Clinical trial results:
Safety and efficacy of repeated low dose D-lysergic acid diethylamide (LSD) D-Tartrate (MM-120) as treatment for ADHD in adults: a multi-center, randomized, double- blind, placebo-controlled Phase 2a Proof of Concept Trial

Summary

EudraCT number	2020-001098-55
Trial protocol	NL
Global end of trial date	04 December 2023

Results information

Result version number	v1 (current)
This version publication date	14 November 2024
First version publication date	14 November 2024

Trial information

Trial identification

Sponsor protocol code	MMED007

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT05200936
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Mind Medicine, Inc.
Sponsor organisation address	One World Trade Center, Suite 8500, New York, United States, NY1007
Public contact	Dan Karlin, Mind Medicine, Inc., +1 917-699-6564, dkarlin@mindmed.co
Scientific contact	Dan Karlin, Mind Medicine, Inc., +1 917-699-6564, dkarlin@mindmed.co

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	04 December 2023
Is this the analysis of the primary completion data?	Yes
Primary completion date	04 December 2023
Global end of trial reached?	Yes
Global end of trial date	04 December 2023
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

To assess the treatment efficacy vs placebo of repeated low doses (20 µg) of MM120 for six weeks in adult subjects with attention-deficit/hyperactivity disorder (ADHD) measured by Adult Attention Deficit Investigator Symptom Rating Scale (AISRS).

Protection of trial subjects:

The conduct of this clinical study met all local legal and regulatory requirements. The study was conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki and the International Council for Harmonization (ICH) guideline E6: Good Clinical Practice (GCP). Before a subject participated in the study, written informed consent was obtained. The subject was asked to read a subject information section of the consent form prospectively approved by the Ethics Committee and to sign it to indicate consent to participate in the study. Informed consent was obtained before the initiation of any study procedures for each subject. If the subject was not capable of providing a signature, an oral statement of consent could be given in the presence of a witness.

Background therapy: -

Evidence for comparator:

Placebo used as a comparator to assess the efficacy of the IMP.

Actual start date of recruitment	20 December 2021
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	No

Notes:

Population of trial subjects

Subjects enrolled per country

Country: Number of subjects enrolled	Netherlands: 3
Country: Number of subjects enrolled	Switzerland: 50
Worldwide total number of subjects	53
EEA total number of subjects	3

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)	53
From 65 to 84 years	0
85 years and over	0

Subject disposition

Recruitment

Recruitment details:

A total of 52 subjects were planned to be enrolled in this study, in the Netherlands and in Switzerland, of which 26 are expected to be recruited in Basel. Advertisement flyers that were hung around UHB and Maastricht University were used early in the study in May 2020 to June 2023.

Pre-assignment

Screening details:

A total of 74 subjects were screened, 21 out of 74 subjects failed screening. The reason for subjects failing screening was not meeting the inclusion/exclusion criteria. 53 subjects were randomized in the study. A total of 53 subjects were analysed in the Full Analysis Set (FAS) and Safety Set (SAF).

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

Arms

Are arms mutually exclusive?	Yes
Arm title	MM120

Arm description:

Subjects receive 20 µg of MM120 administered orally twice weekly for 6 weeks.

Arm type	Experimental
Investigational medicinal product name	D-Lysergic Acid Diethylamide (LSD) D-Tartrate
Investigational medicinal product code	MM120
Other name	LSD D-tartrate
Pharmaceutical forms	Oral solution
Routes of administration	Oral use

Dosage and administration details:

LSD-tartrate 0.029mg (corresp. 0.020 mg LSD), ethanol 0.16 g, aqua pur ad 1 mL
Subjects to receive MM120 twice weekly for 6 weeks.

Arm title	Placebo

Arm description:

Subjects receive Placebo administered orally twice weekly for 6 weeks.

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

Dosage and administration details:

Ethanol 0.16 g aqua pur ad 1 mL
Subjects to receive Placebo twice weekly for 6 weeks.

Number of subjects in period 1	MM120	Placebo
Started	27	26
Completed	23	23
Not completed	4	3
Consent withdrawn by subject	2	2
Pregnancy	-	1
Lost to follow-up	2	-

Baseline characteristics

Reporting groups	
Reporting group title	MM120
Reporting group description:	
Subjects receive 20 µg of MM120 administered orally twice weekly for 6 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects receive Placebo administered orally twice weekly for 6 weeks.	

Reporting group values	MM120	Placebo	Total
Number of subjects	27	26	53
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)	27	26	53
From 65-84 years	0	0	0
85 years and over	0	0	0
Age continuous			
Units: years			
arithmetic mean	40.3	33.1	
standard deviation	± 12.82	± 11.00	-
Gender categorical			
Units: Subjects			
Female	13	9	22
Male	14	17	31
Country			
Units: Subjects			
Switzerland	25	25	50
Netherlands	2	1	3
AISRS Score			
AISRS - Adult ADHD investigator symptom rating scale			
Units: score on a scale			
arithmetic mean	37.3	36.9	
standard deviation	± 5.83	± 5.10	-
CGI - Severity			
CGI - Clinical Global Impression			
Units: Score on a scale			
arithmetic mean	4.9	4.7	
standard deviation	± 0.72	± 0.62	-
ASRS Score			
ASRS - Adult attention-deficit/hyperactivity disorder self-reporting rating scale			

N= 26 for MM120 group			
Units: Score on a scale			
arithmetic mean	47.3	43.9	
standard deviation	± 7.72	± 7.33	-
CAARS-L-SR: ADHD Index			
ADHD = Attention-deficit/hyperactivity disorder; CAARS-L-SR = Connors' adult ADHD rating scale self-report long form			
Units: Score on a scale			
arithmetic mean	27.1	22.3	
standard deviation	± 13.32	± 9.25	-

End points

End points reporting groups	
Reporting group title	MM120
Reporting group description:	
Subjects receive 20 µg of MM120 administered orally twice weekly for 6 weeks.	
Reporting group title	Placebo
Reporting group description:	
Subjects receive Placebo administered orally twice weekly for 6 weeks.	

Primary: Change from Baseline to Week 6 in AISRS score

End point title	Change from Baseline to Week 6 in AISRS score

End point description:

AISRS = Adult ADHD investigator symptom rating scale
The AISRS total score consists of 18 items from the original Attention-deficit/hyperactivity Disorder Rating Scale (ADHD-RS), which were derived based on DSM-5 criteria for ADHD. The ADHD-RS includes 9 items that address symptoms of inattention, and 9 items that address symptoms of impulsivity and hyperactivity. Each item is rated from 0 to 3. The AISRS total score can range from 0 to 54. A higher score corresponds to a worse severity of ADHD.

End point type	Primary

End point timeframe:

Baseline to Week 6

End point values	MM120	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: score on a scale				
least squares mean (standard error)	-7.68 (± 1.59)	-8.96 (± 1.60)		

Statistical analyses

Statistical analysis title	Change from Baseline to Week 6 in AISRS score
Comparison groups	MM120 v Placebo
Number of subjects included in analysis	53
Analysis specification	Pre-specified
Analysis type	superiority
P-value	= 0.7145 [1]
Method	Mixed model for repeated measures
Parameter estimate	Least Squares Mean
Point estimate	1.28

Confidence interval	
level	95 %
sides	2-sided
lower limit	-3.14
upper limit	5.69
Variability estimate	Standard error of the mean
Dispersion value	2.25

Notes:

[1] - p-value is one-sided

Secondary: Summary of Change from Baseline to Week 2 (predose) in AISRS score

End point title	Summary of Change from Baseline to Week 2 (predose) in AISRS score

End point description:

AISRS = Adult ADHD investigator symptom rating scale
The AISRS total score consists of 18 items from the original Attention-deficit/hyperactivity Disorder Rating Scale (ADHD-RS), which were derived based on DSM-5 criteria for ADHD. The ADHD-RS includes 9 items that address symptoms of inattention, and 9 items that address symptoms of impulsivity and hyperactivity. Each item is rated from 0 to 3. The AISRS total score can range from 0 to 54. A higher score corresponds to a worse severity of ADHD.

End point type	Secondary

End point timeframe:

Baseline to Week 2

End point values	MM120	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: Score on a scale				
arithmetic mean (standard deviation)	-3.3 (± 3.62)	-4.8 (± 3.24)		

Statistical analyses

No statistical analyses for this end point

Secondary: Occurrence of subjects who experienced at least a 1-point decrease in the CGI-S

End point title	Occurrence of subjects who experienced at least a 1-point decrease in the CGI-S

End point description:

CGI-S = Clinical global impression-severity scale
The Clinical Global Impression – Severity scale (CGI-S) is a 7-point scale that requires the clinician to rate the severity of the patient's illness at the time of assessment. Possible ratings are:
1. Normal, not at all ill
2. Borderline mentally ill
3. Mildly ill
4. Moderately ill
5. Markedly ill
6. Severely ill
7. Among the most extremely ill patients

End point type	Secondary

End point timeframe:

Baseline to Week 6

End point values	MM120	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Subjects	18	15		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Change from Baseline to Week 2 (predose) of CGI-S

End point title	Summary of Change from Baseline to Week 2 (predose) of CGI-S

End point description:

CGI-S = Clinical global impression-severity scale
The Clinical Global Impression – Severity scale (CGI-S) is a 7-point scale that requires the clinician to rate the severity of the patient's illness at the time of assessment. Possible ratings are:
1. Normal, not at all ill
2. Borderline mentally ill
3. Mildly ill
4. Moderately ill
5. Markedly ill
6. Severely ill
7. Among the most extremely ill patients

End point type	Secondary

End point timeframe:

Baseline to Week 2

End point values	MM120	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	26	26		
Units: Score on a scale				
arithmetic mean (standard deviation)	-0.3 (± 0.47)	-0.4 (± 0.50)		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Change from Baseline to Week 6 of CGI-S

End point title	Summary of Change from Baseline to Week 6 of CGI-S

End point description:

CGI-S = Clinical global impression-severity scale
The Clinical Global Impression – Severity scale (CGI-S) is a 7-point scale that requires the clinician to rate the severity of the patient's illness at the time of assessment. Possible ratings are:
1. Normal, not at all ill
2. Borderline mentally ill
3. Mildly ill
4. Moderately ill
5. Markedly ill
6. Severely ill
7. Among the most extremely ill patients

End point type	Secondary

End point timeframe:

Baseline to Week 6

End point values	MM120	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	23	23		
Units: Score on a scale				
arithmetic mean (standard deviation)	-0.9 (± 0.69)	-1.0 (± 0.95)		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Change from Baseline to Week 6 (Day 40) of ASRS Score

End point title	Summary of Change from Baseline to Week 6 (Day 40) of ASRS Score

End point description:

ASRS = Adult attention-deficit/hyperactivity disorder self-reporting rating scale
The Adult Attention-Deficit/Hyperactivity Disorder Self-Reporting Rating Scale (ASRS) is composed of 18 questions, and uses a scale that ranges from 0-4 based on the individuals mark in either the "never, rarely, sometimes, often, very often" column for a possible total score of 72.

End point type	Secondary

End point timeframe:

Baseline to Week 6

End point values	MM120	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	17	22		
Units: Score on a scale				
arithmetic mean (standard deviation)	-18.6 (± 10.66)	-12.3 (± 10.93)		

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of Change from Baseline to Week 6 (Day 40) of CAARS

End point title	Summary of Change from Baseline to Week 6 (Day 40) of CAARS

End point description:

ADHD = Attention-deficit/hyperactivity disorder; CAARS = Connors' adult ADHD rating scale; DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Ed

The CAARS Self-Report Long Form is a 66-item measure of ADHD symptoms that was designed as a self-report assessment for adult ADHD. Responses are scored on a 4-point scale, where 0 = not at all, 1 = just a little, 2 = pretty much, and 3 = very much.

End point type	Secondary

End point timeframe:

Baseline to Week 6

End point values	MM120	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	18[2]	21		
Units: Score on a scale				
arithmetic mean (full range (min-max))				
DSM-IV Inattentive Symptoms Week 6	-6.3 (-15 to 5)	-4.3 (-16 to 6)		
DSM-IV Hyperactive/ Impulsive symptoms Week 6	-5.3 (-15 to 3)	-2.4 (-15 to 5)		
DSM-IV ADHD Symptoms Total Week 6	-11.6 (-30 to 7)	-6.8 (-30 to 6)		
ADHD Index Week 6	-7.8 (-18 to 2)	-4.8 (-16 to 1)		
Inattention/ Memory problems Week 6	-7.8 (-16 to 1)	-6.0 (-22 to 3)		
Hyperactivity/ Restlessness Week 6	-8.0 (-17 to 1)	-4.4 (-21 to 7)		
Impulsivity/ Emotional lability Week 6	-7.9 (-20 to 6)	-5.0 (-21 to 6)		
Problems with self-concept Week 6	-3.6 (-10 to 1)	-1.9 (-9 to 4)		

Notes:

[2] - N=17 Inattention problem, Hyperactivity Restlessness,Impulsivity/ Emotional ability and problems wSC

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of 5D-ASC Total Score at Week 1 Day 1 and Week 6

End point title	Summary of 5D-ASC Total Score at Week 1 Day 1 and Week 6

End point description:

5D-ASC = 5 dimensions of altered states of consciousness scale
The 5 dimensions of altered states of consciousness (5D-ASC) scale is a visual analog scale consisting of 94 items (Dittrich, 1998; Studerus et al., 2010). The instrument is constructed of five scales, and allows assessing mood, anxiety, derealization, depersonalization, changes in perception, auditory alterations, and reduced vigilance.

End point type	Secondary

End point timeframe:

From Week 1 Day 1 to Week 6

End point values	MM120	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27[3]	26[4]		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Oceanic boundlessness Week 1 Day 1	479.6 (± 511.47)	161.3 (± 334.52)		
Anxious ego dissolution Week 1 Day 1	103.6 (± 171.94)	19.0 (± 32.53)		
Visionary destructuralization Week 1 Day 1	233.4 (± 247.17)	94.8 (± 188.58)		
Auditory alterations Week 1 Day 1	71.0 (± 148.54)	32.7 (± 77.09)		
Vigilance reduction Week 1 Day 1	288.5 (± 228.77)	155.2 (± 187.82)		
Total score Week 1 Day 1	1176.0 (± 997.40)	463.0 (± 733.11)		
Oceanic boundlessness Week 6	403.3 (± 483.36)	70.2 (± 125.32)		
Anxious ego dissolution Week 6	41.0 (± 96.29)	4.2 (± 10.53)		
Visionary destructuralization Week 6	199.7 (± 260.91)	32.9 (± 61.36)		
Auditory alterations Week 6	18.4 (± 42.26)	4.2 (± 9.75)		
Vigilance reduction Week 6	90.3 (± 88.27)	20.0 (± 30.40)		
Total Score Week 6	752.9 (± 845.69)	131.4 (± 188.21)		

Notes:

[3] - N = 23 for Week 6

[4] - N = 23 for Week 6

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of MEQ30 at Week 1 Day 1 and Week 6

End point title	Summary of MEQ30 at Week 1 Day 1 and Week 6

End point description:

MEQ30 = Mystical experience questionnaire 30 items
This 30-item questionnaire is rated on a six-point scale.

End point type	Secondary

End point timeframe:

From Week 1 Day 1 to Week 6

End point values	MM120	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27[5]	26[6]		
Units: Score on a scale				
arithmetic mean (standard deviation)				
Week 1 Day 1	22.37 (± 19.720)	10.40 (± 15.929)		
Week 6	20.50 (± 19.791)	5.20 (± 8.585)		

Notes:

[5] - N= 23 for Week 6

[6] - N= 22 for Week 6

Statistical analyses

No statistical analyses for this end point

Secondary: Summary of VAS Scores Before and After the First Dose

End point title	Summary of VAS Scores Before and After the First Dose

End point description:

VAS = Visual analog scale
The boundaries blur = The boundaries between myself and my surroundings seem to blur

End point type	Secondary

End point timeframe:

Time between 0 to 6 hours post first dose

End point values	MM120	Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	27	26		
Units: Score on a scale				
arithmetic mean (full range (min-max))				
Time 0 (predose) - Any drug effect	0.0 (0 to 0)	0.0 (0 to 0)		
Time 0 (predose) - Drug liking	37.1 (0 to 55)	44.9 (0 to 52)		
Time 0 (predose) - Fear	2.7 (0 to 36)	1.4 (0 to 23)		
Time 0 (predose) - Nausea	1.1 (0 to 30)	0.0 (0 to 0)		
Time 0 (predose) - Alteration of vision	0.0 (0 to 0)	0.0 (0 to 0)		
Time 0 (predose) - Alteration of sense of time	0.0 (0 to 0)	0.0 (0 to 0)		
Time 0 (predose) - The boundaries blur	0.0 (0 to 0)	0.0 (0 to 0)		
0.5 hours post dose - Any drug effect	8.9 (0 to 78)	11.3 (0 to 75)		
0.5 hours post dose - Drug liking	44.4 (0 to 78)	48.1 (0 to 83)		
0.5 hours post dose - Fear	2.0 (0 to 54)	2.2 (0 to 48)		
0.5 hours post dose - Nausea	2.0 (0 to 53)	0.2 (0 to 3)		
0.5 hours post dose - Alteration of vision	3.5 (0 to 54)	7.4 (0 to 81)		
0.5 hours post dose - Alteration of sense of time	2.5 (0 to 41)	3.2 (0 to 35)		
0.5 hours post dose - The boundaries blur	3.0 (0 to 71)	0.8 (0 to 12)		
1 hour post dose - Any drug effect	24.1 (0 to 100)	12.7 (0 to 64)		
1 hour post dose - Drug liking	49.7 (0 to 97)	51.8 (2 to 97)		

1 hour post dose - Fear	1.4 (0 to 32)	0.1 (0 to 2)		
1 hour post dose - Nausea	2.7 (0 to 37)	1.0 (0 to 23)		
1 hour post dose - Alteration of vision	4.0 (0 to 56)	6.9 (0 to 72)		
1 hour post dose - Alteration of sense of time	8.1 (0 to 73)	6.3 (0 to 68)		
1 hour post dose - The boundaries blur	6.0 (0 to 87)	1.5 (0 to 24)		
2 hours post dose - Any drug effect	38.1 (0 to 97)	12.8 (0 to 72)		
2 hours post dose - Drug liking	57.3 (0 to 100)	53.3 (3 to 100)		
2 hours post dose - Fear	4.1 (0 to 68)	0.1 (0 to 2)		
2 hours post dose - Nausea	8.2 (0 to 60)	0.1 (0 to 2)		
2 hours post dose - Alteration of vision	13.0 (0 to 84)	6.2 (0 to 88)		
2 hours post dose - Alteration of sense of time	13.5 (0 to 78)	4.4 (0 to 53)		
2 hours post dose - The boundaries blur	12.3 (0 to 83)	1.3 (0 to 14)		
3 hours post dose - Any drug effect	44.3 (0 to 97)	11.1 (0 to 65)		
3 hours post dose - Drug liking	61.6 (0 to 100)	53.1 (3 to 96)		
3 hours post dose - Fear	2.9 (0 to 54)	0.2 (0 to 2)		
3 hours post dose - Nausea	8.0 (0 to 56)	0.2 (0 to 3)		
3 hours post dose - Alteration of vision	13.9 (0 to 84)	6.5 (0 to 76)		
3 hours post dose - Alteration of sense of time	12.3 (0 to 89)	4.9 (0 to 74)		
3 hours post dose - The boundaries blur	12.7 (0 to 88)	1.4 (0 to 31)		
4 hours post dose - Any drug effect	38.5 (0 to 97)	15.1 (0 to 100)		
4 hours post dose - Drug liking	60.7 (0 to 100)	48.0 (2 to 100)		
4 hours post dose - Fear	2.7 (0 to 50)	0.1 (0 to 2)		
4 hours post dose - Nausea	6.9 (0 to 65)	0.1 (0 to 2)		
4 hours post dose - Alteration of vision	12.4 (0 to 86)	3.2 (0 to 37)		
4 hours post dose - Alteration of sense of time	12.1 (0 to 92)	7.0 (0 to 57)		
4 hours post dose - The boundaries blur	6.9 (0 to 69)	0.2 (0 to 2)		
6 hours post dose - Any drug effect	16.7 (0 to 75)	9.6 (0 to 72)		
6 hours post dose - Drug liking	54.8 (0 to 100)	49.6 (0 to 100)		
6 hours post dose - Fear	2.3 (0 to 52)	2.1 (0 to 48)		
6 hours post dose - Nausea	3.6 (0 to 52)	0.2 (0 to 4)		
6 hours post dose - Alteration of vision	4.1 (0 to 59)	5.8 (0 to 59)		
6 hours post dose - Alteration of sense of time	6.3 (0 to 69)	3.0 (0 to 55)		
6 hours post dose - The boundaries blur	4.1 (0 to 61)	0.1 (0 to 2)		

Statistical analyses

No statistical analyses for this end point

Secondary: Maximum Plasma Concentration (Cmax) of MM120

End point title	Maximum Plasma Concentration (Cmax) of MM120[7]
End point description:	
Cmax = maximum plasma concentration	
End point type	Secondary
End point timeframe:	
Between 0 -6 hours after first dose	

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic parameters were only studied for MM120 administered subjects.

End point values	MM120			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: ng/mL				
arithmetic mean (standard deviation)	0.4811 (± 0.14279)			

Statistical analyses

No statistical analyses for this end point

Secondary: Time to maximum plasma concentration (tmax) of MM120

End point title	Time to maximum plasma concentration (tmax) of MM120[8]

End point description:

Tmax = time to peak plasma concentration

End point type	Secondary

End point timeframe:

Between 0 -6 hours after first dose

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic parameters were only studied for MM120 administered subjects.

End point values	MM120			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: hour				
median (full range (min-max))	1.00 (0.5 to 3.0)			

Statistical analyses

No statistical analyses for this end point

Secondary: The half- life (t½) of MM120 Plasma concentration

End point title	The half- life (t½) of MM120 Plasma concentration[9]

End point description:

t1/2 = half-life,
The PK parameters AUC0-inf and t½ are not reported for the individual PK profiles where lambda was not measured (e.g., fewer than 3 non-zero concentrations in the terminal elimination phase or adjusted Rsq <0.8).

End point type	Secondary

End point timeframe:

Between 0 -6 hours after first dose

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic parameters were only studied for MM120 administered subjects.

End point values	MM120			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: hour				
arithmetic mean (standard deviation)	3.8187 (± 1.27269)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the Plasma Concentration time curve from time 0 to Infinity (AUC 0-inf) of MM120

End point title	Area under the Plasma Concentration time curve from time 0 to Infinity (AUC 0-inf) of MM120[10]

End point description:

AUC = area under the plasma concentration curve
The PK parameters AUC0-inf and t½ are not reported for the individual PK profiles where lambda was not measured (e.g., fewer than 3 non-zero concentrations in the terminal elimination phase or adjusted Rsq <0.8).

End point type	Secondary

End point timeframe:

Between 0 -6 hours after first dose

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic parameters were only studied for MM120 administered subjects.

End point values	MM120			
Subject group type	Reporting group			
Number of subjects analysed	21			
Units: ng·hr/mL				
arithmetic mean (standard deviation)	3.2450 (± 1.58494)			

Statistical analyses

No statistical analyses for this end point

Secondary: Area under the Plasma Concentration-time Curve from Time 0 to 6 hours (AUC 0-6h) of MM120

End point title	Area under the Plasma Concentration-time Curve from Time 0 to 6 hours (AUC 0-6h) of MM120[11]

End point description:

AUC = area under the plasma concentration curve

End point type	Secondary

End point timeframe:

Between 0 -6 hours after first dose

Notes:

[11] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: Pharmacokinetic parameters were only studied for MM120 administered subjects.

End point values	MM120			
Subject group type	Reporting group			
Number of subjects analysed	24			
Units: ng·hr/mL				
arithmetic mean (standard deviation)	1.9411 (± 0.63490)			

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information	
Timeframe for reporting adverse events:	
Overall trial	
Assessment type	Systematic

Dictionary used	
Dictionary name	MedDRA
Dictionary version	25.1

Reporting groups	
Reporting group title	MM120
Reporting group description:	
MM120 - LSD D-tartrate A total of 26 subjects were planned to receive 20 µg of MM120 twice weekly for 6 weeks.	
Reporting group title	Placebo
Reporting group description:	
Placebo identical in appearance to the investigational medicinal product (IMP) administered orally twice weekly for 6 weeks	

Serious adverse events	MM120	Placebo	
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 27 (0.00%)	0 / 26 (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: 1 %

Non-serious adverse events	MM120	Placebo	
Total subjects affected by non-serious adverse events			
subjects affected / exposed	21 / 27 (77.78%)	23 / 26 (88.46%)	
Vascular disorders			
Hot flush			
subjects affected / exposed	2 / 27 (7.41%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Hypertension			
subjects affected / exposed	2 / 27 (7.41%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Surgical and medical procedures			

Tooth extraction			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	4 / 27 (14.81%)	1 / 26 (3.85%)	
occurrences (all)	4	1	
Feeling abnormal			
subjects affected / exposed	2 / 27 (7.41%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Swelling			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Social circumstances			
High risk sexual behaviour			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Substance use			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Reproductive system and breast disorders			
Premenstrual pain			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Respiratory, thoracic and mediastinal disorders			
Oropharyngeal pain			
subjects affected / exposed	0 / 27 (0.00%)	2 / 26 (7.69%)	
occurrences (all)	0	2	
Epistaxis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Nasal congestion			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Throat tightness			

subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Psychiatric disorders			
Illusion			
subjects affected / exposed	4 / 27 (14.81%)	0 / 26 (0.00%)	
occurrences (all)	4	0	
Insomnia			
subjects affected / exposed	3 / 27 (11.11%)	1 / 26 (3.85%)	
occurrences (all)	3	1	
Apathy			
subjects affected / exposed	1 / 27 (3.70%)	2 / 26 (7.69%)	
occurrences (all)	1	2	
Euphoric mood			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Flashback			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Hypersomnia			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Sleep disorder			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Investigations			
Full blood count normal			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Heart rate increased			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Pregnancy test positive			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
SARS-CoV-2 test positive			

subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Urine cannabinoids increased			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Injury, poisoning and procedural complications			
Contusion			
subjects affected / exposed	1 / 27 (3.70%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Ankle fracture			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Palate injury			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Wound			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Cardiac disorders			
Palpitations			
subjects affected / exposed	1 / 27 (3.70%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Syncope			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Nervous system disorders			
Headache			
subjects affected / exposed	13 / 27 (48.15%)	9 / 26 (34.62%)	
occurrences (all)	13	9	
Disturbance in attention			
subjects affected / exposed	2 / 27 (7.41%)	2 / 26 (7.69%)	
occurrences (all)	2	2	
Akathisia			
subjects affected / exposed	1 / 27 (3.70%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Dizziness postural			

subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Restless legs syndrome			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Somnolence			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Blood and lymphatic system disorders			
Anaemia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Ear and labyrinth disorders			
Ear pain			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Eye disorders			
Vision blurred			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Gastrointestinal disorders			
Nausea			
subjects affected / exposed	5 / 27 (18.52%)	1 / 26 (3.85%)	
occurrences (all)	5	1	
Abdominal pain			
subjects affected / exposed	1 / 27 (3.70%)	2 / 26 (7.69%)	
occurrences (all)	1	2	
Abdominal pain upper			
subjects affected / exposed	1 / 27 (3.70%)	2 / 26 (7.69%)	
occurrences (all)	1	2	
Diarrhoea			
subjects affected / exposed	1 / 27 (3.70%)	1 / 26 (3.85%)	
occurrences (all)	1	1	
Flatulence			
subjects affected / exposed	2 / 27 (7.41%)	0 / 26 (0.00%)	
occurrences (all)	2	0	
Abdominal pain lower			

subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Vomiting			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Hepatobiliary disorders			
Liver disorder			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Skin and subcutaneous tissue disorders			
Hyperhidrosis			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Rash			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Renal and urinary disorders			
Urethritis noninfective			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 27 (0.00%)	1 / 26 (3.85%)	
occurrences (all)	0	1	
Back pain			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Muscle tightness			
subjects affected / exposed	1 / 27 (3.70%)	0 / 26 (0.00%)	
occurrences (all)	1	0	
Infections and infestations			
Nasopharyngitis			
subjects affected / exposed	5 / 27 (18.52%)	5 / 26 (19.23%)	
occurrences (all)	5	5	
Urinary tract infection			

subjects affected / exposed occurrences (all)	0 / 27 (0.00%) 0	1 / 26 (3.85%) 1	
Metabolism and nutrition disorders Hypophosphataemia subjects affected / exposed occurrences (all)	1 / 27 (3.70%) 1	0 / 26 (0.00%) 0	

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 July 2022	There was one substantial amendment filed both in Netherlands (submitted 18MAY2022/approved 07JUL2022) and Switzerland (16MAY2022/Approved 03JUN2022). The main reason for the update of the protocol was due to health authorities feedback during the review. A brief summary of the changes are noted below. Study population number decreased from approximately 87 to 52 Add Inclusion criteria 1, 4, 7, 8, 12, 8, 9, 10, 11, 19 and 20. Updated exclusion criteria 16: Women of childbearing potential (WOCBP) (i.e., physiologically capable of becoming pregnant) who are unwilling or unable to use a highly effective method of contraception, as defined in Appendix 2, for the duration of the study, OR Men physiologically capable of fathering a child who are sexually active with WOCBP but are unwilling or unable to use barrier contraception (e.g., condom with or without spermicidal cream or jelly) for the duration of the study NOTE: See Appendix 2 for definitions of WOCBP and highly effective methods of contraception and for information about unacceptable methods of contraception

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported