

WHAT IS CLAIMED:

1. An isolated antibody that specifically binds to human CD73, the antibody comprising a heavy chain variable region comprising complementarity determining regions (CDRs) CDRH1, CDRH2, and CDRH3, and a light chain variable region comprising complementarity determining regions CDRL1, CDRL2, and CDRL3, wherein:

(a) CDRH1 comprises the amino acid sequence of X₁X₂WX₃X₄ (SEQ ID NO: 13), wherein

X₁ is S or N;

X₂ is S or Y;

X₃ is I or M; and

X₄ is N or H;

(b) CDRH2 comprises the amino acid sequence of X₁IYPRX₂X₃DTNYX₄X₅KFKX₆ (SEQ ID NO: 14), wherein

X₁ is R or T;

X₂ is N, A, or S;

X₃ is G or S;

X₄ is N, A, or S;

X₅ is G or Q; and

X₆ is D or G;

(c) CDRH3 comprises the amino acid sequence of LLDYSMDY (SEQ ID NO: 7);

(d) CDRL1 comprises the amino acid sequence of RASQDISX₁X₂LN (SEQ ID NO: 16),

wherein

X₁ is N or I; and

X₂ is Y or S;

(e) CDRL2 comprises the amino acid sequence of YTSRLHS (SEQ ID NO: 10); and/or

(f) CDRL3 comprises the amino acid sequence of QQGNTLPXT (SEQ ID NO: 17), wherein:

X is L or W.

2. The isolated antibody of claim 1, wherein CDRH1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 1 and 2.

3. The isolated antibody of claim 1 or 2, wherein CDRH2 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 3-6.

4. The isolated antibody of any one of the preceding claims, wherein CDRL1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 8 and 9.

5. The isolated antibody of any one of the preceding claims, wherein CDRL3 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 11 and 12.

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6. The isolated antibody of any one of the preceding claims, wherein:

(a) CDRH1 comprises the amino acid sequence of SSWIN (SEQ ID NO: 2);

(b) CDRH2 comprises the amino acid sequence of RIYPRX₁GDTNYX₂GKFKD (SEQ ID NO: 15), wherein

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X₁ is N, A, or S; and

X₂ is N, A, or S;

(c) CDRL1 comprises the amino acid sequence of RASQDISX₁X₂LN (SEQ ID NO: 16), wherein

X₁ is N or I; and

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X₂ is Y or S; and/or

(d) CDRL3 comprises the amino acid sequence of QQGNTLPLT (SEQ ID NO: 12).

7. The isolated antibody of claim 6, wherein CDRH2 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 4-6.

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8. The isolated antibody of claim 6 or 7, wherein CDRL1 comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 8 and 9.

9. The isolated antibody of any one of the preceding claims, wherein CDRH1, CDRH2, and CDRH3 comprise the CDRH1, CDRH2, and CDRH3 amino acid sequences, respectively, set forth in SEQ ID NOs: 2, 4, and 7; 2, 5, and 7; 1, 3, and 7; or 2, 6, and 7.

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10. The isolated antibody of any one of the preceding claims, wherein CDRL1, CDRL2, and CDRL3 comprise the CDRL1, CDRL2, and CDRL3 amino acid sequences, respectively, set forth in SEQ ID NOs: 8, 10, and 12; 9, 10, and 12; or 8, 10, and 11.

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11. The isolated antibody of any one of the preceding claims, wherein CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 comprise the CDRH1, CDRH2, CDRH3,

CDRL1, CDRL2, and CDRL3 amino acid sequences, respectively, set forth in SEQ ID NOs: 2, 4, 7, 8, 10, and 12; 2, 5, 7, 8, 10, and 12; 1, 3, 7, 8, 10, and 11; 2, 4, 7, 8, 10, and 11; 2, 4, 7, 9, 10, and 12; 2, 6, 7, 8, 10, and 12; 2, 5, 7, 9, 10, and 12; or 2, 6, 7, 9, 10, and 12.

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12. The isolated antibody of claim 11, wherein CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 comprise the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences, respectively, set forth in SEQ ID NOs: 2, 4, 7, 8, 10, and 12; or 2, 5, 7, 8, 10, and 12.

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13. An isolated antibody that specifically binds to human CD73, the antibody comprising a heavy chain variable region comprising CDRs CDRH1, CDRH2, and CDRH3, and a light chain variable region comprising complementarity determining regions CDRL1, CDRL2, and CDRL3, wherein CDRH3 comprises the amino acid sequence of LLDYSMDY (SEQ ID NO: 7); and/or CDRL3 comprises the amino acid sequence of QQGNTLPLT (SEQ ID NO: 12) or QQGNTLPWT (SEQ ID NO: 11).

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14. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 31.

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15. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a heavy chain variable region comprising an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 19-21 and 23-30.

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16. The isolated antibody of claim 15, wherein the heavy chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 19-21 and 23-30.

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17. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a heavy chain variable region comprising an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100%

identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 23-30.

5 18. The isolated antibody of claim 17, wherein the heavy chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 23-30.

19. The isolated antibody of claim 18, wherein the heavy chain variable region comprises the amino acid sequence of SEQ ID NO: 24 or 27.

10 20. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a heavy chain variable region comprising an amino acid sequence derived from a human germline sequence as set forth in SEQ ID NO: 22.

15 21. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a light chain variable region comprising an amino acid sequence of SEQ ID NO: 41 or 42.

20 22. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a light chain variable region comprising an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 33-35 and 37-40.

25 23. The isolated antibody of claim 22, wherein the light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 33-35 and 37-40.

30 24. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a light chain variable region comprising an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 37-40.

25. The isolated antibody of claim 24, wherein the light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 37-40.

26. The isolated antibody of claim 25, wherein the light chain variable region comprises the amino acid sequence of SEQ ID NO: 37.

27. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a light chain variable region comprising an amino acid sequence derived from a human germline sequence as set forth in SEQ ID NO: 36.

28. The isolated antibody of any one of the preceding claims, wherein the heavy chain variable region and the light chain variable region, respectively, comprise the amino acid sequences set forth in SEQ ID NOs: 24 and 37; 27 and 37; 19 and 33; 20 and 34; 21 and 35; 23 and 37; 23 and 38; 24 and 38; 25 and 37; 26 and 37; 28 and 37; 25 and 38; 26 and 38; 27 and 38; 28 and 38; 29 and 37; 30 and 37; 23 and 39; or 23 and 40.

29. The isolated antibody of claim 28, wherein the heavy chain variable region and the light chain variable region, respectively, comprise the amino acid sequences set forth in SEQ ID NOs: 24 and 37; or 27 and 37.

30. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a heavy chain constant region selected from the group consisting of human IgG₁, IgG₂, IgG₃, IgG₄, IgA₁, and IgA₂.

31. The isolated antibody of claim 30, wherein the heavy chain constant region is IgG₁.

32. The isolated antibody of claim 31, wherein the amino acid sequence of IgG₁ comprises a N297A mutation, numbered according to the EU numbering system.

33. The isolated antibody of claim 32, wherein the heavy chain constant region comprises the amino acid sequence of SEQ ID NO: 50, 49, 46, 45, 55, or 56.

34. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a heavy chain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 63-88.

5 35. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a light chain constant region selected from the group consisting of human Igκ and Igλ.

36. The isolated antibody of claim 35, wherein the light chain constant region is Igκ.

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37. The isolated antibody of claim 36, wherein the light chain constant region comprises the amino acid sequence of SEQ ID NO: 93 or 89.

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38. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a light chain comprising the amino acid sequence selected from the group consisting of SEQ ID NO: 92 and 94-98.

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39. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a heavy chain and a light chain comprising the amino acid sequences set forth in any row of Table 4, preferably the amino acid sequence selected from the group consisting of SEQ ID NOs: 79 and 97; 85 and 97; 77 and 97; 80 and 97; 86 and 97; 64 and 92; 70 and 96; or 78 and 97, respectively.

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40. The isolated antibody of any one of claims 15-39, wherein the X in any one of SEQ ID NOs: 19, 20, and 65-68 is glutamine.

41. The isolated antibody of any one of claims 15-39, wherein the X in any one of SEQ ID NOs: 21, 23-30, 63, 64, 69-88 is glutamate.

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42. The isolated antibody of any one of claims 15-39, wherein the X in any one of SEQ ID NOs: 19-21, 23-30, and 63-88 is pyroglutamate.

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43. An isolated antibody that binds to the same epitope of human CD73 as the antibody of any one of the preceding claims.

44. The isolated antibody of any one of the preceding claims, wherein the antibody is a humanized antibody.

5 45. The isolated antibody of any one of the preceding claims, wherein the antibody is antagonistic to human CD73.

46. The isolated antibody of claim 45, wherein the antibody deactivates, reduces, or inhibits an activity of human CD73.

10 47. The isolated antibody of claim 45 or 46, wherein the antibody attenuates the ability of human CD73 to convert adenosine monophosphate to adenosine.

15 48. The isolated antibody of any one of the preceding claims, wherein the antibody is internalized upon binding to cells expressing human CD73.

49. The isolated antibody of any one of claims 1-48, further comprising a TGF β -binding moiety.

20 50. The isolated antibody of claim 49, wherein the TGF β -binding moiety is linked to the heavy chain variable region.

51. The isolated antibody of claim 50, wherein the TGF β -binding moiety is linked to the heavy chain variable region via a peptide linker.

25 52. The isolated antibody of any one of claims 30-48, further comprising a TGF β -binding moiety linked to the heavy chain constant region.

53. The isolated antibody of claim 52, wherein the TGF β -binding moiety is linked to the C-terminal residue of the heavy chain constant region.

30 54. The isolated antibody of claim 52 or 53, wherein the N-terminal residue of the TGF β -binding moiety is linked to the C-terminal residue of the heavy chain constant region via a peptide linker.

55. The isolated antibody of claim 51 or 54, wherein the peptide linker comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 103-108.

56. The isolated antibody of any one of claims 49-55, wherein the TGF β -binding moiety specifically binds to human TGF β .

57. The isolated antibody of any one of claims 49-56, wherein the TGF β -binding moiety comprises an extracellular domain of a human TGF β receptor.

58. The isolated antibody of claim 57, wherein the human TGF β receptor is selected from the group consisting of human TGF β R1, TGF β R2, and TGF β R3.

59. The isolated antibody of claim 57 or 58, wherein the human TGF β receptor is human TGF β R2.

60. The isolated antibody of any one of claims 49-59, wherein the TGF β -binding moiety comprises an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence selected from the group consisting of SEQ ID NOs: 109-112.

61. The isolated antibody of any one of claims 49-60, wherein the TGF β -binding moiety consists of an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence selected from the group consisting of SEQ ID NOs: 109-112.

62. The isolated antibody of any one of claims 49-61, wherein the TGF β -binding moiety comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 109-112, preferably SEQ ID NO: 111.

63. The isolated antibody of any one of claims 49-62, wherein the TGF β -binding moiety consists of an amino acid sequence selected from the group consisting of SEQ ID NOs: 109-112, preferably SEQ ID NO: 111.

64. The isolated antibody of any one of claims 49-63, the antibody comprising a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 113-121, preferably SEQ ID NO: 114 or 115.

5 65. The isolated antibody of any one of claims 49-64, wherein the antibody comprises a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 113-121 and a polypeptide comprising the amino acid sequence of SEQ ID NO: 92 or 97.

10 66. The isolated antibody of any one of claims 49-65, wherein the antibody comprises two polypeptides each comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 113-121 and two polypeptides each comprising the amino acid sequence of SEQ ID NO: 92 or 97.

15 67. The isolated antibody of any one of claims 49-66, wherein the antibody comprises two polypeptides each comprising the amino acid sequence of SEQ ID NO: 115 and two polypeptides each comprising the amino acid sequence of SEQ ID NO: 97.

20 68. An isolated antibody that specifically binds to human CD73, the antibody comprising a TGF β -binding moiety.

69. The isolated antibody of claim 68, wherein the antibody is antagonistic to human CD73.

25 70. The isolated antibody of claim 69, wherein the antibody deactivates, reduces, or inhibits an activity of human CD73.

71. The isolated antibody of claim 69 or 70, wherein the antibody attenuates the ability of human CD73 to convert adenosine monophosphate to adenosine.

30 72. The isolated antibody of any one of claims 68-71, wherein the antibody, when bound to TGF β , is antagonistic to human CD73.

73. The isolated antibody of any one of claims 68-72, wherein the TGF β -binding moiety specifically binds to human TGF β .

5 74. The isolated antibody of any one of claims 68-73, wherein the TGF β -binding moiety comprises an extracellular domain of a human TGF β receptor.

75. The isolated antibody of any one of claims 68-74, wherein the human TGF β receptor is selected from the group consisting of human TGF β R1, TGF β R2, and TGF β R3.

10 76. The isolated antibody of claim 74 or 75, wherein the human TGF β receptor is human TGF β R2.

15 77. The isolated antibody of any one of claims 68-76, wherein the TGF β -binding moiety comprises an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence selected from the group consisting of SEQ ID NOs: 109-112.

20 78. The isolated antibody of any one of claims 68-77, wherein the TGF β -binding moiety consists of an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence selected from the group consisting of SEQ ID NOs: 109-112.

25 79. The isolated antibody of any one of claims 68-78, wherein the TGF β -binding moiety comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 109-112, preferably SEQ ID NO: 111.

30 80. The isolated antibody of any one of claims 68-79, wherein the TGF β -binding moiety consists of an amino acid sequence selected from the group consisting of SEQ ID NOs: 109-112, preferably SEQ ID NO: 111.

81. The isolated antibody of any one of claims 1-48, further comprising a VEGF-binding moiety.

82. The isolated antibody of claim 81, wherein the VEGF-binding moiety is linked to the heavy chain variable region.

5 83. The isolated antibody of claim 82, wherein the VEGF-binding moiety is linked to the heavy chain variable region via a peptide linker.

84. The isolated antibody of any one of claims 30-48, further comprising a VEGF-binding moiety linked to the heavy chain constant region.

10 85. The isolated antibody of claim 84, wherein the VEGF-binding moiety is linked to the C-terminal residue of the heavy chain constant region.

15 86. The isolated antibody of claim 84 or 85, wherein the N-terminal residue of the VEGF-binding moiety is linked to the C-terminal residue of the heavy chain constant region via a peptide linker.

87. The isolated antibody of claim 83 or 86, wherein the peptide linker comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 103-108.

20 88. The isolated antibody of any one of claims 81-87, wherein the VEGF-binding moiety specifically binds to human VEGF.

89. The isolated antibody of any one of claims 81-88, wherein the VEGF-binding moiety comprises an extracellular domain of a human VEGF receptor.

25 90. The isolated antibody of any one of claims 81-89, wherein the human VEGF receptor is selected from the group consisting of human VEGFR1, VEGFR2, and VEGFR3.

30 91. The isolated antibody of claim 89 or 90, wherein the human VEGF receptor is human VEGFR1.

92. The isolated antibody of any one of claims 81-91, wherein the VEGF-binding moiety comprises an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%,

94%, 95%, 96%, 97%, 98%, or 99% identical to the sequence set forth in SEQ ID NO: 122.

5 93. The isolated antibody of any one of claims 81-92, wherein the VEGF-binding moiety consists of an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the sequence set forth in SEQ ID NO: 122.

10 94. The isolated antibody of any one of claims 81-93, wherein the VEGF-binding moiety comprises the sequence set forth in SEQ ID NO: 122.

95. The isolated antibody of any one of claims 81-94, wherein the VEGF-binding moiety consists of the sequence set forth in SEQ ID NO: 122.

15 96. The isolated antibody of any one of claims 81-92, the antibody comprising a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 123-127.

20 97. The isolated antibody of any one of claims 81-96, wherein the antibody comprises a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 123-127 and a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 92, 128, and 97.

25 98. The isolated antibody of any one of claims 81-97, wherein the antibody comprises two polypeptides comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 123-127 and two polypeptides comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 92, 128, and 97.

30 99. An isolated antibody that specifically binds to human CD73, the antibody comprising a VEGF-binding moiety.

100. The isolated antibody of claim 99, wherein the antibody is antagonistic to human CD73.

101. The isolated antibody of claim 100, wherein the antibody deactivates, reduces, or inhibits an activity of human CD73.

102. The isolated antibody of claim 100, wherein the antibody attenuates the ability of human CD73 to convert adenosine monophosphate to adenosine.

103. The isolated antibody of any one of claims 99-102, wherein the antibody, when bound to VEGF, is antagonistic to human CD73.

104. The isolated antibody of any one of claims 99-103, wherein the VEGF-binding moiety specifically binds to human VEGF.

105. The isolated antibody of any one of claims 99-104, wherein the VEGF-binding moiety comprises an extracellular domain of a human VEGF receptor.

106. The isolated antibody of any one of claims 99-105, wherein the human VEGF receptor is selected from the group consisting of human VEGFR1, VEGFR2, and VEGFR3.

107. The isolated antibody of claim 105 or 106, wherein the human VEGF receptor is human VEGFR1.

108. The isolated antibody of any one of claims 99-107, wherein the VEGF-binding moiety comprises an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the sequence set forth in SEQ ID NO: 122.

109. The isolated antibody of any one of claims 99-108, wherein the VEGF-binding moiety consists of an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the sequence set forth in SEQ ID NO: 122.

110. The isolated antibody of any one of claims 99-109, wherein the VEGF-binding moiety comprises the amino acid sequence as set forth in SEQ ID NO: 122.

111. The isolated antibody of any one of claims 99-110, wherein the VEGF-binding moiety consists of the amino acid sequence as set forth in SEQ ID NO: 122.

5 112. The isolated antibody of any one of the preceding claims, further comprising a conjugated cytotoxic agent, cytostatic agent, toxin, radionuclide, or detectable label.

10 113. The isolated antibody of any one of the preceding claims, wherein the antibody binds to an epitope located within a region of human CD73, the amino acid sequence of the region consisting of the amino acid sequence of SEQ ID NOs: 90 and/or 91.

15 114. The isolated antibody of any one of the preceding claims, wherein the antibody binds to at least one residue in the amino acid sequence of SEQ ID NOs: 90 and/or 91.

20 115. The isolated antibody of any one of the preceding claims, wherein the antibody binds to one or more amino acid residues of human CD73 selected from the group consisting of Y158, Y161, P165, or D168, numbered according to the amino acid sequence of SEQ ID NO: 99.

25 116. The isolated antibody of any one of the preceding claims, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 133 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.

30 117. The isolated antibody of any one of the preceding claims, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 134 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.

35 118. The isolated antibody of any one of the preceding claims, wherein the antibody binds to amino acid residue Y158 of human CD73, numbered according to the amino acid sequence of SEQ ID NO: 99.

119. The isolated antibody of any one of the preceding claims, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 59 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.

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120. The isolated antibody of any one of the preceding claims, wherein the antibody binds to amino acid residue Y161 of human CD73, numbered according to the amino acid sequence of SEQ ID NO: 99.

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121. The isolated antibody of any one of the preceding claims, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 60 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.

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122. The isolated antibody of any one of the preceding claims, wherein the antibody binds to amino acid residue P165 of human CD73, numbered according to the amino acid sequence of SEQ ID NO: 99.

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123. The isolated antibody of any one of the preceding claims, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 139 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.

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124. The isolated antibody of any one of the preceding claims, wherein the antibody binds to amino acid residue D168 of human CD73, numbered according to the amino acid sequence of SEQ ID NO: 99.

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125. The isolated antibody of any one of the preceding claims, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 140 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.

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126. The isolated antibody of any one of the preceding claims, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 135 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.

127. The isolated antibody of any one of the preceding claims, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 136 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.

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128. The isolated antibody of any one of the preceding claims, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 142 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141, and wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 137 is not substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.

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129. The isolated antibody of any one of the preceding claims, wherein the binding affinity of the antibody to a protein comprising the amino acid sequence of SEQ ID NO: 142 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141, and wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 138 is not substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.

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130. An isolated antibody that specifically binds to human CD73, wherein the antibody binds to an epitope located within a region of human CD73, the amino acid sequence of the region consisting of the amino acid sequence of SEQ ID NOs: 90 and/or 91.

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131. An isolated antibody that specifically binds to human CD73, wherein the antibody binds to at least one residue in the amino acid sequence of SEQ ID NOs: 90 and/or 91.

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132. An isolated antibody that specifically binds to human CD73, wherein the antibody binds to one or more amino acid residues of human CD73 selected from the group consisting of Y158, Y161, P165, or D168, numbered according to the amino acid sequence of SEQ ID NO: 99.

- 5 133. An isolated antibody that specifically binds to human CD73, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 133 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.
- 10 134. An isolated antibody that specifically binds to human CD73, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 134 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.
- 15 135. An isolated antibody that specifically binds to human CD73, wherein the antibody binds to amino acid residue Y158 of human CD73, numbered according to the amino acid sequence of SEQ ID NO: 99.
- 20 136. An isolated antibody that specifically binds to human CD73, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 59 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.
- 25 137. An isolated antibody that specifically binds to human CD73, wherein the antibody binds to amino acid residue Y161 of human CD73, numbered according to the amino acid sequence of SEQ ID NO: 99.
- 30 138. An isolated antibody that specifically binds to human CD73, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 60 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.
139. An isolated antibody that specifically binds to human CD73, wherein the antibody binds to amino acid residue P165 of human CD73, numbered according to the amino acid sequence of SEQ ID NO: 99.

140. An isolated antibody that specifically binds to human CD73, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 139 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.

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141. An isolated antibody that specifically binds to human CD73, wherein the antibody binds to amino acid residue D168 of human CD73, numbered according to the amino acid sequence of SEQ ID NO: 99.

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142. An isolated antibody that specifically binds to human CD73, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 140 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.

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143. An isolated antibody that specifically binds to human CD73, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 135 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.

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144. An isolated antibody that specifically binds to human CD73, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 136 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.

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145. An isolated antibody that specifically binds to human CD73, wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 142 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141, and wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 137 is not substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.

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- 5 146. An isolated antibody that specifically binds to human CD73, wherein the binding affinity of the antibody to a protein comprising the amino acid sequence of SEQ ID NO: 142 is substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141, and wherein the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 138 is not substantially reduced relative to the binding affinity of the antibody for a protein comprising the amino acid sequence of SEQ ID NO: 141.
- 10 147. A compound or molecule comprising a CD73-binding moiety and a TGF β -binding moiety.
- 15 148. An isolated polynucleotide encoding a polypeptide of the antibody of any one of claims 1-146.
149. The polynucleotide of claim 148, wherein the polynucleotide comprises cDNA or mRNA.
- 20 150. A vector comprising the polynucleotide of claim 148 or 149.
151. The vector of claim 150, wherein the vector is a plasmid vector or a viral vector.
- 25 152. A recombinant host cell comprising the polynucleotide of claim 148 or 149, or the vector of claim 150 or 151.
153. A lipid nanoparticle comprising the polynucleotide of claim 148 or 149, or the vector of claim 150 or 151.
- 30 154. A pharmaceutical composition comprising the antibody, polynucleotide, vector, or lipid nanoparticle of any one of claims 1-146 or 148-153 and a pharmaceutically acceptable carrier or excipient.

155. A method of producing an antibody, the method comprising culturing the host cell of claim 152 under suitable conditions so that the polynucleotide is expressed and the antibody is produced.

5 156. A method of treating cancer in a subject, the method comprising administering to the subject an effective amount of the antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition of any one of claims 1-146, 148-151, 153, or 154.

10 157. A method of inhibiting cancer metastasis in a subject, the method comprising administering to the subject an effective amount of the antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition of any one of claims 1-146, 148-151, 153, or 154.

15 158. The method of claim 156 or 157, wherein the antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition is administered intravenously, intratumorally, subcutaneously, intradermally, intramuscularly, intravesically, intracranially, intracavitary or intraventricularly.

20 159. The method of claim 156 or 157, wherein the antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition is administered intratumorally.

160. The method of any one of claims 156-159, further comprising administering one or more additional therapeutic agents to the subject.

25 161. The method of any one of claims 156-160, wherein the antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition, and the one or more additional therapeutic agents are co-administered according to the same schedule (*e.g.*, co-administered at the same time intervals).

30 162. The method of any one of claims 156-160, wherein the antibody, polynucleotide vector, lipid nanoparticle, or pharmaceutical composition, and the one or more additional therapeutic agents are co-administered according to different schedules (*e.g.*, co-administered at different time intervals).

163. The method of any one of claims 156-162, wherein the antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition is co-administered with one or more additional therapeutic agents comprising an activator or agonist of a fms related tyrosine kinase 3 (FLT3; CD135) receptor, a toll-like receptor (TLR) or a stimulator of interferon genes (STING) receptor.
164. The method of claim 163, wherein the TLR agonist or activator is selected from the group consisting of a TLR2 agonist, a TLR3 agonist, a TLR7 agonist, a TLR8 agonist and a TLR9 agonist.
165. The method of claim 163, wherein the STING receptor agonist or activator is selected from the group consisting of ADU-S100 (MIW-815), SB-11285, MK-1454, SR-8291, AdvCA0848, GSK-532, SYN-STING, MSA-1, SR-8291, 5,6-dimethylxanthenone-4-acetic acid (DMXAA), cyclic-GAMP (cGAMP) and cyclic-di-AMP.
166. The method of any one of claims 156-165, wherein the antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition is co-administered with one or more additional therapeutic agents comprising an inhibitor or antagonist of: protein tyrosine phosphatase, non-receptor type 11 (PTPN11 or SHP2), myeloid cell leukemia sequence 1 (MCL1) apoptosis regulator; mitogen-activated protein kinase kinase kinase kinase 1 (MAP4K1) (also called Hematopoietic Progenitor Kinase 1 (HPK1)); diacylglycerol kinase alpha (DGKA, DAGK, DAGK1 or DGK-alpha); 5'-nucleotidase ecto (NT5E or CD73); transforming growth factor beta 1 (TGFB1 or TGFβ); heme oxygenase 1 (HMOX1, HO-1 or HO1); vascular endothelial growth factor A (VEGFA or VEGF); erb-b2 receptor tyrosine kinase 2 (ERBB2 HER2, HER2/neu or CD340); epidermal growth factor receptor (EGFR, ERBB, ERBB1 or HER1); ALK receptor tyrosine kinase (ALK, CD246); poly(ADP-ribose) polymerase 1 (PARP1 or PARP); cyclin dependent kinase 4 (CDK4); cyclin dependent kinase 6 (CDK6); C-C motif chemokine receptor 8 (CCR8, CDw198); CD274 molecule (CD274, PDL1 or PD-L1); programmed cell death 1 (PDCD1, PD1 or PD-1); and/or cytotoxic T-lymphocyte associated protein 4 (CTLA4, CTLA-4, CD152).

167. The method of claim 166, wherein the inhibitor comprises an antigen binding molecule, an antibody or an antigen-binding fragment thereof.

5 168. The method of claim 166, wherein the inhibitor comprises a small organic molecule.

169. The method of claim 166, wherein the inhibitor of MCL1 is selected from the group consisting of AMG-176, AMG-397, S-64315, AZD-5991, 483-LM, A
10 1210477, UMI-77, and JKY-5-037.

170. The method of claim 166, wherein the inhibitor of PTPN11 or SHP2 is selected from the group consisting of TNO155 (SHP-099), RMC-4550, JAB-3068 and RMC-4630.

15 171. The method of claim 160, wherein the additional therapeutic agent is a chemotherapeutic, an anti-neoplastic, a radiotherapeutic, or a checkpoint targeting agent.

20 172. The method of claim 160, wherein the one or more anti-neoplastic or chemotherapeutic agents are selected from the group consisting of a nucleoside analog (*e.g.*, 5-fluorouracil, gemcitabine, cytarabine), a taxane (*e.g.*, paclitaxel, nab-paclitaxel, docetaxel, cabazitaxel), a platinum coordination complex (cisplatin, carboplatin, oxaliplatin, nedaplatin, triplatin tetranitrate, phenanthriplatin, picoplatin, satraplatin, dicycloplatin, eptaplatin, lobaplatin, miriplatin), a dihydrofolate reductase (DHFR) inhibitor (*e.g.*, methotrexate, trimetrexate, pemetrexed), a topoisomerase inhibitor (*e.g.*, doxorubicin, daunorubicin, dactinomycin, eniposide, epirubicin, etoposide, idarubicin, irinotecan, mitoxantrone, pixantrone, sobuzoxane, topotecan, irinotecan, MM-398 (liposomal irinotecan), vosaroxin and GPX-150, aldexorubicin,
25 AR-67, mavelertinib, AST-2818, avitinib (ACEA-0010), irofulven (MGI-114)), an alkylating agent (*e.g.*, a nitrogen mustard (*e.g.*, cyclophosphamide, chlormethine, uramustine or uracil mustard, melphalan, chlorambucil, ifosfamide, bendamustine, temozolomide, carmustine), a nitrosourea (*e.g.*, carmustine, lomustine, streptozocin),
30 an alkyl sulfonate (*e.g.*, busulfan)), and mixtures thereof.

173. The method of claim 160, wherein the checkpoint targeting agent is selected from the group consisting of an antagonist anti-PD-1 antibody, an antagonist anti-PD-L1 antibody, an antagonist anti-PD-L2 antibody, an antagonist anti-CTLA-4 antibody, an antagonist anti-TIM-3 antibody, an antagonist anti-LAG-3 antibody, an antagonist anti-CEACAM1 antibody, an agonist anti-GITR antibody, an antagonist anti-TIGIT antibody, an antagonist anti-VISTA antibody, an agonist anti-CD137 antibody, and an agonist anti-OX40 antibody.

174. The method of claim 173, wherein the additional therapeutic agent is an anti-PD-1 antibody, optionally wherein the anti-PD-1 antibody is pembrolizumab or nivolumab.

175. The method of claim 160, wherein the additional therapeutic agent is an inhibitor of indoleamine-2,3-dioxygenase (IDO).

176. The method of claim 175, wherein the inhibitor is selected from the group consisting of epacadostat, F001287, indoximod, and NLG919.

177. The method of claim 176, wherein the inhibitor is epacadostat.

178. The method of claim 160, wherein the additional therapeutic agent is a vaccine.

179. The method of claim 178, wherein the vaccine comprises a heat shock protein peptide complex (HSPPC) comprising a heat shock protein complexed with an antigenic peptide.

180. The method of claim 179, wherein the heat shock protein is hsc70 and is complexed with a tumor-associated antigenic peptide.

181. The method of claim 179, wherein the heat shock protein is gp96 and is complexed with a tumor-associated antigenic peptide, wherein the HSPPC is derived from a tumor obtained from a subject.

182. The method of claim 160, wherein the additional therapeutic agent is etoposide or doxorubicin.

183. The method of any one of claims 156-182, wherein the antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition is co-administered with a FOLFOX regimen, a FOLFOXIRI regimen or a FOLFIRINOX regimen.

184. The method of claims 156-183, wherein the antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition is co-administered with an immunotherapy, an immunostimulatory therapy, a cellular therapy or a gene therapy.

185. The method of any one of claims 156-184, wherein the cancer is selected from the group consisting of a solid tumor, a hematological cancer, and a metastatic lesion.

186. The method of claim 185, wherein the solid tumor is selected from the group consisting of a sarcoma, a fibroblastic sarcoma, a carcinoma, and an adenocarcinoma.

187. The method of claim 185, wherein the hematological cancer is selected from the group consisting of a leukemia, a lymphoma, and a myeloma.

188. The method of any one of claims 156-184, wherein the cancer is selected from the group consisting of a lung cancer, a melanoma, a renal cancer, a liver cancer, a myeloma, a prostate cancer, a breast cancer, an ovarian cancer, a colorectal cancer, a pancreatic cancer, a head and neck cancer, an anal cancer, a gastro-esophageal cancer, a mesothelioma, a nasopharyngeal cancer, a thyroid cancer, a cervical cancer, an epithelial cancer, a peritoneal cancer, a lymphoproliferative disease, an acute lymphoblastic leukemia (ALL), an acute myelogenous leukemia (AML), a chronic lymphocytic leukemia (CLL), a chronic myelogenous leukemia (CML), a chronic myelomonocytic leukemia (CMML), a hairy cell leukemia, a B cell lymphoma, a diffuse large B-cell lymphoma (DLBCL), an activated B-cell like (ABC) diffuse large B cell lymphoma, a germinal center B cell (GCB) diffuse large B cell lymphoma, a mantle cell lymphoma, a Hodgkin lymphoma, a non-Hodgkin lymphoma, a relapsed

non-Hodgkin lymphoma, a refractory non-Hodgkin lymphoma, a recurrent follicular non-Hodgkin lymphoma, a Burkitt lymphoma, a small lymphocytic lymphoma, a follicular lymphoma, a lymphoplasmacytic lymphoma, and an extranodal marginal zone lymphoma.

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189. The method of any one of claims 156-184, wherein the cancer is selected from the group consisting of an epithelial tumor (*e.g.*, a carcinoma, a squamous cell carcinoma, a basal cell carcinoma, a squamous intraepithelial neoplasia), a glandular tumor (*e.g.*, an adenocarcinoma, an adenoma, an adenomyoma), a mesenchymal or soft tissue tumor (*e.g.*, a sarcoma, a rhabdomyosarcoma, a leiomyosarcoma, a liposarcoma, a fibrosarcoma, a dermatofibrosarcoma, a neurofibrosarcoma, a fibrous histiocytoma, an angiosarcoma, an angiomyxoma, a leiomyoma, a chondroma, a chondrosarcoma, an alveolar soft-part sarcoma, an epithelioid hemangioendothelioma, a Spitz tumor, a synovial sarcoma), and a lymphoma.

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190. The method of any one of claims 156-184, wherein the cancer is a solid tumor in or arising from a tissue or organ selected from the group consisting of: bone (*e.g.*, adamantinoma, aneurysmal bone cysts, angiosarcoma, chondroblastoma, chondroma, chondromyxoid fibroma, chondrosarcoma, chordoma, dedifferentiated chondrosarcoma, enchondroma, epithelioid hemangioendothelioma, fibrous dysplasia of the bone, giant cell tumour of bone, haemangiomas and related lesions, osteoblastoma, osteochondroma, osteosarcoma, osteoid osteoma, osteoma, periosteal chondroma, Desmoid tumor, Ewing sarcoma); lips and oral cavity (*e.g.*, odontogenic ameloblastoma, oral leukoplakia, oral squamous cell carcinoma, primary oral mucosal melanoma); salivary glands (*e.g.*, pleomorphic salivary gland adenoma, salivary gland adenoid cystic carcinoma, salivary gland mucoepidermoid carcinoma, salivary gland Warthin's tumors); esophagus (*e.g.*, Barrett's esophagus, dysplasia and adenocarcinoma); gastrointestinal tract, including stomach (*e.g.*, gastric adenocarcinoma, primary gastric lymphoma, gastrointestinal stromal tumors (GISTs), metastatic deposits, gastric carcinoids, gastric sarcomas, neuroendocrine carcinoma, gastric primary squamous cell carcinoma, gastric adenoacanthomas), intestines and smooth muscle (*e.g.*, intravenous leiomyomatosis), colon (*e.g.*, colorectal adenocarcinoma), rectum, anus; pancreas (*e.g.*, serous neoplasms, including microcystic or macrocystic serous cystadenoma, solid serous cystadenoma, Von

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Hippel-Landau (VHL)-associated serous cystic neoplasm, serous cystadenocarcinoma, mucinous cystic neoplasms (MCN), intraductal papillary mucinous neoplasms (IPMN), intraductal oncocytic papillary neoplasms (IOPN), intraductal tubular neoplasms, cystic acinar neoplasms, including acinar cell cystadenoma, acinar cell cystadenocarcinoma, pancreatic adenocarcinoma, invasive pancreatic ductal adenocarcinomas, including tubular adenocarcinoma, adenosquamous carcinoma, colloid carcinoma, medullary carcinoma, hepatoid carcinoma, signet ring cell carcinoma, undifferentiated carcinoma, undifferentiated carcinoma with osteoclast-like giant cells, acinar cell carcinoma, neuroendocrine neoplasms, neuroendocrine microadenoma, neuroendocrine tumors (NET), neuroendocrine carcinoma (NEC), including small cell or large cell NEC, insulinoma, gastrinoma, glucagonoma, serotonin-producing NET, somatostatinoma, VIPoma, solid-pseudopapillary neoplasms (SPN), pancreatoblastoma); gall bladder (*e.g.* carcinoma of the gallbladder and extrahepatic bile ducts, intrahepatic cholangiocarcinoma); neuro-endocrine (*e.g.*, adrenal cortical carcinoma, carcinoid tumors, pheochromocytoma, pituitary adenomas); thyroid (*e.g.*, anaplastic (undifferentiated) carcinoma, medullary carcinoma, oncocytic tumors, papillary carcinoma, adenocarcinoma); liver (*e.g.*, adenoma, combined hepatocellular and cholangiocarcinoma, fibrolamellar carcinoma, hepatoblastoma, hepatocellular carcinoma, mesenchymal, nested stromal epithelial tumor, undifferentiated carcinoma, hepatocellular carcinoma, intrahepatic cholangiocarcinoma, bile duct cystadenocarcinoma, epithelioid hemangioendothelioma, angiosarcoma, embryonal sarcoma, rhabdomyosarcoma, solitary fibrous tumor, teratoma, York sac tumor, carcinosarcoma, rhabdoid tumor); kidney (*e.g.*, ALK-rearranged renal cell carcinoma, chromophobe renal cell carcinoma, clear cell renal cell carcinoma, clear cell sarcoma, metanephric adenoma, metanephric adenofibroma, mucinous tubular and spindle cell carcinoma, nephroma, nephroblastoma (Wilms tumor), papillary adenoma, papillary renal cell carcinoma, renal oncocytoma, renal cell carcinoma, succinate dehydrogenase-deficient renal cell carcinoma, collecting duct carcinoma); breast (*e.g.*, invasive ductal carcinoma, including without limitation, acinic cell carcinoma, adenoid cystic carcinoma, apocrine carcinoma, cribriform carcinoma, glycogen-rich/clear cell, inflammatory carcinoma, lipid-rich carcinoma, medullary carcinoma, metaplastic carcinoma, micropapillary carcinoma, mucinous carcinoma, neuroendocrine carcinoma, oncocytic carcinoma, papillary carcinoma, sebaceous

carcinoma, secretory breast carcinoma, tubular carcinoma, lobular carcinoma,
 including without limitation, pleomorphic carcinoma, signet ring cell carcinoma,
 peritoneum (*e.g.*, mesothelioma, primary peritoneal cancer)); female sex organ
 tissues, including ovary (*e.g.*, choriocarcinoma, epithelial tumors, germ cell tumors,
 sex cord-stromal tumors), Fallopian tubes (*e.g.*, serous adenocarcinoma, mucinous
 adenocarcinoma, endometrioid adenocarcinoma, clear cell adenocarcinoma,
 transitional cell carcinoma, squamous cell carcinoma, undifferentiated carcinoma,
 müllerian tumors, adenosarcoma, leiomyosarcoma, teratoma, germ cell tumors,
 choriocarcinoma, trophoblastic tumors), uterus (*e.g.*, carcinoma of the cervix,
 endometrial polyps, endometrial hyperplasia, intraepithelial carcinoma (EIC),
 endometrial carcinoma (*e.g.*, endometrioid carcinoma, serous carcinoma, clear cell
 carcinoma, mucinous carcinoma, squamous cell carcinoma, transitional carcinoma,
 small cell carcinoma, undifferentiated carcinoma, mesenchymal neoplasia),
 leiomyoma (*e.g.*, endometrial stromal nodule, leiomyosarcoma, endometrial stromal
 sarcoma (ESS), mesenchymal tumors), mixed epithelial and mesenchymal tumors
 (*e.g.*, adenofibroma, carcinosarcoma, adenosarcoma, carcinosarcoma (malignant
 mixed mesodermal sarcoma - MMMT)), endometrial stromal tumors, endometrial
 malignant müllerian mixed tumours, gestational trophoblastic tumors (partial
 hydatiform mole, complete hydatiform mole, invasive hydatiform mole, placental site
 tumour)), vulva, vagina; male sex organ tissues, including prostate, testis (*e.g.*, germ
 cell tumors, spermatocytic seminoma), penis; bladder (*e.g.*, squamous cell carcinoma,
 urothelial carcinoma, bladder urothelial carcinoma); brain, (*e.g.*, gliomas (*e.g.*,
 astrocytomas, including non-infiltrating, low-grade, anaplastic, glioblastomas;
 oligodendrogliomas, ependymomas), meningiomas, gangliogliomas, schwannomas
 (neurilemmomas), craniopharyngiomas, chordomas, Non-Hodgkin lymphomas,
 pituitary tumors; eye (*e.g.*, retinoma, retinoblastoma, ocular melanoma, posterior
 uveal melanoma, iris hamartoma); head and neck (*e.g.*, nasopharyngeal carcinoma,
 Endolymphatic Sac Tumor (ELST), epidermoid carcinoma, laryngeal cancers
 including squamous cell carcinoma (SCC) (*e.g.*, glottic carcinoma, supraglottic
 carcinoma, subglottic carcinoma, transglottic carcinoma), carcinoma in situ,
 verrucous, spindle cell and basaloid SCC, undifferentiated carcinoma, laryngeal
 adenocarcinoma, adenoid cystic carcinoma, neuroendocrine carcinomas, laryngeal
 sarcoma), head and neck paragangliomas (*e.g.*, carotid body, jugulotympanic, vagal);
 thymus (*e.g.*, thymoma); heart (*e.g.*, cardiac myxoma); lung (*e.g.*, small cell

carcinoma (SCLC), non-small cell lung carcinoma (NSCLC), including squamous cell carcinoma (SCC), adenocarcinoma and large cell carcinoma, carcinoids (typical or atypical), carcinosarcomas, pulmonary blastomas, giant cell carcinomas, spindle cell carcinomas, pleuropulmonary blastoma); lymph (e.g., lymphomas, including Hodgkin's lymphoma, non-Hodgkin's lymphoma, Epstein-Barr virus (EBV)-associated lymphoproliferative diseases, including B cell lymphomas and T cell lymphomas (e.g., Burkitt lymphoma, large B cell lymphoma, diffuse large B-cell lymphoma (DLBCL), mantle cell lymphoma, indolent B-cell lymphoma, low grade B cell lymphoma, fibrin-associated diffuse large cell lymphoma; primary effusion lymphoma; plasmablastic lymphoma; extranodal NK/T cell lymphoma, nasal type; peripheral T cell lymphoma, cutaneous T cell lymphoma, angioimmunoblastic T cell lymphoma; follicular T cell lymphoma; systemic T cell lymphoma), lymphangiomyomatosis); central nervous system (CNS) (e.g., gliomas including astrocytic tumors (e.g., pilocytic astrocytoma, pilomyxoid astrocytoma, subependymal giant cell astrocytoma, pleomorphic xanthoastrocytoma, diffuse astrocytoma, fibrillary astrocytoma, gemistocytic astrocytoma, protoplasmic astrocytoma, anaplastic astrocytoma, glioblastoma (e.g., giant cell glioblastoma, gliosarcoma, glioblastoma multiforme) and gliomatosis cerebri), oligodendroglial tumors (e.g., oligodendroglioma, anaplastic oligodendroglioma), oligoastrocytic tumors (e.g., oligoastrocytoma, anaplastic oligoastrocytoma), ependymal tumors (e.g., subependymoma, myxopapillary ependymoma, ependymomas (e.g., cellular, papillary, clear cell, tanycytic), anaplastic ependymoma), optic nerve glioma, and non-gliomas (e.g., choroid plexus tumors, neuronal and mixed neuronal-glial tumors, pineal region tumors, embryonal tumors, medulloblastoma, meningeal tumors, primary CNS lymphomas, germ cell tumors, pituitary adenomas, cranial and paraspinal nerve tumors, stellar region tumors), neurofibroma, meningioma, peripheral nerve sheath tumors, peripheral neuroblastic tumours (including without limitation neuroblastoma, ganglioneuroblastoma, ganglioneuroma), trisomy 19 ependymoma); neuroendocrine tissues (e.g., paraganglionic system including adrenal medulla (pheochromocytomas) and extra-adrenal paraganglia ((extra-adrenal) paragangliomas); skin (e.g., clear cell hidradenoma, cutaneous benign fibrous histiocytomas, cylindroma, hidradenoma, melanoma (including cutaneous melanoma, mucosal melanoma), pilomatricoma, Spitz tumors); and soft tissues (e.g., aggressive angiomyxoma, alveolar rhabdomyosarcoma, alveolar soft part sarcoma, angiofibroma, angiomatoid fibrous

histiocytoma, synovial sarcoma, biphasic synovial sarcoma, clear cell sarcoma, dermatofibrosarcoma protuberans, desmoid-type fibromatosis, small round cell tumor, desmoplastic small round cell tumor, elastofibroma, embryonal rhabdomyosarcoma, Ewing's tumors/primitive neuroectodermal tumors (PNET), extraskeletal myxoid chondrosarcoma, extraskeletal osteosarcoma, paraspinal sarcoma, inflammatory myofibroblastic tumor, lipoblastoma, lipoma, chondroid lipoma, liposarcoma / malignant lipomatous tumors, liposarcoma, myxoid liposarcoma, fibromyxoid sarcoma, lymphangioleiomyoma, malignant myoepithelioma, malignant melanoma of soft parts, myoepithelial carcinoma, myoepithelioma, myxoinflammatory fibroblastic sarcoma, undifferentiated sarcoma, pericytoma, rhabdomyosarcoma, non-rhabdomyosarcoma soft tissue sarcoma (NRSTS), soft tissue leiomyosarcoma, undifferentiated sarcoma, well-differentiated liposarcoma.

191. The method of any one of claims 156-184, wherein the cancer is selected from the group consisting of a melanoma, a gastric cancer, a triple-negative breast cancer (TNBC), a non-small cell lung cancer (NSCLC), a rectal adenocarcinoma, a colorectal cancer, a renal cell carcinoma, an ovarian cancer, a prostate cancer, an oral squamous cell carcinoma (SCC), a head and neck squamous cell carcinoma (HNSCC), a urothelial bladder cancer, a glioblastoma (GBM), a meningioma, adrenal cancer, and an endometrial cancer.

192. The isolated antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition of any one of claims 1-146, 148-151, 153, or 154 for use in the treatment of cancer.

193. The isolated antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition for use of claim 192, wherein the cancer is selected from the group consisting of a solid tumor, a hematological cancer, and a metastatic lesion.

194. The isolated antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition for use of claim 192, wherein the solid tumor is selected from the group consisting of a sarcoma, a fibroblastic sarcoma, a carcinoma, and an adenocarcinoma.

195. The isolated antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition for use of claim 192, wherein the hematological cancer is selected from the group consisting of a leukemia, a lymphoma, and a myeloma.

196. The isolated antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition for use of any one of claims 192-195, wherein the cancer is selected from the group consisting of a lung cancer, a melanoma, a renal cancer, a liver cancer, a myeloma, a prostate cancer, a breast cancer, an ovarian cancer, a colorectal cancer, a pancreatic cancer, a head and neck cancer, an anal cancer, a gastro-esophageal cancer, a mesothelioma, a nasopharyngeal cancer, a thyroid cancer, a cervical cancer, an epithelial cancer, a peritoneal cancer, a lymphoproliferative disease, an acute lymphoblastic leukemia (ALL), an acute myelogenous leukemia (AML), a chronic lymphocytic leukemia (CLL), a chronic myelogenous leukemia (CML), a chronic myelomonocytic leukemia (CMML), a hairy cell leukemia, a B cell lymphoma, a diffuse large B-cell lymphoma (DLBCL), an activated B-cell like (ABC) diffuse large B cell lymphoma, a germinal center B cell (GCB) diffuse large B cell lymphoma, a mantle cell lymphoma, a Hodgkin lymphoma, a non-Hodgkin lymphoma, a relapsed non-Hodgkin lymphoma, a refractory non-Hodgkin lymphoma, a recurrent follicular non-Hodgkin lymphoma, a Burkitt lymphoma, a small lymphocytic lymphoma, a follicular lymphoma, a lymphoplasmacytic lymphoma, and an extranodal marginal zone lymphoma.

197. The isolated antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition of any one of claims 192-195, wherein the cancer is selected from the group consisting of a melanoma, a gastric cancer, a triple-negative breast cancer (TNBC), a non-small cell lung cancer (NSCLC), a rectal adenocarcinoma, a colorectal cancer, a renal cell carcinoma, an ovarian cancer, a prostate cancer, an oral squamous cell carcinoma (SCC), a head and neck squamous cell carcinoma (HNSCC), a urothelial bladder cancer, a glioblastoma (GBM), a meningioma, adrenal cancer, and an endometrial cancer.

198. Use of the isolated antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition of any one of claims 1-146, 148-151, 153, or 154 for the preparation of a medicament for treating cancer.

199. The use of claim 198, wherein the cancer is selected from the group consisting of a solid tumor, a hematological cancer, and a metastatic lesion.

200. The use of claim 199, wherein the solid tumor is selected from the group consisting of a sarcoma, a fibroblastic sarcoma, a carcinoma, and an adenocarcinoma.

201. The use of claim 199, wherein the hematological cancer is selected from the group consisting of a leukemia, a lymphoma, and a myeloma.

202. The use of any one of claims 198-201, wherein the cancer is selected from the group consisting of a lung cancer, a melanoma, a renal cancer, a liver cancer, a myeloma, a prostate cancer, a breast cancer, an ovarian cancer, a colorectal cancer, a pancreatic cancer, a head and neck cancer, an anal cancer, a gastro-esophageal cancer, a mesothelioma, a nasopharyngeal cancer, a thyroid cancer, a cervical cancer, an epithelial cancer, a peritoneal cancer, a lymphoproliferative disease, an acute lymphoblastic leukemia (ALL), an acute myelogenous leukemia (AML), a chronic lymphocytic leukemia (CLL), a chronic myelogenous leukemia (CML), a chronic myelomonocytic leukemia (CMML), a hairy cell leukemia, a B cell lymphoma, a diffuse large B-cell lymphoma (DLBCL), an activated B-cell like (ABC) diffuse large B cell lymphoma, a germinal center B cell (GCB) diffuse large B cell lymphoma, a mantle cell lymphoma, a Hodgkin lymphoma, a non-Hodgkin lymphoma, a relapsed non-Hodgkin lymphoma, a refractory non-Hodgkin lymphoma, a recurrent follicular non-Hodgkin lymphoma, a Burkitt lymphoma, a small lymphocytic lymphoma, a follicular lymphoma, a lymphoplasmacytic lymphoma, and an extranodal marginal zone lymphoma.

203. The use of any one of claims 198-201, wherein the cancer is selected from the group consisting of a melanoma, a gastric cancer, a triple-negative breast cancer (TNBC), a non-small cell lung cancer (NSCLC), a rectal adenocarcinoma, a colorectal cancer, a renal cell carcinoma, an ovarian cancer, a prostate cancer, an oral squamous cell carcinoma (SCC), a head and neck squamous cell carcinoma (HNSCC), a urothelial bladder cancer, a glioblastoma (GBM), a meningioma, adrenal cancer, and an endometrial cancer.

204. The isolated antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition of any one of claims 1-146, 148-151, 153, or 154, for use in the method of any one of claims 156-191.

5 205. Use of the isolated antibody, polynucleotide, vector, lipid nanoparticle, or pharmaceutical composition of any one of claims 1-146, 148-151, 153, or 154 in the method of any one of claims 156-191.

WHAT IS CLAIMED:

1. An isolated antibody that specifically binds to human CD73, the antibody comprising a heavy chain variable region comprising complementarity determining regions (CDRs) CDRH1, CDRH2, and CDRH3, and a light chain variable region comprising complementarity determining regions CDRL1, CDRL2, and CDRL3, wherein: CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 comprise the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences, respectively, set forth in SEQ ID NOs: 2, 4, 7, 8, 10, and 12; 2, 5, 7, 8, 10, and 12; 1, 3, 7, 8, 10, and 11; 2, 4, 7, 8, 10, and 11; 2, 4, 7, 9, 10, and 12; 2, 6, 7, 8, 10, and 12; 2, 5, 7, 9, 10, and 12; or 2, 6, 7, 9, 10, and 12.
2. The isolated antibody of claim 1, wherein CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 comprise the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 amino acid sequences, respectively, set forth in SEQ ID NOs: 2, , 5, 7, 8, 10, and 12.
3. The isolated antibody of claim 1 or 2, wherein the heavy chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 19-21 and 23-30; and/or the light chain variable region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 33-35 and 37-40.
4. The isolated antibody of any one of the preceding claims, wherein the heavy chain variable region and the light chain variable region, respectively, comprise the amino acid sequences set forth in SEQ ID NOs: 24 and 37; 27 and 37; 19 and 33; 20 and 34; 21 and 35; 23 and 37; 23 and 38; 24 and 38; 25 and 37; 26 and 37; 28 and 37; 25 and 38; 26 and 38; 27 and 38; 28 and 38; 29 and 37; 30 and 37; 23 and 39; or 23 and 40.
5. The isolated antibody of claim 4, wherein the heavy chain variable region and the light chain variable region, respectively, comprise the amino acid sequences set forth in SEQ ID NOs: 27 and 37.

6. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a heavy chain comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 63-88.
- 5 7. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a human kappa or human lambda light chain constant region.
8. The isolated antibody of claim 7, wherein the light chain constant region comprises the amino acid sequence of SEQ ID NO: 93 or 89.
- 10 9. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a light chain comprising the amino acid sequence selected from the group consisting of SEQ ID NO: 92 and 94-98.
- 15 10. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a heavy chain chain constant region, wherein the heavy chain constant region:
 - (a) is selected from the group consisting of human IgG1, IgG2, IgG3, IgG4, IgA1, and IgA2;
 - 20 (b) is an IgG1 heavy chain constant region;
 - (c) is an IgG1 heavy chain constant region comprising a N297A mutation, numbered according to the EU numbering system;
 - (d) comprises the amino acid sequence of SEQ ID NO: 50, 49, 46, 45, 55, or 56.
- 25 11. The isolated antibody of any one of the preceding claims, wherein the antibody comprises a heavy chain and a light chain comprising the amino acid sequences set forth in SEQ ID NOs: 79 and 97; 85 and 97; 77 and 97; 80 and 97; 86 and 97; 64 and 92; 70 and 96; or 78 and 97, respectively.
- 30 12. The isolated antibody of claim 11, wherein the heavy chain and light chain comprise the amino acid sequences set forth in SEQ ID NOs: 85 and 97, respectively.

13. The isolated antibody of any one of claims 1-12, further comprising a TGF β -binding moiety.
14. The isolated antibody of claim 13, wherein the TGF β -binding moiety is linked to a peptide linker.
15. The isolated antibody of claim 14, wherein the peptide linker comprises an amino acid sequence that is at least 95% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 103-108.
16. The isolated antibody of claim 14 or 15, wherein the peptide linker comprises the amino acid sequence of SEQ ID NO: 103.
17. The isolated antibody of claim 13, wherein the TGF β -binding moiety comprises an extracellular domain of a human TGF β receptor.
18. The isolated antibody of any one of claims 13-17, wherein the TGF β -binding moiety comprises an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence selected from the group consisting of SEQ ID NOs: 109-112.
19. The isolated antibody of any one of claims 13-18, wherein the the TGF β -binding moiety comprises the amino acid sequence of SEQ ID NO: 111.
20. The isolated antibody of any one of claims 1-19, the antibody comprising a polypeptide comprising an amino acid sequence that is at least 95% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 113-121; and/or a light chain comprising an amino acid sequence that is at least 95% identical to the amino acid sequence of SEQ ID NO: 97.
21. The isolated antibody of any one of claims 1-20, wherein the antibody comprises two polypeptides each comprising the amino acid sequence of SEQ ID NO: 115, and a light chain comprising the amino acid sequence of SEQ ID NO: 97.

22. The isolated antibody of any one of claims 1-12, further comprising a VEGF-binding moiety.

5 23. The isolated antibody of claim 22, wherein the VEGF-binding moiety is linked via a peptide linker.

24. The isolated antibody of claim 23, wherein the peptide linker comprises an amino acid sequence that is at least 95% identical to an amino acid sequence selected from the group consisting of SEQ ID NOs: 103-108.

10 25. The isolated antibody of claim 23 or 24, wherein the peptide linker comprises the amino acid sequence of SEQ ID NO: 103.

15 26. The isolated antibody of claim 22, wherein the VEGF-binding moiety comprises an extracellular domain of a human VEGF receptor.

27. The isolated antibody of any one of claims 22-26, wherein the VEGF-binding moiety comprises an amino acid sequence at least 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to the sequence set forth in SEQ ID NO: 122.

28. The isolated antibody of any one of claims 22-27, wherein the VEGF-binding moiety comprises the sequence set forth in SEQ ID NO: 122.

29. The isolated antibody of any one of claims 1-12 or 22-28, wherein the antibody comprises a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 123-127 and a polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 92, 128, and 97.

30. The isolated antibody of any one of claims 1-12 or 22-29, wherein the antibody comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 127, and/or a light chain comprising the amino acid sequence of SEQ ID NO: 97.

5 31. The isolated antibody of any one of the preceding claims, further comprising a conjugated cytotoxic agent, cytostatic agent, toxin, radionuclide, or detectable label.

32. An isolated polynucleotide encoding:

(a) a VH and/or a VL of the antibody of any one of claims 1-31;

10 (b) a heavy chain and/or a light chain of the antibody of any one of claims 1-31; or

(c) the amino acid sequence of any one of SEQ ID NOs: 19-21, 23-30, 33-35, 37-40, 63-88, 92, 94-98, 113-121, or 123-127.

33. A vector comprising the polynucleotide of claim 32.

15 34. A recombinant host cell comprising:

(a) the polynucleotide of claim 32;

(b) the vector of claim 33; or

20 (c) a first polynucleotide encoding the VH or the heavy chain of the antibody of any one of claims 1-31, and a second polynucleotide encoding the VL or the light chain of the antibody of any one of claims 1-31.

25 35. A pharmaceutical composition comprising the antibody, polynucleotide, vector, or host cell of any one of claims 1-34 and a pharmaceutically acceptable carrier or excipient.

36. A method of producing an antibody, the method comprising culturing the host cell of claim 34 under suitable conditions so that the polynucleotide is expressed and the antibody is produced.

30 37. Use of the isolated antibody, polynucleotide, vector, host cell, or pharmaceutical composition of any one of claims 1-35 for the preparation of a medicament for

treating a CD73 expressing cancer or inhibiting metastasis of a CD73 expressing cancer in a subject.

38. The use of claim 37, wherein:

(a) the medicament is to be administered intravenously, intratumorally, subcutaneously, intradermally, intramuscularly, intravesically, intracranially, intracavitary or intraventricularly;

(b) the subject is be administered one or more additional therapeutic agents, wherein:

(i) the additional therapeutic agent is an activator or agonist of a fms related tyrosine kinase 3 (FLT3; CD135) receptor, a toll-like receptor (TLR) or a stimulator of interferon genes (STING) receptor;

(ii) the additional therapeutic agent is an inhibitor or antagonist of: protein tyrosine phosphatase, non-receptor type 11 (PTPN11 or SHP2), myeloid cell leukemia sequence 1 (MCL1) apoptosis regulator; mitogen-activated protein kinase kinase kinase 1 (MAP4K1) (also called Hematopoietic Progenitor Kinase 1 (HPK1)); diacylglycerol kinase alpha (DGKA, DAGK, DAGK1 or DGK-alpha); 5'-nucleotidase ecto (NT5E or CD73); transforming growth factor beta 1 (TGFB1 or TGFβ); heme oxygenase 1 (HMOX1, HO-1 or HO1); vascular endothelial growth factor A (VEGFA or VEGF); erb-b2 receptor tyrosine kinase 2 (ERBB2 HER2, HER2/neu or CD340); epidermal growth factor receptor (EGFR, ERBB, ERBB1 or HER1); ALK receptor tyrosine kinase (ALK, CD246); poly(ADP-ribose) polymerase 1 (PARP1 or PARP); cyclin dependent kinase 4 (CDK4); cyclin dependent kinase 6 (CDK6); C-C motif chemokine receptor 8 (CCR8, CDw198); CD274 molecule (CD274, PDL1 or PD-L1); programmed cell death 1 (PDCD1, PD1 or PD-1); and/or cytotoxic T-lymphocyte associated protein 4 (CTLA4, CTLA-4, CD152);

(iii) the additional therapeutic agent is a chemotherapeutic, an anti-neoplastic, a radiotherapeutic, or a checkpoint targeting agent;

(iv) the additional therapeutic agent is a checkpoint targeting agent selected from the group consisting of an antagonist anti-PD-1 antibody, an antagonist anti-PD-L1 antibody, an antagonist anti-PD-L2 antibody, an antagonist anti-CTLA-4 antibody, an antagonist anti-TIM-3 antibody, an antagonist anti-LAG-3

antibody, an antagonist anti-CEACAM1 antibody, an agonist anti-GITR antibody, an antagonist anti-TIGIT antibody, an antagonist anti-VISTA antibody, an agonist anti-CD137 antibody, and an agonist anti-OX40 antibody;

(v) the additional therapeutic agent is an inhibitor of indoleamine-2,3-dioxygenase (IDO);

(vi) the additional therapeutic agent is an inhibitor of IDO selected from the group consisting of epacadostat, F001287, indoximod, and NLG919;

(vii) the additional therapeutic agent is a vaccine;

(viii) the additional therapeutic agent is a vaccine comprising a heat shock protein peptide complex (HSPPC) comprising a heat shock protein complexed with an antigenic peptide;

(ix) the additional therapeutic agent is a vaccine comprising a heat shock protein peptide complex (HSPPC) comprising hsc70 complexed with a tumor-associated antigenic peptide; or

(x) the additional therapeutic agent is a vaccine comprising a heat shock protein peptide complex (HSPPC) comprising gp96 protein complexed with a tumor-associated antigenic peptide, wherein the HSPPC is derived from a tumor obtained from a subject;

(xi) the additional therapeutic agent is etoposide or doxorubicin;

(c) the medicament is to be co-administered with a FOLFOX regimen, a FOLFOXIRI regimen or a FOLFIRINOX regimen; or

(d) the medicament is to be co-administered with an immunotherapy, an immunostimulatory therapy, a cellular therapy or a gene therapy.

39. Use of the isolated antibody, polynucleotide, vector, host cell, or pharmaceutical composition of any one of claims 1-35 for the preparation of a medicament for treating a CD73 expressing cancer.