CLAIMS

1. An isolated monoclonal antibody or antigen-binding fragment thereof comprising a heavy chain complementarity determining region 1 (HCDR1), HCDR2, and HCDR3, a light chain complementarity determining region 1 (LCDR1), LCDR2, and LCDR3, having the polypeptide sequences of:

a. SEQ ID NOs:89, 90, 91, 149, 150 and 151, respectively, or SEQ ID NOs:209, 210, 211, 269, 270 and 271, respectively;

b. SEQ ID NOs:41, 42, 43, 101, 102 and 103, respectively, or SEQ ID NOs:161, 162, 163, 221, 222 and 223, respectively;

c. SEQ ID NOs:44, 45, 46, 104, 105 and 106, respectively, or SEQ ID NOs:164, 165, 166, 224, 225 and 226, respectively;

d. SEQ ID NOs:47, 48, 49, 107, 108 and 109, respectively, or SEQ ID NOs:167, 168, 169, 227, 228 and 229, respectively;

e. SEQ ID NOs:50, 51, 52, 110, 111 and 112, respectively, or SEQ ID NOs:170, 171, 172, 230, 231 and 232, respectively;

f. SEQ ID NOs:53, 54, 55, 113, 114 and 115, respectively, or SEQ ID NOs:173, 174, 175, 233, 234 and 235, respectively;

g. SEQ ID NOs:56, 57, 58, 116, 117 and 118, respectively, or SEQ ID NOs:176, 177, 178, 236, 237 and 238, respectively;

h. SEQ ID NOs:59, 60, 61, 119, 120 and 121, respectively, or SEQ ID NOs:179, 180, 181, 239, 240 and 241, respectively;

i. SEQ ID NOs:62, 63, 64, 122, 123 and 124, respectively, or SEQ ID NOs:182, 183, 184, 242, 243 and 244, respectively;

j. SEQ ID NOs:65, 66, 67, 125, 126 and 127, respectively, or SEQ ID NOs:185, 186, 187, 245, 246 and 247, respectively;

k. SEQ ID NOs:68, 69, 70, 128, 129 and 130, respectively, or SEQ ID NOs:188, 189, 190, 248, 249 and 250, respectively;

l. SEQ ID NOs:71, 72, 73, 131, 132 and 133, respectively, or SEQ ID NOs:191, 192, 193, 251, 252 and 253, respectively;

m. SEQ ID NOs:74, 75, 76, 134, 135 and 136, respectively, or SEQ ID NOs:194, 195, 196, 254, 255 and 256, respectively;

n. SEQ ID NOs:77, 78, 79, 137, 138 and 139, respectively, or SEQ ID NOs:197, 198, 199, 257, 258 and 259, respectively;

o. SEQ ID NOs:80, 81, 82, 140, 141 and 142, respectively, or SEQ ID NOs:200, 201, 202, 260, 261 and 262, respectively;

p. SEQ ID NOs:83, 84, 85, 143, 144 and 145, respectively, or SEQ ID NOs:203, 204, 205, 263, 264 and 265, respectively;

q. SEQ ID NOs:86, 87, 88, 146, 147 and 148, respectively, or SEQ ID NOs:206, 207, 208, 266, 267 and 268, respectively;

r. SEQ ID NOs:92, 93, 94, 152, 153 and 154, respectively, or SEQ ID NOs:212, 213, 214, 272, 273 and 274, respectively;

s. SEQ ID NOs:95, 96, 97, 155, 156 and 157, respectively, or SEQ ID NOs:215, 216, 217, 275, 276 and 277, respectively; or

t. SEQ ID NOs:98, 99, 100, 158, 159 and 160, respectively, or SEQ ID NOs:218, 219, 220, 278, 279 and 280, respectively;

wherein the antibody or antigen-binding fragment thereof specifically binds to CD73.

2. The isolated monoclonal antibody or antigen-binding fragment thereof of claim 1, comprising a heavy chain variable region having a polypeptide sequence at least 95% identical to SEQ ID NO:286, 33, 1, 3, 5, 7, 9, 11, 13, 15, 17, 19, 21, 23, 25, 27, 29, 31, 35, 37, 39, 282, 283, 284, 285, 287, 288, 289, 295, 296, 297, or 298, or a light chain variable region having a polypeptide sequence at least 95% identical to SEQ ID NO:293, 34, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 22, 24, 26, 28, 30, 32, 36, 38, 40, 290, 291, 292, 294, or 299.

3. The isolated monoclonal antibody or antigen-binding fragment thereof of claim 1 or 2, comprising:

a. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:286, and a light chain variable region having the polypeptide sequence of SEQ ID NO:293;

b. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:33, and a light chain variable region having the polypeptide sequence of SEQ ID NO:34;

c. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:1, and a light chain variable region having the polypeptide sequence of SEQ ID NO:2;

d. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:3, and a light chain variable region having the polypeptide sequence of SEQ ID NO:4;
e. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:5, and a light chain variable region having the polypeptide sequence of SEQ ID NO:6;
f. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:7, and a light chain variable region having the polypeptide sequence of SEQ ID NO:8;
g. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:9, and a light chain variable region having the polypeptide sequence of SEQ ID NO:10;
h. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:11, and a light chain variable region having the polypeptide sequence of SEQ ID NO:12;
i. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:13, and a light chain variable region having the polypeptide sequence of SEQ ID NO:14;
j. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:15, and a light chain variable region having the polypeptide sequence of SEQ ID NO:16;
k. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:17, and a light chain variable region having the polypeptide sequence of SEQ ID NO:18;
l. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:19, and a light chain variable region having the polypeptide sequence of SEQ ID NO:20;
m. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:21, and a light chain variable region having the polypeptide sequence of SEQ ID NO:22;
n. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:23, and a light chain variable region having the polypeptide sequence of SEQ ID NO:24;
o. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:25, and a light chain variable region having the polypeptide sequence of SEQ ID NO:26;
p. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:27, and a light chain variable region having the polypeptide sequence of SEQ ID NO:28;
q. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:29, and a light chain variable region having the polypeptide sequence of SEQ ID NO:30;
r. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:31, and a light chain variable region having the polypeptide sequence of SEQ ID NO:32;

s. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:35, and a light chain variable region having the polypeptide sequence of SEQ ID NO:36;

t. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:37, and a light chain variable region having the polypeptide sequence of SEQ ID NO:38;

u. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:39, and a light chain variable region having the polypeptide sequence of SEQ ID NO:40;

v. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:282, and a light chain variable region having the polypeptide sequence of SEQ ID NO:290;

w. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:282, and a light chain variable region having the polypeptide sequence of SEQ ID NO:291;

x. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:282, and a light chain variable region having the polypeptide sequence of SEQ ID NO:292;

y. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:283, and a light chain variable region having the polypeptide sequence of SEQ ID NO:290;

z. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:283, and a light chain variable region having the polypeptide sequence of SEQ ID NO:291;

aa. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:283, and a light chain variable region having the polypeptide sequence of SEQ ID NO:292;

bb. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:284, and a light chain variable region having the polypeptide sequence of SEQ ID NO:290;

cc. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:284, and a light chain variable region having the polypeptide sequence of SEQ ID NO:291;

dd. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:284, and a light chain variable region having the polypeptide sequence of SEQ ID NO:292;

ee. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:285, and a light chain variable region having the polypeptide sequence of SEQ ID NO:290;

ff. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:285, and a light chain variable region having the polypeptide sequence of SEQ ID NO:291;

gg. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:285, and a light chain variable region having the polypeptide sequence of SEQ ID NO:292;

hh. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:283, and a light chain variable region having the polypeptide sequence of SEQ ID NO:293;

ii. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:284, and a light chain variable region having the polypeptide sequence of SEQ ID NO:293;

jj. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:285, and a light chain variable region having the polypeptide sequence of SEQ ID NO:293;

kk. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:286, and a light chain variable region having the polypeptide sequence of SEQ ID NO:290;

ll. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:286, and a light chain variable region having the polypeptide sequence of SEQ ID NO:291;

mm. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:286, and a light chain variable region having the polypeptide sequence of SEQ ID NO:292;

nn. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:287, and a light chain variable region having the polypeptide sequence of SEQ ID NO:294;

oo. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:288, and a light chain variable region having the polypeptide sequence of SEQ ID NO:294;

pp. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:289, and a light chain variable region having the polypeptide sequence of SEQ ID NO:294;

qq. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:284, and a light chain variable region having the polypeptide sequence of SEQ ID NO:299;

rr. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:295, and a light chain variable region having the polypeptide sequence of SEQ ID NO:299;

ss. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:296, and a light chain variable region having the polypeptide sequence of SEQ ID NO:299;

tt. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:297, and a light chain variable region having the polypeptide sequence of SEQ ID NO:299; or

uu. a heavy chain variable region having the polypeptide sequence of SEQ ID NO:298, and a light chain variable region having the polypeptide sequence of SEQ ID NO:299.

4. The isolated monoclonal antibody or antigen-binding fragment thereof of any one of claims 1-3, wherein the monoclonal antibody or antigen-binding fragment thereof inhibits the

enzyme activity of soluble and/or cell-surface CD73, prevents the dimerization of CD73, induces the internalization of CD73, and/or is capable of activating T cells.

5. The isolated monoclonal antibody or antigen-binding fragment thereof of any one of claims 1-4, wherein the antibody or antigen-binding fragment thereof is chimeric or human or humanized.

6. An isolated bispecific antibody or antigen-binding fragment thereof comprising the monoclonal antibody or antigen-binding fragment thereof of any one of claims 1-5.

7. An isolated nucleic acid encoding the monoclonal antibody or antigen-binding fragment thereof of any one of claims 1-5 ~~1-6~~.

8. A vector comprising the isolated nucleic acid of claim 7.

9. A host cell comprising the vector of claim 8.

10. A pharmaceutical composition, comprising the isolated monoclonal antibody or antigen-binding fragment thereof of any one of claims 1-5 and a pharmaceutically acceptable carrier.

11. The pharmaceutical composition of claim 10 for use in a method of inhibiting the nucleotidase activity of CD73, preventing the dimerization of CD73, inducing the internalization of CD73, or treating cancer in a subject in need thereof, wherein the pharmaceutical composition is to be administered to the subject.

12. Use of the pharmaceutical composition of claim 10 in the manufacture of a medicament for the treatment of cancer in a subject in need thereof, wherein the medicament is to be administered to the subject.

13. A method of producing the monoclonal antibody or antigen-binding fragment thereof of any one of claims 1-5, comprising culturing a cell comprising a nucleic acid encoding the monoclonal antibody or antigen-binding fragment thereof under conditions to produce the monoclonal antibody or antigen-binding fragment thereof, and recovering the monoclonal antibody or antigen-binding fragment thereof from the host cell.

14. A method of producing a pharmaceutical composition comprising the monoclonal antibody or antigen-binding fragment thereof of any one of claims 1-5, comprising combining the monoclonal antibody or antigen-binding fragment thereof with a pharmaceutically acceptable carrier to obtain the pharmaceutical composition.

15. A method of determining a level of CD73 or determining the ecto-5’ nucleotidase activity of CD73 in a subject, the method comprising:

a. obtaining a sample from the subject;

b. contacting the sample with an isolated monoclonal antibody or antigen-binding fragment thereof of any one of claims 1-5; and

~~c.~~ determining a level of CD73 or determining the ecto-5’ nucleotidase activity of CD73 in the subject.

16. The method of claim 15, wherein the sample is a tissue sample or a blood sample.

17. The method of claim 16, wherein the tissue sample is a cancer tissue sample.

18. An isolated nucleic acid encoding the bispecific antibody or antigen-binding fragment thereof of claim 6.

19. A vector comprising the isolated nucleic acid of claim 18.

20. A host cell comprising the vector of claim 19.

21. A pharmaceutical composition comprising the isolated bispecific antibody or antigen-binding fragment thereof of claim 6 and a pharmaceutically acceptable carrier.