CLAIMS

1. A pharmaceutical composition comprising a bispecific single chain antibody construct~~,~~ ~~binding~~ that binds to a target cell surface antigen selected from CD19, CD33, FAPalpha, MSLN, FLT3 and BCMA via a first binding domain and to the T cell surface antigen CD3 via a second binding domain, a β-cyclodextrin and a buffer, ~~wherein the composition is stable.~~

wherein the binding domains have pairs of VH regions and VL regions in the format of a single chain antibody (scFv), and wherein the bispecific single chain antibody construct optionally comprises a domain for extending serum half-life which binds to Fc domains,

wherein the composition is characterized by a reduction or prevention of the formation of protein aggregates (high molecular weight species (HMWS)), and

wherein the β-cyclodextrin is not hydroxypropyl-β-cyclodextrin.

2. The composition according to claim 1, wherein the β-cyclodextrin is selected from the group consisting of β-cyclodextrin, methyl-β-cyclodextrin, hydroxyethyl~~-β-cyclodextrin, hydroxypropyl~~-β-cyclodextrin, ethyl-β-cyclodextrin, butyl-β-cyclodextrin Succinyl-(2-hydroxypropyl)-β-cyclodextrin, heptakis(2,3,6-tri-O-methyl)-β-cyclodextrin, heptakis(2,3,6-tri-O-benzoyl)-β-cyclodextrin, β-cyclodextrin phosphate sodium salt, β-cyclodextrin sulphate sodium salt, triacetyl-β-cyclodextrin, heptakis(6-O-sulfo)-β-cyclodextrin heptasodium salt, carboxymethyl-β-cyclodextrin sodium salt, sulfobutylether-β-cyclodextrin sodium salt, and 6-O-p-toluenesulfonyl-β-cyclodextrin.

3. The composition according to claim 1~~ or 2~~, wherein the β-cyclodextrin is present in a concentration in the range of 0.1% to 20% (w/v~~), preferably of 0.5% to 2% (w/v) and more preferably of 0.8% to 1.5% (w/v).~~).

4. The composition according to ~~any one of the preceding claims~~claim 1, wherein the β-cyclodextrin is ~~selected from the group consisting of~~ sulfobutylether-β-cyclodextrin sodium salt~~, hydroxypropyl-β-cyclodextrin~~.

5. The composition according to ~~any one of the preceding claims~~claim 1, wherein the bispecific single chain antibody construct is present in a concentration range of 0.1-5mg/ml~~,~~ ~~preferably of 0.2-2.5 mg/ml, more preferably of 0.25-1.0 mg/ml.~~.

6. The composition according to ~~any one of the preceding claims~~claim 1, wherein the buffer is selected from the group consisting of potassium phosphate, acetic acid/sodium acetate, citric acid/sodium citrate, succinic acid/sodium succinate, tartaric acid/sodium tartrate, histidine/histidine HCl, glycine, Tris, glutamate, acetate and mixtures thereof.

7. The composition according to claim 6, wherein the buffer is selected from the group consisting of potassium phosphate, citric acid/sodium citrate, succinic acid, histidine, glutamate, acetate and combinations thereof.

8. The composition according to ~~any of the preceding claims~~claim 1, wherein the pH of the composition is in the range of 4-7.5.

9. The composition according to ~~any one of the preceding claims~~claim 1, further comprising one or more excipients selected from the group consisting of sucrose, trehalose, mannitol, sorbitol, arginine, lysine, polysorbate 20, polysorbate 80, poloxamer 188, pluronic and combinations thereof.

10. The composition according to ~~any of the preceding claims, which comprises~~claim 1, further comprising one or more preservatives.

11. The composition according to claim 10, wherein the one or more preservative is selected from the group consisting of benzyl alcohol, chlorobutanol, phenol, meta-cresol, methylparaben, phenoxyethanol, propylparaben and thiomerosal.

12. The composition according to ~~any of claims~~ claim 1 ~~to 10~~, wherein the first binding domain ~~of the bispecific single chain antibody construct binds to CD19, CD33, MSLN, FLT3 or BCMA.~~

comprises the

~~13. The composition according to claim 12, wherein the~~ amino acid sequence ~~of the first binding domain of the bispecific single chain construct is~~ selected ~~form~~from the group consisting of SEQ ID NO: 99, 109, 119, 128, 137, 146, 155, 164, 173, 183, 185 and 187, and the ~~amino acid sequence of the~~ second binding domain ~~of~~comprises the ~~bispecific single chain construct is~~amino acid sequence selected ~~form~~from the group consisting of SEQ ID NO: 9, 18, 27, 36, 45, 54, 63, 72, 81, 179 and 90.

~~14.~~

13. The composition according to claim ~~13~~12, wherein the ~~formulation~~composition is free of preservatives, wherein the first and second binding domains of the antibody comprise the amino acid sequence ~~of the bispecific single chain antibody construct is~~ set forth in SEQ ID NO 100 or 110 and the ~~construct~~antibody is ~~in~~present at a concentration of about 0.5 mg/ml, wherein the β-cyclodextrin is sulfobutylether-β-cyclodextrin sodium salt ~~in~~and is present at a

concentration of about 1% (w/v), wherein the buffer is potassium phosphate ~~in~~and is present at a concentration of about 10 mM, and wherein the ~~formulation~~composition further comprises sucrose ~~in~~at a concentration of about 8% (w/v) ~~of~~ and polysorbate 80 ~~in~~at a concentration of about 0.01% (w/v) at a pH of about 6.0.

14. The composition according to claim 3, wherein the β-cyclodextrin is present in a concentration in the range of 0.5% to 2% (w/v).

15. The composition according to claim 14, wherein the β-cyclodextrin is present in a concentration in the range of 0.8% to 1.5% (w/v).

16. The composition according to claim 5, wherein the bispecific single chain antibody construct is present in a concentration range of 0.2-2.5 mg/ml.

17. The composition according to claim 16, wherein the bispecific single chain antibody construct is present in a concentration range of 0.25-1.0 mg/ml.

18. The composition according to claim 1, wherein the amino acid sequence of the bispecific single chain antibody construct is SEQ ID NO: 174.

19. The composition according to claim 12, wherein the cyclodextrin is sulfobutylether-β-cyclodextrin sodium salt in a concentration of about 1% (w/v) and the buffer is potassium phosphate in concentration of about 10 mM, and wherein the composition further comprises mannitol in a concentration of about 42%, sucrose in a concentration of about 2% (w/v), and polysorbate 80 in concentration of about 0.01% (w/v) at a pH of about 6.0.