

CLAIMS

~~What is claimed is:~~

1. An isolated dual binding antibody comprising three complementarity determining regions (CDRs) on a heavy chain (HCDR1, HCDR2, and HCDR3) and three CDRs on a light chain (LCDR1, LCDR2, and LCDR3), wherein
 - (i) the HCDR1 comprises the amino acid sequence set forth in any one of SEQ ID NOs: 349, 355, 149 or 136~~of SEQ ID NO:349 or 355, or the amino acid sequence of SEQ ID NO:149 or SEQ ID NO:136;~~
 - (ii) the HCDR2 comprises the amino acid sequence set forth in any one of SEQ ID NOs: 350, 352, 354, 356, or 150, or the sequence set forth as: I HX1 Y D G S N K (SEQ ID NO:142), wherein HX1 is any amino acid~~of one of SEQ ID NOs:350, 352, 354 and 356, or the amino acid sequence of SEQ ID NO:150 or the sequence set forth as: I HX1 Y D G S N K (SEQ ID NO:142), wherein HX1 is any amino acid;~~
 - (iii) the HCDR3 comprises the amino acid sequence set forth in any one of SEQ ID NOs: 351, 353, 357, 358, or 151, or the sequence set forth as: A R HX2 HX3 HX4 HX5 HX6 HX7 HX8 HX9 HX10 HX11 F D HX12 (SEQ ID NO:143), wherein HX2, HX3, HX4, HX5, HX6, HX7, HX8, HX9, HX10, HX11, and HX12 are any amino acid~~of one of SEQ ID NOs:351, 353, 357, and 358, or the amino acid sequence of SEQ ID NO:151 or the sequence set forth as: A R HX2 HX3 HX4 HX5 HX6 HX7 HX8 HX9 HX10 HX11 F D HX12 (SEQ ID NO:143), wherein HX2, HX3, HX4, HX5, HX6, HX7, HX8, HX9, HX10, HX11, and HX12 are any amino acid;~~
 - (iv) the LCDR1 comprises the amino acid sequence set forth in any one of SEQ ID NOs: 364, 359, 362, 366, 369, 375, or 152, or the sequence set forth as LX1, LX2, G S K LX3 V (SEQ ID NO:144), wherein LX1, LX2, and LX3 are any amino acid~~of one of SEQ ID NOs:359, 362, 364, 366, 369, and 375, or the amino acid sequence of SEQ ID NO:152 or the sequence set forth as LX1, LX2, G S K LX3 V (SEQ ID NO:144), wherein LX1, LX2, and LX3 are any amino acid;~~

(v) the LCDR2 comprises the amino acid sequence set forth in any one of SEQ ID NOs: 360, or 367, or the amino acid sequence of SEQ ID NO:153, or the sequence set forth as D D LX4 (SEQ ID NO:145), wherein LX4 is any amino acid; and

(vi) the LCDR3 comprises the amino acid sequence set forth in any of one of SEQ ID NOs: 384, 361, 363, 365, 368, 370-374, 376-383, 385-407, or 154, or the sequence set forth as Q V W D LX5 LX6 S D LX7 V V (SEQ ID NO:146), wherein LX5, LX6, and LX7 are any amino acid~~361, 363, 365, 368, 370-374, 376-407, or the amino acid sequence of SEQ ID NO:154 or the sequence set forth as Q V W D LX5 LX6 S D LX7 V V (SEQ ID NO:146), wherein LX5, LX6, and LX7 are any amino acid.~~

2. ~~The isolated dual binding antibody of claim 1, wherein~~

~~the HCDR1, HCDR2 and HCDR3 comprise the amino acid sequences of SEQ ID NOs:349, 350 and 351 respectively, and the LCDR1, LCDR2 and LCDR3 comprise the amino acid sequences of SEQ ID NOs:359, 360 and 361 respectively; or~~

~~the HCDR1, HCDR2 and HCDR3 comprise the amino acid sequences of SEQ ID NOs:349, 356 and 351 respectively, and the LCDR1, LCDR2 and LCDR3 comprise the amino acid sequences of SEQ ID NOs:364, 360 and 371 respectively; or~~

~~the HCDR1, HCDR2 and HCDR3 comprise the amino acid sequences of SEQ ID NOs:349, 350 and 351 respectively, and the LCDR1, LCDR2 and LCDR3 comprise the amino acid sequences of SEQ ID NOs:362, 360 and 384 respectively; or~~

~~the HCDR1, HCDR2 and HCDR3 comprise the amino acid sequences of SEQ ID NOs:349, 350 and 351 respectively, and the LCDR1, LCDR2 and LCDR3 comprise the amino acid sequences of SEQ ID NOs:364, 360 and 384 respectively.~~

32. The isolated dual binding antibody of claim 1, wherein the HCDR1, HCDR2 and HCDR3 comprise the amino acid sequences as shown in Table 8 or Table 4, wherein the LCDR1, LCDR2 and LCDR3 comprise the amino acid sequences as shown in Table 9 or Table 5 amino acid sequences of the HCDRs and the LCDRs of said antibody are selected from any one of the following sets:
- (a) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 349, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 364, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 360, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 384;
 - (b) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 349, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 359, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 360, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 361;
 - (c) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 349, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 356, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 364, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 360, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 371;
 - (d) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 349, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 362, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 360, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 384;

- (e) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 349,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 352,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 353,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 362,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 360, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 363;
- (f) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 349,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 354,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 364,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 360, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 365;
- (g) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 349,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 352,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 366,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 368;
- (h) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 356,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 370;
- (i) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 349,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 352,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 353,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 362,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 372;

- (j) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 349,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 359,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 360, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 373;
- (k) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 349,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 364,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 360, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 374;
- (l) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 357,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 375,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 376;
- (m) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 349,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 362,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 360, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 377;
- (n) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 356,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 378;

- (o) HCDR1 comprises the amino acid sequences amino acid sequence set forth in SEQ ID NO: 355, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 356, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 379;
- (p) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 349, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 359, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 360, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 380;
- (q) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 356, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 379;
- (r) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 352, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 381;
- (s) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 357, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 370;

- (t) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 356,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 366,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 382;
- (u) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 370;
- (v) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 356,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 383;
- (w) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 352,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 366,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 385;
- (x) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350,

- HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 386;
- (y) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 352,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 387;
- (z) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 356,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 388;
- (aa) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 356,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 389;
- (bb) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 352,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 379;

- (cc) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 352,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 390;
- (dd) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 366,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 391;
- (ee) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 375,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 392;
- (ff) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 354,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 393;
- (gg) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 356,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 394;

- (hh) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 356,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 395;
- (ii) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 396;
- (jj) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 352,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 397;
- (kk) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 398;
- (ll) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 388;

- (mm) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 394;
- (nn) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 375, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 398;
- (oo) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 352, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 357, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 375, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 399;
- (pp) HCDR1 is set forth in SEQ ID NO: 355, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 375, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 400;
- (qq) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 357, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 375, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 398;

- (rr) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 349, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 378;
- (ss) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 375, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 401;
- (tt) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 356, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 358, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 402;
- (uu) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 349, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 356, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 358, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 403;
- (vv) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355, HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 356, HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 358, LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 375, LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 376;

- (wy) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 402;
- (xx) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 349,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 353,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 359,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 360, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 404;
- (yy) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 357,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 375,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 405;
- (zz) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 366,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 406;
- (aaa) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 350,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 375,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 407; and

(bbb) HCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 355,
HCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 354,
HCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 351,
LCDR1 comprises the amino acid sequence set forth in SEQ ID NO: 369,
LCDR2 comprises the amino acid sequence set forth in SEQ ID NO: 367, and
LCDR3 comprises the amino acid sequence set forth in SEQ ID NO: 379.

4. ~~The isolated dual binding antibody of claim 1,~~

~~wherein HX1 is W or S; HX2 is A or S; HX3 is P; HX4 is Q; HX5 is W; HX6 is E, Q, M, L, or V; HX7 is L, W, or Y; HX8 is V or T; HX9 is H, A, or S; HX10 is E; HX11 is A; HX12 is I, L, or M;~~

~~wherein LX1 is N, L, or I; LX2 is L or I; LX3 is S or L; LX4 is S or G; LX5 is S or T; LX6 is S or G; LX7 is H or G.~~
5. ~~The isolated dual binding antibody of claim 4, wherein HX1 is W, HX2 is A or S, HX6 is E or M, HX7 is L or W, HX8 is V or T, HX9 is H or A, HX12 is I or L, LX1 is L, LX2 is I, LX3 is L, LX4 is S or G, LX5 is S, LX6 is S, LX7 is H or G.~~
6. ~~The isolated dual binding antibody of claim 5, wherein~~

~~a. HX1 is W, HX2 is A, HX6 is E, HX7 is L, HX8 is T, HX9 is A, HX12 is I, LX4 is S, and LX7 is G; or~~

~~b. HX1 is W, HX2 is A, HX6 is M, HX7 is L, HX8 is V, HX9 is A, HX12 is L, LX4 is S, and LX7 is H; or~~

~~c. HX1 is W, HX2 is S, HX6 is E, HX7 is W, HX8 is V, HX9 is H, HX12 is L, LX4 is G, and LX7 is G.~~
73. The isolated dual binding antibody of claim 1 or claim 2, wherein said VH and said VL comprise the amino acid sequences set forth in SEQ ID Nos:337 and 338, respectively; SEQ ID NOs:209 and 210, respectively; SEQ ID NOs:219 and 220, respectively; SEQ ID NOs:249 and 250, respectively; , respectively; SEQ ID NOs:155 and 156, respectively; SEQ ID NOs:157 and 158, respectively; SEQ ID NOs:4 and 3, respectively; SEQ ID NOs:6 and 5, respectively; SEQ ID NOs:8

and 7, respectively; SEQ ID NOs:10 and 9, respectively; SEQ ID NOs:12 and 11, respectively; SEQ ID NOs:14 and 13, respectively; SEQ ID NOs:16 and 15, respectively; SEQ ID NOs:18 and 17, respectively; SEQ ID NOs:20 and 19, respectively; SEQ ID NOs:22 and 21, respectively; SEQ ID NOs:24 and 23, respectively; SEQ ID NOs:26 and 25, respectively; SEQ ID NOs:28 and 27, respectively; SEQ ID NOs:30 and 29, respectively; SEQ ID NOs:32 and 31, respectively; SEQ ID NOs:34 and 33, respectively; SEQ ID NOs:36 and 35, respectively; SEQ ID NOs:38 and 37, respectively; SEQ ID NOs:40 and 39, respectively; SEQ ID NOs:42 and 41, respectively; SEQ ID NOs:44 and 43, respectively; SEQ ID NOs:46 and 45, respectively; SEQ ID NOs:48 and 47, respectively; SEQ ID NOs:50 and 49, respectively; SEQ ID NOs:52 and 51, respectively; or SEQ ID NOs:54 and 53, respectivelywherein the antibody comprises a heavy chain variable domain (VH) and a light chain variable domain (VL), said VH and VL comprise the amino acid sequences of SEQ ID Nos:209 and 210, SEQ ID Nos:219 and 220, SEQ ID Nos:249 and 250, SEQ ID Nos:337 and 338, SEQ ID Nos:155 and 156, SEQ ID Nos:157 and 158, SEQ ID Nos:4 and 3, SEQ ID Nos:6 and 5, SEQ ID Nos:8 and 7, SEQ ID Nos:10 and 9, SEQ ID Nos:12 and 11, SEQ ID Nos:14 and 13, SEQ ID Nos:16 and 15, SEQ ID Nos:18 and 17, SEQ ID Nos:20 and 19, SEQ ID Nos:22 and 21, SEQ ID Nos:24 and 23, SEQ ID Nos:26 and 25, SEQ ID Nos:28 and 27, SEQ ID Nos:30 and 29, SEQ ID Nos:32 and 31, SEQ ID Nos:34 and 33, SEQ ID Nos:36 and 35, SEQ ID Nos:38 and 37, SEQ ID Nos:40 and 39, SEQ ID Nos:42 and 41, SEQ ID Nos:44 and 43, SEQ ID Nos:46 and 45, SEQ ID Nos:48 and 47, SEQ ID Nos:50 and 49, SEQ ID Nos:52 and 51, or SEQ ID Nos:54 and 53.

8. ~~The isolated dual binding antibody of claim 1, wherein the antibody comprises a heavy chain variable domain (VH) and a light chain variable domain (VL), said VH and VL comprise the amino acid sequences as shown in Table 10 or Table 1.~~
9. ~~The isolated dual binding antibody of claim 1, comprising a heavy chain variable domain (VH) and a light chain variable domain (VL), wherein~~

- ~~(c) said VH domain comprises the amino acid sequence set forth in SEQ ID NO: 1 with amino acid variants at two or more of positions 52, 99, 100, 101, 102, 103, 104, 105, 106, 107, 108, or 111, or any combination thereof (IMGT positions: 57, 107, 108, 109, 110, 111, 111A, 112A, 112, 113, 114, or 117, or a combination thereof); and~~
- ~~(d) said VL domain comprises the amino acid sequence set forth in SEQ ID NO: 2 with amino acid variants at two or more of positions 26, 27, 31, 51, 56, 77, 92, 93, or 96, or any combination thereof (IMGT positions: 27, 28, 38, 65, 70, 94, 109, 110, or 115, or a combination thereof).~~
104. The isolated dual binding antibody of any of claims 1-3, wherein said antibody comprises an IgG, an Fv, an scFv, an Fab, an F(ab')₂, a minibody, a diabody, or a triabody.
115. The isolated dual binding antibody of claim 410, wherein said IgG is IgG1, IgG2, IgG3, or IgG4.
126. The isolated dual binding antibody of claim 4 or claim 510, wherein said IgG comprises a heavy chain (HC) comprising a mutation that reduces binding to an Fc receptor, wherein said dual binding antibody comprising this mutation is unable to bind to antibody-dependent cellular cytotoxicity components~~a mutated IgG, said mutant IgG is unable to bind to antibody dependent cellular cytotoxicity components.~~
7. The isolated dual binding antibody according to claim 6, wherein said mutation is a L234A L235A (LALA) mutation or a L234A L235AP329G (LALAPG) mutation.
8. The isolated dual binding antibody according to any of claims 6-7, wherein said VH and said VL comprise the amino acid sequences set forth in SEQ ID Nos:337 and 338, respectively, and said antibody comprises said L234A L235A (LALA) mutation.

9. The isolated dual binding antibody according to any of claims 6-7, wherein said VH and said VL comprise the amino acid sequences set forth in SEQ ID Nos:337 and 338, respectively, and said antibody comprises said L234A L235A P329G (LALAPG) mutation.
- ~~13~~10. A composition comprising the isolated dual binding antibody of any of claims 1-9 and a pharmaceutically acceptable carrier.
- ~~14~~11. An isolated polynucleotide construct encoding the isolated dual binding antibody of any of claims 1-9.
- ~~15~~12. An expression vector comprising the polynucleotide construct of claim ~~14~~11.
- ~~16~~13. A host cell comprising the expression vector of claim ~~15~~12.
- ~~17.~~ ~~A method of treating a subject suffering from a disease or condition, said method comprises administering to said subject a composition comprising the isolated dual binding antibody of claim 1.~~
14. The isolated dual binding antibody of any one of claims 1-9 for use as a medicament.
15. Use of a composition comprising an isolated dual binding antibody of any of claims 1-9 in the preparation of a medicament for the treatment of a disease or condition.
- ~~18~~16. The ~~method~~use of claim ~~17~~15, wherein said disease or condition is an allergic or respiratory condition, an inflammatory or autoimmune condition, or tumors or cancers.
- ~~19~~17. The ~~method~~use of claim ~~17~~15, wherein said disease or condition is asthma, allergic asthma, nonallergic asthma, severe asthma, mild asthma, chronic obstructive pulmonary disease (COPD), a condition involving airway inflammation, cystic fibrosis, allergic lung disease, airway hyperresponsiveness, goblet cell metaplasia, mucus hypersecretion, airway remodeling, pulmonary fibrosis, atopic dermatitis, urticaria, eczema, allergic enterogastritis, allergic

rhinitis, inflammatory bowel diseases, liver cirrhosis or fibrosis, or a combination thereof.

20. ~~The method of claim 17, wherein said dual binding antibody comprises three complementarity determining regions (CDRs) on a heavy chain (HCDR1, HCDR2, and HCDR3) and three CDRs on a light chain (LCDR1, LCDR2, and LCDR3), wherein~~
- ~~the HCDR1, HCDR2 and HCDR3 comprise the amino acid sequence of SEQ ID NOs:349, 350 and 351 respectively, and the LCDR1, LCDR2 and LCDR3 comprise the amino acid sequence of SEQ ID NOs:359, 360 and 361 respectively;~~
- ~~or~~
- ~~the HCDR1, HCDR2 and HCDR3 comprise the amino acid sequence of SEQ ID NOs:349, 356 and 351 respectively, and the LCDR1, LCDR2 and LCDR3 comprise the amino acid sequence of SEQ ID NOs:364, 360 and 371 respectively;~~
- ~~or~~
- ~~the HCDR1, HCDR2 and HCDR3 comprise the amino acid sequence of SEQ ID NOs:349, 350 and 351 respectively, and the LCDR1, LCDR2 and LCDR3 comprise the amino acid sequence of SEQ ID NOs:362, 360 and 384 respectively;~~
- ~~or~~
- ~~the HCDR1, HCDR2 and HCDR3 comprise the amino acid sequence of SEQ ID NOs:349, 350 and 351 respectively, and the LCDR1, LCDR2 and LCDR3 comprise the amino acid sequence of SEQ ID NOs:364, 360 and 384 respectively;~~
- ~~or~~
- ~~the CDRs having the sequences of SEQ ID NOs:149-154.~~

21. ~~The method of claim 17, wherein said dual binding antibody comprises three complementarity determining regions (CDRs) on a heavy chain (HCDR1, HCDR2, and HCDR3) and three CDRs on a light chain (LCDR1, LCDR2, and LCDR3), wherein the HCDR1, HCDR2 and HCDR3 comprise the amino acid~~

~~sequences as shown in Table 8 or Table 4, wherein the LCDR1, LCDR2 and LCDR3 comprise the amino acid sequences as shown in Table 9 or Table 5.~~

~~22. The method of claim 17, wherein said dual binding antibody comprises VH and VL having the sequences of SEQ ID Nos:209 and 210, SEQ ID Nos:219 and 220, SEQ ID Nos:249 and 250, SEQ ID Nos:337 and 338, SEQ ID NOs:155 and 156, SEQ ID Nos:157 and 158.~~

~~23. The method of claim 17, wherein said dual binding antibody comprises VH and VL having the sequences as shown in Table 10 or Table 1.~~