ISRCTN45090913 https://doi.org/10.1186/ISRCTN45090913

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

Submission date
08/11/2025

Recruitment status
Recruiting

Registration date
19/01/2026

Overall study status
Ongoing

Last Edited
06/11/2026

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 (Part A), and adults aged 18 – 60 years old (Part B) with Factor V Leiden or prothrombin G20210A mutation. In Part C, adults aged 18-65 years with Factor V Leiden or prothrombin G20210A mutation and/or a history of provoked VTE.

What does the study involve?
This study will be comprised of three parts (Part A, Part B and Part C).
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.
Part C will include participants who have been diagnosed with Factor V Leiden (FVL), or prothrombin G20210A mutations and/or a history of provoked VTE. 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 (Parts A and B) or 16 months (Part C), 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) and in Part C (adults with Factor V Leiden or prothrombin G20210A mutation and/or a history of provoked VTE) 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 becomes 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 March 2028

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

Type(s)
Principal investigator, Scientific

Contact name
Dr Ulrike Lorch

Contact details
1A Newcomen Street, London Bridge
London
United Kingdom
SE1 1YR
+44 20 7042 5800
u.lorch@richmondpharmacology.com

Type(s)
Public

Contact name
None - City Therapeutics

Contact details
399 Binney St.
Cambridge
United States of America
MA 02142
+1-857-219-5440
clinicaltrials@citytx.com

Additional identifiers

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 and multiple dose study to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of CITY-FXI, a FXI targeting siRNA, administered subcutaneously in healthy adults, adults with Factor V Leiden (FVL) or prothrombin G20210A mutation, and adults with a history of provoked venous thromboembolism (VTE)

Study objectives
Current study objectives as of 29/09/2026:
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, and of a multiple dose regimen of CITY-FXI in adults with FVL or prothrombin G20210A mutation and/or a history of provoked venous thromboembolism (VTE)

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)

Previous 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, London – London Bridge Research Ethics Committee (REC) (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; -; londonbridge.rec@hra.nhs.uk), ref: 25/LO/0803

Primary study design
Interventional

Study design
Interventional double-blind randomized sequential-group placebo-controlled trial

Study type(s)
Efficacy, Safety

Health condition(s) or problem(s) studied
Adults with Factor V Leiden or prothrombin G20210A mutation, and/or a history of provoked venous thromboembolism

Interventions
Current interventions as of 29/09/2026:
The study will be conducted in three 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 C: Multiple dose in Adults with FVL or Prothrombin G20210A Mutation and/or a History of Provoked Venous Thromboembolism (VTE)

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.

Part C will include participants who have been diagnosed with Factor V Leiden (FVL) or prothrombin G20210A mutations and/or a history of provoked VTE. Participants will be randomly assigned to receive the investigational drug (CITY-FXI) or placebo.

Previous 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)
Current secondary outcomes as of 06/10/2026:
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 (Parts A and B); Days 1, 8, 15, 29, 57, 85, 91, 98, 105, 119, 147, 203, 231, 270, up to two additional follow-up visits on Day 360 and 450, and at the end of the study (Part C).
2. Plasma and urine single dose PK parameters of CITY-FXI (Parts A and B) and plasma PK parameters of CITY-FXI (Part C) measured using validated LC/MS drug analysis methods on study Days 1, 2, and 3 (Parts A and B), and Days 1, 2, 91, and 92 (Part C).

Previous secondary outcomes:
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
06/03/2028

Eligibility

Key inclusion criteria
Current key inclusion criteria as of 06/11/2026:

1. Males and women of non-childbearing potential (WONCBP) aged 18 to 45 years (inclusive) (Part A only)
2. Male and female participants aged 18 to 60 years (inclusive) (Part B only), and aged 18 to 65 years (inclusive) (Part C only)
3. Body Mass Index (BMI) between 18 and 25 kg/m² (inclusive, for Parts A and B only) and 18 and 35 kg/m² (inclusive, for Part C only) and a minimum weight of 50 kg (Parts A, B, and C)
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 (Parts B and C)
7. History of provoked venous thromboembolism (VTE) within the last 10 years and/or confirmed diagnosis of heterozygosity for FVL or prothrombin G20210A mutation via genetic testing (Part C only)

———

Previous key inclusion criteria as of 29/09/2026:

1. Males and women of non-childbearing potential (WONCBP) aged 18 to 45 years (inclusive) (Part A only)
2. Male and female participants aged 18 to 60 years (inclusive) (Part B only), and aged 18 to 65 years (inclusive) (Part C only)
3. Body Mass Index (BMI) between 18 and 25 kg/m2 (inclusive, for Part B only) and 18 and 35 kg /m2 (inclusive, for Part C only) and a minimum weight of 50 kg (Parts A, B, and C)
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 (Parts B and C)
7. History of provoked venous thromboembolism (VTE) within the last 10 years and/or confirmed diagnosis of heterozygosity for FVL or prothrombin G20210A mutation via genetic testing (Part C only)

———

Previous 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
Mixed

Lower age limit
18 Years

Upper age limit
65 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
31/01/2027

Locations

Countries of recruitment
United Kingdom

England

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