Claims

1. A bispecific antibody that comprises a first variable domain that can bind an extracellular part of human epidermal growth factor receptor (EGFR) and a second variable domain that can bind an extracellular part of human MET Proto-Oncogene, Receptor Tyrosine Kinase (cMET),

wherein the first variable domain comprises a heavy chain variable region with a CDR1 sequence SYGIS; a CDR2 sequence WISAYX_1X_2NTNYAQKLQG and a CDR3 comprising the sequence $X_3X_4X_5X_6$HWWLX_7A,

wherein

X1 = N; X2 = G; X3 = D; X4 = S; X5 = Y; X6 = W and X7 = G;
X1 = N; X2 = A; X3 = D; X4 = S; X5 = Y; X6 = W and X7 = G;
X1 = S; X2 = G; X3 = D; X4 = S; X5 = Y; X6 = W and X7 = G;
X1 = N; X2 = G; X3 = D; X4 = R; X5 = H; X6 = W and X7 = D;
X1 = N; X2 = A; X3 = D; X4 = R; X5 = H; X6 = W and X7 = D;
X1 = S; X2 = G; X3 = D; X4 = R; X5 = H; X6 = W and X7 = D;
X1 = N; X2 = G; X3 = G; X4 = Y; X5 = L; X6 = D and X7 = G;
X1 = N; X2 = A; X3 = G; X4 = Y; X5 = L; X6 = D and X7 = G; or
X1 = S; X2 = G; X3 = G; X4 = Y; X5 = L; X6 = D and X7 = G,

wherein the second variable domain comprises a CDR1 sequence selected from TYSLN, SYAMN, TYSMN, DYAMN, NYAMN, SFGMS, SYAMN, SYAVN, TYAIN, TYAMN and SYSMN; a CDR2 sequence selected from WINTYTGNPTYAQGFTG, WINTNTGNPTYAQGFTG, WINTNTGNPTYAQDFTG, WINTYTGNPTYVQGFTG, WINTYTGDPTYVQGFTG, WINTYTGSPTYAQGFTG, WINTYTGDPTYAQGFTG, WINTNTGTPTYAQGFTG, and a CDR3 sequence selected from ETYYYDSSGYPFDP, ETYYYDRGGYPFDP, ETYYYDSSGFPFDP, ETYYYQSSGYLFDP, ESYYYDRNDYPFDP, ETYYYDVGGYPFDP, ETYYYDSGGYPFDP, ETYFYDSSGYPFDP, ETYFYDRGGYPFDP, ETYYYDSSAYPFDP, ETFYFDSGGYPFDP, ETYYYATSGYPFDP, ETSYYDRTGYPFDP, ETYYYGSSGYPFAP, ETYYYESSGYPFDP, ETYYFDSGDYPFDP, and ETYYFDSGGYPFDP, and

wherein the first and second variable domain comprise a light chain comprising a CDR1 sequence QSISSY, a CDR2 sequence AAS, and a CDR3 sequence QQSYSTP.

2. The bispecific antibody of claim 1, wherein the second variable domain comprises a heavy chain variable region with the amino acid sequence of one of the sequences of SEQ ID NO: 1-23 with 0-10 amino acid insertions, deletions, substitutions, additions or a combination thereof, outside the indicated CDR sequences.

3. The bispecific antibody of claims 1 or 2, wherein the second variable domain comprises a heavy chain variable region with the amino acid sequence of one of the sequences of SEQ ID NO: 1-23 with 0-5 amino acid insertions, deletions, substitutions, additions or a combination thereof, outside the indicated CDR sequences.

4. The bispecific antibody of any one of claims 1 to 3, that is a human antibody.

5. The bispecific antibody of any one of claims 1 to 4, that is a full-length antibody.

6. The bispecific antibody of any one of claims 1 to 5, that is an IgG1 format antibody having an anti-EGFR, anti-cMET stoichiometry of 1:1.

7. The bispecific antibody of any one of claims 1 to 6, wherein the variable domain that can bind human EGFR can also bind cynomolgus and mouse EGFR.

8. The bispecific antibody of any one of claims 1 to 7, wherein the variable domain that can bind human EGFR binds to domain III of human EGFR.

9. The bispecific antibody of any one of claims 1 to 8, wherein the amino acids at positions 405 and 409 in one CH3 domain are the same as the amino acids at the corresponding positions in the other CH3 domain (EU-numbering).

10. The bispecific antibody of any one of claims 1 to 9 wherein:
X_1 = N; X_2 = G; X_3 = D; X_4 = R; X_5 = H; X_6 = W and X_7 = D;
X_1 = N; X_2 = A; X_3 = D; X_4 = R; X_5 = H; X_6 = W and X_7 = D; or
X_1 = S; X_2 = G; X_3 = D; X_4 = R; X_5 = H; X_6 = W and X_7 = D.

11. The bispecific antibody of any one of claims 1 to 10, wherein:
X_1 = N; X_2 = G; X_3 = D; X_4 = R; X_5 = H; X_6 = W and X_7 = D; or
X_1 = N; X_2 = A; X_3 = D; X_4 = R; X_5 = H; X_6 = W and X_7 = D.

12. The bispecific antibody of any one of claims 1 to 11, wherein the heavy chain variable region of the second variable domain comprises the amino acid sequence of one of the sequences of SEQ ID NO: 13 or 23 with 0-10 amino acid insertions, deletions, substitutions, additions or a combination thereof, outside the indicated CDR sequences.

13. The bispecific antibody of claim 12, wherein the heavy chain variable region of the second variable domain comprises the amino acid sequence of one of the sequences of SEQ ID NO: 13 or 23 with 0-5 amino acid insertions, deletions, substitutions, additions or a combination thereof, outside the indicated CDR sequences.

14. The bispecific antibody of any one of claims 1 to 13, wherein the heavy chain variable region of the first variable domain comprises the amino acid sequence of one of the sequences of SEQ ID NO: 78, 79 or 80 with 0-10 amino acid insertions, deletions, substitutions, additions or a combination thereof, outside the indicated CDR sequences.

15. The bispecific antibody of claim 14, wherein the heavy chain variable region of the first variable domain comprises the amino acid sequence of one of the sequences of SEQ ID NO: 78, 79 or 80 with 0-5 amino acid insertions, deletions, substitutions, additions or a combination thereof, outside the indicated CDR sequences.

16. The bispecific antibody of any one of claims 1 to 15, wherein the first variable domain comprises a heavy chain variable region with a CDR1 sequence SYGIS; a CDR2 sequence WISAYNGNTNYAQKLQG and a CDR3 comprising the sequence DRHWHWWLDAFDY and wherein the second variable domain comprises a heavy chain variable region with a CDR1 sequence SYSMN; a CDR2 sequence WINTYTGDPTYAQGFTG and a CDR3 sequence ETYYYDRGGYPFDP.

17. The bispecific antibody of any one of claims 1 to 15, wherein the first variable domain comprises a heavy chain variable region with a CDR1 sequence SYGIS; a CDR2 sequence WISAYNANTNYAQKLQG and a CDR3 comprising the sequence DRHWHWWLDAFDY and wherein the second variable domain comprises a heavy chain variable region with a CDR1 sequence TYSMN; a CDR2 sequence WINTYTGDPTYAQGFTG and a CDR3 comprising the sequence ETYFYDRGGYPFDP.

18. The bispecific antibody of any one of claims 1 to 15, wherein the first variable domain comprises a heavy chain variable region with a CDR1 sequence SYGIS; a CDR2 sequence WISAYSGNTNYAQKLQG and a CDR3 comprising the sequence DRHWHWWLDAFDY and wherein the second variable domain comprises a heavy chain variable region with a CDR1 sequence TYSMN; a CDR2 sequence WINTYTGDPTYAQGFTG and a CDR3 comprising the sequence ETYFYDRGGYPFDP.

19. The bispecific antibody of any one of claims 1 to 15, wherein the first variable domain comprises a heavy chain variable region with a CDR1 sequence SYGIS; a CDR2 sequence WISAYSGNTNYAQKLQG and a CDR3 comprising the sequence DRHWHWWLDAFDY and wherein the second variable domain comprises a heavy chain variable region with a CDR1 sequence SYSMN; a CDR2 sequence WINTYTGDPTYAQGFTG and a CDR3 sequence ETYYYDRGGYPFDP.

20. The bispecific antibody of any one of claims 1 to 15, wherein the first variable domain comprises a heavy chain variable region with a CDR1 sequence SYGIS; a CDR2 sequence WISAYNANTNYAQKLQG and a CDR3 comprising the sequence DRHWHWWLDAFDY and wherein the second variable domain comprises a heavy chain variable region with a CDR1 sequence SYSMN; a CDR2 sequence WINTYTGDPTYAQGFTG and a CDR3 sequence ETYYYDRGGYPFDP.

21. The bispecific antibody of any one of claims 1 to 15, wherein the first variable domain comprises a heavy chain variable region with a CDR1 sequence SYGIS; a CDR2 sequence WISAYNGNTNYAQKLQG and a CDR3 comprising the sequence DRHWHWWLDAFDY and wherein the second variable domain comprises a heavy chain variable region with a CDR1 sequence TYSMN; a CDR2 sequence WINTYTGDPTYAQGFTG and a CDR3 comprising the sequence ETYFYDRGGYPFDP.

22. The bispecific antibody of claim 1, wherein the first variable domain comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 79 and wherein the second variable domain comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 13.

23. The bispecific antibody of any one of claims 1 to 22, wherein the first and second variable domain comprise a common light chain.

24. The bispecific antibody of claim 23, wherein the first and second variable domain comprise a common light chain having the amino acid sequence:

DIQMTQSPSSLSASVGDRVTITCRASQSISSYLNWYQQKPGKAPKLLIYAASSLQ
SGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQSYSTPPTFGQGTKVEIK.

25. Use of the bispecific antibody of any one of claims 1 to 24 in the manufacture of a medicament for the treatment of a disease involving aberrant cells, wherein the aberrant cells express EGFR, cMET, or EGFR and cMET.

26. Use of the bispecific antibody of any one of claims 1 to 24, in the manufacture of a medicament for the treatment of a subject that has a tumor.

27. Use of claim 26, wherein the tumor is an EGFR positive tumor, a cMET positive tumor or an EGFR and cMET positive tumor.

28. The use of claim 26 or 27, wherein the tumor is a breast cancer; colon cancer, pancreatic cancer, gastric cancer, ovarian cancer, colorectal cancer, head- and neck cancer, lung cancer including non-small cell lung cancer or bladder cancer.

29. The use of any one of claims 26 to 28, wherein the tumor is resistant to treatment with an EGFR tyrosine kinase inhibitor.

30. The use of claim 29, wherein the EGFR tyrosine kinase inhibitor is erlotinib, gefitinib, or afatinib, or a combination of one or more of the respective compounds.

31. The use of claim 30, wherein the EGFR tyrosine kinase inhibitor is erlotinib.

32. The use of any one of claims 25 to 31, wherein the medicament is to be administered in combination with an EGFR tyrosine kinase inhibitor.

33. The use of claim 32, wherein the EGFR tyrosine kinase inhibitor is erlotinib.

34. The use of claim 32 or 33, wherein the bispecific antibody is to be administered simultaneously, sequentially or separately with the said EGFR tyrosine kinase inhibitor.

35. Use of the bispecific antibody of any one of claims 1 to 24, in the manufacture of a medicament for treating a disease involving aberrant cells, wherein the aberrant cells express EGFR, cMET, or EGFR and cMET, wherein the said bispecific antibody is to be administered simultaneously, sequentially or separately with an EGFR tyrosine kinase inhibitor.