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A study to test the safety and effects of a new CB1 antagonist ANEB-001 in healthy occasional cannabis users

Submission date	Recruitment status	[X] Prospectively registered
15/12/2021	No longer recruiting	[ ] Protocol
Registration date	**Overall study status**	[ ] Statistical analysis plan
16/12/2021	Completed	[ ] Results
Last Edited	**Condition category**	[ ] Individual participant data
15/12/2021	Other	[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Cannabis is the most widely used recreational drug worldwide. Effects of cannabis include excitement, euphoria, sensory distortion, sedation, drowsiness and increased heart rate. Some unpleasant effects of acute cannabis intoxication include anxiety and postural hypotension. High doses can produce more severe symptoms including hypotension, panic, myoclonic jerking /hyperkinesis, delirium, respiratory depression, and ataxia. Currently, there are no targeted therapies available for the treatment of acute cannabis intoxication.
ANEB-001 is a cannabinoid CB1 receptor antagonist that was originally developed for the treatment of obesity and potentially other disorders of the metabolic system and CNS. In previous research, ANEB-001 has been shown to be safe, well tolerated and efficacious in reducing caloric intake in humans.
The aim of this study is to investigate whether ANEB-001 effectively penetrates the brain and acts as a central CB1 antagonist during a THC challenge, inhibiting the psychotropic effects of THC.

Who can participate?
Adult healthy volunteers who are recreational cannabis users.

What does the study involve?
For participants, the study involves a screening (duration: 2h). Eligible subjects will present to the research facility on day -1. On the morning of day 1, baseline measurements will be performed and subject will receive the study treatments (THC and ANEB-001 or placebo), followed by multiple rounds of measurements. Measurements include blood pressure, temperature, EKG, attention and reaction tests, questionnaires. On the morning of day 2, some measurements will be repeated and subjects will be discharged. Subject will return for a follow-up visit 7-14 days post-dose (duration: 1h).

What are the possible benefits and risks of participating?
There are no benefits.

THC
THC has potential side effects, but is generally considered safe, even in high dosages. Possible side effects include confusion, hallucinations, delusions, decreased coordination, dizziness, drowsiness, elevated or relaxed mood, anxiety, headache, nausea, stomach pain, trouble concentrating, vomiting and weakness.

ANEB-001
A number of side effects related to ANEB-001 have been observed previously in humans. Nausea, abdominal discomfort, diarrhoea, headache, dizziness and loss of appetite are side effects that regularly occurred after a single intake of ANEB-001. In addition, vomiting sometimes occurred. Some side effects were not seen after a single administration of ANEB-001, but were seen after multiple administrations: feeling hot or cold, sweating excessively, weight loss, muscle stiffness and hiccups. All of these side effects were temporary and resolved during or after the study. Research into drugs similar to ANEB-001 has also shown that long-term treatment with these drugs can cause a gloomy or anxious mood. However, this was not seen after a single administration of ANEB-001. ANEB-001 may also have side effects that we don't know about yet.

Blood draw may be unpleasant or painful for some subjects. No benefit for the subjects is expected from participation in the study.

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?
December 2020 to August 2022

Who is funding the study?
Anebulo Pharmaceuticals, Inc. (USA)

Who is the main contact?
A. Gorbenko, agorbenko@chdr.nl

Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
2021-000305-24

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
AN01AC11 / CHDR2039

Study information

Scientific Title
A randomized, double-blind, placebo-controlled study to assess the safety, tolerability, pharmacokinetics and pharmacodynamics of single oral doses of CB1 antagonist ANEB-001 in healthy occasional cannabis users

Study objectives
ANEB-001 reduces THC effects more than placebo

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved, 18/03/2021, The Independent Ethics Committee (Medisch Ethische ToetsingsCommissie) of the 'Stichting Beoordeling Ethiek Biomedisch Onderzoek' (Doctor Nassaulaan 10, 9401 HK Assen, The Netherlands; +31 592 405 871; info@stbebo.nl), ref:

Study design
Single centre randomized double blind placebo-controlled parallel dose finding study

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Effects of ANEB-001 in healthy occasional users of cannabis

Interventions
The study will consist of two parts, called “Phase 1” and “Phase II”.
In phase I, 20 subjects will be randomized to receive single doses of 50 mg ANEB-001, or 100 mg ANEB-001, or placebo each (60 subjects in total in phase I).
In phase II, up to 6 extension cohorts of 15 subjects each (10 active and 5 placebo each) may be conducted following the completion of the initial phase based on emerging PK, PD, safety and tolerability data. The subject in the extension cohorts may receive single doses ranging from 10 mg to 150 mg of ANEB-001 or matching placebo, based on emerging data.

Each subject in both phase I and phase II will receive a single dose of 10.5 mg THC (NB: no placebo THC in the study) together with the single dose of ANEB-001 or placebo ANEB-001.

The duration of treatment and follow-up is identical for phase I and phase II. The total duration of the study for each subject will be up to 56 days divided as follows:
Screening: Up to 42 days before dosing;
In Clinic period: Days -1 to 2;
Follow-up visit: 7 to 14 days after dosing
Subjects will be admitted to the study unit on Day -1. The study drugs will be administered in the morning of day 1. Subjects will be discharged approximately 24 hours after study drug administration

Intervention Type
Drug

Phase
Phase I

Drug/device/biological/vaccine name(s)
ANEB-001, Namisol

Primary outcome(s)
Measured at pre-dose to 8 hours post-dose (unless noted otherwise):
1. Visual Analogue Scale (VAS) “Feeling High” according to modified Bowdle psychedelic scale (mm)
2. VAS “Alertness” according to Bond and Lader (mm)
3. Body sway: antero-posterior sway (mm)
4. Heart rate (bpm) measured pre-dose to 24 hours post-dose, and at follow up 7-15 days post-dose

Key secondary outcome(s))
Measured at pre-dose to 8 hours post-dose (unless noted otherwise):
1. VAS Bond and Lader: mood (mm), calmness (mm).
2. VAS Bowdle Internal perception, External perception
3. State-Trait Anxiety Inventory (STAI) State anxiety score measured pre-dose to 4 hours post-dose
4. Saccadic eye movements: saccadic reaction time (second), saccadic peak velocity (degrees /second), and saccadic inaccuracy (%);
5. Smooth pursuit eye movements: percentage of time the eyes of the subjects are in smooth pursuit of the target (%);
6. Adaptive tracking: average performance (%);
7. Pupillometry (mm)
8. N-Back, Average reaction time for zero, one and two-back (ms), (nr correct – nr incorrect)/total for zero, one and two-back
9. PK parameters of ANEB-001, THC and 11-OH-THC by non-compartmental analysis of the plasma concentration-time data measured pre-dose to 24 hours post-dose, and at follow up 7-15 days post-dose:
9.1 AUCinf, AUClast, CL/F, Cmax, t1/2, tlag, tmax, Vz/F
9.2 Dose-normalized PK parameters: AUCinf, AUClast, Cmax
10. Treatment-emergent (serious) adverse events ((S)AEs) throughout the study at every study visit

11. Concomitant medication throughout the study at every study visit
12. Vital signs (Pulse Rate (bpm), Systolic blood pressure (mmHg), Diastolic blood pressure (mmHg)) as per assessment schedule measured pre-dose to 24 hours post-dose, and at follow up 7-15 days post-dose
13. Clinical laboratory tests (Hematology, blood chemistry and urinalysis) measured pre-dose to 24 hours post-dose, and at follow up 7-15 days post-dose
14. ECG parameters (Heart Rate (HR) (bpm), PR, QRS, QT, QTcB, QTcF) measured pre-dose to 24 hours post-dose, and at follow up 7-15 days post-dose
15. VAS Nausea
16. Suicidality as assessed by the Columbia Suicide Severity Rating Scale (C-SSRS) measured pre-dose to 24 hours post-dose, and at follow up 7-15 days post-dose
17. Depressive symptoms as assessed by Beck Depression Inventory-II measured pre-dose to 24 hours post-dose, and at follow up 7-15 days post-dose
18. Dissociative symptoms as assessed by Clinician Administered Dissociative States Scale (CADSS) measured pre-dose to 24 hours post-dose, and at follow up 7-15 days post-dose

Completion date
01/08/2022

Eligibility

Key inclusion criteria
1. Signed informed consent prior to any study-mandated procedure
2. Healthy subjects, 18 to 45 years of age, inclusive at screening
3. Body mass index (BMI) between 18 and 30 kg/m², inclusive at screening, and with a minimum weight of 50kg
4. All males must practice effective contraception during the study and be willing and able to continue contraception for at least 90 days after their last dose of study treatment
5. Has the ability to communicate well with the Investigator in the Dutch language and willing to comply with the study restrictions
6. Occasional cannabis users

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
1. Evidence of any active or chronic disease or condition that could interfere with, or for which the treatment of might interfere with, the conduct of the study, or that would pose an

unacceptable risk to the subject in the opinion of the investigator (following a detailed medical history, physical examination, vital signs (systolic and diastolic blood pressure, pulse rate, body temperature) and12-lead electrocardiogram (ECG)). Minor deviations from the normal range may be accepted, if judged by the Investigator to have no clinical relevance.
2. Clinically significant abnormalities, as judged by the investigator, in laboratory test results (including hepatic and renal panels, complete blood count, chemistry panel and urinalysis). In the case of uncertain or questionable results, tests performed during screening may be repeated before randomization to confirm eligibility or judged to be clinically irrelevant for healthy subjects.
3. Positive Hepatitis B surface antigen (HBsAg), Hepatitis C antibody (HCV Ab), or human immunodeficiency virus antibody (HIV Ab) at screening.
4. Systolic blood pressure (SBP) greater than 140 or less than 90 mmHg, and diastolic blood pressure (DBP) greater than 95 or less than 50 mmHg at screening.
5. Abnormal findings in the resting ECG at screening defined as:
a. QTcF> 450 or < 300 msec for men and QTcF >470 or <300 msec for women
b. Notable resting bradycardia (HR < 40 bpm) or tachycardia (HR >100 bpm)
c. Personal or family history of congenital long QT syndrome or sudden death;
d. ECG with QRS and/or T wave judged to be unfavourable for a consistently accurate QT measurement (e.g., neuromuscular artefact that cannot be readily eliminated, arrhythmias, indistinct QRS onset, low amplitude T wave, merged T- and U-waves, prominent U waves);
e. Evidence of atrial fibrillation, atrial flutter, complete branch block, Wolf-Parkinson-White Syndrome, or cardiac pacemaker
6. Use of any medications (prescription or over-the-counter [OTC]), within 7 days of study drug administration, or less than 5 half-lives (whichever is longer). Exceptions are paracetamol (up to 4 g/day) and ibuprofen (up to 1g/day) and topical medications that are not expected to reach a meaningful systemic exposure, as judged by the investigator. Other exceptions will only be made if the rationale is clearly documented by the investigator.
7. Use of any vitamin, mineral, herbal, and dietary supplements within 7 days of study drug administration, or less than 5 half-lives (whichever is longer). Exceptions will only be made if the rationale is clearly documented by the investigator.
8. Participation in an investigational drug or device study (last dosing of previous study was within 90 days prior to first dosing of this study).
9. History of abuse of addictive substances (alcohol, illegal substances) or current use of more than 21 units alcohol per week, drug abuse, or regular user of sedatives, hypnotics, tranquillisers, or any other addictive agent other than recreative use of THC
10. Positive test for drugs of abuse (other than THC) at screening.
11. Positive test for drugs of abuse pre-dose.
12. Alcohol will not be allowed from at least 24 hours before screening or pre-dose.
13. Smoker of more than 10 cigarettes per day prior to screening or who use tobacco products equivalent to more than 10 cigarettes per day and unable to abstain from smoking whilst in the unit.
14. Is demonstrating excess in caffeine consumption (more than eight cups of coffee or equivalent per day.
15. Any confirmed significant allergic reactions (urticaria or anaphylaxis) against any drug, or multiple drug allergies (non-active hay fever is acceptable).
16. Loss or donation of blood over 500 mL within three months (males) or four months (females) prior to screening or intention to donate blood or blood products during the study.
17. Women of child bearing potential (WOCBP), or non-WOCBP who are breast feeding will not be allowed to participate in the study.
18. Any known factor, condition, or disease that might interfere with treatment compliance, study conduct or interpretation of the results such as drug or alcohol dependence or psychiatric disease.

19. Clinically significant suicidal ideation in the past 5 years as judged by the investigator or any life-time suicide attempts.
20. History of cannabis-induced psychosis, schizophrenia or other clinically relevant psychiatric disorders, as judged by the investigator.
21. History of a clinically significant mood disorder, including but not limited to major depressive disorder, as judged by the investigator.

Date of first enrolment
20/12/2021

Date of final enrolment
01/08/2022

Locations

Countries of recruitment
Netherlands

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

Sponsor information

Organisation
Anebulo Pharmaceuticals, Inc.

Funder(s)

Funder type
Industry

Funder Name
Anebulo Pharmaceuticals, 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
Study website	Study website	11/11/2025	11/11/2025	No	Yes