Clinical trial results:
The Effect of Psilocybin on MDD Symptom Severity and Synaptic Density – A Single Dose Randomized, Double Blind, Placebo-Controlled Phase 2 Positron Emission Tomography Study

Summary

EudraCT number	2020-002790-94
Trial protocol	SE
Global end of trial date	20 June 2025

Results information

Result version number	v1 (current)
This version publication date	22 November 2026
First version publication date	22 November 2026

Trial information

Trial identification

Sponsor protocol code	200828

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT04630964
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Norra Stockholms Psykiatri
Sponsor organisation address	Vårdvägen 3, Stockholm, Sweden, 112 19
Public contact	PSIPET information, SLSO, johanna.evengard@sll.se
Scientific contact	PSIPET information, SLSO, johanna.evengard@sll.se

Notes:

Paediatric regulatory details

Is trial part of an agreed paediatric investigation plan (PIP)	No
Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial?	No
Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial?	No

Notes:

Results analysis stage

Analysis stage	Final
Date of interim/final analysis	20 June 2025
Is this the analysis of the primary completion data?	Yes
Primary completion date	20 June 2025
Global end of trial reached?	Yes
Global end of trial date	20 June 2025
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective of this study is to evaluate the efficacy of a single 25 mg oral dose of psilocybin for major depressive disorder (MDD) compared to an active placebo (niacin) in otherwise medically-healthy participants between the ages of 20 and 65, assessed as the difference between groups in changes in depressive symptoms.

Protection of trial subjects:

screening including psychiatric assessment, medical examination, ECG, toxicology, pregnancy test and MR
Close follow-up

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	04 January 2021
Long term follow-up planned	Yes
Long term follow-up rationale	Safety, Efficacy
Long term follow-up duration	1 Years
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Sweden: 35
Worldwide total number of subjects	35
EEA total number of subjects	35

Notes:

Subjects enrolled per age group

In utero	0
Preterm newborn - gestational age < 37 wk	0
Newborns (0-27 days)	0
Infants and toddlers (28 days-23 months)	0
Children (2-11 years)	0
Adolescents (12-17 years)	0

Adults (18-64 years)	35
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

Recruitment took place between january 2021 and january 2023 in Stockholm, Sweden.

Pre-assignment

Screening details:

Participants were recruited via social media and Google Ads. Digital prescreening was followed by an in-person screening visit.
Incl/excl criteria can be found at https://clinicaltrials.gov/study/NCT04630964
748 potential participants registered on the study homepage, 63 proceeded to in-person screening, 39 were included.

Period 1

Period 1 title	overall trial (overall period)
Is this the baseline period?	Yes
Allocation method	Randomised - controlled
Blinding used	Double blind
Roles blinded	Subject, Investigator, Monitor, Data analyst, Carer, Assessor

Arms

Are arms mutually exclusive?	Yes
Arm title	Psilocybin

Arm description: -

Arm type	Experimental
Investigational medicinal product name	Psilocybin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

25 mg

Arm title	Niacin

Arm description: -

Arm type	Placebo
Investigational medicinal product name	Niacin
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

100mg

Number of subjects in period 1	Psilocybin	Niacin
Started	17	18
Completed	17	17
Not completed	0	1
Consent withdrawn by subject	-	1

Baseline characteristics

Reporting groups	
Reporting group title	Psilocybin
Reporting group description: -	
Reporting group title	Niacin
Reporting group description: -	

Reporting group values	Psilocybin	Niacin	Total
Number of subjects	17	18	35
Age categorical Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	17	18	35
85 years and over	0	0	0
Age continuous			
Mean age 41 years (40.97), range 22-61 years			
Units: years			
arithmetic mean	39.6	42.2	
full range (min-max)	22 to 58	22 to 61	-
Gender categorical			
14 male,21 female			
Units: Subjects			
Female	10	11	21
Male	7	7	14

End points

End points reporting groups	
Reporting group title	Psilocybin
Reporting group description: -	
Reporting group title	Niacin
Reporting group description: -	

Primary: MADRS score at day 8	
End point title	MADRS score at day 8
End point description:	
Observed MADRS scores at day 8 are presented as arithmetic means. The model-adjusted between-group difference in the primary analysis was −7.27 MADRS points (95% CI −12.89 to −1.65; p = 0.01).	
End point type	Primary
End point timeframe:	
Day 8	

End point values	Psilocybin	Niacin		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	17		
Units: MADRS points				
number (not applicable)	12.59	20.71		

Statistical analyses

Statistical analysis title	MMRM
Statistical analysis description:	
Mixed-effects model for repeated measures (MMRM) comparing MADRS scores between the psilocybin and niacin groups, adjusting for baseline MADRS score and accounting for repeated measurements over time.	
Comparison groups	Psilocybin v Niacin
Number of subjects included in analysis	34
Analysis specification	Pre-specified
Analysis type	superiority[1]
P-value	= 0.01 [2]
Method	Mixed models analysis
Parameter estimate	Median difference (final values)
Point estimate	-7.27
Confidence interval	
level	95 %
sides	2-sided
lower limit	-12.89
upper limit	-1.65

Notes:

[1] - Between-group difference in MADRS change from baseline to day 8, estimated using a mixed model for repeated measures (MMRM), adjusted for baseline MADRS, with fixed effects for treatment, time and treatment-by-time interaction.

[2] - P-value derived from the model-adjusted between-group comparison at day 8.

Adverse events

Adverse events information	
Timeframe for reporting adverse events: Jan 2021- feb 2024	
Assessment type	Systematic
Dictionary used	
Dictionary name	MedDRA
Dictionary version	10.0
Reporting groups	
Reporting group title	Psilocybin
Reporting group description: 48 adverse events reported to be related to study medication	
Reporting group title	Niacin
Reporting group description: 15 AEs reported to be related to study medication	

Serious adverse events	Psilocybin	Niacin	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 17 (0.00%)	0 / 18 (0.00%)	
number of deaths (all causes)	0	0	
number of deaths resulting from adverse events	0	0	

Frequency threshold for reporting non-serious adverse events: 5 %

Non-serious adverse events	Psilocybin	Niacin	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	16 / 17 (94.12%)	11 / 18 (61.11%)	
Vascular disorders			
presyncope			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
thromboembolic event			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Psychiatric disorders			
anxiety			

subjects affected / exposed	7 / 17 (41.18%)	3 / 18 (16.67%)	
occurrences (all)	9	3	
delusion			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Euphoric mood			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
hallucination			
subjects affected / exposed	5 / 17 (29.41%)	0 / 18 (0.00%)	
occurrences (all)	5	0	
insomnia			
subjects affected / exposed	2 / 17 (11.76%)	0 / 18 (0.00%)	
occurrences (all)	2	0	
irritability			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
psychiatric disorders - other specify: vivid dreams			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
suicidal ideation			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Injury, poisoning and procedural complications			
fall			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Cardiac disorders			
Hypertension			
subjects affected / exposed	3 / 17 (17.65%)	0 / 18 (0.00%)	
occurrences (all)	3	0	
sinus tachycardia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Nervous system disorders			

agitation				
subjects affected / exposed	3 / 17 (17.65%)	1 / 18 (5.56%)		
occurrences (all)	3	1		
Ataxia				
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)		
occurrences (all)	1	0		
confusion				
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)		
occurrences (all)	1	0		
dysphasia				
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)		
occurrences (all)	1	0		
headache				
subjects affected / exposed	10 / 17 (58.82%)	6 / 18 (33.33%)		
occurrences (all)	10	9		
hot flashes				
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)		
occurrences (all)	1	0		
movements involuntary				
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)		
occurrences (all)	1	0		
nervous system disorders - other specify: metallic taste				
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)		
occurrences (all)	1	0		
paresthesia				
subjects affected / exposed	3 / 17 (17.65%)	2 / 18 (11.11%)		
occurrences (all)	3	2		
peripheral sensory neuropathy				
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)		
occurrences (all)	0	1		
seizure				
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)		
occurrences (all)	1	0		
Tremor				

subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
vertigo			
subjects affected / exposed	1 / 17 (5.88%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Eye disorders			
blurred vision			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Dyspepsia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
flatulence			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Lower gastrointestinal haemorrhage			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
Nausea			
subjects affected / exposed	2 / 17 (11.76%)	1 / 18 (5.56%)	
occurrences (all)	2	1	
Hepatobiliary disorders			
alanine aminotransferase increased aspartate aminotransferase incr			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Skin and subcutaneous tissue disorders			
Alopecia			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
urinary incontinence			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Musculoskeletal and connective tissue disorders			

Arthralgia			
subjects affected / exposed	1 / 17 (5.88%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
back pain			
subjects affected / exposed	1 / 17 (5.88%)	1 / 18 (5.56%)	
occurrences (all)	1	1	
Infections and infestations			
tooth infection			
subjects affected / exposed	0 / 17 (0.00%)	1 / 18 (5.56%)	
occurrences (all)	0	1	
upper respiratory infection			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	
occurrences (all)	1	0	
Metabolism and nutrition disorders			
weight loss			
subjects affected / exposed	1 / 17 (5.88%)	0 / 18 (0.00%)	
occurrences (all)	1	0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
09 January 2023	Skin biopsy

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported