SUPPLEMENTARY MATERIAL

Clinical Pharmacokinetics and Safety of a New HIV-1 Capsid Inhibitor, VH4004280, After Oral Administration in Adults Without HIV

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Table S1. Participant Demographics and Baseline Characteristics

Parameter	Parts 1 and 3 (N=47)	Part 2 (N=26)
Male sex, n (%)	46 (98)	26 (100)
Age, median (range), y	33 (19-54)	36 (22-54)
Hispanic or Latin American ethnicity, n (%)	14 (30)	7 (27)
Race, n (%)		
Asian	4 (9)	3 (12)
Black or African American	19 (40)	15 (58)
Native Hawaiian or Other Pacific Islander	2 (4)	0
White	20 (43)	8 (31)
Multiple races	2 (4)	0
Body mass index, median (range), kg/m^2	25.6 (20.4-29.9)	26.6 (19.0-29.9)

Table S2. Maximum Grade Increases Post-Baseline Relative to Baseline in Liver and Lipid Parameters in the Safety Population

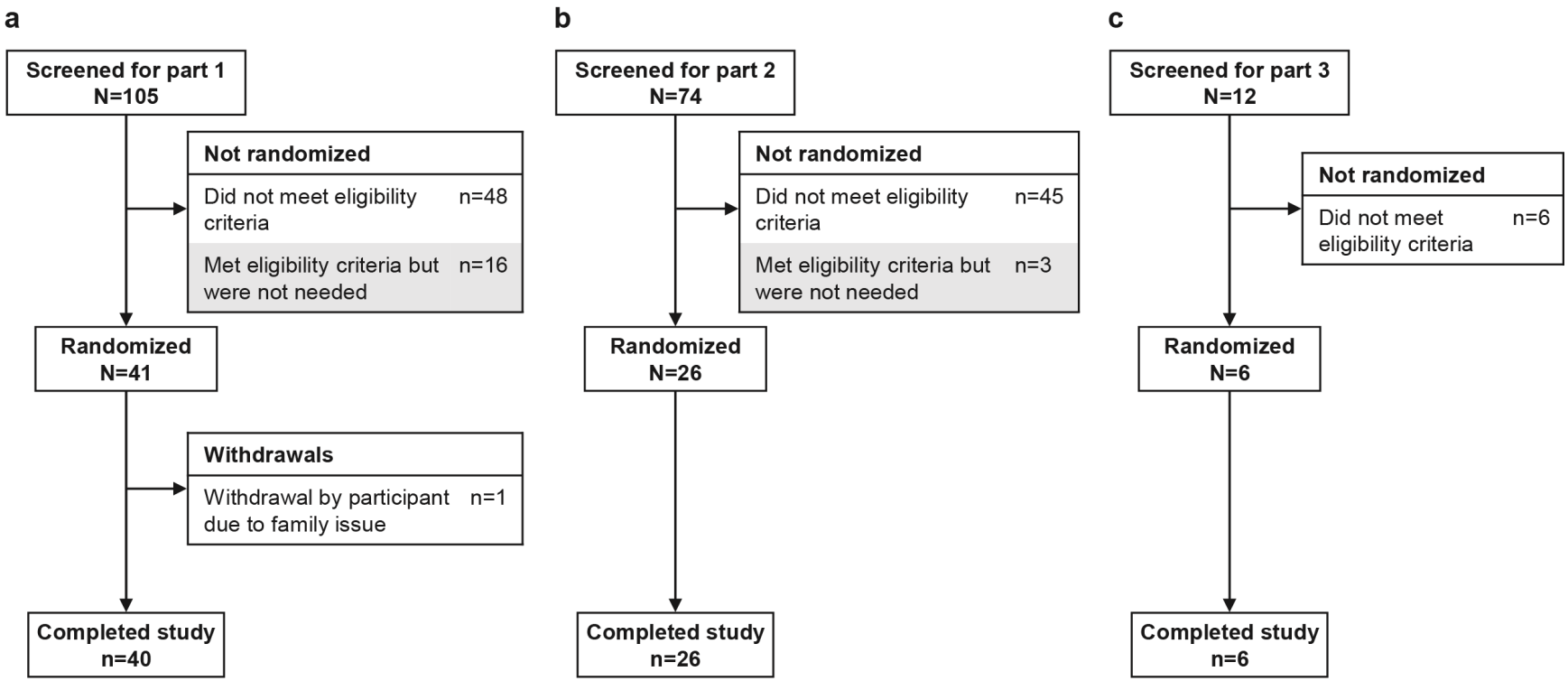
	Parts 1 and 3							
Category, n (%)	**VH-280 10 mg PiB (N=6)**	**VH-280 50 mg PiB (N=7)**	**VH-280 150 mg PiB (N=6)**	**VH-280 450 mg PiB (N=6)**	**VH-280 900 mg PiB (N=6)**	**VH-280 450 mg tablet formulation (N=6)**	**VH-280 total (N=37)**	**Placebo PiB (N=10)**
ALT								
Increase to grade 1	1 (17)	0	1 (17)	0	0	0	2 (5)	1 (10)
Increase to grade 2	0	0	0	0	0	1 (17)[a]	1 (3)	0
Increase to grade 3	0	0	0	0	0	0	0	0
AST								
Increase to grade 1	0	0	0	0	0	1 (17)	1 (3)	0
Increase to grade 2	0	0	0	0	0	0	0	0
Increase to grade 3	0	0	0	0	0	0	0	1 (10)
Total bilirubin								
Increase to grade 1	0	0	0	1 (17)	0	0	1 (3)	0
Increase to grade 2	0	0	0	0	0	0	0	0
Increase to grade 3	0	0	0	0	0	0	0	0
Total cholesterol								
Increase to grade 1	0	0	1 (17)	4 (67)	2 (33)	1 (17)	8 (22)	2 (20)
Increase to grade 2	0	0	0	0	0	0	0	1 (10)
Increase to grade 3	0	0	0	0	0	0	0	0
LDL cholesterol								
Increase to grade 1	0	0	1 (17)	4 (67)	2 (33)	0	7 (19)	0
Increase to grade 2	0	0	0	1 (17)	0	0	1 (3)	2 (20)
Increase to grade 3	0	0	0	0	0	0	0	0

	Part 2				
	VH-280 100 mg PiB (N=6)	**VH-280 250 mg PiB (N=8)**	**VH-280 350 mg PiB (N=6)**	**VH-280 total (N=20)**	**Placebo PiB (N=6)**
ALT					
Increase to grade 1	1 (17)	0	1 (17)	2 (10)	1 (17)
Increase to grade 2	0	0	0	0	0
Increase to grade 3	0	0	0	0	0
AST					
Increase to grade 1	0	1 (13)	0	1 (5)	1 (17)

Increase to grade 2	0	0	0	0	0
Increase to grade 3	0	0	1 (17)[b]	1 (5)	0
Total cholesterol					
Increase to grade 1	0	1 (13)	1 (17)	2 (10)	1 (17)
Increase to grade 2	2 (33)	1 (13)	4 (67)	7 (35)	1 (17)
Increase to grade 3	0	0	0	0	0
LDL cholesterol					
Increase to grade 1	0	0	0	0	1 (17)
Increase to grade 2	0	4 (50)	3 (50)	7 (35)	0
Increase to grade 3[c]	2 (33)	0	2 (33)	4 (20)	0

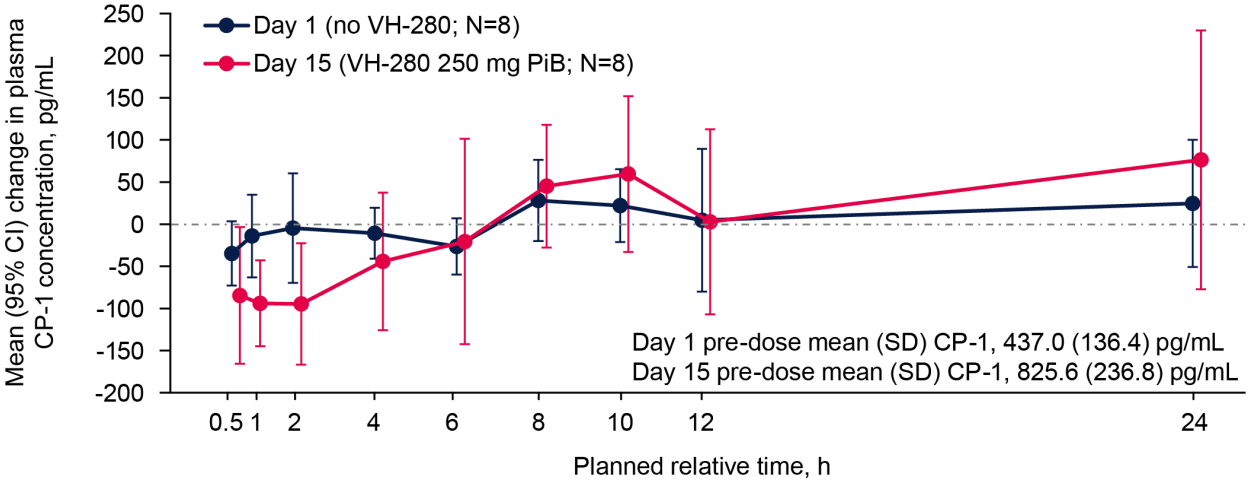
ALT, alanine aminotransferase; AST, aspartate aminotransferase; LDL, low-density-lipoprotein; PiB, powder-in-bottle; VH-280, VH4004280.
[a]Grade 2 increase in ALT on Day 14 was asymptomatic and accompanied by a grade 1 increase in AST, both of which normalized by the final study visit. This participant had elevated ALT (grade 1) at baseline, and a FibroScan® (Echosens, Westborough, MA) showed mild hepatic steatosis. [b]Grade 3 increase in AST on Day 28 accompanied by a grade 1 increase in ALT and grade 4 increase in creatine kinase, all thought to be related to strenuous exercise. All 3 parameters had normalized at the next study visit on Day 35. [c]All 4 participants with a grade 3 increase in LDL cholesterol had elevated total cholesterol and/or LDL cholesterol (grade 1) at baseline, and all returned to grade ≤1 values during follow-up.

Figure S1. Participant disposition for **(a)** part 1, **(b)** part 2, and **(c)** part 3.



Note: the most common reasons for screening failure were not being overtly healthy and inability to comply with study requirements and restrictions.

Figure S2. Mean change from pre-dose plasma CP-1 PK concentration vs time data in part 2 (linear scale) in the CP-1 PK population.



CP-1, coproporphyrin-1; PiB, powder-in-bottle; PK, pharmacokinetics; VH-280, VH4004280.