

CLAIMS

1. ~~_____~~ A polypeptide that comprises ~~or consists of~~ at least three immunoglobulin single variable domains (ISVDs), wherein each of said ISVDs comprises three complementarity determining regions (CDRs), CDR1 to CDR3, respectively), ~~wherein the at least three ISVDs are optionally linked via one or more peptidic linkers~~, and wherein:

a) ~~_____~~ a first ISVD specifically binds to the constant domain of ~~the~~ a T cell receptor (TCR) on a T cell and comprises:

~~i. a CDR1 that iscomprising~~ the amino acid sequence of SEQ ID NO: 6 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 6;~~

~~ii. a CDR2 that iscomprising~~ the amino acid sequence of SEQ ID NO: 10 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 10;~~ and

~~iii. a CDR3 that iscomprising~~ the amino acid sequence of SEQ ID NO: 14 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 14;~~

b) ~~_____~~ a second ISVD specifically binds to Glypican-3 (GPC3) and comprises:

~~iv. a CDR1 that iscomprising~~ the amino acid sequence of SEQ ID NO: 7 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 7;~~

~~v. a CDR2 that iscomprising~~ the amino acid sequence of SEQ ID NO: 11 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 11;~~ and

~~vi. a CDR3 that iscomprising~~ the amino acid sequence of SEQ ID NO: 15 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 15;~~ and

c) ~~_____~~ a third ISVD specifically binds to GPC3 and comprises:

~~vii. a CDR1 that iscomprising~~ the amino acid sequence of SEQ ID NO: 8 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 8;~~

~~viii. a CDR2 that iscomprising~~ the amino acid sequence of SEQ ID NO: 12 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 12;~~ and

~~ix. a CDR3 that iscomprising~~ the amino acid sequence of SEQ ID NO: 16 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 16;~~

wherein the order of the ISVDs indicates their relative position to each other considered from the N-terminus to the C-terminus of said polypeptide, ~~wherein the first ISVDs is optionally located at the N-terminus of said polypeptide.~~

2. ~~_____~~ The polypeptide according to claim 1, wherein:

- a) ~~_____~~ said first ISVD comprises a CDR1 beingconsisting of the amino acid sequence of SEQ ID NO: 6, a CDR2 beingconsisting of the amino acid sequence of SEQ ID NO: 10 and a CDR3 beingconsisting of the amino acid sequence of SEQ ID NO: 14;
- b) said second ISVD comprises a CDR1 beingconsisting of the amino acid sequence of SEQ ID NO: 7, a CDR2 beingconsisting of the amino acid sequence of SEQ ID NO: 11 and a CDR3 beingconsisting of the amino acid sequence of SEQ ID NO: 15; and
- c) ~~_____~~ said third ISVD comprises a CDR1 beingconsisting of the amino acid sequence of SEQ ID NO: 8, a CDR2 beingconsisting of the amino acid sequence of SEQ ID NO: 12 and a CDR3 beingconsisting of the amino acid sequence of SEQ ID NO: 16.
3. ~~_____~~ The polypeptide according to any of claimsclaim 1-or 2, wherein:
- a) ~~_____~~ ~~the amino acid sequence of~~ said first ISVD exhibits-acomprises the amino acid sequence identity-of more than 90% with SEQ ID NO: 2;
- b) ~~_____~~ ~~said second ISVD comprises~~ the amino acid sequence of ~~said second ISVD exhibits a sequence identity of more than 90% with~~ SEQ ID NO: 3; and
- c) ~~_____~~ ~~the amino acid sequence of~~ said third ISVD exhibits-acomprises the amino acid sequence identity of more than 90% identity with SEQ ID NO: 4.
4. ~~_____~~ The polypeptide according to any of claimsclaim 1-to 3, wherein:
- a) ~~_____~~ said first ISVD consists of the amino acid sequence of SEQ ID NO: 2;
- b) ~~_____~~ said second ISVD consists of the amino acid sequence of SEQ ID NO: 3; and
- c) ~~_____~~ said third ISVD consists of the amino acid sequence of SEQ ID NO: 4.
5. ~~_____~~ The polypeptide according to any of claimsclaim 1-to 4, wherein the first ISVD and the second ISVD are linked to each other via a linker consisting of less than 10 amino acids, preferably a linker consisting of less than 6 amino acids, ~~wherein the linker most preferably is or~~ a 5GS linker.
6. ~~_____~~ The polypeptide according to any of claimsclaim 1-to 5, wherein said polypeptide further comprises one or more other groups, residues, moieties or binding units, optionally linked via one or more peptidic linkers, in which said one or more other groups, residues, moieties or binding units provide the polypeptide with increased half-life, compared to the corresponding polypeptide without said one or more other groups, residues, moieties or binding units.
7. ~~_____~~ The polypeptide according to claim 6, in which said one or more other groups, residues, moieties or binding units that provide the polypeptide with increased half-life is chosen from the group consisting of a polyethylene glycol molecule, serum proteins or fragments thereof, binding units that can bind to serum proteins, an Fc portion, and small proteins or peptides that can bind to serum proteins.

8. ~~_____~~ The polypeptide according to ~~any one of claims 6 or~~ claim 7, in which said one or more other groups, residues, moieties or binding units that provide the polypeptide with increased half-life ~~is chosen from the group consisting of binding units that can bind to serum albumin (such as human serum albumin) or a serum immunoglobulin (such as IgG).~~

9. ~~_____~~ The polypeptide according to ~~claim 8, in which said binding unit that provides the polypeptide with increased half-life~~ comprise an ISVD that binds to human serum albumin.

10. ~~_____~~

9. The polypeptide according to claim 98, wherein the ISVD binding to human serum albumin comprises

i. ~~_____~~ a CDR1 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 9 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 9;~~

ii. ~~_____~~ a CDR2 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 13 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 13; and~~

iii. ~~_____~~ and a CDR3 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 17 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 17.~~

11. ~~The polypeptide according to any of claims 9 or 10, wherein the ISVD binding to human serum albumin comprises a CDR1 being the amino acid sequence of SEQ ID NO: 9, a CDR2 being the amino acid sequence of SEQ ID NO: 13 and a CDR3 being the amino acid sequence of SEQ ID NO: 17.~~

12. ~~The polypeptide according to any of claims 9 to 11, wherein the amino acid sequence of said ISVD binding to human serum albumin exhibits a sequence identity of more than 90% with SEQ ID NO: 5.~~

13. ~~_____~~ The polypeptide according to ~~any of claims 9 to 12~~

10. The polypeptide according to claim 8, wherein said ISVD binding to human serum albumin consists of the amino acid sequence of SEQ ID NO: 5.

14. ~~_____~~

11. The polypeptide according to ~~any of claims~~ claim 1 to 13, wherein the polypeptide comprises ~~or consists of an the~~ amino acid sequence ~~exhibiting a sequence identity of more than 90% with of~~ SEQ ID NO: 1.

15. ~~_____~~

12. The polypeptide according to ~~any of claims~~ claim 1 to 14, wherein the polypeptide ~~comprises or~~ consists of the amino acid sequence of SEQ ID NO: 1.

16. ~~_____~~

13. A polypeptide that comprises ~~or consists of~~ at least one immunoglobulin single variable domain (ISVD) that specifically binds Glypican-3 (GPC3), wherein said ISVD comprises three

complementarity determining regions (CDRs, CDR1 to CDR3, respectively)~~7_z~~ and wherein the at least one ISVD comprises:

~~a)~~ a) a CDR1 ~~that is~~consisting of the amino acid sequence of SEQ ID NO: 7 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 7;~~_z

a CDR2 ~~that is~~consisting of the amino acid sequence of SEQ ID NO: 11 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 11;~~ and

a CDR3 ~~that is~~consisting of the amino acid sequence of SEQ ID NO: 15 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 15;~~_z or

~~b)~~ b) a CDR1 ~~that is~~consisting of the amino acid sequence of SEQ ID NO: 8 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 8;~~_z

a CDR2 ~~that is~~consisting of the amino acid sequence of SEQ ID NO: 12 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 12;~~ and

a CDR3 ~~that is~~consisting of the amino acid sequence of SEQ ID NO: 16 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 16;~~_z

~~17.~~ The polypeptide according to claim 16, wherein the at least one ISVD comprises:

~~a) a CDR1 being the amino acid sequence of SEQ ID NO: 7, a CDR2 being the amino acid sequence of SEQ ID NO: 11 and a CDR3 being the amino acid sequence of SEQ ID NO: 15, or~~

~~b) a CDR1 being the amino acid sequence of SEQ ID NO: 8, a CDR2 being the amino acid sequence of SEQ ID NO: 12 and a CDR3 being the amino acid sequence of SEQ ID NO: 16.~~

~~18.~~ The polypeptide according to any of claims 16 or 17, wherein the amino acid sequence of the at least one ISVD comprises or consists of:

~~a) an amino acid sequence with a sequence identity of more than 90% with SEQ ID NO: 3, or~~

~~b) an amino acid sequence with a sequence identity of more than 90% identity with SEQ ID NO: 4.~~

~~19.~~ The polypeptide according to any of claims 16 to 18, wherein said at least one ISVD comprises or consists of:

~~a) the amino acid sequence of SEQ ID NO: 3, or~~

~~b) the amino acid sequence of SEQ ID NO: 4.~~

~~20. —~~

~~14. A polypeptide that comprises ~~or consists of~~ at least two immunoglobulin single variable domains (ISVDs), wherein each of said ISVDs comprises three complementarity determining regions (CDRs), CDR1 to CDR3, respectively), ~~and~~ wherein:~~

~~a) each of a first and a second ISVD specifically binds to Glypican-3 (GPC3) and comprises:~~

~~i. a CDR1 consisting of the ~~at least two~~ ISVDs are optionally linked via one or more peptidic linkers, amino acid sequence of SEQ ID NO: 7;~~

~~ii. a CDR2 consisting of the amino acid sequence of SEQ ID NO: 11; and wherein:~~

~~a) —~~

~~iii. a CDR3 consisting of the amino acid sequence of SEQ ID NO: 15;~~

~~b) each of~~ a first and a second ISVD specifically binds to GPC3 and comprises:

~~i. i. a CDR1 that is the amino acid sequence consisting of SEQ ID NO: 7 or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 7;~~

~~ii. a CDR2 that is the amino acid sequence of SEQ ID NO: 11 or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 11; and~~

~~iii. a CDR3 that is the amino acid sequence of SEQ ID NO: 15 or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 15;~~

~~b) —~~ a first and a second ISVD specifically binds to GPC3 and comprises

~~i. a CDR1 that is the amino acid sequence of SEQ ID NO: 8 or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 8;~~

~~ii. ii. a CDR2 that is consisting of the amino acid sequence of SEQ ID NO: 12 or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 12; and, and~~

~~iii. iii. a CDR3 that is consisting of the amino acid sequence of SEQ ID NO: 16 or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 16;~~

~~c) —~~ a first ISVD specifically binds to GPC3 and comprises:

~~i. i. a CDR1 that is consisting of the amino acid sequence of SEQ ID NO: 7 or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 7;~~

~~ii. ii. a CDR2 that is consisting of the amino acid sequence of SEQ ID NO: 11 or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 11; and~~

~~iii. iii. a CDR3 that is consisting of the amino acid sequence of SEQ ID NO: 15 or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 15;~~ and

a second ISVD specifically binds to GPC3 and comprises:

iv. ~~i.~~ a CDR1 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 8 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 8;~~_i

~~v.~~ v. a CDR2 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 12 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 12;~~ and

~~vi.~~ vi. a CDR3 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 16 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 16;~~_i

d) ~~—~~ a first ISVD specifically binds to GPC3 and comprises:

~~i.~~ i. a CDR1 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 8 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 8;~~_i

~~ii.~~ ii. a CDR2 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 12 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 12;~~ and

~~iii.~~ iii. a CDR3 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 16 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 16;~~_i and

a second ISVD specifically binds to GPC3 and comprises:

~~iv.~~ iv. a CDR1 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 7 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 7;~~_i

~~v.~~ v. a CDR2 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 11 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 11;~~ and

~~vi.~~ vi. a CDR3 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 15 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 15;~~_i

~~a)~~ e) a first ISVD specifically binds to the constant domain of ~~the~~_a T cell receptor (TCR) on a T cell ~~and comprises~~ and comprises:

~~i.~~ i. a CDR1 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 6 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 6;~~_i

~~ii.~~ ii. a CDR2 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 10 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 10;~~ and ~~and~~

~~iii.~~ iii. a CDR3 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 14 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 14;~~_i and

a second ISVD specifically binds to GPC3 and comprises:

~~iv.~~ iv. a CDR1 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 7 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 7;~~_i

v- ~~v.~~ a CDR2 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 11 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 11~~; and

vi- ~~vi.~~ a CDR3 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 15 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 15~~;

b) ~~f)~~ a first ISVD specifically binds to GPC3 and comprises:

i- ~~i.~~ a CDR1 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 7 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 7~~;

ii- ~~ii.~~ a CDR2 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 11 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 11~~; and

iii- ~~iii.~~ a CDR3 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 15 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 15~~; and

a second ISVD specifically binds to the constant domain of ~~the~~ TCR on a T cell and comprises:

iv- ~~iv.~~ a CDR1 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 6 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 6~~;

v- ~~v.~~ a CDR2 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 10 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 10~~; and

vi- ~~vi.~~ a CDR3 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 14 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 14~~;

e) ~~g)~~ a first ISVD specifically binds to the constant domain of ~~the~~ TCR on a T cell and comprises:

i- ~~i.~~ a CDR1 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 6 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 6~~;

ii- ~~ii.~~ a CDR2 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 10 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 10~~; and

iii- ~~iii.~~ a CDR3 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 14 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 14~~; and

a second ISVD specifically binds to GPC3 and comprises:

iv- ~~iv.~~ a CDR1 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 8 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 8~~;

v- ~~v.~~ a CDR2 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 12 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 12~~; and

~~vi.~~ vi. a CDR3 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 16 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 16;~~ or

~~d)~~ h) a first ISVD specifically binds to GPC3 and comprises:

~~i.~~ i. a CDR1 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 8 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 8;~~

~~ii.~~ ii. a CDR2 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 12 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 12;~~ and

~~iii.~~ iii. a CDR3 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 16 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 16;~~ and

a second ISVD specifically binds to the constant domain of ~~the~~ a TCR on a T cell and comprises:

~~iv.~~ iv. a CDR1 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 6 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 6;~~

~~v.~~ v. a CDR2 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 10 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 10;~~ and

~~vi.~~ vi. a CDR3 ~~that is consisting of~~ the amino acid sequence of SEQ ID NO: 14 ~~or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 14;~~

~~vi.~~

wherein the order of the ISVDs indicates their relative position to each other considered from the N-terminus to the C-terminus of said polypeptide.

~~21.~~ 21. The polypeptide according to claim 20, wherein:

~~a) the first and the second ISVD specifically binds to GPC3 and comprises a CDR1 being the amino acid sequence of SEQ ID NO: 7, a CDR2 being the amino acid sequence of SEQ ID NO: 11 and a CDR3 being the amino acid sequence of SEQ ID NO:~~

~~15;~~

~~b) the first and the second ISVD specifically binds to GPC3 and comprises a CDR1 being the amino acid sequence of SEQ ID NO: 8, a CDR2 being the amino acid sequence of SEQ ID NO: 12 and a CDR3 being the amino acid sequence of SEQ ID NO: 16;~~

~~c) the first ISVD specifically binds to GPC3 and comprises a CDR1 being the amino acid sequence of SEQ ID NO: 7, a CDR2 being the amino acid sequence of SEQ ID NO: 11 and a CDR3 being the amino acid sequence of SEQ ID NO: 15, and the second ISVD specifically binds to GPC3 and comprises a CDR1 being the amino acid sequence of SEQ ID NO: 8, a CDR2 being the amino acid sequence of SEQ ID NO: 12 and a CDR3 being the amino acid sequence of SEQ ID NO: 16;~~

- d) ~~the first ISVD specifically binds to GPC3 and comprises a CDR1 being the amino acid sequence of SEQ ID NO: 8, a CDR2 being the amino acid sequence of SEQ ID NO: 12 and a CDR3 being the amino acid sequence of SEQ ID NO: 16, and the second ISVD specifically binds to GPC3 and comprises a CDR1 being the amino acid sequence of SEQ ID NO: 7, a CDR2 being the amino acid sequence of SEQ ID NO: 11 and a CDR3 being the amino acid sequence of SEQ ID NO: 15,~~
- e) ~~the first ISVD specifically binds to the constant domain of the TCR on a T cell and comprises a CDR1 being the amino acid sequence of SEQ ID NO: 6, a CDR2 being the amino acid sequence of SEQ ID NO: 10 and a CDR3 being the amino acid sequence of SEQ ID NO: 14, and the second ISVD specifically binds to GPC3 and comprises a CDR1 being the amino acid sequence of SEQ ID NO: 7, a CDR2 being the amino acid sequence of SEQ ID NO: 11 and a CDR3 being the amino acid sequence of SEQ ID NO: 15,~~
- f) ~~the first ISVD specifically binds to GPC3 and comprises a CDR1 being the amino acid sequence of SEQ ID NO: 7, a CDR2 being the amino acid sequence of SEQ ID NO: 11 and a CDR3 being the amino acid sequence of SEQ ID NO: 15, and the second ISVD specifically binds to the constant domain of the TCR on a T cell and comprises a CDR1 being the amino acid sequence of SEQ ID NO: 6, a CDR2 being the amino acid sequence of SEQ ID NO: 10 and a CDR3 being the amino acid sequence of SEQ ID NO: 14,~~
- g) ~~the first ISVD specifically binds to the constant domain of the TCR on a T cell and comprises a CDR1 being the amino acid sequence of SEQ ID NO: 6, a CDR2 being the amino acid sequence of SEQ ID NO: 10 and a CDR3 being the amino acid sequence of SEQ ID NO: 14, and the second ISVD specifically binds to GPC3 and comprises a CDR1 being the amino acid sequence of SEQ ID NO: 8, a CDR2 being the amino acid sequence of SEQ ID NO: 12 and a CDR3 being the amino acid sequence of SEQ ID NO: 16, or~~
- h) ~~the first ISVD specifically binds to GPC3 and comprises a CDR1 being the amino acid sequence of SEQ ID NO: 8, a CDR2 being the amino acid sequence of SEQ ID NO: 12 and a CDR3 being the amino acid sequence of SEQ ID NO: 16, and the second ISVD specifically binds to the constant domain of the TCR on a T cell and comprises a CDR1 being the amino acid sequence of SEQ ID NO: 6, a CDR2 being the amino acid sequence of SEQ ID NO: 10 and a CDR3 being the amino acid sequence of SEQ ID NO: 14.~~

22. ~~The polypeptide according to any of claims 20 or 21, wherein:~~

- a) ~~the amino acid sequence of the first and the second ISVD that specifically binds to GPC3 exhibits a sequence identity of more than 90% with SEQ ID NO: 3,~~
- b) ~~the amino acid sequence of the first and the second ISVD that specifically binds to GPC3 exhibits a sequence identity of more than 90% with SEQ ID NO: 4,~~
- c) ~~the amino acid sequence of the first ISVD that specifically binds to GPC3 exhibits a sequence identity of more than 90% with SEQ ID NO: 3, and the second ISVD that specifically binds to GPC3 exhibits a sequence identity of more than 90% identity with SEQ ID NO: 4,~~
- d) ~~the amino acid sequence of the first ISVD that specifically binds to GPC3 exhibits a sequence identity of more than 90% with SEQ ID NO: 4, and the second ISVD that specifically binds to GPC3 exhibits a sequence identity of more than 90% identity with SEQ ID NO: 3,~~
- e) ~~the amino acid sequence of the first ISVD that specifically binds to the constant domain of the TCR on a T cell exhibits a sequence identity of more than 90% with SEQ ID NO: 2, and the second ISVD that specifically binds to GPC3 exhibits a sequence identity of more than 90% identity with SEQ ID NO: 3,~~
- f) ~~the amino acid sequence of the first ISVD that specifically binds to GPC3 exhibits a sequence identity of more than 90% with SEQ ID NO: 3, and the second ISVD that specifically binds to the constant domain of the TCR on a T cell exhibits a sequence identity of more than 90% identity with SEQ ID NO: 2~~
- g) ~~the amino acid sequence of the first ISVD that specifically binds to the constant domain of the TCR on a T cell exhibits a sequence identity of more than 90% with SEQ ID NO: 2, and the second ISVD that specifically binds to GPC3 exhibits a sequence identity of more than 90% identity with SEQ ID NO: 4, or~~
- h) ~~the amino acid sequence of the first ISVD that specifically binds to GPC3 exhibits a sequence identity of more than 90% with SEQ ID NO: 4, and the second ISVD that specifically binds to the constant domain of the TCR on a T cell exhibits a sequence identity of more than 90% identity with SEQ ID NO: 2.~~

23. ~~The polypeptide according to any of claims 20 to 22, wherein:~~

- a) ~~the first and the second ISVD that specifically binds to GPC3 consist of the amino acid sequence of SEQ ID NO: 3,~~
- b) ~~the first and the second ISVD that specifically binds to GPC3 consist of the amino acid sequence of SEQ ID NO: 4,~~
- c) ~~the first ISVD that specifically binds to GPC3 consists of the amino acid sequence of SEQ ID NO: 3, and the second ISVD that specifically binds to GPC3 consists of the amino acid sequence of SEQ ID NO: 4,~~
- d) ~~the first ISVD that specifically binds to GPC3 consists of the amino acid sequence of SEQ ID NO: 4, and the second ISVD that specifically binds to GPC3 consists of the amino acid sequence of SEQ ID NO: 3,~~
- e) ~~the first ISVD that specifically binds to the constant domain of the TCR on a T cell consists of the amino acid sequence of SEQ ID NO: 2, and the second ISVD that specifically binds to GPC3 consists of the amino acid sequence of SEQ ID NO: 3,~~
- f) ~~the first ISVD that specifically binds to GPC3 consists of the amino acid sequence of SEQ ID NO: 3, and the second ISVD that specifically binds to the constant domain of the TCR on a T cell consists of the amino acid sequence of SEQ ID NO: 2,~~
- g) ~~the first ISVD that specifically binds to the constant domain of the TCR on a T cell consists of the amino acid sequence of SEQ ID NO: 2, and the second ISVD that specifically binds to GPC3 consists of the amino acid sequence of SEQ ID NO: 4, or~~
- h) ~~the first ISVD that specifically binds to GPC3 consists of the amino acid sequence of SEQ ID NO: 4, and the second ISVD that specifically binds to the constant domain of the TCR on a T cell consists of the amino acid sequence of SEQ ID NO: 2.~~

~~24. The polypeptide according to any of claims 20 to 23, wherein the polypeptide comprises or consists of an amino acid sequence selected from SEQ ID NOs: 1, 49-72 and 78-81.~~

~~25. The polypeptide according to any of claims 16 to 24, wherein said polypeptide further comprises one or more other groups, residues, moieties or binding units, optionally linked via one or more peptidic linkers, in which said one or more other groups, residues, moieties or binding units provide the polypeptide with increased half-life, compared to the corresponding polypeptide without said one or more other groups, residues, moieties or binding units.~~

~~26. The polypeptide according to claim 25, in which said one or more other groups, residues, moieties or binding units that provide the polypeptide with increased half-life is chosen from the group consisting of a polyethylene glycol molecule, serum proteins or fragments thereof, binding units that can bind to serum proteins, an Fc portion, and small proteins or peptides that can bind to serum proteins.~~

~~27. The polypeptide according to any one of claims 25 to 26, in which said one or more other binding units that provide the polypeptide with increased half-life is chosen from the group consisting of binding units that can bind to serum albumin (such as human serum albumin) or a serum immunoglobulin (such as IgG).~~

~~28. The polypeptide according to claim 27, in which said binding unit that provides the polypeptide with increased half-life is an ISVD that binds to human serum albumin.~~

~~29. The polypeptide according to claim 28, wherein the ISVD binding to human serum albumin comprises~~

- ~~i. — a CDR1 that is the amino acid sequence of SEQ ID NO: 9 or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 9;~~
- ~~ii. — a CDR2 that is the amino acid sequence of SEQ ID NO: 13 or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 13; and~~
- ~~iii. — a CDR3 that is the amino acid sequence of SEQ ID NO: 17 or an amino acid sequence with 2 or 1 amino acid difference(s) with SEQ ID NO: 17.~~

~~30. The polypeptide according to any of claims 28 to 29, wherein the ISVD binding to human serum albumin comprises a CDR1 that is the amino acid sequence of SEQ ID NO: 9, a CDR2 being the amino acid sequence of SEQ ID NO: 13 and a CDR3 being the amino acid sequence of SEQ ID NO: 17.~~

~~31. The polypeptide according to any of claims 28 to 30, wherein the amino acid sequence of said ISVD binding to human serum albumin exhibits a sequence identity of more than 90% with SEQ ID NO: 5.~~

~~32. The polypeptide according to any of claims 28 to 31, wherein said ISVD binding to human serum albumin consists of the amino acid sequence of SEQ ID NO: 5.~~

~~33. A nucleic acid comprising a nucleotide sequence that encodes a polypeptide according to any of claims 1 to 32, preferably according to any of claims 1 to 15 claim 1.~~

~~34. —~~

~~16. A host or host cell comprising a nucleic acid according to claim 33 15.~~

~~35. —~~

~~17. A method for producing a polypeptide according to any of claims 1 to 32, preferably according to any of claims 1 to 15, said method at least comprising the steps of:~~

~~a) —~~

~~expressing, in a suitable host cell or host organism or in another suitable expression system, a nucleic acid according to claim 33; optionally followed by: 15.~~

~~b) — isolating and/or purifying the polypeptide according to any of claims 1 to 32, preferably according to any of claims 1 to 15.~~

~~36. —~~

~~18. A composition comprising at least one polypeptide according to any of claims 1 to 32, preferably according to any of claims 1 to 15, or a nucleic acid according to claim 33 1.~~

~~37. —~~

~~19. The composition according to claim 36 18, which is a pharmaceutical composition which further comprises at least one pharmaceutically acceptable carrier, diluent or excipient and/or adjuvant; and optionally comprises one or more further pharmaceutically active polypeptides and/or compounds.~~

~~38. A polypeptide according to any of claims 1 to 32, preferably according to any of claims 1 to 15, or a composition according to claim 36 or 37, for use as a medicament.~~

~~39. A polypeptide according to any of claims 1 to 32, preferably according to any of claims 1 to 15, or a composition according to claim 36 or 37, for use in the treatment of cancer, preferably liver cancer or lung cancer.~~

~~40. The polypeptide or composition for use according to claim 39, wherein the liver cancer is hepatocellular carcinoma.~~

~~41. —~~

~~20. Use of a pharmaceutically active amount of a polypeptide according to claim 1 in the manufacture of a medicament for A method of treating cancer, preferably liver cancer or lung cancer in, wherein said method comprises administering, to a subject in need thereof, a pharmaceutically active amount of a polypeptide according to any of claims 1 to 32, preferably according to any of claims 1 to 15, or a composition according to claim 36 or 37.~~

~~42. —~~

~~21. The method according to claim 41, wherein the liver cancer is hepatocellular carcinoma.~~

~~43. — Use of a polypeptide according to any of claims claim 1 to 32, preferably according to any of claims 1 to 15, wherein the at least three ISVDs are linked via one or a composition according to claim 36 or 37, in the preparation of a medicament more peptidic linkers.~~

~~44. — Use of a~~

22. The polypeptide according to ~~any~~claim 1, wherein the first ISVD is located at the N-terminus of claims 1 to 32, preferably said polypeptide.

23. The polypeptide according to claim 6, wherein the one or more other groups, residues, moieties or binding units are linked via one or more peptidic linkers.

24. The polypeptide according to ~~claims 1~~claim 7, wherein said one or more other groups, residues, moieties or binding units that provide the polypeptide with increased half-life comprise a binding units that can bind to 15, or a serum albumin or a serum immunoglobulin.

25. The polypeptide according to claim 14, wherein the at least two ISVDs are linked via one or more peptidic linkers.

26. The method according to claim 17, further comprising:

isolating and/or purifying the polypeptide encoded by the nucleic acid.

27. The composition according to claim ~~36 or 37, in~~19, wherein the ~~preparation of a pharmaceutical composition for treating cancer, preferably liver cancer comprises one or more further pharmaceutically active polypeptides and/or lung cancer compounds.~~

~~45. Use of the polypeptide or a composition~~

28. The use according to ~~claims 44~~claim 20, wherein the liver cancer is hepatocellular carcinoma.