding or lactating and must use, with their partner, a condom with or without spermicide plus a highly effective birth control method from the time of informed consent and for 120 days following last administered dose.
9. Male patients who are sexually active with a partner of childbearing potential must use, with their partner, a condom with or without spermicide plus an approved method of highly effective contraception from the time of informed consent until 120 days after their last dose of IMP.
10. Patients must agree not to donate semen or ova/oocytes during the study and for 120 days after the last dose of IMP.
11. Patients must have a Body Mass Index (BMI) ≥ 18 and ≤ 36 kg/m² and weigh at least 45kg at screening.
12. Patients must be in good health as determined by medical history, physical examination, vital signs, 12-lead ECG and clinical laboratory assessments at the time of screening, as judged by the Investigator.

Participant type(s)

Mixed

Age group

Adult

Lower age limit

18 Years

Upper age limit

55 Years

Sex

Both

Target number of participants

58

Total final enrolment

58

Key exclusion criteria

Current exclusion criteria as of 03/03/2023:

Part A

1. History/presence of any clinically relevant acute or chronic medical or psychiatric condition that could interfere with the subject's safety or expose the subject to undue risk as judged by the Investigator.
2. Current or previous use of tobacco, nicotine products or e-cigarettes in the past 6 months.
3. Smoking history of > 5 pack years.
4. Positive urine cotinine test at screening or Day -1.

Part B

1. History/presence of any clinically relevant acute or chronic medical or psychiatric condition other than psoriasis that could interfere with the patient's safety or expose the patient to undue risk as judged by the Investigator.
2. A diagnosis of non-plaque psoriasis.
3. Plaque psoriasis restricted to the scalp, palms, soles and face.
4. Pustular, erythrodermic, inverse and guttate psoriasis.
5. Drug-induced psoriasis.
6. Diagnosis of psoriatic arthritis, uveitis, inflammatory bowel disease, or other immune-mediated conditions that are commonly associated with psoriasis for which a patient requires current systemic immunosuppressant medical treatment.
7. Presence of other skin conditions that could interfere with psoriasis evaluation or assessments.
8. Sunbed use in the 4 weeks prior to screening or planned use prior to the final study visit.
9. Any clinically significant infection requiring antimicrobial treatment in the 2 weeks prior to Day 1.

Parts A & B

1. After a min 10 minutes supine rest at the time of screening or on Day -1:
 - 1.1. Systolic blood pressure <90 or >140 mmHg, or
 - 1.2. Diastolic blood pressure <50 or >90 mmHg, or
 - 1.3. Pulse <40 or >90 bpm
2. Any clinically significant abnormalities in ECG at the time of screening or on Day -1 incl. prolonged QTcF (>450 ms for males; >470 ms for females) and cardiac arrhythmias, as judged by the Investigator.
3. Clinically significant abnormalities in renal function at screening including: eGFR <60 mL/min
4. Clinically significant abnormalities in liver function at screening including:
 - 4.1. Bilirubin >1.0 x ULN
 - 4.2. Aminotransferases >1.0 x ULN
 - 4.3. ALP >1.0 x ULN
5. Haemoglobin <130 g/l for males or <120 g/l for females at screening
6. Any clinically significant illness, medical/surgical procedure or trauma within 4 weeks of the first dose of IMP.
7. Malignancy within the past 5 years of screening with the exception of in situ removal of basal cell carcinoma or resected benign colonic polyps.
8. Any planned major surgery within the duration of the study or in the 30 days following study completion.
9. History of latent or active tuberculosis or a positive Quantiferon test at screening. Patients with an indeterminate result at screening will be allowed one retest; if not negative on retesting, the subject will be excluded.

10. Females who are pregnant, breastfeeding, lactating or plan to be pregnant during the study period or 120 days after.
11. Female subjects with a positive serum or urine pregnancy test at screening or on Day -1.
12. Positive serum HBsAg, HCVAb or HIV 1 and/or 2 antibodies at screening.
13. A Positive test for active COVID-19 prior to dosing on Day 1.
14. History of any drug and/or alcohol abuse in the 2 years prior to screening.
15. Regular alcohol consumption of >14 units per week.
16. Positive urine drugs of abuse test and/or alcohol breath test at screening or on Day -1 that cannot be accounted for by concomitant medication in the opinion of the Investigator.
17. Receiving any of the prohibited concomitant medications.
18. Plasma donation within one month of screening, blood donation (or corresponding blood loss) ≥ 400 ml during the three months prior to screening or planned donation during the study until 4 months after the final study visit.
19. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the Investigator or designee at screen.
20. Subject has dietary restrictions incompatible with the diet that can be provided by the study site, in the opinion of the Investigator or is unwilling to refrain from consuming restricted foods and beverages during the study.
21. Regular excessive caffeine consumption defined as a daily intake of >5 cups of caffeine-containing beverages.
22. Known history of intolerance or hypersensitivity to AX-202 or to any other component of the formulation.
23. Known history of intolerance to placebo or excipients.
24. Clinically significant serious adverse reaction, allergy or serious hypersensitivity, including to any drug or food, as judged by the Investigator.
25. Involvement in the planning and conduct of the study.
26. Participation in another clinical study with an experimental drug within 3 months (non-biologic), 6 months (biologic) or 5 half-lives, whichever is longer, before the administration of IMP.
27. Considered unsuitable for entry into the study in any other way at the discretion of the Investigator, e.g. Investigator considers the patient unlikely to comply with study procedures, restrictions and requirements.

Previous exclusion criteria:

Part A

1. History/presence of any clinically relevant acute or chronic medical or psychiatric condition that could interfere with the subject's safety or expose the subject to undue risk as judged by the Investigator.
2. Current or previous use of tobacco, nicotine products or e-cigarettes in the past 6 months.
3. Smoking history of > 5 pack years.
4. Positive urine cotinine test at screening or Day -1.

Part B

1. History/presence of any clinically relevant acute or chronic medical or psychiatric condition other than psoriasis that could interfere with the patient's safety or expose the patient to undue risk as judged by the Investigator.
2. A diagnosis of non-plaque psoriasis.
3. Plaque psoriasis restricted to the scalp, palms, soles and face.
4. Pustular, erythrodermic, inverse and guttate psoriasis.
5. Drug-induced psoriasis.
6. Diagnosis of psoriatic arthritis, uveitis, inflammatory bowel disease, or other immune-mediated conditions that are commonly associated with psoriasis for which a patient requires

current systemic immunosuppressant medical treatment.

7. Presence of other skin conditions that could interfere with psoriasis evaluation or assessments.

8. Sunbed use in the 4 weeks prior to screening or planned use prior to the final study visit.

9. Any clinically significant infection requiring antimicrobial treatment in the 2 weeks prior to Day 1.

Parts A & B

1. After a min 10 minutes supine rest at the time of screening or on Day -1:

1.1. Systolic blood pressure <90 or >150 mmHg, or

1.2. Diastolic blood pressure <50 or >95 mmHg, or

1.3. Pulse <40 or >90 bpm

2. Any clinically significant abnormalities in ECG at the time of screening or on Day -1 incl. prolonged QTcF (>450 ms for males; >470 ms for females) and cardiac arrhythmias, as judged by the Investigator.

3. Clinically significant abnormalities in renal function at screening including: eGFR <60 mL/min

4. Clinically significant abnormalities in liver function at screening including:

4.1. Bilirubin $>1.5 \times$ ULN

4.2. Aminotransferases $>1.5 \times$ ULN (Part A) or $> 2 \times$ ULN (Part B)

4.3 ALP $>1.5 \times$ ULN

5. Haemoglobin < 10 g/dL at screening.

6. Any clinically significant illness, medical/surgical procedure or trauma within 4 weeks of the first dose of IMP.

7. Malignancy within the past 5 years of screening with the exception of in situ removal of basal cell carcinoma or resected benign colonic polyps.

8. Any planned major surgery within the duration of the study or in the 30 days following study completion.

9. History of latent or active tuberculosis or a positive Quantiferon test at screening. Patients with an indeterminate result at screening will be allowed one retest; if not negative on retesting, the subject will be excluded.

10. Females who are pregnant, breastfeeding, lactating or plan to be pregnant during the study period or 120 days after.

11. Female subjects with a positive serum or urine pregnancy test at screening or on Day -1.

12. Positive serum HBsAg, HCVAb or HIV 1 and/or 2 antibodies at screening.

13. A Positive test for active COVID-19 prior to dosing on Day 1.

14. History of any drug and/or alcohol abuse in the 2 years prior to screening.

15. Regular alcohol consumption of >14 units per week.

16. Positive urine drugs of abuse test and/or alcohol breath test at screening or on Day -1 that cannot be accounted for by concomitant medication in the opinion of the Investigator.

17. Receiving any of the prohibited concomitant medications.

18. Plasma donation within one month of screening, blood donation (or corresponding blood loss) ≥ 400 ml during the three months prior to screening or planned donation during the study until 4 months after the final study visit.

19. Subjects who do not have suitable veins for multiple venepunctures/cannulation as assessed by the Investigator or designee at screen.

20. Subject has dietary restrictions incompatible with the diet that can be provided by the study site, in the opinion of the Investigator or is unwilling to refrain from consuming restricted foods and beverages during the study.

21. Regular excessive caffeine consumption defined as a daily intake of >5 cups of caffeine-containing beverages.

22. Known history of intolerance or hypersensitivity to AX-202 or to any other component of the

formulation.

23. Known history of intolerance to placebo or excipients.

24. Clinically significant serious adverse reaction, allergy or serious hypersensitivity, including to any drug or food, as judged by the Investigator.

25. Involvement in the planning and conduct of the study.

26. Participation in another clinical study with an experimental drug within 3 months (non-biologic), 6 months (biologic) or 5 half-lives, whichever is longer, before the administration of IMP.

27. Considered unsuitable for entry into the study in any other way at the discretion of the Investigator, e.g. Investigator considers the patient unlikely to comply with study procedures, restrictions and requirements.

Date of first enrolment

17/04/2023

Date of final enrolment

24/01/2024

Locations

Countries of recruitment

England

United Kingdom

Study participating centre

Medical Evaluations Unit Ltd

The Langley Building

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Sponsor information

Organisation

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Sponsor type

Industry

Website

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Funder(s)

Funder type

Industry

Funder Name

Arxx Therapeutics

Results and Publications

Publication and dissemination plan

1. Peer-reviewed scientific journals
2. Internal report
3. Conference presentation
4. Submission to regulatory authorities
5. Study results will be disseminated in peer-reviewed scientific journals, internal reports, and by submission to regulatory authorities; future arrangements for sharing data will be decided by the sponsor but only anonymised data would be shared.

Intention to publish date

21/03/2025

Individual participant data (IPD) sharing plan

The datasets generated and/or analysed during the current study will be available upon request from Arxx Therapeutics, contact details can be found at the following website: <https://arxxtx.com/>.

Deidentified individual participant data will be available after the study has been reported, approximately 12 months after the study's concluded. These data will be available for 36 months. These data will be shared with Investigators whose proposed use of the data has been approved by Arxx Therapeutics. Proposals may be submitted up to 36 months following reporting of the study.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			26/07/2023	No	No