

## **SUPPLEMENTARY MATERIAL**

### **Clinical Pharmacokinetics and Safety of Orally Administered VH4011499, a New HIV-1 Capsid Inhibitor, in Adults Without HIV**

Nilay Thakkar,<sup>1\*</sup> Rulan Griesel,<sup>2\*</sup> Amy Pierce,<sup>3</sup> Veronica Bainbridge,<sup>4</sup> Bronagh Shepherd,<sup>4</sup> Konstantinos Angelis,<sup>4</sup> Andrew Tomlinson,<sup>4</sup> Yash Gandhi,<sup>1</sup> Darin Brimhall,<sup>5</sup> Brian Spears,<sup>6</sup> Daijha Anderson,<sup>3</sup> Emma Pinnick,<sup>4</sup> Carolina Acupil,<sup>3</sup> Cynthia McCoig,<sup>7</sup> Mark Baker,<sup>8</sup> Paul Benn<sup>2</sup>

<sup>1</sup>GSK, 1250 S Collegeville Road, Collegeville, PA, USA 19426; <sup>2</sup>ViiV Healthcare, 79 New Oxford Street, London WC1A 1DG, UK; <sup>3</sup>ViiV Healthcare, 410 Blackwell Street, Durham, NC, USA 27701; <sup>4</sup>GSK, 79 New Oxford Street, London WC1A 1DG, UK; <sup>5</sup>PPD-Thermo Fisher Scientific, 8285 W Arby Avenue, Suite 331, Las Vegas, NV, USA 89113; <sup>6</sup>PPD-Thermo Fisher Scientific, 7551 Metro Center Drive, Suite 300, Austin, TX, USA 78744; <sup>7</sup>ViiV Healthcare, P.T.M., Severo Ochoa 2, 28760 Tres Cantos, Madrid, Spain; <sup>8</sup>ViiV Healthcare, Route de l'Etraz 2, Case postale 1279, Nyon 1, CH-1260, Switzerland

\*Nilay Thakkar and Rulan Griesel served as co-first authors and contributed equally to the work.

**Corresponding author:** Nilay Thakkar, PhD; [nilay.x.thakkar@gsk.com](mailto:nilay.x.thakkar@gsk.com)

## Table of Contents

|                 |   |
|-----------------|---|
| Table S1.....   | 3 |
| Table S2.....   | 4 |
| Figure S1. .... | 5 |
| Figure S2. .... | 6 |
| Figure S3. .... | 8 |

**Table S1.** Participant Demographics and Baseline Characteristics

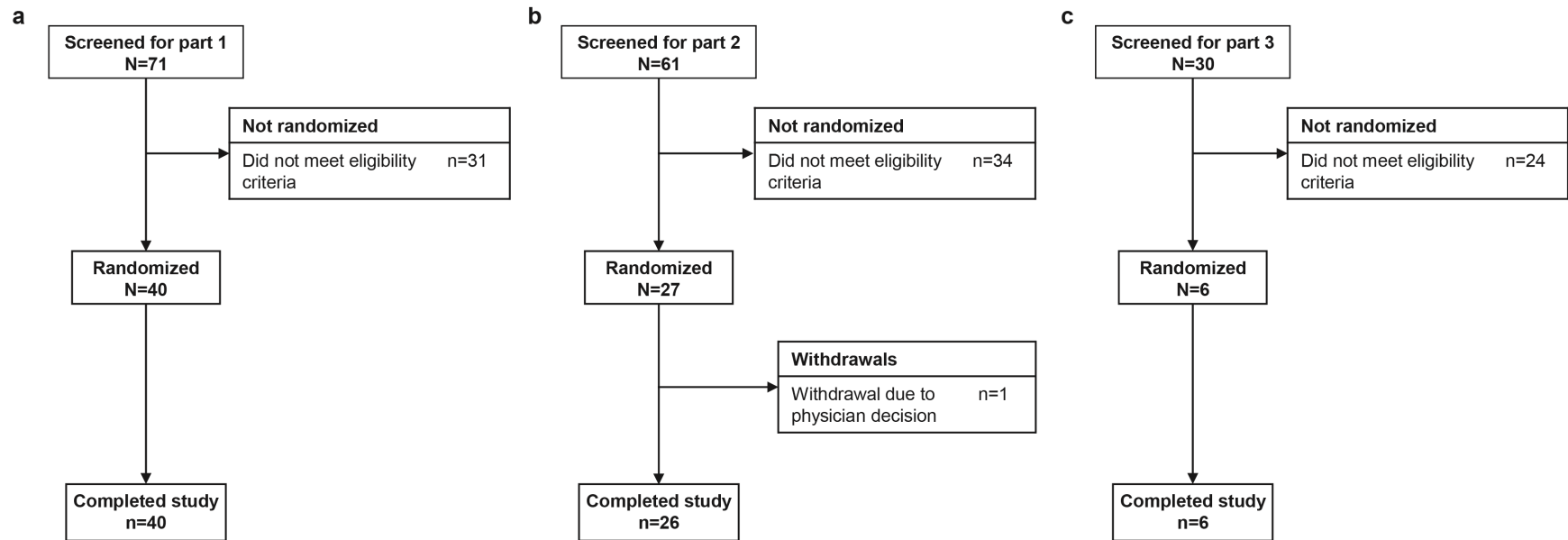
| <b>Parameter</b>                                   | <b>Parts 1 and 3<br/>(N=46)</b> | <b>Part 2<br/>(N=27)</b> |
|----------------------------------------------------|---------------------------------|--------------------------|
| Male sex, n (%)                                    | 43 (93)                         | 25 (93)                  |
| Age, median (range), y                             | 37 (24-55)                      | 34 (21-54)               |
| Hispanic or Latin American ethnicity, n (%)        | 14 (30)                         | 9 (33)                   |
| Race, n (%)                                        |                                 |                          |
| Asian                                              | 6 (13)                          | 1 (4)                    |
| Black or African American                          | 14 (30)                         | 15 (56)                  |
| Native Hawaiian or Other Pacific Islander          | 1 (2)                           | 0                        |
| White                                              | 19 (41)                         | 11 (41)                  |
| Multiple races                                     | 6 (13)                          | 0                        |
| Body mass index, median (range), kg/m <sup>2</sup> | 26.9 (20.3-30.7)                | 25.6 (19.4-32.0)         |

**Table S2.** Summary of Maximum Grade Increase Post-Baseline Relative to Baseline in Lipid Parameters: Safety Population

| <b>Parts 1 and 3</b>   |                                           |                                            |                                            |                                            |                                             |                                                           |                                    |                                   |
|------------------------|-------------------------------------------|--------------------------------------------|--------------------------------------------|--------------------------------------------|---------------------------------------------|-----------------------------------------------------------|------------------------------------|-----------------------------------|
| <b>Category, n (%)</b> | <b>VH-499<br/>25 mg<br/>PiB<br/>(N=6)</b> | <b>VH-499<br/>125 mg<br/>PiB<br/>(N=6)</b> | <b>VH-499<br/>200 mg<br/>PiB<br/>(N=6)</b> | <b>VH-499<br/>625 mg<br/>PiB<br/>(N=6)</b> | <b>VH-499<br/>1875 mg<br/>PiB<br/>(N=6)</b> | <b>VH-499<br/>200 mg tablet<br/>formulation<br/>(N=6)</b> | <b>VH-499<br/>total<br/>(N=36)</b> | <b>Placebo<br/>PiB<br/>(N=10)</b> |
| Total cholesterol      |                                           |                                            |                                            |                                            |                                             |                                                           |                                    |                                   |
| Increase to grade 1    | 0                                         | 0                                          | 1 (17)                                     | 1 (17)                                     | 1 (17)                                      | 0                                                         | 3 (8)                              | 2 (20)                            |
| Increase to grade 2    | 0                                         | 1 (17)                                     | 0                                          | 1 (17)                                     | 0                                           | 0                                                         | 2 (6)                              | 0                                 |
| Increase to grade 3    | 0                                         | 0                                          | 0                                          | 0                                          | 1 (17)                                      | 0                                                         | 1 (3)                              | 1 (10)                            |
| LDL cholesterol        |                                           |                                            |                                            |                                            |                                             |                                                           |                                    |                                   |
| Increase to grade 1    | 1 (17)                                    | 0                                          | 0                                          | 1 (17)                                     | 1 (17)                                      | 1 (17)                                                    | 4 (11)                             | 2 (20)                            |
| Increase to grade 2    | 0                                         | 0                                          | 1 (17)                                     | 1 (17)                                     | 0                                           | 0                                                         | 2 (6)                              | 0                                 |
| Increase to grade 3    | 0                                         | 1 (17)                                     | 0                                          | 0                                          | 1 (17)                                      | 0                                                         | 2 (6)                              | 1 (10)                            |
| <b>Part 2</b>          |                                           |                                            |                                            |                                            |                                             |                                                           |                                    |                                   |
|                        | <b>VH-499<br/>200 mg PiB<br/>(N=6)</b>    | <b>VH-499<br/>300 mg PiB<br/>(N=8)</b>     | <b>VH-499<br/>400 mg PiB<br/>(N=6)</b>     | <b>VH-499<br/>total<br/>(N=20)</b>         | <b>Placebo<br/>PiB<br/>(N=7)</b>            |                                                           |                                    |                                   |
| Total cholesterol      |                                           |                                            |                                            |                                            |                                             |                                                           |                                    |                                   |
| Increase to grade 1    | 0                                         | 3 (38)                                     | 0                                          | 3 (15)                                     | 1 (14)                                      |                                                           |                                    |                                   |
| Increase to grade 2    | 1 (17)                                    | 1 (13)                                     | 0                                          | 2 (10)                                     | 1 (14)                                      |                                                           |                                    |                                   |
| Increase to grade 3    | 0                                         | 1 (13)                                     | 0                                          | 1 (5)                                      | 0                                           |                                                           |                                    |                                   |
| LDL cholesterol        |                                           |                                            |                                            |                                            |                                             |                                                           |                                    |                                   |
| Increase to grade 1    | 1 (17)                                    | 2 (25)                                     | 0                                          | 3 (15)                                     | 1 (14)                                      |                                                           |                                    |                                   |
| Increase to grade 2    | 1 (17)                                    | 1 (13)                                     | 0                                          | 2 (10)                                     | 0                                           |                                                           |                                    |                                   |
| Increase to grade 3    | 0                                         | 1 (13)                                     | 0                                          | 1 (5)                                      | 0                                           |                                                           |                                    |                                   |

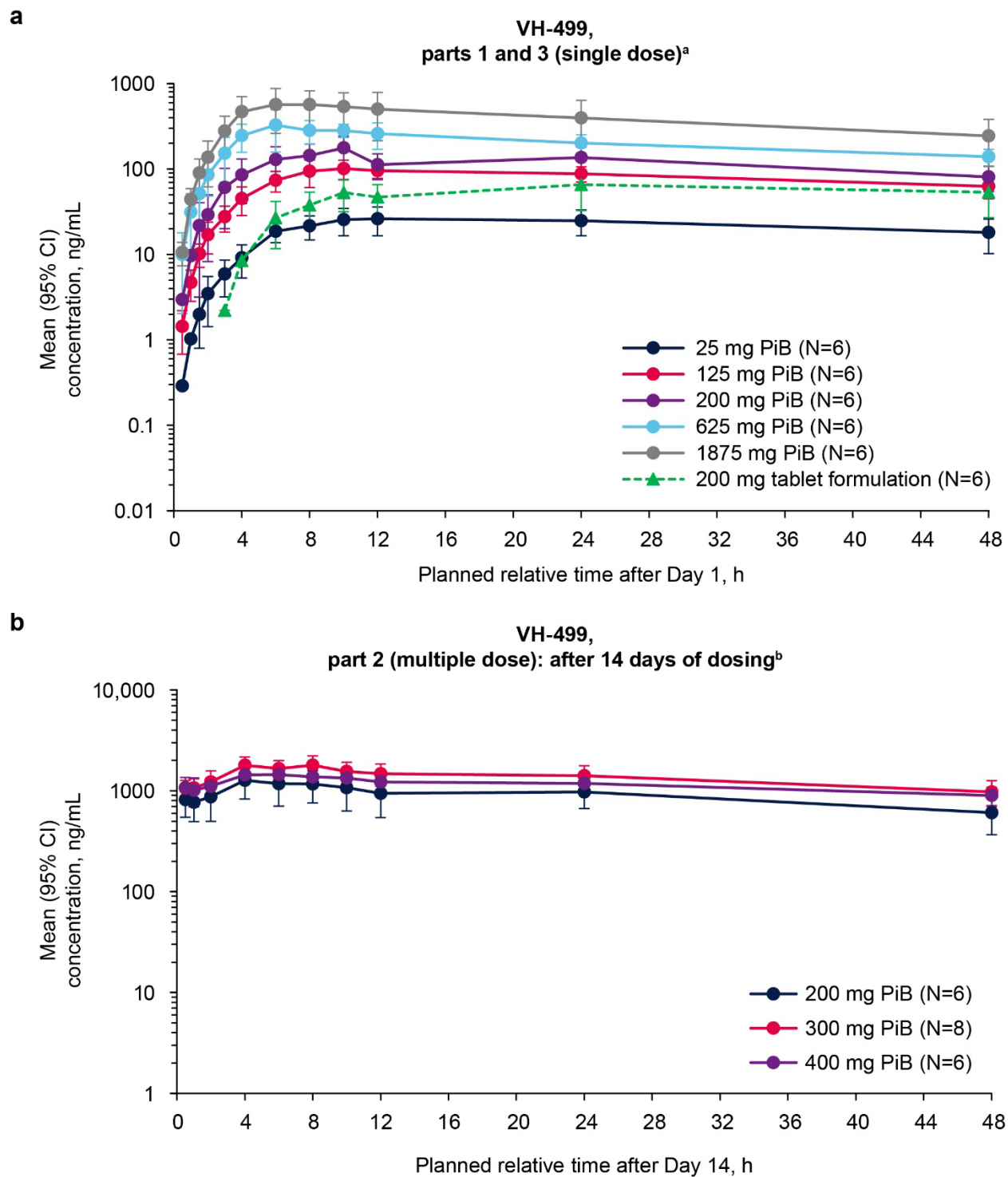
LDL, low-density-lipoprotein; PiB, powder-in-bottle; VH-499, VH4011499.

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



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

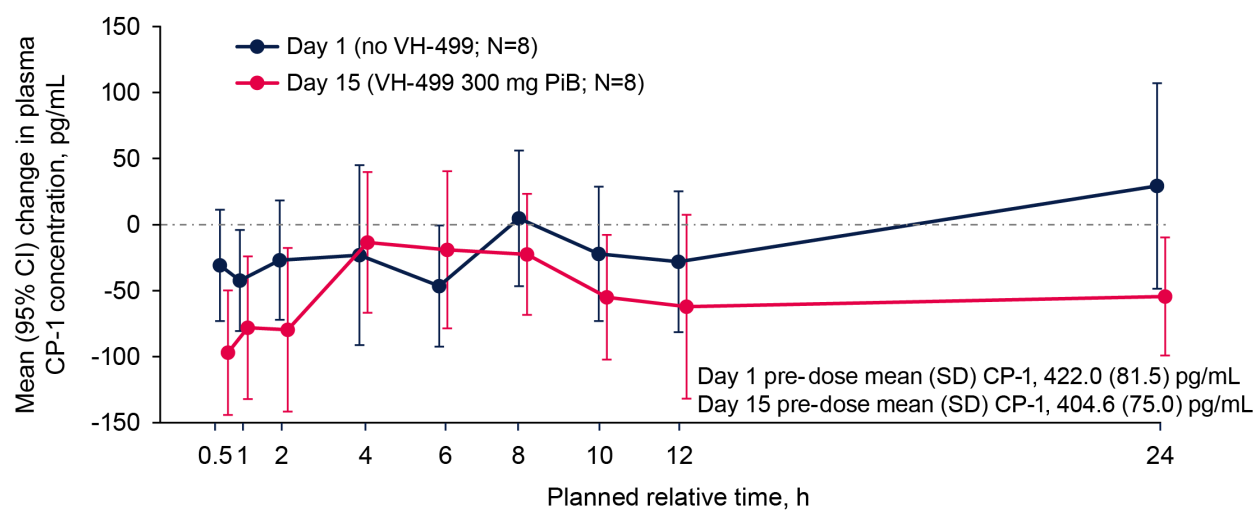
**Figure S2.** Mean plasma VH-499 concentration vs time plots through 48 hours after **(a)** single-dose oral administration of VH-499 in parts 1 and 3 and **(b)** multiple-dose oral administration of VH-499 in part 2: PK population.



PiB, powder-in-bottle; PK, pharmacokinetics; VH-499, VH4011499. <sup>a</sup>Lower limit of quantitation was 0.5 ng/mL for PiB formulation and 5 ng/mL for tablet formulation. Participants with concentrations below these limits had concentration values imputed to 0 and thus are not displayed. All values were below the limit of quantitation before 3 hours for 200 mg tablet formulation. If imputed values were >30%, then 95% CI was not calculated. <sup>b</sup>Lower limit of quantitation was 0.5 ng/mL.

**Figure S3.** Mean change from pre-dose plasma CP-1 PK concentration vs time data in part 2

(linear scale): CP-1 PK population.



CP-1, coproporphyrin-1; PiB, powder-in-bottle; PK, pharmacokinetics; VH-499, VH4011499.