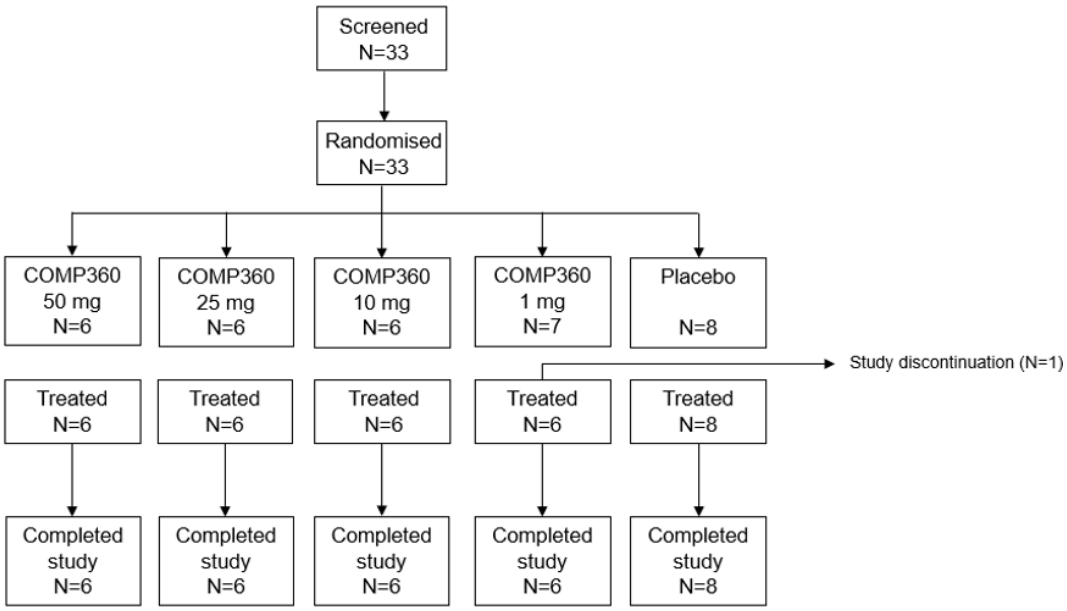
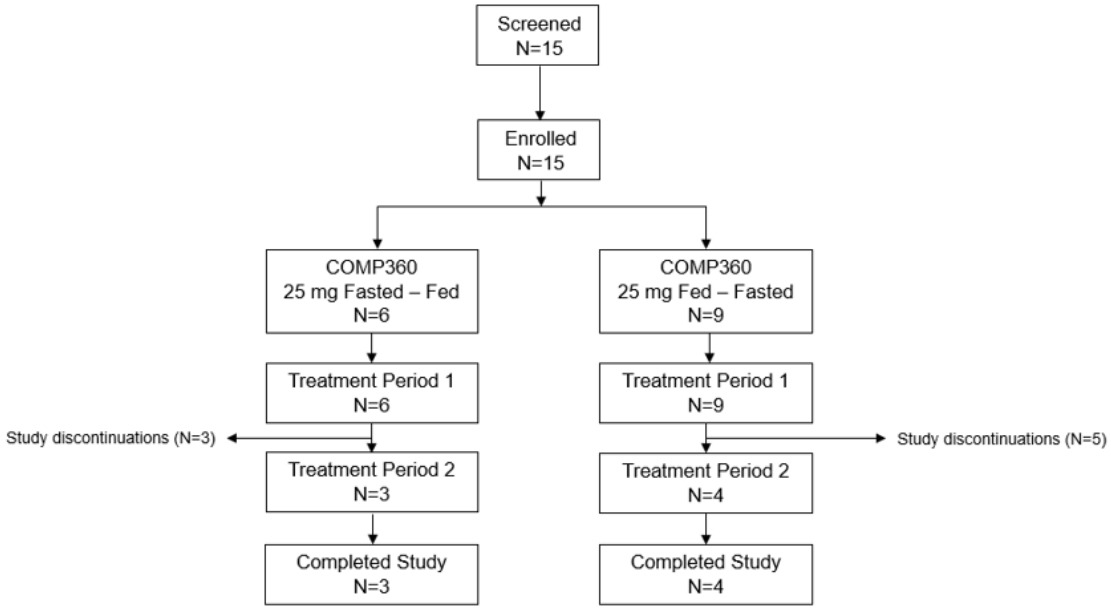
Participant flow

Single Dose Pharmacokinetic (PK) Component:



1 participant discontinued from the study due to the study staff being unable to cannulate.

Food Effect (FE) Component:



2 participants failed to meet continuation criteria; 1 participant withdrew consent; 5 participants discontinued for "other" reasons such as withdrawing due to not enough time between the first and second dose, requiring more than 2 weeks between the first and second dose, and not being able to attend the second dosing visit.

Baseline characteristics

Single Dose Pharmacokinetic (PK) Component:

	COMP360						
Characteristic	**50 mg**	**25 mg**	**10 mg**	**1 mg**	**All COMP360**	**Placebo**	**Overall**
Statistic	**N=6**	**N=6**	**N=6**	**N=6**	**N=24**	**N=8**	**N=32**
Age at Screening (years)							
Mean	23.5	33.5	30.0	32.3	29.8	31.5	30.3
SD	4.68	11.57	11.12	11.55	10.26	7.95	9.64
Min, max	21, 33	18, 50	20, 48	22, 48	18, 50	26, 50	18, 50
Median	22.0	35.0	26.5	29.0	24.0	28.5	27.0
Sex, n (%)							
Male	5 (83.3)	2 (33.3)	3 (50.0)	4 (66.7)	14 (58.3)	4 (50.0)	18 (56.3)
Female	1 (16.7)	4 (66.7)	3 (50.0)	2 (33.3)	10 (41.7)	4 (50.0)	14 (43.8)
Race, n (%)							
White	6 (100)	6 (100)	6 (100)	6 (100)	24 (100)	5 (62.5)	29 (90.6)
Mixed/other	0	0	0	0	0	3 (37.5)	3 (9.4)
Ethnicity, n (%)							
Hispanic or Latino	0	0	0	0	0	1 (12.5)	1 (3.1)
Not Hispanic or Latino	6 (100)	6 (100)	6 (100)	6 (100)	24 (100)	5 (62.5)	29 (90.6)
Unknown	0	0	0	0	0	2 (25.0)	2 (6.3)
BMI (kg/m^2)							
Mean	23.32	25.18	24.73	24.68	24.48	23.49	24.23
SD	2.885	3.610	3.876	1.965	3.043	2.622	2.934
Min, max	19.3, 28.1	18.8, 29.1	19.9, 29.3	21.7, 27.1	18.8, 29.3	20.3, 28.3	18.8, 29.3
Median	23.50	25.80	25.20	25.35	24.45	23.05	24.10

BMI=body mass index; Max=maximum; min=minimum; N=number of participants; SD=standard deviation.

Food Effect (FE) Component:

	COMP360		
Characteristic	**25 mg Fasted**	**25 mg Fasted**	**Overall**
Statistic	**25 mg Fed**	**25 mg Fed**	
	N=6	**N=9**	**N=15**
Age at Screening (years)			
Mean	35.2	30.4	32.3
SD	11.20	8.85	9.76
Min, max	21, 49	23, 51	21, 51
Median	39.5	28.0	31.0
Sex, n (%)			
Male	1 (16.7)	3 (33.3)	4 (26.7)
Female	5 (83.3)	6 (66.7)	11 (73.3)

	COMP360		
Characteristic **Statistic**	**25 mg Fasted** **25 mg Fed**	**25 mg Fasted** **25 mg Fed**	**Overall**
Race, n (%)			
Asian	0	1 (11.1)	1 (6.7)
Black or African American	0	2 (22.2)	2 (13.3)
White	6 (100)	6 (66.7)	12 (80.0)
Ethnicity, n (%)			
Not Hispanic or Latino	6 (100)	8 (88.9)	14 (93.3)
Unknown	0	1 (11.1)	1 (6.7)
BMI (kg/m^2)			
Mean	25.00	25.11	25.07
SD	1.334	2.855	2.301
Min, max	23.8, 27.4	19.6, 29.3	19.6, 29.3
Median	24.40	25.70	24.90

BMI=body mass index; Max=maximum; min=minimum; N=number of participants; SD=standard deviation.

Outcome measures

The primary objective of this study was to investigate the safety and tolerability of increasing doses of orally administered COMP360 (1 mg, 10 mg, 25 mg, and 50 mg) in healthy volunteers for the single dose PK and FE components.

Key safety conclusions are summarised below.

• COMP360 (50 mg, 25 mg, 10 mg and 1 mg) appeared to have an acceptable safety profile and was well tolerated in both the single dose PK and FE components.

• No serious treatment emergent adverse events (TEAEs) were identified in this study.

• The majority of TEAEs had on onset within the first 2 days following COMP360 administration and resolved within either 1 or 2 days.

• In the single dose PK component, related TEAEs were reported in 5 participants (83.3%) in the 50 mg group, 3 participants (50.0%) in the 25 mg group, 3 participants (50.0%) in the 10 mg group, and 1 participant (12.5%) in the placebo group. No related TEAEs were reported in the 1 mg group. In the FE component, 10 participants experienced TEAEs considered by the investigator to be related to study treatment (6 participants [60.0%] in fasted condition and 5 participants [41.7%] in the fed condition).

• In the single dose PK component, of participants treated with COMP360, 12 (50.0%) had mild TEAEs and 2 (8.3%) had moderate TEAEs. One participant (12.5%) treated with placebo experienced a mild TEAE. In the FE component, overall, 9 participants (60.0%) experienced mild TEAEs, and 3 participants (20.0%) experienced moderate TEAEs. No severe TEAEs were reported in either component.

• In the FE component, 2 participants in the fed condition had TEAEs that led to study discontinuation;1 participant (8.3%) had TEAEs of emotional distress, nausea, panic attack, and vomiting, and 1 participant (8.3%) had a TEAE of liver function test increased. No TEAEs leading to study discontinuation occurred in the single dose PK component.

• There was no increase in suicidal ideation or behaviour throughout the study, as assessed by the C-SSRS.

• No clinically significant trends were observed in the laboratory results.

• Transient elevations in systolic BP, diastolic BP, and HR were seen in most participants, with effects peaking 2 to 3 hours post-dose. However, there were limitations related to access of data that prevented review of all continuous BP data.

• The results from the cardiodynamic evaluation demonstrated that COMP360 has no clinically relevant effect on cardiac conduction but an effect on HR could not be excluded. The effect on the QTc interval was either small or negative and an effect on ΔΔQTcF exceeding 10 ms can be excluded within the full observed ranges of plasma concentrations of psilocin, 4-HIAA, and psilocin-O-glucuronide.

Adverse events

There were no serious adverse events (SAEs) reported in this study.