Study Title:
Efficacy and safety of COMP360 psilocybin therapy in anorexia nervosa: a proof-of-concept study.
Description (purpose of the study):
This study aims to explore the efficacy and safety of COMP360 25 mg as compared to COMP360 1 mg (control condition) administered with psychological support in participants with AN.
Primary Objective
• To assess the efficacy of COMP360 with psychological support in improving AN symptoms.
Secondary Objectives
• To assess the effects of COMP360 on associated obsessive-compulsive symptoms typical of AN.
• To assess effects of COMP360 on weight gain in participants with AN.
Safety Objective
• To assess the safety and tolerability of COMP360 delivered under supportive conditions.
Exploratory Objectives
• To assess the effects of COMP360 psilocybin therapy on changes in quality of life, psychosocial impairment, anxiety, and depressive symptoms.
• To assess the overall severity of AN symptoms and improvement according to clinical judgment.
• To assess readiness and motivation to change and eating disorder-related preoccupations and rituals.
• To assess acceptability of the treatment
Number of Participants: Up to 60 participants with AN will be randomised with a 2: I ratio to either 25 mg or I mg COMP360 with psychological support **(Our site target is to enroll 5 subjects)**
Eligibility criteria for Qualified participants:
Inclusion Criteria
To be eligible for the study, participants must meet the following criteria:

1. Signed ICF.
2. Any sex and aged 18 years or above at screening.
3. Meeting criteria for AN either restrictive or binge-purging type, according to the DSM-5, based on medical records, clinical assessment, BMI, and documented completion of MINI 7.0.2 and EDE at screening.
4. Have successfully discontinued all prohibited medications for a period of at least two weeks prior to baseline. For fluoxetine (Prozac), immediate cessation at screening period visit I a followed by at least four weeks of washout will be required prior to baseline.
5. Has a history of disordered eating with duration of at least 3 years prior to screening, that is consistent with AN.
6. BMI >15 kg/m2 and ≤ 20 kg/m2 For participants with a BMI <16 kg/m2 and> 18.5 kg/m2 at screening, approval from the Medical Monitor will be required. Any participant with a BMI > 18.5 kg/m2 must meet all of the criteria for AN except that, despite significant weight loss, the individual's weight is within or above the normal range.
7. Being otherwise medically stable at screening determined by clinical interview, clinical laboratory values, vital signs, ECG, and medical history.
8. Have at least one documented prior attempt at treatment in the past 3 years.
9. Agree to have the study team maintain contact with an identified companion for the duration of the study.
10. Able to complete all protocol required assessment tools without any assistance or alteration to the copyrighted assessments, and to comply with all study visits.

Exclusion Criteria

Exclusion of potentially confounding psychiatric diseases and therapies:

1. Prior or ongoing bipolar disorder, any psychotic disorder, including schizophrenia, schizophreniform disorder, schizoaffective disorder, brief psychotic disorder (unless substance induced or due to a medical condition), antisocial personality disorder, or any serious psychiatric comorbidity as assessed by medical history and a structured clinical interview (MINI 7.0.2).
2. Prior or ongoing paranoid, schizoid, schizotypal, histrionic, narcissistic personality disorder based on medical history and clinical judgment.
3. Borderline personality disorder as demonstrated by medical history, the MINI Plus – BPD and clinical judgment.
4. Significant suicide risk as defined by (I) suicidal ideation as endorsed on items 4 or 5 on the C-SSRS within the past year, at screening or at baseline, or; (2) suicidal behaviours within the past year or; (3) clinical assessment of significant suicidal risk during participant interview.
5. Current (within last year) alcohol or substance use disorder as informed by the DSM-5 assessed via the MINI 7.0.2, and urine toxicology at screening.
6. Other personal circumstances and behaviour judged to be incompatible with establishment of rapport or safe exposure to psilocybin.
7. Exposure to psilocybin, or any other psychedelics, such as ayahuasca, mescaline, LSD, or peyote within the past year.

General medical exclusion criteria:

1. Significant weight loss (> I kg per week) between screening and baseline.
2. Abnormal and clinically significant results on the physical examination.
3. A participant who is pregnant, nursing, or planning to conceive. Males and females who engage in sexual intercourse which could result in pregnancy, must agree to use a highly effective contraceptive method (as listed in Section I 0.1.2) throughout their participation in the study. Participants of childbearing potential must have a negative serum pregnancy test at screening, and negative urine pregnancy test at baseline. Participants should be informed not to donate sperm during the study period or for at least three months after COMP360 administration.
4. Clinically significant laboratory test abnormalities at screening including full blood count (hemoglobin <l O g/dL), alanine aminotransferase (ALT) or aspartate aminotransferase (AST) $\geq$ 3 x upper limit of normal (ULN), total bilirubin $\geq$ 1.5 x ULN or alkaline Phosphatase $\geq$ 2.5 x ULN, reduced glomerular filtration rate (GFR< 60) or creatinine > 1.5 x ULN.
5. Gilbert's syndrome.
6. Cardiovascular conditions: recent stroke (< l year prior to signing ICF), recent myocardial infarction (<1 year prior to signing ICF), uncontrolled hypertension (blood pressure > 140/90 mm Hg), bradycardia (<50 beats per minute [bpm]), elongated corrected QT interval by Fredericia (QTcF; >450 ms for men and >470 ms for women), clinically significant arrhythmia (<1 year prior to signing the ICF) based on vital signs and ECG measurement at screening and baseline and medical history.

7. Diabetes type I or uncontrolled diabetes type 2.
8. Epilepsy or history of seizures.
9. Positive urine drug screen for illicit drugs or drugs of abuse at screening and/or baseline.

Any positive urine drug test will be reviewed with participants to determine the pattern of use and eligibility will be determined at the investigator's discretion in conjunction with the medical monitor.

COMPENSATION PER VISIT

Visit#	Intervention Period (Weeks)	Stipend Amount
Visit-I	Screening	$90.00
Phone call-I	Screening Period	$60.00
Visit IA	Screening Period	$60.00
Phone call-2	Screening Period	$60.00
Visit IB	Screening Period	$60.00
Phone call-3	Screening Period	$60.00
Visit- 2	Baseline	$80
Visit- 3	Administration day	$170.00
Visit- 4	Day2	$100.00
Visit- 5	Week1	$60.00
Visit- 6	Week2	$60.00
Visit- 7	Week3	$30.00
Visit- 8	Week4	$80.00
Visit- 9	Week6	$30.00
Visit- 10	Week8	$30.00
Visit- 11	Week10	$30.00
Visit-12/Early Termination	Week 12	$80.00
Unscheduled Visit	Unscheduled Visit	$0.00
Any extra screening visit/phone call	Screening Period	$60.00 for each screening visit/phone call

CONTACT : email: psychclinicaltrials@austin.utexas.edu ; fouzia.sheikh@austin.utexas.edu

Phone# 512-495-5566