Pharmacokinetics and Evaluation of Potential Dosing Regimens for Long-Acting VH4524184

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Background

- Advancing long-acting antiretrovirals is essential to expanding complete treatment options, providing more convenient and sustainable choices that improve adherence, ensuring a good tolerability profile, enhancing quality of life, and driving progress toward ending the HIV epidemic[1,2]
- VH-184 is a third-generation INSTI based on its enhanced resistance profile versus second-generation INSTIs[3,4] and is in development as a potential long-acting injectable antiretroviral for HIV-1
- Oral VH-184 monotherapy demonstrated highly potent antiviral activity in a proof-of-concept study, with up to a mean reduction in viral load of 2.31 $\log_{10}$ c/mL, similar to dolutegravir, and had a favorable safety, tolerability, and PK profile[5]
- Here we present the following interim data from a first-time-in-human study of long-acting injectable VH-184:
  - Safety and PK observations
  - Predicted PK profile of VH-184 for long-acting and ultra-long-acting dosing

INSTI, integrase strand transfer inhibitor; PK, pharmacokinetics; VH-184, VH4524184.

1. Ullah Nayan et al. *Adv Drug Deliv Rev*. 2023;200:115009. **2.** Vinay et al. *HIV Med*. 2025;26:1343-1355. **3.** Rogg et al. *Clin Infect Dis*. 2025;81:510-520. **4.** Underwood et al. CROI 2026; Denver, CO. Poster 554. **5.** Rogg et al. CROI 2025; San Francisco, CA. Oral presentation 152.

Study Design

An ongoing double-blind, randomized, placebo-controlled, phase 1 study (NCT06310551)

Inclusion criteria

- Aged 18-55 years
- Adults without HIV-1
- Body weight ≥45 kg[a]
- BMI 18.5-32.0 kg/m^2

Single ascending doses of SC or IM VH-184 or matching placebo (N=7 to 8 per cohort)

	Route	VH-184 doses (injection volume)
Formulation A	SC	240 mg (0.8 mL), 420 mg (1.4 mL), 750 mg (2.5 mL)
	IM thigh	450 mg (1.5 mL), 900 mg (3 mL)
Formulation B	SC	400 mg (1 mL), 800 mg (2 mL)
	IM thigh	400 mg (1 mL), 800 mg (2 mL)
	IM gluteal	400 mg (1 mL)

Endpoints

- Safety, tolerability, and PK were assessed post-dose for up to 52 weeks[b]

PK analyses

- Single-dose PK parameters using available data were evaluated by non-compartmental analyses
- Observed PK data were integrated into a PopPK model to simulate dosing regimens

BMI, body mass index; IM, intramuscular; PK, pharmacokinetics; PopPK, population PK; SC, subcutaneous; VH-184, VH4524184.

[a]For female participants, ≥45 kg; for male participants, ≥50 kg. [b]Follow-up duration varies across cohorts due to staggered start-up timelines, with data collection ongoing.

Participant Demographics and Baseline Characteristics

- Across cohorts, participants were primarily male, with median age ranging from 33 to 51 years

	Formulation A					Formulation B				
	SC			IM thigh		SC		IM thigh		IM gluteal
Parameter[a]	240 mg 0.8 mL (N=8)	420 mg 1.4 mL (N=8)	750 mg 2.5 mL (N=7)	450 mg 1.5 mL (N=8)	900 mg 3 mL (N=8)	400 mg 1 mL (N=7)	800 mg 2 mL (N=8)	400 mg 1 mL (N=7)	800 mg 2 mL (N=7)	400 mg 1 mL (N=8)
Age, median (range), y	34 (22-55)	42 (21-54)	34 (25-40)	36 (23-45)	34 (18-53)	33 (24-46)	36 (19-43)	51 (40-55)	46 (33-52)	44 (35-48)
Male, n (%)[b]	7 (88)	8 (100)	6 (86)	8 (100)	7 (88)	6 (86)	6 (75)	2 (29)	7 (100)	7 (88)
Race, n (%)										
Asian or Hispanic	1 (12)	0	1 (14)	0	0	0	0	1 (14)	2 (29)	0
Black or African American	4 (50)	3 (38)	1 (14)	2 (25)	2 (25)	4 (57)	1 (12)	3 (43)	2 (29)	1 (12)
White	3 (38)	5 (62)	5 (71)	6 (75)	6 (75)	3 (43)	7 (88)	3 (43)	3 (43)	7 (88)
BMI, mean (range), kg/m^2	26.2 (20.9-30.2)	26.6 (21.2-31.4)	28.0 (24.5-31.5)	28.2 (23.0-31.6)	25.2 (20.1-29.7)	25.8 (21.2-30.1)	26.5 (23.4-30.3)	27.0 (20.6-31.1)	26.9 (22.8-30.3)	28.0 (20.8-31.5)

BMI, body mass index; IM, intramuscular; SC, subcutaneous; VH-184, VH4524184.

[a]Cohorts are currently blinded and include participants who received VH-184 and placebo. [b]Assigned male sex at birth.

ISRs Generally Well Tolerated and Predominantly Mild in Severity

- Overall, 80% (61/76) of participants had ≥1 ISR; the most common ISR was injection-site pain (68% [52/76])
- Most ISRs were grade 1 (84% [113/134]),[a] and the median duration of ISRs was 4 to 8 days across cohorts, excluding nodules

	Formulation A					Formulation B				
	SC			IM thigh		SC		IM thigh		IM gluteal
ISR, n (%)[b]	240 mg 0.8 mL (N=8)	420 mg 1.4 mL (N=8)	750 mg 2.5 mL (N=7)	450 mg 1.5 mL (N=8)	900 mg 3 mL (N=8)	400 mg 1 mL (N=7)	800 mg 2 mL (N=8)	400 mg 1 mL (N=7)	800 mg 2 mL (N=7)	400 mg 1 mL (N=8)
Any ISR	8 (100)	8 (100)	6 (86)	6 (75)	8 (100)	5 (71)	5 (62)	5 (71)	4 (57)	6 (75)
Maximum grade 1	5 (62)	6 (75)	1 (14)	6 (75)	7 (88)	4 (57)	4 (50)	4 (57)	2 (29)	6 (75)
Maximum grade 2	3 (38)	2 (25)	3 (43)	0	1 (12)	1 (14)	1 (12)	1 (14)	2 (29)	0
Maximum grade 3	0	0	2 (29)[c]	0	0	0	0	0	0	0
Maximum grade 4	0	0	0	0	0	0	0	0	0	0
Most common ISRs[d]										
Injection-site pain	5 (62)	8 (100)	6 (86)	6 (75)	8 (100)	3 (43)	4 (50)	2 (29)	4 (57)	6 (75)
Injection-site erythema	5 (62)	7 (88)	6 (86)	1 (12)	2 (25)	5 (71)	3 (38)	3 (43)	0	1 (12)
Injection-site nodule[e]	7 (88)	6 (75)	4 (57)	0	0	5 (71)	2 (25)	1 (14)	0	0
Injection-site pruritus	3 (38)	3 (38)	3 (43)	0	1 (12)	0	0	0	0	0

IM, intramuscular; ISR, injection-site reaction; SC, subcutaneous; VH-184, VH4524184.

[a]Event-level data. [b]Cohorts are currently blinded and include participants who received VH-184 and placebo. [c]Grade 3 ISRs in the formulation A SC 750-mg cohort were pain and erythema (duration 8 and 14 days, respectively); pain resolved with acetaminophen. [d]Other ISRs included injection-site swelling (n=2 [25%] each in the formulation A SC 240- and 420-mg cohorts and 1 [14%] in the formulation A SC 750-mg cohort), injection-site induration (n=2 [25%] in the formulation B SC 800-mg cohort), and muscle tightness (n=2 [29%] in the formulation A SC 750-mg cohort). [e]The median duration of ISR nodules was 84 days.

VH-184 Was Well Tolerated and Had a Favorable Safety Profile

- Most VH-184–related non-ISR AEs were mild, none were serious, and none led to withdrawal[a]
- No clinically significant trends in laboratory abnormalities, vital signs, or electrocardiogram parameters were observed

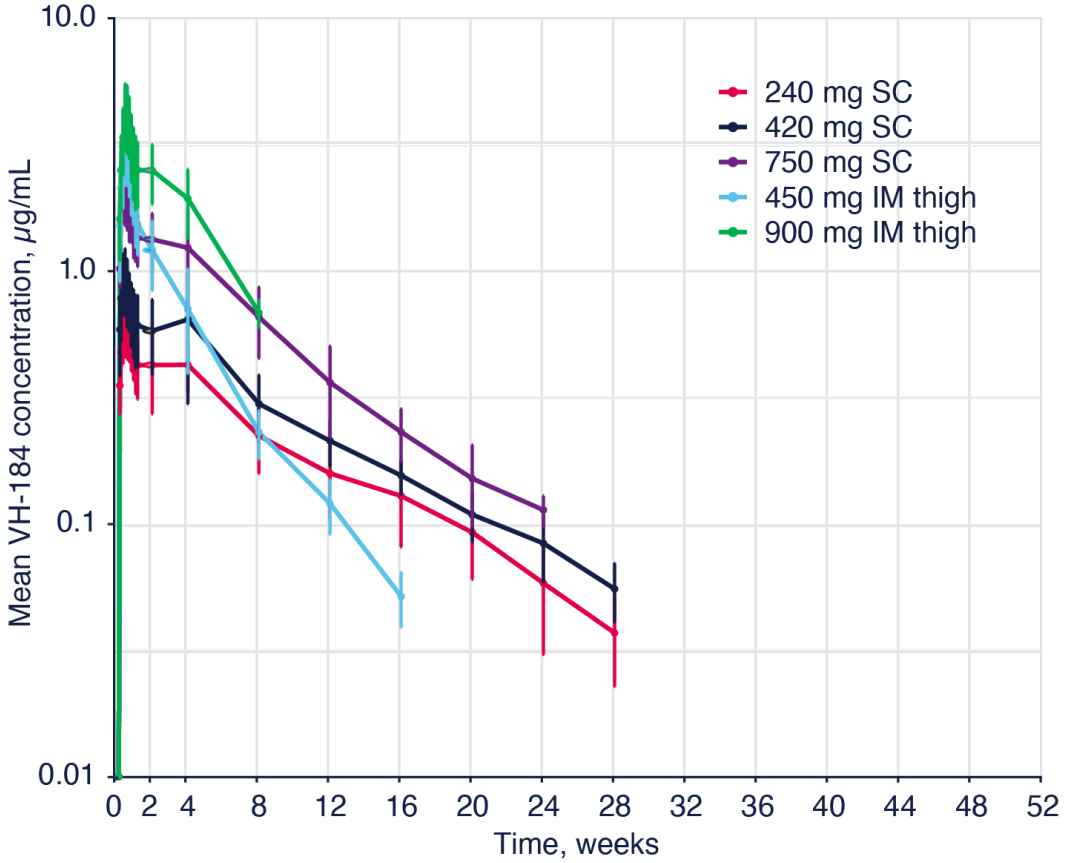
	Formulation A					Formulation B				
	SC			IM thigh		SC		IM thigh		IM gluteal
VH-184–related non-ISR AEs, n (%)[b]	240 mg 0.8 mL (N=8)	420 mg 1.4 mL (N=8)	750 mg 2.5 mL (N=7)	450 mg 1.5 mL (N=8)	900 mg 3 mL (N=8)	400 mg 1 mL (N=7)	800 mg 2 mL (N=8)	400 mg 1 mL (N=7)	800 mg 2 mL (N=7)	400 mg 1 mL (N=8)
Any non-ISR AE	0	1 (12)	4 (57)	0	0	1 (14)	1 (12)	0	2 (29)	0
Grade 1	0	0	4 (57)	0	0	1 (14)	1 (12)	0	2 (29)	0
Grade 2	0	1 (12)	0	0	0	0	0	0	0	0
Grade 3	0	0	0	0	0	0	0	0	0	0
Any SAE	0	0	0	0	0	0	0	0	0	0
Any AE leading to withdrawal	0	0	0	0	0	0	0	0	0	0

AE, adverse event; IM, intramuscular; ISR, injection-site reaction; SAE, serious AE; SC, subcutaneous; VH-184, VH4524184.

[a]The only non-ISR VH-184–related AE reported in more than 1 participant was headache. [b]Cohorts are currently blinded and include participants who received VH-184 and placebo.

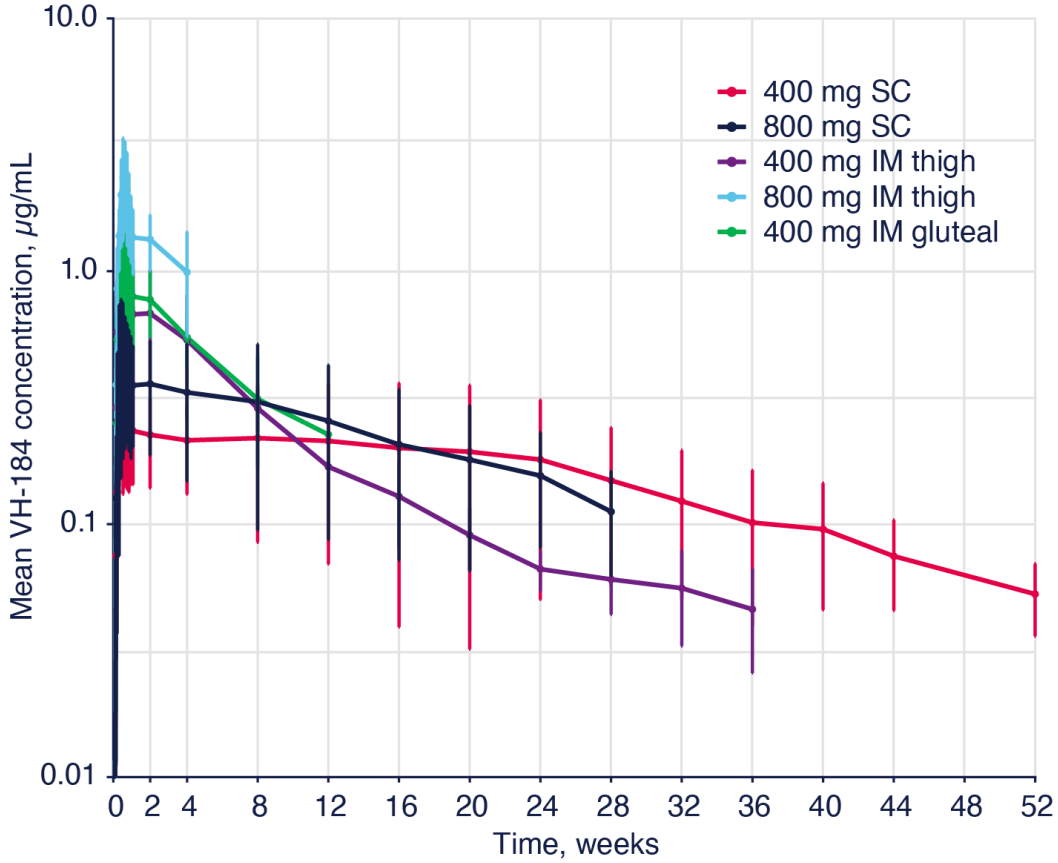
Observed PK Profile Supports Ultra-Long-Acting Potential of VH-184

Formulation A



- Median $t_{1/2}$ ranged from 3.5 (IM thigh) to 7.8 (SC) weeks across doses
- Median Tmax of 3 days after SC or IM administration

Ultra-Long-Acting: Formulation B

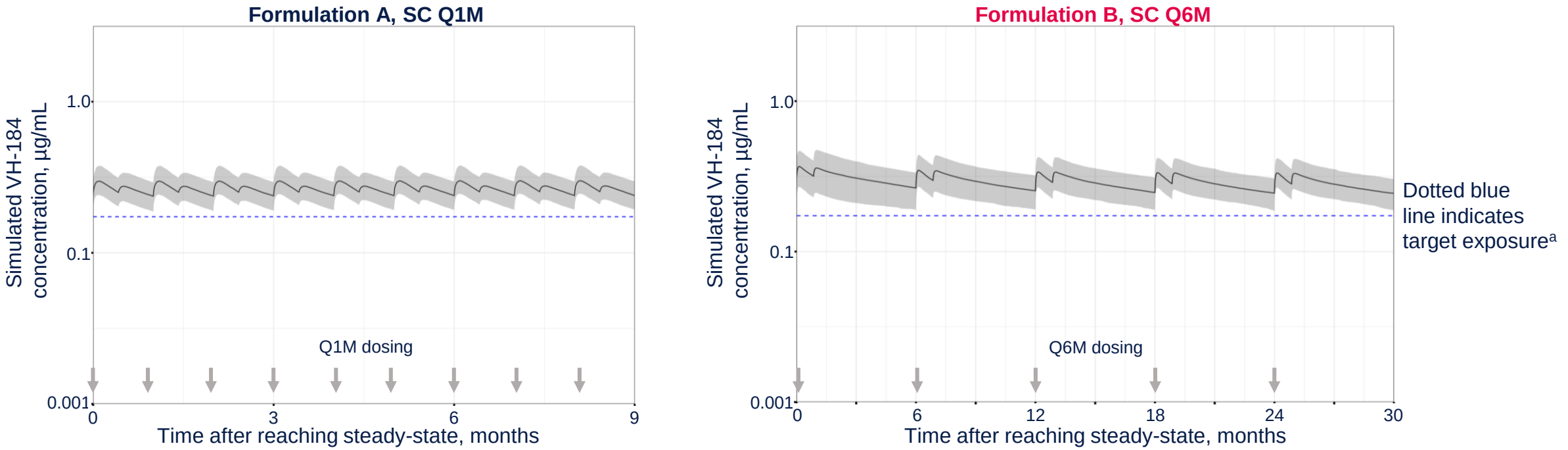


- Median $t_{1/2}$ ranged from 14.9 (IM thigh) to 19.8 (SC) weeks across doses
- Tmax variable due to flat PK profile

IM, intramuscular; PK, pharmacokinetics; SC, subcutaneous; $t_{1/2}$, terminal half-life; Tmax, time to maximum plasma concentration; VH-184, VH4524184.

VH-184 Simulations Support Twice-Yearly Dosing

- A PopPK analysis informed by data from this ongoing study adequately characterized the observed PK profile for both formulations and was used to simulate multiple VH-184 regimens
- VH-184 long-acting injectable formulations are predicted to maintain VH-184 PK above clinically effective concentrations, covering a wide range of long-acting dosing: Q1M or Q2M dosing for formulation A and Q4M or Q6M dosing for formulation B



PK, pharmacokinetics; PopPK, population PK; Q1M, every month; Q2M, every 2 months; Q4M, every 4 months; Q6M, every 6 months; VH-184, VH4524184.

[a]Target exposure is 4 × protein-adjusted 90% inhibitory concentration.

Conclusions

Twice-yearly dosing of the third-generation INSTI VH-184 is achievable based on data from this ongoing study and PopPK analysis

- VH-184 has a promising safety, tolerability, and PK profile suitable for long-acting dosing regimens
  - Both SC and IM single-dose injections of VH-184 were associated with predominantly mild ISRs
- VH-184 is being evaluated in the phase 2b INNOVATE study (NCT07202546) in adults with HIV
- VH-184 is part of ViiV Healthcare's broader efforts to develop innovative ultra-long-acting therapies that address the diverse needs of people affected by HIV and transform HIV care

For information on the enhanced resistance profile of VH-184 versus bictegravir, see Underwood et al. CROI 2026; Denver, CO. Poster 554

Plain language summary

VH-184 is an experimental medicine being studied for HIV. In this study, we found that it can stay in the body for a long time, which means it might only need to be given twice a year as an injection into the muscle or under the skin. It was also generally well tolerated and had a good safety profile

IM, intramuscular; INSTI, integrase strand transfer inhibitor; ISR, injection-site reaction; PK, pharmacokinetics; PopPK, population PK; SC, subcutaneous; VH-184, VH4524184.

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