

WHAT IS CLAIMED IS:

1. An isolated polypeptide that specifically binds to HER2 protein, said polypeptide comprising a heavy chain variable region including three complementarity determining regions, said regions having sequences H1, H2, and H3, wherein:

the H1 sequence is GFX₁IKDITYIH (SEQ ID NO: 1);

the H2 sequence is X₂IX₃PTX₄X₅YX₆X₇YADSVKG (SEQ ID NO: 2); and

the H3 sequence is WGGDGFYX₈MDY (SEQ ID NO: 3);

wherein X₁ is N or W, X₂ is R or K, X₃ is Y or K or D, X₄ is N or A, X₅ is G or K, X₆ is T or D, X₇ is R or E and X₈ is A or E; and

a light chain variable region including three complementarity determining regions having sequences L1, L2, and L3, wherein:

the L1 sequence is RASQDVNTX₉VA (SEQ ID NO: 4);

the L2 sequence is SASFLYS (SEQ ID NO: 5); and

the L3 sequence is QQX₁₀YTPPT (SEQ ID NO: 6),

wherein X₉ is A or D and X₁₀ is H or D or E;

provided that when X₁-X₈ are N, R, Y, N, G, T, R and A, respectively, X₉ is not A and X₁₀ is not H.

2. An isolated polypeptide that specifically binds to HER2 protein and CD3 protein, said polypeptide comprising a heavy chain variable region including three anti-HER2 complementarity determining regions, said regions having sequences H1, H2, and H3, wherein:

the H1 sequence is GFX₁IKDITYIH (SEQ ID NO: 1);

the H2 sequence is X₂IX₃PTX₄X₅YX₆X₇YADSVKG (SEQ ID NO: 2); and

the H3 sequence is WGGDGFYX₈MDY (SEQ ID NO: 3);

wherein X₁ is N or W, X₂ is R or K, X₃ is Y or K or D, X₄ is N or A, X₅ is G or K, X₆ is T or D, X₇ is R or E and X₈ is A or E; and

a light chain variable region including three anti-HER2 complementarity determining regions having sequences L1, L2, and L3 wherein:

the L1 sequence is RASQDVNTX₉VA (SEQ ID NO: 4);

the L2 sequence is SASFLYS (SEQ ID NO: 5); and

the L3 sequence is QQX₁₀YTPPT (SEQ ID NO: 6),

wherein X₉ is A or D and X₁₀ is H or D or E; provided that when X₁-X₈ are N, R, Y, N, G, T, R and A, respectively, X₉ is not A and X₁₀ is not H; and

six anti-CD3 complementarity determining regions L4, L5, L6, L7, L8, and L9 wherein:

the L4 sequence is GFTFNTYAMN (SEQ ID NO: 54),
the L5 sequence is RIRSKYNNYATYYADSVKD (SEQ ID NO: 55),
the L6 sequence is HX₁₁NFX₁₂NSKVSWSFX₁₃Y (SEQ ID NO: 70),
the L7 sequence is RSSX₁₄GAVTTSNYDN (SEQ ID NO: 71),
the L8 sequence is GTNKRAP (SEQ ID NO: 58), and
the L9 sequence is ALWYSNLWV (SEQ ID NO: 59),
wherein X₁₁ is G, S, A or T, X₁₂ is G or P, X₁₃ is A or Q, and X₁₄ is T or A.

3. The isolated polypeptide of claim 1 or 2, wherein the H1 sequence is GFWIKDTYIH (SEQ ID NO: 7) or GFNIKDTYIH (SEQ ID NO: 50).

4. The isolated polypeptide of claim 1 or 2, wherein the H2 sequence is selected from the group consisting of:

KIYPTNGYTRYADSVKG (SEQ ID NO: 8)
RIKPTNGYTRYADSVKG (SEQ ID NO: 9)
RIDPTNGYTRYADSVKG (SEQ ID NO: 10)
RIYPTAGYTRYADSVKG (SEQ ID NO: 11)
RIYPTNKYTRYADSVKG (SEQ ID NO: 12)
RIYPTNGYDRYADSVKG (SEQ ID NO: 13)
RIYPTNGYTEYADSVKG (SEQ ID NO: 14) and
RIYPTNGYTRYADSVKG (SEQ ID NO: 49).

5. The isolated polypeptide of claim 1 or 2, wherein the H3 sequence is WGGDGFYEMDY (SEQ ID NO: 15) or WGGDGFYAMDY (SEQ ID NO: 51).

6. The isolated polypeptide of claim 1 or 2, wherein the L1 sequence is RASQDVNTDVA (SEQ ID NO: 16) or RASQDVNTAVA (SEQ ID NO: 52).

7. The isolated polypeptide of claim 1 or 2, wherein the L3 sequence is QQDYTTPPT (SEQ ID NO: 17), QQEYTPPT (SEQ ID NO: 18) or QQHYTPPT (SEQ ID NO: 53).

8. The isolated polypeptide of claim 2, wherein the the L6 sequence is any one of SEQ ID NOs: 56 and 60-67 and the L7 sequence is SEQ ID NO: 57, 68 or 69.

9. An isolated polypeptide that specifically binds to HER2 protein, said polypeptide comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region is one of:

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVAKIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 19)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTEYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 20)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIKPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 21)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIDPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 22)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
AGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 23)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NKYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 24)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYDRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 25)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYEMDYW
GQGTLVTVSS (SEQ ID NO: 26)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVES (SEQ ID NO: 27), or

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 28), and

the light chain variable region is one of:

DIQMTQSPSSLSASVGDRVTTTCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:
29)

DIQMTQSPSSLSASVGDRVTTTCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:
30)

DIQMTQSPSSLSASVGDRVTTTCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQDYTTPPTFGQGTKVEIK (SEQ ID NO:
31) or

DIQMTQSPSSLSASVGDRVTTTCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQEYTPPTFGQGTKVEIK (SEQ ID NO:
32).

10. An isolated polypeptide that specifically binds to HER2 protein, said polypeptide comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region is one of:

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLLTVSS (SEQ ID NO: 33)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVAKIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLLTVSS (SEQ ID NO: 19)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTEYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLLTVSS (SEQ ID NO: 20)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIKPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLLTVSS (SEQ ID NO: 21)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIDPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLLTVSS (SEQ ID NO: 22)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
AGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLLTVSS (SEQ ID NO: 23)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
 NKYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
 GQGTLVTVSS (SEQ ID NO: 24)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
 NGYDRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
 GQGTLVTVSS (SEQ ID NO: 25)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
 NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYEMDYW
 GQGTLVTVSS (SEQ ID NO: 26)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
 NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
 GQGTLVTVES (SEQ ID NO: 27), or

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
 NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
 GQGTLVTVSS (SEQ ID NO: 28), and

the light chain variable region is one of:

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
 SGVPSRFSGSRSGDFTLTISSLQPEDFATYYCQQHYYTPPTFGQGGTKVEIK (SEQ ID NO:
 30)

DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
 SGVPSRFSGSRSGDFTLTISSLQPEDFATYYCQQDYTPPTFGQGGTKVEIK (SEQ ID NO:
 31) or

DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
 SGVPSRFSGSRSGDFTLTISSLQPEDFATYYCQQEYTPPTFGQGGTKVEIK (SEQ ID NO:
 32).

11. The isolated polypeptide of claim 9, wherein the heavy chain variable region and the light chain variable region are selected from:

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVAKIYPT
 NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
 GQGTLVTVSS (SEQ ID NO: 19) and

DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
 SGVPSRFSGSRSGDFTLTISSLQPEDFATYYCQQHYYTPPTFGQGGTKVEIK (SEQ ID NO:
 29), or

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTEYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLLTVSS (SEQ ID NO: 20) and

DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQHYYTPPTFGQGTKVEIK (SEQ ID
NO:29).

12. The isolated polypeptide of claim 10, wherein the heavy chain variable region is:

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLLTVSS (SEQ ID NO: 33), and

the light chain variable region is one of:

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQHYYTPPTFGQGTKVEIK (SEQ ID NO:
30),

DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQDYTPPTFGQGTKVEIK (SEQ ID NO:
31), or

DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQEYTPPTFGQGTKVEIK (SEQ ID NO:
32).

13. The isolated polypeptide of claim 9, wherein the light chain variable region is:

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQHYYTPPTFGQGTKVEIK (SEQ ID NO:
30); and

the heavy chain variable region is one of:

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLLTVSS (SEQ ID NO: 33),

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVAKIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLLTVSS (SEQ ID NO: 19)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTEYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 20)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIKPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 21)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIDPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 22)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
AGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 23)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NKYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 24)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYDRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 25)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYEMDYW
GQGTLVTVSS (SEQ ID NO: 26)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVES (SEQ ID NO: 27), or

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 28).

14. An isolated polypeptide that specifically binds to HER2 protein, said polypeptide comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region is one of:

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIKPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG

VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHHKPSNTKVDKKVEPKSCDKTHTC
PPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP
REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGD
SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 35);

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NKYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHHKPSNTKVDKKVEPKSCDKTHTC
PPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP
REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGD
SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 36);

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYDRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHHKPSNTKVDKKVEPKSCDKTHTC
PPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP
REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGD
SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 37);

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYEMDYW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHHKPSNTKVDKKVEPKSCDKTHTC
PPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP
REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGD
SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 38); or

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVESASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHHKPSNTKVDKKVEPKSCDKTHTC
PPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH

NAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP
REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDG
SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 39);
and

the light chain variable region is one of:

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFGSRSGTDFTLTISLQPEDFATYYCQQHYYTPPTFGQGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSL
STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECSSRSGGGGEVQLVESGGGLVQ
PGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF
TISRDDSKNSLYLQMNSLKTEDTAVYYCVRHSNFGNSKVSWFQYWGQGLTVTVSSGGS
GGSGGSGGSGGQAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTSNYDNWVQQKPGQAPR
GLIGGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCALWYSNLWVFGGGTK
LTVLSR (SEQ ID NO: 41);

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFGSRSGTDFTLTISLQPEDFATYYCQQHYYTPPTFGQGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSL
STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECSSRSGGGGEVQLVESGGGLVQ
PGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF
TISRDDSKNSLYLQMNSLKTEDTAVYYCVRHGNFGNSKVSWFQYWGQGLTVTVSSGG
SGGSGGSGGSGGQAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTSNYDNWVQQKPGQAP
RGLIGGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCALWYSNLWVFGGGT
KLTVLSR (SEQ ID NO: 42);

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFGSRSGTDFTLTISLQPEDFATYYCQQHYYTPPTFGQGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDYSL
STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECSSRSGGGGEVQLVESGGGLVQ
PGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF
TISRDDSKNSLYLQMNSLKTEDTAVYYCVRHGNFPNSKVSWFQYWGQGLTVTVSSGGS
GGSGGSGGSGGQAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTSNYDNWVQQKPGQAPR
GLIGGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCALWYSNLWVFGGGTK
LTVLSR (SEQ ID NO: 43);

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFGSRSGTDFTLTISLQPEDFATYYCQQHYYTPPTFGQGTKVEIKRTVAAPSVFI

FPPSDEQLKSGTASVVCLLNNFYPPREAKVQWKVDNALQSGNSQESVTEQDSKDYSL
STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECSSRSGGGGEVQLVESGGGLVQ
PGGSLRLSCAASGFTFTNYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF
TISRDDSKNSLYLQMNSLKTEDTAVYYCVRHANFGNSKVSWFAYWGQGLTVTVSSGG
SGSGSGSGSGGQAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTSNYDNWVQKPGQAP
RGLIGGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCALWYSNLWVFGGGT
KLTVLSR (SEQ ID NO: 44);

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFTLTISLQPEDFATYYCQHHYTPPTFGQGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPPREAKVQWKVDNALQSGNSQESVTEQDSKDYSL
STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECSSRSGGGGEVQLVESGGGLVQ
PGGSLRLSCAASGFTFTNYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF
TISRDDSKNSLYLQMNSLKTEDTAVYYCVRHGFPNSKVSWFAYWGQGLTVTVSSGG
GGSGSGSGSGGQAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTSNYDNWVQKPGQAPR
GLIGGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCALWYSNLWVFGGGTK
LTVLSR (SEQ ID NO: 45);

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFTLTISLQPEDFATYYCQHHYTPPTFGQGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPPREAKVQWKVDNALQSGNSQESVTEQDSKDYSL
STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECSSRSGGGGEVQLVESGGGLVQ
PGGSLRLSCAASGFTFTNYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF
TISRDDSKNSLYLQMNSLKTEDTAVYYCVRHFNFGNSKVSWFAYWGQGLTVTVSSGG
GGSGSGSGSGGQAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTSNYDNWVQKPGQAPR
GLIGGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCALWYSNLWVFGGGTK
LTVLSR (SEQ ID NO: 46);

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFTLTISLQPEDFATYYCQHHYTPPTFGQGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPPREAKVQWKVDNALQSGNSQESVTEQDSKDYSL
STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECSSRSGGGGEVQLVESGGGLVQ
PGGSLRLSCAASGFTFTNYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF
TISRDDSKNSLYLQMNSLKTEDTAVYYCVRHFNFGNSKVSWFAYWGQGLTVTVSSGG
GGSGSGSGSGGQAVVTQEPSLTVSPGGTVTLTCRSSAGAVTTSNYDNWVQKPGQAPR
GLIGGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCALWYSNLWVFGGGTK
LTVLSR (SEQ ID NO: 47); or

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQHYTTPPTFGQGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDESTYSL
STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECSSRSGGGGEVQLVESGGGLVQ
PGGSLRLSCAASGFTFTNYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF
TISRDDSKNSLYLQMNSLKTEDTAVYYCVRHTNFGNSKVSWFAYWGQGLTVTVSSGGS
GGSGGSGGSGGQAVVTQEPSLTVSPGGTVTLTCRSSAGAVTTSNYDNWVQQKPGQAPR
GLIGGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCALWYNLWVFGGGGTK
LTVLSR (SEQ ID NO: 48).

15. The isolated polypeptide of claim 14, wherein the heavy chain variable region is SEQ ID NO: 35 and the light chain variable region is any one of SEQ ID NOs: 41-48.

16. The isolated polypeptide of claim 14, wherein the heavy chain variable region is SEQ ID NO: 36 and the light chain variable region is any one of SEQ ID NOs: 41-48.

17. The isolated polypeptide of claim 14, wherein the heavy chain variable region is SEQ ID NO: 37 and the light chain variable region is any one of SEQ ID NOs: 41-48.

18. The isolated polypeptide of claim 14, wherein the heavy chain variable region is SEQ ID NO: 38 and the light chain variable region is any one of SEQ ID NOs: 41-48.

19. The isolated polypeptide of claim 14, wherein the heavy chain variable region is SEQ ID NO: 39 and the light chain variable region is any one of SEQ ID NOs: 41-48.

20. An anti-HER2 antibody or antibody fragment comprising the isolated polypeptide of any one of claims 1-19.

21. The antibody or antibody fragment of claim 20, wherein the antibody or antibody fragment has a higher binding affinity to HER2 protein at a pH in a tumor microenvironment in comparison with a different pH that occurs in a non-tumor microenvironment.

22. The antibody or antibody fragment of claim 21, wherein the pH in the tumor microenvironment is in a range of from 5.0 to 6.8 and the pH in the non-tumor microenvironment is in a range of from 7.0 to 7.6.

23. An antibody or antibody fragment comprising a heavy chain variable region including three complementarity determining regions, said regions having sequences H1, H2, and H3, wherein:

the H1 sequence is GFX₁IKDTYIH (SEQ ID NO: 1);

the H2 sequence is X₂IX₃PTX₄X₅YX₆X₇YADSVKG (SEQ ID NO: 2); and

the H3 sequence is WGGDGFYX₈MDY (SEQ ID NO: 3);

wherein X₁ is N or W, X₂ is R or K, X₃ is Y or K or D, X₄ is N or A, X₅ is G or K, X₆ is T or D, X₇ is R or E and X₈ is A or E; and

a light chain variable region including three complementarity determining regions having sequences L1, L2, and L3, wherein:

the L1 sequence is RASQDVNTX₉VA (SEQ ID NO: 4);

the L2 sequence is SASFLYS (SEQ ID NO: 5); and

the L3 sequence is QQX₁₀YTTPT (SEQ ID NO: 6),

wherein X₉ is A or D and X₁₀ is H, D or E;

provided that when X₁-X₈ are N, R, Y, N, G, T, R and A, respectively, X₉ is not A and X₁₀ is not H.

24. A bispecific antibody or antibody fragment that specifically binds to HER2 protein and CD3 protein, said antibody or antibody fragment comprising a heavy chain variable region including three anti-HER2 complementarity determining regions, said regions having sequences H1, H2, and H3, wherein:

the H1 sequence is GFX₁IKDTYIH (SEQ ID NO: 1);

the H2 sequence is X₂IX₃PTX₄X₅YX₆X₇YADSVKG (SEQ ID NO: 2); and

the H3 sequence is WGGDGFYX₈MDY (SEQ ID NO: 3);

wherein X₁ is N or W, X₂ is R or K, X₃ is Y or K or D, X₄ is N or A, X₅ is G or K, X₆ is T or D, X₇ is R or E and X₈ is A or E; and

a light chain variable region including three anti-HER2 complementarity determining regions having sequences L1, L2, and L3 wherein:

the L1 sequence is RASQDVNTX₉VA (SEQ ID NO: 4);

the L2 sequence is SASFLYS (SEQ ID NO: 5); and

the L3 sequence is QQX₁₀YTPPT (SEQ ID NO: 6),
 wherein X₉ is A or D and X₁₀ is H or D or E; provided that when X₁-X₈ are N, R, Y, N, G, T, R
 and A, respectively, X₉ is not A and X₁₀ is not H; and
 six anti-CD3 complementarity determining regions L4, L5, L6, L7, L8, and L9 wherein:
 the L4 sequence is GFTFNTYAMN (SEQ ID NO: 54),
 the L5 sequence is RIRSKYNNYATYYADSVKD (SEQ ID NO: 55),
 the L6 sequence is HX₁₁NFX₁₂NSKVSXFX₁₃Y (SEQ ID NO: 70),
 the L7 sequence is RSSX₁₄GAVTTSNYDN (SEQ ID NO: 71),
 the L8 sequence is GTNKRAP (SEQ ID NO: 58), and
 the L9 sequence is ALWYSNLWV (SEQ ID NO: 59),
 wherein X₁₁ is G, S, A or T, X₁₂ is G or P, X₁₃ is A or Q, and X₁₄ is T or A.

25. The antibody or antibody fragment of claim 24, wherein the H1 sequence is
 GFWIKDTYIH (SEQ ID NO: 7) or GFNIKDTYIH (SEQ ID NO: 50).

26. The antibody or antibody fragment of claim 24, wherein the H2 sequence is selected from
 the group consisting of:

KIYPTNGYTRYADSVKG (SEQ ID NO: 8)
 RIKPTNGYTRYADSVKG (SEQ ID NO: 9)
 RIDPTNGYTRYADSVKG (SEQ ID NO: 10)
 RIYPTAGYTRYADSVKG (SEQ ID NO: 11)
 RIYPTNKYTRYADSVKG (SEQ ID NO: 12)
 RIYPTNGYDRYADSVKG (SEQ ID NO: 13)
 RIYPTNGYTEYADSVKG (SEQ ID NO: 14) and
 RIYPTNGYTRYADSVKG (SEQ ID NO: 49).

27. The antibody or antibody fragment of claim 24, wherein the H3 sequence is
 WGGDGFYEMDY (SEQ ID NO: 15) or WGGDGFYAMDY (SEQ ID NO: 51).

28. The antibody or antibody fragment of claim 24, wherein the L1 sequence is
 RASQDVNTDVA (SEQ ID NO: 16) or RASQDVNTAVA (SEQ ID NO: 52).

29. The antibody or antibody fragment claim 24, wherein the L3 sequence is QQDYTPPT
 (SEQ ID NO: 17), QQEYTPPT (SEQ ID NO: 18), or QQHYTPPT (SEQ ID NO: 53).

30. An antibody or antibody fragment comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region is one of:

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVAKIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 19)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTEYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 20)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIKPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 21)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIDPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 22)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
AGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 23)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NKYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 24)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYDRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 25)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYEMDYW
GQGTLVTVSS (SEQ ID NO: 26)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVES (SEQ ID NO: 27), or

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 28), and

the light chain variable region is one of:

DIQMTQSPSSLSASVGDRVITTCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:
29)

DIQMTQSPSSLSASVGDRVITTCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQHYTTPPTFGQGTKVEIK (SEQ ID NO:
30)

DIQMTQSPSSLSASVGDRVITTCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQDYTTPPTFGQGTKVEIK (SEQ ID NO:
31) or

DIQMTQSPSSLSASVGDRVITTCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQEYTPPTFGQGTKVEIK (SEQ ID NO:
32).

31. An antibody or antibody fragment comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region is one of:

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 33)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVAKIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 19)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTEYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 20)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIKPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 21)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIDPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 22)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
AGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 23)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
 NKYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
 GQGTLVTVSS (SEQ ID NO: 24)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
 NGYDRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
 GQGTLVTVSS (SEQ ID NO: 25)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
 NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYEMDYW
 GQGTLVTVSS (SEQ ID NO: 26)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
 NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
 GQGTLVTVES (SEQ ID NO: 27), or

EVQLVESGGGLVQPGGSLRLSCAASGFWIKDTYIHWVRQAPGKGLEWVARIYPT
 NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
 GQGTLVTVSS (SEQ ID NO: 28), and

the light chain variable region is one of:

DIQMTQSPSSLSASVGDRVITTCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
 SGVPSRFSGRSGTDFTLTISLQPEDFATYYCQQHYYTPPTFGQGGTKVEIK (SEQ ID NO:
 30)

DIQMTQSPSSLSASVGDRVITTCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
 SGVPSRFSGRSGTDFTLTISLQPEDFATYYCQQDYTPPTFGQGGTKVEIK (SEQ ID NO:
 31) or

DIQMTQSPSSLSASVGDRVITTCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
 SGVPSRFSGRSGTDFTLTISLQPEDFATYYCQQEYTPPTFGQGGTKVEIK (SEQ ID NO:
 32).

32. The antibody or antibody fragment of claim 30, wherein the heavy chain variable region and the light chain variable region are:

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVAKIYPT
 NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
 GQGTLVTVSS (SEQ ID NO: 19) and

DIQMTQSPSSLSASVGDRVITTCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
 SGVPSRFSGRSGTDFTLTISLQPEDFATYYCQQHYYTPPTFGQGGTKVEIK (SEQ ID NO:
 29), or

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTEYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 20) and

DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQHYYTPPTFGQGTKVEIK (SEQ ID
NO:29).

33. The antibody or antibody fragment of claim 31, wherein the heavy chain variable region is:

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 33), and

the light chain variable region is one of:

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQHYYTPPTFGQGTKVEIK (SEQ ID NO:
30),

DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQDYTPPTFGQGTKVEIK (SEQ ID NO:
31), or

DIQMTQSPSSLSASVGDRVTITCRASQDVNTAVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQEYTPPTFGQGTKVEIK (SEQ ID NO:
32).

34. The antibody or antibody fragment of claim 30, wherein the light chain variable region is:

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTISLQPEDFATYYCQQHYYTPPTFGQGTKVEIK (SEQ ID NO:
30); and

the heavy chain variable region is one of:

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 33),

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVAKIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 19)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTEYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 20)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIKPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 21)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIDPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 22)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
AGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 23)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NKYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 24)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYDRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 25)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYEMDYW
GQGTLVTVSS (SEQ ID NO: 26)

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVES (SEQ ID NO: 27), or

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSS (SEQ ID NO: 28).

35. An antibody or antibody fragment comprising a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region is one of:

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIKPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTC

PPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP
REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGD
SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 35);

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NKYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTC
PPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP
REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGD
SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 36);

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYDRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTC
PPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP
REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGD
SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 37);

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYEMDYW
GQGTLVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTC
PPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP
REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGD
SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 38); or

EVQLVESGGGLVQPGGSLRLSCAASGFNIKDTYIHWVRQAPGKGLEWVARIYPT
NGYTRYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCSRWGGDGFYAMDYW
GQGTLVTVESASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSG
VHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTC
PPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVH
NAKTKPREEQYQSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQP

REPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDS DG
SFFLYSKLTVDKSRWQQGNV FSCSV MHEALHNHYTQKSLSLSPGK (SEQ ID NO: 39);
and

the light chain variable region is one of:

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFGSRSGTDFTLTIS SLQPEDFATYYCQQHYTTPPTFGQGTKVEIKRTVAAPS VFI
FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSK DSTYSL S
STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC SRSGGGGEVQLVESGGGLVQ
PGGSLRLS CAASGFTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF
TISRDDSKNSLYLQMNSLKTEDTAVYYCVRHSNFGNSKVS WFQYWGQGLTVTVSSGGS
GGSGGSGGGGQAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTSNYDNWVQQKPGQAPR
GLIGGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCALWYSNLWVFGGGTK
LTVLSR (SEQ ID NO: 41);

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFGSRSGTDFTLTIS SLQPEDFATYYCQQHYTTPPTFGQGTKVEIKRTVAAPS VFI
FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSK DSTYSL S
STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC SRSGGGGEVQLVESGGGLVQ
PGGSLRLS CAASGFTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF
TISRDDSKNSLYLQMNSLKTEDTAVYYCVRHGNFGNSKVS WFQYWGQGLTVTVSSGG
SGGSGGSGGGGQAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTSNYDNWVQQKPGQAP
RGLIGGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCALWYSNLWVFGGGT
KLTVLSR (SEQ ID NO: 42);

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFGSRSGTDFTLTIS SLQPEDFATYYCQQHYTTPPTFGQGTKVEIKRTVAAPS VFI
FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSK DSTYSL S
STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC SRSGGGGEVQLVESGGGLVQ
PGGSLRLS CAASGFTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF
TISRDDSKNSLYLQMNSLKTEDTAVYYCVRHGNFPNSKVS WFQYWGQGLTVTVSSGGS
GGSGGSGGGGQAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTSNYDNWVQQKPGQAPR
GLIGGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCALWYSNLWVFGGGTK
LTVLSR (SEQ ID NO: 43);

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFGSRSGTDFTLTIS SLQPEDFATYYCQQHYTTPPTFGQGTKVEIKRTVAAPS VFI
FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSK DSTYSL S

STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECRSRSGGGGEVQLVESGGGLVQ
PGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF
TISRDDSKNSLYLQMNSLKTEDTAVYYCVRHANFGNSKVSWFAYWGQGLTVTVSSGG
SGGSGGSGGSGGQAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTSNYDNWVQQKPGQAP
RGLIGGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCALWYSNLWVFGGGT
KLTVLSR (SEQ ID NO: 44);

DIQMTQSPSSLSASVGDRVITTCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFTLTISLQPEDFATYYCQQHYYTPPTFGQGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDYSL
STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECRSRSGGGGEVQLVESGGGLVQ
PGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF
TISRDDSKNSLYLQMNSLKTEDTAVYYCVRHGNFNSKVSWFAYWGQGLTVTVSSGGS
GGSGGSGGSGGQAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTSNYDNWVQQKPGQAPR
GLIGGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCALWYSNLWVFGGGTK
LTVLSR (SEQ ID NO: 45);

DIQMTQSPSSLSASVGDRVITTCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFTLTISLQPEDFATYYCQQHYYTPPTFGQGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDYSL
STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECRSRSGGGGEVQLVESGGGLVQ
PGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF
TISRDDSKNSLYLQMNSLKTEDTAVYYCVRHTNFGNSKVSWFAYWGQGLTVTVSSGGS
GGSGGSGGSGGQAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTSNYDNWVQQKPGQAPR
GLIGGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCALWYSNLWVFGGGTK
LTVLSR (SEQ ID NO: 46);

DIQMTQSPSSLSASVGDRVITTCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFTLTISLQPEDFATYYCQQHYYTPPTFGQGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPRKAKVQWKVDNALQSGNSQESVTEQDSKDYSL
STLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGECRSRSGGGGEVQLVESGGGLVQ
PGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF
TISRDDSKNSLYLQMNSLKTEDTAVYYCVRHSNFGNSKVSWFAYWGQGLTVTVSSGGS
GGSGGSGGSGGQAVVTQEPSLTVSPGGTVTLTCRSSAGAVTTSNYDNWVQQKPGQAPR
GLIGGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCALWYSNLWVFGGGTK
LTVLSR (SEQ ID NO: 47); or

DIQMTQSPSSLSASVGDRVTITCRASQDVNTDVAWYQQKPGKAPKLLIYSASFLY
SGVPSRFSGSRSGTDFLTITSLQPEDFATYYCQHHYTPPTFGQGTKVEIKRTVAAPSVFI
FPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTYSLS
STLTLSKADYEKHKVYACEVTHQGLSPVTKSFNRGECSSRSGGGGEVQLVESGGGLVQ
PGGSLRLSCAASGFTFTNYAMNWRQAPGKGLEWVARIRSKYNNYATYYADSVKDRF
TISRDDSKNSLYLQMNSLKTEDTAVYYCVRHNTNFGNSKVSWFAYWGQGLTVTVSSGGS
GGSGGSGGSGGQAVVTQEPSLTVSPGGTVTLTCRSSAGAVTTSNYDNWVQQKPGQAPR
GLIGGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCALWYSNLWVFGGGGTK
LTVLSR (SEQ ID NO: 48).

36. The antibody or antibody fragment of claim 35, wherein the heavy chain variable region sequence is SEQ ID NO: 35 and the light chain variable region is any one of SEQ ID NOs: 41-48.

37. The antibody or antibody fragment of claim 35, wherein the heavy chain variable region sequence is SEQ ID NO: 36 and the light chain variable region is any one of SEQ ID NOs: 41-48.

38. The antibody or antibody fragment of claim 35, wherein the heavy chain variable region sequence is SEQ ID NO: 37 and the light chain variable region is any one of SEQ ID NOs: 41-48.

39. The antibody or antibody fragment of claim 35, wherein the heavy chain variable region is SEQ ID NO: 38 and the light chain variable region is any one of SEQ ID NOs: 41-48.

40. The antibody or antibody fragment of claim 35, wherein the heavy chain variable region sequence is SEQ ID NO: 39 and the light chain variable region is any one of SEQ ID NOs: 41-48.

41. The antibody or antibody fragment of any one of claims 20-40, wherein the antibody or antibody fragment has a higher binding affinity to HER2 protein at a pH in a tumor microenvironment in comparison with a different pH that occurs in a non-tumor microenvironment.

42. The antibody or antibody fragment of claim 41, wherein the pH in the tumor microenvironment is in a range of from 5.0 to 6.8 and the pH in the non-tumor microenvironment is in a range of from 7.0 to 7.6.
43. The antibody or antibody fragment of any one of claims 20-40, wherein the antibody or antibody fragment has a ratio of binding affinity to the HER2 protein at a pH in a tumor microenvironment to a binding affinity to the HER2 protein at a different pH in a non-tumor microenvironment of at least about 1.5:1, at least about 2:1, at least about 3:1, at least about 4:1, at least about 5:1, at least about 6:1, at least about 7:1, at least about 8:1, at least about 9:1, at least about 10:1, at least about 20:1, at least about 30:1, at least about 50:1, at least about 70:1, or at least about 100:1.
44. An immunoconjugate comprising the antibody or antibody fragment of any one of claims 20-40.
45. The immunoconjugate of claim 44, wherein the immunoconjugate comprises at least one agent selected from a chemotherapeutic agent, a radioactive atom, a cytostatic agent and a cytotoxic agent.
46. The immunoconjugate of claim 45, comprising at least two said agents.
47. The immunoconjugate of any one of claims 45-46, wherein the at least one agent is a radioactive agent.
48. The immunoconjugate of claim 47, wherein the radioactive agent is selected from an alpha emitter, a beta emitter and a gamma emitter.
49. The immunoconjugate of any one of claims 45-48, wherein the antibody or antibody fragment and the at least one agent are covalently bonded to a linker molecule.
50. The immunoconjugate of any one of claims 45-49, wherein one said at least one agent is selected from maytansinoids, auristatins, dolastatins, calicheamicin, pyrrolobenzodiazepines, and anthracyclines.

51. A pharmaceutical composition comprising:
the polypeptide of any one of claims 1-19, the antibody or antibody fragment of any one of claims 20-43, or the immunoconjugate of any one of claims 44-50; and
a pharmaceutically acceptable carrier.
52. The pharmaceutical composition of claim 51, further comprising a tonicity agent.
53. The pharmaceutical composition of any one of claims 51-52, further comprising an immune checkpoint inhibitor molecule.
54. The pharmaceutical composition of claim 53, wherein the immune checkpoint inhibitor molecule is an antibody or antibody fragment against an immune checkpoint.
55. The pharmaceutical composition of any one of claims 53-54, wherein the immune checkpoint is selected from CTLA4, LAG3, TIM3, TIGIT, VISTA, BTLA, OX40, CD40, 4-1BB, PD-1, PD-L1, GITR, B7-H3, B7-H4, KIR, A2aR, CD27, CD70, DR3, and ICOS.
56. The pharmaceutical composition of any one of claims 53-55, wherein the immune checkpoint is CTLA4, PD-1 or PD-L1.
57. The pharmaceutical composition of any one of claims 51-56, further comprising an antibody or antibody fragment against an antigen selected from CTLA4, PD1, PD-L1, AXL, ROR2, CD3, EpCAM, B7-H3, ROR1, SFRP4 and a WNT protein.
58. A method of treating cancer comprising a step of administering the polypeptide of any one of claims 1-19, the antibody or antibody fragment of any one of claims 20-43, the immunoconjugate of any one of claims 44-50 or the pharmaceutical composition of any one of claims 51-56 to a patient with cancer.
59. A kit for diagnosis or treatment, said kit comprising the polypeptide of any one of claims 1-19, the antibody or antibody fragment of any one of claims 20-43, or the immunoconjugate of any one of claims 44-50 or the pharmaceutical composition of any one of claims 51-56 and instructions for using the antibody or antibody fragment, the immunoconjugate and/or the pharmaceutical composition for diagnosis or treatment.