

Claims

- [Claim 1] A binding agent comprising:
a CDR-L1, a CDR-L2 and a CDR-L3 which are three polypeptide sequences of a light chain complementarity determining region (CDR-L),
wherein the CDR-L1 is selected from SEQ ID Nos 1-15, the CDR-L2 is selected from SEQ ID Nos 16-25 and the CDR-L3 is selected from SEQ ID Nos 26-36, and
wherein the binding agent specifically binds to an extracellular domain of mesenchymal epithelial transition factor (cMET).
- [Claim 2] A binding agent comprising:
a CDR-H1, a CDR-H2 and a CDR-H3 which are three polypeptide sequences of a heavy chain complementarity determining region (CDR-H),
wherein the CDR-H1 is selected from SEQ ID Nos 50-61, the CDR-H2 is selected from SEQ ID Nos 62-78 and the CDR-H3 is selected from SEQ ID Nos 79-93, and
wherein the binding agent specifically binds to an extracellular domain of mesenchymal epithelial transition factor (cMET).
- [Claim 3] A binding agent comprising:
a CDR-L1 selected from SEQ ID NOs. 1-15, a CDR-L2 selected from SEQ ID NOs. 16-25, a CDR-L3 selected from SEQ ID NOs. 26-36, a CDR-H1 selected from SEQ ID Nos 50-61, a CDR-H2 selected from SEQ ID Nos 62-78, and a CDR-H3 selected from SEQ ID Nos 79-93
wherein the binding agent specifically binds to an extracellular domain of mesenchymal epithelial transition factor (cMET).
- [Claim 4] The binding agent of claim 1 or 3, wherein the CDR-L1 is selected from SEQ ID NOs 2, 4, 6, 8, 10, 12 and 14.
- [Claim 5] The binding agent of claim 1, 3 or 4, wherein the CDR-L2 is selected from SEQ ID NOs 17, 19, 21, 23 and 25.
- [Claim 6] The binding agent of claim 1, 3, 4 or 5, wherein the CDR-L3 is selected from SEQ ID NOs 27, 29, 31, 33 and 35.
- [Claim 7] The binding agent of claim 2 or 3, wherein the CDR-H1 is selected from SEQ ID NOs 51, 53, 55, 57 and 59.
- [Claim 8] The binding agent of claim 2, 3 or 7, wherein the CDR-H2 selected from SEQ ID Nos 62-78 is selected from SEQ ID NOs 63, 65, 67, 69, 73 and 75.

- [Claim 9] The binding agent of claim 2, 3 or 8, wherein the CDR-H3 is selected from SEQ ID NOs 80, 82, 84, 86, 88, 91 and 93.
- [Claim 10] The binding agent of any one of claims 1 to 9, wherein the binding agent is an antibody, or a binding fragment thereof.
- [Claim 11] The binding agent of claim 10, wherein the binding agent is a monoclonal antibody, or binding fragment thereof.
- [Claim 12] The binding agent of any one of claims 1 to 11, wherein the binding agent comprises a constant region of an IgG₁, IgG₂, IgG₃, or IgG₄.
- [Claim 13] The binding agent of any one of claims 1 to 11, wherein the binding agent comprises a constant region of an IgD, IgE, IgA or IgM.
- [Claim 14] The binding agent of any one of claims 1 to 13, wherein the binding agent is humanized.
- [Claim 15] The binding agent of any one of claims 1 to 13, wherein the binding agent comprises at least one humanized or human framework region.
- [Claim 16] The binding agent of claim 15, wherein the binding agent comprises at least three humanized or human framework regions.
- [Claim 17] The binding agent of any one of claims 1 to 13, wherein the binding agent comprises at least one mouse framework region.
- [Claim 18] The binding agent of claim 17, wherein the binding agent comprises at least three mouse framework regions.
- [Claim 19] The binding agent of any one of claims 1 to 18, wherein the binding agent is a Fab, Fab', F(ab')₂, Fv or scFV fragment of an antibody.
- [Claim 20] The binding agent of any one of claims 1 to 19, wherein the binding agent consists of a single chain polypeptide.
- [Claim 21] The binding agent of any one of claims 1 to 13, wherein the binding agent comprises a variable light chain region having an amino acid sequence selected from SEQ ID NOS 37-44.
- [Claim 22] The binding agent of any one of claims 1 to 13, wherein the binding agent comprises a variable heavy chain region having an amino acid sequence selected from SEQ ID NOS 94-103.
- [Claim 23] The binding agent of any one of claims 1 to 13, wherein the binding agent comprises a light chain sequence selected from SEQ ID NOS 45-49.
- [Claim 24] The binding agent of any one of claims 1 to 13, wherein the binding agent comprises a heavy chain sequence selected from SEQ ID NOS 104-108.
- [Claim 25] The binding agent of claim 23 or 24, wherein the light chain sequence selected from SEQ ID NOS 45-49 and/or the heavy chain sequence

- selected from SEQ ID NOS 104-108 comprises one to five amino acid modifications selected from an amino acid addition, an amino acid deletion and an amino acid substitution.
- [Claim 26] The binding agent of any one of claims 1 to 25, wherein the binding agent induces internalization of cMET on a human cancer cell.
- [Claim 27] The binding agent of any one of claims 1 to 25, wherein the binding agent induces degradation of cMET on a human cancer cell.
- [Claim 28] The binding agent of any one of claims 1 to 25, wherein the binding agent is not a cMET agonist.
- [Claim 29] The binding agent of any one of claims 1 to 28, wherein the binding agent binds specifically to a mammalian cMET.
- [Claim 30] The binding agent of claim 29, wherein the mammalian cMET is a human cMET, monkey cMET or rat cMET.
- [Claim 31] The binding agent of claim 30, wherein the binding agent binds specifically to a human cMET, monkey cMET and rat cMET.
- [Claim 32] The binding agent of claim 30, wherein the binding agent binds specifically to human cMET.
- [Claim 33] The binding agent of any one of claims 1 to 32, wherein the binding agent specifically binds to the extracellular domain of a wild type cMET.
- [Claim 34] The binding agent of any one of claims 1 to 32, wherein the binding agent specifically binds to the extracellular domain of a cMET variant.
- [Claim 35] The binding agent of claim 34, wherein the cMET variant comprises an E168D or an N375S variant of cMET.
- [Claim 36] The binding agent of any one of claims 1 to 34, wherein the binding agent specifically binds the extracellular domain of human cMET with a KD of 10 nM or less.
- [Claim 37] The binding agent of claim 36, wherein the binding agent specifically binds the extracellular domain of human cMET with a KD of 1 nM or less.
- [Claim 38] The binding agent of any one of claims 1 to 37, wherein the binding agent comprises an anti-neoplastic agent.
- [Claim 39] A composition comprising a first binding agent that is the binding agent of any one of claims 1 to 38, and a second binding agent that does not bind specifically to cMET.
- [Claim 40] The composition of claim 39, wherein a first binding agent is the binding agent that specifically binds to the extracellular domain of cMET and the second binding agent is conjugated to the first binding

- agent.
- [Claim 41] A method of treating a subject having a neoplastic disorder or cancer comprising:
- a) providing a subject having, or suspected of having, a neoplastic disorder; and
 - b) administering a therapeutically effective amount of the binding agent of any one of claims 1 to 38 or the composition of any one of claims 39 to 40 to the subject.
- [Claim 42] The method of claim 41, wherein the binding agent specifically binds to the extracellular domain of cMET expressed on one or more cells of the subject.
- [Claim 43] The method of claim 41 or 42, wherein the binding agent inhibits mitosis of, and/or induces death of the one or more cells expressing cMET.
- [Claim 44] The method of any one of claims 41 to 43, wherein the neoplastic disorder or cancer comprises a lung carcinoma, breast carcinoma, ovarian carcinoma, kidney carcinoma, colorectal carcinoma, gastric carcinoma, thyroid carcinoma, pancreas carcinoma, neuroblastoma, or a squamous cell carcinoma of the head and neck, cervical cancer, hepatocellular cancer, sarcomas, mesothelioma, glioblastoma, multiple myeloma, melanoma, prostate and esophageal carcinoma.
- [Claim 45] A pharmaceutical composition comprising the binding agent of any one of claims 1 to 38, and a pharmaceutically acceptable excipient, diluent, additive or carrier.
- [Claim 46] The pharmaceutical composition of claim 45, wherein the additive comprises a preservative.
- [Claim 47] The pharmaceutical composition of claim 45 or 46, wherein the diluent comprises phosphate buffered saline.
- [Claim 48] The pharmaceutical composition of any one of claims 45 to 47, wherein the excipient comprises sodium citrate dehydrate or polyoxyethylene-sorbitan-20 mono-oleate (polysorbate 80).
- [Claim 49] The pharmaceutical composition any one of claims 45 to 48, wherein the carrier comprises a recombinant protein.
- [Claim 50] The pharmaceutical composition of any one of claims 45 to 49, wherein the composition is sterile.
- [Claim 51] The pharmaceutical composition of any one of claims 45 to 50, wherein the composition is formulated as a sterile, lyophilized powder suitable for intravenous administration to a mammal.