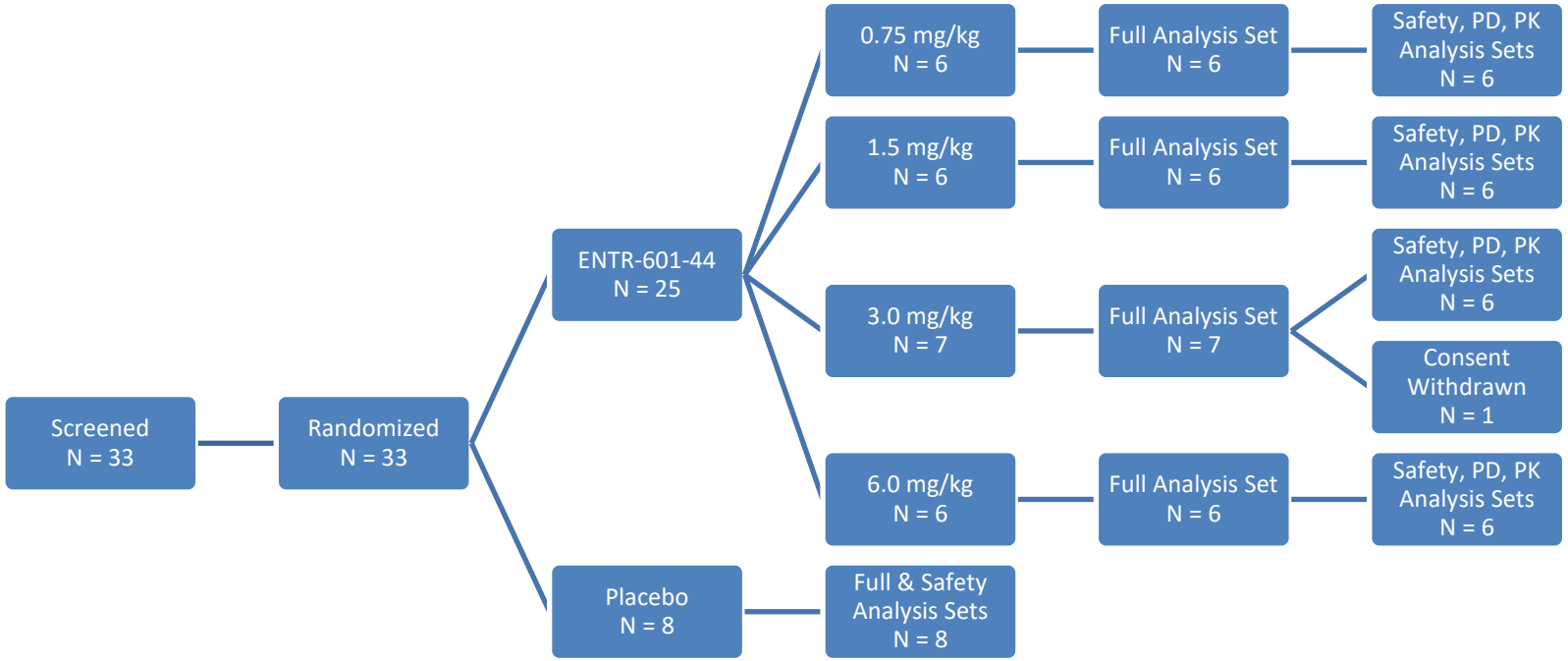
1. STUDY ENTR-601-44-101 BASIC RESULTS

1.1. Participant Flow



Abbreviations: N – number of participants in each group.

1.2. Baseline Characteristics

Table 1: Baseline characteristics for Study ENTR-601-44-101

Characteristic		**ENTR-601-44 (N = 25)**	**Placebo (N = 8)**	**Overall (N = 33)**
Race	Asian	2 (8.0%)	1 (12.5%)	3 (9.1%)
	White	19 (76.0%)	7 (87.5%)	26 (78.8%)
	Multiple	2 (8.0%)	0	2 (6.1%)
	Other: Black African	1 (4.0%)	0	1 (3.0%)
	Other: African	1 (4.0%)	0	1 (3.0%)
	Missing Values	0	0	0
Age at Screening (years; mean)		32.96	31.25	32.55
Ethnicity	Not Hispanic or Latino	24 (96.0%)	8 (100.0%)	32 (97.0%)
	Not Reported	1 (4.0%)	0	1 (3.0%)
	Missing Values	0	0	0
Height at Screening (m; mean)		1.78	1.76	1.77
Weight at Screening (kg/m^2; mean)		77.74	83.26	79.08 (mean)
Body Mass Index at Screening (kg/m^2; mean)		24.66	26.88	25.2 (mean)
Sex	Male	25 (100.0%)	8 (100.0%)	33 (100.0%)

Abbreviations: kg – kilograms; m – meters; N – the number of participants who were randomized to the stated treatment group.

1.3. Outcome Measures

Table 2: Primary outcome measure: Incidence and severity of treatment-emergent adverse events (TEAEs) and serious adverse events (SAEs) at Day 1 to end of study

Dose Level (mg/kg)	Number of TEAEs n (%), e	Number of Serious TEAEs n (%), e	Number of Life-Threatening or Fatal TEAEs n (%), e
0.75 (N = 6)	5 (83.3%), 12 • Mild: 1 (16.7%), 2 • Moderate: 4 (66.7%), 6 • Severe: 0	0	0
1.5 (N = 6)	2 (33.3%), 3 • Mild: 0 • Moderate: 2 (33.3%), 2 • Severe: 0	0	0
3.0 (N = 6)	3 (50.0%), 3 • Mild: 2 (33.3%), 2 • Moderate: 1 (16.7%), 1 • Severe: 0	0	0
6.0 (N = 6)	3 (50.0%), 4 • Mild: 2 (33.3%), 3 • Moderate: 1 (16.7%), 1 • Severe: 0	0	0
Placebo (N = 8)	1 (12.5%), 1 • Mild: 0 • Moderate: 1 (12.5%), 1 • Severe: 0	0	0

Abbreviations: kg – kilogram; mg – milligram, N – the number of participants who received at least one dose in the stated treatment group; SAE – serious adverse event; TEAE – treatment-emergent adverse event.
n (%), e – number of participants with events (percentage of participant with events), number of events

Table 3: Primary outcome measure: Incidence of abnormalities in laboratory parameters, electrocardiogram (ECG) parameters, vital sign measurements, and physical examinations at Day 1 to end of study

Assessment	Summary
Clinical laboratory parameters	Overall, there were no clinically significant changes in safety laboratory assessments, including no clinically significant changes in coagulation-related-tests (platelet counts, PT, INR, aPTT), renal-related tests (cystatin C, BUN, creatinine, magnesium, or phosphorous levels), or liver function tests (ALT, AST, GGT, and ALP; alanine transaminase, aspartate aminotransferase, gamma-glutamyl transferase, and alkaline phosphatase, respectively).
Electrocardiogram (ECG) parameters	There were no significant treatment- or dose-related trends in the mean or individual participant ECG parameters during the study, including no clinically meaningful changes in QT intervals seen at any dose level. Although some ECG parameters were outside appropriate reference ranges at some timepoints, these findings were determined to be transient and of no clinical significance.
Vital sign measurements	There were no significant treatment- or dose-related trends in the mean or individual participant vital sign values during the study for systolic and diastolic BP, temperature, HR and respiratory rate. Although some vital sign parameters were outside the appropriate reference ranges, these findings were observed at isolated timepoints, transient and held no clinical significance.
Physical examinations	There were no clinically significant abnormal findings in the physical examinations performed during the study.

Abbreviations: ALP – alkaline phosphatase; ALT – alanine aminotransferase; aPTT – activated partial thromboplastin time; AST -aspartate aminotransferase; BP – blood pressure; BUN – blood urea nitrogen; ECG – electrocardiogram; GGT – gamma-glutamyl transferase; HR – heart rate; INR – international normalized ratio; PT – preferred term.

Table 4: Secondary outcome measures for Study ENTR-601-44-101

Outcome Measure	Parameter	Dose Level (mg/kg)	ENTR-601-44 Mean (SD), N	Metabolite Mean (SD), N
Plasma PK of ENTR-601-44 and its final metabolite, including but not limited to maximum concentration (C_{max}), area under the curve (AUC_{last}), and the half-life ($t_{½}$) from Day 1 to end of study	C_{max} (ng/mL)	0.75	3570 (571), N = 6	No measurable concentration[1]
		1.5	7400 (475), N = 6	NC; only 3 participants at this dose level had two measurable concentrations.
		3.0	15500 (2070), N = 6	10.1 (3.90), N = 6
		6.0	31100 (3760), N = 6	15.4 (5.24), N = 6
	AUC_{last} (h*ng/mL)	0.75	4630 (794), N = 6	No measurable concentration[1]
		1.5	11900 (1000), N = 6	NC; only 3 participants at this dose level had two measurable concentrations.
		3.0	27800 (3500), N = 6	947 (422), N = 4
		6.0	59900 (8060), N = 6	1560 (521), N = 6
	$t_{½}$ (h)	0.75	2.63 (0.230), N = 6	No measurable concentration[1]
		1.5	3.24 (1.13), N = 6	NC
		3.0	3.86 (0.428), N = 6	172 (NC), N = 1
		6.0	5.16 (1.93), N = 6	102 (30.3), N = 6

Table 4: Secondary outcome measures for Study ENTR-601-44-101 (Continued)

Outcome Measure	Parameter	Dose Level (mg/kg)	ENTR-601-44 Mean (SD), N	Metabolite Mean (SD), N
Amounts of ENTR-601-44 and its final metabolite excreted in urine at Day 1 to end of study	$A_{e\ (000\text{-}144)}$ (mg)	0.75	Not observed	5.29 (1.20), N = 6
		1.5	Not observed	14.9 (1.51), N = 6
		3.0	0.00566 (NC), N = 1	25.7 (10.2), N = 6
		6.0	0.583 (0.538), N = 5	130 (11.3), N = 6

[1]Concentration was near the lower limit of quantification (LLOQ; 5 ng/mL).
Abbreviations: AUC – area under curve; Ae(000-144) = Cumulative amount excreted (Ae) over the time interval from the start of infusion through end of collection interval in hours; AUC_{last} – AUC from start of infusion to time of the last quantifiable concentration; C_{max} – maximum observed concentration; h – hours; mg – milligram; mL – milliliter; ng – nanogram; N – number of participants in analysis; NC – not calculated; PK – pharmacokinetic; SD – standard deviation; $t_{½}$ – observed terminal half-life.

1.4. Adverse Events

Table 5: Incidence of adverse events in Study ENTR-601-44-101

System Organ Class	ENTR-601-44 0.75 mg/kg	ENTR-601-44 1.5 mg/kg	ENTR-601-44 3.0 mg/kg	ENTR-601-44 6.0 mg/kg	Placebo	Overall
Ear and labyrinth	0	1	0	0	0	1
Gastrointestinal	1	1	0	1	0	3
General, administration site conditions	0	0	0	2	0	2
Infections and infestations	3	1	1	0	0	5
Injury, poisoning, and procedural complications	2	0	0	0	1	3
Nervous system	2	0	2	2	1	7
Renal and urinary	1	0	0	0	0	1
Respiratory, thoracic, and mediastinal	1	0	0	0	0	1

Abbreviations: kg – kilogram; mg – milligram.

There were no deaths, SAEs, significant AEs, or AEs (including treatment-emergent AEs) which required a participant to be withdrawn during the study.