# Safety and Tolerability of VH3810109 (N6LS) Among Antiretroviral Therapy–Naive Adults Living With HIV-1: Results From the Monotherapy Phase of the Phase 2a BANNER Study

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# Presenter Disclosure Information

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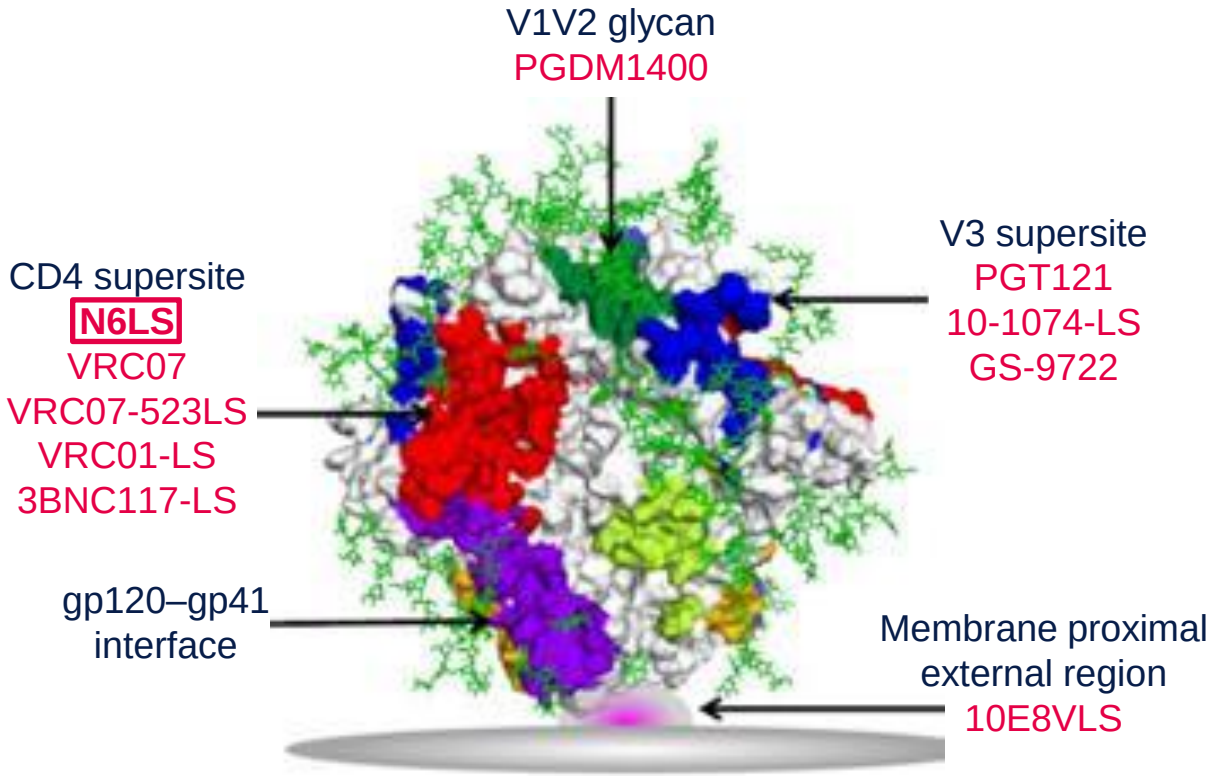
discloses the following pertaining to this presentation:

Stock/Shareholder: GSK
Employee: ViiV Healthcare

# Introduction

- VH3810109 (N6LS) is a novel bNAb with broad and potent neutralization activity in vitro, which targets the CD4 binding site of the HIV-1 envelope protein
- N6LS has demonstrated robust antiviral effect in adults with HIV-1 in part 1 of the proof-of-concept phase 2a BANNER study[1]
  - N6LS led to virologic response in 13/14 participants, with a median decline in viremia of 1.72 $log_{10}$ c/mL and maximum viral nadir from baseline of −2.60 $log_{10}$ c/mL
- Here we report the safety and tolerability of N6LS from parts 1 and 2 of BANNER when given IV or SC in ART-naive adults with HIV-1

**bNAbs target 5 conserved regions on the envelope[2-10]**




LS-containing bNAbs have been engineered to have long half-lives[11]

ART, antiretroviral therapy; bNAb, broadly neutralizing antibody; IV, intravenous; N6LS, VH3810109; SC, subcutaneous.

**1.** Leone et al. HIV Drug Therapy Glasgow 2022; Glasgow, Scotland. Slides O34. **2.** Bar et al. *N Engl J Med.* 2016;375:2037-2050. **3.** Kwon et al. *Retrovirology.* 2012;9(suppl 2):O34. **4.** Scheid et al. *Science.* 2011;333:1633-1637. **5.** Mouquet et al. *Proc Natl Acad Sci U S A.* 2012;109:E3268-E3277. **6.** Walker et al. *Nature.* 2011;477:466-470. **7.** Caskey. *Curr Opin HIV AIDS*. 2020;15:49-55. **8.** Doria-Rose et al. *J Virol.* 2015;90:76-91. **9.** Kwon et al. *J Virol.* 2016;90:5899-5914. **10.** Gaudinski et al. *Lancet HIV*. 2019;6:e667-e679. **11.** Huang et al. *Immunity.* 2016;45:1108-1121.

# BANNER Study Design

**Randomized, open-label, 2-part, multicenter study assessing safety, PK, and antiviral activity of N6LS in ART-naive adults**

**Inclusion criteria**
- Age 18-65 years
- HIV-1 RNA ≥5000 c/mL
- CD4+ cell count ≥250 cells/mm$^3$
- ART-naive

**Randomized 1:1**

**Single N6LS infusion**

**Part 1**
- N6LS 40 mg/kg IV (n=8)
- N6LS 280 mg (~4 mg/kg[a]) IV (n=6)

**Planned interim analysis[b]**
- To determine whether to proceed to part 2 and to determine dose selection in part 2

**Inclusion criteria**
- Age 18-65 years
- HIV-1 RNA ≥5000 c/mL
- CD4+ cell count ≥250 cells/mm$^3$
- ART-naive

**Randomized 1:1**

**Part 2**
- N6LS 700 mg (~10 mg/kg[a]) IV (n=16)
- N6LS 70 mg (~1 mg/kg[a]) IV (n=16)
- N6LS 700 mg (~10 mg/kg[a]) SC (n=16)

**Monotherapy endpoint criteria (Days 11-84)**
- Virologic non-response (viral nadir decline <0.5 $\log_{10}$ c/mL at Day 11)
- Virologic rebound (VL rebound of ≥1.0 $\log_{10}$ c/mL increase from nadir or to <0.5 $\log_{10}$ c/mL from baseline)
- Missing/Delayed data from previous visits
- Reached Day 84

**Participants receive INI-based SOC**

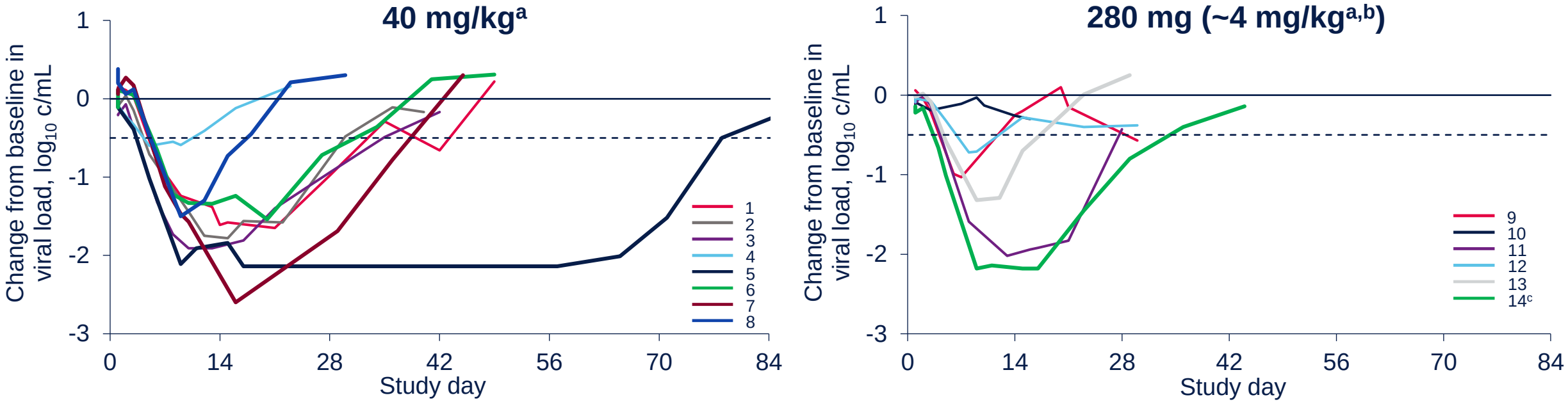
**Day 1** | **Day 11** | **Monotherapy** | **Day 84** | **SOC[c] 48 weeks**

- Safety endpoints included incidence of adverse events and infusion/injection site reactions, vital signs, electrocardiograms, and clinical laboratory tests monitored through date of last participant completing the monotherapy phase

ART, antiretroviral therapy; INI, integrase inhibitor; IV, intravenous; N6LS, VH3810109; PK, pharmacokinetics; SC, subcutaneous; SOC, standard of care; VL, viral load.

[a]For a 70-kg individual. [b]A planned interim analysis was performed to evaluate virologic response, safety, and PK from the monotherapy and SOC periods in part 1. [c]A SOC INI-based regimen (dolutegravir/lamivudine) was provided at the end of the monotherapy periods in parts 1 and 2.

# N6LS Led to Virologic Response in 13/14 Participants




| Viral dynamic measures | N6LS 40 mg/kg IV (n=8) | N6LS 280 mg IV (~4 mg/kg[b]; n=6) |
|---|---|---|
| Median (range) viral nadir from baseline, $log_{10}$ c/mL | −1.72 (−0.60, −2.60) | −1.18 (−0.30, −2.18) |
| Median (range) time to viral nadir, days | 16 (5-21) | 9 (7-16) |
| Maximum viral nadir from baseline, $log_{10}$ c/mL | −2.60 | −2.18 |
| Median (range) time to viral rebound among responders, days | 35 (12-78) [n=8] | 18 (14-29) [n=5] |

Solid line represents no change from baseline and dashed line represents virologic non-response (viral nadir decline <0.5 $log_{10}$ c/mL at Day 11). IV, intravenous; N6LS, VH3810109.
[a]Each line represents an individual participant. [b]For a 70-kg individual. [c]Participant 14 is the only female participant in the study.
Leone et al. HIV Drug Therapy Glasgow 2022; Virtual and Glasgow, Scotland. Slides O34.



Leone et al. EACS 2023; Warsaw, Poland. Slides PS8.O5.

# BANNER Demographics and Baseline Characteristics

| Parameter | Part 1 | | Part 2 | | | Total (N=62) |
|---|---|---|---|---|---|---|
| | 40 mg/kg IV (N=8) | 280 mg IV (~4 mg/kg[a]) (N=6) | 700 mg IV (~10 mg/kg[a]) (N=16) | 70 mg IV (~1 mg/kg[a]) (N=16) | 700 mg SC (~10 mg/kg[a]) (N=16) | |
| Age, median (range), y[b] | 30.5 (24-51) | 28.0 (18-54) | 28.5 (20-61) | 30.5 (21-57) | 26.5 (19-57) | 29.0 (18-61) |
| Sex, male, n (%) | 8 (100) | 5 (83) | 14 (88) | 16 (100) | 15 (94) | 58 (94) |
| Race, n (%) | | | | | | |
| Black/African American | 2 (25) | 1 (17) | 3 (19) | 3 (19) | 2 (13) | 11 (18) |
| White/Caucasian/European heritage | 6 (75) | 5 (83) | 10 (63) | 8 (50) | 9 (56) | 38 (61) |
| Other races[c] | 0 | 0 | 3 (19) | 5 (31) | 5 (31) | 13 (21) |
| Ethnicity, Hispanic/Latin American, n (%) | 6 (75) | 4 (67) | 14 (88) | 14 (88) | 13 (81) | 51 (82) |
| HIV-1 RNA, median (range), $log_{10}$ c/mL | 4.1 (3.1-5.2) | 4.5 (3.8-5.0) | 4.4 (3.9-5.0) | 4.4 (3.9-5.8) | 4.4 (2.1-5.3) | 4.4 (2.1-5.8) |
| CD4+ cell count, median (range), cells/$mm^3$ | 313.0 (190-700) | 374.5 (265-601) | 389.0 (202-842) | 438.5 (179-850) | 440.5 (263-774) | 383.0 (179-850) |
| Body mass index, mean (SD), $kg/m^2$ | 27.0 (5.7) | 27.4 (4.3) | 23.6 (2.7) | 25.7 (4.9) | 24.2 (4.2) | 25.1 (4.4) |

IV, intravenous; SC, subcutaneous; SD, standard deviation.
[a]For a 70-kg individual. [b]Age was imputed when full date of birth was not provided. [c]Included American Indian or Alaska Native (n=3), Native Hawaiian or Other Pacific Islander (n=1), White Arabic/North African heritage (n=4), and individuals of multiple races (n=5).



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# Safety Summary: Monotherapy Phase

- N6LS was well tolerated, with few drug-related AEs and no serious AEs
  - Across dose groups, no noteworthy differences in overall AE incidences were observed
- Grade 3-4 AEs were reported in 10/62 (16%) participants; none were drug-related
  - Increased blood creatine phosphokinase and neutropenia were the only grade 3-4 AEs reported in >1 participant overall
- No clinically significant safety trends in vital signs, electrocardiograms, or laboratory tests were observed across dose groups

| | Part 1 | | Part 2 | | | |
|---|---|---|---|---|---|---|
| Participants, n (%) | 40 mg/kg IV (N=8) | 280 mg IV (~4 mg/kg) (N=6) | 700 mg IV (~10 mg/kg) (N=16) | 70 mg IV (~1 mg/kg) (N=16) | 700 mg SC (~10 mg/kg) (N=16) | Total (N=62) |
| Any AE | 7 (88) | 4 (67) | 9 (56) | 8 (50) | 11 (69) | 39 (63) |
| Drug-related | 2 (25) | 2 (33) | 1 (6) | 2 (13) | 6 (38) | 13 (21) |
| Grade 3-4 AEs | 1 (13) | 0 | 2 (13) | 3 (19) | 4 (25) | 10 (16) |
| Drug-related | 0 | 0 | 0 | 0 | 0 | 0 |
| Serious AEs | 0 | 0 | 0 | 0 | 0 | 0 |
| Drug-related | 0 | 0 | 0 | 0 | 0 | 0 |
| Deaths | 0 | 0 | 0 | 0 | 0 | 0 |

AE, adverse event; IV, intravenous; N6LS, VH3810109; SC, subcutaneous.

# Summary of Drug-Related Adverse Events: Monotherapy Phase

- All drug-related adverse events were grade 1 or 2
- Drug-related adverse events occurring in ≥2 participants were headache (n=3), infusion site pain (n=3), infusion site bruising (n=2), and abdominal pain (n=2)

| | Part 1 | | Part 2 | | | |
|---|---|---|---|---|---|---|
| Participants, n (%) | 40 mg/kg IV (N=8) | 280 mg IV (~4 mg/kg) (N=6) | 700 mg IV (~10 mg/kg) (N=16) | 70 mg IV (~1 mg/kg) (N=16) | 700 mg SC (~10 mg/kg) (N=16) | Total (N=62) |
| Drug-related adverse events | 2 (25) | 2 (33) | 1 (6) | 2 (13) | 6 (38) | 13 (21) |
| Drug-related adverse events by system organ class | | | | | | |
| Gastrointestinal disorders | 1 (13) | 1 (17) | 0 | 0 | 1 (6) | 3 (5) |
| General disorders and administration site conditions[a] | 1 (13) | 1 (17) | 1 (6) | 1 (6) | 4 (25) | 8 (13) |
| Skin and subcutaneous tissue disorders | 1 (13) | 0 | 0 | 0 | 0 | 1 (2) |
| Musculoskeletal and connective tissue disorders | 0 | 1 (17) | 0 | 0 | 0 | 1 (2) |
| Nervous system disorders | 0 | 0 | 0 | 1 (6) | 2 (13) | 3 (5) |
| Investigations[b] | 0 | 0 | 0 | 0 | 1 (6) | 1 (2) |

IV, intravenous; SC, subcutaneous.
[a]System organ class of general disorders and administration site conditions includes application site pain, asthenia, fatigue, and infusion/injection site reactions. [b]System organ class of investigations includes clinical laboratory test abnormalities.



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# Summary of Infusion/Injection Site Reactions: Monotherapy Phase

- 7/62 (11%) participants experienced 9 infusion/injection site reactions, all grade 1, with a maximum duration of 10 days
- No infusion/injection site nodules were reported

| Parameter | Part 1 | | Part 2 | | | Total (N=62) |
|---|---|---|---|---|---|---|
| | 40 mg/kg IV (N=8) | 280 mg IV (~4 mg/kg) (N=6) | 700 mg IV (~10 mg/kg) (N=16) | 70 mg IV (~1 mg/kg) (N=16) | 700 mg SC (~10 mg/kg) (N=16) | |
| Number of participants with infusion/injection site reactions, n (%) | 2 (25) | 0 | 1 (6) | 1 (6) | 3 (19) | 7 (11) |
| Number of infusion/injection site reaction adverse events, n | 2 | 0 | 1 | 2 | 4 | 9 |
| Grade 1, n (%) of events[a] | 2 (100) | 0 | 1 (100) | 2 (100) | 4 (100) | 9 (100) |
| Grade 2-4, n (%) of events | 0 | 0 | 0 | 0 | 0 | 0 |

IV, intravenous; SC, subcutaneous.
[a]40 mg/kg IV: 1 infusion site erythema, 1 infusion site pain; 700 mg IV: 1 infusion site pain; 70 mg IV: 2 infusion site bruising (same participant); 700 mg SC: 1 injection site bruising and 1 injection site discoloration (same participant), 1 injection site pain, 1 injection site pruritus.



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# Conclusions

- A single dose of N6LS was well tolerated, with few drug-related adverse events, including mild infusion/injection site reactions, and no serious adverse events during the monotherapy phase, at both high and low doses and with IV and SC administration
- No clinically significant changes in vital signs, electrocardiograms, or laboratory tests were observed over the course of the study
- Safety data from parts 1 and 2 of BANNER support the ongoing development of N6LS into phase 2b for the treatment of HIV-1

Additional data on the pharmacokinetics, pharmacodynamics, and virologic activity of N6LS from the BANNER study are presented in Poster eP.A.099[1]

IV, intravenous; N6LS, VH3810109; SC, subcutaneous.

**1.** Edwards et al. EACS 2023; Warsaw, Poland. Poster eP.A.099.

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