

CLAIMS

What is claimed is:

1. An antibody comprising a heavy chain variable region comprising a heavy chain CDR1 (HCDR1), CDR2 (HCDR2), and CDR3 (HCDR3), and a light chain variable region comprising a light chain CDR1 (LCDR1), CDR2 (LCDR2), and CDR3 (LCDR3), and wherein the antibody has:
 - a HCDR1 of SEQ ID NO: 62, HCDR2 of SEQ ID NO: 125, and HCDR3 of SEQ ID NO: 66, a LCDR1 of SEQ ID NO: 64; a LCDR2 of SEQ ID NO: 59; and a LCDR3 of SEQ ID NO: 60;
 - a HCDR1 of SEQ ID NO: 62, HCDR2 of SEQ ID NO: 125, and HCDR3 of SEQ ID NO: 65, a LCDR1 of SEQ ID NO: 64; a LCDR2 of SEQ ID NO: 59; and a LCDR3 of SEQ ID NO: 60;
 - a HCDR1 of SEQ ID NO: 62, HCDR2 of SEQ ID NO: 125, and HCDR3 of SEQ ID NO: 67, a LCDR1 of SEQ ID NO: 64; a LCDR2 of SEQ ID NO: 59; and a LCDR3 of SEQ ID NO: 60;
 - a HCDR1 of SEQ ID NO: 62, HCDR2 of SEQ ID NO: 125, and HCDR3 of SEQ ID NO: 69, a LCDR1 of SEQ ID NO: 58; a LCDR2 of SEQ ID NO: 68; and a LCDR3 of SEQ ID NO: 60;
 - a HCDR1 of SEQ ID NO: 53, HCDR2 of SEQ ID NO: 54, and HCDR3 of SEQ ID NO: 33, a LCDR1 of SEQ ID NO: 50; a LCDR2 of SEQ ID NO: 51; and a LCDR3 of SEQ ID NO: 52;
 - a HCDR1 of SEQ ID NO: 139, HCDR2 of SEQ ID NO: 140, and HCDR3 of SEQ ID NO: 82, a LCDR1 of SEQ ID NO: 83; a LCDR2 of SEQ ID NO: 84; and a LCDR3 of SEQ ID NO: 85;
 - a HCDR1 of SEQ ID NO: 141, HCDR2 of SEQ ID NO: 142, and HCDR3 of SEQ ID NO: 57, a LCDR1 of SEQ ID NO: 87; a LCDR2 of SEQ ID NO: 88; and a LCDR3 of SEQ ID NO: 89;
 - a HCDR1 of SEQ ID NO: 143, HCDR2 of SEQ ID NO: 144, and HCDR3 of SEQ ID NO: 92, a LCDR1 of SEQ ID NO: 93; a LCDR2 of SEQ ID NO: 88; and a LCDR3 of SEQ ID NO: 94;
 - a HCDR1 of SEQ ID NO: 145, HCDR2 of SEQ ID NO: 146, and HCDR3 of SEQ ID NO:

97, a LCDR1 of SEQ ID NO: 98; a LCDR2 of SEQ ID NO: 99; and a LCDR3 of SEQ ID NO: 100;

a HCDR1 of SEQ ID NO: 25, HCDR2 of SEQ ID NO: 26, and HCDR3 of SEQ ID NO: 27, a LCDR1 of SEQ ID NO: 22; a LCDR2 of SEQ ID NO: 23; and a LCDR3 of SEQ ID NO: 24;

a HCDR1 of SEQ ID NO: 31, HCDR2 of SEQ ID NO: 32, and HCDR3 of SEQ ID NO: 33, a LCDR1 of SEQ ID NO: 28; a LCDR2 of SEQ ID NO: 29; and a LCDR3 of SEQ ID NO: 30;

a HCDR1 of SEQ ID NO: 37, HCDR2 of SEQ ID NO: 38, and HCDR3 of SEQ ID NO: 39, a LCDR1 of SEQ ID NO: 34; a LCDR2 of SEQ ID NO: 29; and a LCDR3 of SEQ ID NO: 36;

a HCDR1 of SEQ ID NO: 43, HCDR2 of SEQ ID NO: 44, and HCDR3 of SEQ ID NO: 45, a LCDR1 of SEQ ID NO: 40; a LCDR2 of SEQ ID NO: 41; and a LCDR3 of SEQ ID NO: 43;

a HCDR1 of SEQ ID NO: 25, HCDR2 of SEQ ID NO: 26, and HCDR3 of SEQ ID NO: 27, a LCDR1 of SEQ ID NO: 22; a LCDR2 of SEQ ID NO: 23; and a LCDR3 of SEQ ID NO: 24;

a HCDR1 of SEQ ID NO: 31, HCDR2 of SEQ ID NO: 46, and HCDR3 of SEQ ID NO: 33, a LCDR1 of SEQ ID NO: 28; a LCDR2 of SEQ ID NO: 29; and a LCDR3 of SEQ ID NO: 30;

a HCDR1 of SEQ ID NO: 37, HCDR2 of SEQ ID NO: 48, and HCDR3 of SEQ ID NO: 39, a LCDR1 of SEQ ID NO: 47; a LCDR2 of SEQ ID NO: 29; and a LCDR3 of SEQ ID NO: 36;

a HCDR1 of SEQ ID NO: 43, HCDR2 of SEQ ID NO: 49, and HCDR3 of SEQ ID NO: 45, a LCDR1 of SEQ ID NO: 40; a LCDR2 of SEQ ID NO: 41; and a LCDR3 of SEQ ID NO: 42;

a HCDR1 of SEQ ID NO: 55, HCDR2 of SEQ ID NO: 54, and HCDR3 of SEQ ID NO: 33, a LCDR1 of SEQ ID NO: 50; a LCDR2 of SEQ ID NO: 51; and a LCDR3 of SEQ ID NO: 52;

a HCDR1 of SEQ ID NO: 56, HCDR2 of SEQ ID NO: 125, and HCDR3 of SEQ ID NO: 57, a LCDR1 of SEQ ID NO: 58; a LCDR2 of SEQ ID NO: 59; and a LCDR3 of

- SEQ ID NO: 60;
- a HCDR1 of SEQ ID NO: 56, HCDR2 of SEQ ID NO: 125, and HCDR3 of SEQ ID NO: 61, a LCDR1 of SEQ ID NO: 58; a LCDR2 of SEQ ID NO: 59; and a LCDR3 of SEQ ID NO: 60;
- a HCDR1 of SEQ ID NO: 62, HCDR2 of SEQ ID NO: 125, and HCDR3 of SEQ ID NO: 63, a LCDR1 of SEQ ID NO: 64; a LCDR2 of SEQ ID NO: 59; and a LCDR3 of SEQ ID NO: 60;
- a HCDR1 of SEQ ID NO: 62, HCDR2 of SEQ ID NO: 125, and HCDR3 of SEQ ID NO: 65, a LCDR1 of SEQ ID NO: 58; a LCDR2 of SEQ ID NO: 68; and a LCDR3 of SEQ ID NO: 60;
- a HCDR1 of SEQ ID NO: 62, HCDR2 of SEQ ID NO: 125, and HCDR3 of SEQ ID NO: 126, a LCDR1 of SEQ ID NO: 58; a LCDR2 of SEQ ID NO: 68; and a LCDR3 of SEQ ID NO: 60;
- a HCDR1 of SEQ ID NO: 62, HCDR2 of SEQ ID NO: 125, and HCDR3 of SEQ ID NO: 69, a LCDR1 of SEQ ID NO: 64; a LCDR2 of SEQ ID NO: 59; and a LCDR3 of SEQ ID NO: 70;
- a HCDR1 of SEQ ID NO: 71, HCDR2 of SEQ ID NO: 72, and HCDR3 of SEQ ID NO: 73, a LCDR1 of SEQ ID NO: 74; a LCDR2 of SEQ ID NO: 59; and a LCDR3 of SEQ ID NO: 75;
- a HCDR1 of SEQ ID NO: 76, HCDR2 of SEQ ID NO: 77, and HCDR3 of SEQ ID NO: 78, a LCDR1 of SGGSGSYGYYG SEQ ID NO: 147; a LCDR2 of SEQ ID NO: 59; and a LCDR3 of SEQ ID NO: 79;
- a HCDR1 of SEQ ID NO: 80, HCDR2 of SEQ ID NO: 81, and HCDR3 of SEQ ID NO: 82, a LCDR1 of SEQ ID NO: 83; a LCDR2 of SEQ ID NO: 84; and a LCDR3 of SEQ ID NO: 85;
- a HCDR1 of SEQ ID NO: 62, HCDR2 of SEQ ID NO: 86, and HCDR3 of SEQ ID NO: 57, a LCDR1 of SEQ ID NO: 87; a LCDR2 of SEQ ID NO: 88; and a LCDR3 of SEQ ID NO: 89;
- a HCDR1 of SEQ ID NO: 90, HCDR2 of SEQ ID NO: 91, and HCDR3 of SEQ ID NO: 92, a LCDR1 of SEQ ID NO: 93; a LCDR2 of SEQ ID NO: 88; and a LCDR3 of SEQ ID NO: 94;

a HCDR1 of SEQ ID NO: 95, HCDR2 of SEQ ID NO: 96, and HCDR3 of SEQ ID NO: 97, a LCDR1 of SEQ ID NO: 98; a LCDR2 of SEQ ID NO: 99; and a LCDR3 of SEQ ID NO: 100;

a HCDR1 of SEQ ID NO: 62, HCDR2 of SEQ ID NO: 125, and HCDR3 of SEQ ID NO: 57, a LCDR1 of SEQ ID NO: 58; a LCDR2 of SEQ ID NO: 59; and a LCDR3 of SEQ ID NO: 60; or

a HCDR1 of SEQ ID NO: 62, HCDR2 of SEQ ID NO: 102, and HCDR3 of SEQ ID NO: 57, a LCDR1 of SEQ ID NO: 87; a LCDR2 of SEQ ID NO: 88; and a LCDR3 of SEQ ID NO: 89, and wherein the antibody binds to claudin 6 with an affinity of less than 10 nM and with at least a 100-fold greater EC₅₀ than claudin 9, claudin 3, and/or claudin 4.

2. ~~An peptide or antibody, wherein the peptide or the antibody comprises~~ comprising a sequence of SEQ ID NO: 62, SEQ ID NO: 125, SEQ ID NO: 66, SEQ ID NO: 64; SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 65, SEQ ID NO: 69, SEQ ID NO: 58, SEQ ID NO: 68, SEQ ID NO: 67, SEQ ID NO: 53, SEQ ID NO: 54 SEQ ID NO: 33, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 2-32, 34-49, 55-57, 61, 63, 70-100, and 102-135, ~~or a variant thereof.~~

~~3. A peptide or antibody comprising a sequence that is 90-99% identical to a protein comprising a sequence of SEQ ID NO: 62, SEQ ID NO: 125, SEQ ID NO: 66, SEQ ID NO: 64; SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 65, SEQ ID NO: 69, SEQ ID NO: 58, SEQ ID NO: 68, SEQ ID NO: 67, SEQ ID NO: 53, SEQ ID NO: 54 SEQ ID NO: 33, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 2-32, 34-49, 55-57, 61, 63, 70-100, and 102-135.~~

~~4. The peptide of claim 3, wherein the peptide comprises 1, 2, 3, 4, or 5 substitutions, deletions, or insertions as compared to a sequence of SEQ ID NO: 62, SEQ ID NO: 125, SEQ ID NO: 66, SEQ ID NO: 64; SEQ ID NO: 59, SEQ ID NO: 60, SEQ ID NO: 65, SEQ ID NO: 69, SEQ ID NO: 58, SEQ ID NO: 68, SEQ ID NO: 67, SEQ ID NO: 53, SEQ ID NO: 54 SEQ ID NO: 33, SEQ ID NO: 50, SEQ ID NO: 51, SEQ ID NO: 52, SEQ ID NO: 2-32, 34-49, 55-57, 61, 63, 70-100, and 102-135.~~

~~5. An antibody, such as a monoclonal antibody or scFv, that binds to an epitope on Claudin 6 whose residues include T33, N38, D68, P74, D76, D146, V152, A153, E154, Q156, R158, or any combination thereof.~~

~~6. An antibody, such as a monoclonal antibody or a scFv, that binds preferentially to Claudin 6 as compared to Claudin 9, wherein the antibody binds to an epitope on Claudin 6 that comprises Q156.~~

37. A bi-specific antibody comprising a first V_H peptide that binds to Claudin 6 and second V_H peptide that binds to a different moiety, optionally wherein the antibody comprises heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 53, 62, 25, 31, 37, 43, 55, 56, 71, 76, 80, 90, or 95; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 54, 125, 26, 32, 38, 44, 46, 48, 49, 72, 77, 81, 86, 91, 96, or 102 and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 33, 65, 66, 67, 69, 27, 39, 45, 57, 61, 63, 66, 126, 73, 82, 57, 92, or 97 ~~or variants of any of the foregoing.~~

48. The bi-specific antibody of claims 37, wherein the antibody comprises a light chain variable region comprising a sequence of any one of sequences as set forth in SEQ ID NOs: 127-135, or wherein the antibody comprises a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 50, 58, 64, 22, 28, 34, 40, 47, 74, 83, 87, 93, or 98; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 51, 59, 68, 23, 29, 41, 84, 88, or 99, and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 52, 60, 24, 30, 36, 42, 70, 75, 79, 85, 89, or 94, ~~or variants of any of the foregoing.~~

59. A nucleic acid molecule encoding an antibody of claim 1 or claim 2, or a bi-specific antibody of claim 3 or claim 4 ~~an amino acid sequence of claims 2-8.~~

610. A vector comprising the nucleic acid molecule of claim 59.

~~711.~~ A cell ~~comprising the nucleic~~ comprising the nucleic acid molecule of claim ~~59~~, or the vector of claim ~~610~~.

~~812.~~ A pharmaceutical composition comprising the antibody, ~~or bi-specific antibody peptide, or protein~~, of any one of claims ~~1-4 1-8, or a nucleic acid molecule encoding the same~~.

~~913.~~ Use of a Claudin 6 antibody in the manufacture of a medicament for the treatment of a Claudin 6 mediated disorder, wherein the Claudin 6 antibody is an antibody ~~or protein~~ of any one of claims ~~1-41-8, or a nucleic acid molecule encoding the same, wherein the Claudin 6 mediated disorder is benign or metastatic cancer, ovarian cancer, ovarian carcinoma, reproductive cancer, breast cancer, cervical cancer, testicular cancer, uterine cancer, placental cancer, lung cancer, gastric cancer, hepatic cancer, pancreatic cancer, bile duct cancer, cancer of the urinary bladder, kidney cancer, colon cancer, small bowel cancer, skin cancer, head and neck cancer, sarcoma, or germ cell tumor.~~

~~14.—The use of claim 13, wherein the disorder is benign or metastatic cancer, for example, ovarian cancer, ovarian carcinoma, reproductive cancer, breast cancer, cervical cancer, testicular cancer, uterine cancer, placental cancer, lung cancer, gastric cancer, hepatic cancer, pancreatic cancer, bile duct cancer, cancer of the urinary bladder, kidney cancer, colon cancer, small bowel cancer, skin cancer, head and neck cancer, sarcoma, or germ cell tumor.~~

~~1015.~~ The antibody of claim 1, wherein the antibody comprises a light chain variable region having at least 95% identity to the amino acid sequence of SEQ ID NO: 110, and ~~/or~~ a heavy chain variable region having at least 95% identity to the amino acid sequence of SEQ ID NO: 109.

~~1116.~~ The antibody of claim 1, wherein the antibody comprises a light chain variable region having at least 95% identity to the amino acid sequence of SEQ ID NO: 108, and ~~/or~~ a heavy chain variable region having at least 95% identity to the amino acid sequence of SEQ ID NO: 107.

~~1217.~~ The antibody of claim 1, wherein the antibody comprises a light chain variable region having at least 95% identity to the amino acid sequence of SEQ ID NO: 118, and ~~/or~~ a heavy chain

variable region having at least 95% identity to the amino acid sequence of SEQ ID NO: 117.

1318. The antibody of claim 1, wherein the antibody comprises a light chain variable region having at least 95% identity to the amino acid sequence of SEQ ID NO: 112, and ~~or~~ a heavy chain variable region having at least 95% identity to the amino acid sequence of SEQ ID NO: 111.

1419. The antibody of claim 1, wherein the antibody comprises a light chain variable region having at least 95% identity to the amino acid sequence of SEQ ID NO: 19, and ~~or~~ a heavy chain variable region having at least 95% identity to the amino acid sequence of SEQ ID NO: 18.

1520. A method of making the antibody of claim 1, the method comprising culturing a cell comprising a nucleic acid molecule encoding the antibody of claim 1 under conditions to produce the antibody.

1624. An antibody or bi-specific antibody ~~or protein~~ of any one of claims 1-4,1-8, or a nucleic acid molecule encoding the same, for use as a medicament.

1722. An antibody or bi-specific antibody ~~protein~~ of any one of claims 1-4,1-8, or a nucleic acid molecule encoding the same, for use in the treatment of a Claudin 6 mediated disorder, wherein the Claudin 6 mediated disorder is benign or metastatic cancer, ovarian cancer, ovarian carcinoma, reproductive cancer, breast cancer, cervical cancer, testicular cancer, uterine cancer, placental cancer, lung cancer, gastric cancer, hepatic cancer, pancreatic cancer, bile duct cancer, cancer of the urinary bladder, kidney cancer, colon cancer, small bowel cancer, skin cancer, head and neck cancer, sarcoma, or germ cell tumor.

~~23. — The antibody or protein, or a nucleic acid molecule encoding the same, for use of claim 22, wherein the disorder is benign or metastatic cancer, for example, ovarian cancer, ovarian carcinoma, reproductive cancer, breast cancer, cervical cancer, testicular cancer, uterine cancer, placental cancer, lung cancer, gastric cancer, hepatic cancer, pancreatic cancer, bile duct cancer, cancer of the urinary bladder, kidney cancer, colon cancer, small bowel cancer, skin cancer, head and neck cancer, sarcoma, or germ cell tumor.~~