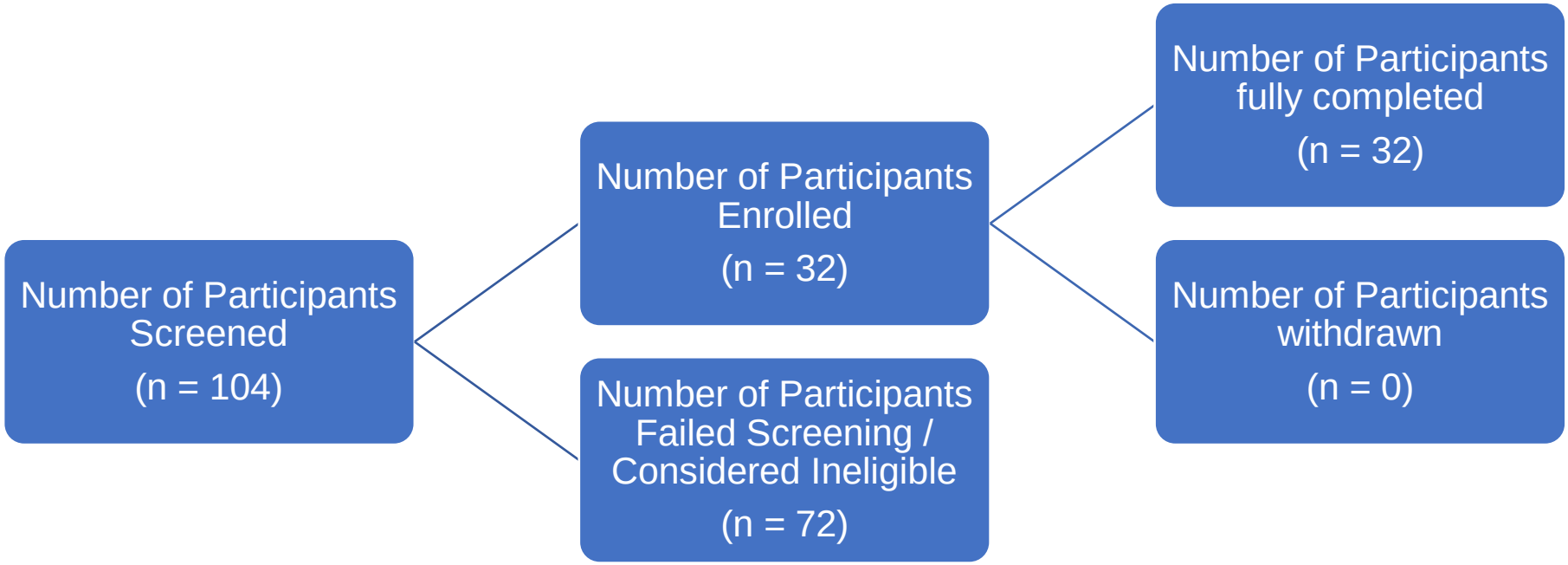
Participant Flow



Baseline Characteristics

Summary of Participant Demographics (Safety Set)

Parameter	Statistics	Placebo (N=8)	Cohort 1: OCT461201 10 mg (N=6)	Cohort 2: OCT461201 50 mg (N=6)	Cohort 3: OCT461201 150 mg (N=6)	Cohort 4: OCT461201 450 mg (N=6)	OCT461201 Overall (N=24)	Overall (N=32)
Age (yrs)	Mean	36.8	37.2	40.3	34.8	36.7	37.3	37.1
	SD	6.45	4.62	6.86	7.81	9.40	7.17	6.90
Height (m)	Mean	1.666	1.675	1.677	1.712	1.810	1.718	1.705
	SD	0.0605	0.0596	0.0653	0.0752	0.1285	0.0983	0.0923
Screening Weight (kg)	Mean	73.16	71.63	72.55	75.25	86.32	76.44	75.62
	SD	9.189	8.377	9.513	17.785	16.103	13.995	12.902
Post-Study Weight (kg)	Mean	73.16	71.95	72.92	75.30	86.72	76.72	75.83
	SD	9.268	8.339	10.128	18.156	17.317	14.511	13.345
Screening BMI (kg/m^2)	Mean	26.310	25.518	25.748	25.392	26.172	25.708	25.858
	SD	2.5458	2.6879	2.3924	3.9035	1.9979	2.6622	2.6061
Gender:								
Male	n (%)	3 (37.5)	1 (16.7)	3 (50.0)	4 (66.7)	5 (83.3)	13 (54.2)	16 (50.0)
Female	n (%)	5 (62.5)	5 (83.3)	3 (50.0)	2 (33.3)	1 (16.7)	11 (45.8)	16 (50.0)
Ethnicity:								
Not Hispanic or Latino	n (%)	8 (100.0)	6 (100.0)	6 (100.0)	6 (100.0)	6 (100.0)	24 (100.0)	32 (100.0)
Hispanic or Latino	n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Race:								
Asian	n (%)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	1 (4.2)	1 (3.1)
White	n (%)	8 (100.0)	6 (100.0)	5 (83.3)	4 (66.7)	6 (100.0)	21 (87.5)	29 (90.6)

Treatment: Single oral dose of OCT461201 capsule or placebo in the fasted state.
Percentages calculated from the number of participants in the Safety Set within a treatment group.

Outcome Measures

Table 1: Summary of Derived OCT461201 PK Parameters (PK Set)

Treatment	Summary Statistic	T_{max} (h)	C_{max} (ng/mL)	AUC_{0-t} (h*ng/mL)	AUC_{0-24} (h*ng/mL)	AUC_{0-inf} (h*ng/mL)	$AUC_{\%extrap}$ (%)	CL/F (L/h)	Vz/F (L)	$t_{1/2}$ (h)	Ae_{0*24} (ng)	Fe_{0-24} (%)	CL_R (L/h)
Cohort 1: 10 mg OCT461201 (N=6)	n	2	2	0	0	0	0	0	0	0	6	6	0
	Geo. Mean	*0.750	11.0	NC	NC	NC	NC	NC	NC	NC	824000	8.24	NC
	Geo. SD	(0.5 – 1.0)	1.01	NC	NC	NC	NC	NC	NC	NC	1.30	1.30	NC
	Geo. CV%	N/A	1.0	NC	NC	NC	NC	NC	NC	NC	26.6	26.6	NC
Cohort 2: 50 mg OCT461201 (N=6)	n	6	6	6	6	6	6	6	6	6	6	6	6
	Geo. Mean	*0.500	84.7	314	390	419	25.0	119	1050	6.08	4230000	8.45	10.8
	Geo. SD	(0.5 – 1.0)	1.50	1.30	1.25	1.30	1.11	1.30	1.12	1.33	1.58	1.58	1.70
	Geo. CV%	N/A	42.4	26.6	22.8	26.8	10.2	26.8	11.2	28.9	48.2	48.2	57.1
Cohort 3: 150 mg OCT461201 (N=6)	n	6	6	6	6	6	6	6	6	6	6	6	6
	Geo. Mean	*0.750	174	1020	1040	1200	14.5	125	1610	8.90	19300000	12.8	18.5
	Geo. SD	(0.5 – 3.0)	1.56	1.45	1.39	1.44	1.22	1.44	1.31	1.31	1.46	1.46	1.40
	Geo. CV%	N/A	46.5	38.4	34.0	37.9	19.8	37.9	27.2	27.5	39.1	39.1	34.5
Cohort 4: 450 mg OCT461201 (N=6)	n	6	6	6	6	6	6	6	6	6	6	6	6
	Geo. Mean	*1.00	647	4570	3890	4950	7.73	90.9	2160	16.4	60500000	13.4	15.5
	Geo. SD	(1.0 – 2.0)	1.38	1.28	1.27	1.29	1.18	1.29	1.28	1.10	1.52	1.52	1.58
	Geo. CV%	N/A	33.1	24.9	24.6	25.5	16.7	25.5	24.8	9.4	43.9	43.9	47.9

***** Median (min-max) presented for T_{max}

Treatment: Single oral dose of OCT461201 capsule in the fasted state.

LLOQ = 9.87 ng/mL. For the purposes of PK parameter calculation, BLQ values were set to zero at pre-dose and missing for post-dose timepoints.

AUCs and associated parameters non-calculable due to insufficient data.

Table 2: Summary of Statistical Analysis of Plasma OCT461201 Dose Proportionality (PK Set)

Parameter	Geometric LSMeans (95% CI)				Intercept	Slope (95% C.I.)
	Cohort 1: OCT461201 10 mg (N=6)	Cohort 2: OCT461201 50 mg (N=6)	Cohort 3: OCT461201 150 mg (N=6)	Cohort 4: OCT461201 450 mg (N=6)		
C_{max} (ng/mL)	11.0 (6.22, 19.5)	84.7 (60.9, 118)	174 (125, 242)	647 (465, 899)	0.2983	1.005 (0.845, 1.164)
AUC_{0-t} (h*ng/mL)	NC	314 (242, 407)	1020 (788, 1320)	4570 (3520, 5920)	0.9291	1.219 (1.052, 1.385)
AUC_{0-inf} (h*ng/mL)	NC	419 (323, 543)	1200 (925, 1550)	4950 (3820, 6420)	1.5806	1.124 (0.955, 1.293)

Treatment: Single oral dose of OCT461201 capsule in the fasted state.
Results obtained using a regression analysis on log-transformed values versus log-transformed dose using the power model.
NC = Non-calculable due to insufficient data

Table 3: Summary of Statistical Analysis of Plasma OCT461201 Dose Independence (PK Set)

Parameter	LSMeans (95% CI)				Intercept	Slope (95% C.I.)
	Cohort 1: OCT461201 10 mg (N=6)	Cohort 2: OCT461201 50 mg (N=6)	Cohort 3: OCT461201 150 mg (N=6)	Cohort 4: OCT461201 450 mg (N=6)		
$t_{1/2}$ (h)	NC	6.29 (4.56, 8.02)	9.17 (7.44, 10.9)	16.5 (14.8, 18.2)	5.1774	0.025 (0.020, 0.031)
CL/F (L/h)	NC	123 (87.4, 158)	133 (97.7, 169)	93.3 (57.8, 129)	135.41	-0.088 (-0.206, 0.031)

Treatment: Single oral dose of OCT461201 capsule in the fasted state.
Results obtained using a fixed effects ANOVA on non-transformed data with a fixed effect of dose.

ANOVA = analysis of variance, NC = non-calculable due to insufficient data.

Adverse Events

A total of 7 treatment emergent adverse events (TEAEs) were reported by 7 (21.9%) participants during the study. All were mild or moderate and were considered of no reasonable possible relationship to IMP. A higher percentage of participants reported TEAEs in the OCT461201 treatment groups overall when compared to placebo (29.2% vs 0%). This appeared to be driven by increased reporting of individual TEAEs (preferred term) in the 50 mg and 150 mg dose groups, although overall the incidence was low and there were no clear dose-related trends. The most commonly occurring TEAE was headache reported by 3 (9.4%) participants overall. There were no SAEs, deaths or withdrawals due to AEs. All TEAEs resolved before the end of the study.

Table 4: Overall Summary of TEAEs by Severity and Relationship (Safety Set)

	Placebo (N=8)	Cohort 1: OCT461201 10 mg (N=6)	Cohort 2: OCT461201 50 mg (N=6)	Cohort 3: OCT461201 150 mg (N=6)	Cohort 4: OCT461201 450 mg (N=6)	OCT461201 Overall (N=24)	Overall (N=32)
Number of TEAEs	0	1	2	3	1	7	7
Number (%) of participants reporting at least one:							
TEAE	0 (0.0)	1 (16.7)	2 (33.3)	3 (50.0)	1 (16.7)	7 (29.2)	7 (21.9)
Serious TEAE	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TEAE Leading to Withdrawal	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
TEAE Leading to Death	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Number (%) of participants with TEAE by severity:							
Mild	0 (0.0)	1 (16.7)	2 (33.3)	2 (33.3)	1 (16.7)	6 (25.0)	6 (18.8)
Moderate	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (4.2)	1 (3.1)
Severe	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Number (%) of participants with TEAE by relationship to study drug:							
Reasonable Possibility	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
No Reasonable Possibility	0 (0.0)	1 (16.7)	2 (33.3)	3 (50.0)	1 (16.7)	7 (29.2)	7 (21.9)

Treatment: Single oral dose of OCT461201 capsule or placebo in the fasted state.
A participant with multiple adverse events is counted only once at the maximum level of severity or the strongest relationship to study drug within a treatment group.
Percentages calculated from the number of participants in the Safety Set within a treatment group.

Table 5: TEAEs in Each Treatment Group by Preferred Term (Safety Set)

Preferred Term	Number of Events / Number (%) of Participants						
	Placebo (N=8)	Cohort 1: OCT461201 10 mg (N=6)	Cohort 2: OCT461201 50 mg (N=6)	Cohort 3: OCT461201 150 mg (N=6)	Cohort 4: OCT461201 450 mg (N=6)	OCT461201 Overall (N=24)	Overall (N=32)
Headache	0 / 0 (0.0)	0 / 0 (0.0)	2 / 2 (33.3)	1 / 1 (16.7)	0 / 0 (0.0)	3 / 3 (12.5)	3 / 3 (9.4)
Arthralgia	0 / 0 (0.0)	0 / 0 (0.0)	0 / 0 (0.0)	1 / 1 (16.7)	0 / 0 (0.0)	1 / 1 (4.2)	1 / 1 (3.1)
Dizziness	0 / 0 (0.0)	0 / 0 (0.0)	0 / 0 (0.0)	1 / 1 (16.7)	0 / 0 (0.0)	1 / 1 (4.2)	1 / 1 (3.1)
Lip swelling	0 / 0 (0.0)	1 / 1 (16.7)	0 / 0 (0.0)	0 / 0 (0.0)	0 / 0 (0.0)	1 / 1 (4.2)	1 / 1 (3.1)
Oropharyngeal pain	0 / 0 (0.0)	0 / 0 (0.0)	0 / 0 (0.0)	0 / 0 (0.0)	1 / 1 (16.7)	1 / 1 (4.2)	1 / 1 (3.1)

Treatment: Single oral dose of OCT461201 capsule or placebo in the fasted state.
A participant is counted only once per preferred term within a treatment group.
Percentages calculated from the number of participants in the Safety Set within a treatment group.