

## Supplementary Figure Legends.

**Supplementary Figure 1. Interferon-stimulated gene expression following GS-9620 administration.** The RNA expression level in PBMC of each of the indicated interferon-stimulated genes (ISGs) was determined immediately prior to and at 24 h following each of the first 8 doses of GS-9620 (doses 1.1—1.8) for all six study animals. For each animal, dose, and gene, the fold change in expression at 24 h post-dose compared with the corresponding pre-dose time point is shown, with upregulation expressed as positive values and downregulation expressed as negative values.

**Supplementary Figure 2. Change in plasma TNF $\alpha$  concentration following GS-9620 administration.** The concentration of TNF $\alpha$  in plasma was determined immediately prior to and at 24 h following each of the indicated GS-9620 doses. The fold change in plasma TNF $\alpha$  at 24 h relative to the corresponding pre-dose time measurement is shown for each animal. GS-9620 treated animals are shown with red plot symbols and vehicle control animals are shown with blue plot symbols. Mean fold increase for each dose is shown for each group.

**Supplementary Figure 3. Expression of lymphoid homing markers on CD8<sup>+</sup> T cells and NK cells in blood.** Shown are the frequency of CD8<sup>+</sup> T cells (A) and NK cells (B) in blood expressing CCR7 and CXCR5 immediately prior to and at 24 h post-dose for GS-9620 doses 1.1 and 1.12. GS-9620 treated animals are shown with red plot symbols and vehicle control animals are shown with blue plot symbols.

**Supplementary Figure 4. Change in co-expression of CD38 and HLA-DR on CD8<sup>+</sup> T cells.** Fold change in the percentage of CD8<sup>+</sup> T cells co-expressing CD38 and HLA-DR at 24 h and 48 h post-dose compared with the corresponding pre-dose value for each of the 12 doses of the first course of GS-9620. \*,  $p < 0.006$

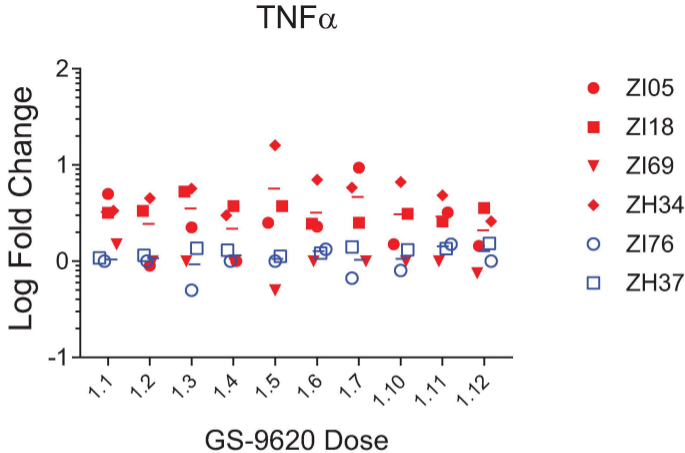
**Supplementary Figure 5. Frequency of CD56<sup>-</sup>CD16<sup>+</sup> NK cells that express HLA-DR.** Shown are the frequency of HLA-DR expressing CD56<sup>-</sup>CD16<sup>+</sup> NK cells in blood immediately prior to (Pre) and at 24 h and 48 h following each of the 12 doses of the first course of GS-9620 (doses 1.1 through 1.12). GS-9620 treated animals are shown with red plot symbols and vehicle control animals are shown with blue plot symbols.

**Supplementary Figure 6. CD4-normalized cell-associated viral RNA levels in PBMC.** Cell-associated vRNA content was quantified by qRT-PCR in PBMC samples collected immediately prior to (Pre) and at 24 h and 48 h following each of the 12 doses of the first course of GS-9620 (doses 1.1 through 1.12). Values were normalized based on input cell numbers, determined by independent qPCR measurements of a host cell gene within each sample, and on flow cytometric analyses of the frequency of CD4<sup>+</sup> cells within matched blood samples. GS-9620 treated animals are shown with red plot symbols and vehicle control animals are shown with blue plot symbols.

**Supplementary Figure 7. Gag-specific CD8<sup>+</sup> T cell responses to SIV gag peptide pools.** Shown are the results of intracellular staining of the indicated cytokines in CD8<sup>+</sup> T cells collected at the indicated time points and stimulated with a peptide pool derived from SIV gag.

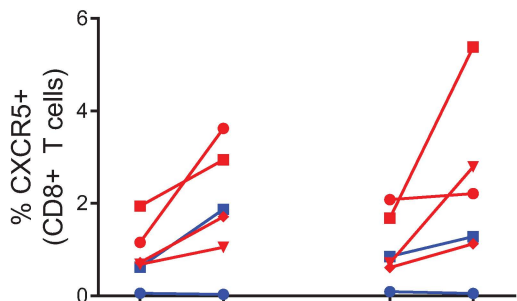
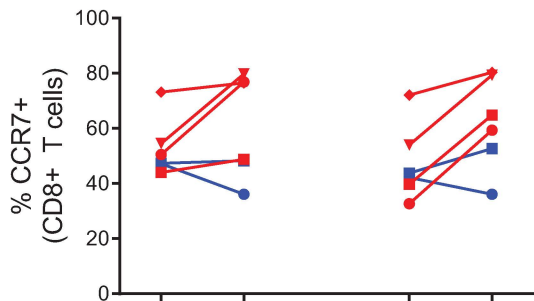
GS-9620 treated animals are shown with red plots and vehicle control animals are shown with blue plots.





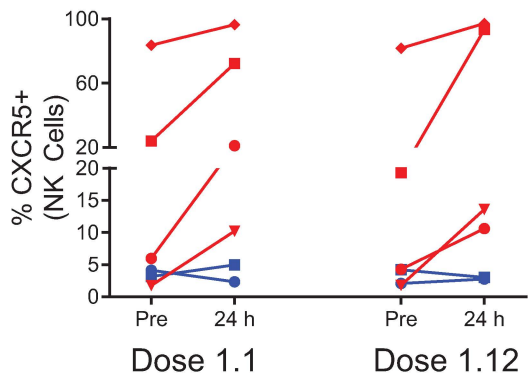
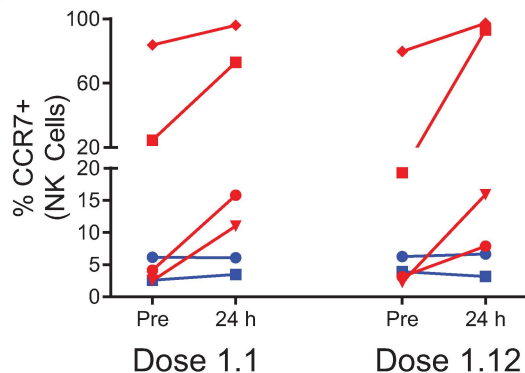
Supplementary Figure 2

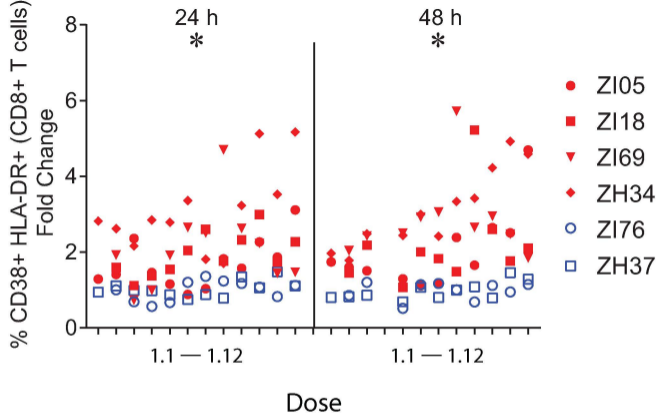
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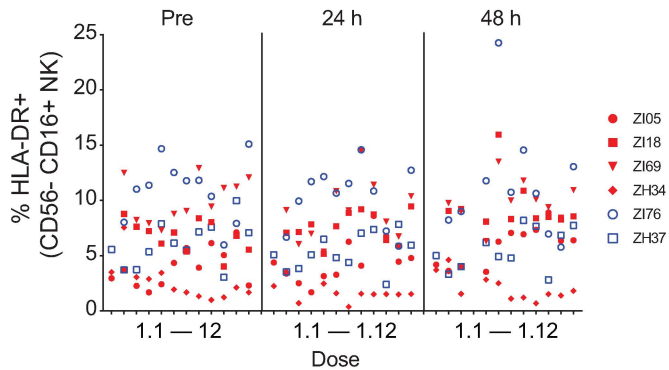
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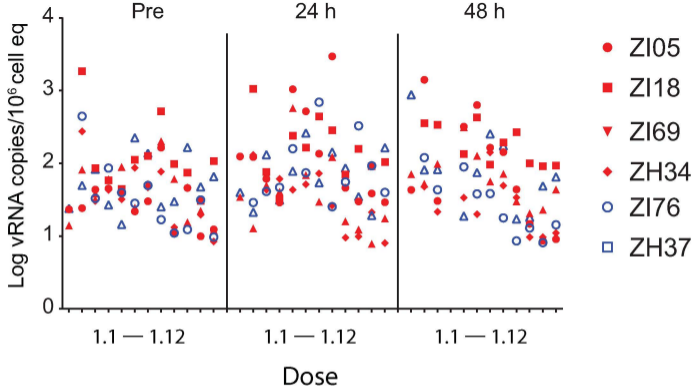




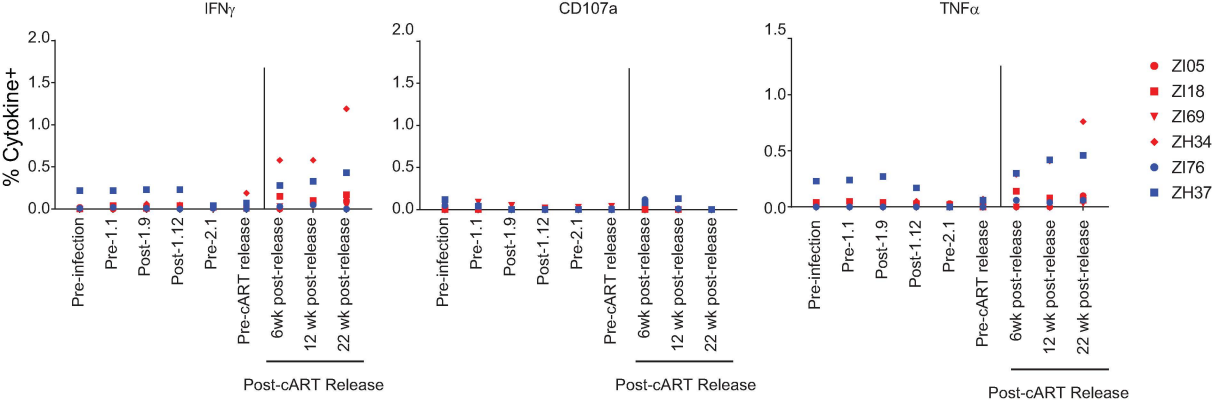
Supplementary Figure 4



Supplementary Figure 5



Supplementary Figure 6



Supplementary Figure 7