CLAIMS

1. A polypeptide for use in the treatment of Glypican-3-positive (GPC3+) solid tumours wherein the polypeptide comprises or consists of at least three immunoglobulin single variable domains (ISVDs), wherein each of said ISVDs comprises three complementarity determining regions (CDR1 to CDR3, respectively), and wherein:

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

i. a CDR1 that is the amino acid sequence of SEQ ID NO: 6;
ii. a CDR2 that is the amino acid sequence of SEQ ID NO: 10; and
iii. a CDR3 that is the amino acid sequence of SEQ ID NO: 14;

b) a second ISVD specifically binds to GPC3 and comprises

iv. a CDR1 that is the amino acid sequence of SEQ ID NO: 7;
v. a CDR2 that is the amino acid sequence of SEQ ID NO: 11; and
vi. a CDR3 that is the amino acid sequence of SEQ ID NO: 15; and

c) a third ISVD specifically binds to GPC3 and comprises

vii. a CDR1 that is the amino acid sequence of SEQ ID NO: 8;
viii. a CDR2 that is the amino acid sequence of SEQ ID NO: 12; and
ix. a CDR3 that is the amino acid sequence of SEQ ID NO: 16,

wherein the CDRs are defined according to AbM annotation, and

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.

2. The polypeptide for use according to claim 1, wherein the first ISVDs is located at the N-terminus of said polypeptide.

3. The polypeptide for use according to claim 1 or 2, wherein

a) the amino acid sequence of said first ISVD comprised in the polypeptide exhibits a sequence identity of more than 90% with SEQ ID NO: 2, or said first ISVD comprised in the polypeptide consists of the amino acid sequence of SEQ ID NO: 2;

b) the amino acid sequence of said second ISVD comprised in the polypeptide exhibits a sequence identity of more than 90% with SEQ ID NO: 3, or said second ISVD comprised in the polypeptide consists of the amino acid sequence of SEQ ID NO: 3; and

c) the amino acid sequence of said third ISVD comprised in the polypeptide exhibits a sequence identity of more than 90% identity with SEQ ID NO: 4, or said third ISVD comprised in the polypeptide consists of the amino acid sequence of SEQ ID NO: 4,

wherein the CDRs are defined according to AbM annotation.

4. The polypeptide for use according to any one of claims 1-3, wherein the at least three ISVDs are linked via one or more peptidic linkers, optionally wherein the first ISVD and the second ISVD comprised in the polypeptide are linked to each other via the peptidic linker consisting of less than 10 amino acids, preferably less than 6 amino acids, wherein the linker most preferably is a 5GS linker.

5. The polypeptide for use according to any one of claims 1-4, wherein the 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.

6. The polypeptide for use according to claim 5, wherein 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.

7. The polypeptide for use according to claim 5 or 6, 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 or a serum immunoglobulin, preferably said binding

unit is an ISVD that binds to human serum albumin, further preferably wherein the ISVD binding to human serum albumin comprises:

i. a CDR1 that is the amino acid sequence of SEQ ID NO: 9;

ii. a CDR2 that is the amino acid sequence of SEQ ID NO: 13; and

iii. a CDR3 that is the amino acid sequence of SEQ ID NO: 17,

wherein the CDRs are defined according to AbM annotation.

8. The polypeptide for use according to claim 7, 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, or said ISVD binding to human serum albumin consists of the amino acid sequence of SEQ ID NO: 5.

9. The polypeptide for use according to any one of claims 1-8, wherein the polypeptide comprises or consists of an amino acid sequence exhibiting a sequence identity of more than 90% with SEQ ID NO: 1, or the polypeptide comprises or consists of the amino acid sequence of SEQ ID NO: 1.

10. Composition for use in the treatment of GPC3+ solid tumours, wherein the composition comprises the polypeptide as defined in any one of claims 1-9, optionally comprising pharmaceutically acceptable excipients, and preferably wherein the composition is provided as a liquid formulation.

11. The polypeptide or composition for use according to any one of claims 1-10, wherein the polypeptide or composition is to be administered to a subject in need thereof together with a PD-L1 inhibitor, preferably wherein the PD-L1 inhibitor is an anti-PD-L1 monoclonal antibody, further preferably Atezolizumab.

12. The polypeptide or composition for use according to any one of claims 1-11, wherein the GPC3+ solid tumour is selected from hepatocellular carcinoma (HCC) and non-small cell lung cancer (NSCLC), preferably wherein NSCLC is metastatic NSCLC.

13. The polypeptide or composition for use according to any one of claims 1-12, wherein the polypeptide and/or composition is to be administered to a subject in need thereof:

(a) intravenously or subcutaneously;

(b) at a dosage of between 1 and 200 mg, preferably between 1 and 70 mg, or 1 to 72 mg, or about 1 mg, or about 3 mg, or in an amount of between 1 and 36 mg;

(c) at a dosage of between 15 and 3500 μg/kg, preferably between 45 and 1100 μg/kg; and/or

(d) at most twice a week to a subject in need thereof, preferably once a week.

14. The polypeptide or composition for use according to any one of claims 1-13, wherein the administration of the polypeptide to a subject in need thereof results in a decrease in alpha-fetoprotein (AFP) level of at least 20% from baseline, preferably in a decrease in AFP level of at least 30% from baseline, more preferably in a decrease in AFP level of at least 40% from baseline, such as a decrease in AFP level of at least 50%, at least 55%, at least 59%, at least 60%, or at least 70% from baseline, wherein a decrease in AFP levels of at least 20% from baseline is maintained for at least two, preferably for at least three, more preferably for at least six weeks or more of treatment.

15. Use of a peptide or composition as defined in any one of claims 1-14 for the manufacture of a medicament for the treatment of Glypican-3-positive (GPC3+) solid tumours.