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A study to investigate the safety, tolerability, and concentration in the blood of different dose strengths of ENX-102 in healthy volunteers

Submission date
12/03/2025

Recruitment status
No longer recruiting

Registration date
28/04/2025

Overall study status
Completed

Last Edited
28/04/2025

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[X] Results
[ ] Individual participant data

Plain English summary of protocol

Background and study aims
The purpose of this study is to investigate the study drug ENX-102.

The main objectives of this study are as follows:
- To determine the safety and tolerability (degree to which side effects of a drug can be tolerated) of ENX-102 when it is administered as a single dose at different dose strengths on one occasion.
- To investigate the amount of ENX-102 in the blood after a single oral dose, how the amount of ENX-102 in the blood changes over time, and whether there are differences in the amount of ENX-102 in the blood when ENX-102 is given at different dose strengths.

Who can participate?
A total of up to 56 participants are needed to fully complete this study. Participants must be healthy adult females or males aged between 18 and 55.

What does the study involve?
The study is a double-blind, randomised, placebo-controlled single ascending dose (SAD) study. The study will be split into 7 different groups with 8 participants in each group; each group will evaluate a different dose strength of ENX-102 starting at the lowest dose of 0.5 milligrams (mg) in Group 1. The doses in the study will range from 0.5 mg up to 10 mg in Group 7.

The study will consist of a screening visit (between 28 and 2 days prior to first dose), 1 treatment period (consisting of up to 7 days with 6 overnight stays) and a post-study follow-up visit 7 days after discharge from the clinical unit.

In this study, participants will either be given ENX-102 or a placebo (which contains no active drug). Both ENX-102 and the placebo will be administered in the form of an oral capsule or multiple capsules (dependent on dose strength). 6 participants in each group will receive active ENX-102 and the remaining 2 participants will receive the placebo. Blood samples will be taken at set time points throughout the study in order to measure the amount of ENX-102 in the blood.

We will compare the results from each of the groups to determine if there are any significant differences in the safety of ENX-102, the amount of ENX-102 in the blood, how this changes over time and whether there are any differences between the different dose strengths.

What are the possible benefits and risks of participating?
Taking part in the study is not expected to provide any direct medical benefit. However, the information we get from this study may help improve the treatment of diseases including CNS conditions like epilepsy, spasticity, and anxiety.

Possible risks include the following:
Blood Sampling: The procedure for blood collection either by direct venepuncture or indwelling cannula may cause mild pain and bruising at the collection site. Placement of an indwelling catheter is proposed in order to minimise these effects for rapid PK sampling. Very rarely, a blockage of a vein or a small nerve injury can occur, resulting in numbness and pain. If this occurs, it will resolve with time.

Blood pressure and pulse rate: The participants blood pressure and pulse will be measured using an inflatable cuff which will be placed on the arm. They may experience mild discomfort in the arm whilst the cuff is inflated.

ECG: Small sticky pads will be placed on the participants' upper body before the ECG and an ECG machine will measure the electrical activity of the participants' heart. Before the pads are applied, the skin needs to be cleaned. Trained staff may need to shave/clip small patches of the participants hair in these areas. Like Elastoplast® these sticky pads may be uncomfortable to remove.

COVID-19 Risks: Participants should also be aware of the risks of exposure to COVID-19. When participants attend the clinical unit at each visit, they may be asked to complete a self-declaration form and temperature check to confirm that they are not showing any early signs of COVID-19 infection and that they have not had any contact with individuals who are currently self-isolating or have tested positive (dependent on risk mitigation measures employed at the clinical unit at the time of clinical conduct).

Participants may also be required to have a negative COVID-19 test prior to admission to the clinical unit for any overnight stays as defined within the study protocol. This procedure may cause some mild discomfort in the nose or throat when the swab is being taken but this should resolve after the procedure has been completed.

Additionally, at the clinical unit, participants may be asked to wear a facemask during procedures where clinical staff cannot maintain a 2 m distance. It is noted that if participants have a medical exemption from wearing a face mask, they will not be required to do so. In any circumstance, to prevent risk of transmission between staff and participants, all staff will be wearing appropriate personal protective equipment i.e., face masks, face shields etc during the course of the study.

Harm to the unborn child:
For men:
For male participants (of childbearing potential), they will be required to use a highly effective or 2 effective methods of contraception (including a condom) with their partner (of childbearing potential) during the trial from Day -1 and for at least 3 months following the last dose of ENX-102.

For Women:
For female participants, they should not take part in this study if they are pregnant, breast-feeding or intended to become pregnant 3 months following the last dose of ENX-102. If a woman who might become pregnant participates, she will be asked to have a pregnancy test (blood) before taking part and at set time points throughout the study. For female participants (of childbearing potential), they will be required to use a highly effective or 2 effective methods of contraception (including a condom) with their partner (of childbearing potential) during the trial from Day -1 and for at least 3 months following the last dose of ENX-102.

Throughout the study the health of the participants will be regularly monitored and appropriate treatment for any medical condition will be provided if required. All doctors employed by Simbec-Orion are trained and certified in Advanced Life Support Procedures in order to deal with a medical emergency. Nurses and other clinical staff are also trained in emergency procedures. Simbec-Orion also has an agreement with Prince Charles Hospital for referral of participants if required following a medical emergency.

Where is the study run from?
The study will be conducted at Simbec-Orion Clinical Pharmacology Unit, an MHRA Phase 1 accredited CRO based in South Wales.

When is the study starting and how long is it expected to run for?
November 2020 to November 2021.

Who is funding the study?
This study is funded and sponsored by a pharmaceutical company called Engrail Therapeutics Inc., based and headquartered in the United States.

Who is the main contact?
Eve Taylor, Senior Vice President, Clinical Development, Engrail Therapeutics inc. Eve. Taylor@engrail.com

Contact information

Type(s)
Public, Scientific

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-000406-24

Integrated Research Application System (IRAS)
293950

Protocol serial number
ENX-102-001

Study information

Scientific Title
A single ascending dose study to evaluate safety, tolerability, and pharmacokinetics of ENX-102 in healthy volunteers

Acronym
ENX-102-001

Study objectives
The primary objective of this study is:
- To evaluate the safety and tolerability of ENX-102 after single administration of increasing doses in comparison with placebo.

The secondary objective of this study is:
- To evaluate the pharmacokinetics (PK) of ENX-102 after single administration of increasing doses of ENX-102.

Ethics approval required
Ethics approval required

Ethics approval(s)
1. Approved 12/03/2021, Wales Research Ethics Committee 2 (Health and Care Research Wales, Castlebridge 4. 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 2920 230457; Wales.REC2@wales.nhs.uk), ref: 21.WA.0065

2. Approved 26/03/2021, MHRA (10 South Colonnade, Canary Wharf, London, E14 4PU, United Kingdom; +44 (0) 20 3080 6000; info@mhra.gov.uk), ref: CTA 54507/0001/001-0001

Primary study design
Interventional

Study design
Randomized double-blind placebo-controlled single ascending dose study

Study type(s)
Other, Safety

Health condition(s) or problem(s) studied
Epilepsy, anxiety, spasticity or other CNS disorders

Interventions
This is a randomised, double-blind, placebo-controlled, SAD study in healthy volunteers. Each subject will be screened up to 28 days prior to Day 1. Eligible subjects will be admitted to the Clinical Unit 1 day before dosing (Day –1) and remain confined for at least 5 days (Day 4).

On Day –1, eligibility will be confirmed and baseline physical examination, vital signs, 12-lead electrocardiogram (ECG), and clinical laboratory assessments including COVID-19 polymerase chain reaction (PCR) antigen testing (if required) will be performed. An additional optional blood sample may be collected for potential genotyping. On Day 1, subjects will be randomly assigned to receive either a single dose of ENX-102 (n=6) or placebo (n=2). Pre-dose vital signs, 12-lead ECG, and plasma PK samples will be collected.

After study drug administration, serial PK plasma samples will be collected through 72 hours after dosing and up to 120 hours after dosing if the in-house treatment period of the study is extended. Safety assessments will be conducted through the End-of-Study Visit (7 ± 1 days after discharge). Within each cohort, 2 sentinel subjects (i.e., 1 subject on active and 1 on placebo) will be dosed and followed for at least 24 hours before the remainder of the cohort is dosed. The following doses of ENX-102 are planned and will be tested in sequential cohorts: 0.5 mg, 1 mg, 1.5 mg, 2 mg, 3 mg, 5 mg, and up to 10 mg.

The study end is defined as last subject last visit.

The study will take place in the Clinical Unit of Simbec-Orion Clinical Pharmacology (Clinical Unit) under full medical and nursing supervision.

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
ENX-102 Oral Capsules

Primary outcome(s)
1. Adverse Events (AEs) including serious AEs (SAEs) and treatment emergent AEs (TEAEs) will be recorded from the point of informed consent up to final post-study follow up visit.
2. A full Physical examination (including weight measurement) at screening, Day -1 and end of study. A Symptom-directed physical examination will be performed on Day 1 and last day of

treatment period (Day 4, Day 5 or Day 6).
3. Laboratory safety (biochemistry, haematology, coagulation and urinalysis) at screening, Day -1, last day of treatment period (Day 4, 5 or 6) & End of Study.
4. Vital signs (systolic/diastolic blood pressure, pulse, oral body temperature and respiratory rate) at screening, Day -1, Day 1 (pre-dose and 0.5, 1, 2, 4, 6, 8 and 12 hr post dose), Day 2 (24 hr & 36 hr post-dose), Day 3 (48 hr post-dose), Day 4 (72 hr post-dose), Day 5 (96 hr post-dose), Day 6 (120 hr post-dose) and End-of Study Visit.
5. 12-lead ECG (heart rate, PR interval, QRS width, QT interval and QTcF interval) at screening, Day -1, Day 1 (pre-dose and 0.5, 1, 2, 4, 6, 8 and 12 hr post dose), Day 2 (24 hr & 36 hr post-dose), Day 3 (48 hr post-dose), Day 4 (72 hr post-dose), Day 5 (96 hr post-dose), Day 6 (120 hr post-dose) and End-of Study Visit.

Key secondary outcome(s)
Pharmacokinetic/pharmacodynamic parameters derived from analysis of plasma for concentrations of ENX-102.
PK Endpoints are defined as follows:
- Cmax - maximum observed concentration.
- Tmax – Time taken to reach Cmax
- AUC0-24 - area under the concentration-time curve from 0 to 24 hours.
- AUC 0-t - the area under the concentration-time curve from dosing (time 0) to time t.
- AUC0-Inf - Area under the plasma concentration time curve extrapolated to infinity.
- t½ - half-life.

Plasma samples for PK evaluation of ENX-102 will be taken at the following time points:
Day 1: prior to dose, 15 mins, 30 mins, 45 mins, 1 hr, 1 hr 30 mins, 2 hr, 4 hr, 6 hr, 8 hr & 12 hr following dose
Day 2: 24 hr & 36 hr post-dose
Day 3: 48 hr post-dose
Day 4: 72 hr post-dose
Day 5: 96 hr post-dose
Day 6: 120 hr post-dose
End of Study

Completion date
23/11/2021

Eligibility

Key inclusion criteria
1. Participants who are able to provide informed consent indicating they understand the purpose of, and procedures required, for the study and are willing to participate.
2. Healthy males/females aged 18 to 55 years at Screening.
3. Female subjects:
a. Of non-childbearing potential, defined as either permanently sterilized (at least 4 months after surgical sterilization including bilateral salpingectomy, tubal ligation, or oophorectomy with or without hysterectomy) or post-menopausal (defined as amenorrhea for 12 consecutive months and documented plasma follicle-stimulating hormone [FSH] level >40 IU/mL; in the event a subject's menopausal status has been clearly established and yet serum FSH levels are not consistent with a post-menopausal status, determination of the subject’s eligibility to be included in the study will be at the Investigator’s discretion following consultation with the Sponsor); OR

b. Of childbearing potential willing to use both a highly effective method of contraception and a condom with any partner or remain abstinent if abstaining from sexual intercourse is in line with the preferred and usual lifestyle of the participant, from the Day –1 until 3 months after Day 1; AND
c. Of childbearing potential or non-childbearing potential with a negative pregnancy test at Screening and Day –1.
4. Male subjects who, if fertile (defined as post-pubertal and not permanently sterile by orchidectomy or vasectomy), are willing to use both a highly effective method of contraception and a condom with any partner of childbearing potential or remain abstinent if abstaining from sexual intercourse is in line with the preferred and usual lifestyle of the subject, from Day –1 until 3 months after Day 1.
5. Body mass index of 18 to 35 kg/m².
6. Willing and able to comply with all study-related restrictions.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
55 Years

Sex
All

Total final enrolment
56

Key exclusion criteria
1. Clinically significant abnormality within 2 years of Screening that in the Investigator's opinion may place the subject at risk or interfere with study outcome variables; this includes, but is not limited to, history of or current cardiac, renal, neurologic, gastrointestinal, pulmonary, endocrinologic, hematologic, or immunologic disease or history of malignancy.
2. History of convulsions (other than benign febrile convulsions of childhood) including epilepsy, or personal history of significant cerebral trauma or CNS infections (e.g.,meningitis).
3. History or evidence of any medical condition potentially altering the absorption, metabolism, or elimination of drugs; this includes a surgical history of the gastrointestinal tract affecting gastric motility or altering the gastrointestinal tract.
4. Any of the following cardiovascular conditions at Screening or Day –1:
a. History or evidence of any of the following:
i. Myocardial infarction
ii. Cardiac valvulopathy
iii. Cardiac surgery revascularization (coronary artery bypass grafting or percutaneous transluminal coronary angioplasty)

iv. Unstable angina
v. Cerebrovascular accident or stroke or transient ischemic attack
vi. Pacemaker
vii. Atrial fibrillation, flutter, or non-sustained or sustained ventricular tachycardia
viii. Pulmonary arterial hypertension
ix. Sick sinus syndrome, second- or third-degree atrioventricular block
x. Uncontrolled hypertension
xi. Congestive heart failure
xii. Family history of sudden death or personal history of long QT syndrome
xiii. Hypokalemia
xiv. Unexplained syncope or syncope within the last 3 years regardless of etiology
b. Electrographically and clinically significant abnormalities, as judged by the Investigator, that might interfere with ECG analysis at Screening and on Day –1, including evidence of a previous myocardial infarction, significant left ventricular hypertrophy, flat T-waves (particularly in the inferior leads), or more than minor non-specific ST-T wave changes.
c. Rhythm other than sinus rhythm
d. Heart rate <40 beats per minute (bpm) or >100 bpm
e. Systolic blood pressure >140 mm Hg; mean diastolic blood pressure >90 mm Hg
f. QT interval corrected using Fridericia's formula (QTcF) >450 msec in males or >470 msec in females
g. QRS interval ≥120 msec
h. PR interval >220 msec
5. Self-reported or documented medical history of having experienced suicidal ideation within 30 days prior to Screening, any suicidal behaviour within 2 years prior to Screening, and/or the Investigator assesses the subject to be a safety risk to him/herself or others.
6. Diagnosis of any sleep disorder in the last 6 months or current complaints of sleep disturbance or daytime symptoms attributable to unsatisfactory sleep or shift worker whose routine work hours overlap with the typical sleep period.
7. History or evidence of moderate or severe substance use disorder as defined by the Diagnostic and Statistical Manual of Mental Disorders (5th Edition) or intake of more than14 units of alcohol weekly.
8. Is a smoker or has used nicotine or nicotine-containing products within 90 days of Screening and/or will not agree to abstain from nicotine use during the study from Screening through to the end of study visit; this includes cigarettes, e-cigarettes, and nicotine replacement or nicotine-containing products.
9. Has a positive qualitative drug or alcohol test at Screening or Day -1.
10. Has ingested any concomitant medication (excluding hormonal birth control and ibuprofen [maximum daily dose of 1200 mg] and acetaminophen [maximum daily dose of 4000 mg]) within 5 half-lives or 30 days (whichever is longer) prior to Day 1.
11. Has received any known hepatic- or renal-clearance-altering agents (e.g., erythromycin, cimetidine, barbiturates, phenothiazines) within 90 days prior to Day 1.
12. Has clinically significant abnormal findings in serum chemistry, coagulation, haematology, or urinalysis results at Screening or Day –1.
13. Has elevated (>1.5 × upper limit of normal [ULN]) liver enzymes (alanine aminotransferase and/or aspartate aminotransferase) and/or bilirubin.
14. Has clinically significant abnormal findings in vital sign assessments, at Screening or Day –1.
15. Is pregnant (i.e., positive pregnancy test), breastfeeding, or lactating.
16. Clinically significant history of previous allergy/sensitivity to the study drug, any drugs in the same or similar class, or any of the excipients contained within the study drug.
17. Participated in a New Chemical Entity clinical study within the previous 3 months or five half-lives, whichever is longer, or a marketed drug clinical study within the 30 days or five half-lives, whichever is longer, prior to Day 1. Washout period between studies is defined as the period of

time elapsed between the last dose of the previous study and the first dose of the next study.
18. History of hepatitis B or hepatitis C or demonstration of hepatitis B surface antigen or hepatitis C antibody at Screening.
19. History of HIV infection or demonstration of HIV antibodies at Screening.
20. History of any confirmed significant allergic reactions (urticaria or anaphylaxis) against any drug or any multiple drug allergies (non-active hay fever is acceptable).
21. Donated >500 mL blood or plasma within 30 days prior to Day 1 or has lost >1200 mL of blood within 4 months prior to Day 1.
22. Any other condition that, in the Investigator's opinion, might indicate that the subject is unsuitable for the study (e.g., information provided by the general practitioner, if available).
23. Subject is unable or unwilling to comply with the requirements of the study or, in the opinion of the Investigator, should not participate in the study.
24. Positive COVID-19 PCR test prior to/on admission (if required).

Date of first enrolment
08/04/2021

Date of final enrolment
20/10/2021

Locations

Countries of recruitment
United Kingdom

Wales

Study participating centre
Simbec Research Limited
Simbec House Merthyr Tydfil Industrial Park
Merthyr Tydfil Industrial Park
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CF48 4DR

Sponsor information

Organisation
Engrail Therapeutics, Inc.

Funder(s)

Funder type
Industry

Funder Name
Engrail Therapeutics Inc.

Results and Publications

Individual participant data (IPD) sharing plan
The study data will be shared with relevant research groups and external stakeholders collaborating with the study sponsor to support the future development of the IMP within the boundaries of strict confidentiality agreements.

The data sharing plans for the current study are unknown and will be made available at a later date.

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?
Basic results	version 1.0	28/04/2025	28/04/2025	No	No