

WHAT IS CLAIMED IS:

- 1.—An antibody or antigen-binding fragment which specifically binds to Claudin-18 (CLDN 18), wherein the antibody or antigen-binding fragment comprises ~~at least one heavy or light chain complementarity determining region (CDR) having an amino acid sequence selected from the group consisting of GDY, SEQ ID NOs: 18, 20, 22, 27, 29, 31, 36, 38, 40, 45, 47, 49, 54, 56, 58, 63, 65, 67, 72, 74, 81, 83, 85, 90, 92, 94, 99, 101, 103, 108, 110, 112, 117, 119, 121, 126, 128, 130, 135, 137, 139, 144, 146, 148, 153, 155, 157, 163, 165, 167, 172, 174, 176, 181, 183, 185, 190, 192, 194, 198, 200, 202, 207, 209, 211, 216, 218, 220, 225, 227, 229, 234, 236, 238, 243, 245, 247, 252, 254, 256, 261, 263, 265, 270, 272, 274, 279, 281, 283, 288, 290, 292, 297, 299, 301, 306, 308, 310, 315, 317, 319, 324, 326, 328, 333, 335, 337, 342, 344, 346, 351, 353, 355, 360, 362, 364, 369, 371, 373, 378, 380, 382, 387, 389, 391, 396, 398, 400, 405, 407, 409, 414, 416, 418, 423, 425, 427, 432, 434, 436, 441, 443, 445, 450, 452, 454, 459, 461, 463, 468, 470, 472, 477, 479, 481, 486, 488, 490, 495, 497, 499, 504, 506, 508, 513, 515, 517, 522, 524, 526, 531, 533, 535, 540, 542, 544, 549, 551, 553, 558, 560, 562, 567, 569, 571, 576, 578, 580, 585, 587, 589, 594, 596, 598, 603, 605, 607, 612, 614, 616, 621, 623, 625, 630, 632, 634, 639, 641, 643, 648, 650, 652, 657, 659, 661, 666, 668, 670, 675, 677, 679, 684, 686, 688, 693, 695, 726, 727, 728 and 697.~~
- 2.—The antibody or antigen-binding fragment of claim 1, comprising: a heavy chain variable (VH) region comprising ~~1, 2 or 3 VH CDR having an amino acid sequence selected from the group consisting of GDY, SEQ ID NOs: 18, 20, 22, 36, 38, 40, 54, 56, 58, 72, 74, 90, 92, 94, 108, 110, 112, 126, 128, 130, 144, 146, 148, 163, 165, 167, 181, 183, 185, 198, 200, 202, 216, 218, 220, 234, 236, 238, 252, 254, 256, 270, 272, 274, 288, 290, 292, 206, 308, 310, 324, 326, 328, 342, 344, 346, 360, 362, 364, 378, 380, 382, 396, 398, 400, 414, 416, 418, 432, 434, 436, 450, 452, 454, 468, 470, 472, 486, 488, 490, 504, 506, 508, 522, 524, 526, 540, 542, 544, 558, 560, 562, 576, 578, 580, 594, 596, 598, 612, 614, 616, 630, 632, 634, 648, 650, 652, 666, 668, 670, 684, 686, 726, 727 and 688.~~
- 3.—The antibody or antigen-binding fragment of claim 2, further comprising a light chain variable (VL) region comprising ~~1, 2 or 3 VL CDR having an amino acid sequence selected from the group consisting of SEQ ID NOs: 27, 29, 31, 45, 47, 49, 63, 65, 67, 81, 83, 85, 99, 101, 103, 117, 119, 121, 135, 137, 139, 153, 155, 157, 172, 174, 176, 190, 192, 194, 207, 209, 211, 225, 227, 229, 243, 245, 247, 261, 263, 265, 279, 281, 283, 297, 299, 301, 315, 317, 319, 333, 335, 337, 351, 353, 355, 369, 371, 373, 387, 389, 391, 405, 407, 409, 423, 425, 427, 441, 443, 445, 459, 461, 463, 477, 479, 481, 495, 497, 499, 513, 515, 517, 531, 533, 535, 549, 551, 553, 567,~~

~~569, 571, 585, 587, 589, 603, 605, 607, 621, 623, 625, 639, 641, 643, 657, 659, 661, 675, 677, 679, 693, 695, 728 and 697.~~

~~4. The antibody or antigen binding fragment of any of the preceding claims, comprising:~~

~~i. a VH CDR 1 having an amino acid sequence selected from the group consisting of GDY, SEQ ID NOs: 18, 36, 54, 72, 90, 108, 126, 144, 163, 181, 198, 216, 234, 252, 270, 288, 206, 324, 342, 360, 378, 396, 414, 432, 450, 468, 486, 504, 522, 540, 558, 576, 594, 612, 630, 648, 666 and 684;~~

~~ii. a VH CDR2 having an amino acid sequence selected from the group consisting of SEQ ID NOs: 20, 38, 56, 74, 92, 110, 128, 146, 165, 183, 200, 218, 236, 254, 272, 290, 308, 326, 344, 362, 380, 398, 416, 434, 452, 470, 488, 506, 524, 542, 560, 578, 596, 614, 632, 650, 668, 726, 727 and 686; and~~

~~iii. a VH CDR3 having an amino acid sequence selected from the group consisting of GDY and SEQ ID NOs: 22, 40, 58, 94, 112, 130, 148, 167, 185, 202, 220, 238, 256, 274, 292, 310, 328, 346, 364, 382, 400, 418, 436, 454, 472, 490, 508, 526, 544, 562, 580, 598, 616, 634, 652, 670 and 688.~~

~~5. The antibody or antigen binding fragment of claim 4, comprising:~~

~~i. a VL CDR 1 having an amino acid sequence selected from the group consisting of SEQ ID NOs: 27, 45, 63, 81, 99, 117, 135, 153, 172, 190, 207, 225, 243, 261, 279, 297, 315, 333, 351, 369, 387, 405, 423, 441, 459, 477, 495, 513, 531, 549, 567, 585, 603, 621, 639, 657, 675, 728 and 693;~~

~~ii. a VL CDR2 having an amino acid sequence selected from the group consisting of SEQ ID NOs: 29, 47, 65, 83, 101, 119, 137, 155, 174, 192, 209, 227, 245, 263, 281, 299, 317, 335, 353, 371, 389, 407, 425, 443, 461, 479, 497, 515, 533, 551, 569, 587, 605, 623, 641, 659, 677 and 695; and~~

~~iii. a VL CDR3 having an amino acid sequence selected from the group consisting of SEQ ID NOs: 31, 49, 67, 85, 103, 121, 139, 157, 176, 194, 211, 229, 247, 265, 283, 301, 319, 337, 355, 373, 391, 409, 427, 445, 463, 481, 499, 517, 535, 553, 571, 589, 607, 625, 643, 661, 679 and 697.~~

~~6. The antibody or antigen binding fragment of any of the preceding claims, comprising:~~

- i. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 18, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 20, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 22;~~
- ii. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 36, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 38, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 40;~~
- iii. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 54, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 56, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 58;~~
- iv. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 72, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 74, and a VH-CDR 3 having an amino acid sequence of GDY;~~
- v. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 90, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 92, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 94;~~
- vi. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 108, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 110, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 112;~~
- vii. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 126, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 128, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 130;~~
- viii. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 144, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 146, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 148;~~
- ix. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 163, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 165, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 167;~~
- x. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 181, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 183, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 185;~~

- xi. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 198, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 200, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 202;~~
- xii. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 216, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 218, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 220;~~
- xiii. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 234, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 236, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 238;~~
- xiv. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 252, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 254, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 256;~~
- xv. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 270, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 272, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 274;~~
- xvi. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 288, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 290, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 292;~~
- xvii. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 306, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 308, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 310;~~
- xviii. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 324, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 326, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 328;~~
- xix. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 342, a VH-CDR 2 having an amino acid sequence selected from the group consisting of SEQ ID NOs: 344, 726 and 727, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 346;~~
- xx. ~~a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 360, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 362, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 364;~~

- ~~xxi. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 378, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 380, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 382;~~
- ~~xxii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 396, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 398, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 400;~~
- ~~xxiii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 414, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 416, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 418;~~
- ~~xxiv. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 432, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 434, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 436;~~
- ~~xxv. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 450, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 452, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 454;~~
- ~~xxvi. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 468, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 470, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 472;~~
- ~~xxvii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 486, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 488, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 490;~~
- ~~xxviii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 504, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 506, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 508;~~
- ~~xxix. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 522, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 524, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 526;~~
- ~~xxx. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 540, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 542, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 544;~~

- ~~xxxi. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 558, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 560, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 562;~~
- ~~xxxii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 576, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 578, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 580;~~
- ~~xxxiii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 594, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 596, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 598;~~
- ~~xxxiv. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 612, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 614, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 616;~~
- ~~xxxv. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 630, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 632, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 634;~~
- ~~xxxvi. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 648, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 650, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 652;~~
- ~~xxxvii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 666, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 668, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 670; or~~
- ~~xxxviii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 684, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 686, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 688.~~

7. The antibody or antigen-binding fragment of claim 6, further comprising:

- ~~i. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 27, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 29, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 31;~~
- ~~ii. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 45, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 47, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 49;~~

- iii. ~~a VL CDR 1 having an amino acid sequence of SEQ ID NO: 63, a VL CDR 2 having an amino acid sequence of SEQ ID NO: 65, and a VL CDR 3 having an amino acid sequence of SEQ ID NO: 67;~~
- iv. ~~a VL CDR 1 having an amino acid sequence of SEQ ID NO: 81, a VL CDR 2 having an amino acid sequence of SEQ ID NO: 83, and a VL CDR 3 having an amino acid sequence of SEQ ID NO: 85; or~~
- v. ~~a VL CDR 1 having an amino acid sequence of SEQ ID NO: 99, a VL CDR 2 having an amino acid sequence of SEQ ID NO: 101, and a VL CDR 3 having an amino acid sequence of SEQ ID NO: 103;~~
- vi. ~~a VL CDR 1 having an amino acid sequence of SEQ ID NO: 117, a VL CDR 2 having an amino acid sequence of SEQ ID NO: 119, and a VL CDR 3 having an amino acid sequence of SEQ ID NO: 121;~~
- vii. ~~a VL CDR 1 having an amino acid sequence of SEQ ID NO: 135, a VL CDR 2 having an amino acid sequence of SEQ ID NO: 137, and a VL CDR 3 having an amino acid sequence of SEQ ID NO: 139;~~
- viii. ~~a VL CDR 1 having an amino acid sequence of SEQ ID NO: 153, a VL CDR 2 having an amino acid sequence of SEQ ID NO: 155, and a VL CDR 3 having an amino acid sequence of SEQ ID NO: 157;~~
- ix. ~~a VL CDR 1 having an amino acid sequence of SEQ ID NO: 172, a VL CDR 2 having an amino acid sequence of SEQ ID NO: 174, and a VL CDR 3 having an amino acid sequence of SEQ ID NO: 176;~~
- x. ~~a VL CDR 1 having an amino acid sequence of SEQ ID NO: 190, a VL CDR 2 having an amino acid sequence of SEQ ID NO: 192, and a VL CDR 3 having an amino acid sequence of SEQ ID NO: 194;~~
- xi. ~~a VL CDR 1 having an amino acid sequence of SEQ ID NO: 207, a VL CDR 2 having an amino acid sequence of SEQ ID NO: 209, and a VL CDR 3 having an amino acid sequence of SEQ ID NO: 211;~~
- xii. ~~a VL CDR 1 having an amino acid sequence of SEQ ID NO: 225, a VL CDR 2 having an amino acid sequence of SEQ ID NO: 227, and a VL CDR 3 having an amino acid sequence of SEQ ID NO: 229;~~

- ~~xiii. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 243, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 245, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 247;~~
- ~~xiv. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 261, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 263, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 265;~~
- ~~xv. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 279, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 281, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 283;~~
- ~~xvi. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 297, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 299, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 301;~~
- ~~xvii. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 315, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 317, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 319;~~
- ~~xviii. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 333, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 335, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 337;~~
- ~~xix. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 351 or SEQ ID NO: 728, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 353, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 355;~~
- ~~xx. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 369, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 371, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 373;~~
- ~~xxi. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 387, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 389, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 391;~~
- ~~xxii. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 405, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 407, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 409; or~~

- xxiii. ~~a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 423, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 425, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 427;~~
- xxiv. ~~a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 441, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 443, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 445;~~
- xxv. ~~a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 459, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 461, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 463;~~
- xxvi. ~~a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 477, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 479, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 481;~~
- xxvii. ~~a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 495, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 497, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 499;~~
- xxviii. ~~a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 513, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 515, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 517;~~
- xxix. ~~a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 531, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 533, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 535;~~
- xxx. ~~a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 549, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 551, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 553;~~
- xxxi. ~~a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 567, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 569, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 571;~~
- xxxii. ~~a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 585, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 587, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 589;~~

- ~~xxxiii. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 603, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 605, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 607;~~
- ~~xxxiv. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 621, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 623, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 625;~~
- ~~xxxv. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 639, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 641, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 643;~~
- ~~xxxvi. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 657, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 659, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 661;~~
- ~~xxxvii. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 675, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 677, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 679; or~~
- ~~xxxviii. a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 693, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 695, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 697.~~

~~8.1. The antibody or antigen-binding fragment of any of the preceding claims, comprising:~~

- i. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 18, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 20, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 22, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 27, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 29, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 31;
- ii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 36, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 38, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 40, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 45, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 47, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 49;
- iii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 54, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 56, and a VH-CDR 3 having an amino acid

- sequence of SEQ ID NO: 58, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 63, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 65, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 67;
- iv. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 72, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 74, and a VH-CDR 3 having an amino acid sequence of GDY, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 81, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 83, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 85;
 - v. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 90, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 92, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 94, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 99, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 101, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 103;
 - vi. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 108, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 110, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 112, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 117, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 119, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 121;
 - vii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 126, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 128, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 130, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 135, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 137, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 139;
 - viii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 144, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 146, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 148, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 153, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 155, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 157;
 - ix. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 163, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 165, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 167, a VL-CDR 1 having an amino acid sequence of SEQ ID

- NO: 172, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 174, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 176;
- x. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 181, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 183, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 185, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 190, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 192, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 194;
 - xi. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 198, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 200, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 202, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 207, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 209, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 211;
 - xii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 216, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 218, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 220, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 225, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 227, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 229;
 - xiii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 234, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 236, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 238, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 243, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 245, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 247;
 - xiv. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 252, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 254, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 256, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 261, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 263, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 265;
 - xv. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 270, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 272, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 274, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 279, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 281, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 283;

- xvi. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 288, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 290, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 292, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 297, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 299, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 301;
- xvii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 306, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 308, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 310, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 315, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 317, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 319;
- xviii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 324, a VH-CDR 2 having an amino acid sequence selected from the group consisting of SEQ ID NOs: 326, 726 and 727, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 328, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 333 or 728, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 335, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 337;
- xix. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 342, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 344, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 346, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 351, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 353, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 355;
- xx. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 360, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 362, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 364, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 369, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 371, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 373;
- xxi. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 378, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 380, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 382, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 387, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 389, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 391;

- xxii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 396, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 398, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 400, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 405, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 407, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 409;
- xxiii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 414, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 416, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 418, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 423, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 425, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 427;
- xxiv. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 432, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 434, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 436, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 441, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 443, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 445;
- xxv. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 450, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 452, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 454, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 459, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 461, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 463;
- xxvi. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 468, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 470, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 472, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 477, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 479, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 481;
- xxvii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 486, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 488, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 490, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 495, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 497, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 499;
- xxviii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 504, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 506, and a VH-CDR 3 having an amino acid

sequence of SEQ ID NO: 508, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 513, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 515, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 517;

- xxix. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 522, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 524, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 526, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 531, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 533, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 535;
- xxx. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 540, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 542, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 544, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 549, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 551, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 553;
- xxxi. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 558, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 560, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 562, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 567, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 569, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 571;
- xxxii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 576, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 578, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 580, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 585, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 587, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 589;
- xxxiii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 594, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 596, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 598, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 603, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 605, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 607;
- xxxiv. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 612, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 614, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 616, a VL-CDR 1 having an amino acid sequence of SEQ ID

NO: 621, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 623, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 625;

xxxv. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 630, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 632, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 634, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 639, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 641, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 643;

xxxvi. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 648, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 650, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 652, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 657, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 659, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 661;

xxxvii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 666, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 668, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 670, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 675, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 677, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 679; or

xxxviii. a VH-CDR 1 having an amino acid sequence of SEQ ID NO: 684, a VH-CDR 2 having an amino acid sequence of SEQ ID NO: 686, and a VH-CDR 3 having an amino acid sequence of SEQ ID NO: 688, a VL-CDR 1 having an amino acid sequence of SEQ ID NO: 693, a VL-CDR 2 having an amino acid sequence of SEQ ID NO: 695, and a VL-CDR 3 having an amino acid sequence of SEQ ID NO: 697.

9.2. The antibody or antigen-binding fragment of ~~any of the preceding claims~~ 1, comprising a pair of heavy chain variable region and light chain variable region sequences selected from the group consisting of: SEQ ID NOs: 25/34, SEQ ID NOs: 43/52, SEQ ID NOs: 61/70, SEQ ID NOs: 79/88, SEQ ID NOs: 97/106, SEQ ID NOs: 115/124, SEQ ID NOs: 133/142, SEQ ID NOs: 151/160, SEQ ID NOs: 205/214, SEQ ID NOs: 223/232, SEQ ID NOs: 241/250, SEQ ID NOs: 259/268, SEQ ID NOs: 277/286, SEQ ID NOs: 295/304, SEQ ID NOs: 313/322, SEQ ID NOs: 331/340, SEQ ID NOs: 349/358, SEQ ID NOs: 367/376, SEQ ID NOs: 385/394, SEQ ID NOs: 403/412, SEQ ID NOs: 421/430, SEQ ID NOs: 439/448, SEQ ID NOs: 457/466, SEQ ID NOs: 475/484, SEQ ID NOs: 493/502, SEQ ID NOs: 511/520, SEQ ID NOs: 529/538, SEQ ID NOs: 547/556, SEQ ID NOs: 565/574, SEQ ID NOs: 583/592, SEQ ID NOs: 601/610, SEQ ID

NOs: 619/628, SEQ ID NOs: 637/646, SEQ ID NOs: 655/664, SEQ ID NOs: 673/682, SEQ ID NOs: 691/161, SEQ ID NOs: 170/179, SEQ ID NOs: 188/76, or a pair of homologous sequences thereof having at least 80%, 85%, 90%, 95%, 97%, 98%, or 99% sequence identity yet retains specific binding affinity to CLDN 18.

~~10.3.~~ The antibody or antigen-binding fragment of ~~any of~~ claims 1-8, comprising:

- a) a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 704, SEQ ID NO: 705, SEQ ID NO: 706 and SEQ ID NO: 707, and a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 708, SEQ ID NO: 709 and SEQ ID NO: 710; or
- b) a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 711, SEQ ID NO: 712, SEQ ID NO: 713 and SEQ ID NO: 714, and a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 715, SEQ ID NO: 716 and SEQ ID NO: 717; or
- ~~e)~~—a heavy chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 718, SEQ ID NO: 719, SEQ ID NO: 720, SEQ ID NO: 721 -and SEQ ID NO: 722, -and a light chain variable region comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 723, SEQ ID NO: 724 and SEQ ID NO: 725.

~~c)~~

~~11.4.~~ The antibody or antigen-binding fragment of any of the preceding claims, further comprising one or more amino acid residue substitutions or modifications that yet retains specific binding affinity to CLDN 18.

~~12.~~ The antibody or antigen-binding fragment of claim 11, wherein at least one of the substitutions or modifications is in one or more of the CDR sequences, and/or in one or more of the non-CDR sequences of the heavy chain variable region or light chain variable region.

~~13.~~ The antibody or antigen-binding fragment of the preceding claims, further comprising one or more non-natural amino acid (NNAA) substitution.

~~14.~~ The antibody or antigen-binding fragment of claim 13, wherein the NNAA is capable of being conjugated.

- ~~15. An antibody or antigen-binding fragment thereof, recognizing the same antigenic determinant site as that of the antibody or antigen-binding fragment of any of the preceding claims.~~
- ~~16. The antibody or antigen-binding fragment of any of the preceding claims, the antibody or antigen-binding fragment is a monoclonal antibody or antigen-binding fragment thereof, a polyclonal antibody or antigen-binding fragment thereof, a bispecific antibody or antigen-binding fragment thereof, a chimeric antibody or antigen-binding fragment thereof, a humanized antibody or antigen-binding fragment thereof, a recombinant antibody or antigen-binding fragment thereof, a human antibody or antigen-binding fragment thereof, a labeled antibody or antigen-binding fragment thereof, a bivalent antibody or antigen-binding fragment thereof, or an anti-idiotypic antibody or antigen-binding fragment thereof, or~~
- ~~17.5. The antibody or antigen-binding fragment of any of the preceding claims, the antibody or antigen-binding fragment is a camelized single domain antibody, a diabody, a scFv, an scFv dimer, a dsFv, a (dsFv)₂, a dsFv-dsFv', an Fv fragment, a Fab, a Fab', a F(ab')₂, a ds-diabody, a nanobody, a domain antibody, or a bivalent domain antibody.~~
- ~~18.6. The antibody or antigen-binding of any of the preceding claims, further comprising an immunoglobulin constant region.~~
- ~~19. The antibody or antigen-binding fragment of claim 18, wherein the immunoglobulin constant region is a λ light chain, κ light chain, γ 1 heavy chain, γ 2 heavy chain, γ 3 heavy chain, or γ 4 heavy chain constant region.~~
- ~~20. The antibody or antigen-binding fragment of any of the preceding claims, wherein the antibody or antigen-binding fragment is human IgG1 isotype.~~
- ~~21.7. The antibody or antigen-binding fragment of claim 18~~6~~, wherein the immunoglobulin constant region comprises an Fc region having an amino acid sequence selected from the group consisting of SEQ ID NOs: 700-703.~~
- ~~22. The antibody or antigen-binding fragment of any of the preceding claims, wherein the antibody or antigen-binding fragment specifically binds to CLDN 18.1 protein and/or CLDN 18.2 protein.~~
- ~~23. The antibody or antigen-binding fragment of any of claims 1-21, wherein the antibody or antigen-binding fragment binds to both CLDN 18.1 protein and CLDN 18.2 protein.~~

- ~~24.8.~~ The antibody or antigen-binding fragment of any of the preceding claims 22, wherein the binding affinity or the max MFI of the antibody or antigen-binding fragment to a cell expressing CLDN 18.2 is higher than or comparable with ~~a reference antibody~~ IMAB362.
- ~~25.~~ The antibody or antigen-binding fragment of claim 24, wherein the max MFI of the antibody or antigen-binding fragment to a cell expressing CLDN 18.2 is higher than IMAB362, the reference antibody
- ~~26.~~ The antibody or antigen-binding fragment of claim 24 or 25, wherein the reference antibody is IMAB362.
- ~~27.~~ The antibody or antigen-binding fragment of any of claims 24-26, wherein the surface expression of CLDN 18.2 on the cell is low.
- ~~28.~~ The antibody or antigen-binding fragment of any one of claims 24-26, wherein the binding affinity is determined by FACS or ELISA.
- ~~29.9.~~ The antibody or antigen-binding fragment of any one of the preceding claims 22-28, wherein the antibody or antigen-binding fragment binds to the CLDN 18.2 protein with an EC₅₀ of less than about 10 nM, less than about 8 nM, less than about 6 nM, less than about 4 nM, or less than about 2 nM.
- ~~30.10.~~ The antibody or antigen-binding fragment of any of the preceding claims, being linked to one or more conjugate moieties.
- ~~31.11.~~ The antibody or antigen-binding fragment of claim ~~30~~10, wherein the conjugate moiety comprises an active agent, a radioactive isotope, a detectable label, a pharmacokinetic modifying moiety, or a purifying moiety.
- ~~32.~~ The antibody or antigen-binding fragment of claim 30, wherein the conjugate moiety is covalently attached either directly or via a linker.
- ~~33.12.~~ A chimeric antigen receptor, comprising the antibody or antigen-binding fragment of any one of claims 1-~~32~~11, a transmembrane region and an intracellular signal region.
- ~~34.~~ The chimeric antigen receptor of claim 33, wherein the intracellular signal region is selected from the group consisting of: an intracellular signal regions sequence of CD3, FcγRI, CD27, CD28, CD137, CD134, MyD88, CD40, CD278, TLRs, or a combination thereof.
- ~~35.~~ The chimeric antigen receptor of claim 33 or 34, wherein the transmembrane region comprises a transmembrane region of CD3, CD4, CD8 or CD28.

- ~~36.13.~~ 36.13. An isolated polynucleotide encoding the antibody or antigen-binding fragment of any one of claims ~~1-32~~ 11 or the chimeric antigen receptor of ~~any one of claims 33-35~~ 12.
- ~~37.14.~~ 37.14. The isolated polynucleotide of claim ~~36~~ 13, comprising a nucleotide sequence selected from a group consisting of: SEQ ID NOs: 24, 42, 60, 78, 96, 114, 132, 150, 204, 222, 240, 258, 276, 294, 312, 330, 348, 366, 384, 402, 420, 438, 456, 474, 492, 510, 528, 546, 564, 582, 600, 618, 636, 654, 672, 690, 169, 187, or a homologous sequence thereof having at least 80% sequence identity.
- ~~38.15.~~ 38.15. The isolated polynucleotide of claim ~~37~~ 14, further comprising a nucleotide sequence selected from a group consisting of: SEQ ID NOs: 33, 51, 69, 87, 105, 123, 141, 159, 213, 231, 249, 267, 285, 303, 321, 339, 357, 375, 393, 411, 429, 447, 465, 483, 501, 519, 537, 555, 573, 591, 609, 627, 645, 663, 681, 699, 178, 196, or a homologous sequence thereof having at least 80% sequence identity.
- ~~39.16.~~ 39.16. A vector comprising the polynucleotide of any of claims ~~37-38~~ 14-15.
- ~~40.17.~~ 40.17. A host expression system comprising the vector of claim ~~39~~ 16 or having the polynucleotide of any of claims ~~37-38~~ 14-15 integrated into genome thereof.
- ~~41.~~ 41. ~~The host expression system of 40, being a microorganism, a yeast, or a mammalian cell, wherein the microorganism is selected from the group consisting of *E. coli* and *B. subtilis*, wherein the yeast is *Saccharomyces*, and wherein the mammalian cell is selected from the group consisting of COS, CHO-S, CHO-K1, HEK 293, and 3T3 cells.~~
- ~~42.18.~~ 42.18. A virus comprising the vector of claim ~~39~~ 16.
- ~~43.19.~~ 43.19. A method of expressing the antibody or antigen-binding fragment of any one of claims ~~1-32~~ 11 or the chimeric antigen receptor of ~~any one of claims 33-35~~ 12, comprising culturing the host expression system of claim ~~40 or 41~~ 17 under conditions in which the antibody or antigen-binding fragment of any one of claims ~~1-32~~ 11 or the chimeric antigen receptor of ~~any one of claims 33-35~~ 12 is expressed.
- ~~44.20.~~ 44.20. An antibody-drug conjugate comprising the antibody or antigen-binding fragment thereof of any one of claims ~~1-32~~ 11, linked to one or more therapeutic agents directly or via a linker.
- ~~45.21.~~ 45.21. The antibody-drug conjugate of claim ~~44~~ 20, wherein the one or more therapeutic agents comprise cytotoxic agent, such as Monomethylauristatin F (MMAF).
- ~~46.22.~~ 46.22. A modified immune cell targeting cells expressing CLDN 18.2, comprising the antibody or antigen-binding fragment thereof of any one of claims ~~1-32~~ 11 or the chimeric antigen receptor

of ~~any one of claims 33-35~~12, the polynucleotide of any of claims ~~35~~13-3715, the vector of claim ~~38~~16 or the virus of claim ~~42~~18.

~~47. The modified immune cell of claim 46, wherein the cells expressing CLDN 18.2 are selected from the group consisting of: gastric cancer cells, pancreatic cancer cells, esophageal cancer cells, lung cancer cells, gallbladder cancer cells, colorectal cancer, and liver cancer cells.~~

~~48.23. The modified immune cell of claim 46 or 47~~22, wherein the immune cell is T lymphocyte, NK cell, monocyte, macrophage or NKT lymphocyte.

~~49. The modified immune cell of any of claims 46-48, further having one or more features selected from the group consisting of:~~

- ~~i. carrying an encoding sequence for an exogenous cytokine,~~
- ~~ii. expressing another chimeric antigen receptor, or a combination thereof,~~
- ~~iii. expressing a chemokine receptor~~
- ~~iv. expressing an siRNA that reduces expression of an immune checkpoint inhibitor or a protein that blocks the immune checkpoint inhibitor,~~
- ~~v. having endogenous immune checkpoint inhibitor knocked out~~
- ~~vi. expressing secretable antibody sc fv~~
- ~~vii. expressing a co-stimulatory protein~~
- ~~viii. expressing a safety switch.~~

~~50. The modified immune cell of claim 49, wherein the immune checkpoint inhibitor is selected from the group consisting of PD 1, CTLA 4, LAG 3, TIM 3.~~

~~51.24. A pharmaceutical composition comprising the antibody or antigen-binding fragment of any one of claims 1-3~~211, the chimeric antigen receptor of ~~any one of claims 33-35~~12, the polynucleotide of any of claims ~~36~~13-3815, the vector of claim ~~39~~16, the virus of claim ~~42~~18, or the modified immune cell of any one of claims ~~46~~22-5023, and one or more pharmaceutically acceptable carriers.

~~52. The pharmaceutical composition of claim 51, wherein said one or more pharmaceutical acceptable carriers are selected from the group consisting of pharmaceutically acceptable liquid, gel, solid carriers, aqueous vehicles, nonaqueous vehicles, antimicrobial agents, isotonic agents, buffers, antioxidants, anesthetics, suspending/dispersing agents, sequestering or chelating agents, diluents, adjuvants, excipients, and non-toxic auxiliary substances.~~

~~53. The pharmaceutical composition of claim 51 or 52, further comprises one or more therapeutic agents.~~

~~54. The pharmaceutical composition of claim 44 or 53, wherein the one or more therapeutic agents are selected from the group consisting of amrubicin, apatinib mesylate, atrasentan batabulin, calcitriol, capecitabine, cilengitide, dasatinib, decatanib, edotecarin, enzastaurin, erlotinib, everolimus, gimatecan, gossypol ipilimumab, lonafarnib, lucanthone, neuradiab, nolatrexed, oblimersen, olaparib, ofatumumab, oregovomab, panitumumab, pazopanibrubitecan, regorafenib talampanel, tegafur, temsirolimus, tesmilifene, tetrandrine, ticilimumab, trametinib, trabectedin, vandetanib, vitespan, zanolimumab, zolendronate, histrelin, azacitidine, dexrazoxane, alemtuzumab, lenalidomide, gemtuzumab, ketoconazole, nitrogen mustard, ibritumomab tiuxetan, decitabine, hexamethylmelamine, bexarotene, tositumomab, arsenic trioxide, editronate, cyclosporine, Edwina asparaginase, epirubicin, oxaliplatin, an anti-PD1 antibody, an anti-PDL1 antibody, an anti-HER2 antibody, an anti-HER2 ADC, 5-fluorouracil and strontium 89.~~

~~55.25. A kit comprising:~~

~~a container, and the pharmaceutical composition of any one of claims 51-54~~24; or

~~a container, and the antibody or antigen-binding fragment of any one of claims 1-32~~11, the chimeric antigen receptor of ~~any one of claims 33-35~~12, the polynucleotide of any of claims ~~36~~13-~~38~~15, the vector of claim ~~39~~16, the virus of claim ~~42~~18, or the modified immune cell of any one of claims ~~46~~22-~~50~~23.

~~56. A method for treating or preventing a CLDN-related condition in a subject, comprising administering a therapeutically effective amount of the antibody or antigen-binding fragment of any one of claims 1-32, the chimeric antigen receptor of any one of claims 33-35, the polynucleotide of any of claims 36-38, the vector of claim 39, the virus of claim 42, or the modified immune cell of any one of claims 46-50 to the subject.~~

~~57. The method of claim 56, wherein the CLDN-related condition is cancerous condition.~~

~~58. The method of claim 57, wherein the cancerous condition is selected from the group consisting of lung cancer (e.g., small cell lung cancer, non-small cell lung cancer (NSCLC), adenocarcinoma of the lung, or squamous cell carcinoma of the lung), gastric or stomach cancer (e.g., gastrointestinal cancer), pancreatic cancer, esophageal cancer, liver cancer (e.g., hepatocellular carcinoma/hepatoma), squamous cell cancer, cancer of the peritoneum, brain tumor (e.g., glioblastoma/glioblastoma multiforme (GBM), non-glioblastoma brain tumor, or~~

meningioma), glioma (e.g., ependymoma, astrocytoma, anaplastic astrocytoma, oligodendroglioma, or mixed glioma such as oligoastrocytoma), cervical cancer, ovarian cancer, liver cancer (e.g., hepatoblastoma, hepatocellular carcinoma/hepatoma, or hepatic carcinoma), bladder cancer (e.g., urothelial cancer), breast cancer, colon cancer, colorectal cancer, rectal cancer, endometrial or uterine carcinoma, salivary gland carcinoma, kidney or renal cancer (e.g., rhabdoid tumor of the kidney), prostate cancer, vulval cancer, penile cancer, anal cancer (e.g., anal squamous cell carcinoma), thyroid cancer, head and neck cancer (e.g., nasopharyngeal cancer), skin cancer (e.g., melanoma or squamous cell carcinoma), osteosarcoma, Ewing's sarcoma, chondrosarcoma, soft tissue sarcoma (e.g., rhabdomyosarcoma, fibrosarcoma, Kaposi's sarcoma), carcinoid cancer, eye cancer (e.g., retinoblastoma), mesothelioma, lymphocytic/lymphoblastic leukemia (e.g., acute lymphocytic/lymphoblastic leukemia (ALL) of both T-cell lineage and B-cell precursor lineage, chronic lymphoblastic/lymphocytic leukemia (CLL), acute myelogenous/myeloblastic leukemia (AML), including mast cell leukemia, chronic myelogenous/myelocytic/myeloblastic leukemia (CML), hairy cell leukemia (HCL), Hodgkin's disease, non-Hodgkin's lymphoma, chronic myelomonocytic leukemia (CMML), follicular lymphoma (FL), diffuse large B-cell lymphoma (DLCL), mantle cell lymphoma (MCL), Burkitt's lymphoma (BL), mycosis fungoides, Sezary syndrome, cutaneous T-cell lymphoma, mast cell neoplasm, medulloblastoma, nephroblastoma, solitary plasmacytoma, myelodysplastic syndrome, chronic and non-chronic myeloproliferative disorder, central nervous system tumor, pituitary adenoma, vestibular schwannoma, primitive neuroectodermal tumor, ependymoma, choroid plexus papilloma, polycythemia vera, thrombocythemia, gallbladder cancer, idiopathic myelofibrosis, and pediatric cancers such as pediatric sarcomas (e.g., neuroblastoma, rhabdomyosarcoma, and osteosarcoma).

59. The method of any one of claims 56-58, wherein the administration is through a parenteral route comprising subcutaneous, intraperitoneal, intravenous, intramuscular, or intradermal injection; or a non-parenteral route comprising transdermal, oral, intranasal, intraocular, sublingual, rectal, or topical.
60. The method of any one of claims 56-59, wherein the method further includes administering to the subject in need thereof an additional therapeutic agent.
61. The method of claim 60, wherein the additional therapeutic agent is selected from the group consisting of: an active agent, an imaging agent, a cytotoxic agent, and angiogenesis inhibitor, a kinase inhibitor, a co-stimulation molecule agonist, a co-inhibition molecule blocker, an

~~adhesion molecule blocker, an anti-cytokine antibody or functional fragment thereof, a detectable label or reporter, an antimicrobial, a gene editing agent, a beta agonist, an viral RNA inhibitor, a polymerase inhibitor, an interferon, and a microRNA.~~

~~62. The method of claim 60 or 61, wherein the additional therapeutic agent is administered to the subject in need before administration of the composition of any one of claims 51-54, after administration of the composition of any one of claims 51-54, and/or at the same time as the composition of any one of claims 51-54.~~

~~63. A method for diagnosing a CLDN-related condition, comprising detecting the CLDN by using the antibody or antigen binding fragment of any one of claims 1-32, the chimeric antigen receptor of any one of claims 33-35, the polynucleotide of any of claims 36-38, the vector of claim 39, the virus of claim 42, the modified immune cell of any one of claims 46-50, the antibody-drug conjugate of claim 44, the pharmaceutical composition of any one of claims 49-52, or the kit of claim 55.~~

~~64. The method of claim 63, wherein the CLDN is CLDN 18.2 or CLDN 18.1.~~

~~65. The method of claim 63, wherein condition is selected from the group consisting of: gastric cancer, pancreatic cancer, esophageal cancer, lung cancer, gallbladder cancer, colorectal cancer and liver cancer.~~

~~66.26. A method for inducing the death of a cell expressing CLDN 18.2, comprising contacting the cell expressing CLDN 18.2 with the antibody or antigen-binding fragment of any one of claims 1-1132, the chimeric antigen receptor of any one of claims 1233-35, the polynucleotide of any of claims 1336-1538, the vector of claim 1639, the virus of claim 1842, the modified immune cell of any one of claims 22 or 2346-50, the antibody-drug conjugate of claim 2044, the pharmaceutical composition of any one of claims 2449-52, or the kit of claim 2555, *in vitro*.~~

~~67. The method of claim 66, wherein the cell is contacted with the antibody or antigen-binding fragment of any one of claims 1-32, the chimeric antigen receptor of any one of claims 33-35, the polynucleotide of any of claims 36-38, the vector of claim 39, the virus of claim 42, the modified immune cell of any one of claims 46-50, the antibody-drug conjugate of claim 44, the pharmaceutical composition of any one of claims 49-52, or the kit of claim 55, *in vitro* or *in vivo*.~~

~~68. The method of claim 66 or 67, wherein the cell is a cancer cell or a solid tumor cell.~~

~~69. The method of claim 66 or 67, wherein the cell is a solid tumor cell.~~

~~70. Use of the antibody or antigen-binding fragment of any one of claims 1-32, the chimeric antigen receptor of any one of claims 33-35, the polynucleotide of any of claims 36-38, the vector of claim 39, the virus of claim 42, the modified immune cell of any one of claims 46-50, the antibody drug conjugate of claim 44, the pharmaceutical composition of any one of claims 49-52, or the kit of claim 55 in the manufacture of a medicament for treating CLDN-related condition in a subject in need thereof.~~

~~71. Use of the antibody or antigen-binding fragment of any one of claims 1-32, the chimeric antigen receptor of any one of claims 33-35, the polynucleotide of any of claims 36-38, the vector of claim 39, the virus of claim 42, the modified immune cell of any one of claims 46-50, the antibody drug conjugate of claim 44, the pharmaceutical composition of any one of claims 49-52, or the kit of claim 55 in the manufacture of a diagnostic reagent for detecting CLDN-related condition.~~

~~72.27. The antibody or antigen-binding fragment of any one of claims 1-1132, the chimeric antigen receptor of any one of claims 1233-35, the polynucleotide of any of claims 1336-1538, the vector of claim 1639, the virus of claim 1842, the modified immune cell of any one of claims 22 or 2346-50, the antibody-drug conjugate of claim 2044, the pharmaceutical composition of any one of claims 2449-52, or the kit of claim 2555 for use in a method for treating or preventing a CLDN-related condition in a subject in need thereof.~~

~~73.28. The antibody or antigen-binding fragment of any one of claims 1-1132, the chimeric antigen receptor of any one of claims 1233-35, the polynucleotide of any of claims 1336-1538, the vector of claim 1639, the virus of claim 1842, the modified immune cell of any one of claims 22 or 2346-50, the antibody-drug conjugate of claim 2044, the pharmaceutical composition of any one of claims 2449-52, or the kit of claim 2555 for use in a method for diagnosing or detecting a CLDN-related condition, wherein the antibody or antigen-binding fragment, the chimeric antigen receptor, the polynucleotide, the vector, the virus, the modified immune cell, the antibody-drug conjugate, the pharmaceutical composition, or the kit is to be used to detect the CLDN.~~

29. The antibody or antigen-binding fragment of any one of claims 1-11, the chimeric antigen receptor of claim 12, the polynucleotide of any of claims 13-15, the vector of claim 16, the virus of claim 18, the modified immune cell of claims 22 or 23, the antibody-drug conjugate of claim 20, the pharmaceutical composition of claim 24, or the kit of claim 25 for use in a method for inducing the death of a cell expressing CLDN 18.2, wherein the antibody or

antigen-binding fragment, the chimeric antigen receptor, the polynucleotide, the vector, the virus, the modified immune cell, the antibody-drug conjugate, the pharmaceutical composition, or the kit is to be contacted with the cell expressing CLDN 18.2.