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Safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD) and effects of intravenous (IV) and intramuscular (IM) dosing of SPL028 (deuterated DMT fumarate [a serotonergic psychedelic]) in healthy volunteers and participants with major depressive disorder (MDD)

Submission date
15/07/2024

Recruitment status
No longer recruiting

Registration date
13/08/2024

Overall study status
Completed

Last Edited
16/12/2024

Condition category
Other

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

Plain English Summary
Background and study aims
This is a study investigating a modified version of N, N-dimethyltryptamine (DMT) – DMT is a psychedelic substance that occurs naturally in many plants and animals. Psychedelic substances, also known as hallucinogens, act on the brain causing temporary changes to perception, sensations, and emotions, which can be intense. DMT is best known for being the main psychedelic substance in ayahuasca (a hallucinogenic brew that has been used for centuries in religious ceremonies in some South American countries). DMT is a Class A illegal drug – we have a special licence to be able to give this modified version of DMT to participants in this study. The modified version of DMT being investigated in this study is called SPL028 (also known as the 'study drug').
The modification that has been made to the DMT molecule is predicted to cause SPL028 to have a longer duration of effect compared to standard DMT; other than the predicted longer duration of effect, SPL028 is very similar to standard DMT. We're testing the study drug as an experimental treatment for Major Depressive Disorder (MDD) in combination with therapy sessions. In Part A of this study, we're investigating how safe and tolerated SPL028 is in healthy volunteers.

The main aims of this study are:
• To assess the safety and tolerability of the study drug, given as a slow injection into a vein in the arm or given as a quick injection into a muscle. The safety and tolerability will be compared

between these different ways of giving the study drug.
• To see how the body absorbs and removes the study drug.
• To assess the effect of the study drug on the body, mood, feelings, thoughts and beliefs.

Who can participate?
To take part in Cohorts 1 and 2 of this study, you must:
• Be 25 to 65 years of age.
• Have a body mass index (BMI) between 18 and 33.9 – your BMI may be too high if you're overweight or if you're very muscular; you can ask us to explain how we work out your BMI.
• Have suitable veins (so we can easily inject the study drug and/or take blood samples).
• Be registered with a General Practitioner (GP).
• Be willing to be contacted by email, telephone and video call, and have internet access.
• Have not taken any monoamine oxidase inhibitors for at least 3 months before the Screening visit.
• Agree to follow the contraception requirements of the study.
• Be willing to follow the study lifestyle restrictions .
• Have had at least two previous 'breakthrough' experiences with serotonergic psychedelic drugs, including but not limited to: DMT, ayahausca, LSD, LSA (morning glory seeds), amphetamine-class drugs, mescaline, peyote, san pedro, ibogaine and psilocybin (including mushroom species containing psilocybin). A breakthrough experience is an immersive and intense experience, in which almost all connection to the real world is lost.
• Match all the other characteristics required to enter this study.

To take part in Cohorts 3, 4 and 5 of this study, you must:
• Be 25 to 65 years of age.
• Have a body mass index (BMI) between 18 and 33.9 – your BMI may be too high if you're overweight or if you're very muscular; you can ask us to explain how we work out your BMI.
• Have suitable veins (so we can easily inject the study drug and/or take blood samples).
• Be registered with a General Practitioner (GP).
• Be willing to be contacted by email, telephone and video call, and have internet access.
• Have not taken any monoamine oxidase inhibitors for at least 3 months before the Screening visit. Have not taken any monoamine oxidase inhibitors for at least 3 months before the Screening visit.
• Agree to follow the contraception requirements of the study.
• Be willing to follow the study lifestyle restrictions.
• Have had a maximum of 2 previous experiences with serotonergic psychedelic drugs with no 'breakthrough' experiences, including but not limited to: DMT, ayahausca, LSD, LSA (morning glory seeds), amphetamine-class drugs, mescaline, peyote, san pedro, ibogaine and psilocybin (including mushroom species containing psilocybin). A breakthrough experience is an immersive and intense experience, in which almost all connection to the real world is lost.
• Match all the other characteristics required to enter this study.

What does the study involve?
Cohorts 1&2:
Your maximum length of participation in this study will be approximately 15 weeks and you will be given two doses of the study medication. You will be required to attend study visits on 3 occasions in total, consisting of a Screening visit and 2 inpatient periods (2-night periods), and 2 video calls.
You will attend the clinic on the day prior to the day of dosing (Day -1) of each Treatment Period and stay until Day 2 of each Treatment Period (2-night period). You will be administered study medication on Day 1 of each Treatment Period. On Day 2, you will be discharged from the clinic following completion of safety assessments and a session to discuss your experience with the

therapist team. You will be contacted on Day 15 (±2 days) of each Treatment Period by video call for an Integration session with the therapist team and completion of safety assessments (which may be separate telephone or video calls). Alternatively, you may be asked to come to the clinic to complete one or both of the Follow-up visits in person, instead of by video call. In addition, you will be required to self-complete multiple other questionnaires regarding your attitudes, moods and relationships. There will be a 3 to 6 week period between Treatment Periods; all assessments performed in the Treatment Periods will be the same.

We'll give you information about a psychedelic participant advocacy network and community run psychedelic Integration groups that you may wish to attend after your End-of-Study video call. The clinic visits will take place at the MAC Clinical Research Unit (CRU) located in Manchester. You will visit the same CRU for all study visits.

Cohorts 3-5:
Your maximum length of participation in this study will be approximately 8 weeks and you will be given one dose of the study medication. You will be required to attend study visits on 3 occasions in total, consisting of a Screening visit, 1 inpatient period (2-night period) and 1 video call. Following your Screening visit, you will attend the clinic on the day prior to the day of dosing (Day -1) and stay until Day 2 (2-night period). You will be administered study medication on Day 1. On Day 2, you will be discharged from the clinic following completion of safety assessments and a session to discuss your experience with the therapist team. You will be contacted on Day 15 (±2 days) by video call for an Integration session with the therapist team and completion of safety assessments (which may be separate telephone or video calls). Alternatively, you may be asked to come to the clinic to complete the Follow-up visit in person, instead of by video call. In addition, you will be required to self-complete multiple other questionnaires regarding your attitudes, moods and relationships. We'll give you information about a psychedelic participant advocacy network and community run psychedelic Integration groups that you may wish to attend after your End-of-Study video call. The clinic visits will take place at the MAC Clinical Research Unit (CRU) located in Manchester. You will visit the same CRU for all study visits.

What are the possible risks and benefits of participating?
The dose of SPL028 you'll receive is likely to cause a psychedelic experience or 'trip', which could last a maximum of 4 hours, although it will likely be much shorter than this (expected to last about 1 hour following IV infusion in your arm and about 2 hours following IM injection into a muscle). Typically, standard DMT causes an experience that lasts a maximum of 30 minutes. Due to a small modification of the DMT molecule, this may be longer for SPL028. Administration by injection into a muscle may also extend the duration of effect.

You may experience: visual imagery or hallucinations (seeing colourful patterns, or seeing or hearing things that aren't real), a sense of being detached from your thoughts or feelings, changes in your sense of time and space, out-of-body experiences, disorientation or confusion, anxiety, intense emotions such as happiness or grief. Sometimes people experience unpleasant images and sounds and may also 'relive' painful memories or traumas. You'll have the support and guidance of expert therapists to help you interpret and deal with any experiences you may have during your trip. If you become very upset or agitated after your dose, the study doctor may give you a licensed medicine to help you relax.

Before you take part in the study, we'll explain what you should expect from a psychedelic trip and how to respond to it (while on the ward and once you've gone home), and you'll have an interview with a psychiatrist to make sure you're suitable to take part. We'll monitor you closely during and after your dose – the therapist team and a nurse will be with you, and a psychiatrist

will be available if needed. If you are being dosed by IV infusion, we'll stop the infusion of study medicine early if you ask us to, or if we think it's necessary. We will not be able to stop dosing early when you are being given the study medicine by injection into a muscle. Before and after your dose, the study therapist team will talk to you about your experience.
If you were to have a challenging experience or negative reaction to SPL028 during or after the session, our research team will be able to help you. Challenging experiences can be triggered by psychedelic drugs, such as DMT, and are usually temporary and resolve with reassurance and support. The chances are that we won't need to use any medication at all, and any psychedelic effects will be short-lived and resolve of their own accord. Your experience with SPL028 might make you feel differently about yourself and your life, so we'll advise you not to make any life changing decisions for 6 weeks following the session.
As with any new medicine, we don't yet know all its side effects. In any clinical trial, there is a risk of an unexpected, serious reaction to the study drug, which could be potentially life-threatening.

In clinical studies of DMT, some people had physical effects, such as increased blood pressure and heart rate, feeling sick, and headaches. We'll monitor your heart rate and blood pressure during the study. In the unlikely event that your heart rate or rhythm or your blood pressure changes significantly, the study doctor will take the appropriate steps to reverse this side effect. If deemed necessary, you may be referred to the hospital emergency department and/or a cardiologist for further investigations and/or treatments.

You will be closely monitored throughout the study, and questions about suicidal thoughts and feelings will be frequently asked throughout the study using a rating scale. If your mental health were to deteriorate significantly during any point of the study and we had serious concerns about your safety, then we would be obliged to involve local mental health services to determine how best to manage your condition.
The study drug's effect on the body may change when the drug is taken in combination with another drug, which can result in either a decrease or increase in the effects of either, or both, drugs. This could have potential side effects. The study team will carefully evaluate any prescription or non-prescription medications that you are taking at your Screening visit. For further details on medications that are not allowed during this study.

So called 'flashbacks', or a sense of re-experiencing psychedelic drug effects when no drug has been taken has been described in scientific literature with recreational use of drugs such as DMT. If this occurs it is usually not a problem but please do let the research team know, who can support or guide you.
A very rarely reported side effect of taking psychedelics as recreational drugs is something called hallucinogen-induced persistent perceptual disorder (HPPD). People who report symptoms of HPPD may see haloes around objects, light trails and alterations in the colour and shape of objects. This effect is seen very rarely following recreational use of psychedelic drugs and has not been reported when psychedelic drugs have been taken in scientific and clinical studies.

As with any new medicine, the study drug might affect an unborn child. You must not take part in the study if you are pregnant or want to become pregnant at the time of the study. Please tell us straight away if you think you or your partner might be pregnant. We would want to keep in touch with you until the end of the pregnancy, to find out if the study drug had affected your unborn child – we'd ask your permission to do that.
The study drug may affect your concentration or judgement, so you shouldn't drive or operate machinery for 24 hours after your dose (if you leave MAC for any reason, before the scheduled time).

You will be carefully monitored during your time on the study, although this does not mean these side effects could not occur. It is important that you report to your study doctor all symptoms and side effects that you may experience, as soon as they appear, whether or not you think they are related to the study medication. You will always be closely looked after throughout the study.

Although all possible precautions are taken to prevent serious side effects, if such a side effect occurs, you may need to be admitted into hospital. Depending on the type of side effect, a medical specialist may be asked to take over your care. If you're ill while you're on the ward, we'll give you any immediate treatment you need. If you're ill after leaving the ward, call us as soon as you can. We might need to see you again, but if you weren't well enough to travel, you'd need help from a local doctor or hospital. One of our doctors is always available on the telephone to discuss medical problems with you or with other doctors.

We'll give you a medical alert card with some information about the study and contact numbers of MAC doctors. When you've left the ward, carry the card with you at all times until your End-of-Study video call. If you visit other healthcare professionals (such as a doctor, nurse or dentist), show them the card. Bring your medical alert card with you whenever you visit the ward. We will also provide you with an out of hours emergency contact number for a member of staff.
This drug will not be available for use after you have completed the study. It is not anticipated that there will be any benefit to you, but you are contributing to the scientific knowledge which may lead to the expansion of treatment options for people with MDD.

DMT is a Class A illegal drug, as is SPL028 (modified DMT) – we have a special licence to be able to give SPL028 to volunteers in this study.
The Sponsor, and/or others working with the Sponsor, will own the results of this study. The results might have commercial or intellectual property value and might be used to apply for patents. You won't receive any financial benefit that might come from the study.

Where is the study run from?
The study is run from a commercial clinical research centre in Manchester (UK)

When is the study starting and how long is it expected to run for?
June 2022 to December 2023

Who is funding the study?
The study is funded by a company called Cybin UK Ltd, based in England (UK)

Who is the main contact?
Ellen James, ellen@cybin.com

Contact information

Type(s)
Public, Scientific, Principal Investigator

Contact name
Dr Ezanul Wahab

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Additional identifiers

EudraCT/CTIS number
2022-002618-17

IRAS number
1006153

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CT028_001, IRAS 1006153

Study information

Scientific Title
A phase 1, double-blind study investigating the safety, tolerability, pharmacokinetics (PK) and pharmacodynamics (PD) of intravenous (IV) and intramuscular (IM) dosing of SPL028 (deuterated DMT fumarate [a serotonergic psychedelic]) in healthy participants (Part A); followed by an open-label study investigating the safety, tolerability, pharmacokinetics, pharmacodynamics and exploratory efficacy of SPL028 in participants with major depressive disorder (Part B)

Study hypothesis
SPL028 with support therapy is safe and well tolerated following intravenous (IV) and intramuscular (IM) administration in healthy participants.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 27/10/2022, Wales Research Ethics Committee 1 (Health and Care Research Wales, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, United Kingdom; +44 2920 785738; wales.REC1@wales.nhs.uk), ref: 22/WA/0220

Study design
Interventional randomized controlled trial

Primary study design

Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Pharmaceutical testing facility

Study type(s)
Safety, Efficacy

Participant information sheet
Not available in web format, please use contact details to request a participant information sheet.

Condition
Healthy participants

Interventions
Part A: Part A of this study is a Phase 1, double-blind study to determine the safety, tolerability, PK profile and PD of IV and IM dosing of SPL028 in healthy participants.

It is planned to enrol up to 40 healthy participants (excluding replacements) into up to 5 cohorts, comprising 8 participants each. Cohorts 1 and 2 will recruit psychedelic-experienced healthy participants, whereas Cohorts 3, 4 and 5 will recruit healthy participants with little to no psychedelic experience.

In each cohort in Part A of this study, 6 healthy participants will be randomised to receive SPL028, and 2 healthy participants will be randomised to receive placebo. SPL028 (deuterated dimethyltryptamine) by intramuscular injection or intravenous infusion or matched placebo. Participants in Cohorts 1 and 2 will each take part in two Treatment Periods spaced 3 to 6 weeks apart. Participants in Cohorts 1 and 2 will either be given two doses of the study drug, or one dose of study drug and one dose of placebo; they will not be given placebo in both Treatment Periods. In each of Cohorts 3-5, 6 participants will receive the study drug and 2 participants will receive placebo.

Part B: This was an optional part with patients with MDD, but it did not take place.

Intervention Type
Drug

Pharmaceutical study type(s)
Pharmacokinetic, Pharmacodynamic, Dose response

Phase
Phase I

Drug/device/biological/vaccine name(s)
SPL028 (deuterated N,N-dimethyltryptamine fumarate; d-DMT)

Primary outcome measure

Safety and tolerability of SPL028 with support therapy following intravenous (IV) and intramuscular (IM) administration:
1. Safety will be evaluated by monitoring of adverse events (AEs), vital signs (blood pressure [BP], heart rate [HR] and temperature), 12-lead electrocardiogram (ECG) evaluations cannulation and injection site reactions, clinical laboratory assessments (haematology, clinical chemistry, coagulation and urinalysis) and physical examination findings. Baseline to Day 29
2. Suicidal ideation and behaviour will be evaluated using the Beck Scale for Suicidal Ideation (BSS). Baseline to Day 15
3. Tolerability will be evaluated by reviewing the therapist's notes that document the subjective psychedelic effects and a tolerability assessment. At Day 1

Secondary outcome measures
1. PK IV using frequent blood sampling from pre-dose to 2 hours post-dose
2. PK IM using frequent blood sampling from pre-dose to 4 hours post-dose
3. PD – Wellbeing using The Warwick-Edinburgh Mental Well-being Scale (WEMWBS) on day -1 and at Day 15
4. PD – Anxiety using Spielberger's State-Trait Anxiety Inventory Trait Subscale (STAI-T) on day -1 and at Day 15
5. PD – Post-treatment changes using Post-Treatment Changes Scale (PTCS) and The Psychedelic Predictor Scale at Day 15
6. PD – Subjective experience using Mystical Experience Questionnaire (MEQ), The Ego Dissolution Inventory (EDI), Emotional Breakthrough Inventory (EBI), Challenging Experience Questionnaire (CEQ) at Day 1 post-dose (before the first post-dose integration session) and using Intensity Rating Visual Analogue Scale (IRVAS) at Day 1 post-dose (after the first post-dose integration session)
7. PD – arrythmia measured using continuous 12-lead Holter electrocardiogram (ECG) on Day -1, pre-dose, during-dosing, until at least 10 min after the 4 h (IV) and 5h (IM) post-dose PK blood sample, and at Day 2.
8. The degree of blinding measured using a Blinding Integrity Questionnaire (BIQ) at Day 1 post-dose, prior to the Integrations session

Overall study start date
29/06/2022

Overall study end date
15/12/2023

Eligibility

Participant inclusion criteria
1. Participant has a body mass index (BMI) of 18 to 33.9 kg/m², inclusive.
2. Participant has not been administered any Monoamine Oxidase (MAO) inhibitor class antidepressants for at least 3 months prior to Screening.
3. Registered with a GP in the UK.
4. Sufficient intelligence to understand the nature of the trial and any hazards of participation in it. Ability to communicate satisfactorily with the Investigator and therapist team to participate in, and comply with the requirements of, the entire trial.
5. Healthy as determined by a responsible physician, based on no clinically significant findings from medical evaluation including medical history, a physical examination, concomitant medication, vital signs, 12-lead ECG and clinical laboratory evaluations (including haematology, coagulation, biochemistry and urinalysis) at the Screening visit and admission.

6. Agree to follow the contraception requirements of the trial.
7. Willing to be contacted by email and telephone and video call.
8. Proficient in reading and writing English sufficient to complete questionnaires.
9. Willing to give written consent to have data entered into The Over-volunteering Prevention System.
10. Provision of giving written informed consent, which includes compliance with the requirements and restrictions listed in the consent form, after having the opportunity to discuss the trial with the Investigator or their delegate.

Part A – Cohorts 1 and 2 Only
1. Healthy participants aged 25 to 65 years, inclusive.
2. Healthy psychedelic-experienced participants (psychedelic-experienced is defined as having at least two previous experiences, with breakthrough [see Section 3.3.1 for definition], of serotonergic psychedelic drugs, including but not limited to: DMT, ayahausca, LSD, LSA [morning glory seeds], 2,5-Dimethoxy-4-iodoamphetamine [DOI], dimethoxybromoamphetamine [DOB], 2,5-Dimethoxy-4 chloroamphetamine [DOC], 2-(4-bromo-2,5-dimethoxyphenyl)ethanamine [2CB], 1-(2,5-Dimethoxy-4-ethylphenyl)-2-aminoethane [2CE], mescaline, peyote, san pedro, ibogaine and psilocybin [including mushroom species containing psilocybin]).
3. No psychedelic drug use 6 weeks prior to dosing (excluding the study drug) until the end of the study.

Part A – Cohorts 3, 4 and 5 Only
1. Healthy participants aged 25 to 65 years, inclusive.
2. Healthy participants with little to no psychedelic experience (defined as a maximum of two previous experiences that weren't breakthrough, including but not limited to: DMT, ayahausca, LSD, LSA, DOI, DOB, DOC, 2CB, 2CE, mescaline, peyote, san pedro, ibogaine and psilocybin [including mushroom species containing psilocybin]).
3. No psychedelic drug use 6 months prior to dosing (excluding the study drug) until the end of the study.

Participant type(s)
Healthy volunteer

Age group
Adult

Lower age limit
25 Years

Upper age limit
65 Years

Sex
Both

Target number of participants
40

Total final enrolment
38

Participant exclusion criteria

Psychiatric Exclusion Criteria

Participants with any of the following will be excluded from study participation:

1. Participant meets the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition (DSM-5) criteria for substance abuse disorder, as assessed by the Mini International Neuropsychiatric Interview (MINI) Version 7.0.2 at Screening, or a positive urine drugs of abuse result at Screening or Day -1 (excluding cannabis which is permitted to be taken up to 24 hours before each trial visit, but which may be detected in urine). Repeat tests may be considered by the Investigator with justification.
2. Current or clinically relevant history of a psychotic disorder, including schizophrenia, psychosis, bipolar disorder, delusional disorder, paranoid personality disorder, schizoaffective disorder, borderline personality disorder, emotionally unstable personality disorder or panic disorder, as assessed by a structured clinical interview (including the MINI Version 7.0.2).
3. In first-degree relatives, a clinically relevant history of a psychotic disorder, including schizophrenia, psychosis, bipolar disorder, delusional disorder, paranoid personality disorder or schizoaffective disorder. Significant history of mania (as determined by the Investigator and medical records, in agreement with the Sponsor's Medical Monitor).
4. Significant history of mania (as determined by the Investigator and medical records, in agreement with the Sponsor's Medical Monitor).
5. Psychiatric condition judged to be incompatible with establishment of rapport with the therapy team and/or safe exposure to DMT, based on the Investigator's clinical evaluation (e.g., borderline personality disorder).
6. Significant suicide risk, as defined by:

6.1. Suicidal ideation as endorsed on the BSS within 1 year prior to Screening or on Day -1, or
6.2. Suicidal behaviours within 1 year prior to Screening, or
6.3. History of serious suicide attempts in lifetime (i.e., those that require hospitalisation), or
6.4. Clinical assessment of significant suicide risk during Participant interview

General Medical Exclusion Criteria

Participants with any of the following will be excluded from study participation:

1. Clinically relevant history of abnormal physical or mental health interfering with the study as determined by medical history and physical examinations obtained during Screening, as judged by the Investigator (including [but not limited to]: neurological, psychiatric, endocrine, thyroid, cardiovascular, respiratory, GI, hepatic, haematological, musculoskeletal, immunological, renal, connective tissue diseases or disorders or any other medically relevant condition as judged by the Investigator).
2. Clinically relevant abnormal laboratory results (including hepatic and renal panels, complete blood count, chemistry panel and urinalysis), 12-lead ECG and vital signs, or physical findings at Screening and/or Day -1 as judged by the Investigator, that in the Investigator's opinion may constitute a risk for an individual who is exposed to DMT.

In case of uncertain or questionable results, tests performed during Screening may be repeated to confirm eligibility or judged to be clinically irrelevant for healthy participants.

3. Any acute condition or infection, or history of chronic illness or condition, that could interfere with, or for which the treatment might interfere with, the conduct of the study as outlined in this Protocol, or that would, in the opinion of the Investigator, pose an unacceptable risk to the participant in this study.
4. Current or previous medical history of any significant cardiovascular conditions, such as: coronary heart disease, arrhythmia, clinically significant ECG abnormality, artificial heart valve or current hypertension. In addition, any family history of long QT syndrome or sudden death (due to a cardiac event).
5. AST, ALT, gamma-glutamyl transferase (GGT) or total bilirubin levels >1 × ULN at Screening or

Day -1. Isolated raised bilirubin for participants suspected or confirmed to have Gilbert's syndrome can be permitted at the Investigator's discretion up to a total bilirubin level of 35 µmol /L. These laboratory evaluations may be repeated once per planned testing occasion(Screening and Day -1) at the discretion of the Investigator. If the repeat test is within the reference range of 1 × ULN, the participant may be included only if the Investigator considers that the previous finding will not introduce additional risk factors and will not interfere with interpretation of safety data.
6. Psychological or neurological (e.g., medical conditions associated with seizures or convulsions) chronic illness or condition, as deemed relevant by the Investigator, in agreement with the Sponsor's Medical Monitor.
7. Blood pressure and HR in the supine and standing position outside of the following ranges at Screening:
a. Systolic BP: 90 to 140 mmHg.
b. Diastolic BP: 40 to 90 mmHg.
c. Heart rate: 40 to 100 bpm.
Borderline values (i.e., values that are within 5 mmHg of the range for BP, or 5 bpm of the range for HR) will be repeated. Participants can be included if the repeat value is within the specified range or still borderline but deemed not clinically significant by the Investigator.
8. QT interval corrected for HR using Fridericia's formula (QTcF) values ≥450 msec (males) or ≥470 msec (females) at Screening or predose on Day 1. Triplicatemeasurements will be made; mean QTcF values ≥450 msec (males) or ≥470 msec (females) will lead to exclusion. A repeat (in triplicate) is permitted on one occasion for determination of eligibility at the discretion of the Investigator. If the repeat test is within the reference range, the participant may be included only if the Investigator considers that the previous finding will not introduce additional risk factors and will not interfere with interpretation of safety data.
9. Presence of clinically significant ECG abnormalities at the Screening visit, as defined by medical judgement.
10. Positive test for hepatitis B surface antigen (HBsAg), anti-hepatitis C antibody (anti-HCV) or human immunodeficiency virus I and II (anti-HIV I/II) at Screening.
11. Intake of >21 units of alcohol weekly, the inability to refrain from alcohol use from 24 hours prior to each visit during the study or a positive breath alcohol test result at Screening or Day -1. One unit is equivalent to a 285 mL glass of full-strength beer or 1 (30 mL) measure of spirits or 1 glass (100 mL) of wine.
12. Receipt of an investigational product (including prescription medicines) as part of another clinical trial within 3 months prior to Day -1 or in the Follow-up period of another clinical trial at the time of Screening for this study.
13. Use of prescription or non-prescription medications (except hormonal contraception and HRT), including herbal and nutritional supplements, or OTC medications taken within 28 days of dosing and throughout the study will be assessed on a case-by-case basis to determine if its use would compromise participant safety or interfere with study procedures or data interpretation. The participant may take paracetamol (less or equal to 4 g/day) or ibuprofen (less or equal to 1.6 g/day) for up to 4 hours prior to dosing.
14. Current use of a long-term prescription medicine and/or acute medicine deemed to pose a risk of interaction with the study drug, as assessed by the Investigator and in agreement with the Sponsor's Medical Monitor.
15. History of severe adverse reaction to any drug or history of severe adverse reaction to or sensitivity to serotonergic psychedelic drugs.
16. Participant of childbearing potential (POCBP) who are pregnant, lactating or planning to conceive, or who are sexually active with a partner capable of fathering a child, and not using a reliable method of contraception. A POCBP must have a negative serum pregnancy test at Screening, and a negative urine pregnancy test on Day -1. If a urine test cannot be confirmed as negative, a serum pregnancy test is required.

17. Donation of blood or plasma (more than 400 mL) within 3 months prior to dosing.
18. A phobia of needles or blood.
19. Unsuitable veins for venepuncture and/or cannulation.
20. Unlikely to cooperate with the requirements of the study, in the opinion of the Investigator or designee.
21. Objection by GP to participant entering the trial.

Part A - Cohorts 1 and 2 Only
1. Use of any serotonergic psychedelics (e.g., mescaline, LSD, psilocybin and DMT) within 6 weeks prior to dosing.
2. Unable to refrain from smoking cigarettes and e-cigarettes from 24 hours prior to dosing, and while in the CRU.

Part A – Cohorts 3, 4 and 5 Only
1. Use of any serotonergic psychedelics (e.g., mescaline, LSD, psilocybin and DMT) within 6 months prior to dosing.
2. Unable to refrain from smoking cigarettes and e-cigarettes from 24 hours prior to dosing, and while in the CRU.

Recruitment start date
16/01/2023

Recruitment end date
20/11/2023

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
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Sponsor information

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Sponsor type
Industry

Funder(s)

Funder type
Industry

Funder Name
Cybin UK Ltd

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal.

Intention to publish date
15/12/2024

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study are not expected to be made available due to commercial sensitivity.

IPD sharing plan summary
Not expected to be made available

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Other unpublished results	version 1.0	02/12/2024	16/12/2024	No	No