Safety, Pharmacokinetics, and Pharmacodynamics of MSD-001 after Single Dosing in Healthy Adults: A Randomized, Double-Blind, Placebo-Controlled Study

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LEGEND FOR ALL GRAPHS

Placebo · Part 1: 0.5 mg · Part 1: 1.0 mg · Part 1: 3.0 mg · Part 1: 6.0 mg · Part 1: 10.0 mg · Part 2: 0.5 mg · Part 2: 3.0 mg

1 – PURPOSE

Recent clinical trials have provided robust evidence for the therapeutic potential of serotonergic psychedelics such as psilocybin, lysergic acid diethylamide (LSD), and dimethyltryptamine (DMT) in the treatment of various mental health disorders following acute or intermittent dosing.[1,2]

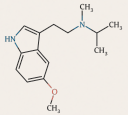


Figure 1. MSD-001

MSD-001 (5-MeO-MiPT) is a short-acting orally available serotonergic tryptamine that primarily engages 5-HT_{1A}, 5-HT_{7}, 5-HT_{1D} receptors. The aim of this single ascending dose study was to evaluate the safety, pharmacokinetic (PK), and pharmacodynamic (PD) profile of MSD-001 (0.5–10mg) in healthy adult male and female participants.

2 – METHODS

In this double-blind, placebo-controlled trial, CYP2D6 extensive metabolizers (EM)[3] received single doses of MSD-001 or placebo across 5 cohorts (0.5, 1, 3, 6, and 10mg); CYP2D6 poor metabolizers (PM) were similarly evaluated (MSD-001 0.5 and 3mg).

Part 1 (N=40): CYP2D6 Intermediate and Extensive Metabolizers (IM/EM; gene activity score 1–2.5), randomized, placebo-controlled, and double-blind.

Part 2 (N=7): CYP2D6 Poor Metabolizers (PMs), open-label.

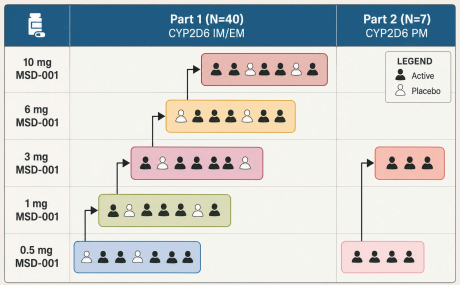


Figure 2. Study Cohorts

Procedures and Assessments

Eligible participants received a single dose of MSD-001 on Day 1 and were evaluated for safety, PK sampling and PD assessments. Participants were clinically monitored for the entirety of the dosing session (Day 1). Participants then returned to the clinic 14–16 days later for a clinical follow-up visit and contacted by phone 27–31 days thereafter.

Safety was assessed via evaluation of adverse events (AEs), vital signs, ECGs, laboratory tests, and suicidality risk. PK was analyzed using a non-compartmental model.[3] PD measures included assessments of subjective effect intensity, dimensions of subjective experience as well as associated changes in qEEG/fMRI and neurophysiological/psychological effects.

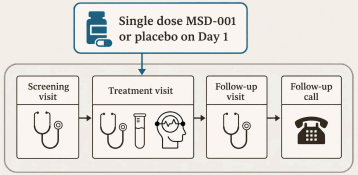
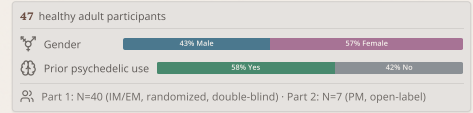


Figure 3. Study periods

Demographics & Baseline Characteristics

Cohorts were well balanced with no clinically meaningful differences across cohorts in baseline physical parameters including age, height, weight, and BMI.



3 – RESULTS

Safety

MSD-001 was safe and generally well-tolerated. No serious adverse events (SAEs) were reported, and most (98%) AEs were of mild intensity. The AEs reported in the highest proportion of participants dosed with MSD-001 were:

- Sensory processing disorder (e.g., visual effects; 49%)
- Feeling of relaxation (35%)
- Euphoric mood (32%)

No clinically meaningful cardiovascular, laboratory, physical, or psychiatric abnormalities were observed.

Pharmacokinetics

In **Part 1** (CYP2D6 IM/EMs), MSD-001 was rapidly absorbed (median T_{max} 1–2 h; median $t_{1/2}$ ~2–3 h) with dose-related exposure, except for a plateau between 6–10 mg MSD-001.

In **Part 2** (CYP2D6 PMs), median C_{max} increased ~1.6–1.8-fold and $t_{1/2}$ ~2-fold relative to IM/EMs.

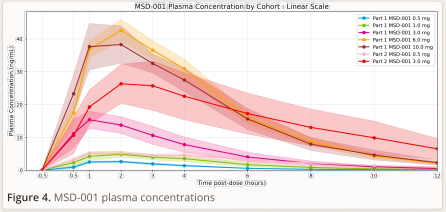


Figure 4. MSD-001 plasma concentrations

Pharmacodynamics

MSD-001 produced eyes-closed resting state EEG changes across frontal (Fz–Cz) and parietal–occipital (Pz–O1, Pz–O2) channels, showing suppression of delta and theta signals in the absence of any changes in alpha with the most pronounced effects at 6 and 10 mg.

MSD-001 showed elevations in saccadic peak velocity (SPV) at doses ≥3 mg, suggesting heightened arousal with no concomitant changes observed for attentional or psychomotor impairment.

MSD-001 increased ratings of feel drug effects, high, and liking relative to placebo, with the largest subjective drug-effect signal generally observed at the 6–10 mg doses suggesting that MSD-001 produced measurable acute subjective effects, including positive drug effects, without a consistent increase in desire for more drug.

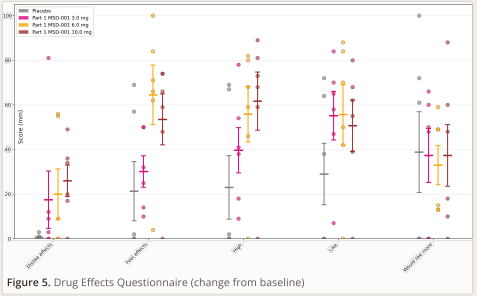


Figure 5. Drug Effects Questionnaire (change from baseline)

Exposure-related increases in 5D-ASC outcomes were observed at doses of ≥3 mg, most prominently in Reductions of Vigilance and Visionary Restructuralization. No effect was observed for Anxious Ego Dissolution and Auditory Alterations.

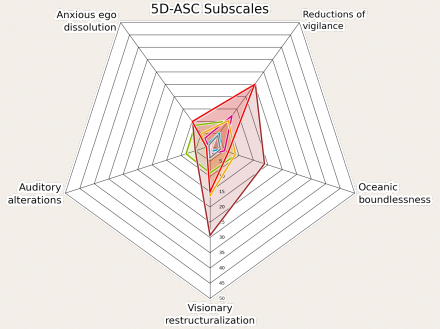


Figure 6. 5D-ASC Subscales

4 – CONCLUSION AND CLINICAL IMPLICATIONS

This first-in-human study demonstrates single oral doses of MSD-001 up to 10 mg in healthy participants to be safe and generally well tolerated with dose-proportional increases in PK observed across the dose range studied. The impact of CYP2D6 activity on its PK profile suggests the potential need for genotype informed dosing in future clinical trials. MSD-001 elicited mild dose-dependent alterations in subjective experience without evidence of anxious ego dissolution. Based on these findings, a dose range of 6–10 mg is supported for future clinical investigations of MSD-001.

REFERENCES

[1] Fernandes-Nascimento et al., 2025.
[2] Yao et al., 2024.
[3] Marasanapalle, V. P., et al. (2024). Investigation of the differences in the pharmacokinetics of drugs in individuals with different CYP2D6 genotypes. *Journal of Clinical Pharmacology*. Advance online publication.

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