

Claims

1. A bispecific polypeptide comprising a first binding domain, designated B1, which is capable of binding specifically to CD40, and a second binding domain, designated B2, which is capable of specifically binding to carcinoembryonic antigen (CEA).

2. The bispecific polypeptide according to Claim 1, wherein the first and/or second binding domains are/is selected from the group consisting of antibodies and antigen-binding fragments thereof, and CD40 ligands, optionally wherein the antigen-binding fragment is selected from the group consisting of: Fv fragments (such as a single chain Fv fragment, or a disulphide-bonded Fv fragment), Fab-like fragments (such as a Fab fragment; a Fab' fragment or a F(ab)₂ fragment) and domain antibodies,

optionally wherein the polypeptide is a bispecific antibody,
and/or wherein:

- (a) binding domain B1 and/or binding domain B2 is an intact IgG antibody;
- (b) binding domain B1 and/or binding domain B2 is an Fv fragment;
- (c) binding domain B1 and/or binding domain B2 is a Fab fragment; and/or
- (d) binding domain B1 and/or binding domain B2 is a single domain antibody,

optionally the bispecific polypeptide comprises a human Fc region or a variant of a said region, where the region is an IgG1, IgG2, IgG3 or IgG4 region, preferably an IgG1 or IgG4 region,

optionally wherein the Fc exhibits no or very low affinity for FcγR,

optionally wherein the Fc region is a variant of a human IgG1 Fc region comprising a mutation at one or more of the following positions:

L234, L235, P239, D265, N297 and/or P329,

optionally wherein alanine is present at the mutated position(s),

further optionally wherein the Fc region is a variant of a human IgG1 Fc region comprising the double mutations L234A and L235A.

3. The bispecific polypeptide according to any one of Claim 2, wherein the bispecific polypeptide is selected from the groups consisting of:

- (a) bivalent bispecific antibodies, such as IgG-scFv bispecific antibodies (for example, wherein B1 is an intact IgG and B2 is an scFv attached to B1 at the N-terminus of a light chain and/or at the C-terminus of a light chain and/or at the N-terminus of a heavy chain and/or at the C-terminus of a heavy chain of the IgG, or vice versa);
- (b) monovalent bispecific antibodies, such as a DuoBody® or a 'knob-in-hole' bispecific antibody (for example, an scFv-KIH, scFv-KIHr, a BiTE-KIH or a BiTE- KIHr);
- (c) scFv2-Fc bispecific antibodies (for example, ADAPTIR™ bispecific antibodies);
- (d) BiTE/scFv2 bispecific antibodies;
- (e) DVD-Ig bispecific antibodies;
- (f) DART-based bispecific antibodies (for example, DART2-Fc or DART);
- (g) DNL-Fab3 bispecific antibodies; and
- (h) scFv-HSA-scFv bispecific antibodies,

optionally wherein the bispecific polypeptide is an IgG-scFv bispecific antibody.

4. The bispecific polypeptide according to any one of the preceding claims, wherein binding domain B1 and binding domain B2 are fused directly to each other,

or wherein binding domain B1 and binding domain B2 are joined via a polypeptide linker,

optionally wherein the linker is selected from the group consisting of the amino acid sequence SGGGSGGGGS (SEQ ID NO: 337), SGGGSGGGGSAP (SEQ ID NO: 338), NFSQP (SEQ ID NO: 339), KRTVA (SEQ ID NO: 340), GGGSGGGG (SEQ ID NO: 341), GGGSGGGGS (SEQ ID NO: 342), GGGSGGGGSGGGGS (SEQ ID NO: 343), GSTSGSGKPGSGEGSTKG (SEQ ID NO: 344), THTCPPCPKSSDK (SEQ ID NO: 345), GGGG (SEQ ID NO: 346), EAAKEAAKGGGGS (SEQ ID NO: 347), EAAKEAAK (SEQ ID NO: 348), or (SG)m, where m = 1 to 7.

5. The bispecific polypeptide according to any one of the preceding claims, wherein one of B1 or B2 is an immunoglobulin molecule, and one of B1 or B2 is a Fab fragment, wherein the Fab fragment is fused to the C-terminus of the heavy chain of the immunoglobulin via the light chain of the Fab fragment.

6. The bispecific polypeptide according to any one of the preceding claims, wherein the bispecific polypeptide comprises one or more mutations to promote association of the

heavy chain polypeptide of the immunoglobulin with the light chain polypeptide of the immunoglobulin and/or to promote association of the heavy chain polypeptide of the Fab with the light chain polypeptide of the Fab,

optionally wherein the one or more mutations prevent the formation of aggregates and a Fab by-product,

and/or wherein the mutations prevent formation of aggregates and Fab by-products by generating steric hindrance and/or incompatibility between charges,

and/or wherein the polypeptide comprises one or more mutation pairs each comprising two functionally compatible mutations.

7. The bispecific polypeptide according to any one of the preceding claims, wherein the polypeptide can modulate the activity of and/or activate myeloid cells,

and/or wherein the polypeptide is incapable of inducing antibody-dependent cell cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP) and/or complement-dependent cytotoxicity (CDC),

and/or wherein the polypeptide is capable of:

- a) inducing tumour immunity; and/or
- b) inducing tumour-specific immune activation; and/or
- c) inducing activation of dendritic cells; and/or
- d) inducing internalisation of associated tumour debris and/or extracellular vesicles containing CEA antigens as well as tumour neoantigens; and/or
- e) inducing cross-presentation of peptides derived from internalised tumour antigens on MHC; and/or
- f) inducing priming and activation of effector T cells; and/or
- g) inducing direct tumoricidal effects, selected from the list consisting of: apoptosis, necroptosis, antibody-dependent cellular cytotoxicity (ADCC) and complement-dependent cytotoxicity (CDC); and/or
- h) activation of a B-cell, in the presence of a CEA; and/or
- i) activation of dendritic cells in the presence of CEA; and/or
- j) capable of increased dendritic cell cross-presentation of neoantigens; and/or
- k) inducing proliferation of neoantigen specific T cells; and/or
- l) promoting uptake of tumor derived material, derived from tumor cells expressing CEA

optionally wherein the B-cell activation is characterised by CD86 upregulation.

8. The bispecific polypeptide according to any one of the preceding claims wherein binding domain B1 binds to human CD40 with a K_D of less than $2 \times 10^{-7}M$ or less than $1.5 \times 10^{-7}M$ or less than $8.5 \times 10^{-8}M$ or less than $8 \times 10^{-8}M$ or less than $7.5 \times 10^{-8}M$ or less than $7 \times 10^{-8}M$ or less than $9 \times 10^{-8}M$ or less than $9 \times 10^{-9}M$ or less than $5 \times 10^{-10}M$ or less than $3 \times 10^{-10}M$, preferably less than $8.5 \times 10^{-8}M$, more preferably less than $5 \times 10^{-10}M$ or less than $3 \times 10^{-10}M$.

9. The bispecific polypeptide according to any one of the preceding claims, wherein binding domain B1 comprises one or more heavy chain CDR sequences selected from those in Table C(1) and/or wherein binding domain B1 comprises one or more light chain CDR sequences selected from those in Table C(2),

optionally wherein binding domain B1 comprises one, two or three light chain CDR sequences from a particular row for an individual antibody reference in Table C(2), and/or one, two or three heavy chain CDR sequences from the corresponding row for the antibody with the same reference in Table C(1),

further optionally wherein binding domain B1 comprises all three heavy chain CDR sequences of a particular antibody reference as shown in Table C(1), and/or all three light chain CDR sequences of an antibody reference as shown in Table C(2), or wherein binding domain B1 comprises a heavy chain VH sequence and/or a light chain VL sequence as shown in Table A.

10. The bispecific polypeptide according to any one of the preceding claims, wherein B1 comprises any one, two, three, four, five or all six features independently selected from the following:

- (a) a heavy chain CDR1 sequence which consists of the sequence "G, F, T, F, S, S, Y, A";
- (b) a heavy chain CDR2 sequence which is 8 amino acids in length and comprises the consensus sequence: "I, G/S, S/G, Y/S, G/S, G/S, G/Y/S, T";
- (c) a heavy chain CDR3 sequence which is 9 to 12 amino acids in length and which comprises the consensus sequence of : "A, R, Y/R/G, Y/P/V/-, N/S/V, F/Y/W, G/H/S, -/S, -/V, M/F, D, Y"
- (d) a light chain CDR1 sequence which consists of the sequence: "Q, S, I, S, S, Y";
- (e) a light chain CDR2 sequence which consists of the sequence: "A, A, S";

(f) a light chain CDR3 sequence which is 9 amino acids in length and comprises the consensus sequence: "Q, Q, Y/S, G/Y, R/S/V, N/A/Y/T, P, P/F/Y, T".

optionally wherein binding domain B1 comprises:

- (a) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody 1132/1133 (SEQ ID NOs: 73, 74 and 75; and/or 90, 91 and 92); or
- (b) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody 1107/1108 (SEQ ID NOs: 73, 78 and 80; and/or SEQ ID NOs: 90, 91 and 95); or
- (c) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody 1150/1151 (SEQ ID NOs: 73, 76 and 77; and/or SEQ ID NOs: 90, 91 and 93); or
- (d) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody 1140/1135 (SEQ ID NOs: 73, 78 and 79; and/or SEQ ID NOs: 90, 91 and 94); or
- (e) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody G12 or G12_mut or ffAC_05337 (SEQ ID NOs: 81, 82 and 83; and/or SEQ ID NOs: 96, 97, and 98); or
- (f) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody APX005 (SEQ ID NOs: 84, 85 and 86; and/or SEQ ID NOs: 99, 100, and 101); or
- (g) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody 21.4.1 (SEQ ID NOs: 87, 88 and 89; and/or SEQ ID NOs: 102, 103, and 104).

optionally wherein binding domain B1 comprises:

- (a) the heavy chain variable region and/or the light chain variable region of antibody 1132/1133 (SEQ ID NOs: 3 and 1); or
- (b) the heavy chain variable region and/or the light chain variable region of antibody 1107/1108 (SEQ ID NOs: 15 and 13); or
- (c) the heavy chain variable region and/or the light chain variable region of antibody 1150/1151 (SEQ ID NOs: 7 and 5); or
- (d) the heavy chain variable region and/or the light chain variable region of antibody 1140/1135 (SEQ ID NOs: 11 and 9); or
- (e) the heavy chain variable region and/or the light chain variable region of antibody G12 (SEQ ID NOs: 19 and 17); or
- (f) the heavy chain variable region and/or the light chain variable region of antibody APX005 (SEQ ID NOs: 23 and 21); or
- (g) the heavy chain variable region and/or the light chain variable region of antibody 21.4.1 (SEQ ID NOs: 27 and 25); or
- (h) the heavy chain variable region and/or the light chain variable region of antibody G12_mut (SEQ ID NOs: 29 and 17); or

(i) the heavy chain variable region and/or the light chain variable region of antibody ffAC_05337 (SEQ ID NOs: 431 and 430),

further optionally wherein binding domain B1 comprises the light chain of antibody 1132/1133 (SEQ ID NO: 372 or 379) and/or the heavy chain of antibody 1132/1133 (SEQ ID NO: 371 or 378).

further optionally wherein binding domain B1 comprises the light chain of antibody G12 (SEQ ID NO: 381) and/or the heavy chain of antibody G12 (SEQ ID NO: 380) or the light chain of antibody G12_mut (SEQ ID NO: 383) and/or the heavy chain of antibody G12_mut (SEQ ID NO: 382).

further optionally wherein binding domain B1 comprises the light chain of antibody ffAC_05337 (SEQ ID NO: 430) and/or the heavy chain of antibody ffAC_05337 (SEQ ID NO: 431).

11. The bispecific polypeptide according to any one of the preceding claims, wherein the CEA is a tumor-associated CEA,

and/or wherein the CEA is a carcinoembryonic antigen-related cell adhesion molecule (CEACAM),

optionally wherein the CEACAM is one or more selected from the listing consisting of: CEACAM1; CEACAM6; and CEACAM5,

preferably wherein the CEACAM is CEACAM5.

12. The bispecific polypeptide according to any one of the preceding claims, wherein B2 is capable of specifically binding to CEA on a target cell,

optionally wherein the target cell is a cancer cell and/or a tumour cell,

optionally wherein the CEA on the target cell is an intermediate level of CEA or a high level of CEA,

optionally wherein the intermediate level of CEA is characterised by the target cell expressing about 10,000 or more CEA receptors per target cell, preferably about 50,000 or more CEA receptors per target cell,

or wherein the high level of CEA is characterised by the target cell expressing about 200,000 of more CEA receptors per target cell, preferably about 300,000 of more CEA receptors per target cell,

optionally wherein binding domain B2 binds to human CEA with a K_D of less than $2 \times 10^{-6}M$ or less than $1.5 \times 10^{-8}M$ or less than $2.5 \times 10^{-9}M$ or less than $2 \times 10^{-9}M$ or less than $1.5 \times 10^{-12}M$ or less than $1 \times 10^{-12}M$, preferably less than $1.5 \times 10^{-8}M$ or less than $2.5 \times 10^{-9}M$ or less than $1.5 \times 10^{-12}M$,

and optionally wherein binding domain B2 binds preferentially to CEA on a cell over soluble CEA.

13. The bispecific polypeptide according to any one of the preceding claims, wherein binding domain B2 comprises one or more heavy chain CDR sequences selected from those in Table D(1a) and/or Table D(1b) and/or wherein binding domain B2 comprises one or more light chain CDR sequences selected from those in Table D(2) optionally wherein binding domain B2 comprises one, two or three light chain CDR sequences from a particular row for an individual antibody reference in Table D(2), and/or one, two or three heavy chain CDR sequences from the corresponding row for the antibody with the same reference in Table D(1a) and/or Table D(1b),

optionally wherein binding domain B2 comprises all three heavy chain CDR sequences of a particular antibody reference as shown in Table D(1a) and/or Table D(1b), and/or all three light chain CDR sequences of an antibody reference as shown in Table D(2), or wherein binding domain B1 comprises a heavy chain VH sequence and/or a light chain VL sequence as shown in Table B.

14. The bispecific polypeptide according to any one of the preceding claims, wherein B2 comprises any one, two, three, four, five or all six features independently selected from the following:

- (a) a heavy chain CDR1 sequence which consists of the sequence: "G, F, T, F, S, S, S, Y" or which comprises the consensus sequence of: "G, F, T, F, G/S, S, Y, Y/A";
- (b) a heavy chain CDR2 sequence which consists of the sequence: "I, G, S, G, S, Y, S, T" or which comprises the consensus sequence of: "I, S, G, Y/S, G, Y/G, S, T";
- (c) a heavy chain CDR3 sequence which comprises the consensus sequence of: "A, R, Y, P, S, V, P/L, F, P, Q, S, P/H/L, H/P/L, L/F/V/W, D, Y" or which comprises the consensus sequence of: "A, R, H/Y, G, Y, G/S/T, V/ H, L/F, D, Y";

- (d) a light chain CDR1 sequence which consists of the sequence: "Q, S, I, S, S, Y" or which comprises the consensus sequence of: "Q, S, I, R/S, S, Y";
- (e) a light chain CDR2 sequence which consists of the sequence: "A, A, S";
- (f) a light chain CDR3 sequence which consists of the sequence: "Q, Q, A, G, N, P, H, T" or which comprises the consensus sequence of: "Q, Q, G/Y, T/P/A, W/-, Y/-, F/V, P, F/Y, T", optionally wherein binding domain B2 comprises:
 - (a) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05059 (SEQ ID NOs: 216, 217 and 218 or 280, 281 and 218 and/or SEQ ID NOs: 90, 91 and 311)
 - (b) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05060 (SEQ ID NOs: 219, 220 and 221 or 282, 283 and 221 and/or SEQ ID NOs: 312, 91 and 313)
 - (c) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05061 (SEQ ID NOs: 222, 223 and 224 or 284, 285 and 224 and/or SEQ ID NOs: 90, 91 and 314)
 - (d) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05062 (SEQ ID NOs: 222, 223 and 225 or 284, 285 and 225 and/or SEQ ID NOs: 315, 316 and 94)
 - (e) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05064 (SEQ ID NOs: 222, 223 and 226 or 284, 285 and 226 and/or SEQ ID NOs: 90, 91 and 317)
 - (f) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05079 (SEQ ID NOs: 216, 217 and 227 or 280, 281 and 227 and/or SEQ ID NOs: 90, 91 and 311)
 - (g) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05080 (SEQ ID NOs: 216, 217 and 228 or 280, 281 and 228 and/or SEQ ID NOs: 90, 91 and 311)
 - (h) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05081 (SEQ ID NOs: 216, 217 and 229 or 280, 281 and 229 and/or SEQ ID NOs: 90, 91 and 311)
 - (i) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05082 (SEQ ID NOs: 222, 223 and 230 or 284, 285 and 230 and/or SEQ ID NOs: 90, 91 and 311)
 - (j) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05083 (SEQ ID NOs: 222, 223 and 231 or 284, 285 and 231 and/or SEQ ID NOs: 318, 91 and 319)

- (k) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05084 (SEQ ID NOs: 222, 223 and 232 or 284, 285 and 232 and/or SEQ ID NOs: 90, 91 and 320)
- (l) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05085 (SEQ ID NOs: 219, 233 and 234 or 286, 287 and 234 and/or SEQ ID NOs: 90, 91 and 311)
- (m) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05086 (SEQ ID NOs: 216, 217 and 235 or 280, 281 and 235 and/or SEQ ID NOs: 90, 91 and 311)
- (n) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05087 (SEQ ID NOs: 216, 217 and 236 or 280, 281 and 236 and/or SEQ ID NOs: 90, 91 and 311)
- (o) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05088 (SEQ ID NOs: 216, 217 and 237 or 280, 281 and 237 and/or SEQ ID NOs: 90, 91 and 311)
- (p) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05089 (SEQ ID NOs: 216, 217 and 238 or 280, 281 and 238 and/or SEQ ID NOs: 90, 91 and 311)
- (q) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05090 or ffAC_05337 (SEQ ID NOs: 216, 217 and 239 or 280, 281 and 239 and/or SEQ ID NOs: 90, 91 and 311)
- (r) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05091 (SEQ ID NOs: 216, 217 and 240 or 280, 281 and 240 and/or SEQ ID NOs: 90, 91 and 311)
- (s) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05092 (SEQ ID NOs: 216, 217 and 218 or 280, 281 and 218 and/or SEQ ID NOs: 321, 91 and 311)
- (t) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05093 (SEQ ID NOs: 216, 217 and 241 or 280, 281 and 241 and/or SEQ ID NOs: 90, 91 and 311)
- (u) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05094 (SEQ ID NOs: 216, 217 and 242 or 280, 281 and 242 and/or SEQ ID NOs: 90, 91 and 311)
- (v) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05095 (SEQ ID NOs: 216, 217 and 243 or 280, 281 and 243 and/or SEQ ID NOs: 90, 91 and 311)

- (w) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05096 (SEQ ID NOs: 216, 217 and 244 or 280, 281 and 244 and/or SEQ ID NOs: 90, 91 and 311)
- (x) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05097 (SEQ ID NOs: 217, 216 and 245 or 280, 281 and 245 and/or SEQ ID NOs: 90, 91 and 311)
- (y) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05098 (SEQ ID NOs: 219, 220 and 246 or 282, 283 and 246 and/or SEQ ID NOs: 312, 91 and 313)
- (z) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05099 (SEQ ID NOs: 222, 223 and 224 or 288, 285 and 224 and/or SEQ ID NOs: 90, 91 and 311)
- (aa) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody AC_05100 (SEQ ID NOs: 222, 223 and 247 or 288, 285 and 247 and/or SEQ ID NOs: 90, 91 and 311)
- (ab) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody Fab1 (SEQ ID NOs: 248, 249 and 250 or 289, 290 and 250 and/or SEQ ID NOs: 90, 91 and 322)
- (ac) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody Fab2 (SEQ ID NOs: 251, 252 and 253 or 291, 292 and 253 and/or SEQ ID NOs: 90, 91 and 323)
- (ad) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody Fab3 (SEQ ID NOs: 254, 255 and 256 or 293, 294 and 256 and/or SEQ ID NOs: 324, 325 and 326)
- (ae) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody Fab4 (SEQ ID NOs: 257, 258 and 259 or 295, 296 and 259 and/or SEQ ID NOs: 90, 91 and 327)
- (af) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody Fab5 (SEQ ID NOs: 260, 261 and 262 or 297, 298 and 262 and/or SEQ ID NOs: 324, 325 and 328)
- (ag) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody Fab6 (SEQ ID NOs: 263, 264 and 265 or 299, 300 and 265 and/or SEQ ID NOs: 324, 325 and 329)
- (ah) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody Fab7 (SEQ ID NOs: 266, 267 and 268 or 301, 302 and 268 and/or SEQ ID NOs: 90, 91 and 330)

- (ai) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody Fab8 (SEQ ID NOs: 269, 270 and 271 or 303, 304 and 271 and/or SEQ ID NOs: 90, 91 and 331)
- (aj) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody Fab9 (SEQ ID NOs: 272, 335 and 273 or 305, 306 and 273 and/or SEQ ID NOs: 90, 91 and 332)
- (ak) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody Fab10 (SEQ ID NOs: 274, 275 and 276 or 307, 308 and 276 and/or SEQ ID NOs: 90, 91 and 333) and/or
- (al) the three CDRs of the heavy chain and/or the three CDRs of the light chain of antibody Fab11 (SEQ ID NOs: 277, 278 and 279 or 309, 310 and 279 and/or SEQ ID NOs: 324, 325 and 334),

further optionally wherein binding domain B2 comprises:

- (a) the heavy chain variable region and/or the light chain variable region of antibody AC_05059 (SEQ ID NO: 33 and/or SEQ ID NO: 31)
- (b) the heavy chain variable region and/or the light chain variable region of antibody AC_05060 (SEQ ID NO: 37 and/or SEQ ID NO: 35)
- (c) the heavy chain variable region and/or the light chain variable region of antibody AC_05061 (SEQ ID NO: 41 and/or SEQ ID NO: 39)
- (d) the heavy chain variable region and/or the light chain variable region of antibody AC_05062 (SEQ ID NO: 45 and/or SEQ ID NO: 43)
- (e) the heavy chain variable region and/or the light chain variable region of antibody AC_05064 (SEQ ID NO: 49 and/or SEQ ID NO: 47)
- (f) the heavy chain variable region and/or the light chain variable region of antibody AC_05079 (SEQ ID NO: 53 and/or SEQ ID NO: 51)
- (g) the heavy chain variable region and/or the light chain variable region of antibody AC_05080 (SEQ ID NO: 57 and/or SEQ ID NO: 55)
- (h) the heavy chain variable region and/or the light chain variable region of antibody AC_05081 (SEQ ID NO: 61 and/or SEQ ID NO: 59)
- (i) the heavy chain variable region and/or the light chain variable region of antibody AC_05082 (SEQ ID NO: 65 and/or SEQ ID NO: 63)
- (j) the heavy chain variable region and/or the light chain variable region of antibody AC_05083 (SEQ ID NO: 69 and/or SEQ ID NO: 67)
- (k) the heavy chain variable region and/or the light chain variable region of antibody AC_05084 (SEQ ID NO: 106 and/or SEQ ID NO: 71)
- (l) the heavy chain variable region and/or the light chain variable region of antibody AC_05085 (SEQ ID NO: 110 and/or SEQ ID NO: 108)

- (m) the heavy chain variable region and/or the light chain variable region of antibody AC_05086 (SEQ ID NO: 114 and/or SEQ ID NO: 112)
- (n) the heavy chain variable region and/or the light chain variable region of antibody AC_05087 (SEQ ID NO: 118 and/or SEQ ID NO: 116)
- (o) the heavy chain variable region and/or the light chain variable region of antibody AC_05088 (SEQ ID NO: 122 and/or SEQ ID NO: 120)
- (p) the heavy chain variable region and/or the light chain variable region of antibody AC_05089 (SEQ ID NO: 126 and/or SEQ ID NO: 124)
- (q) the heavy chain variable region and/or the light chain variable region of antibody AC_05090 (SEQ ID NO: 130 and/or SEQ ID NO: 128)
- (r) the heavy chain variable region and/or the light chain variable region of antibody AC_05091 (SEQ ID NO: 134 and/or SEQ ID NO: 132)
- (s) the heavy chain variable region and/or the light chain variable region of antibody AC_05092 (SEQ ID NO: 138 and/or SEQ ID NO: 136)
- (t) the heavy chain variable region and/or the light chain variable region of antibody AC_05093 (SEQ ID NO: 142 and/or SEQ ID NO: 140)
- (u) the heavy chain variable region and/or the light chain variable region of antibody AC_05094 (SEQ ID NO: 146 and/or SEQ ID NO: 144)
- (v) the heavy chain variable region and/or the light chain variable region of antibody AC_05095 (SEQ ID NO: 150 and/or SEQ ID NO: 148)
- (w) the heavy chain variable region and/or the light chain variable region of antibody AC_05096 (SEQ ID NO: 154 and/or SEQ ID NO: 152)
- (x) the heavy chain variable region and/or the light chain variable region of antibody AC_05097 (SEQ ID NO: 158 and/or SEQ ID NO: 156)
- (y) the heavy chain variable region and/or the light chain variable region of antibody AC_05098 (SEQ ID NO: 162 and/or SEQ ID NO: 160)
- (z) the heavy chain variable region and/or the light chain variable region of antibody AC_05099 (SEQ ID NO: 166 and/or SEQ ID NO: 164)
- (aa) the heavy chain variable region and/or the light chain variable region of antibody AC_05100 (SEQ ID NO: 170 and/or SEQ ID NO: 168)
- (ab) the heavy chain variable region and/or the light chain variable region of antibody Fab1 (SEQ ID NO: 174 and/or SEQ ID NO: 172)
- (ac) the heavy chain variable region and/or the light chain variable region of antibody Fab2 (SEQ ID NO: 178 and/or SEQ ID NO: 176)
- (ad) the heavy chain variable region and/or the light chain variable region of antibody Fab3 (SEQ ID NO: 182 and/or SEQ ID NO: 180)
- (ae) the heavy chain variable region and/or the light chain variable region of antibody Fab4 (SEQ ID NO: 186 and/or SEQ ID NO: 184)

- (af) the heavy chain variable region and/or the light chain variable region of antibody Fab5 (SEQ ID NO: 190 and/or SEQ ID NO: 188)
- (ag) the heavy chain variable region and/or the light chain variable region of antibody Fab6 (SEQ ID NO: 194 and/or SEQ ID NO: 192)
- (ah) the heavy chain variable region and/or the light chain variable region of antibody Fab7 (SEQ ID NO: 198 and/or SEQ ID NO: 196)
- (ai) the heavy chain variable region and/or the light chain variable region of antibody Fab8 (SEQ ID NO: 202 and/or SEQ ID NO: 200)
- (aj) the heavy chain variable region and/or the light chain variable region of antibody Fab9 (SEQ ID NO: 206 and/or SEQ ID NO: 204)
- (ak) the heavy chain variable region and/or the light chain variable region of antibody Fab10 (SEQ ID NO: 210 and/or SEQ ID NO: 208)
- (al) the heavy chain variable region and/or the light chain variable region of antibody Fab11 (SEQ ID NO: 214 and/or SEQ ID NO: 212)
- (am) the heavy chain variable region and/or the light chain variable region of antibody mAb2 (SEQ ID NO: 387 and /or SEQ ID NO: 385) and/or
- (an) the heavy chain variable region and/or the light chain variable region of antibody ffAC_05337 (SEQ ID NO: 433 and /or SEQ ID NO: 432), further optionally wherein binding domain B2 comprises:
 - (a) the light chain and/or the heavy chain of antibody AC_05059 (SEQ ID NO: 388 and/or SEQ ID NO: 389)
 - (b) the light chain and/or the heavy chain of antibody AC_05060 (SEQ ID NO: 390 and/or SEQ ID NO: 391)
 - (c) the light chain and/or the heavy chain of antibody AC_05061 (SEQ ID NO: 392 and/or (SEQ ID NO: 393)
 - (d) the light chain and/or the heavy chain of antibody AC_05062 (SEQ ID NO: 394 and/or SEQ ID NO: 395)
 - (e) the light chain and/or the heavy chain of antibody AC_05064 (SEQ ID NO: 396 and/or SEQ ID NO: 397)
 - (f) the light chain and/or the heavy chain of antibody AC_05079 (SEQ ID NO: 398 and/or SEQ ID NO: 399)
 - (g) the light chain and/or the heavy chain of antibody AC_05081 (SEQ ID NO: 400 and/or SEQ ID NO: 401)
 - (h) the light chain and/or the heavy chain of antibody AC_05088 (SEQ ID NO: 402 and/or SEQ ID NO: 403)
 - (i) the light chain and/or the heavy chain of antibody AC_05089 (SEQ ID NO: 404 and/or SEQ ID NO: 405)

- (j) the light chain and/or the heavy chain of antibody AC_05090 (SEQ ID NO: 406 and/or SEQ ID NO: 407)
- (k) the light chain and/or the heavy chain of antibody AC_05091 (SEQ ID NO: 408 and/or SEQ ID NO: 409)
- (l) the light chain and/or the heavy chain of antibody AC_05093 (SEQ ID NO: 410 and/or SEQ ID NO: 411)
- (m) the light chain and/or the heavy chain of antibody AC_05094 (SEQ ID NO: 412 and/or SEQ ID NO: 413)
- (n) the light chain and/or the heavy chain of antibody AC_05096 (SEQ ID NO: 414 and/or SEQ ID NO: 415)
- (o) the light chain and/or the heavy chain of antibody AC_05097 (SEQ ID NO: 416 and/or SEQ ID NO: 417)
- (p) the light chain and/or the heavy chain of antibody Fab1 (SEQ ID NO: 418 and/or SEQ ID NO: 419)
- (q) the light chain and/or the heavy chain of antibody Fab3 (SEQ ID NO: 420 and/or (SEQ ID NO: 421).

15. The bispecific polypeptide according to any one of the preceding claims wherein the bispecific polypeptide:

comprises a Chain H1 comprising a sequence selected from the listing consisting of: SEQ ID NO: 359; SEQ ID NO: 362; SEQ ID NO: 365; and/or SEQ ID NO: 367; and/or

comprises a Chain L1 comprising a sequence selected from the listing consisting of: SEQ ID NO: 360; SEQ ID NO: 363; SEQ ID NO: 372; and/or SEQ ID NO: 368; and/or

comprises a Chain H2 comprising a sequence selected from the listing consisting of: SEQ ID NO: 361; SEQ ID NO: 364; SEQ ID NO: 366; and/or SEQ ID NO: 369.

16. A polypeptide comprising a binding domain, designated B2, as defined in any one of Claims 1 to 15, which is capable of specifically binding to CEA.

17. A bispecific polypeptide comprising a first binding domain, designated B3, which is capable of binding specifically to a target antigen that is not CD40, and a second binding domain, designated B2, as defined in any of Claims 1 to 16, which is capable of specifically binding to CEA.

18. An isolated nucleic acid molecule encoding a bispecific polypeptide according to any one of Claims 1-15 or 17 or a polypeptide according to Claim 16, or a component polypeptide chain thereof,

optionally wherein the molecule is a cDNA molecule,

and/or wherein the nucleic acid molecule encodes an antibody heavy chain or variable region thereof,

and/or wherein the nucleic acid molecule encodes an antibody light chain or variable region thereof.

19. The vector comprising a nucleic acid molecule according to Claim 18,

optionally wherein the vector is an expression vector.

20. A recombinant host cell comprising a nucleic acid molecule according to Claim 18 or a vector according to Claim 19,

optionally wherein the host cell is a bacterial cell,

or wherein the host cell is a mammalian cell,

optionally wherein the host cell is a human cell.

21. A method for producing bispecific polypeptide according to any one of Claims 1-15 or 17 or a polypeptide according to Claim 16, the method comprising culturing a host cell as defined in Claim 20 under conditions which permit expression of the bispecific polypeptide or component polypeptide chain thereof.

22. A pharmaceutical composition comprising an effective amount of bispecific polypeptide according to any one of Claims 1-15 or 17 or an effective amount of a polypeptide according to Claim 16, and a pharmaceutically-acceptable diluent, carrier or excipient,

optionally wherein the pharmaceutical composition is adapted for parenteral delivery

or adapted for intravenous delivery.

23. A bispecific polypeptide according to any one of Claims 1-15 or 17 or a polypeptide according to Claim 16, for use in medicine,

optionally for use in treating cancer and/or a tumour and/or a non-cancer condition in a subject, optionally wherein the subject is a human and/or, optionally for administration systemically,

and/or wherein the polypeptide is for use in combination with one or more additional therapeutic agents,

optionally wherein the one or more additional therapeutic agents is/are an immunotherapeutic agent that binds a target selected from the group consisting of PD-1/PD-L1, VGFR, EGFR, HER2, CTLA-4, CD137, OX40, GITR, LAG3, TIM3, CD27, VISTA and KIR.

24. The bispecific polypeptide or polypeptide for use according to Claim 23 wherein the cancer and/or the tumour comprises target cells comprising expression of CEA,

optionally wherein the expression of CEA is an intermediate level of CEA expression or a high level of CEA expression,

optionally wherein the intermediate level of CEA expression is characterised by the target cell expressing about 10,000 or more CEA receptors per target cell, preferably about 50,000 or more CEA receptors per target cell, optionally wherein the high level of CEA expression is characterised by the target cell expressing about 200,000 or more CEA receptors per target cell, preferably about 300,000 or more CEA receptors per target cell.

25. The bispecific polypeptide or polypeptide for use according to Claim 23 or 24, wherein the cancer and/or the tumour is one or more cancer and/or tumour selected from the list consisting of: prostate cancer and/or a prostate tumour; breast cancer and/or a breast tumour; lung cancer and/or a lung tumour; colorectal cancer and/or a colorectal tumour; melanomas; bladder cancer and/or a bladder tumour; brain/CNS cancer and/or a brain/CNS tumour; cervical cancer and/or a cervical tumour; oesophageal cancer and/or a oesophageal tumour; gastric cancer and/or a gastric tumour; head/neck cancer and/or a head/neck tumour; kidney cancer and/or a kidney tumour; liver cancer and/or a liver tumour; carcinoma; leukaemia; lymphomas; ovarian cancer and/or an ovarian tumour; pancreatic cancer and/or a pancreatic tumour; tonsil cancer and/or a tonsil tumour; and sarcomas,

optionally wherein the one or more cancer and/or tumour selected from the list consisting of: breast cancer and/or a breast tumour; lung cancer and/or a lung tumour; colorectal cancer and/or a colorectal tumour; gastric cancer and/or a gastric tumour; and/or pancreatic cancer and/or a pancreatic tumour,

and/or wherein the tumour is a solid tumour,

or wherein the one or more non-cancer condition is selected from the list consisting of: ulcerative colitis, pancreatitis; cirrhosis; COPD; Crohn's disease; and/or hypothyroidism.