

(2002)). The use of a clearing or blocking agent allows for sufficient levels of radioactivity to be administered for an efficient treatment while limiting adverse toxicity, but the timing and dosage must be chosen with care, and there is the possibility of the clearing agent introducing risks of adverse effects such as immune reactions. Thus, the use of a clearing phase is a complicating aspect in pre-targeting methods.

SUMMARY

The present ~~invention~~disclosure provides sets of antibodies useful in pre-targeting methods, and methods of using the same.

~~In one aspect, the~~The present ~~invention~~disclosure provides a set of antibodies comprising:

i) a first antibody comprising an antigen binding moiety that binds to an antigen expressed on the surface of a target cell, and further comprising a V_H domain of an antigen binding site for a radiolabelled compound, but not comprising a V_L domain of an antigen binding site for the radiolabelled compound; and

ii) a second antibody comprising an antigen binding moiety that binds to an antigen expressed on the surface of a target cell, and further comprising a V_L domain of an antigen binding site for the radiolabelled compound, but not comprising a V_H domain of the antigen binding site for the radiolabelled compound,

wherein said V_H domain of the first antibody and said V_L domain of the second antibody are together capable of forming a functional antigen binding site for the radiolabelled compound.

In a particular ~~embodiment~~example, the first and second antibody each comprise an Fc domain. In some ~~embodiments~~examples, each of the first and second antibody may comprise a) an Fc domain b) at least one antigen-binding moiety, comprising a binding site for the target antigen and c) a polypeptide comprising either a V_L domain or a V_H domain of the antigen binding site for the radiolabelled compound (but not both), wherein the C-terminus of the antigen binding moiety of (b) is fused to the N-terminus of one subunit of the Fc domain, and the C-terminus of the polypeptide of (c) is fused to the N-terminus of the other subunit of the Fc domain.

Thus, the first antibody may comprise or consist of:

- a) an Fc domain comprising a first and second subunit;
- b) an antigen binding moiety comprising a binding site for a target antigen; and

c) a polypeptide comprising or consisting of an antibody heavy chain variable domain (VH) of an antigen binding site for the radiolabelled compound;

wherein the antigen binding moiety of (b) is fused to the N-terminus of the first subunit of the Fc domain of (a), and the polypeptide of (c) is fused by its C-terminus to the N-terminus of the second subunit of the Fc domain of (a),

and wherein the first antibody does not comprise a VL domain of an antigen binding site for the radiolabelled compound.

The second antibody may comprise or consist of:

- 10 a) an Fc domain comprising a first and second subunit;
 b) an antigen binding moiety comprising a binding site for a target antigen; and
 c) a polypeptide comprising or consisting of an antibody light chain variable domain (VL) of an antigen binding site for the radiolabelled compound;

wherein the antigen binding moiety of (b) is fused to the N-terminus of the first subunit of the Fc domain of (a), and the polypeptide of (c) is fused by its C-terminus to the N-terminus of the second subunit of the Fc domain of (a),

and wherein the second antibody does not comprise a VH domain of an antigen binding site for the radiolabelled compound.

- 20 Neither the first nor the second antibody comprise, on their own, a functional antigen binding site for a radiolabelled compound. The first antibody has only a V_H domain from the functional binding site for the radiolabelled compound, and not the V_L domain. The second antibody has only the V_L domain, and not the V_H domain.

In one aspect, the present disclosure provides a set of antibodies comprising:
i) a first antibody comprising an antibody fragment comprising an antigen binding site specific for an antigen expressed on the surface of a target cell, an Fc domain, and a polypeptide comprising a VH domain of an antigen binding site for a radiolabelled compound, wherein the C-terminus of the antibody fragment is fused to the N-terminus of one chain of the Fc domain, and the C-terminus of the polypeptide is fused to the N-terminus of the other chain of the Fc domain, and wherein said first antibody does not comprise a VL domain of an antigen binding site for the radiolabelled compound; and

ii) a second antibody comprising an antibody fragment comprising an antigen binding site specific for an antigen expressed on the surface of a target cell, an Fc domain, and a polypeptide comprising a VL domain of an antigen binding site for the radiolabelled compound, wherein the C-terminus of the antibody fragment is fused to the N-terminus of one chain of the Fc domain, and the C-terminus of the polypeptide is fused to the N-terminus of the other chain of the Fc domain, and wherein the second antibody does not comprise a VH domain of the antigen binding site for the radiolabelled compound;

wherein said VH domain of the first antibody and said VL domain of the second antibody are together capable of forming a functional antigen binding site for the radiolabelled compound.

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A functional antigen binding site for the radiolabelled compound is formed when the V_H and V_L domains of the first and second antibodies are associated. This may occur, for example, when the first and second antibodies are bound to the same individual target cell or to adjacent cells.

The first and second antibodies described herein may be referred to herein as “single domain split antibodies”, “SPLITs”, “split antibodies”, hemibodies” or “demibodies”. The V_H and V_L domain which together form an antigen binding site capable of binding to the radiolabelled compound are split between two antibodies, and not present as part of the same antibody.

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The split domain format means that the radiolabelled compound cannot bind to either the first antibody on its own or to the second antibody on its own. In the blood, there is little

or no stable association between the first and the second antibody, and so little or no stable binding of the radiolabelled compound.

An antigen expressed on the surface of a target cell may be referred to herein as a “target antigen”, “target cell antigen” or “TA”. According to the present ~~invention~~disclosure, the first and the second antibody described above may have a binding site for different target antigens, or for the same target antigen. (For the avoidance of doubt, where it stated that the antibodies bind the same target antigen, this means that they have a binding site capable of binding to the same target antigen and includes the possibility that the antibodies may bind to two individual antigen molecules that are the same as each other). For example, in one embodimentexample, both the first and the second antibody bind to CEA.

In some embodimentexamples, the first and second antibody may bind to (have a binding site for) the same epitope of the same target antigen. In other embodimentexamples, the first antibody may bind to (have a binding site for) a different epitope of the target antigen from the second antibody.

In some embodimentexamples, the first and second antibody may comprise the same antigen binding site for the target antigen. That is, they may comprise an antigen binding site capable of binding to the target antigen, comprising a V_L and V_H sequence, where the V_L and V_H sequences forming this antigen binding site are the same in the first and in the second antibodies.

In some embodimentexamples, each of the first and the second antibodies are monovalent for the target antigen. In other embodimentexamples, each of the first and the second antibodies are bivalent for the target antigen. In some embodimentexamples they are each bivalent and monospecific for an epitope. In other embodimentexamples, each of the first and second antibodies are biparatopic for the target antigen, i.e., the first and the second antibodies each have binding sites for two different epitopes of the target antigen.

The presence of an Fc region has benefits in the context of radioimmunotherapy and radioimaging, e.g. prolonging the protein’s circulating half-life and/or resulting in higher tumour uptake than may be observed with smaller fragments. The “split domain” format described herein may be particularly advantageous in this context, as it mitigates against the greater possibility of association with radiolabelled compound that would otherwise occur due to the prolonged presence of the circulating antibody.

In some embodimentexamples, the Fc domain is modified to reduce or eliminate effector function.

~~In another aspect, the~~The present ~~invention~~disclosure provides a pharmaceutical composition comprising the set of antibodies as described herein. ~~In another aspect, the~~The present ~~invention~~disclosure provides a kit comprising two separate pharmaceutical compositions, each comprising one of the antibodies described herein (i.e., the first and second antibody respectively).

~~In a further aspect, the~~The present ~~invention~~disclosure relates to a polynucleotide or set of polynucleotides encoding any of the antibodies or sets of antibodies described herein. In another aspect, the present disclosure provides a set of nucleic acids expressing the set of antibodies as described herein. ~~In another aspect, the~~The present ~~invention~~disclosure relates to a vector or set of vectors comprising said polynucleotide or polynucleotides, optionally an expression vector or set of expression vectors. In another aspect, the present disclosure provides an expression vector or set of expression vectors comprising the set of nucleic acids as described herein. In a further object the present ~~invention~~disclosure relates to a prokaryotic or eukaryotic host cell or a set of host cells comprising a vector or set of vectors of the present ~~invention~~disclosure. In another aspect, the present disclosure provides a host cell or set of host cells comprising the expression vector or set of expression vectors as described herein. In addition there is provided a method of producing an antibody comprising culturing the host cell(s) so that the antibody is produced.

In some ~~embodiment~~examples, antibodies as described herein find use in a method of pre-targeted radioimmunotherapy (PRIT) or in a method of pre-targeted radioimaging.

~~In one aspect, the~~The present ~~invention~~disclosure provides a method of pre-targeted radioimmunotherapy which comprises:

- i) administering to a subject a first antibody and a second antibody as described above; and
- ii) subsequently administering to said subject a radiolabelled compound.

In another aspect, the present disclosure provides use of a set of antibodies as described herein in the manufacture of a medicament for pretargeting radioimmunotherapy, the pretargeting radioimmunotherapy comprising

i) that the set of antibodies as described herein is to be administered to a subject, wherein the first and second antibodies are to be administered simultaneously or sequentially, in either order, wherein the antibodies bind to the target antigen and localise to the surface of a cell expressing the target antigen; and wherein association of the first and second antibody forms a functional binding site for the radiolabelled compound;
and

ii) that a radiolabelled compound is to be administered subsequently, wherein the radiolabelled compound binds to functional binding site for the radiolabelled compound, optionally wherein:

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a) the pretargeting radioimmunotherapy does not comprise a step of administration of a clearing or blocking agent; and/or

b) the subject is human; and/or

c) the target antigen is a cancer- or tumour-associated antigen and the method is a method of radioimmunotherapy of a tumour or cancer.

~~In another aspect, the~~The present ~~invention~~disclosure provides a first and a second antibody described above for use in a method of treatment comprising administering the first antibody and the second antibody to a subject, and subsequently administering to said subject a radiolabelled compound. ~~In another aspect, the invention~~The disclosure provides a first antibody as described above for use in a method of treatment comprising administering the first antibody and the second antibody to a subject, and subsequently administering to said subject a radiolabelled compound. ~~In another aspect the invention~~The disclosure provides the second antibody as described above for use in a method of treatment comprising administering the first antibody and the second antibody to a subject, and subsequently administering to said subject a radiolabelled compound.

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~~In another aspect, the~~The present ~~invention~~disclosure provides a method of radioimaging which comprises:

- i) administering to a subject a first and a second antibody as described herein, wherein the antibodies bind to the target antigen and localise to the surface of a cell expressing the target antigen;
- ii) subsequently administering a radiolabelled compound; and optionally
- iii) imaging the tissue or organ where the radionuclide has localised.

In another aspect, the present disclosure provides use of a set of antibodies as described herein in the manufacture of a medicament for targeting a radioisotope to a tissue or organ for radioimaging, the targeting comprising:

i) that a set of antibodies as described herein is to be administered to a subject, wherein the first and second antibodies are to be administered simultaneously or sequentially, in either order, wherein the antibodies bind to a target antigen and localise to the surface of a cell expressing the target antigen, wherein association of the first and second antibody forms a functional binding site for the radiolabelled compound;

and

ii) that a radiolabelled compound is to be administered subsequently, wherein the radiolabelled compound binds to the functional binding site for the radiolabelled compound, optionally wherein:

a) the targeting does not comprise a step of administration of a clearing or blocking agent; and/or

b) the method further comprises a step of imaging, optionally wherein the target antigen is a cancer or tumour-associated antigen and the step of imaging is imaging tumours or cancer.

~~In another aspect, the~~The present ~~invention~~disclosure provides a first and a second antibody as described herein for use in a method of diagnosis carried out on the human or animal body, wherein the method comprises

- i) administering to subject a first and a second antibody as described herein, wherein the antibodies bind to the target antigen and localise to the surface of a cell expressing the target antigen;
- ii) subsequently administering a radiolabelled compound; and optionally

iii) imaging the tissue or organ where the radionuclide has localised.

The imaging step may be followed by a step of forming a diagnosis and optionally a step of delivering that diagnosis to the subject. In some ~~embodiment~~examples the method may further comprise determining an appropriate treatment and optionally administering that treatment to the subject.

In each of the above methods/uses, binding of the first and the second antibody to the same or adjacent target cells results in association of the V_H and V_L domains of an antigen binding site for a radiolabelled compound and the formation of a functional antigen binding site for the radiolabelled compound. Thus, after administration of the radiolabelled
10 compound, the radiolabelled compound binds to the functional antigen binding site formed by association of the V_H and V_L .

In any of the methods and uses described herein, the first and second antibodies can be administered simultaneously or sequentially, in either order.

Frequently in the art, methods of PRIT or radioimaging involve a clearing step. The clearing step comprises administering an agent between the administration of the antibody and the administration of the radiolabelled compound, wherein the agent increases the rate of removal of the antibody from blood and/or blocks binding of radiolabelled compound to the antibody.

In an ~~embodiment~~example of the methods and uses described herein, the method does
20 not comprise a clearing step. That is, it does not comprise a step of administering a clearing agent or a blocking agent between the administration of the first and second antibodies and

the administration of radiolabelled compound (i.e., after the administration of the antibodies but before administration of the radiolabelled compound). In another ~~embodiment~~example, no agent is administered between the administration of the first and second antibodies and the administration of radiolabelled compound, other than optionally a radiosensitizer, immunotherapeutic and/or a chemotherapeutic agent. In another ~~embodiment~~example, no agent is administered between the administration of the first and second antibodies and the administration of radiolabelled compound.

In some ~~embodiment~~examples, the antibodies described herein may be administered as part of a combination therapy. For example, they may be administered in combination with one or more radiosensitizers, immunotherapeutics and/or chemotherapeutic agents: the radiosensitizer, immunotherapeutic or chemotherapeutic agent and the antibodies may be administered simultaneously or sequentially, in either order.

The methods of radioimaging and radioimmunotherapy described herein may optionally be combined as discussed further herein.

~~In a further aspect, the~~The present ~~invention~~disclosure provides a kit comprising:

- i) a first and a second antibody as described herein;
- ii) a radiolabelled compound which binds to the antigen binding site formed by association of the first and the second antibody.

Optionally the kit may exclude (i.e., does not comprise) a clearing agent or a blocking agent as described herein.

Optionally the kit may further comprise a radiosensitizer, immunotherapeutic or chemotherapeutic agent.

In some ~~embodiment~~examples, the first and the second antibody may be present in the same pharmaceutical composition. In other ~~embodiment~~examples, the first and second antibody may be present in separate pharmaceutical compositions. In some ~~embodiment~~examples, the radiolabelled compound is present in a pharmaceutical composition separate from the antibodies.

~~In another aspect, the~~The present ~~invention~~disclosure relates to a novel peptide linker. The present inventors have determined that in a peptide linker consisting of y amino acids, a Ser in the y position (i.e., a Ser as the last/C-terminal amino acid of the linker) may induce glycosylation of the y+2 amino acid (i.e., of the amino acid positioned 2 residues in the C-terminal direction from the last amino acid in the linker), depending on the nature of this y+2 amino acid. Therefore it may be preferred that the last serine residue of the linker is placed in the y-2 or y-3 position (i.e., that the last serine residue of the linker is at a position 2 or 3 amino

acids in the N-terminal direction from the last amino acid in the linker). In some embodimentsexamples, the linker may consist of y consecutive amino acid residues selected from the group consisting of Gly and Ser, e.g., wherein y= 5 or more, e.g., y=5 to 100, 5 to 70, 5 to 60 or 5 to 50; or y=10 to 100; 10 to 70, 10 to 60 or 10 to 50; e.g., 15 to 31 or 15 to 30; e.g., y=15, 16, 17, 18, 19, 20, 21, 22, 23, 24 or 25; and wherein the last serine is in the y-2 or y-3 position. (Thus, there may be a serine in the y-2 position and a glycine in the y-1 and y position; or there may be a serine in the y-3 position and a glycine in the y-2, y-1 and y positions). In some embodimentsexamples it may be preferred that y=20 or 21. In some embodimentsexamples, it may be preferred that the linker is (GxS)_n(GGSGG) or (GxS)_n(GGSGGG) with G = glycine, S = serine, x = 4 and n= 1 to 20 or 2 to 20 or 1 to 10 or 2 to 10, e.g., n= 2, 3, 4 or 5, 6, 7, 8 or 9, e.g., n=2 to 5 or 2 to 4. For instance, the linker may be GGGGSGGGGSGGGGSGGSGG (SEQ ID NO: 150) or GGGGSGGGGSGGGGSGGSGGG (SEQ ID NO: 151).

In another aspect, the present disclosure provides a peptide linker consisting of y consecutive residues selected from the group consisting of Gly and Ser, wherein y= 5 to 100, 5 to 70, 5 to 60, 5 to 50 or 10 to 100, 10 to 70, 10 to 60, or 10 to 50, and wherein the last serine is in the y-2 or y-3 position, optionally:

i) wherein y=10 to 50;

ii) wherein y= 15 to 31 or 15 to 30, optionally wherein y= 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 or 25, optionally wherein y= 20 or 21;

iii) consisting of the sequence (GxS)_n(GGSGG) or (GxS)_n(GGSGGG), wherein G = glycine, S = serine, x = 4 and n=1 to 20, 2 to 20, 1 to 10 or 2 to 10, optionally wherein n= 2, 3, 4 or 5 or wherein n=2, 3 or 4; or

iv) consisting of the sequence GGGGSGGGGSGGGGSGGSGG (SEQ ID NO: 150) or GGGGSGGGGSGGGGSGGSGGG (SEQ ID NO: 151).

In another aspect of the invention, the present inventiondisclosure relates to the use of said peptide linker to join two domains of a multi-domain protein. In another aspect, the present disclosure provides use of a peptide linker as described herein to join a first and a second domain of a multi-domain protein. In another aspect, the present ~~invention~~disclosure

relates to a multi-domain protein comprising at least a first and a second domain, wherein said first and second domains are connected by ~~said linker~~ a peptide linker as described herein. ~~In another aspect the invention~~ The disclosure relates to a method of connecting two domains in a multi-domain protein, comprising connecting said domains via the linker. In some ~~embodiment~~ examples, the method may comprise expressing the multi-domain protein from a nucleic acid which encodes the first domain, the linker, and the second domain, wherein the linker connects the first and second domains.

10 In some ~~embodiment~~ examples, the first and domains may be independently selected from i) an Fc domain of an antibody; ii) an antigen binding moiety; and iii) a VL or VH domain (e.g., as may be found in a split antibody or hemibody).

In some ~~embodiment~~ examples, an antigen binding moiety may be an antibody fragment such as a Fv, Fab, cross-Fab, Fab', Fab'-SH, F(ab')₂; diabody; linear antibody; single-chain antibody molecule (e.g., scFv or scFab); or single domain antibody (dAbs) such as VHH; or may be a non-antibody binding scaffold such as a DARPin (designed ankyrin repeat protein); affibody; Sso7d; monobody or anticalin.

In some ~~embodiment~~ examples, the multi-domain protein may be a multispecific antibody e.g., a bispecific antibody. The first and second domains may each be an antibody fragment

capable of binding to an antigen. In another [embodimentexample](#), the linker may be used to connect an antibody fragment to an Fc domain in a multi-specific antibody.

In some [embodimentexamples](#), the multi-domain protein may comprise a first domain which is an antigen binding moiety (such as antibody fragment capable of binding to an antigen), and a second domain which is either a VH or VL domain. In some [embodimentexamples](#), the linker may be used to connect the antigen binding moiety (e.g., antibody fragment) to the VH or VL domain. For instance, in some [embodimentexamples](#) the C-terminus of the antibody fragment (or one chain thereof where the antibody fragment comprises more than one chain, e.g., in the case of a Fab) is connected to the N-terminus of the VH or VL domain. In some [embodimentexamples](#), multi-domain protein may further comprise an Fc domain comprising a first and second subunit, and the linker may be used to connect the first or second subunit of the Fc domain to the VH or VL domain. In one [embodimentexample](#), the C-terminus of the first or second subunit of the Fc domain is connected to the N-terminus of the VH or VL domain. In another [embodimentexample](#), the C-terminus of the VH or VL domain is connected to the N-terminus of the first or second subunit of the Fc domain.

In some [embodimentexamples](#), the multi-domain protein may be any antibody as described herein.

BRIEF DESCRIPTION OF THE FIGURES

Figure 1 shows the schematic structure of a target antigen (TA)-DOTAM bispecific antibody (TA-DOTAM BsAb) belonging to the comparative examples, and exemplary TA-split-DOTAM-VH/VL antibodies.

Figure 2 is a schematic diagram showing the assembly of a split-VH/VL DOTAM binder on tumour cells. The TA-split-DOTAM-VH/VL antibodies will not significantly bind ^{212}Pb -DOTAM unless bound to tumour antigen (TA) on targeted cells, where the two domains of the DOTAM binder are assembled.

Figure 3 shows a schematic overview of an example of the Three-Step TA-PRIT concept, involving use of a clearing agent.

Figure 4 shows a schematic overview of an example of the Two-Step TA-PRIT concept, in which a clearing agent is not used.

Figure 5 shows binding of split antibodies to MKN45 cells to demonstrate CEA binding competence. Detection of antibodies is done using human IgG specific secondary antibodies.

WHAT IS CLAIMED IS:

1. A set of antibodies comprising:

- i) a first antibody comprising an antibody fragment comprising an antigen binding site specific for an antigen expressed on the surface of a target cell, an Fc domain, and a polypeptide comprising a VH domain of an antigen binding site for a radiolabelled compound, wherein the C-terminus of the antibody fragment is fused to the N-terminus of one chain of the Fc domain, and the C-terminus of the polypeptide is fused to the N-terminus of the other chain of the Fc domain, and wherein said first antibody does not comprise a VL domain of an antigen binding site for the radiolabelled compound; and
- ii) a second antibody comprising an antibody fragment comprising an antigen binding site specific for an antigen expressed on the surface of a target cell, an Fc domain, and a polypeptide comprising a VL domain of an antigen binding site for the radiolabelled compound, wherein the C-terminus of the antibody fragment is fused to the N-terminus of one chain of the Fc domain, and the C-terminus of the polypeptide is fused to the N-terminus of the other chain of the Fc domain, and wherein the second antibody does not comprise a VH domain of the antigen binding site for the radiolabelled compound;

wherein said VH domain of the first antibody and said VL domain of the second antibody are together capable of forming a functional antigen binding site for the radiolabelled compound.

2. The set of antibodies of claim 1, wherein the antibody fragment is selected from at least one Fv, scFv, or Fab or cross-Fab fragment, optionally wherein the antibody fragment is a Fab.

~~3. The set of antibodies of claim 2, wherein the antibody fragment is a Fab.~~

~~43.~~ The set of antibodies of ~~any one of claims 1 to 3~~claim 1 or claim 2, wherein the Fc domain is modified to reduce or eliminate effector function.

~~54.~~ The set of antibodies of any one of claims 1 to ~~43~~, wherein the first antibody comprises:

- i) a complete light chain;
- ii) a complete heavy chain;

iii) an additional Fc chain; and

iv) a polypeptide comprising or consisting of the VH domain of the antigen binding site for the radiolabeled compound;

wherein the light chain of (i) and the heavy chain of (ii) together provide an antigen binding site for a target antigen; and wherein the polypeptide comprising or consisting of the VH domain of the antigen binding site for the radiolabeled compound is fused by its C-terminus via a linker to the N-terminus of (iii); and

the second antibody comprises:

v) a complete light chain;

vi) a complete heavy chain;

vii) an additional Fc chain; and

viii) a polypeptide comprising or consisting of the VL domain of the antigen binding site for the radiolabeled compound;

wherein the light chain of (v) and the heavy chain of (vi) together provide an antigen binding site for a target antigen; and wherein the polypeptide comprising or consisting of the VL domain of the antigen binding site for the radiolabeled compound is fused by its C-terminus via a linker to the N-terminus of (vii).

65. The set of antibodies of any one of the preceding claims, wherein the radiolabelled compound comprises radiolabelled DOTA or a salt or functional variant thereof, optionally wherein the radiolabelled DOTA or a salt or functional variant thereof is radiolabelled with a Lu or Y radioisotope.

~~7. The set of antibodies of any one of the preceding claims, wherein the radiolabelled compound is DOTA or a salt or functional variant thereof radiolabelled with a Lu or Y radioisotope.~~

86. The set of antibodies according to claim ~~6 or 75~~, wherein:

i) the VH domain of the antigen binding site for the radiolabelled compound comprises (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO: 35; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO: 36; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO: 37;

- ii) the VH domain of the antigen binding site for the radiolabelled compound comprises the amino acid sequence of SEQ ID NO: 41, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO: 41;
- iii) the VL domain of the antigen binding site for the radiolabelled compound comprises (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 38; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 39; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO: 40; and/or
- iv) the VL domain of the antigen binding site for the radiolabelled compound comprises an amino acid sequence of SEQ ID NO: 42 or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO: 42.

~~9. — The set of antibodies according to any one of claims 6 to 8, wherein the VH domain of the antigen binding site for the radiolabelled compound comprises the amino acid sequence of SEQ ID NO: 41, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO: 41.~~

~~10. — The set of antibodies of any one of claims 6 to 9, wherein the VL domain of the antigen binding site for the radiolabelled compound comprises (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO: 38; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO: 39; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO: 40.~~

~~11. — The set of antibodies of any one of claims 6 to 10, wherein the VL domain of the antigen binding site for the radiolabelled compound comprises an amino acid sequence of SEQ ID NO: 42 or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO: 42.~~

~~127.~~ The set of antibodies of any one of claims 1 to ~~54~~, wherein the radiolabelled compound comprises Pb-DOTAM, optionally wherein the functional binding site for Pb-DOTAM binds with a K_D value of the binding affinity of 100pM, 50pM, 20pM, 10pM, 5pM, 1pM or less, e.g. 0.9pM or less, 0.8pM or less, 0.7pM or less, 0.6pM or less or 0.5pM or less, optionally wherein the functional binding site for Pb-DOTAM binds to Pb-DOTAM and to Bi-DOTAM.

~~13. The set of antibodies according to claim 12, wherein the functional binding site for Pb-DOTAM binds with a K_D value of the binding affinity of 100pM, 50pM, 20pM, 10pM, 5pM, 1pM or less, e.g. 0.9pM or less, 0.8pM or less, 0.7pM or less, 0.6pM or less or 0.5pM or less.~~

~~14. The set of antibodies according to claim 12 or claim 13, wherein the functional binding site for Pb-DOTAM binds to Pb-DOTAM and to Bi-DOTAM.~~

~~158.~~ The set of antibodies ~~of any one of claims 12 to 14~~according to claim 7, wherein the VH domain of the antigen binding site for the radiolabelled compound comprises:

a) heavy chain CDR2 comprising the amino acid sequence FIGSRGDTYYASWAKG (SEQ ID NO:2), or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 2, wherein these substitutions do not include Phe50, Asp56 and/or Tyr58, and optionally also do not include Gly52 and/or Arg54;

b) heavy chain CDR3 comprising the amino acid sequence ERDPYGGGAYPPHL (SEQ ID NO:3), or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 3, wherein these substitutions do not include Glu95, Arg96, Asp97, Pro98, and optionally also do not include Ala100C, Tyr100D, and/or Pro100E and/or optionally also do not include Tyr99;

and a heavy chain CDR1 which is optionally:

c) a heavy chain CDR1 comprising the amino acid sequence GFSLSTYSMS (SEQ ID NO:1) or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 1;
optionally wherein the VH domain of the antigen binding site for the radiolabelled compound comprises (a) CDR-H1 comprising the amino acid sequence of GFSLSTYSMS (SEQ ID NO:1); (b) CDR-H2 comprising the amino acid sequence of FIGSRGDTYYASWAKG (SEQ ID NO:2) and (c) CDR-H3 comprising the amino acid sequence of ERDPYGGGAYPPHL (SEQ ID NO:3)

~~16. The set of antibodies of claim 15, wherein the VH domain of the antigen binding site for the radiolabelled compound comprises (a) CDR-H1 comprising the amino acid sequence of GFSLSTYSMS (SEQ ID NO:1); (b) CDR-H2 comprising the amino acid sequence of~~

~~FIGSRGDTYYASWAKG (SEQ ID NO:2) and (c) CDR H3 comprising the amino acid sequence of ERDPYGGGAYPPHL (SEQ ID NO:3).~~

~~179.~~ The set of antibodies ~~of any one of claims 12 to 16~~ according to claim 7 or 8, wherein:

~~a)~~ the VH domain of the antigen binding site for the radiolabelled compound comprises:

~~i) an amino acid sequence of SEQ ID NO: 143; or~~

~~ii) a variant of SEQ ID NO: 143 comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:143, optionally wherein the N-terminal Q residue remains invariant or is substituted by a residue selected from the group consisting of E, K, R, S, T, A, L, Y, D, N and V; or~~

~~iii) a variant of SEQ ID NO: 143 comprising an amino acid sequence which varies from SEQ ID NO: 143 only by one or more substitutions, and which has at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:143; optionally wherein the N-terminal Q residue remains invariant; or~~

~~b) the VH domain of the antigen binding site for the radiolabelled compound comprises an amino acid sequence of SEQ ID NO: 7, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO: 7, optionally wherein the VH domain of the antigen binding site for the radiolabelled compound further comprises an additional N-terminal residue, e.g., Q or a residue selected from the group consisting of E, K, R, S, T, A, L, Y, D, N and V; or~~

~~c) the VH domain of the antigen binding site for the radiolabelled compound comprises an amino acid sequence of SEQ ID NO: 9, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO: 9, and optionally further comprises an N-terminal residue, e.g., Q or a residue selected from the group consisting of E, K, R, S, T, A, L, Y, D, N and V.~~

~~18.—The set of antibodies of any one of claims 12 to 16, wherein the VH domain of the antigen binding site for the radiolabelled compound comprises an amino acid sequence of SEQ ID NO: 7, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO: 7, optionally wherein the VH domain of the antigen binding site for the radiolabelled compound further comprises an~~

~~additional N-terminal residue, e.g., Q or a residue selected from the group consisting of E, K, R, S, T, A, L, Y, D, N and V.~~

~~19. The set of antibodies of any one of claims 12 to 16, wherein the VH domain of the antigen binding site for the radiolabelled compound comprises an amino acid sequence of SEQ ID NO: 9, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO: 9, and optionally further comprises an N-terminal residue, e.g., Q or a residue selected from the group consisting of E, K, R, S, T, A, L, Y, D, N and V.~~

~~2010.~~ The set of antibodies of any one of claims ~~12 to 197~~ to 9, wherein the VL domain of the antigen binding site for the radiolabelled compound comprises

d) light chain CDR1 comprising the amino acid sequence QSSHSVYSDNDLA (SEQ ID NO:4) or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 4, wherein these substitutions do not include Tyr28 and Asp32;

e) light chain CDR3 comprising the amino acid sequence LGGYDDESPTYG (SEQ ID NO:6) or a variant thereof having up to 1, 2, or 3 substitutions in SEQ ID NO: 6, wherein these substitutions do not include Gly91, Tyr92, Asp93, Thr95c and Tyr96, and a light chain CDR2₁ which is optionally

f) light chain CDR 2 comprising the amino acid sequence QASKLAS (SEQ ID NO: 5) or a variant thereof having at least 1, 2 or 3 substitutions in SEQ ID NO: 5, optionally not including Gln50₁,

and optionally wherein the VL domain of the antigen binding site for the radiolabelled compound comprises (d) CDR-L1 comprising the amino acid sequence of QSSHSVYSDNDLA (SEQ ID NO:4); (e) CDR-L2 comprising the amino acid sequence of QASKLAS (SEQ ID NO:5); and (f) CDR-L3 comprising the amino acid sequence of LGGYDDESPTYG (SEQ ID NO:6).

~~21. The set of antibodies of claim 20, wherein the VL domain of the antigen binding site for the radiolabelled compound comprises (d) CDR-L1 comprising the amino acid sequence of QSSHSVYSDNDLA (SEQ ID NO:4); (e) CDR-L2 comprising the amino acid sequence of QASKLAS (SEQ ID NO:5); and (f) CDR-L3 comprising the amino acid sequence of LGGYDDESPTYG (SEQ ID NO:6).~~

~~2211.~~ The set of antibodies of any one of claims ~~12 to 21~~ 7 to 10, wherein the VL domain of the antigen binding site for the radiolabelled compound comprises

- i) an amino acid sequence of SEQ ID NO: 144, or
- ii) a variant of SEQ ID NO: 144 comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:144, optionally wherein the N-terminal A residue remains invariant or is substituted by another amino acid selected from the group consisting of D, N, E, Q, S, A, V, L, T, Y, K and R; or
- iii) a variant of SEQ ID NO: 144 comprising an amino acid sequence which varies from SEQ ID NO: 144 only by one or more substitutions, and which has at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:144; optionally wherein the N-terminal A residue remains invariant

or

wherein the VL domain of the antigen binding site for the radiolabelled compound comprises an amino acid sequence of SEQ ID NO: 8, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO: 8, and optionally further comprises an additional N-terminal residue such as A or a residue selected from the group consisting of D, N, E, Q, S, A, V, L, T, Y, K and R.

~~23.—The set of antibodies of any one of claims 12 to 21, wherein the VL domain of the antigen binding site for the radiolabelled compound comprises an amino acid sequence of SEQ ID NO: 8, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO: 8, and optionally further comprises an additional N-terminal residue such as A or a residue selected from the group consisting of D, N, E, Q, S, A, V, L, T, Y, K and R.~~

2412. The set of antibodies according to any one of the preceding claims, wherein the first and second antibody bind to the same target antigen, optionally wherein the first and second antibody bind to the same epitope of the target antigen or wherein the first antibody binds to a different epitope of the target antigen from the second antibody.

~~25.—The set of antibodies of claim 24, wherein the first and second antibody bind to the same epitope of the target antigen.~~

~~26. — The set of antibodies of claim 24, wherein the first antibody binds to a different epitope of the target antigen from the second antibody.~~

~~27~~13. The set of antibodies of any one of the preceding claims, wherein the antigen expressed on the surface of a target cell is:

i) a tumour-associated antigen;

ii) selected from the group consisting of carcinoembryonic antigen (CEA), CD20, HER2, EGP-1 (epithelial glycoprotein-1, also known as trophoblast-2), colon-specific antigen-p (CSAp), a pancreatic mucin MUC1, GPRC5D and FAP; or

iii) selected from the group consisting of CEA, GPRC5D and FAP.

~~28. — The set of antibodies of any one of the preceding claims, wherein the antigen expressed on the surface of a target cell is selected from the group consisting of carcinoembryonic antigen (CEA), CD20, HER2, EGP-1 (epithelial glycoprotein-1, also known as trophoblast-2), colon-specific antigen-p (CSAp), a pancreatic mucin MUC1, GPRC5D and FAP.~~

~~29. — The set of antibodies of any one of the preceding claims, wherein the antigen expressed on the surface of a target cell is selected from the group consisting of CEA, GPRC5D and FAP.~~

~~30~~14. The set of antibodies of any one of the preceding claims, wherein the antigen expressed on the surface of a target cell is CEA.

~~31~~15. The set of antibodies according to claim ~~30~~14, wherein the first antibody comprises an antigen-binding site which binds to CEA, comprising

i) _____ a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:19; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:20; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:21; and a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:22; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:23; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:24; and/or

wherein the first antibody comprises an antigen-binding site for CEA comprising a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 25, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:25, and/or wherein the first antibody comprises an antigen-binding site for CEA comprising a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 26, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:26;

or

ii) a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:43; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:44; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:45; and a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:46; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:47; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:48, and/or wherein the first antibody comprises an antigen-binding site for CEA comprising a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 49, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:49, and/or wherein the first antibody comprises an antigen-binding site for CEA comprising a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 50, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:50;

or

iii) a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:11; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:12; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:13; and a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:14; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:15; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:16, and/or wherein the first antibody comprises an antigen-binding site for CEA comprising a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 17, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:17, and/or wherein the first antibody comprises an antigen-

binding site for CEA comprising a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 18, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:18;

or

iv) a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:59; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:60; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:61; and a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:62; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:63; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:64, and/or wherein the first antibody comprises an antigen-binding site for CEA comprising a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 65, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:65, and/or wherein the first antibody comprises an antigen-binding site for CEA comprising a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 66, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:66;

or

v) a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:116; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:117 or 118; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:119; and a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:120, 121 or 122; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:123, 124 or 125; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:126, and/or wherein the first antibody comprises an antigen-binding site which binds to CEA, comprising a heavy chain variable region (VH) comprising an amino acid sequence selected from SEQ ID NO: 129, 130, 131, 132, 133 or 134, or a sequence with 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity thereto; and a light chain variable region (VL) comprising an amino acid sequence selected from SEQ ID NO: 135, 136, 137, 138, 139 or 140, or a sequence with 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity thereto, and/or wherein the first antibody comprises an antigen-binding site which binds to CEA, comprising:
(a) a VH domain comprising an amino acid sequence of SEQ ID NO:129 and a VL domain comprising an amino acid sequence of SEQ ID NO:139, or

(b) a VH domain comprising an amino acid sequence of SEQ ID NO:133 and a VL domain comprising an amino acid sequence of SEQ ID NO:139, or
(c) a VH domain comprising an amino acid sequence of SEQ ID NO:130 and a VL domain comprising an amino acid sequence of SEQ ID NO:139, or
(d) a VH domain comprising an amino acid sequence of SEQ ID NO:134 and a VL domain comprising an amino acid sequence of SEQ ID NO:138, or
(e) a VH domain comprising an amino acid sequence of SEQ ID NO:133 and a VL domain comprising an amino acid sequence of SEQ ID NO:138, or
(f) a VH domain comprising an amino acid sequence of SEQ ID NO:131 and a VL domain comprising an amino acid sequence of SEQ ID NO:138, or
(g) a VH domain comprising an amino acid sequence of SEQ ID NO:129 and a VL domain comprising an amino acid sequence of SEQ ID NO:138.

~~32.—The set of antibodies according to claim 30 or 31, wherein the first antibody comprises an antigen-binding site for CEA comprising a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 25, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:25.~~

~~33.—The set of antibodies according to any one of claims 30-32, wherein the first antibody comprises an antigen-binding site for CEA comprising a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 26, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:26.~~

~~34.—The set of antibodies according to claim 30, wherein the first antibody comprises an antigen-binding site which binds to CEA, comprising a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:43; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:44; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:45; and a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:46; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:47; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:48.~~

~~35.—The set of antibodies according to claim 30 or 34, wherein the first antibody comprises an antigen-binding site for CEA comprising a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 49, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:49.~~

~~36.—The set of antibodies according to any one of claims 30, 34 or 35, wherein the first antibody comprises an antigen-binding site for CEA comprising a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 50, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:50.~~

~~37.—The set of antibodies according to claim 30, wherein the first antibody comprises an antigen-binding site which binds to CEA, comprising~~

~~a heavy chain variable region comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO:11; (b) CDR H2 comprising the amino acid sequence of SEQ ID NO:12; and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO:13; and~~

~~a light chain variable region comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NO:14; (e) CDR L2 comprising the amino acid sequence of SEQ ID NO:15; and (f) CDR L3 comprising the amino acid sequence of SEQ ID NO:16.~~

~~38.—The set of antibodies according to claim 30 or 37, wherein the first antibody comprises an antigen-binding site for CEA comprising a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 17, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:17.~~

~~39.—The set of antibodies according to claim 30, 37 or 38, wherein the first antibody comprises an antigen-binding site for CEA comprising a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 18, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:18.~~

40. — ~~The set of antibodies according to claim 30, wherein the first antibody comprises an antigen-binding site which binds to CEA, comprising~~

~~a heavy chain variable region comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO:59; (b) CDR H2 comprising the amino acid sequence of SEQ ID NO:60; and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO:61; and a light chain variable region comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NO:62; (e) CDR L2 comprising the amino acid sequence of SEQ ID NO:63; and (f) CDR L3 comprising the amino acid sequence of SEQ ID NO:64.~~

41. — ~~The set of antibodies according to claim 30 or claim 40, wherein the first antibody comprises an antigen-binding site for CEA comprising a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 65, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:65.~~

42. — ~~The set of antibodies according to claim 30, 40 or 41, wherein the first antibody comprises an antigen-binding site for CEA comprising a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 66, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:66.~~

43. — ~~The set of antibodies according to claim 40, wherein the first antibody comprises an antigen-binding site which binds to CEA, comprising a heavy chain variable region comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO:116; (b) CDR H2 comprising the amino acid sequence of SEQ ID NO:117 or 118; (c) CDR H3 comprising the amino acid sequence of SEQ ID NO:119; and a light chain variable region comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NO:120, 121 or 122; (e) CDR L2 comprising the amino acid sequence of SEQ ID NO:123, 124 or 125; and (f) CDR L3 comprising the amino acid sequence of SEQ ID NO:126.~~

44. — ~~The set of antibodies according to claim 30 or 43, wherein the first antibody comprises an antigen-binding site which binds to CEA, comprising a heavy chain variable~~

~~region (VH) comprising an amino acid sequence selected from SEQ ID NO: 129, 130, 131, 132, 133 or 134, or a sequence with 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity thereto; and a light chain variable region (VL) comprising an amino acid sequence selected from SEQ ID NO: 135, 136, 137, 138, 139 or 140, or a sequence with 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity thereto.~~

~~45. —The set of antibodies according to claim 30, 43 or 44, wherein the first antibody comprises an antigen-binding site which binds to CEA, comprising:~~

- ~~(a) a VH domain comprising an amino acid sequence of SEQ ID NO:129 and a VL domain comprising an amino acid sequence of SEQ ID NO:139, or~~
- ~~(b) a VH domain comprising an amino acid sequence of SEQ ID NO:133 and a VL domain comprising an amino acid sequence of SEQ ID NO:139, or~~
- ~~(c) a VH domain comprising an amino acid sequence of SEQ ID NO:130 and a VL domain comprising an amino acid sequence of SEQ ID NO:139, or~~
- ~~(d) a VH domain comprising an amino acid sequence of SEQ ID NO:134 and a VL domain comprising an amino acid sequence of SEQ ID NO:138, or~~
- ~~(e) a VH domain comprising an amino acid sequence of SEQ ID NO:133 and a VL domain comprising an amino acid sequence of SEQ ID NO:138, or~~
- ~~(f) a VH domain comprising an amino acid sequence of SEQ ID NO:131 and a VL domain comprising an amino acid sequence of SEQ ID NO:138, or~~
- ~~(g) a VH domain comprising an amino acid sequence of SEQ ID NO:129 and a VL domain comprising an amino acid sequence of SEQ ID NO:138.~~

~~46~~16. The set of antibodies according to ~~any one of claims 30 to 45~~claim 14 or claim 15, wherein the second antibody comprises an antigen-binding site which binds to CEA, comprising

i) _____ a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:19; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:20; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:21; and a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:22; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:23; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:24; and/or wherein the second antibody comprises an antigen-binding site for CEA comprising a VH

sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 25, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:25, and/or wherein the second antibody comprises an antigen-binding site for CEA comprising a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 26, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:26;

or

ii) a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:43; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:44; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:45; and a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:46; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:47; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:48, and/or wherein the second antibody comprises an antigen-binding site for CEA comprising a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 49, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:49, and/or wherein the second antibody comprises an antigen-binding site for CEA comprising a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 50, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:50;

or

iii) a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:11; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:12; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:13; and a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:14; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:15; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:16, and/or wherein the second antibody comprises an antigen-binding site for CEA comprising a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 17, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:17, and/or wherein the second antibody comprises an antigen-binding site for CEA comprising a VL sequence comprising an amino acid sequence selected

from the group consisting of SEQ ID NO: 18, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:18;

or

iv) a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:59; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:60; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:61; and a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:62; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:63; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:64, and/or wherein the second antibody comprises an antigen-binding site for CEA comprising a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 65, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:65, and/or wherein the second antibody comprises an antigen-binding site for CEA comprising a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 66, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:66;

or

v) a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:116; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:117 or 118; (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:119; and a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:120, 121 or 122; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:123, 124 or 125; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:126, and/or wherein the second antibody comprises an antigen-binding site which binds to CEA, comprising a heavy chain variable region (VH) comprising an amino acid sequence selected from SEQ ID NO: 129, 130, 131, 132, 133 or 134, or a sequence with 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity thereto; and a light chain variable region (VL) comprising an amino acid sequence selected from SEQ ID NO: 135, 136, 137, 138, 139 or 140, or a sequence with 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity thereto, and/or wherein the second antibody comprises an antigen-binding site which binds to CEA, comprising:
(a) a VH domain comprising an amino acid sequence of SEQ ID NO:129 and a VL domain comprising an amino acid sequence of SEQ ID NO:139, or

(b) a VH domain comprising an amino acid sequence of SEQ ID NO:133 and a VL domain comprising an amino acid sequence of SEQ ID NO:139, or
(c) a VH domain comprising an amino acid sequence of SEQ ID NO:130 and a VL domain comprising an amino acid sequence of SEQ ID NO:139, or
(d) a VH domain comprising an amino acid sequence of SEQ ID NO:134 and a VL domain comprising an amino acid sequence of SEQ ID NO:138, or
(e) a VH domain comprising an amino acid sequence of SEQ ID NO:133 and a VL domain comprising an amino acid sequence of SEQ ID NO:138, or
(f) a VH domain comprising an amino acid sequence of SEQ ID NO:131 and a VL domain comprising an amino acid sequence of SEQ ID NO:138, or
(g) a VH domain comprising an amino acid sequence of SEQ ID NO:129 and a VL domain comprising an amino acid sequence of SEQ ID NO:138.

~~47. — The set of antibodies according to any one of claims 30-46, wherein the second antibody comprises an antigen-binding site for CEA comprising a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 25, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:25.~~

~~48. — The set of antibodies according to any one of claims 30-47, wherein the second antibody comprises an antigen-binding site for CEA comprising a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 26, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:26.~~

~~49. — The set of antibodies according to any one of claim 30 to 45, wherein the second antibody comprises an antigen-binding site which binds to CEA, comprising a heavy chain variable region comprising (a) CDR-H1 comprising the amino acid sequence of SEQ ID NO:43; (b) CDR-H2 comprising the amino acid sequence of SEQ ID NO:44; and (c) CDR-H3 comprising the amino acid sequence of SEQ ID NO:45; and a light chain variable region comprising (d) CDR-L1 comprising the amino acid sequence of SEQ ID NO:46; (e) CDR-L2 comprising the amino acid sequence of SEQ ID NO:47; and (f) CDR-L3 comprising the amino acid sequence of SEQ ID NO:48.~~

~~50. —The set of antibodies according to any one of claims 30 to 45 or 49, wherein the second antibody comprises an antigen-binding site for CEA comprising a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 49, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:49.~~

~~51. —The set of antibodies according to any one of claims 30 to 45, 49 or 50, wherein the second antibody comprises an antigen-binding site for CEA comprising a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 50, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:50.~~

~~52. —The set of antibodies according to any one of claims 30 to 45, wherein the second antibody comprises an antigen-binding site which binds to CEA, comprising a heavy chain variable region comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO:11; (b) CDR H2 comprising the amino acid sequence of SEQ ID NO:12; and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO:13; and a light chain variable region comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NO:14; (e) CDR L2 comprising the amino acid sequence of SEQ ID NO:15; and (f) CDR L3 comprising the amino acid sequence of SEQ ID NO:16.~~

~~53. —The set of antibodies according to any one of claims 30 to 45 or 52, wherein the second antibody comprises an antigen-binding site for CEA comprising a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 17, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:17.~~

~~54. —The set of antibodies according to any one of claims 30 to 45, 52 or 53, wherein the second antibody comprises an antigen-binding site for CEA comprising a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 18, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:18.~~

55. — ~~The set of antibodies according to any one of claim 30 to 45, wherein the second antibody comprises an antigen-binding site which binds to CEA, comprising~~
a heavy chain variable region comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO:59; (b) CDR H2 comprising the amino acid sequence of SEQ ID NO:60; and (c) CDR H3 comprising the amino acid sequence of SEQ ID NO:61; and
a light chain variable region comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NO:62; (e) CDR L2 comprising the amino acid sequence of SEQ ID NO:63; and (f) CDR L3 comprising the amino acid sequence of SEQ ID NO:64.

56. — ~~The set of antibodies according to any one of claims 30 to 45 or 55, wherein the second antibody comprises an antigen-binding site for CEA comprising a VH sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 65, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:65.~~

57. — ~~The set of antibodies according to claim 30 to 45, 55 or 56, wherein the second antibody comprises an antigen-binding site for CEA comprising a VL sequence comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 66, or a variant thereof comprising an amino acid sequence having at least 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to SEQ ID NO:66.~~

58. — ~~The set of antibodies according to claim 30 to 45, wherein the second antibody comprises an antigen-binding site which binds to CEA, comprising a heavy chain variable region comprising (a) CDR H1 comprising the amino acid sequence of SEQ ID NO:116; (b) CDR H2 comprising the amino acid sequence of SEQ ID NO:117 or 118; (c) CDR H3 comprising the amino acid sequence of SEQ ID NO:119; and a light chain variable region comprising (d) CDR L1 comprising the amino acid sequence of SEQ ID NO:120, 121 or 122; (e) CDR L2 comprising the amino acid sequence of SEQ ID NO:123, 124 or 125; and (f) CDR L3 comprising the amino acid sequence of SEQ ID NO:126.~~

59. — ~~The set of antibodies according to claim 30 to 45 or 58, wherein the second antibody comprises an antigen-binding site which binds to CEA, comprising a heavy chain variable~~

~~region (VH) comprising an amino acid sequence selected from SEQ ID NO: 129, 130, 131, 132, 133 or 134, or a sequence with 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity thereto; and a light chain variable region (VL) comprising an amino acid sequence selected from SEQ ID NO: 135, 136, 137, 138, 139 or 140, or a sequence with 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity thereto.~~

~~60. —The set of antibodies according to claim 30 to 45, 58 or 59, wherein the second antibody comprises an antigen-binding site which binds to CEA, comprising:~~

- ~~(a) a VH domain comprising an amino acid sequence of SEQ ID NO:129 and a VL domain comprising an amino acid sequence of SEQ ID NO:139, or~~
- ~~(b) a VH domain comprising an amino acid sequence of SEQ ID NO:133 and a VL domain comprising an amino acid sequence of SEQ ID NO:139, or~~
- ~~(c) a VH domain comprising an amino acid sequence of SEQ ID NO:130 and a VL domain comprising an amino acid sequence of SEQ ID NO:139, or~~
- ~~(d) a VH domain comprising an amino acid sequence of SEQ ID NO:134 and a VL domain comprising an amino acid sequence of SEQ ID NO:138, or~~
- ~~(e) a VH domain comprising an amino acid sequence of SEQ ID NO:133 and a VL domain comprising an amino acid sequence of SEQ ID NO:138, or~~
- ~~(f) a VH domain comprising an amino acid sequence of SEQ ID NO:131 and a VL domain comprising an amino acid sequence of SEQ ID NO:138, or~~
- ~~(g) a VH domain comprising an amino acid sequence of SEQ ID NO:129 and a VL domain comprising an amino acid sequence of SEQ ID NO:138.~~

~~61~~17. The set of antibodies according to claim ~~30~~14, wherein the first antibody is an antibody according to ~~any one of claims 31 to 33~~claim 14(i) and the second antibody is an antibody according to ~~any one of claims 46 to 48~~claim 15(i).

~~62~~18. The set of antibodies according to claim 1, wherein:

- i) the first antibody comprises a first heavy chain of SEQ ID NO:112, a second heavy chain of SEQ ID NO: 146 and a light chain of SEQ ID NO: 115; and
- ii) the second antibody comprises a first heavy chain of SEQ ID NO:112, a second heavy chain of SEQ ID NO: 145 and a light chain of SEQ ID NO: 115.

~~6319.~~ A set of nucleic acids expressing the set of antibodies of any one of the preceding claims.

~~6420.~~ An expression vector or set of expression vectors comprising the set of nucleic acids according to claim ~~6319~~.

~~6521.~~ A host cell or set of host cells comprising the expression vector or set of expression vectors of claim ~~6420~~.

~~6622.~~ ~~A method of~~Use of a set of antibodies according to any one of claims 1 to 18 in the manufacture of a medicament for pretargeting radioimmunotherapy, the pretargeting radioimmunotherapy comprising

i) ~~administering to a subject~~that the set of antibodies according to any one of claims 1 to ~~6218 is to be administered to a subject~~, wherein the first and second antibodies are to be administered simultaneously or sequentially, in either order, wherein the antibodies bind to the target antigen and localise to the surface of a cell expressing the target antigen; and wherein association of the first and second antibody forms a functional binding site for the radiolabelled compound;
and

ii) ~~subsequently administering~~that a radiolabelled compound is to be administered subsequently, wherein the radiolabelled compound binds to functional binding site for the radiolabelled compound, optionally wherein:

a) the pretargeting radioimmunotherapy does not comprise a step of administration of a clearing or blocking agent; and/or

b) the subject is human; and/or

c) the target antigen is a cancer- or tumour-associated antigen and the method is a method of radioimmunotherapy of a tumour or cancer.

~~67.—The method of claim 66, wherein the method does not comprise a step of administering a clearing or blocking agent.~~

~~68.—The method of claim 66 or 67, wherein the subject is human.~~

~~69.—The method of any one of claims 66 to 67, wherein the target antigen is a cancer or tumour-associated antigen and the method is a method of radioimmunotherapy of a tumour or cancer.~~

~~70.—The set of antibodies according to any one of claims 1 to 62, for use in a method of pretargeting radioimmunotherapy according to any one of claims 66 to 69.~~

~~7123. A method of~~Use of a set of antibodies according to any one of claims 1 to 18 in the manufacture of a medicament for targeting a radioisotope to a tissue or organ for radioimaging, the targeting comprising:

i) ~~administering to a subject~~that a set of antibodies according to any one of claims 1 to ~~62~~18 is to be administered to a subject, wherein the first and second antibodies are to be administered simultaneously or sequentially, in either order, wherein the antibodies bind to a target antigen and localise to the surface of a cell expressing the target antigen, wherein association of the first and second antibody forms a functional binding site for the radiolabelled compound;

and

ii) ~~subsequently administering~~that a radiolabelled compound is to be administered subsequently, wherein the radiolabelled compound binds to the functional binding site for the radiolabelled compound,
optionally wherein:

a) the targeting does not comprise a step of administration of a clearing or blocking agent; and/or

b) the method further comprises a step of imaging, optionally wherein the target antigen is a cancer or tumour-associated antigen and the step of imaging is imaging tumours or cancer.

~~72.—The method of claim 71, wherein the method does not comprise a step of administering a clearing or blocking agent.~~

~~73.—The method of claim 71 or 72, wherein the method further comprises a step of imaging.~~

~~74. — The method of claim 73, wherein the target antigen is a cancer or tumour-associated antigen and the method is a method of imaging tumours or cancer.~~

~~75~~24. A peptide linker consisting of y consecutive residues selected from the group consisting of Gly and Ser, wherein y= 5 to 100, 5 to 70, 5 to 60, 5 to 50 or 10 to 100, 10 to 70, 10 to 60, or 10 to 50, and wherein the last serine is in the y-2 or y-3 position,

optionally:

i) wherein y=10 to 50;

ii) wherein y= 15 to 31 or 15 to 30, optionally wherein y= 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 or 25, optionally wherein y= 20 or 21;

iii) consisting of the sequence (GxS)_n(GGSGG) or (GxS)_n(GGSGGG), wherein G = glycine, S = serine, x = 4 and n=1 to 20, 2 to 20, 1 to 10 or 2 to 10, optionally wherein n= 2, 3, 4 or 5 or wherein n=2, 3 or 4; or

iv) consisting of the sequence GGGGSGGGSGGGSGGSGG (SEQ ID NO: 150) or GGGGSGGGSGGGSGGSGGG (SEQ ID NO: 151).

~~76. — The peptide linker of claim 75, wherein y=10 to 50.~~

~~77. — The peptide linker of claim 75, wherein y= 15 to 31 or 15 to 30;~~

~~78. — The peptide linker of claim 77, wherein y= 15, 16, 17, 18, 19, 20, 21, 22, 23, 24 or 25.~~

~~79. — The peptide linker of claim 78, wherein y= 20 or 21.~~

~~80. — The peptide linker of claim 75, consisting of the sequence (GxS)_n(GGSGG) or (GxS)_n(GGSGGG), wherein G = glycine, S = serine, x = 4 and n=1 to 20, 2 to 20, 1 to 10 or 2 to 10.~~

~~81. — The peptide linker of claim 80, wherein n= 2, 3, 4 or 5.~~

~~82. — The peptide linker of claim 80, wherein n=2, 3 or 4.~~

~~83. The peptide linker of claim 75 consisting of the sequence GGGGSGGGGSGGGSGGSGG (SEQ ID NO: 150) or GGGGSGGGGSGGGSGGSGGG (SEQ ID NO: 151).~~

~~84~~25. Use of a peptide linker of ~~any one of claims 75 to 83~~claim 24, to join a first and a second domain of a multi-domain protein.

~~85~~26. A multi-domain protein comprising at least a first and a second domain, wherein said first and second domains are connected by a peptide linker of ~~any one of claims 75 to 83~~claim 24.

~~86~~27. The use of claim ~~84~~25 or the multi-domain protein of claim ~~85~~26, wherein:

- ~~i) the multi-domain protein is an antibody~~
- ~~ii) the multi-domain protein is a bispecific antibody;~~
- ~~iii) the first domain is an antigen binding moiety, and the second domain is a VH or VL domain, optionally wherein the antigen binding moiety is an antibody fragment; or~~
- ~~iv) the first domain is an Fc domain, and the second domain is a VH or VL domain.~~

~~87. The use of claim 84 or the multi-domain protein of claim 85, wherein the multi-domain protein is a bispecific antibody.~~

~~88. The use of claim 84 or the multi-domain protein of claim 85, wherein the first domain is an antigen binding moiety, and the second domain is a VH or VL domain.~~

~~89. The use of the multi-domain binding protein of claim 88, wherein the antigen binding moiety is an antibody fragment.~~

~~90. The use of claim 84 or the multi-domain protein of claim 85, wherein the first domain is an Fc domain, and the second domain is a VH or VL domain.~~