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A study on the safety, tolerability, and effects of GM-2505

Submission date	Recruitment status
14/11/2022	No longer recruiting
Registration date	**Overall study status**
04/07/2024	Completed
Last Edited	**Condition category**
23/10/2025	Mental and Behavioural Disorders

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

Plain English summary of protocol

Background and study aims
A psychedelic experience (also called a trip) is a temporary altered state of consciousness caused by the ingestion of a psychedelic substance. Psychedelics cause a trip by increasing the serotonin signal in the brain. Serotonin is present in many areas of the brain and has various functions. It plays an important role in regulating mood, sleep, emotions and memory. An increase in serotonin can ensure that people with psychiatric disorders experience fewer complaints. For example, a study has shown that hallucinogenic substances that increase serotonin can be used, in combination with psychotherapy, to treat anxiety disorders, depressive disorders and substance dependence. New research drugs that improve the medical effects of classic psychedelics are currently under investigation. The investigational drug GM-2505 is comparable to other psychedelics that have previously been studied in a medical research setting, such as, for example, lysergic acid diethylamide (LSD), dimethyltryptamine (DMT) or psilocybin. However, GM-2505 has not been tested in humans before, so its effects on humans have yet to be characterized. This study aims to evaluate the safety, pharmacokinetics (PK; the study of the time course of drug absorption, distribution, metabolism, and excretion in the human body) and pharmacodynamics (PD; the study of a drug's molecular, biochemical, and physiologic effects or actions in the human body) of single ascending intravenous doses of GM-2505 in healthy volunteers.

Who can participate?
Healthy female or male subjects, aged 18 to 55 years old

What does the study involve?
Single GM-2505 doses will be administered, to achieve the main study objective. Up to 6 cohorts of 8 subjects may be recruited for this study. All 6 cohorts will be dosed with an IV dose. For each cohort, sentinel dosing in 2 subjects will be performed.

What are the possible benefits and risks of participating?
No benefit is expected for the healthy volunteers participating in this study. Given the drug's effect profile, the research team take into account the potential occurrence of the following side effects:
1. Hypertension (blood pressure increase)

2. Nausea - Headache
3. Orthotasis (dizziness when standing up)
4. Fatigue
5. Decreased muscle tension
6. Anxiety
Participation may increase the knowledge about the safety and effects of the investigated drug.

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?
August 2022 to July 2023

Who is funding the study?
Gilgamesh Pharmaceuticals (USA)

Who is the main contact?
S Makai-Bölöni (Project Leader), SMBoloni@chdr.nl (Netherlands)

Contact information

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Public, Scientific

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Clinical Trials Information System (CTIS)
2022-003014-37

Protocol serial number
CHDR2209 / GLG-2501

Study information

Scientific Title
An adaptive, randomized, double-blind, placebo-controlled, single ascending dose (SAD) study to evaluate safety, pharmacokinetics (PK) and pharmacodynamics (PD) of GM-2505 in healthy volunteers

Study objectives
This study aims to evaluate the safety, pharmacokinetics (PK) and pharmacodynamics (PD) of single ascending intravenous doses of GM-2505 in healthy volunteers

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 01/11/2022, The Independent Ethics Committee (Medisch Ethische ToetsingsCommissie) of the 'Stichting Beoordeling Ethiek Biomedisch Onderzoek' (Doctor Nassaulaan 10, HK Assen, 9401, Netherlands; +31 592-405871; info@stbebo.nl), ref: NL82521.056.22

Primary study design
Interventional

Study design
Adaptive single-ascending-dose randomized placebo-controlled double-blind safety and tolerability study

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Major depressive disorder, depression

Interventions
Single dose of GM-2505 or placebo

Intervention Type
Drug

Phase
Not Applicable

Drug/device/biological/vaccine name(s)
GM-2505

Primary outcome(s)
Safety and tolerability outcomes after single intravenous (IV) doses of GM-2505 measured pre-dose and several times post-dose up to 24h post-dose:
1. Adverse events measured using clinical logs monitored continuously from signing ICF to the last follow-up
2. Hematology measured using a standard laboratory clinical safety panel upon admission to the clinical unit, before discharge, and during the follow-up visit
3. Serum chemistry measured using a standard laboratory clinical safety panel upon admission to the clinical unit, before discharge, and during the follow-up visit
4. Urinalysis measured using a standard laboratory clinical safety panel upon admission to the clinical unit, before discharge, and during the follow-up visit
5. Vital signs measured using pulse and blood pressure taken after 5 minutes in the supine position at screening, upon admission, 5 pre-dose, and 5, 40, 1h, 2h, 4h, 8h, 24h post-dose. Automated oscillometric blood pressures were used.
6. 12-lead ECG measured using standard ECG procedures obtained during the study with a Marquette 2000/5500 and stored using the MUSE Cardiology Information System. ECGs were taken after at least 5 minutes in the supine position at screening, upon admission, 5 pre-dose, and 5, 40, 1h, 2h, 4h, 8h, and 24h post-dose.
7. Occurrence of psychotic symptoms measured using the Brief Psychiatric Rating Scale (BPRS) at screening, upon admission to the clinical unit, 2, 6, and 24h post-dose, and during the follow-up visit
8. Occurrence of suicidal thoughts and ideations measured using the Columbia–Suicide Severity Rating Scale (C-SSRS) at screening, upon admission to the clinical unit, and 24h post-dose, and during the follow-up visit
9. Occurrence of central serotonergic toxicity measured using Hunter's Serotonin Toxicity Criteria (HSTC) only in the suspected cases of serotonergic toxicity signs throughout the study
10. Safety-EEG measured using continuous recording standard procedures with continuous recording 4 min pre-dose and 40 min post-dose

Key secondary outcome(s)
1. To assess the the pharmacokinetics (PK) of GM-2505, AUCinf, AUCinf(%extrap), AUClast, CL, Cmax, t1/2, tmax, Vss, Vz, CLR, Aelast, Aelast% will be measured in plasma and urine, pre-dose and several times post dose, up to 24h. 15 pre-dose, and 10, 20, 40, 1h, 1h 30, 2h, 3h, 4h, 6h, 12h, 24h post-dose.
2. To characterize the pharmacodynamics (PD) of GM-2505:
2.1. The NeuroCart test battery on Day 1 pre-dose and 40, 2h, 6h, 24h post-dose
2.2. Clinical rating scales:
2.2.1. Real Time Intensity on Day 1, 15 pre-dose, and 10, 20, 40, 1h, 1h 30, 2h, 3h, 4h, 6h, 12h, 24h post-dose
2.2.2. VAS Bond & Lader, VAS Bowdle, Drug effects Questionnaire on Day 1, pre-dose, and 20, 40, 1h, 2h, 3h, 4h, 5h, 8h post-dose
2.2.3. 5 Dimension Altered States of Consciousness rating scale (5DASC), Mystical Effects Questionnaire (MEQ-30): ~ 4 h post-dose
2.2.4. Pharmaco-EEG, resting state: pre-dose, 30 min, 1h, 1.5h, 3h, 6h, and 25h post-dose
2.3. Computerized tests:

2.3.1. N-Back task, Sustained Attention to Response Task, Probabilistic learning task, a reinforcement learning and working memory task, and an effort cost-benefit task at baseline, 6h post-dose, and 24h post-dose

Completion date
01/07/2023

Eligibility

Key inclusion criteria
1. Healthy female or male subjects, aged 18 to 55 years old, inclusive. Healthy status is defined by absence of evidence of any active or chronic disease following a detailed medical, surgical a complete physical examination including vital signs, 12-lead ECG, hematology, blood chemistry, and urinalysis. If the results of the serum chemistry panel, hematology, or urinalysis are outside the normal reference ranges, the subject may be included only if the investigator judges the abnormalities to be not clinically significant.
2. Subject has a body mass index (BMI) between 18.0 and 30.0 kg/m2 inclusive (BMI=weight /height2) at screening.
3. Self-report of at least one prior hallucinogen drug experience that included a meaningful altered state of consciousness (a state in which the subject experienced phenomena that altered his psychological functioning, such as loss of ego boundaries, impaired control of actions and cognition, disembodiment, changed meaning of perception, visual alterations, and audio–visual synesthesia) in the past 5 years. Hallucinogenic substances can include psilocybin, LSD, DMT, ayahuasca, mescaline, ibogaine, 2C-drugs (such as 2CB, 2CI and 2CE) and/or ketamine.
4. Subjects must be willing to adhere to the prohibitions and restrictions specified in the protocol, including attending all study visits, preparatory and follow-up sessions, and completing all study evaluations.
5. Each subject must sign an informed consent form (ICF) indicating that he or she understands the purpose and procedures required for the study and are willing to participate in the study. Agree to refrain from using any psychoactive drugs from 30 days before first dosing and until the last follow-up visit and to refrain from using alcoholic beverages within 48 hours prior to admission of each treatment period.

Participant type(s)
Healthy volunteer

Healthy volunteers allowed
No

Age group
Adult

Sex
All

Key exclusion criteria
1. Clinically significant current or previous liver or renal insufficiency, cardiac, vascular, pulmonary, gastrointestinal, endocrine, neurologic, hematologic, rheumatologic, metabolic or inflammatory illness, or any other illness that would compromise the well-being of the subject or the study or prevent the subject from meeting or performing study requirements according to the investigator.

3. Subject has a history of or current hypertension (resting systolic blood pressure > 130 mmHg or diastolic blood pressure >90 mmHg) at screening.
5. Resting heart rate (HR) greater than 100 or less than 45 beats per minute (bpm) at screening.
7. Clinically significant personal or familial history of epilepsy, seizures, convulsions, or other seizure disorder(excluding febrile seizures as a child), previous head trauma or other risk factor for seizure.
8. Clinically significant current or previous psychiatric disorder according to DSM 5. Specifically, current or previous psychotic disorders and bipolar disorder will be excluded.
9. Family history of a psychotic disorder (whether in the context of bipolar disorder, schizophrenia or schizoaffective disorder) in first-degree and second-degree relatives.
10. Clinically significant current or previous suicidality based on the C-SSRS and psychiatric history indicating current suicidal ideation or a history of active suicidal ideation or suicide attempts
11. Subject has a current or history of drug or alcohol use disorder according to the to DSM-IV and/or DSM 5within the past 12 months.
12. Use of psychoactive substances (including ketamine, esketamine, MDMA, cannabinoids), during the 6 weeks prior to screening. Single/occasional use may be allowed at the discretion of investigator.
13. Ingestion of psychedelics (including psilocybin, DMT/ayahuasca, LSD, another serotonergic psychedelic)during 4 weeks prior to screening.
14. Persistent psychological effects following the previous use of psilocybin, LSD, DMT, ayahuasca, mescaline, ibogaine, 2C-drugs (such as 2CB, 2CI and 2CE) and/or ketamine. Such effects might include but are not limited to anxiety, depressed mood, paranoid ideation and/or hallucinations (including hallucinogen persisting perception disorder – HPPD) or recurrent flashbacks related to use.
15. Subject has a positive test result(s) for alcohol and/or drugs of abuse (including opiates (including methadone),cocaine, amphetamines, methamphetamines, cannabinoids, barbiturates, and benzodiazepines) at screening or admission to the clinical unit.

Date of first enrolment
14/11/2022

Date of final enrolment
01/06/2023

Locations

Countries of recruitment
Netherlands

Study participating centre
Centre for Human Drug Research
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Sponsor information

Organisation
Gilgamesh Pharmaceuticals

Funder(s)

Funder type
Industry

Funder Name
Gilgamesh Pharmaceuticals

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?
Results article		16/10/2025	23/10/2025	Yes	No