

necessarily induce effective cell killing, an observation that may at least in part arise from differential endosomal/lysosomal processing pathways in different types of cancer cells.

Therapeutic antibodies may require substantial quantities of product over multiple dosages to be clinically effective (e.g. 200–350mg/m² per dose). A therapeutic dose of ADC may often be marginally less than that of naked therapeutic monoclonal antibodies (TMAs) (e.g. at 160 mg per dose). However, ADC construction involves additional technologies such as chemical conjugation steps that complicate production streams and can raise the cost of manufacture significantly. It is therefore desirable to provide therapeutic dose ADCs at lower cost where possible.

Despite the promise that antibodies offer as therapeutic agents, a need continues to exist for effective therapeutic antibodies to treat prostate, bladder, and/or pancreatic cancer.

Summary of the Invention

The present inventors have surprisingly identified that the BLCA-38 antibody referred to and used in the aforementioned prior art is a combination of two distinct monoclonal antibodies in a mixed population. It has been determined that only one of these antibody species is capable of binding strongly to the relevant target antigen present on prostate cancer cells, whilst the second species cannot. Moreover, it has been unexpectedly discovered that the antibody species is capable of binding to the relevant target antigen present on prostate cancer cells is internalised upon doing so, despite the aforementioned prior art indicating to the contrary. Moreover, the present inventors have demonstrated effective internalisation in prostate, bladder and pancreatic cancer cells providing a means of targeting and killing these cancer cell types.

Accordingly, in a first aspect the present invention provides a use of an anti-glypican-1 (anti-GPC1) antibody and/or an antigen-binding fragment thereof in the preparation of a medicament for treating prostate, bladder, and/or pancreatic cancer in a subject, wherein the antibody and/or fragment is conjugated to at least one cytotoxic agent that is toxic to a prostate, bladder, and/or pancreatic cancer cell in the subject. Also disclosed is a method for treating prostate, bladder, and/or pancreatic cancer in a subject, the method comprising administering to the subject a pharmaceutical preparation comprising an anti-glypican-1 (anti-GPC1) antibody and/or an antigen-binding fragment thereof, wherein the antibody and/or fragment is conjugated to at least one cytotoxic agent that is toxic to a prostate, bladder, and/or pancreatic cancer cell in the subject.

Also disclosed is a method for killing a prostate, bladder, and/or pancreatic cancer cell in a subject, the method comprising administering to the subject a pharmaceutical preparation comprising an anti-glypican-1 (anti-GPC1) antibody and/or an antigen-binding fragment thereof, wherein the antibody and/or fragment is

conjugated to at least one cytotoxic agent that is toxic to the prostate, bladder, and/or pancreatic cancer cell in the subject.

Also disclosed is a method for treating a prostate, bladder, and/or pancreatic cancer tumour in a subject, the method comprising administering to the subject a pharmaceutical preparation comprising an anti-glypican-1 (anti-GPC1) antibody and/or an antigen-binding fragment thereof, wherein the antibody and/or fragment is conjugated to at least one cytotoxic agent that is toxic to a prostate, bladder, and/or pancreatic cancer cell in the tumour.

Also disclosed is a use of an anti-glypican-1 (anti-GPC1) antibody and/or an antigen-binding fragment thereof in the preparation of a medicament for treating prostate, bladder, and/or pancreatic cancer in a subject, wherein the antibody and/or fragment is conjugated to at least one cytotoxic agent that is toxic to a prostate, bladder, and/or pancreatic cancer cell in the subject.

Also disclosed is a use of an anti-glypican-1 (anti-GPC1) antibody and/or an antigen-binding fragment thereof in the preparation of a medicament for killing a prostate, bladder, and/or pancreatic cancer cell in a subject, wherein the antibody and/or fragment is conjugated to at least one cytotoxic agent that is toxic to a prostate, bladder, and/or pancreatic cancer cell in the subject.

Also disclosed is a use of an anti-glypican-1 (anti-GPC1) antibody and/or an antigen-binding fragment thereof in the preparation of a medicament treating a prostate, bladder, and/or pancreatic cancer tumour in a subject, wherein the antibody and/or fragment is conjugated to at least one cytotoxic agent that is toxic to a prostate, bladder, and/or pancreatic cancer cell in the subject.

Also disclosed is an anti-glypican-1 (anti-GPC1) antibody and/or an antigen-binding fragment thereof for use in treating prostate, bladder, and/or pancreatic cancer in a subject, wherein the antibody and/or fragment is conjugated to at least one cytotoxic agent that is toxic to a prostate, bladder, and/or pancreatic cancer cell in the subject.

Also disclosed is an anti-glypican-1 (anti-GPC1) antibody and/or an antigen-binding fragment thereof for use in killing a prostate, bladder, and/or pancreatic cancer cell in a subject, wherein the antibody and/or fragment is conjugated to at least one cytotoxic agent that is toxic to the prostate, bladder, and/or pancreatic cancer cell in the subject.

Also disclosed is an anti-glypican-1 (anti-GPC1) antibody and/or an antigen-binding fragment thereof for use in treating a prostate, bladder, and/or pancreatic cancer tumour in a subject, wherein the antibody and/or fragment is conjugated to at least one cytotoxic agent that is toxic to a prostate, bladder, and/or pancreatic cancer cell in the subject.

Also disclosed is a method of radioimaging a prostate, bladder, and/or pancreas in a subject, the method comprising:

administering to the subject a pharmaceutical preparation comprising an anti-glypican-1 (anti-GPC1) antibody and/or an antigen-binding fragment thereof, wherein the antibody and/or fragment is conjugated to at least one radioimaging agent,

detecting radiation emitted by the radioimaging agent, and

using the detected radiation to form a radioimage of the prostate, bladder, and/or pancreas.

In one example, the prostate of the subject is characterised by benign prostatic hyperplasia (BPH).

In one example, the prostate, bladder and/or pancreas of the subject is cancerous. In one embodiment of the tenth aspect, the subject suffers from prostate, bladder and/or pancreatic cancer.

In one example, the radiomaging agent is selected from the group consisting of: ^{18}F , ^{67}Ga , ^{68}Ga , ^{81}mKr , ^{82}Rb , ^{13}N , ^{99}mTc , ^{111}In , ^{123}I , ^{124}I , ^{133}Xe , ^{201}Tl , ^{177}Lu , ^{89}Zr , ^{64}Cu , ^{67}Cu , ^{32}P , and any combination thereof.

In one example, the radiomaging is single-photon emission computed tomography (SPECT) and the radioimaging agent is selected from the group consisting of: ^{99}mTc , ^{111}In , ^{67}Ga , ^{123}I , and any combination thereof.

In one example, the radiomaging is positron emission tomography (PET) and the radioimaging agent is selected from the group consisting of: ^{18}F , ^{68}Ga , ^{64}Cu , ^{86}Y , ^{124}I , ^{89}Zr , and any combination thereof.

In one example, the pharmaceutical preparation does not comprise an antibody with a light chain variable region comprising:

a complementarity determining region 1 (CDR1) comprising or consisting of an amino acid sequence defined by positions 48-58 of **SEQ ID NO: 11**;

a complementarity determining region 2 (CDR2) comprising or consisting of an amino acid sequence defined by positions 74-80 of **SEQ ID NO: 11**;

a complementarity determining region 3 (CDR3) comprising or consisting of an amino acid sequence defined by positions 113-121 of **SEQ ID NO: 11**.

In another example, the cytotoxic agent is a prodrug designed for activation upon uptake into an endosome or lysosome of said prostate, bladder, and/or pancreatic cancer cell.

In another example, the prodrug is conjugated to the antibody and/or an antigen-binding fragment thereof by:

an acid sensitive-linker susceptible to cleavage at a pH that is less than: pH 7.2, pH 7.0, pH 6.5, pH 6.0, pH 5.5, pH 5.0, pH 4.5, or pH 4.

an enzyme-cleavable linker, wherein the enzyme capable of cleaving the linker exists within the endosome or lysosome.

In another example, the cytotoxic agent is linked to the antibody and/or antigen binding fragment thereof by binding to a chelating agent conjugated to the antibody and/or antigen binding fragment thereof.

In an additional example, the antibody comprises:

(a) a heavy chain variable region comprising:

a complementarity determining region 1 (CDR1) comprising or consisting of an amino acid sequence defined by positions 50-54 of **SEQ ID NO: 3**;

a complementarity determining region 2 (CDR2) comprising or consisting of an amino acid sequence defined by positions 69-85 of **SEQ ID NO: 3**;

a complementarity determining region 3 (CDR3) comprising or consisting of an amino acid sequence defined by positions 118-126 of **SEQ ID NO: 3**; and

(b) a light chain variable region comprising:

a complementarity determining region 1 (CDR1) comprising or consisting of an amino acid sequence defined by positions 44-54 of **SEQ ID NO: 4**;

a complementarity determining region 2 (CDR2) comprising or consisting of an amino acid sequence defined by positions 70-76 of **SEQ ID NO: 4**;

a complementarity determining region 3 (CDR3) comprising or consisting of an amino acid sequence defined by positions 109-117 of **SEQ ID NO: 4**.

In one example, the antibody is produced by a hybridoma cell as deposited at Cellbank Australia under accession number CBA20140026, or progeny thereof.

In a further example, the antibody is:

(i) a humanised anti-GPC1 antibody,

- (ii) a chimeric anti-GPC1 antibody,
- (i) a human anti-GPC1 antibody,
- (ii) a monoclonal anti-GPC1 antibody,
- (iii) a multimeric anti-GPC1 antibody, or
- (iv) a synthetic anti-GPC1 antibody.

In one example, the antibody is a chimeric antibody comprising:

(a) a heavy chain constant region comprising or consisting of an amino acid sequence as defined in residues 138-467 of **SEQ ID NO: 7**; and

(b) a light chain constant region comprising or consisting of an amino acid sequence as defined in residues of 128-234 **SEQ ID NO: 8**.

In another example, the antigen-binding fragment thereof is: a single chain variable fragment (scFv), a variable domain (Fv) fragment, a fragment antigen binding (Fab) fragment, a F(ab)₂ fragment, a peptide, or a proteolytic fragment containing an epitope binding region.

In yet another example, the antigen-binding fragment thereof is: a single chain variable fragment (scFv) comprising a sequence as defined in **SEQ ID NO: 9**.

In still another example, the cytotoxic agent is selected from the group consisting of: an adrenocortical suppressant, an alkylating agent, an alkyl sulfonate, an anthracycline, an anti-angiogenic agent, an antibiotic, an antimetabolite, an antimitotic, an auristatin, a calicheamycin, a camptothecin, a COX-2 inhibitor, an enzyme inhibitor, an epipodophyllotoxin, an ethylenimine derivative, a folic acid analog, an HDAC inhibitor, a heat shock protein (HSP90) inhibitor, a hormone antagonist, a maytansinoid, a methylhydrazine derivative, an mTOR inhibitor, a nitrogen mustard, a nitrosourea, a platinum coordination complex, a pro-apoptotic agent, a proteasome inhibitor, a purine analog, a pyrimidine analog, a radioisotope, a substituted urea, a taxane, triazene, a tubulin inhibitor, a tyrosine kinase inhibitor, and a vinca alkaloid.

In still another example, the cytotoxic agent is selected from the group consisting of: afatinib, aplidin, anastrozole, anthracyclines, AVL-101, AVL-291, axitinib, azaribine, bendamustine, bleomycin, bortezomib, bosutinib, bryostatin-1, busulfan, camptothecins, carboplatin, calicheamycin, camptothecin, carboplatin, carmustine, celecoxib, chlorambucil, cisplatin, cladribine, COX-2 inhibitors, crizotinib, cyano-morpholino doxorubicin, cyclophosphamide, cytarabine, dacarbazine, dactinomycin, dasatinib,

daunorubicin, dinaciclib, 3',5'-O-dioleoyl-FudR (FudR-d0), DM1, DM3, DM4, docetaxel, doxorubicin, doxorubicin glucuronide, duocarmycin, endostatin, entinostat, epidophyllotoxin, epirubicin glucuronide, erlotinib, estramustine, estrogen receptor binding agents, etoposide
5 glucuronide, etoposide phosphate, etoposide (VP16), exemestane, farnesyl-protein transferase inhibitors, fingolimod, flavopiridol, floxuridine (FUdR), fludarabine, 5-fluorouracil, flutamide, fostamatinib, ganetespib, GDC-0834, gefitinib, gemcitabine, GS-1101, 10-hydroxycamptothecin, hydroxyurea, ibrutinib, idarubicin, idelalisib, ifosfamide, imatinib, irinotecan (CPT-11), lapatinib, lenolidamide, leucovorin, LFM-A13, lomustine,
10 mechlorothamine, melphalan, mercaptopurine, 6-mercaptopurine, methotrexate, mithramycin, mitomycin, mitotane, mitoxantrone, monomethylauristatin D (MMAD), monomethylauristatin E (MMAE), monomethylauristatin F (MMAF), navelbine, neratinib, nilotinib, nitrosurea, olaparib, paclitaxel, PCI-32765, pentostatin, plicomycin, a 2-PDox pro-drug (pro-2-PDox), procarbazine, PSI-341, 2-pyrrolinodoxorubicine (2-PDox), raloxifene,
15 semustine, SN-38, sorafenib, streptozocin, SU1 1248, sunitinib, tamoxifen, temazolomide, teniposide, thalidomide, thioguanine, thiotepa, topotecan, transplatinum, uracil mustard, vatalanib, vinblastine, vinca alkaloids, vincristine, vinorelbine, and ZD 1839.

In still another example, the cytotoxic agent is a radioisotope selected from the group consisting of: ^{90}Y , ^{188}Re , ^{166}Ho , ^{165}Dy , ^{109}Pd , ^{111}Ag , ^{186}Re , ^{198}Au , ^{153}Sm , ^{64}Cu , ^{177}Lu , ^{131}I , ^{125}I ,
20 ^{67}Cu , ^{175}Yb , ^{166}Dy , ^{169}Er , ^{212}Bi , ^{213}Bi , ^{225}Ac , ^{212}Pb , ^{66}Ga , ^{67}Ga , ^{68}Ga , ^{86}Y , $^{94\text{m}}\text{Tc}$, and ^{89}Zr .

In still another example, the antibody or antigen-binding fragment thereof is conjugated with a chelating agent selected from the group consisting of: DOTA, DTPA, NOTA, NODAGA, MeCOSAR, TETA, TRAP, TE2A, CBTE2A.

In still another example, the cytotoxic agent and the antibody or antigen-binding
25 fragment thereof are conjugated with a chelating agent selected from the group consisting of: DOTA, DTPA, NOTA, NODAGA, MeCOSAR, TETA, TRAP, TE2A, CBTE2A.

In a further example, the subject is a mammalian subject or a human subject.

In a second aspect, the present invention provides an isolated antibody population comprising:

30 first antibodies and/or antigen binding fragments thereof, that are conjugated to at least one cytotoxic agent which is toxic to a prostate, bladder, and/or pancreatic cancer cell, wherein the first antibodies comprise:

- (a) a heavy chain variable region comprising:
a complementarity determining region 1 (CDR1) comprising or consisting of an amino acid sequence defined by positions 50-54 of **SEQ ID NO: 3**;
5 a complementarity determining region 2 (CDR2) comprising or consisting of an amino acid sequence defined by positions 69-85 of **SEQ ID NO: 3**;
a complementarity determining region 3 (CDR3) comprising or consisting of an amino acid sequence defined by positions 118-126 of **SEQ ID NO: 3**; and
- (b) a light chain variable region comprising:
10 a complementarity determining region 1 (CDR1) comprising or consisting of an amino acid sequence defined by positions 44-54 of **SEQ ID NO: 4**;
a complementarity determining region 2 (CDR2) comprising or consisting of an amino acid sequence defined by positions 70-76 of **SEQ ID NO: 4**;
a complementarity determining region 3 (CDR3) comprising or consisting of
15 an amino acid sequence defined by positions 109-117 of **SEQ ID NO: 4**;
and wherein the antibody population does not contain second antibodies comprising a light chain variable region comprising:
a complementarity determining region 1 (CDR1) comprising or consisting of an amino acid sequence defined by positions 48-58 of **SEQ ID NO: 11**;
20 a complementarity determining region 2 (CDR2) comprising or consisting of an amino acid sequence defined by positions 74-80 of **SEQ ID NO: 11**;
a complementarity determining region 3 (CDR3) comprising or consisting of an amino acid sequence defined by positions 113-121 of **SEQ ID NO: 11**.
- In one example, the first antibodies and/or antigen binding fragments thereof are any
25 one or more of monoclonal antibodies, humanised antibodies, chimeric antibodies, multimeric antibodies, and/or synthetic antibodies.
- In another example, the antigen binding fragments are any one or more of single chain variable fragments (scFv), variable domain (Fv) fragments, fragment antigen binding (Fab) fragments, F(ab)₂ fragments, peptides, or proteolytic fragments containing an epitope binding
30 region.
- In an additional example, the first antibodies comprise or consist of a heavy chain sequence as defined by positions 20-461 of **SEQ ID NO: 3** and a light chain sequence as defined by positions 21-234 of **SEQ ID NO: 4**.
- In a further example, the first antibodies and/or antigen binding fragments thereof are
35 chimeric.

In a further example, the first antibodies and/or antigen binding fragments thereof are chimeric antibodies comprising:

(a) a heavy chain constant region comprising or consisting of an amino acid sequence as defined in residues 138-467 of **SEQ ID NO: 7**; and

(b) a light chain constant region comprising or consisting of an amino acid sequence as defined in residues of 128-234 **SEQ ID NO: 8**.

In another example, the antigen binding fragments are single chain variable fragments (scFv) comprising a sequence as defined in **SEQ ID NO: 9**.

In yet another example, the cytotoxic agent is selected from the group consisting of: an adrenocortical suppressant, an alkylating agent, an alkyl sulfonate, an anthracycline, an anti-angiogenic agent, an antibiotic, an antimetabolite, an antimitotic, an auristatin, a calicheamycin, a camptothecin, a COX-2 inhibitor, an enzyme inhibitor, an epipodophyllotoxin, an ethylenimine derivative, a folic acid analog, an HDAC inhibitor, a heat shock protein (HSP90) inhibitor, a hormone antagonist, a maytansinoid, a methylhydrazine derivative, an mTOR inhibitor, a nitrogen mustard, a nitrosourea, a platinum coordination complex, a pro-apoptotic agent, a proteasome inhibitor, a purine analog, a pyrimidine analog, a radioisotope, a substituted urea, a taxane, triazene, a tubulin inhibitor, a tyrosine kinase inhibitor, and a vinca alkaloid.

In another example, the cytotoxic agent is selected from the group consisting of: afatinib, aplidin, anastrozole, anthracyclines, AVL-101, AVL-291, axitinib, azaribine, bendamustine, bleomycin, bortezomib, bosutinib, bryostatin-1, busulfan, camptothecins, carboplatin, calicheamycin, camptothecin, carboplatin, carmustine, celecoxib, chlorambucil, cisplatin, cladribine, COX-2 inhibitors, crizotinib, cyano-morpholino doxorubicin, cyclophosphamide, cytarabine, dacarbazine, dactinomycin, dasatinib, daunorubicin, dinaciclib, 3',5'-O-dioleoyl-FudR (FUDR-d0), DM1, DM3, DM4, docetaxel, doxorubicin, doxorubicin glucuronide, duocarmycin, endostatin, entinostat, epipodophyllotoxin, epirubicin glucuronide, erlotinib, estramustine, estrogen receptor binding agents, etoposide glucuronide, etoposide phosphate, etoposide (VP16), exemestane, farnesyl-protein transferase inhibitors, fingolimod, flavopiridol, floxuridine (FUDR), fludarabine, 5-fluorouracil, flutamide, fostamatinib, ganetespib, GDC-0834, gefitinib, gemcitabine, GS-1101, 10-hydroxycamptothecin, hydroxyurea, ibrutinib, idarubicin, idelalisib, ifosfamide, imatinib, irinotecan (CPT-11), lapatinib, lenolidamide, leucovorin, LFM-A13, lomustine, mechlorethamine, melphalan, mercaptopurine, 6-mercaptopurine, methotrexate, mithramycin, mitomycin, mitotane, mitoxantrone, monomethylauristatin D (MMAD),

monomethylauristatin E (MMAE), monomethylauristatin F (MMAF), navelbine, neratinib, nilotinib, nitrosurea, olaparib, paclitaxel, PCI-32765, pentostatin, plicomycin, a 2-PDox pro-drug (pro-2-PDox), procarbazine, PSI-341, 2-pyrrolinodoxorubicine (2-PDox), raloxifene, semustine, SN-38, sorafenib, streptozocin, SU1 1248, sunitinib, tamoxifen, temazolomide, 5 teniposide, thalidomide, thioguanine, thiotepa, topotecan, transplatinum, uracil mustard, vatalanib, vinblastine, vinca alkaloids, vincristine, vinorelbine, and ZD 1839.

In yet another example, the cytotoxic agent is a prodrug designed for activation upon uptake into an endosome or lysosome of said prostate, bladder, and/or pancreatic cancer cell.

In one example, the prodrug is conjugated to the antibody and/or an antigen-binding 10 fragment thereof by:

an acid sensitive-linker susceptible to cleavage at a pH that is less than: pH 7.2, pH 7.0, pH 6.5, pH 6.0, pH 5.5, pH 5.0, pH 4.5, or pH 4; or

an enzyme-cleavable linker, wherein the enzyme capable of cleaving the linker exists within the endosome or lysosome.

15 In one example, the cytotoxic agent is linked to the antibody and/or antigen binding fragment thereof by binding to a chelating agent conjugated to the antibody and/or antigen binding fragment thereof.

In still another example, the cytotoxic agent and the antibody or antigen-binding fragment thereof are conjugated with a chelating agent selected from the group consisting of: 20 DOTA, DTPA, NOTA, NODAGA, MeCOSAR, TETA, TRAP, TE2A, CBTE2A.

In still another example, the cytotoxic agent is a radioisotope selected from the group consisting of: ^{90}Y , ^{188}Re , ^{166}Ho , ^{165}Dy , ^{109}Pd , ^{111}Ag , ^{186}Re , ^{198}Au , ^{153}Sm , ^{64}Cu , ^{177}Lu , ^{131}I , ^{125}I , ^{67}Cu , ^{175}Yb , ^{166}Dy , ^{169}Er , ^{212}Bi , ^{213}Bi , ^{225}Ac , ^{212}Pb , ^{66}Ga , ^{67}Ga , ^{68}Ga , ^{86}Y , $^{94\text{m}}\text{Tc}$, and ^{89}Zr .

In still another example, the antibody or antigen-binding fragment thereof is conjugated 25 with a chelating agent selected from the group consisting of: DOTA, DTPA, NOTA, NODAGA, MeCOSAR, TETA, TRAP, TE2A, and CBTE2A.

Brief Description of the Drawings

Preferred embodiments of the present invention will now be described, by way of 30 example only, with reference to the accompanying figures wherein:

CLAIMS

1. Use of an anti-glypican-1 (anti-GPC1) antibody and/or an antigen-binding fragment thereof in the preparation of a medicament for treating prostate, bladder, and/or pancreatic cancer in a subject, wherein the antibody and/or fragment is conjugated to at least one cytotoxic agent that is toxic to a prostate, bladder, and/or pancreatic cancer cell in the subject.
2. The use according to claim 1, wherein the pharmaceutical preparation does not comprise an antibody with a light chain variable region comprising:
 - a complementarity determining region 1 (CDR1) comprising or consisting of an amino acid sequence defined by positions 48-58 of **SEQ ID NO: 11**;
 - a complementarity determining region 2 (CDR2) comprising or consisting of an amino acid sequence defined by positions 74-80 of **SEQ ID NO: 11**;
 - a complementarity determining region 3 (CDR3) comprising or consisting of an amino acid sequence defined by positions 113-121 of **SEQ ID NO: 11**.
3. The use according to claim 1 or claim 2, wherein the antibody comprises:
 - (a) a heavy chain variable region comprising:
 - a complementarity determining region 1 (CDR1) comprising or consisting of an amino acid sequence defined by positions 50-54 of **SEQ ID NO: 3**;
 - a complementarity determining region 2 (CDR2) comprising or consisting of an amino acid sequence defined by positions 69-85 of **SEQ ID NO: 3**;
 - a complementarity determining region 3 (CDR3) comprising or consisting of an amino acid sequence defined by positions 118-126 of **SEQ ID NO: 3**; and
 - (b) a light chain variable region comprising:
 - a complementarity determining region 1 (CDR1) comprising or consisting of an amino acid sequence defined by positions 44-54 of **SEQ ID NO: 4**;
 - a complementarity determining region 2 (CDR2) comprising or consisting of an amino acid sequence defined by positions 70-76 of **SEQ ID NO: 4**;

a complementarity determining region 3 (CDR3) comprising or consisting of an amino acid sequence defined by positions 109-117 of **SEQ ID NO: 4**.

4. The use according to claim 3, wherein the antibody is produced by a hybridoma cell as deposited at Cellbank Australia under accession number CBA20140026, or progeny thereof.

5. The use according to any one of claims 1 to 4, wherein the antibody is:

- (i) a humanised anti-GPC1 antibody,
- (ii) a chimeric anti-GPC1 antibody,
- (i) a human anti-GPC1 antibody,
- (ii) a monoclonal anti-GPC1 antibody,
- (iii) a multimeric anti-GPC1 antibody,
- (iv) a synthetic anti-GPC1 antibody, or
- (v) a chimeric antibody comprising a heavy chain constant region comprising or consisting of an amino acid sequence as defined in residues 138-467 of **SEQ ID NO: 7**; and a light chain constant region comprising or consisting of an amino acid sequence as defined in residues of 128-234 **SEQ ID NO: 8**.

6. The use according to any one of claims 1 to 5, wherein the antigen-binding fragment thereof is: a single chain variable fragment (scFv), a single chain variable fragment (scFv) comprising a sequence as defined in **SEQ ID NO: 9**, a variable domain (Fv) fragment, a fragment antigen binding (Fab) fragment, a F(ab)₂ fragment, a peptide, or a proteolytic fragment containing an epitope binding region.

7. The use according to any one of claims 1 to 6, wherein the cytotoxic agent is selected from the group consisting of:

- (a) an adrenocortical suppressant, an alkylating agent, an alkyl sulfonate, an anthracycline, an anti-angiogenic agent, an antibiotic, an antimetabolite, an antimitotic, an auristatin, a calicheamycin, a camptothecin, a COX-2 inhibitor, an enzyme inhibitor, an epipodophyllotoxin, an ethylenimine derivative, a folic acid analog, an HDAC inhibitor, a heat shock protein (HSP90) inhibitor, a hormone

antagonist, a maytansinoid, a methyl hydrazine derivative, an mTOR inhibitor, a nitrogen mustard, a nitrosourea, a platinum coordination complex, a pro-apoptotic agent, a proteasome inhibitor, a purine analog, a pyrimidine analog, a radioisotope, a substituted urea, a taxane, triazene, a tubulin inhibitor, a tyrosine kinase inhibitor, and a vinca alkaloid;

(b) afatinib, aplidin, anastrozole, anthracyclines, AVL-101, AVL-291, axitinib, azaribine, bendamustine, bleomycin, bortezomib, bosutinib, bryostatin-1, busulfan, camptothecans, carboplatin, calicheamycin, camptothecin, carboplatin, carmustine, celecoxib, chlorambucil, cisplatin, cladribine, COX-2 inhibitors, crizotinib, cyanomorpholino doxorubicin, cyclophosphamide, cytarabine, dacarbazine, dactinomycin, dasatinib, daunorubicin, dinaciclib, 3',5'-O-dioleoyl-FudR (FudR-dO), DM1, DM3, DM4, docetaxel, doxorubicin, doxorubicin glucuronide, duocarmycin, endostatin, entinostat, epidophyllotoxin, epirubicin glucuronide, erlotinib, estramustine, estrogen receptor binding agents, etoposide glucuronide, etoposide phosphate, etoposide (VP16), exemestane, farnesyl-protein transferase inhibitors, fingolimod, flavopiridol, floxuridine (FudR), fludarabine, 5-fluorouracil, flutamide, fostamatinib, ganetespib, GDC-0834, gefitinib, gemcitabine, GS-1101, 10-hydroxycamptothecin, hydroxyurea, ibrutinib, idarubicin, idelalisib, ifosfamide, imatinib, irinotecan (CPT-11), lapatinib, lenolidamide, leucovorin, LFM-A13, lomustine, mechlorethamine, melphalan, mercaptopurine, 6-mercaptopurine, methotrexate, mithramycin, mitomycin, mitotane, mitoxantrone, monomethylauristatin D (MMAD), monomethylauristatin E (MMAE), monomethylauristatin F (MMAF), navelbine, neratinib, nilotinib, nitrosourea, olaparib, paclitaxel, PCI-32765, pentostatin, plicomycin, a 2-PDox pro-drug (pro-2-PDox), procarbazine, PSI-341, 2-pyrrolinodoxorubicine (2-PDox), raloxifene, semustine, SN-38, sorafenib, streptozocin, SU1 1248, sunitinib, tamoxifen, temazolomide, teniposide, thalidomide, thioguanine, thiotepa, topotecan, transplatin, uracil mustard, vatalanib, vinblastine, vinca alkaloids, vincristine, vinorelbine, and ZD 1839.

8. The use according to any one of claims 1 to 7, wherein the cytotoxic agent is:

- (a) a radioisotope;
- (b) a radioisotope selected from the group consisting of: ^{90}Y , ^{188}Re , ^{166}Ho , ^{165}Dy , ^{109}Pd , ^{111}Ag , ^{186}Re , ^{198}Au , ^{153}Sm , ^{64}Cu , ^{177}Lu , ^{131}I , ^{125}I , ^{67}Cu , ^{175}Yb , ^{166}Dy , ^{169}Er , ^{212}Bi , ^{213}Bi , ^{225}Ac , ^{212}Pb , ^{66}Ga , ^{67}Ga , ^{68}Ga , ^{64}Cu , ^{86}Y , $^{94\text{m}}\text{Tc}$, and ^{89}Zr .

9. The use according to any one of claims 1 to 8, wherein the subject is a mammalian subject or a human subject.

10. An isolated antibody population comprising:

first antibodies and/or antigen binding fragments thereof, that are conjugated to at least one cytotoxic agent which is toxic to a prostate, bladder, and/or pancreatic cancer cell, wherein the first antibodies comprise:

(a) a heavy chain variable region comprising:

a complementarity determining region 1 (CDR1) comprising or consisting of an amino acid sequence defined by positions 50-54 of **SEQ ID NO: 3**;

a complementarity determining region 2 (CDR2) comprising or consisting of an amino acid sequence defined by positions 69-85 of **SEQ ID NO: 3**;

a complementarity determining region 3 (CDR3) comprising or consisting of an amino acid sequence defined by positions 118-126 of **SEQ ID NO: 3**; and

(b) a light chain variable region comprising:

a complementarity determining region 1 (CDR1) comprising or consisting of an amino acid sequence defined by positions 44-54 of **SEQ ID NO: 4**;

a complementarity determining region 2 (CDR2) comprising or consisting of an amino acid sequence defined by positions 70-76 of **SEQ ID NO: 4**;

a complementarity determining region 3 (CDR3) comprising or consisting of an amino acid sequence defined by positions 109-117 of **SEQ ID NO: 4**;

and wherein the antibody population does not contain second antibodies comprising a light chain variable region comprising:

a complementarity determining region 1 (CDR1) comprising or consisting of an amino acid sequence defined by positions 48-58 of **SEQ ID NO: 11**;

a complementarity determining region 2 (CDR2) comprising or consisting of an amino acid sequence defined by positions 74-80 of **SEQ ID NO: 11**;

a complementarity determining region 3 (CDR3) comprising or consisting of an amino acid sequence defined by positions 113-121 of **SEQ ID NO: 11**.

11. The antibody population according to claim 10, wherein the first antibodies and/or antigen binding fragments thereof are any one or more of monoclonal antibodies, humanised antibodies, chimeric antibodies, multimeric antibodies, synthetic antibodies, and/or chimeric antibodies comprising:

(a) a heavy chain constant region comprising or consisting of an amino acid sequence as defined in residues 138-467 of **SEQ ID NO: 7**; and

(b) a light chain constant region comprising or consisting of an amino acid sequence as defined in residues of 128-234 **SEQ ID NO: 8**..

12. The antibody population according to claim 10 or claim 11, wherein the antigen binding fragments are any one or more of single chain variable fragments (scFv), single chain variable fragments (scFv) comprising a sequence as defined in **SEQ ID NO: 9**, variable domain (Fv) fragments, fragment antigen binding (Fab) fragments, F(ab)₂ fragments, peptides, or proteolytic fragments containing an epitope binding region.

13. The antibody population according to any one of claims 10 to 12, wherein the first antibodies comprise or consist of a heavy chain sequence as defined by positions 20-461 of **SEQ ID NO: 3** and a light chain sequence as defined by positions 21-234 of **SEQ ID NO: 4**.

14. The antibody population according to any one of claims 10 to 13, wherein the cytotoxic agent is selected from the group consisting of:

(a) an adrenocortical suppressant, an alkylating agent, an alkyl sulfonate, an anthracycline, an anti-angiogenic agent, an antibiotic, an antimetabolite, an antimitotic, an auristatin, a calicheamycin, a camptothecin, a COX-2 inhibitor, an enzyme inhibitor, an epipodophyllotoxin, an ethylenimine derivative, a folic acid analog, an HDAC inhibitor, a heat shock protein (HSP90) inhibitor, a hormone antagonist, a maytansinoid, a methyl hydrazine derivative, an mTOR inhibitor, a nitrogen mustard, a nitrosourea, a platinum coordination complex, a pro-apoptotic agent, a proteasome inhibitor, a purine analog, a pyrimidine analog, a radioisotope, a substituted urea, a taxane, triazene, a tubulin inhibitor, a tyrosine kinase inhibitor, and a vinca alkaloid;

(b) afatinib, aplidin, anastrozole, anthracyclines, AVL-101, AVL-291, axitinib, azaribine, bendamustine, bleomycin, bortezomib, bosutinib, bryostatin-1, busulfan, camptothecans, carboplatin, calicheamycin, camptothecin, carboplatin, carmustine, celecoxib, chlorambucil, cisplatin, cladribine, COX-2 inhibitors, crizotinib, cyanomorpholino doxorubicin, cyclophosphamide, cytarabine, dacarbazine, dactinomycin, dasatinib, daunorubicin, dinaciclib, 3',5'-O-dioleoyl-FudR (FudR-d0), DM1, DM3, DM4, docetaxel, doxorubicin, doxorubicin glucuronide, duocarmycin, endostatin, entinostat, epidophyllotoxin, epirubicin glucuronide, erlotinib, estramustine, estrogen receptor binding agents, etoposide glucuronide, etoposide phosphate, etoposide (VP16), exemestane, farnesyl-protein transferase inhibitors, fingolimod, flavopiridol, floxuridine (FudR), fludarabine, 5-fluorouracil, flutamide, fostamatinib, ganetespib, GDC-0834, gefitinib, gemcitabine, GS-1101, 10-hydroxycamptothecin, hydroxyurea, ibrutinib, idarubicin, idelalisib, ifosfamide, imatinib, irinotecan (CPT-11), lapatinib, lenolidamide, leucovorin, LFM-A13, lomustine, mechlorethamine, melphalan, mercaptopurine, 6-mercaptopurine, methotrexate, mithramycin, mitomycin, mitotane, mitoxantrone, monomethylauristatin D (MMAD), monomethylauristatin E (MMAE), monomethylauristatin F (MMAF), navelbine, neratinib, nilotinib, nitrosurea, olaparib, paclitaxel, PCI-32765, pentostatin, plicomycin, a 2-PDox pro-drug (pro-2-PDox), procarbazine, PSI-341, 2-pyrrolinodoxorubicine (2-PDox), raloxifene, semustine, SN-38, sorafenib, streptozocin, SU1 1248, sunitinib, tamoxifen, temazolomide, teniposide, thalidomide, thioguanine, thiotepa, topotecan, transplatinum, uracil mustard, vatalanib, vinblastine, vinca alkaloids, vincristine, vinorelbine, and ZD 1839.

15. The antibody population according to any one of claims 10 to 14, wherein the cytotoxic agent is:

(a) a radioisotope;

(b) a radioisotope selected from the group consisting of: ^{90}Y , ^{188}Re , ^{166}Ho , ^{165}Dy , ^{109}Pd , ^{111}Ag , ^{186}Re , ^{198}Au , ^{153}Sm , ^{64}Cu , ^{177}Lu , ^{131}I , ^{125}I , ^{67}Cu , ^{175}Yb , ^{166}Dy , ^{169}Er , ^{212}Bi , ^{213}Bi , ^{225}Ac , ^{212}Pb , ^{66}Ga , ^{67}Ga , ^{68}Ga , ^{64}Cu , ^{86}Y , $^{94\text{m}}\text{Tc}$, and ^{89}Zr .