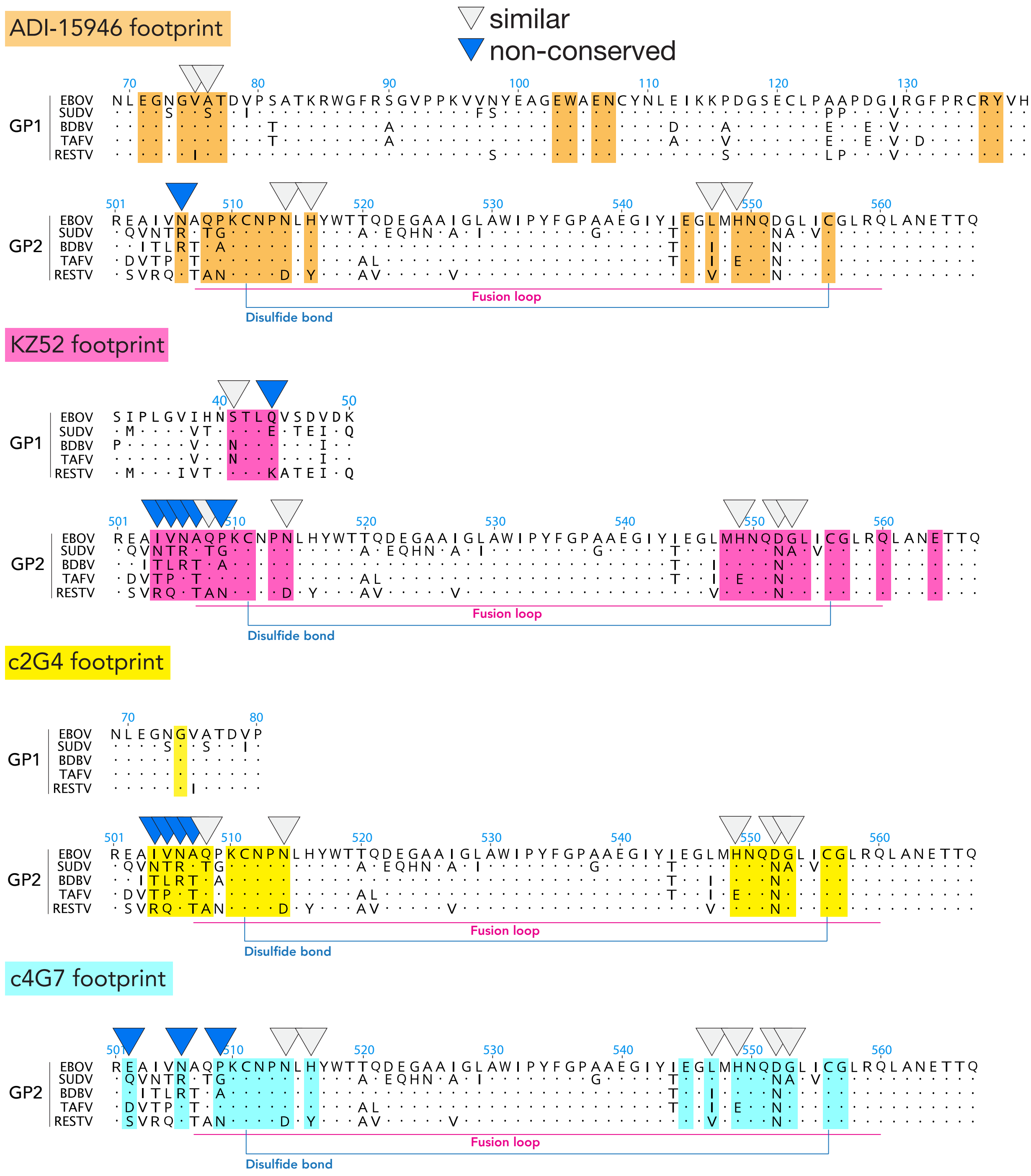
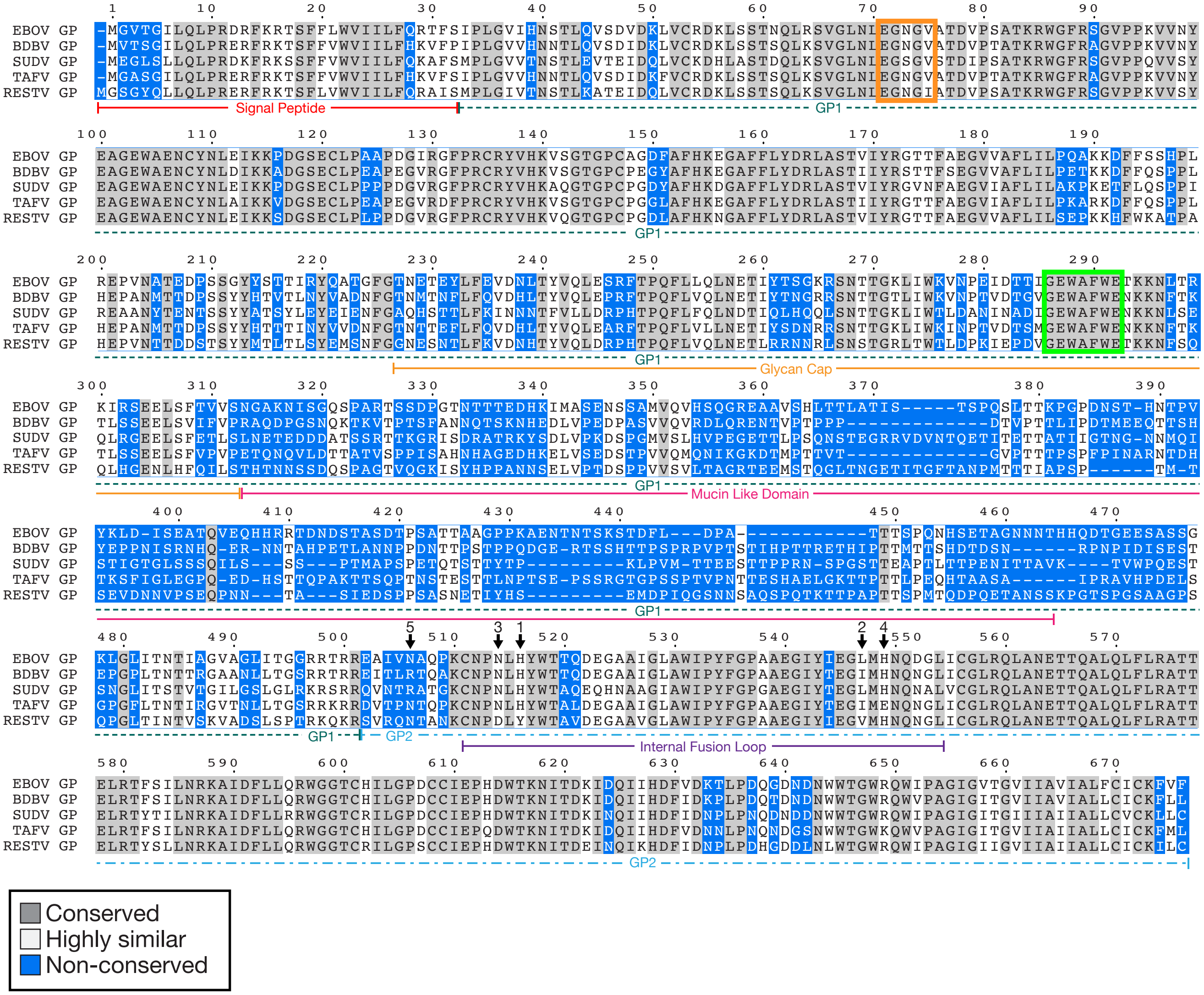
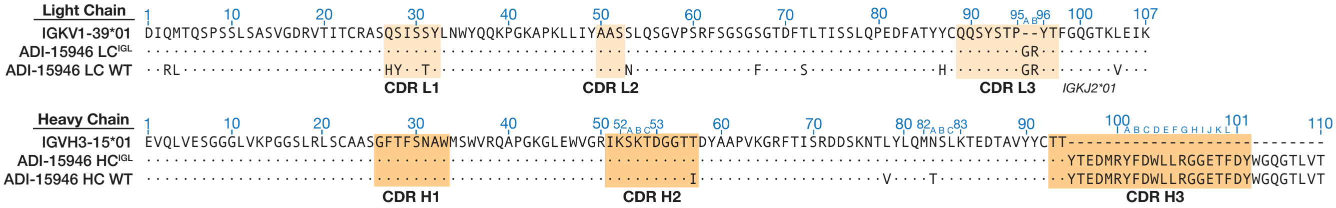


Supplementary Note 1. Comparison of the epitopes of ADI-15946 and EBOV mono-specific base binders. Each footprint is shown on a partial amino acid sequence alignment of EBOV, SUDV, BDBV, Taï Forest Virus (TAFV) and RESTV, with the residues that contain atoms located within 4 Å of each antibody when bound highlighted in the appropriate color (ADI-15946 contacts are orange, KZ52 contacts are pink, etc.). Within each footprint, grey inverted triangles indicate those contact residues that are similar across the ebolaviruses, while blue inverted triangles indicate those contact residues that differ more significantly across the ebolaviruses. Residues not indicated by triangles are either identical across the genus or not involved in the interface.



Supplementary Note 2. Ebolavirus conservation alignment. Sequence alignment of ebolavirus GPs colored by conservation as indicated in the legend. The location of the five residues that differ in the ADI-15946 epitope between EBOV and SUDV are indicated with arrowheads above their location in the sequence alignment (the numbering is consistent with Fig. 6F). The region of the β17-β18 loop that binds to the 3_{10} pocket is boxed in green, and residues 71-75 of the 3_{10} helix are boxed in orange.



Supplementary Note 3. Genesis of ADI-15946. Alignment of mature VH and VL sequences for ADI-15946 with their closest human germline V and J gene segments, and reconstruction of an inferred germline ancestor (IGL) bearing mature CDR-H3. Conserved residues are indicated with dots. Light and heavy chain sequences are numbered according to the Kabat scheme.