SUMMARY ~~OF THE INVENTION~~

[006a] In a first aspect, the present invention refers to an isolated antibody capable of binding at least one polypeptide selected from

- SEQ ID NO: 164;
- SEQ ID NO: 165;
- SEQ ID NO: 123;
- amino acids 495-556 of HGF;
- amino acids 507-585 of HGF; and
- amino acids 506-728 of HGF,

wherein the antibody is capable of neutralizing binding of HGF to c-Met.

[006b] In a second aspect, the present invention refers to an isolated antibody, wherein the antibody is capable of binding hepatocyte growth factor (HGF), wherein the antibody is capable of neutralizing binding of HGF to c-Met, and the antibody is selected from:

an antibody comprising a light chain comprising SEQ ID NOs: 60, 70, and 80, and a heavy chain comprising SEQ ID NOs: 90, 100, and 110;

an antibody comprising a light chain comprising SEQ ID NOs: 61, 71, and 81, and a heavy chain comprising SEQ ID NOs: 91, 101, and 111;

an antibody comprising a light chain comprising SEQ ID NOs: 62, 72, and 82, and a heavy chain comprising SEQ ID NOs: 92, 102, and 112;

an antibody comprising a light chain comprising SEQ ID NOs: 63, 73, and 83, and a heavy chain comprising SEQ ID NOs: 93, 103, and 113;

an antibody comprising a light chain comprising SEQ ID NOs: 64, 74, and 84, and a heavy chain comprising SEQ ID NOs: 94, 104, and 114;

an antibody comprising a light chain comprising SEQ ID NOs: 65, 75, and 85, and a heavy chain comprising SEQ ID NOs: 95, 105, and 115;

an antibody comprising a light chain comprising SEQ ID NOs: 66, 76, and 86, and a heavy chain comprising SEQ ID NOs: 96, 106, and 116;

an antibody comprising a light chain comprising SEQ ID NOs: 67, 77, and 87, and a heavy chain comprising SEQ ID NOs: 97, 107, and 117;

an antibody comprising a light chain comprising SEQ ID NOs: 68, 78, and 88, and a heavy chain comprising SEQ ID NOs: 98, 108, and 118; and

an antibody comprising a light chain comprising SEQ ID NOs: 69, 79, and 89, and a heavy chain comprising SEQ ID NOs: 99, 109, and 119.

[006c] In a third aspect, the present invention refers to an isolated antibody which is capable of neutralizing binding of HGF to c-Met and which competes for binding to HGF with at least one antibody selected from:

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 24 from residue 23 to residue 129 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 25 from residue 20 to residue 141;

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 26 from residue 21 to residue 133 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 27 from residue 20 to residue 137;

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 28 from residue 23 to residue 129 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 29 from residue 20 to residue 139;

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 30 from residue 23 to residue 129 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 31 from residue 20 to residue 148;

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 32 from residue 23 to residue 129 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 33 from residue 20 to residue 139;

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 34 from residue 23 to residue 129 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 35 from residue 20 to residue 144;

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 36 from residue 21 to residue 133 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 37 from residue 20 to residue 142;

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 38 from residue 21 to residue 128 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 39 from residue 20 to residue 139;

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 40 from residue 23 to residue 129 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 41 from residue 20 to residue 140; and

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 42 from residue 21 to residue 128 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 43 from residue 20 to residue 139.

[007] In certain ~~embodiments~~examples, ~~the invention provides~~described herein is an isolated polypeptide comprising at least one complementarity determining region (CDR) selected from CDR1a, CDR2a, and CDR3a

wherein CDR1a comprises the amino acid sequence a b c d e f g h i j k l m n o p q, wherein amino acid a is selected from lysine, arginine, or glutamine; amino acid b is selected from serine or alanine; amino acid c is serine, amino acid d is glutamine; amino acid e is selected from serine, glycine, or aspartic acid; amino acid f is selected from valine or isoleucine or is not present; amino acid g is selected from leucine or phenylalanine or is not present; amino acid h is selected from phenylalanine or tyrosine or is not present; amino acid i is serine or not present; amino acid j is serine or not present; amino acid k is selected from asparagine, threonine, or not present; amino acid l is selected from asparagine, isoleucine, or valine; amino acid m is selected from lysine, arginine, asparagine, or aspartic acid; amino acid n is selected from asparagine or serine; amino acid o is selected from tyrosine, aspartic acid, tryptophan, or asparagine; amino acid p is leucine; and amino acid q is selected from alanine, glycine, or asparagine;

wherein CDR2a comprises the amino acid sequence r s t u v w x, wherein amino acid r is selected from tryptophan, alanine, valine, glutamic acid, or glycine; amino acid s is alanine, amino acid t is serine, amino acid u is selected from threonine, serine, or aspartic acid; amino acid v is selected from

arginine or leucine; amino acid w is selected from glutamic acid, glutamine, or alanine; and amino acid x is selected from serine, asparagine, or threonine;

wherein CDR3a comprises the amino acid sequence y z a' b' c' d' e' f' g' h', wherein amino acid y is selected from glutamine or leucine; amino acid z is selected from glutamine, asparagine, or arginine; amino acid a' is selected from tyrosine, histidine, alanine, or serine; amino acid b' is selected from phenylalanine, tyrosine, aspartic acid, asparagine, or isoleucine; amino acid c' is selected from serine, glycine, or asparagine; amino acid d' is selected from proline, tyrosine, threonine, phenylalanine, aspartic acid, leucine, or tryptophan; amino acid e' is proline; amino acid f' is proline or is not present; amino acid g' is tryptophan, leucine, proline, tyrosine, or isoleucine; and amino acid h' is threonine or asparagine; and

wherein the polypeptide, in association with an antibody heavy chain, is capable of binding hepatocyte growth factor (HGF).

[008] In certain ~~embodiments~~examples, ~~the invention provides~~there is described an isolated polypeptide comprising at least one complementarity determining region (CDR) selected from CDR1b, CDR2b, and CDR3b

wherein CDR1b comprises the amino acid sequence a b c d e f g, wherein amino acid a is serine or is not present; amino acid b is selected from aspartic acid or glycine, or is not present; amino acid c is selected from aspartic acid, glycine, serine, valine, threonine, or isoleucine; amino acid d is tyrosine; amino acid e is selected from tyrosine or glycine; amino acid f is selected from isoleucine, methionine, or tryptophan; and amino acid g is selected from histidine, asparagine, or serine;

phenylalanine, or is not present; amino acid d' is glycine or is not present; amino acid e' is selected from tryptophan or tyrosine, or is not present; amino acid f' is aspartic acid or is not present; amino acid g' is selected from serine or arginine, or is not present; amino acid h' is serine or is not present; amino acid i' is selected from glycine or tyrosine, or is not present; amino acid j' is selected from tyrosine, glutamic acid, or aspartic acid, or is not present; amino acid k' is selected from tyrosine, phenylalanine, or aspartic acid, or is not present; amino acid l' is selected from tyrosine, aspartic acid, histidine, or tryptophan, or is not present; amino acid m' is selected from tyrosine, glycine, aspartic acid, proline, or serine, or is not present; amino acid n' is selected from glycine, valine, tyrosine, or aspartic acid, or is not present; amino acid o' is selected from leucine, alanine, glycine, or tyrosine, or is not present; amino acid p' is selected from methionine, phenylalanine, or tyrosine; amino acid q' is aspartic acid, and amino acid r' is selected from valine, tyrosine, isoleucine, or proline; and

wherein the polypeptide, in association with an antibody light chain, is capable of binding HGF.

[009] In certain ~~embodiments~~examples, ~~the invention provides~~there is described an isolated specific binding agent, wherein the specific binding agent comprises:

(i) a first polypeptide comprising at least one complementarity determining region (CDR) selected from CDR1a, CDR2a, and CDR3a

wherein CDR1a comprises the amino acid sequence a b c d e f g h i j k l m n o p q, wherein amino acid a is selected from lysine, arginine, or glutamine; amino acid b is selected from serine or alanine; amino acid c is

from glycine, valine, tyrosine, or aspartic acid, or is not present; amino acid o' is selected from leucine, alanine, glycine, or tyrosine, or is not present; amino acid p' is selected from methionine, phenylalanine, or tyrosine; amino acid q' is aspartic acid, and amino acid r' is selected from valine, tyrosine, isoleucine, or proline; and

wherein the second polypeptide, in association with an antibody light chain, is capable of binding HGF.

[010] In certain ~~embodiments~~examples, ~~the invention provides~~there is described an isolated polypeptide comprising at least one amino acid sequence selected from SEQ ID NO: 24, 26, 28, 30, 32, 34, 36, 38, 40, and 42.

[011] In certain ~~embodiments~~examples, ~~the invention provides~~there is described an isolated polypeptide comprising at least one amino acid sequence selected from SEQ ID NO: 25, 27, 29, 31, 33, 35, 37, 39, 41, and 43.

[012] In certain ~~embodiments~~examples, ~~the invention provides~~there is described an isolated nucleic acid molecule comprising at least one nucleotide sequence selected from SEQ ID NO: 1, 3, 5, 7, 9, 11, 13, 15, 17, and 19.

[013] In certain ~~embodiments~~examples, ~~the invention provides~~there is described an isolated nucleic acid molecule comprising at least one nucleotide sequence selected from SEQ ID NO: 2, 4, 6, 8, 10, 12, 14, 16, 18, and 20.

[014] In certain ~~embodiments~~examples, ~~the invention provides~~there is described an isolated nucleic acid molecule that encodes a polypeptide comprising at least one complementarity determining region (CDR) selected from CDR1a, CDR2a, and CDR3a

phenylalanine, tyrosine, aspartic acid, asparagine, or isoleucine; amino acid c' is selected from serine, glycine, or asparagine; amino acid d' is selected from proline, tyrosine, threonine, phenylalanine, aspartic acid, leucine, or tryptophan; amino acid e' is proline; amino acid f' is proline or is not present; amino acid g' is tryptophan, leucine, proline, tyrosine, or isoleucine; and amino acid h' is threonine or asparagine; and

wherein the polypeptide, in association with an antibody heavy chain, is capable of binding hepatocyte growth factor (HGF).

[015] In certain ~~embodiments~~examples, ~~the invention provides~~there is described an isolated nucleic acid molecule that encodes a polypeptide comprising at least one complementarity determining region (CDR) selected from CDR1b, CDR2b, and CDR3b

wherein CDR1b comprises the amino acid sequence a b c d e f g, wherein amino acid a is serine or is not present; amino acid b is selected from aspartic acid or glycine, or is not present; amino acid c is selected from aspartic acid, glycine, serine, valine, threonine, or isoleucine; amino acid d is tyrosine; amino acid e is selected from tyrosine or glycine; amino acid f is selected from isoleucine, methionine, or tryptophan; and amino acid g is selected from histidine, asparagine, or serine;

wherein CDR2b comprises the amino acid sequence h i j k l m n o p q r s t u v w x, wherein amino acid h is selected from tryptophan, tyrosine, valine, asparagine, or glutamic acid; amino acid i is selected from isoleucine, phenylalanine, or valine; amino acid j is selected from asparagine, serine, tryptophan, or tyrosine; amino acid k is selected from proline, serine, tyrosine,

selected from tyrosine, glutamic acid, or aspartic acid, or is not present; amino acid k' is selected from tyrosine, phenylalanine, or aspartic acid, or is not present; amino acid l' is selected from tyrosine, aspartic acid, histidine, or tryptophan, or is not present; amino acid m' is selected from tyrosine, glycine, aspartic acid, proline, or serine, or is not present; amino acid n' is selected from glycine, valine, tyrosine, or aspartic acid, or is not present; amino acid o' is selected from leucine, alanine, glycine, or tyrosine, or is not present; amino acid p' is selected from methionine, phenylalanine, or tyrosine; amino acid q' is aspartic acid, and amino acid r' is selected from valine, tyrosine, isoleucine, or proline; and

wherein the polypeptide, in association with an antibody light chain, is capable of binding HGF.

[016] In certain ~~embodiments~~examples, ~~the invention provides~~there is described an isolated cell line that produces an antibody selected from 1.24.1, 1.29.1, 1.60.1, 1.61.3, 1.74.3, 1.75.1, 2.4.4, 2.12.1, 2.40.1, and 3.10.1.

[017] In certain ~~embodiments~~examples, ~~the invention provides~~there is described a method of inhibiting binding of HGF to Met comprising administering a specific binding agent to HGF.

[018] In certain ~~embodiments~~examples, ~~the invention provides~~there is described a polypeptide comprising at least one amino acid sequence selected from SEQ ID NO: 164 and 165.

[019] In certain ~~embodiments~~examples, ~~the invention provides~~there is described a polypeptide consisting essentially of at least one amino acid sequence selected from SEQ ID NO: 164 and 165.

[020] In certain ~~embodiments~~examples, ~~the invention provides~~there is described a specific binding agent which is capable of binding at least one amino acid sequence selected from SEQ ID NO: 164 and 165.

[021] In certain ~~embodiments~~examples, ~~the invention provides~~there is described an antibody or antigen binding domain which is capable of binding at least one amino acid sequence selected from SEQ ID NO: 164 and 165.

[022] In certain ~~embodiments~~examples, ~~the invention provides~~there is described a method of obtaining an antibody capable of binding hepatocyte growth factor (HGF) comprising administering at least one polypeptide selected from SEQ ID NO: 164 and 165 to an animal and obtaining an antibody capable of binding HGF from the animal.

[023] In certain ~~embodiments~~examples, ~~the invention provides~~there is described a method of decreasing or preventing binding of a specific binding agent to hepatocyte growth factor (HGF) by administering a polypeptide comprising at least one amino acid sequence selected from SEQ ID NO: 164 and 165.

[024] In certain ~~embodiments~~examples, ~~the invention provides~~there is described a method of decreasing or preventing binding of a specific binding agent to hepatocyte growth factor (HGF) by administering a polypeptide consisting of at least one amino acid sequence selected from SEQ ID NO: 164 and 165.

[024a] In a fourth aspect, the present invention refers to a composition comprising an antibody as defined above and a pharmaceutically acceptable carrier.

[024b] In a fifth aspect, the present invention refers to the antibody as defined above and at least one chemotherapy agent for use in treating cancer in a patient.

[024c] In a sixth aspect, the present invention refers to the antibody as defined above and radiation therapy for use in treating cancer in a patient.

[024d] In a seventh aspect, the present invention refers to an *in vitro* method of detecting the level of hepatocyte growth factor (HGF) in a sample, comprising contacting the sample with the antibody as defined above.

[024e] In an eighth aspect, the present invention refers to a method of obtaining an antibody as defined above capable of binding hepatocyte growth factor (HGF) comprising administering at least one polypeptide consisting of an amino acid sequence selected from

- SEQ ID NO: 164;
- SEQ ID NO: 165;
- SEQ ID NO: 123;
- amino acids 495-556 of HGF; and
- amino acids 507-585 of HGF

to a non-human animal and obtaining an antibody capable of binding HGF from the animal.

[024f] In a ninth aspect, the present invention refers to a host cell comprising a first polynucleotide that encodes a light chain and a second polynucleotide that encodes a heavy chain, wherein the light chain and the heavy chain form an antibody that is capable of binding hepatocyte growth factor (HGF), and the antibody is selected from:

an antibody comprising a light chain comprising SEQ ID NOs: 60, 70, and 80, and a heavy chain comprising SEQ ID NOs: 90, 100, and 110;

an antibody comprising a light chain comprising SEQ ID NOs: 61, 71, and 81, and a heavy chain comprising SEQ ID NOs: 91, 101, and 111;

an antibody comprising a light chain comprising SEQ ID NOs: 62, 72, and 82, and a heavy chain comprising SEQ ID NOs: 92, 102, and 112;

an antibody comprising a light chain comprising SEQ ID NOs: 63, 73, and 83, and a heavy chain comprising SEQ ID NOs: 93, 103, and 113;

an antibody comprising a light chain comprising SEQ ID NOs: 64, 74, and 84, and a heavy chain comprising SEQ ID NOs: 94, 104, and 114;

an antibody comprising a light chain comprising SEQ ID NOs: 65, 75, and 85, and a heavy chain comprising SEQ ID NOs: 95, 105, and 115;

an antibody comprising a light chain comprising SEQ ID NOs: 66, 76, and 86, and a heavy chain comprising SEQ ID NOs: 96, 106, and 116;

an antibody comprising a light chain comprising SEQ ID NOs: 67, 77, and 87, and a heavy chain comprising SEQ ID NOs: 97, 107, and 117;

an antibody comprising a light chain comprising SEQ ID NOs: 68, 78, and 88, and a heavy chain comprising SEQ ID NOs: 98, 108, and 118; and

an antibody comprising a light chain comprising SEQ ID NOs: 69, 79, and 89, and a heavy chain comprising SEQ ID NOs: 99, 109, and 119.

[024g] In a tenth aspect, the present invention refers to a host cell comprising a first polynucleotide that encodes a light chain and a second polynucleotide that encodes a heavy chain, wherein the light chain and the heavy chain form an antibody that is capable of binding a human/mouse chimeric HGF polypeptide,

wherein the chimeric polypeptide comprises a mouse HGF molecule having amino acids 506-728 of human HGF in place of the homologous mouse sequence,

wherein the antibody does not bind significantly to mouse HGF, and

wherein the antibody is capable of neutralizing binding of HGF to c-Met.

[024h] In an eleventh aspect, the present invention refers to a host cell comprising a first polynucleotide that encodes a light chain and a second polynucleotide that encodes a heavy chain, wherein the light chain and the heavy chain form an antibody that is capable of neutralizing binding of HGF to c-Met and which competes for binding to HGF with at least one antibody selected from:

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 24 from residue 23 to residue 129 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 25 from residue 20 to residue 141;

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 26 from residue 21 to residue 133 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 27 from residue 20 to residue 137;

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 28 from residue 23 to residue 129 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 29 from residue 20 to residue 139;

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 30 from residue 23 to residue 129 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 31 from residue 20 to residue 148;

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 32 from residue 23 to residue 129 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 33 from residue 20 to residue 139;

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 34 from residue 23 to residue 129 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 35 from residue 20 to residue 144;

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 36 from residue 21 to residue 133 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 37 from residue 20 to residue 142;

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 38 from residue 21 to residue 128 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 39 from residue 20 to residue 139;

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 40 from residue 23 to residue 129 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 41 from residue 20 to residue 140; and

an antibody comprising a light chain comprising the amino acid sequence of SEQ ID NO: 42 from residue 21 to residue 128 and a heavy chain comprising the amino acid sequence of SEQ ID NO: 43 from residue 20 to residue 139.

[024i] In a twelfth aspect, the present invention refers to a method of producing an antibody that is capable of binding hepatocyte growth factor (HGF), comprising expressing a first polynucleotide and a second polynucleotide in an isolated host cell, wherein the first polynucleotide encodes a light chain and the second polynucleotide encodes a heavy chain, wherein the light chain and heavy chain form an antibody as defined above.

[025] Other ~~embodiments~~examples of this invention will be readily apparent from the disclosure provided herewith.

BRIEF DESCRIPTION OF THE FIGURES

[026] Figure 1A shows a dendrogram of kappa light chains of certain antibodies to HGF showing their germ line relationships. Germ line gene identifications are indicated to the right of the antibody designation. Figure 1B shows an amino acid sequence alignment of kappa light chain variable regions of certain antibodies to HGF. Germ line gene identifications are indicated at the left. The CDR regions are indicated as bold lines above the aligned sequences.

[027] Figure 2A shows a dendrogram of gamma heavy chains of certain antibodies to HGF showing their germ line relationships. Germ line gene identifications are indicated to the right of the antibody designation. Figure 2B shows an amino acid sequence alignment of gamma heavy chain variable regions of certain antibodies to HGF. Germ line gene identifications are indicated at the left. The CDR regions are indicated as bold lines above the aligned sequences.

[028] Figure 3 shows DNA sequences encoding variable regions from both the light and the heavy chains of certain antibodies to HGF. Antibody name, germ line designation, and sequence ID are indicated for each sequence. The natural signal peptide sequence is underlined. The