

WHAT IS CLAIMED IS:

1. An antibody, wherein the antibody comprises:
 - (a) a heavy chain variable domain and a light chain variable domain selected from the group of:
 - (i) SEQ ID NO: 5 and SEQ ID NO: 6, respectively;
 - (ii) SEQ ID NO: 7 and SEQ ID NO: 8, respectively;
 - (iii) SEQ ID NO: 9 and SEQ ID NO: 10, respectively;
 - (iv) SEQ ID NO: 11 and SEQ ID NO: 12, respectively;
 - (v) SEQ ID NO: 13 and SEQ ID NO: 14, respectively;
 - (vi) SEQ ID NO: 15 and SEQ ID NO: 16, respectively;
 - (vii) SEQ ID NO: 17 and SEQ ID NO: 18, respectively;
 - (viii) SEQ ID NO: 19 and SEQ ID NO: 20, respectively;
 - (ix) SEQ ID NO: 21 and SEQ ID NO: 22, respectively;
 - (x) SEQ ID NO: 23 and SEQ ID NO: 24, respectively;
 - (xi) SEQ ID NO: 25 and SEQ ID NO: 26, respectively;
 - (xii) SEQ ID NO: 27 and SEQ ID NO: 28, respectively;
 - (xiii) SEQ ID NO: 29 and SEQ ID NO: 30, respectively;
 - (xiv) SEQ ID NO: 31 and SEQ ID NO: 32, respectively;
 - (xv) SEQ ID NO: 33 and SEQ ID NO: 34, respectively; and
 - (b) a heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 155 or SEQ ID NO: 189 comprising one or more of the following:
 - (i) a lysine to cysteine substitution at amino acid position 105 and deletion of a threonine at amino acid positions 106 and 108;
 - (ii) a methionine to tyrosine substitution at amino acid position 135, a serine to threonine substitution at amino acid position 137, and a threonine to glutamic acid substitution at amino acid position 139;
 - (iii) a methionine to leucine substitution at amino acid position 311 and an asparagine to serine substitution at amino acid position 317; and
 - (iv) an alanine to a cysteine substitution at amino acid position 1;and/or
- a light chain C_L sequence of SEQ ID NO: 157 comprising a valine to cysteine substitution at amino acid position 98.

2. The antibody of claim 1, wherein the heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 155 or SEQ ID NO: 189 comprises a lysine to cysteine substitution at amino acid position 105 and deletion of a threonine at amino acid positions 106 and 108.

3. The antibody of claim 2, wherein the antibody comprises heavy chain and light chain sequences selected from the group of:

- (i) SEQ ID NO: 35 and SEQ ID NO: 41, respectively;
- (ii) SEQ ID NO: 43 and SEQ ID NO: 49, respectively;
- (iii) SEQ ID NO: 51 and SEQ ID NO: 57, respectively;
- (iv) SEQ ID NO: 59 and SEQ ID NO: 65, respectively;
- (v) SEQ ID NO: 67 and SEQ ID NO: 73, respectively;
- (vi) SEQ ID NO: 75 and SEQ ID NO: 81, respectively;
- (vii) SEQ ID NO: 83 and SEQ ID NO: 89, respectively;
- (viii) SEQ ID NO: 91 and SEQ ID NO: 97, respectively;
- (ix) SEQ ID NO: 99 and SEQ ID NO: 105, respectively;
- (x) SEQ ID NO: 107 and SEQ ID NO: 113, respectively;
- (xi) SEQ ID NO: 115 and SEQ ID NO: 121, respectively;
- (xii) SEQ ID NO: 123 and SEQ ID NO: 129, respectively;
- (xiii) SEQ ID NO: 131 and SEQ ID NO: 137, respectively;
- (xiv) SEQ ID NO: 139 and SEQ ID NO: 145, respectively; or
- (xv) SEQ ID NO: 147 and SEQ ID NO: 153, respectively.

4. The antibody of claim 1, wherein the heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 155 or SEQ ID NO: 189 comprises:

a lysine to cysteine substitution at amino acid position 105 and deletion of a threonine at amino acid positions 106 and 108; and

a methionine to leucine substitution at amino acid position 311 and an asparagine to serine substitution at amino acid position 317.

5. The antibody of claim 4, wherein the antibody comprises heavy chain and light chain sequences selected from the group of:

- (i) SEQ ID NO: 36 and SEQ ID NO: 41, respectively;
- (ii) SEQ ID NO: 44 and SEQ ID NO: 49, respectively;

- (iii) SEQ ID NO: 52 and SEQ ID NO: 57, respectively;
- (iv) SEQ ID NO: 60 and SEQ ID NO: 65, respectively;
- (v) SEQ ID NO: 68 and SEQ ID NO: 73, respectively;
- (vi) SEQ ID NO: 76 and SEQ ID NO: 81, respectively;
- (vii) SEQ ID NO: 84 and SEQ ID NO: 89, respectively;
- (viii) SEQ ID NO: 92 and SEQ ID NO: 97, respectively;
- (ix) SEQ ID NO: 100 and SEQ ID NO: 105, respectively;
- (x) SEQ ID NO: 108 and SEQ ID NO: 113, respectively;
- (xi) SEQ ID NO: 116 and SEQ ID NO: 121, respectively;
- (xii) SEQ ID NO: 124 and SEQ ID NO: 129, respectively;
- (xiii) SEQ ID NO: 132 and SEQ ID NO: 137, respectively;
- (xiv) SEQ ID NO: 140 and SEQ ID NO: 145, respectively; or
- (xv) SEQ ID NO: 148 and SEQ ID NO: 153, respectively.

6. The antibody of claim 1, wherein the heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 155 or SEQ ID NO: 189 comprises:

a lysine to cysteine substitution at amino acid position 105 and deletion of a threonine at amino acid positions 106 and 108; and

a methionine to tyrosine substitution at amino acid position 135, a serine to threonine substitution at amino acid position 137, and a threonine to glutamic acid substitution at amino acid position 139.

7. The antibody of claim 6, wherein the antibody comprises heavy chain and light chain sequences selected from the group of:

- (i) SEQ ID NO: 37 and SEQ ID NO: 41, respectively;
- (ii) SEQ ID NO: 45 and SEQ ID NO: 49, respectively;
- (iii) SEQ ID NO: 53 and SEQ ID NO: 57, respectively;
- (iv) SEQ ID NO: 61 and SEQ ID NO: 65, respectively;
- (v) SEQ ID NO: 69 and SEQ ID NO: 73, respectively;
- (vi) SEQ ID NO: 77 and SEQ ID NO: 81, respectively;
- (vii) SEQ ID NO: 85 and SEQ ID NO: 89, respectively;
- (viii) SEQ ID NO: 93 and SEQ ID NO: 97, respectively;
- (ix) SEQ ID NO: 101 and SEQ ID NO: 105, respectively;

- (x) SEQ ID NO: 109 and SEQ ID NO: 113, respectively;
- (xi) SEQ ID NO: 117 and SEQ ID NO: 121, respectively;
- (xii) SEQ ID NO: 125 and SEQ ID NO: 129, respectively;
- (xiii) SEQ ID NO: 133 and SEQ ID NO: 137, respectively;
- (xiv) SEQ ID NO: 141 and SEQ ID NO: 145, respectively; or
- (xv). SEQ ID NO: 149 and SEQ ID NO: 153, respectively.

8. The antibody of claim 1, wherein:

the heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 155 or SEQ ID NO: 189 comprises a lysine to cysteine substitution at amino acid position 105 and deletion of a threonine at amino acid positions 106 and 108; and

the light chain C_L sequence of SEQ ID NO: 157 comprises a valine to cysteine substitution at amino acid position 98.

9. The antibody of claim 8, wherein the antibody comprises heavy chain and light chain sequences selected from the group of:

- (i) SEQ ID NO: 35 and SEQ ID NO: 42, respectively;
- (ii) SEQ ID NO: 43 and SEQ ID NO: 50, respectively;
- (iii) SEQ ID NO: 51 and SEQ ID NO: 58, respectively;
- (iv) SEQ ID NO: 59 and SEQ ID NO: 66, respectively;
- (v) SEQ ID NO: 67 and SEQ ID NO: 74, respectively;
- (vi) SEQ ID NO: 75 and SEQ ID NO: 82, respectively;
- (vii) SEQ ID NO: 83 and SEQ ID NO: 90, respectively;
- (viii) SEQ ID NO: 91 and SEQ ID NO: 98, respectively;
- (ix) SEQ ID NO: 99 and SEQ ID NO: 106, respectively;
- (x) SEQ ID NO: 107 and SEQ ID NO: 114, respectively;
- (xi) SEQ ID NO: 115 and SEQ ID NO: 122, respectively;
- (xii) SEQ ID NO: 123 and SEQ ID NO: 130, respectively;
- (xiii) SEQ ID NO: 131 and SEQ ID NO: 138, respectively;
- (xiv) SEQ ID NO: 139 and SEQ ID NO: 146, respectively; or
- (xv) SEQ ID NO: 147 and SEQ ID NO: 154, respectively.

10. The antibody of claim 1, wherein:

the heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 155 or SEQ ID NO: 189 comprises:

a lysine to cysteine substitution at amino acid position 105 and deletion of a threonine at amino acid positions 106 and 108; and

a methionine to leucine substitution at amino acid position 311 and an asparagine to serine substitution at amino acid position 317; and

the light chain C_L sequence of SEQ ID NO: 157 comprises a valine to cysteine substitution at amino acid position 98.

11. The antibody of claim 10, wherein the antibody comprises heavy chain and light chain sequences selected from the group of:

- (i) SEQ ID NO: 36 and SEQ ID NO: 42, respectively;
- (ii) SEQ ID NO: 44 and SEQ ID NO: 50, respectively;
- (iii) SEQ ID NO: 52 and SEQ ID NO: 58, respectively;
- (iv) SEQ ID NO: 60 and SEQ ID NO: 66, respectively;
- (v) SEQ ID NO: 68 and SEQ ID NO: 74, respectively;
- (vi) SEQ ID NO: 76 and SEQ ID NO: 82, respectively;
- (vii) SEQ ID NO: 84 and SEQ ID NO: 90, respectively;
- (viii) SEQ ID NO: 92 and SEQ ID NO: 98, respectively;
- (ix) SEQ ID NO: 100 and SEQ ID NO: 106, respectively;
- (x) SEQ ID NO: 108 and SEQ ID NO: 114, respectively;
- (xi) SEQ ID NO: 116 and SEQ ID NO: 122, respectively;
- (xii) SEQ ID NO: 124 and SEQ ID NO: 130, respectively;
- (xiii) SEQ ID NO: 132 and SEQ ID NO: 138, respectively;
- (xiv) SEQ ID NO: 140 and SEQ ID NO: 146, respectively; or
- (xv) SEQ ID NO: 148 and SEQ ID NO: 154, respectively.

12. The antibody of claim 1, wherein:

the heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 155 or SEQ ID NO: 189 comprises:

a lysine to cysteine substitution at amino acid position 105 and deletion of a threonine at amino acid positions 106 and 108; and

a methionine to tyrosine substitution at amino acid position 135, a serine to threonine substitution at amino acid position 137, and a threonine to glutamic acid substitution at amino acid position 139; and

the light chain C_L sequence of SEQ ID NO: 157 comprises a valine to cysteine substitution at amino acid position 98.

13. The antibody of claim 12, wherein the antibody comprises heavy chain and light chain sequences selected from the group of:

- (i) SEQ ID NO: 37 and SEQ ID NO: 42, respectively;
- (ii) SEQ ID NO: 45 and SEQ ID NO: 50, respectively;
- (iii) SEQ ID NO: 53 and SEQ ID NO: 58, respectively;
- (iv) SEQ ID NO: 61 and SEQ ID NO: 66, respectively;
- (v) SEQ ID NO: 69 and SEQ ID NO: 74, respectively;
- (vi) SEQ ID NO: 77 and SEQ ID NO: 82, respectively;
- (vii) SEQ ID NO: 85 and SEQ ID NO: 90, respectively;
- (viii) SEQ ID NO: 93 and SEQ ID NO: 98, respectively;
- (ix) SEQ ID NO: 101 and SEQ ID NO: 106, respectively;
- (x) SEQ ID NO: 109 and SEQ ID NO: 114, respectively;
- (xi) SEQ ID NO: 117 and SEQ ID NO: 122, respectively;
- (xii) SEQ ID NO: 125 and SEQ ID NO: 130, respectively;
- (xiii) SEQ ID NO: 133 and SEQ ID NO: 138, respectively;
- (xiv) SEQ ID NO: 141 and SEQ ID NO: 146, respectively; or
- (xv) SEQ ID NO: 149 and SEQ ID NO: 154, respectively.

14. The antibody of claim 1, wherein the heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 155 or SEQ ID NO: 189 comprises:

amino acid a lysine to cysteine substitution at amino acid position 105 and deletion of a threonine at positions 106 and 108; and

an alanine to a cysteine substitution at amino acid position 1.

15. The antibody of claim 14, wherein the antibody comprises heavy chain and light chain sequences selected from the group of:

- (i) SEQ ID NO: 38 and SEQ ID NO: 41, respectively;

- (ii) SEQ ID NO: 46 and SEQ ID NO: 49, respectively;
- (iii) SEQ ID NO: 54 and SEQ ID NO: 57, respectively;
- (iv) SEQ ID NO: 62 and SEQ ID NO: 65, respectively;
- (v) SEQ ID NO: 70 and SEQ ID NO: 73, respectively;
- (vi) SEQ ID NO: 78 and SEQ ID NO: 81, respectively;
- (vii) SEQ ID NO: 86 and SEQ ID NO: 89, respectively;
- (viii) SEQ ID NO: 94 and SEQ ID NO: 97, respectively;
- (ix) SEQ ID NO: 102 and SEQ ID NO: 105, respectively;
- (x) SEQ ID NO: 110 and SEQ ID NO: 113, respectively;
- (xi) SEQ ID NO: 118 and SEQ ID NO: 121, respectively;
- (xii) SEQ ID NO: 126 and SEQ ID NO: 129, respectively;
- (xiii) SEQ ID NO: 134 and SEQ ID NO: 137, respectively;
- (xiv) SEQ ID NO: 142 and SEQ ID NO: 145, respectively; or
- (xv) SEQ ID NO: 150 and SEQ ID NO: 153, respectively.

16. The antibody of claim 1, wherein the heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 155 or SEQ ID NO: 189 comprises:

a lysine to cysteine substitution at amino acid position 105 and deletion of a threonine at amino acid positions 106 and 108;

a methionine to leucine substitution at amino acid position 311 and an asparagine to serine substitution at amino acid position 317; and

an alanine to a cysteine substitution at amino acid position 1.

17. The antibody of claim 16, wherein the antibody comprises a heavy chain and a light chain sequence selected from the group of:

- (i) SEQ ID NO: 39 and SEQ ID NO: 41, respectively;
- (ii) SEQ ID NO: 47 and SEQ ID NO: 49, respectively;
- (iii) SEQ ID NO: 55 and SEQ ID NO: 57, respectively;
- (iv) SEQ ID NO: 63 and SEQ ID NO: 65, respectively;
- (v) SEQ ID NO: 71 and SEQ ID NO: 73, respectively;
- (vi) SEQ ID NO: 79 and SEQ ID NO: 81, respectively;
- (vii) SEQ ID NO: 87 and SEQ ID NO: 89, respectively;
- (viii) SEQ ID NO: 95 and SEQ ID NO: 97, respectively;

- (ix) SEQ ID NO: 103 and SEQ ID NO: 105, respectively;
- (x) SEQ ID NO: 111 and SEQ ID NO: 113, respectively;
- (xi) SEQ ID NO: 119 and SEQ ID NO: 121, respectively;
- (xii) SEQ ID NO: 127 and SEQ ID NO: 129, respectively;
- (xiii) SEQ ID NO: 135 and SEQ ID NO: 137, respectively;
- (xiv) SEQ ID NO: 143 and SEQ ID NO: 145, respectively; or
- (xv) SEQ ID NO: 151 and SEQ ID NO: 153, respectively.

18. The antibody of claim 1, wherein the heavy chain CH1-CH2-CH3 sequence of SEQ ID NO: 155 or SEQ ID NO: 189 comprises:

a lysine to cysteine substitution at amino acid position 105 and deletion of a threonine at amino acid positions 106 and 108;

a methionine to tyrosine substitution at amino acid position 135, a serine to threonine substitution at amino acid position 137, and a threonine to glutamic acid substitution at amino acid position 139; and

an alanine to a cysteine substitution at amino acid position 1.

19. The antibody of claim 18, wherein the antibody comprises a heavy chain and a light chain sequence selected from the group of:

- (i) SEQ ID NO: 40 and SEQ ID NO: 41, respectively;
- (ii) SEQ ID NO: 48 and SEQ ID NO: 49, respectively;
- (iii) SEQ ID NO: 56 and SEQ ID NO: 57, respectively;
- (iv) SEQ ID NO: 64 and SEQ ID NO: 65, respectively;
- (v) SEQ ID NO: 72 and SEQ ID NO: 73, respectively;
- (vi) SEQ ID NO: 80 and SEQ ID NO: 81, respectively;
- (vii) SEQ ID NO: 88 and SEQ ID NO: 89, respectively;
- (viii) SEQ ID NO: 96 and SEQ ID NO: 97, respectively;
- (ix) SEQ ID NO: 104 and SEQ ID NO: 105, respectively;
- (x) SEQ ID NO: 112 and SEQ ID NO: 113, respectively;
- (xi) SEQ ID NO: 120 and SEQ ID NO: 121, respectively;
- (xii) SEQ ID NO: 128 and SEQ ID NO: 129, respectively;
- (xiii) SEQ ID NO: 136 and SEQ ID NO: 137, respectively;
- (xiv) SEQ ID NO: 144 and SEQ ID NO: 145, respectively; or

(xv) SEQ ID NO: 152 and SEQ ID NO: 153, respectively.

20. The antibody of any one of claims 2-19, wherein the antibody further comprises a cytotoxic drug conjugated to one or more of the following:

(a) a heavy chain CH1-CH2-CH3 of SEQ ID NO: 155 or SEQ ID NO: 189 comprising one or more of the following:

- (i) the cysteine at amino acid position 103;
- (ii) the cysteine of a lysine to cysteine substitution at amino acid position 105;
- (iii) the cysteine at amino acid position 109;
- (iv) the cysteine at amino acid position 112; and/or

(b) the cysteine at amino acid position 107 of SEQ ID NO: 157.

21. The antibody of any one of claims 8-13 and 20, wherein the antibody further comprises a cytotoxic or cytostatic agent is conjugated to the cysteine at position 98 of SEQ ID NO: 157.

22. The antibody of any one of claims 14-20, wherein the antibody further comprises a cytotoxic or cytostatic agent is conjugated to the cysteine at position 1 of SEQ ID NO: 155 or SEQ ID NO: 189.

23. The antibody of claim 20-22, wherein the cytotoxic or cytostatic agent is a conjugated toxin, a radioisotope, drug, or a small molecule.

24. The antibody of any one of claims 1-23,
wherein:

(a) the dissociation rate of the antibody at a pH of about 4.0 to about 6.5 is faster than the dissociation rate at a pH of about 7.0 to about 8.0; or

(b) the dissociation constant (K_D) of the antibody at a pH of about 4.0 to about 6.5 is greater than the K_D at a pH of about 7.0 to about 8.0.

25. The antibody of any one of claims 20-24, wherein a composition comprising the antibody:

provides for one or more of:

an increase in toxin liberation in a target mammalian cell as compared to a composition comprising the same amount of a control antibody;
an increase in target mammalian cell killing as compared to a composition comprising the same amount of a control antibody; and
an increase in endolysosomal delivery in the target mammalian cell as compared to a composition comprising the same amount of a control antibody.

26. The antibody of any one of claims 1-25, wherein a composition comprising the antibody:

results in a less of a reduction in the level of MET presented on the surface of a target mammalian cell as compared to a composition comprising the same amount of a control antibody; or

does not result in a detectable reduction in the level of MET presented on the surface of the target mammalian cell.

27. The antibody of claim 25 or 26, wherein the antibody is degraded in a target mammalian cell following internalization of the antibody by a target mammalian cell.

28. The antibody of any one of claims 25-27, wherein the target mammalian cell is a cancer cell.

29. The antibody of any one of claims 25-28, wherein the antibody is cytotoxic or cytostatic to the target mammalian cell.

30. The antibody of any one of claims 1-29, wherein the antibody has an avidity that results in increased selectivity for cancer cells over non-cancerous cells.

31. The antibody of any one of claims 1-30, wherein the antibody is:
cross-reactive with a non-human primate MET and human MET; or
cross-reactive with a non-human primate MET, a human MET, and one or both of rat MET and a mouse MET.

32. The antibody of any one of claims 1-31, wherein the half-life of the antibody in vivo is increased as compared to the half-life of a control antibody in vivo.

33. A pharmaceutical composition comprising an effective amount of any one of the antibodies of claims 1-32.

34. A kit comprising at least one dose of the antibody of any one of claims 1-32 or the pharmaceutical composition of claim 33.

35. Use of a therapeutically effective amount of the antibody of any one of claims 1-32 or the pharmaceutical composition of claim 33 in the manufacture of a medicament for treating cancer to a subject identified as having a cancer characterized by having the population of cancer cells that have MET or an epitope of MET presented on their surface.

36. Use of a therapeutically effective amount of the antibody of any one of claims 1-32 or the pharmaceutical composition of claim 33 in the manufacture of a medicament for reducing the volume of a tumor in a subject, wherein the tumor is characterized by having a population of cancer cells that have MET or an epitope of MET presented on their surface, wherein the subject is identified as having a cancer characterized by having the population of cancer cells.

37. Use of an effective amount of the antibody of any one of claims 1-32 or the pharmaceutical composition of claim 33 in the manufacture of a medicament for inducing cell death in a cancer cell in a subject, wherein the cancer cell has MET or an epitope of MET presented on its surface, and wherein the subject is identified as having a cancer characterized by having a population of the cancer cells.

38. Use of a therapeutically effective amount of the antibody of any one of claims 1-32 or the pharmaceutical composition of claim 33 in the manufacture of a medicament for decreasing the risk of developing a metastasis or decreasing the risk of developing an additional metastasis in a subject having a cancer, wherein the cancer is characterized by having a population of cancer cells that have MET or an epitope of MET presented on their

surface, and wherein the subject is identified as having a cancer characterized by having the population of cancer cells.