Description of Additional Supplementary Files

File Name: Supplementary Data 1

Description: Neutralization breadth and potency of V3 directed DARPins and antibodies

File Name: Supplementary Data 2

Description: Neutralization fingerprint analysis of V3-Crown bnDs and bnAbs

File Name: Supplementary Data 3

Description: Env binding properties of V3-crown DARPins and V3 specific antibodies

File Name: Supplementary Data 4

Description: Protective effect of the V1V2 domain against V3-directed DARPins and antibodies

File Name: Supplementary Data 5

Description: Data collection and structure refinement statistics of DARPin:V3 co-crystal structures

File Name: Supplementary Data 6

Description: Distribution of the buried surface area (BSA) on V3 in DARPin:V3 co-crystal structures

File Name: Supplementary Data 7

Description: Envelope mutational scanning identifies key residues that determine sensitivity to V3 bnDs.

File Name: Supplementary Data 8

Description: Repetitive testing of JR-CSF Env alanine point mutants in a pseudovirus inhibition assay for

identification of DARPin resistance mutations.

File Name: Supplementary Data 9

Description: Effect of size and valency on V3-crown bnD Env binding and neutralization activity

File Name: Supplementary Data 10

Description: All raw data related to Figure 6 and Supplementary Figures 14 and 15

File Name: Supplementary Data 11

Description: Overview of results from the linear regression analysis presented in Figure 6c and

Supplementary Figure 14c

File Name: Supplementary Data 12

Description: Sources and references for antibodies and recombinant proteins used in the study