WHAT IS CLAIMED

1. An isolated bispecific epidermal growth factor receptor (EGFR)/ hepatocyte growth factor receptor (c-Met) antibody, comprising:
   a) a first heavy chain (HC1) comprising a HC1 constant domain 3 (HC1 CH3) and a HC1 variable region 1 (VH1);
   b) a second heavy chain (HC2) comprising a HC2 constant domain 3 (HC2 CH3) and a HC2 variable region 2 (VH2);
   c) a first light chain (LC1) comprising a light chain variable region 1 (VL1); and
   d) a second light chain (LC2) comprising a light chain variable region 2 (VL2), wherein the VH1 and the VL1 pair to form a first antigen-binding site that specifically binds EGFR, the VH2 and the VL2 pair to form a second antigen-binding site that specifically binds c-Met, the HC1 comprises at least one substitution in the HC1 CH3 and the HC2 comprises at least one substitution in the HC2 CH3, and the substitution in the HC1 CH3 and the substitution in the HC2 CH3 occur at different amino acid residue positions, when residue numbering is according to the EU index.
2. The bispecific antibody of claim 1,

wherein the antibody inhibits phosphorylation of extracellular signal-related kinases 1 and 2 (ERK1/2) in NCI-H292, NCI-H1975 or SKMES-1 cell line with an IC_{50} value that is at least about 10-fold less, at least about 20-fold less, at least about 30-fold less, at least about 40-fold less, at least about 50-fold less or at least about 60-fold less when compared to the IC_{50} value of inhibition of phosphorylation of ERK1/2 in NCI-H292, NCI-H1975 or SKMES-1 cell lines with a mixture of a control monovalent EGFR antibody comprising a heavy chain 3 (HC3) and a light chain 3 (LC3) and a control monovalent c-Met antibody comprising a heavy chain 4 (HC4) and a light chain 4 (LC4), wherein

the HC3 and the HC1, the LC3 and the LC1, the HC4 and the HC2, and the LC4 and the LC2 have identical amino acid sequences, respectively, and

the phosphorylation of ERK1/2 is measured in whole cell lysates by sandwich immunoassay using an anti-phosphoERK1/2 antibody as a capture antibody and an antibody binding to unphosphorylated and phosphorylated ERK1/2 conjugated with an electrochemiluminescent compound as a detection antibody.

3. The bispecific antibody of claims 1 or 2, wherein the antibody inhibits phosphorylation of ERK1/2 with an IC_{50} value of about $2x10^{-9}$ M or less, about $1x10^{-9}$ M or less, or about $1x10^{-10}$ M or less.
4. The bispecific antibody of claim 2 or 3, wherein ERK1 is phosphorylated at residues Thr202 and Tyr204, and ERK2 is phosphorylated at residues Thr185 and Tyr197.
5. The bispecific antibody of any of the claims 1-4,

wherein the antibody inhibits phosphorylation of protein kinase B (AKT) at Ser473 in NCI-H1975 cell line with an IC_{50} value that is at least about 70-fold less when compared to the IC_{50} value of inhibition of phosphorylation of AKT at Ser473 in NCI- H1975 cell line with the mixture of control monovalent EGFR antibody comprising the HC3 and the LC3 and control monovalent c-Met antibody comprising the HC4 and the LC4, wherein

the HC3 and the HC1, the LC3 and the LC1, the HC4 and the HC2, and the LC4 and the LC2 have identical amino acid sequences, respectively, and

phosphorylation of AKT at Ser473 is measured in whole cell lysates by sandwich immunoassay using an antibody binding to unphosphorylated and phosphorylated AKT as a capture antibody and an anti-phospho AKT Ser473 antibody conjugated with an electrochemiluminescent compound as a detection antibody.
6. The bispecific antibody of any of the claims 1-5,

wherein the antibody inhibits phosphorylation of AKT at Thr308 in NCI-H1975 cell line with an IC_{50} value that is at least about 100-fold less when compared to the IC_{50} value of inhibition of phosphorylation of AKT at Thr308 in NCI-H1975 cell line with the mixture of the control monovalent EGFR antibody comprising the HC3 and the LC3 and the control monovalent c-Met antibody comprising the HC4 and the LC4, wherein

the HC3 and the HC1, the LC3 and the LC1, the HC4 and the HC2, and the LC4 and the LC2 have identical amino acid sequences, respectively, and

the phosphorylation of AKT at Thr308 is measured in whole cell lysates by sandwich immunoassay using an antibody binding to unphosphorylated and phosphorylated AKT as a capture antibody and an anti-phospho AKT Thr308 antibody conjugated to an electrochemiluminescent compound as a detection antibody.
7. The bispecific antibody of claim 5 or 6, wherein the antibody inhibits phosphorylation of AKT at Ser473 or at Thr308 with an IC_{50} value of about $1x10^{-9}$ M or less.
8. The bispecific antibody of any of the claims 1-7, wherein the HC1, the LC1, the HC2 and the LC2 comprise the amino acid sequences of SEQ ID NOs: 199, 200, 201 and

202, respectively, optionally having a C-terminal lysine removed from the HC1, the HC2, or both the HC1 and the HC2.

9. The bispecific antibody any of the claims 1-8, wherein the bispecific antibody binds EGFR having the amino acid sequence shown in SEQ ID NO: 73 at EGFR residues K489, I491, K467 and S492 and c-Met at residues PEFRDSYPIKYVHAF (SEQ ID NO: 238) and FAQSKPDSAEPMDRSA (SEQ ID NO: 239).

10. The bispecific antibody of of any of the claims 1-9, wherein the antibody inhibits growth of NCI-H292 or NCI-H1975 cells with an IC_{50} value that is at least about 300-fold less, at least about 400-fold less, at least about 500-fold less, at least about 600-fold less, at least about 700-fold less or at least about 800-fold less when compared to the IC_{50} value of inhibition of growth of NCI-H292 or NCI-H1975 cells with cetuximab when NCI-H292 or NCI-H1975 cells are grown in low attachment conditions.

11. The bispecific antibody of any of the claims 1-10, wherein the antibody inhibits growth of HGF-expressing SKMES-1 cell tumor in SCID Beige mice with a percentage (%) T/C value of at least 500-fold less on day 36 when compared to cetuximab, when the bispecific antibody and cetuximab are administered at 20 mg/kg dose.

12. The bispecific antibody of any of the claims 1-11, wherein the antibody neutralizes EGFR and c-Met signaling.

13. The bispecific antibody of any of the claims 1-12, wherein the HC1 and the HC2 are of IgG1, IgG2, IgG3 or IgG4 isotype.

14. The bispecific antibody of claim 13, wherein the HC1 and the HC2 are of IgG1 isotype.

15. The bispecific antibody of claim 13 or 14, wherein the HC1 CH3 comprises at least one, two, three, four, five, six, seven or eight substitutions and the HC2 CH3 comprises at least one, two, three, four, five, six, seven or eight substitutions at residue positions 350, 366, 368, 370, 399, 405, 407 or 409, when residue numbering is according to the EU index.

16. The bispecific antibody of claim 15, wherein the HC1 CH3 comprises at least one, two, three or four substitutions and the HC2 CH3 comprises at least one, two, three or four substitutions at residue positions 350, 370, 405 or 409.

17. The bispecific antibody of claim 16, wherein the HC1 CH3 comprises at least one substitution and the HC2 CH3 comprises at least one substitution at residue positions 405 or 409.
18. The bispecific antibody of claim 17, wherein the HC1 CH3 comprises a K409R or F405L substitution and the HC2 CH3 comprises a K409R or F405L substitution.
19. The bispecific antibody of claim 18, wherein the HC1 CH3 comprises the F405L substitution and the HC2 CH3 comprises the K409R substitution.
20. The bispecific antibody any of the claims 1-19, wherein
    a) the VH1 comprises the heavy chain complementarity determining region (HCDR) 1 (HCDR1), HCDR2 and HCDR3 amino acid sequences of SEQ ID NOs: 210, 211 and 212, respectively; and
    b) the VL1 comprises the light chain complementarity determining region (LCDR) 1 (LCDR1), LCDR2 and LCDR3 amino acid sequences of SEQ ID NOs: 213, 214 and 215, respectively.
21. The bispecific antibody of claim 20, wherein
    a) the VH2 comprises the HCDR1, the HCDR2, and the HCDR3 amino acid sequences of SEQ ID NOs: 216, 217 and 218, respectively; and
    b) the VL2 comprises the LCDR1, the LCDR2 and the LCDR3 amino acid sequences of SEQ ID NOs: 219, 220 and 221, respectively.
22. The bispecific antibody of claim 21, wherein the VH1, the VL1, the VH2 and the VL2 comprise the amino acid sequences of SEQ ID NOs: 189, 190, 193 and 194, respectively.

23. The bispecific antibody of any of the claims 1-7 or 9-18, wherein
    a) VH1 comprises the HCDR1, the HCDR2, and the HCDR3 amino acid sequences of SEQ ID NOs: 222, 223 and 224, respectively; and
    b) VL1 comprises the LCDR1, the LCDR2 and the LCDR3 amino acid sequences of SEQ ID NOs: 225, 226 and 227, respectively.
24. The bispecific antibody of claim 23, wherein
    a) VH2 comprises the HCDR1, the HCDR2, and the HCDR3 amino acid sequences of SEQ ID NOs: 228, 229 and 230, respectively; and
    b) VL2 comprises the LCDR1, the LCDR2 and the LCDR3 amino acid sequences of SEQ ID NOs: 231, 232 and 233, respectively.

25. The bispecific antibody of claim 24, wherein the VH1, the VL1, the VH2 and the VL2 comprise the amino acid sequences of SEQ ID NOs: 191, 192, 195 and 196, respectively.
26. The bispecific antibody of claim 25, wherein the HC1, the LC1, the HC2 and the LC2 comprise the amino acid sequences of SEQ ID NOs: 234, 235, 236 and 237, respectively, and the C-terminal lysine is optionally removed from the HC1, the HC2, or both the HC1 and the HC2.
27. The bispecific antibody of claim 22 or 26, further comprising 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14 or 15 conservative amino acid substitutions in the HC1, the LC1, the HC2 or the LC2.
28. The bispecific antibody of claim 27, comprising a substitution M252Y/S254T/T256E in the HC1 and/or the HC2, wherein residue numbering is according to the EU index.
29. The bispecific antibody of any of the claims 1-29, wherein the antibody has a biantennary glycan structure with a fucose content of about between 1% to about 15%.
30. The bispecific antibody of claim 2, wherein HC1, LC1, HC2 and LC2 are encoded by synthetic polynucleotides comprising the sequence of SEQ ID NOs: 205, 206, 207 and 208, respectively.
31. An isolated synthetic polynucleotide encoding the HC1, the HC2, the LC1 or the LC2 of claim 8 or 26.
32. The isolated polynucleotide of claim 31 comprising the polynucleotide sequence of SEQ ID NOs: 205, 206, 207 or 208.
33. A vector comprising the polynucleotide of claim 31 or 32.
34. An isolated host cell comprising the vector of claim 33.
35. A method of producing the isolated bispecific EGFR/c-Met antibody of claim 8, comprising:
    a) combining an isolated monospecific bivalent anti-EGFR antibody comprising two heavy chains of SEQ ID NO: 199 and two light chains of SEQ ID NO: 200 and an isolated monospecific bivalent anti-c-Met antibody comprising two heavy chains of SEQ ID NO: 201 and two light chains of SEQ ID NO: 202 in a mixture of about 1:1 molar ratio;
    b) introducing a reducing agent into the mixture;
    c) incubating the mixture about ninety minutes to about six hours;
    d) removing the reducing agent; and
    e) purifying the bispecific EGFR/c-Met antibody that comprises a first heavy chain of SEQ ID NO: 199 and a second heavy chain of SEQ ID NO: 201, a first light

chain of SEQ ID NO: 200 and a second light chain of SEQ ID NO: 202, wherein the first heavy chain of SEQ ID NO: 199 pairs with the first light chain of SEQ ID NO: 200 to form the first binding domain that specifically binds EGFR, and the second heavy chain of SEQ ID NO: 201 pairs with the second light chain of SEQ ID NO: 202 to form the second binding domain that specifically binds c-Met.

36. The method of claim 35, wherein the reducing agent is 2- mercaptoethanolamine (2-MEA).
37. The method of claim 36, wherein the 2-MEA is present at a concentration of about 25 mM to about 75 mM.
38. The method of claim 37, wherein the incubating step is performed at a temperature of about 25°C to about 37°C.
39. A pharmaceutical composition comprising the bispecific antibody of any of the claims 1-30 and a pharmaceutically acceptable carrier.
40. A method of treating a subject having cancer, comprising administering a therapeutically effective amount of the bispecific EGFR/c-Met antibody of claim 2, 8 or 26 to a patient in need thereof for a time sufficient to treat the cancer.
41. The method of claim 40, wherein the cancer is associated with an EGFR activating mutation, an EGFR gene amplification, increased levels of circulating HGF, a c-Met activating mutation, a c-Met gene amplification or a mutant KRAS.
42. The method of claim 41, wherein the EGFR activating mutation is G719A, G719X (X being any amino acid), L861X (X being any amino acid), L858R, E746K, L747S, E749Q, A750P, A755V, V765M, L858P or T790M substitution, deletion of E746-A750, deletion of R748-P753, insertion of Ala (A) between M766 and A767, insertion of Ser, Val and Ala (SVA) between S768 and V769, and insertion of Asn and Ser (NS) between P772 and H773.
43. The method of claim 42, wherein the EGFR activating mutation is L858R, del(E476, A750) and/or T790M substitution.
44. The method of claim 41, wherein the mutant KRAS has a G12V or G12C substitution.
45. The method of claim 44, wherein the mutant KRAS has a G12V substitution.
46. The method of claim 41, wherein the subject is resistant or has acquired resistance to treatment with erlotinib, gefitinib, afatinib, CO-1686, AZD9192 or cetuximab.
47. The method of claim 41, wherein the cancer is an epithelial cell cancer, breast cancer, ovarian cancer, lung cancer, non-small cell lung cancer (NSCLC), lung adenocarcinoma, small cell lung cancer, colorectal cancer, anal cancer, prostate

cancer, kidney cancer, bladder cancer, head and neck cancer, pharynx cancer, cancer of the nose, pancreatic cancer, skin cancer, oral cancer, cancer of the tongue, esophageal cancer, vaginal cancer, cervical cancer, cancer of the spleen, testicular cancer, gastric cancer, cancer of the thymus, colon cancer, thyroid cancer, liver cancer, hepatocellular carcinoma (HCC) or sporadic or hereditary papillary renal cell carcinoma (PRCC).

48. The method of claim 40, wherein the subject is homozygous for phenylalanine at position 158 of CD16 or heterozygous for valine and pheynylalanine at position 158 of CD16.
49. The method of claim 47, comprising administering a second therapeutic agent.
50. The method of claim 49, wherein the second therapeutic agent is a chemotherapeutic agent or a targeted anti-cancer therapy.
51. The method of claim 50, wherein the chemotherapeutic agent is cisplatin or vinblastine.
52. The method of claim 50, wherein the chemotherapeutic agent or the targeted anti-cancer therapy is a tyrosine kinase inhibitor of EGFR, c-Met, HER2, HER3, HER4 or VEGFR.
53. The method of claim 52, wherein the tyrosine kinase inhibitor is erlotinib, gefitinib or afatinib.
54. The method of claim 49, wherein the second therapeutic agent is administered simultaneously, sequentially or separately.
55. A method of inhibiting growth or proliferation of cells that express EGFR and/or c-Met, comprising contacting the cells with the bispecific antibody of claim 2, 8 or 26.
56. A method of inhibiting growth or metastasis of EGFR and/or c-Met expressing tumor or cancer cells in a subject comprising administering to the subject an effective amount of the bispecific antibody of claim 2, 8 or 26 to inhibit the growth or metastasis of EGFR and/or c-Met expressing tumor or cancer cells.
57. The method of claim 56, wherein the EGFR and/or c-Met expressing tumor is an epithelial cell cancer, breast cancer, ovarian cancer, lung cancer, non-small cell lung cancer (NSCLC), lung adenocarcinoma, small cell lung cancer, colorectal cancer, anal cancer, prostate cancer, kidney cancer, bladder cancer, head and neck cancer, pharynx cancer, cancer of the nose, pancreatic cancer, skin cancer, oral cancer, cancer of the tongue, esophageal cancer, vaginal cancer, cervical cancer, cancer of the spleen, testicular cancer, gastric cancer, cancer of the thymus, colon cancer, thyroid cancer,

liver cancer, hepatocellular carcinoma (HCC) or sporadic or hereditary papillary renal cell carcinoma (PRCC).

58. The method of claim 57, wherein the EGFR and/or c-Met expressing tumor is associated with an EGFR activating mutation, an EGFR gene amplification, increased levels of circulating HGF, a c-Met activating mutation, a c-Met gene amplification or a mutant KRAS.
59. The method of claim 58, wherein the EGFR activating mutation is G719A, G719X (X being any amino acid), L861X (X being any amino acid), L858R, E746K, L747S, E749Q, A750P, A755V, V765M, L858P or T790M substitution, deletion of E746-A750, deletion of R748-P753, insertion of Ala (A) between M766 and A767, insertion of Ser, Val and Ala (SVA) between S768 and V769, and insertion of Asn and Ser (NS) between P772 and H773.
60. The method of claim 59, wherein the EGFR activating mutation is L858R, del(E476, A750) and/or T790M substitution.
61. The method of claim 58, wherein the mutant KRAS has a G12V or G12C substitution.
62. The method of claim 61, wherein the mutant KRAS has a G12V substitution.
63. Use of a bispecific antibody of any of the claims 1-30 for therapy.
64. A bispecific antibody according to any of the claims 1-30 for use in treatment of cancer.
65. A bispecific antibody according to any of the claims 1-30 for use according to claim 64, wherein cancer is an epithelial cell cancer, breast cancer, ovarian cancer, lung cancer, non-small cell lung cancer (NSCLC), lung adenocarcinoma, small cell lung cancer, colorectal cancer, anal cancer, prostate cancer, kidney cancer, bladder cancer, head and neck cancer, pharynx cancer, cancer of the nose, pancreatic cancer, skin cancer, oral cancer, cancer of the tongue, esophageal cancer, vaginal cancer, cervical cancer, cancer of the spleen, testicular cancer, gastric cancer, cancer of the thymus, colon cancer, thyroid cancer, liver cancer, hepatocellular carcinoma (HCC) or sporadic or hereditary papillary renal cell carcinoma (PRCC).

WHAT IS CLAIMED

1. An isolated bispecific epidermal growth factor receptor (EGFR)/ hepatocyte growth factor receptor (c-Met) antibody, comprising:
   a) a first heavy chain (HC1) comprising a HC1 constant domain 3 (HC1 CH3) and a HC1 variable region 1 (VH1);
   b) a second heavy chain (HC2) comprising a HC2 constant domain 3 (HC2 CH3) and a HC2 variable region 2 (VH2);
   c) a first light chain (LC1) comprising a light chain variable region 1 (VL1); and
   d) a second light chain (LC2) comprising a light chain variable region 2 (VL2), wherein the VH1 and the VL1 pair to form a first antigen-binding site that specifically binds EGFR, the VH2 and the VL2 pair to form a second antigen- binding site that specifically binds c-Met, the HC1 comprises a F405L or a K409R substitution in the HC1 CH3, the HC2 comprises at a F405L or a K409R substitution in the HC2 CH3, the substitution in the HC1 CH3 and the substitution in the HC2 CH3 occurring at different amino acid residue positions, when residue numbering is according to the EU index, and the VH1, the VL1, the VH2 and the VL2 comprise the amino acid sequences of SEQ ID NOs: 189, 190, 193 and 194, respectively.
2. The bispecific antibody of claim 1,

   wherein the antibody inhibits phosphorylation of extracellular signal-related kinases 1 and 2 (ERK1/2) in NCI-H1975 cell line with an IC_{50} value that is at least about 60-fold less when compared to the IC_{50} value of inhibition of phosphorylation of ERK1/2 in NCI-H1975 cell line with a mixture of a control monovalent EGFR antibody comprising a heavy chain 3 (HC3) and a light chain 3 (LC3) and a control monovalent c-Met antibody comprising a heavy chain 4 (HC4) and a light chain 4 (LC4), wherein

   the HC3 and the HC1, the LC3 and the LC1, the HC4 and the HC2, and the LC4 and the LC2 have identical amino acid sequences, respectively, and

   the phosphorylation of ERK1/2 is measured in whole cell lysates by sandwich immunoassay using an anti-phosphoERK1/2 antibody as a capture antibody and an antibody binding to unphosphorylated and phosphorylated ERK1/2 conjugated with an electrochemiluminescent compound as a detection antibody.

3. The bispecific antibody of claims 1 or 2, wherein the antibody inhibits phosphorylation of ERK1/2 with an IC_{50} value of about $2x10^{-9}$ M or less.
4. The bispecific antibody of claim 2 or 3, wherein ERK1 is phosphorylated at residues Thr202 and Tyr204, and ERK2 is phosphorylated at residues Thr185 and Tyr197.
5. The bispecific antibody of any of the claims 1-4,

wherein the antibody inhibits phosphorylation of protein kinase B (AKT) at Ser473 in NCI-H1975 cell line with an IC_{50} value that is at least about 70-fold less when compared to the IC_{50} value of inhibition of phosphorylation of AKT at Ser473 in NCI- H1975 cell line with the mixture of control monovalent EGFR antibody comprising the HC3 and the LC3 and control monovalent c-Met antibody comprising the HC4 and the LC4, wherein

the HC3 and the HC1, the LC3 and the LC1, the HC4 and the HC2, and the LC4 and the LC2 have identical amino acid sequences, respectively, and

phosphorylation of AKT at Ser473 is measured in whole cell lysates by sandwich immunoassay using an antibody binding to unphosphorylated and phosphorylated AKT as a capture antibody and an anti-phospho AKT Ser473 antibody conjugated with an electrochemiluminescent compound as a detection antibody.
6. The bispecific antibody of any of the claims 1-5,

wherein the antibody inhibits phosphorylation of AKT at Thr308 in NCI-H1975 cell line with an IC_{50} value that is at least about 100-fold less when compared to the IC_{50} value of inhibition of phosphorylation of AKT at Thr308 in NCI-H1975 cell line with the mixture of the control monovalent EGFR antibody comprising the HC3 and the LC3 and the control monovalent c-Met antibody comprising the HC4 and the LC4, wherein

the HC3 and the HC1, the LC3 and the LC1, the HC4 and the HC2, and the LC4 and the LC2 have identical amino acid sequences, respectively, and

the phosphorylation of AKT at Thr308 is measured in whole cell lysates by sandwich immunoassay using an antibody binding to unphosphorylated and phosphorylated AKT as a capture antibody and an anti-phospho AKT Thr308 antibody conjugated to an electrochemiluminescent compound as a detection antibody.
7. The bispecific antibody of claim 5 or 6, wherein the antibody inhibits phosphorylation of AKT at Ser473 or at Thr308 with an IC_{50} value of about $1x10^{-9}$ M or less.

8. The bispecific antibody of any of the claims 1-7, wherein the HC1 CH3 comprises the F405L substitution and the HC2 CH3 comprises the K409R substitution.
9. The bispecific antibody of any of the claims 1-8, wherein the HC1 and the HC2 are of IgG1, IgG2, IgG3 or IgG4 isotype.
10. The bispecific antibody of claim 9, wherein the HC1 and the HC2 are of IgG1 isotype.
11. The bispecific antibody of any of the claims 1-10, wherein the HC1, the LC1, the HC2 and the LC2 comprise the amino acid sequences of SEQ ID NOs: 199, 200, 201 and 202, respectively, optionally having a C-terminal lysine removed from the HC1, the HC2, or both the HC1 and the HC2.
12. The bispecific antibody of any of the claims 1-11, wherein the antibody has a biantennary glycan structure with a fucose content of about between 1% to about 15%.
13. The bispecific antibody of claim 1, wherein HC1, LC1, HC2 and LC2 are encoded by synthetic polynucleotides comprising the sequence of SEQ ID NOs: 205, 206, 207 and 208, respectively.
14. An isolated synthetic polynucleotide encoding the HC1, the HC2, the LC1 or the LC2 of claim 1 or 11 or 26.
15. An isolated synthetic polynucleotide comprising the polynucleotide sequence of SEQ ID NOs: 205, 206, 207 or 208.
16. A vector comprising the polynucleotide of claim 14 or 15.
17. An isolated host cell comprising the vector of claim 16.
18. A method of producing the isolated bispecific EGFR/c-Met antibody of claim11, comprising:
    a) combining an isolated monospecific bivalent anti-EGFR antibody comprising two heavy chains of SEQ ID NO: 199 and two light chains of SEQ ID NO: 200 and an isolated monospecific bivalent anti-c-Met antibody comprising two heavy chains of SEQ ID NO: 201 and two light chains of SEQ ID NO: 202 in a mixture of about 1:1 molar ratio;
    b) introducing a reducing agent into the mixture;
    c) incubating the mixture about ninety minutes to about six hours;
    d) removing the reducing agent; and
    e) purifying the bispecific EGFR/c-Met antibody that comprises a first heavy chain of SEQ ID NO: 199 and a second heavy chain of SEQ ID NO: 201, a first light chain of SEQ ID NO: 200 and a second light chain of SEQ ID NO: 202, wherein the first heavy chain of SEQ ID NO: 199 pairs with the first light chain of SEQ ID NO: 200 to form the first binding domain that specifically binds

EGFR, and the second heavy chain of SEQ ID NO: 201 pairs with the second light chain of SEQ ID NO: 202 to form the second binding domain that specifically binds c-Met.

19. The method of claim 18, wherein the reducing agent is 2- mercaptoethanolamine (2-MEA).
20. The method of claim 19, wherein the 2-MEA is present at a concentration of about 25 mM to about 75 mM.
21. The method of claim 20, wherein the incubating step is performed at a temperature of about 25°C to about 37ºC.
22. A pharmaceutical composition comprising the bispecific antibody of any of the claims 1-11 and a pharmaceutically acceptable carrier.
23. A bispecific antibody of any of the claims 1-11 for therapy.