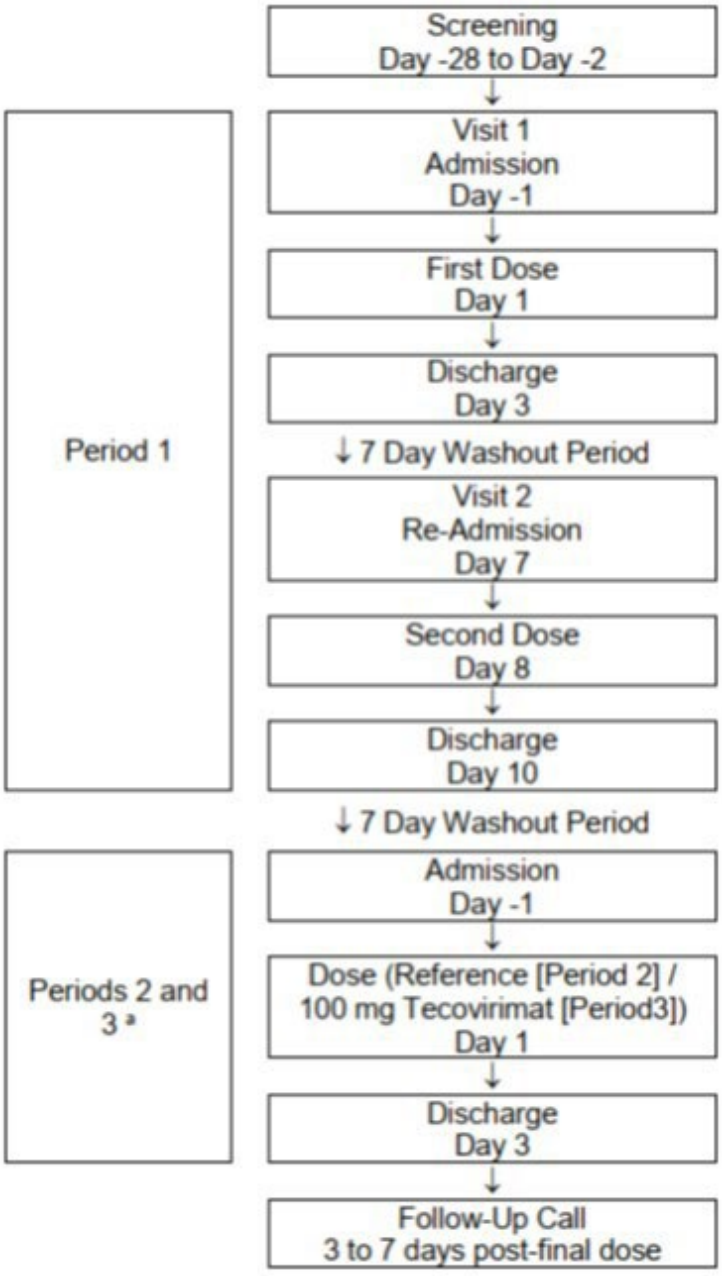
Participant Flow



Baseline Characteristics

Study Demographics

		Overall (N=11) n (%)
Age (years)	n	11
	Mean	32.3
	SD	10.1

	Median	30.0
	Min	21
	Max	50
Ethnicity n (%)	NOT HISPANIC OR LATINO	11 (100)
Race n (%)	ASIAN	1 (9.1)
	BLACK OR AFRICAN AMERICAN	1 (9.1)
	WHITE	9 (81.8)
Sex n (%)	MALE	8 (72.7)
	FEMALE	3 (27.3)
Height (cm)	n	11
	Mean	175.6
	SD	7.7
	Median	176.0
	Min	164
	Max	189
Weight (kg)	n	11
	Mean	78.50
	SD	16.16
	Median	76.60
	Min	58.0
	Max	100.7
BMI (kg/m²)	n	11
	Mean	25.34
	SD	4.31
	Median	25.90
	Min	20.0
	Max	31.5

Outcome Measures

Parameter	Definition
$AUC_{(0\text{-}24)}$	Area under the curve from time 0 to 24 hours post-dose
$AUC_{(0\text{-}inf)}$	Area under the curve from time 0 extrapolated to infinity
$AUC_{(0\text{-}last)}$	Area under the curve from time 0 to the time of last measurable concentration
AUC_{extrap}	Area under the curve from time of the last measurable concentration to infinity as a percentage of the area under the curve extrapolated to infinity
C_{24}	Concentration at 24 hours post-dose
CL/F	Total body clearance calculated after a single extravascular administration where F (fraction of dose bioavailable) is unknown

C_{max}	Maximum observed concentration
Frel AUC(0-inf)	Relative bioavailability based on AUC(0-inf)
F_{rel} AUC(0-last)	Relative bioavailability based on AUC(0-last)
F_{rel} C_{max}	Relative bioavailability based on Cmax
Lambda-z	First order rate constant associated with the terminal (log-linear) portion of the curve
$T_{1/2}$	Terminal elimination half-life
T_{lag}	Time prior to the first measurable concentration
T_{max}	Time of maximum observed concentration
Vz/F	Apparent volume of distribution based on the terminal phase calculated using AUC(0-inf) after a single extravascular administration where F (fraction of dose bioavailable) is unknown

Pharmacokinetics

Dose level and formulation Status Subjects	600 mg Prototype 1 Day 1 Fed N=11	600 mg Prototype 1 Day 8 Fed N=11	600 mg TPOXX reference capsule Fed N=10	100 mg Prototype 1 Fed N=10
T_{lag}[a] (h)	0.000 (0.00-0.00)	0.000 (0.00-0.00)	0.000 (0.00-0.50)	0.000 (0.00-0.50)
T_{max}[a] (h)	4.000 (1.50-5.00)	3.008 (1.00-5.00)	4.517 (3.02-6.00)	3.500 (1.50-5.03)
C_{max}[b] (ng/mL)	1550 (51.0)	1530 (36.6)	1130 (35.4)	308 (21.3)
C_{24}[b] (ng/mL)	183 (37.3)	167 (20.4)	154 (19.0)	62.5 (31.1)
$AUC_{(0-24)}$[b] (ng.h/mL)	12800 (38.2)	11600 (26.2)	8980 (29.8)	2530 (19.8)
$AUC_{(0-last)}$[b] (ng.h/mL)	16800 (32.6)	15100 (19.9)	12100 (22.9)	3750 (20.3)
$AUC_{(0-inf)}$[b] (ng.h/mL)	17500 [n=1]	16300 [n=1]	NC	NC
$T_{1/2}$[b] (h)	19.309 [n=1]	38.634 (58.6) [n=3]	26.20, 28.20 [n=2]	26.476 (14.8) [n=3]
Lambda-z [b] (1/h)	0.03590 [n=1]	1794 (58.6) [n=3]	246, 0.0265 [n=2]	2618 (14.8) [n=3]
CL/F [b] (mL/min)	571 [n=1]	613 [n=1]	NC	NC
Vz/F[b] (L)	954 [n=1]	1270 [n=1]	NC	NC
F_{rel} C_{max}[b] (%)	5.989 (43.1) [n=10]	99.909 (25.9)	NA	NA
F_{rel} $AUC_{(0-24)}$[b] (%) 24)	8.700 (26.9) [n=10]	93.387 (20.8)	NA	NA
F_{rel} $AUC_{(0-last)}$[b] (%)	4.311 (24.0) [n=10]	92.997 (18.9)	NA	NA
F_{rel} $AUC_{(0-inf)}$[b] (%)	NC	NC	NA	NA

NA = not applicable, NC = not calculated, [n] = number of subjects with an observation, h=hour
[a] Median (range)
[b] Geometric Mean (Geometric CV%)
F_{rel} values for 600 mg Prototype 1 Day 1 and 600 mg Prototype 1 Day 8 capture the comparisons 600 mg Prototype 1 Day 1 vs. 600 mg TPOXX and 600 mg Prototype 1 Day 8 vs 600 mg Prototype 1 Day 1, respectively

Bioavailability

Comparison	Pharmacokinetic Parameter	Geometric Mean Ratio (%)	90% Confidence Interval of Geometric Mean Ratio (%)
600 mg Prototype 1 Day 1 vs. 600 mg TPOXX reference capsule	C_{max}	135.99	(113.37, 163.12)
	$AUC_{(0-24)}$	138.70	(123.00, 156.41)
	$AUC_{(0-last)}$	134.31	(120.61, 149.57)
600 mg Prototype 1 Day 8 vs. 600 mg Prototype 1 Day 1	C_{max}	99.91	(83.29, 119.84)
	$AUC_{(0-24)}$	93.39	(82.82, 105.31)
	$AUC_{(0-last)}$	93.00	(83.51, 103.56)

Dose Proportionality

Comparison	Pharmacokinetic Parameter	Geometric Mean Ratio (%)	90% Confidence Interval of Geometric Mean Ratio (%)
600 mg Prototype 1 Day 1 vs. 100 mg Prototype 1	C_{max}	498.97	(388.27, 641.23)
	$AUC_{(0-24)}$	491.69	(412.80, 585.65)
	$AUC_{(0-last)}$	432.55	(372.85, 501.80)

Taste

Taste Attribute	Overall Liking	Smell	Sweetness	Bitterness	Flavour	Mouth Feel / Texture	Grittiness	Aftertaste
N	11	11	11	11	11	11	11	11
n	11	6	11	10	11	11	9	10
Median (range)	6.0 (3-9)	5.0 (5-9)	6.0 (4-9)	5.0 (3-9)	6.0 (3-9)	6.0 (2-9)	5.0 (3-9)	5.5 (2-9)
Grade 1 n (%)	0	0	0	0	0	0	0	0
Grade 2 n (%)	0	0	0	0	0	1 (9.1)	0	1 (9.1)
Grade 3 n (%)	1 (9.1)	0	0	1 (9.1)	2 (18.2)	0	1 (9.1)	1 (9.1)
Grade 4 n (%)	2 (18.2)	0	1 (9.1)	2 (18.2)	1 (9.1)	1 (9.1)	0	2 (18.2)
Grade 5 n (%)	0	5 (45.5)	1 (9.1)	4 (36.4)	1 (9.1)	2 (18.2)	6 (54.5)	1 (9.1)
Grade 6 n (%)	3 (27.3)	0	4 (36.4)	0	4 (36.4)	2 (18.2)	0	1 (9.1)
Grade 7 n (%)	2 (18.2)	0	1 (9.1)	0	0	3 (27.3)	1 (9.1)	1 (9.1)
Grade 8 n (%)	2 (18.2)	0	2 (18.2)	1 (9.1)	2 (18.2)	1 (9.1)	0	1 (9.1)
Grade 9 n (%)	1 (9.1)	1 (9.1)	2 (18.2)	2 (18.2)	1 (9.1)	1 (9.1)	1 (9.1)	2 (18.2)
N/A n (%)	0	5 (45.5)	0	1 (9.1)	0	0	2 (18.2)	1 (9.1)

Adverse Events

Overall Summary of Adverse Events

(subjects)	600 MG P1 Day 1 (N=11)	600 MG P1 Day 8 (N=10)	600 MG TPOXX (N=10)	100 MG Prototype 1 (N=10)	Overall (N=11)
	n (%)	n (%)	n (%)	n (%)	n (%)
Adverse Event	3 (27.3)	2 (20.0)	3 (30.0)	1 (1.0)	6 (54.5)
Severe AE	0	0	0	0	0

Adverse Drug Reaction	0	1 (10.0)	1 (10.0)	0	1 (9.1)
Serious AE	0	0	0	0	0
AE leading to Subject withdrawal	1 (9.1)	0	0	0	1 (9.1)
AE leading to death	0	0	0	0	0

Incidence of Adverse Events

(subjects)	**600 mg Prototype 1 Day 1 (N=11)**	**600 mg Prototype 1 Day 8 (N=10)**	**600 mg TPOXX reference capsule (N=10)**	**100 mg Prototype 1 (N=10)**	**Overall (N=11)**
System Organ Class Preferred Term	n(%)	n(%)	n(%)	n(%)	n(%)
TEAE's	3 (27.3)	2 (20.2)	3 (30.0)	1 (10.0)	6 (54.5)
Nervous System Disorders	2 (18.2)	1 (10.0)	2 (20.0)	0	3 (27.3)
Headache	1 (9.1)	1 (10.0)	2 (20.0)	0	2 (18.2)
Dizziness	1 (9.1)	0	0	0	1 (9.1)
Gastrointestinal disorders	0	0	1 (10.0)	1 (10.0)	2 (18.2)
Abdominal pain upper	0	0	1 (10.0)	0	1 (9.1)
Gingival pain	0	0	0	1 (10.0)	1 (9.1)
Infections and infestations	1 (9.1)	1 (10.0)	0	0	2 (18.2)

COVID-19	1 (9.1)	0	0	0	1 (9.1)
Viral upper respiratory tract infection	0	1 (10.0)	0	0	1 (9.1)
Reproductive system and breast disorders	0	0	1 (10.0)	0	1 (9.1)
Dysmenorrhea	0	0	1 (10.0)	0	1 (10.0)

There were 10 Adverse Events reported by 6 subjects. The most common Adverse Events reported was headache (4/10). Of reported Adverse Events, 2/10 were considered possibly related to Investigational Medicinal Product.