

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.
- 5 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.
- 10 16. The isolated antibody of claim 14 or 15, wherein the peptide linker comprises the amino acid sequence of SEQ ID NO: 103.
- 15 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.
- 20 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.
- 25 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.
- 30 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.
- 20 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.
- 25 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.
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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:
- 10 (a) a VH and/or a VL of the antibody of any one of claims 1-31;
- (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
- (c)) a first polynucleotide encoding the VH or the heavy chain of the antibody of any
- 20 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.
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
- 25 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:

- 5 (a) the medicament is to be administered intravenously, intratumorally, subcutaneously, intradermally, intramuscularly, intravesically, intracranially, intracavitary or intraventricularly;
- (b) the subject is to be administered one or more additional therapeutic agents, wherein:
 - 10 (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
 - 15 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
 - 20 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);
 - 25 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
 - 30 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.