

expressing tumors are available, and there remains an unmet need unaddressed by current approaches.

For example, colorectal cancer (CRC) shows a high prevalence and predictable expression of B7-H6. It is one of the leading causes of cancer morbidity and mortality worldwide.

5 Approximately 25 % of CRC patients initially present with overt metastasis and metastatic disease develops in 40 – 50 % of newly diagnosed patients. Although recent improvements in chemotherapy and targeted therapies have extended survival durations of metastatic CRC, most patients will succumb to their disease.

10 In view of the poor outlook for cancer patients with advanced disease, there is a need to identify more efficacious therapies, particularly efficacious therapies with improved tolerability.

Thus, it is an object of the invention to provide pharmacologically active agents, compositions and/or methods of treatment that provide certain advantages compared to the agents, compositions and/or methods currently used and/or known in the art. These
15 advantages include improved therapeutic and pharmacological properties, such as *in vivo* efficacy, less side effects, reduced immunogenicity, improved therapeutic window, reduced administration (e.g. infusion) times, lower dosage, extended half-life to allow less frequent dosing and other advantageous properties such as improved ease of preparation, stability, compatibility with conventional antibody processes or reduced costs of goods,
20 especially as compared to candidate drugs already known in the art.

~~BRIEF SUMMARY OF THE INVENTION~~

The present ~~invention~~disclosure is based on a bispecific T cell engaging approach employing multi-specific binding proteins with a binding arm to CD3, which is expressed
25 on T cells, and a binding arm to B7H6, which is expressed on the cell surface of tumor cells. Through simultaneously binding to T cells and tumors cells, the T cell engagers of the present ~~invention~~disclosure force the formation of a cytolytic synapse between the two cells and thereby redirect the T cell activity selectively to the targeted tumor cells.

~~In one aspect, the invention~~The disclosure provides a multi-specific binding protein
30 comprising a first antigen binding unit specifically binding to B7H6 and a second antigen binding unit specifically binding to CD3, wherein said first antigen binding unit specifically binding to B7H6 is selected from the group consisting of i) to xxiv):

SEQ ID NO:136 (CDR1), SEQ ID NO:137 (CDR2) and SEQ ID NO:138 (CDR3);
and

- xxiv) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:139 (CDR1), SEQ ID NO:140 (CDR2) and SEQ ID NO:141 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:142 (CDR1), SEQ ID NO:143 (CDR2) and SEQ ID NO:144 (CDR3).

In one aspect, the present disclosure provides a protein comprising a first antigen binding unit specifically binding to B7H6 and a second antigen binding unit specifically binding to CD3, wherein said first antigen binding unit specifically binding to B7H6 is selected from the group consisting of i) to xxiv):

- i) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:1 (CDR1), SEQ ID NO:2 (CDR2) and SEQ ID NO:3 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:4 (CDR1), SEQ ID NO:5 (CDR2) and SEQ ID NO:6 (CDR3);
- ii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:7 (CDR1), SEQ ID NO:8 (CDR2) and SEQ ID NO:9 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:10 (CDR1), SEQ ID NO:11 (CDR2) and SEQ ID NO:12 (CDR3);
- iii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:13 (CDR1), SEQ ID NO:14 (CDR2) and SEQ ID NO:15 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:16 (CDR1), SEQ ID NO:17 (CDR2) and SEQ ID NO:18 (CDR3);
- iv) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:19 (CDR1), SEQ ID NO:20 (CDR2) and SEQ ID NO:21 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:22 (CDR1), SEQ ID NO:23 (CDR2) and SEQ ID NO:24 (CDR3);

- v) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:25 (CDR1), SEQ ID NO:26 (CDR2) and SEQ ID NO:27 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:28 (CDR1), SEQ ID NO:29 (CDR2) and SEQ ID NO:30 (CDR3);
- 5 vi) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:31 (CDR1), SEQ ID NO:32 (CDR2) and SEQ ID NO:33 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:34 (CDR1), SEQ ID NO:35 (CDR2) and SEQ ID NO:36 (CDR3);
- vii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:37 (CDR1), SEQ ID NO:38 (CDR2) and SEQ ID NO:39 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:40 (CDR1), SEQ ID NO:41 (CDR2) and SEQ ID NO:42 (CDR3);
- 10 viii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:43 (CDR1), SEQ ID NO:44 (CDR2) and SEQ ID NO:45 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:46 (CDR1), SEQ ID NO:47 (CDR2) and SEQ ID NO:48 (CDR3);
- 15 ix) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:49 (CDR1), SEQ ID NO:50 (CDR2) and SEQ ID NO:51 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:52 (CDR1), SEQ ID NO:53 (CDR2) and SEQ ID NO:54 (CDR3);
- 20 x) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:55 (CDR1), SEQ ID NO:56 (CDR2) and SEQ ID NO:57 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:58 (CDR1), SEQ ID NO:59 (CDR2) and SEQ ID NO:60 (CDR3);
- 25 xi) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:61 (CDR1), SEQ ID NO:62 (CDR2) and SEQ ID NO:63 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:64 (CDR1), SEQ ID NO:65 (CDR2) and SEQ ID NO:66 (CDR3);

- xii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:67 (CDR1), SEQ ID NO:68 (CDR2) and SEQ ID NO:69 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:70 (CDR1), SEQ ID NO:71 (CDR2) and SEQ ID NO:72 (CDR3);
- 5 xiii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:73 (CDR1), SEQ ID NO:74 (CDR2) and SEQ ID NO:75 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:76 (CDR1), SEQ ID NO:77 (CDR2) and SEQ ID NO:78 (CDR3);
- 10 xiv) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:79 (CDR1), SEQ ID NO:80 (CDR2) and SEQ ID NO:81 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:82 (CDR1), SEQ ID NO:83 (CDR2) and SEQ ID NO:84 (CDR3);
- 15 xv) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:85 (CDR1), SEQ ID NO:86 (CDR2) and SEQ ID NO:87 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:88 (CDR1), SEQ ID NO:89 (CDR2) and SEQ ID NO:90 (CDR3);
- 20 xvi) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:91 (CDR1), SEQ ID NO:92 (CDR2) and SEQ ID NO:93 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:94 (CDR1), SEQ ID NO:95 (CDR2) and SEQ ID NO:96 (CDR3);
- xvii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:97 (CDR1), SEQ ID NO:98(CDR2) and SEQ ID NO:99 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:100 (CDR1), SEQ ID NO:101 (CDR2) and SEQ ID NO:102 (CDR3);
- 25 xviii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:103 (CDR1), SEQ ID NO:104 (CDR2) and SEQ ID NO:105 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:106 (CDR1), SEQ ID NO:107 (CDR2) and SEQ ID NO:108 (CDR3);

xix) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:109 (CDR1), SEQ ID NO:110 (CDR2) and SEQ ID NO:111 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:112 (CDR1), SEQ ID NO:113 (CDR2) and SEQ ID NO:114 (CDR3);

5 xx) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:115 (CDR1), SEQ ID NO:116 (CDR2) and SEQ ID NO:117 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:118 (CDR1), SEQ ID NO:119 (CDR2) and SEQ ID NO:120 (CDR3);

10 xxi) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:121 (CDR1), SEQ ID NO:122 (CDR2) and SEQ ID NO:123 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:124 (CDR1), SEQ ID NO:125 (CDR2) and SEQ ID NO:126 (CDR3);

15 xxii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:127 (CDR1), SEQ ID NO:128 (CDR2) and SEQ ID NO:129 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:130 (CDR1), SEQ ID NO:131 (CDR2) and SEQ ID NO:132 (CDR3);

20 xxiii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:133 (CDR1), SEQ ID NO:134 (CDR2) and SEQ ID NO:135 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:136 (CDR1), SEQ ID NO:137 (CDR2) and SEQ ID NO:138 (CDR3);
and

25 xxiv) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:139 (CDR1), SEQ ID NO:140 (CDR2) and SEQ ID NO:141 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:142 (CDR1), SEQ ID NO:143 (CDR2) and SEQ ID NO:144 (CDR3).

In some ~~embodiment~~examples of the binding protein of the ~~invention~~disclosure, the first antigen binding unit specifically binding to B7H6 is selected from the group consisting of i) to xxiv):

- i) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:145 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:146;
- 5 ii) a light chain variable domain comprising the amino acid sequences of SEQ ID NO:147 and heavy chain variable domain comprising the amino acid sequences of SEQ ID NO:148;
- iii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:149 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:150;
- 10 iv) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:151 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:152;
- v) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:153 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:154;
- 15 vi) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:155 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:156;
- vii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:157 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:158;
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xviii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:179 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:180;

5 xix) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:181 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:182;

xx) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:183 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:184;

10 xxi) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:185 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:186;

15 xxii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:187 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:188;

xxiii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:189 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:190; and

20 xxiv) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:191 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:192.

| In some embodimentsexamples of the binding protein of the inventiondisclosure, the second antigen binding unit specifically binding to CD3 is selected from the group consisting of i)-vi):

25 i) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:257 (CDR1), SEQ ID NO:258 (CDR2) and SEQ ID NO:259 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:260 (CDR1), SEQ ID NO:261 (CDR2) and SEQ ID NO:262 (CDR3);

30 ii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:263 (CDR1), SEQ ID NO:264 (CDR2) and SEQ ID NO:265 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:266 (CDR1), SEQ ID NO:267 (CDR2) and SEQ ID NO:268 (CDR3);

- iii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:269 (CDR1), SEQ ID NO:270 (CDR2) and SEQ ID NO:271 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:272 (CDR1), SEQ ID NO:273 (CDR2) and SEQ ID NO:274 (CDR3);
- 5 iv) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:275 (CDR1), SEQ ID NO:276 (CDR2) and SEQ ID NO:277 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:278 (CDR1), SEQ ID NO:279 (CDR2) and SEQ ID NO:280 (CDR3);
- v) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:281 (CDR1), SEQ ID NO:282 (CDR2) and SEQ ID NO:283 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:284 (CDR1), SEQ ID NO:285 (CDR2) and SEQ ID NO:286 (CDR3);
- 10 and
- vi) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:287 (CDR1), SEQ ID NO:288 (CDR2) and SEQ ID NO:289 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:290 (CDR1), SEQ ID NO:291 (CDR2) and SEQ ID NO:292 (CDR3).
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In some embodimentsexamples of the binding protein of the inventiondisclosure, the second antigen binding unit specifically binding to CD3 is selected from the group consisting of i)

20 to vi):

- i) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:293 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:294;
- ii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:295 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:296;
- 25 iii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:297 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:298;
- iv) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:299 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:300;
- 30

- v) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:301 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:302; and
- vi) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:303 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:304.

In some embodimentsexamples of the binding protein of the inventiondisclosure, the first antigen binding unit specifically binding to B7H6 comprises from its N- to C-terminus a first light chain variable domain, a first light chain constant domain, a first peptide linker, a first heavy chain variable domain and a first heavy chain constant CH1 domain; and the second antigen binding unit specifically binding to CD3 comprises from its N- to C-terminus a second light chain variable domain, a second light chain constant domain, a second peptide linker, a second heavy chain variable domain and a second heavy chain constant CH1 domain. In some embodimentsexamples of the binding protein of the inventiondisclosure, the first and/or second peptide linker comprises 26 to 42 amino acids, preferably any one of 30 to 40 amino acids, 34 to 40 amino acids, or 36 to 39 amino acids, more preferably 38 amino acids. In some embodimentsexamples of the inventiondisclosure, the first linker and/or second linker is a Gly-Ser linker, preferably comprising the amino acid sequence of SEQ ID NO:250, more preferably said first and second peptide linker comprise the same sequence (e.g. SEQ ID NO:250). In some embodimentsexamples of the inventiondisclosure, the first light chain constant domain and the second light chain constant domain comprise independently a human kappa or lambda domain.

In some embodimentsexamples, the first antigen binding unit specific for B7H6 of the binding protein of the inventiondisclosure comprises an amino acid sequence selected from the group consisting of SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196 SEQ ID NO:197 SEQ ID NO:198 SEQ ID NO:199 SEQ ID NO:200 SEQ ID NO:201 SEQ ID NO:202 SEQ ID NO:203 SEQ ID NO:204 SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, and SEQ ID NO:216 and the second antigen binding unit specific for CD3 comprises an amino acid sequence selected from the group consisting of SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, and SEQ ID NO:310, preferably SEQ ID NO:305.

In some ~~embodiment~~examples, the binding protein of the ~~invention~~disclosure further comprises a first and a second Fc domain, wherein said first Fc domain is covalently linked to said first antigen binding unit, preferably to the C-terminus of said first antigen binding unit, and said second Fc domain is covalently linked to said second antigen binding unit, preferably to the C-terminus of said second antigen binding unit.

In some ~~embodiment~~examples of the ~~invention~~disclosure,

- i) the first Fc domain comprises a tyrosine (Y) at position 366 [T366Y], and the second Fc domain comprises a threonine (T) at position 407 [Y407T], or
- ii) the first Fc domain comprises a tryptophan (W) at position 366 [T366W], and the second Fc domain comprises a serine (S) at position 366 [T366S], an alanine (A) at position 368 [L368A] and a valine (V) at position 407 [Y407V], or
- iii) the second Fc domain comprises a tyrosine (Y) at position 366 [T366Y], and the first Fc domain comprises a threonine (T) at position 407 [Y407T], or
- iv) the second Fc domain comprises a tryptophan (W) at position 366 [T366W], and the first Fc domain comprises a serine (S) at position 366 [T366S], an alanine (A) at position 368 [L368A] and a valine (V) at position 407 [Y407V],

preferably wherein the first or the second Fc domain further comprises an arginine at position 435 [H435R] and a phenylalanine at position 436 [Y436F]. In some

~~embodiment~~examples, the first and/or second Fc domain comprises an alanine at position 234[L234A] and at position 235 [L235A].

In some ~~embodiment~~examples, the binding protein of the ~~invention~~disclosure comprises a first polypeptide chain specifically binding to B7H6 comprising an amino acid sequence selected from the group consisting of SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO: 224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, and SEQ ID NO:240 and a second polypeptide chain specifically binding to CD3 comprising the amino acid sequence selected from the group consisting of SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, and SEQ ID NO:316, preferably SEQ ID NO:311.

~~In a further aspect, the invention~~The disclosure provides an isolated nucleic acid molecule i) encoding a first antigen binding unit and/or a second antigen binding unit of a binding protein of the ~~invention~~disclosure, optionally further encoding a first and/or a second Fc domain, or ii) encoding the first and/or the second polypeptide chain of binding protein of the ~~invention~~disclosure. In a further aspect, the disclosure provides an isolated nucleic acid molecule encoding the first antigen binding unit and/or the second antigen binding unit of a protein of the disclosure, optionally further encoding a first and/or a second Fc domain. In a further aspect, the disclosure provides an isolated nucleic acid molecule encoding the first and/or the second polypeptide chain of the disclosure. In further aspects provided herein~~are~~The disclosure provides expression vectors comprising the nucleic acid molecule of the ~~invention~~disclosure, host cells transfected with such expression vectors, and methods of manufacturing a protein of the ~~invention~~disclosure. In a further aspect, the disclosure provides an expression vector comprising the nucleic acid molecule of the disclosure. In a further aspect, the disclosure provides a host cell transfected with the expression vector of the disclosure. In a further aspect, the disclosure provides a method of manufacturing a protein of the disclosure comprising

i) cultivating the host cell of the disclosure under conditions allowing expression of the protein of the disclosure; and,

ii) recovering the protein; and optionally

iii) further purifying and/or modifying and/or formulating the protein.

~~In a further aspect of the invention, provided herein is~~The disclosure provides a multi-specific binding protein comprising a first polypeptide chain specifically binding to B7H6 and a second polypeptide chain specifically binding to CD3, where the first polypeptide chain comprises a first light chain, a first linker, and a first heavy chain and the second polypeptide chain comprises a second light chain, a second linker, and a second heavy chain, preferably the C-terminus of the first light chain is covalently bound to the N-terminus of the first heavy chain via the first peptide linker and the C-terminus of the second light chain is covalently bound to the N-terminus of the second heavy chain via the second peptide linker. The skilled person would understand that any reference herein to a “light chain” or “heavy chain” refers to an antibody light chain or antibody heavy chain, respectively.

In some ~~embodiment~~examples of the protein of the ~~invention~~disclosure, the first polypeptide chain specifically binding to B7H6 comprises a light chain variable and heavy chain variable domain comprising CDR sequences, VH/VL sequences and/or single chain Fab sequences as defined for the antigen binding units of any one of B7H6#1, B7H6#2, B7H6#3, B7H6#4, B7H6#5, B7H6#12, B7H6#13, B7H6#14, B7H6#15, B7H6#16, B7H6#17, B7H6#18, B7H6#19, B7H6#20, B7H6#21, B7H6#22, B7H6#23 and B7H6#24 described herein. In some ~~embodiment~~examples, the second polypeptide chain specifically binding to CD3 comprises a light chain variable and heavy chain variable domain comprising CDR sequences, VH/VL sequences and/or scFab sequences as defined for the antigen binding units of CD3#1, as described herein.

~~Further aspects, embodiments,~~The disclosure provides uses and methods involving the binding proteins of the ~~invention~~disclosure will become clear from the following detailed description of the ~~invention~~disclosure and from the appended claims.

The ~~invention~~disclosure provides for novel binding proteins that allow a more efficient treatment of B7H6 expressing cancers, such as (metastatic) colorectal cancer ((m)CRC), non-small cell lung cancer (NSCLC), or head and neck squamous cell carcinoma (HNSCC).

5 In a further aspect, the disclosure provides the protein of the disclosure for use in medicine.

In a further aspect, the disclosure provides a pharmaceutical composition comprising the protein of the disclosure and a pharmaceutically acceptable carrier.

In a further aspect, the disclosure provides use of the protein of the disclosure in the manufacture of a pharmaceutical composition for treating cancer.

10 In a further aspect, the disclosure provides the protein of the disclosure for use in treating cancer.

BRIEF DESCRIPTION OF THE DRAWINGS

Figure 1: Schematic representation of a bispecific binding protein of the invention

15 **Figure 2:** Schematic representation of the extracellular B7H6 protein expressed on the cell surface of CHO-K1 cells.

Figure 3: Binding of 34 exemplary B7H6/CD3 binding proteins to recombinant human B7H6 extracellular protein.

20 **Figure 4:** Binding of 34 exemplary B7H6/CD3 binding proteins to recombinant human Alanine-mutated B7H6 extracellular protein.

Figure 5: Binding of 34 exemplary B7H6/CD3 binding proteins to HCT-15 cells expressing endogenous human B7H6.

Figure 6: Binding of 23 exemplary B7H6/CD3 binding proteins to recombinant CHO-K1 cells expressing cynomolgus monkey B7H6.

25 **Figure 7:** Binding of 23 exemplary B7H6/CD3 binding proteins to human T-cells expressing CD3.

Figure 8: Binding of 23 exemplary B7H6/CD3 binding proteins to B7H6-negative CHO-K1 cells.

Figure 9: Inhibitory activity of 17 exemplary B7H6/CD3 binding proteins of B7H6-dependent IFN γ secretion by NK-92MI cells.

5 **Figure 10:** Potency in lysing target cells of 11 exemplary B7H6/CD3 binding proteins redirecting non-stimulated T-cells towards human HCT-15 cells.

Figure 11: Potency in lysing target cells of 23 exemplary B7H6/CD3 binding proteins redirecting non-stimulated T-cells towards human HCT-15 cells.

10 **Figure 12:** Potency in lysing target cells of an exemplary B7H6/CD3 binding protein at various effector to target (E:T) cell ratios.

CLAIMS

1. A protein comprising a first antigen binding unit specifically binding to B7H6 and a second antigen binding unit specifically binding to CD3, wherein said first antigen binding unit specifically binding to B7H6 is selected from the group consisting of i) to xxiv):
 - i) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:1 (CDR1), SEQ ID NO:2 (CDR2) and SEQ ID NO:3 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:4 (CDR1), SEQ ID NO:5 (CDR2) and SEQ ID NO:6 (CDR3);
 - ii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:7 (CDR1), SEQ ID NO:8 (CDR2) and SEQ ID NO:9 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:10 (CDR1), SEQ ID NO:11 (CDR2) and SEQ ID NO:12 (CDR3);
 - iii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:13 (CDR1), SEQ ID NO:14 (CDR2) and SEQ ID NO:15 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:16 (CDR1), SEQ ID NO:17 (CDR2) and SEQ ID NO:18 (CDR3);
 - iv) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:19 (CDR1), SEQ ID NO:20 (CDR2) and SEQ ID NO:21 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:22 (CDR1), SEQ ID NO:23 (CDR2) and SEQ ID NO:24 (CDR3);
 - v) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:25 (CDR1), SEQ ID NO:26 (CDR2) and SEQ ID NO:27 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:28 (CDR1), SEQ ID NO:29 (CDR2) and SEQ ID NO:30 (CDR3);
 - vi) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:31 (CDR1), SEQ ID NO:32 (CDR2) and SEQ ID NO:33 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:34 (CDR1), SEQ ID NO:35 (CDR2) and SEQ ID NO:36 (CDR3);

- vii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:37 (CDR1), SEQ ID NO:38 (CDR2) and SEQ ID NO:39 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:40 (CDR1), SEQ ID NO:41 (CDR2) and SEQ ID NO:42 (CDR3);
- viii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:43 (CDR1), SEQ ID NO:44 (CDR2) and SEQ ID NO:45 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:46 (CDR1), SEQ ID NO:47 (CDR2) and SEQ ID NO:48 (CDR3);
- ix) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:49 (CDR1), SEQ ID NO:50 (CDR2) and SEQ ID NO:51 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:52 (CDR1), SEQ ID NO:53 (CDR2) and SEQ ID NO:54 (CDR3);
- x) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:55 (CDR1), SEQ ID NO:56 (CDR2) and SEQ ID NO:57 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:58 (CDR1), SEQ ID NO:59 (CDR2) and SEQ ID NO:60 (CDR3);
- xi) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:61 (CDR1), SEQ ID NO:62 (CDR2) and SEQ ID NO:63 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:64 (CDR1), SEQ ID NO:65 (CDR2) and SEQ ID NO:66 (CDR3);
- xii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:67 (CDR1), SEQ ID NO:68 (CDR2) and SEQ ID NO:69 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:70 (CDR1), SEQ ID NO:71 (CDR2) and SEQ ID NO:72 (CDR3);
- xiii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:73 (CDR1), SEQ ID NO:74 (CDR2) and SEQ ID NO:75 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:76 (CDR1), SEQ ID NO:77 (CDR2) and SEQ ID NO:78 (CDR3);
- xiv) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:79 (CDR1), SEQ ID NO:80 (CDR2) and SEQ ID NO:81

- (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:82 (CDR1), SEQ ID NO:83 (CDR2) and SEQ ID NO:84 (CDR3);
- xv) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:85 (CDR1), SEQ ID NO:86 (CDR2) and SEQ ID NO:87 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:88 (CDR1), SEQ ID NO:89 (CDR2) and SEQ ID NO:90 (CDR3);
 - xvi) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:91 (CDR1), SEQ ID NO:92 (CDR2) and SEQ ID NO:93 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:94 (CDR1), SEQ ID NO:95 (CDR2) and SEQ ID NO:96 (CDR3);
 - xvii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:97 (CDR1), SEQ ID NO:98 (CDR2) and SEQ ID NO:99 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:100 (CDR1), SEQ ID NO:101 (CDR2) and SEQ ID NO:102 (CDR3);
 - xviii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:103 (CDR1), SEQ ID NO:104 (CDR2) and SEQ ID NO:105 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:106 (CDR1), SEQ ID NO:107 (CDR2) and SEQ ID NO:108 (CDR3);
 - xix) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:109 (CDR1), SEQ ID NO:110 (CDR2) and SEQ ID NO:111 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:112 (CDR1), SEQ ID NO:113 (CDR2) and SEQ ID NO:114 (CDR3);
 - xx) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:115 (CDR1), SEQ ID NO:116 (CDR2) and SEQ ID NO:117 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:118 (CDR1), SEQ ID NO:119 (CDR2) and SEQ ID NO:120 (CDR3);
 - xxi) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:121 (CDR1), SEQ ID NO:122 (CDR2) and SEQ ID NO:123 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:124 (CDR1), SEQ ID NO:125 (CDR2) and SEQ ID NO:126 (CDR3);

- xxii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:127 (CDR1), SEQ ID NO:128 (CDR2) and SEQ ID NO:129 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:130 (CDR1), SEQ ID NO:131 (CDR2) and SEQ ID NO:132 (CDR3);
- xxiii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:133 (CDR1), SEQ ID NO:134 (CDR2) and SEQ ID NO:135 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:136 (CDR1), SEQ ID NO:137 (CDR2) and SEQ ID NO:138 (CDR3);
and
- xxiv) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:139 (CDR1), SEQ ID NO:140 (CDR2) and SEQ ID NO:141 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:142 (CDR1), SEQ ID NO:143 (CDR2) and SEQ ID NO:144 (CDR3).

2. The protein of claim 1, wherein said first antigen binding unit specifically binding to B7H6 is selected from the group consisting of i) to xxiv):

- i) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:145 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:146;
- ii) a light chain variable domain comprising the amino acid sequences of SEQ ID NO:147 and heavy chain variable domain comprising the amino acid sequences of SEQ ID NO:148;
- iii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:149 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:150;
- iv) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:151 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:152;
- v) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:153 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:154;

- vi) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:155 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:156;
- vii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:157 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:158;
- viii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:159 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:160;
- ix) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:161 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:162;
- x) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:163 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:164;
- xi) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:165 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:166;
- xii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:167 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:168;
- xiii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:169 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:170;
- xiv) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:171 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:172;
- xv) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:173 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:174;

- xvi) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:175 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:176;
 - xvii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:177 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:178;
 - xviii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:179 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:180;
 - xix) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:181 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:182;
 - xx) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:183 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:184;
 - xxi) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:185 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:186;
 - xxii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:187 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:188;
 - xxiii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:189 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:190; and
 - xxiv) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:191 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:192.
3. The protein of claim 1 or 2, wherein said second antigen binding unit specifically binding to CD3 is selected from the group consisting of i)-vi):
- i) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:257 (CDR1), SEQ ID NO:258 (CDR2) and SEQ ID

- NO:259 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:260 (CDR1), SEQ ID NO:261 (CDR2) and SEQ ID NO:262 (CDR3);
- ii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:263 (CDR1), SEQ ID NO:264 (CDR2) and SEQ ID NO:265 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:266 (CDR1), SEQ ID NO:267 (CDR2) and SEQ ID NO:268 (CDR3);
 - iii) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:269 (CDR1), SEQ ID NO:270 (CDR2) and SEQ ID NO:271 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:272 (CDR1), SEQ ID NO:273 (CDR2) and SEQ ID NO:274 (CDR3);
 - iv) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:275 (CDR1), SEQ ID NO:276 (CDR2) and SEQ ID NO:277 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:278 (CDR1), SEQ ID NO:279 (CDR2) and SEQ ID NO:280 (CDR3);
 - v) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:281 (CDR1), SEQ ID NO:282 (CDR2) and SEQ ID NO:283 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:284 (CDR1), SEQ ID NO:285 (CDR2) and SEQ ID NO:286 (CDR3); and
 - vi) an antigen binding unit comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:287 (CDR1), SEQ ID NO:288 (CDR2) and SEQ ID NO:289 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:290 (CDR1), SEQ ID NO:291 (CDR2) and SEQ ID NO:292 (CDR3).
4. The protein of any one of claims 1 to 3, wherein said second antigen binding unit specifically binding to CD3 is selected from the group consisting of i) to vi):
- i) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:293 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:294;

- ii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:295 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:296;
- iii) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:297 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:298;
- iv) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:299 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:300;
- v) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:301 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:302; and
- vi) a light chain variable domain comprising the amino acid sequence of SEQ ID NO:303 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:304.

5. The protein of any one of claims 1 to 4, wherein

- i) said first antigen binding unit specifically binding to B7H6 comprises from its N- to C-terminus a first light chain variable domain, a first light chain constant domain, a first peptide linker, a first heavy chain variable domain and a first heavy chain constant CH1 domain; and
- ii) said second antigen binding unit specifically binding to CD3 comprises from its N- to C-terminus a second light chain variable domain, a second light chain constant domain, a second peptide linker, a second heavy chain variable domain and a second heavy chain constant CH1 domain.

6. The protein of claim 5, wherein

- i) said first antigen binding unit comprises light chain CDRs comprising the amino acid sequences of SEQ ID NO:67 (CDR1), SEQ ID NO:68 (CDR2) and SEQ ID NO:69 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:70 (CDR1), SEQ ID NO:71 (CDR2) and SEQ ID NO:72 (CDR3), and said second antigen binding unit comprises light chain CDRs comprising the amino

acid sequences of SEQ ID NO:257 (CDR1), SEQ ID NO:258 (CDR2) and SEQ ID NO:259 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:260 (CDR1), SEQ ID NO:261 (CDR2) and SEQ ID NO:262 (CDR3);
or

ii) said first antigen binding unit comprises light chain CDRs comprising the amino acid sequences of SEQ ID NO:79 (CDR1), SEQ ID NO:80 (CDR2) and SEQ ID NO:81 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:82 (CDR1), SEQ ID NO:83 (CDR2) and SEQ ID NO:84 (CDR3) and said second antigen binding unit comprises light chain CDRs comprising the amino acid sequences of SEQ ID NO:257 (CDR1), SEQ ID NO:258 (CDR2) and SEQ ID NO:259 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:260 (CDR1), SEQ ID NO:261 (CDR2) and SEQ ID NO:262 (CDR3);
or

iii) said first antigen binding unit comprises light chain CDRs comprising the amino acid sequences of SEQ ID NO:85 (CDR1), SEQ ID NO:86 (CDR2) and SEQ ID NO:87 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:88 (CDR1), SEQ ID NO:89 (CDR2) and SEQ ID NO:90 (CDR3) and said second antigen binding unit comprises light chain CDRs comprising the amino acid sequences of SEQ ID NO:257 (CDR1), SEQ ID NO:258 (CDR2) and SEQ ID NO:259 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:260 (CDR1), SEQ ID NO:261 (CDR2) and SEQ ID NO:262 (CDR3);
or

iv) said first antigen binding unit comprises light chain CDRs comprising the amino acid sequences of SEQ ID NO:91 (CDR1), SEQ ID NO:92 (CDR2) and SEQ ID NO:93 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:94 (CDR1), SEQ ID NO:95 (CDR2) and SEQ ID NO:96 (CDR3) and said second antigen binding unit comprises light chain CDRs comprising the amino acid sequences of SEQ ID NO:257 (CDR1), SEQ ID NO:258 (CDR2) and SEQ ID NO:259 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:260 (CDR1), SEQ ID NO:261 (CDR2) and SEQ ID NO:262 (CDR3).

7. The protein of claim 5 or 6, wherein

- i) said first antigen binding unit comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:167 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:168, and said second antigen binding unit comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:293 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:294; or
 - ii) said first antigen binding unit comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:171 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:172, and said second antigen binding unit comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:293 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:294; or
 - iii) said first antigen binding unit comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:173 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:174, and said second antigen binding unit comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:293 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:294; or
 - iv) said first antigen binding unit comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:175 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:176, and said second antigen binding unit comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:293 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:294.
8. The protein of any one of claims 5 to 7, wherein said first and/or second peptide linker comprises 26 to 42 amino acids, preferably any one of 30 to 40 amino acids, 34 to 40 amino acids, or 36 to 39 amino acids, more preferably 38 amino acids.
9. The protein of any one of claims 5 to 8, wherein said first linker and/or second linker is a Gly-Ser linker, preferably comprising the amino acid sequence of SEQ ID NO:250, more preferably said first and second peptide linker comprise the same sequence (e.g., SEQ ID NO:250).

10. The protein of any one of claims 5 to 9, wherein the first light chain constant domain and the second light chain constant domain comprise a human kappa or lambda domain.
11. The protein of any one of claims 5 to 10, wherein said first antigen binding unit specific for B7H6 comprises an amino acid sequence selected from the group consisting of SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196, SEQ ID NO:197, SEQ ID NO:198, SEQ ID NO:199, SEQ ID NO:200, SEQ ID NO:201, SEQ ID NO:202, SEQ ID NO:203, SEQ ID NO:204, SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, and SEQ ID NO:216 and said second antigen binding unit specific for CD3 comprises an amino acid sequence selected from the group consisting of SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, and SEQ ID NO:310.
12. The protein of claim 11, wherein
 - (i) said first antigen binding unit specific for B7H6 comprises an amino acid sequence of SEQ ID NO: 204 and said second antigen binding unit specific for CD3 comprises an amino acid sequence of SEQ ID NO:305; or
 - (ii) said first antigen binding unit specific for B7H6 comprises an amino acid sequence of SEQ ID NO: 206 and said second antigen binding unit specific for CD3 comprises an amino acid sequence of SEQ ID NO.305;
 - (iii) said first antigen binding unit specific for B7H6 comprises an amino acid sequence of SEQ ID NO: 207 and said second antigen binding unit specific for CD3 comprises an amino acid sequence of SEQ ID NO.305; or
 - (iv) said first antigen binding unit specific for B7H6 comprises an amino acid sequence of SEQ ID NO: 208 and said second antigen binding unit specific for CD3 comprises an amino acid sequence of SEQ ID NO.305.
13. The protein of any one of claims 5 to 12 further comprising a first and a second Fc domain, said first Fc domain being covalently linked to said first antigen binding unit, preferably to the C-terminus of said first antigen binding unit, and said second Fc domain being covalently linked to said second antigen binding unit, preferably to the C-terminus of said second antigen binding unit.
14. The protein of claim 13, wherein

- i) said first Fc domain comprises a tyrosine (Y) at position 366 [T366Y], and said second Fc domain comprises a threonine (T) at position 407 [Y407T], or
- ii) said first Fc domain comprises a tryptophan (W) at position 366 [T366W], and said second Fc domain comprises a serine (S) at position 366 [T366S], an alanine (A) at position 368 [L368A] and a valine (V) at position 407 [Y407V], or
- iii) said second Fc domain comprises a tyrosine (Y) at position 366 [T366Y], and said first Fc domain comprises a threonine (T) at position 407 [Y407T], or
- iv) said second Fc domain comprises a tryptophan (W) at position 366 [T366W], and said first Fc domain comprises a serine (S) at position 366 [T366S], an alanine (A) at position 368 [L368A] and a valine (V) at position 407 [Y407V],

preferably wherein said first or said second Fc domain further comprises an arginine at position 435 [H435R] and a phenylalanine at position 436 [Y436F].

15. The protein of claim 13 or 14, wherein said first and/or said second Fc domain comprises an alanine at position 234[L234A] and at position 235 [L235A], preferably said first Fc domain comprises an amino acid sequence of SEQ ID NO:242 and said second Fc domain comprises an amino acid sequence of SEQ ID NO:243.
16. The protein of any one of claims 5 to 15 comprising a first polypeptide chain specifically binding to B7H6 comprising an amino acid sequence selected from the group consisting of SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO: 224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, and SEQ ID NO:240 and a second polypeptide chain specifically binding to CD3 comprising the amino acid sequence selected from the group consisting of SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, and SEQ ID NO:316.
17. The protein of claim 16, wherein
 - (i) said first polypeptide chain specifically binding to B7H6 comprises an amino acid sequence of SEQ ID NO: 228 and said second polypeptide chain specifically binding to CD3 comprises and amino acid sequence of SEQ ID NO:311; or

- (ii) said first polypeptide chain specifically binding to B7H6 comprises an amino acid sequence of SEQ ID NO: 230 and said second polypeptide chain specifically binding to CD3 comprises an amino acid sequence of SEQ ID NO:311, or
 - (iii) said first polypeptide chain specifically binding to B7H6 comprises an amino acid sequence of SEQ ID NO: 231 and said second polypeptide chain specifically binding to CD3 comprises an amino acid sequence of SEQ ID NO:311; or
 - (iv) said first polypeptide chain specifically binding to B7H6 comprises an amino acid sequence of SEQ ID NO: 232 and said second polypeptide chain specifically binding to CD3 comprises an amino acid sequence of SEQ ID NO:311.
18. The protein of any one of claims 16 to 17, wherein said first and said second polypeptide chain are linked via disulfide bonds forming a bispecific, bivalent and heterodimeric protein.
 19. An isolated nucleic acid molecule encoding the first antigen binding unit and/or the second antigen binding unit of a protein of any one of claims 1 to 12, optionally further encoding a first and/or a second Fc domain.
 20. An isolated nucleic acid molecule encoding the first and/or the second polypeptide chain of claim 16 or 17.
 21. An expression vector comprising the nucleic acid molecule of claim 19 or 20.
 22. A host cell transfected with the expression vector of claim 21.
 23. A method of manufacturing a protein of any one of claims 1 to 18 comprising
 - i) cultivating the host cell of claim 22 under conditions allowing expression of the protein of any one of items 1 to 18; and,
 - ii) recovering the protein; and optionally
 - iii) further purifying and/or modifying and/or formulating the protein.
 - ~~24. A protein comprising a first polypeptide chain specifically binding to B7H6 (a B7H6 chain) and a second polypeptide chain specifically binding to CD3 (a CD3 chain), wherein said first polypeptide chain comprises a first light chain, a first linker, and a first heavy chain and said second polypeptide chain comprises a second light chain, a second linker, and a second heavy chain, preferably wherein the C-terminus of said first light chain is covalently linked to the N-terminus of said first heavy chain via said first peptide linker and wherein the C-terminus of said second light chain is covalently linked to the N-terminus of said second heavy chain via said second peptide linker.~~

- ~~25. The protein of claim 20, wherein said first and said second polypeptide chain are linked via disulfide bonds forming a bispecific, bivalent and heterodimeric protein.~~
- ~~26. The protein of claim 24, wherein said first polypeptide chain specifically binding to B7H6 comprises a light chain variable domain and heavy chain variable domain comprising CDR sequences selected from the group consisting of i) to xxiv):~~
- ~~i) — light chain CDRs comprising the amino acid sequences of SEQ ID NO:1 (CDR1), SEQ ID NO:2 (CDR2) and SEQ ID NO:3 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:4 (CDR1), SEQ ID NO:5 (CDR2) and SEQ ID NO:6 (CDR3);~~
 - ~~ii) — light chain CDRs comprising the amino acid sequences of SEQ ID NO:7 (CDR1), SEQ ID NO:8 (CDR2) and SEQ ID NO:9 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:10 (CDR1), SEQ ID NO:11 (CDR2) and SEQ ID NO:12 (CDR3);~~
 - ~~iii) — light chain CDRs comprising the amino acid sequences of SEQ ID NO:13 (CDR1), SEQ ID NO:14 (CDR2) and SEQ ID NO:15 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:16 (CDR1), SEQ ID NO:17 (CDR2) and SEQ ID NO:18 (CDR3);~~
 - ~~iv) — light chain CDRs comprising the amino acid sequences of SEQ ID NO:19 (CDR1), SEQ ID NO:20 (CDR2) and SEQ ID NO:21 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:22 (CDR1), SEQ ID NO:23 (CDR2) and SEQ ID NO:24 (CDR3);~~
 - ~~v) — light chain CDRs comprising the amino acid sequences of SEQ ID NO:25 (CDR1), SEQ ID NO:26 (CDR2) and SEQ ID NO:27 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:28 (CDR1), SEQ ID NO:29 (CDR2) and SEQ ID NO:30 (CDR3);~~
 - ~~vi) — light chain CDRs comprising the amino acid sequences of SEQ ID NO:31 (CDR1), SEQ ID NO:32 (CDR2) and SEQ ID NO:33 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:34 (CDR1), SEQ ID NO:35 (CDR2) and SEQ ID NO:36 (CDR3);~~

- ~~vii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:37 (CDR1), SEQ ID NO:38 (CDR2) and SEQ ID NO:39 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:40 (CDR1), SEQ ID NO:41 (CDR2) and SEQ ID NO:42 (CDR3);~~
- ~~viii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:43 (CDR1), SEQ ID NO:44 (CDR2) and SEQ ID NO:45 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:46 (CDR1), SEQ ID NO:47 (CDR2) and SEQ ID NO:48 (CDR3);~~
- ~~ix) light chain CDRs comprising the amino acid sequences of SEQ ID NO:49 (CDR1), SEQ ID NO:50 (CDR2) and SEQ ID NO:51 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:52 (CDR1), SEQ ID NO:53 (CDR2) and SEQ ID NO:54 (CDR3);~~
- ~~x) light chain CDRs comprising the amino acid sequences of SEQ ID NO:55 (CDR1), SEQ ID NO:56 (CDR2) and SEQ ID NO:57 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:58 (CDR1), SEQ ID NO:59 (CDR2) and SEQ ID NO:60 (CDR3);~~
- ~~xi) light chain CDRs comprising the amino acid sequences of SEQ ID NO:61 (CDR1), SEQ ID NO:62 (CDR2) and SEQ ID NO:63 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:64 (CDR1), SEQ ID NO:65 (CDR2) and SEQ ID NO:66 (CDR3);~~
- ~~xii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:67 (CDR1), SEQ ID NO:68 (CDR2) and SEQ ID NO:69 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:70 (CDR1), SEQ ID NO:71 (CDR2) and SEQ ID NO:72 (CDR3);~~
- ~~xiii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:73 (CDR1), SEQ ID NO:74 (CDR2) and SEQ ID NO:75 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:76 (CDR1), SEQ ID NO:77 (CDR2) and SEQ ID NO:78 (CDR3);~~
- ~~xiv) light chain CDRs comprising the amino acid sequences of SEQ ID NO:79 (CDR1), SEQ ID NO:80 (CDR2) and SEQ ID NO:81 (CDR3) and heavy chain~~

- CDRs comprising the amino acid sequences of SEQ ID NO:82 (CDR1), SEQ ID NO:83 (CDR2) and SEQ ID NO:84 (CDR3);
- xv) ~~light chain CDRs comprising the amino acid sequences of SEQ ID NO:85 (CDR1), SEQ ID NO:86 (CDR2) and SEQ ID NO:87 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:88 (CDR1), SEQ ID NO:89 (CDR2) and SEQ ID NO:90 (CDR3);~~
- xvi) ~~light chain CDRs comprising the amino acid sequences of SEQ ID NO:91 (CDR1), SEQ ID NO:92 (CDR2) and SEQ ID NO:93 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:94 (CDR1), SEQ ID NO:95 (CDR2) and SEQ ID NO:96 (CDR3);~~
- xvii) ~~light chain CDRs comprising the amino acid sequences of SEQ ID NO:97 (CDR1), SEQ ID NO:98 (CDR2) and SEQ ID NO:99 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:100 (CDR1), SEQ ID NO:101 (CDR2) and SEQ ID NO:102 (CDR3);~~
- xviii) ~~light chain CDRs comprising the amino acid sequences of SEQ ID NO:103 (CDR1), SEQ ID NO:104 (CDR2) and SEQ ID NO:105 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:106 (CDR1), SEQ ID NO:107 (CDR2) and SEQ ID NO:108 (CDR3);~~
- xix) ~~light chain CDRs comprising the amino acid sequences of SEQ ID NO:109 (CDR1), SEQ ID NO:110 (CDR2) and SEQ ID NO:111 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:112 (CDR1), SEQ ID NO:113 (CDR2) and SEQ ID NO:114 (CDR3);~~
- xx) ~~light chain CDRs comprising the amino acid sequences of SEQ ID NO:115 (CDR1), SEQ ID NO:116 (CDR2) and SEQ ID NO:117 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:118 (CDR1), SEQ ID NO:119 (CDR2) and SEQ ID NO:120 (CDR3);~~
- xxi) ~~light chain CDRs comprising the amino acid sequences of SEQ ID NO:121 (CDR1), SEQ ID NO:122 (CDR2) and SEQ ID NO:123 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:124 (CDR1), SEQ ID NO:125 (CDR2) and SEQ ID NO:126 (CDR3);~~

~~xxii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:127 (CDR1), SEQ ID NO:128 (CDR2) and SEQ ID NO:129 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:130 (CDR1), SEQ ID NO:131 (CDR2) and SEQ ID NO:132 (CDR3);~~

~~xxiii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:133 (CDR1), SEQ ID NO:134 (CDR2) and SEQ ID NO:135 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:136 (CDR1), SEQ ID NO:137 (CDR2) and SEQ ID NO:138 (CDR3); and~~

~~xxiv) light chain CDRs comprising the amino acid sequences of SEQ ID NO:139 (CDR1), SEQ ID NO:140 (CDR2) and SEQ ID NO:141 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:142 (CDR1), SEQ ID NO:143 (CDR2) and SEQ ID NO:144 (CDR3).~~

~~27. The protein of claim 24 or 26, wherein said second polypeptide chain specifically binding to CD3 comprises a light chain variable domain and heavy chain variable domain comprising CDR sequences selected from the group consisting of i) to vi):~~

~~i) light chain CDRs comprising the amino acid sequences of SEQ ID NO:257 (CDR1), SEQ ID NO:258 (CDR2) and SEQ ID NO:259 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:260 (CDR1), SEQ ID NO:261 (CDR2) and SEQ ID NO:262 (CDR3);~~

~~ii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:263 (CDR1), SEQ ID NO:264 (CDR2) and SEQ ID NO:265 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:266 (CDR1), SEQ ID NO:267 (CDR2) and SEQ ID NO:268 (CDR3);~~

~~iii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:269 (CDR1), SEQ ID NO:270 (CDR2) and SEQ ID NO:271 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:272 (CDR1), SEQ ID NO:273 (CDR2) and SEQ ID NO:274 (CDR3);~~

~~iv) light chain CDRs comprising the amino acid sequences of SEQ ID NO:275 (CDR1), SEQ ID NO:276 (CDR2) and SEQ ID NO:277 (CDR3) and heavy chain~~

CDRs comprising the amino acid sequences of SEQ ID NO:278 (CDR1), SEQ ID NO:279 (CDR2) and SEQ ID NO:280 (CDR3);

v) ~~light chain CDRs comprising the amino acid sequences of SEQ ID NO:281 (CDR1), SEQ ID NO:282 (CDR2) and SEQ ID NO:283 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:284 (CDR1), SEQ ID NO:285 (CDR2) and SEQ ID NO:286 (CDR3); and~~

vi) ~~light chain CDRs comprising the amino acid sequences of SEQ ID NO:287 (CDR1), SEQ ID NO:288 (CDR2) and SEQ ID NO:289 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:290 (CDR1), SEQ ID NO:291 (CDR2) and SEQ ID NO:292 (CDR3).~~

28. — The protein of any one of claims 24 to 27, wherein

i) ~~said first polypeptide chain specifically binding to B7H6 light chain comprises CDRs comprising the amino acid sequences of SEQ ID NO:67 (CDR1), SEQ ID NO:68 (CDR2) and SEQ ID NO:69 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:70 (CDR1), SEQ ID NO:71 (CDR2) and SEQ ID NO:72 (CDR3); and said second polypeptide chain specifically binding to CD3 comprises light chain CDRs comprising the amino acid sequences of SEQ ID NO:257 (CDR1), SEQ ID NO:258 (CDR2) and SEQ ID NO:259 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:260 (CDR1), SEQ ID NO:261 (CDR2) and SEQ ID NO:262 (CDR3); or~~

ii) ~~said first polypeptide chain specifically binding to B7H6 light chain comprises light chain CDRs comprising the amino acid sequences of SEQ ID NO:79 (CDR1), SEQ ID NO:80 (CDR2) and SEQ ID NO:81 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:82 (CDR1), SEQ ID NO:83 (CDR2) and SEQ ID NO:84 (CDR3), and said second polypeptide chain specifically binding to CD3 comprises light chain CDRs comprising the amino acid sequences of SEQ ID NO:257 (CDR1), SEQ ID NO:258 (CDR2) and SEQ ID NO:259 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:260 (CDR1), SEQ ID NO:261 (CDR2) and SEQ ID NO:262 (CDR3); or~~

iii) ~~said first polypeptide chain specifically binding to B7H6 light chain comprises light chain CDRs comprising the amino acid sequences of SEQ ID NO:85 (CDR1), SEQ~~

~~ID NO:86 (CDR2) and SEQ ID NO:87 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:88 (CDR1), SEQ ID NO:89 (CDR2) and SEQ ID NO:90 (CDR3), and said second polypeptide chain specifically binding to CD3 comprises light chain CDRs comprising the amino acid sequences of SEQ ID NO:257 (CDR1), SEQ ID NO:258 (CDR2) and SEQ ID NO:259 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:260 (CDR1), SEQ ID NO:261 (CDR2) and SEQ ID NO:262 (CDR3); or~~

~~iv) said first polypeptide chain specifically binding to B7H6 light chain comprises light chain CDRs comprising the amino acid sequences of SEQ ID NO:91 (CDR1), SEQ ID NO:92 (CDR2) and SEQ ID NO:93 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:94 (CDR1), SEQ ID NO:95 (CDR2) and SEQ ID NO:96 (CDR3), and said second polypeptide chain specifically binding to CD3 comprises light chain CDRs comprising the amino acid sequences of SEQ ID NO:257 (CDR1), SEQ ID NO:258 (CDR2) and SEQ ID NO:259 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:260 (CDR1), SEQ ID NO:261 (CDR2) and SEQ ID NO:262 (CDR3).~~

~~29. The protein of any one of claims 24 to 27, wherein said first polypeptide chain specifically binding to B7H6 comprises a light chain variable domain and a heavy chain variable domain selected from the group consisting of i) to xxiv):~~

- ~~i) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:145 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:146;~~
- ~~ii) — a light chain variable domain comprising the amino acid sequences of SEQ ID NO:147 and heavy chain variable domain comprising the amino acid sequences of SEQ ID NO:148;~~
- ~~iii) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:149 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:150;~~
- ~~iv) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:151 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:152;~~

- v) ~~a light chain variable domain comprising the amino acid sequence of SEQ ID NO:153 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:154;~~
- vi) ~~a light chain variable domain comprising the amino acid sequence of SEQ ID NO:155 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:156;~~
- vii) ~~a light chain variable domain comprising the amino acid sequence of SEQ ID NO:157 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:158;~~
- viii) ~~a light chain variable domain comprising the amino acid sequence of SEQ ID NO:159 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:160;~~
- ix) ~~a light chain variable domain comprising the amino acid sequence of SEQ ID NO:161 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:162;~~
- x) ~~a light chain variable domain comprising the amino acid sequence of SEQ ID NO:163 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:164;~~
- xi) ~~a light chain variable domain comprising the amino acid sequence of SEQ ID NO:165 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:166;~~
- xii) ~~a light chain variable domain comprising the amino acid sequence of SEQ ID NO:167 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:168;~~
- xiii) ~~a light chain variable domain comprising the amino acid sequence of SEQ ID NO:169 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:170;~~
- xiv) ~~a light chain variable domain comprising the amino acid sequence of SEQ ID NO:171 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:172;~~

- ~~xv) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:173 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:174;~~
- ~~xvi) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:175 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:176;~~
- ~~xvii) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:177 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:178;~~
- ~~xviii) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:179 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:180;~~
- ~~xix) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:181 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:182;~~
- ~~xx) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:183 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:184;~~
- ~~xxi) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:185 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:186;~~
- ~~xxii) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:187 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:188;~~
- ~~xxiii) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:189 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:190; and~~
- ~~xxiv) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:191 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:192.~~

~~30. The protein of any one of claims 24 to 29, wherein said second polypeptide chain specifically binding to CD3 comprises a light chain variable domain and a heavy chain variable domain selected from the group consisting of i) - vi):~~

- ~~i) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:293 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:294;~~
- ~~ii) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:295 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:296;~~
- ~~iii) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:297 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:298;~~
- ~~iv) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:299 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:300;~~
- ~~v) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:301 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:302; and~~
- ~~vi) — a light chain variable domain comprising the amino acid sequence of SEQ ID NO:303 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:304.~~

~~31. The protein of any one of claims 24 to 30, wherein~~

- ~~i) — said first polypeptide chain specifically binding to B7H6 comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:167 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:168, and said second polypeptide chain specifically binding to CD3 comprises light chain variable domain comprising the amino acid sequence of SEQ ID NO:293 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:294 ; or~~
- ~~ii) — said first polypeptide chain specifically binding to B7H6 comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:171 and heavy~~

- ~~chain variable domain comprising the amino acid sequence of SEQ ID NO:172, and said second polypeptide chain specifically binding to CD3 comprises light chain variable domain comprising the amino acid sequence of SEQ ID NO:293 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:294; or~~
- ~~iii) said first polypeptide chain specifically binding to B7H6 comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:173 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:174, and said second polypeptide chain specifically binding to CD3 comprises light chain variable domain comprising the amino acid sequence of SEQ ID NO:293 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:294; or~~
- ~~iv) said first polypeptide chain specifically binding to B7H6 comprises a light chain variable domain comprising the amino acid sequence of SEQ ID NO:175 and heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:176, and said second polypeptide chain specifically binding to CD3 comprises light chain variable domain comprising the amino acid sequence of SEQ ID NO:293 and a heavy chain variable domain comprising the amino acid sequence of SEQ ID NO:294;~~
- ~~32. The protein of any one of claims 24 to 31, wherein said first and/or second peptide linker comprises 26 to 42 amino acids, preferably any one of 30 to 40 amino acids, 34 to 40 amino acids, or 36 to 39 amino acids, more preferably 38 amino acids.~~
- ~~33. The protein of claim 32, wherein said first linker and/or second linker is a Gly-Ser linker, preferably comprising the amino acid sequence of SEQ ID NO:250, more preferably said first and second peptide linker comprise the same sequence (e.g., SEQ ID NO:250).~~
- ~~34. The protein of any one of claims 24 to 33, wherein said first light chain and said second light chain independently comprise a human kappa or lambda domain.~~
- ~~35. The protein of any one of claims 24 to 34, wherein said first polypeptide chain comprises a scFab binding to B7H6 comprising an amino acid sequence selected from the group consisting of SEQ ID NO:193, SEQ ID NO:194, SEQ ID NO:195, SEQ ID NO:196 SEQ ID NO:197 SEQ ID NO:198 SEQ ID NO:199 SEQ ID NO:200 SEQ ID NO:201 SEQ ID NO:202 SEQ ID NO:203 SEQ ID NO:204 SEQ ID NO:205, SEQ ID NO:206, SEQ ID NO:207, SEQ ID NO:208, SEQ ID NO:209, SEQ ID NO:210, SEQ ID NO:211, SEQ ID NO:212, SEQ ID NO:213, SEQ ID NO:214, SEQ ID NO:215, and SEQ ID NO:216 and said second polypeptide chain comprises a scFab binding to CD3~~

~~comprising an amino acid sequence selected from the group consisting of SEQ ID NO:305, SEQ ID NO:306, SEQ ID NO:307, SEQ ID NO:308, SEQ ID NO:309, and SEQ ID NO: 310.~~

~~36. The protein of claim 35, wherein~~

- ~~i) said first polypeptide chain comprises a scFab binding to B7H6 comprising an amino acid sequence of SEQ ID NO:204 and said second polypeptide chain comprises a scFab binding to CD3 comprising an amino acid sequence of SEQ ID NO:305; or~~
- ~~ii) said first polypeptide chain comprises a scFab binding to B7H6 comprising an amino acid sequence of SEQ ID NO:206 and said second polypeptide chain comprises a scFab binding to CD3 comprising an amino acid sequence of SEQ ID NO:305; or~~
- ~~iii) said first polypeptide chain comprises a scFab binding to B7H6 comprising an amino acid sequence of SEQ ID NO:207 and said second polypeptide chain comprises a scFab binding to CD3 comprising an amino acid sequence of SEQ ID NO:305; or~~
- ~~iv) said first polypeptide chain comprises a scFab binding to B7H6 comprising an amino acid sequence of SEQ ID NO:208 and said second polypeptide chain comprises a scFab binding to CD3 comprising an amino acid sequence of SEQ ID NO:305.~~

~~37. The protein of any one of items 24 to 36, wherein~~

- ~~i) said first heavy chain comprises a tyrosine (Y) at position 366 [T366Y], and said second heavy chain comprises a threonine (T) at position 407 [Y407T], or~~
- ~~ii) said first heavy chain comprises a tryptophan (W) at position 366 [T366W], and said second heavy chain comprises a serine (S) at position 366 [T366S], an alanine (A) at position 368 [L368A] and a valine (V) at position 407 [Y407V], or~~
- ~~iii) said second heavy chain comprises a tyrosine (Y) at position 366 [T366Y], and said first heavy chain comprises a threonine (T) at position 407 [Y407T], or~~
- ~~iv) said second heavy chain comprises a tryptophan (W) at position 366 [T366W], and said first heavy chain comprises a serine (S) at position 366 [T366S], an alanine (A) at position 368 [L368A] and a valine (V) at position 407 [Y407V], preferably wherein said first or said second heavy chain further comprises an arginine at position 435 [H435R] and a phenylalanine at position 436 [Y436F].~~

~~38. The protein of any one of items 24 to 37, wherein said first and/or said second heavy chain comprises an alanine at position 234 [L234A] and at position 235 [L235A] preferably said first heavy chain comprises Fc domain with an amino acid sequence of~~

~~SEQ ID NO:242 and said second heavy chain domain comprises an Fc domain with an amino acid sequence of SEQ ID NO:243.~~

~~39. The protein of any one of items 24 to 38 comprising a first polypeptide chain specifically binding to B7H6 comprising an amino acid sequence selected from the group consisting of SEQ ID NO:217, SEQ ID NO:218, SEQ ID NO:219, SEQ ID NO:220, SEQ ID NO:221, SEQ ID NO:222, SEQ ID NO:223, SEQ ID NO: 224, SEQ ID NO:225, SEQ ID NO:226, SEQ ID NO:227, SEQ ID NO:228, SEQ ID NO:229, SEQ ID NO:230, SEQ ID NO:231, SEQ ID NO:232, SEQ ID NO:233, SEQ ID NO:234, SEQ ID NO:235, SEQ ID NO:236, SEQ ID NO:237, SEQ ID NO:238, SEQ ID NO:239, and SEQ ID NO:240 and a second polypeptide chain specifically binding to CD3 comprising the amino acid sequence selected from the group consisting of SEQ ID NO:311, SEQ ID NO:312, SEQ ID NO:313, SEQ ID NO:314, SEQ ID NO:315, and SEQ ID NO:316.~~

~~40. The protein of claim 38, wherein~~

- ~~i) said first polypeptide chain comprises an amino acid sequence of SEQ ID NO:228 and said second polypeptide chain comprises an amino acid sequence of SEQ ID NO:311; or~~
- ~~ii) said first polypeptide chain comprises an amino acid sequence of SEQ ID NO:230 and said second polypeptide chain comprises an amino acid sequence of SEQ ID NO:311; or~~
- ~~iii) said first polypeptide chain comprises an amino acid sequence of SEQ ID NO:231 and said second polypeptide chain comprises an amino acid sequence of SEQ ID NO:311; or~~
- ~~iv) said first polypeptide chain comprises an amino acid sequence of SEQ ID NO:232 and said second polypeptide chain comprises an amino acid sequence of SEQ ID NO:311.~~

~~41. An isolated nucleic acid molecule encoding the first and/or the second polypeptide chain of any one of claims 24 to 40.~~

~~42. An expression vector comprising the nucleic acid molecule of claim 41.~~

~~43. A host cell transfected with the expression vector of claim 42.~~

~~44~~24. The protein of any one of claims 1 to 18 ~~or 24 to 40~~ for use in medicine.

~~45~~25. A pharmaceutical composition comprising the protein of any one of claims 1 to 18 ~~or 24 to 40~~ and a pharmaceutically acceptable carrier.

~~46. A method of treating cancer comprising administering to a patient in need thereof a therapeutically effective amount of the protein of any one of claims 1 to 18 or 24 to 40.~~

~~47~~26. Use of the protein of any one of claims 1 to 18 ~~or 24 to 40 for preparing~~ in the manufacture of a pharmaceutical composition for treating cancer.

~~48~~27. The protein of any one of claims 1 to 18 ~~or 24 to 40~~ for use in ~~a method of~~ treating cancer.

~~49~~28. The ~~method of claim 46, the~~ use of claim ~~47~~26 or the protein for use of claim ~~48~~27, wherein the cancer is a B7H6 expressing tumor, preferably wherein the cancer is (metastatic) colorectal cancer ((m)CRC), non-small cell lung cancer (NSCLC), or head and neck squamous cell carcinoma (HNSCC).

~~50~~29. The ~~method of claim 46 or 49, the~~ use of claim ~~47 or 49~~26 or 28, or the protein for use of claim ~~48 or 49~~27 or 28, wherein said protein is used in combination with a cytotoxic or cytostatic chemotherapeutic agent, a therapeutically active compound that inhibits angiogenesis, a signal transduction pathway inhibitor (e.g., an EGFR inhibitor), an immune modulator, an immune checkpoint inhibitor, a mitotic checkpoint inhibitor or a hormonal therapy agent.

~~51~~30. The ~~method,~~ use or protein for use of claim ~~50~~29, wherein said protein is used in combination with an immune checkpoint inhibitor, preferably an anti- PD-1 antibody or an anti-PD-L1 antibody.

~~52~~31. The ~~method,~~ use or protein for use of claim ~~51~~30, wherein the anti-PD-1 antibody is selected from the group consisting of PD1-1, PD1-2, PD1-3, PD1-4, and PD1-5.

~~53. An anti-B7H6 antibody molecule comprising~~

~~i) — light chain CDRs comprising the amino acid sequences of SEQ ID NO:1 (CDR1), SEQ ID NO:2 (CDR2) and SEQ ID NO:3 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:4 (CDR1), SEQ ID NO:5 (CDR2) and SEQ ID NO:6 (CDR3); or~~

~~ii) — light chain CDRs comprising the amino acid sequences of SEQ ID NO:7 (CDR1), SEQ ID NO:8 (CDR2) and SEQ ID NO:9 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:10 (CDR1), SEQ ID NO:11 (CDR2) and SEQ ID NO:12 (CDR3); or~~

- ~~iii) —light chain CDRs comprising the amino acid sequences of SEQ ID NO:13 (CDR1), SEQ ID NO:14 (CDR2) and SEQ ID NO:15 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:16 (CDR1), SEQ ID NO:17 (CDR2) and SEQ ID NO:18 (CDR3); or~~
- ~~iv) —light chain CDRs comprising the amino acid sequences of SEQ ID NO:19 (CDR1), SEQ ID NO:20 (CDR2) and SEQ ID NO:21 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:22 (CDR1), SEQ ID NO:23 (CDR2) and SEQ ID NO:24 (CDR3); or~~
- ~~v) —light chain CDRs comprising the amino acid sequences of SEQ ID NO:25 (CDR1), SEQ ID NO:26 (CDR2) and SEQ ID NO:27 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:28 (CDR1), SEQ ID NO:29 (CDR2) and SEQ ID NO:30 (CDR3); or~~
- ~~vi) —light chain CDRs comprising the amino acid sequences of SEQ ID NO:31 (CDR1), SEQ ID NO:32 (CDR2) and SEQ ID NO:33 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:34 (CDR1), SEQ ID NO:35 (CDR2) and SEQ ID NO:36 (CDR3); or~~
- ~~vii) —light chain CDRs comprising the amino acid sequences of SEQ ID NO:37 (CDR1), SEQ ID NO:38 (CDR2) and SEQ ID NO:39 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:40 (CDR1), SEQ ID NO:41 (CDR2) and SEQ ID NO:42 (CDR3); or~~
- ~~viii) —light chain CDRs comprising the amino acid sequences of SEQ ID NO:43 (CDR1), SEQ ID NO:44 (CDR2) and SEQ ID NO:45 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:46 (CDR1), SEQ ID NO:47 (CDR2) and SEQ ID NO:48 (CDR3); or~~
- ~~ix) —light chain CDRs comprising the amino acid sequences of SEQ ID NO:49 (CDR1), SEQ ID NO:50 (CDR2) and SEQ ID NO:51 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:52 (CDR1), SEQ ID NO:53 (CDR2) and SEQ ID NO:54 (CDR3); or~~
- ~~x) —light chain CDRs comprising the amino acid sequences of SEQ ID NO:55 (CDR1), SEQ ID NO:56 (CDR2) and SEQ ID NO:57 (CDR3) and heavy chain CDRs~~

- ~~comprising the amino acid sequences of SEQ ID NO:58 (CDR1), SEQ ID NO:59 (CDR2) and SEQ ID NO:60 (CDR3); or~~
- ~~xi) light chain CDRs comprising the amino acid sequences of SEQ ID NO:61 (CDR1), SEQ ID NO:62 (CDR2) and SEQ ID NO:63 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:64 (CDR1), SEQ ID NO:65 (CDR2) and SEQ ID NO:66 (CDR3); or~~
- ~~xii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:67 (CDR1), SEQ ID NO:68 (CDR2) and SEQ ID NO:69 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:70 (CDR1), SEQ ID NO:71 (CDR2) and SEQ ID NO:72 (CDR3); or~~
- ~~xiii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:73 (CDR1), SEQ ID NO:74 (CDR2) and SEQ ID NO:75 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:76 (CDR1), SEQ ID NO:77 (CDR2) and SEQ ID NO:78 (CDR3); or~~
- ~~xiv) comprising light chain CDRs comprising the amino acid sequences of SEQ ID NO:79 (CDR1), SEQ ID NO:80 (CDR2) and SEQ ID NO:81 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:82 (CDR1), SEQ ID NO:83 (CDR2) and SEQ ID NO:84 (CDR3); or~~
- ~~xv) light chain CDRs comprising the amino acid sequences of SEQ ID NO:85 (CDR1), SEQ ID NO:86 (CDR2) and SEQ ID NO:87 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:88 (CDR1), SEQ ID NO:89 (CDR2) and SEQ ID NO:90 (CDR3); or~~
- ~~xvi) light chain CDRs comprising the amino acid sequences of SEQ ID NO:91 (CDR1), SEQ ID NO:92 (CDR2) and SEQ ID NO:93 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:94 (CDR1), SEQ ID NO:95 (CDR2) and SEQ ID NO:96 (CDR3); or~~
- ~~xvii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:97 (CDR1), SEQ ID NO:98 (CDR2) and SEQ ID NO:99 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:100 (CDR1), SEQ ID NO:101 (CDR2) and SEQ ID NO:102 (CDR3); or~~
- ~~xviii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:103 (CDR1), SEQ ID NO:104 (CDR2) and SEQ ID NO:105 (CDR3) and heavy chain~~

CDRs comprising the amino acid sequences of SEQ ID NO:106 (CDR1), SEQ ID NO:107 (CDR2) and SEQ ID NO:108 (CDR3); or

~~xix) light chain CDRs comprising the amino acid sequences of SEQ ID NO:109 (CDR1), SEQ ID NO:110 (CDR2) and SEQ ID NO:111 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:112 (CDR1), SEQ ID NO:113 (CDR2) and SEQ ID NO:114 (CDR3); or~~

~~xx) light chain CDRs comprising the amino acid sequences of SEQ ID NO:115 (CDR1), SEQ ID NO:116 (CDR2) and SEQ ID NO:117 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:118 (CDR1), SEQ ID NO:119 (CDR2) and SEQ ID NO:120 (CDR3); or~~

~~xxi) light chain CDRs comprising the amino acid sequences of SEQ ID NO:121 (CDR1), SEQ ID NO:122 (CDR2) and SEQ ID NO:123 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:124 (CDR1), SEQ ID NO:125 (CDR2) and SEQ ID NO:126 (CDR3); or~~

~~xxii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:127 (CDR1), SEQ ID NO:128 (CDR2) and SEQ ID NO:129 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:130 (CDR1), SEQ ID NO:131 (CDR2) and SEQ ID NO:132 (CDR3); or~~

~~xxiii) light chain CDRs comprising the amino acid sequences of SEQ ID NO:133 (CDR1), SEQ ID NO:134 (CDR2) and SEQ ID NO:135 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:136 (CDR1), SEQ ID NO:137 (CDR2) and SEQ ID NO:138 (CDR3); or~~

~~xxiv) light chain CDRs comprising the amino acid sequences of SEQ ID NO:139 (CDR1), SEQ ID NO:140 (CDR2) and SEQ ID NO:141 (CDR3) and heavy chain CDRs comprising the amino acid sequences of SEQ ID NO:142 (CDR1), SEQ ID NO:143 (CDR2) and SEQ ID NO:144 (CDR3).~~