specific delivery platform components. The alpha particle emitting radioisotope-delivery platforms of the present invention provide shorter half-lives compared to traditional IgGs, but longer half-lives than smaller monomeric antibody fragment formats. Such half-lives allow for a reduction in toxicity due to the alpha emitter, while preserving the antibody fragment long enough in the body to exert therapeutic activity. For example, the alpha particle emitting radioisotope-delivery platforms of the current disclosure exhibit enhanced tumor targeting and reduced accumulation in radiosensitive tissues such as the bone-marrow and kidney. Further and surprisingly, the alpha particle emitting radioisotope-delivery platforms of the present invention exhibit excellent tumor binding and labeling properties for tumors with different antigen densities, which can be a limitation for some use of some immunoconjugates.

[0007a] Described herein, in one aspect, is an immunoconjugate comprising an: a) antigen binding region; b) an immunoglobulin heavy chain constant region; and c) a chelating agent; wherein the molecular weight of the immunoconjugate is between 60 and 110 kDa, wherein the antigen binding region comprises a VHH polypeptide, wherein the immunoglobulin heavy chain constant region comprises an alteration to one or more amino acid residues that reduces binding of the immunoconjugate to the neonatal Fc receptor (FcRn) , wherein the alteration to one or more amino acid residues that reduces binding of the immunoconjugate to the neonatal Fc receptor (FcRn) is to an amino acid residue selected from the list consisting of I253A, H310A, H435Q, and combinations thereof per EU numbering.

[0007b] In another aspect, described herein is the use of the immunoconjugate provided herein in the manufacture of a pharmaceutical composition for treating a cancer or a tumor in an individual, wherein the cancer or the tumor in the individual expresses an antigen specifically bound to the immunoconjugate.

[0007c] In another aspect, described herein is the use of the immunoconjugate provided herein in the manufacture of a pharmaceutical composition for delivering a radioisotope to a cancer cell or a tumor cell in an individual wherein the cancer cell or the tumor cell in the individual expresses an antigen specifically bound to the immunoconjugate.

[0007d] In yet another aspect, described herein is the use of the immunoconjugate provided herein in the manufacture of a pharmaceutical composition for imaging a tumor in an individual, wherein the tumor in the individual expresses an antigen specifically bound to the immunoconjugate.

[0007e] In another aspect, described herein is the immunoconjugate provided herein for use in therapy.

[0007f] In another aspect, described herein is a pharmaceutical composition comprising the immunoconjugate as described herein and a pharmaceutically acceptable carrier.

[0007g] In another aspect, described herein is a nucleic acid encoding the antigen binding region and immunoglobulin heavy chain constant region of the immunoconjugate as described herein.

[0007h] In yet another aspect, described herein is a cell comprising the nucleic acid of as described herein.

[0007i] In yet another aspect, described herein is a method of making the immunoconjugate as described herein, the method comprising culturing a host cell comprising a nucleic acid encoding the antigen binding region and immunoglobulin heavy chain constant region of the immunoconjugate under conditions suitable for expression of the immunoconjugate, and optionally recovering the antigen binding region and immunoglobulin heavy chain constant region of the immunoconjugate from the host cell, a lysate thereof, or a host cell culture medium thereof.

[0008] Described herein in one aspect is an immunoconjugate comprising an: a) antigen binding region; b) an immunoglobulin heavy chain constant region; and c) a chelating agent; wherein the molecular weight of the immunoconjugate is between 60 and 110 kDa. In certain embodiments, the antigen binding region comprises an scFv polypeptide or a VHH polypeptide. In certain embodiments, the antigen binding region comprises an scFv polypeptide. In certain embodiments, the antigen binding region comprises a VHH polypeptide. In certain embodiments, the antigen binding region is humanized. In certain embodiments, rein the antigen binding region specifically binds to HER2 or to DLL3. In certain embodiments, the antigen binding region specifically binds to HER2. In certain embodiments, the antigen binding region of the immunoconjugate comprises: a) a heavy chain CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 21; b) a heavy chain CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 22; and c) a heavy chain CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 23 and that binds to HER2. In certain embodiments, the antigen binding region of the immunoconjugate comprises a sequence that is at least 85%, 90%, 95%, 97%, 98%, 99%, or 100% identical to the sequence set forth in SEQ ID NO: 20 and that binds to HER2. In certain embodiments, the antigen binding region specifically binds to DLL3. In certain embodiments, the antigen binding region of the immunoconjugate comprises: a) a heavy chain CDR1 comprising the amino acid sequence set forth in SEQ ID NO: 31; b) a heavy chain CDR2 comprising the amino acid sequence set forth in SEQ ID NO: 32; and c) a heavy chain CDR3

comprising the amino acid sequence set forth in SEQ ID NO: 33 and that binds to DLL3. In certain embodiments, the antigen binding region of the immunoconjugate comprises a sequence that is at least 85%, 90%, 95%, 97%, 98%, 99%, or 100% identical to the sequence set forth in SEQ ID NO: 30 and that binds to DLL3. In certain embodiments, the immunoglobulin heavy chain constant region comprises a CH2 domain of an immunoglobulin, CH3 domain of an

CLAIMS

What is claimed is:

1. An immunoconjugate comprising an: a) antigen binding region; b) an immunoglobulin heavy chain constant region; and c) a chelating agent; wherein the molecular weight of the immunoconjugate is between 60 and 110 kDa, wherein the antigen binding region comprises a VHH polypeptide, wherein the immunoglobulin heavy chain constant region comprises an alteration to one or more amino acid residues that reduces binding of the immunoconjugate to the neonatal Fc receptor (FcRn), wherein the alteration to one or more amino acid residues that reduces binding of the immunoconjugate to the neonatal Fc receptor (FcRn) is to an amino acid residue selected from the list consisting of I253A, H310A, H435Q, and combinations thereof per EU numbering.

2. The immunoconjugate of claim 1, wherein the antigen binding region specifically binds to HER2 or to DLL3.

3. The immunoconjugate of claims 1 or 2, wherein the immunoglobulin chain constant region further comprises an alteration to one or more amino acid residues that reduces effector function of the immunoglobulin heavy chain constant region; and optionally wherein the alteration to one or more amino acid residues that reduces the effector function of the immunoglobulin heavy chain constant region comprises L234A, L235E, G237A, A330S, and/or P331S per EU numbering.

4. The immunoconjugate of any one of claims 1 to 3, wherein the amino acid alteration to one or more amino acid residues that reduces binding of the immunoconjugate to the neonatal Fc receptor (FcRn) reduces the serum half-life of the immunoconjugate.

5. The immunoconjugate of any one of claims 1 to 4, wherein the immunoconjugate has a serum half-life of less than 72 hours.

6. The immunoconjugate of any one of claims 1 to 5, wherein the chelating agent is a alpha emitter chelating agent or a beta- or gamma-emitter chelating agent, optionally wherein the chelating agent is selected from the list consisting of: DOTA, DO3A, DOTAGA, DOTAGA anhydride, Py4Pa, Py4Pa-NCS, Crown, Macropa, Macropa-NCS, HEHA, CHXoctapa, Bispa, Noneunpa, and combinations thereof.

7. The immunoconjugate of any one of claims 1 to 6, wherein the chelating agent is a beta- or gamma-emitter chelating agent.

8. The immunoconjugate of any one of claims 1 to 7, wherein the chelating agent is coupled to the antigen binding region and/or the immunoglobulin heavy chain constant region by a linker, wherein the. linker or a linker precursor used to form the linker is selected from: 6-maleimidocaproyl (MC), maleimidopropanoyl (MP), valine-citrulline (val-cit), alanine-phenylalanine (ala-phe), p-aminobenzyloxycarbonyl (PAB), and those resulting from conjugation with linker reagents: N-Succinimidyl 4-(2-pyridylthio) pentanoate forming linker moiety 4-mercaptopentanoic acid (SPP), Succinimidyl 4-(N-maleimidomethyl)cyclohexane-1-carboxylate (SMCC), N-Succinimidyl 4-(2-pyridyldithio)butanoate (SPDB), N-Succinimidyl (4-iodo-acetyl) aminobenzoate (SIAB), polyethylene glycol (PEG), a polyethylene glycol polymers (PEGn), and S-2-(4-Isothiocyanatobenzyl) (SCN).

9. The immunoconjugate of any one of claims 1 to 8, further comprising a radioisotope.

10. The immunoconjugate of claim 9, wherein the radioisotope is selected for use in radio-imaging, and wherein the radioisotope is selected from the list consisting of 111-In, 89-Zr, 64-Cu, 68-Ga, and 134-Ce.

11. The immunoconjugate of claim 9, wherein the radioisotope is an alpha emitter selected from the list consisting of 225-Ac, 223-Ra, 224-Ra, 227-Th, 212-Pb, 212-Bi, and 213-Bi.

12. The immunoconjugate of claim 9, wherein the radioisotope is a beta emitter selected from 177-Lu, 90-Y, 67-Cu, and 153-Sm.

13. The immunoconjugate of any one of claims 1 to 12, wherein the molecular weight of the immunoconjugate is between 60 and 90 kDa.

14. Use of the immunoconjugate of any one of claims 9 to 13 in the manufacture of a medicament for treating a cancer or a tumor in an individual, wherein the cancer or the tumor in the individual expresses an antigen specifically bound to the immunoconjugate.

15. Use of the immunoconjugate of any one of claims 9 to 13 in the manufacture of a medicament for delivering a radioisotope to a cancer cell or a tumor cell in an individual, wherein the cancer cell or the tumor cell in the individual expresses an antigen specifically bound to the immunoconjugate.

16. Use of the immunoconjugate of any one of claims 9 to 13, in the manufacture of a medicament for imaging a tumor in an individual, wherein the tumor in the individual expresses an antigen specifically bound to the immunoconjugate.

17. The immunoconjugate of any of claims 9 to 13 for use in therapy.

18. A pharmaceutical composition comprising the immunoconjugate of any one of claims 9 to 13 and a pharmaceutically acceptable carrier.

19. A nucleic acid encoding the antigen binding region and immunoglobulin heavy chain constant region of the immunoconjugate of any one of claims 9 to 13.

20. A cell comprising the nucleic acid of claim 19.

21. A method of making the immunoconjugate of any one of claims 9 to 13, the method comprising culturing a host cell comprising a nucleic acid encoding the antigen binding region and immunoglobulin heavy chain constant region of the immunoconjugate under conditions suitable for expression of the immunoconjugate, and optionally recovering the antigen binding region and immunoglobulin heavy chain constant region of the immunoconjugate from the host cell, a lysate thereof, or a host cell culture medium thereof.