### Supplemental Table 1. Summary of Baseline Resistance-Associated Substitutions in B/F/TAF-treated Participants

| Baseline Genotype of Participants, % (n/N) | Pooled B/F/TAF n=2034 |
|------------------------------------------|------------------------|
| PR/RT data available (historical and/or proviral) | 90 (1825/2034) |
| NRTI-R<sup>a</sup> | 16 (288/1825) |
| M184V/I | 10 (182/1825) |
| K65R/N | 1 (18/1825) |
| ≥1 TAM | 9 (167/1825) |
| NNRTI-R<sup>b</sup> | 22 (397/1825) |
| RPV-R<sup>c</sup> | 9 (170/1825) |
| K103N/S | 11 (205/1825) |
| PI-R<sup>d</sup> | 11 (201/1825) |
| IN data available (historical and/or proviral) | 85 (1731/2034) |
| Primary INSTI-R<sup>e</sup> | 2 (30/1731) |

<sup>a</sup> Nucleoside reverse transcriptase inhibitor resistance (NRTI-R) substitutions were K65R/E/N, T69 insertions, K70E, L74V/I, Y115F, Q151M, M184V/I, and thymidine analog mutations (TAMs; M41L, D67N, K70R, L210W, T215F/Y, and K219E/N/Q/R) in reverse transcriptase.

<sup>b</sup> Nonnucleoside reverse transcriptase inhibitor resistance (NNRTI-R) substitutions were L100I, K101E/P, K103N/S, V106M/A, V108I, E138A/G/K/Q/R, V179L, Y181C/I/V, Y188C/H/L, G190A/E/Q/S, H221Y, P225H, F227C and M230L/I in reverse transcriptase.

<sup>c</sup> Rilpivirine resistance (RPV-R) substitutions were L100I, K101E/P, E138A/G/K/Q/R, V179L, Y181C/I/V, Y188L, H221Y, F227C, and M230I/L in RT.

<sup>d</sup> Protease inhibitor resistance (PI-R) substitutions were D30N, V32I, M46I/L, I47V/A, G48V, I50V/L, I54M/L, Q58E, T74P, L76V, V82A/F/L/S/T, N83D, I84V, N88S and L90M in protease.

<sup>e</sup> Primary integrase strand transfer inhibitor resistance (INSTI-R) substitutions were T66I/A/K, E92Q/G, F121Y, Y143R/H/C, S147G, Q148H/K/R, N155H/S and R263K in integrase.
Supplemental Table 2. Detection of Baseline M184V/I by Historical or Baseline DNA Genotype and Viral Suppression at Last Visit Among B/F/TAF-treated Participants

| Participants, % (n/N) | Historical Genotype n=956 | Baseline DNA Genotype n=1712 |
|------------------------|---------------------------|-----------------------------|
|                        | Detection Frequency       | HIV-1 RNA <50 copies/mL at Last Visit [median B/F/TAF duration, weeks] | Detection Frequency | HIV-1 RNA <50 copies/mL at Last Visit [median B/F/TAF duration, weeks] |
| M184V/I                | 4% (38/956)               | 100% (38/38) [55]           | 10% (167/1712)      | 98% (164/167) [71] |
| M184V only             | 4% (35/956)               | 100% (35/35) [56]           | 9% (148/1712)       | 99% (146/148) [71] |
| M184I                  | <1% (2/956)               | 100% (2/2) [62]             | 1% (10/1712)        | 100% (10/10) [94]  |
| M184V and M184I mixture| <1% (1/956)               | 100% (1/1) [40]             | 1% (9/1712)         | 89% (8/9) [47]      |
| M184V/I alone (no other resistance substitution) | 1% (9/956) | 100% (9/9) [60] | 2% (34/1712) | 97% (33/34) [71] |
| M184V/I + ≥1 other resistance substitution | 3% (29/956) | 100% (29/29) [54] | 8% (133/1712) | 98% (131/133) [71] |
| M184V/I + other NRTI-R | 1% (13/956) | 100% (13/13) [54] | 5% (81/1712) | 99% (80/81) [64]  |
| M184V/I + K65N/R/N     | <1% (3/956)               | 100% (3/3) [50]             | <1% (7/1712)        | 100% (7/7) [53]    |
| M184V/I + 1-2 TAMs     | 1% (10/956)               | 100% (10/10) [55]           | 4% (68/1712)        | 99% (67/68) [64]   |
| M184V/I + ≥2 TAMs      | 1% (8/956)                | 100% (8/8) [56]             | 2% (29/1712)        | 97% (28/29) [69]   |
| M184V/I + K65E, L74V/I, Y115F, and/or Q151M | <1% (2/956) | 100% (2/2) [53] | 2% (39/1712) | 100% (39/39) [62] |
| M184V/I + NNRTI-R      | 3% (25/956)               | 100% (25/25) [54]           | 5% (85/1712)        | 99% (84/85) [72]   |
| M184V/I + K103N        | 2% (15/956)               | 100% (15/15) [51]           | 3% (58/1712)        | 98% (57/58) [72]   |
| M184V/I + RPV-R        | 1% (11/956)               | 100% (11/11) [58]           | 3% (45/1712)        | 100% (45/45) [72]  |
| M184V/I + E138A/G/K/Q/R| 1% (5/956)                | 100% (5/5) [51]             | <1% (8/1712)        | 100% (8/8) [88]    |
| M184V/I + PI-R         | 1% (8/956)                | 100% (8/8) [67]             | 3% (46/1712)        | 100% (46/46) [64]  |
| M184V/I + Primary INSTI-R | 0 | NA | <1 % (4/1712) | 100% (4/4) [63] |
### Supplemental Table 3. Discovery of M184V/I by Retrospective Baseline DNA Genotyping by M184V/I Enrollment Criteria

#### A. All Studies (M184V/I n=182)

| Baseline DNA Genotype, % (n) | Historical Genotype at Enrollment | Total n=1825 |
|-----------------------------|----------------------------------|-------------|
|                            | M184V/I n=38                     | Wild-type M184 n=918 | No data n=869 |
| M184V/I                    | 61% (23)                         | 3% (31)       | 13% (113)    | 9% (167) |
| Wild-type M184             | 24% (9)                          | 85% (780)     | 87% (756)    | 85% (1545) |
| No data                    | 16% (6)                          | 12% (107)     | 0            | 6% (113) |

#### B. Studies 4030 and 4580 only (M184V/I n=97): M184V/I Allowed

| Baseline DNA Genotype, % (n) | Historical Genotype at Enrollment | Total n=705 |
|-----------------------------|----------------------------------|-------------|
|                            | M184V/I n=37                     | Wild-type M184 n=338 | No data n=330 |
| M184V/I                    | 59% (22)                         | 5% (17)      | 13% (43)     | 12% (82) |
| Wild-type M184             | 24% (9)                          | 81% (273)    | 87% (287)    | 81% (569) |
| No data                    | 16% (6)                          | 14% (48)     | 0            | 54% (8) |

#### C. Studies 1844, 1878, 4449, and 1474 only (M184V/I n=85): M184V/I Excluded if Known Prior to Switch

| Baseline DNA Genotype, % (n) | Historical Genotype at Enrollment | Total n=1120 |
|-----------------------------|----------------------------------|-------------|
|                            | M184V/I n=1                      | Wild-type M184 n=580 | No data n=539 |
| M184V/I                    | 100% (1)                         | 2% (14)      | 13% (70)     | 8% (85) |
| Wild-type M184             | 0                                | 87% (507)    | 87% (469)    | 87% (976) |
| No data                    | 0                                | 10% (59)     | 0            | 5% (59) |
Supplemental Table 4. Demographics, Clinical Characteristics, and Resistance at Baseline for Participants With and Without Preexisting M184V/I

|                          | M184V/I n=216 | Wild-type M184V/I n=216 | P-value  |
|--------------------------|---------------|--------------------------|----------|
| From USA, % (n)          |               |                          |          |
| Median age, years (IQR)  | 80% (173)     | 70% (1311)               | 0.003    |
|                          | 52.5 (47.75–59) | 48 (38–56)               | <0.0001  |
| <50 years, % (n)         | 35% (76)      | 54% (1014)               |          |
| ≥50 years, % (n)         | 65% (140)     | 46% (849)                | <0.0001  |
| Sex at birth, % (n)      |               |                          |          |
| Male                     | 78% (168)     | 82% (1534)               | 0.100    |
| Female                   | 22% (48)      | 18% (329)                |          |
| Race/ethnicity           |               |                          |          |
| Black or African decent  | 47% (100)     | 37% (678)                | 0.003    |
| Hispanic/Latino          | 19% (41)      | 14% (264)                | 0.049    |
| Baseline BMI, % (n)      |               |                          |          |
| Underweight & normal: <25 kg/m² | 32% (69) | 35% (654) | 0.634 |
| Overweight: ≥25–<30 kg/m² | 40% (87)    | 37% (683)            |          |
| Obese: ≥30 kg/m²         | 28% (60)      | 28% (526)                |          |
| Baseline CKD stage (based on eGFR [CG]), % (n) | | | |
| Stage 1: ≥90 mL/min      | 58% (125)     | 68% (1263)               | 0.004    |
| Stage 2: ≥60–<90 mL/min  | 36% (76)      | 29% (534)                |          |
| Stage 3A: ≥45–<60 mL/min | 6% (13)      | 3% (55)                  |          |
| Stage 3B: ≥30–<45 mL/min | 0            | <1% (11)                 |          |
| Stage 4: ≥15–<30 mL/min  | 0            | 0                       |          |
| Stage 5: <15 mL/min      | 0            | 0                       |          |
| Median CD4 count, cells/µL (IQR) | 638.5 (460–839.5) | 681 (495–884) | 0.038 |
| CD4 <500 cells/µL, % (n) | 34% (73)      | 25% (473)                | 0.008    |
| CD4 ≥500 cells/µL, % (n) | 66% (143)     | 75% (1390)               |          |
| Baseline HIV-1 RNA, % (n) |             |                          |          |
| <50 copies/mL            | 97% (210)     | 98% (1823)               | 0.551    |
| ≥50 copies/mL            | 3% (6)        | 2% (40)                  |          |
| HIV acquisition factor, % (n) |             |                          |          |
| Injection drug use       | 8% (18)       | 3% (61)                  | 0.0002   |
| Homosexual sex           | 55% (119)     | 65% (1210)               | 0.004    |
| Heterosexual sex         | 38% (81)      | 31% (586)                | 0.072    |
| HIV disease status, % (n) |             |                          |          |
| Symptomatic or AIDS      | 23% (50)      | 15% (280)                | 0.002    |
| Asymptomatic             | 77% (166)     | 85% (1583)               |          |
| Median time since ART start, years (IQR) | 19.0 (11.1–22.4) | 7.3 (3.9–13.6) | <0.0001 |
Sax, Andreatta, et al, "High Efficacy of Switching to Bictegravir/Emtricitabine/Tenofovir Alafenamide in People with Suppressed HIV and Preexisting M184V/I," Supplemental Data

|                                | M184V/I n=216 | Wild-type M184V/I n=216 | P-value\(^a\) |
|--------------------------------|---------------|--------------------------|---------------|
| Median duration of baseline ARV regimen (IQR) | 2.1 (1.0−4.1) | 1.7 (1.0−3.4) | 0.127        |
| Median number of prior third agents (IQR) | 3.0 (2.0−4.0) | 2.0 (1.0−2.0) | <0.0001      |
| Median number of prior third agent classes (IQR) | 2.0 (1.0−3.0) | 1.0 (1.0−2.0) | <0.0001      |

Prior third agents, % (n)

| Prior third agents | M184V/I (n) | Wild-type M184V/I (n) | P-value\(^b\) |
|--------------------|-------------|-----------------------|---------------|
| Any INSTI          | 63% (137)   | 67% (1242)            | 0.340         |
| DTG                | 52% (112)   | 54% (999)             | 0.621         |
| EVG                | 13% (29)    | 17% (325)             | 0.137         |
| RAL                | 20% (44)    | 10% (178)             | <0.0001       |
| Any NNRTI          | 48% (103)   | 38% (704)             | <0.0001       |
| Any PI             | 79% (171)   | 52% (973)             | <0.0001       |

Baseline resistance substitutions, % (n)

| Baseline resistance substitutions | M184V/I (n) | Wild-type M184V/I (n) | P-value\(^b\) |
|-----------------------------------|-------------|-----------------------|---------------|
| NRTI-R (other than M184V/I)       | 49% (105)   | 7% (132)              | <0.0001       |
| ≥1 TAM                            | 40% (87)    | 6% (119)              | <0.0001       |
| NNRTI-R                           | 54% (116)   | 18% (344)             | <0.0001       |
| RPV-R                             | 27% (59)    | 8% (144)              | <0.0001       |
| PI-R                              | 27% (59)    | 9% (169)              | <0.0001       |
| Primary INSTI-R                   | 2% (5)      | 1% (26)               | 0.324         |
| Secondary INSTI-R\(^c\)           | 41% (86)    | 51% (890)             | 0.007         |

Clinical trial, % (n)

| Clinical trial | M184V/I (n) | Wild-type M184V/I (n) | P-value |
|----------------|-------------|-----------------------|---------|
| Study 4030     | 38% (81)    | 21% (389)             |         |
| Study 4580     | 24% (51)    | 23% (422)             |         |
| Study 1844     | 8% (17)     | 27% (511)             | <0.0001 |
| Study 1878     | 30% (64)    | 25% (460)             |         |
| Study 4449     | 1% (3)      | 4% (81)               |         |

\(a\) P-value derived from the CMH test for categorical data (general association statistic was used for nominal data; row mean scores differ statistic was used for ordinal data) or the 2-sided Wilcoxon rank sum test for continuous data.

\(b\) Versus not from USA, non-Black race, not Hispanic or Latino ethnicity, no injection drug use, no homosexual or heterosexual sex, no prior treatment with listed third agents, or no baseline resistance to listed drug classes, as applicable.

\(c\) Secondary INSTI-R substitutions are M50I, H51Y, L68V/I, V72A/N/T, L74M, Q95K/R, T97A, G118R, S119P/R/T, F121C, A128T, E138K/A, G140A/C/S, P145S, Q146R/I/K/L/P, V151L/A, S153A/F/Y, E157K/Q, G163K/R and E170A in integrase.

ART, antiretroviral treatment; BMI, body mass index; CDK, chronic kidney disease; DTG, dolutegravir; eGFR (CG), estimated glomerular filtration rate by Cockcroft-Gault; EVG, elvitegravir; IQR, interquartile range; R, resistance; RAL, raltegravir; RPV, rilpivirine;