

**Supplementary Table 1.** Gag-Protease genotype and phenotype of baseline (pre-ART) samples relative to p8.MJ4GP

| Patient no. | Protease amino acid changes <sup>a</sup>                   | Gag CS amino acid changes <sup>a</sup> | LPV<br>(FC) <sup>b</sup> S≤ 3.8 | RTV<br>(FC) <sup>b</sup> S≤ 3.2 |
|-------------|--|--|---------------------------------|---------------------------------|
| 1           | K20R, E35D, M36I, S37N, S39P, I62V, P63L, T74S, I77V       | S373N, T374A                           | 0.5                             | 0.3                             |
| 2           | M36I, S37N, S39P, P63L, I77V, P81T                         | S373N, T374S, M378V                    | 0.2                             | 0.4                             |
| 3           | E35D, M36I, S37N, S39P, I77V                               | I134V, S373G, T374G                    | 0.4                             | 0.6                             |
| 4           | E35D, M36I, S37N, S39P, P63L, T74S, I77V                   | V128T, T374N, S451N                    | 2.7                             | 2.4                             |
| 5           | S12T, I19L, M36I, S37N, S39P, P63L, I77V, T80N, P81T       | S373N, T374N, S451N                    | 0.3                             | 0.2                             |
| 6           | S12T, V15I, I19T, M36I, S37N, S39P, I62V, I64L, K70R, I77V | T374G, S451N                           | 0.6                             | 0.6                             |
| 7           | E35D, M36I, S37N, S39P, A71T, I77V                         | S373N, T374S, S451N                    | 1.8                             | 2.2                             |
| 8           | L10I, K20R, E35D, M36I, S37N, S39P, P63L, C67Y, I77V       | S373N, T374S, S451N                    | 0.4                             | 0.3                             |
| 9           | M36I S37N, S39P, P63A, T74S, I77V                          | V128I, S373N, T374P                    | 1.9                             | 2.1                             |
| 10          | S12T, V15I, S39P   | S373N, T374V                           | <b>4.5</b>                      | <b>3.8</b>                      |
| 11          | V15I, M36I, S39P, P63S, I77V, V82I                         | V128I, T374A                           | 0.7                             | 0.7                             |
| 12          | I19V, K20R, E35D, M36I, S37N, S39P, R57K, D60E, Q61E, I77V | S451N                                  | <b>6.4</b>                      | <b>4.0</b>                      |
| 13          | E35D, M36I, S37N, S39P, P63V, T74S, I77V                   | T374V, E428K, L449P, P453L             | <b>9.5</b>                      | <b>7.8</b>                      |
| 14          | L10M, S37K, S39P, K41I, P63T, I77V                         | S373N, T374G, S451N                    | 1.4                             | 0.8                             |
| 15          | I19T, K20R, E35D, M36I, S37N, S39T, P63V, I77V             | S373H, T374G, S451N                    | 2.3                             | 0.4                             |
| 16          | S37N, S39P, K41R, P63L, T74S                               | S373N, T374S, I437L, S451N             | 1.7                             | 1.2                             |
| 17          | S12A, I19T, M36I, S37N, S39P, D60G, P63V, I64M, I77V       | S373N, T374A, S451N                    | 3.2                             | 2.3                             |
| 18          | M36I, S37N, S39P, P63L, I77V, V82I                         | Y132F, S373K, T374G                    | <b>4.3</b>                      | <b>4.8</b>                      |
| 19          | M36L, S37E, S39P, K41R, P63V, I77V                         | S373T, P453L                           | 1.5                             | 1.9                             |
| 20          | I19T, M36I, S37N, S39P, I77V                               | S373N, T374S, S451N                    | 1.9                             | <b>4.9</b>                      |

<sup>a</sup> The Protease and Gag CS amino acid changes are reported as changes relative to p8.MJ4GP

<sup>b</sup> The fold change in susceptibility for LPV and RTV is based on the EC<sub>50</sub> of the baseline sample relative to p8.MJ4GP

**Supplementary Table 2.** Comparison of phenotypic fold changes calculated using the baseline sample and reference plasmid

| Patient ID | Stanford Predicted Phenotype | Actual Phenotype (FC): |           |
|------------|------------------------------|------------------------|-----------|
|            |                              | Baseline               | p8.9MJ4GP |
| 1          | High                         | 191                    | 74        |
| 2*         | Intermediate                 | 109                    | 27        |
| 3*         | Intermediate                 | 68                     | 31        |
| 4*         | High                         | 5.2                    | 20        |
| 5*         | Susceptible                  | 4.2                    | 1.3       |
| 6          | Susceptible                  | 1.3                    | 0.5       |
| 7          | Susceptible                  | 0.8                    | 1.7       |
| 8          | Intermediate                 | 12                     | 5.3       |
| 9          | Intermediate                 | 6.0                    | 12        |
| 10         | Intermediate                 | 7.6                    | 24        |
| 11*        | Susceptible                  | 5.9                    | 3.9       |
| 12*        | Intermediate                 | 1.2                    | 6.5       |
| 13         | Susceptible                  | 0.1                    | 1.2       |
| 14         | Susceptible                  | 2.6                    | 3.2       |
| 15         | Susceptible                  | 0.4                    | 0.6       |
| 16         | Susceptible                  | 1.3                    | 2.1       |
| 17         | Susceptible                  | 0.4                    | 1.2       |
| 18         | Susceptible                  | 2.1                    | 9.9       |
| 19         | Susceptible                  | 1.0                    | 1.5       |
| 20         | Susceptible                  | 0.1                    | 0.7       |

\*Samples showing discordance with Stanford.