# VH3810109 (N6LS) in Antiretroviral Therapy–Naive Adults With HIV-1: Phase 2a BANNER Efficacy Data

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# Introduction

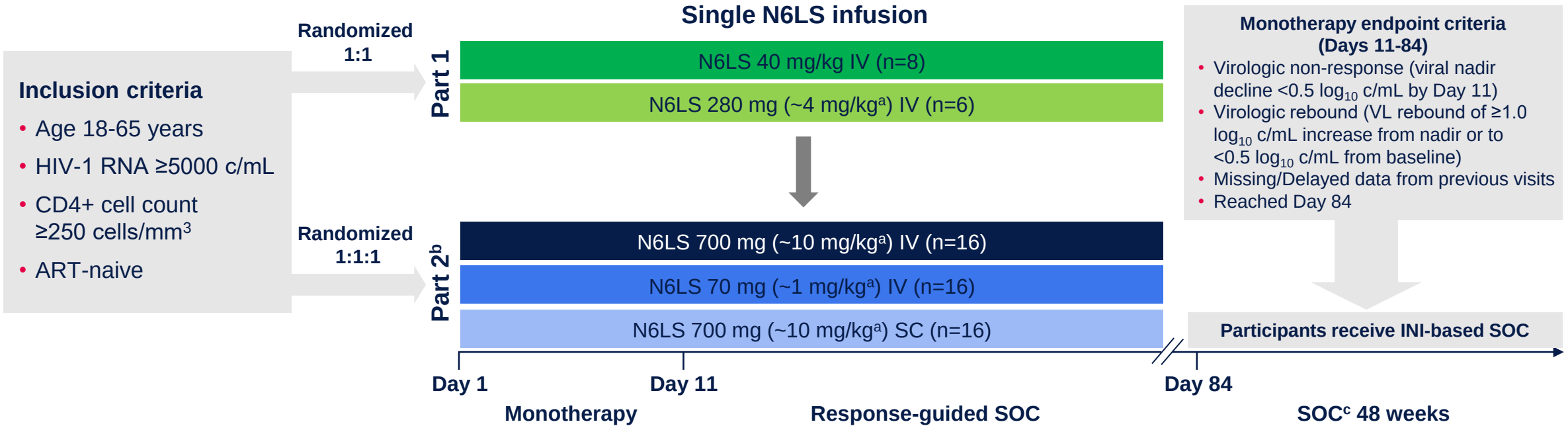
- The broadly neutralizing antibody N6LS is a CD4-binding site antibody with broad and potent neutralizing activity against the viral envelope in vitro
- N6LS demonstrated robust antiviral effect when given at 40 mg/kg IV in people living with HIV-1 in part 1 of the BANNER study[1]
  - Median viral nadir from baseline was −1.72 $\log_{10}$ c/mL and maximum viral nadir from baseline was −2.60 $\log_{10}$ c/mL
- N6LS administered IV or SC showed a good safety profile and was well tolerated across dosing groups (~1, ~4, ~10, and 40 mg/kg IV; ~10 mg/kg SC) in BANNER parts 1 and 2[2]
- We report efficacy data for N6LS administered IV or SC in parts 1 and 2 of BANNER

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

**1.** Leone et al. HIV Drug Therapy Glasgow 2022; Glasgow, Scotland. Oral Presentation O34. **2.** Leone et al. EACS 2023; Warsaw, Poland. Oral Presentation PS8.O5.

# BANNER Study Design

**Randomized, open-label, 2-part, multicenter study of N6LS in ART-naive adults**




- N6LS antibody susceptibility screening was not performed; instead, N6LS susceptibility was determined retrospectively using the PhenoSense® monoclonal antibody assay (Monogram Biosciences, South San Francisco, CA)

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

[a]For a 70-kg individual. [b]Part 2, with doses described above, was triggered after a planned interim analysis of part 1 data was performed and demonstrated acceptable virologic response, safety, and pharmacokinetics from the monotherapy and SOC periods. [c]An SOC INI-based regimen (dolutegravir/lamivudine) was provided at the end of the monotherapy periods in parts 1 and 2.

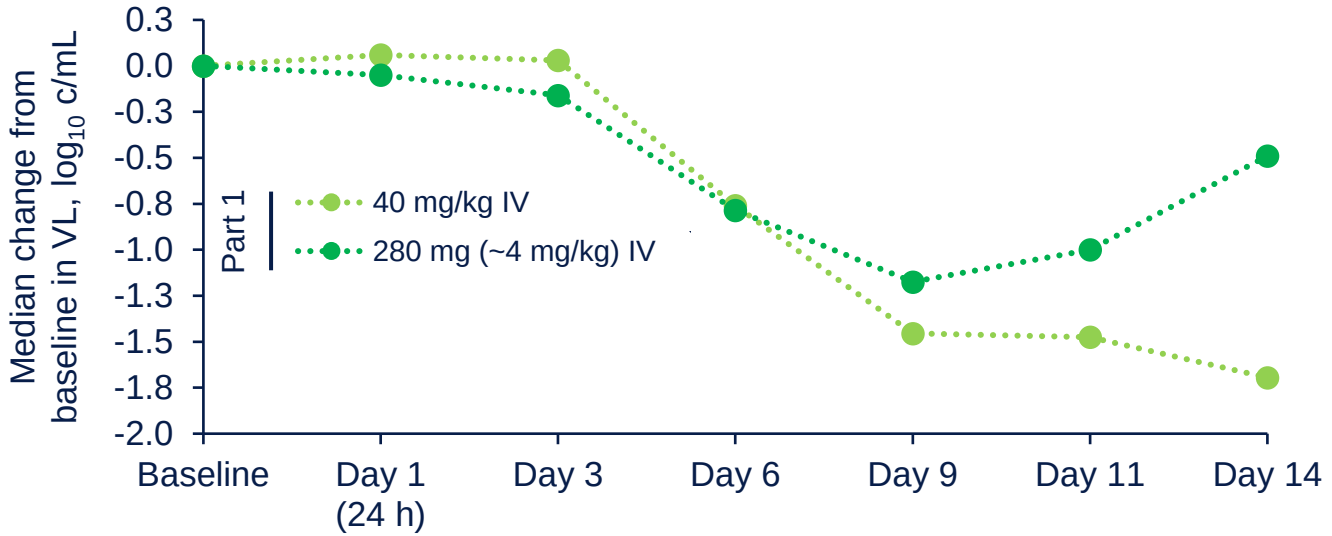
# Demographics and Baseline Characteristics

| Parameter | Part 1 | | Part 2 | | | Total (N=62) |
|---|---|---|---|---|---|---|
| | N6LS 40 mg/kg IV (N=8) | N6LS 280 mg IV (~4 mg/kg[a]) (N=6) | N6LS 700 mg IV (~10 mg/kg[a]) (N=16) | N6LS 70 mg IV (~1 mg/kg[a]) (N=16) | N6LS 700 mg SC (~10 mg/kg[a]) (N=16) | |
| Age, median (range), years[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 (190-700) | 375 (265-601) | 389 (202-842) | 439 (179-850) | 441 (263-774) | 383 (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; N6LS, VH3810109; 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).

# BANNER Part 1: Dose-Dependent Antiviral Activity

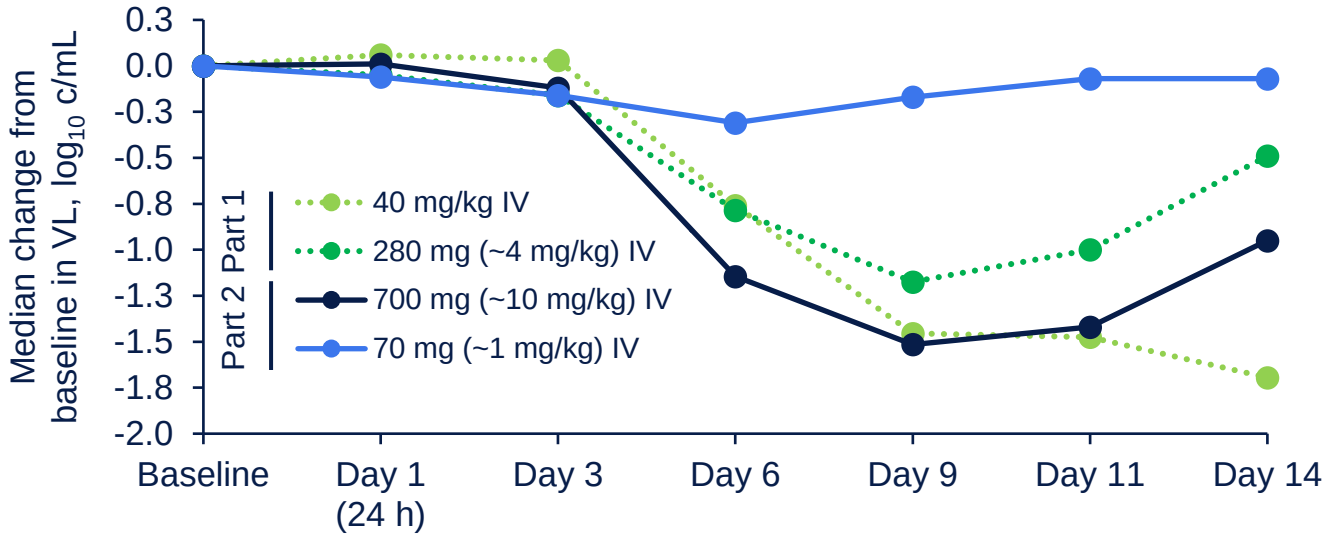



| Viral dynamic measures, median (range) | Part 1 | | Part 2 | | |
|---|---|---|---|---|---|
| | N6LS 40 mg/kg IV (N=8) | N6LS 280 mg IV (~4 mg/kg[a]) (N=6) | N6LS 700 mg IV (~10 mg/kg[a]) (N=16) | N6LS 70 mg IV (~1 mg/kg[a]) (N=16) | N6LS 700 mg SC (~10 mg/kg[a]) (N=16) |
| Viral nadir from baseline, $log_{10}$ c/mL | −1.72 (−2.60, −0.60) | −1.18 (−2.18, −0.30) | −1.54 (−2.22, −0.41) | −0.43 (−1.29, −0.12) | −0.50 (−2.13, −0.09) |
| Time to viral nadir, days | 16 (5-21) | 9 (7-16) | 9 (6-27) | 7 (2-23) | 9 (1-50) |
| Time to viral rebound among responders, days | 35 (12-78) [n=8] | 18 (14-29) [n=5] | 22 (14-43) [n=14] | 13 (10-22) [n=7] | 17 (11-63) [n=8] |

IV, intravenous; N6LS, VH3810109; SC, subcutaneous; VL, viral load.

[a]For a 70-kg individual.

# BANNER Part 2: Dose-Dependent Antiviral Activity




| Viral dynamic measures, median (range) | Part 1 | | Part 2 | | |
|---|---|---|---|---|---|
| | N6LS 40 mg/kg IV (N=8) | N6LS 280 mg IV (~4 mg/kg[a]) (N=6) | N6LS 700 mg IV (~10 mg/kg[a]) (N=16) | N6LS 70 mg IV (~1 mg/kg[a]) (N=16) | N6LS 700 mg SC (~10 mg/kg[a]) (N=16) |
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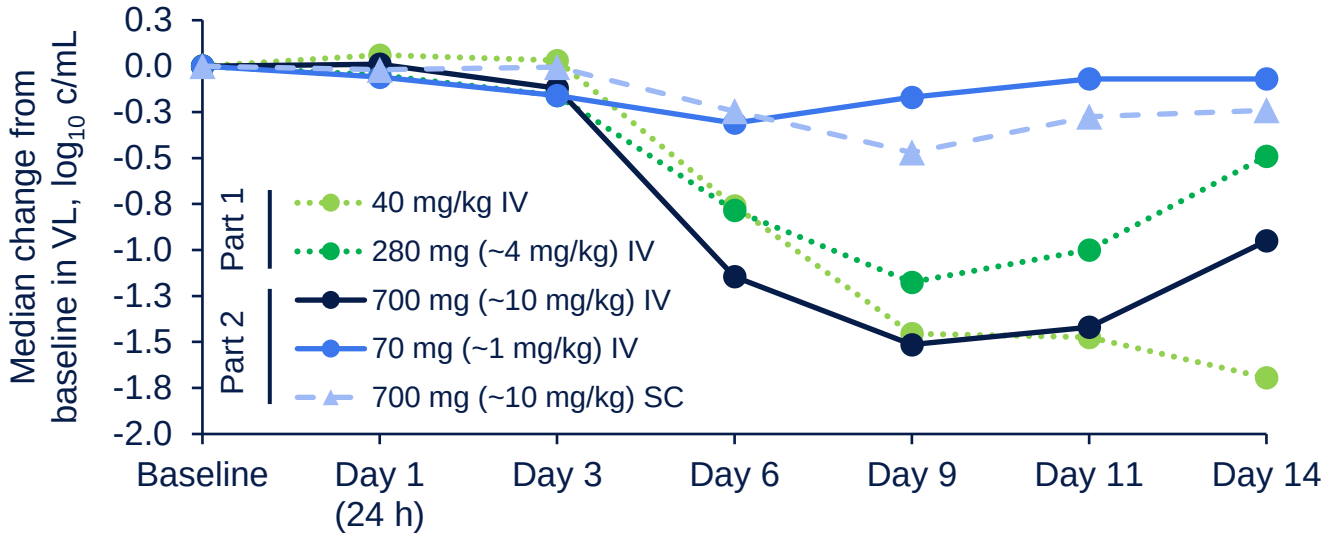
IV, intravenous; N6LS, VH3810109; SC, subcutaneous; VL, viral load.

[a]For a 70-kg individual.

# BANNER Part 2: SC Antiviral Activity




- Lower exposures were observed with SC vs IV administration using the same N6LS dose
- Lower SC exposure due to first-pass lymphatic elimination
- The SC response was as expected when considering N6LS exposures achieved

| | Part 1 | | | | Part 2 |
|---|---|---|---|---|---|
| **Viral dynamic measures, median (range)** | **N6LS 40 mg/kg IV (N=8)** | **N6LS 280 mg IV (~4 mg/kg[a]) (N=6)** | **N6LS 700 mg IV (~10 mg/kg[a]) (N=16)** | **N6LS 70 mg IV (~1 mg/kg[a]) (N=16)** | **N6LS 700 mg SC (~10 mg/kg[a]) (N=16)** |
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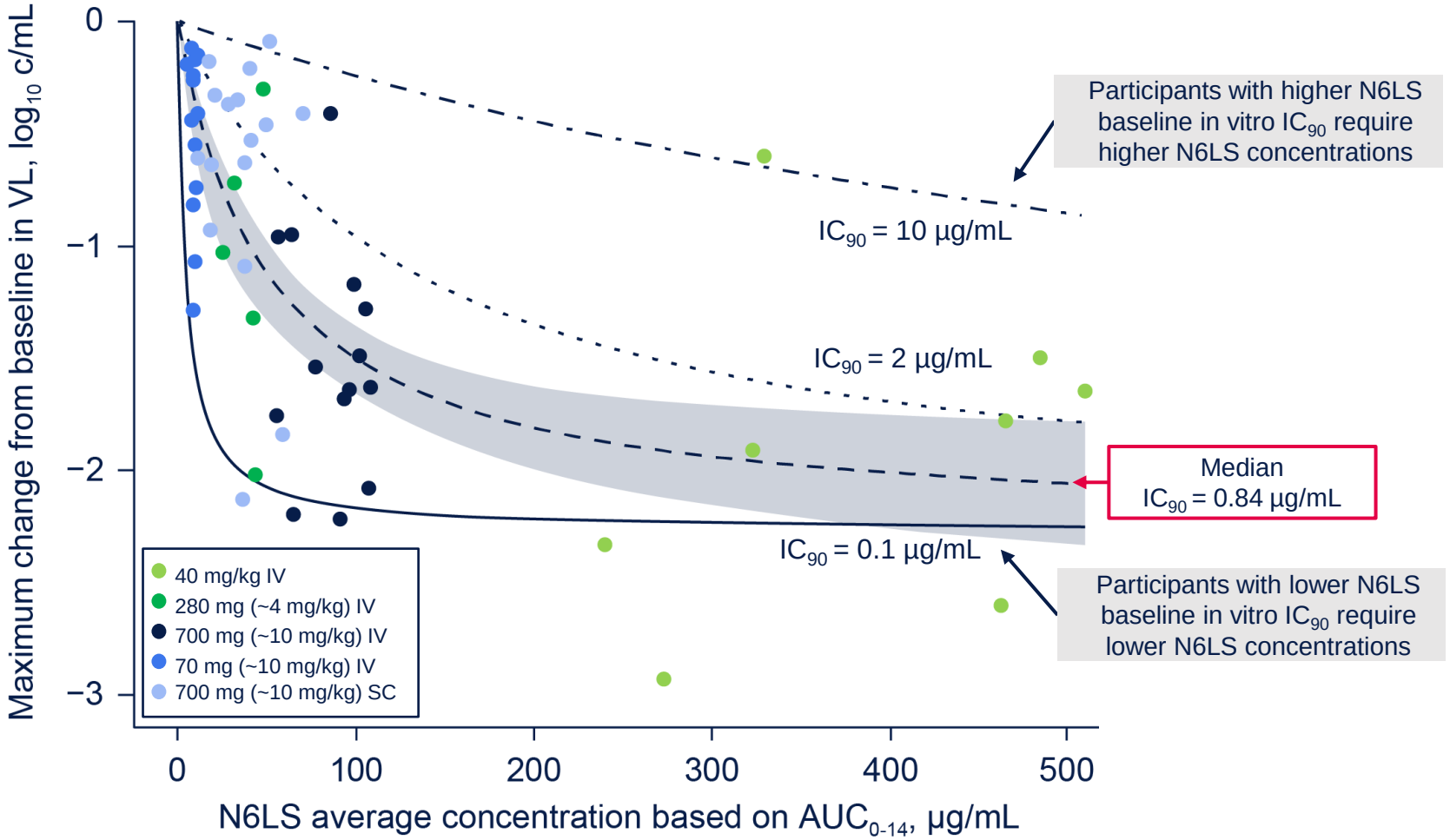
| Time to viral nadir, days | 16 (5-21) | 9 (7-16) | 9 (6-27) | 7 (2-23) | 9 (1-50) |
| Time to viral rebound among responders, days | 35 (12-78) [n=8] | 18 (14-29) [n=5] | 22 (14-43) [n=14] | 13 (10-22) [n=7] | 17 (11-63) [n=8] |

IV, intravenous; N6LS, VH3810109; SC, subcutaneous; VL, viral load.

[a]For a 70-kg individual.

# N6LS Antiviral Activity Correlated With Drug Exposure




*95% PI based on 1000 samplings from variance-covariance matrix*

- Emax model describes the relationship between the maximum change from baseline in VL and the observed N6LS concentration
- A clear exposure-response relationship was observed; higher N6LS exposures give greater VL declines

AUC, area under the plasma concentration–time curve; Emax, maximum effect; $IC_{90}$, 90% inhibitory concentration; IV, intravenous; N6LS, VH3810109; PI, prediction interval; SC, subcutaneous; VL, viral load.


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

Leone et al. CROI 2024; Denver, CO. Oral Presentation 117.

# Conclusions

- Robust antiviral response was observed with N6LS and was correlated with N6LS exposure[1]; this exposure-dependent antiviral activity was consistent with reports for other bNAbs[2]
  - Baseline viral sensitivity to N6LS was an important predictor of N6LS concentrations required to achieve antiviral effect[1]
  - Lower SC viral response was as expected when considering N6LS exposures achieved
- The SPAN study explores the safety and tolerability of higher doses of N6LS, including SC with rHuPH20 in HIV-negative adults and is presented in Poster 639[3]
- Results from BANNER and SPAN support the ongoing clinical development of N6LS as an ultra-long dosing strategy into phase 2b (EMBRACE, NCT05996471)

bNAb, broadly neutralizing antibody; Cmax, maximum plasma concentration; IV, intravenous; N6LS, VH3810109; SC, subcutaneous.

**1.** Edwards et al. EACS 2023; Warsaw, Poland. Poster eP.A.099. **2.** Caskey et al. *Nature*. 2015;522:487-491. **3.** Win et al. CROI 2024; Denver, CO. Poster 639.

# Acknowledgments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