

**MindMed**

**Corporate Presentation**

August 2024

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## Cautionary Note Regarding Regulatory Matters

The United States federal government regulates drugs through the Controlled Substances Act. MM120 is a proprietary, pharmaceutically optimized form of lysergide D-tartrate and MM402, or R(-)-MDMA, is our proprietary form of the R-enantiomer of MDMA (3,4-methylenedioxymethamphetamine). Lysergide and MDMA are Schedule I substances under the Controlled Substances Act. While the Company is focused on programs using psychedelic or hallucinogenic compounds and non-hallucinogenic derivatives of these compounds, including in its MM120, MM402 and other product candidates, the Company does not have any direct or indirect involvement with the illegal selling, production or distribution of any substances in the jurisdictions in which it operates. The Company is a neuro-pharmaceutical drug development company and does not deal with psychedelic or hallucinogenic substances except within laboratory and clinical trial settings conducted within approved regulatory frameworks. The Company's products will not be commercialized prior to applicable regulatory approval, which will only be granted if clinical evidence of safety and efficacy for the intended uses is successfully developed.

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# We Aim To Be A Global Leader In Brain Health



# Experienced Leadership with a Proven Track Record



**Robert Barrow**  
Chief Executive Officer and Board Director



**Daniel Karlin, MD, MA**  
Chief Medical Officer



**Miri Halperin Wernli, PhD**  
Executive President



**Mark Sullivan, JD**  
Chief Legal Officer and Corporate Secretary



**Francois Lilienthal, MD, MBA**  
Chief Commercial Officer



**Carrie Liao, CPA**  
Chief Accounting Officer

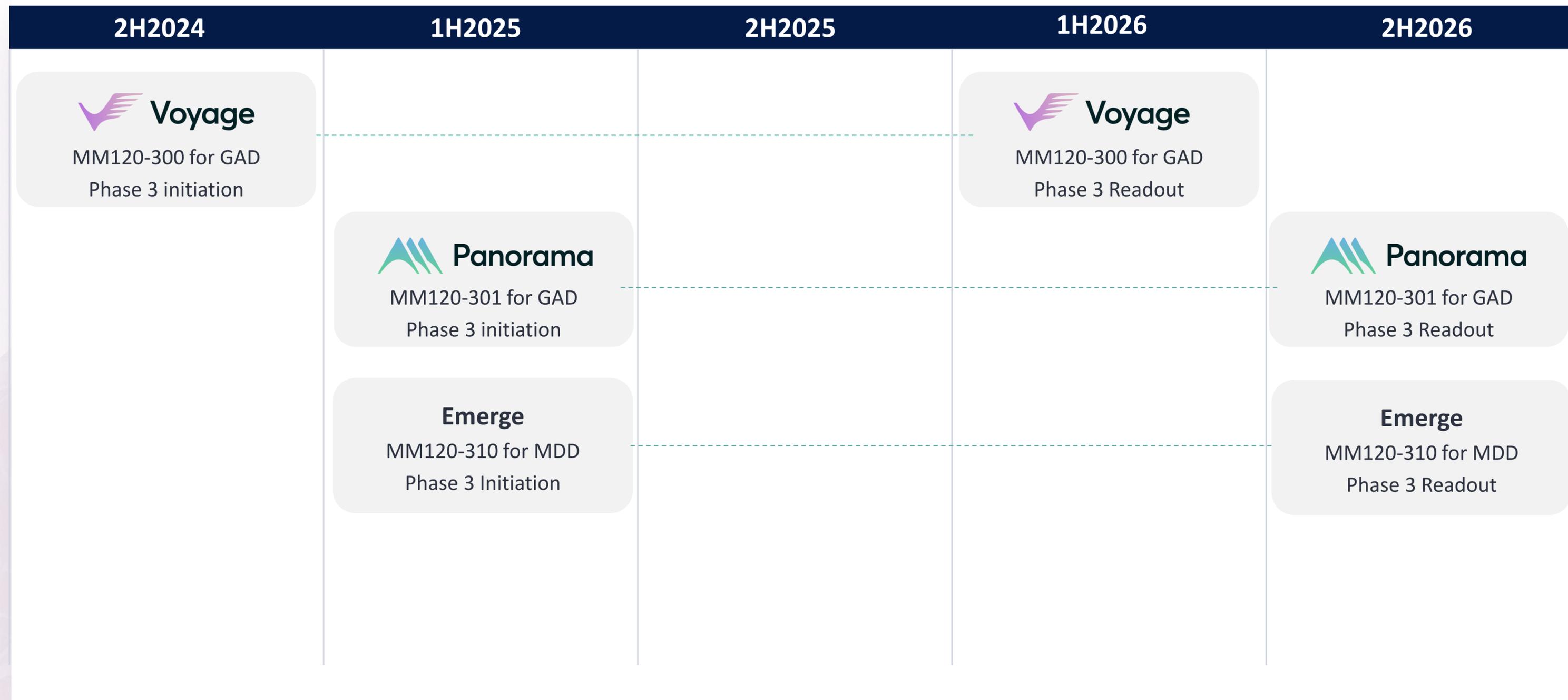
## Strong Experience in Brain Health Innovation<sup>1</sup>



# MindMed Research & Development Pipeline

Product Candidate	Indication	Preclinical	Phase 1	Phase 2	Pivotal / Phase 3	Registration
<b>MM120 ODT</b> <i>(Lysergide D-tartrate)</i>	Generalized Anxiety Disorder (GAD) <sup>1</sup>	[Progress bar spanning Preclinical, Phase 1, and Phase 2]				
	Major Depressive Disorder (MDD) <sup>1,2</sup>	[Progress bar spanning Preclinical, Phase 1, and Phase 2]				
	Additional Indication(s) <sup>2</sup>	[Progress bar spanning Preclinical and Phase 1]				
<b>MM402</b> <i>(R(-)-MDMA)</i>	Autism Spectrum Disorder (ASD) <sup>1</sup>	[Progress bar spanning Preclinical]				

# Next Steps and Anticipated Milestones for R&D Pipeline





**MindMed**

**MM120 ODT**  
**LSD D-tartrate**  
**Program Overview**

# Key Highlights of MM120 Program



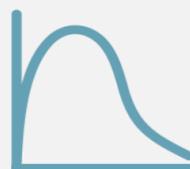
## Positive 12-Week Durability in Phase 2b Trial of GAD<sup>1</sup>

- Primary and secondary endpoints met with statistical significance
- 7.7-point improvement over placebo ( $d=0.81$ ;  $p=0.003$ )
- 48% clinical remission rate at Week 12



## Breakthrough Therapy Designation for GAD<sup>2</sup>

- Recognizes preliminary evidence of substantial improvement over SOC
- FDA organizational commitment and efficient development support



## Enhanced Product Profile of MM120 ODTs

- Results from PK bridging study demonstrate differentiated profile
- Rapid absorption, better bioavailability & greater therapeutic AUC



## Market Protection Strategies and IP Portfolio

- IP-driven R&D strategies to maximize market protection potential
- Advancing IP portfolio with recent and near-term potential grants

# MM120 Has the Potential to Address Large Unmet Needs in Major Brain Health Disorders

## Potential Best-in-Class Therapy with Novel MOA

**Preliminary Clinical Evidence**

**Large Market Opportunities**

**Significant Need for New Treatments**

### Generalized Anxiety Disorder (GAD)

**Effect size (d=0.8) more than double SOC<sup>1</sup>**  
**48% remission rate 12 weeks after single dose<sup>1</sup>**

**20 million US adults with GAD<sup>2</sup>**  
**13 million treated for GAD each year<sup>2</sup>**

**SSRI/SNRIs<sup>3</sup>: 50% failure rate with frequent undesirable AEs**  
**Benzodiazepines: dependence & tolerance; appropriate for short-term use**

### Major Depressive Disorder (MDD)

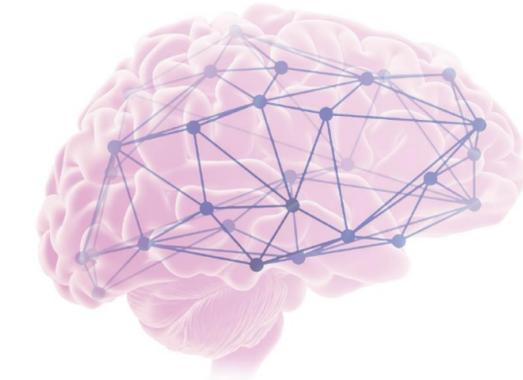
**Significant, rapid and durable effects in comorbid depression symptoms in GAD<sup>1</sup>**  
**Extensive body of historical evidence**

**31 million US adults with MDD<sup>2</sup>**  
**18 million treated for MDD each year<sup>2</sup>**

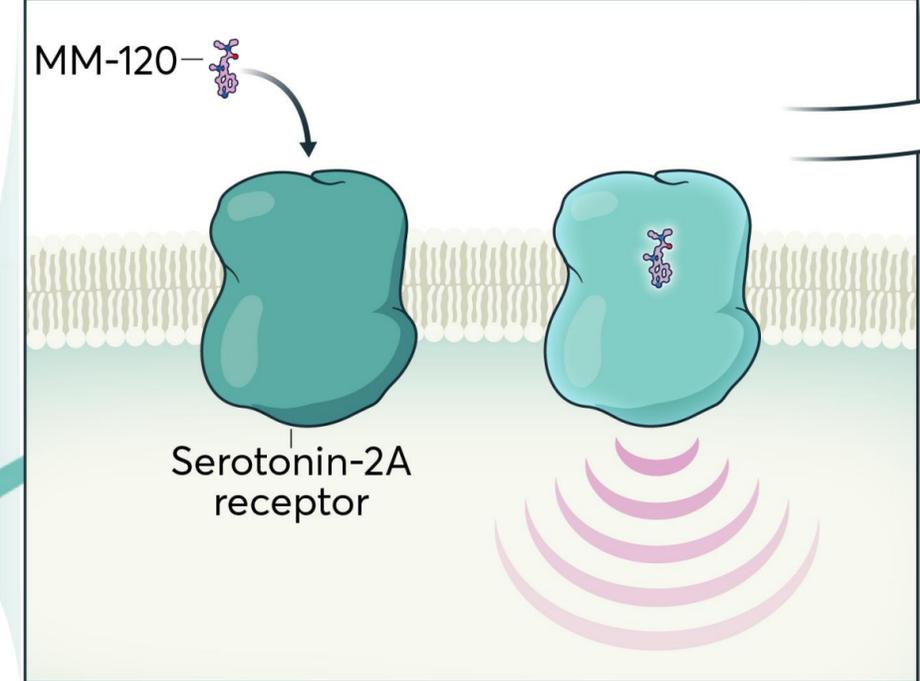
**SSRI/SNRIs<sup>4</sup>: 31% resistant to 1<sup>st</sup> and 2<sup>nd</sup> line treatments**  
**3<sup>rd</sup> line treatments: intensive, time-consuming and poor tolerability**

# Clinical Rationale and Mechanism of Action

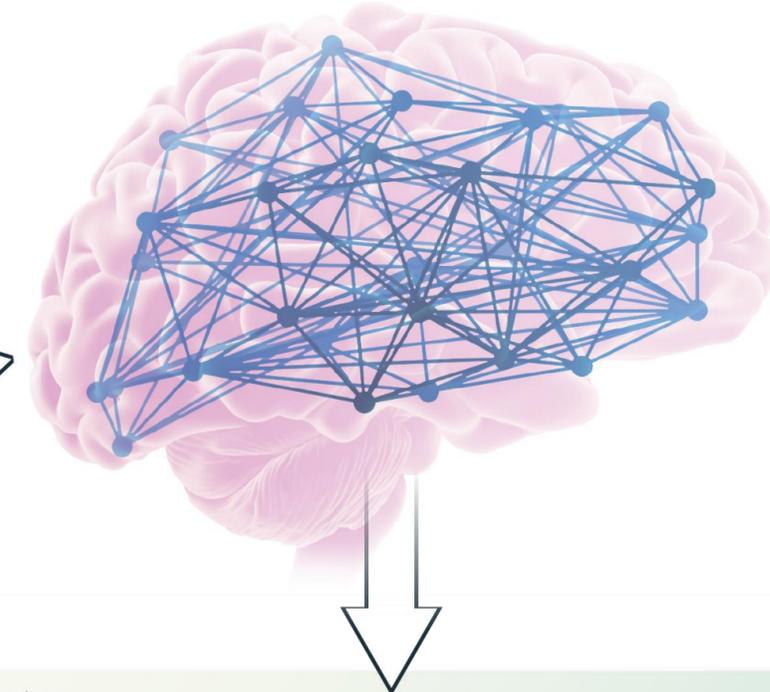
Baseline connectivity between brain regions



MM-120 activates serotonin-2A receptors



Increased connectivity between brain regions



-  ↑ Transiently and powerfully alters perception, behavior, and mood
-  ↑ Intensifies thoughts, emotions, and sensorium
-  ↑ Durable anxiolytic effects and neurogenesis
-  ↓ Rumination, anxiety

# MM120 ODT Program Overview



## Generalized Anxiety Disorder (GAD)

## Major Depressive Disorder (MDD)



MM120-300



MM120-301

Emerge

MM120-310

*Study name to be announced*

MM120-311

**N=200<sup>1,2</sup>**  
(1:1 randomization)

MM120 100 µg vs. Placebo

- **Part A:** 12-week DB, RCT
- **Part B:** 40-week Extension with OL Treatment

*Initiation: 2H2024<sup>3</sup>*

**N=240<sup>1,2</sup>**  
(5:2:5 randomization)

MM120 100 µg vs. Placebo  
(including 50 µg control)

- **Part A:** 12-week DB, RCT
- **Part B:** 40-week Extension with OL Treatment

*Initiation: 1H2025<sup>3</sup>*

**N=140<sup>2</sup>**  
(1:1 randomization)

MM120 100 µg vs. Placebo

- **Part A:** 12-week DB, RCT
- **Part B:** 40-week Extension with OL Treatment

*Initiation: 1H2025<sup>3</sup>*

*Study design to be disclosed*

# Strategies to Address Key Drug Class Methodological Considerations



Expectancy  
Bias &  
Functional  
Unblinding

- Blinded centralized raters for primary outcome measure
- Dose-response in Phase 2 across ‘functionally active’ doses
- Complementary studies with multiple ‘functionally masking’ arms
- Pre- and post-dose expectancy questionnaire (participants)
- Post-dose blinding questionnaire (participants and raters)
- Drug effect isolated from psychotherapeutic intervention



Cardiovascular  
Safety

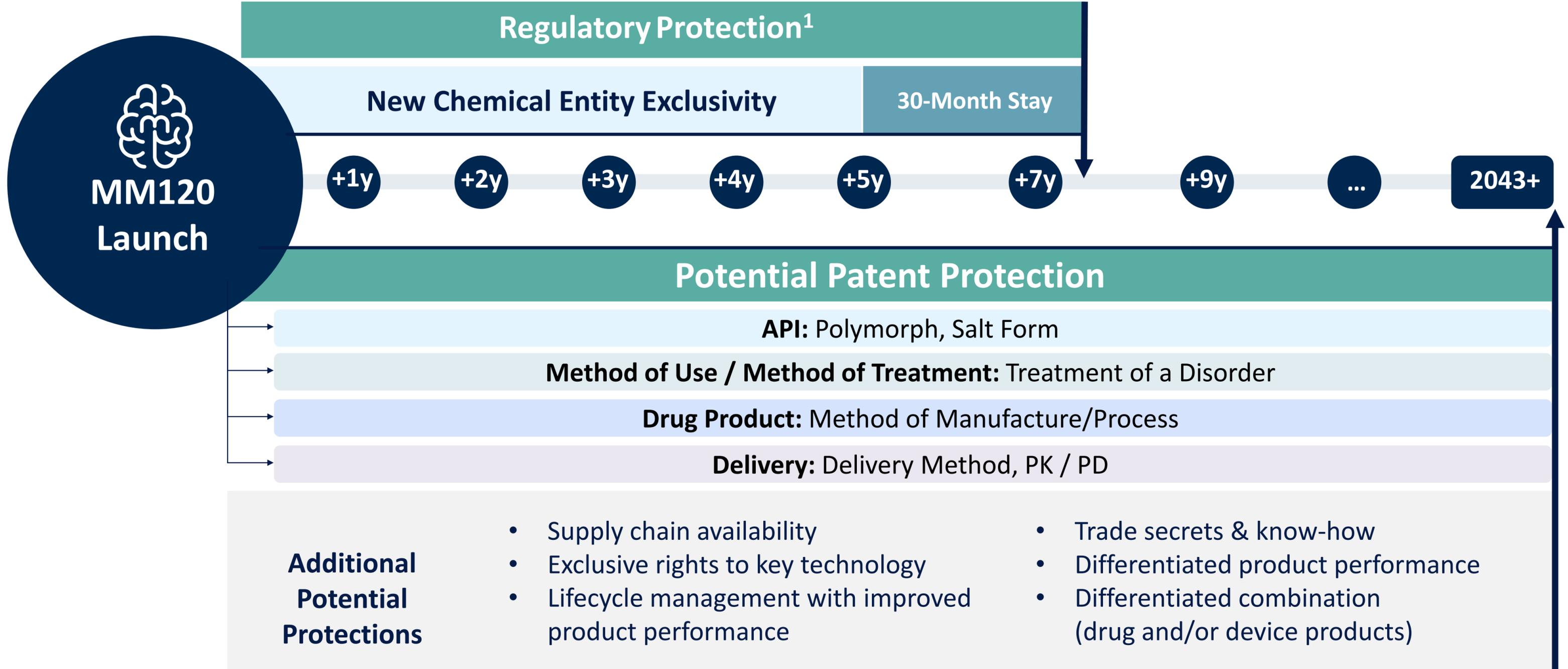
- Collection of ECGs in Phase 3 clinical trials
- Dedicated TQT study in parallel with Phase 3



Adverse Event  
Collection

- Collection of all AEs, including “positive” and MOA-related
- Frequent assessment to define time course for resolution of drug effects

# MM120 | Multiple Layers of Intellectual Property and Protection





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**MM120 ODT**

**LSD D-tartrate**

*Phase 3 Program in GAD*

# MM120 for GAD | Phase 3 Program Overview



## Phase 3 Program

### Two Phase 3 pivotal clinical trials in GAD<sup>1</sup>

- 12-week randomized, placebo-controlled primary efficacy study design
- 40-week extension phase to characterize safety and define retreatment parameters



## Consistent Protocol Design & Conduct

### Key design elements largely consistent between Phase 2b and Phase 3 studies

- Hamilton Anxiety Scale (HAM-A) primary outcome measure
  - Primary endpoint: change from baseline to Week 12<sup>2</sup>
- Limited changes to key inclusion/exclusion criteria
  - No planned change in dosing session monitoring protocol
- Duration of treatment session monitoring reduced to 8 hours<sup>3</sup>



## Program Alignment

### Alignment with FDA on program design reached at EOP2 meeting

- Study designs believed to be consistent with FDA guidance
- Program initiation expected in 2H2024

# Phase 2 Results in GAD Demonstrated 12-Week Durability with Effect Size Over Double the Standard of Care<sup>1,3</sup>

## Comparative Effect Sizes in GAD



## Key Highlights of Phase 2b 12 Week Results

- Maximum **effect size  $d=0.81$**  more than **double** the standard of care<sup>2,3</sup>
- **Rapid and durable clinical response** after single administration<sup>3</sup>
- Clinical activity with **no psychotherapeutic intervention** beyond study drug

# Phase 2 Results in GAD Delivered on Target Product Profile after Single Dose and Support Phase 3 Advancement<sup>1,2</sup>

Fast Acting



1.8-point reduction in CGI-S within 24 hours (p<0.0001)

Durable Activity



21.9-point improvement in HAM-A at Week 12 (p=0.003) represents further improvement from Week 4

Response / Remission



48% of participants in remission at Week 12<sup>3</sup>

Limited Side Effect Burden



Favorable tolerability profile with most AEs limited to dosing day

Scalability, Access & Value



Results achieved with no additional therapy

# MM120 for GAD | Phase 3 Study Designs

## PHASE 3 STUDY<sup>1</sup>



**Voyage**  
Study MM120-300

### Part A 12 Week Randomized, Double-Blind

*Single Dose*

- N=100** MM120 ODT 100 µg
- N=100** Placebo

*Single Dose*

- N=100** MM120 ODT 100 µg
- N=40** MM120 ODT 50 µg
- N=100** Placebo

### Part B 40 Week Extension with Opportunity for Open-Label Treatment

*Potential retreatment if HAM-A ≥ 16*

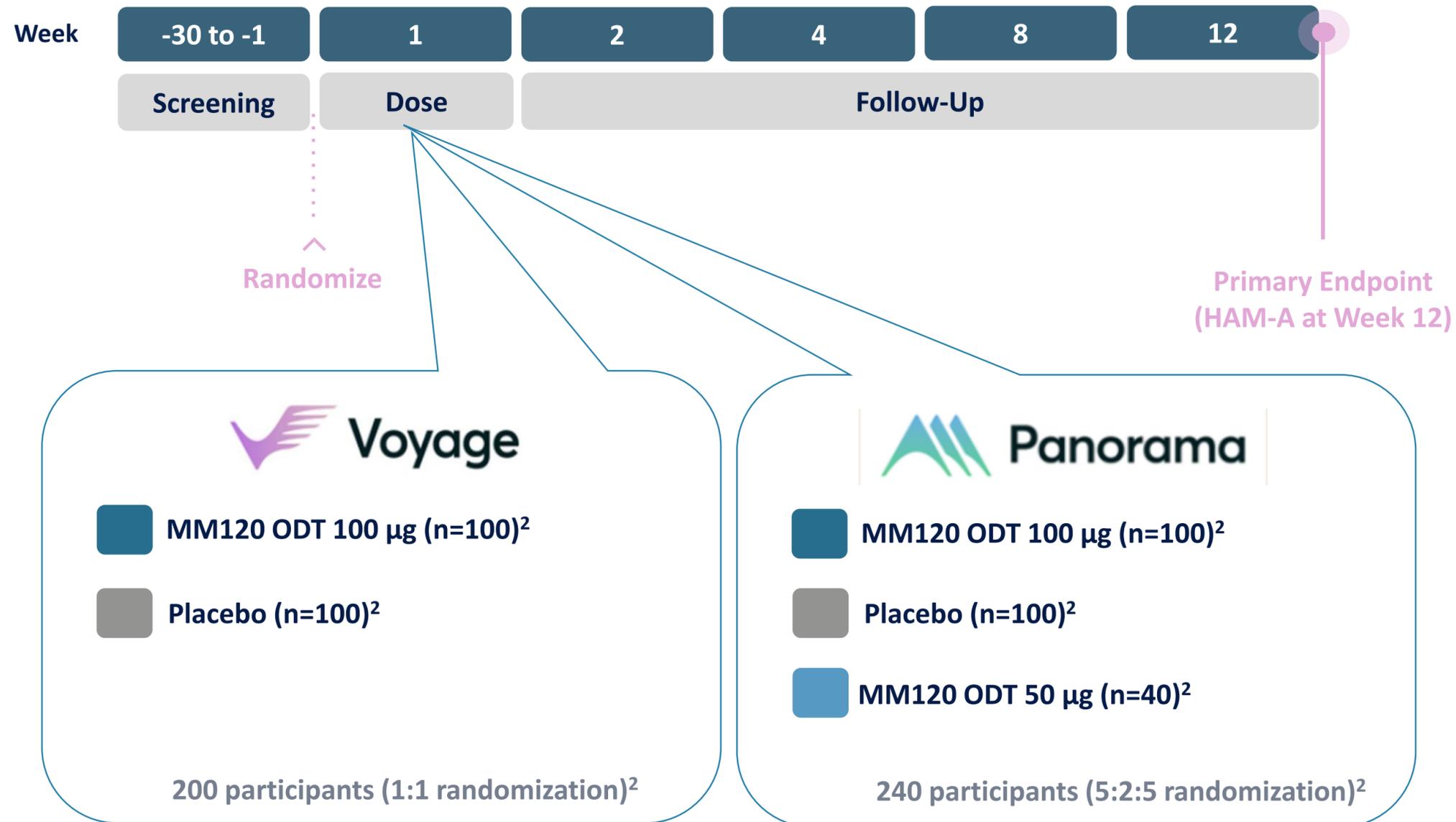


*Potential retreatment if HAM-A ≥ 16*



Primary Endpoint  
(HAM-A at Week 12)

# Phase 3 GAD Part A Trial Schematics: Two Pivotal Studies with Complementary Designs<sup>1</sup>



## STUDY MM120-300 & MM120-301 | Part A

A Phase 3 Study of a Single Dose of MM120 for Generalized Anxiety Disorder

### SELECT ENTRY CRITERIA

- Men and Women
- Ages 18-74
- Diagnosis of GAD
- HAM-A  $\geq$  20

### KEY SECONDARY ENDPOINTS

- HAM-A at Week 1
- CGI-S at Day 2
- Time to retreatment / inefficacy

# Phase 3 GAD Part B Trial Schematics: Extension Phase



Study Month

4

5

6

7

8

9

10

11

12

## Follow-up Observation

*GAD-7 (ePRO): biweekly*  
*HAM-A (central rater): monthly or when GAD-7  $\geq 10$*

## Potential Retreatment

*Eligible for open-label treatment with MM120 ODT 100  $\mu\text{g}$  if HAM-A  $\geq 16$ ; maximum of 4 doses during Part B*

MM120-300 & -301 | Part B

## Part B Outcomes:

- Safety of repeated treatment
- Time to retreatment / inefficacy
- Average treatments/year
- Response to re-treatment

# Phase 3 GAD Part A Trials: Primary & Key Secondary Endpoints<sup>1</sup>



Primary

Change in HAM-A  
from Baseline to Week 12  
MM120 ODT 100 µg vs. placebo

Key  
Secondaries

Change in HAM-A from Baseline to Week 1  
MM120 ODT 100 µg vs. placebo

Change in CGI-S from Baseline to Day 2  
MM120 ODT 100 µg vs. placebo

Time to Retreatment / Inefficacy  
MM120 ODT 100 µg vs. placebo

**Phase 2b  
HAM-A Results at Week 12<sup>2</sup>**

-21.9 points from Baseline  
-7.7 points vs. placebo (p=0.003)

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***Phase 3 studies have 90% power to detect a 5.0-point difference vs. placebo<sup>3</sup>***

1. Clinical study designs subject to ongoing regulatory discussion and review, including of Phase 3 clinical trial protocols.  
2. 100 µg dose group.  
3. Based on assumption of n=85 evaluable subjects per arm; standard deviation of 10 and resulting effect size of d=0.5. Studies will employ an adaptive design with interim blinded sample size re-estimation based on nuisance parameters (e.g. patient retention rate, variability of primary outcome measure) allowing for up to 50% more subjects in each arm to maintain statistical power.



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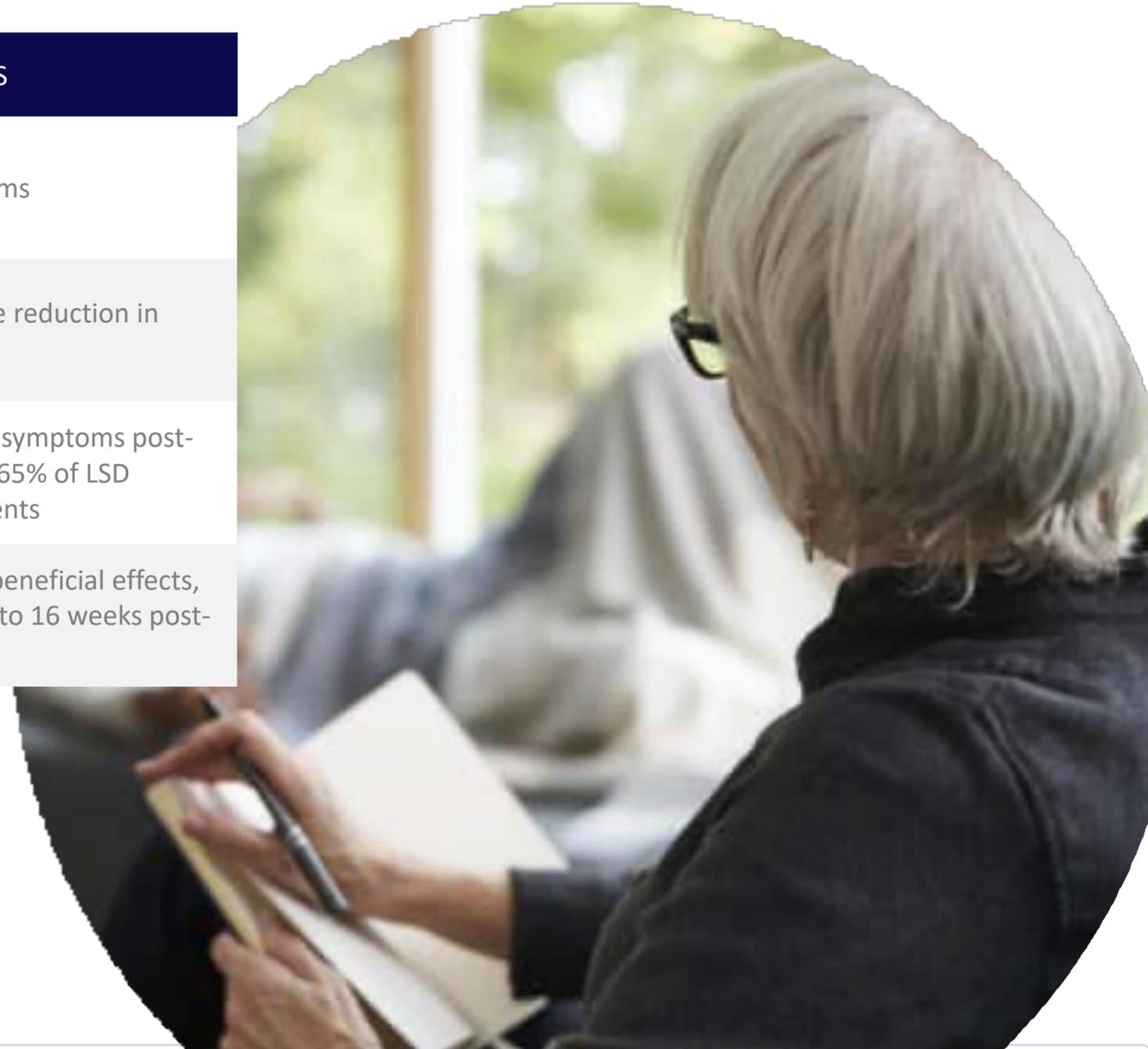
**MM120 ODT**

**LSD D-tartrate**

*Phase 3 Program in MDD*

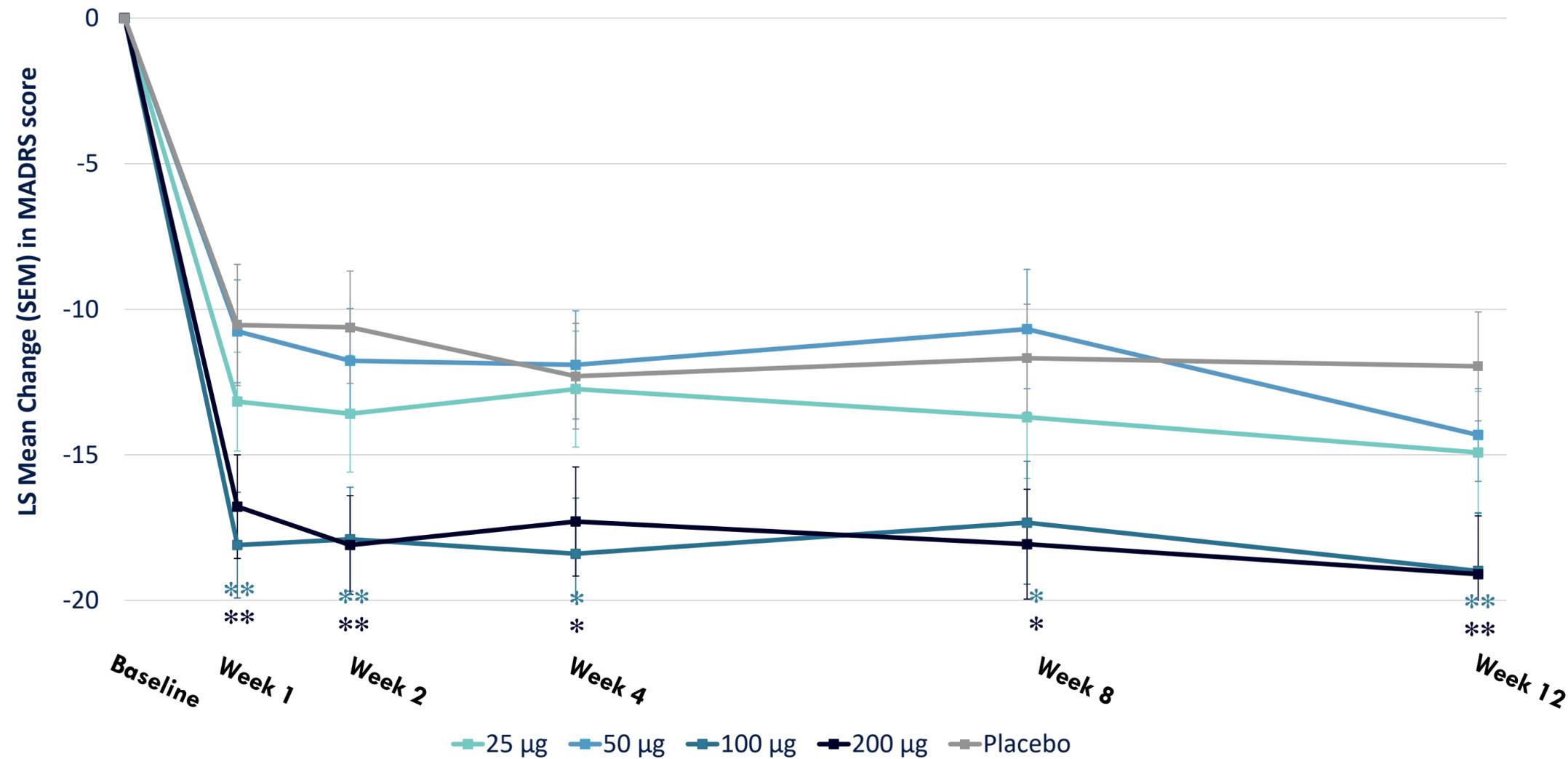
# Decades of LSD Clinical Research in Psychiatric Disorders Supports its Unique Potential

STUDIES	INDICATION(S)	SAMPLE SIZE	KEY FINDINGS
<b>21 STUDIES PRIOR TO 1974</b>	Anxiety, depression & neurotic illnesses	512 patients	Up to 95% reduction in symptoms
<b>GASSER 2014</b>	Anxiety in terminal illness	12 patients	Effect size of $d=1.1$ with durable reduction in anxiety at 1 year
<b>HOLZE 2023</b>	Anxiety	42 patients	Rapid and durable reduction in symptoms post-treatment. Clinical response in 65% of LSD patients vs. 9% of placebo patients
<b>MULLER 2023</b>	Major Depressive Disorder	61 patients	Significant, rapid, durable and beneficial effects, with benefit maintained for up to 16 weeks post-treatment ( $p=0.008$ )



# MM120 Antidepressant Potential Demonstrated in GAD Patients with Comorbid Depression (MADRS) <sup>1,2</sup>

## MADRS Change from Baseline<sup>3</sup>



### Change from Baseline<sup>2,3</sup>

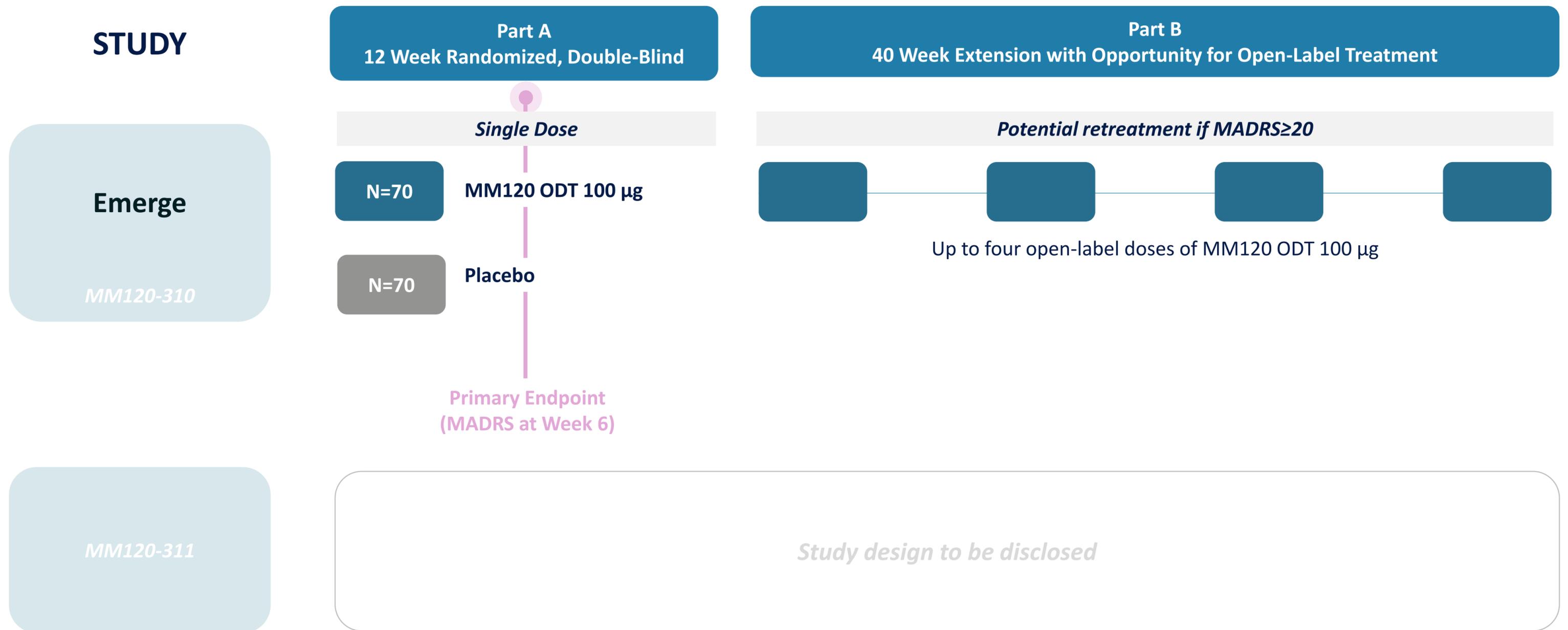
- Week 4: -18.1 points
- Week 12: -18.7 points

### Improvement over Placebo<sup>2,3</sup>

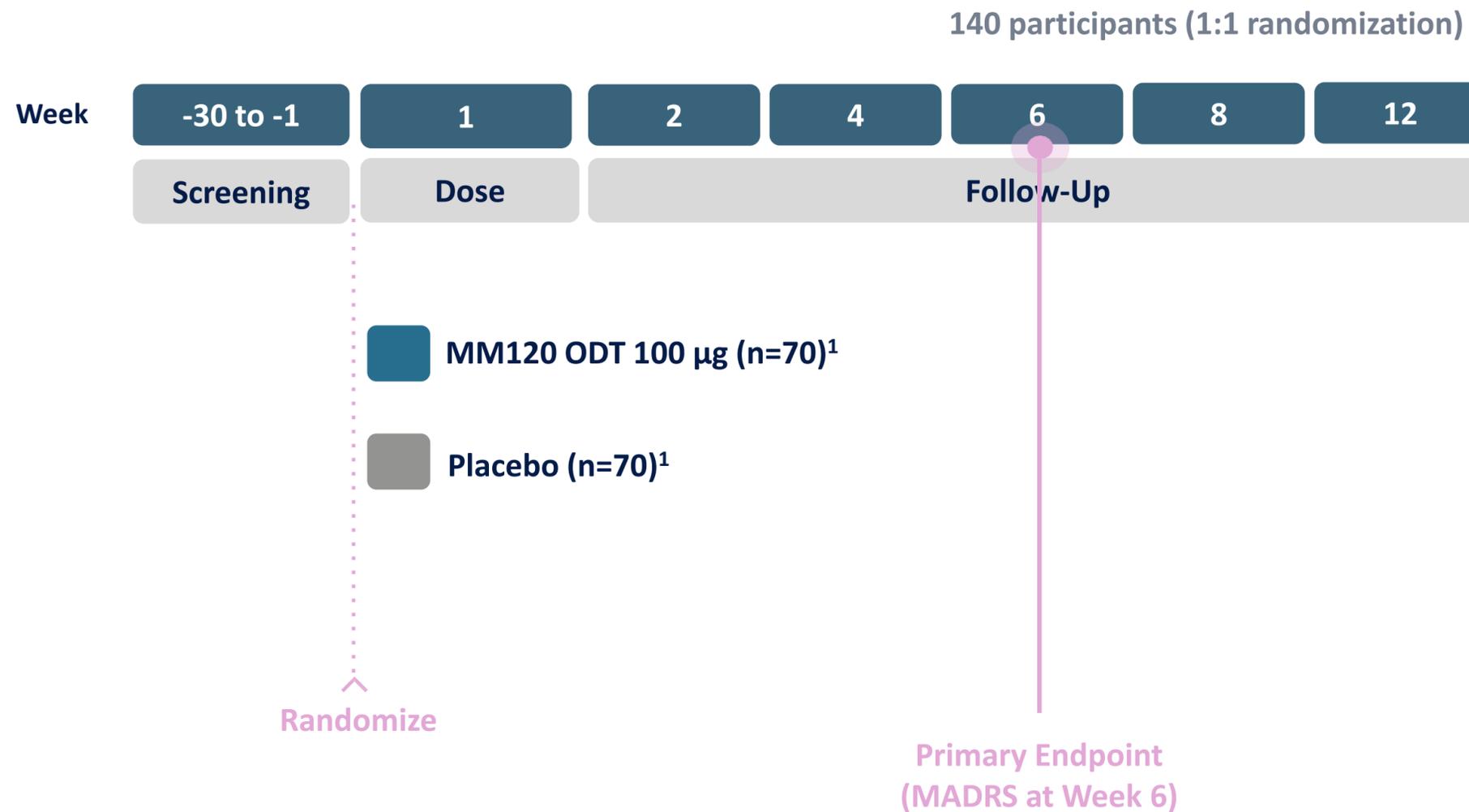
- Week 4: -5.7 points, p<0.05
- Week 12: -6.4 points, p<0.01

\*p<0.05  
\*\*p≤0.01

# MM120 for MDD | Phase 3 Study Design<sup>1</sup>



# Phase 3 MDD Trial Schematic: Emerge Study<sup>1</sup>



## MM120-310 | Part A

A Phase 3 Study of a Single Dose of MM120 for Major Depressive Disorder

### KEY ENTRY CRITERIA

- Men and Women
- Ages 18-74
- Diagnosis of MDD
- MADRS ≥ 26

### SECONDARY ENDPOINTS<sup>2</sup>

- MADRS at Week 12
- MADRS at Week 1
- CGI-S at Day 2
- Time to retreatment / inefficacy



**MindMed**

**MM120 ODT**

**LSD D-tartrate**

*Phase 2b Results in GAD*

# Phase 2b Trial of MM120 Utilized Standard GAD Design and Endpoints and was Aligned with FDA Draft Guidance for Drug Class<sup>1</sup>

- **Standard GAD study design with endpoints that have supported registration for approved drugs**
- **Randomized, double-blind, placebo-controlled, 12-week trial**
  - Single administration of MM120 or placebo
  - No psychotherapeutic intervention
  - Trial design closely aligned with subsequently issued FDA 2023 Draft Guidance<sup>2</sup>
  - Patients washed out of anxiety pharmacotherapy prior to randomization
- **Enrolled 198 patients with GAD**
- **Five-arm dose optimization design with 1:1:1:1:1 randomization**
- **Primary endpoint: change in Hamilton Anxiety Scale (HAM-A) at week 4**
  - Assessed by central rater blinded to treatment assignment and visit number

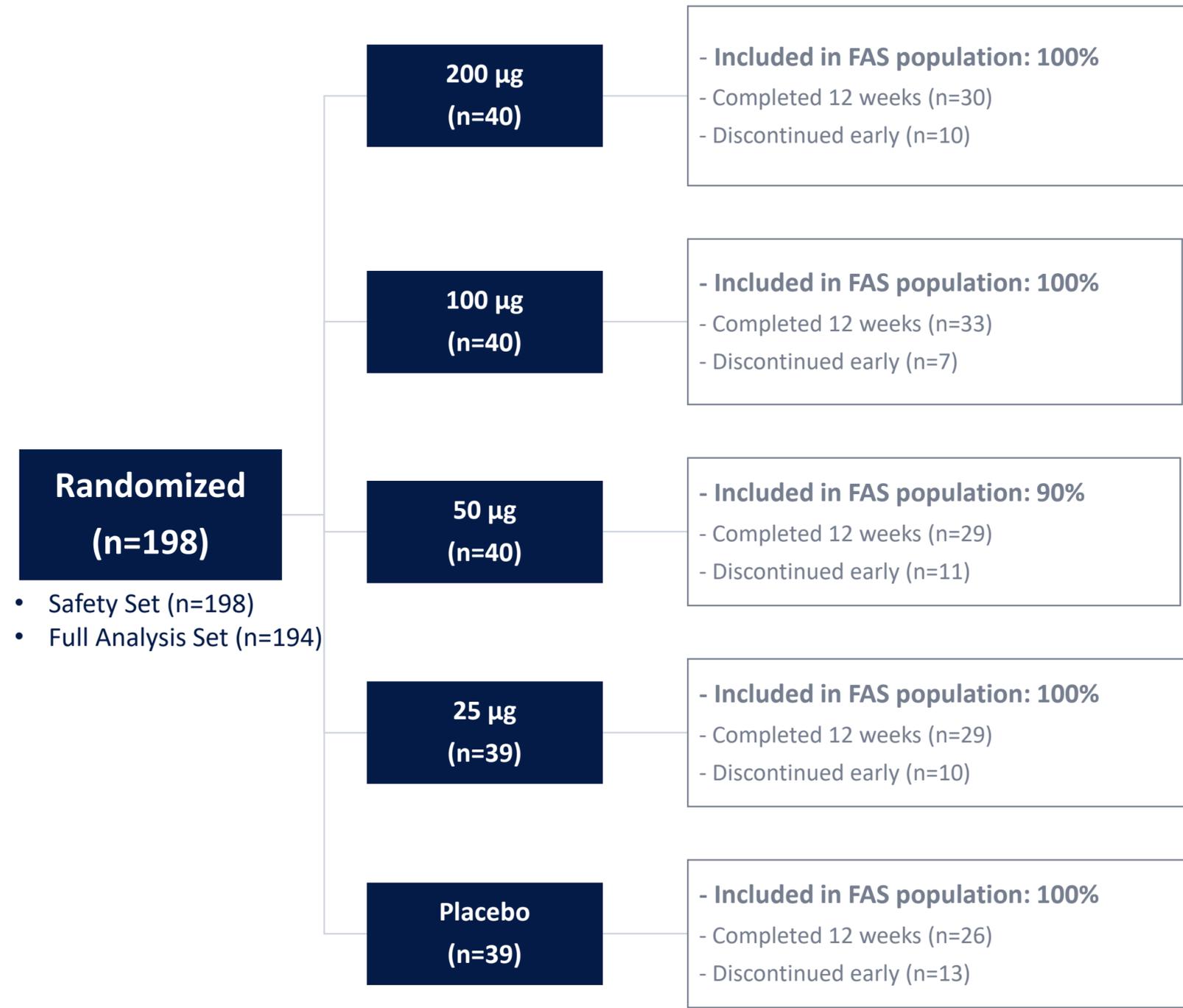


# Treatment Paradigm: Standalone Drug Effects with No Psychotherapeutic Intervention<sup>1</sup>

- Dosing session monitors (DSMs) in the room provide no psychotherapeutic intervention
- Delivery protocol consistent with 2023 FDA Draft Guidance<sup>2</sup>
- No significant changes planned to treatment session delivery between Phase 2 and Phase 3

	Pre-treatment	During treatment	Post-treatment
Patient Journey in MMED008	<ul style="list-style-type: none"> <li>✓ Comprehensive informed consent process</li> <li>✓ Eligibility evaluation</li> </ul>	<ul style="list-style-type: none"> <li>✓ Continuous monitoring by DSMs</li> <li>✓ Music, eye shades, reading, writing</li> <li>✓ Concludes when discharge criteria met</li> </ul>	<ul style="list-style-type: none"> <li>✓ Follow-up visits for assessment only</li> </ul>
Not Part of Patient Journey in MMED008	<ul style="list-style-type: none"> <li>✗ No “preparation”</li> <li>✗ Pre-treatment activities consisted of a comprehensive informed consent process</li> </ul>	<ul style="list-style-type: none"> <li>✗ No “assisted therapy”</li> <li>✗ No psychotherapy and no therapeutic intervention beyond study drug</li> </ul>	<ul style="list-style-type: none"> <li>✗ No “integration”</li> <li>✗ No ongoing therapeutic engagement as part of clinical trial activities</li> </ul>

# Participant Disposition Aligned with Historical Expectations<sup>1</sup>



**79% 12-week completion rate**  
in high dose groups<sup>2</sup> despite need for follow-up visits with no additional treatment

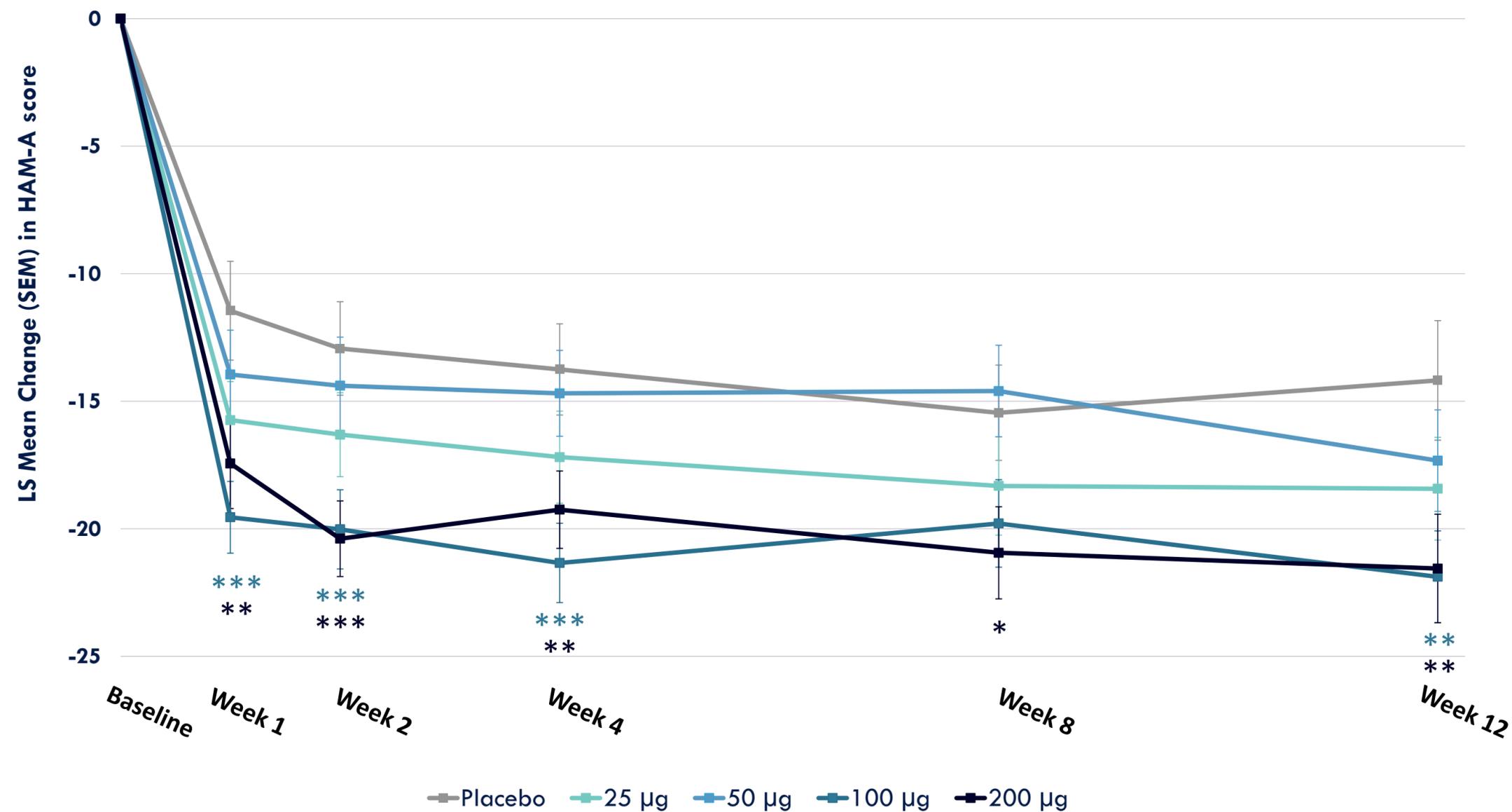
**74% 12-week completion rate**  
of all randomized participants which is consistent with other studies in drug class

# Participant Demographics and Baseline Characteristics Generally Balanced Across Groups<sup>1</sup>

Demographic (n=194)	MM120				Placebo (n=39)
	25 µg (n=39)	50 µg (n=36)	100 µg (n=40)	200 µg (n=40)	
Mean age (years)	38.0	45.3	42.7	42.1	38.7
Sex, female (%)	51.3%	55.6%	40.0%	70.0%	66.7%
Race (% white)	84.6%	80.6%	90.0%	82.5%	76.9%
Baseline HAM-A score	30.2	30.3	29.3	31.0	30.3
Baseline CGI-S score	4.9	4.9	4.8	5.1	4.9

# Statistically and Clinically Significant Reductions in HAM-A Score Continued at Week 12<sup>1,2</sup>

## HAM-A Change from Baseline



### Change from Baseline<sup>2</sup>

- Week 4: -21.3 points
- Week 12: -21.9 points

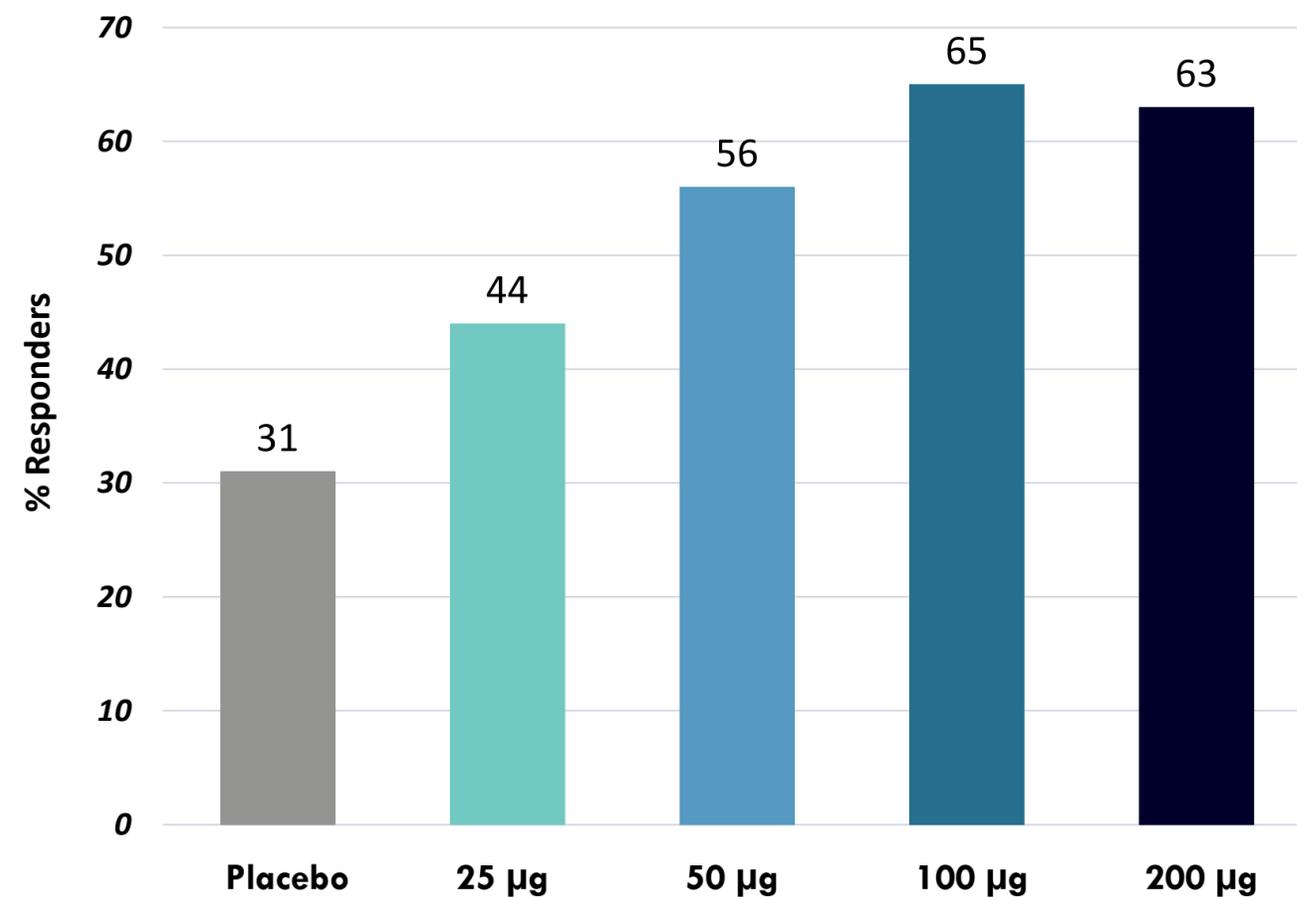
### Improvement over Placebo<sup>2</sup>

- Week 4: -7.6 pts, p=0.0004
- Week 12: -7.7 pts, p=0.003

\* p < 0.05  
 \*\* p < 0.01  
 \*\*\* p < 0.001

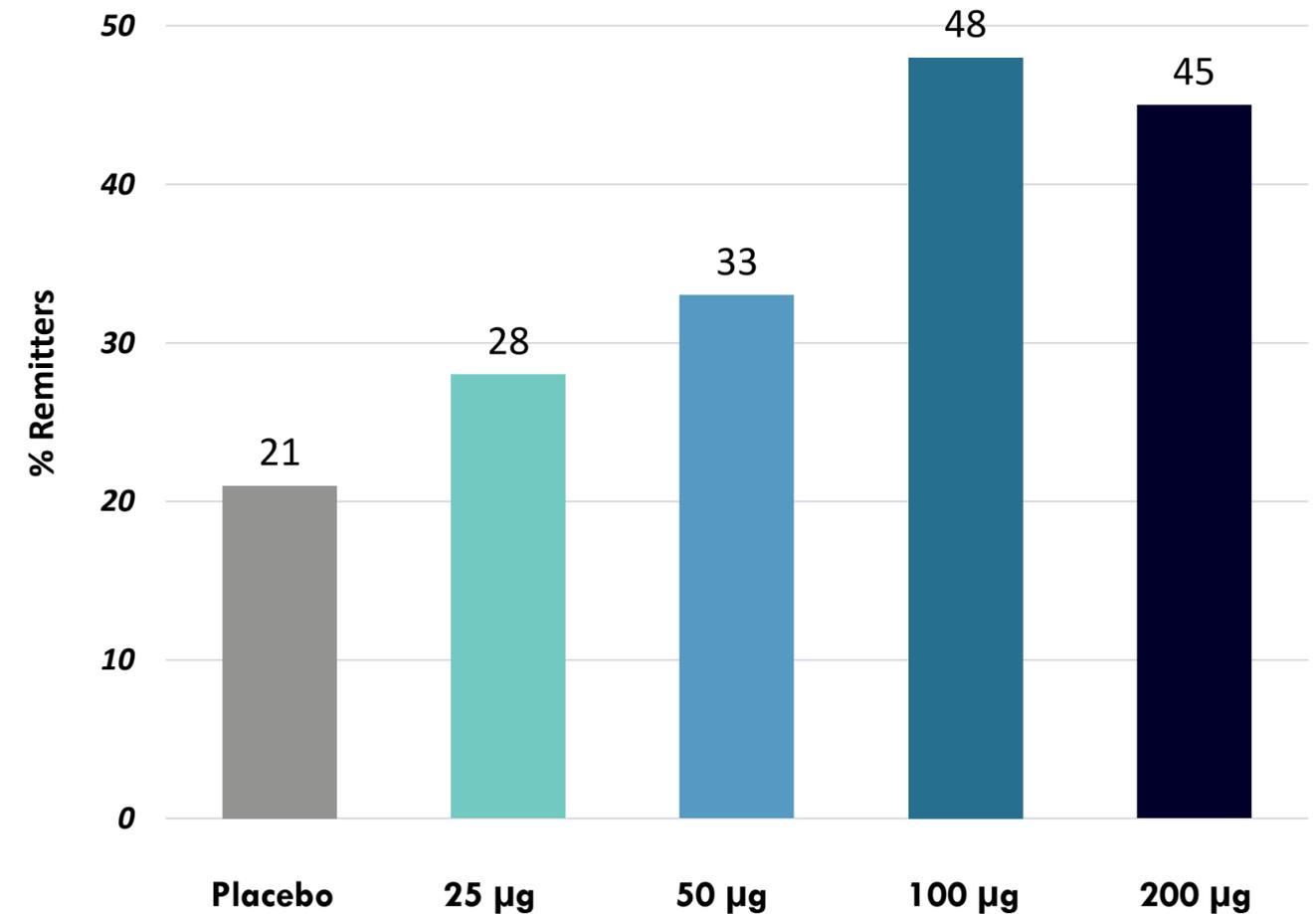
# Continued Response and Remission through Week 12 with 65% Clinical Responder Rate and 48% Clinical Remission Rate<sup>1</sup>

## HAM-A Response Rate at Week 12<sup>2</sup>



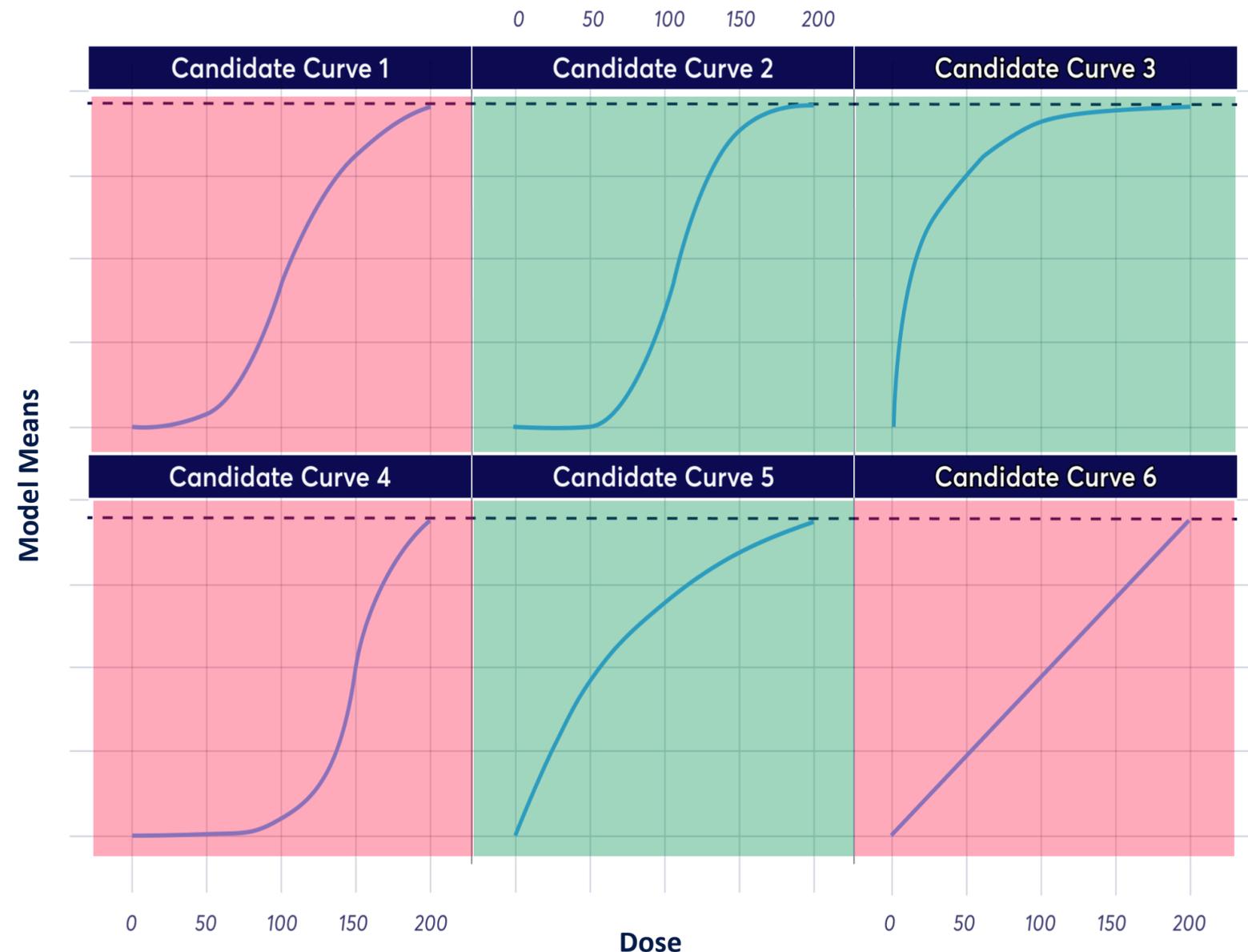
p-values not calculated

## HAM-A Remission Rate at Week 12<sup>2</sup>



p-values not calculated

# Primary & Key Secondary Analysis (MCP-Mod) Support Dose Response Relationship for MM120 in GAD<sup>1</sup>



## Key Takeaways from MCP-Mod Analysis<sup>2</sup>

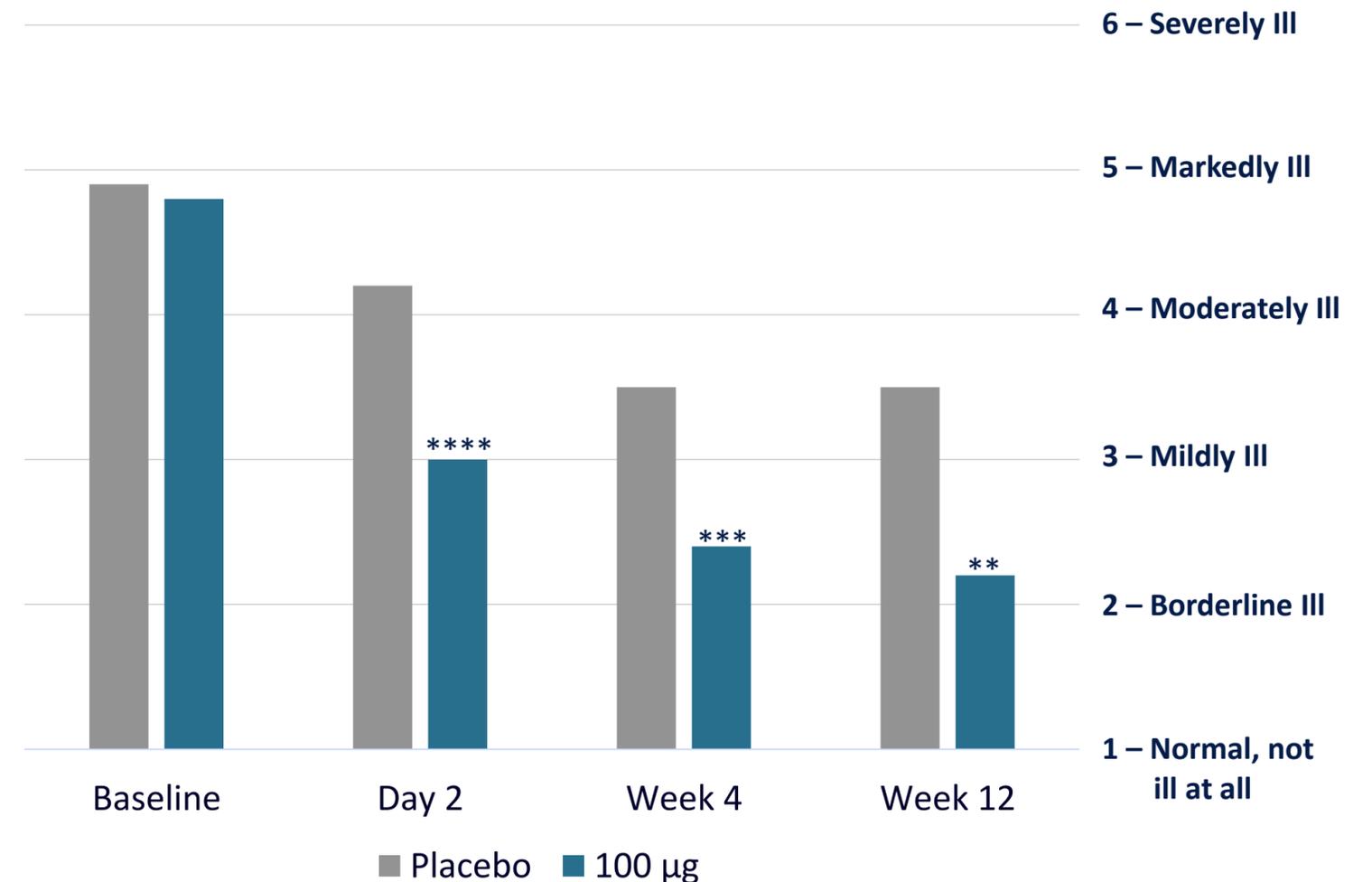
- Statistically significant dose response relationship with multiple model fits
- Supports dose selection of 100  $\mu\text{g}$  for subsequent studies in GAD
- Pre-specified model estimates and observed responses drive dose selection for Phase 3 studies

# Rapid and Sustained Improvements in Clinical Global Impressions – Severity (CGI-S) Starting on Day 2 and Continuing through Week 12<sup>1</sup>

## CGI-S Improvement in 100 µg Group

- Statistically and clinically significant improvement by Day 2 and maintained through Week 12
- Greater than 2-unit improvement in CGI-S score through Week 12
- Participants on average only borderline-to-mildly ill at Week 12

## CGI-S Scores at Week 12<sup>2</sup>



\*p<0.05  
 \*\*p≤0.01  
 \*\*\*p≤0.001  
 \*\*\*\*p≤0.0001

# MM120 was Well-tolerated with Mostly Transient, Mild-to-Moderate Adverse Events Consistent with Drug Class Expectations<sup>1</sup>

## Favorable tolerability profile

- Virtually all AEs (99%) were mild-to-moderate in severity
- Minimal (2.5%) TEAEs led to study withdrawal
- No drug-related serious adverse events (SAEs)<sup>2</sup>

## No SAEs related to study drug

- Only SAE was in 50 µg dose group and deemed unrelated
- Adverse event profile consistent with historical studies and drug class

## No suicidal behavior or suicidality signal<sup>3</sup>

- No suicidal or self-injurious behavior
- ≤ 2 participant per arm reported suicidal ideation during the study
- No indication of increased suicidality or suicide-related risk

# Most Common ( $\geq 10\%$ ) TEAEs in High-Dose Groups Demonstrate Favorable Tolerability Profile<sup>1,2</sup>

Preferred Term	MM120								Placebo (n=39)	
	25 $\mu$ g (n=39)		50 $\mu$ g (n=40)		100 $\mu$ g (n=40)		200 $\mu$ g (n=40)		DD	AFT
	DD	AFT	DD	AFT	DD	AFT	DD	AFT		
Illusion	12 (31)	1 (2.6)	18 (45)	1 (2.5)	24 (60)	1 (2.5)	30 (75)	–	3 (7.7)	–
Nausea	3 (7.7)	–	11 (28)	–	16 (40)	1 (2.5)	24 (60)	2 (5.0)	1 (2.6)	2 (5.1)
Headache	4 (10)	2 (5.1)	9 (23)	2 (5.0)	10 (25)	4 (10)	10 (25)	1 (2.5)	8 (21)	1 (2.6)
Hallucination, visual	6 (15)	1 (2.6)	9 (23)	–	9 (23)	–	6 (15)	–	1 (2.6)	–
Euphoric mood	2 (5.1)	–	5 (13)	–	11 (28)	–	6 (15)	–	1 (2.6)	–
Anxiety	1 (2.6)	3 (7.7)	3 (7.5)	3 (7.5)	4 (10)	–	5 (13)	1 (2.5)	–	2 (5.1)
Mydriasis	1 (2.6)	–	7 (18)	–	8 (20)	–	4 (10)	–	1 (2.6)	–
Hyperhidrosis	1 (2.6)	–	4 (10)	–	9 (23)	–	5 (13)	–	–	–
Paraesthesia	2 (5.1)	–	2 (5.0)	–	2 (5.0)	–	8 (20)	–	2 (5.1)	1 (2.6)
Blood pressure increased	3 (7.7)	–	5 (13)	–	4 (10)	–	4 (10)	–	–	–
Dizziness	3 (7.7)	–	2 (5.0)	–	3 (7.5)	–	5 (13)	–	1 (2.6)	–
Tremor	–	–	3 (7.5)	–	2 (5.0)	1 (2.5)	8 (20)	–	–	–
Thinking abnormal	1 (2.6)	–	2 (5.0)	–	4 (10)	1 (2.5)	5 (13)	–	–	–
Pseudohallucination	–	–	3 (7.5)	–	3 (7.5)	–	4 (10)	–	–	–
Feeling abnormal	1 (2.6)	–	2 (5.0)	–	–	–	–	4 (10)	1 (2.6)	1 (2.6)
COVID-19	–	1 (2.6)	–	2 (5.0)	–	1 (2.5)	–	4 (10)	–	–

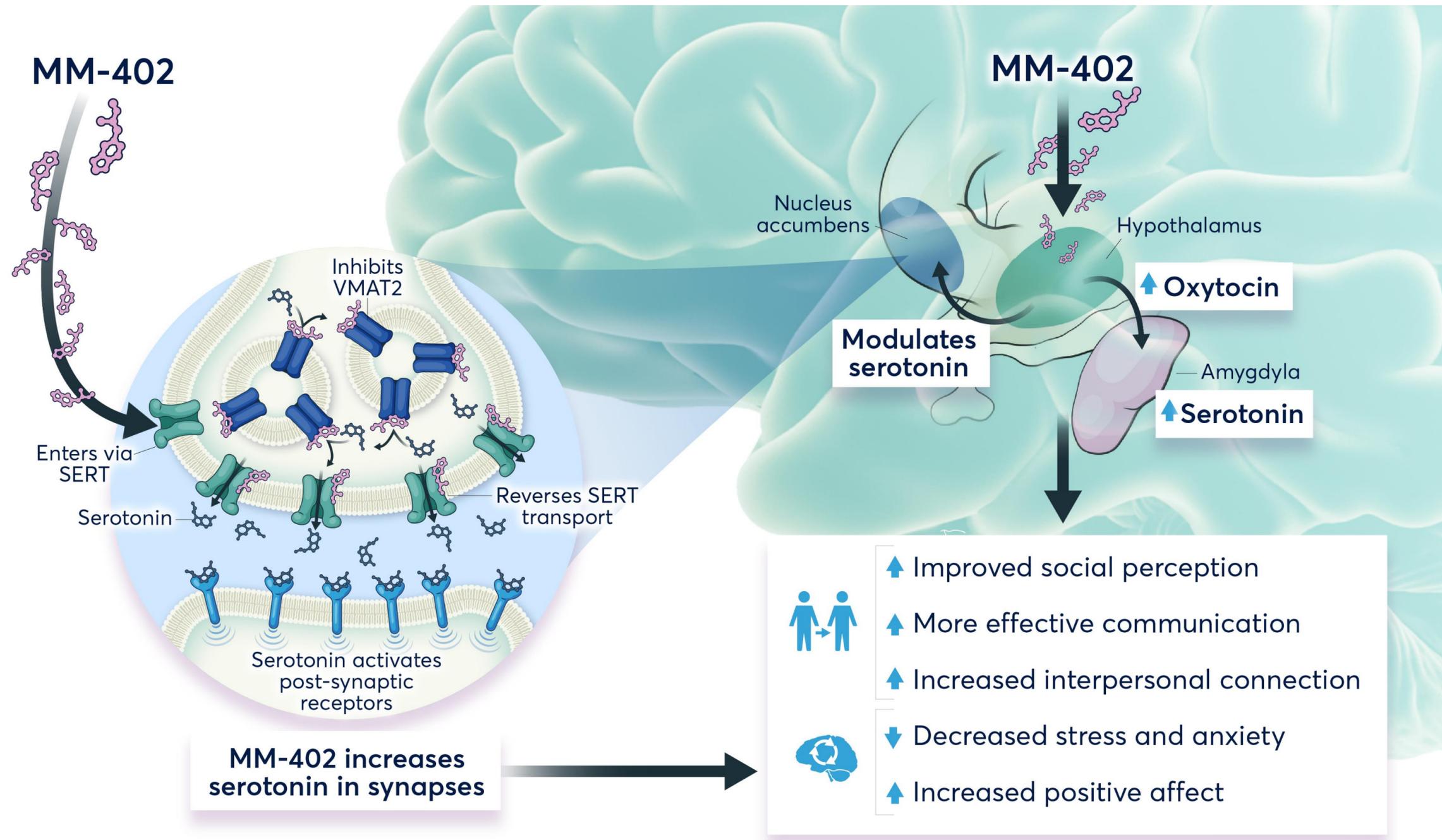


**MindMed**

**MM402**

**R(-)-MDMA**

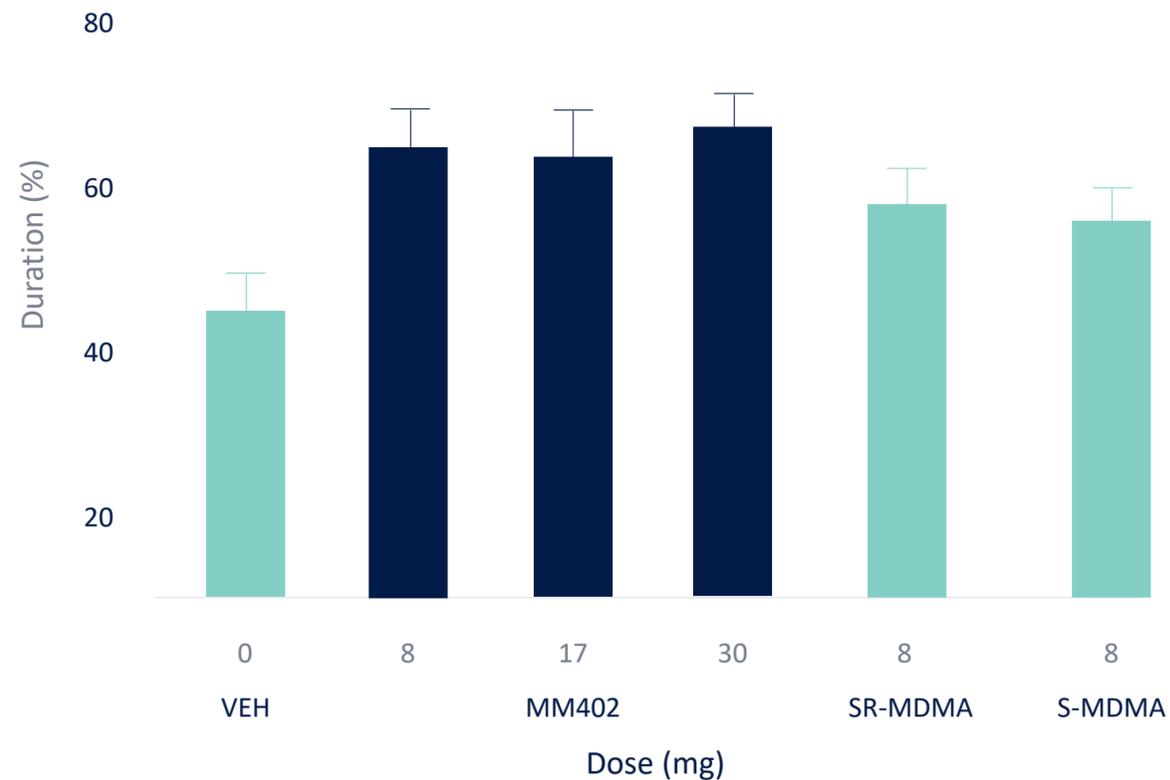
# Differentiated Mechanism of Action Targets Key Pathways



# Addressing the Urgent Need For Novel ASD Therapies

- MM402 is the serotonergic enantiomer of MDMA
- Potential first-in-class therapy for core symptoms of ASD
- Intend to develop for daily, at-home use

Increased duration of interaction in the three-chamber social interaction test<sup>1</sup>



Enhanced pro-social effects with potentially **reduced side effects** compared to MDMA



less stimulant activity



increased social interaction<sup>2</sup>



increasing feelings of connectedness



reduced dopamine-related adverse effects<sup>2</sup>



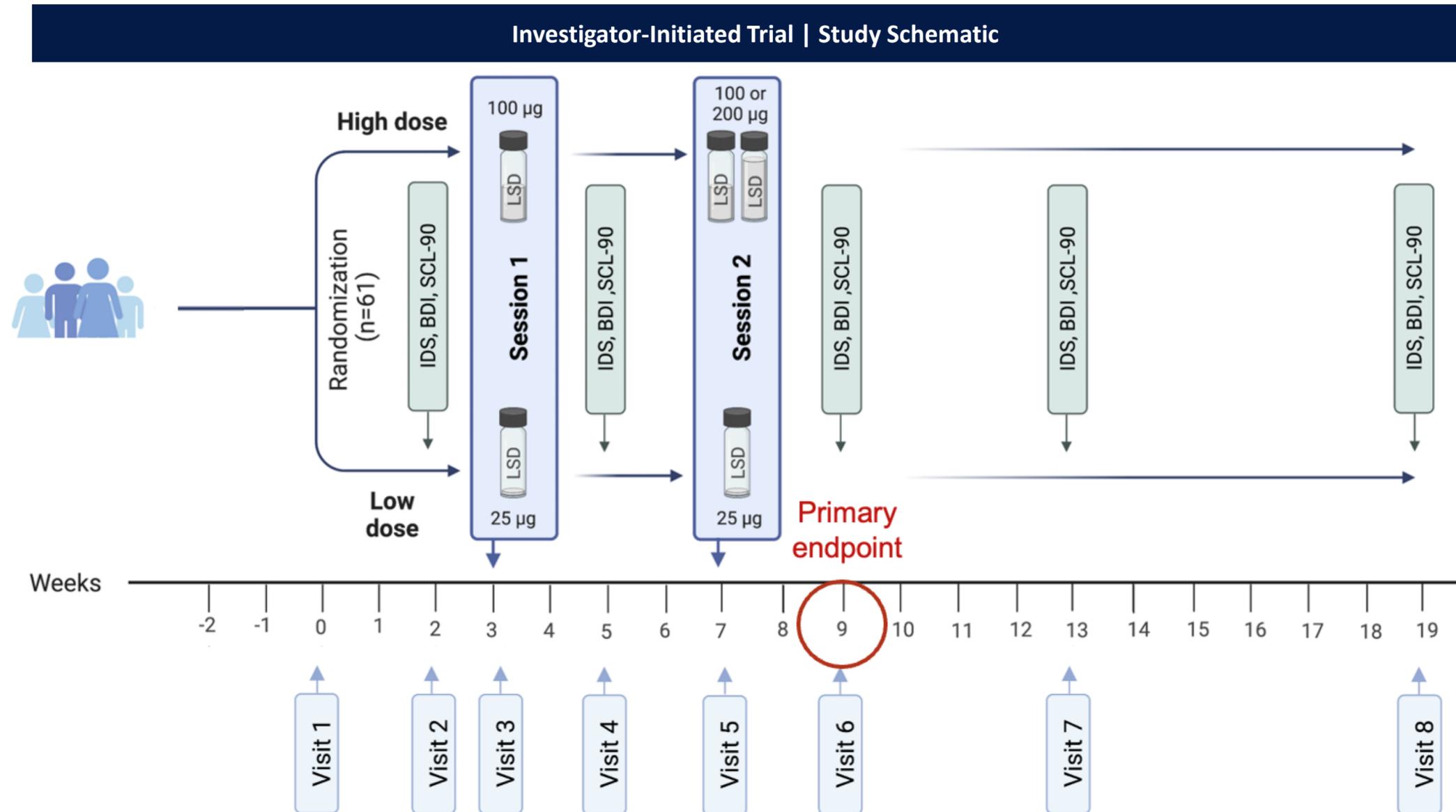
**MindMed**



**MindMed**

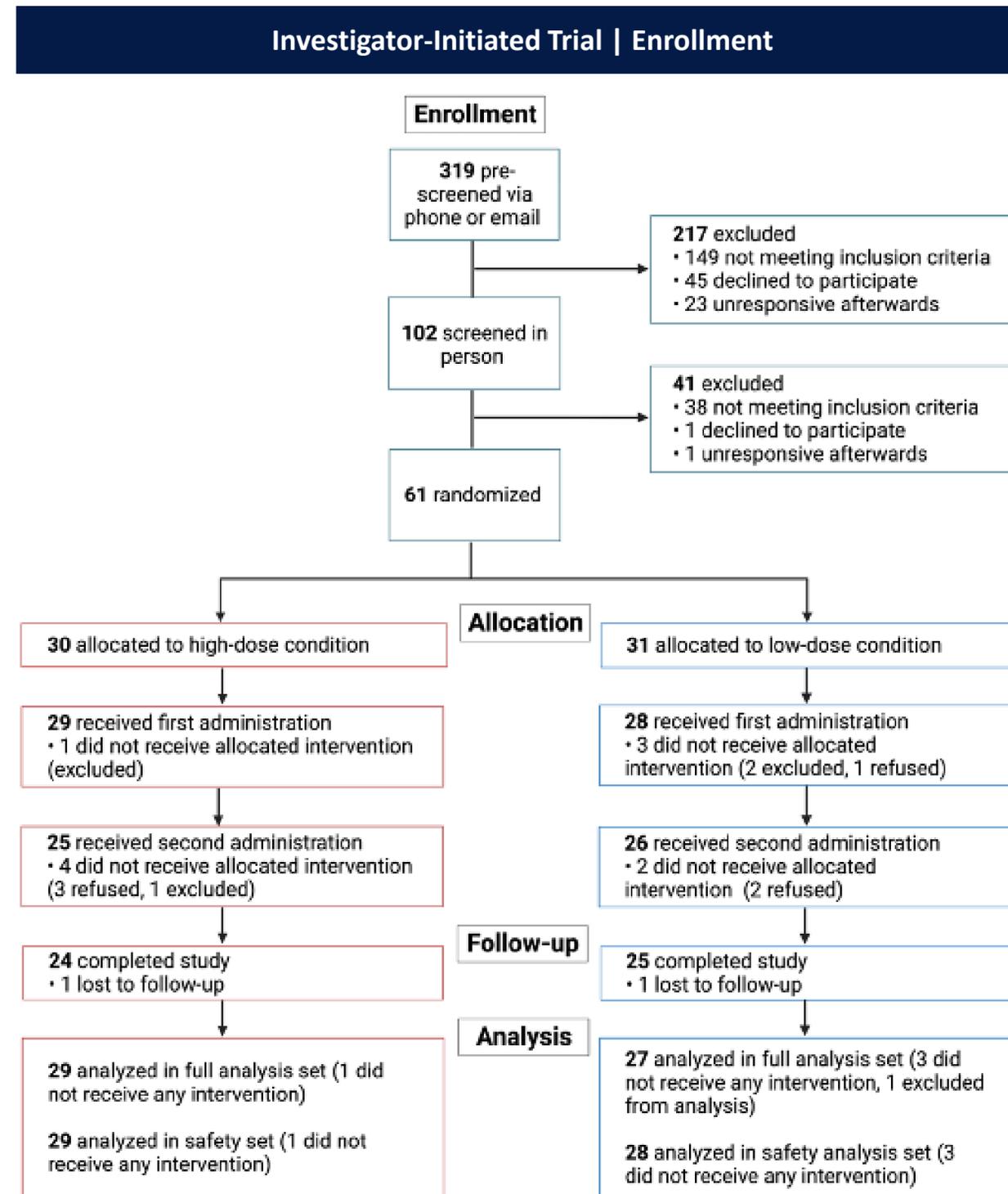
**Appendix**

# Investigator Initiated Trial of LSD for Depressive Disorders



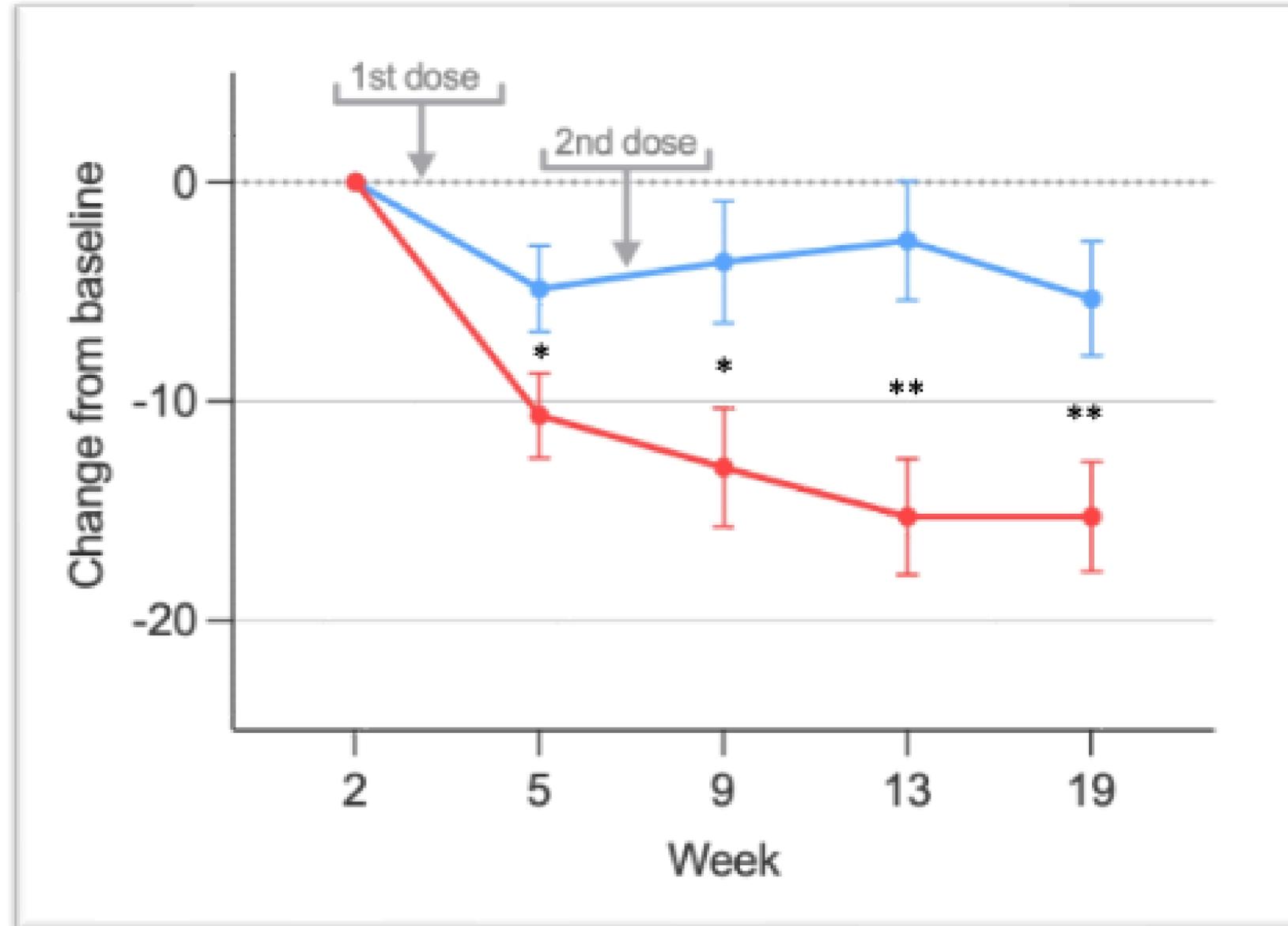
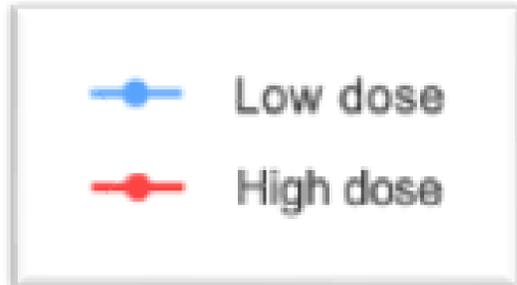
Study Design Overview
<p><b>KEY ENTRY CRITERIA</b></p> <ul style="list-style-type: none"> <li>• Men and Women</li> <li>• Ages 25 and older</li> <li>• Diagnosis of MDD</li> </ul>
<p><b>STUDY ENDPOINTS</b></p> <ul style="list-style-type: none"> <li>• IDS-C (primary at Week 9)</li> <li>• IDS-SR</li> <li>• BDI</li> <li>• SCL-90</li> </ul>

# Investigator Initiated Trial of LSD for Depressive Disorders



# Investigator Initiated Trial of LSD for Depressive Disorders

Primary Outcome Measure | Change in IDS-C over Time



## Change from Baseline to Week 9

- Low dose control: -3.6 points
- High dose: -12.9 points

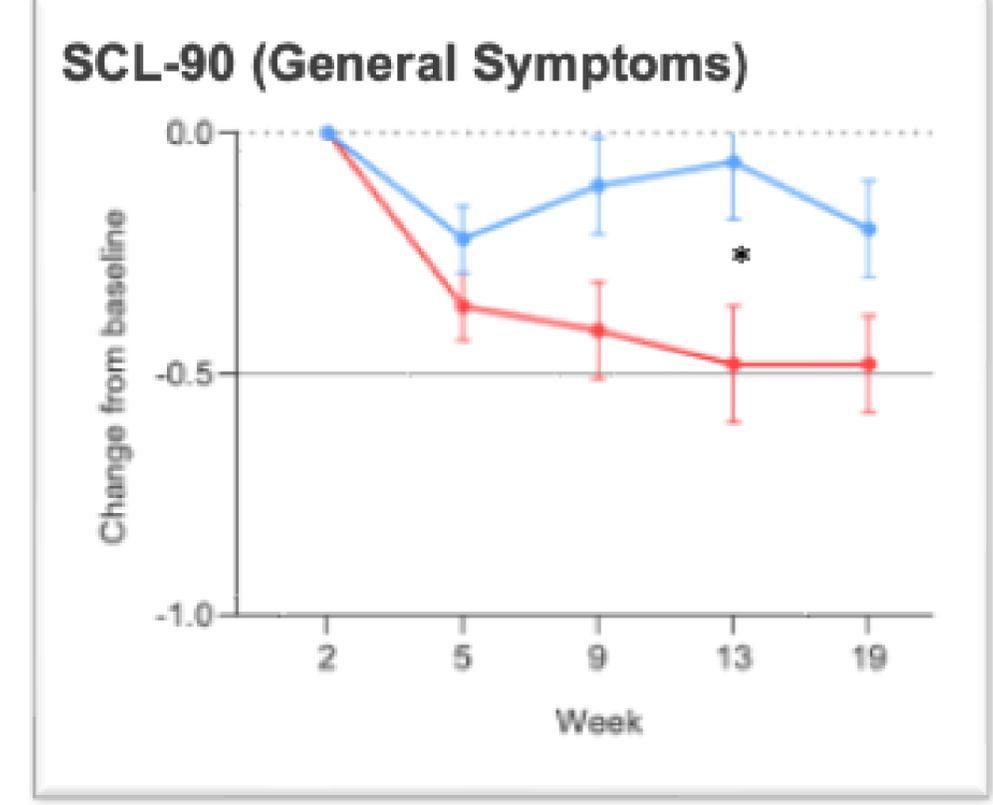
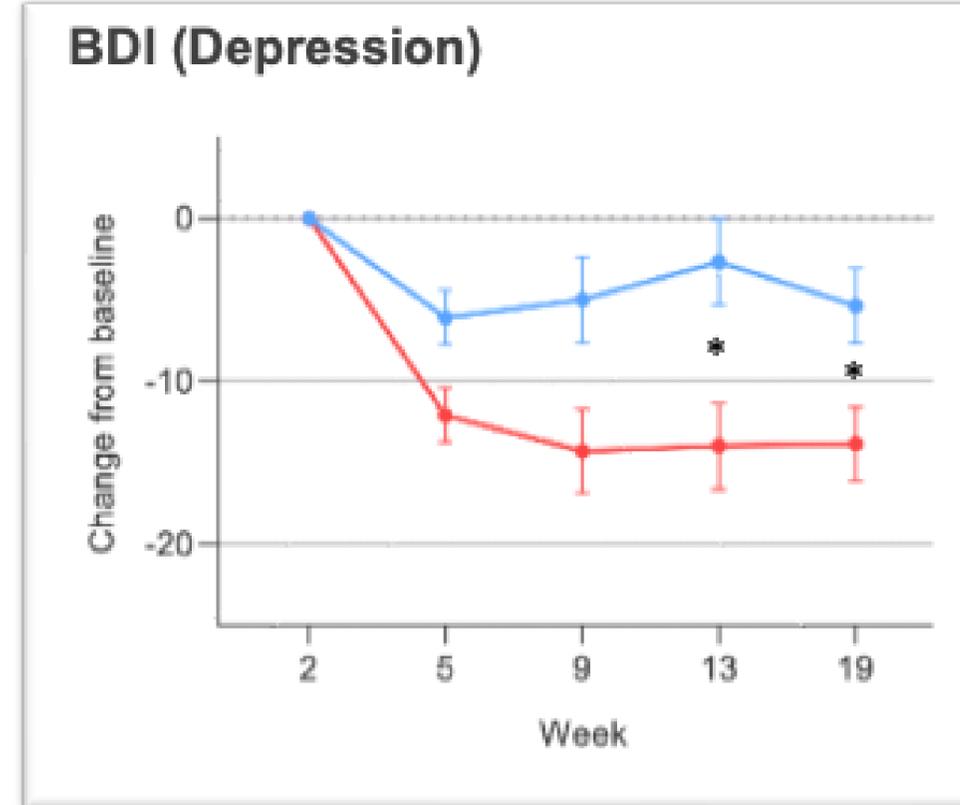
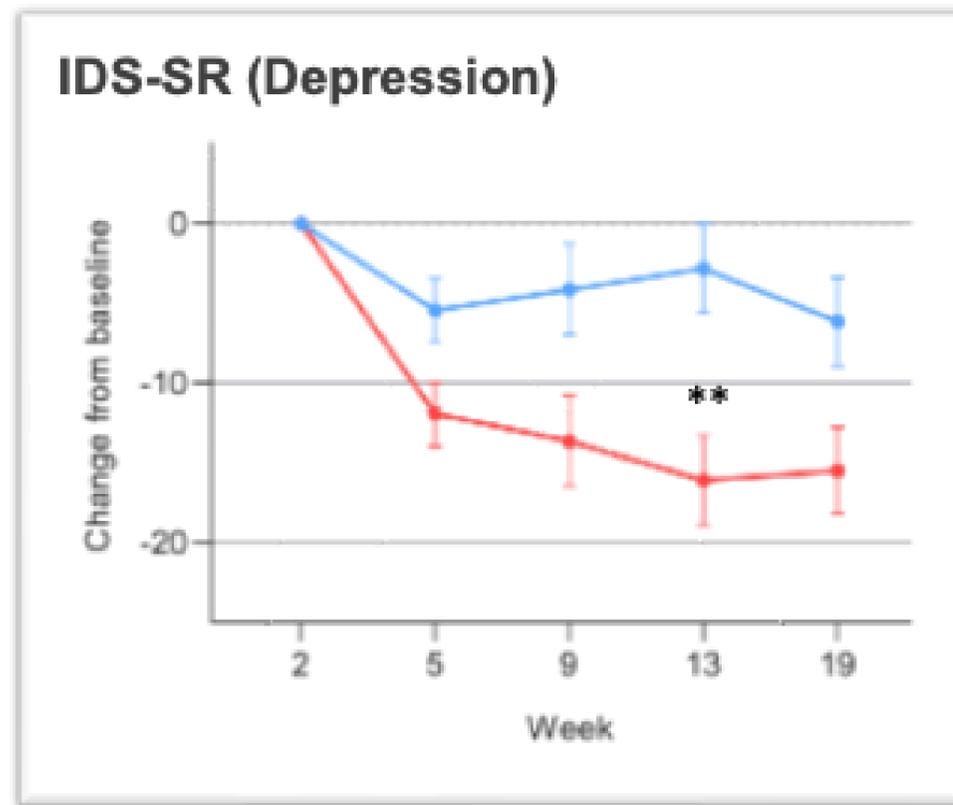
## Other Highlights

- 50% reduction from baseline in high dose group

\*p<0.05  
\*\*p≤0.01

# Investigator Initiated Trial of LSD for Depressive Disorders

## Secondary Outcome Measures



\*p<0.05  
\*\*p≤0.01