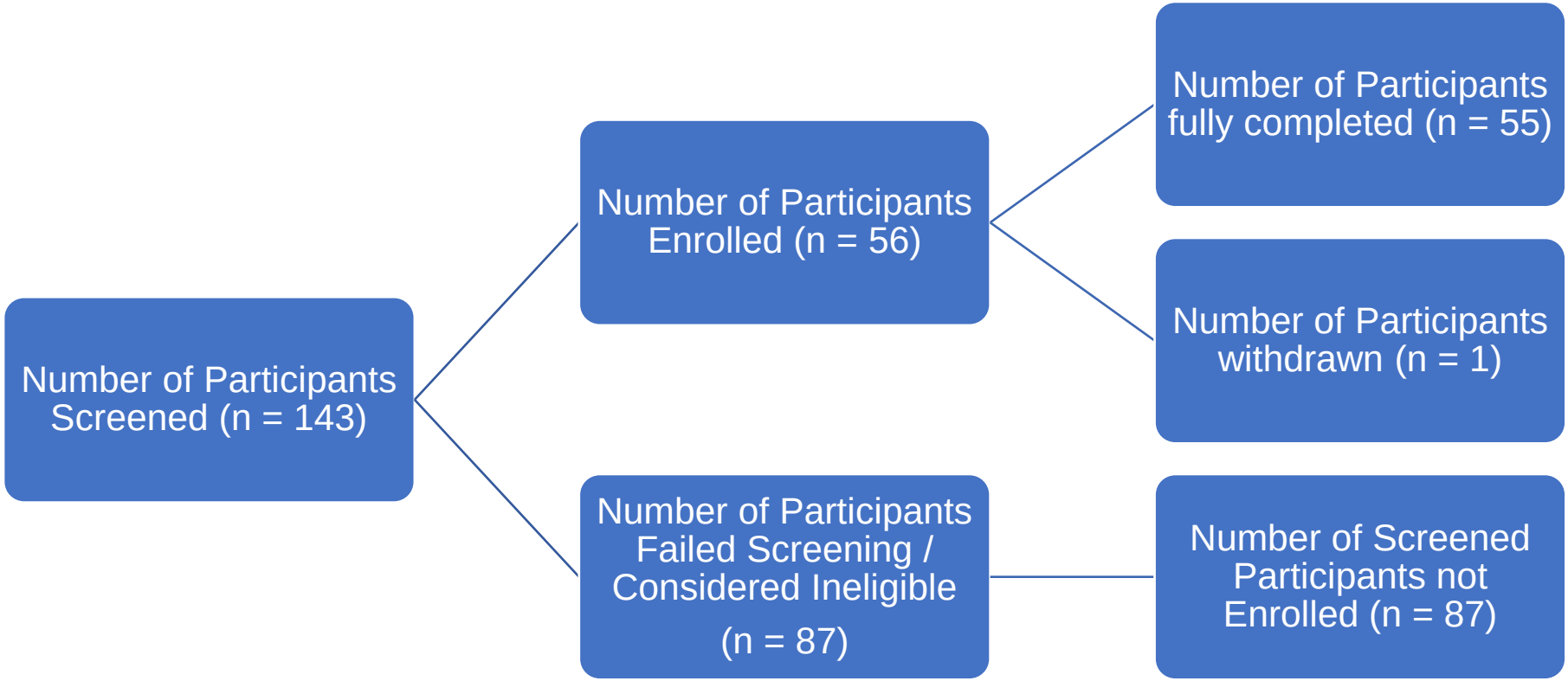
Participant Flow



Baseline Characteristics

Summary of Subject Demographics and Baseline Data (Safety Analysis Set)

		Cohort 1		Cohort 2		Cohort 3		Cohort 4		Cohort 5		Cohort 6		Cohort 7		PL Total (N=14)	ENX-102 Total (N=42)
		0.5mg ENX-102 (N=6)	PL (N=2)	1.0mg ENX-102 (N=6)	PL (N=2)	1.5mg ENX-102 (N=6)	PL (N=2)	2.0mg ENX-102 (N=6)	PL (N=2)	3.0mg ENX-102 (N=6)	PL (N=2)	5.0mg ENX-102 (N=6)	PL (N=2)	10mg ENX-102 (N=6)	PL (N=2)		
Age (years)	Mean	35.5	37.0	39.8	38.0	33.3	24.5	32.0	38.0	28.2	30.0	26.8	31.5	31.0	28.0	32.4	32.4
Height (cm)	Mean	176.8	183.0	172.3	176.0	177.8	176.0	170.3	177.0	162.7	178.5	167.2	169.5	164.5	184.0	177.7	170.2
Weight (kg)	Mean	78.47	90.55	77.88	69.20	81.40	79.65	77.38	91.35	73.47	86.00	58.73	85.70	64.62	83.15	83.66	73.14
BMI (kg/m^2)	Mean	24.92	27.10	26.13	22.30	25.77	25.75	26.37	29.20	27.90	26.90	21.00	29.85	23.72	24.65	26.54	25.11
Sex: Male	n (%)	5 (83.3%)	2 (100%)	3 (50.0%)	2 (100%)	5 (83.3%)	2 (100%)	2 (33.3%)	2 (100%)	1 (16.7%)	2 (100%)	1 (16.7%)	1 (50.0%)	0	2 (100%)	13 (92.9%)	17 (40.5%)
Female	n (%)	1 (16.7%)	0	3 (50.0%)	0	1 (16.7%)	0	4 (66.7%)	0	5 (83.3%)	0	5 (83.3%)	1 (50.0%)	6 (100%)	0	1 (7.1%)	25 (59.5%)
Ethnicity:																	
Hispanic/Latino	n (%)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Not Hispanic/Latino	n (%)	3 (50.0%)	1 (50.0%)	5 (83.3%)	2 (100%)	4 (66.7%)	2 (100%)	4 (66.7%)	2 (100%)	5 (83.3%)	2 (100%)	5 (83.3%)	2 (100%)	6 (100%)	2 (100%)	13 (92.9%)	32 (76.2%)
Not reported	n (%)	3 (50.0%)	1 (50.0%)	1 (16.7%)	0	2 (33.3%)	0	2 (33.3%)	0	1 (16.7%)	0	1 (16.7%)	0	0	0	1 (7.1%)	10 (23.8%)
Race:																	
American Indian/Alaska Native	n (%)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
Asian	n (%)	0	0	0	0	0	0	0	0	1 (16.7%)	0	0	0	0	0	0	1 (2.4%)
Black/African American	n (%)	0	0	0	0	1 (16.7%)	0	0	0	0	0	0	0	0	0	0	1 (2.4%)
Native Hawaiian/Other Pacific Islander	n (%)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
White	n (%)	5 (83.3%)	2 (100%)	6 (100%)	2 (100%)	5 (83.3%)	2 (100%)	6 (100%)	2 (100%)	5 (83.3%)	2 (100%)	6 (100%)	2 (100%)	6 (100%)	2 (100%)	14 (100%)	39 (92.9%)
Multiple Races Checked	n (%)	1 (16.7%)	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1 (2.4%)

PL = placebo

Outcome Measures

Table 1: Summary of Derived *ENX-102* PK Parameters (PK Analysis Set)

Parameter	Statistic	Cohort 1 0.5mg ENX-102 (N = 6)	Cohort 2 1mg ENX-102 (N = 6)	Cohort 3 1.5mg ENX-102 (N = 6)	Cohort 4 2mg ENX-102 (N = 6)	Cohort 5 3mg ENX-102 (N = 6)	Cohort 6 5mg ENX-102 (N = 6)	Cohort 7 10mg ENX-102 (N = 6)
C_{max} (ng/mL)	n	6	6	6	6	6	6	6
	Geo. Mean	6.929	13.141	14.857	20.319	32.006	55.972	95.023
T_{max} (h)	n	6	6	6	6	6	6	6
	Median	1.250	1.500	1.250	1.500	3.000	4.000	4.000
K_{el} (1/h)	n	6	6	6	6	6	6	6
	Geo. Mean	0.012	0.014	0.013	0.011	0.010	0.017	0.013
$t_{1/2}$ (h)	n	6	6	6	6	6	6	6
	Geo. Mean	59.342	50.200	53.190	60.559	72.479	40.960	51.432
AUC_{0-t} (h*ng/mL)	n	6	6	6	6	6	6	6
	Geo. Mean	237.674	370.833	517.328	807.109	1498.136	2345.840	4104.739
AUC_{0-24} (h*ng/mL)	n	6	6	6	6	6	6	6
	Geo. Mean	74.393	125.803	186.779	232.952	403.111	813.385	1350.152
AUC_{0-inf} (h*ng/mL)	n	6	6	6	6	6	6	6
	Geo. Mean	269.798	394.907	551.669	842.816	1682.124	2368.372	4553.557
CL/F (L/h)	n	6	6	6	6	6	6	6
	Geo. Mean	1.853	2.532	2.719	2.373	1.783	2.111	2.196
Vz/F (L)	n	6	6	6	6	6	6	6
	Geo. Mean	158.661	183.394	208.650	207.324	186.488	124.753	162.950

Table 2: Dose Proportionality Assessment (PK Analysis Set)

Dose Normalised Parameter	Statistic	Cohort 1 0.5mg ENX-102 (N = 6)	Cohort 2 1mg ENX-102 (N = 6)	Cohort 3 1.5mg ENX-102 (N = 6)	Cohort 4 2mg ENX-102 (N = 6)	Cohort 5 3mg ENX-102 (N = 6)	Cohort 6 5mg ENX-102 (N = 6)	Cohort 7 10mg ENX-102 (N = 6)
C_{max} (ng/mL/mg)	n	6	6	6	6	6	6	6
	Geo. LSMean[1]	13.8578	13.1410	9.9043	10.1593	10.6688	11.1945	9.5023
	Dose X/Dose 0.5mg		0.9483	0.7147	0.7331	0.7699	0.8078	0.6857
	90% CI of Ratio[1]		0.7874, 1.1420	0.5935, 0.8607	0.6087, 0.8829	0.6393, 0.9272	0.6708, 0.9729	0.5694, 0.8258
	p-value[2]		0.6323	0.0043	0.0078	0.0231	0.0605	0.0016
AUC_{0-inf} (h*ng/mL/mg)	n	6	6	6	6	6	6	6
	Geo. LSMean[1]	539.5962	394.9073	367.7796	421.4080	560.7081	473.6743	455.3557
	Dose X/Dose 0.5mg		0.7319	0.6816	0.7810	1.0391	0.8778	0.8439
	90% CI of Ratio[1]		0.5444, 0.9838	0.5070, 0.9162	0.5810, 1.0498	0.7730, 1.3968	0.6530, 1.1800	0.6278, 1.1344
	p-value[2]		0.0833	0.0353	0.1668	0.8278	0.4617	0.3390
AUC_{0-24} (h*ng/mL/mg)	n	6	6	6	6	6	6	6
	Geo. LSMean[1]	148.7852	125.8028	124.5194	116.4761	134.3702	162.6770	135.0152
	Dose X/Dose 0.5mg		0.8455	0.8369	0.7828	0.9031	1.0934	0.9075
	90% CI of Ratio[1]		0.7139, 1.0015	0.7066, 0.9912	0.6610, 0.9272	0.7625, 1.0697	0.9231, 1.2950	0.7662, 1.0748
	p-value[2]		0.1028	0.0842	0.0197	0.3160	0.3790	0.3389

[1] Analysis was performed on log-transformed values. Geometric means and CIs were converted to the original scale by taking the anti-log.

[2] P value was obtained using an ANOVA model with treatment as a main effect.

If 100% was included within the CIs, then linearity was concluded.

Adverse Events

A total of 28 adverse events were reported by participants across all dose levels within the study. There was an identified trend of higher incidences of reported adverse events (side effects) as the dose strength increased; however the reported effects were aligned with the types of effects reported for the study drug in previous clinical trials using an alternative form of ENX-102. All adverse events which were reported were considered to be mild to moderate in severity and resolved before the study completed.

Table 3: TEAEs in each Treatment Group by System Organ Class and Preferred Term (Safety Analysis Set)

SYSTEM ORGAN CLASS Preferred term [n (%) m]	Cohort 1 0.5mg ENX-102 (N = 6)	Cohort 2 1mg ENX-102 (N = 6)	Cohort 3 1.5mg ENX-102 (N = 6)	Cohort 4 2mg ENX-102 (N = 6)	Cohort 5 3mg ENX-102 (N = 6)	Cohort 6 5mg ENX-102 (N = 6)	Cohort 7 10mg ENX-102 (N = 6)	Placebo Total* (N=14)	ENX-102 Total (N = 42)
Any AE	0	3 (50.0%) 5	0	1 (16.7%) 1	3 (50.0%) 3	5 (83.3%) 8	4 (66.7%) 9	1 (7.1%) 1	16 (38.1%) 26
NERVOUS SYSTEM DISORDERS:	0	2 (33.3%) 3	0	1 (16.7%) 1	2 (33.3%) 2	3 (50.0%) 3	4 (66.7%) 7	1 (7.1%) 1	12 (28.6%) 16
Dizziness	0	1 (16.7%) 1	0	0	2 (33.3%) 2	2 (33.3%) 2	3 (50.0%) 3	0	8 (19.0%) 8
Dizziness Postural	0	1 (16.7%) 2	0	0	0	1 (16.7%) 1	1 (16.7%) 1	1 (7.1%) 1	3 (7.1%) 4
Somnolence	0	0	0	1 (16.7%) 1	0	0	2 (33.3%) 2	0	3 (7.1%) 3
Lethargy	0	0	0	0	0	0	1 (16.7%) 1	0	1 (2.4%) 1
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS:	0	1 (16.7%) 1	0	0	1 (16.7%) 1	3 (50.0%) 3	1 (16.7%) 2	0	6 (14.3%) 7
Fatigue	0	1 (16.7%) 1	0	0	0	3 (50.0%) 3	0	0	4 (9.5%) 4
Catheter Site Pain	0	0	0	0	1 (16.7%) 1	0	0	0	1 (2.4%) 1
Vessel Puncture Site Pain	0	0	0	0	0	0	1 (16.7%) 1	0	1 (2.4%) 1
Vessel Puncture Site Swelling	0	0	0	0	0	0	1 (16.7%) 1	0	1 (2.4%) 1
MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS:	0	1 (16.7%) 1	0	0	0	1 (16.7%) 1	0	0	2 (4.8%) 2
Back Pain	0	0	0	0	0	1 (16.7%) 1	0	0	1 (2.4%) 1
Pain in Extremity	0	1 (16.7%) 1	0	0	0	0	0	0	1 (2.4%) 1
GASTROINTESTINAL DISORDERS:	0	0	0	0	0	1 (16.7%) 1	0	0	1 (2.4%) 1
Nausea	0	0	0	0	0	1 (16.7%) 1	0	0	1 (2.4%) 1

* One subject experienced postural dizziness after receiving placebo in Cohort 5 (3 mg ENX-102/placebo).

n = Number of subjects; m = Number of events

AEs were coded using MedDRA version 24.0. At each level of summation (system organ class, preferred term) subjects reporting more than 1 event were included only once. Table was sorted by descending subject count in the total column across all subjects (not displayed) by system organ class and preferred term.

Percentages were based on total number of subjects in each treatment group. Treatment-emergence was defined as any AE that had an onset on or after the dose of study drug or any pre-existing condition that had worsened on or after the dose of study drug.

Table 4: Treatment Related TEAEs in each Treatment Group by System Organ Class, Preferred Term and Maximum Severity (Safety Analysis Set)

SYSTEM ORGAN CLASS Preferred Term Maximum Intensity [n (%)]	Cohort 1 0.5mg ENX-102 (N = 6)	Cohort 2 1mg ENX-102 (N = 6)	Cohort 3 1.5mg ENX-102 (N = 6)	Cohort 4 2mg ENX-102 (N = 6)	Cohort 5 3mg ENX-102 (N = 6)	Cohort 6 5mg ENX-102 (N = 6)	Cohort 7 10mg ENX-102 (N = 6)	Placebo Total* (N=14)	ENX-102 Total (N = 42)
Any AE:	0	3 (50.0%)	0	1 (16.7%)	2 (33.3%)	4 (66.7%)	4 (66.7%)	1 (7.1%)	14 (33.3%)
Mild	0	3 (50.0%)	0	1 (16.7%)	2 (33.3%)	3 (50.0%)	2 (33.3%)	0	11 (26.2%)
Moderate	0	0	0	0	0	1 (16.7%)	2 (33.3%)	1 (7.1%)	3 (7.1%)
Severe	0	0	0	0	0	0	0	0	0
NERVOUS SYSTEM DISORDERS:	0	2 (33.3%)	0	1 (16.7%)	2 (33.3%)	3 (50.0%)	4 (66.7%)	1 (7.1%)	12 (28.6%)
Mild	0	2 (33.3%)	0	1 (16.7%)	2 (33.3%)	2 (33.3%)	2 (33.3%)	0	9 (21.4%)
Moderate	0	0	0	0	0	1 (16.7%)	2 (33.3%)	1 (7.1%)	3 (7.1%)
Severe	0	0	0	0	0	0	0	0	0
Dizziness:	0	1 (16.7%)	0	0	2 (33.3%)	2 (33.3%)	3 (50.0%)	0	8 (19.0%)
Mild	0	1 (16.7%)	0	0	2 (33.3%)	2 (33.3%)	3 (50.0%)	0	8 (19.0%)
Moderate	0	0	0	0	0	0	0	0	0
Severe	0	0	0	0	0	0	0	0	0
Dizziness Postural:	0	1 (16.7%)	0	0	0	1 (16.7%)	1 (16.7%)	1 (7.1%)	3 (7.1%)
Mild	0	1 (16.7%)	0	0	0	0	0	0	1 (2.4%)
Moderate	0	0	0	0	0	1 (16.7%)	1 (16.7%)	1 (7.1%)	2 (4.8%)
Severe	0	0	0	0	0	0	0	0	0
Somnolence:	0	0	0	1 (16.7%)	0	0	2 (33.3%)	0	3 (7.1%)
Mild	0	0	0	1 (16.7%)	0	0	0	0	1 (2.4%)
Moderate	0	0	0	0	0	0	2 (33.3%)	0	2 (4.8%)
Severe	0	0	0	0	0	0	0	0	0
Lethargy:	0	0	0	0	0	0	1 (16.7%)	0	1 (2.4%)
Mild	0	0	0	0	0	0	1 (16.7%)	0	1 (2.4%)
Moderate	0	0	0	0	0	0	0	0	0
Severe	0	0	0	0	0	0	0	0	0
GENERAL DISORDERS AND ADMINISTRATION SITE CONDITIONS:	0	1 (16.7%)	0	0	0	3 (50.0%)	0	0	4 (9.5%)
Mild	0	1 (16.7%)	0	0	0	3 (50.0%)	0	0	4 (9.5%)
Moderate	0	0	0	0	0	0	0	0	0
Severe	0	0	0	0	0	0	0	0	0

SYSTEM ORGAN CLASS Preferred Term Maximum Intensity [n (%)]	Cohort 1 0.5mg ENX-102 (N = 6)	Cohort 2 1mg ENX-102 (N = 6)	Cohort 3 1.5mg ENX-102 (N = 6)	Cohort 4 2mg ENX-102 (N = 6)	Cohort 5 3mg ENX-102 (N = 6)	Cohort 6 5mg ENX-102 (N = 6)	Cohort 7 10mg ENX-102 (N = 6)	Placebo Total* (N=14)	ENX-102 Total (N = 42)
Fatigue:	0	1 (16.7%)	0	0	0	3 (50.0%)	0	0	4 (9.5%)
Mild	0	1 (16.7%)	0	0	0	3 (50.0%)	0	0	4 (9.5%)
Moderate	0	0	0	0	0	0	0	0	0
Severe	0	0	0	0	0	0	0	0	0
GASTROINTESTINAL DISORDERS:	0	0	0	0	0	1 (16.7%)	0	0	1 (2.4%)
Mild	0	0	0	0	0	1 (16.7%)	0	0	1 (2.4%)
Moderate	0	0	0	0	0	0	0	0	0
Severe	0	0	0	0	0	0	0	0	0
Nausea:	0	0	0	0	0	1 (16.7%)	0	0	1 (2.4%)
Mild	0	0	0	0	0	1 (16.7%)	0	0	1 (2.4%)
Moderate	0	0	0	0	0	0	0	0	0
Severe	0	0	0	0	0	0	0	0	0

* One subject experienced moderate postural dizziness after receiving placebo in Cohort 5 (3 mg ENX-102/placebo).

Treatment related included all events experienced as ‘Definitely’, ‘Probably’ or ‘Potentially’ related. Events with missing relationship were counted as related in this summary.

n = Number of subjects.

AEs were coded using MedDRA version 24.0. At each level of summation (system organ class, preferred term) subjects reporting more than 1 event were included only once at the maximum severity. AEs with missing severity were considered severe in this summary.

Table was sorted by descending subject count in the total column across all subjects (not displayed) by system organ class and preferred term.

Percentages were based on total number of subjects in each treatment group.

Treatment-emergence was defined as any AE that had an onset on or after the dose of study drug or any pre-existing condition that had worsened on or after the dose of study drug.