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(54) Title: STABILIZED POLYPEPTIDES

|      |      |      |      |      |      |      |
|------|------|------|------|------|------|------|
| FWR1 | CDR1 | FWR2 | CDR2 | FWR3 | CDR3 | FWR4 |
|------|------|------|------|------|------|------|

Fig. 1

(57) Abstract: The disclosure provides a polypeptide comprising an antibody heavy chain variable domain (VH) variant comprising a plurality of antigen-binding regions and a framework comprising framework region 1, framework region 2 and framework region 3 (FWR3), wherein the VH variant has an amino acid sequence in which at least eight of the following criteria i) to x) are fulfilled: i) the residue in Kabat position 19 is R, S, K or T; ii) the residue in Kabat position 23 is T, V, A or S; iii) the residue in Kabat position 24 is I, V or S; iv) the residue in Kabat position 40 is selected from R, I, T or K; v) the residue in Kabat position 43 is R, K, Q, E or G; vi) the residue in Kabat position 44 is E, Q, A, D or G; vii) the residue in Kabat position 45 is R, I or L; viii) the residue in Kabat position 76 is N or Q; ix) the residue in Kabat position 79 is Y, W or F; and x) the residue in Kabat position 89 is V, or I. The VH variants have improved alkaline stability and are useful as a scaffold for an affinity binder for *in vitro* applications, such as detection, analysis or separation of an analyte based on affinity interactions.