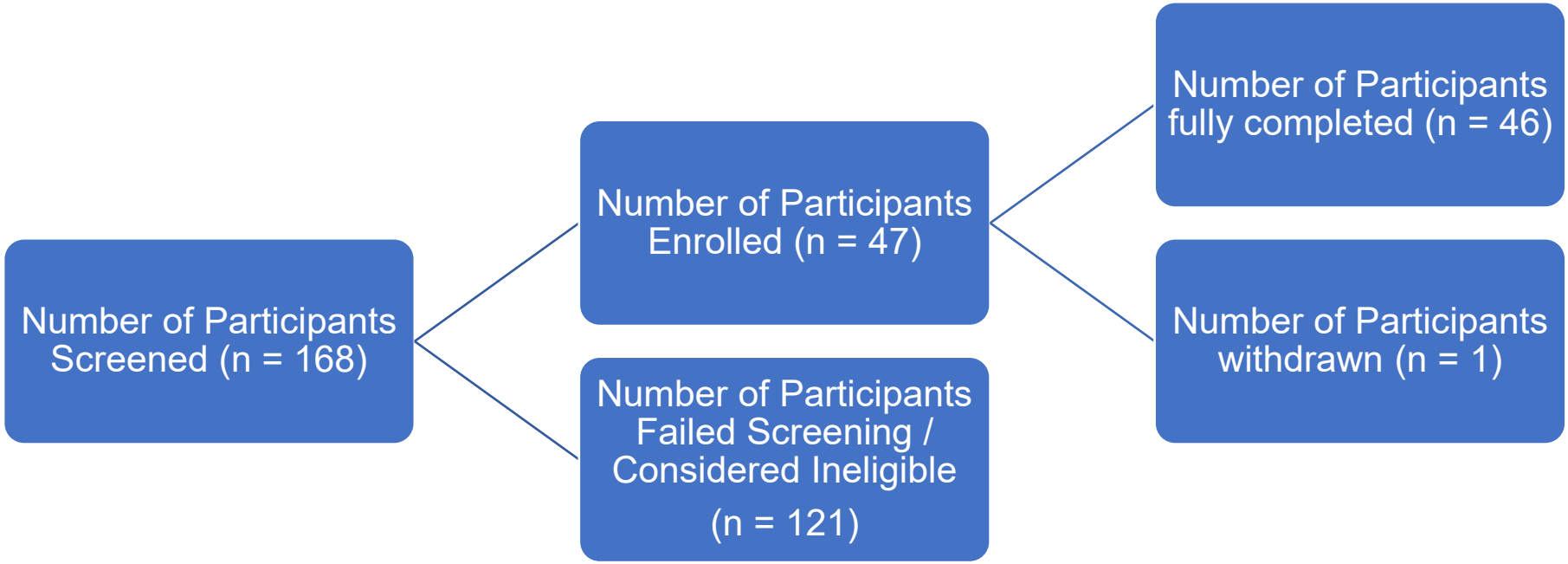
Participant Flow



Baseline Characteristics

Table 10.4.1 Summary of Participant Demographics – Period 1

		WVE-006					
	Pooled Placebo (N=10)	30 mg (N=6)	100 mg (N=5)	200 mg (N=6)	400 mg (N=6)	600 mg (N=6)	Total (N=39)
Age at informed consent (years)							
n	10	6	5	6	6	6	39
Mean	35.8	34.0	44.4	34.0	36.8	34.8	36.4
SD	9.0	8.7	11.9	10.2	9.3	8.9	9.5
Median	35.5	31.0	44.0	34.0	34.0	36.0	34.0
Q1, Q3	28.0, 39.0	28.0, 43.0	42.0, 55.0	24.0, 41.0	31.0, 42.0	26.0, 43.0	28.0, 43.0
Min, Max	26, 56	25, 46	26, 55	22, 49	27, 53	24, 44	22, 56
Sex							
n	10	6	5	6	6	6	39
Male	6 (60.0)	2 (33.3)	5 (100)	2 (33.3)	4 (66.7)	4 (66.7)	23 (59.0)
Female	4 (40.0)	4 (66.7)	0	4 (66.7)	2 (33.3)	2 (33.3)	16 (41.0)
Ethnicity							
n	10	6	5	6	6	6	39
Hispanic/Latino	0	0	1 (20.0)	0	0	0	1 (2.6)
Not Hispanic/Latino	10 (100)	6 (100)	4 (80.0)	6 (100)	6 (100)	6 (100)	38 (97.4)
Race							
n	10	6	5	6	6	6	39
American Indian or Alaska Native	0	0	0	0	0	0	0
Asian	0	0	0	0	0	0	0
Black or African American	0	0	0	0	0	0	0
Native Hawaiian or Other Pacific Islander	0	0	0	0	0	0	0
White	10 (100)	6 (100)	5 (100)	6 (100)	6 (100)	6 (100)	39 (100)
Mixed	0	0	0	0	0	0	0
Unknown	0	0	0	0	0	0	0
Other	0	0	0	0	0	0	0

		WVE-006					
	Pooled Placebo (N=10)	30 mg (N=6)	100 mg (N=5)	200 mg (N=6)	400 mg (N=6)	600 mg (N=6)	Total (N=39)
Weight (kg)							
n	10	6	5	6	6	6	39
Mean	77.57	82.38	89.60	65.40	73.95	82.45	78.17
SD	11.61	14.75	8.78	10.88	8.45	9.59	12.54
Median	80.65	80.45	93.40	65.40	72.75	82.05	78.40
Q1, Q3	68.50, 84.10	72.40, 94.60	81.00, 95.80	58.30, 76.00	69.10, 81.70	76.40, 88.00	69.10, 85.70
Min, Max	60.7, 93.5	63.3, 103.1	79.4, 98.4	49.2, 78.1	62.1, 85.3	69.6, 96.6	49.2, 103.1
Height (m)							
n	10	6	5	6	6	6	39
Mean	1.740	1.678	1.792	1.677	1.722	1.742	1.725
SD	0.103	0.113	0.064	0.078	0.083	0.037	0.089
Median	1.775	1.670	1.780	1.655	1.735	1.735	1.740
Q1, Q3	1.620, 1.800	1.570, 1.780	1.760, 1.840	1.610, 1.730	1.640, 1.790	1.710, 1.750	1.620, 1.790
Min, Max	1.56, 1.88	1.56, 1.82	1.71, 1.87	1.61, 1.80	1.61, 1.82	1.71, 1.81	1.56, 1.88
BMI (kg/m^2)							
n	10	6	5	6	6	6	39
Mean	25.496	29.048	28.000	23.123	24.892	27.157	26.161
SD	1.853	2.369	3.513	2.294	1.371	2.687	2.913
Median	25.595	29.555	27.400	23.795	25.170	27.940	25.750
Q1, Q3	24.270, 26.450	26.760, 31.130	26.150, 31.060	22.210, 24.570	23.510, 25.750	25.530, 29.310	24.100, 29.070
Min, Max	22.66, 29.30	25.68, 31.61	23.45, 31.94	18.98, 25.39	23.09, 26.66	22.73, 29.49	18.98, 31.94

Abbreviations: BMI = body mass index; n = number of participants with available data at the specific timepoint; SD = Standard Deviation; Q1 = 25% percentile; Q3 = 75% percentile; Min = Minimum; Max = Maximum.

Data Source: Table 14.1.2.1, Listing 16.2.4.1.1

Table 10.4.2 Summary of Participant Demographics – Period 2

	Placebo (N=2)	600 mg MD (N=6)	Total (N=8)
Age at informed consent (years)			
n	2	6	8
Mean	39.5	39.0	39.1
SD	7.8	12.1	10.7
Median	39.5	41.0	40.5
Q1, Q3	34.0, 45.0	33.0, 50.0	33.5, 48.0
Min, Max	34, 45	19, 50	19, 50
Sex			
n	2	6	8
Male	1 (50.0)	5 (83.3)	6 (75.0)
Female	1 (50.0)	1 (16.7)	2 (25.0)
Ethnicity			
n	2	6	8
Hispanic/Latino	0	0	0
Not Hispanic/Latino	2 (100)	6 (100)	8 (100)
Race			
n	2	6	8
American Indian or Alaska Native	0	0	0
Asian	1 (50.0)	0	1 (12.5)
Black or African American	0	1 (16.7)	1 (12.5)
Native Hawaiian or Other Pacific Islander	0	0	0
White	1 (50.0)	4 (66.7)	5 (62.5)
Mixed	0	1 (16.7)	1 (12.5)
Unknown	0	0	0
Other	0	0	0
Weight (kg)			
n	2	6	8
Mean	91.20	74.10	78.38
SD	28.43	16.61	19.37
Median	91.20	74.05	77.20
Q1, Q3	71.10, 111.30	64.40, 86.10	64.60, 90.55
Min, Max	71.1, 111.3	51.0, 95.0	51.0, 111.3
Height (m)			
n	2	6	8
Mean	1.770	1.748	1.754
SD	0.184	0.100	0.110
Median	1.770	1.790	1.790
Q1, Q3	1.640, 1.900	1.740, 1.810	1.690, 1.810
Min, Max	1.64, 1.90	1.55, 1.81	1.55, 1.90
BMI (kg/m^2)			
n	2	6	8
Mean	28.635	24.000	25.159
SD	3.104	3.567	3.882
Median	28.635	23.635	26.140
Q1, Q3	26.440, 30.830	21.230, 26.280	21.250, 27.720
Min, Max	26.44, 30.83	20.22, 29.00	20.22, 30.83

Abbreviations: BMI = body mass index; n = number of participants with available data at the specific timepoint; SD = Standard Deviation; Q1 = 25% percentile; Q3 = 75% percentile; Min = Minimum; Max = Maximum.

Data Source: Table 14.1.2.2, Listing 16.2.4.1.2

Outcome Measures

Table 11.1.1 Summary of WVE-006 Single-Dose Plasma PK Parameters – Period 1

	WVE-006				
	30 mg (N=6)	100 mg (N=5)	200 mg (N=6)	400 mg (N=6)	600 mg (N=6)
Parameter: AUC_{0-24h} (h*ng/mL)					
Day 1					
n	6	5	6	6	6
Mean	588	1713	7044	27799	48833
SD	138	384	4634	11520	13659
%CV [a]	23.6	22.4	65.8	41.4	28.0
Parameter: AUC_{0-48h} (h*ng/mL)					
Day 1					
n	5	5	6	6	6
Mean	602	1981	7418	28457	51050
SD	106	358	4422	11120	12943
%CV [a]	17.5	18.1	59.6	39.1	25.4
Parameter: AUC_{inf} (h*ng/mL)					
Day 1					
n	5	5	6	6	6
Mean	607	2012	7546	29844	53621
SD	101	388	4440	10444	13217
%CV [a]	16.7	19.3	58.8	35.0	24.6
Parameter: AUC_{last} (h*ng/mL)					
Day 1					
n	6	5	6	6	6
Mean	626	1978	7507	29466	53342
SD	115	357	4427	10688	13166
%CV [a]	18.3	18.1	59.0	36.3	24.7
Parameter: C_{max} (ng/mL)					
Day 1					
n	6	5	6	6	6
Mean	40.4	112	562	2038	3718
SD	11.6	42.2	440	864	963
%CV [a]	28.7	37.7	78.3	42.4	25.9
Parameter: $t_{1/2}$ (h)					
Day 1					
n	5	5	4	5	5
Mean	5.10	6.40	12.8	292	321
SD	2.35	2.60	12.5	274	186
%CV [a]	46.0	40.7	97.1	93.9	58.0
Parameter: T_{last} (h)					
Day 1					
n	6	5	6	6	6
Median	36.0	48.0	108	504	721
Min, Max	24.0, 48.0	24.0, 48.1	48.0, 169	336, 2016	504, 1344
Parameter: t_{max} (h)					
Day 1					
n	6	5	6	6	6
Median	8.00	8.00	7.01	10.0	8.04
Min, Max	4.00, 12.0	4.03, 8.08	4.00, 12.0	8.00, 12.0	8.00, 12.0
Parameter: CL/F (mL/h)					
Day 1					
n	5	5	6	6	6
Mean	50434	51138	34082	14827	11755
SD	7788	9410	16873	5086	2826
%CV [a]	15.4	18.4	49.5	34.3	24.0

[a] %CV = 100% x (SD/Mean)

Note: Values for $t_{1/2}$, Lambda Z, and Vz/F are excluded if the corresponding value of R2 Adjusted is less than 0.8.

Abbreviations: C_{max}=maximum observed concentration; CV = coefficient of variation; n = number of participants with available data; SD = Standard Deviation; Min = Minimum; Max = Maximum.

Data Source: Table 14.3.9.2.1, Listing 16.2.5.4.2.1

Table 11.1.2 Summary of WVE-006 Multiple-Dose (Biweekly) Plasma PK Parameters – Period 2

	WVE-006 600 mg MD (N=6)	
	Day 1	Day 29
Parameter: AUC_{0-24h} (h*ng/mL)		
n	6	6
Mean	70637	66140
SD	46241	47469
%CV [a]	65.5	71.8
Parameter: AUC_{0-48h} (h*ng/mL)		
n	6	6
Mean	73783	68785
SD	44244	45331
%CV [a]	60.0	65.9
Parameter: AUC_{inf} (h*ng/mL)		
n	6	6
Mean	76137	78191
SD	44286	44350
%CV [a]	58.2	56.7
Parameter: AUC_{last} (h*ng/mL)		
n	6	6
Mean	75678	75824
SD	44053	44437
%CV [a]	58.2	58.6
Parameter: AUC_{tau} (h*ng/mL)		
n	6	6
Mean	75679	72131
SD	44053	45043
%CV [a]	58.2	62.4
Parameter: C_{max} (ng/mL)		
n	6	6
Mean	5929	5995
SD	4933	5419
%CV [a]	83.2	90.4
Parameter: T_{last} (h)		
n	6	6
Median	336	2015
Min, Max	336, 336	1345, 2017
Parameter: t_{max} (h)		
n	6	6
Median	10.0	8.00
Min, Max	4.00, 12.0	4.00, 24.0
Parameter: R_AUC_{tau}		
n	N/A	6

	WVE-006 600 mg MD (N=6)	
Mean	N/A	0.938
SD	N/A	0.208
%CV [a]	N/A	22.1
Parameter: R_C_{max}		
Day 29		
n	N/A	6
Mean	N/A	0.935
SD	N/A	0.341
%CV [a]	N/A	36.5

[a] %CV = 100% x (SD/Mean)

Note: Values for $t_{1/2}$, Lambda Z, and Vz/F are excluded if the corresponding value of R2 Adjusted is less than 0.8.

Abbreviations: C_{max}=maximum observed concentration; CV = coefficient of variation; n = number of participants with available data; SD = Standard Deviation; Min = Minimum; Max = Maximum, N/A = not applicable.

Data Source: **Table 14.3.9.2.2, Listing 16.2.5.4.2.2**

Adverse Events

Period 1: There were no Grade 3, 4 or 5 treatment-emergent adverse events (TEAEs), no serious adverse events (SAEs), and no participants discontinued treatment, were withdrawn or died as a result of TEAEs. A total of 8 (80%) of participants who received placebo and 18 (62.1%) of participants who received WVE-006 experienced Grade 1 or 2 TEAEs, of which 1 participant experienced mild injection site reaction that was considered related to the study drug (200 mg WVE-006). There were no other injection site reactions during Period 1. The most common TEAEs in the WVE-006 treatment group overall were increased blood creatine phosphokinase (CPK) and rash each occurred in 4 (13.8%) participants. The blood CPK increases and rashes were considered unrelated to study drug and were also observed in the placebo group (1 [10%] of placebo participants). Out of the 5 participants who had raised blood CPK (all Grade 2), 4 (1 [10%] placebo; 3 [10.3%] WVE-006 overall) also had increased transaminases (alanine aminotransferase [ALT] and/or aspartate transaminase [AST]). The increases in both were attributed to exercise and completely resolved. Review of the TEAE profiles for Period 1 demonstrated no treatment, or dose related trends in TEAEs following WVE-006 or placebo, and all TEAEs resolved during the study.

Period 2: There were no Grade 3, 4 or 5 TEAEs, no SAEs and no participants discontinued treatment, were withdrawn or died as a result of TEAEs. A total of 1 (50%) of participants who received placebo and 2 (33.3%) of participants who received WVE-006 experienced a Grade 2 TEAE, all of which were considered unrelated to study drug. There were no injection site reactions during Period 2. The most common TEAE in the WVE-006 treatment group overall was influenza-like illness (2 [33.3%] of participants). The events were considered unrelated to study drug. There were no treatment-related TEAEs during Period 2. Review of the TEAE profiles for Period 2 demonstrated no treatment, or dose related trends in TEAEs following WVE-006 or placebo, and all TEAEs resolved during the study.

Table 12.1.1 Overall Summary of TEAEs – Period 1

		WVE-006					
	Pooled Placebo (N=10)	30 mg (N=6)	100 mg (N=5)	200 mg (N=6)	400 mg (N=6)	600 mg (N=6)	Pooled WVE-006 (N=29)
Participants with a TEAE [a]	8 (80.0)	5 (83.3)	4 (80.0)	3 (50.0)	3 (50.0)	3 (50.0)	18 (62.1)
Grade 1	2 (20.0)	3 (50.0)	0	2 (33.3)	1 (16.7)	2 (33.3)	8 (27.6)
Grade 2	6 (60.0)	2 (33.3)	4 (80.0)	1 (16.7)	2 (33.3)	1 (16.7)	10 (34.5)
Grade 3	0	0	0	0	0	0	0
Grade 4	0	0	0	0	0	0	0
Grade 5	0	0	0	0	0	0	0
Participants with a TEAE related to study drug	0	0	0	1 (16.7)	0	0	1 (3.4)
Participants with a Grade 3/4/5 TEAE related to study drug	0	0	0	0	0	0	0
Participants with a Serious TEAE	0	0	0	0	0	0	0
Participants with a Serious TEAE related to study drug	0	0	0	0	0	0	0
Participants discontinuing treatment due to a TEAE	0	0	0	0	0	0	0
Participants withdrawing from the study due to a TEAE	0	0	0	0	0	0	0
Participants died due to a TEAE	0	0	0	0	0	0	0

Note: Numbers in parentheses are percentages based on the number of participants in the safety population.
Note: Participants are counted only once in each category.
[a] Participants in the Grade 1 - Grade 5 categories below are reported by their maximum severity.
Data Source: Table 14.3.1.1.1, Listing 16.2.7.1.1

Table 12.1.2 Overall Summary of TEAEs – Period 2

	Placebo (N=2)	WVE-006 600 mg MD (N=6)
Participants with a TEAE [a]	1 (50.0)	2 (33.3)
Grade 1	0	0
Grade 2	1 (50.0)	2 (33.3)
Grade 3	0	0
Grade 4	0	0
Grade 5	0	0
Participants with a TEAE related to study drug	0	0
Participants with a Grade 3/4/5 TEAE related to study drug	0	0
Participants with a Serious TEAE	0	0
Participants with a Serious TEAE related to study drug	0	0
Participants discontinuing treatment due to a TEAE	0	0
Participants withdrawing from the study due to a TEAE	0	0
Participants died due to a TEAE	0	0

Note: Numbers in parentheses are percentages based on the number of participants in the safety population.
Note: Participants are counted only once in each category.
[a] Participants in the Grade 1 - Grade 5 categories below are reported by their maximum severity.
Data Source: Table 14.3.1.1.2, Listing 16.2.7.1.2

Table 12.1.3 TEAEs in each Treatment Group by Preferred Term – Period 1

		WVE-006					
	Pooled Placebo (N=10)	30 mg (N=6)	100 mg (N=5)	200 mg (N=6)	400 mg (N=6)	600 mg (N=6)	Pooled WVE-006 (N=29)
Participants with a TEAE	8 (80.0)	5 (83.3)	4 (80.0)	3 (50.0)	3 (50.0)	3 (50.0)	18 (62.1)
Blood creatine phosphokinase increased	1 (10.0)	1 (16.7)	2 (40.0)	0	0	1 (16.7)	4 (13.8)
Rash	1 (10.0)	1 (16.7)	2 (40.0)	1 (16.7)	0	0	4 (13.8)
Headache	2 (20.0)	1 (16.7)	0	0	1 (16.7)	1 (16.7)	3 (10.3)
Influenza like illness	1 (10.0)	0	0	0	1 (16.7)	2 (33.3)	3 (10.3)
Nasopharyngitis	2 (20.0)	2 (33.3)	1 (20.0)	0	0	0	3 (10.3)
Transaminases increased	1 (10.0)	1 (16.7)	2 (40.0)	0	0	0	3 (10.3)
Abdominal discomfort	0	1 (16.7)	0	0	0	0	1 (3.4)
Arthralgia	1 (10.0)	0	1 (20.0)	0	0	0	1 (3.4)
Catheter site pain	0	0	0	0	0	1 (16.7)	1 (3.4)
Dysmenorrhoea	0	0	0	0	1 (16.7)	0	1 (3.4)
Dyspepsia	0	0	0	0	1 (16.7)	0	1 (3.4)
Fatigue	0	0	0	0	1 (16.7)	0	1 (3.4)
Injection site reaction	0	0	0	1 (16.7)	0	0	1 (3.4)
Oropharyngeal pain	0	1 (16.7)	0	0	0	0	1 (3.4)
Pollakiuria	0	0	0	1 (16.7)	0	0	1 (3.4)
Pruritus	0	1 (16.7)	0	0	0	0	1 (3.4)
Thermal burn	0	0	0	1 (16.7)	0	0	1 (3.4)
Toothache	0	0	1 (20.0)	0	0	0	1 (3.4)
Back pain	1 (10.0)	0	0	0	0	0	0
Dizziness	1 (10.0)	0	0	0	0	0	0

Note: Numbers in parentheses are percentages based on the number of participants in the safety population.
Note: Preferred terms are sorted by decreasing incidence in the Pooled WVE-006 column.
Note: Participants are counted once within each preferred term.
Note: Adverse events are coded using MedDRA Version 26.1.
Data Source: Table 14.3.1.2.1.1, Listing 16.2.7.1.1

Table 12.1.4 TEAEs in each Treatment Group by Preferred Term– Period 2

	Placebo (N=2)	WVE-006 600 mg MD (N=6)
Participants with a TEAE	1 (50.0)	2 (33.3)
Influenza like illness	0	2 (33.3)
Arthralgia	0	1 (16.7)
Back pain	0	1 (16.7)
Headache	0	1 (16.7)
Rash erythematous	0	1 (16.7)
Skin abrasion	1 (50.0)	0

Note: Numbers in parentheses are percentages based on the number of participants in the safety population.
Note: Preferred terms are sorted by decreasing incidence in the Pooled WVE-006 column.
Note: Participants are counted once within each preferred term.
Note: Adverse events are coded using MedDRA Version 26.1.
Data Source: Table 14.3.1.2.1.2, Listing 16.2.7.1.2