

WHAT IS CLAIMED IS:

1. An antigen-binding protein that binds STEAP1 of SEQ ID NO: 2 and comprises:

(a1) heavy chain CDRs comprising amino acid sequences that differ by no more than 3, 2, or 1 amino acid from i) vhCDR1 SEQ ID NO: 14, vhCDR2 SEQ ID NO: 15 or vhCDR2 SEQ ID NO: 21, and vhCDR3 SEQ ID NO: 16, or ii) vhCDR1 SEQ ID NO: 33, vhCDR2 SEQ ID NO: 34, and vhCDR3 SEQ ID NO: 35; and

(a2) light chain CDRs comprising amino acid sequences that differ by no more than 3, 2, or 1 amino acid from i) vlCDR1 SEQ ID NO: 11, vlCDR2 SEQ ID NO: 12, and vlCDR3 SEQ ID NO: 13; or ii) vlCDR1 SEQ ID NO: 30, vlCDR2 SEQ ID NO: 31, and vlCDR3 SEQ ID NO: 32; or

(b1) a light chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO: 183 or SEQ ID NO: 186; and

(b2) a heavy chain variable domain comprising an amino acid sequence at least 90% identical to SEQ ID NO: 182, SEQ ID NO: 184, or SEQ ID NO: 185.

2. The antigen-binding protein of claim 1, comprising CDR sequences

a) vhCDR1 comprising SEQ ID NO: 14, vhCDR2 comprising SEQ ID NO: 15 or SEQ ID NO: 21, and vhCDR3 comprising SEQ ID NO: 16; or

b) vhCDR1 comprising SEQ ID NO: 33, vhCDR2 comprising SEQ ID NO: 34, and vhCDR3 comprising SEQ ID NO: 35.

3. The antigen-binding protein of any one of claims 1-2, comprising

vhCDR1 comprising SEQ ID NO: 14,

vhCDR2 comprising SEQ ID NO: 15,

vhCDR3 comprising SEQ ID NO: 16,

vlCDR1 comprising SEQ ID NO: 11,

vlCDR2 comprising SEQ ID NO: 12, and

vlCDR3 comprising SEQ ID NO: 13.

4. The antigen-binding protein of any one of claims 1-2, comprising
vhCDR1 comprising SEQ ID NO: 33,
vhCDR2 comprising SEQ ID NO: 34,
vhCDR3 comprising SEQ ID NO: 35,
vlCDR1 comprising SEQ ID NO: 30,
vlCDR2 comprising SEQ ID NO: 31, and
vlCDR3 comprising SEQ ID NO: 32.
5. The antigen-binding protein of any one of claims 1-2, comprising a variable heavy domain comprising SEQ ID NO: 182, SEQ ID NO: 184, or SEQ ID NO: 185.
6. The antigen-binding protein of any one of claims 1-2, comprising a variable light domain comprising SEQ ID NO: 183 or SEQ ID NO: 186.
7. The antigen-binding protein of any one of claims 1-2, comprising a variable heavy domain comprising SEQ ID NO: 182 and a variable light domain comprising SEQ ID NO: 183.
8. An antigen-binding protein that cross-blocks the binding of a reference antigen-binding protein of any one of claims 1-7 to STEAP1 or which is cross-blocked from binding to STEAP1 by a reference antigen-binding protein any one of claims 1-7.
9. The antigen-binding protein of claim 8, wherein the cross-blocking is detected by surface plasmon resonance or ELISA.
10. The antigen-binding protein of claim 8, which does not bind extracellular loop 2 of STEAP1.
11. The antigen-binding protein of claim 8, which preferentially mediates T cell dependent killing of cells with a surface density of STEAP1 of greater than 10,000 STEAP receptors per cell.

12. An antigen-binding protein which binds a region of STEAP1 within amino acids 92-118 and amino acids 279-290.
13. The antigen-binding protein of any one of claims 1-12, wherein the antigen-binding protein is an antibody.
14. The antigen-binding protein of claim 13, which is a monoclonal antibody, a chimeric antibody, or a humanized antibody.
15. The antigen-binding protein of any one of claims 1-14, wherein the antigen-binding protein is an antigen-binding antibody fragment.
16. The antigen-binding protein of any one of claims 1-12, comprising a single chain antibody, a diabody, a triabody, a tetrabody, or a domain antibody.
17. A pharmaceutical composition comprising the antigen-binding protein of any one of claims 1-16 and a physiologically acceptable carrier.
18. The pharmaceutical composition of claim 17, further comprising an anti-PD-1 antigen-binding protein comprising a vhCDR1 comprising the amino acid sequence set forth in SEQ ID NO: 189, a vhCDR2 comprising the amino acid sequence set forth in SEQ ID NO: 190, a vhCDR3 comprising the amino acid sequence set forth in SEQ ID NO: 191, a vlCDR1 comprising the amino acid sequence set forth in SEQ ID NO: 192, a vhCDR2 comprising the amino acid sequence set forth in SEQ ID NO: 193, and a vl CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 194.
19. Use of the pharmaceutical composition of claim 17 or claim 18 in the preparation of a medicament for treating cancer in a subject in need thereof.
20. The use of claim 19, further comprising an anti-PD-1 antigen-binding protein to be administered to the subject.

21. Use of the antigen-binding protein of any one of claims 1-16 in the preparation of a medicament for treating cancer in a subject in need thereof.
22. The use of claim 21, wherein the medicament is for administering an effective amount of the anti-STEAP1 antigen-binding protein in association with an effective amount of an anti-PD-1 antigen-binding protein.
23. A polynucleotide comprising a nucleic acid sequence encoding the light chain variable domain and/or heavy chain variable domain of the antigen-binding protein of any one of claims 1-12.
24. An expression vector comprising the polynucleotide of claim 23.
25. A composition comprising a polynucleotide comprising a nucleic acid sequence encoding the light chain variable domain of the antigen-binding protein of any one of claims 1-12 and a polynucleotide comprising a nucleic acid sequence encoding the heavy chain variable domain of the antigen-binding protein of any one of claims 1-12.
26. A method of making an antigen-binding protein, the method comprising contacting a host cell with the polynucleotide of claim 23 or the composition of claim 25 under conditions that allow expression of the light chain variable domain and the heavy chain variable domain.
27. A bispecific antigen-binding protein comprising the antigen-binding protein of any one of claims 1-12.
28. The bispecific antigen-binding protein of claim 27, which binds STEAP1 and CD3.
29. The bispecific antigen-binding protein of claim 28, comprising a CD3 binding domain comprising CDR sequences of SEQ ID NOs: 170-172 and 174-176.

30. A heterodimeric antibody comprising:

a) a first monomer comprising a first heavy chain comprising:

1) a first variable heavy domain;

2) a first constant heavy chain comprising a first CH1 domain and a first Fc domain;

3) a scFv that binds human CD3 and comprises a scFv variable light domain, an scFv linker and a scFv variable heavy domain; wherein said scFv is covalently attached between the C-terminus of said CH1 domain and the N-terminus of said first Fc domain using domain linker(s);

b) a second monomer comprising a second heavy chain comprising a second variable heavy domain and a second constant heavy chain comprising a second Fc domain; and

c) a common light chain comprising a variable light domain and a constant light domain;

wherein said first variable heavy domain and said variable light domain bind human STEAP1, said second variable heavy domain and said variable light domain bind human STEAP1, and wherein

(i) the first variable heavy domain and the second variable heavy domain comprise heavy chain CDRs comprising amino acid sequences that differ by no more than 3, 2, or 1 amino acid from (a) vhCDR1 SEQ ID NO: 14, (b) vhCDR2 SEQ ID NO: 15 or SEQ ID NO: 21, and (3) vhCDR3 SEQ ID NO: 16, and the variable light domain comprises light chain CDRs comprising amino acid sequences that differ by no more than 3, 2, or 1 amino acid from vlCDR1 SEQ ID NO: 11, vlCDR2 SEQ ID NO: 12, and vlCDR3 SEQ ID NO: 13; or

(ii) the first variable heavy domain and the second variable heavy domain comprise heavy chain CDRs comprising amino acid sequences that differ by no more than 3, 2, or 1 amino acid from vhCDR1 SEQ ID NO: 33, vhCDR2 SEQ ID NO: 34, and vhCDR3 SEQ ID NO: 35, and the variable light domain comprises light chain CDRs comprising amino acid sequences that differ by no more than 3, 2, or 1 amino acid from vlCDR1 SEQ ID NO: 30, vlCDR2 SEQ ID NO: 31, and vlCDR3 SEQ ID NO: 32; or

(iii) the first variable heavy domain and the second variable heavy domain comprise an amino acid sequence at least 90% identical to SEQ ID NO: 182 or 184 and the variable light domain comprises an amino acid sequence at least 90% identical to SEQ ID NO: 183.

31. The heterodimeric antibody of claim 30, wherein the first monomer comprises amino acid substitutions E233P, L235V, G236A, S267K, R292C, N297G, V302C, E357Q, and S364K; the second monomer comprises the amino acid substitutions N208D, E233P, L235V, G236A, S267K, R292C, Q295E, N297G, V302C, L368D, K370S, N384D, Q418E, and N421D; and both monomers comprise a deletion at position 234.

32. The heterodimeric antibody of claim 30 or claim 31, wherein said scFv comprises

(i) a variable heavy domain comprising heavy chain CDRs comprising amino acid sequences that differ by no more than 3, 2, or 1 amino acid from vhCDR1 SEQ ID NO: 170, vhCDR2 SEQ ID NO: 171, and vhCDR3 SEQ ID NO: 172, and a variable light domain comprising light chain CDRs comprising amino acid sequences that differ by no more than 3, 2, or 1 amino acid from vlCDR1 SEQ ID NO: 174, vlCDR2 SEQ ID NO: 175, and vlCDR3 SEQ ID NO: 176; or

(ii) a variable heavy domain comprising an amino acid sequence at least 90% identical to SEQ ID NO: 169 and a variable light domain comprising an amino acid sequence at least 90% identical to SEQ ID NO: 173.

33. The heterodimeric antibody of claim 30 or claim 32, wherein said scFv comprises CDRs comprising vhCDR1 comprising SEQ ID NO: 170, vhCDR2 comprising SEQ ID NO: 171, vhCDR3 comprising SEQ ID NO: 172, vlCDR1 comprising SEQ ID NO: 174, vlCDR2 comprising SEQ ID NO: 175, and vlCDR3 comprising SEQ ID NO: 176.

34. The heterodimeric antibody of any one of claims 30-32, wherein said scFv comprises a variable heavy region and a variable light region of SEQ ID NO: 169 and SEQ ID NO: 173.

35. The heterodimeric antibody of any one of claims 30-34, wherein said scFv has a charged scFv linker.

36. The heterodimeric antibody of claim 35, wherein the charged scFv linker has a positive charge from 3 to 8 and is selected from the group consisting of SEQ ID NOs: 143 to 153.

37. The heterodimeric antibody of claim 35, wherein the scFv linker comprises SEQ ID NO: 152.
38. The heterodimeric antibody of any one of claims 30-34, wherein said scFv comprises the sequence of SEQ ID NO: 44.
39. The heterodimeric antibody of any one of claims 30-38, wherein the first variable heavy domain and the second variable heavy domain comprise CDR sequences vhCDR1 comprising SEQ ID NO: 14, vhCDR2 comprising SEQ ID NO: 15, vhCDR3 comprising SEQ ID NO: 16, and wherein the variable light domain comprises CDR sequences vlCDR1 comprising SEQ ID NO: 11, vlCDR2 comprising SEQ ID NO: 12, and vlCDR3 comprising SEQ ID NO: 13.
40. The heterodimeric antibody of any of claims 30-38, wherein the first variable heavy domain and the second variable heavy domain comprise SEQ ID NO: 182 and the variable light domain comprises SEQ ID NO: 183.
41. The heterodimeric antibody of claim 39 comprising the amino acid substitution N67Q and/or a substitution at one or more of positions 292, 297, or 302.
42. The heterodimeric antibody of claim 30, wherein the first monomer comprises the sequence of SEQ ID NO: 19, the second monomer comprises the sequence of SEQ ID NO: 18, and the common light chain comprises the sequence of SEQ ID NO: 17.
43. The heterodimeric antibody of claim 30, wherein the first monomer comprises the sequence of SEQ ID NO: 202, the second monomer comprises the sequence of SEQ ID NO: 201, and the common light chain comprises the sequence of SEQ ID NO: 200.
44. A nucleic acid composition comprising:
- a) a first nucleic acid encoding the first monomer of any one of claims 30-43;
 - b) a second nucleic acid encoding the second monomer of any one of claims 30-43 and
 - c) a third nucleic acid encoding the common light chain of any one of claims 30-43.

45. A nucleic acid composition comprising:

a) a first expression vector comprising a first nucleic acid encoding the first monomer of any one of claims 30-43;

b) a second expression vector comprising a second nucleic acid encoding the second monomer of any one of claims 30-43; and

c) a third expression vector comprising a third nucleic acid encoding the common light chain of any one of claims 30-43.

46. A host cell comprising the nucleic acid composition of claim 44 or claim 45.

47. A pharmaceutical composition comprising the heterodimeric antibody of any one of claims 30-43.

48. The heterodimeric antibody of any one of claims 30-43 or the pharmaceutical composition of claim 47 for use in treating a subject in need thereof.

49. Use of the heterodimeric antibody of any one of claims 30-43 or the pharmaceutical composition of claim 47 in the preparation of a medicament for treating cancer in a subject in need thereof.

50. The heterodimeric antibody or the pharmaceutical composition for use of claim 48, or the use of claim 49, further comprising an anti-PD-1 antigen-binding protein to be administered to the subject.

51. The use, or the heterodimeric antibody or the pharmaceutical composition for use of any one of claims 20, 22, and 50, wherein the anti-PD1 antigen-binding protein comprises a vhCDR1 comprising the amino acid sequence set forth in SEQ ID NO: 189, a vhCDR2 comprising the amino acid sequence set forth in SEQ ID NO: 190, a vhCDR3 comprising the amino acid sequence set forth in SEQ ID NO: 191, a vlCDR1 comprising the amino acid sequence set forth

in SEQ ID NO: 192, a vhCDR2 comprising the amino acid sequence set forth in SEQ ID NO: 193, and a vl CDR3 comprising the amino acid sequence set forth in SEQ ID NO: 194.

52. The use, or the heterodimeric antibody or the pharmaceutical composition for use of claim 51, wherein the anti-PD1 antigen-binding protein comprises a heavy chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 195 and a light chain variable domain comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 196.

53. The use, or the heterodimeric antibody or the pharmaceutical composition for use of claim 52, wherein the anti-PD1 antigen-binding protein comprises a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO: 195 and a light chain variable domain comprising the amino acid sequence of SEQ ID NO: 196.

54. The use, or the heterodimeric antibody or the pharmaceutical composition for use of any one of claims 51-53, wherein the anti-PD-1 antigen-binding protein is an antigen-binding antibody fragment.

55. The use, or the heterodimeric antibody or the pharmaceutical composition for use of any one of claims 51-53, wherein the anti-PD-1 antigen-binding protein is an antibody.

56. The use, or the heterodimeric antibody or the pharmaceutical composition for use of any one of claims 51-53, wherein the anti-PD-1 antigen-binding protein is a monoclonal antibody, a chimeric antibody, or a humanized antibody.

57. The use, or the heterodimeric antibody or the pharmaceutical composition for use of any one of claims 51-56, wherein the anti-PD1 antigen-binding protein comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 197 and a light chain comprising the amino acid sequence of SEQ ID NO: 198.

58. The use, or the heterodimeric antibody or the pharmaceutical composition for use of any one of claims 51-56, wherein the anti-PD1 antigen-binding protein comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 208 and a light chain comprising the amino acid sequence of SEQ ID NO: 209.

59. The use, or the heterodimeric antibody or the pharmaceutical composition for use of any one of claims 49-58, wherein the cancer is prostate cancer.

60. The use, or the heterodimeric antibody or the pharmaceutical composition for use of any one of claims 49-58, wherein the cancer is Ewing sarcoma.