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A phase 1 trial in healthy adults and adults with increased inherited risk of developing blood clots

Submission date
08/11/2025

Recruitment status
Recruiting

Registration date
19/01/2026

Overall study status
Ongoing

Last Edited
02/02/2026

Condition category
Haematological Disorders

[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
We are conducting this study to learn more about an investigational drug called CITY-FXI. This is not yet approved for use by drug regulatory agencies and can only be given in clinical studies. This clinical study will be the first time CITY-FXI will be given to humans. CITY-FXI is being investigated in this study to see if it is safe, tolerable, and how it affects the body.
CITY-FXI is being developed to help prevent the occurrence of thromboembolic diseases (formation of harmful blood clots). A blood clot is when blood becomes thick and sticky and forms a lump that can block blood flow. These blood clots can sometimes be life-threatening, for example, when formed in the legs (known as deep vein thrombosis) or lungs (known as pulmonary embolism).
Current medicines for thromboembolic diseases are effective but may increase the risk of serious bleeding, so there is a need for safer medicines that prevent clots without causing excess bleeding.
CITY-FXI is an investigational drug that uses a type of molecule called small interfering ribonucleic acid (siRNA). It is designed to reduce the amount of a specific protein called Factor XI (FXI). By lowering FXI, CITY-FXI could help prevent harmful blood clots with a lower bleeding risk than with currently available drugs. It is not yet known whether CITY-FXI will have this effect.

Who can participate?
Healthy volunteers aged 18 – 45 years old, and adults aged 18 – 60 years old with Factor V Leiden or Prothrombin G20210A mutation

What does the study involve?
This study will be comprised of two parts (Part A and Part B).
Part A will include healthy participants who will be randomly assigned to receive the investigational drug (CITY-FXI) or placebo (placebo is a product that looks like and is administered in the same way as the investigational drug but does not contain the active ingredient).
Part B will include participants who have been diagnosed with Factor V Leiden (FVL) or Prothrombin G20210A mutations (variations in your genes that increase the risk of blood clot

formation). Participants will be randomly assigned to receive the investigational drug (CITY-FXI) or placebo.
The planned duration of study participation could be approximately 13 months, depending on how each participant's body responds to CITY-FXI from screening to the last visit.

What are the possible benefits and risks of participating?
There is no medical benefit to the participants of Part A of the study, as they are healthy volunteers. However, they will receive free regular health checks by participating in this study. It is hoped that the information collected in this study will help patients at risk of or with thromboembolic diseases (formation of harmful blood clots) in the future.
Participants in Part B (adults with factor V Leiden or prothrombin G20210A mutation) may or may not have a temporary reduction in thrombotic (formation of blood clots) risk. The data we get from this study will help us understand how safe the study drug is in preventing the formation of harmful blood clots. Participants will also receive free regular health checks in this study.
There are potential risks related to the investigational drug and procedures, such as bleeding, allergic reactions, and soreness or pain from the blood samples or the study drug or placebo injection. It is currently unknown if CITY-FXI will have any effects on pregnancy, breastfeeding, or unborn foetus. As this drug has not been given to humans before, the understanding of risks is based on earlier studies that were mainly conducted in animals. The Study Doctor understands these risks and can provide guidance on how these risks relate to participants when choosing to participate in the study.
If a participant gets new symptoms of an illness or become unwell during the study, they will be examined by a Study Doctor. This may involve additional safety tests (including urine and blood tests, vital signs, and electrocardiograms). The Study Doctor will perform a clinical assessment and ensure the condition is managed appropriately. The risks and benefits of any additional treatment will be explained to participants.

Where is the study run from?
Richmond Pharmacology (London, UK)

When is the study starting and how long is it expected to run for?
January 2026 through October 2027

Who is funding the study?
City Therapeutics, a biopharmaceutical company based in Massachusetts in the United States of America (USA)

Who is the main contact?
City Therapeutics, clinicaltrials@citytx.com

Contact information

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Scientific

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Integrated Research Application System (IRAS)
1013145

Protocol serial number
FXI-1101

Study information

Scientific Title
A phase 1, randomised, double-blind, placebo-controlled single ascending dose study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of CITY-FXI, a FXI targeting siRNA, administered subcutaneously in healthy adults and adults with factor V Leiden or prothrombin G20210A mutation

Study objectives
Primary objective:
To evaluate the safety and tolerability of a single dose of investigational drug (CITY-FXI) in healthy adults and adults that have genetic conditions of Factor V Leiden or prothrombin G20210A mutation

Secondary objectives:
1. To characterise how the investigational drug (CITY-FXI) affects the body (known as pharmacodynamics).
2. To characterise how the investigational drug (CITY-FXI) moves throughout the body (known as pharmacokinetics)

Ethics approval required
Ethics approval required

Ethics approval(s)
approved 23/12/2025, - (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; -; -), ref: 25/LO/0803

Study design
Interventional double blind randomized parallel group placebo controlled trial

Primary study design
Interventional

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Factor V Leiden or prothrombin G20210A mutation in healthy adults and adults

Interventions
The study will be conducted in two parts:
Part A: Single Ascending Dose in Healthy Adults
Part B: Single Ascending Dose in Adults with Factor V Leiden (FVL) or Prothrombin G20210A Mutation

Part A will include healthy participants who will be randomly assigned to receive the investigational drug (CITY-FXI) or placebo.

Part B will include participants who have been diagnosed with Factor V Leiden (FVL) or Prothrombin G20210A mutations. Participants will be randomly assigned to receive the investigational drug (CITY-FXI) or placebo.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
CITY-FXI

Primary outcome(s)
Incidence, severity, and relationship of treatment emergent adverse events (TEAEs) measured using data collected from electronic Case Report Forms (eCRF) throughout and up to the end of the study.

Key secondary outcome(s))
1. Change from baseline in levels of plasma Factor XI (FXI) antigen, FXI activity, and activated partial thromboplastin time (aPTT) measured using validated FXI antigen, FXI activity, and aPTT assays, respectively, on Days -1, 1, 3, 8, 15, 22, 29, 36, 43, 50, 57, 85, 113, 141, 180, up to two additional follow-up visits on Day 270 and 360, and at the end of the study
2. Plasma and urine single dose PK parameters of CITY-FXI measured using validated LC/MS drug analysis methods on study Days 1, 2, and 3

Completion date
31/10/2026

Eligibility

Key inclusion criteria
1. Males and women of non-childbearing potential (WONCBP) aged 18 to 45 years (Part A only)
2. Male and female participants aged 18 to 60 years (Part B only)
3. Body Mass Index (BMI) between 18 and 25 kg/m2 (inclusive) and a minimum weight of 50 kg
4. Ability and willingness to comply fully with all study procedures and lifestyle considerations
5. Confirmed diagnosis of FVL or prothrombin G20210A mutation via genetic testing (Part B only)
6. Women of childbearing potential (WOCBP) must agree to use acceptable highly effective contraceptive methods (Part B only)

Participant type(s)
All

Healthy volunteers allowed
Yes

Age group

Adult

Lower age limit
18 years

Upper age limit
60 years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Any clinically significant systemic disease or disorder, including but not limited to cardiovascular, hepatic, or oncological conditions
2. History or evidence of any bleeding disorders
3. History of clinically significant spontaneous bleeding
4. Prior treatment with an investigational agent
5. Confirmed diagnosis of homozygous mutations, or combined thrombophilic defects of (Part B only)

Date of first enrolment
22/01/2026

Date of final enrolment
01/08/2026

Locations

Countries of recruitment
United Kingdom

Study participating centre
Richmond Pharmacology Limited
1a Newcomen Street, London Bridge
London
England
SE1 1YR

Sponsor information

Organisation
City Therapeutics Inc.

Funder(s)

Funder type

Funder Name
City Therapeutics, Inc

Results and Publications

Individual participant data (IPD) sharing plan

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