

~~WHAT IS CLAIMED IS:~~

1. An ~~isolated fully human~~ anti-human CLDN18.2 antibody, wherein the antibody does not bind to human CLDN18.1 and the antibody comprises:

- (a) a heavy chain variable region comprising CDR1: SEQ ID NO: 221, CDR2: SEQ ID NO: 222, CDR3: SEQ ID NO: 223 and a light chain variable region comprising CDR1: SEQ ID NO: 224, CDR2: SEQ ID NO: 225, CDR3: SEQ ID NO: 226;
- (b) a heavy chain variable region comprising CDR1: SEQ ID NO: 227, CDR2: SEQ ID NO: 228, CDR3: SEQ ID NO: 229 and a light chain variable region comprising CDR1: SEQ ID NO: 230, CDR2: SEQ ID NO: 231, CDR3: SEQ ID NO: 232;
- (c) a heavy chain variable region comprising CDR1: SEQ ID NO: 233, CDR2: SEQ ID NO: 234, CDR3: SEQ ID NO: 235 and a light chain variable region comprising CDR1: SEQ ID NO: 236, CDR2: SEQ ID NO: 237, CDR3: SEQ ID NO: 238;
- (d) a heavy chain variable region comprising CDR1: SEQ ID NO: 239, CDR2: SEQ ID NO: 240, CDR3: SEQ ID NO: 241 and a light chain variable region comprising CDR1: SEQ ID NO: 242, CDR2: SEQ ID NO: 243, CDR3: SEQ ID NO: 244;
- (e) a heavy chain variable region comprising CDR1: SEQ ID NO: 245, CDR2: SEQ ID NO: 246, CDR3: SEQ ID NO: 247 and a light chain variable region comprising CDR1: SEQ ID NO: 248, CDR2: SEQ ID NO: 249, CDR3: SEQ ID NO: 250;
- (f) a heavy chain variable region comprising CDR1: SEQ ID NO: 251, CDR2: SEQ ID NO: 252, CDR3: SEQ ID NO: 253 and a light chain variable region comprising CDR1: SEQ ID NO: 254, CDR2: SEQ ID NO: 255, CDR3: SEQ ID NO: 256;
- (g) a heavy chain variable region comprising CDR1: SEQ ID NO: 257, CDR2: SEQ ID NO: 258, CDR3: SEQ ID NO: 259 and a light chain variable region comprising CDR1: SEQ ID NO: 260, CDR2: SEQ ID NO: 261, CDR3: SEQ ID NO: 262;
- (h) a heavy chain variable region comprising CDR1: SEQ ID NO: 263, CDR2: SEQ ID NO: 264, CDR3: SEQ ID NO: 265 and a light chain variable region comprising CDR1: SEQ ID NO: 266, CDR2: SEQ ID NO: 267, CDR3: SEQ ID NO: 268;
- (i) a heavy chain variable region comprising CDR1: SEQ ID NO: 269, CDR2: SEQ ID NO: 270, CDR3: SEQ ID NO: 271 and a light chain variable region comprising CDR1: SEQ ID NO: 272, CDR2: SEQ ID NO: 273, CDR3: SEQ ID NO: 274;

- (j) a heavy chain variable region comprising CDR1: SEQ ID NO: 275, CDR2: SEQ ID NO: 276, CDR3: SEQ ID NO: 277 and a light chain variable region comprising CDR1: SEQ ID NO: 278, CDR2: SEQ ID NO: 279, CDR3: SEQ ID NO: 280;
- (k) a heavy chain variable region comprising CDR1: SEQ ID NO: 281, CDR2: SEQ ID NO: 282, CDR3: SEQ ID NO: 283 and a light chain variable region comprising CDR1: SEQ ID NO: 284, CDR2: SEQ ID NO: 285, CDR3: SEQ ID NO: 286;
- (l) a heavy chain variable region comprising CDR1: SEQ ID NO: 287, CDR2: SEQ ID NO: 288, CDR3: SEQ ID NO: 289 and a light chain variable region comprising CDR1: SEQ ID NO: 290, CDR2: SEQ ID NO: 291, CDR3: SEQ ID NO: 292;
- (m) a heavy chain variable region comprising CDR1: SEQ ID NO: 293, CDR2: SEQ ID NO: 294, CDR3: SEQ ID NO: 295 and a light chain variable region comprising CDR1: SEQ ID NO: 296, CDR2: SEQ ID NO: 297, CDR3: SEQ ID NO: 298;
- (n) a heavy chain variable region comprising CDR1: SEQ ID NO: 299, CDR2: SEQ ID NO: 300, CDR3: SEQ ID NO: 301 and a light chain variable region comprising CDR1: SEQ ID NO: 302, CDR2: SEQ ID NO: 303, CDR3: SEQ ID NO: 304;
- (o) a heavy chain variable region comprising CDR1: SEQ ID NO: 311, CDR2: SEQ ID NO: 312, CDR3: SEQ ID NO: 313 and a light chain variable region comprising CDR1: SEQ ID NO: 314, CDR2: SEQ ID NO: 315, CDR3: SEQ ID NO: 316;
- (p) a heavy chain variable region comprising CDR1: SEQ ID NO: 317, CDR2: SEQ ID NO: 318, CDR3: SEQ ID NO: 319 and a light chain variable region comprising CDR1: SEQ ID NO: 320, CDR2: SEQ ID NO: 321, CDR3: SEQ ID NO: 322; or
- (q) a heavy chain variable region comprising CDR1: SEQ ID NO: 323, CDR2: SEQ ID NO: 324, CDR3: SEQ ID NO: 325 and a light chain variable region comprising CDR1: SEQ ID NO: 326, CDR2: SEQ ID NO: 327, CDR3: SEQ ID NO: 328.

2. An ~~isolated~~ anti-human CLDN18.2 antibody, wherein the antibody does not bind to human CLDN18.1 and the antibody comprises:

- (a) a heavy chain variable region comprising CDR1: SEQ ID NO: 47, CDR2: SEQ ID NO: 48, CDR3: SEQ ID NO: 49 and a light chain variable region comprising CDR1: SEQ ID NO: 50, CDR2: SEQ ID NO: 51, CDR3: SEQ ID NO: 52;

- (b) a heavy chain variable region comprising CDR1: SEQ ID NO: 53, CDR2: SEQ ID NO: 54, CDR3: SEQ ID NO: 55 and a light chain variable region comprising CDR1: SEQ ID NO: 56, CDR2: SEQ ID NO: 57, CDR3: SEQ ID NO: 58;
- (c) a heavy chain variable region comprising CDR1: SEQ ID NO: 59, CDR2: SEQ ID NO: 60, CDR3: SEQ ID NO: 61 and a light chain variable region comprising CDR1: SEQ ID NO: 62, CDR2: SEQ ID NO: 63, CDR3: SEQ ID NO: 64;
- (d) a heavy chain variable region comprising CDR1: SEQ ID NO: 65, CDR2: SEQ ID NO: 66, CDR3: SEQ ID NO: 67 and a light chain variable region comprising CDR1: SEQ ID NO: 68, CDR2: SEQ ID NO: 69, CDR3: SEQ ID NO: 70;
- (e) a heavy chain variable region comprising CDR1: SEQ ID NO: 71, CDR2: SEQ ID NO: 72, CDR3: SEQ ID NO: 73 and a light chain variable region comprising CDR1: SEQ ID NO: 74, CDR2: SEQ ID NO: 75, CDR3: SEQ ID NO: 76;
- (f) a heavy chain variable region comprising CDR1: SEQ ID NO: 77, CDR2: SEQ ID NO: 78, CDR3: SEQ ID NO: 79 and a light chain variable region comprising CDR1: SEQ ID NO: 80, CDR2: SEQ ID NO: 81, CDR3: SEQ ID NO: 82;
- (g) a heavy chain variable region comprising CDR1: SEQ ID NO: 83, CDR2: SEQ ID NO: 84, CDR3: SEQ ID NO: 85 and a light chain variable region comprising CDR1: SEQ ID NO: 86, CDR2: SEQ ID NO: 87, CDR3: SEQ ID NO: 88;
- (h) a heavy chain variable region comprising CDR1: SEQ ID NO: 89, CDR2: SEQ ID NO: 90, CDR3: SEQ ID NO: 91 and a light chain variable region comprising CDR1: SEQ ID NO: 92, CDR2: SEQ ID NO: 93, CDR3: SEQ ID NO: 94;
- (i) a heavy chain variable region comprising CDR1: SEQ ID NO: 95, CDR2: SEQ ID NO: 96, CDR3: SEQ ID NO: 97 and a light chain variable region comprising CDR1: SEQ ID NO: 98, CDR2: SEQ ID NO: 99, CDR3: SEQ ID NO: 100;
- (j) a heavy chain variable region comprising CDR1: SEQ ID NO: 101, CDR2: SEQ ID NO: 102, CDR3: SEQ ID NO: 103 and a light chain variable region comprising CDR1: SEQ ID NO: 104, CDR2: SEQ ID NO: 105, CDR3: SEQ ID NO: 106;
- (k) a heavy chain variable region comprising CDR1: SEQ ID NO: 107, CDR2: SEQ ID NO: 108, CDR3: SEQ ID NO: 109 and a light chain variable region comprising CDR1: SEQ ID NO: 110, CDR2: SEQ ID NO: 111, CDR3: SEQ ID NO: 112;

- (l) a heavy chain variable region comprising CDR1: SEQ ID NO: 113, CDR2: SEQ ID NO: 114, CDR3: SEQ ID NO: 115 and a light chain variable region comprising CDR1: SEQ ID NO: 116, CDR2: SEQ ID NO: 117, CDR3: SEQ ID NO: 118;
- (m) a heavy chain variable region comprising CDR1: SEQ ID NO: 119, CDR2: SEQ ID NO: 120, CDR3: SEQ ID NO: 121 and a light chain variable region comprising CDR1: SEQ ID NO: 122, CDR2: SEQ ID NO: 123, CDR3: SEQ ID NO: 124;
- (n) a heavy chain variable region comprising CDR1: SEQ ID NO: 125, CDR2: SEQ ID NO: 126, CDR3: SEQ ID NO: 127 and a light chain variable region comprising CDR1: SEQ ID NO: 128, CDR2: SEQ ID NO: 129, CDR3: SEQ ID NO: 130;
- (o) a heavy chain variable region comprising CDR1: SEQ ID NO: 131, CDR2: SEQ ID NO: 132, CDR3: SEQ ID NO: 133 and a light chain variable region comprising CDR1: SEQ ID NO: 134, CDR2: SEQ ID NO: 135, CDR3: SEQ ID NO: 136;
- (p) a heavy chain variable region comprising CDR1: SEQ ID NO: 137, CDR2: SEQ ID NO: 138, CDR3: SEQ ID NO: 139 and a light chain variable region comprising CDR1: SEQ ID NO: 140, CDR2: SEQ ID NO: 141, CDR3: SEQ ID NO: 142;
- (q) a heavy chain variable region comprising CDR1: SEQ ID NO: 143, CDR2: SEQ ID NO: 144, CDR3: SEQ ID NO: 145 and a light chain variable region comprising CDR1: SEQ ID NO: 146, CDR2: SEQ ID NO: 147, CDR3: SEQ ID NO: 148;
- (r) a heavy chain variable region comprising CDR1: SEQ ID NO: 149, CDR2: SEQ ID NO: 150, CDR3: SEQ ID NO: 151 and a light chain variable region comprising CDR1: SEQ ID NO: 152, CDR2: SEQ ID NO: 153, CDR3: SEQ ID NO: 154;
- (s) a heavy chain variable region comprising CDR1: SEQ ID NO: 155, CDR2: SEQ ID NO: 156, CDR3: SEQ ID NO: 157 and a light chain variable region comprising CDR1: SEQ ID NO: 158, CDR2: SEQ ID NO: 159, CDR3: SEQ ID NO: 160;
- (t) a heavy chain variable region comprising CDR1: SEQ ID NO: 161, CDR2: SEQ ID NO: 162, CDR3: SEQ ID NO: 163 and a light chain variable region comprising CDR1: SEQ ID NO: 164, CDR2: SEQ ID NO: 165, CDR3: SEQ ID NO: 166;
- (u) a heavy chain variable region comprising CDR1: SEQ ID NO: 167, CDR2: SEQ ID NO: 168, CDR3: SEQ ID NO: 169 and a light chain variable region comprising CDR1: SEQ ID NO: 170, CDR2: SEQ ID NO: 171, CDR3: SEQ ID NO: 172;

(v) a heavy chain variable region comprising CDR1: SEQ ID NO: 173, CDR2: SEQ ID NO: 174, CDR3: SEQ ID NO: 175 and a light chain variable region comprising CDR1: SEQ ID NO: 176, CDR2: SEQ ID NO: 177, CDR3: SEQ ID NO: 178; or

(w) a heavy chain variable region comprising CDR1: SEQ ID NO: 179, CDR2: SEQ ID NO: 180, CDR3: SEQ ID NO: 181 and a light chain variable region comprising CDR1: SEQ ID NO: 182, CDR2: SEQ ID NO: 183, CDR3: SEQ ID NO: 184.

3. An ~~isolated~~ anti-human CLDN18.2 antibody, wherein the antibody does not bind to human CLDN18.1 and the antibody comprises:

(a) a heavy chain variable region sequence of SEQ ID NO: 1 and a light chain variable region sequence of SEQ ID NO: 2;

(b) a heavy chain variable region sequence of SEQ ID NO: 3 and a light chain variable region sequence of SEQ ID NO: 4;

(c) a heavy chain variable region sequence of SEQ ID NO: 5 and a light chain variable region sequence of SEQ ID NO: 6;

(d) a heavy chain variable region sequence of SEQ ID NO: 7 and a light chain variable region sequence of SEQ ID NO: 8;

(e) a heavy chain variable region sequence of SEQ ID NO: 9 and a light chain variable region sequence of SEQ ID NO: 10;

(f) a heavy chain variable region sequence of SEQ ID NO: 11 and a light chain variable region sequence of SEQ ID NO: 12;

(g) a heavy chain variable region sequence of SEQ ID NO: 13 and a light chain variable region sequence of SEQ ID NO: 14;

(h) a heavy chain variable region sequence of SEQ ID NO: 15 and a light chain variable region sequence of SEQ ID NO: 16;

(i) a heavy chain variable region sequence of SEQ ID NO: 17 and a light chain variable region sequence of SEQ ID NO: 18;

(j) a heavy chain variable region sequence of SEQ ID NO: 19 and a light chain variable region sequence of SEQ ID NO: 20;

(k) a heavy chain variable region sequence of SEQ ID NO: 21 and a light chain variable region sequence of SEQ ID NO: 22;

- (l) a heavy chain variable region sequence of SEQ ID NO: 23 and a light chain variable region sequence of SEQ ID NO: 24;
- (m) a heavy chain variable region sequence of SEQ ID NO: 25 and a light chain variable region sequence of SEQ ID NO: 26;
- (n) a heavy chain variable region sequence of SEQ ID NO: 27 and a light chain variable region sequence of SEQ ID NO: 28;
- (o) a heavy chain variable region sequence of SEQ ID NO: 29 and a light chain variable region sequence of SEQ ID NO: 30;
- (p) a heavy chain variable region sequence of SEQ ID NO: 31 and a light chain variable region sequence of SEQ ID NO: 32;
- (q) a heavy chain variable region sequence of SEQ ID NO: 33 and a light chain variable region sequence of SEQ ID NO: 34;
- (r) a heavy chain variable region sequence of SEQ ID NO: 35 and a light chain variable region sequence of SEQ ID NO: 36;
- (s) a heavy chain variable region sequence of SEQ ID NO: 37 and a light chain variable region sequence of SEQ ID NO: 38;
- (t) a heavy chain variable region sequence of SEQ ID NO: 39 and a light chain variable region sequence of SEQ ID NO: 40;
- (u) a heavy chain variable region sequence of SEQ ID NO: 41 and a light chain variable region sequence of SEQ ID NO: 42;
- (v) a heavy chain variable region sequence of SEQ ID NO: 43 and a light chain variable region sequence of SEQ ID NO: 44; or
- (w) a heavy chain variable region sequence of SEQ ID NO: 45 and a light chain variable region sequence of SEQ ID NO: 46.

4. The anti-human CLDN18.2 antibody of claim 3, wherein the antibody is a humanized antibody.
5. The anti-human CLDN18.2 antibody of claim 3, wherein the antibody is a chimeric antibody.
6. An ~~isolated fully human~~ anti-human CLDN18.2 antibody, wherein the antibody does not bind to human CLDN18.1 and the antibody comprises:

- (a) a heavy chain variable region sequence of SEQ ID NO: 185 and a light chain variable region sequence of SEQ ID NO: 186;
- (b) a heavy chain variable region sequence of SEQ ID NO: 187 and a light chain variable region sequence of SEQ ID NO: 188;
- (c) a heavy chain variable region sequence of SEQ ID NO: 189 and a light chain variable region sequence of SEQ ID NO: 190;
- (d) a heavy chain variable region sequence of SEQ ID NO: 191 and a light chain variable region sequence of SEQ ID NO: 192;
- (e) a heavy chain variable region sequence of SEQ ID NO: 193 and a light chain variable region sequence of SEQ ID NO: 194;
- (f) a heavy chain variable region sequence of SEQ ID NO: 195 and a light chain variable region sequence of SEQ ID NO: 196;
- (g) a heavy chain variable region sequence of SEQ ID NO: 197 and a light chain variable region sequence of SEQ ID NO: 198;
- (h) a heavy chain variable region sequence of SEQ ID NO: 199 and a light chain variable region sequence of SEQ ID NO: 200;
- (i) a heavy chain variable region sequence of SEQ ID NO: 201 and a light chain variable region sequence of SEQ ID NO: 202;
- (j) a heavy chain variable region sequence of SEQ ID NO: 203 and a light chain variable region sequence of SEQ ID NO: 204;
- (k) a heavy chain variable region sequence of SEQ ID NO: 205 and a light chain variable region sequence of SEQ ID NO: 206;
- (l) a heavy chain variable region sequence of SEQ ID NO: 207 and a light chain variable region sequence of SEQ ID NO: 208;
- (m) a heavy chain variable region sequence of SEQ ID NO: 209 and a light chain variable region sequence of SEQ ID NO: 210;
- (n) a heavy chain variable region sequence of SEQ ID NO: 211 and a light chain variable region sequence of SEQ ID NO: 212;
- (o) a heavy chain variable region sequence of SEQ ID NO: 215 and a light chain variable region sequence of SEQ ID NO: 216;

- (p) a heavy chain variable region sequence of SEQ ID NO: 217 and a light chain variable region sequence of SEQ ID NO: 218; or
- (q) a heavy chain variable region sequence of SEQ ID NO: 219 and a light chain variable region sequence of SEQ ID NO: 220.

7. An ~~isolated~~ Fc-modified anti-human CLDN18.2 antibody comprising VH and VL sequences selected from:

- (a) a heavy chain variable region sequence of SEQ ID NO: 1 and a light chain variable region sequence of SEQ ID NO: 2;
- (b) a heavy chain variable region sequence of SEQ ID NO: 3 and a light chain variable region sequence of SEQ ID NO: 4;
- (c) a heavy chain variable region sequence of SEQ ID NO: 201 and a light chain variable region sequence of SEQ ID NO: 202; and
- (d) a heavy chain variable region sequence of SEQ ID NO: 203 and a light chain variable region sequence of SEQ ID NO: 204

wherein the antibody does not bind to CLDN18.1 and further wherein the Fc-modified antibody is characterized by enhanced ADCC activity relative to the ADCC activity of an antibody comprising the same variable VH and VL regions in combination with a wild-type human IgG1 Fc domain.

8. An ~~isolated~~ Fc-modified anti-human CLDN18.2 antibody comprising a recombinant heavy chain having the amino acid sequence SEQ ID NO :336 and a light chain comprising the sequence set for in SEQ ID NO: 337, wherein the Fc-modified antibody is characterized by enhanced ADCC activity relative to the ADCC activity of an antibody comprising the same variable VH and VL regions in combination with a wild-type human IgG1 Fc domain.

9. An isolated Fc-modified anti-human CLDN18.2 antibody comprising a recombinant heavy chain having the amino acid sequence SEQ ID NO :338 and a light chain comprising the sequence set for in SEQ ID NO: 337, wherein the Fc-modified antibody is characterized by enhanced ADCC activity relative to the ADCC activity of an antibody comprising the same variable VH and VL regions in combination with a wild-type human IgG1 Fc domain.

10. The ~~isolated~~ anti-human CLDN18.2 antibody ~~according to~~ claim 6, wherein the Fc-modified antibody is characterized by enhanced ADCC activity relative to the ADCC activity of an antibody comprising the same variable VH and VL regions in combination with a wild-type human IgG1 Fc domain.

11. The anti-human CLDN18.2 antibody of any one of claims 1-6, wherein the antibody is a fully human anti-human CLDN18.2 antibody.

12. The anti-human CLDN18.2 antibody of any one of claims 1-11, wherein the antibody is an isolated anti-human CLDN18.2 antibody.