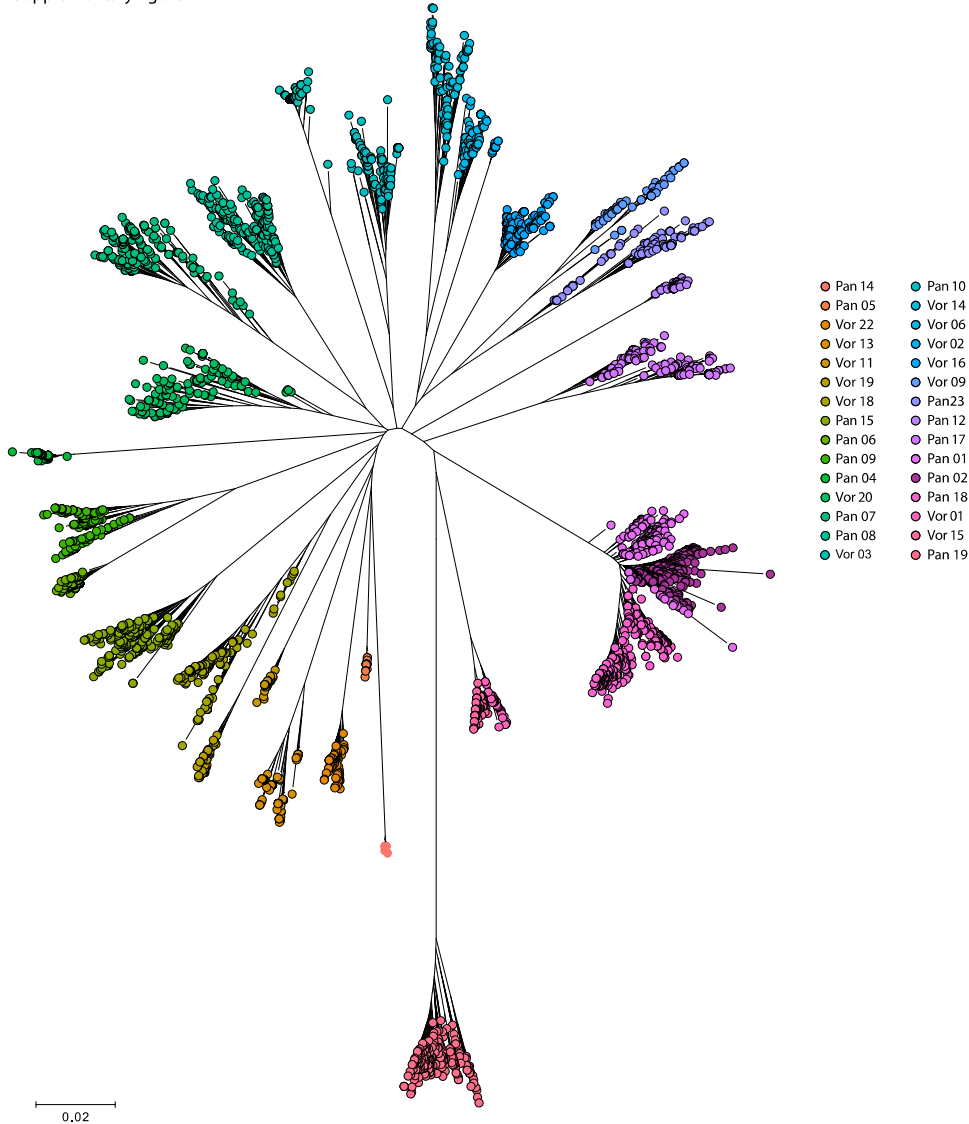


Supplementary figure 1



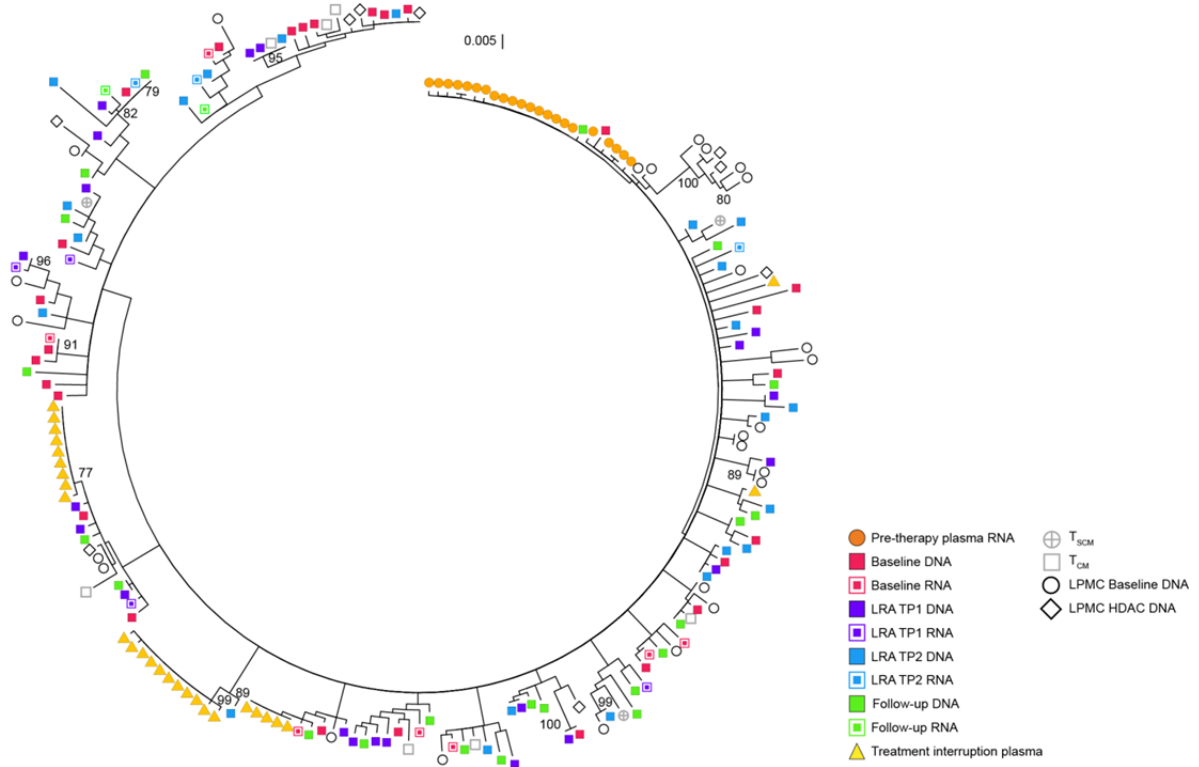
1

2

3 **Supplementary Figure 1** Sequences from individual study participants segregate
4 independently A neighbor-joining tree of sequences from all participants in both the
5 panobinostat and vorinostat trials is shown. Sequences that were classified as defective
6 (containing stop codons or hypermutation) were not included. The phylogenetic analysis
7 and tree construction were conducted using MEGA-CC.

8

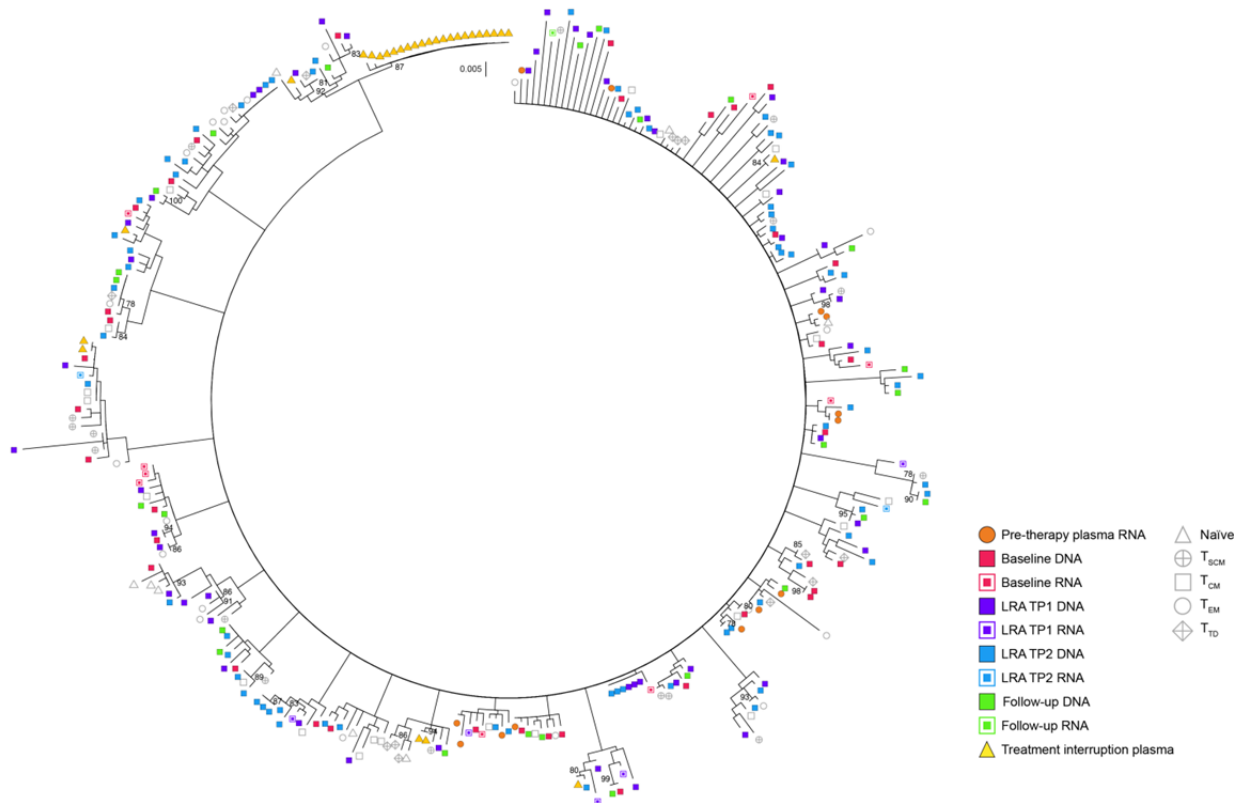
Supplementary figure 2



9

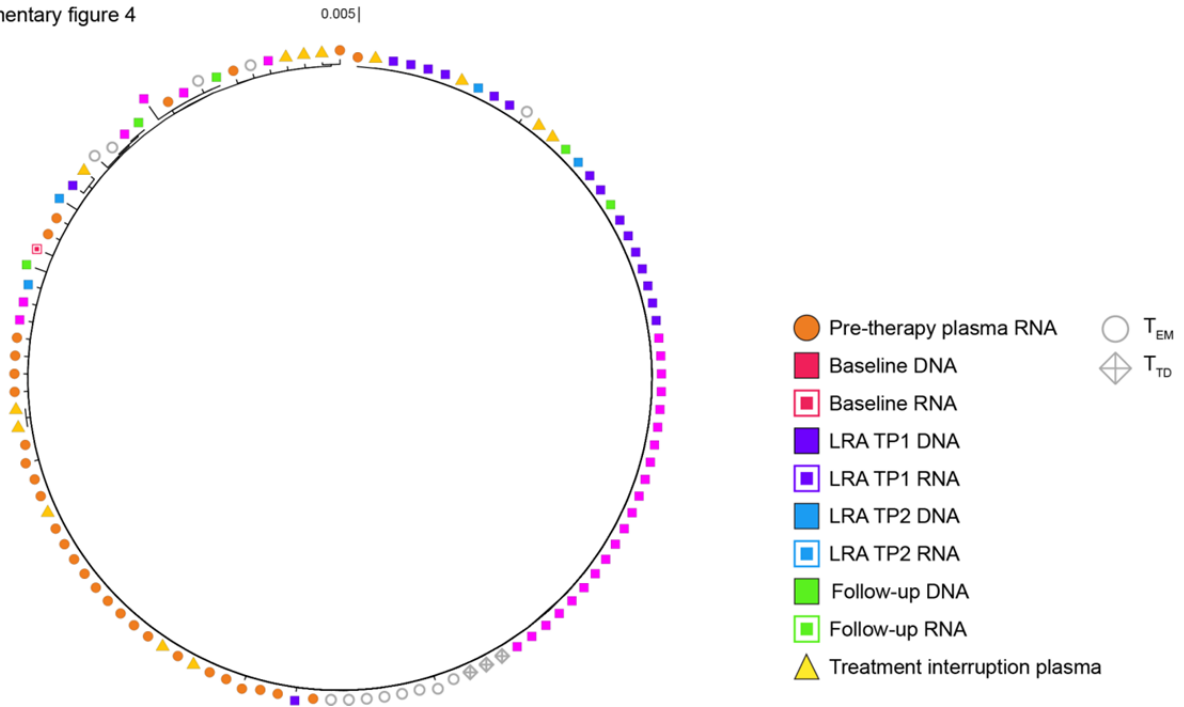
10

11 **Supplementary Figure 2** Panobinostat participant 1 phylogenetic tree. Maximum-
12 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
13 genome sequencing on isolated CD4+ T cells for participant 1 from the panobinostat
14 trial. The phylogenetic analysis and tree construction were conducted using MEGA-CC.
15 Defective sequences (hypermutants or containing stop codons) were excluded from the
16 phylogenetic tree analysis. The plasma samples were collected approximately 2 months
17 prior to initiation of anti-retroviral therapy and 14 days following the analytical treatment
18 interruption. Peripheral blood samples were collected at baseline, 28 days after the first
19 dose of panobinostat (TP1), 32 days after the first dose of panobinostat (TP2), and 38
20 days after the final panobinostat dose. Intestinal lamina propria mononuclear cells were
21 collected at baseline (1 week prior to the first panobinostat dose) and during week 4 of
22 the panobinostat trial. Cell subsets were sorted from peripheral blood samples collected
23 38 days after the final panobinostat dose.



24

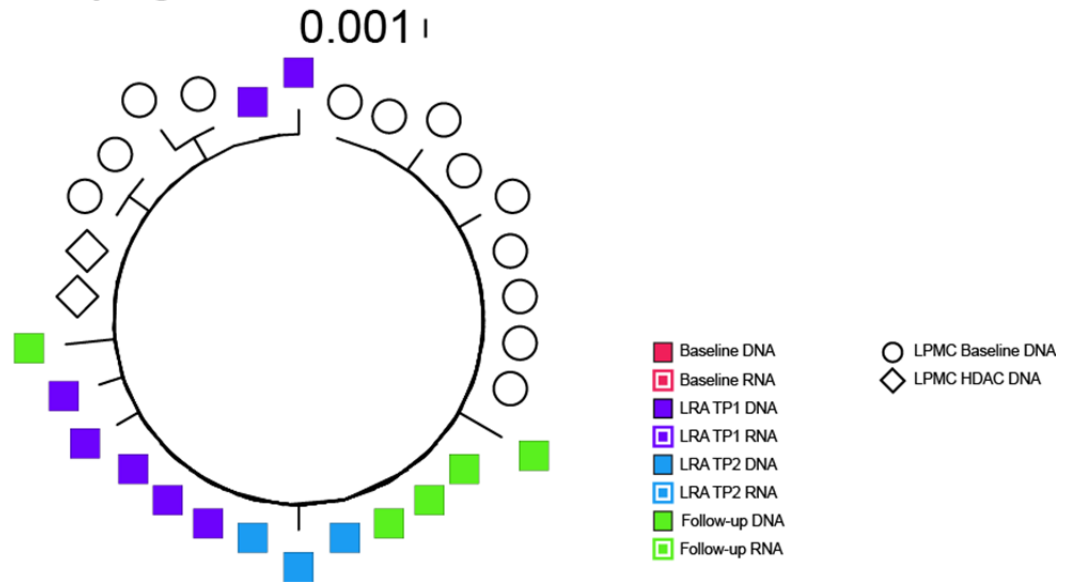
25 **Supplementary Figure 3** Panobinostat participant 2 phylogenetic tree. Maximum-
 26 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
 27 genome sequencing on isolated CD4+ T cells for participant 2 from the panobinostat
 28 trial. The phylogenetic analysis and tree construction were conducted using MEGA-CC.
 29 Defective sequences (hypermutants or containing stop codons) were excluded from the
 30 phylogenetic tree analysis. The plasma samples were collected approximately 1 year
 31 and 5 months prior to initiation of anti-retroviral therapy and 14 days following the
 32 analytical treatment interruption. Peripheral blood samples were collected at baseline, 2
 33 hours after the first dose of panobinostat (TP1), 14 days and 42 days after the first dose
 34 of panobinostat (sequences from these two time points are both labeled as TP2), and
 35 38 days after the final panobinostat dose. Cell subsets were sorted from peripheral
 36 blood samples collected 38 days after the final panobinostat dose.



37

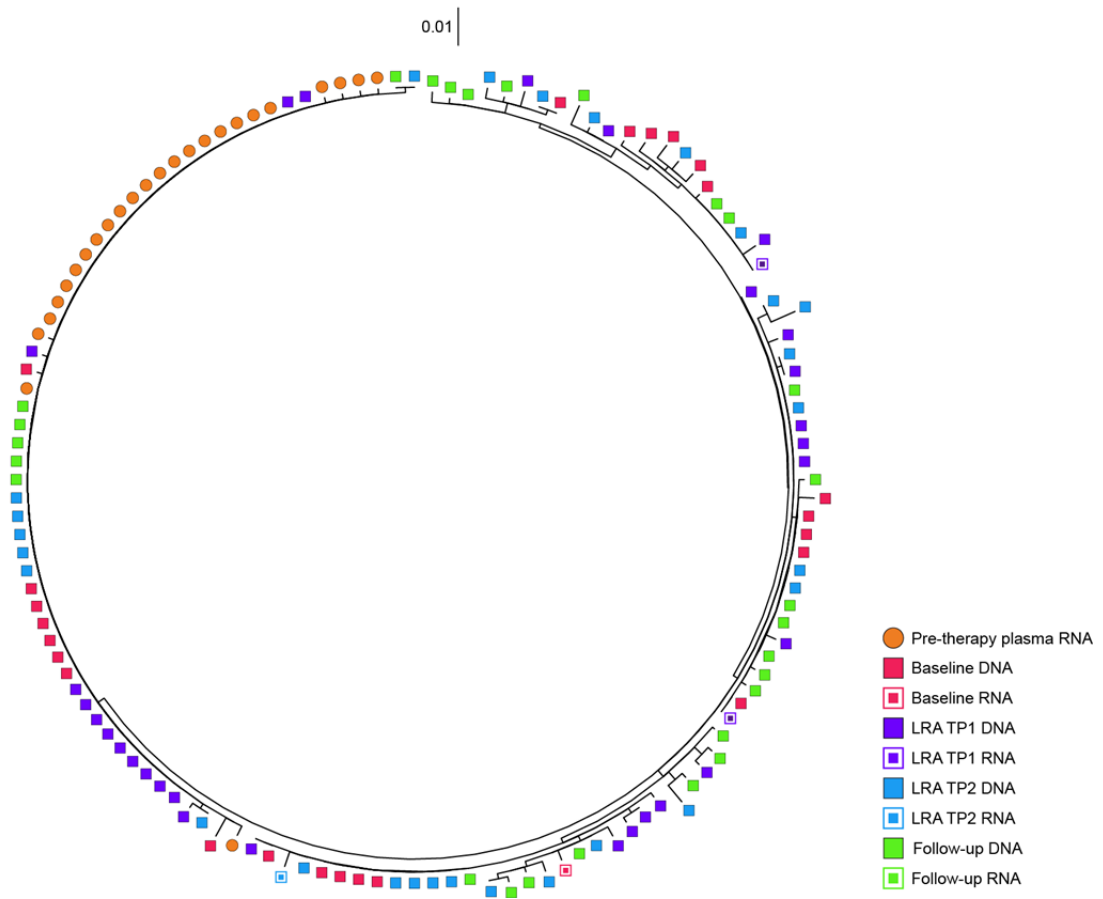
38 **Supplementary Figure 4** Panobinostat participant 4 phylogenetic tree. Maximum-
 39 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
 40 genome sequencing on isolated CD4+ T cells for participant 4 from the panobinostat
 41 trial. The phylogenetic analysis and tree construction were conducted using MEGA-CC.
 42 Defective sequences (hypermutants or containing stop codons) were excluded from the
 43 phylogenetic tree analysis. The plasma samples were collected the day of anti-retroviral
 44 therapy initiation and 46 and 55 days following the analytical treatment interruption.
 45 Peripheral blood samples were collected at baseline, 1 day after the first dose of
 46 panobinostat (TP1), 28 days after the first dose of panobinostat (TP2), and 38 days
 47 after the final panobinostat dose. Cell subsets were sorted from peripheral blood
 48 samples collected 38 days after the final panobinostat dose.

Supplementary figure 5



49

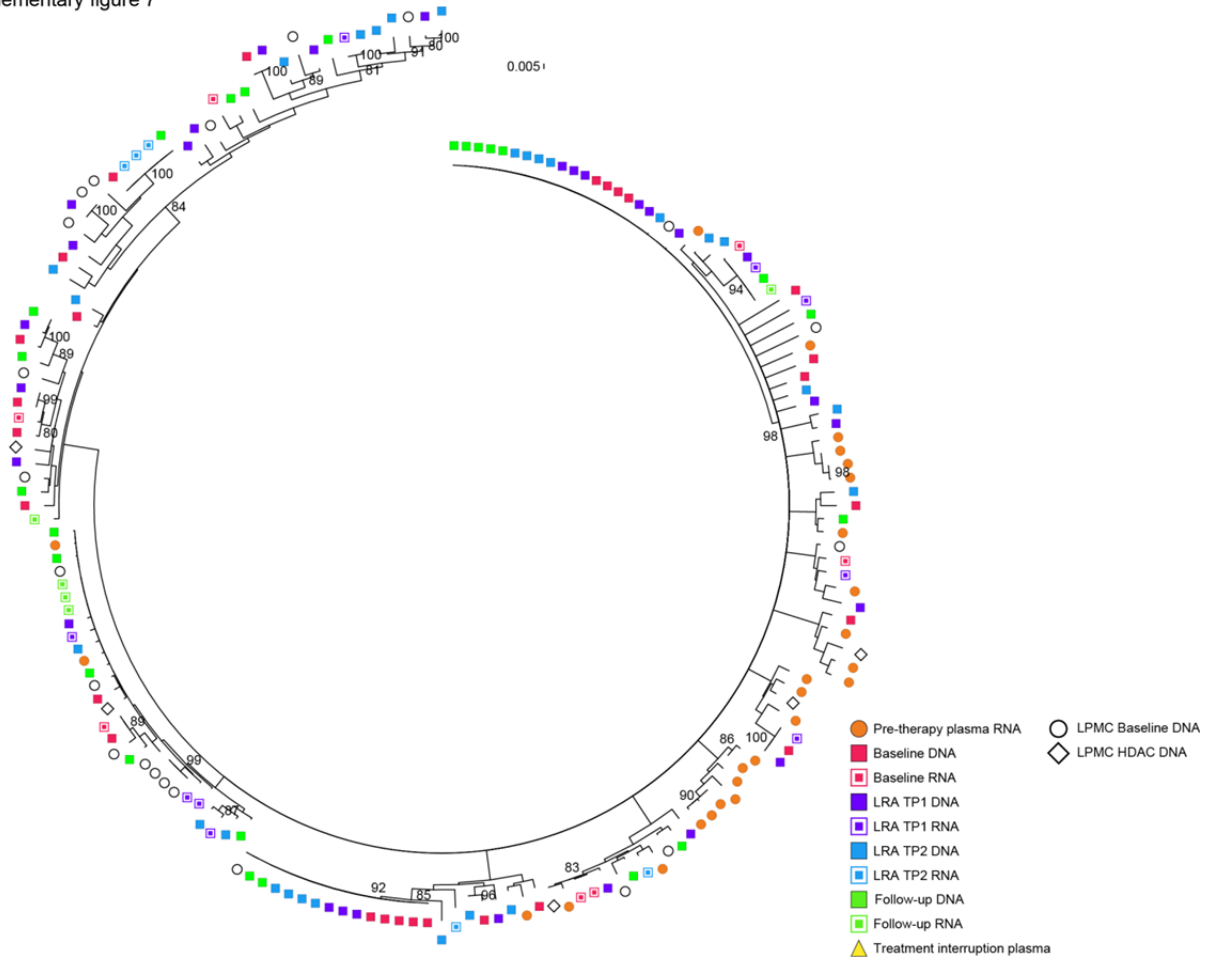
50 **Supplementary Figure 5** Panobinostat participant 5 phylogenetic tree. Maximum-
51 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
52 genome sequencing on isolated CD4+ T cells for participant 5 from the panobinostat
53 trial. The phylogenetic analysis and tree construction were conducted using MEGA-CC.
54 Defective sequences (hypermutants or containing stop codons) were excluded from the
55 phylogenetic tree analysis. Peripheral blood samples were collected at baseline, 2
56 hours after the first dose of panobinostat (TP1), 28 days after the first dose of
57 panobinostat (TP2), and 38 days after the final panobinostat dose. Intestinal lamina
58 propria mononuclear cells were collected at baseline (1 week prior to the first
59 panobinostat dose) and during week 4 of the panobinostat trial.



60

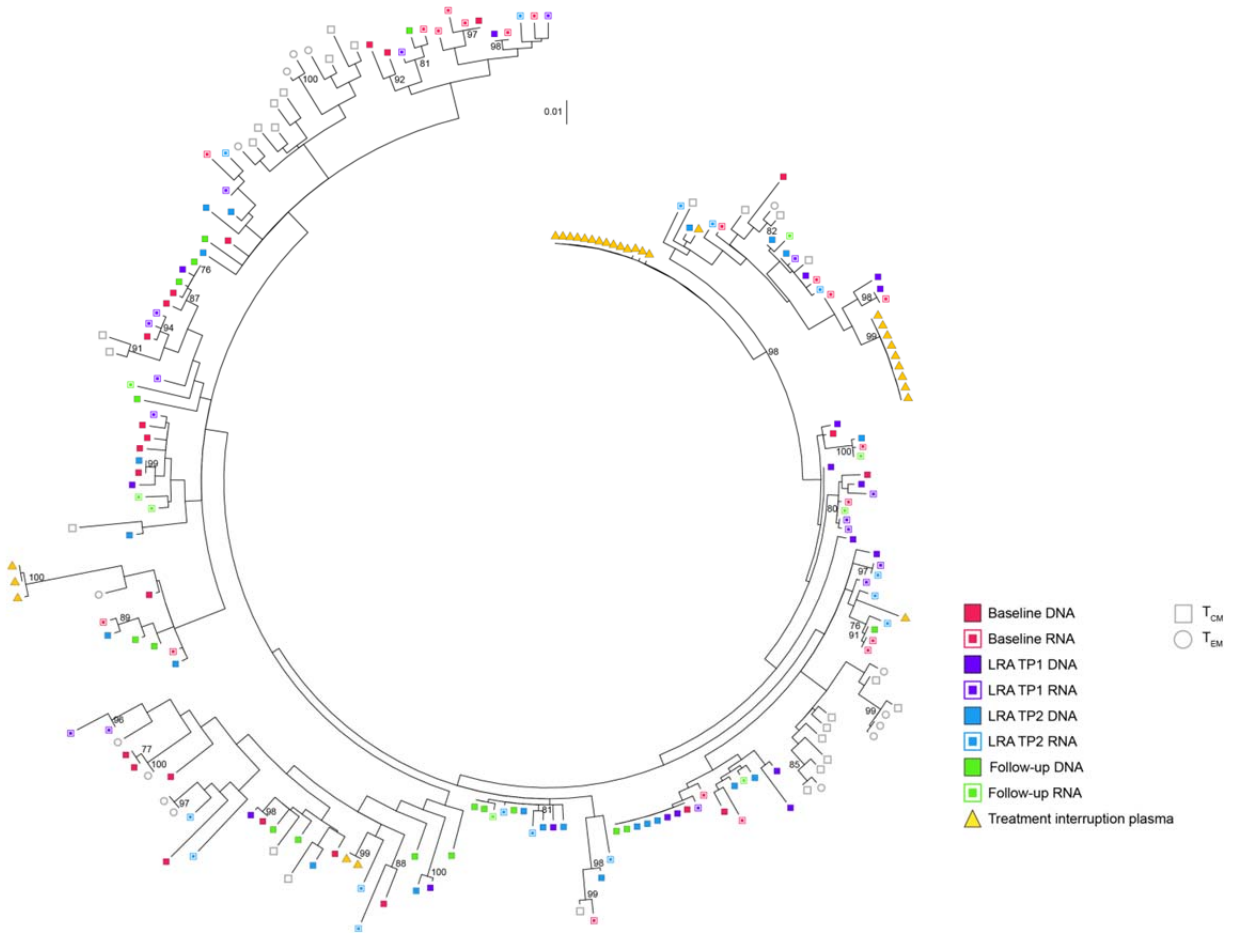
61 **Supplementary Figure 6** Panobinostat participant 6 phylogenetic tree. Maximum-
 62 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
 63 genome sequencing on isolated CD4+ T cells for participant 6 from the panobinostat
 64 trial. The phylogenetic analysis and tree construction were conducted using MEGA-CC.
 65 Defective sequences (hypermutants or containing stop codons) were excluded from the
 66 phylogenetic tree analysis. The plasma sample was collected approximately 8 months
 67 prior to initiation of anti-retroviral therapy. Peripheral blood samples were collected at
 68 baseline, 2 hours after the first dose of panobinostat (TP1), 1 day after the first dose of
 69 panobinostat (TP2), and 38 days after the final panobinostat dose.

Supplementary figure 7



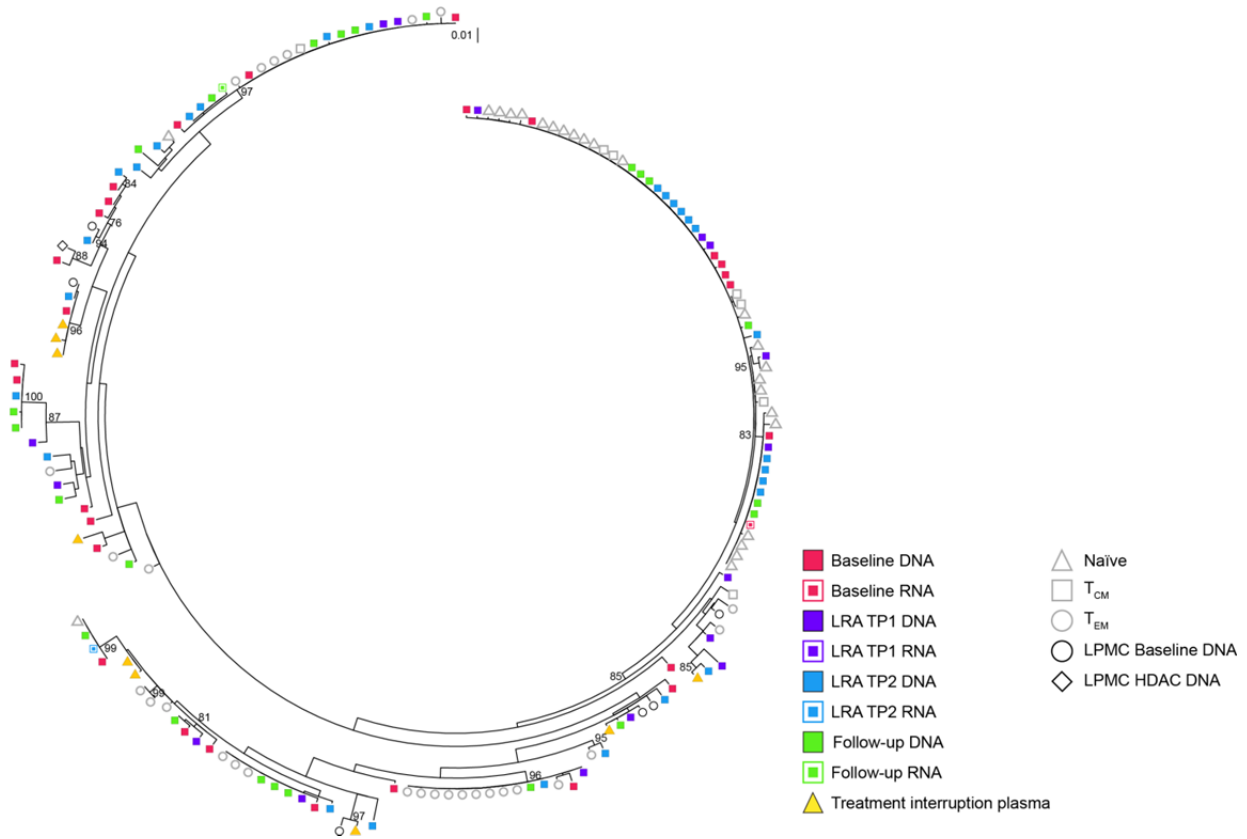
70

71 **Supplementary Figure 7** Panobinostat participant 7 phylogenetic tree. Maximum-
72 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
73 genome sequencing on isolated CD4+ T cells for participant 7 from the panobinostat
74 trial. The phylogenetic analysis and tree construction were conducted using MEGA-CC.
75 Defective sequences (hypermutants or containing stop codons) were excluded from the
76 phylogenetic tree analysis. The plasma sample was collected approximately 1 year prior
77 to initiation of anti-retroviral therapy. Peripheral blood samples were collected at
78 baseline, 2 hours after the first dose of panobinostat (TP1), 28 days after the first dose
79 of panobinostat (TP2), and 38 days after the final panobinostat dose. Intestinal lamina
80 propria mononuclear cells were collected at baseline (1 week prior to the first
81 panobinostat dose) and during week 4 of the panobinostat trial.



82

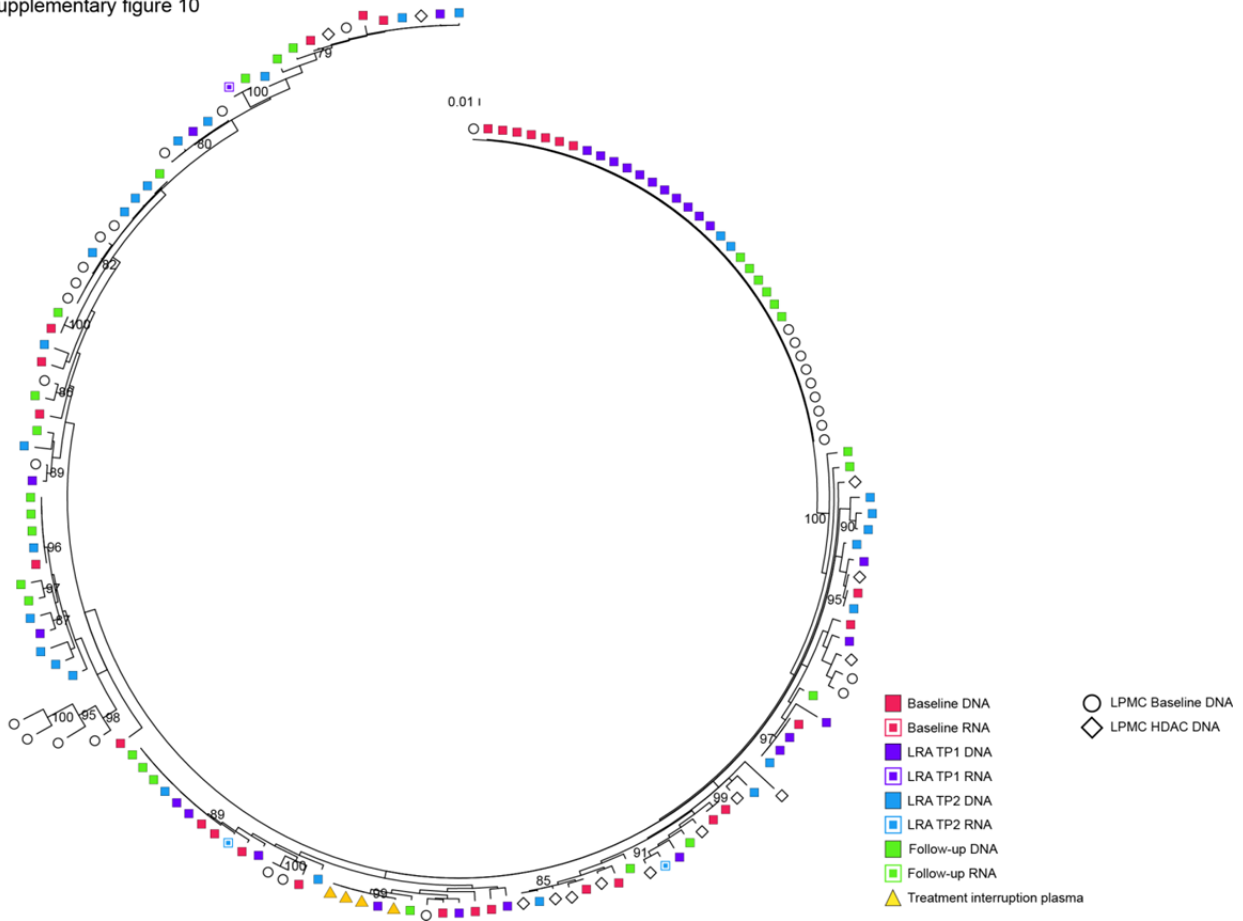
83 **Supplementary Figure 8** Panobinostat participant 8 phylogenetic tree. Maximum-
 84 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
 85 genome sequencing on isolated CD4+ T cells for participant 8 from the panobinostat
 86 trial. The phylogenetic analysis and tree construction were conducted using MEGA-CC.
 87 Defective sequences (hypermutants or containing stop codons) were excluded from the
 88 phylogenetic tree analysis. The plasma sample was collected 14 days following the
 89 analytical treatment interruption. Peripheral blood samples were collected at baseline, 2
 90 hours after the first dose of panobinostat (TP1), 32 days after the first dose of
 91 panobinostat (TP2), and 38 days after the final panobinostat dose. Cell subsets were
 92 sorted from peripheral blood samples collected 38 days after the final panobinostat
 93 dose.



94

95 **Supplementary Figure 9** Panobinostat participant 9 phylogenetic tree. Maximum-
 96 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
 97 genome sequencing on isolated CD4+ T cells for participant 9 from the panobinostat
 98 trial. The phylogenetic analysis and tree construction were conducted using MEGA-CC.
 99 Defective sequences (hypermutants or containing stop codons) were excluded from the
 100 phylogenetic tree analysis. The plasma sample was collected 24 days following the
 101 analytical treatment interruption. Peripheral blood samples were collected at baseline,
 102 14 days after the first dose of panobinostat (TP1), 28 days after the first dose of
 103 panobinostat (TP2), and 38 days after the final panobinostat dose. Intestinal lamina
 104 propria mononuclear cells were collected at baseline (1 week prior to the first
 105 panobinostat dose) and during week 4 of the panobinostat trial. Cell subsets were
 106 sorted from peripheral blood samples collected 38 days after the final panobinostat
 107 dose.

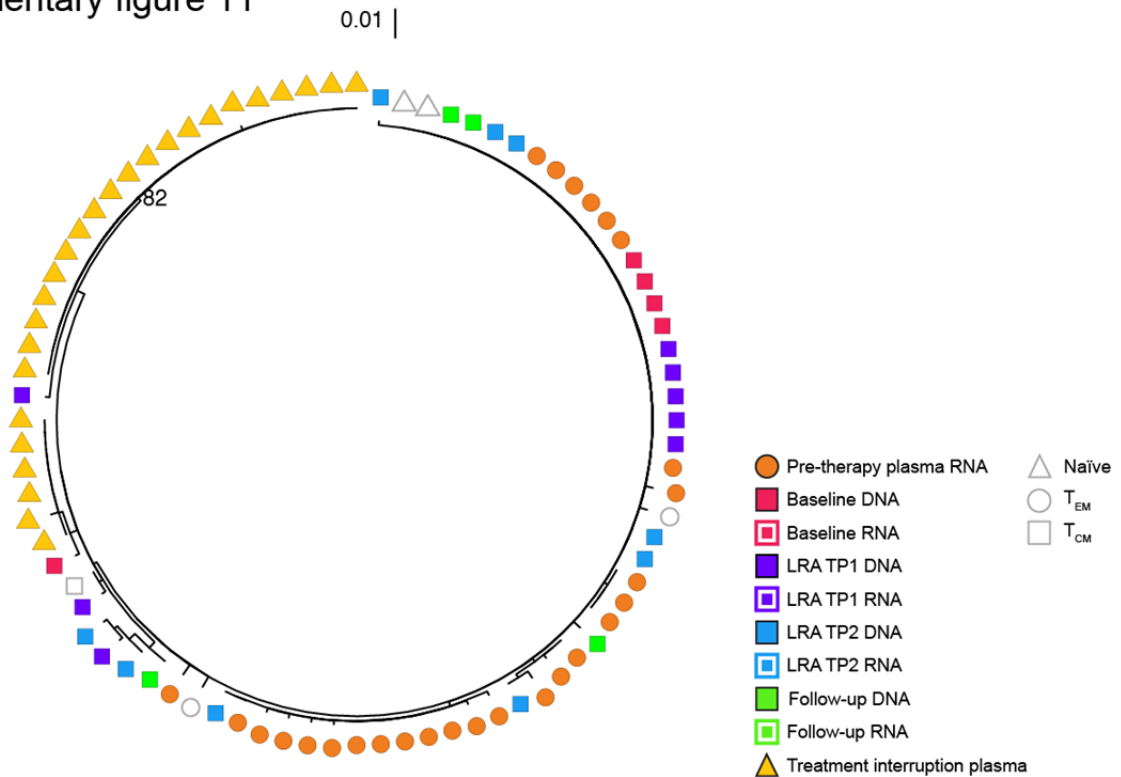
Supplementary figure 10



108

109 **Supplementary Figure 10** Panobinostat participant 10 phylogenetic tree. Maximum-
110 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
111 genome sequencing on isolated CD4+ T cells for participant 10 from the panobinostat
112 trial. The phylogenetic analysis and tree construction were conducted using MEGA-CC.
113 Defective sequences (hypermutants or containing stop codons) were excluded from the
114 phylogenetic tree analysis. The plasma sample was collected 145 days following the
115 analytical treatment interruption. Peripheral blood samples were collected at baseline, 1
116 day after the first dose of panobinostat (TP1), 28 days after the first dose of
117 panobinostat (TP2), and 38 days after the final panobinostat dose. Intestinal lamina
118 propria mononuclear cells were collected at baseline (1 week prior to the first
119 panobinostat dose) and during week 4 of the panobinostat trial.

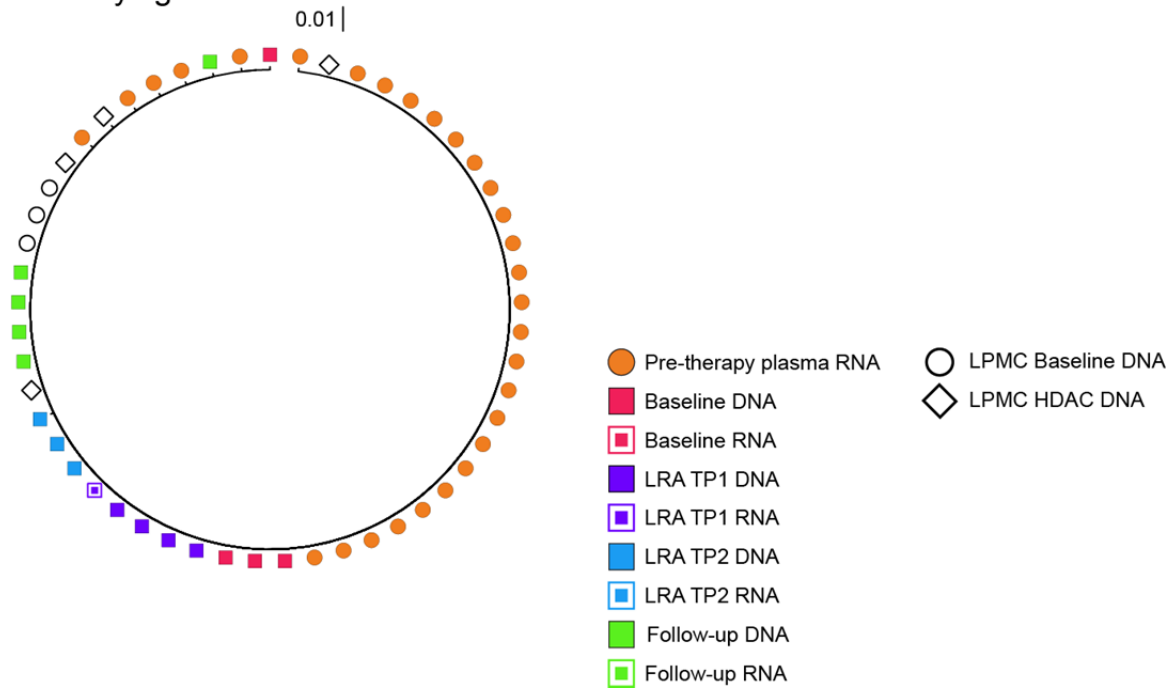
Supplementary figure 11



120

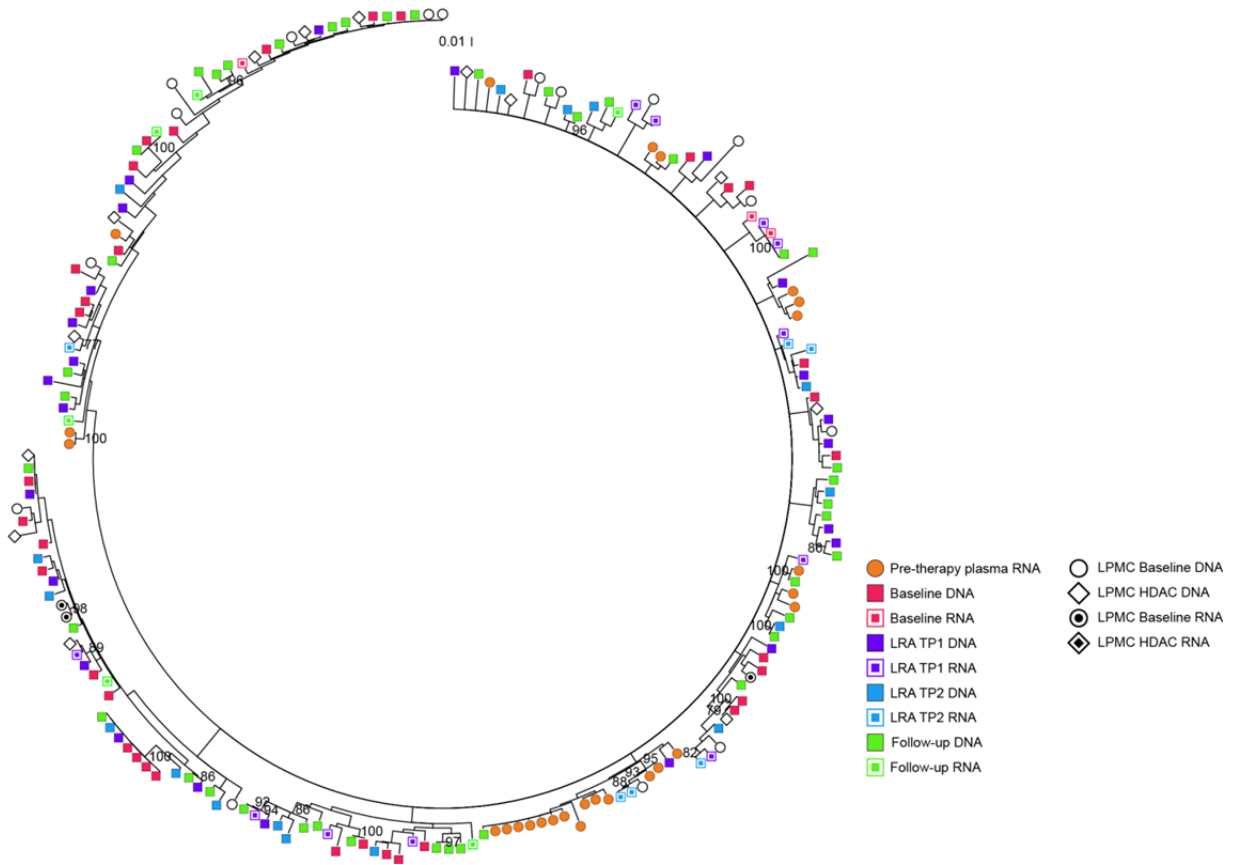
121 **Supplementary Figure 11** Panobinostat participant 12 phylogenetic tree. Maximum-
 122 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
 123 genome sequencing on isolated CD4+ T cells for participant 12 from the panobinostat
 124 trial. The phylogenetic analysis and tree construction were conducted using MEGA-CC.
 125 Defective sequences (hypermutants or containing stop codons) were excluded from the
 126 phylogenetic tree analysis. The plasma samples were collected approximately 1 year
 127 and 2 months prior to initiation of anti-retroviral therapy and 17 days following the
 128 analytical treatment interruption. Peripheral blood samples were collected at baseline,
 129 28 days after the first dose of panobinostat (TP1), 46 days after the first dose of
 130 panobinostat (TP2), and 38 days after the final panobinostat dose. Cell subsets were
 131 sorted from peripheral blood samples collected 38 days after the final panobinostat
 132 dose.

Supplementary figure 12



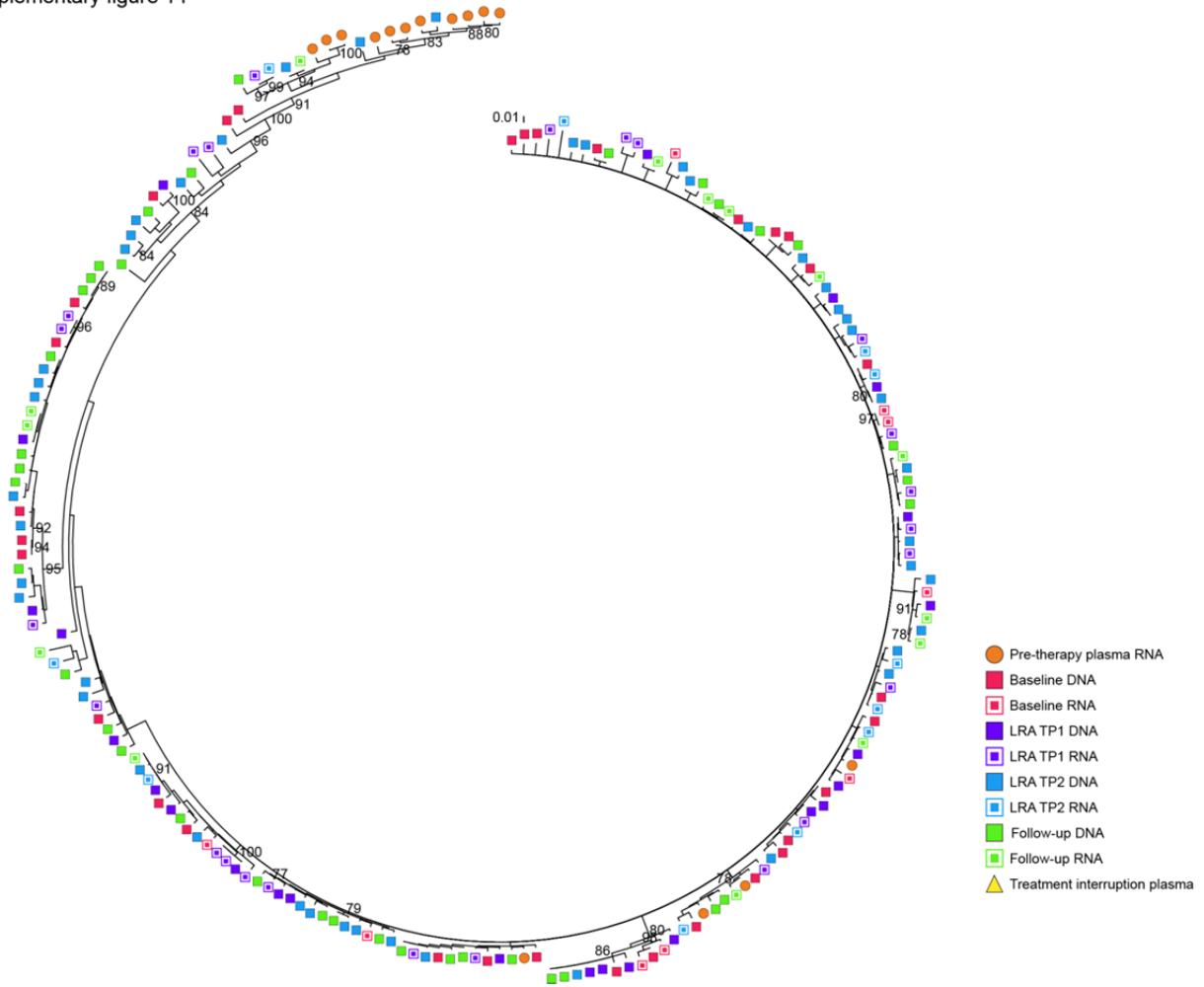
133

134 **Supplementary Figure 12** Panobinostat participant 14 phylogenetic tree. Maximum-
135 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
136 genome sequencing on isolated CD4+ T cells for participant 14 from the panobinostat
137 trial. The phylogenetic analysis and tree construction were conducted using MEGA-CC.
138 Defective sequences (hypermutants or containing stop codons) were excluded from the
139 phylogenetic tree analysis. The plasma samples was collected 2 days prior to initiation
140 of anti-retroviral therapy. Peripheral blood samples were collected at baseline, 9 days
141 after the first dose of panobinostat (TP1), 18 days after the first dose of panobinostat
142 (TP2), and 38 days after the final panobinostat dose. Intestinal lamina propria
143 mononuclear cells were collected at baseline (1 week prior to the first panobinostat
144 dose) and during week 4 of the panobinostat trial.



145

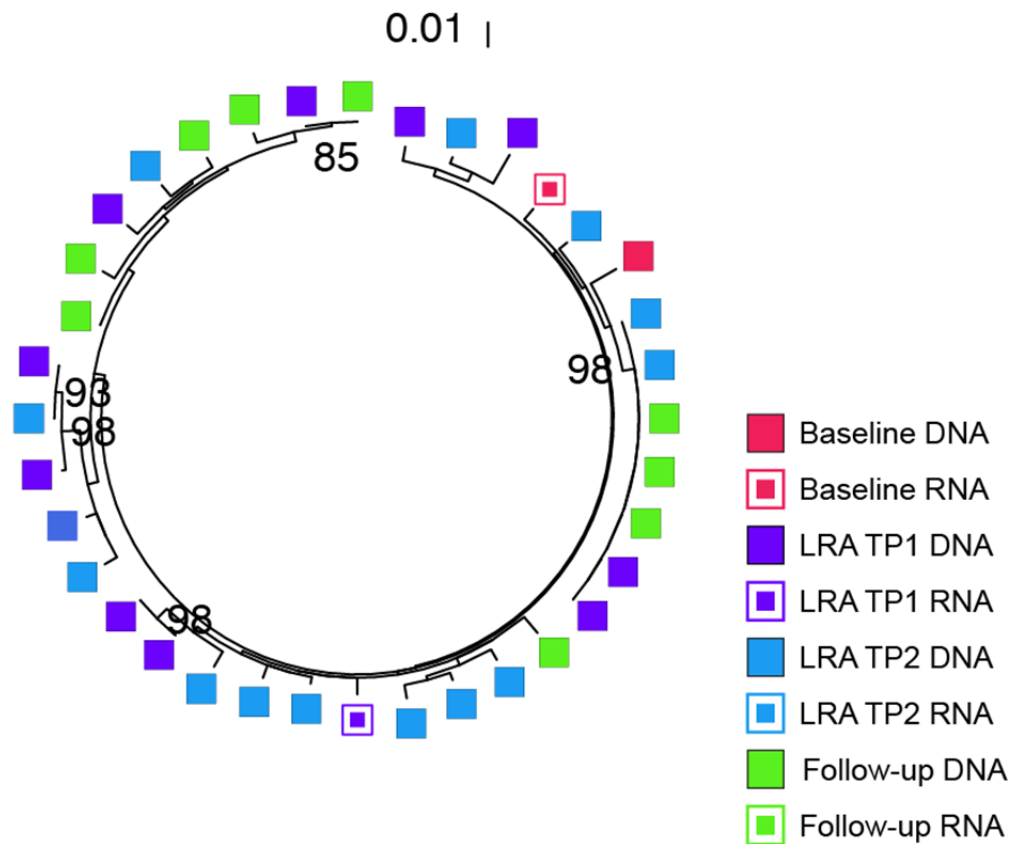
146 **Supplementary Figure 13** Panobinostat participant 15 phylogenetic tree. Maximum-
 147 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
 148 genome sequencing on isolated CD4+ T cells for participant 15 from the panobinostat
 149 trial. The phylogenetic analysis and tree construction were conducted using MEGA-CC.
 150 Defective sequences (hypermutants or containing stop codons) were excluded from the
 151 phylogenetic tree analysis. The plasma sample was collected approximately 2 years
 152 and 1 month prior to initiation of anti-retroviral therapy. Peripheral blood samples were
 153 collected at baseline, 32 days after the first dose of panobinostat (TP1), 46 days after
 154 the first dose of panobinostat (TP2), and 38 days after the final panobinostat dose.
 155 Intestinal lamina propria mononuclear cells were collected at baseline (1 week prior to
 156 the first panobinostat dose) and during week 4 of the panobinostat trial.



157

158 **Supplementary Figure 14** Panobinostat participant 19 phylogenetic tree. Maximum-
 159 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
 160 genome sequencing on isolated CD4+ T cells for participant 19 from the panobinostat
 161 trial. The phylogenetic analysis and tree construction were conducted using MEGA-CC.
 162 Defective sequences (hypermutants or containing stop codons) were excluded from the
 163 phylogenetic tree analysis. The plasma sample was collected approximately 9 months
 164 prior to initiation of anti-retroviral therapy. Peripheral blood samples were collected at
 165 baseline, 23 days after the first dose of panobinostat (TP1), 32 days after the first dose
 166 of panobinostat (TP2), and 38 days after the final panobinostat dose.

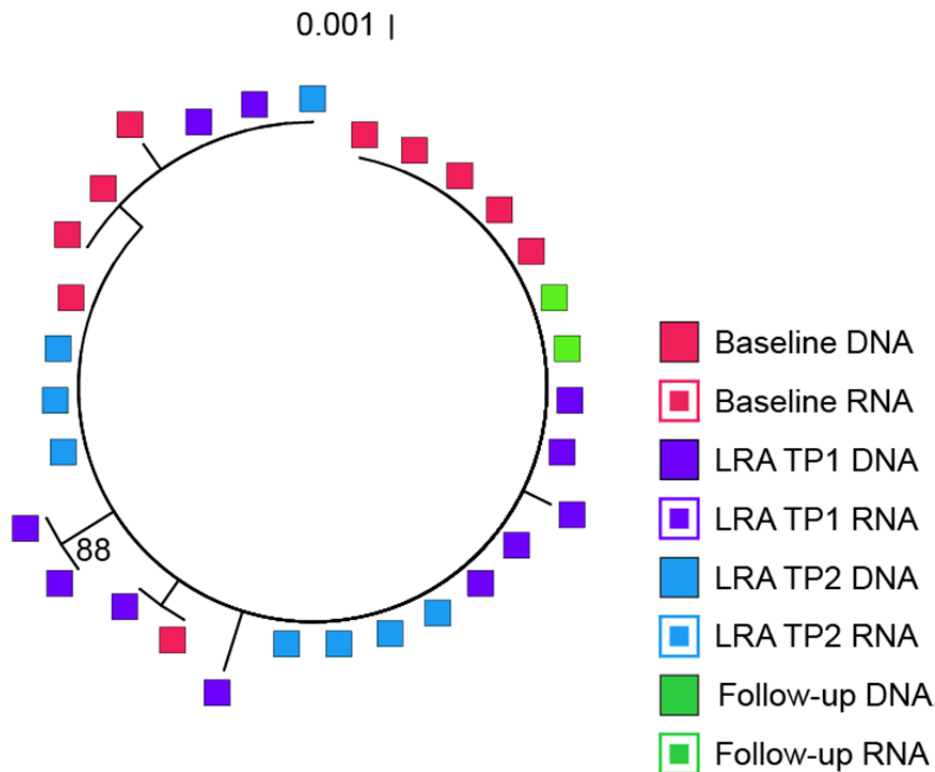
Supplementary figure 15



167

168 **Supplementary Figure 15** Vorinostat participant VOR001 phylogenetic tree. Maximum-
169 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
170 genome sequencing on isolated CD4+ T cells for participant VOR001 from the
171 vorinostat trial. The phylogenetic analysis and tree construction were conducted using
172 MEGA-CC. Defective sequences (hypermutants or containing stop codons) were
173 excluded from the phylogenetic tree analysis. Peripheral blood samples were collected
174 at baseline, 8 hours after the first dose of vorinostat (TP1), 14 days after the first dose of
175 vorinostat (TP2), and 7 days after the final vorinostat dose.

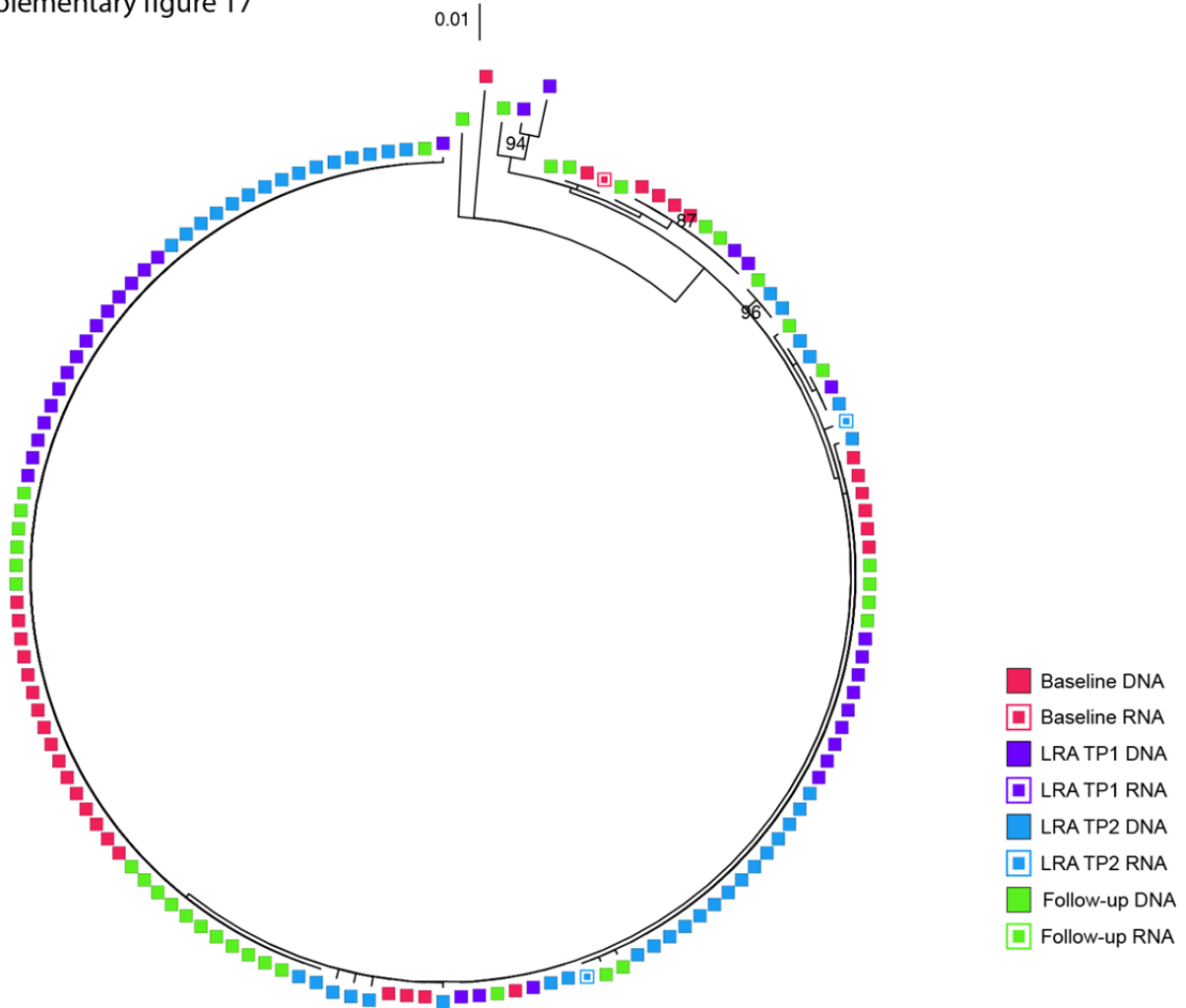
Supplementary figure 16



176

177 **Supplementary Figure 16** Vorinostat participant VOR002 phylogenetic tree. Maximum-
178 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
179 genome sequencing on isolated CD4+ T cells for participant VOR002 from the
180 vorinostat trial. The phylogenetic analysis and tree construction were conducted using
181 MEGA-CC. Defective sequences (hypermutants or containing stop codons) were
182 excluded from the phylogenetic tree analysis. Peripheral blood samples were collected
183 at baseline, 24 hours after the first dose of vorinostat (TP1), 7 days after the first dose of
184 vorinostat (TP2), and 7 days after the final vorinostat dose.

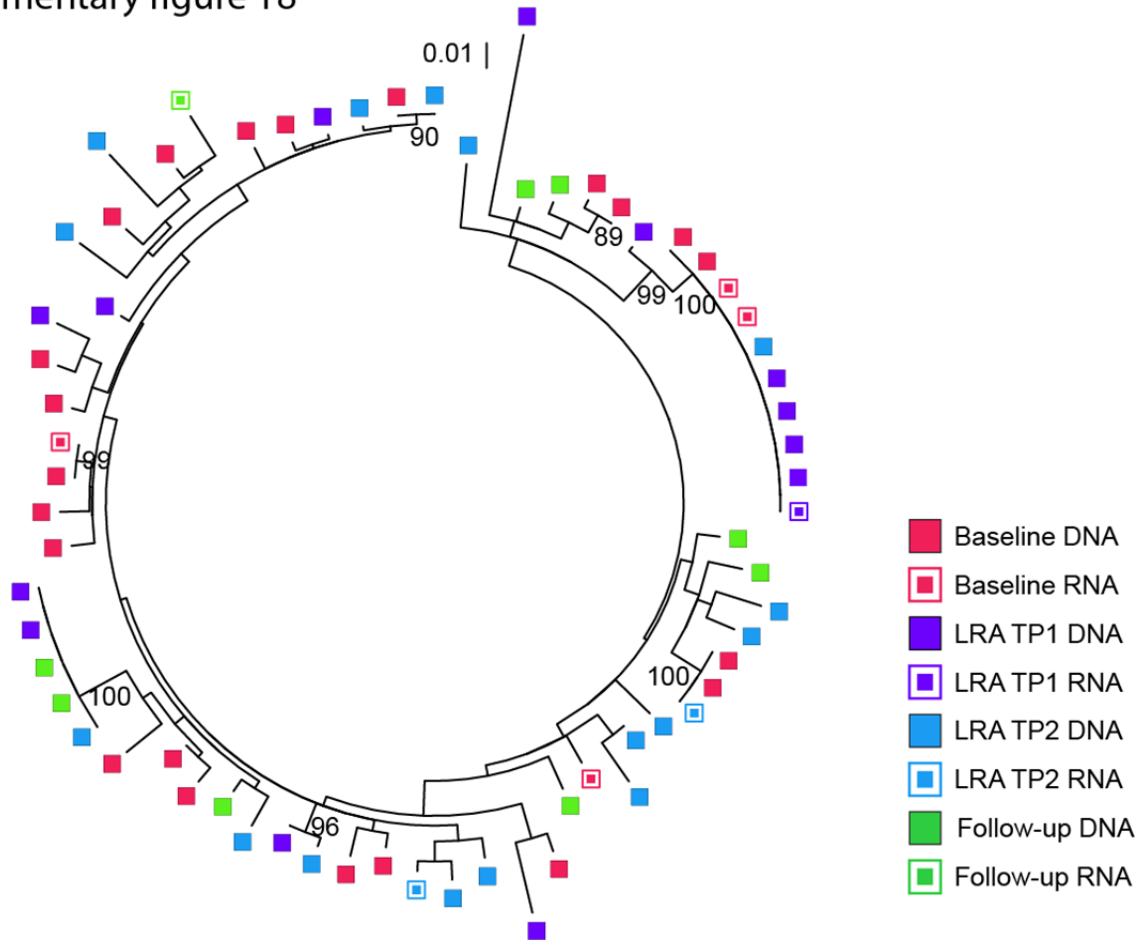
Supplementary figure 17



185

186 **Supplementary Figure 17** Vorinostat participant VOR003 phylogenetic tree. Maximum-
187 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
188 genome sequencing on isolated CD4+ T cells for participant VOR003 from the
189 vorinostat trial. The phylogenetic analysis and tree construction were conducted using
190 MEGA-CC. Defective sequences (hypermutants or containing stop codons) were
191 excluded from the phylogenetic tree analysis. Peripheral blood samples were collected
192 at baseline, 2 hours after the first dose of vorinostat (TP1), 24 hours after the first dose
193 of vorinostat (TP2), and 7 days after the final vorinostat dose.

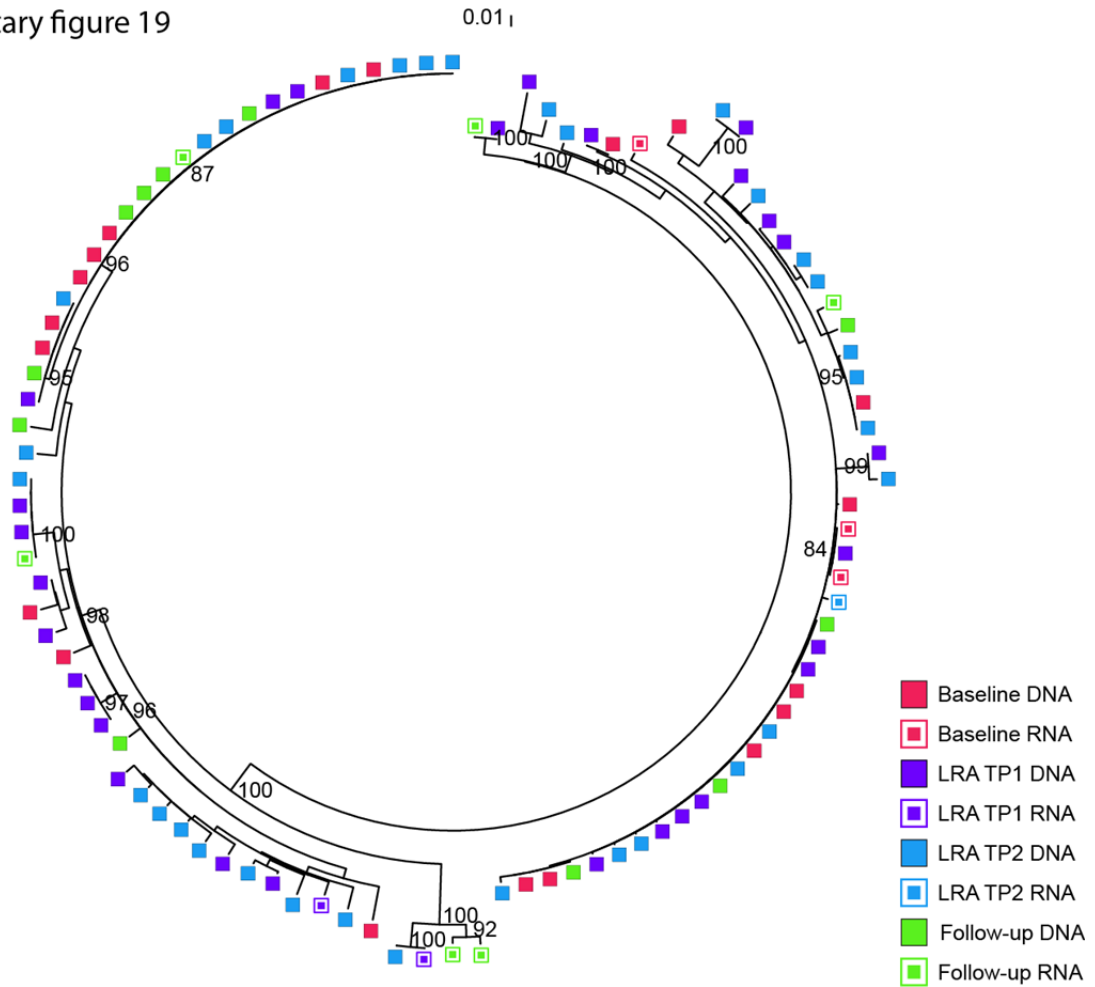
Supplementary figure 18



194

195 **Supplementary Figure 18** Vorinostat participant VOR006 phylogenetic tree. Maximum-
196 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
197 genome sequencing on isolated CD4+ T cells for participant VOR006 from the
198 vorinostat trial. The phylogenetic analysis and tree construction were conducted using
199 MEGA-CC. Defective sequences (hypermutants or containing stop codons) were
200 excluded from the phylogenetic tree analysis. Peripheral blood samples were collected
201 at baseline, 7 days after the first dose of vorinostat (TP1), 14 days after the first dose of
202 vorinostat (TP2), and 7 days after the final vorinostat dose.

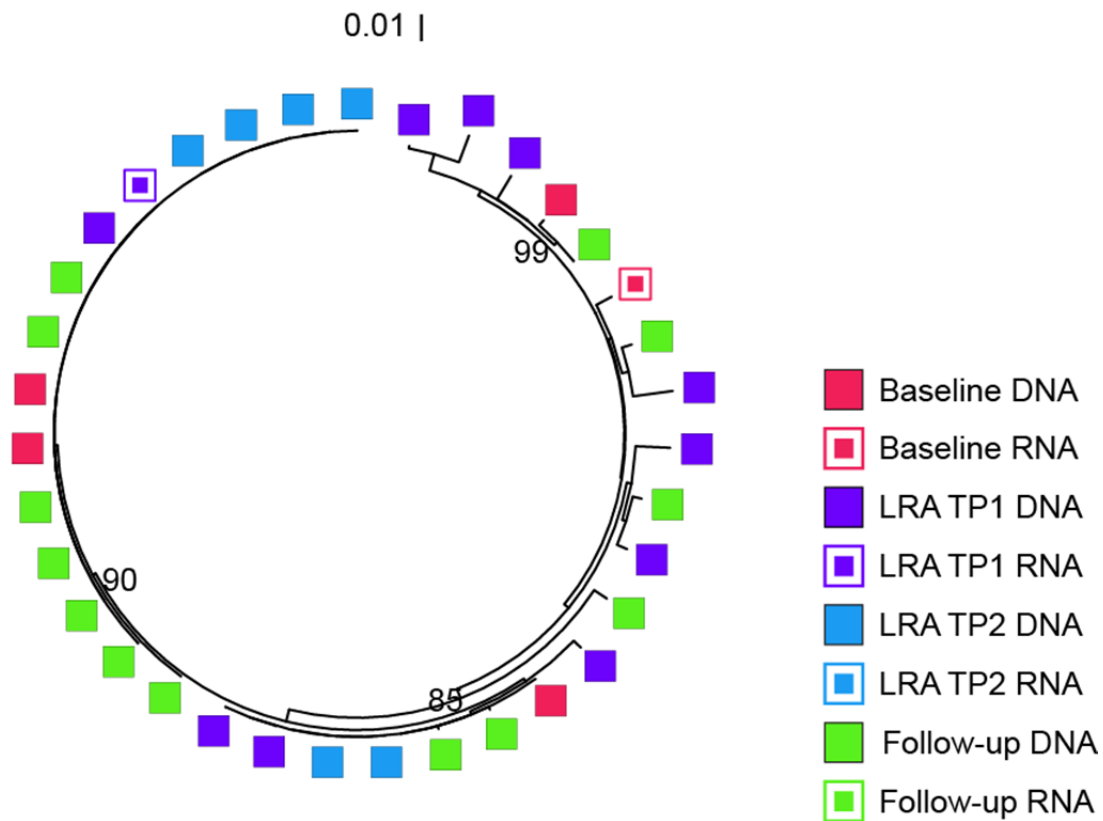
Supplementary figure 19



203

204 **Supplementary Figure 19** Vorinostat participant VOR009 phylogenetic tree. Maximum-
205 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
206 genome sequencing on isolated CD4+ T cells for participant VOR009 from the
207 vorinostat trial. The phylogenetic analysis and tree construction were conducted using
208 MEGA-CC. Defective sequences (hypermutants or containing stop codons) were
209 excluded from the phylogenetic tree analysis. Peripheral blood samples were collected
210 at baseline, 24 hours after the first dose of vorinostat (TP1), 7 days after the first dose of
211 vorinostat (TP2), and 7 days after the final vorinostat dose.

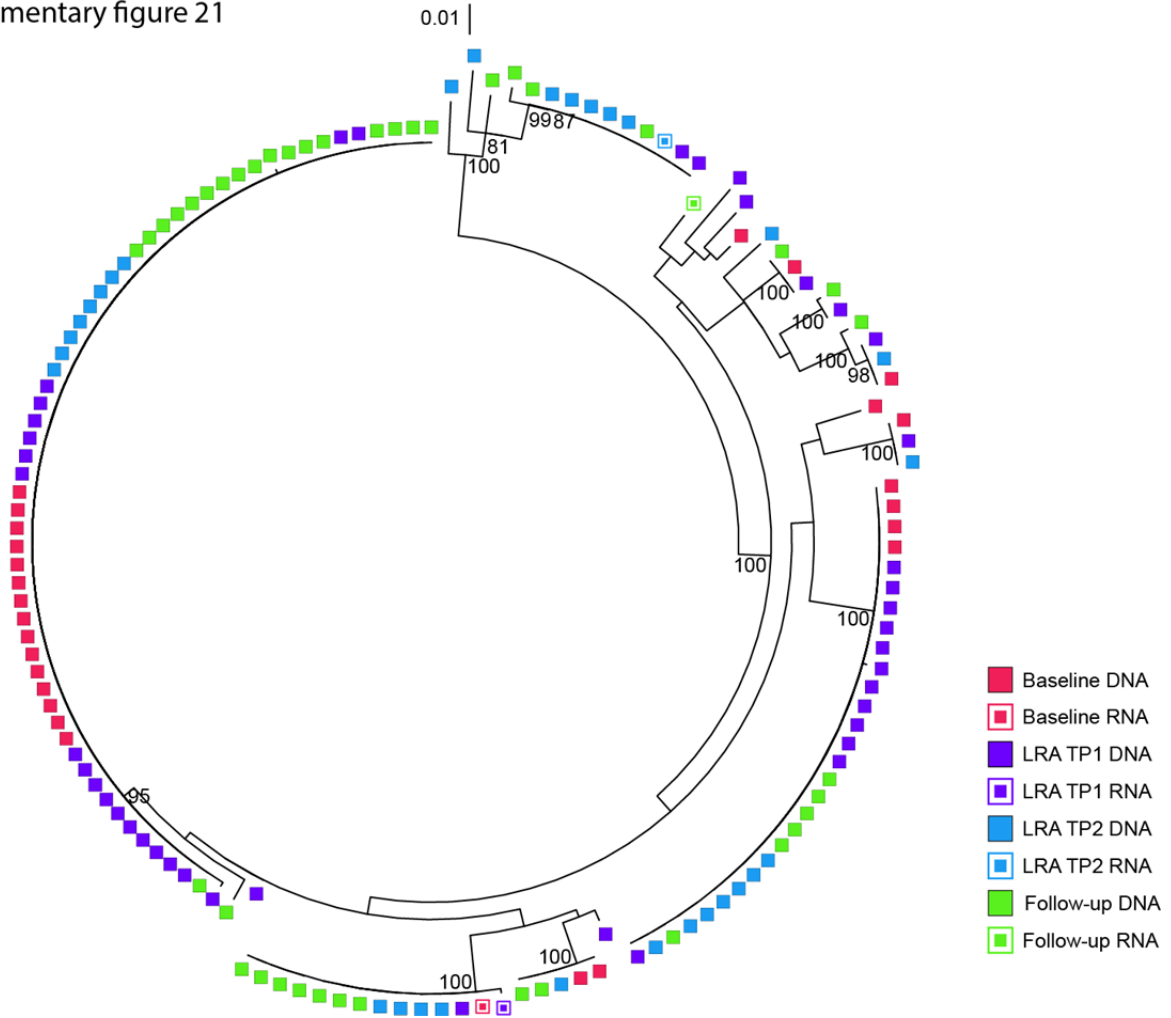
Supplementary figure 20



212

213 **Supplementary Figure 20** Vorinostat participant VOR011 phylogenetic tree. Maximum-
214 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
215 genome sequencing on isolated CD4+ T cells for participant VOR011 from the
216 vorinostat trial. The phylogenetic analysis and tree construction were conducted using
217 MEGA-CC. Defective sequences (hypermutants or containing stop codons) were
218 excluded from the phylogenetic tree analysis. Peripheral blood samples were collected
219 at baseline, 8 hours after the first dose of vorinostat (TP1), 14 days after the first dose of
220 vorinostat (TP2), and 7 days after the final vorinostat dose.

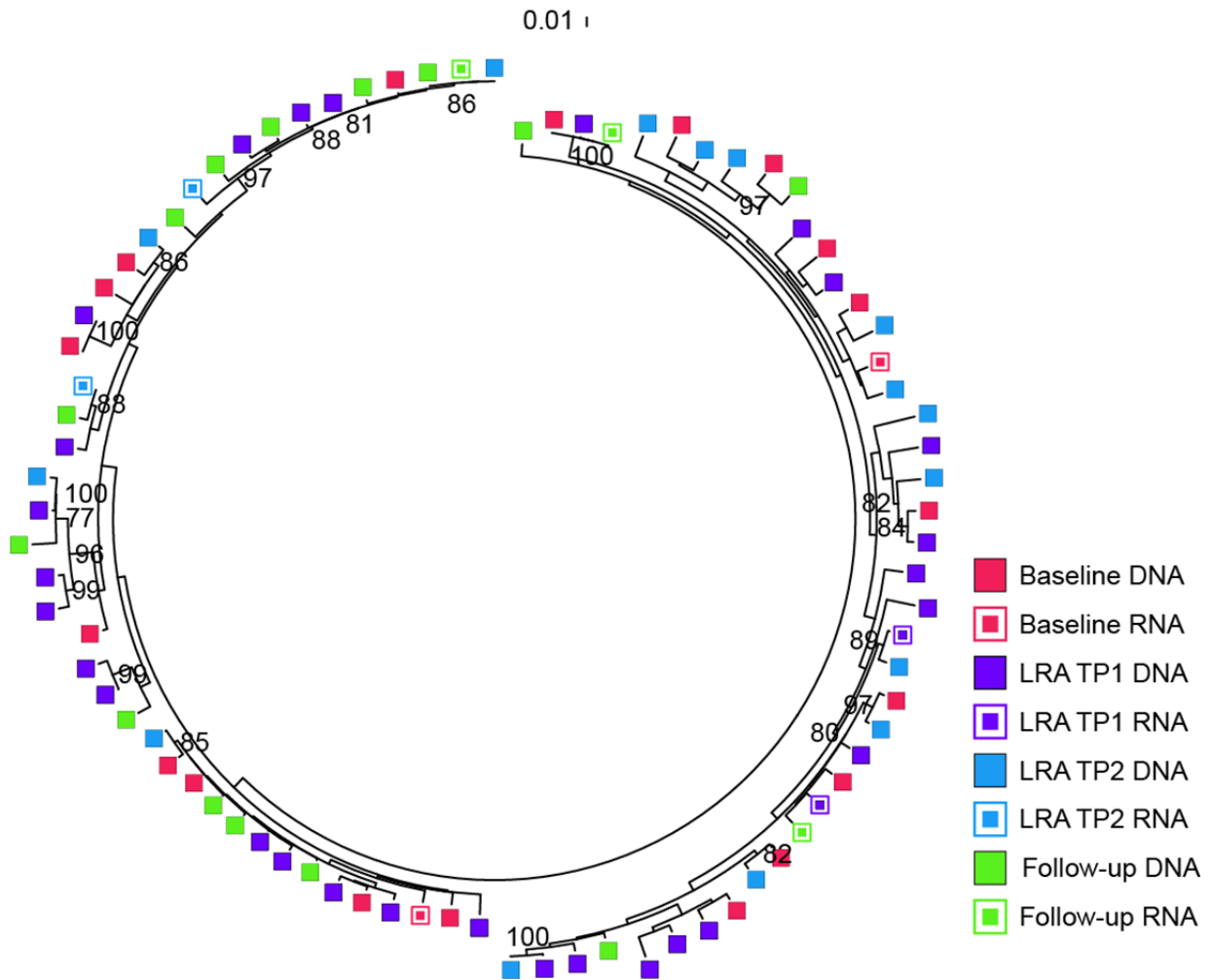
Supplementary figure 21



221

222 **Supplementary Figure 21** Vorinostat participant VOR013 phylogenetic tree. Maximum-
223 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
224 genome sequencing on isolated CD4+ T cells for participant VOR013 from the
225 vorinostat trial. The phylogenetic analysis and tree construction were conducted using
226 MEGA-CC. Defective sequences (hypermutants or containing stop codons) were
227 excluded from the phylogenetic tree analysis. Peripheral blood samples were collected
228 at baseline, 24 hours after the first dose of vorinostat (TP1), 7 days after the first dose of
229 vorinostat (TP2), and 7 days after the final vorinostat dose.

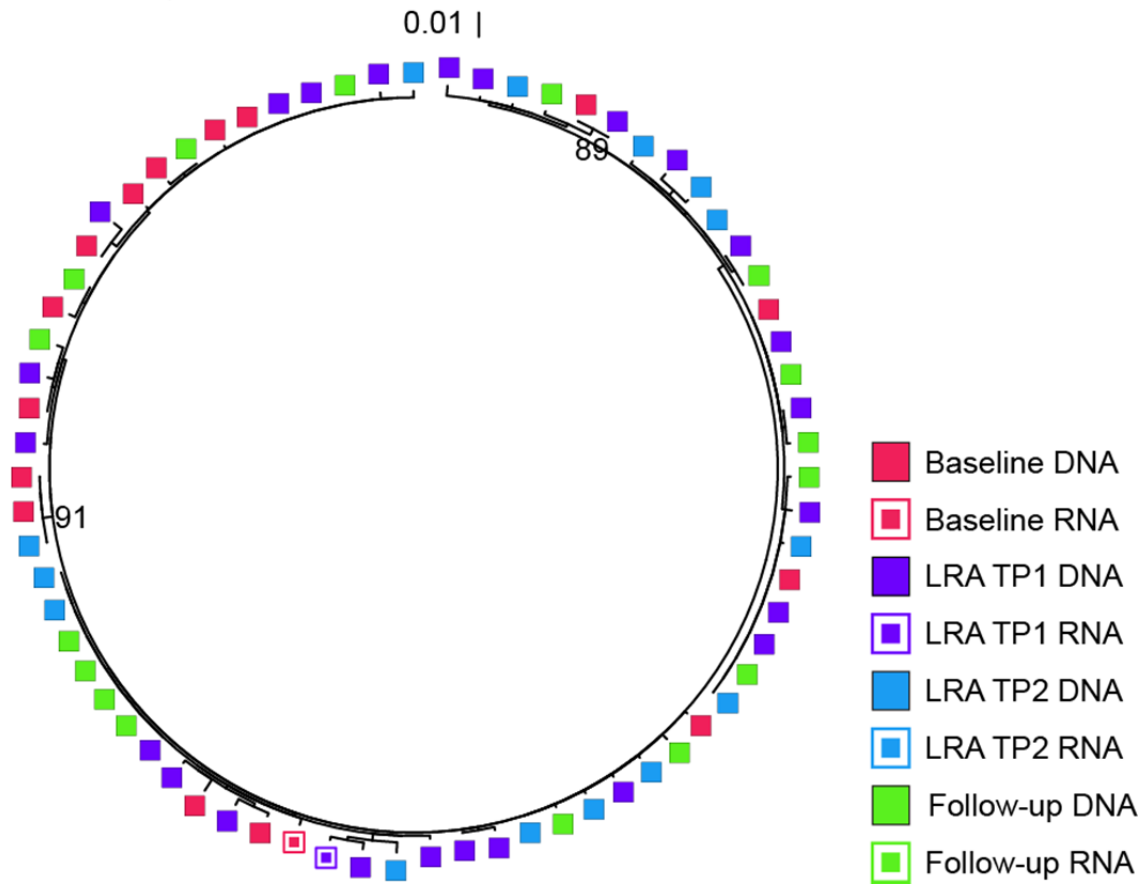
Supplementary figure 22



230

231 **Supplementary Figure 22** Vorinostat participant VOR014 phylogenetic tree. Maximum-
 232 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
 233 genome sequencing on isolated CD4+ T cells for participant VOR014 from the
 234 vorinostat trial. The phylogenetic analysis and tree construction were conducted using
 235 MEGA-CC. Defective sequences (hypermutants or containing stop codons) were
 236 excluded from the phylogenetic tree analysis. Peripheral blood samples were collected
 237 at baseline, 24 hours after the first dose of vorinostat (TP1), 7 days after the first dose of
 238 vorinostat (TP2), and 7 days after the final vorinostat dose.

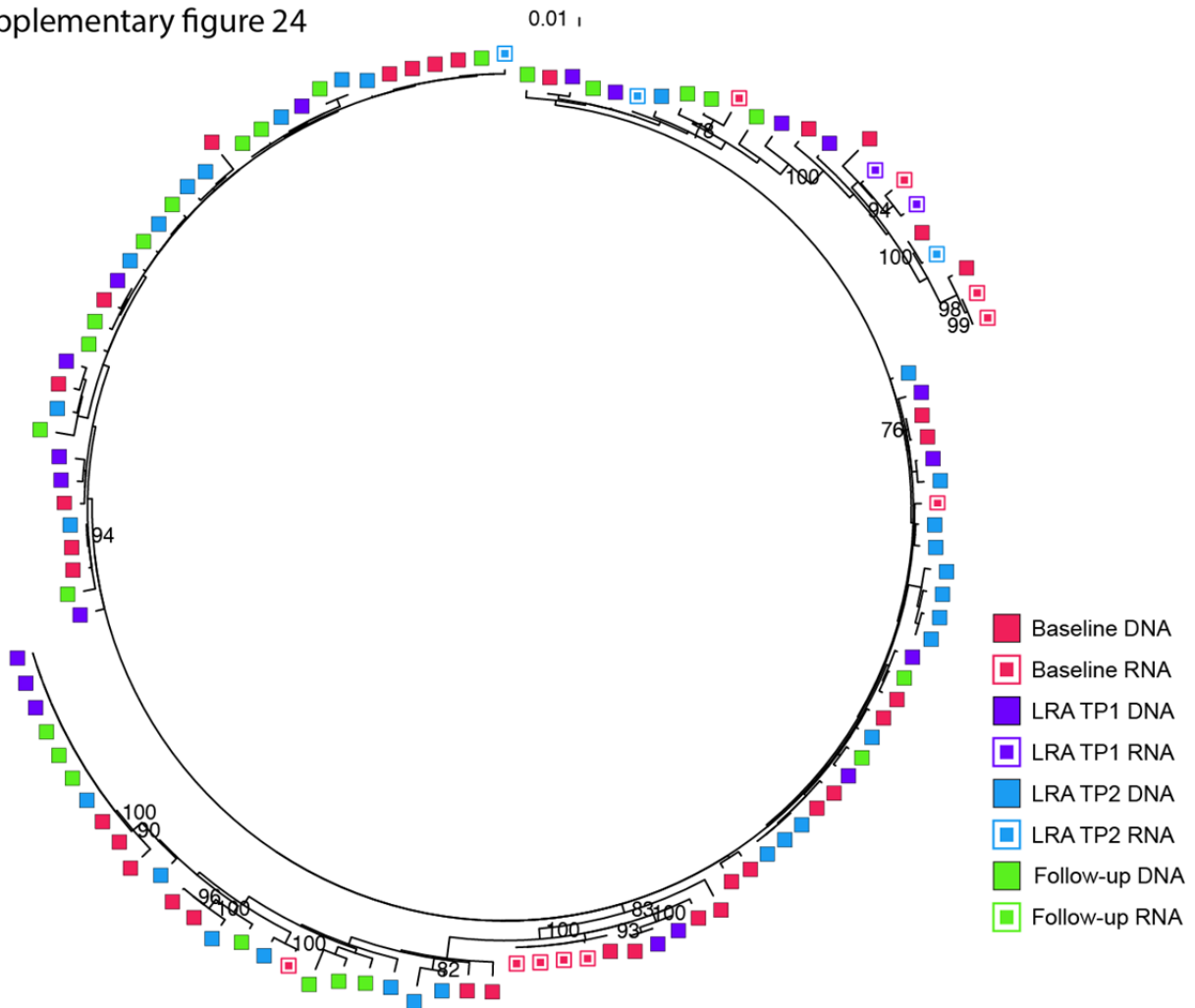
Supplementary figure 23



239

240 **Supplementary Figure 23** Vorinostat participant VOR015 phylogenetic tree. Maximum-
241 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
242 genome sequencing on isolated CD4+ T cells for participant VOR015 from the
243 vorinostat trial. The phylogenetic analysis and tree construction were conducted using
244 MEGA-CC. Defective sequences (hypermutants or containing stop codons) were
245 excluded from the phylogenetic tree analysis. Peripheral blood samples were collected
246 at baseline, 24 hours after the first dose of vorinostat (TP1), 7 days after the first dose of
247 vorinostat (TP2), and 7 days after the final vorinostat dose.

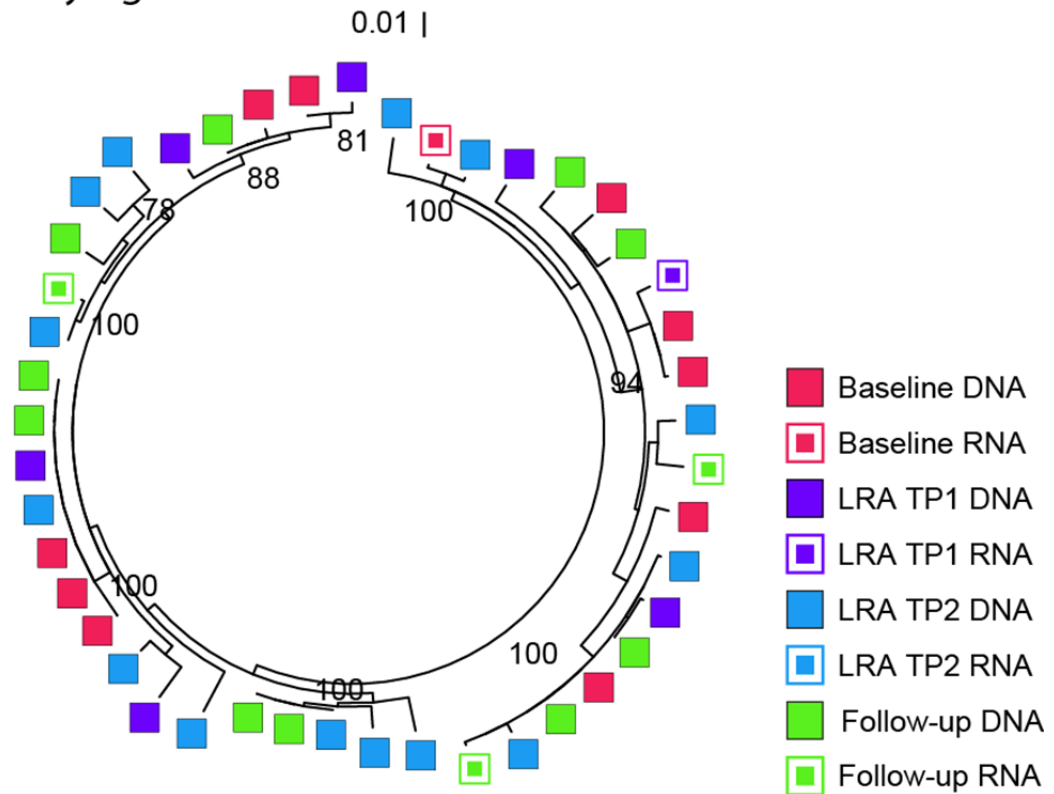
Supplementary figure 24



248

249 **Supplementary Figure 24** Vorinostat participant VOR018 phylogenetic tree. Maximum-
250 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
251 genome sequencing on isolated CD4+ T cells for participant VOR018 from the
252 vorinostat trial. The phylogenetic analysis and tree construction were conducted using
253 MEGA-CC. Defective sequences (hypermutants or containing stop codons) were
254 excluded from the phylogenetic tree analysis. Peripheral blood samples were collected
255 at baseline, 8 hours after the first dose of vorinostat (TP1), 14 days after the first dose of
256 vorinostat (TP2), and 7 days after the final vorinostat dose.

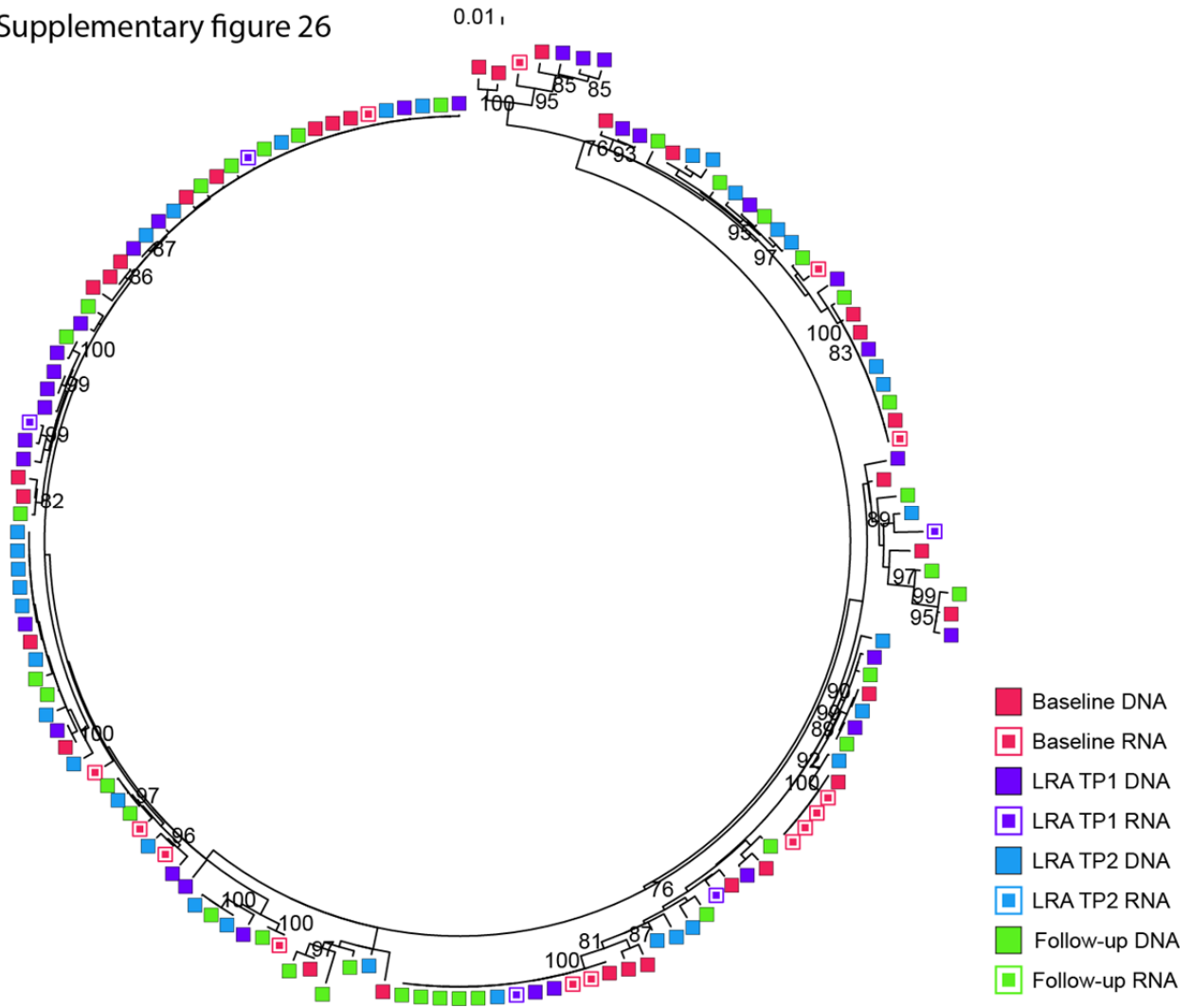
Supplementary figure 25



257

258 **Supplementary Figure 25** Vorinostat participant VOR019 phylogenetic tree. Maximum-
259 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
260 genome sequencing on isolated CD4+ T cells for participant VOR019 from the
261 vorinostat trial. The phylogenetic analysis and tree construction were conducted using
262 MEGA-CC. Defective sequences (hypermutants or containing stop codons) were
263 excluded from the phylogenetic tree analysis. Peripheral blood samples were collected
264 at baseline, 24 hours after the first dose of vorinostat (TP1), 14 days after the first dose
265 of vorinostat (TP2), and 7 days after the final vorinostat dose.

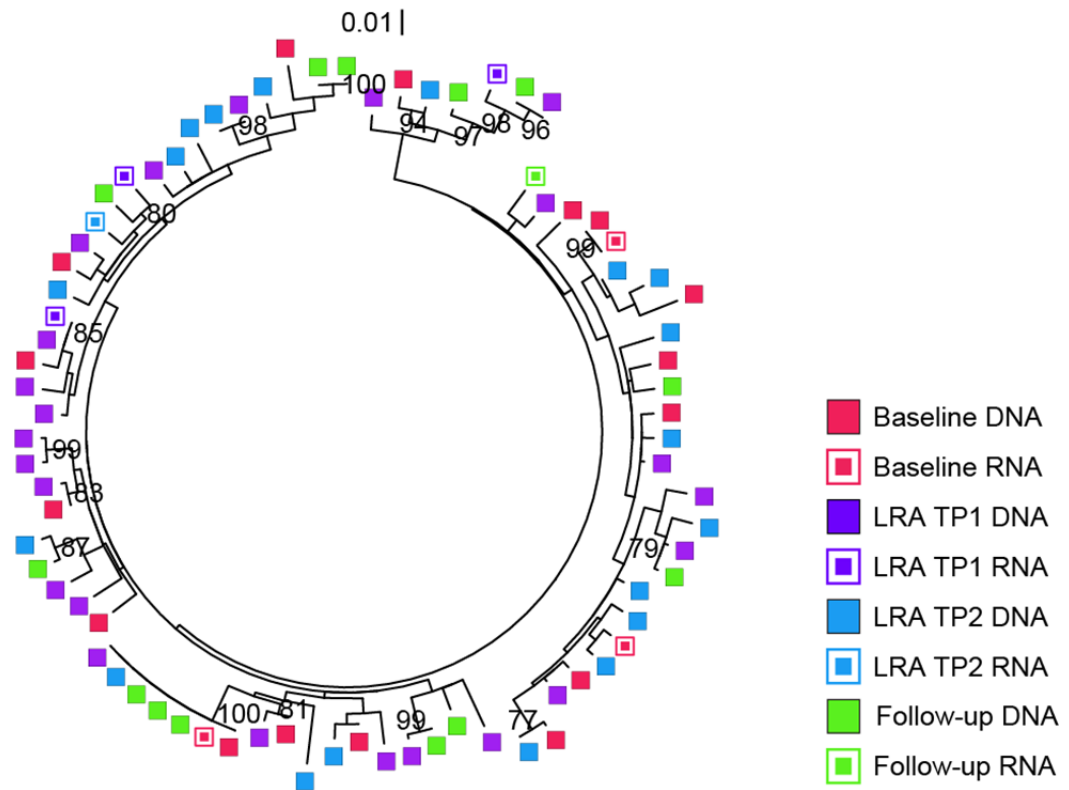
Supplementary figure 26



266

267 **Supplementary Figure 26** Vorinostat participant VOR020 phylogenetic tree. Maximum-
268 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
269 genome sequencing on isolated CD4+ T cells for participant VOR020 from the
270 vorinostat trial. The phylogenetic analysis and tree construction were conducted using
271 MEGA-CC. Defective sequences (hypermutants or containing stop codons) were
272 excluded from the phylogenetic tree analysis. Peripheral blood samples were collected
273 at baseline, 24 hours after the first dose of vorinostat (TP1), 7 days after the first dose of
274 vorinostat (TP2), and 7 days after the final vorinostat dose.

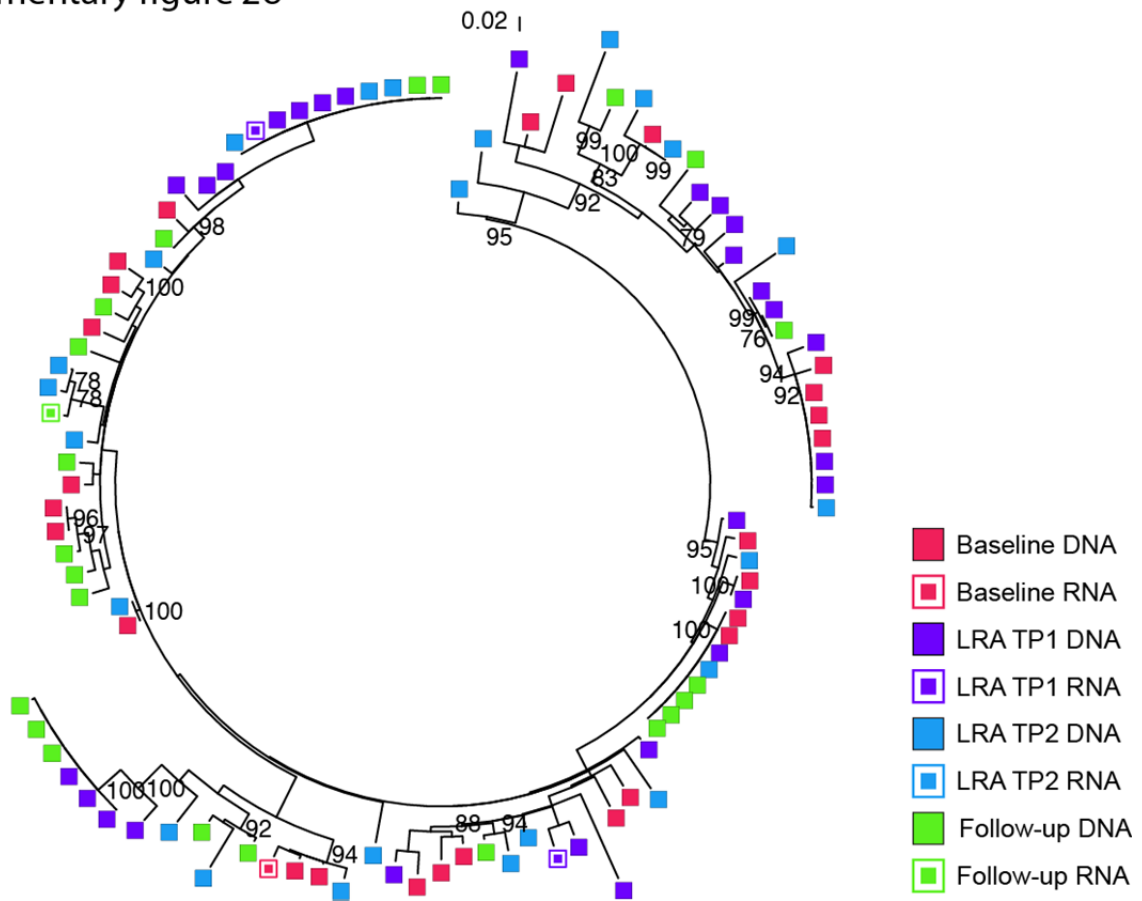
Supplementary figure 27



275

276 **Supplementary Figure 27** Vorinostat participant VOR022 phylogenetic tree. Maximum-
277 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
278 genome sequencing on isolated CD4+ T cells for participant VOR022 from the
279 vorinostat trial. The phylogenetic analysis and tree construction were conducted using
280 MEGA-CC. Defective sequences (hypermutants or containing stop codons) were
281 excluded from the phylogenetic tree analysis. Peripheral blood samples were collected
282 at baseline, 2 hours after the first dose of vorinostat (TP1), 7 days after the first dose of
283 vorinostat (TP2), and 7 days after the final vorinostat dose.

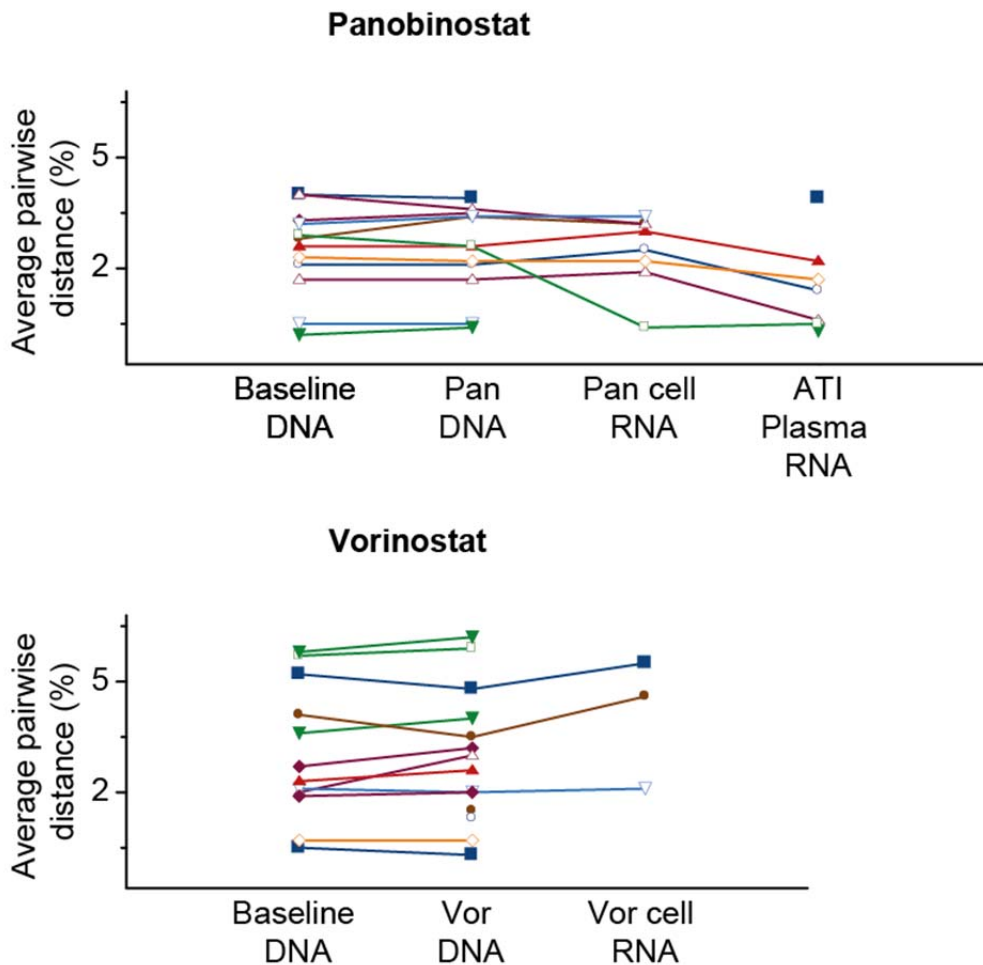
Supplementary figure 28



284

285 **Supplementary Figure 28** Vorinostat participant VOR023 phylogenetic tree. Maximum-
286 likelihood tree of the V1-V3 region of HIV-1 *env* sequences obtained using single-
287 genome sequencing on isolated CD4+ T cells for participant VOR023 from the
288 vorinostat trial. The phylogenetic analysis and tree construction were conducted using
289 MEGA-CC. Defective sequences (hypermutants or containing stop codons) were
290 excluded from the phylogenetic tree analysis. Peripheral blood samples were collected
291 at baseline, 7 days after the first dose of vorinostat (TP1), 14 days after the first dose of
292 vorinostat (TP2), and 7 days after the final vorinostat dose.

Supplementary figure 29



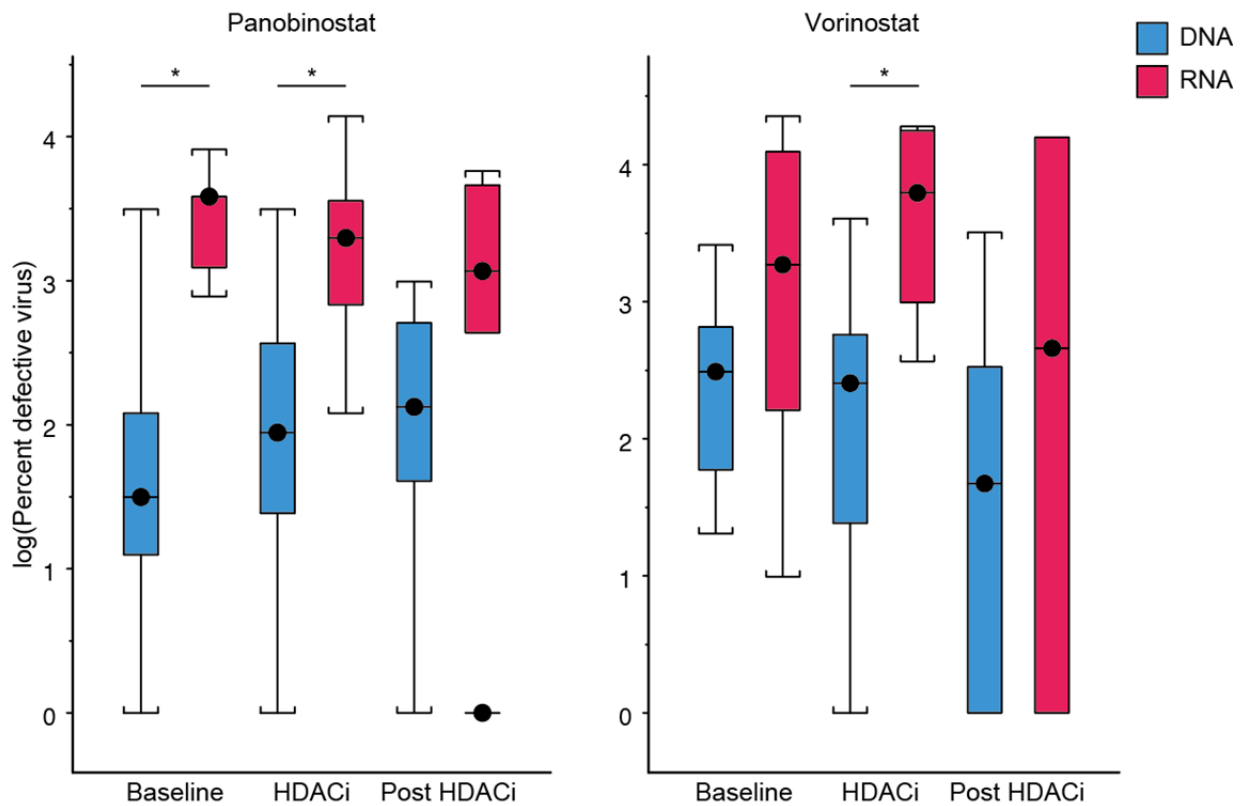
293

294 **Supplementary Figure 29** Linear mixed effects model of the average pairwise
 295 distance. A linear mixed effect model was used to compare the average pairwise
 296 distance (%) of the baseline DNA, on HDACi DNA, on HDAC RNA, and analytical
 297 treatment interruption plasma RNA within each drug trial. Patient identifier was
 298 considered as a random effect and the sample type factor as both a fixed effect and as
 299 a random effect with a general positive definite covariance structure. In the
 300 Panobinostat drug trial, there was a statistically significant within patient difference in
 301 average pairwise distance (%) across the four sample types ($p < 0.001$). There was no
 302 statistically significant within patient difference between the baseline and on trial DNA
 303 samples (mean change 0.02%, SE 0.08%, $p = 0.741$), nor between the on trial DNA and
 304 RNA samples (mean difference 0.11%, SE 0.33%, $p = 0.748$). There was however a
 305 statistically significant within patient difference between the on trial RNA measurement

306 and that following treatment interruption (mean change -0.72%, SE 0.55%, $p=0.043$). In
 307 the Vorinostat drug trial, only 3 of the 14 subjects had measurable on trial RNA values
 308 and no RNA measurements were taken following treatment interruption. There was no
 309 statistically significant within patient difference in average pairwise distance (%) across
 310 the baseline or on trial sample types ($p=0.2$). There was no statistically significant within
 311 patient difference between the baseline and on trial DNA samples (mean change
 312 0.13%, SE 0.12%, $p=0.298$), nor between the on trial RNA and DNA samples (mean
 313 difference 0.35%, SE 0.23%, $p=0.154$). The linear mixed effect model was used to
 314 generate the p values.

315

Supplementary figure 30



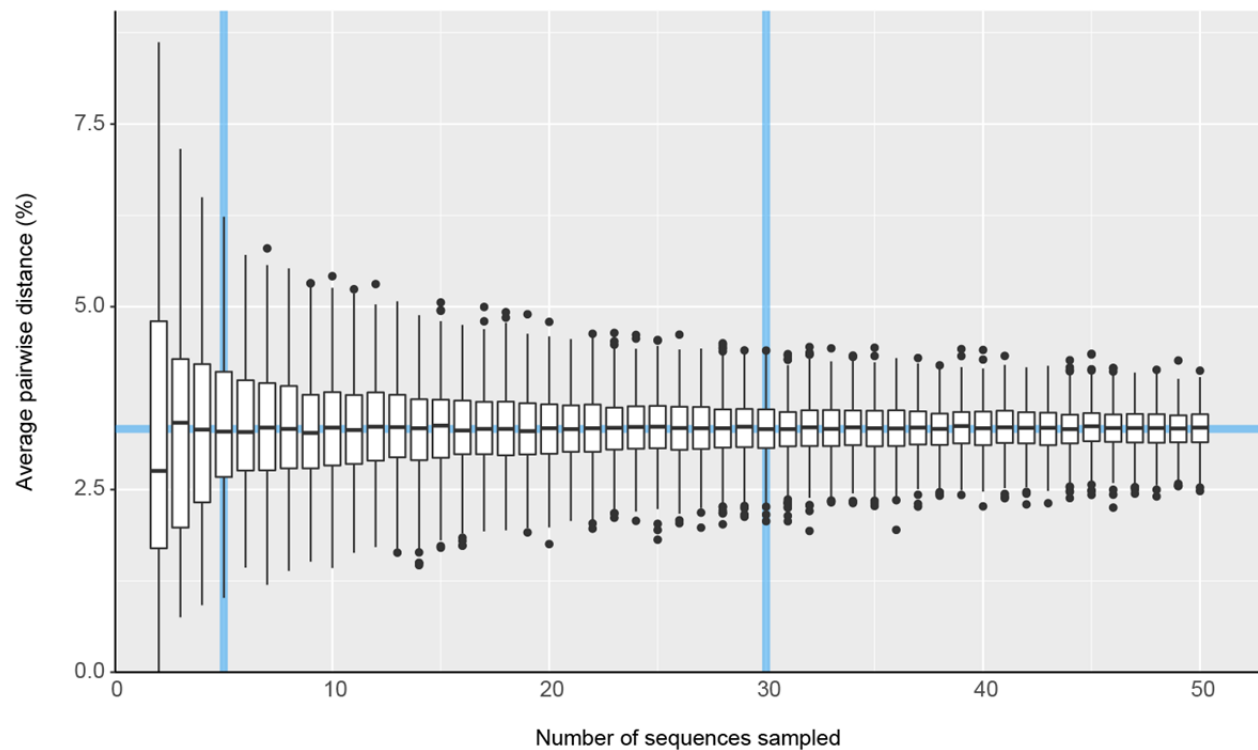
316

317 **Supplementary figure 30** Linear mixed effect model of the percent defective virus. The
 318 percentage of defective virus was log transformed to approximate normality and to
 319 stabilize the variance prior to analysis. Linear mixed effects models were used to
 320 investigate the joint effects of time (treated as a 3-level factor) and type (DNA or RNA)
 321 on log(percentage of defective virus) within each drug trial. Patient identifier, time, and

322 type were considered as random effects with a general positive definite covariance
323 structure, and time, type, and their 2-way interaction as fixed effects. Parameter
324 estimates and their 95% confidence intervals (95%CI) for the log(percentage of dead-
325 end virus) analyses were back- transformed to present results using the original scale of
326 measurement. In the Panobinostat drug trial, there was no statistically significant
327 interaction between the within patient effects of the time factor (baseline, on trial,
328 followup) and type (DNA, RNA) on log(percentage defective virus) ($p=0.267$). The linear
329 mixed effect model was used to generate p values.

330

Supplementary figure 31



331

332 **Supplementary figure 31** Simulation of sampling for the average pairwise distances.
333 Box plot illustrating the results of a simulation of 1,000 replicate comparisons of the
334 average pairwise distance for 2-50 sequences. Five sequences can be used to
335 generate an accurate measure of the average pairwise distance (mean simulation 3.345
336 vs. actual mean 3.327, variance 1.07, 95% CI 3.281-3.410).

337

338 **Supplementary table 1** Number of intact sequences obtained for each sample for each
 339 participant in the panobinostat trial.

Participant	Pre-ART plasma RNA	Baseline DNA	Baseline RNA	Time point 1 DNA	Time point 1 RNA	Time point 2 DNA	Time point 2 RNA	Follow-up DNA	Follow-up RNA	Treatment Interruption plasma RNA	Baseline LPMC DNA	Baseline LPMC RNA	Week 4 LPMC DNA	Week 4 LPMC RNA	Naive	Central Memory	Effector Memory	Stem cell Memory	Terminally differentiated
Pan01	22	27	7	21	4	22	3	22	2	27	26	0	9	0	0	7	0	3	0
Pan02	13	36	9	49	5	69	2	25	1	29	-	-	-	-	8	21	20	16	13
Pan04	30	27	1	17	0	4	0	5	0	13	-	-	-	-	0	0	13	0	3
Pan05	-	0	0	7	0	3	0	5	0	-	13	0	2	0	-	-	-	-	-
Pan06	26	24	1	29	2	27	1	27	0	-	-	-	-	-	-	-	-	-	-
Pan07	26	27	7	28	9	27	5	24	5	-	21	0	5	0	-	-	-	-	-
Pan08	-	24	20	18	16	22	15	17	8	30	-	-	-	-	0	26	15	0	0
Pan09	-	28	1	16	0	28	1	23	1	9	6	0	1	0	24	7	28	0	0
Pan10	-	29	0	27	1	28	2	27	0	4	29	0	13	0	0	0	0	0	0
Pan12	27	5	0	8	0	9	0	4	0	26	-	-	-	-	2	1	2	0	0
Pan14	29	4	0	4	1	3	0	5	0	-	3	0	4	0	-	-	-	-	-
Pan15	26	36	3	24	11	16	6	41	6	-	16	3	13	0	0	0	0	0	0
Pan17	-	24	1	21	22	14	0	30	4	13	8	1	14	1	0	4	7	16	0
Pan18	28	28	7	27	15	29	18	28	6	24	25	14	28	8	-	-	-	-	-
Pan19	15	32	9	24	24	45	11	36	14	-	0	0	0	0	-	-	-	-	-

340

341 **Supplementary table 2** Number of intact sequences obtained for each sample for each
 342 participant in the vorinostat trial as well as whether the participant began ART treatment
 343 during acute or chronic infection.

Participant	Acute/Chronic	Baseline DNA	Baseline RNA	Time point 1 DNA	Time point 1 RNA	Time point 2 DNA	Time point 2 RNA	Follow-up DNA	Follow-up RNA
Vor01	C	1	1	10	1	13	1	9	0
Vor02	A	10	0	11	0	8	0	2	0
Vor03	C	32	1	33	0	43	2	35	0
Vor06	C	22	4	13	1	16	2	8	1
Vor09	C	19	3	28	2	32	1	11	6
Vor11	C	4	1	10	1	6	0	13	0
Vor13	C	26	1	42	1	30	1	41	1
Vor14	C	19	2	28	2	15	2	14	3
Vor15	C	15	1	24	1	14	0	16	0
Vor16	C	29	36	31	13	41	7	24	8
Vor18	C	34	10	19	2	29	3	24	0
Vor19	C	10	1	6	1	14	0	10	3
Vor20	C	32	14	31	5	33	0	35	0
Vor22	C	16	3	23	3	19	1	13	1
Vor23	C	26	1	28	2	24	0	22	1
	1/14	295	79	337	35	337	20	277	24

344

345 **Supplementary table 3** Linear mixed effects model of the percent defective virus for
 346 the panobinostat trial.

Time	RNA/DNA	Lower CI	Upper CI	p-value	n
Baseline	5.0	2.7	9.4	0.001	7
On trial	3.6	1.6	8.0	0.007	9
Follow up	2.1	0.2	19.2	0.416	6

347 CI-confidence interval

348 **Supplementary table 4** Linear mixed effects model of the percent defective virus for
 349 the vorinostat trial.

Time	RNA/DNA	Lower CI	Upper CI	p-value	n
Baseline	1.4	0.3	6.3	0.616	5
On trial	3.2	1.3	8.2	0.024	6
Follow up	2.0	0.0	>30	0.697	3

350 CI-confidence interval

