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Study to investigate the effects and safety of ENX-102 in healthy volunteers.

Submission date
06/09/2022

Recruitment status
No longer recruiting

Registration date
01/11/2022

Overall study status
Completed

Last Edited
01/11/2022

Condition category
Nervous System Diseases

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
This Phase 1 study is looking at how this drug works in the human body and the safety of the drug ENX-102 in healthy volunteers. This trial does not test if the drug helps to improve health. This trial will investigate the safety, tolerability, how the drug affects and interacts with the body, and how the drug moves through the body.

Who can participate?
Healthy male and female volunteers aged 18 to 55 years who are deemed eligible for participation by in and exclusion criteria.

What does the study involve?
Subjects will be screened within 28 days of Day 1. Eligible subjects will be admitted to the inpatient unit on Day –1 and subjects are expected to remain confined for 14 days. The 14-day inpatient period includes a 1-day Baseline Period (Day -1), a 12-day Treatment Period (Day 1 through Day 12), and a 1-day Follow-up Period (Day 13). Discharge is planned for Day 13. Subjects will return to the clinic for follow-up visits on Day 19, and Day 26.

What are the possible benefits and risks of participating?
No medical benefit can be expected from this study for the participants. ENX-102 has been used in a clinical trial before and was well tolerated, with the most common side effects being fatigue, dizziness and light-headedness.

Where is the study run from?
Centre for Human Drug Research (Netherlands)

When is the study starting and how long is it expected to run for?
March 2021 to September 2022

Who is funding the study?
Engrail Therapeutics, Inc. (USA)

Who is the main contact?
P. Nettesheim (Project Leader), pnettesheim@chdr.nl

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-004112-25

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
CHDR2057

Study information

Scientific Title
A multiple ascending dose study to evaluate safety, tolerability, pharmacokinetics, and pharmacodynamics of ENX-102 at plasma steady state in healthy volunteers

Acronym
ENX-102

Study objectives
ENX102 shows pharmacokinetic and pharmacodynamic preferable profile for future in clinic use

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 28/09/2021, Stichting BEBO (Doctor Nassaulaan 10, 9401 HK Assen, The Netherlands; +31 592-405871; info@stbebo.nl), ref: NL78813.056.21

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

Primary study design
Interventional

Study type(s)
Other

Health condition(s) or problem(s) studied
ENX-102 is a new research drug that is being developed for the treatment of neuropsychiatric disorders.

Interventions
This is a randomized, double blind, placebo controlled, multiple ascending dose study in healthy volunteers. Subjects will be screened within 28 days of Day 1. Eligible subjects will be admitted to the inpatient unit on Day –1 and subjects are expected to remain confined for 14 days; discharge will be contingent upon clinical assessment and judgment of the Investigator. The 14 day inpatient period includes a 1-day Baseline Period (Day 1), a 12 day Treatment Period (Day 1 through Day 12), and a 1 day Follow up Period (Day 13). Discharge is planned for Day 13. Subjects will return to the clinic for follow up visits on Day 19, and Day 26. A total of 40 subjects based on the anticipated 5 cohorts of 8 subjects (6 active, 2 placebo per cohort) were enrolled. Randomization will occur on Day 1. Subjects will be randomly assigned to receive ENX-¬102 or placebo in a ratio of 6:2.
Randomization will be based on a randomization schedule prepared by the Sponsor statistician or designee prior the start of the study. The randomization schedule will be provided to the unblinded pharmacist. Subjects will be considered randomized once the subject's randomization number has been assigned.

Intervention Type
Drug

Drug/device/biological/vaccine name(s)
ENX 102

Primary outcome(s)
The safety and tolerability of ENX-102 will be assessed by the following:
1. AEs (day 1 to day 26) measured using patient records
2. Vital signs (2 positional blood pressure and HR, respiratory rate, and tympanic body temperature) at screening, day -1 to day 13, day 19 day 26
3. 12 lead ECG at screening, day -1, day 1, day 12, day 13, day 26
4. Clinical laboratory tests (hematology, serum chemistry, urinalysis) at screening, day -1, day 6, day 13, day 26
5. Physical examination at screening, day -1, day 13, day 26
6. Pregnancy test (where applicable)
7. C SSRS at screening, day -1, day 1, day 6, day 13, day 26
8. MOAA/S at day 1, day 2, day 12, day 13, day 19, day 26

Key secondary outcome(s))
Pharmacokinetic Measures at Day 1: Pre-dose and at 0.5, 1, 1.5, 2, 3, 6, 8, 10, and 12 hours after dosing; Days 2-11: Pre-dose (24 hours after the previous day's dose); Day 12: Pre-dose (24 hours

after Day 13 dosing) and at 0.5, 1, 1.5, 2, 3, 6, 8, 10, and 12 hours after dosing; Days 13: 24 hours after Day 12 dosing; Day 19: 168 hours after Day 12 dosing; Day 26: 312 hours after Day 12 dosing:
1. Maximum plasma concentration (Cmax)
2. Time to reach maximum plasma concentration (Tmax)
3. Area under the plasma concentration time curve (AUC) from administration to the end of dosing (AUC0 t),
4. AUC from administration to 24 h after dosing (AUC0 24), AUC extrapolated to infinite time (AUC0 ∞),
5. Plasma concentration half life (t1/2),
6. Terminal rate constant (λz),
7. Apparent total clearance of the drug from plasma after oral administration (CL/F),
8. Apparent volume of distribution during terminal phase after non intravenous administration (Vz/F).

Pharmacodynamic Measures at Baseline, Single dose (Day 1), Steady state (Day 12):
NeuroCart assessments
1. Saccadic eye movements, saccadic reaction time (seconds), saccadic peak velocity (degrees /second), and saccadic inaccuracy (%)
2. Smooth pursuit eye movements (percentage of time the eyes of the subject are in smooth pursuit of the target) (%)
3. Adaptive tracking (average performance) (%)
4. Body sway (antero posterior sway) (mm)
5. Pupil size
6. VAS according to Bond and Lader to assess mood, alertness, and calmness (mm)
7. Cognitive assessment: VVLT (Learning and Immediate Recall, Delayed Recall, and Delayed Recognition)
8. qEEG

Completion date
05/09/2022

Eligibility

Key inclusion criteria
1. Healthy male and female volunteers aged 18 to 55 years, inclusive, at Screening
2. Capable of giving written informed consent
3. Willing to give written consent to have data entered into "Verified Clinical Trials"
4. Female subjects
4.1. 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 level >40 IU/mL; in the event a subject's menopausal status has been clearly established and yet serum follicle stimulating hormone 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), and with a negative pregnancy test at Screening and Day –1; OR
4.2. Of childbearing potential and willing to use 2 effective methods of contraception (i.e., established method of contraception + condom) or remain abstinent (where abstaining from sexual intercourse is in line with the preferred and usual lifestyle of the subject) from Day –1 through 3 months after the last dose of study drug, and with a negative pregnancy test at

Screening and Day –1
5. Male subjects who, if fertile (defined as post pubertal and not permanently sterile by orchidectomy or vasectomy)
6. must be willing to use a condom or remain abstinent (where abstaining from sexual intercourse is in line with the preferred and usual lifestyle of the subject) from Day –1 through 3 months after the last dose of study drug
7. Body mass index of 18 to 35 kg/m² at Screening
8. Willing and able to comply with all study requirements including the following:
8.1. Reside in the inpatient unit from Day –1 until discharge on Day 13
8.2. Refrain from strenuous exercise from Day –4 until Day 26
8.3. Abstain from grapefruit, alcohol, caffeine, or xanthine containing products from Day –4 through Day 26

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
40

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
2. study outcome variables; this includes, but is not limited to, history of or current cardiac, renal, neurologic, gastrointestinal, pulmonary,
3. endocrinologic, hematologic, or immunologic disease or history of malignancy
4. Reports having experienced suicidal ideation (Type 4 or 5 on the CSSRS) within 30 days prior to Screening, any suicidal behavior within 2
5. years prior to Screening (any "Yes" answers on Suicidal Behavior section of CSSRS), and/or the Investigator assesses the subject to be a safety risk to him/herself or others
6. History or evidence of moderate or severe Substance Use Disorder as defined by the Diagnostic and Statistical Manual of Mental Disorders (5th Edition)
7. Clinically significant abnormal findings in serum chemistry, coagulation, hematology, or urinalysis results at Screening or Day –1
8. Clinically significant abnormal findings in vital sign assessments at Screening or Day –1
9. History of hepatitis B or hepatitis C or demonstration of hepatitis B surface antigen or hepatitis C antibody at Screening
10. History of HIV infection or demonstration of HIV antibodies at Screening
11. Receipt of an investigational drug within 90 days or 5 halflives, whichever is longer, prior to Day 1 or currently in the followup period of another clinical trial at the time of Screening

12. Any other condition that, in the Investigator's opinion, might indicate that the subject is unsuitable for the study

Date of first enrolment
03/11/2021

Date of final enrolment
10/08/2022

Locations

Countries of recruitment
Netherlands

Study participating centre
Centre for Human Drug Research
Zernikedreef 8
Leiden
Netherlands
2333 CL

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 current data sharing plans for this study are unknown and will be 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?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes