

HETERODIMERIC ANTIBODIES THAT BIND CD3 AND CLDN6**PRIORITY CLAIM**

[0001] This application claims the benefit of U.S. Provisional Patent Application No. 63/158,584, filed March 9, 2021, which is hereby incorporated by reference in its entirety.

SEQUENCE LISTING

[0002] The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on February 24, 2022, is named 067461-5281-WO_SL.txt and is 991,664 bytes in size

BACKGROUND

[0003] Antibody-based therapeutics have been used successfully to treat a variety of diseases, including cancer. An increasingly prevalent avenue being explored is the engineering of single immunoglobulin molecules that co-engage two different antigens. Such alternate antibody formats that engage two different antigens are often referred to as bispecific antibodies. Because the considerable diversity of the antibody variable region (Fv) makes it possible to produce an Fv that recognizes virtually any molecule, the typical approach to bispecific antibody generation is the introduction of new variable regions into the antibody.

[0004] A particularly useful approach for bispecific antibodies is to engineer a first binding domain which engages CD3 and a second binding domain which engages an antigen associated with or upregulated on cancer cells so that the bispecific antibody redirects CD3+ T cells to destroy the cancer cells. Claudin 6 (CLDN6) has been determined to be upregulated in gastric, lung, and ovarian cancers. In view of this, it is believed that anti-CLDN6 antibodies are useful, for example, for localizing anti-tumor therapeutics (e.g., chemotherapeutic agents and T cells) to such CLDN6 expressing tumors. The present invention provides novel bispecific antibodies to CD3 and CLDN6 that are capable of localizing CD3+ effector T cells to CLDN6 expressing tumors.

SUMMARY

[0005] Provided herein are novel CLDN6 binding domains, and anti-CLDN6 x anti-CD3 antibodies that include such CLDN6 binding domains. Also provided herein are methods of using such antibodies for the treatment of CLDN6-associated cancers.

[0006] In a first aspect, provided herein are compositions comprising a CLDN6 antigen binding domain. In some embodiments, the CLDN6 antigen binding domain comprises a set of 6 CDRs (vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2 and vlCDR3) from a variable heavy domain (VH)/variable light domain (VL) pair selected from the group consisting:

H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1, H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1, H2.12_L1, H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1, H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1, H1.9_L1.1, H1.19_L1.1, H1.22_L1.1, H1.24_L1.1, H2_L1.1, H2.1_L1.1, H2.2_L1.1, H2.3_L1.1, H2.4_L1.1, H2.5_L1.1, H2.6_L1.1, H2.7_L1.1, H2.8_L1.1, H2.9_L1.1, H2.11_L1.1, H2.12_L1.1, H2.71_L1.1, H2.75_L1.1, H2.90_L1.1, H2.91_L1.1, H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4, H1.2_L1.4, H1.3_L1.4, H1.4_L1.4, H1.5_L1.4, H1.6_L1.4, H1.7_L1.4, H1.8_L1.4, H1.9_L1.4, H1.19_L1.4, H1.22_L1.4, H1.24_L1.4, H2_L1.4, H2.1_L1.4, H2.2_L1.4, H2.3_L1.4, H2.4_L1.4, H2.5_L1.4, H2.6_L1.4, H2.7_L1.4, H2.8_L1.4, H2.9_L1.4, H2.11_L1.4, H2.12_L1.4, H2.71_L1.4, H2.75_L1.4, H2.90_L1.4, H2.91_L1.4, H2.118_L1.4, H2.119_L1.4, H1_L1.7, H1.1_L1.7, H1.2_L1.7, H1.3_L1.7, H1.4_L1.7, H1.5_L1.7, H1.6_L1.7, H1.7_L1.7, H1.8_L1.7, H1.9_L1.7, H1.19_L1.7, H1.22_L1.7, H1.24_L1.7, H2_L1.7, H2.1_L1.7, H2.2_L1.7, H2.3_L1.7, H2.4_L1.7, H2.5_L1.7, H2.6_L1.7, H2.7_L1.7, H2.8_L1.7, H2.9_L1.7, H2.11_L1.7, H2.12_L1.7, H2.71_L1.7, H2.75_L1.7, H2.90_L1.7, H2.91_L1.7, H2.118_L1.7, H2.119_L1.7, H1_L1.16, H1.1_L1.16, H1.2_L1.16, H1.3_L1.16, H1.4_L1.16, H1.5_L1.16, H1.6_L1.16, H1.7_L1.16, H1.8_L1.16, H1.9_L1.16, H1.19_L1.16, H1.22_L1.16, H1.24_L1.16, H2_L1.16, H2.1_L1.16, H2.2_L1.16, H2.3_L1.16, H2.4_L1.16, H2.5_L1.16, H2.6_L1.16, H2.7_L1.16, H2.8_L1.16, H2.9_L1.16, H2.11_L1.16, H2.12_L1.16, H2.71_L1.16, H2.75_L1.16, H2.90_L1.16, H2.91_L1.16, H2.118_L1.16, H2.119_L1.16, H1_L1.18, H1.1_L1.18, H1.2_L1.18, H1.3_L1.18, H1.4_L1.18, H1.5_L1.18, H1.6_L1.18, H1.7_L1.18, H1.8_L1.18, H1.9_L1.18, H1.19_L1.18, H1.22_L1.18, H1.24_L1.18, H2_L1.18, H2.1_L1.18, H2.2_L1.18, H2.3_L1.18, H2.4_L1.18, H2.5_L1.18,

L1.18, H2.6_L1.18, H2.7_L1.18, H2.8_L1.18, H2.9_L1.18, H2.11_L1.18, H2.12_L1.18, H2.71_L1.18, H2.75_L1.18, H2.90_L1.18, H2.91_L1.18, H2.118_L1.18, H2.119_L1.18, H1_L1.19, H1.1_L1.19, H1.2_L1.19, H1.3_L1.19, H1.4_L1.19, H1.5_L1.19, H1.6_L1.19, H1.7_L1.19, H1.8_L1.19, H1.9_L1.19, H1.19_L1.19, H1.22_L1.19, H1.24_L1.19, H2_L1.19, H2.1_L1.19, H2.2_L1.19, H2.3_L1.19, H2.4_L1.19, H2.5_L1.19, H2.6_L1.19, H2.7_L1.19, H2.8_L1.19, H2.9_L1.19, H2.11_L1.19, H2.12_L1.19, H2.71_L1.19, H2.75_L1.19, H2.90_L1.19, H2.91_L1.19, H2.118_L1.19, H2.119_L1.19, H1_L1.21, H1.1_L1.21, H1.2_L1.21, H1.3_L1.21, H1.4_L1.21, H1.5_L1.21, H1.6_L1.21, H1.7_L1.21, H1.8_L1.21, H1.9_L1.21, H1.19_L1.21, H1.22_L1.21, H1.24_L1.21, H2_L1.21, H2.1_L1.21, H2.2_L1.21, H2.3_L1.21, H2.4_L1.21, H2.5_L1.21, H2.6_L1.21, H2.7_L1.21, H2.8_L1.21, H2.9_L1.21, H2.11_L1.21, H2.12_L1.21, H2.71_L1.21, H2.75_L1.21, H2.90_L1.21, H2.91_L1.21, H2.118_L1.2, H2.119_L1.21, H1_L1.22, H1.1_L1.22, H1.2_L1.22, H1.3_L1.22, H1.4_L1.22, H1.5_L1.22, H1.6_L1.22, H1.7_L1.22, H1.8_L1.22, H1.9_L1.22, H1.19_L1.22, H1.22_L1.22, H1.24_L1.22, H2_L1.22, H2.1_L1.22, H2.2_L1.22, H2.3_L1.22, H2.4_L1.22, H2.5_L1.22, H2.6_L1.22, H2.7_L1.22, H2.8_L1.22, H2.9_L1.22, H2.11_L1.22, H2.12_L1.22, H2.71_L1.22, H2.75_L1.22, H2.90_L1.22, H2.91_L1.22, H2.118_L1.22, H2.119_L1.22, H1_L1.23, H1.1_L1.23, H1.2_L1.23, H1.3_L1.23, H1.4_L1.23, H1.5_L1.23, H1.6_L1.23, H1.7_L1.23, H1.8_L1.23, H1.9_L1.23, H1.19_L1.23, H1.22_L1.23, H1.24_L1.23, H2_L1.23, H2.1_L1.23, H2.2_L1.23, H2.3_L1.23, H2.4_L1.23, H2.5_L1.23, H2.6_L1.23, H2.7_L1.23, H2.8_L1.23, H2.9_L1.23, H2.11_L1.23, H2.12_L1.23, H2.71_L1.23, H2.75_L1.23, H2.90_L1.23, H2.91_L1.23, H2.118_L1.23, H2.119_L1.23, H1_L1.27, H1.1_L1.27, H1.2_L1.27, H1.3_L1.27, H1.4_L1.27, H1.5_L1.27, H1.6_L1.27, H1.7_L1.27, H1.8_L1.27, H1.9_L1.27, H1.19_L1.27, H1.22_L1.27, H1.24_L1.27, H2_L1.27, H2.1_L1.27, H2.2_L1.27, H2.3_L1.27, H2.4_L1.27, H2.5_L1.27, H2.6_L1.27, H2.7_L1.27, H2.8_L1.27, H2.9_L1.27, H2.11_L1.27, H2.12_L1.27, H2.71_L1.27, H2.75_L1.27, H2.90_L1.27, H2.91_L1.27, H2.118_L1.27, H2.119_L1.27, H1_L1.60, H1.1_L1.60, H1.2_L1.60, H1.3_L1.60, H1.4_L1.60, H1.5_L1.60, H1.6_L1.60, H1.7_L1.60, H1.8_L1.60, H1.9_L1.60, H1.19_L1.60, H1.22_L1.60, H1.24_L1.60, H2_L1.60, H2.1_L1.60, H2.2_L1.60, H2.3_L1.60, H2.4_L1.60, H2.5_L1.60, H2.6_L1.60, H2.7_L1.60, H2.8_L1.60, H2.9_L1.60, H2.11_L1.60, H2.12_L1.60, H2.71_L1.60, H2.75_L1.60, H2.90_L1.60, H2.91_L1.60, H2.118_L1.60, H2.119_L1.60, H1_L1.107, H1.1_L1.107, H1.2_L1.107, H1.3_L1.107, H1.4_L1.107, H1.5_L1.107, H1.6_L1.107, H1.7_L1.107, H1.8_L1.107, H1.9_L1.107, H1.19_L1.107, H1.22_L1.107, H1.24_L1.107, H2_L1.107, H2.1_L1.107, H2.2_L1.107, H2.3_L1.107,

H2.4_L1.107, H2.5_L1.107, H2.6_L1.107, H2.7_L1.107, H2.8_L1.107, H2.9_L1.107, H2.11_L1.107, H2.12_L1.107, H2.71_L1.107, H2.75_L1.107, H2.90_L1.107, H2.91_L1.107, H2.118_L1.107, H2.119_L1.107, H1_L1.114, H1.1_L1.114, H1.2_L1.114, H1.3_L1.114, H1.4_L1.114, H1.5_L1.114, H1.6_L1.114, H1.7_L1.114, H1.8_L1.114, H1.9_L1.114, H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114, H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114, H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114, H2.90_L1.114, H2.91_L1.114, H2.118_L1.114, H2.119_L1.114, H1_L1.187, H1.1_L1.187, H1.2_L1.187, H1.3_L1.187, H1.4_L1.187, H1.5_L1.187, H1.6_L1.187, H1.7_L1.187, H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187, H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187, H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187, H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187, H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189, H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189, H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189, H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189, H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189, H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2, H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2.

[0007] In some embodiments, the CLDN6 antigen binding domain comprises a VH/VL pair selected from the group consisting of: H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1, H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1, H2.12_L1, H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1, H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1, H1.9_L1.1, H1.19_L1.1, H1.22_L1.1, H1.24_L1.1, H2_L1.1, H2.1_L1.1, H2.2_L1.1, H2.3_L1.1, H2.4_L1.1, H2.5_L1.1, H2.6_L1.1, H2.7_L1.1, H2.8_L1.1, H2.9_L1.1, H2.11_L1.1, H2.12_L1.1, H2.71_L1.1, H2.75_L1.1, H2.90_L1.1, H2.91_L1.1, H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4, H1.2_L1.4, H1.3_L1.4, H1.4_L1.4, H1.5_L1.4, H1.6_L1.4, H1.7_L1.4, H1.8_L1.4, H1.9_L1.4,

H1.19_L1.4, H1.22_L1.4, H1.24_L1.4, H2_L1.4, H2.1_L1.4, H2.2_L1.4, H2.3_L1.4,
H2.4_L1.4, H2.5_L1.4, H2.6_L1.4, H2.7_L1.4, H2.8_L1.4, H2.9_L1.4, H2.11_L1.4,
H2.12_L1.4, H2.71_L1.4, H2.75_L1.4, H2.90_L1.4, H2.91_L1.4, H2.118_L1.4,
H2.119_L1.4, H1_L1.7, H1.1_L1.7, H1.2_L1.7, H1.3_L1.7, H1.4_L1.7, H1.5_L1.7,
H1.6_L1.7, H1.7_L1.7, H1.8_L1.7, H1.9_L1.7, H1.19_L1.7, H1.22_L1.7, H1.24_L1.7,
H2_L1.7, H2.1_L1.7, H2.2_L1.7, H2.3_L1.7, H2.4_L1.7, H2.5_L1.7, H2.6_L1.7,
H2.7_L1.7, H2.8_L1.7, H2.9_L1.7, H2.11_L1.7, H2.12_L1.7, H2.71_L1.7, H2.75_L1.7,
H2.90_L1.7, H2.91_L1.7, H2.118_L1.7, H2.119_L1.7, H1_L1.16, H1.1_L1.16, H1.2_
L1.16, H1.3_L1.16, H1.4_L1.16, H1.5_L1.16, H1.6_L1.16, H1.7_L1.16, H1.8_L1.16,
H1.9_L1.16, H1.19_L1.16, H1.22_L1.16, H1.24_L1.16, H2_L1.16, H2.1_L1.16, H2.2_
L1.16, H2.3_L1.16, H2.4_L1.16, H2.5_L1.16, H2.6_L1.16, H2.7_L1.16, H2.8_L1.16,
H2.9_L1.16, H2.11_L1.16, H2.12_L1.16, H2.71_L1.16, H2.75_L1.16, H2.90_L1.16,
H2.91_L1.16, H2.118_L1.16, H2.119_L1.16, H1_L1.18, H1.1_L1.18, H1.2_L1.18,
H1.3_L1.18, H1.4_L1.18, H1.5_L1.18, H1.6_L1.18, H1.7_L1.18, H1.8_L1.18, H1.9_
L1.18, H1.19_L1.18, H1.22_L1.18, H1.24_L1.18, H2_L1.18, H2.1_L1.18, H2.2_L1.18,
H2.3_L1.18, H2.4_L1.18, H2.5_L1.18, H2.6_L1.18, H2.7_L1.18, H2.8_L1.18, H2.9_
L1.18, H2.11_L1.18, H2.12_L1.18, H2.71_L1.18, H2.75_L1.18, H2.90_L1.18, H2.91_
L1.18, H2.118_L1.18, H2.119_L1.18, H1_L1.19, H1.1_L1.19, H1.2_L1.19, H1.3_L1.19,
H1.4_L1.19, H1.5_L1.19, H1.6_L1.19, H1.7_L1.19, H1.8_L1.19, H1.9_L1.19, H1.19_L1.19,
H1.22_L1.19, H1.24_L1.19, H2_L1.19, H2.1_L1.19, H2.2_L1.19, H2.3_L1.19, H2.4_L1.19,
H2.5_L1.19, H2.6_L1.19, H2.7_L1.19, H2.8_L1.19, H2.9_L1.19, H2.11_L1.19,
H2.12_L1.19, H2.71_L1.19, H2.75_L1.19, H2.90_L1.19, H2.91_L1.19, H2.118_L1.19,
H2.119_L1.19, H1_L1.21, H1.1_L1.21, H1.2_L1.21, H1.3_L1.21, H1.4_L1.21, H1.5_L1.21,
H1.6_L1.21, H1.7_L1.21, H1.8_L1.21, H1.9_L1.21, H1.19_L1.21, H1.22_L1.21,
H1.24_L1.21, H2_L1.21, H2.1_L1.21, H2.2_L1.21, H2.3_L1.21, H2.4_L1.21, H2.5_L1.21,
H2.6_L1.21, H2.7_L1.21, H2.8_L1.21, H2.9_L1.21, H2.11_L1.21, H2.12_L1.21,
H2.71_L1.21, H2.75_L1.21, H2.90_L1.21, H2.91_L1.21, H2.118_L1.21, H2.119_L1.21,
H1_L1.22, H1.1_L1.22, H1.2_L1.22, H1.3_L1.22, H1.4_L1.22, H1.5_L1.22, H1.6_L1.22,
H1.7_L1.22, H1.8_L1.22, H1.9_L1.22, H1.19_L1.22, H1.22_L1.22, H1.24_L1.22,
H2_L1.22, H2.1_L1.22, H2.2_L1.22, H2.3_L1.22, H2.4_L1.22, H2.5_L1.22, H2.6_L1.22,
H2.7_L1.22, H2.8_L1.22, H2.9_L1.22, H2.11_L1.22, H2.12_L1.22, H2.71_L1.22,
H2.75_L1.22, H2.90_L1.22, H2.91_L1.22, H2.118_L1.22, H2.119_L1.22, H1_L1.23,
H1.1_L1.23, H1.2_L1.23, H1.3_L1.23, H1.4_L1.23, H1.5_L1.23, H1.6_L1.23, H1.7_L1.23,
H1.8_L1.23, H1.9_L1.23, H1.19_L1.23, H1.22_L1.23, H1.24_L1.23, H2_L1.23,

H2.1_L1.23, H2.2_L1.23, H2.3_L1.23, H2.4_L1.23, H2.5_L1.23, H2.6_L1.23, H2.7_L1.23, H2.8_L1.23, H2.9_L1.23, H2.11_L1.23, H2.12_L1.23, H2.71_L1.23, H2.75_L1.23, H2.90_L1.23, H2.91_L1.23, H2.118_L1.23, H2.119_L1.23, H1_L1.27, H1.1_L1.27, H1.2_L1.27, H1.3_L1.27, H1.4_L1.27, H1.5_L1.27, H1.6_L1.27, H1.7_L1.27, H1.8_L1.27, H1.9_L1.27, H1.19_L1.27, H1.22_L1.27, H1.24_L1.27, H2_L1.27, H2.1_L1.27, H2.2_L1.27, H2.3_L1.27, H2.4_L1.27, H2.5_L1.27, H2.6_L1.27, H2.7_L1.27, H2.8_L1.27, H2.9_L1.27, H2.11_L1.27, H2.12_L1.27, H2.71_L1.27, H2.75_L1.27, H2.90_L1.27, H2.91_L1.27, H2.118_L1.27, H2.119_L1.27, H1_L1.60, H1.1_L1.60, H1.2_L1.60, H1.3_L1.60, H1.4_L1.60, H1.5_L1.60, H1.6_L1.60, H1.7_L1.60, H1.8_L1.60, H1.9_L1.60, H1.19_L1.60, H1.22_L1.60, H1.24_L1.60, H2_L1.60, H2.1_L1.60, H2.2_L1.60, H2.3_L1.60, H2.4_L1.60, H2.5_L1.60, H2.6_L1.60, H2.7_L1.60, H2.8_L1.60, H2.9_L1.60, H2.11_L1.60, H2.12_L1.60, H2.71_L1.60, H2.75_L1.60, H2.90_L1.60, H2.91_L1.60, H2.118_L1.60, H2.119_L1.60, H1_L1.107, H1.1_L1.107, H1.2_L1.107, H1.3_L1.107, H1.4_L1.107, H1.5_L1.107, H1.6_L1.107, H1.7_L1.107, H1.8_L1.107, H1.9_L1.107, H1.19_L1.107, H1.22_L1.107, H1.24_L1.107, H2_L1.107, H2.1_L1.107, H2.2_L1.107, H2.3_L1.107, H2.4_L1.107, H2.5_L1.107, H2.6_L1.107, H2.7_L1.107, H2.8_L1.107, H2.9_L1.107, H2.11_L1.107, H2.12_L1.107, H2.71_L1.107, H2.75_L1.107, H2.90_L1.107, H2.91_L1.107, H2.118_L1.107, H2.119_L1.107, H1_L1.114, H1.1_L1.114, H1.2_L1.114, H1.3_L1.114, H1.4_L1.114, H1.5_L1.114, H1.6_L1.114, H1.7_L1.114, H1.8_L1.114, H1.9_L1.114, H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114, H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114, H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114, H2.90_L1.114, H2.91_L1.114, H2.118_L1.114, H2.119_L1.114, H1_L1.187, H1.1_L1.187, H1.2_L1.187, H1.3_L1.187, H1.4_L1.187, H1.5_L1.187, H1.6_L1.187, H1.7_L1.187, H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187, H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187, H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187, H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187, H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189, H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189, H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189, H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189, H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189, H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2,

H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2.

[0008] 3. In some embodiments, the VH/VL pair is selected from the group consisting of H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187.

[0009] In some embodiments, the composition is a monoclonal antibody.

[0010] In another aspect, provided herein is a heterodimeric antibody comprising: a) a first monomer, b) a second monomer, and c) a light chain. The first monomer comprises: i) an anti-CD3 scFv comprising a first variable light domain, an scFv linker and a first variable heavy domain; and ii) a first Fc domain, wherein the scFv is covalently attached to the N-terminus of the first Fc domain using a domain linker. The second monomer comprises a VH2-CH1-hinge-CH2-CH3 monomer, wherein VH is a second variable heavy domain and CH2-CH3 is a second Fc domain. The light chain comprises a second variable light domain. In this embodiment, the second variable heavy domain and the second variable light domain form a CLDN6 antigen binding domain (ABD).

[0011] In some embodiments, the CLDN6 binding domain comprises a set of 6 CDRs (vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2 and vlCDR3) from a variable heavy domain/variable light domain pair selected from the group consisting of: H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1, H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1, H2.12_L1, H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1, H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1, H1.9_L1.1, H1.19_L1.1, H1.22_L1.1, H1.24_L1.1, H2_L1.1, H2.1_L1.1, H2.2_L1.1, H2.3_L1.1, H2.4_L1.1, H2.5_L1.1, H2.6_L1.1, H2.7_L1.1, H2.8_L1.1, H2.9_L1.1, H2.11_L1.1, H2.12_L1.1, H2.71_L1.1, H2.75_L1.1, H2.90_L1.1, H2.91_L1.1, H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4, H1.2_L1.4, H1.3_L1.4, H1.4_L1.4, H1.5_L1.4, H1.6_L1.4, H1.7_L1.4, H1.8_L1.4, H1.9_L1.4, H1.19_L1.4, H1.22_L1.4, H1.24_L1.4, H2_L1.4, H2.1_L1.4, H2.2_L1.4, H2.3_L1.4, H2.4_L1.4, H2.5_L1.4, H2.6_L1.4, H2.7_L1.4, H2.8_L1.4, H2.9_L1.4, H2.11_L1.4, H2.12_L1.4, H2.71_L1.4, H2.75_L1.4, H2.90_L1.4, H2.91_L1.4, H2.118_L1.4, H2.119_L1.4, H1_L1.7, H1.1_L1.7, H1.2_L1.7, H1.3_L1.7, H1.4_L1.7, H1.5_L1.7, H1.6_L1.7, H1.7_L1.7, H1.8_L1.7, H1.9_L1.7, H1.19_L1.7, H1.22_L1.7,

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H1.1_L1.27, H1.2_L1.27, H1.3_L1.27, H1.4_L1.27, H1.5_L1.27, H1.6_L1.27, H1.7_L1.27,
H1.8_L1.27, H1.9_L1.27, H1.19_L1.27, H1.22_L1.27, H1.24_L1.27, H2_L1.27,

H2.1_L1.27, H2.2_L1.27, H2.3_L1.27, H2.4_L1.27, H2.5_L1.27, H2.6_L1.27, H2.7_L1.27, H2.8_L1.27, H2.9_L1.27, H2.11_L1.27, H2.12_L1.27, H2.71_L1.27, H2.75_L1.27, H2.90_L1.27, H2.91_L1.27, H2.118_L1.27, H2.119_L1.27, H1_L1.60, H1.1_L1.60, H1.2_L1.60, H1.3_L1.60, H1.4_L1.60, H1.5_L1.60, H1.6_L1.60, H1.7_L1.60, H1.8_L1.60, H1.9_L1.60, H1.19_L1.60, H1.22_L1.60, H1.24_L1.60, H2_L1.60, H2.1_L1.60, H2.2_L1.60, H2.3_L1.60, H2.4_L1.60, H2.5_L1.60, H2.6_L1.60, H2.7_L1.60, H2.8_L1.60, H2.9_L1.60, H2.11_L1.60, H2.12_L1.60, H2.71_L1.60, H2.75_L1.60, H2.90_L1.60, H2.91_L1.60, H2.118_L1.60, H2.119_L1.60, H1_L1.107, H1.1_L1.107, H1.2_L1.107, H1.3_L1.107, H1.4_L1.107, H1.5_L1.107, H1.6_L1.107, H1.7_L1.107, H1.8_L1.107, H1.9_L1.107, H1.19_L1.107, H1.22_L1.107, H1.24_L1.107, H2_L1.107, H2.1_L1.107, H2.2_L1.107, H2.3_L1.107, H2.4_L1.107, H2.5_L1.107, H2.6_L1.107, H2.7_L1.107, H2.8_L1.107, H2.9_L1.107, H2.11_L1.107, H2.12_L1.107, H2.71_L1.107, H2.75_L1.107, H2.90_L1.107, H2.91_L1.107, H2.118_L1.107, H2.119_L1.107, H1_L1.114, H1.1_L1.114, H1.2_L1.114, H1.3_L1.114, H1.4_L1.114, H1.5_L1.114, H1.6_L1.114, H1.7_L1.114, H1.8_L1.114, H1.9_L1.114, H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114, H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114, H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114, H2.90_L1.114, H2.91_L1.114, H2.118_L1.114, H2.119_L1.114, H1_L1.187, H1.1_L1.187, H1.2_L1.187, H1.3_L1.187, H1.4_L1.187, H1.5_L1.187, H1.6_L1.187, H1.7_L1.187, H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187, H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187, H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187, H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187, H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189, H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189, H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189, H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189, H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189, H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2, H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2.

[0012] In some embodiments, the CLDN6 binding domain comprises a VH/VL pair selected from the group consisting of: H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1, H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1, H2.12_L1, H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1, H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1, H1.9_L1.1, H1.19_L1.1, H1.22_L1.1, H1.24_L1.1, H2_L1.1, H2.1_L1.1, H2.2_L1.1, H2.3_L1.1, H2.4_L1.1, H2.5_L1.1, H2.6_L1.1, H2.7_L1.1, H2.8_L1.1, H2.9_L1.1, H2.11_L1.1, H2.12_L1.1, H2.71_L1.1, H2.75_L1.1, H2.90_L1.1, H2.91_L1.1, H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4, H1.2_L1.4, H1.3_L1.4, H1.4_L1.4, H1.5_L1.4, H1.6_L1.4, H1.7_L1.4, H1.8_L1.4, H1.9_L1.4, H1.19_L1.4, H1.22_L1.4, H1.24_L1.4, H2_L1.4, H2.1_L1.4, H2.2_L1.4, H2.3_L1.4, H2.4_L1.4, H2.5_L1.4, H2.6_L1.4, H2.7_L1.4, H2.8_L1.4, H2.9_L1.4, H2.11_L1.4, H2.12_L1.4, H2.71_L1.4, H2.75_L1.4, H2.90_L1.4, H2.91_L1.4, H2.118_L1.4, H2.119_L1.4, H1_L1.7, H1.1_L1.7, H1.2_L1.7, H1.3_L1.7, H1.4_L1.7, H1.5_L1.7, H1.6_L1.7, H1.7_L1.7, H1.8_L1.7, H1.9_L1.7, H1.19_L1.7, H1.22_L1.7, H1.24_L1.7, H2_L1.7, H2.1_L1.7, H2.2_L1.7, H2.3_L1.7, H2.4_L1.7, H2.5_L1.7, H2.6_L1.7, H2.7_L1.7, H2.8_L1.7, H2.9_L1.7, H2.11_L1.7, H2.12_L1.7, H2.71_L1.7, H2.75_L1.7, H2.90_L1.7, H2.91_L1.7, H2.118_L1.7, H2.119_L1.7, H1_L1.16, H1.1_L1.16, H1.2_L1.16, H1.3_L1.16, H1.4_L1.16, H1.5_L1.16, H1.6_L1.16, H1.7_L1.16, H1.8_L1.16, H1.9_L1.16, H1.19_L1.16, H1.22_L1.16, H1.24_L1.16, H2_L1.16, H2.1_L1.16, H2.2_L1.16, H2.3_L1.16, H2.4_L1.16, H2.5_L1.16, H2.6_L1.16, H2.7_L1.16, H2.8_L1.16, H2.9_L1.16, H2.11_L1.16, H2.12_L1.16, H2.71_L1.16, H2.75_L1.16, H2.90_L1.16, H2.91_L1.16, H2.118_L1.16, H2.119_L1.16, H1_L1.18, H1.1_L1.18, H1.2_L1.18, H1.3_L1.18, H1.4_L1.18, H1.5_L1.18, H1.6_L1.18, H1.7_L1.18, H1.8_L1.18, H1.9_L1.18, H1.19_L1.18, H1.22_L1.18, H1.24_L1.18, H2_L1.18, H2.1_L1.18, H2.2_L1.18, H2.3_L1.18, H2.4_L1.18, H2.5_L1.18, H2.6_L1.18, H2.7_L1.18, H2.8_L1.18, H2.9_L1.18, H2.11_L1.18, H2.12_L1.18, H2.71_L1.18, H2.75_L1.18, H2.90_L1.18, H2.91_L1.18, H2.118_L1.18, H2.119_L1.18, H1_L1.19, H1.1_L1.19, H1.2_L1.19, H1.3_L1.19, H1.4_L1.19, H1.5_L1.19, H1.6_L1.19, H1.7_L1.19, H1.8_L1.19, H1.9_L1.19, H1.19_L1.19, H1.22_L1.19, H1.24_L1.19, H2_L1.19, H2.1_L1.19, H2.2_L1.19, H2.3_L1.19, H2.4_L1.19, H2.5_L1.19, H2.6_L1.19, H2.7_L1.19, H2.8_L1.19, H2.9_L1.19, H2.11_L1.19, H2.12_L1.19, H2.71_L1.19, H2.75_L1.19, H2.90_L1.19, H2.91_L1.19, H2.118_L1.19, H2.119_L1.19, H1_L1.21, H1.1_L1.21, H1.2_L1.21, H1.3_L1.21, H1.4_L1.21, H1.5_L1.21, H1.6_L1.21,

H1.7_L1.21, H1.8_L1.21, H1.9_L1.21, H1.19_L1.21, H1.22_L1.21, H1.24_L1.21,
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H2.7_L1.21, H2.8_L1.21, H2.9_L1.21, H2.11_L1.21, H2.12_L1.21, H2.71_L1.21,
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H2.8_L1.22, H2.9_L1.22, H2.11_L1.22, H2.12_L1.22, H2.71_L1.22, H2.75_L1.22,
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H1.9_L1.23, H1.19_L1.23, H1.22_L1.23, H1.24_L1.23, H2_L1.23, H2.1_L1.23,
H2.2_L1.23, H2.3_L1.23, H2.4_L1.23, H2.5_L1.23, H2.6_L1.23, H2.7_L1.23, H2.8_L1.23,
H2.9_L1.23, H2.11_L1.23, H2.12_L1.23, H2.71_L1.23, H2.75_L1.23, H2.90_L1.23,
H2.91_L1.23, H2.118_L1.23, H2.119_L1.23, H1_L1.27, H1.1_L1.27, H1.2_L1.27,
H1.3_L1.27, H1.4_L1.27, H1.5_L1.27, H1.6_L1.27, H1.7_L1.27, H1.8_L1.27, H1.9_L1.27,
H1.19_L1.27, H1.22_L1.27, H1.24_L1.27, H2_L1.27, H2.1_L1.27, H2.2_L1.27,
H2.3_L1.27, H2.4_L1.27, H2.5_L1.27, H2.6_L1.27, H2.7_L1.27, H2.8_L1.27, H2.9_L1.27,
H2.11_L1.27, H2.12_L1.27, H2.71_L1.27, H2.75_L1.27, H2.90_L1.27, H2.91_L1.27,
H2.118_L1.27, H2.119_L1.27, H1_L1.60, H1.1_L1.60, H1.2_L1.60, H1.3_L1.60,
H1.4_L1.60, H1.5_L1.60, H1.6_L1.60, H1.7_L1.60, H1.8_L1.60, H1.9_L1.60, H1.19_L1.60,
H1.22_L1.60, H1.24_L1.60, H2_L1.60, H2.1_L1.60, H2.2_L1.60, H2.3_L1.60, H2.4_L1.60,
H2.5_L1.60, H2.6_L1.60, H2.7_L1.60, H2.8_L1.60, H2.9_L1.60, H2.11_L1.60,
H2.12_L1.60, H2.71_L1.60, H2.75_L1.60, H2.90_L1.60, H2.91_L1.60, H2.118_L1.60,
H2.119_L1.60, H1_L1.107, H1.1_L1.107, H1.2_L1.107, H1.3_L1.107, H1.4_L1.107,
H1.5_L1.107, H1.6_L1.107, H1.7_L1.107, H1.8_L1.107, H1.9_L1.107, H1.19_L1.107,
H1.22_L1.107, H1.24_L1.107, H2_L1.107, H2.1_L1.107, H2.2_L1.107, H2.3_L1.107,
H2.4_L1.107, H2.5_L1.107, H2.6_L1.107, H2.7_L1.107, H2.8_L1.107, H2.9_L1.107,
H2.11_L1.107, H2.12_L1.107, H2.71_L1.107, H2.75_L1.107, H2.90_L1.107,
H2.91_L1.107, H2.118_L1.107, H2.119_L1.107, H1_L1.114, H1.1_L1.114, H1.2_L1.114,
H1.3_L1.114, H1.4_L1.114, H1.5_L1.114, H1.6_L1.114, H1.7_L1.114, H1.8_L1.114,
H1.9_L1.114, H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114,
H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114,
H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114,
H2.90_L1.114, H2.91_L1.114, H2.118_L1.114, H2.119_L1.114, H1_L1.187, H1.1_L1.187,

H1.2_L1.187, H1.3_L1.187, H1.4_L1.187, H1.5_L1.187, H1.6_L1.187, H1.7_L1.187, H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187, H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187, H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187, H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187, H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189, H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189, H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189, H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189, H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189, H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2, H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2.

[0013] In certain embodiments, the CLDN6 binding domain comprises a VH/VL pair selected from the group consisting of: H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187.

[0014] In some embodiments of the heterodimeric antibody, the anti-CD3 scFv comprises a VH/VL pair selected from the group consisting of H1.30_L1.47, H1.32_L1.47, H1.89_L1.47, H1.90_L1.47, H1.33_L1.47, H1.31_L1.47, L1.47_H1.30, L1.47_H1.30, L1.47_H1.32, L1.47_H1.89, L1.47_H1.90, L1.47_H1.33, and L1.47_H1.31.

[0015] In some embodiments of the heterodimeric antibody, the scFv linker is a charged scFv linker.

[0016] In some embodiments, the first and second Fc domains are variant Fc domains. In some embodiments, the first and second Fc domains comprise a set of heterodimerization variants selected from the group consisting of those depicted in Figures 1A-1E. In some embodiments, the set of heterodimerization variants selected is from the group consisting of S364K/E357Q : L368D/K370S; S364K : L368D/K370S; S364K : L368E/K370S; D401K : T411E/K360E/Q362E; and T366W : T366S/L368A/Y407V, wherein numbering is according to EU numbering.

[0017] In some embodiments, the first and second monomers further comprise one or more ablation variants. In some embodiments, the one or more ablation variants are E233P/L234V/L235A/G236del/S267K, wherein numbering is according to EU numbering.

[0018] In exemplary embodiments, one of the first or second monomer comprises one or more pI variants. In some embodiments, the one or more pI variants are N208D/Q295E/N384D/Q418E/N421D, wherein numbering is according to EU numbering.

[0019] In exemplary embodiments of the heterodimeric antibody, the first monomer comprises amino acid variants S364K/E357Q/ E233P/L234V/L235A/G236del/S267K, the second monomer comprises amino acid variants L368D/K370S/N208D/Q295E/N384D/Q418E/N421D/E233P/L234V/L235A/G236del/S267K, and wherein numbering is according to EU numbering.

[0020] In some embodiments, the first and second monomers each further comprise amino acid variants 428/434S, wherein numbering is according to EU numbering.

[0021] In another aspect, provided herein is a heterodimeric antibody comprising: a) a first monomer comprising, from N-terminal to C-terminal, a scFv-linker-CH2-CH3, wherein scFv is an anti-CD3 scFv and CH2-CH3 is a first Fc domain; b) a second monomer comprising, from N-terminal to C-terminal, a VH-CH1-hinge-CH2-CH3, wherein CH2-CH3 is a second Fc domain; and c) a light chain comprising VL-CL. The first variant Fc domain comprises amino acid variants S364K/E357Q, the second variant Fc domain comprises amino acid variants L368D/K370S, the first and second variant Fc domains each comprises amino acid variants E233P/L234V/L235A/G236del/S267K, and the CH1-hinge-CH2-CH3 of the second monomer comprises amino acid variants N208D/Q295E/N384D/Q418E/N421D (EU numbering). Further, the VH and VL form an CLDN6 binding domain comprising the variable heavy domain and the variable light domain, respectively, of an CLDN6 binding domain selected from H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187; and the anti-CD3 scFv comprises the variable heavy domain and the variable light domain of a CD3 binding domain selected from H1.30_L1.47, H1.32_L1.47, H1.89_L1.47, H1.90_L1.47, H1.33_L1.47, H1.31_L1.47, L1.47_H1.30, L1.47_H1.30, L1.47_H1.32, L1.47_H1.89, L1.47_H1.90, L1.47_H1.33, and L1.47_H1.31.

[0022] In some embodiments, the first and second variant Fc domains each further comprise amino acid variants 428/434S, wherein numbering is according to EU numbering.

[0023] In another aspect, provided herein is a heterodimeric antibody comprising: a) a first monomer, b) a second monomer, and c) a common light chain. The first monomer comprises, from N-terminal to C-terminal, a VH1-CH1-linker 1-scFv-linker 2-CH2-CH3, wherein VH1 is a first variable heavy domain, scFv is an anti-CD3 scFv, linker 1 and linker 2 are a first domain linker and second domain linker, respectively, and CH2-CH3 is a first Fc domain. The second monomer comprises, from N-terminal to C-terminal, a VH2-CH1-hinge-CH2-CH3, wherein VH2 is a second variable heavy domain and CH2-CH3 is a second Fc domain; and c) a common light chain comprising a variable light domain. The first variable heavy domain and the variable light domain form a first CLDN6 ABD, and the second variable heavy domain and the variable light domain form a second CLDN6 ABD.

[0024] In some embodiments, the first and second CLDN6 binding domains each comprise a set of 6 CDRs (vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2 and vlCDR3) from a VH/VL pair selected from the group consisting of: H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1, H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1, H2.12_L1, H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1, H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1, H1.9_L1.1, H1.19_L1.1, H1.22_L1.1, H1.24_L1.1, H2_L1.1, H2.1_L1.1, H2.2_L1.1, H2.3_L1.1, H2.4_L1.1, H2.5_L1.1, H2.6_L1.1, H2.7_L1.1, H2.8_L1.1, H2.9_L1.1, H2.11_L1.1, H2.12_L1.1, H2.71_L1.1, H2.75_L1.1, H2.90_L1.1, H2.91_L1.1, H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4, H1.2_L1.4, H1.3_L1.4, H1.4_L1.4, H1.5_L1.4, H1.6_L1.4, H1.7_L1.4, H1.8_L1.4, H1.9_L1.4, H1.19_L1.4, H1.22_L1.4, H1.24_L1.4, H2_L1.4, H2.1_L1.4, H2.2_L1.4, H2.3_L1.4, H2.4_L1.4, H2.5_L1.4, H2.6_L1.4, H2.7_L1.4, H2.8_L1.4, H2.9_L1.4, H2.11_L1.4, H2.12_L1.4, H2.71_L1.4, H2.75_L1.4, H2.90_L1.4, H2.91_L1.4, H2.118_L1.4, H2.119_L1.4, H1_L1.7, H1.1_L1.7, H1.2_L1.7, H1.3_L1.7, H1.4_L1.7, H1.5_L1.7, H1.6_L1.7, H1.7_L1.7, H1.8_L1.7, H1.9_L1.7, H1.19_L1.7, H1.22_L1.7, H1.24_L1.7, H2_L1.7, H2.1_L1.7, H2.2_L1.7, H2.3_L1.7, H2.4_L1.7, H2.5_L1.7, H2.6_L1.7, H2.7_L1.7, H2.8_L1.7, H2.9_L1.7, H2.11_L1.7, H2.12_L1.7, H2.71_L1.7, H2.75_L1.7, H2.90_L1.7, H2.91_L1.7, H2.118_L1.7, H2.119_L1.7, H1_L1.16, H1.1_L1.16, H1.2_L1.16, H1.3_L1.16, H1.4_L1.16, H1.5_L1.16, H1.6_L1.16, H1.7_L1.16, H1.8_L1.16, H1.9_L1.16, H1.19_L1.16, H1.22_L1.16, H1.24_L1.16, H2_L1.16, H2.1_L1.16, H2.2_L1.16, H2.3_L1.16, H2.4_L1.16, H2.5_L1.16, H2.6_L1.16, H2.7_L1.16, H2.8_L1.16,

H2.9_L1.16, H2.11_L1.16, H2.12_L1.16, H2.71_L1.16, H2.75_L1.16, H2.90_L1.16, H2.91_L1.16, H2.118_L1.16, H2.119_L1.16, H1_L1.18, H1.1_L1.18, H1.2_L1.18, H1.3_L1.18, H1.4_L1.18, H1.5_L1.18, H1.6_L1.18, H1.7_L1.18, H1.8_L1.18, H1.9_L1.18, H1.19_L1.18, H1.22_L1.18, H1.24_L1.18, H2_L1.18, H2.1_L1.18, H2.2_L1.18, H2.3_L1.18, H2.4_L1.18, H2.5_L1.18, H2.6_L1.18, H2.7_L1.18, H2.8_L1.18, H2.9_L1.18, H2.11_L1.18, H2.12_L1.18, H2.71_L1.18, H2.75_L1.18, H2.90_L1.18, H2.91_L1.18, H2.118_L1.18, H2.119_L1.18, H1_L1.19, H1.1_L1.19, H1.2_L1.19, H1.3_L1.19, H1.4_L1.19, H1.5_L1.19, H1.6_L1.19, H1.7_L1.19, H1.8_L1.19, H1.9_L1.19, H1.19_L1.19, H1.22_L1.19, H1.24_L1.19, H2_L1.19, H2.1_L1.19, H2.2_L1.19, H2.3_L1.19, H2.4_L1.19, H2.5_L1.19, H2.6_L1.19, H2.7_L1.19, H2.8_L1.19, H2.9_L1.19, H2.11_L1.19, H2.12_L1.19, H2.71_L1.19, H2.75_L1.19, H2.90_L1.19, H2.91_L1.19, H2.118_L1.19, H2.119_L1.19, H1_L1.21, H1.1_L1.21, H1.2_L1.21, H1.3_L1.21, H1.4_L1.21, H1.5_L1.21, H1.6_L1.21, H1.7_L1.21, H1.8_L1.21, H1.9_L1.21, H1.19_L1.21, H1.22_L1.21, H1.24_L1.21, H2_L1.21, H2.1_L1.21, H2.2_L1.21, H2.3_L1.21, H2.4_L1.21, H2.5_L1.21, H2.6_L1.21, H2.7_L1.21, H2.8_L1.21, H2.9_L1.21, H2.11_L1.21, H2.12_L1.21, H2.71_L1.21, H2.75_L1.21, H2.90_L1.21, H2.91_L1.21, H2.118_L1.2, H2.119_L1.21, H1_L1.22, H1.1_L1.22, H1.2_L1.22, H1.3_L1.22, H1.4_L1.22, H1.5_L1.22, H1.6_L1.22, H1.7_L1.22, H1.8_L1.22, H1.9_L1.22, H1.19_L1.22, H1.22_L1.22, H1.24_L1.22, H2_L1.22, H2.1_L1.22, H2.2_L1.22, H2.3_L1.22, H2.4_L1.22, H2.5_L1.22, H2.6_L1.22, H2.7_L1.22, H2.8_L1.22, H2.9_L1.22, H2.11_L1.22, H2.12_L1.22, H2.71_L1.22, H2.75_L1.22, H2.90_L1.22, H2.91_L1.22, H2.118_L1.22, H2.119_L1.22, H1_L1.23, H1.1_L1.23, H1.2_L1.23, H1.3_L1.23, H1.4_L1.23, H1.5_L1.23, H1.6_L1.23, H1.7_L1.23, H1.8_L1.23, H1.9_L1.23, H1.19_L1.23, H1.22_L1.23, H1.24_L1.23, H2_L1.23, H2.1_L1.23, H2.2_L1.23, H2.3_L1.23, H2.4_L1.23, H2.5_L1.23, H2.6_L1.23, H2.7_L1.23, H2.8_L1.23, H2.9_L1.23, H2.11_L1.23, H2.12_L1.23, H2.71_L1.23, H2.75_L1.23, H2.90_L1.23, H2.91_L1.23, H2.118_L1.23, H2.119_L1.23, H1_L1.27, H1.1_L1.27, H1.2_L1.27, H1.3_L1.27, H1.4_L1.27, H1.5_L1.27, H1.6_L1.27, H1.7_L1.27, H1.8_L1.27, H1.9_L1.27, H1.19_L1.27, H1.22_L1.27, H1.24_L1.27, H2_L1.27, H2.1_L1.27, H2.2_L1.27, H2.3_L1.27, H2.4_L1.27, H2.5_L1.27, H2.6_L1.27, H2.7_L1.27, H2.8_L1.27, H2.9_L1.27, H2.11_L1.27, H2.12_L1.27, H2.71_L1.27, H2.75_L1.27, H2.90_L1.27, H2.91_L1.27, H2.118_L1.27, H2.119_L1.27, H1_L1.60, H1.1_L1.60, H1.2_L1.60, H1.3_L1.60, H1.4_L1.60, H1.5_L1.60, H1.6_L1.60, H1.7_L1.60, H1.8_L1.60, H1.9_L1.60, H1.19_L1.60, H1.22_L1.60, H1.24_L1.60, H2_L1.60, H2.1_L1.60, H2.2_L1.60, H2.3_L1.60, H2.4_L1.60, H2.5_L1.60, H2.6_L1.60, H2.7_L1.60, H2.8_L1.60, H2.9_L1.60,

H2.11_L1.60, H2.12_L1.60, H2.71_L1.60, H2.75_L1.60, H2.90_L1.60, H2.91_L1.60, H2.118_L1.60, H2.119_L1.60, H1_L1.107, H1.1_L1.107, H1.2_L1.107, H1.3_L1.107, H1.4_L1.107, H1.5_L1.107, H1.6_L1.107, H1.7_L1.107, H1.8_L1.107, H1.9_L1.107, H1.19_L1.107, H1.22_L1.107, H1.24_L1.107, H2_L1.107, H2.1_L1.107, H2.2_L1.107, H2.3_L1.107, H2.4_L1.107, H2.5_L1.107, H2.6_L1.107, H2.7_L1.107, H2.8_L1.107, H2.9_L1.107, H2.11_L1.107, H2.12_L1.107, H2.71_L1.107, H2.75_L1.107, H2.90_L1.107, H2.91_L1.107, H2.118_L1.107, H2.119_L1.107, H1_L1.114, H1.1_L1.114, H1.2_L1.114, H1.3_L1.114, H1.4_L1.114, H1.5_L1.114, H1.6_L1.114, H1.7_L1.114, H1.8_L1.114, H1.9_L1.114, H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114, H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114, H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114, H2.90_L1.114, H2.91_L1.114, H2.118_L1.114, H2.119_L1.114, H1_L1.187, H1.1_L1.187, H1.2_L1.187, H1.3_L1.187, H1.4_L1.187, H1.5_L1.187, H1.6_L1.187, H1.7_L1.187, H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187, H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187, H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187, H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187, H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189, H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189, H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189, H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189, H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189, H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2, H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2.

[0025] In exemplary embodiments, each of the first and second CLDN6 binding domains comprise a VH/VL pair selected from the group consisting of: H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1, H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1, H2.12_L1, H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1, H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1, H1.9_L1.1, H1.19_L1.1, H1.22_L1.1,

H1.24_L1.1, H2_L1.1, H2.1_L1.1, H2.2_L1.1, H2.3_L1.1, H2.4_L1.1, H2.5_L1.1,
H2.6_L1.1, H2.7_L1.1, H2.8_L1.1, H2.9_L1.1, H2.11_L1.1, H2.12_L1.1, H2.71_L1.1,
H2.75_L1.1, H2.90_L1.1, H2.91_L1.1, H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4,
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H2_L1.7, H2.1_L1.7, H2.2_L1.7, H2.3_L1.7, H2.4_L1.7, H2.5_L1.7, H2.6_L1.7,
H2.7_L1.7, H2.8_L1.7, H2.9_L1.7, H2.11_L1.7, H2.12_L1.7, H2.71_L1.7, H2.75_L1.7,
H2.90_L1.7, H2.91_L1.7, H2.118_L1.7, H2.119_L1.7, H1_L1.16, H1.1_L1.16, H1.2_L1.16,
H1.3_L1.16, H1.4_L1.16, H1.5_L1.16, H1.6_L1.16, H1.7_L1.16, H1.8_L1.16,
H1.9_L1.16, H1.19_L1.16, H1.22_L1.16, H1.24_L1.16, H2_L1.16, H2.1_L1.16, H2.2_L1.16,
H2.3_L1.16, H2.4_L1.16, H2.5_L1.16, H2.6_L1.16, H2.7_L1.16, H2.8_L1.16,
H2.9_L1.16, H2.11_L1.16, H2.12_L1.16, H2.71_L1.16, H2.75_L1.16, H2.90_L1.16,
H2.91_L1.16, H2.118_L1.16, H2.119_L1.16, H1_L1.18, H1.1_L1.18, H1.2_L1.18,
H1.3_L1.18, H1.4_L1.18, H1.5_L1.18, H1.6_L1.18, H1.7_L1.18, H1.8_L1.18, H1.9_L1.18,
H1.19_L1.18, H1.22_L1.18, H1.24_L1.18, H2_L1.18, H2.1_L1.18, H2.2_L1.18,
H2.3_L1.18, H2.4_L1.18, H2.5_L1.18, H2.6_L1.18, H2.7_L1.18, H2.8_L1.18, H2.9_L1.18,
H2.11_L1.18, H2.12_L1.18, H2.71_L1.18, H2.75_L1.18, H2.90_L1.18, H2.91_L1.18,
H2.118_L1.18, H2.119_L1.18, H1_L1.19, H1.1_L1.19, H1.2_L1.19, H1.3_L1.19,
H1.4_L1.19, H1.5_L1.19, H1.6_L1.19, H1.7_L1.19, H1.8_L1.19, H1.9_L1.19, H1.19_L1.19,
H1.22_L1.19, H1.24_L1.19, H2_L1.19, H2.1_L1.19, H2.2_L1.19, H2.3_L1.19, H2.4_L1.19,
H2.5_L1.19, H2.6_L1.19, H2.7_L1.19, H2.8_L1.19, H2.9_L1.19, H2.11_L1.19,
H2.12_L1.19, H2.71_L1.19, H2.75_L1.19, H2.90_L1.19, H2.91_L1.19, H2.118_L1.19,
H2.119_L1.19, H1_L1.21, H1.1_L1.21, H1.2_L1.21, H1.3_L1.21, H1.4_L1.21, H1.5_L1.21,
H1.6_L1.21, H1.7_L1.21, H1.8_L1.21, H1.9_L1.21, H1.19_L1.21, H1.22_L1.21,
H1.24_L1.21, H2_L1.21, H2.1_L1.21, H2.2_L1.21, H2.3_L1.21, H2.4_L1.21, H2.5_L1.21,
H2.6_L1.21, H2.7_L1.21, H2.8_L1.21, H2.9_L1.21, H2.11_L1.21, H2.12_L1.21,
H2.71_L1.21, H2.75_L1.21, H2.90_L1.21, H2.91_L1.21, H2.118_L1.21, H2.119_L1.21,
H1_L1.22, H1.1_L1.22, H1.2_L1.22, H1.3_L1.22, H1.4_L1.22, H1.5_L1.22, H1.6_L1.22,
H1.7_L1.22, H1.8_L1.22, H1.9_L1.22, H1.19_L1.22, H1.22_L1.22, H1.24_L1.22,
H2_L1.22, H2.1_L1.22, H2.2_L1.22, H2.3_L1.22, H2.4_L1.22, H2.5_L1.22, H2.6_L1.22,

H2.7_L1.22, H2.8_L1.22, H2.9_L1.22, H2.11_L1.22, H2.12_L1.22, H2.71_L1.22,
H2.75_L1.22, H2.90_L1.22, H2.91_L1.22, H2.118_L1.22, H2.119_L1.22, H1_L1.23,
H1.1_L1.23, H1.2_L1.23, H1.3_L1.23, H1.4_L1.23, H1.5_L1.23, H1.6_L1.23, H1.7_L1.23,
H1.8_L1.23, H1.9_L1.23, H1.19_L1.23, H1.22_L1.23, H1.24_L1.23, H2_L1.23,
H2.1_L1.23, H2.2_L1.23, H2.3_L1.23, H2.4_L1.23, H2.5_L1.23, H2.6_L1.23, H2.7_L1.23,
H2.8_L1.23, H2.9_L1.23, H2.11_L1.23, H2.12_L1.23, H2.71_L1.23, H2.75_L1.23,
H2.90_L1.23, H2.91_L1.23, H2.118_L1.23, H2.119_L1.23, H1_L1.27, H1.1_L1.27,
H1.2_L1.27, H1.3_L1.27, H1.4_L1.27, H1.5_L1.27, H1.6_L1.27, H1.7_L1.27, H1.8_L1.27,
H1.9_L1.27, H1.19_L1.27, H1.22_L1.27, H1.24_L1.27, H2_L1.27, H2.1_L1.27,
H2.2_L1.27, H2.3_L1.27, H2.4_L1.27, H2.5_L1.27, H2.6_L1.27, H2.7_L1.27, H2.8_L1.27,
H2.9_L1.27, H2.11_L1.27, H2.12_L1.27, H2.71_L1.27, H2.75_L1.27, H2.90_L1.27,
H2.91_L1.27, H2.118_L1.27, H2.119_L1.27, H1_L1.60, H1.1_L1.60, H1.2_L1.60,
H1.3_L1.60, H1.4_L1.60, H1.5_L1.60, H1.6_L1.60, H1.7_L1.60, H1.8_L1.60, H1.9_L1.60,
H1.19_L1.60, H1.22_L1.60, H1.24_L1.60, H2_L1.60, H2.1_L1.60, H2.2_L1.60,
H2.3_L1.60, H2.4_L1.60, H2.5_L1.60, H2.6_L1.60, H2.7_L1.60, H2.8_L1.60, H2.9_L1.60,
H2.11_L1.60, H2.12_L1.60, H2.71_L1.60, H2.75_L1.60, H2.90_L1.60, H2.91_L1.60,
H2.118_L1.60, H2.119_L1.60, H1_L1.107, H1.1_L1.107, H1.2_L1.107, H1.3_L1.107,
H1.4_L1.107, H1.5_L1.107, H1.6_L1.107, H1.7_L1.107, H1.8_L1.107, H1.9_L1.107,
H1.19_L1.107, H1.22_L1.107, H1.24_L1.107, H2_L1.107, H2.1_L1.107, H2.2_L1.107,
H2.3_L1.107, H2.4_L1.107, H2.5_L1.107, H2.6_L1.107, H2.7_L1.107, H2.8_L1.107,
H2.9_L1.107, H2.11_L1.107, H2.12_L1.107, H2.71_L1.107, H2.75_L1.107, H2.90_L1.107,
H2.91_L1.107, H2.118_L1.107, H2.119_L1.107, H1_L1.114, H1.1_L1.114, H1.2_L1.114,
H1.3_L1.114, H1.4_L1.114, H1.5_L1.114, H1.6_L1.114, H1.7_L1.114, H1.8_L1.114,
H1.9_L1.114, H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114,
H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114,
H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114,
H2.90_L1.114, H2.91_L1.114, H2.118_L1.114, H2.119_L1.114, H1_L1.187, H1.1_L1.187,
H1.2_L1.187, H1.3_L1.187, H1.4_L1.187, H1.5_L1.187, H1.6_L1.187, H1.7_L1.187,
H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187,
H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187,
H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187,
H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187,
H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189,
H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189,

H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189, H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189, H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189, H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2, H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2.

[0026] In some embodiments, the VH/VL pairs are selected from the group consisting of H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187.

[0027] In some embodiments, the scFv comprises a set of 6 CDRs (vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2 and vlCDR3) from VH/VL pairs selected from the group consisting of: H1.30_L1.47, H1.32_L1.47, H1.89_L1.47, H1.90_L1.47, H1.33_L1.47, H1.31_L1.47, L1.47_H1.30, L1.47_H1.30, L1.47_H1.32, L1.47_H1.89, L1.47_H1.90, L1.47_H1.33, and L1.47_H1.31. In exemplary embodiments, the scFv comprises the variable heavy domain and variable light domain of any of the following CD3 binding domains: H1.30_L1.47, H1.32_L1.47, H1.89_L1.47, H1.90_L1.47, H1.33_L1.47, H1.31_L1.47, L1.47_H1.30, L1.47_H1.30, L1.47_H1.32, L1.47_H1.89, L1.47_H1.90, L1.47_H1.33, and L1.47_H1.31.

[0028] In some embodiments of the heterodimeric antibody, the scFv linker is a charged scFv linker. In some embodiments, the scFv linker is a charged scFv linker having the amino acid sequence (GKPGS)₄ (SEQ ID NO: 1).

[0029] In some embodiments, the first and second Fc domains are variant Fc domains. In some embodiments, the first and second Fc domains comprise a set of heterodimerization variants selected from the group consisting of those depicted in Figures 1A-1E. In some embodiments, the set of heterodimerization variants selected is from the group consisting of S364K/E357Q : L368D/K370S; S364K : L368D/K370S; S364K : L368E/K370S; D401K : T411E/K360E/Q362E; and T366W : T366S/L368A/Y407V, wherein numbering is according to EU numbering.

[0030] In some embodiments, the first and second monomers further comprise one or more ablation variants. In some embodiments, the one or more ablation variants are E233P/L234V/L235A/G236del/S267K, wherein numbering is according to EU numbering.

[0031] In exemplary embodiments, one of the first or second monomer comprises one or more pI variants. In some embodiments, the one or more pI variants are N208D/Q295E/N384D/Q418E/N421D, wherein numbering is according to EU numbering.

[0032] In exemplary embodiments of the heterodimeric antibody, the first monomer comprises amino acid variants S364K/E357Q/E233P/L234V/L235A/G236del/S267K, the second monomer comprises amino acid variants L368D/K370S/N208D/Q295E/N384D/Q418E/N421D/E233P/L234V/L235A/G236del/S267K, and wherein numbering is according to EU numbering.

[0033] In some embodiments, the first and second monomers each further comprise amino acid variants 428/434S, wherein numbering is according to EU numbering.

[0034] In another aspect, provided herein is heterodimeric antibody comprising: a) a first monomer, b) a second monomer, and c) a common light chain. The first monomer comprises, from N-terminal to C-terminal, a VH1-CH1-linker 1-scFv-linker 2-CH2-CH3, wherein scFv is an anti-CD3 scFv and CH2-CH3 is a first Fc domain. The second monomer comprises, from N-terminal to C-terminal, a VH1-CH1-hinge-CH2-CH3, wherein CH2-CH3 is a second Fc domain. The common light chain comprising VL-CL. The first variant Fc domain comprises amino acid variants S364K/E357Q, the second variant Fc domain comprises amino acid variants L368D/K370S, the first and second variant Fc domains each comprises amino acid variants E233P/L234V/L235A/G236del/S267K, and the CH1-hinge-CH2-CH3 of the second monomer comprises amino acid variants N208D/Q295E/N384D/Q418E/N421D (EU numbering). The VH and VL comprise the variable heavy domain and the variable light domain of a CLDN6 ABD selected from H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187; and the anti-CD3 scFv comprises the variable heavy domain and the variable light domain of a CD3 binding domain selected from H1.30_L1.47, H1.32_L1.47, H1.89_L1.47, H1.90_L1.47, H1.33_L1.47, H1.31_L1.47, L1.47_H1.30, L1.47_H1.30, L1.47_H1.32, L1.47_H1.89, L1.47_H1.90, L1.47_H1.33, and L1.47_H1.31.

[0035] Also provided herein are nucleic acid compositions comprising nucleic acids encoding the antibodies described herein, expression vector compositions that include such nucleic acids, host cells for making the antibodies that comprise the expression vector compositions, and methods of making the antibodies.

BRIEF DESCRIPTION OF THE DRAWINGS

[0036] Figures 1A – 1E depict useful pairs of Fc heterodimerization variant sets (including skew and pI variants) that lead to Fc heterodimerization. There are variants for which there are no corresponding “monomer 2” variants; these are pI variants which can be used alone on either monomer.

[0037] Figure 2 depicts a list of isosteric variant antibody constant regions and their respective substitutions. pI₋(-) indicates lower pI variants, while pI₊(+) indicates higher pI variants. These can be optionally and independently combined with other heterodimerization variants of the inventions (and other variant types as well, as outlined herein.)

[0038] Figure 3 depicts useful ablation variants that ablate FcγR binding (sometimes referred to as “knock outs” or “KO” variants). Generally, ablation variants are found on both monomers, although in some cases they may be on only one monomer

[0039] Figure 4 depicts particularly useful embodiments of “non-Fv” components of the invention.

[0040] Figure 5 depicts a number of charged scFv linkers that find use in increasing or decreasing the pI of the subject heterodimeric bsAbs that utilize one or more scFv as a component, as described herein. The (+H) positive linker finds particular use herein, particularly with anti-CD3 V_L and V_H sequences shown herein. A single prior art scFv linker with a single charge is referenced as “Whitlow”, from Whitlow et al., Protein Engineering 6(8):989-995 (1993). It should be noted that this linker was used for reducing aggregation and enhancing proteolytic stability in scFvs. Such charged scFv linkers can be used in any of the subject antibody formats disclosed herein that include scFvs (e.g., 1 + 1 Fab-scFv-Fc and 2 + 1 Fab₂-scFv-Fc formats).

[0041] Figure 6 depicts a number of exemplary domain linkers. In some embodiments, these linkers find use linking a single-chain Fv to an Fc chain. In some embodiments, these linkers may be combined. For example, a GGGGS linker (SEQ ID NO: 5) may be combined with a “half hinge” linker.

[0042] Figure 7A – 7D depicts the sequences of several useful 1 + 1 Fab-scFv-Fc bispecific antibody format heavy chain backbones based on human IgG1, without the Fv sequences (e.g. the scFv and the VH for the Fab side). Backbone 1 is based on human IgG1 (356E/358M allotype), and includes the S364K/E357Q : L368D/K370S skew variants,

C220S on the chain with the S364K/E357Q skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 2 is based on human IgG1 (356E/358M allotype), and includes S364K : L368D/K370S skew variants, C220S on the chain with the S364K skew variant, the N208D/Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants, and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 3 is based on human IgG1 (356E/358M allotype), and includes S364K : L368E/K370S skew variants, C220S on the chain with the S364K skew variant, the N208D/Q295E/N384D/Q418E/N421D pI variants on the chain with L368E/K370S skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 4 is based on human IgG1 (356E/358M allotype), and includes D401K : K360E/Q362E/T411E skew variants, C220S on the chain with the D401K skew variant, the N208D/Q295E/N384D/Q418E/N421D pI variants on the chain with K360E/Q362E/T411E skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 5 is based on human IgG1 (356D/358L allotype), and includes S364K/E357Q : L368D/K370S skew variants, C220S on the chain with the S364K/E357Q skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 6 is based on human IgG1 (356E/358M allotype), and includes S364K/E357Q : L368D/K370S skew variants, C220S on the chain with the S364K/E357Q skew variants, N208D/Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains, as well as an N297A variant on both chains. Backbone 7 is identical to 6 except the mutation is N297S. Backbone 8 is based on human IgG4, and includes the S364K/E357Q : L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants, as well as a S228P (EU numbering, this is S241P in Kabat) variant on both chains that ablates Fab arm exchange as is known in the art. Backbone 9 is based on human IgG2, and includes the S364K/E357Q : L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants. Backbone 10 is based on human IgG2, and includes the S364K/E357Q : L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants as well as a S267K variant on both chains. Backbone 11 is identical to backbone 1, except it includes M428L/N434S Xtend

mutations. Backbone 12 is based on human IgG1 (356E/358M allotype), and includes S364K/E357Q : L368D/K370S skew variants, C220S and the P217R/P229R/N276K pI variants on the chain with S364K/E357Q skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Included within each of these backbones are sequences that are 90, 95, 98 and 99% identical (as defined herein) to the recited sequences, and/or contain from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 additional amino acid substitutions (as compared to the “parent” of the Figure, which, as will be appreciated by those in the art, already contain a number of amino acid modifications as compared to the parental human IgG1 (or IgG2 or IgG4, depending on the backbone). That is, the recited backbones may contain additional amino acid modifications (generally amino acid substitutions) in addition to the skew, pI and ablation variants contained within the backbones of this figure.

[0043] Figures 8A – 8C depict the sequences of several useful 2 + 1 Fab₂-scFv-Fc bispecific antibody format heavy chain backbones based on human IgG1, without the Fv sequences (e.g. the scFv and the VH for the Fab side). Backbone 1 is based on human IgG1 (356E/358M allotype), and includes the S364K/E357Q : L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 2 is based on human IgG1 (356E/358M allotype), and includes S364K : L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants, and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 3 is based on human IgG1 (356E/358M allotype), and includes S364K : L368E/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the chain with L368E/K370S skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 4 is based on human IgG1 (356E/358M allotype), and includes D401K : K360E/Q362E/T411E skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the chain with K360E/Q362E/T411E skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 5 is based on human IgG1 (356D/358L allotype), and includes S364K/E357Q : L368D/K370S skew variants, the N208D/Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Backbone 6 is based on human IgG1 (356E/358M allotype), and includes

S364K/E357Q : L368D/K370S skew variants, N208D/Q295E/N384D/Q418E/N421D pI variants on the chain with L368D/K370S skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains, as well as an N297A variant on both chains. Backbone 7 is identical to 6 except the mutation is N297S. Backbone 8 is identical to backbone 1, except it includes M428L/N434S Xtend mutations. Backbone 9 is based on human IgG1 (356E/358M allotype), and includes S364K/E357Q : L368D/K370S skew variants, the P217R/P229R/N276K pI variants on the chain with S364K/E357Q skew variants and the E233P/L234V/L235A/G236del/S267K ablation variants on both chains. Included within each of these backbones are sequences that are 90, 95, 98 and 99% identical (as defined herein) to the recited sequences, and/or contain from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 additional amino acid substitutions (as compared to the “parent” of the Figure, which, as will be appreciated by those in the art, already contain a number of amino acid modifications as compared to the parental human IgG1 (or IgG2 or IgG4, depending on the backbone). That is, the recited backbones may contain additional amino acid modifications (generally amino acid substitutions) in addition to the skew, pI and ablation variants contained within the backbones of this figure.

[0044] Figure 9 depicts the sequences of several useful constant light domain backbones based on human IgG1, without the Fv sequences (e.g. the scFv or the Fab). Included herein are constant light backbone sequences that are 90, 95, 98 and 99% identical (as defined herein) to the recited sequences, and/or contain from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 additional amino acid modifications.

[0045] Figure 10A-10F depicts sequences for exemplary anti-CD3 scFvs suitable for use in the bispecific antibodies of the invention. The CDRs are underlined, the scFv linker is double underlined (in the sequences, the scFv linker is a positively charged scFv (GKPGS)₄ linker (SEQ ID NO: 1), although as will be appreciated by those in the art, this linker can be replaced by other linkers, including uncharged or negatively charged linkers, some of which are depicted in Figure 5), and the slashes indicate the border(s) of the variable domains. In addition, the naming convention illustrates the orientation of the scFv from N- to C-terminus. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 2, and thus included herein are not only the CDRs that are underlined but also CDRs included within the V_H and V_L domains using other numbering

systems. Furthermore, as for all the sequences in the Figures, these V_H and V_L sequences can be used either in a scFv format or in a Fab format.

[0046] Figure 11 depicts the antigen sequences for a number of antigens of use in the invention, including both human and cyno, to facilitate the development of antigen binding domains that bind to both for ease of clinical development.

[0047] Figure 12 depicts alignment of human CLDN6 and CLDN9 sequences and highlights the 3 differences in their respective extracellular loops. Figure 12 discloses SEQ ID NOS 173-174, respectively, in order of appearance.

[0048] Figure 13 depicts the variable heavy and variable light chain sequences for exemplary murine CLDN6 binding domain referred to herein as mC6-30 as well as sequences for XENP34243, a bivalent IgG1 mAb based on mC6-30 and with E233P/L234V/L235A/G236del/S267K ablation variant. CDRs are underlined and slashes indicate the border(s) between the variable regions and constant domain. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 2, and thus included herein are not only the CDRs that are underlined but also CDRs included within the V_H and V_L domains using other numbering systems. Furthermore, as for all the sequences in the Figures, these V_H and V_L sequences can be used either in a scFv format or in a Fab format.

[0049] Figure 14 depicts the variable heavy and variable light chain sequences for humanized C6-30 variants. CDRs are underlined and slashes indicate the border(s) between the variable regions and constant domain. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 2, and thus included herein are not only the CDRs that are underlined but also CDRs included within the V_H and V_L domains using other numbering systems. Further, as for all the sequences in the Figures, these V_H and V_L sequences can be used either in a scFv format or in a Fab format. Furthermore, each of the variable heavy domains depicted herein can be paired with any other α CLDN6 variable light domain; and each of the variable light domains depicted herein can be paired with any other α CLDN6 variable heavy domain.

[0050] Figure 15A-15J depicts the variable heavy and variable light chain sequences for C6-30 variants engineered for reduced degradation (e.g. aspartic acid isomerization and

deamidation) liability, enhanced selectivity for CLDN6, and/or modulated CLDN6 binding affinity. CDRs are underlined and slashes indicate the border(s) between the variable regions and constant domain. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 2, and thus included herein are not only the CDRs that are underlined but also CDRs included within the V_H and V_L domains using other numbering systems. Further, as for all the sequences in the Figures, these V_H and V_L sequences can be used either in a scFv format or in a Fab format. Furthermore, each of the variable heavy domains depicted herein can be paired with any other α CLDN6 variable light domain; and each of the variable light domains depicted herein can be paired with any other α CLDN6 variable heavy domain.

[0051] Figures 16A-16V depict illustrative C6-30[CLDN6] variants (parental humanized variants and further engineered variants) formatted as bivalent anti-CLDN6 mAb and IgG1 backbone with E233P/L234V/L235A/G236del/S267K ablation variant. CDRs are underlined and slashes indicate the border(s) between the variable regions and constant domain. As noted herein and is true for every sequence herein containing CDRs, the exact identification of the CDR locations may be slightly different depending on the numbering used as is shown in Table 2, and thus included herein are not only the CDRs that are underlined but also CDRs included within the V_H and V_L domains using other numbering systems. Furthermore, as for all the sequences in the Figures, these V_H and V_L sequences can be used either in a scFv format or in a Fab format.

[0052] Figures 17A and 17B depict a couple of formats of the present invention. Figure 17A depicts the “1 + 1 Fab-scFv-Fc” format, with a first Fab arm binding CLDN6 and a second scFv arm binding CD3. Figure 17B depicts the “2 + 1 Fab₂-scFv-Fc” format, with a first Fab arm binding CLDN6 and a second Fab-scFv arm, wherein the Fab binds CLDN6 and the scFv binds CD3.

[0053] Figure 18 depicts sequences of a comparator CLDN6 binding domain (sequences as disclosed in US Patent No. 10,233,253) formatted as a bivalent anti-CLDN6 IgG1 mAb with E233P/L234V/L235A/G236del/S267K ablation variant (XENP26863), and formatted as a 1 + 1 Fab-scFv-Fc bsAb with CD3 High (XENP26849).

[0054] Figure 19 depicts the sequences for illustrative α CLDN6 x α CD3 bsAbs in the 1 + 1 Fab-scFv-Fc format and comprising a CD3 High scFv (H1.30_L1.47 in either the VHVL

orientation or the VLVH orientation). CDRs are underlined and slashes indicate the border(s) between the variable regions and other chain components (e.g. constant region and domain linkers). It should be noted that the α CLDN6 x α CD3 bsAbs can utilize variable region, Fc region, and constant domain sequences that are 90, 95, 98 and 99% identical (as defined herein), and/or contain from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions. In addition, each sequence outlined herein can include or exclude the M428L/N434S variants in one or preferably both Fc domains, which results in longer half-life in serum

[0055] Figure 20 depicts the sequences for illustrative α CLDN6 x α CD3 bsAbs in the 1 + 1 Fab-scFv-Fc format and comprising a CD3 High-Int #1 scFv (H1.32_L1.47 in either the VHVL orientation or the VLVH orientation). CDRs are underlined and slashes indicate the border(s) between the variable regions and other chain components (e.g. constant region and domain linkers). It should be noted that the α CLDN6 x α CD3 bsAbs can utilize variable region, Fc region, and constant domain sequences that are 90, 95, 98 and 99% identical (as defined herein), and/or contain from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions. In addition, each sequence outlined herein can include or exclude the M428L/N434S variants in one or preferably both Fc domains, which results in longer half-life in serum

[0056] Figures 21A and 21B depict the sequences for illustrative α CLDN6 x α CD3 bsAbs in the 2 + 1 Fab₂-scFv-Fc format and comprising a CD3 High scFv (H1.30_L1.47 in either the VHVL orientation or the VLVH orientation). CDRs are underlined and slashes indicate the border(s) between the variable regions and other chain components (e.g. constant region and domain linkers). It should be noted that the α CLDN6 x α CD3 bsAbs can utilize variable region, Fc region, and constant domain sequences that are 90, 95, 98 and 99% identical (as defined herein), and/or contain from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions. In addition, each sequence outlined herein can include or exclude the M428L/N434S variants in one or preferably both Fc domains, which results in longer half-life in serum.

[0057] Figures 22A-22H depict the sequences for illustrative α CLDN6 x α CD3 bsAbs in the 2 + 1 Fab₂-scFv-Fc format and comprising a CD3 High-Int #1 scFv (H1.32_L1.47 in either the VHVL orientation or the VLVH orientation). CDRs are underlined and slashes indicate the border(s) between the variable regions and other chain components (e.g. constant region and domain linkers). It should be noted that the α CLDN6 x α CD3 bsAbs can utilize variable region, Fc region, and constant domain sequences that are 90, 95, 98 and 99% identical (as defined herein), and/or contain from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions. In

addition, each sequence outlined herein can include or exclude the M428L/N434S variants in one or preferably both Fc domains, which results in longer half-life in serum.

[0058] Figure 23 depicts binding of six murine anti-human CLDN6 bivalent mAbs designated A) C6-10, B) C6-11, C) C6-15, D) C6-21, E) C6-24, and F) C6-30 to HEK293-Trex cells that have been transfected to stably express human CLDN6, CLDN3, CLDN4, or CLDN9 as well as parental HEK293-Trex cells. Clones C6-11, C6-24, and C6-30 showed selectivity for CLDN6 over CLDN9.

[0059] Figure 24 depicts binding of humanized variants of C6-30 in different humanization frameworks – (A) H1L1, (B) H1L2, (C) H2L1, (D) H2L2, and (E) the original mouse mAb to HEK293-Trex cells that have been transfected to stably express human CLDN6, CLDN3, CLDN4, or CLDN9 as well as parental HEK293-Trex cells. Clones C6-11, C6-24, and C6-30 showed selectivity for CLDN6 over CLDN9. Each of the humanized variants of C6-30 retained selectivity for CLDN6 over CLDN9 (as well as over CLDN3 and CLDN4).

[0060] Figure 25 depicts binding of humanized variants of C6-11 in different humanization frameworks – (A) H1L1, (B) H1L2, (C) H2L1, (D) H2L2, and (E) the original mouse mAb to HEK293-Trex cells that have been transfected to stably express human CLDN6, CLDN3, CLDN4, or CLDN9 as well as parental HEK293-Trex cells. Clones C6-11, C6-24, and C6-30 showed selectivity for CLDN6 over CLDN9. Each of the humanized variants of C6-30 retained selectivity for CLDN6 over CLDN9 (as well as over CLDN3 and CLDN4).

[0061] Figure 26 depicts binding of humanized variants of C6-24 in different humanization frameworks – (A) H1L1, (B) H1L2, (C) H2L1, (D) H2L2, and (E) the original mouse mAb to HEK293-Trex cells that have been transfected to stably express human CLDN6, CLDN3, CLDN4, or CLDN9 as well as parental HEK293-Trex cells. Clones C6-11, C6-24, and C6-30 showed selectivity for CLDN6 over CLDN9. Each of the humanized variants of C6-30 retained selectivity for CLDN6 over CLDN9 (as well as over CLDN3 and CLDN4).

[0062] Figure 27 depicts variants of humanized C6-30 engineered with substitutions in the variable heavy domain to remove degradation (e.g. deamidation and aspartic acid isomerization) liabilities and their binding potency to CLDN6 and CLDN9. XENP35093 (having C6-30 H1.9_L1) maintained selectivity with minimal loss to CLDN6 binding.

[0063] Figure 28 depicts binding of A) XENP34228 (C6-24_H1L1 x CD3 bsAb in the 1 + 1 Fab-scFv-Fc format), B) XENP34232 (C6-24_H1L1 x CD3 bsAb in the 2 + 1 Fab₂-scFv-Fc format), C) XENP34229 (C6-30_H1L1 x CD3 bsAb in the 1 + 1 Fab-scFv-Fc format), D)

XENP34233 (C6-30_H1L1 x CD3 bsAb in the 2 + 1 Fab₂-scFv-Fc format), E) XENP34637 (C6-30_H2L1 x CD3 bsAb in the 1 + 1 Fab-scFv-Fc format), and F) XENP34638 (C6-30_H2L1 x CD3 bsAb in the 2 + 1 Fab₂-scFv-Fc format) to HEK293E cells expressing human, cynomolgus, and mouse CLDN6. Each of the variants were cross-reactive for human, cynomolgus, and mouse CLDN6 irrespective of bispecific format.

[0064] Figure 29 depicts binding of A) XENP34228 (C6-24_H1L1 x CD3 bsAb in the 1 + 1 Fab-scFv-Fc format), B) XENP34232 (C6-24_H1L1 x CD3 bsAb in the 2 + 1 Fab₂-scFv-Fc format), C) XENP34229 (C6-30_H1L1 x CD3 bsAb in the 1 + 1 Fab-scFv-Fc format), D) XENP34233 (C6-30_H1L1 x CD3 bsAb in the 2 + 1 Fab₂-scFv-Fc format), E) XENP34637 (C6-30_H2L1 x CD3 bsAb in the 1 + 1 Fab-scFv-Fc format), and F) XENP34638 (C6-30_H2L1 x CD3 bsAb in the 2 + 1 Fab₂-scFv-Fc format) to HEK293E cells expressing CLDN6, CLDN6 I143V isotype, CLDN9, CLDN3, and CLDN4. Each of the humanized C6-30 variants demonstrated enhanced selectivity in the 2 + 1 Fab₂-scFv-Fc format, in contrast to the humanized C6-24 variant which demonstrated similar selectivity in the 1 + 1 Fab-scFv-Fc format and the 2 + 1 Fab₂-scFv-Fc format.

[0065] Figure 30 depicts the binding of variants from a single point mutation library of humanized C6-30 to 293 cells expressing CLDN6 or CLDN9. Each point on the plot represents a test article which was screened for binding at a single dose (30 ug/ml) to CLDN6 and CLDN9 and then analyzed with flow cytometry to obtain an MFI value. Test articles that skewed toward higher CLDN6 MFI values and lower CLDN9 MFI values, such as those circled on the scatter plot, were selected for further development.

[0066] Figures 31A and 31B depict EC₅₀ of binding of illustrative C6-30 variants (in the context of bivalent mAbs) from the library combining the favorite variable heavy domain and variable light domain variants to HEK293E cells expressing CLDN6 or CLDN9 in A) a first and b) a second experiment. XENP26863 is a bivalent mAb based on a comparator CLDN6 binding domain. It should be noted that binding data from the experiments cannot be compared head-to-head as antigen density on the transfected cells vary between experiments. Nonetheless, several variants were enhanced in selectivity in comparison to the parental humanized clone (i.e. XENP34218_H1L1 and XENP34220_H2L1) and in comparison to comparator XENP26863.

[0067] Figure 32 depicts binding of illustrative C6-30 variants from library combining favorite variable heavy domain and variable light domain variants to HEK293E cells expressing A) CLDN6 or B) CLDN9.

[0068] Figure 33 depicts EC50 of binding of illustrative C6-30 variants (in the context of bivalent mAbs) from the library combining the favorite variable heavy domain and variable light domain variants to HEK293E cells expressing CLDN6 or CLDN9. XENP26863 is a bivalent mAb based on a comparator CLDN6 binding domain. Each of the 16 combination variants were enhanced in selectivity in comparison to the parental humanized clone (i.e. XENP34218_H1L1 and XENP34220_H2L1). 10 of the 16 combination variants demonstrated enhanced selectivity in comparison to comparator XENP26863.

[0069] Figure 34 depicts binding of select C6-30 variants formatted as bivalent monospecific mAbs and 2 + 1 Fab₂-scFv-Fc bsAbs to HEK293E cells expressing A) CLDN6 or B) CLDN9.

[0070] Figure 35 depicts binding of C6-24_H1L1, C6-30_H1L1, and C6-30_H2L1 in 1 + 1 Fab-scFv-Fc and 2 + 1 Fab₂-scFv-Fc to cells transfected to express human A) CLDN5, B) CLDN8, and C) CLDN17. None of the clones were cross-reactive for the additional claudins investigated.

[0071] Figures 36A to 36J depict several formats of the present invention. The first is the 1+1 Fab-scFv-Fc format, with a first and a second anti-antigen binding domain. Additionally, mAb-Fv, mAb-scFv, Central-scFv, Central-Fv, one-armed central-scFv, one scFv-mAb, scFv-mAb and a dual scFv format are all shown. For all of the scFv domains depicted, they can be either N- to C-terminus variable heavy-(optional linker)-variable light, or the opposite. In addition, for the one-armed scFv-mAb, the scFv can be attached either to the N-terminus of a heavy chain monomer or to the N-terminus of the light chain.

[0072] Figure 37 depicts induction of RTCC on PA-1 (CLDN6^{high}) cells by C6-24_H1L1, C6-30_H1L1, and C6-30_H2L1 in 1 + 1 Fab-scFv-Fc and 2 + 1 Fab₂-scFv-Fc bsAbs (CD3 High). The 2 + 1 Fab₂-scFv-Fc constructs showed 20-100 fold lower EC50 in comparison to 1 + 1 constructs. Additionally, potency shifts between the 2 + 1 vs. 1 + 1 construct were ~half-log more for C6-30_H2L1 in comparison to C6-30_H1L1.

[0073] Figure 38 depicts activation of CD8 T cells in the presence of PA-1 (CLDN6^{high}) cells by C6-24_H1L1, C6-30_H1L1, and C6-30_H2L1 in 1 + 1 Fab-scFv-Fc and 2 + 1 Fab₂-scFv-

Fc bsAbs with CD3 High as indicated by A) percentage CD8 T cells expressing CD69 and B) percentage of CD8 T cells expressing CD107a.

[0074] Figure 39 depicts induction of RTCC on A) HUTU-80 (CLDN6^{high}) and B) CLDN293-Trex stably transfected to express CLDN9 (CLDN9^{high}) by C6-30 formatted as 1 + 1 Fab-scFv-Fc or 2 + 1 Fab₂-scFv-Fc bsAbs with CD3 High or CD3 High-Int#1. The 2 + 1 format enabled much more potent RTCC activity on CLDN6⁺ cells in comparison to the 1 + 1 format. The bsAbs based on C6-30 demonstrated much weaker induction of RTCC on CLDN9⁺ cells in comparison to comparator bsAb XENP26849. 2 + 1 Fab₂-scFv-Fc bsAb having the lower affinity CD3_High-Int#1 induced RTCC on off-target CLDN9⁺ cells less potently than 2 + 1 bsAbs having high affinity CD3_High.

[0075] Figure 40 depicts activation of CD8 T cells in the presence of A) HUTU-80 (CLDN6^{high}) and B) CLDN293-Trex stably transfected to express CLDN9 (CLDN9^{high}) by C6-30 formatted as 1 + 1 Fab-scFv-Fc or 2 + 1 Fab₂-scFv-Fc bsAbs with CD3 High or CD3 High-Int#1 (as indicated by CD107a expression).

[0076] Figure 41 depicts induction of RTCC on A) PA-1 (1.1x10⁶ CLDN6 density), B) OV-90 (195K CLDN6 density), C) NEC-8 (175K CLDN6 density), and D) COV-318 (11K CLDN6 density) cells by C6-30_H1L1 or C6-30_H2L1 in 1 + 1 Fab-scFv-Fc or 2 + 1 Fab₂-scFv-Fc bsAbs with CD3 High or CD3 High-Int#1. Cell killing activity correlates with CLDN6 antigen density and affinity of the CD3 binding domain.

[0077] Figure 42 depicts EC50 of RTCC induction on PA-1 (1.1x10⁶ CLDN6 density) and B) OV-90 (195K CLDN6 density) by C6-30_H1L1 or C6-30_H2L1 in 1 + 1 Fab-scFv-Fc or 2 + 1 Fab₂-scFv-Fc bsAbs with CD3 High or CD3 High-Int#1.

[0078] Figure 43 depicts activation of CD8 T cells in the presence of A) PA-1 (1.1x10⁶ CLDN6 density), B) OV-90 (195K CLDN6 density), C) NEC-8 (175K CLDN6 density), and D) COV-318 (11K CLDN6 density) cells by C6-30_H1L1 or C6-30_H2L1 in 1 + 1 Fab-scFv-Fc or 2 + 1 Fab₂-scFv-Fc bsAbs with CD3 High or CD3 High-Int#1 (as indicated by CD107a expression). T cell activation correlates with CLDN6 antigen density and affinity of the CD3 binding domain.

[0079] Figure 44 depicts EC50 of CD8 T cell activation in the presence of A) PA-1 (1.1x10⁶ CLDN6 density), B) OV-90 (195K CLDN6 density), C) NEC-8 (175K CLDN6 density), and D) COV-318 (11K CLDN6 density) cells by C6-30_H1L1 or C6-30_H2L1 in 1

+ 1 Fab-scFv-Fc or 2 + 1 Fab₂-scFv-Fc bsAbs with CD3 High or CD3 High-Int#1 (as indicated by CD107a expression).

[0080] Figure 45 depicts induction of RTCC on A) HUTU-80 (CLDN6^{high}) and B) CLDN293-Trex stably transfected to express CLDN9 (CLDN9^{high}) by C6-30 variants formatted as 2 + 1 Fab₂-scFv-Fc bsAbs with CD3 High-Int#1 at a 10:1 effector:target ratio. The bsAbs having selectivity-engineered CLDN6 binding domains demonstrated modulated activity on CLDN6⁺ cells and/or modulated activity on CLDN9⁺ cells in comparison to bsAbs having the parental C6-30_H1L1 and C6-30_H2L1. XENP37233 demonstrated similar activity on CLDN9⁺ cells but significantly enhanced activity on CLDN6⁺ cells in comparison to the parental clones. XENP37227 demonstrated reduced activity on CLDN9⁺ cells and enhanced activity on CLDN6⁺ cells (albeit, less enhanced in comparison to XENP37233) in comparison to the parental clones. XENP37231 demonstrated little to no activity on CLDN9⁺ cells but slightly reduced activity on CLDN6⁺ cells in comparison to the parental clones.

[0081] Figure 46 depicts induction of RTCC on A) HUTU-80 (CLDN6^{high}) and B) CLDN293-Trex stably transfected to express CLDN9 (CLDN9^{high}) by C6-30 variants formatted as 2 + 1 Fab₂-scFv-Fc bsAbs with CD3 High-Int#1 at a 1:1 effector:target ratio.

[0082] Figure 47 depicts activation of CD8 T cells in the presence of A) HUTU-80 (CLDN6^{high}) and B) CLDN293-Trex stably transfected to express CLDN9 (CLDN9^{high}) by C6-30 formatted as 1 + 1 Fab-scFv-Fc or 2 + 1 Fab₂-scFv-Fc bsAbs with CD3 High or CD3 High-Int#1 (as indicated by CD69 expression).

[0083] Figure 48 depicts activation of CD8 T cells in the presence of A) HUTU-80 (CLDN6^{high}) and B) CLDN293-Trex stably transfected to express CLDN9 (CLDN9^{high}) by C6-30 formatted as 1 + 1 Fab-scFv-Fc or 2 + 1 Fab₂-scFv-Fc bsAbs with CD3 High or CD3 High-Int#1 (as indicated by CD107a expression).

[0084] Figure 49 depicts IFN γ secretion by T cells in the presence of A) HUTU-80 (CLDN6^{high}) and B) CLDN293-Trex stably transfected to express CLDN9 (CLDN9^{high}) by C6-30 formatted as 1 + 1 Fab-scFv-Fc or 2 + 1 Fab₂-scFv-Fc bsAbs with CD3 High or CD3 High-Int#1 (as indicated by IFN γ secretion).

[0085] Figure 50 depicts IL-2 secretion by T cells in the presence of A) HUTU-80 (CLDN6^{high}) and B) CLDN293-Trex stably transfected to express CLDN9 (CLDN9^{high}) by C6-30 formatted as 1 + 1 Fab-scFv-Fc or 2 + 1 Fab₂-scFv-Fc bsAbs with CD3 High or CD3 High-Int#1 (as indicated by IL-2 secretion).

[0086] Figure 51 depicts TNF α secretion by T cells in the presence of A) HUTU-80 (CLDN6^{high}) and B) CLDN293-Trex stably transfected to express CLDN9 (CLDN9^{high}) by C6-30 formatted as 1 + 1 Fab-scFv-Fc or 2 + 1 Fab₂-scFv-Fc bsAbs with CD3 High or CD3 High-Int#1 (as indicated by TNF α secretion).

[0087] Figures 52A-52H depict overlay of induction of RTCC on HUTU-80 (CLDN6^{high}) and CLDN293-Trex stably transfected to express CLDN9 (CLDN9^{high}) by A) XENP37227 (C6-30_H1.9_L1.187), B) XENP37228 (C6-30_H1.19_L1.187), C) XENP37229 (C6-30_H1.22_L1.187), D) XENP37230 (C6-30_H1.22_L1.189), E) XENP37231 (C6-30_H1.24_L1.187), F) XENP37232 (C6-30_H1.24_L1.189), G) XENP37233 (C6-30_H2.91_L1.187), and H) XENP35386 (C6-30_H1L1) each of which are bispecific antibodies in the 2 + 1 Fab₂-scFv-Fc format with CD3 High-Int#1. Each bsAb can be dosed at high concentrations to achieve efficacious killing of CLDN6⁺ cells while avoiding killing of CLDN9⁺ cells.

[0088] Figure 53 depicts A) induction of RTCC (including EC50 values) on PA-1 (CLDN6^{high}) cells by XENP37233, XENP37227, XENP37231, and XENP37630 at a 1:1 effector:target ratio, as well a CD8⁺ T cell activation as indicated by B) CD25 expression and C) CD107a expression.

[0089] Figure 54 depicts the ability of XENP37541 to bind cells expressing CLDN6 in a density dependent manner. PA-1 cells were engineered to stably express a range of CLDN6 antigen densities. XENP37541 was incubated with cells at a range of doses. Cells were washed, stained with a secondary antibody, and washed again prior to being analyzed using flow cytometry. XENP37541 was able to bind cells with lower levels of CLDN6 expression, even down to 47k CLDN6 antigens per cell.

[0090] Figure 55 depicts the induction of RTCC on PA-1 cells engineered to express a range of CLDN6 antigen levels, which are annotated in the EC50 chart in the figure. A 1:1 effector:target cell ratio and 72 hour incubation time was used before measuring RTCC. The results show that XENP37541, XENP37634, and XENP37545 were all able to induce RTCC in a CLDN6 density dependent manner, while negative control RSV x CD3 bsAb XENP32140 was not. XENP37541 displayed the strongest potency and lowest EC50 values across all different levels of CLDN6 expression.

[0091] Figure 56 depict the change in tumor volume (as determined by caliper measurements) A) over time, B) by Day 14 and C) by Day 20 (after 1st dose on Day 0) in PA-

1 and huPBMG-engrafted NSG mice dosed with PBS and XENP37233, XENP37227, XENP37630, or XENP37231 at 0.3, 1.0, or 3.0 mg/kg* indicates $p < 0.05$ vs. PBS group (statistical analysis performed using Mann-Whitney test on baseline corrected tumor volume). By Day 14, each of the bispecific antibodies enhanced anti-tumor activity in comparison to PBS control.

[0092] Figure 57 depicts dose response observed in pharmacokinetics for each of A) XENP37541, B) XENP37545, C) XENP37547, and D) XENP37634.

[0093] Figure 58 depicts overlay of blood concentration of for each of XENP37541, XENP37545, XENP37547, and XENP37634 following 60X dose.

[0094] Figures 59A and 59B depict the sequences for illustrative α CLDN6 x α CD3 bsAbs in the 2 + 1 Fab₂-scFv-Fc format and comprising a CD3 High-Int #2 scFv (H1.89_L1.47 in either the VHVL orientation or the VLVH orientation). CDRs are underlined and slashes indicate the border(s) between the variable regions and other chain components (e.g. constant region and domain linkers). It should be noted that the α CLDN6 x α CD3 bsAbs can utilize variable region, Fc region, and constant domain sequences that are 90, 95, 98 and 99% identical (as defined herein), and/or contain from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid substitutions. In addition, each sequence outlined herein can include or exclude the M428L/N434S variants in one or preferably both Fc domains, which results in longer half-life in serum.

[0095] Figures 60A and 60B depict sequences comprising a comparator CLDN6 binding domain Comp_CHO02. XENP37217 comprises this comparator CLDN6 binding domain in the 2 + 1 Fab₂-scFv-Fc format, while XENP38084 comprises the binding domain in the bivalent antibody format.

[0096] Figures 61A-61C depict the binding of C6-30 variants, as well as comparator CLDN6 x CD3 bsAb XENP37217, to other claudin family members CLDN3, CLDN4, CLDN8 and CLDN17. 293 cells were transiently transfected to express CLDN3, CLDN4, CLDN8, or CLDN17. Cells were plated and each test article was added to each cell line at a 100 μ g/ml dose. After 1 hour incubation at 4°C, cells were washed and a secondary AF647 antibody was added. Cells were incubated at 4°C for another hour, followed by additional washing and then analysis by flow cytometry. Comparator molecule XENP37217 showed significantly higher binding to CLDN8 and CLDN17 than any of the C6-30 variants.

DETAILED DESCRIPTION

[0097] The present invention provides heterodimeric bispecific antibodies that bind to human CD3 ϵ and human CLDN6.

I. Overview

[0098] Anti-bispecific antibodies that co-engage CD3 and a tumor antigen target are used to redirect T cells to attack and lyse targeted tumor cells. Examples include the BiTE® and DART formats, which monovalently engage CD3 and a tumor antigen. While the CD3-targeting approach has shown considerable promise, a common side effect of such therapies is the associated production of cytokines, often leading to toxic cytokine release syndrome. Because the anti-CD3 binding domain of the bispecific antibody engages all T cells, the high cytokine-producing CD4 T cell subset is recruited. Moreover, the CD4 T cell subset includes regulatory T cells, whose recruitment and expansion can potentially lead to immune suppression and have a negative impact on long-term tumor suppression. In addition, these formats do not contain Fc domains and show very short serum half-lives in patients.

[0099] Provided herein are novel anti-CD3 x anti-CLDN6 (also referred to as anti-CLDN6 x anti-CD3, α CD3 x α CLDN6, α CLDN6 x α CD3 or sometimes just CLDN6 X CD3) heterodimeric bispecific antibodies and methods of using such antibodies for the treatment of cancers. In particular, provided herein are anti-CD3, anti-CLDN6 bispecific antibodies in a variety of formats. These bispecific antibodies are useful for the treatment of cancers, particularly those with increased CLDN6 expression such as renal cell carcinoma. Such antibodies are used to direct CD3⁺ effector T cells to CLDN6⁺ tumors, thereby allowing the CD3⁺ effector T cells to attack and lyse the CLDN6⁺ tumors.

[00100] Additionally, the bispecific antibodies of the invention additionally distinguish between CLDN6 and other members of the CLDN family. While CLDN6 is expressed on cancers, CLDN9 is more highly expressed in healthy tissues (e.g. the cervix and the esophagus), so cross-reactivity of CLDN6 therapeutic with CLDN9 could lead to off-target toxicity. However, CLDN6 is 96% identical to CLDN9, differing by only 3 residues in their extracellular loops (as depicted in Figure 12); therefore, it is a significant challenge to develop an antibody capable of binding CLDN6 selectively over CLDN9, as well as selectivity of CLDN6 antigen binding domains (ABDs) that bind CLDN6 preferentially over other members of the CLDN family, including CLDN3 and CLDN4. Thus, included in the

present invention are antibodies and/or antigen binding domains that bind CLDN6 preferentially over CLDN9 as well as these ABDs in anti-CLDN6 X anti-CD3 bispecific antibodies.

[00101] Additionally, in some embodiments, the disclosure provides bispecific antibodies that have different binding affinities to human CD3 that can alter or reduce the potential side effects of anti-CD3 therapy. That is, in some embodiments the antibodies described herein provide antibody constructs comprising anti-CD3 antigen binding domains that are “strong” or “high affinity” binders to CD3 (e.g. one example are heavy and light variable domains depicted as H1.30_L1.47 (optionally including a charged linker as appropriate)) and also bind to CLDN6. In other embodiments, the antibodies described herein provide antibody constructs comprising anti-CD3 antigen binding domains that are “lite” or “lower affinity” binders to CD3. Additional embodiments provides antibody constructs comprising anti-CD3 antigen binding domains that have intermediate or “medium” affinity to CD3 that also bind to CLDN6. While a very large number of anti-CD3 antigen binding domains (ABDs) can be used, particularly useful embodiments use 6 different anti-CD3 ABDs, although they can be used in two scFv orientations as discussed herein. Affinity is generally measured using a Biacore assay.

[00102] It should be appreciated that the “high, medium, low” anti-CD3 sequences provided herein can be used in a variety of heterodimerization formats as discussed herein. In general, due to the potential side effects of T cell recruitment, exemplary embodiments utilize formats that only bind CD3 monovalently, such as depicted in Figure 17A and 17B, and in the formats depicted herein, it is the CD3 ABD that is a scFv as more fully described herein. In contrast, the subject bispecific antibodies can bind CLDN6 either monovalently (e.g. Figure 17A) or bivalently (e.g. Figure 17B).

[00103] Provided herein are compositions that include CLDN6 binding domains, including antibodies with such CLDN6 binding domains (e.g., CLDN6 x CD3 bispecific antibodies). Subject antibodies that include such CLDN6 binding domains advantageously elicit a range of different immune responses, depending on the particular CLDN6 binding domain used. For example, the subject antibodies exhibit differences in selectivity for cells with different CLDN6 expression, potencies for CLDN6 expressing cells, ability to elicit cytokine release, and sensitivity to soluble CLDN6. Such CLDN6 binding domains and related antibodies find use, for example, in the treatment of CLDN6-associated cancers.

[00104] Accordingly, in one aspect, provided herein are heterodimeric antibodies that bind to two different antigens, e.g. the antibodies are “bispecific”, in that they bind two different target antigens, generally CLDN6 and CD3 as described herein. These heterodimeric antibodies can bind these target antigens either monovalently (e.g. there is a single antigen binding domain such as a variable heavy and variable light domain pair) or bivalently (there are two antigen binding domains that each independently bind the antigen). In some embodiments, the heterodimeric antibody provided herein includes one CD3 binding domain and one CLDN6 binding domain (e.g., heterodimeric antibodies in the “1 + 1 Fab-scFv-Fc” format described herein). In other embodiments, the heterodimeric antibody provided herein includes one CD3 binding domain and two CLDN6 binding domains (e.g., heterodimeric antibodies in the “2 + 1 Fab₂-scFv-Fc” formats described herein). The heterodimeric antibodies provided herein are based on the use different monomers which contain amino acid substitutions that “skew” formation of heterodimers over homodimers, as is more fully outlined below, coupled with “pI variants” that allow simple purification of the heterodimers away from the homodimers, as is similarly outlined below. The heterodimeric bispecific antibodies provided generally rely on the use of engineered or variant Fc domains that can self-assemble in production cells to produce heterodimeric proteins, and methods to generate and purify such heterodimeric proteins.

II. Nomenclature

[00105] The antibodies provided herein are listed in several different formats. In some instances, each monomer of a particular antibody is given a unique “XENP” number, although as will be appreciated in the art, a longer sequence might contain a shorter one. For example, a “scFv-Fc” monomer of a 1 + 1 Fab-scFv-Fc format antibody may have a first XENP number, while the scFv domain itself will have a different XENP number. Some molecules have three polypeptides, so the XENP number, with the components, is used as a name. Thus, the molecule XENP37630, which is in 2 + 1 Fab₂-scFv-Fc format, comprises three sequences (see Figure 59A) a “Fab-Fc Heavy Chain” monomer (“Chain 1”); 2) a “Fab-scFv-Fc Heavy Chain” monomer (“Chain 2”); and 3) a “Light Chain” monomer (“Chain 3”) or equivalents, although one of skill in the art would be able to identify these easily through sequence alignment. These XENP numbers are in the sequence listing as well as identifiers, and used in the Figures. In addition, one molecule, comprising the three components, gives rise to multiple sequence identifiers. For example, the listing of the Fab includes, the full heavy chain sequence, the variable heavy domain sequence and the three CDRs of the

variable heavy domain sequence, the full light chain sequence, a variable light domain sequence and the three CDRs of the variable light domain sequence. A Fab-scFv-Fc monomer includes a full length sequence, a variable heavy domain sequence, 3 heavy CDR sequences, and an scFv sequence (include scFv variable heavy domain sequence, scFv variable light domain sequence and scFv linker). Note that some molecules herein with a scFv domain use a single charged scFv linker (+H), although others can be used. In addition, the naming nomenclature of particular antigen binding domains (e.g., CLDN6 and CD3 binding domains) use a “Hx.xx_Ly.yy” type of format, with the numbers being unique identifiers to particular variable chain sequences. Thus, an Fv domain of the antigen binding domain is “H1 L1”, which indicates that the variable heavy domain, H1, was combined with the light domain L1. In the case that these sequences are used as scFvs, the designation “H1 L1”, indicates that the variable heavy domain, H1 is combined with the light domain, L1, and is in VH-linker-VL orientation, from N- to C-terminus. This molecule with the identical sequences of the heavy and light variable domains but in the reverse order (VL-linker-VH orientation, from N- to C-terminus) would be designated “L1_H1.1”. Similarly, different constructs may “mix and match” the heavy and light chains as will be evident from the sequence listing and the figures.

[00106] Additionally, the bispecific antibodies of the invention are referred to herein as “anti-CD3 x anti-CLDN6”, “ α CD3 x α CLDN6”, “ α CLDN6 x α CD3” or sometimes just “CLDN6 X CD3”. The order of the antigens is not determinative as will be discussed below, although the majority of the formats that utilize as scFv have the an anti-CD3 ABD as the scFv.

III. Definitions

[00107] In order that the application may be more completely understood, several definitions are set forth below. Such definitions are meant to encompass grammatical equivalents.

[00108] By “CLDN6” herein is meant a protein belonging to the claudin family. CLDN6 sequences are depicted, for example, in Figure 11. The ABDs of the invention bind to human CLDN6.

[00109] By “ablation” herein is meant a decrease or removal of activity. Thus for example, “ablating Fc γ R binding” means the Fc region amino acid variant has less than 50%

starting binding as compared to an Fc region not containing the specific variant, with more than 70-80-90-95-98% loss of activity being preferred, and in general, with the activity being below the level of detectable binding in a Biacore, SPR or BLI assay. Of particular use in the ablation of FcγR binding are those shown in Figure 3, which generally are added to both monomers.

[00110] By "ADCC" or "antibody dependent cell-mediated cytotoxicity" as used herein is meant the cell-mediated reaction wherein nonspecific cytotoxic cells that express FcγRs recognize bound antibody on a target cell and subsequently cause lysis of the target cell. ADCC is correlated with binding to FcγRIIIa; increased binding to FcγRIIIa leads to an increase in ADCC activity.

[00111] By "ADCP" or antibody dependent cell-mediated phagocytosis as used herein is meant the cell-mediated reaction wherein nonspecific phagocytic cells that express FcγRs recognize bound antibody on a target cell and subsequently cause phagocytosis of the target cell.

[00112] As used herein, term "antibody" is used generally. Antibodies described herein can take on a number of formats as described herein, including traditional antibodies as well as antibody derivatives, fragments and mimetics, including a number of bispecific formats described herein.

[00113] Traditional immunoglobulin (Ig) antibodies are "Y" shaped tetramers. Each tetramer is typically composed of two identical pairs of polypeptide chains, each pair having one "light chain" monomer (typically having a molecular weight of about 25 kDa) and one "heavy chain" monomer (typically having a molecular weight of about 50-70 kDa).

[00114] Other useful antibody formats include, but are not limited to, the 1 + 1 Fab-scFv-Fc format and 2 + 1 Fab-scFv-Fc antibody formats described herein, as well as "mAb-Fv," "mAb-scFv," "central-Fv," "one-armed scFv-mAb," "scFv-mAb," "dual scFv," and "trident" format antibodies, as discussed below.

[00115] Antibody heavy chains typically include a variable heavy (VH) domain, which includes vhCDR1-3, and an Fc domain, which includes a CH2-CH3 monomer. In some embodiments, antibody heavy chains include a hinge and CH1 domain. Traditional antibody heavy chains are monomers that are organized, from N- to C-terminus: VH-CH1-hinge-CH2-CH3. The CH1-hinge-CH2-CH3 is collectively referred to as the heavy chain "constant domain" or "constant region" of the antibody, of which there are five different categories or

“isotypes”: IgA, IgD, IgG, IgE and IgM. Thus, “isotype” as used herein is meant any of the subclasses of immunoglobulins defined by the chemical and antigenic characteristics of their constant regions. It should be understood that therapeutic antibodies can also comprise hybrids of isotypes and/or subclasses. For example, as shown in US Publication 2009/0163699, incorporated by reference, the antibodies described herein include the use of human IgG1/G2 hybrids.

[00116] In some embodiments, the antibodies provided herein include IgG isotype constant domains, which has several subclasses, including, but not limited to IgG1, IgG2, IgG3, and IgG4. In the IgG subclass of immunoglobulins, there are several immunoglobulin domains in the heavy chain. By “immunoglobulin (Ig) domain” herein is meant a region of an immunoglobulin having a distinct tertiary structure. Of interest in the antibodies described herein are the heavy chain domains, including, the constant heavy (CH) domains and the hinge domains. In the context of IgG antibodies, the IgG isotypes each have three CH regions. Accordingly, “CH” domains in the context of IgG are as follows: “CH1” refers to positions 118-220 according to the EU index as in Kabat. “CH2” refers to positions 237-340 according to the EU index as in Kabat, and “CH3” refers to positions 341-447 according to the EU index as in Kabat. As shown herein and described below, the pI variants can be in one or more of the CH regions, as well as the hinge region, discussed below.

[00117] It should be noted that IgG1 has different allotypes with polymorphisms at 356 (D or E) and 358 (L or M). The sequences depicted herein use the 356D/358M allotype, however the other allotype is included herein. That is, any sequence inclusive of an IgG1 Fc domain included herein can have 356E/358L replacing the 356D/358M allotype. It should be understood that therapeutic antibodies can also comprise hybrids of isotypes and/or subclasses. For example, as shown in US Publication 2009/0163699, incorporated by reference, the present antibodies, in some embodiments, include IgG1/IgG2 hybrids.

[00118] By “Fc” or “Fc region” or “Fc domain” as used herein is meant the polypeptide comprising the constant region of an antibody, in some instances, excluding all of the first constant region immunoglobulin domain (e.g., CH1) or a portion thereof, and in some cases, optionally including all or part of the hinge. For IgG, the Fc domain comprises immunoglobulin domains CH2 and CH3 (C γ 2 and C γ 3), and optionally all or a portion of the hinge region between CH1 (C γ 1) and CH2 (C γ 2). Thus, in some cases, the Fc domain includes, from N- to C-terminal, CH2-CH3 and hinge-CH2-CH3. In some embodiments, the Fc domain is that from human IgG1, IgG2, IgG3 or IgG4, with human IgG1 hinge-CH2-CH3

and IgG4 hinge-CH2-CH3 finding particular use in many embodiments. Additionally, in the case of human IgG1 Fc domains, frequently the hinge includes a C220S amino acid substitution. Furthermore, in the case of human IgG4 Fc domains, frequently the hinge includes a S228P amino acid substitution. Although the boundaries of the Fc region may vary, the human IgG heavy chain Fc region is usually defined to include residues E216, C226, or A231 to its carboxyl-terminal, wherein the numbering is according to the EU index as in Kabat. In some embodiments, as is more fully described below, amino acid modifications are made to the Fc region, for example to alter binding to one or more FcγR or to the FcRn.

[00119] By “heavy chain constant region” herein is meant the CH1-hinge-CH2-CH3 portion of an antibody (or fragments thereof), excluding the variable heavy domain; in EU numbering of human IgG1 this is amino acids 118-447. By “heavy chain constant region fragment” herein is meant a heavy chain constant region that contains fewer amino acids from either or both of the N- and C-termini but still retains the ability to form a dimer with another heavy chain constant region.

[00120] Another type of Ig domain of the heavy chain is the hinge region. By “hinge” or “hinge region” or “antibody hinge region” or “hinge domain” herein is meant the flexible polypeptide comprising the amino acids between the first and second constant domains of an antibody. Structurally, the IgG CH1 domain ends at EU position 215, and the IgG CH2 domain begins at residue EU position 231. Thus for IgG the antibody hinge is herein defined to include positions 216 (E216 in IgG1) to 230 (p230 in IgG1), wherein the numbering is according to the EU index as in Kabat. In some cases, a “hinge fragment” is used, which contains fewer amino acids at either or both of the N- and C-termini of the hinge domain. As noted herein, pI variants can be made in the hinge region as well. Many of the antibodies herein have at least one of the cysteines at position 220 according to EU numbering (hinge region) replaced by a serine. Generally, this modification is on the “scFv monomer” side for most of the sequences depicted herein, although it can also be on the “Fab monomer” side, or both, to reduce disulfide formation. Specifically included within the sequences herein are one or both of these cysteines replaced (C220S).

[00121] As will be appreciated by those in the art, the exact numbering and placement of the heavy constant region domains can be different among different numbering systems. A useful comparison of heavy constant region numbering according to EU and Kabat is as below, see Edelman et al., 1969, Proc Natl Acad Sci USA 63:78-85 and Kabat et al., 1991,

Sequences of Proteins of Immunological Interest, 5th Ed., United States Public Health Service, National Institutes of Health, Bethesda, entirely incorporated by reference.

TABLE 1

	<u>EU Numbering</u>	<u>Kabat Numbering</u>
<i>CH1</i>	118-215	114-223
<i>Hinge</i>	216-230	226-243
<i>CH2</i>	231-340	244-360
<i>CH3</i>	341-447	361-478

[00122] The antibody light chain generally comprises two domains: the variable light domain (VL), which includes light chain CDRs vLCDR1-3, and a constant light chain region (often referred to as CL or C κ). The antibody light chain is typically organized from N- to C-terminus: VL-CL.

[00123] By “antigen binding domain” or “ABD” herein is meant a set of six Complementary Determining Regions (CDRs) that, when present as part of a polypeptide sequence, specifically binds a target antigen (e.g., CLDN6 or CD3) as discussed herein. As is known in the art, these CDRs are generally present as a first set of variable heavy CDRs (vhCDRs or VHCDRs) and a second set of variable light CDRs (vLCDRs or VLCDRs), each comprising three CDRs: vhCDR1, vhCDR2, vhCDR3 variable heavy CDRs and vLCDR1, vLCDR2 and vLCDR3 variable light CDRs. The CDRs are present in the variable heavy domain (vhCDR1-3) and variable light domain (vLCDR1-3). The variable heavy domain and variable light domain from an Fv region.

[00124] The antibodies described herein provide a large number of different CDR sets. In this case, a “full CDR set” comprises the three variable light and three variable heavy CDRs, e.g., a vLCDR1, vLCDR2, vLCDR3, vhCDR1, vhCDR2 and vhCDR3. These can be part of a larger variable light or variable heavy domain, respectfully. In addition, as more fully outlined herein, the variable heavy and variable light domains can be on separate polypeptide chains, when a heavy and light chain is used (for example when Fabs are used), or on a single polypeptide chain in the case of scFv sequences.

[00125] As will be appreciated by those in the art, the exact numbering and placement of the CDRs can be different among different numbering systems. However, it should be understood that the disclosure of a variable heavy and/or variable light sequence includes the disclosure of the associated (inherent) CDRs. Accordingly, the disclosure of each variable heavy region is a disclosure of the vhCDRs (e.g., vhCDR1, vhCDR2 and vhCDR3) and the disclosure of each variable light region is a disclosure of the vlCDRs (e.g., vlCDR1, vlCDR2 and vlCDR3). A useful comparison of CDR numbering is as below, *see Lafranc et al., Dev. Comp. Immunol.* 27(1):55-77 (2003):

TABLE 2

	Kabat+ Chothia	IMGT	Kabat	AbM	Chothia	Contact	Xencor
vhCDR1	26-35	27-38	31-35	26-35	26-32	30-35	27-35
vhCDR2	50-65	56-65	50-65	50-58	52-56	47-58	54-61
vhCDR3	95-102	105-117	95-102	95-102	95-102	93-101	103-116
vlCDR1	24-34	27-38	24-34	24-34	24-34	30-36	27-38
vlCDR2	50-56	56-65	50-56	50-56	50-56	46-55	56-62
vlCDR3	89-97	105-117	89-97	89-97	89-97	89-96	97-105

[00126] Throughout the present specification, the Kabat numbering system is generally used when referring to a residue in the variable domain (approximately, residues 1-107 of the light chain variable region and residues 1-113 of the heavy chain variable region) and the EU numbering system for Fc regions (e.g., Kabat et al., *supra* (1991)).

[00127] The CDRs contribute to the formation of the antigen-binding, or more specifically, epitope binding site of the antigen binding domains and antibodies. “Epitope” refers to a determinant that interacts with a specific antigen binding site in the variable region of an antibody molecule known as a paratope. Epitopes are groupings of molecules such as amino acids or sugar side chains and usually have specific structural characteristics, as well as specific charge characteristics. A single antigen may have more than one epitope.

[00128] The epitope may comprise amino acid residues directly involved in the binding (also called immunodominant component of the epitope) and other amino acid

residues, which are not directly involved in the binding, such as amino acid residues which are effectively blocked by the specifically antigen binding peptide; in other words, the amino acid residue is within the footprint of the specifically antigen binding peptide.

[00129] Epitopes may be either conformational or linear. A conformational epitope is produced by spatially juxtaposed amino acids from different segments of the linear polypeptide chain. A linear epitope is one produced by adjacent amino acid residues in a polypeptide chain. Conformational and nonconformational epitopes may be distinguished in that the binding to the former but not the latter is lost in the presence of denaturing solvents.

[00130] An epitope typically includes at least 3, and more usually, at least 5 or 8-10 amino acids in a unique spatial conformation. Antibodies that recognize the same epitope can be verified in a simple immunoassay showing the ability of one antibody to block the binding of another antibody to a target antigen, for example "binning." As outlined below, the disclosure not only includes the enumerated antigen binding domains and antibodies herein, but those that compete for binding with the epitopes bound by the enumerated antigen binding domains.

[00131] In some embodiments, the six CDRs of the antigen binding domain are contributed by a variable heavy and a variable light domain. In a "Fab" format, the set of 6 CDRs are contributed by two different polypeptide sequences, the variable heavy domain (vh or VH; containing the vhCDR1, vhCDR2 and vhCDR3) and the variable light domain (vl or VL; containing the vlCDR1, vlCDR2 and vlCDR3), with the C-terminus of the vh domain being attached to the N-terminus of the CH1 domain of the heavy chain and the C-terminus of the vl domain being attached to the N-terminus of the constant light domain (and thus forming the light chain). In a scFv format, the vh and vl domains are covalently attached, generally through the use of a linker (a "scFv linker") as outlined herein, into a single polypeptide sequence, which can be either (starting from the N-terminus) vh-linker-vl or vl-linker-vh, with the former being generally preferred (including optional domain linkers on each side, depending on the format used (e.g., from Figure 36). In general, the C-terminus of the scFv domain is attached to the N-terminus of the hinge in the second monomer.

[00132] By "variable region" or "variable domain" as used herein is meant the region of an immunoglobulin that comprises one or more Ig domains substantially encoded by any of the V κ , V λ , and/or VH genes that make up the kappa, lambda, and heavy chain immunoglobulin genetic loci respectively, and contains the CDRs that confer antigen

specificity. Thus, a “variable heavy domain” pairs with a “variable light domain” to form an antigen binding domain (“ABD”). In addition, each variable domain comprises three hypervariable regions (“complementary determining regions,” “CDRs”) (VHCDR1, VHCDR2 and VHCDR3 for the variable heavy domain and VLCDR1, VLCDR2 and VLCDR3 for the variable light domain) and four framework (FR) regions, arranged from amino-terminus to carboxy-terminus in the following order: FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4. The hypervariable region generally encompasses amino acid residues from about amino acid residues 24-34 (LCDR1; “L” denotes light chain), 50-56 (LCDR2) and 89-97 (LCDR3) in the light chain variable region and around about 31-35B (HCDR1; “H” denotes heavy chain), 50-65 (HCDR2), and 95-102 (HCDR3) in the heavy chain variable region; Kabat et al., SEQUENCES OF PROTEINS OF IMMUNOLOGICAL INTEREST, 5th Ed. Public Health Service, National Institutes of Health, Bethesda, Md. (1991) and/or those residues forming a hypervariable loop (e.g. residues 26-32 (LCDR1), 50-52 (LCDR2) and 91-96 (LCDR3) in the light chain variable region and 26-32 (HCDR1), 53-55 (HCDR2) and 96-101 (HCDR3) in the heavy chain variable region; Chothia and Lesk (1987) J. Mol. Biol. 196:901-917. Specific CDRs of the invention are described in Table 2.

[00133] By “Fab” or “Fab region” as used herein is meant the polypeptide that comprises the VH, CH1, VL, and CL immunoglobulin domains, generally on two different polypeptide chains (e.g. VH-CH1 on one chain and VL-CL on the other). Fab may refer to this region in isolation, or this region in the context of a bispecific antibody described herein. In the context of a Fab, the Fab comprises an Fv region in addition to the CH1 and CL domains.

[00134] By “Fv” or “Fv fragment” or “Fv region” as used herein is meant a polypeptide that comprises the VL and VH domains of an ABD. Fv regions can be formatted as both Fabs (as discussed above, generally two different polypeptides that also include the constant regions as outlined above) and scFvs, where the VL and VH domains are combined (generally with a linker as discussed herein) to form an scFv.

[00135] By “single chain Fv” or “scFv” herein is meant a variable heavy domain covalently attached to a variable light domain, generally using a scFv linker as discussed herein, to form a scFv or scFv domain. A scFv domain can be in either orientation from N- to C-terminus (VH-linker-VL or VL-linker-VH). In the sequences depicted in the sequence listing and in the figures, the order of the VH and VL domain is indicated in the name, e.g. H.X_L.Y means N- to C-terminal is VH-linker-VL, and L.Y_H.X is VL-linker-VH.

[00136] Some embodiments of the subject antibodies provided herein comprise at least one scFv domain, which, while not naturally occurring, generally includes a variable heavy domain and a variable light domain, linked together by a scFv linker. As outlined herein, while the scFv domain is generally from N- to C-terminus oriented as VH-scFv linker-VL, this can be reversed for any of the scFv domains (or those constructed using vh and vl sequences from Fabs), to VL-scFv linker-VH, with optional linkers at one or both ends depending on the format.

[00137] By "modification" herein is meant an amino acid substitution, insertion, and/or deletion in a polypeptide sequence or an alteration to a moiety chemically linked to a protein. For example, a modification may be an altered carbohydrate or PEG structure attached to a protein. By "amino acid modification" herein is meant an amino acid substitution, insertion, and/or deletion in a polypeptide sequence. For clarity, unless otherwise noted, the amino acid modification is always to an amino acid coded for by DNA, e.g. the 20 amino acids that have codons in DNA and RNA.

[00138] By "amino acid substitution" or "substitution" herein is meant the replacement of an amino acid at a particular position in a parent polypeptide sequence with a different amino acid. In particular, in some embodiments, the substitution is to an amino acid that is not naturally occurring at the particular position, either not naturally occurring within the organism or in any organism. For example, the substitution E272Y refers to a variant polypeptide, in this case an Fc variant, in which the glutamic acid at position 272 is replaced with tyrosine. For clarity, a protein which has been engineered to change the nucleic acid coding sequence but not change the starting amino acid (for example exchanging CGG (encoding arginine) to CGA (still encoding arginine) to increase host organism expression levels) is not an "amino acid substitution"; that is, despite the creation of a new gene encoding the same protein, if the protein has the same amino acid at the particular position that it started with, it is not an amino acid substitution.

[00139] By "amino acid insertion" or "insertion" as used herein is meant the addition of an amino acid sequence at a particular position in a parent polypeptide sequence. For example, -233E or 233E designates an insertion of glutamic acid after position 233 and before position 234. Additionally, -233ADE or A233ADE designates an insertion of AlaAspGlu after position 233 and before position 234.

[00140] By "amino acid deletion" or "deletion" as used herein is meant the removal of an amino acid sequence at a particular position in a parent polypeptide sequence. For example, E233- or E233#, E233() or E233del designates a deletion of glutamic acid at position 233. Additionally, EDA233- or EDA233# designates a deletion of the sequence GluAspAla that begins at position 233.

[00141] By "variant protein" or "protein variant", or "variant" as used herein is meant a protein that differs from that of a parent protein by virtue of at least one amino acid modification. The protein variant has at least one amino acid modification compared to the parent protein, yet not so many that the variant protein will not align with the parental protein using an alignment program such as that described below. In general, variant proteins (such as variant Fc domains, etc., outlined herein, are generally at least 75, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98 or 99% identical to the parent protein, using the alignment programs described below, such as BLAST. "Variant" as used herein also refers to particular amino acid modifications that confer particular function (e.g., a "heterodimerization variant," "pI variant," "ablation variant," etc.).

[00142] As described below, in some embodiments the parent polypeptide, for example an Fc parent polypeptide, is a human wild-type sequence, such as the heavy constant domain or Fc region from IgG1, IgG2, IgG3 or IgG4, although human sequences with variants can also serve as "parent polypeptides", for example the IgG1/2 hybrid of US Publication 2006/0134105 can be included. The protein variant sequence herein will preferably possess at least about 80% identity with a parent protein sequence, and most preferably at least about 90% identity, more preferably at least about 95-98-99% identity. Accordingly, by "antibody variant" or "variant antibody" as used herein is meant an antibody that differs from a parent antibody by virtue of at least one amino acid modification, "IgG variant" or "variant IgG" as used herein is meant an antibody that differs from a parent IgG (again, in many cases, from a human IgG sequence) by virtue of at least one amino acid modification, and "immunoglobulin variant" or "variant immunoglobulin" as used herein is meant an immunoglobulin sequence that differs from that of a parent immunoglobulin sequence by virtue of at least one amino acid modification. "Fc variant" or "variant Fc" as used herein is meant a protein comprising an amino acid modification in an Fc domain as compared to an Fc domain of human IgG1, IgG2 or IgG4.

[00143] "Fc variant" or "variant Fc" as used herein is meant a protein comprising an amino acid modification in an Fc domain. The modification can be an addition, deletion, or

substitution. The Fc variants are defined according to the amino acid modifications that compose them. Thus, for example, N434S or 434S is an Fc variant with the substitution for serine at position 434 relative to the parent Fc polypeptide, wherein the numbering is according to the EU index. Likewise, M428L/N434S defines an Fc variant with the substitutions M428L and N434S relative to the parent Fc polypeptide. The identity of the WT amino acid may be unspecified, in which case the aforementioned variant is referred to as 428L/434S. It is noted that the order in which substitutions are provided is arbitrary, that is to say that, for example, 428L/434S is the same Fc variant as 434S/428L, and so on. For all positions discussed herein that relate to antibodies or derivatives and fragments thereof (e.g., Fc domains), unless otherwise noted, amino acid position numbering is according to the EU index. The "EU index" or "EU index as in Kabat" or "EU numbering" scheme refers to the numbering of the EU antibody (Edelman et al., 1969, Proc Natl Acad Sci USA 63:78-85, hereby entirely incorporated by reference).

[00144] In general, variant Fc domains have at least about 80, 85, 90, 95, 97, 98 or 99 percent identity to the corresponding parental human IgG Fc domain (using the identity algorithms discussed below, with one embodiment utilizing the BLAST algorithm as is known in the art, using default parameters). Alternatively, the variant Fc domains can have from 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acid modifications as compared to the parental Fc domain. Alternatively, the variant Fc domains can have up to 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19 or 20 amino acid modifications as compared to the parental Fc domain. Additionally, as discussed herein, the variant Fc domains described herein still retain the ability to form a dimer with another Fc domain as measured using known techniques as described herein, such as non-denaturing gel electrophoresis.

[00145] By "protein" herein is meant at least two covalently attached amino acids, which includes proteins, polypeptides, oligopeptides and peptides. In addition, polypeptides that make up the antibodies described herein may include synthetic derivatization of one or more side chains or termini, glycosylation, PEGylation, circular permutation, cyclization, linkers to other molecules, fusion to proteins or protein domains, and addition of peptide tags or labels.

[00146] By "residue" as used herein is meant a position in a protein and its associated amino acid identity. For example, Asparagine 297 (also referred to as Asn297 or N297) is a residue at position 297 in the human antibody IgG1.

[00147] By "IgG subclass modification" or "isotype modification" as used herein is meant an amino acid modification that converts one amino acid of one IgG isotype to the corresponding amino acid in a different, aligned IgG isotype. For example, because IgG1 comprises a tyrosine and IgG2 a phenylalanine at EU position 296, a F296Y substitution in IgG2 is considered an IgG subclass modification.

[00148] By "non-naturally occurring modification" as used herein is meant an amino acid modification that is not isotypic. For example, because none of the human IgGs comprise a serine at position 434, the substitution 434S in IgG1, IgG2, IgG3, or IgG4 (or hybrids thereof) is considered a non-naturally occurring modification.

[00149] By "amino acid" and "amino acid identity" as used herein is meant one of the 20 naturally occurring amino acids that are coded for by DNA and RNA.

[00150] By "effector function" as used herein is meant a biochemical event that results from the interaction of an antibody Fc region with an Fc receptor or ligand. Effector functions include but are not limited to ADCC, ADCP, and CDC.

[00151] By "IgG Fc ligand" as used herein is meant a molecule, preferably a polypeptide, from any organism that binds to the Fc region of an IgG antibody to form an Fc/Fc ligand complex. Fc ligands include but are not limited to FcγRIs, FcγRIIs, FcγRIII_s, FcRn, C1q, C3, mannan binding lectin, mannose receptor, staphylococcal protein A, streptococcal protein G, and viral FcγR. Fc ligands also include Fc receptor homologs (FcRH), which are a family of Fc receptors that are homologous to the FcγRs (Davis et al., 2002, Immunological Reviews 190:123-136, entirely incorporated by reference). Fc ligands may include undiscovered molecules that bind Fc. Particular IgG Fc ligands are FcRn and Fc gamma receptors. By "Fc ligand" as used herein is meant a molecule, preferably a polypeptide, from any organism that binds to the Fc region of an antibody to form an Fc/Fc ligand complex.

[00152] By "Fc gamma receptor", "FcγR" or "FcγgammaR" as used herein is meant any member of the family of proteins that bind the IgG antibody Fc region and is encoded by an FcγR gene. In humans this family includes but is not limited to FcγRI (CD64), including isoforms FcγRIa, FcγRIb, and FcγRIc; FcγRII (CD32), including isoforms FcγRIIa (including allotypes H131 and R131), FcγRIIb (including FcγRIIb-1 and FcγRIIb-2), and FcγRIIc; and FcγRIII (CD16), including isoforms FcγRIIIa (including allotypes V158 and F158) and FcγRIIIb (including allotypes FcγRIIb-NA1 and FcγRIIb-NA2) (Jefferis et al.,

2002, Immunol Lett 82:57-65, entirely incorporated by reference), as well as any undiscovered human FcγRs or FcγR isoforms or allotypes. An FcγR may be from any organism, including but not limited to humans, mice, rats, rabbits, and monkeys. Mouse FcγRs include but are not limited to FcγRI (CD64), FcγRII (CD32), FcγRIII (CD16), and FcγRIII-2 (CD16-2), as well as any undiscovered mouse FcγRs or FcγR isoforms or allotypes.

[00153] By "FcRn" or "neonatal Fc Receptor" as used herein is meant a protein that binds the IgG antibody Fc region and is encoded at least in part by an FcRn gene. The FcRn may be from any organism, including but not limited to humans, mice, rats, rabbits, and monkeys. As is known in the art, the functional FcRn protein comprises two polypeptides, often referred to as the heavy chain and light chain. The light chain is beta-2-microglobulin and the heavy chain is encoded by the FcRn gene. Unless otherwise noted herein, FcRn or an FcRn protein refers to the complex of FcRn heavy chain with beta-2-microglobulin. A variety of FcRn variants used to increase binding to the FcRn receptor, and in some cases, to increase serum half-life. An "FcRn variant" is one that increases binding to the FcRn receptor, and suitable FcRn variants are shown below.

[00154] By "parent polypeptide" as used herein is meant a starting polypeptide that is subsequently modified to generate a variant. The parent polypeptide may be a naturally occurring polypeptide, or a variant or engineered version of a naturally occurring polypeptide. Accordingly, by "parent immunoglobulin" as used herein is meant an unmodified immunoglobulin polypeptide that is modified to generate a variant, and by "parent antibody" as used herein is meant an unmodified antibody that is modified to generate a variant antibody. It should be noted that "parent antibody" includes known commercial, recombinantly produced antibodies as outlined below. In this context, a "parent Fc domain" will be relative to the recited variant; thus, a "variant human IgG1 Fc domain" is compared to the parent Fc domain of human IgG1, a "variant human IgG4 Fc domain" is compared to the parent Fc domain human IgG4, etc.

[00155] By "position" as used herein is meant a location in the sequence of a protein. Positions may be numbered sequentially, or according to an established format, for example the EU index for antibody numbering.

[00156] By "target antigen" as used herein is meant the molecule that is bound specifically by the antigen binding domain comprising the variable regions of a given antibody.

[00157] By "strandedness" in the context of the monomers of the heterodimeric antibodies described herein is meant that, similar to the two strands of DNA that "match", heterodimerization variants are incorporated into each monomer so as to preserve the ability to "match" to form heterodimers. For example, if some pI variants are engineered into monomer A (e.g. making the pI higher) then steric variants that are "charge pairs" that can be utilized as well do not interfere with the pI variants, e.g. the charge variants that make a pI higher are put on the same "strand" or "monomer" to preserve both functionalities. Similarly, for "skew" variants that come in pairs of a set as more fully outlined below, the skilled artisan will consider pI in deciding into which strand or monomer one set of the pair will go, such that pI separation is maximized using the pI of the skews as well.

[00158] By "target cell" as used herein is meant a cell that expresses a target antigen.

[00159] By "host cell" in the context of producing a bispecific antibody according to the antibodies described herein is meant a cell that contains the exogenous nucleic acids encoding the components of the bispecific antibody and is capable of expressing the bispecific antibody under suitable conditions. Suitable host cells are discussed below.

[00160] By "wild type or WT" herein is meant an amino acid sequence or a nucleotide sequence that is found in nature, including allelic variations. A WT protein has an amino acid sequence or a nucleotide sequence that has not been intentionally modified.

[00161] Provided herein are a number of antibody domains that have sequence identity to human antibody domains. Sequence identity between two similar sequences (e.g., antibody variable domains) can be measured by algorithms such as that of Smith, T.F. & Waterman, M.S. (1981) "Comparison Of Biosequences," Adv. Appl. Math. 2:482 [local homology algorithm]; Needleman, S.B. & Wunsch, CD. (1970) "A General Method Applicable To The Search For Similarities In The Amino Acid Sequence Of Two Proteins," J. Mol. Biol. 48:443 [homology alignment algorithm], Pearson, W.R. & Lipman, D.J. (1988) "Improved Tools For Biological Sequence Comparison," Proc. Natl. Acad. Sci. (U.S.A.) 85:2444 [search for similarity method]; or Altschul, S.F. et al, (1990) "Basic Local Alignment Search Tool," J. Mol. Biol. 215:403-10, the "BLAST" algorithm, see <https://blast.ncbi.nlm.nih.gov/Blast.cgi>. When using any of the aforementioned algorithms,

the default parameters (for Window length, gap penalty, etc.) are used. In one embodiment, sequence identity is done using the BLAST algorithm, using default parameters

[00162] The antibodies described herein are generally isolated or recombinant. “Isolated,” when used to describe the various polypeptides disclosed herein, means a polypeptide that has been identified and separated and/or recovered from a cell or cell culture from which it was expressed. Ordinarily, an isolated polypeptide will be prepared by at least one purification step. An “isolated antibody,” refers to an antibody which is substantially free of other antibodies having different antigenic specificities. “Recombinant” means the antibodies are generated using recombinant nucleic acid techniques in exogenous host cells, and they can be isolated as well.

[00163] “Specific binding” or “specifically binds to” or is “specific for” a particular antigen or an epitope means binding that is measurably different from a non-specific interaction. Specific binding can be measured, for example, by determining binding of a molecule compared to binding of a control molecule, which generally is a molecule of similar structure that does not have binding activity. For example, specific binding can be determined by competition with a control molecule that is similar to the target.

[00164] Specific binding for a particular antigen or an epitope can be exhibited, for example, by an antibody having a KD for an antigen or epitope of at least about 10^{-4} M, at least about 10^{-5} M, at least about 10^{-6} M, at least about 10^{-7} M, at least about 10^{-8} M, at least about 10^{-9} M, alternatively at least about 10^{-10} M, at least about 10^{-11} M, at least about 10^{-12} M, or greater, where KD refers to a dissociation rate of a particular antibody-antigen interaction. Typically, an antibody that specifically binds an antigen will have a KD that is 20-, 50-, 100-, 500-, 1000-, 5,000-, 10,000- or more times greater for a control molecule relative to the antigen or epitope.

[00165] Also, specific binding for a particular antigen or an epitope can be exhibited, for example, by an antibody having a K_A or K_a for an antigen or epitope of at least 20-, 50-, 100-, 500-, 1000-, 5,000-, 10,000- or more times greater for the epitope relative to a control, where K_A or K_a refers to an association rate of a particular antibody-antigen interaction. Binding affinity is generally measured using a Biacore, SPR or BLI assay.

IV. Antibodies of the Invention

[00166] The present invention provides antibodies, including monoclonal antibodies and bispecific antibodies, that bind to human CLDN6 (it should be noted that many, if not most, of the exemplified antibodies also bind to cyno CLDN6 for ease of pre-clinical testing, but this is not required in all embodiments). In particular, bispecific antibodies are provided that bind CD3 and CLDN6 that make take on a variety of formats as more fully described below.

[00167] Of particular interest are anti-CLDN6 antigen binding domains (and antibodies containing them) that preferentially bind CLDN6 over CLDN9.

1. Antibodies

[00168] The antibodies provided herein include different antibody domains as is more fully described below. As described herein and known in the art, the antibodies described herein include different domains within the heavy and light chains, which can be overlapping as well. These domains include, but are not limited to, the Fc domain, the CH1 domain, the CH2 domain, the CH3 domain, the hinge domain, the heavy constant domain (CH1-hinge-Fc domain or CH1-hinge-CH2-CH3), the variable heavy domain, the variable light domain, the light constant domain, Fab domains and scFv domains.

[00169] In particular, the formats depicted in Figures 17 and 36 are usually referred to as “heterodimeric antibodies”, meaning that the protein has at least two associated Fc sequences self-assembled into a heterodimeric Fc domain and at least two Fv regions, whether as Fabs or as scFvs.

a. Chimeric and Humanized Antibodies

[00170] In certain embodiments, the antibodies described herein comprise a heavy chain variable region from a particular germline heavy chain immunoglobulin gene and/or a light chain variable region from a particular germline light chain immunoglobulin gene. For example, such antibodies may comprise or consist of a human antibody comprising heavy or light chain variable regions that are “the product of” or “derived from” a particular germline sequence. A human antibody that is “the product of” or “derived from” a human germline immunoglobulin sequence can be identified as such by comparing the amino acid sequence of the human antibody to the amino acid sequences of human germline immunoglobulins and

selecting the human germline immunoglobulin sequence that is closest in sequence (i.e., greatest % identity) to the sequence of the human antibody (using the methods outlined herein). A human antibody that is "the product of" or "derived from" a particular human germline immunoglobulin sequence may contain amino acid differences as compared to the germline sequence, due to, for example, naturally-occurring somatic mutations or intentional introduction of site-directed mutation. However, a humanized antibody typically is at least 90% identical in amino acids sequence to an amino acid sequence encoded by a human germline immunoglobulin gene and contains amino acid residues that identify the antibody as being derived from human sequences when compared to the germline immunoglobulin amino acid sequences of other species (e.g., murine germline sequences). In certain cases, a humanized antibody may be at least 95, 96, 97, 98 or 99%, or even at least 96%, 97%, 98%, or 99% identical in amino acid sequence to the amino acid sequence encoded by the germline immunoglobulin gene. Typically, a humanized antibody derived from a particular human germline sequence will display no more than 10-20 amino acid differences from the amino acid sequence encoded by the human germline immunoglobulin gene (prior to the introduction of any skew, pI and ablation variants herein; that is, the number of variants is generally low, prior to the introduction of the variants described herein). In certain cases, the humanized antibody may display no more than 5, or even no more than 4, 3, 2, or 1 amino acid difference from the amino acid sequence encoded by the germline immunoglobulin gene (again, prior to the introduction of any skew, pI and ablation variants herein; that is, the number of variants is generally low, prior to the introduction of the variants described herein). In some embodiments, the amino acid differences are in one or more of the 6 CDRs. In some embodiments, the amino acid differences are in a VH and/or VL framework region.

[00171] In one embodiment, the parent antibody has been affinity matured, as is known in the art. Structure-based methods may be employed for humanization and affinity maturation, for example as described in USSN 11/004,590. Selection based methods may be employed to humanize and/or affinity mature antibody variable regions, including but not limited to methods described in Wu et al., 1999, J. Mol. Biol. 294:151-162; Baca et al., 1997, J. Biol. Chem. 272(16):10678-10684; Rosok et al., 1996, J. Biol. Chem. 271(37): 22611-22618; Rader et al., 1998, Proc. Natl. Acad. Sci. USA 95: 8910-8915; Krauss et al., 2003, Protein Engineering 16(10):753-759, all entirely incorporated by reference. Other humanization methods may involve the grafting of only parts of the CDRs, including but not limited to methods described in USSN 09/810,510; Tan et al., 2002, J. Immunol. 169:1119-

1125; De Pascalis et al., 2002, J. Immunol. 169:3076-3084, all entirely incorporated by reference.

2. Heterodimeric Antibodies

[00172] In exemplary embodiments, the bispecific antibodies provided herein are heterodimeric bispecific antibodies that include two variant Fc domain sequences. Such variant Fc domains include amino acid modifications to facilitate the self-assembly and/or purification of the heterodimeric antibodies.

[00173] An ongoing problem in antibody technologies is the desire for “bispecific” antibodies that bind to two different antigens simultaneously, in general thus allowing the different antigens to be brought into proximity and resulting in new functionalities and new therapies. In general, these antibodies are made by including genes for each heavy and light chain into the host cells. This generally results in the formation of the desired heterodimer (A-B), as well as the two homodimers (A-A and B-B (not including the light chain heterodimeric issues)). However, a major obstacle in the formation of bispecific antibodies is the difficulty in biasing the formation of the desired heterodimeric antibody over the formation of the homodimers and/or purifying the heterodimeric antibody away from the homodimers.

[00174] There are a number of mechanisms that can be used to generate the subject heterodimeric antibodies. In addition, as will be appreciated by those in the art, these different mechanisms can be combined to ensure high heterodimerization. Amino acid modifications that facilitate the production and purification of heterodimers are collectively referred to generally as “heterodimerization variants.” As discussed below, heterodimerization variants include “skew” variants (e.g., the “knobs and holes” and the “charge pairs” variants described below) as well as “pI variants,” which allow purification of heterodimers from homodimers. As is generally described in US Patent No. US 9,605,084, hereby incorporated by reference in its entirety and specifically as below for the discussion of heterodimerization variants, useful mechanisms for heterodimerization include “knobs and holes” (“KIH”) as described in US Patent No. US 9,605,084, “electrostatic steering” or “charge pairs” as described in US Patent No. US 9,605,084, pI variants as described in US Patent No. US 9,605,084, and general additional Fc variants as outlined in US Patent No. US 9,605,084 and below.

[00175] Heterodimerization variants that are useful for the formation and purification of the subject heterodimeric antibody (e.g., bispecific antibodies) are further discussed in detailed below.

a. Skew Variants

[00176] In some embodiments, the heterodimeric antibody includes skew variants which are one or more amino acid modifications in a first Fc domain (A) and/or a second Fc domain (B) that favor the formation of Fc heterodimers (Fc dimers that include the first and the second Fc domain; (A-B) over Fc homodimers (Fc dimers that include two of the first Fc domain or two of the second Fc domain; A-A or B-B). Suitable skew variants are included in the Figure 29 of US Publ. App. No. 2016/0355608, hereby incorporated by reference in its entirety and specifically for its disclosure of skew variants, as well as in Figure 1.

[00177] Thus, suitable Fc heterodimerization variant pairs that will permit the formation of heterodimeric Fc regions are shown in Figure 1. Thus a first Fc domain has first Fc heterodimerization variants and the second Fc domain has second Fc heterodimerization variants selected from the pairs in Figure 1.

[00178] One mechanism is generally referred to in the art as “knobs and holes”, referring to amino acid engineering that creates steric influences to favor heterodimeric formation and disfavor homodimeric formation can also optionally be used; this is sometimes referred to as “knobs and holes”, as described in USSN 61/596,846, Ridgway et al., Protein Engineering 9(7):617 (1996); Atwell et al., J. Mol. Biol. 1997 270:26; US Patent No. 8,216,805, all of which are hereby incorporated by reference in their entirety. The Figures identify a number of “monomer A – monomer B” pairs that rely on “knobs and holes”. In addition, as described in Merchant et al., Nature Biotech. 16:677 (1998), these “knobs and hole” mutations can be combined with disulfide bonds to skew formation to heterodimerization.

[00179] An additional mechanism that finds use in the generation of heterodimers is sometimes referred to as “electrostatic steering” as described in Gunasekaran et al., J. Biol. Chem. 285(25):19637 (2010), hereby incorporated by reference in its entirety. This is sometimes referred to herein as “charge pairs”. In this embodiment, electrostatics are used to skew the formation towards heterodimerization. As those in the art will appreciate, these may also have an effect on pI, and thus on purification, and thus could in some cases also be considered pI variants. However, as these were generated to force heterodimerization and

were not used as purification tools, they are classified as “steric variants”. These include, but are not limited to, D221E/P228E/L368E paired with D221R/P228R/K409R (e.g. these are “monomer corresponding sets) and C220E/P228E/368E paired with C220R/E224R/P228R/K409R.

[00180] In some embodiments, the skew variants advantageously and simultaneously favor heterodimerization based on both the “knobs and holes” mechanism as well as the “electrostatic steering” mechanism. In some embodiments, the heterodimeric antibody includes one or more sets of such heterodimerization skew variants. These variants come in “pairs” of “sets”. That is, one set of the pair is incorporated into the first monomer and the other set of the pair is incorporated into the second monomer. It should be noted that these sets do not necessarily behave as “knobs in holes” variants, with a one-to-one correspondence between a residue on one monomer and a residue on the other. That is, these pairs of sets may instead form an interface between the two monomers that encourages heterodimer formation and discourages homodimer formation, allowing the percentage of heterodimers that spontaneously form under biological conditions to be over 90%, rather than the expected 50% (25 % homodimer A/A:50% heterodimer A/B:25% homodimer B/B). Exemplary heterodimerization “skew” variants are depicted in Figure 1. Such “skew” variants include, but are not limited to: S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L; K370S : S364K/E357Q (EU numbering).

[00181] In exemplary embodiments, the heterodimeric antibody includes Fc heterodimerization variants as sets: S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L; K370S : S364K/E357Q; or a T366S/L368A/Y407V : T366W (optionally including a bridging disulfide, T366S/L368A/Y407V/Y349C : T366W/S354C) are all “skew” variant amino acid substitution sets of Fc heterodimerization variants. In an exemplary embodiment, the heterodimeric antibody includes a “S364K/E357Q : L368D/K370S” amino acid substitution set. In terms of nomenclature, the pair “S364K/E357Q : L368D/K370S” means that one of the monomers includes an Fc domain that includes the amino acid substitutions S364K and E357Q and the other monomer includes an Fc domain that includes the amino acid substitutions L368D and K370S; as above, the “strandedness” of these pairs depends on the starting pI.

[00182] In some embodiments, the skew variants provided herein can be optionally and independently incorporated with any other modifications, including, but not limited to, other skew variants (see, e.g., in Figure 37 of US Publ. App. No. 2012/0149876, herein incorporated by reference, particularly for its disclosure of skew variants), pI variants, isotypic variants, FcRn variants, ablation variants, etc. into one or both of the first and second Fc domains of the heterodimeric antibody. Further, individual modifications can also independently and optionally be included or excluded from the subject the heterodimeric antibody.

[00183] Additional monomer A and monomer B variants that can be combined with other variants, optionally and independently in any amount, such as pI variants outlined herein or other steric variants that are shown in Figure 37 of US 2012/0149876, the figure and legend and SEQ ID NOs of which are incorporated expressly by reference herein.

[00184] In some embodiments, the steric variants outlined herein can be optionally and independently incorporated with any pI variant (or other variants such as Fc variants, FcRn variants, etc.) into one or both monomers, and can be independently and optionally included or excluded from the proteins of the antibodies described herein.

[00185] A list of suitable skew variants is found in Figure 1. Of particular use in many embodiments are the pairs of sets including, but not limited to, S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L and K370S : S364K/E357Q. In terms of nomenclature, the pair “S364K/E357Q : L368D/K370S” means that one of the monomers has the double variant set S364K/E357Q and the other has the double variant set L368D/K370S.

b. pI (Isoelectric point) Variants for Heterodimers

[00186] In some embodiments, the heterodimeric antibody includes purification variants that advantageously allow for the separation of heterodimeric antibody (e.g., anti-CLDN6 x anti-CD3 bispecific antibody) from homodimeric proteins.

[00187] There are several basic mechanisms that can lead to ease of purifying heterodimeric antibodies. For example, modifications to one or both of the antibody heavy chain monomers A and B such that each monomer has a different pI allows for the isoelectric purification of heterodimeric A-B antibody from monomeric A-A and B-B proteins. Alternatively, some scaffold formats, such as the “1 + 1 Fab-scFv-Fc” format and the “2 + 1

Fab₂-scFv-Fc” format, also allows separation on the basis of size. As described above, it is also possible to “skew” the formation of heterodimers over homodimers using skew variants. Thus, a combination of heterodimerization skew variants and pI variants find particular use in the heterodimeric antibodies provided herein.

[00188] Additionally, as more fully outlined below, depending on the format of the heterodimeric antibody, pI variants either contained within the constant region and/or Fc domains of a monomer, and/or domain linkers can be used. In some embodiments, the heterodimeric antibody includes additional modifications for alternative functionalities that can also create pI changes, such as Fc, FcRn and KO variants.

[00189] In some embodiments, the subject heterodimeric antibodies provided herein include at least one monomer with one or more modifications that alter the pI of the monomer (i.e., a “pI variant”). In general, as will be appreciated by those in the art, there are two general categories of pI variants: those that increase the pI of the protein (basic changes) and those that decrease the pI of the protein (acidic changes). As described herein, all combinations of these variants can be done: one monomer may be wild type, or a variant that does not display a significantly different pI from wild-type, and the other can be either more basic or more acidic. Alternatively, each monomer is changed, one to more basic and one to more acidic.

[00190] Depending on the format of the heterodimer antibody, pI variants can be either contained within the constant and/or Fc domains of a monomer, or charged linkers, either domain linkers or scFv linkers, can be used. That is, antibody formats that utilize scFv(s) such as “1 + 1 Fab-scFv-Fc”, format can include charged scFv linkers (either positive or negative), that give a further pI boost for purification purposes. As will be appreciated by those in the art, some 1 + 1 Fab-scFv-Fc formats are useful with just charged scFv linkers and no additional pI adjustments, although the antibodies described herein do provide pI variants that are on one or both of the monomers, and/or charged domain linkers as well. In addition, additional amino acid engineering for alternative functionalities may also confer pI changes, such as Fc, FcRn and KO variants.

[00191] In subject heterodimeric antibodies that utilizes pI as a separation mechanism to allow the purification of heterodimeric proteins, amino acid variants are introduced into one or both of the monomer polypeptides. That is, the pI of one of the monomers (referred to herein for simplicity as “monomer A”) can be engineered away from monomer B, or both

monomer A and B change be changed, with the pI of monomer A increasing and the pI of monomer B decreasing. As is outlined more fully below, the pI changes of either or both monomers can be done by removing or adding a charged residue (e.g., a neutral amino acid is replaced by a positively or negatively charged amino acid residue, e.g., glycine to glutamic acid), changing a charged residue from positive or negative to the opposite charge (aspartic acid to lysine) or changing a charged residue to a neutral residue (e.g., loss of a charge; lysine to serine.). A number of these variants are shown in the Figures 1 and 2.

[00192] Thus, in some embodiments, the subject heterodimeric antibody includes amino acid modifications in the constant regions that alter the isoelectric point (pI) of at least one, if not both, of the monomers of a dimeric protein to form “pI antibodies”) by incorporating amino acid substitutions (“pI variants” or “pI substitutions”) into one or both of the monomers. As shown herein, the separation of the heterodimers from the two homodimers can be accomplished if the pIs of the two monomers differ by as little as 0.1 pH unit, with 0.2, 0.3, 0.4 and 0.5 or greater all finding use in the antibodies described herein.

[00193] As will be appreciated by those in the art, the number of pI variants to be included on each or both monomer(s) to get good separation will depend in part on the starting pI of the components, for example in the 1 + 1 Fab-scFv-Fc and 2 + 1 Fab₂-scFv-Fc formats, the starting pI of the scFv and Fab(s) of interest. That is, to determine which monomer to engineer or in which “direction” (e.g., more positive or more negative), the Fv sequences of the two target antigens are calculated and a decision is made from there. As is known in the art, different Fvs will have different starting pIs which are exploited in the antibodies described herein. In general, as outlined herein, the pIs are engineered to result in a total pI difference of each monomer of at least about 0.1 logs, with 0.2 to 0.5 being preferred as outlined herein.

[00194] In the case where pI variants are used to achieve heterodimerization, by using the constant region(s) of the heavy chain(s), a more modular approach to designing and purifying bispecific proteins, including antibodies, is provided. Thus, in some embodiments, heterodimerization variants (including skew and pI heterodimerization variants) are not included in the variable regions, such that each individual antibody must be engineered. In addition, in some embodiments, the possibility of immunogenicity resulting from the pI variants is significantly reduced by importing pI variants from different IgG isotypes such that pI is changed without introducing significant immunogenicity. Thus, an additional problem to be solved is the elucidation of low pI constant domains with high human sequence

content, e.g., the minimization or avoidance of non-human residues at any particular position. Alternatively or in addition to isotypic substitutions, the possibility of immunogenicity resulting from the pI variants is significantly reduced by utilizing isosteric substitutions (e.g. Asn to Asp; and Gln to Glu).

[00195] As discussed below, a side benefit that can occur with this pI engineering is also the extension of serum half-life and increased FcRn binding. That is, as described in US Publ. App. No. US 2012/0028304 (incorporated by reference in its entirety), lowering the pI of antibody constant domains (including those found in antibodies and Fc fusions) can lead to longer serum retention in vivo. These pI variants for increased serum half-life also facilitate pI changes for purification.

[00196] In addition, it should be noted that the pI variants give an additional benefit for the analytics and quality control process of bispecific antibodies, as the ability to either eliminate, minimize and distinguish when homodimers are present is significant. Similarly, the ability to reliably test the reproducibility of the heterodimeric antibody production is important.

[00197] In general, embodiments of particular use rely on sets of variants that include skew variants, which encourage heterodimerization formation over homodimerization formation, coupled with pI variants, which increase the pI difference between the two monomers to facilitate purification of heterodimers away from homodimers.

[00198] Exemplary combinations of pI variants are shown in Figures 4 and 5, and Figure 30 of US Publ. App. No. 2016/0355608, all of which are herein incorporated by reference in its entirety and specifically for the disclosure of pI variants. Preferred combinations of pI variants are shown in Figures 1 and 2. As outlined herein and shown in the figures, these changes are shown relative to IgG1, but all isotypes can be altered this way, as well as isotype hybrids. In the case where the heavy chain constant domain is from IgG2-4, R133E and R133Q can also be used.

[00199] In one embodiment, a preferred combination of pI variants has one monomer (the negative Fab side) comprising 208D/295E/384D/418E/421D variants (N208D/Q295E/N384D/Q418E/N421D when relative to human IgG1) and a second monomer (the positive scFv side) comprising a positively charged scFv linker, including (GKPGS)₄ (SEQ ID NO: 1). However, as will be appreciated by those in the art, the first monomer includes a CH1 domain, including position 208. Accordingly, in constructs that do

not include a CH1 domain (for example for antibodies that do not utilize a CH1 domain on one of the domains), a preferred negative pI variant Fc set includes 295E/384D/418E/421D variants (Q295E/N384D/Q418E/N421D when relative to human IgG1).

[00200] Accordingly, in some embodiments, one monomer has a set of substitutions from Figure 2 and the other monomer has a charged linker (either in the form of a charged scFv linker because that monomer comprises an scFv or a charged domain linker, as the format dictates, which can be selected from those depicted in Figure 5).

[00201] In some embodiments, modifications are made in the hinge of the Fc domain, including positions 216, 217, 218, 219, 220, 221, 222, 223, 224, 225, 226, 227, 228, 229, and 230 based on EU numbering. Thus, pI mutations and particularly substitutions can be made in one or more of positions 216-230, with 1, 2, 3, 4 or 5 mutations finding use. Again, all possible combinations are contemplated, alone or with other pI variants in other domains.

[00202] Specific substitutions that find use in lowering the pI of hinge domains include, but are not limited to, a deletion at position 221, a non-native valine or threonine at position 222, a deletion at position 223, a non-native glutamic acid at position 224, a deletion at position 225, a deletion at position 235 and a deletion or a non-native alanine at position 236. In some cases, only pI substitutions are done in the hinge domain, and in others, these substitution(s) are added to other pI variants in other domains in any combination.

[00203] In some embodiments, mutations can be made in the CH2 region, including positions 233, 234, 235, 236, 274, 296, 300, 309, 320, 322, 326, 327, 334 and 339, based on EU numbering. It should be noted that changes in 233-236 can be made to increase effector function (along with 327A) in the IgG2 backbone. Again, all possible combinations of these 14 positions can be made; e.g., = may include a variant Fc domain with 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 CH2 pI substitutions.

[00204] Specific substitutions that find use in lowering the pI of CH2 domains include, but are not limited to, a non-native glutamine or glutamic acid at position 274, a non-native phenylalanine at position 296, a non-native phenylalanine at position 300, a non-native valine at position 309, a non-native glutamic acid at position 320, a non-native glutamic acid at position 322, a non-native glutamic acid at position 326, a non-native glycine at position 327, a non-native glutamic acid at position 334, a non-native threonine at position 339, and all possible combinations within CH2 and with other domains.

[00205] In this embodiment, the modifications can be independently and optionally selected from position 355, 359, 362, 384, 389, 392, 397, 418, 419, 444 and 447 (EU numbering) of the CH3 region. Specific substitutions that find use in lowering the pI of CH3 domains include, but are not limited to, a non-native glutamine or glutamic acid at position 355, a non-native serine at position 384, a non-native asparagine or glutamic acid at position 392, a non-native methionine at position 397, a non-native glutamic acid at position 419, a non-native glutamic acid at position 359, a non-native glutamic acid at position 362, a non-native glutamic acid at position 389, a non-native glutamic acid at position 418, a non-native glutamic acid at position 444, and a deletion or non-native aspartic acid at position 447.

[00206] In general, as will be appreciated by those in the art, there are two general categories of pI variants: those that increase the pI of the protein (basic changes) and those that decrease the pI of the protein (acidic changes). As described herein, all combinations of these variants can be done: one monomer may be wild type, or a variant that does not display a significantly different pI from wild-type, and the other can be either more basic or more acidic. Alternatively, each monomer is changed, one to more basic and one to more acidic.

[00207] Preferred combinations of pI variants are shown in Figure 2. As outlined herein and shown in the figures, these changes are shown relative to IgG1, but all isotypes can be altered this way, as well as isotype hybrids. In the case where the heavy chain constant domain is from IgG2-4, R133E and R133Q can also be used.

[00208] In one embodiment, for example in the Figure 36 formats, a preferred combination of pI variants has one monomer (the negative Fab side) comprising 208D/295E/384D/418E/421D variants (N208D/Q295E/N384D/Q418E/N421D when relative to human IgG1) and a second monomer (the positive scFv side) comprising a positively charged scFv linker, including (GKPGS)₄ (SEQ ID NO: 1). However, as will be appreciated by those in the art, the first monomer includes a CH1 domain, including position 208. Accordingly, in constructs that do not include a CH1 domain (for example for antibodies that do not utilize a CH1 domain on one of the domains, for example in a dual scFv format or a “one-armed” format such as those depicted in Figure 36B, C or D), a preferred negative pI variant Fc set includes 295E/384D/418E/421D variants (Q295E/N384D/Q418E/N421D when relative to human IgG1).

[00209] Accordingly, in some embodiments, one monomer has a set of substitutions from Figure 4 and the other monomer has a charged linker (either in the form of a charged

scFv linker because that monomer comprises an scFv or a charged domain linker, as the format dictates, which can be selected from those depicted in Figure 5).

c. Isotypic Variants

[00210] In addition, many embodiments of the antibodies described herein rely on the “importation” of pI amino acids at particular positions from one IgG isotype into another, thus reducing or eliminating the possibility of unwanted immunogenicity being introduced into the variants. A number of these are shown in Figure 21 of US Publ. 2014/0370013, hereby incorporated by reference. That is, IgG1 is a common isotype for therapeutic antibodies for a variety of reasons, including high effector function. However, the heavy constant region of IgG1 has a higher pI than that of IgG2 (8.10 versus 7.31). By introducing IgG2 residues at particular positions into the IgG1 backbone, the pI of the resulting monomer is lowered (or increased) and additionally exhibits longer serum half-life. For example, IgG1 has a glycine (pI 5.97) at position 137, and IgG2 has a glutamic acid (pI 3.22); importing the glutamic acid will affect the pI of the resulting protein. As is described below, a number of amino acid substitutions are generally required to significantly affect the pI of the variant antibody. However, it should be noted as discussed below that even changes in IgG2 molecules allow for increased serum half-life.

[00211] In other embodiments, non-isotypic amino acid changes are made, either to reduce the overall charge state of the resulting protein (e.g. by changing a higher pI amino acid to a lower pI amino acid), or to allow accommodations in structure for stability, etc. as is further described below.

[00212] In addition, by pI engineering both the heavy and light constant domains, significant changes in each monomer of the heterodimer can be seen. As discussed herein, having the pIs of the two monomers differ by at least 0.5 can allow separation by ion exchange chromatography or isoelectric focusing, or other methods sensitive to isoelectric point.

d. Calculating pI

[00213] The pI of each monomer can depend on the pI of the variant heavy chain constant domain and the pI of the total monomer, including the variant heavy chain constant domain and the fusion partner. Thus, in some embodiments, the change in pI is calculated on the basis of the variant heavy chain constant domain, using the chart in the Figure 19 of US

Pub. 2014/0370013. As discussed herein, which monomer to engineer is generally decided by the inherent pI of the Fv and scaffold regions. Alternatively, the pI of each monomer can be compared.

e. pI Variants that also confer better FcRn in vivo binding

[00214] In the case where the pI variant decreases the pI of the monomer, they can have the added benefit of improving serum retention in vivo.

[00215] Although still under examination, Fc regions are believed to have longer half-lives in vivo, because binding to FcRn at pH 6 in an endosome sequesters the Fc (Ghetie and Ward, 1997 Immunol Today. 18(12): 592-598, entirely incorporated by reference). The endosomal compartment then recycles the Fc to the cell surface. Once the compartment opens to the extracellular space, the higher pH, ~7.4, induces the release of Fc back into the blood. In mice, Dall'Acqua et al. showed that Fc mutants with increased FcRn binding at pH 6 and pH 7.4 actually had reduced serum concentrations and the same half-life as wild-type Fc (Dall'Acqua et al. 2002, J. Immunol. 169:5171-5180, entirely incorporated by reference). The increased affinity of Fc for FcRn at pH 7.4 is thought to forbid the release of the Fc back into the blood. Therefore, the Fc mutations that will increase Fc's half-life in vivo will ideally increase FcRn binding at the lower pH while still allowing release of Fc at higher pH. The amino acid histidine changes its charge state in the pH range of 6.0 to 7.4. Therefore, it is not surprising to find His residues at important positions in the Fc/FcRn complex.

[00216] Recently it has been suggested that antibodies with variable regions that have lower isoelectric points may also have longer serum half-lives (Igawa et al., 2010 PEDS. 23(5): 385-392, entirely incorporated by reference). However, the mechanism of this is still poorly understood. Moreover, variable regions differ from antibody to antibody. Constant region variants with reduced pI and extended half-life would provide a more modular approach to improving the pharmacokinetic properties of antibodies, as described herein.

f. Additional Fc Variants for Additional Functionality

[00217] In addition to the heterodimerization variants discussed above, there are a number of useful Fc amino acid modifications that can be made for a variety of reasons, including, but not limited to, altering binding to one or more FcγR receptors, altered binding to FcRn receptors, etc., as discussed below.

[00218] Accordingly, the antibodies provided herein (heterodimeric, as well as homodimeric) can include such amino acid modifications with or without the

heterodimerization variants outlined herein (e.g., the pI variants and steric variants). Each set of variants can be independently and optionally included or excluded from any particular heterodimeric protein.

(i) FcγR Variants

[00219] Accordingly, there are a number of useful Fc substitutions that can be made to alter binding to one or more of the FcγR receptors. In certain embodiments, the subject antibody includes modifications that alter the binding to one or more FcγR receptors (i.e., "FcγR variants"). Substitutions that result in increased binding as well as decreased binding can be useful. For example, it is known that increased binding to FcγRIIIa generally results in increased ADCC (antibody dependent cell-mediated cytotoxicity; the cell-mediated reaction wherein nonspecific cytotoxic cells that express FcγRs recognize bound antibody on a target cell and subsequently cause lysis of the target cell). Similarly, decreased binding to FcγRIIb (an inhibitory receptor) can be beneficial as well in some circumstances. Amino acid substitutions that find use in the antibodies described herein include those listed in US Patent Nos. 8,188,321 (particularly Figure 41) and 8,084,582, and US Publ. App. Nos. 20060235208 and 20070148170, all of which are expressly incorporated herein by reference in their entirety and specifically for the variants disclosed therein. Particular variants that find use include, but are not limited to, 236A, 239D, 239E, 332E, 332D, 239D/332E, 267D, 267E, 328F, 267E/328F, 236A/332E, 239D/332E/330Y, 239D/332E/330L, 243A, 243L, 264A, 264V and 299T.

[00220] In addition, there are additional Fc substitutions that find use in increased binding to the FcRn receptor and increased serum half-life, as specifically disclosed in USSN 12/341,769, hereby incorporated by reference in its entirety, including, but not limited to, 434S, 434A, 428L, 308F, 259I, 428L/434S, 428L/434A, 259I/308F, 436I/428L, 436I or V/434S, 436V/428L and 259I/308F/428L. Such modification may be included in one or both Fc domains of the subject antibody.

(ii) Ablation Variants

[00221] Similarly, another category of functional variants are "FcγR ablation variants" or "Fc knock out (FcKO or KO)" variants. In these embodiments, for some therapeutic applications, it is desirable to reduce or remove the normal binding of the Fc domain to one or more or all of the Fcγ receptors (e.g. FcγR1, FcγRIIa, FcγRIIb, FcγRIIIa, etc.) to avoid

additional mechanisms of action. That is, for example, in many embodiments, particularly in the use of bispecific antibodies that bind CD3 monovalently it is generally desirable to ablate Fc γ RIIIa binding to eliminate or significantly reduce ADCC activity. Wherein one of the Fc domains comprises one or more Fc γ receptor ablation variants. These ablation variants are depicted in Figure 3, and each can be independently and optionally included or excluded, with preferred aspects utilizing ablation variants selected from the group consisting of G236R/L328R, E233P/L234V/L235A/G236del/S239K, E233P/L234V/L235A/G236del/S267K, E233P/L234V/L235A/G236del/S239K/A327G, E233P/L234V/L235A/G236del/S267K/A327G and E233P/L234V/L235A/G236del. It should be noted that the ablation variants referenced herein ablate Fc γ R binding but generally not FcRn binding.

[00222] As is known in the art, the Fc domain of human IgG1 has the highest binding to the Fc γ receptors, and thus ablation variants can be used when the constant domain (or Fc domain) in the backbone of the heterodimeric antibody is IgG1. Alternatively, or in addition to ablation variants in an IgG1 background, mutations at the glycosylation position 297 (generally to A or S) can significantly ablate binding to Fc γ RIIIa, for example. Human IgG2 and IgG4 have naturally reduced binding to the Fc γ receptors, and thus those backbones can be used with or without the ablation variants.

B. Combination of Heterodimeric and Fc Variants

[00223] As will be appreciated by those in the art, all of the recited heterodimerization variants (including skew and/or pI variants) can be optionally and independently combined in any way, as long as they retain their “strandedness” or “monomer partition”. In some embodiments, the heterodimeric antibodies provided herein include the combination of heterodimerization skew variants, isosteric pI substitutions and FcKO variants as depicted in Figure 4. In addition, all of these variants can be combined into any of the heterodimerization formats.

[00224] In the case of pI variants, while embodiments finding particular use are shown in the Figures, other combinations can be generated, following the basic rule of altering the pI difference between two monomers to facilitate purification.

[00225] In addition, any of the heterodimerization variants, skew and pI, are also independently and optionally combined with Fc ablation variants, Fc variants, FcRn variants, as generally outlined herein.

[00226] Exemplary combination of variants that are included in some embodiments of the heterodimeric 1+1 Fab-scFv-Fc and 2 + 1 Fab₂-scFv-Fc format antibodies are included in Figure 4. In certain embodiments, the antibody is a heterodimeric 1+1 Fab-scFv-Fc or 2 + 1 Fab₂-scFv-Fc format antibody as shown in Figures 17A and 17B.

C. Anti-CLDN6 x Anti-CD3 Bispecific Antibodies

[00227] In another aspect, provided herein are anti-CLDN6 x anti-CD3 (also referred to herein as “ α CLDN6 x α CD3”) bispecific antibodies. Such antibodies include at least one CLDN6 binding domain and at least one CD3 binding domain. In some embodiments, bispecific α CLDN6 x α CD3 provided herein immune responses selectively in tumor sites that express CLDN6.

[00228] Note that unless specified herein, the order of the antigen list in the name does not confer structure; that is a CLDN6 x CD3 1 + 1 Fab-scFv-Fc antibody can have the scFv bind to CLDN6 or CD3, although in some cases, the order specifies structure as indicated.

[00229] As is more fully outlined herein, these combinations of ABDs can be in a variety of formats, as outlined below, generally in combinations where one ABD is in a Fab format and the other is in an scFv format. Exemplary formats that are used in the bispecific antibodies provided herein include the 1 + 1 Fab-scFv-Fc and 2 + 1 Fab₂-scFv-Fv formats (see, e.g., Figures 17A and 17B). Other useful antibody formats include, but are not limited to, “mAb-Fv,” “mAb-scFv,” “central-Fv,” “one-armed scFv-mAb,” “scFv-mAb,” “dual scFv,” and “trident” format antibodies, as depicted in Figure 36 and more fully described below.

[00230] In addition, in general, one of the ABDs comprises a scFv as outlined herein, in an orientation from N- to C-terminus of VH-scFv linker-VL or VL-scFv linker-VH. One or both of the other ABDs, according to the format, generally is a Fab, comprising a VH domain on one protein chain (generally as a component of a heavy chain) and a VL on another protein chain (generally as a component of a light chain).

[00231] As will be appreciated by those in the art, any set of 6 CDRs or VH and VL domains can be in the scFv format or in the Fab format, which is then added to the heavy and light constant domains, where the heavy constant domains comprise variants (including within the CH1 domain as well as the Fc domain). The scFv sequences contained in the sequence listing utilize a particular charged linker, but as outlined herein, uncharged or other charged linkers can be used, including those depicted in Figure 5.

[00232] In addition, as discussed above, the numbering used in the Sequence Listing for the identification of the CDRs is Kabat, however, different numbering can be used, which will change the amino acid sequences of the CDRs as shown in Table 2.

[00233] For all of the variable heavy and light domains listed herein, further variants can be made. As outlined herein, in some embodiments the set of 6 CDRs can have from 0, 1, 2, 3, 4 or 5 amino acid modifications (with amino acid substitutions finding particular use), as well as changes in the framework regions of the variable heavy and light domains, as long as the frameworks (excluding the CDRs) retain at least about 80, 85 90, 95 or 99 % identity to a human germline sequence selected from those listed in Figure 1 of U.S. Patent No.7,657,380, which Figure and Legend is incorporated by reference in its entirety herein. Thus, for example, the identical CDRs as described herein can be combined with different framework sequences from human germline sequences, as long as the framework regions retain at least 80, 85 90, 95 or 99 % identity to a human germline sequence selected from those listed in Figure 1 of U.S. Patent No.7,657,380. Alternatively, the CDRs can have amino acid modifications (e.g., from 1, 2, 3, 4 or 5 amino acid modifications in the set of CDRs (that is, the CDRs can be modified as long as the total number of changes in the set of 6 CDRs is less than 6 amino acid modifications, with any combination of CDRs being changed; e.g., there may be one change in vLCDR1, two in vhCDR2, none in vhCDR3, etc.)), as well as having framework region changes, as long as the framework regions retain at least 80, 85 90, 95 or 99 % identity to a human germline sequence selected from those listed in Figure 1 of U.S. Patent No.7,657,380.

[00234] As discussed herein, the subject heterodimeric antibodies include two antigen binding domains (ABDs), each of which bind to CLDN6 or CD3. As outlined herein, these heterodimeric antibodies can be bispecific and bivalent (each antigen is bound by a single ABD, for example, in the format depicted in Figure 17A), or bispecific and trivalent (one antigen is bound by a single ABD and the other is bound by two ABDs, for example as depicted in Figure 17B).

[00235] In addition, in general, one of the ABDs comprises a scFv as outlined herein, in an orientation from N- to C-terminus of VH-scFv linker-VL or VL-scFv linker-VH. One or both of the other ABDs, according to the format, generally is a Fab, comprising a VH domain on one protein chain (generally as a component of a heavy chain) and a VL on another protein chain (generally as a component of a light chain).

[00236] The disclosure provides a number of ABDs as outlined below. As will be appreciated by those in the art, any set of 6 CDRs or VH and VL domains can be in the scFv format or in the Fab format, which is then added to the heavy and light constant domains, where the heavy constant domains comprise variants (including within the CH1 domain as well as the Fc domain). The scFv sequences contained in the sequence listing utilize a particular charged linker, but as outlined herein, uncharged or other charged linkers can be used, including those depicted in Figure 5.

[00237] In addition, as discussed above, the numbering used in the Sequence Listing for the identification of the CDRs is Kabat, however, different numbering can be used, which will change the amino acid sequences of the CDRs as shown in Table 2.

[00238] For all of the variable heavy and light domains listed herein, further variants can be made. As outlined herein, in some embodiments the set of 6 CDRs can have from 0, 1, 2, 3, 4 or 5 amino acid modifications (with amino acid substitutions finding particular use), as well as changes in the framework regions of the variable heavy and light domains, as long as the frameworks (excluding the CDRs) retain at least about 80, 85 90, 95 or 99% identity to a human germline sequence selected from those listed in Figure 1 of U.S. Patent No.7,657,380, which Figure and Legend is incorporated by reference in its entirety herein. Thus, for example, the identical CDRs as described herein can be combined with different framework sequences from human germline sequences, as long as the framework regions retain at least 80, 85 90, 95 or 99% identity to a human germline sequence selected from those listed in Figure 1 of U.S. Patent No.7,657,380. Alternatively, the CDRs can have amino acid modifications (e.g. from 1, 2, 3, 4 or 5 amino acid modifications in the set of CDRs (that is, the CDRs can be modified as long as the total number of changes in the set of 6 CDRs is less than 6 amino acid modifications, with any combination of CDRs being changed; e.g. there may be one change in VLCDR1, two in VHCDR2, none in VHCDR3, etc.)), as well as having framework region changes, as long as the framework regions retain at least 80, 85 90, 95 or 99% identity to a human germline sequence selected from those listed in Figure 1 of U.S. Patent No.7,657,380.

1. CLDN6 Antigen Binding Domains

[00239] Herein is provided monoclonal and bispecific antibodies (e.g., the anti-CLDN6 x anti-CD3 antibodies provided herein), and fusion proteins that contain antigen binding domains that bind to human CLDN6. Suitable sets of 6 CDRs and/or VH and VL domains are depicted in Figures 13, 14, 15 and 18. In some embodiments, the heterodimeric antibody is a 1 + 1 Fab-scFv-Fc or 2 + 1 Fab2-scFv-Fv format antibody (see, e.g., Figures 17A and 17B) although any of the formats outlined below can be utilized.

[00240] In some embodiments, the CLDN6 ABD has a set of vhCDRs selected from the vhCDR1, vhCDR2 and vhCDR3 sequences from a VH selected from the group consisting of H1, H1.1, H1.2, H1.3, H1.4, H1.5, H1.6, H1.7, H1.8, H1.9, H1.19, H1.22, H1.24, H2, H2.1, H2.2, H2.3, H2.4, H2.5, H2.6, H2.7, H2.8, H2.9, H2.11, H2.12, H2.71, H2.75, H2.90, H2.91, H2.118 and H2.119, see Figures 14 and 15.

[00241] In some embodiments, the VH domain of the CLDN6 ABD is selected from the group consisting of H1, H1.1, H1.2, H1.3, H1.4, H1.5, H1.6, H1.7, H1.8, H1.9, H1.19, H1.22, H1.24, H2, H2.1, H2.2, H2.3, H2.4, H2.5, H2.6, H2.7, H2.8, H2.9, H2.11, H2.12, H2.71, H2.75, H2.90, H2.91, H2.118 and H2.119, see Figures 14 and 15.

[00242] In some embodiments, the CLDN6 ABD has a set of vlCDRs selected from the vlCDR1, vlCDR2 and vlCDR3 sequences from a VL selected from the group consisting of L1, L1.1, L1.4, L1.7, L1.16, L1.18, L1.19, L1.21, L1.22, L1.23, L1.27, L1.60, L1.107, L1.114, L1.187, L1.189 and L2, see Figures 14 and 15.

[00243] In some embodiments, the VL of the CLDN6 ABD is selected from the group consisting of L1, L1.1, L1.4, L1.7, L1.16, L1.7, L1.16, L1.18, L1.19, L1.21, L1.22, L1.23, L1.27, L1.60, L1.107, L1.114, L1.187, L1.189 and L2, see Figures 14 and 15.

[00244] Accordingly, included herein are CLDN6 ABDs that have a set of 6 CDRs (vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2 and vlCDR3) from VH/VL pairs selected from the group consisting of: H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1, H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1, H2.12_L1, H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1, H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1, H1.9_L1.1, H1.19_L1.1, H1.22_L1.1, H1.24_L1.1, H2_L1.1, H2.1_L1.1,

H2.2_L1.1, H2.3_L1.1, H2.4_L1.1, H2.5_L1.1, H2.6_L1.1, H2.7_L1.1, H2.8_L1.1,
H2.9_L1.1, H2.11_L1.1, H2.12_L1.1, H2.71_L1.1, H2.75_L1.1, H2.90_L1.1, H2.91_L1.1,
H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4, H1.2_L1.4, H1.3_L1.4, H1.4_L1.4,
H1.5_L1.4, H1.6_L1.4, H1.7_L1.4, H1.8_L1.4, H1.9_L1.4, H1.19_L1.4, H1.22_L1.4,
H1.24_L1.4, H2_L1.4, H2.1_L1.4, H2.2_L1.4, H2.3_L1.4, H2.4_L1.4, H2.5_L1.4,
H2.6_L1.4, H2.7_L1.4, H2.8_L1.4, H2.9_L1.4, H2.11_L1.4, H2.12_L1.4, H2.71_L1.4,
H2.75_L1.4, H2.90_L1.4, H2.91_L1.4, H2.118_L1.4, H2.119_L1.4, H1_L1.7, H1.1_L1.7,
H1.2_L1.7, H1.3_L1.7, H1.4_L1.7, H1.5_L1.7, H1.6_L1.7, H1.7_L1.7, H1.8_L1.7,
H1.9_L1.7, H1.19_L1.7, H1.22_L1.7, H1.24_L1.7, H2_L1.7, H2.1_L1.7, H2.2_L1.7,
H2.3_L1.7, H2.4_L1.7, H2.5_L1.7, H2.6_L1.7, H2.7_L1.7, H2.8_L1.7, H2.9_L1.7,
H2.11_L1.7, H2.12_L1.7, H2.71_L1.7, H2.75_L1.7, H2.90_L1.7, H2.91_L1.7,
H2.118_L1.7, H2.119_L1.7, H1_L1.16, H1.1_L1.16, H1.2_L1.16, H1.3_L1.16, H1.4_L1.16,
H1.5_L1.16, H1.6_L1.16, H1.7_L1.16, H1.8_L1.16, H1.9_L1.16, H1.19_L1.16,
H1.22_L1.16, H1.24_L1.16, H2_L1.16, H2.1_L1.16, H2.2_L1.16, H2.3_L1.16, H2.4_L1.16,
H2.5_L1.16, H2.6_L1.16, H2.7_L1.16, H2.8_L1.16, H2.9_L1.16, H2.11_L1.16,
H2.12_L1.16, H2.71_L1.16, H2.75_L1.16, H2.90_L1.16, H2.91_L1.16, H2.118_L1.16,
H2.119_L1.16, H1_L1.18, H1.1_L1.18, H1.2_L1.18, H1.3_L1.18, H1.4_L1.18, H1.5_L1.18,
H1.6_L1.18, H1.7_L1.18, H1.8_L1.18, H1.9_L1.18, H1.19_L1.18, H1.22_L1.18,
H1.24_L1.18, H2_L1.18, H2.1_L1.18, H2.2_L1.18, H2.3_L1.18, H2.4_L1.18, H2.5_L1.18,
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H2.71_L1.18, H2.75_L1.18, H2.90_L1.18, H2.91_L1.18, H2.118_L1.18, H2.119_L1.18,
H1_L1.19, H1.1_L1.19, H1.2_L1.19, H1.3_L1.19, H1.4_L1.19, H1.5_L1.19,
H1.6_L1.19, H1.7_L1.19, H1.8_L1.19, H1.9_L1.19, H1.19_L1.19, H1.22_L1.19,
H1.24_L1.19, H2_L1.19, H2.1_L1.19, H2.2_L1.19, H2.3_L1.19, H2.4_L1.19, H2.5_L1.19,
H2.6_L1.19, H2.7_L1.19, H2.8_L1.19, H2.9_L1.19, H2.11_L1.19, H2.12_L1.19,
H2.71_L1.19, H2.75_L1.19, H2.90_L1.19, H2.91_L1.19, H2.118_L1.19, H2.119_L1.19,
H1_L1.21, H1.1_L1.21, H1.2_L1.21, H1.3_L1.21, H1.4_L1.21, H1.5_L1.21, H1.6_L1.21,
H1.7_L1.21, H1.8_L1.21, H1.9_L1.21, H1.19_L1.21, H1.22_L1.21, H1.24_L1.21,
H2_L1.21, H2.1_L1.21, H2.2_L1.21, H2.3_L1.21, H2.4_L1.21, H2.5_L1.21, H2.6_L1.21,
H2.7_L1.21, H2.8_L1.21, H2.9_L1.21, H2.11_L1.21, H2.12_L1.21, H2.71_L1.21,
H2.75_L1.21, H2.90_L1.21, H2.91_L1.21, H2.118_L1.21, H2.119_L1.21, H1_L1.22,
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H2.119_L1.60, H1_L1.107, H1.1_L1.107, H1.2_L1.107, H1.3_L1.107, H1.4_L1.107,
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H1.9_L1.114, H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114,
H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114,
H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114,
H2.90_L1.114, H2.91_L1.114, H2.118_L1.114, H2.119_L1.114, H1_L1.187, H1.1_L1.187,
H1.2_L1.187, H1.3_L1.187, H1.4_L1.187, H1.5_L1.187, H1.6_L1.187, H1.7_L1.187,
H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187,
H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187,
H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187,
H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187,
H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189,
H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189,

H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189, H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189, H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189, H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2, H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2.

[00245] Additionally, included herein are CLDN6 ABDs that have VH/VL pairs selected from the group consisting of: H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1, H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1, H2.12_L1, H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1, H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1, H1.9_L1.1, H1.19_L1.1, H1.22_L1.1, H1.24_L1.1, H2_L1.1, H2.1_L1.1, H2.2_L1.1, H2.3_L1.1, H2.4_L1.1, H2.5_L1.1, H2.6_L1.1, H2.7_L1.1, H2.8_L1.1, H2.9_L1.1, H2.11_L1.1, H2.12_L1.1, H2.71_L1.1, H2.75_L1.1, H2.90_L1.1, H2.91_L1.1, H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4, H1.2_L1.4, H1.3_L1.4, H1.4_L1.4, H1.5_L1.4, H1.6_L1.4, H1.7_L1.4, H1.8_L1.4, H1.9_L1.4, H1.19_L1.4, H1.22_L1.4, H1.24_L1.4, H2_L1.4, H2.1_L1.4, H2.2_L1.4, H2.3_L1.4, H2.4_L1.4, H2.5_L1.4, H2.6_L1.4, H2.7_L1.4, H2.8_L1.4, H2.9_L1.4, H2.11_L1.4, H2.12_L1.4, H2.71_L1.4, H2.75_L1.4, H2.90_L1.4, H2.91_L1.4, H2.118_L1.4, H2.119_L1.4, H1_L1.7, H1.1_L1.7, H1.2_L1.7, H1.3_L1.7, H1.4_L1.7, H1.5_L1.7, H1.6_L1.7, H1.7_L1.7, H1.8_L1.7, H1.9_L1.7, H1.19_L1.7, H1.22_L1.7, H1.24_L1.7, H2_L1.7, H2.1_L1.7, H2.2_L1.7, H2.3_L1.7, H2.4_L1.7, H2.5_L1.7, H2.6_L1.7, H2.7_L1.7, H2.8_L1.7, H2.9_L1.7, H2.11_L1.7, H2.12_L1.7, H2.71_L1.7, H2.75_L1.7, H2.90_L1.7, H2.91_L1.7, H2.118_L1.7, H2.119_L1.7, H1_L1.16, H1.1_L1.16, H1.2_L1.16, H1.3_L1.16, H1.4_L1.16, H1.5_L1.16, H1.6_L1.16, H1.7_L1.16, H1.8_L1.16, H1.9_L1.16, H1.19_L1.16, H1.22_L1.16, H1.24_L1.16, H2_L1.16, H2.1_L1.16, H2.2_L1.16, H2.3_L1.16, H2.4_L1.16, H2.5_L1.16, H2.6_L1.16, H2.7_L1.16, H2.8_L1.16, H2.9_L1.16, H2.11_L1.16, H2.12_L1.16, H2.71_L1.16, H2.75_L1.16, H2.90_L1.16, H2.91_L1.16, H2.118_L1.16, H2.119_L1.16, H1_L1.18, H1.1_L1.18, H1.2_L1.18, H1.3_L1.18, H1.4_L1.18, H1.5_L1.18, H1.6_L1.18, H1.7_L1.18, H1.8_L1.18, H1.9_L1.18, H1.19_L1.18, H1.22_L1.18, H1.24_L1.18, H2_L1.18, H2.1_L1.18, H2.2_L1.18,

H2.3_L1.18, H2.4_L1.18, H2.5_L1.18, H2.6_L1.18, H2.7_L1.18, H2.8_L1.18, H2.9_L1.18, H2.11_L1.18, H2.12_L1.18, H2.71_L1.18, H2.75_L1.18, H2.90_L1.18, H2.91_L1.18, H2.118_L1.18, H2.119_L1.18, H1_L1.19, H1.1_L1.19, H1.2_L1.19, H1.3_L1.19, H1.4_L1.19, H1.5_L1.19, H1.6_L1.19, H1.7_L1.19, H1.8_L1.19, H1.9_L1.19, H1.19_L1.19, H1.22_L1.19, H1.24_L1.19, H2_L1.19, H2.1_L1.19, H2.2_L1.19, H2.3_L1.19, H2.4_L1.19, H2.5_L1.19, H2.6_L1.19, H2.7_L1.19, H2.8_L1.19, H2.9_L1.19, H2.11_L1.19, H2.12_L1.19, H2.71_L1.19, H2.75_L1.19, H2.90_L1.19, H2.91_L1.19, H2.118_L1.19, H2.119_L1.19, H1_L1.21, H1.1_L1.21, H1.2_L1.21, H1.3_L1.21, H1.4_L1.21, H1.5_L1.21, H1.6_L1.21, H1.7_L1.21, H1.8_L1.21, H1.9_L1.21, H1.19_L1.21, H1.22_L1.21, H1.24_L1.21, H2_L1.21, H2.1_L1.21, H2.2_L1.21, H2.3_L1.21, H2.4_L1.21, H2.5_L1.21, H2.6_L1.21, H2.7_L1.21, H2.8_L1.21, H2.9_L1.21, H2.11_L1.21, H2.12_L1.21, H2.71_L1.21, H2.75_L1.21, H2.90_L1.21, H2.91_L1.21, H2.118_L1.2, H2.119_L1.21, H1_L1.22, H1.1_L1.22, H1.2_L1.22, H1.3_L1.22, H1.4_L1.22, H1.5_L1.22, H1.6_L1.22, H1.7_L1.22, H1.8_L1.22, H1.9_L1.22, H1.19_L1.22, H1.22_L1.22, H1.24_L1.22, H2_L1.22, H2.1_L1.22, H2.2_L1.22, H2.3_L1.22, H2.4_L1.22, H2.5_L1.22, H2.6_L1.22, H2.7_L1.22, H2.8_L1.22, H2.9_L1.22, H2.11_L1.22, H2.12_L1.22, H2.71_L1.22, H2.75_L1.22, H2.90_L1.22, H2.91_L1.22, H2.118_L1.22, H2.119_L1.22, H1_L1.23, H1.1_L1.23, H1.2_L1.23, H1.3_L1.23, H1.4_L1.23, H1.5_L1.23, H1.6_L1.23, H1.7_L1.23, H1.8_L1.23, H1.9_L1.23, H1.19_L1.23, H1.22_L1.23, H1.24_L1.23, H2_L1.23, H2.1_L1.23, H2.2_L1.23, H2.3_L1.23, H2.4_L1.23, H2.5_L1.23, H2.6_L1.23, H2.7_L1.23, H2.8_L1.23, H2.9_L1.23, H2.11_L1.23, H2.12_L1.23, H2.71_L1.23, H2.75_L1.23, H2.90_L1.23, H2.91_L1.23, H2.118_L1.23, H2.119_L1.23, H1_L1.27, H1.1_L1.27, H1.2_L1.27, H1.3_L1.27, H1.4_L1.27, H1.5_L1.27, H1.6_L1.27, H1.7_L1.27, H1.8_L1.27, H1.9_L1.27, H1.19_L1.27, H1.22_L1.27, H1.24_L1.27, H2_L1.27, H2.1_L1.27, H2.2_L1.27, H2.3_L1.27, H2.4_L1.27, H2.5_L1.27, H2.6_L1.27, H2.7_L1.27, H2.8_L1.27, H2.9_L1.27, H2.11_L1.27, H2.12_L1.27, H2.71_L1.27, H2.75_L1.27, H2.90_L1.27, H2.91_L1.27, H2.118_L1.27, H2.119_L1.27, H1_L1.60, H1.1_L1.60, H1.2_L1.60, H1.3_L1.60, H1.4_L1.60, H1.5_L1.60, H1.6_L1.60, H1.7_L1.60, H1.8_L1.60, H1.9_L1.60, H1.19_L1.60, H1.22_L1.60, H1.24_L1.60, H2_L1.60, H2.1_L1.60, H2.2_L1.60, H2.3_L1.60, H2.4_L1.60, H2.5_L1.60, H2.6_L1.60, H2.7_L1.60, H2.8_L1.60, H2.9_L1.60, H2.11_L1.60, H2.12_L1.60, H2.71_L1.60, H2.75_L1.60, H2.90_L1.60, H2.91_L1.60, H2.118_L1.60, H2.119_L1.60, H1_L1.107, H1.1_L1.107, H1.2_L1.107, H1.3_L1.107, H1.4_L1.107, H1.5_L1.107, H1.6_L1.107, H1.7_L1.107, H1.8_L1.107, H1.9_L1.107, H1.19_L1.107, H1.22_L1.107, H1.24_L1.107, H2_L1.107, H2.1_L1.107, H2.2_L1.107,

H2.3_L1.107, H2.4_L1.107, H2.5_L1.107, H2.6_L1.107, H2.7_L1.107, H2.8_L1.107, H2.9_L1.107, H2.11_L1.107, H2.12_L1.107, H2.71_L1.107, H2.75_L1.107, H2.90_L1.107, H2.91_L1.107, H2.118_L1.107, H2.119_L1.107, H1_L1.114, H1.1_L1.114, H1.2_L1.114, H1.3_L1.114, H1.4_L1.114, H1.5_L1.114, H1.6_L1.114, H1.7_L1.114, H1.8_L1.114, H1.9_L1.114, H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114, H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114, H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114, H2.90_L1.114, H2.91_L1.114, H2.118_L1.114, H2.119_L1.114, H1_L1.187, H1.1_L1.187, H1.2_L1.187, H1.3_L1.187, H1.4_L1.187, H1.5_L1.187, H1.6_L1.187, H1.7_L1.187, H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187, H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187, H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187, H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187, H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189, H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189, H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189, H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189, H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189, H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2, H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2.

[00246] In particular embodiments, the VH/VL pairs are selected from the group consisting of H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187.

[00247] In particular embodiments, the VH/VL pairs are Fabs and are selected from the group consisting of H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187.

[00248] As will be appreciated by those in the art, suitable CLDN6 binding domains can comprise a set of 6 CDRs as depicted in the Figures, either as they are underlined or, in the case where a different numbering scheme is used as described herein and as shown in Table 2, as the CDRs that are identified using other alignments within the VH and VL sequences of those depicted in Figures 13, 14 and 15. Suitable ABDs can also include the entire VH and VL sequences as depicted in these sequences and Figures, used as scFvs or as

Fabs. In many of the embodiments herein that contain an Fv to CLDN6, it is the Fab monomer that binds CLDN6.

[00249] In addition to the parental CDR sets disclosed in the figures and sequence listing that form an ABD to CLDN6, provided herein are variant CLDN6 ABDs having CDRs that include at least one modification of the CLDN6 ABD CDRs disclosed herein (e.g., (Figures 13-15 and 18 and the sequence listing). In one embodiment, the CLDN6 ABD of the subject heterodimeric antibody includes a set of 6 CDRs with 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 amino acid modifications as compared to the 6 CDRs of a CLDN6 binding domain VH/VL pair as described herein, including the figures and sequence listing. In exemplary embodiments, the CLDN6 ABD of the subject heterodimeric antibody includes a set of 6 CDRs with 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 amino acid modifications as compared to the 6 CDRs of one of the following CLDN6 binding domain VH/VL pairs: H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187. In certain embodiments, the CLDN6 ABD of the subject antibody is capable of binding to CLDN6, as measured at least one of a Biacore, surface plasmon resonance (SPR), BLI (biolayer interferometry, e.g., Octet assay) assay, and/or flow cytometry, with the latter finding particular use in many embodiments. In particular embodiments, the CLDN6 ABD is capable of binding human CLDN6 (see Figure 11). In some cases, each variant CDR has no more than 1 or 2 amino acid changes, with no more than 1 per CDR being particularly useful.

[00250] In some embodiments, the CLDN6 ABD of the subject antibody includes 6 CDRs that are at least 90, 95, 97, 98 or 99% identical to the 6 CDRs of a CLDN6 ABD as described herein, including the figures and sequence listing. In exemplary embodiments, the CLDN6 ABD of the subject antibody includes 6 CDRs that are at least 90, 95, 97, 98 or 99% identical to the 6 CDRs of one of the following CLDN6 binding domain VH/VL pairs: H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187). In certain embodiments, the CLDN6 ABD of the subject antibody is capable of binding to CLDN6, as measured at least one of a Biacore, surface plasmon resonance (SPR), BLI (biolayer interferometry, e.g., Octet assay) assay, and/or flow cytometry, with the latter finding particular use in many embodiments. In particular embodiments, the CLDN6 ABD is capable of binding human CLDN6 antigen (see Figure 11).

[00251] In another exemplary embodiment, the CLDN6 ABD of the subject antibody includes the variable heavy (VH) domain and variable light (VL) domain of any one of the

CLDN6 binding domain VH/VL pairs described herein, including the figures and sequence listing.

[00252] In some embodiments, the subject antibody includes a CLDN6 ABD that includes a variable heavy domain and/or a variable light domain that are variants of a CLDN6 ABD VH and VL domain disclosed herein. In one embodiment, the variant VH domain and/or VL domain has from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid changes from a VH and/or VL domain of a CLDN6 ABD described herein, including the figures and sequence listing. In exemplary embodiments, the variant VH domain and/or VL domain has from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid changes from a VH and/or VL domain of one of the following CLDN6 binding domain VH/VL pairs: H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187. In some embodiments, the changes are in a VH domain depicted in Figures 13-15 and 18. In some embodiments, the changes are in a VL domain are depicted in Figures 13-15 and 18. In some embodiments, the changes are in a VH and VL domain are depicted in Figures 13-15 and 18. In some embodiments, one or more amino acid changes are in the VH and/or VL framework regions (FR1, FR2, FR3, and/or FR4). In some embodiments, one or more amino acid changes are in one or more CDRs. In certain embodiments, the CLDN6 ABD of the subject antibody is capable of binding to CLDN6, as measured at least one of a Biacore, surface plasmon resonance (SPR), BLI (biolayer interferometry, e.g., Octet assay) assay, and/or flow cytometry, with the latter finding particular use in many embodiments. In particular embodiments, the CLDN6 ABD is capable of binding human CLDN6 antigen (see Figure 11).

[00253] In one embodiment, the variant VH and/or VL domain is at least 90, 95, 97, 98 or 99% identical to the VH and/or VL of a CLDN6 ABD as described herein, including the figures and sequence listing. In exemplary embodiments, the variant VH and/or VL domain is at least 90, 95, 97, 98 or 99% identical to the VH and/or VL of one of the following CLDN6 binding domain VH/VL pairs: H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187. In some embodiments, the CLDN6 ABD includes a VH that is at least 90, 95, 97, 98 or 99% identical to VH domain depicted in Figures 13-15 and 18. In some embodiments, the CLDN6 ABD includes a VL that is at least 90, 95, 97, 98 or 99% identical to VL domain depicted in Figures 13-15 and 18. In some embodiments, the CLDN6 ABD includes a VH and a VL that is at least 90, 95, 97, 98 or 99% identical to a VH domain and a VL domain depicted in Figures 13-15 and 18. In certain embodiments, the CLDN6 ABD of the subject antibody is capable of binding to CLDN6, as measured at least one of a Biacore,

surface plasmon resonance (SPR), BLI (biolayer interferometry, e.g., Octet assay) assay, and/or flow cytometry, with the latter finding particular use in many embodiments. In particular embodiments, the CLDN6 ABD is capable of binding human CLDN6 antigen (see Figure 11).

2. CD3 Antigen Binding Domains

[00254] The heterodimeric bispecific of the invention (e.g., anti-CLDN6 x anti-CD3 antibodies) also include an ABD that binds to human epsilon CD3 (CD3ε).

[00255] Suitable sets of 6 CDRs and/or VH and VL domains, as well as scFv sequences, are depicted in Figure 10. CD3 binding domain sequences that are of particular use include, but are not limited to, anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47, anti-CD3 H1.31_L1.47, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.32, anti-CD3 L1.47_H1.89, anti-CD3 L1.47_H1.90, anti-CD3 L1.47_H1.33, and anti-CD3 L1.47_H1.31 as depicted in Figure 10. As shown in Figure 10, when the anti-CD3 ABD is a scFv domain, the VH and VL domains can be in either orientation.

[00256] As will be appreciated by those in the art, suitable CD3 binding domains can comprise a set of 6 CDRs as depicted in Figure 10, either as they are underlined or, in the case where a different numbering scheme is used as described herein and as shown in Table 2, as the CDRs that are identified using other alignments within the VH and VL sequences of those depicted in Figures 10A-10F. Suitable ABDs can also include the entire VH and VL sequences as depicted in these sequences and Figures, used as scFvs or as Fabs. In many of the embodiments herein that contain an Fv to CD3, it is the scFv monomer that binds CD3.

[00257] In addition to the parental CDR sets disclosed in the figures and sequence listing that form an ABD to CD3, provided herein are variant CD3 ABDS having CDRs that include at least one modification of the CD3 ABD CDRs disclosed herein (e.g., (Figure 10 and the sequence listing). In one embodiment, the CD3 ABD of the subject heterodimeric antibody (e.g., anti-CLDN6 x anti-CD3 antibody) includes a set of 6 CDRs with 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 amino acid modifications as compared to the 6 CDRs of a CD3 ABD as described herein, including the figures and sequence listing. In exemplary embodiments, the CD3 ABD of the subject heterodimeric antibody includes a set of 6 CDRs with 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 amino acid modifications as compared to the 6 CDRs of one of the following

CD3 binding domains: anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47, anti-CD3 H1.31_L1.47, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.32, anti-CD3 L1.47_H1.89, anti-CD3 L1.47_H1.90, anti-CD3 L1.47_H1.33, and anti-CD3 L1.47_H1.31 (Figure 10). In certain embodiments, the CD3 ABD of the subject antibody is capable of binding CD3 antigen, as measured by at least one of a Biacore, surface plasmon resonance (SPR), flow cytometry, and/or BLI (biolayer interferometry, e.g., Octet assay) assay, with the latter finding particular use in many embodiments. In particular embodiments, the CD3ABD is capable of binding human CD3.

[00258] In some embodiments, the CD3 ABD of the subject antibody includes 6 CDRs that are at least 90, 95, 97, 98 or 99% identical to the 6 CDRs of a CD3 ABD as described herein, including the figures and sequence listing. In exemplary embodiments, the CD3 ABD of the subject antibody includes 6 CDRs that are at least 90, 95, 97, 98 or 99% identical to the 6 CDRs of one of the following CD3 binding domains: anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47, anti-CD3 H1.31_L1.47, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.32, anti-CD3 L1.47_H1.89, anti-CD3 L1.47_H1.90, anti-CD3 L1.47_H1.33, and anti-CD3 L1.47_H1.31 (Figure 10). In certain embodiments, the CD3 ABD is capable of binding to the CD3, as measured by at least one of a Biacore, surface plasmon resonance (SPR), flow cytometry, and/or BLI (biolayer interferometry, e.g., Octet assay) assay, with the latter finding particular use in many embodiments. In particular embodiments, the CD3 ABD is capable of binding human CD3 antigen.

[00259] In another exemplary embodiment, the CD3 ABD of the subject antibody includes the variable heavy (VH) domain and variable light (VL) domain of any one of the CD3 binding domains described herein, including the figures and sequence listing.

[00260] In some embodiments, the subject antibody includes a CD3 ABD that includes a variable heavy domain and/or a variable light domain that are variants of a CD3 ABD VH and VL domain disclosed herein. In one embodiment, the variant VH domain and/or VL domain has from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid changes from a VH and/or VL domain of a CD3 ABD described herein, including the figures and sequence listing. In exemplary embodiments, the variant VH domain and/or VL domain has from 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acid changes from a VH and/or VL domain of one of the following CD3 binding domains: anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47,

anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47, anti-CD3 H1.31_L1.47, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.32, anti-CD3 L1.47_H1.89, anti-CD3 L1.47_H1.90, anti-CD3 L1.47_H1.33, and anti-CD3 L1.47_H1.31 (Figure 10). In some embodiments, the changes are in a VH domain depicted in Figure 10. In some embodiments, the changes are in a VL domain are depicted in Figure 10. In some embodiments, the changes are in a VH and VL domain are depicted in Figure 10. In some embodiments, one or more amino acid changes are in the VH and/or VL framework regions (FR1, FR2, FR3, and/or FR4). In some embodiments, one or more amino acid changes are in one or more CDRs. In certain embodiments, the CD3 ABD of the subject antibody is capable of binding to CD3, as measured at least one of a Biacore, surface plasmon resonance (SPR), flow cytometry, and/or BLI (biolayer interferometry, e.g., Octet assay) assay, with the latter finding particular use in many embodiments. In particular embodiments, the CD3 ABD is capable of binding human CD3 antigen.

[00261] In one embodiment, the variant VH and/or VL domain is at least 90, 95, 97, 98 or 99% identical to the VH and/or VL of a CD3 ABD as described herein, including the figures and sequence listing. In exemplary embodiments, the variant VH and/or VL domain is at least 90, 95, 97, 98 or 99% identical to the VH and/or VL of one of the following CD3 binding domains: anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47, anti-CD3 H1.31_L1.47, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.32, anti-CD3 L1.47_H1.89, anti-CD3 L1.47_H1.90, anti-CD3 L1.47_H1.33, and anti-CD3 L1.47_H1.31 (Figure 10). In some embodiments, the CD3 ABD includes a VH that is at least 90, 95, 97, 98 or 99% identical to VH domain depicted in Figure 10. In some embodiments, the CD3 ABD includes a VL that is at least 90, 95, 97, 98 or 99% identical to VL domain depicted in Figure 10. In some embodiments, the CD3 ABD includes a VH and a VL that is at least 90, 95, 97, 98 or 99% identical to a VH domain and a VL domain depicted in Figure 10. In certain embodiments, the CD3 ABD is capable of binding to CD3, as measured by at least one of a Biacore, surface plasmon resonance (SPR), flow cytometry, and/or BLI (biolayer interferometry, e.g., Octet assay) assay, with the latter finding particular use in many embodiments. In particular embodiments, the CD3 ABD is capable of binding human CD3 antigen.

[00262] In addition to the α CD3 ABDs of Figure 10, additional ABDs of use in the invention include those depicted in Figures 14 and 15 of WO2014/145806, hereby expressly incorporated herein in their entirety including the Figures and Legends therein.

3. Linkers

[00263] As shown herein, there are a number of suitable linkers (for use as either domain linkers or scFv linkers) that can be used to covalently attach the recited domains (e.g., scFvs, Fabs, Fc domains, etc.), including traditional peptide bonds, generated by recombinant techniques. Exemplary linkers to attach domains of the subject antibody to each other are depicted in Figure 6. In some embodiments, the linker peptide may predominantly include the following amino acid residues: Gly, Ser, Ala, or Thr. The linker peptide should have a length that is adequate to link two molecules in such a way that they assume the correct conformation relative to one another so that they retain the desired activity. In one embodiment, the linker is from about 1 to 50 amino acids in length, preferably about 1 to 30 amino acids in length. In one embodiment, linkers of 1 to 20 amino acids in length may be used, with from about 5 to about 10 amino acids finding use in some embodiments. Useful linkers include glycine-serine polymers, including for example (GS)_n, (GSGGS)_n (SEQ ID NO: 3), (GGGGS)_n (SEQ ID NO: 2), and (GGGS)_n (SEQ ID NO: 4), where n is an integer of at least one (and generally from 3 to 4), glycine-alanine polymers, alanine-serine polymers, and other flexible linkers, some of which are shown in Figure 5 and Figure 6. Alternatively, a variety of nonproteinaceous polymers, including but not limited to polyethylene glycol (PEG), polypropylene glycol, polyoxyalkylenes, or copolymers of polyethylene glycol and polypropylene glycol, may find use as linkers.

[00264] Other linker sequences may include any sequence of any length of CL/CH1 domain but not all residues of CL/CH1 domain; for example the first 5-12 amino acid residues of the CL/CH1 domains. Linkers can be derived from immunoglobulin light chain, for example C_κ or C_λ. Linkers can be derived from immunoglobulin heavy chains of any isotype, including for example C_γ1, C_γ2, C_γ3, C_γ4, C_α1, C_α2, C_δ, C_ε, and C_μ. Linker sequences may also be derived from other proteins such as Ig-like proteins (e.g. TCR, FcR, KIR), hinge region-derived sequences, and other natural sequences from other proteins.

[00265] In some embodiments, the linker is a “domain linker”, used to link any two domains as outlined herein together. For example, in Figure 17B, there may be a domain linker that attaches the C-terminus of the CH1 domain of the Fab to the N-terminus of the scFv, with another optional domain linker attaching the C-terminus of the scFv to the CH2 domain (although in many embodiments the hinge is used as this domain linker). While any

suitable linker can be used, many embodiments utilize a glycine-serine polymer as the domain linker, including for example (GS)_n, (GSGGS)_n (SEQ ID NO: 3), (GGGGS)_n (SEQ ID NO: 2), and (GGGS)_n (SEQ ID NO: 4), where n is an integer of at least one (and generally from 3 to 4 to 5) as well as any peptide sequence that allows for recombinant attachment of the two domains with sufficient length and flexibility to allow each domain to retain its biological function. In some cases, and with attention being paid to “strandedness”, as outlined below, charged domain linkers, as used in some embodiments of scFv linkers can be used. Exemplary useful domain linkers are depicted in Figure 6.

[00266] With particular reference to the domain linker used to attach the scFv domain to the Fc domain in the “2+1” format, there are several domain linkers that find particular use, including “full hinge C220S variant,” “flex half hinge,” “charged half hinge 1,” and “charged half hinge 2” as shown in Figure 6.

[00267] In some embodiments, the linker is a “scFv linker”, used to covalently attach the VH and VL domains as discussed herein. In many cases, the scFv linker is a charged scFv linker, a number of which are shown in Figure 5. Accordingly, in some embodiments, the antibodies described herein further provide charged scFv linkers, to facilitate the separation in pI between a first and a second monomer. That is, by incorporating a charged scFv linker, either positive or negative (or both, in the case of scaffolds that use scFvs on different monomers), this allows the monomer comprising the charged linker to alter the pI without making further changes in the Fc domains. These charged linkers can be substituted into any scFv containing standard linkers. Again, as will be appreciated by those in the art, charged scFv linkers are used on the correct “strand” or monomer, according to the desired changes in pI. For example, as discussed herein, to make 1+1 Fab-scFv-Fc format heterodimeric antibody, the original pI of the Fv region for each of the desired antigen binding domains are calculated, and one is chosen to make an scFv, and depending on the pI, either positive or negative linkers are chosen.

[00268] Charged domain linkers can also be used to increase the pI separation of the monomers of the antibodies described herein as well, and thus those included in Figure 5 can be used in any embodiment herein where a linker is utilized.

D. Useful Formats of the Invention

[00269] As will be appreciated by those in the art and discussed more fully below, the heterodimeric bispecific antibodies provided herein can take on a wide variety of configurations, as are generally depicted in Figure 17 as well as Figure 36. Some figures depict “single ended” configurations, where there is one type of specificity on one “arm” of the molecule and a different specificity on the other “arm”. Other figures depict “dual ended” configurations, where there is at least one type of specificity at the “top” of the molecule and one or more different specificities at the “bottom” of the molecule. Thus, in some embodiments, the antibodies described herein are directed to novel immunoglobulin compositions that co-engage a different first and a second antigen.

[00270] As will be appreciated by those in the art, the heterodimeric formats of the antibodies described herein can have different valencies as well as be bispecific. That is, heterodimeric antibodies of the antibodies described herein can be bivalent and bispecific, wherein one target tumor antigen (e.g. CD3) is bound by one binding domain and the other target tumor antigen (e.g. CLDN6) is bound by a second binding domain. The heterodimeric antibodies can also be trivalent and bispecific, wherein the first antigen is bound by two binding domains and the second antigen by a second binding domain. As is outlined herein, when CD3 is one of the target antigens, it is preferable that the CD3 is bound only monovalently, to reduce potential side effects.

[00271] The antibodies described herein utilize anti-CD3 antigen binding domains in combination with anti-CLDN6 binding domains. As will be appreciated by those in the art, any collection of anti-CD3 CDRs, anti-CD3 variable light and variable heavy domains, Fabs and scFvs as described herein, and depicted in any of the Figures can be used. Similarly, any of the anti-CLDN6 antigen binding domains can be used, whether CDRs, variable light and variable heavy domains, Fabs and scFvs as described herein, and depicted in any of the Figures can be used, optionally and independently combined in any combination.

1. 1+1 Fab-scFv-Fc Format

[00272] One heterodimeric scaffold that finds particular use in the antibodies described herein is the “1+1 Fab-scFv-Fc” or “bottle-opener” format as shown in Figure 17A with an exemplary combination of a CD3 binding domain and a tumor target antigen (CLDN6) binding domain. In this embodiment, one heavy chain monomer of the antibody contains a single chain Fv (“scFv”, as defined below) and an Fc domain. The scFv includes a variable

heavy domain (VH1) and a variable light domain (VL1), wherein the VH1 is attached to the VL1 using an scFv linker that can be charged (see, e.g., Figure 5). The scFv is attached to the heavy chain using a domain linker (see, e.g., Figure 6). The other heavy chain monomer is a “regular” heavy chain (VH-CH1-hinge-CH2-CH3). The 1 + 1 Fab-scFv-Fc also includes a light chain that interacts with the VH-CH1 to form a Fab. This structure is sometimes referred to herein as the “bottle-opener” format, due to a rough visual similarity to a bottle-opener. The two heavy chain monomers are brought together by the use of amino acid variants (e.g., heterodimerization variants, discussed above) in the constant regions (e.g., the Fc domain, the CH1 domain and/or the hinge region) that promote the formation of heterodimeric antibodies as is described more fully below.

[00273] There are several distinct advantages to the present “1+1 Fab-scFv-Fc” format. As is known in the art, antibody analogs relying on two scFv constructs often have stability and aggregation problems, which can be alleviated in the antibodies described herein by the addition of a “regular” heavy and light chain pairing. In addition, as opposed to formats that rely on two heavy chains and two light chains, there is no issue with the incorrect pairing of heavy and light chains (e.g. heavy 1 pairing with light 2, etc.).

[00274] Many of the embodiments outlined herein rely in general on the 1+1 Fab-scFv-Fc or “bottle opener” format antibody that comprises a first monomer comprising an scFv, comprising a variable heavy and a variable light domain, covalently attached using an scFv linker (charged, in many but not all instances), where the scFv is covalently attached to the N-terminus of a first Fc domain usually through a domain linker. The domain linker can be either charged or uncharged and exogenous or endogenous (e.g., all or part of the native hinge domain). Any suitable linker can be used to attach the scFv to the N-terminus of the first Fc domain. In some embodiments, the domain linker is chosen from the domain linkers in Figure 6. The second monomer of the 1 + 1 Fab-scFv-Fc format or “bottle opener” format is a heavy chain, and the composition further comprises a light chain.

[00275] In general, in many preferred embodiments, the scFv is the domain that binds to the CD3, and the Fab forms an CLDN6 binding domain. An exemplary anti-CLDN6 x anti-CD3 bispecific antibody in the 1 + 1 Fab-scFv-Fc format is depicted in Figure 17A. Exemplary anti-CLDN6 x anti-CD3 bispecific antibodies in the 1+1 Fab-scFv-Fc format are depicted in Figures 19 and 20.

[00276] In addition, the Fc domains of the antibodies described herein generally include skew variants (e.g. a set of amino acid substitutions as shown in Figure 1, with particularly useful skew variants being selected from the group consisting of S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L; K370S : S364K/E357Q; T366S/L368A/Y407V : T366W and T366S/L368A/Y407V/Y349C : T366W/S354C), optionally ablation variants (including those shown in Figure 3), optionally charged scFv linkers (including those shown in Figure 5) and the heavy chain comprises pI variants (including those shown in Figure 2).

[00277] In certain embodiments, the 1 + 1 Fab-scFv-Fc scaffold format includes a first monomer that includes a scFv-domain linker-CH2-CH3 monomer, a second monomer that includes a first variable heavy domain-CH1-hinge-CH2-CH3 monomer and a third monomer that includes a first variable light domain. In some embodiments, the CH2-CH3 of the first monomer is a first variant Fc domain and the CH2-CH3 of the second monomer is a second variant Fc domain. In some embodiments, the scFv includes a scFv variable heavy domain and a scFv variable light domain that form a CD3 binding moiety. In certain embodiments, the scFv variable heavy domain and scFv variable light domain are covalently attached using an scFv linker (charged, in many but not all instances. See, e.g., Figure 5). In some embodiments, the first variable heavy domain and first variable light domain form a CLDN6 binding domain.

[00278] In some embodiments, the 1 + 1 Fab-scFv-Fc format includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments include 1 + 1 Fab-scFv-Fc formats that comprise: a) a first monomer (the “scFv monomer”) that comprises a charged scFv linker (with the +H sequence of Figure 5 being preferred in some embodiments), the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, and an scFv that binds to CD3 as outlined herein; b) a second monomer (the “Fab monomer”) that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, and a variable heavy domain; and c) a light chain that includes a variable light domain light domain (VL) and a constant light domain (CL), wherein numbering is according to EU numbering. The variable heavy domain and variable light domain make up an CLDN6 binding moiety.

[00279] Any suitable CD3 ABD can be included in the 1 + 1 Fab-scFv-Fc format antibody, included those provided herein. CD3 binding domain sequences finding particular

use in these embodiments include, but are not limited to, H1.30_L1.47, H1.32_L1.47, H1.89_L1.47, H1.90_L1.47, H1.33_L1.47, H1.31_L1.47, L1.47_H1.30, L1.47_H1.30, L1.47_H1.32, L1.47_H1.89, L1.47_H1.90, L1.47_H1.33, and L1.47_H1.31 or a variant thereof, as well as those depicted in Figure 10 and those depicted in Figures 14 and 15 of WO2014/145806, hereby incorporated by reference including the Legends.

[00280] Any suitable CLDN6 ABD can be included in the 1 + 1 Fab-scFv-Fc format antibody, included those provided herein. CLDN6 ABDs that are of particular use in these embodiments include, but are not limited to, VH and VL domains selected from have VH/VL pairs selected from the group consisting of: H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1, H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1, H2.12_L1, H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1, H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1, H1.9_L1.1, H1.19_L1.1, H1.22_L1.1, H1.24_L1.1, H2_L1.1, H2.1_L1.1, H2.2_L1.1, H2.3_L1.1, H2.4_L1.1, H2.5_L1.1, H2.6_L1.1, H2.7_L1.1, H2.8_L1.1, H2.9_L1.1, H2.11_L1.1, H2.12_L1.1, H2.71_L1.1, H2.75_L1.1, H2.90_L1.1, H2.91_L1.1, H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4, H1.2_L1.4, H1.3_L1.4, H1.4_L1.4, H1.5_L1.4, H1.6_L1.4, H1.7_L1.4, H1.8_L1.4, H1.9_L1.4, H1.19_L1.4, H1.22_L1.4, H1.24_L1.4, H2_L1.4, H2.1_L1.4, H2.2_L1.4, H2.3_L1.4, H2.4_L1.4, H2.5_L1.4, H2.6_L1.4, H2.7_L1.4, H2.8_L1.4, H2.9_L1.4, H2.11_L1.4, H2.12_L1.4, H2.71_L1.4, H2.75_L1.4, H2.90_L1.4, H2.91_L1.4, H2.118_L1.4, H2.119_L1.4, H1_L1.7, H1.1_L1.7, H1.2_L1.7, H1.3_L1.7, H1.4_L1.7, H1.5_L1.7, H1.6_L1.7, H1.7_L1.7, H1.8_L1.7, H1.9_L1.7, H1.19_L1.7, H1.22_L1.7, H1.24_L1.7, H2_L1.7, H2.1_L1.7, H2.2_L1.7, H2.3_L1.7, H2.4_L1.7, H2.5_L1.7, H2.6_L1.7, H2.7_L1.7, H2.8_L1.7, H2.9_L1.7, H2.11_L1.7, H2.12_L1.7, H2.71_L1.7, H2.75_L1.7, H2.90_L1.7, H2.91_L1.7, H2.118_L1.7, H2.119_L1.7, H1_L1.16, H1.1_L1.16, H1.2_L1.16, H1.3_L1.16, H1.4_L1.16, H1.5_L1.16, H1.6_L1.16, H1.7_L1.16, H1.8_L1.16, H1.9_L1.16, H1.19_L1.16, H1.22_L1.16, H1.24_L1.16, H2_L1.16, H2.1_L1.16, H2.2_L1.16, H2.3_L1.16, H2.4_L1.16, H2.5_L1.16, H2.6_L1.16, H2.7_L1.16, H2.8_L1.16, H2.9_L1.16, H2.11_L1.16, H2.12_L1.16, H2.71_L1.16, H2.75_L1.16, H2.90_L1.16, H2.91_L1.16, H2.118_L1.16, H2.119_L1.16, H1_L1.18, H1.1_L1.18, H1.2_L1.18, H1.3_L1.18, H1.4_L1.18, H1.5_L1.18, H1.6_L1.18, H1.7_L1.18, H1.8_L1.18, H1.9_L1.18, H1.19_L1.18, H1.22_L1.18, H1.24_L1.18, H2_L1.18, H2.1_L1.18, H2.2_L1.18,

H2.3_L1.18, H2.4_L1.18, H2.5_L1.18, H2.6_L1.18, H2.7_L1.18, H2.8_L1.18, H2.9_L1.18, H2.11_L1.18, H2.12_L1.18, H2.71_L1.18, H2.75_L1.18, H2.90_L1.18, H2.91_L1.18, H2.118_L1.18, H2.119_L1.18, H1_L1.19, H1.1_L1.19, H1.2_L1.19, H1.3_L1.19, H1.4_L1.19, H1.5_L1.19, H1.6_L1.19, H1.7_L1.19, H1.8_L1.19, H1.9_L1.19, H1.19_L1.19, H1.22_L1.19, H1.24_L1.19, H2_L1.19, H2.1_L1.19, H2.2_L1.19, H2.3_L1.19, H2.4_L1.19, H2.5_L1.19, H2.6_L1.19, H2.7_L1.19, H2.8_L1.19, H2.9_L1.19, H2.11_L1.19, H2.12_L1.19, H2.71_L1.19, H2.75_L1.19, H2.90_L1.19, H2.91_L1.19, H2.118_L1.19, H2.119_L1.19, H1_L1.21, H1.1_L1.21, H1.2_L1.21, H1.3_L1.21, H1.4_L1.21, H1.5_L1.21, H1.6_L1.21, H1.7_L1.21, H1.8_L1.21, H1.9_L1.21, H1.19_L1.21, H1.22_L1.21, H1.24_L1.21, H2_L1.21, H2.1_L1.21, H2.2_L1.21, H2.3_L1.21, H2.4_L1.21, H2.5_L1.21, H2.6_L1.21, H2.7_L1.21, H2.8_L1.21, H2.9_L1.21, H2.11_L1.21, H2.12_L1.21, H2.71_L1.21, H2.75_L1.21, H2.90_L1.21, H2.91_L1.21, H2.118_L1.2, H2.119_L1.21, H1_L1.22, H1.1_L1.22, H1.2_L1.22, H1.3_L1.22, H1.4_L1.22, H1.5_L1.22, H1.6_L1.22, H1.7_L1.22, H1.8_L1.22, H1.9_L1.22, H1.19_L1.22, H1.22_L1.22, H1.24_L1.22, H2_L1.22, H2.1_L1.22, H2.2_L1.22, H2.3_L1.22, H2.4_L1.22, H2.5_L1.22, H2.6_L1.22, H2.7_L1.22, H2.8_L1.22, H2.9_L1.22, H2.11_L1.22, H2.12_L1.22, H2.71_L1.22, H2.75_L1.22, H2.90_L1.22, H2.91_L1.22, H2.118_L1.22, H2.119_L1.22, H1_L1.23, H1.1_L1.23, H1.2_L1.23, H1.3_L1.23, H1.4_L1.23, H1.5_L1.23, H1.6_L1.23, H1.7_L1.23, H1.8_L1.23, H1.9_L1.23, H1.19_L1.23, H1.22_L1.23, H1.24_L1.23, H2_L1.23, H2.1_L1.23, H2.2_L1.23, H2.3_L1.23, H2.4_L1.23, H2.5_L1.23, H2.6_L1.23, H2.7_L1.23, H2.8_L1.23, H2.9_L1.23, H2.11_L1.23, H2.12_L1.23, H2.71_L1.23, H2.75_L1.23, H2.90_L1.23, H2.91_L1.23, H2.118_L1.23, H2.119_L1.23, H1_L1.27, H1.1_L1.27, H1.2_L1.27, H1.3_L1.27, H1.4_L1.27, H1.5_L1.27, H1.6_L1.27, H1.7_L1.27, H1.8_L1.27, H1.9_L1.27, H1.19_L1.27, H1.22_L1.27, H1.24_L1.27, H2_L1.27, H2.1_L1.27, H2.2_L1.27, H2.3_L1.27, H2.4_L1.27, H2.5_L1.27, H2.6_L1.27, H2.7_L1.27, H2.8_L1.27, H2.9_L1.27, H2.11_L1.27, H2.12_L1.27, H2.71_L1.27, H2.75_L1.27, H2.90_L1.27, H2.91_L1.27, H2.118_L1.27, H2.119_L1.27, H1_L1.60, H1.1_L1.60, H1.2_L1.60, H1.3_L1.60, H1.4_L1.60, H1.5_L1.60, H1.6_L1.60, H1.7_L1.60, H1.8_L1.60, H1.9_L1.60, H1.19_L1.60, H1.22_L1.60, H1.24_L1.60, H2_L1.60, H2.1_L1.60, H2.2_L1.60, H2.3_L1.60, H2.4_L1.60, H2.5_L1.60, H2.6_L1.60, H2.7_L1.60, H2.8_L1.60, H2.9_L1.60, H2.11_L1.60, H2.12_L1.60, H2.71_L1.60, H2.75_L1.60, H2.90_L1.60, H2.91_L1.60, H2.118_L1.60, H2.119_L1.60, H1_L1.107, H1.1_L1.107, H1.2_L1.107, H1.3_L1.107, H1.4_L1.107, H1.5_L1.107, H1.6_L1.107, H1.7_L1.107, H1.8_L1.107, H1.9_L1.107, H1.19_L1.107, H1.22_L1.107, H1.24_L1.107, H2_L1.107, H2.1_L1.107, H2.2_L1.107,

H2.3_L1.107, H2.4_L1.107, H2.5_L1.107, H2.6_L1.107, H2.7_L1.107, H2.8_L1.107, H2.9_L1.107, H2.11_L1.107, H2.12_L1.107, H2.71_L1.107, H2.75_L1.107, H2.90_L1.107, H2.91_L1.107, H2.118_L1.107, H2.119_L1.107, H1_L1.114, H1.1_L1.114, H1.2_L1.114, H1.3_L1.114, H1.4_L1.114, H1.5_L1.114, H1.6_L1.114, H1.7_L1.114, H1.8_L1.114, H1.9_L1.114, H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114, H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114, H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114, H2.90_L1.114, H2.91_L1.114, H2.118_L1.114, H2.119_L1.114, H1_L1.187, H1.1_L1.187, H1.2_L1.187, H1.3_L1.187, H1.4_L1.187, H1.5_L1.187, H1.6_L1.187, H1.7_L1.187, H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187, H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187, H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187, H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187, H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189, H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189, H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189, H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189, H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189, H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2, H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2 or a variant thereof.

[00281] In particular embodiments, the α CLDN6 ABD VH/VL pairs are selected from the group consisting of H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187 or a variant thereof.

[00282] In some embodiments, the 1 + 1 Fab-scFv-Fc format includes skew variants, pI variants, ablation variants and FcRn variants. Accordingly, some embodiments include 1 + 1 Fab-scFv-Fc formats that comprise: a) a first monomer (the “scFv monomer”) that comprises a charged scFv linker (with the +H sequence of Figure 6 being preferred in some embodiments), the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and an scFv that binds to CD3 as outlined herein; b) a second monomer (the “Fab monomer”) that comprises

the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/Q418E/N421D, the ablation variants E233P/L234V/L235A/ G236del/S267K, the FcRn variants M428L/N434S, and a variable heavy domain; and c) a light chain that includes a variable light domain(VL) and a constant light domain (CL), wherein numbering is according to EU numbering. The variable heavy domain and variable light domain make up a CLDN6 binding domain. CD3 binding domain sequences finding particular use in these embodiments include, but are not limited to, H1.30_L1.47, H1.32_L1.47, H1.89_L1.47, H1.90_L1.47, H1.33_L1.47, H1.31_L1.47, L1.47_H1.30, L1.47_H1.30, L1.47_H1.32, L1.47_H1.89, L1.47_H1.90, L1.47_H1.33, and L1.47_H1.31 or a variant thereof, as well as those depicted in Figures 10. CLDN6 binding domain sequences that are of particular use in these embodiments include, but are not limited to, the α CLDN6 ABD VH_VL pairs are selected from the group consisting of H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187 or a variant thereof.

[00283] Particularly useful CLDN6 and CD3 sequence combinations for use with the 1 + 1 format antibody include, for example, are disclosed in Figures 19 and 20.

[00284] Figures 7A-7D show some exemplary Fc domain sequences that are useful in the 1 + 1 Fab-scFv-Fc format antibodies. The “monomer 1” sequences depicted in Figures 7A-7D typically refer to the Fc domain of the “Fab-Fc heavy chain” and the “monomer 2” sequences refer to the Fc domain of the “scFv-Fc heavy chain.” Further, Figure 9 provides useful CL sequences that can be used with this format.

[00285] In some embodiments, any of the VH and VL sequences depicted herein (including all VH and VL sequences depicted in the Figures and Sequence Listings, including those directed to CLDN6) can be added to the bottle opener backbone formats of Figure 7A-7D as the “Fab side”, using any of the anti-CD3 scFv sequences shown in the Figures and Sequence Listings.

[00286] For bottle opener backbone 1 from Figure 7A, (optionally including the 428L/434S variants), CD binding domain sequences finding particular use in these embodiments include, but are not limited to, CD3 binding domain anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47 and anti-CD3 H1.31_L1.47 attached as the scFv side of the backbones shown in Figure 7.

2. mAb-Fv

[00287] One heterodimeric scaffold that finds particular use in the antibodies described herein is the mAb-Fv format (Figure 36G). In this embodiment, the format relies on the use of a C-terminal attachment of an “extra” variable heavy domain to one monomer and the C-terminal attachment of an “extra” variable light domain to the other monomer, thus forming a third antigen binding domain, wherein the Fab portions of the two monomers bind a CLDN6 and the “extra” scFv domain binds CD3.

[00288] In this embodiment, the first monomer comprises a first heavy chain, comprising a first variable heavy domain and a first constant heavy domain comprising a first Fc domain, with a first variable light domain covalently attached to the C-terminus of the first Fc domain using a domain linker (VH1-CH1-hinge-CH2-CH3-[optional linker]-VL2). The second monomer comprises a second variable heavy domain of the second constant heavy domain comprising a second Fc domain, and a third variable heavy domain covalently attached to the C-terminus of the second Fc domain using a domain linker (vh1-CH1-hinge-CH2-CH3-[optional linker]-VH2). The two C-terminally attached variable domains make up a Fv that binds CD3 (as it is less preferred to have bivalent CD3 binding). This embodiment further utilizes a common light chain comprising a variable light domain and a constant light domain that associates with the heavy chains to form two identical Fabs that bind a CLDN6. As for many of the embodiments herein, these constructs include skew variants, pI variants, ablation variants, additional Fc variants, etc. as desired and described herein.

[00289] The antibodies described herein provide mAb-Fv formats where the CD3 binding domain sequences are as shown in Figure 10 or a variant thereof. The antibodies described herein provide mAb-Fv formats wherein the CLDN6 binding domain sequences are as shown in Figures 13, 14 and 15 or a variant thereof.

[00290] In addition, the Fc domains of the mAb-Fv format comprise skew variants (e.g. a set of amino acid substitutions as shown in Figure 1, with particularly useful skew variants being selected from the group consisting of S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L, K370S : S364K/E357Q, T366S/L368A/Y407V : T366W and T366S/L368A/Y407V/Y349C : T366W/S354C), optionally ablation variants (including those shown in Figure 3), optionally charged scFv linkers (including those shown in Figure 5) and the heavy chain comprises pI variants (including those shown in Figure 2).

[00291] In some embodiments, the mAb-Fv format includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments include mAb-Fv formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, and a first variable heavy domain that, with the first variable light domain of the light chain, makes up an Fv that binds to CLDN6, and a second variable heavy domain; b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, and a first variable heavy domain that, with the first variable light domain, makes up the Fv that binds to CLDN6 as outlined herein, and a second variable light chain, that together with the second variable heavy domain forms an Fv (ABD) that binds to CD3; and c) a light chain comprising a first variable light domain and a constant light domain.

[00292] In some embodiments, the mAb-Fv format includes skew variants, pI variants, ablation variants and FcRn variants. Accordingly, some embodiments include mAb-Fv formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a first variable heavy domain that, with the first variable light domain of the light chain, makes up an Fv that binds to CLDN6, and a second variable heavy domain; b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a first variable heavy domain that, with the first variable light domain, makes up the Fv that binds to CLDN6 as outlined herein, and a second variable light chain, that together with the second variable heavy domain of the first monomer forms an Fv (ABD) that binds CD3; and c) a light chain comprising a first variable light domain and a constant light domain.

3. mAb-scFv

[00293] One heterodimeric scaffold that finds particular use in the antibodies described herein is the mAb-scFv format (Figure 36H). In this embodiment, the format relies on the use of a C-terminal attachment of a scFv to one of the monomers, thus forming a third antigen binding domain, wherein the Fab portions of the two monomers bind CLDN6 and the “extra” scFv domain binds CD3. Thus, the first monomer comprises a first heavy chain

(comprising a variable heavy domain and a constant domain), with a C-terminally covalently attached scFv comprising a scFv variable light domain, an scFv linker and a scFv variable heavy domain in either orientation (VH1-CH1-hinge-CH2-CH3-[optional linker]-VH2-scFv linker-VL2 or VH1-CH1-hinge-CH2-CH3-[optional linker]-VL2-scFv linker-VH2). This embodiment further utilizes a common light chain comprising a variable light domain and a constant light domain, that associates with the heavy chains to form two identical Fabs that bind CLDN6. As for many of the embodiments herein, these constructs include skew variants, pI variants, ablation variants, additional Fc variants, etc. as desired and described herein.

[00294] The antibodies described herein provide mAb-scFv formats, where the CD3 binding domain sequences are as shown in Figure 10A-10F or a variant thereof and the CLDN6 binding domain sequences are as shown in Figures 13-15 and 18 or a variant thereof.

[00295] In addition, the Fc domains of the mAb-scFv format comprise skew variants (e.g. a set of amino acid substitutions as shown in Figure 1, with particularly useful skew variants being selected from the group consisting of S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L, K370S : S364K/E357Q, T366S/L368A/Y407V : T366W and T366S/L368A/Y407V/Y349C : T366W/S354C), optionally ablation variants (including those shown in Figure 3), optionally charged scFv linkers (including those shown in Figure 5) and the heavy chain comprises pI variants (including those shown in Figure 2).

[00296] In some embodiments, the mAb-scFv format includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments include mAb-scFv formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, and a variable heavy domain that, with the variable light domain of the common light chain, makes up an Fv that binds to CLDN6 as outlined herein, and a scFv domain that binds to CD3; b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, and a variable heavy domain that, with the variable light domain of the common light chain, makes up an Fv that binds to CLDN6 as outlined herein; and c) a common light chain comprising a variable light domain and a constant light domain.

[00297] In some embodiments, the mAb-scFv format includes skew variants, pI variants, ablation variants and FcRn variants. Accordingly, some embodiments include mAb-scFv formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a variable heavy domain that, with the variable light domain of the common light chain, makes up an Fv that binds to CLDN6 as outlined herein, and a scFv domain that binds to CD3; b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a variable heavy domain that, with the variable light domain of the common light chain, makes up an Fv that binds to CLDN6 as outlined herein; and c) a common light chain comprising a variable light domain and a constant light domain.

4. 2+1 Fab₂-scFv-Fc Format

[00298] One heterodimeric scaffold that finds particular use in the antibodies described herein is the “2+1 Fab₂-scFv-Fc” format (also referred to in previous related filings as “Central-scFv format”) shown in Figure 17B with an exemplary combination of a CD3 binding domain and two tumor target antigen (CLDN6) binding domains. In this embodiment, the format relies on the use of an inserted scFv domain thus forming a third antigen binding domain, wherein the Fab portions of the two monomers bind CLDN6 and the “extra” scFv domain binds CD3. The scFv domain is inserted between the Fc domain and the CH1-Fv region of one of the monomers, thus providing a third antigen binding domain. As described, CLDN6 x CD3 bispecific antibodies having the 2 + 1 Fab₂-scFv-Fc format are potent in inducing redirected T cell cytotoxicity in cellular environments that express low levels of CLDN6. Moreover, as shown in the examples, CLDN6 x CD3 bispecific antibodies having the 2 + 1 Fab₂-scFv-Fc format allow for the “fine tuning” of immune responses as such antibodies exhibit a wide variety of different properties, depending on the CLDN6 and/or CD3 binding domains used. For example, such antibodies exhibit differences in selectivity for cells with different CLDN6 expression, potencies for CLDN6 expressing cells, ability to elicit cytokine release, and sensitivity to soluble CLDN6. These CLDN6 antibodies find use, for example, in the treatment of CLDN6-associated cancers.

[00299] In this embodiment, one monomer comprises a first heavy chain comprising a first variable heavy domain, a CH1 domain (and optional hinge) and Fc domain, with a scFv comprising a scFv variable light domain, an scFv linker and a scFv variable heavy domain. The scFv is covalently attached between the C-terminus of the CH1 domain of the heavy constant domain and the N-terminus of the first Fc domain using optional domain linkers (VH1-CH1-[optional linker]-VH2-scFv linker-VL2-[optional linker including the hinge]-CH2-CH3, or the opposite orientation for the scFv, VH1-CH1-[optional linker]-VL2-scFv linker-VH2-[optional linker including the hinge]-CH2-CH3). The optional linkers can be any suitable peptide linkers, including, for example, the domain linkers included in Figure 6. In some embodiments, the optional linker is a hinge or a fragment thereof. The other monomer is a standard Fab side (i.e., VH1-CH1-hinge-CH2-CH3). This embodiment further utilizes a common light chain comprising a variable light domain and a constant light domain, that associates with the heavy chains to form two identical Fabs that bind CLDN6. As for many of the embodiments herein, these constructs include skew variants, pI variants, ablation variants, additional Fc variants, etc. as desired and described herein.

[00300] In one embodiment, the 2 + 1 Fab₂-scFv-Fc format antibody includes an scFv with the VH and VL of a CD3 binding domain sequence depicted in Figure 10 or a variant thereof. In one embodiment, the 2 + 1 Fab₂-scFv-Fc format antibody includes two Fabs having the VH and VL of a CLDN6 binding domain as shown in Figures 13-15 and 18 or a variant thereof.

[00301] In exemplary embodiments, the CLDN6 binding domain of the 2 + 1 Fab₂-scFv-Fc CLDN6 x CD3 bispecific antibody includes the VH and VL CD3 binding domain sequences finding particular use in these embodiments include, but are not limited to, H1.30_L1.47, H1.32_L1.47, H1.89_L1.47, H1.90_L1.47, H1.33_L1.47, H1.31_L1.47, L1.47_H1.30, L1.47_H1.30, L1.47_H1.32, L1.47_H1.89, L1.47_H1.90, L1.47_H1.33, and L1.47_H1.31 or a variant thereof, as well as those depicted in Figure 10 and those depicted in Figures 14 and 15 of WO2014/145806, hereby incorporated by reference including the Legends.

[00302] Any suitable CLDN6 ABD can be included in the 2 + 1 Fab₂-scFv-Fc format antibody, included those provided herein. CLDN6 ABDs that are of particular use in these embodiments include, but are not limited to, VH and VL domains selected from the group consisting of: H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1,

H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1, H2.12_L1,
H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1,
H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1,
H1.9_L1.1, H1.19_L1.1, H1.22_L1.1, H1.24_L1.1, H2_L1.1, H2.1_L1.1, H2.2_L1.1,
H2.3_L1.1, H2.4_L1.1, H2.5_L1.1, H2.6_L1.1, H2.7_L1.1, H2.8_L1.1, H2.9_L1.1,
H2.11_L1.1, H2.12_L1.1, H2.71_L1.1, H2.75_L1.1, H2.90_L1.1, H2.91_L1.1,
H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4, H1.2_L1.4, H1.3_L1.4, H1.4_L1.4,
H1.5_L1.4, H1.6_L1.4, H1.7_L1.4, H1.8_L1.4, H1.9_L1.4, H1.19_L1.4, H1.22_L1.4,
H1.24_L1.4, H2_L1.4, H2.1_L1.4, H2.2_L1.4, H2.3_L1.4, H2.4_L1.4, H2.5_L1.4,
H2.6_L1.4, H2.7_L1.4, H2.8_L1.4, H2.9_L1.4, H2.11_L1.4, H2.12_L1.4, H2.71_L1.4,
H2.75_L1.4, H2.90_L1.4, H2.91_L1.4, H2.118_L1.4, H2.119_L1.4, H1_L1.7, H1.1_L1.7,
H1.2_L1.7, H1.3_L1.7, H1.4_L1.7, H1.5_L1.7, H1.6_L1.7, H1.7_L1.7, H1.8_L1.7,
H1.9_L1.7, H1.19_L1.7, H1.22_L1.7, H1.24_L1.7, H2_L1.7, H2.1_L1.7, H2.2_L1.7,
H2.3_L1.7, H2.4_L1.7, H2.5_L1.7, H2.6_L1.7, H2.7_L1.7, H2.8_L1.7, H2.9_L1.7,
H2.11_L1.7, H2.12_L1.7, H2.71_L1.7, H2.75_L1.7, H2.90_L1.7, H2.91_L1.7,
H2.118_L1.7, H2.119_L1.7, H1_L1.16, H1.1_L1.16, H1.2_L1.16, H1.3_L1.16, H1.4_L1.16,
H1.5_L1.16, H1.6_L1.16, H1.7_L1.16, H1.8_L1.16, H1.9_L1.16, H1.19_L1.16,
H1.22_L1.16, H1.24_L1.16, H2_L1.16, H2.1_L1.16, H2.2_L1.16, H2.3_L1.16, H2.4_L1.16,
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H2.12_L1.16, H2.71_L1.16, H2.75_L1.16, H2.90_L1.16, H2.91_L1.16, H2.118_L1.16,
H2.119_L1.16, H1_L1.18, H1.1_L1.18, H1.2_L1.18, H1.3_L1.18, H1.4_L1.18, H1.5_L1.18,
H1.6_L1.18, H1.7_L1.18, H1.8_L1.18, H1.9_L1.18, H1.19_L1.18, H1.22_L1.18,
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H2.71_L1.18, H2.75_L1.18, H2.90_L1.18, H2.91_L1.18, H2.118_L1.18, H2.119_L1.18,
H1_L1.19, H1.1_L1.19, H1.2_L1.19, H1.3_L1.19, H1.4_L1.19, H1.5_L1.19,
H1.6_L1.19, H1.7_L1.19, H1.8_L1.19, H1.9_L1.19, H1.19_L1.19, H1.22_L1.19,
H1.24_L1.19, H2_L1.19, H2.1_L1.19, H2.2_L1.19, H2.3_L1.19, H2.4_L1.19, H2.5_L1.19,
H2.6_L1.19, H2.7_L1.19, H2.8_L1.19, H2.9_L1.19, H2.11_L1.19, H2.12_L1.19,
H2.71_L1.19, H2.75_L1.19, H2.90_L1.19, H2.91_L1.19, H2.118_L1.19, H2.119_L1.19,
H1_L1.21, H1.1_L1.21, H1.2_L1.21, H1.3_L1.21, H1.4_L1.21, H1.5_L1.21, H1.6_L1.21,
H1.7_L1.21, H1.8_L1.21, H1.9_L1.21, H1.19_L1.21, H1.22_L1.21, H1.24_L1.21,
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H2.90_L1.22, H2.91_L1.22, H2.118_L1.22, H2.119_L1.22, H1_L1.23, H1.1_L1.23,
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H1.19_L1.27, H1.22_L1.27, H1.24_L1.27, H2_L1.27, H2.1_L1.27, H2.2_L1.27,
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H2.118_L1.27, H2.119_L1.27, H1_L1.60, H1.1_L1.60, H1.2_L1.60, H1.3_L1.60,
H1.4_L1.60, H1.5_L1.60, H1.6_L1.60, H1.7_L1.60, H1.8_L1.60, H1.9_L1.60, H1.19_L1.60,
H1.22_L1.60, H1.24_L1.60, H2_L1.60, H2.1_L1.60, H2.2_L1.60, H2.3_L1.60, H2.4_L1.60,
H2.5_L1.60, H2.6_L1.60, H2.7_L1.60, H2.8_L1.60, H2.9_L1.60, H2.11_L1.60,
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H2.4_L1.107, H2.5_L1.107, H2.6_L1.107, H2.7_L1.107, H2.8_L1.107, H2.9_L1.107,
H2.11_L1.107, H2.12_L1.107, H2.71_L1.107, H2.75_L1.107, H2.90_L1.107,
H2.91_L1.107, H2.118_L1.107, H2.119_L1.107, H1_L1.114, H1.1_L1.114, H1.2_L1.114,
H1.3_L1.114, H1.4_L1.114, H1.5_L1.114, H1.6_L1.114, H1.7_L1.114, H1.8_L1.114,
H1.9_L1.114, H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114,
H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114,
H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114,
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H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187,
H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187,

H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187, H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187, H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189, H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189, H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189, H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189, H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189, H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2, H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2.

[00303] In particular embodiments, the α CLDN6 ABD VH/VL pairs are selected from the group consisting of H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187 or a variant thereof.

[00304] In addition, the Fc domains of the 2 + 1 Fab₂-scFv-Fc format comprise skew variants (e.g. a set of amino acid substitutions as shown in Figure 1, with particularly useful skew variants being selected from the group consisting of S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L, K370S : S364K/E357Q, T366S/L368A/Y407V : T366W and T366S/L368A/Y407V/Y349C : T366W/S354C), optionally ablation variants (including those shown in Figure 3), optionally charged scFv linkers (including those shown in Figure 5) and the heavy chain comprises pI variants (including those shown in Figure 2).

[00305] In some embodiments, the 2 + 1 Fab₂-scFv-Fc format antibody includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments include 2 + 1 Fab₂-scFv-Fc formats that comprise: a) a first monomer (the Fab-scFv-Fc side) that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, and a variable heavy domain that, with the variable light domain of the common light chain, makes up an Fv that binds to CLDN6 as outlined herein, and an scFv domain that binds to CD3; b) a second monomer (the Fab-Fc side) that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, and a variable heavy domain that, with variable light domain of the common light chain, makes up an Fv that binds to CLDN6 as outlined herein; and c) a common light chain comprising the variable

light domain and a constant light domain, where numbering is according to EU numbering. In some embodiments, the α CLDN6 VH_VL pairs are selected from the group consisting of H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187 or a variant thereof.

[00306] In some embodiments, the 2 + 1 Fab₂-scFv-Fc format antibody includes skew variants, pI variants, ablation variants and FcRn variants. Accordingly, some embodiments include 2 + 1 Fab₂-scFv-Fc formats that comprise: a) a first monomer (the Fab-scFv-Fc side) that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a variable heavy domain that, with the variable light domain of the common light chain, makes up an Fv that binds to CLDN6 as outlined herein, and an scFv domain that binds to CD3; b) a second monomer (the Fab-Fc side) that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a variable heavy domain that, with variable light domain of the common light chain, makes up an Fv that binds to CLDN6 as outlined herein; and c) a common light chain comprising a variable light domain and a constant light domain, where numbering is according to EU numbering. In some embodiments, the α CLDN6 VH_VL pairs are selected from the group consisting of H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187 or a variant thereof. CD3 binding domain sequences finding particular use in these embodiments include, but are not limited to, H1.30_L1.47, H1.32_L1.47, H1.89_L1.47, H1.90_L1.47, H1.33_L1.47, H1.31_L1.47, L1.47_H1.30, L1.47_H1.30, L1.47_H1.32, L1.47_H1.89, L1.47_H1.90, L1.47_H1.33, and L1.47_H1.31 or a variant thereof.

[00307] Figures 8A-8C shows some exemplary Fc domain sequences that are useful with the 2 + 1 Fab₂-scFv-Fc format. The “monomer 1” sequences depicted in Figures 8A-8C typically refer to the Fc domain of the “Fab-Fc heavy chain” and the “monomer 2” sequences refer to the Fc domain of the “Fab-scFv-Fc heavy chain.” Further, Figure 9 provides useful CL sequences that can be used with this format.

[00308] Exemplary anti-CLDN6 x anti-CD3 2 + 1 Fab₂-scFv-Fc format antibodies are depicted in Figures 21, 22, 59 and 60.

5. Central-Fv

[00309] One heterodimeric scaffold that finds particular use in the antibodies described herein is the Central-Fv format (Figure 36I). In this embodiment, the format relies on the use of an inserted Fv domain (i.e., the central Fv domain) thus forming an “extra” third antigen binding domain, wherein the Fab portions of the two monomers bind a CLDN6 and the “extra” central Fv domain binds CD3. The “extra” central Fv domain is inserted between the Fc domain and the CH1-Fv region of the monomers, thus providing a third antigen binding domain (i.e., the “extra” central Fv domain), wherein each monomer contains a component of the “extra” central Fv domain (i.e., one monomer comprises the variable heavy domain and the other a variable light domain of the “extra” central Fv domain).

[00310] In this embodiment, one monomer comprises a first heavy chain comprising a first variable heavy domain, a CH1 domain, and Fc domain and an additional variable light domain. The light domain is covalently attached between the C-terminus of the CH1 domain of the heavy constant domain and the N-terminus of the first Fc domain using domain linkers (VH1-CH1-[optional linker]-VL2-hinge-CH2-CH3). The other monomer comprises a first heavy chain comprising a first variable heavy domain, a CH1 domain and Fc domain and an additional variable heavy domain (VH1-CH1-[optional linker]-VH2-hinge-CH2-CH3). The light domain is covalently attached between the C-terminus of the CH1 domain of the heavy constant domain and the N-terminus of the first Fc domain using domain linkers.

[00311] This embodiment further utilizes a common light chain comprising a variable light domain and a constant light domain, that associates with the heavy chains to form two identical Fabs that each bind an CLDN6. As for many of the embodiments herein, these constructs include skew variants, pI variants, ablation variants, additional Fc variants, etc. as desired and described herein.

[00312] The antibodies described herein provide central-Fv formats, where the CD3 binding domain sequences are as shown in Figure 10 or a variant thereof, and the CLDN6 binding domain sequences are as shown in Figures 13, 14 and 15 or a variant thereof.

6. One-armed central-scFv

[00313] One heterodimeric scaffold that finds particular use in the antibodies described herein is the one-armed central-scFv format (Figure 36C). In this embodiment, one monomer

comprises just an Fc domain, while the other monomer includes a Fab domain (a first antigen binding domain), a scFv domain (a second antigen binding domain) and an Fc domain, where the scFv domain is inserted between the Fc domain and the Fc domain. In this format, the Fab portion binds one receptor target and the scFv binds another. In this format, either the Fab portion binds a CLDN6 and the scFv binds CD3 or vice versa.

[00314] In this embodiment, one monomer comprises a first heavy chain comprising a first variable heavy domain, a CH1 domain and Fc domain, with a scFv comprising a scFv variable light domain, an scFv linker and a scFv variable heavy domain. The scFv is covalently attached between the C-terminus of the CH1 domain of the heavy constant domain and the N-terminus of the first Fc domain using domain linkers, in either orientation, VH1-CH1-[optional domain linker]-VH2-scFv linker-VL2-[optional domain linker]-CH2-CH3 or VH1-CH1-[optional domain linker]-VL2-scFv linker-VH2-[optional domain linker]-CH2-CH3. The second monomer comprises an Fc domain (CH2-CH3). This embodiment further utilizes a light chain comprising a variable light domain and a constant light domain that associates with the heavy chain to form a Fab.

[00315] As for many of the embodiments herein, these constructs include skew variants, pI variants, ablation variants, additional Fc variants, etc. as desired and described herein.

[00316] The antibodies described herein provide central-Fv formats where the CD3 binding domain sequences are as shown in Figure 10 or a variant thereof, and the CLDN6 binding domain sequences are as shown in Figures 13, 14 and 15 or a variant thereof.

[00317] In addition, the Fc domains of the one-armed central-scFv format generally include skew variants (e.g. a set of amino acid substitutions as shown in Figure 1, with particularly useful skew variants being selected from the group consisting of S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L, K370S : S364K/E357Q, T366S/L368A/Y407V : T366W and T366S/L368A/Y407V/Y349C : T366W/S354C), optionally ablation variants (including those shown in Figure 3), optionally charged scFv linkers (including those shown in Figure 5) and the heavy chain comprises pI variants (including those shown in Figure 2).

[00318] In some embodiments, the one-armed central-scFv format includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments of the one-armed central-scFv formats comprise: a) a first monomer that comprises the skew variants

S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, and a variable heavy domain that, with the variable light domain of the light chain, makes up an Fv that binds to CLDN6 as outlined herein, and a scFv domain that binds to CD3; b) a second monomer that includes an Fc domain having the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K; and c) a light chain comprising a variable light domain and a constant light domain.

[00319] In some embodiments, the one-armed central-scFv format includes skew variants, pI variants, ablation variants and FcRn variants. Accordingly, some embodiments of the one-armed central-scFv formats comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a variable heavy domain that, with the variable light domain of the light chain, makes up an Fv that binds to CLDN6 as outlined herein, and a scFv domain that binds to CD3; b) a second monomer that includes an Fc domain having the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, and the FcRn variants M428L/N434S; and c) a light chain comprising a variable light domain and a constant light domain.

7. One-armed scFv-mAb

[00320] One heterodimeric scaffold that finds particular use in the antibodies described herein is the one-armed scFv-mAb format (Figure 36D). In this embodiment, one monomer comprises just an Fc domain, while the other monomer uses a scFv domain attached at the N-terminus of the heavy chain, generally through the use of a linker: VH-scFv linker-VL-[optional domain linker]-CH1-hinge-CH2-CH3 or (in the opposite orientation) VL-scFv linker-VH-[optional domain linker]-CH1-hinge-CH2-CH3. In this format, the Fab portions each bind CLDN6 and the scFv binds CD3. This embodiment further utilizes a light chain comprising a variable light domain and a constant light domain, that associates with the heavy chain to form a Fab. As for many of the embodiments herein, these constructs include skew variants, pI variants, ablation variants, additional Fc variants, etc. as desired and described herein.

[00321] The antibodies described herein provide one-armed scFv-mAb formats, where the CD3 binding domain sequences are as shown in Figure 10 or a variant thereof, and wherein the CLDN6 binding domain sequences are as shown in Figures 13, 14 and 15 or a variant thereof.

[00322] In addition, the Fc domains of the one-armed scFv-mAb format generally include skew variants (e.g. a set of amino acid substitutions as shown in Figure 1, with particularly useful skew variants being selected from the group consisting of S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L, K370S : S364K/E357Q, T366S/L368A/Y407V : T366W and T366S/L368A/Y407V/Y349C : T366W/S354C), optionally ablation variants (including those shown in Figure 3), optionally charged scFv linkers (including those shown in Figure 5) and the heavy chain comprises pI variants (including those shown in Figure 2).

[00323] In some embodiments, the one-armed scFv-mAb format includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments of the one-armed scFv-mAb formats comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, and a variable heavy domain that, with the variable light domain of the light chain, makes up an Fv that binds to CLDN6 as outlined herein, and a scFv domain that binds to CD3; b) a second monomer that includes an Fc domain having the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K; and c) a light chain comprising a variable light domain and a constant light domain.

[00324] In some embodiments, the one-armed scFv-mAb format includes skew variants, pI variants, ablation variants and FcRn variants. Accordingly, some embodiments one-armed scFv-mAb formats comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a variable heavy domain that, with the variable light domain of the light chain, makes up an Fv that binds to CLDN6 as outlined herein, and a scFv domain that binds to CD3; b) a second monomer that includes an Fc domain having the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, and the FcRn variants M428L/N434S; and c) a light chain comprising a variable light domain and a constant light domain.

8. scFv-mAb

[00325] One heterodimeric scaffold that finds particular use in the antibodies described herein is the mAb-scFv format (Figure 36E). In this embodiment, the format relies on the use of a N-terminal attachment of a scFv to one of the monomers, thus forming a third antigen binding domain, wherein the Fab portions of the two monomers bind CLDN6 and the “extra” scFv domain binds CD3.

[00326] In this embodiment, the first monomer comprises a first heavy chain (comprising a variable heavy domain and a constant domain), with a N-terminally covalently attached scFv comprising a scFv variable light domain, an scFv linker and a scFv variable heavy domain in either orientation ((VH1-scFv linker-VL1-[optional domain linker]- VH2-CH1-hinge-CH2-CH3) or (with the scFv in the opposite orientation) ((VL1-scFv linker-VH1-[optional domain linker]-VH2-CH1-hinge-CH2-CH3)). This embodiment further utilizes a common light chain comprising a variable light domain and a constant light domain that associates with the heavy chains to form two identical Fabs that bind CLDN6. As for many of the embodiments herein, these constructs include skew variants, pI variants, ablation variants, additional Fc variants, etc. as desired and described herein.

[00327] The antibodies described herein provide scFv-mAb formats, where the CD3 binding domain sequences are as shown in Figure 10 or a variant thereof, and wherein the CLDN6 binding domain sequences are as shown in Figures 13, 14 and 15 or a variant thereof.

[00328] In addition, the Fc domains of the scFv-mAb format generally include skew variants (e.g. a set of amino acid substitutions as shown in Figure 1, with particularly useful skew variants being selected from the group consisting of S364K/E357Q : L368D/K370S; L368D/K370S : S364K; L368E/K370S : S364K; T411T/E360E/Q362E : D401K; L368D/K370S : S364K/E357L, K370S : S364K/E357Q, T366S/L368A/Y407V : T366W and T366S/L368A/Y407V/Y349C : T366W/S354C), optionally ablation variants (including those shown in Figure 3), optionally charged scFv linkers (including those shown in Figure 5) and the heavy chain comprises pI variants (including those shown in Figure 2).

[00329] In some embodiments, the scFv-mAb format includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments include scFv-mAb formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, and a variable heavy domain that,

with the variable light domain of the common light chain, makes up an Fv that binds to CLDN6 as outlined herein, and a scFv domain that binds to CD3; b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, and a variable heavy domain that, with the variable light domain of the common light chain, makes up an Fv that binds to CLDN6 as outlined herein; and c) a common light chain comprising a variable light domain and a constant light domain.

[00330] In some embodiments, the scFv-mAb format includes skew variants, pI variants, ablation variants and FcRn variants. Accordingly, some embodiments include scFv-mAb formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a variable heavy domain that, with the variable light domain of the common light chain, makes up an Fv that binds to CLDN6 as outlined herein, and a scFv domain that binds to CD3; b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a variable heavy domain that, with the variable light domain of the common light chain, makes up an Fv that binds to CLDN6 as outlined herein; and c) a common light chain comprising a variable light domain and a constant light domain.

9. Dual scFv formats

[00331] The antibodies described herein also provide dual scFv formats as are known in the art (Figure 36B). In this embodiment, the CLDN6 x CD3 heterodimeric bispecific antibody is made up of two scFv-Fc monomers (both in either (VH-scFv linker-VL-[optional domain linker]-CH2-CH3) format or (VL-scFv linker-VH-[optional domain linker]-CH2-CH3) format, or with one monomer in one orientation and the other in the other orientation.

[00332] The antibodies described herein provide dual scFv formats where the CD3 binding domain sequences are as shown in Figure 10A-10F or a variant thereof, and wherein the CLDN6 binding domain sequences are as shown in Figures 13-15 and 18 or a variant thereof. In some embodiments, the dual scFv format includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments include dual scFv formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants

E233P/L234V/L235A/G236del/S267K, and a first scFv that binds either CD3 or CLDN6; and b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants

[00333] E233P/L234V/L235A/G236del/S267K, and a second scFv that binds either CD3 or CLDN6. In some embodiments, the dual scFv format includes skew variants, pI variants, ablation variants and FcRn variants. In some embodiments, the dual scFv format includes skew variants, pI variants, and ablation variants. Accordingly, some embodiments include dual scFv formats that comprise: a) a first monomer that comprises the skew variants S364K/E357Q, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a first scFv that binds either CD3 or CLDN6; and b) a second monomer that comprises the skew variants L368D/K370S, the pI variants N208D/Q295E/N384D/ Q418E/N421D, the ablation variants E233P/L234V/L235A/G236del/S267K, the FcRn variants M428L/N434S and a second scFv that binds either CD3 or CLDN6.

10. Non-heterodimeric bispecific antibodies

[00334] As will be appreciated by those in the art, the anti-CLDN6 x anti-CD3 antibodies provided herein can also be included in non-heterodimeric bispecific formats (see Figure 36J). In this format, the anti-CLDN6 x anti-CD3 includes: 1) a first monomer comprising a VH1-CH1-hinge-CH2-CH3; 2) a second monomer comprising a VH2-CH1-hinge-CH2-CH3; 3) a first light chain comprising a VL1-CL; and 4) a second light chain comprising a VL2-CL. In such embodiments, the VH1 and VL1 form a first antigen binding domain and VH2 and VL2 form a second antigen binding domain. One of the first or second antigen binding domains binds CLDN6 and the other antigen binding domain binds CD3.

[00335] Any suitable CLDN6 binding domain and CD3 binding domain can be included in the anti-CLDN6 x anti-CD3 antibody in the non-heterodimeric bispecific antibody format, including any of the CLDN6 binding domains and CD3 binding domains and related VHs and VLs provided herein or a variant thereof (see, e.g., Figures 10, 13-15 and 18).

11. Trident Format

[00336] In some embodiments, the bispecific antibodies described herein are in the “Trident” format as generally described in WO2015/184203, hereby expressly incorporated

by reference in its entirety and in particular for the Figures, Legends, definitions and sequences of “Heterodimer-Promoting Domains” or “HPDs”, including “K-coil” and “E-coil” sequences. Tridents rely on using two different HPDs that associate to form a heterodimeric structure as a component of the structure. In this embodiment, the Trident format include a “traditional” heavy and light chain (e.g., VH1-CH1-hinge-CH2-CH3 and VL1-CL), a third chain comprising a first “diabody-type binding domain” or “DART®”, VH2-(linker)-VL3-HPD1 and a fourth chain comprising a second DART®, VH3-(linker)-(linker)-VL2-HPD2. The VH1 and VL1 form a first ABD, the VH2 and VL2 form a second ABD, and the VH3 and VL3 form a third ABD. In some cases, the second and third ABDs bind the same antigen, in this instance generally CLDN6, e.g., bivalently, with the first ABD binding a CD3 monovalently.

[00337] Any suitable CLDN6 binding domain and CD3 binding domain can be included in the anti-CLDN6 x anti-CD3 antibody in the Trident bispecific antibody format, including any of the CLDN6 binding domains and CD3 binding domains and related VHs and VLs provided herein or a variant thereof (see, e.g., Figures 10, 13-15 and 18).

12. Monospecific, Monoclonal antibodies

[00338] As will be appreciated by those in the art, the novel CLDN6 ABD sequences outlined herein can also be used in both monospecific antibodies (e.g., “traditional monoclonal antibodies”) or non-heterodimeric bispecific formats. Accordingly, in some embodiments, the antibodies described herein provide monoclonal (monospecific) antibodies comprising the 6 CDRs and/or the vh and vl sequences from the figures, generally with IgG1, IgG2, IgG3 or IgG4 constant regions, with IgG1, IgG2 and IgG4 (including IgG4 constant regions comprising a S228P amino acid substitution) finding particular use in some embodiments. That is, any sequence herein with a “H_L” designation can be linked to the constant region of a human IgG1 antibody.

[00339] Any suitable CLDN6 ABD can be included in the monospecific antibody, including any of the CLDN6 ABDs described herein. In some embodiments, the monospecific antibody is an CLDN6 monospecific antibody that has a VH_VL pairs selected from the group consisting of: H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1, H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1,

H2.12_L1, H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1, H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1, H1.9_L1.1, H1.19_L1.1, H1.22_L1.1, H1.24_L1.1, H2_L1.1, H2.1_L1.1, H2.2_L1.1, H2.3_L1.1, H2.4_L1.1, H2.5_L1.1, H2.6_L1.1, H2.7_L1.1, H2.8_L1.1, H2.9_L1.1, H2.11_L1.1, H2.12_L1.1, H2.71_L1.1, H2.75_L1.1, H2.90_L1.1, H2.91_L1.1, H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4, H1.2_L1.4, H1.3_L1.4, H1.4_L1.4, H1.5_L1.4, H1.6_L1.4, H1.7_L1.4, H1.8_L1.4, H1.9_L1.4, H1.19_L1.4, H1.22_L1.4, H1.24_L1.4, H2_L1.4, H2.1_L1.4, H2.2_L1.4, H2.3_L1.4, H2.4_L1.4, H2.5_L1.4, H2.6_L1.4, H2.7_L1.4, H2.8_L1.4, H2.9_L1.4, H2.11_L1.4, H2.12_L1.4, H2.71_L1.4, H2.75_L1.4, H2.90_L1.4, H2.91_L1.4, H2.118_L1.4, H2.119_L1.4, H1_L1.7, H1.1_L1.7, H1.2_L1.7, H1.3_L1.7, H1.4_L1.7, H1.5_L1.7, H1.6_L1.7, H1.7_L1.7, H1.8_L1.7, H1.9_L1.7, H1.19_L1.7, H1.22_L1.7, H1.24_L1.7, H2_L1.7, H2.1_L1.7, H2.2_L1.7, H2.3_L1.7, H2.4_L1.7, H2.5_L1.7, H2.6_L1.7, H2.7_L1.7, H2.8_L1.7, H2.9_L1.7, H2.11_L1.7, H2.12_L1.7, H2.71_L1.7, H2.75_L1.7, H2.90_L1.7, H2.91_L1.7, H2.118_L1.7, H2.119_L1.7, H1_L1.16, H1.1_L1.16, H1.2_L1.16, H1.3_L1.16, H1.4_L1.16, H1.5_L1.16, H1.6_L1.16, H1.7_L1.16, H1.8_L1.16, H1.9_L1.16, H1.19_L1.16, H1.22_L1.16, H1.24_L1.16, H2_L1.16, H2.1_L1.16, H2.2_L1.16, H2.3_L1.16, H2.4_L1.16, H2.5_L1.16, H2.6_L1.16, H2.7_L1.16, H2.8_L1.16, H2.9_L1.16, H2.11_L1.16, H2.12_L1.16, H2.71_L1.16, H2.75_L1.16, H2.90_L1.16, H2.91_L1.16, H2.118_L1.16, H2.119_L1.16, H1_L1.18, H1.1_L1.18, H1.2_L1.18, H1.3_L1.18, H1.4_L1.18, H1.5_L1.18, H1.6_L1.18, H1.7_L1.18, H1.8_L1.18, H1.9_L1.18, H1.19_L1.18, H1.22_L1.18, H1.24_L1.18, H2_L1.18, H2.1_L1.18, H2.2_L1.18, H2.3_L1.18, H2.4_L1.18, H2.5_L1.18, H2.6_L1.18, H2.7_L1.18, H2.8_L1.18, H2.9_L1.18, H2.11_L1.18, H2.12_L1.18, H2.71_L1.18, H2.75_L1.18, H2.90_L1.18, H2.91_L1.18, H2.118_L1.18, H2.119_L1.18, H1_L1.19, H1.1_L1.19, H1.2_L1.19, H1.3_L1.19, H1.4_L1.19, H1.5_L1.19, H1.6_L1.19, H1.7_L1.19, H1.8_L1.19, H1.9_L1.19, H1.19_L1.19, H1.22_L1.19, H1.24_L1.19, H2_L1.19, H2.1_L1.19, H2.2_L1.19, H2.3_L1.19, H2.4_L1.19, H2.5_L1.19, H2.6_L1.19, H2.7_L1.19, H2.8_L1.19, H2.9_L1.19, H2.11_L1.19, H2.12_L1.19, H2.71_L1.19, H2.75_L1.19, H2.90_L1.19, H2.91_L1.19, H2.118_L1.19, H2.119_L1.19, H1_L1.21, H1.1_L1.21, H1.2_L1.21, H1.3_L1.21, H1.4_L1.21, H1.5_L1.21, H1.6_L1.21, H1.7_L1.21, H1.8_L1.21, H1.9_L1.21, H1.19_L1.21, H1.22_L1.21, H1.24_L1.21, H2_L1.21, H2.1_L1.21, H2.2_L1.21, H2.3_L1.21, H2.4_L1.21, H2.5_L1.21, H2.6_L1.21, H2.7_L1.21, H2.8_L1.21, H2.9_L1.21, H2.11_L1.21, H2.12_L1.21, H2.71_L1.21, H2.75_L1.21, H2.90_L1.21, H2.91_L1.21, H2.118_L1.2, H2.119_L1.21, H1_L1.22,

H1.1_L1.22, H1.2_L1.22, H1.3_L1.22, H1.4_L1.22, H1.5_L1.22, H1.6_L1.22, H1.7_L1.22, H1.8_L1.22, H1.9_L1.22, H1.19_L1.22, H1.22_L1.22, H1.24_L1.22, H2_L1.22, H2.1_L1.22, H2.2_L1.22, H2.3_L1.22, H2.4_L1.22, H2.5_L1.22, H2.6_L1.22, H2.7_L1.22, H2.8_L1.22, H2.9_L1.22, H2.11_L1.22, H2.12_L1.22, H2.71_L1.22, H2.75_L1.22, H2.90_L1.22, H2.91_L1.22, H2.118_L1.22, H2.119_L1.22, H1_L1.23, H1.1_L1.23, H1.2_L1.23, H1.3_L1.23, H1.4_L1.23, H1.5_L1.23, H1.6_L1.23, H1.7_L1.23, H1.8_L1.23, H1.9_L1.23, H1.19_L1.23, H1.22_L1.23, H1.24_L1.23, H2_L1.23, H2.1_L1.23, H2.2_L1.23, H2.3_L1.23, H2.4_L1.23, H2.5_L1.23, H2.6_L1.23, H2.7_L1.23, H2.8_L1.23, H2.9_L1.23, H2.11_L1.23, H2.12_L1.23, H2.71_L1.23, H2.75_L1.23, H2.90_L1.23, H2.91_L1.23, H2.118_L1.23, H2.119_L1.23, H1_L1.27, H1.1_L1.27, H1.2_L1.27, H1.3_L1.27, H1.4_L1.27, H1.5_L1.27, H1.6_L1.27, H1.7_L1.27, H1.8_L1.27, H1.9_L1.27, H1.19_L1.27, H1.22_L1.27, H1.24_L1.27, H2_L1.27, H2.1_L1.27, H2.2_L1.27, H2.3_L1.27, H2.4_L1.27, H2.5_L1.27, H2.6_L1.27, H2.7_L1.27, H2.8_L1.27, H2.9_L1.27, H2.11_L1.27, H2.12_L1.27, H2.71_L1.27, H2.75_L1.27, H2.90_L1.27, H2.91_L1.27, H2.118_L1.27, H2.119_L1.27, H1_L1.60, H1.1_L1.60, H1.2_L1.60, H1.3_L1.60, H1.4_L1.60, H1.5_L1.60, H1.6_L1.60, H1.7_L1.60, H1.8_L1.60, H1.9_L1.60, H1.19_L1.60, H1.22_L1.60, H1.24_L1.60, H2_L1.60, H2.1_L1.60, H2.2_L1.60, H2.3_L1.60, H2.4_L1.60, H2.5_L1.60, H2.6_L1.60, H2.7_L1.60, H2.8_L1.60, H2.9_L1.60, H2.11_L1.60, H2.12_L1.60, H2.71_L1.60, H2.75_L1.60, H2.90_L1.60, H2.91_L1.60, H2.118_L1.60, H2.119_L1.60, H1_L1.107, H1.1_L1.107, H1.2_L1.107, H1.3_L1.107, H1.4_L1.107, H1.5_L1.107, H1.6_L1.107, H1.7_L1.107, H1.8_L1.107, H1.9_L1.107, H1.19_L1.107, H1.22_L1.107, H1.24_L1.107, H2_L1.107, H2.1_L1.107, H2.2_L1.107, H2.3_L1.107, H2.4_L1.107, H2.5_L1.107, H2.6_L1.107, H2.7_L1.107, H2.8_L1.107, H2.9_L1.107, H2.11_L1.107, H2.12_L1.107, H2.71_L1.107, H2.75_L1.107, H2.90_L1.107, H2.91_L1.107, H2.118_L1.107, H2.119_L1.107, H1_L1.114, H1.1_L1.114, H1.2_L1.114, H1.3_L1.114, H1.4_L1.114, H1.5_L1.114, H1.6_L1.114, H1.7_L1.114, H1.8_L1.114, H1.9_L1.114, H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114, H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114, H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114, H2.90_L1.114, H2.91_L1.114, H2.118_L1.114, H2.119_L1.114, H1_L1.187, H1.1_L1.187, H1.2_L1.187, H1.3_L1.187, H1.4_L1.187, H1.5_L1.187, H1.6_L1.187, H1.7_L1.187, H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187, H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187, H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187,

H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187, H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189, H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189, H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189, H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189, H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189, H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2, H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2 or a variant thereof.

[00340] In particular monoclonal embodiments, the VH_VL pair is selected from the group consisting of H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187 or a variant thereof.

E. Particular Embodiments of the Invention

[00341] The invention specifically provides 1+1 and 2+1 formats that bind CD3 and CLDN6.

1. 1 + 1 Format

[00342] In particular 1+1 format embodiments, the α CLDN6 ABD is the Fab and has the VH_VL pair H1.9_L1.187 and the α CD3 ABD is a scFv selected from the group consisting of anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47, anti-CD3 H1.31_L1.47, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.32, anti-CD3 L1.47_H1.89, anti-CD3 L1.47_H1.90, anti-CD3 L1.47_H1.33, and anti-CD3 L1.47_H1.31.

[00343] In particular 1+1 format embodiments, the α CLDN6 ABD is the Fab and has the VH_VL pair H1.24_L1.187, and the α CD3 ABD is a scFv selected from the group consisting of anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47, anti-CD3 H1.31_L1.47, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.32, anti-CD3 L1.47_H1.89, anti-CD3 L1.47_H1.90, anti-CD3 L1.47_H1.33, and anti-CD3 L1.47_H1.31.

[00344] In particular 1+1 format embodiments, the α CLDN6 ABD is the Fab and has the VH_VL pair H2.91_L1.187 and the α CD3 ABD is a scFv selected from the group consisting of anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47, anti-CD3 H1.31_L1.47, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.32, anti-CD3 L1.47_H1.89, anti-CD3 L1.47_H1.90, anti-CD3 L1.47_H1.33, and anti-CD3 L1.47_H1.31.

[00345] In particular 1+1 format embodiments, the α CLDN6 ABD is the Fab and has the VH_VL pair H1.9_L1.187. and the α CD3 ABD is a scFv selected from the group consisting of anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47, anti-CD3 H1.31_L1.47, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.32, anti-CD3 L1.47_H1.89, anti-CD3 L1.47_H1.90, anti-CD3 L1.47_H1.33, and anti-CD3 L1.47_H1.31.

2. 2 + 1 Format

[00346] In particular 2+1 format embodiments, the α CLDN6 ABD is the Fab and has the VH_VL pair H1.9_L1.187 and the α CD3 ABD is a scFv selected from the group consisting of anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47, anti-CD3 H1.31_L1.47, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.32, anti-CD3 L1.47_H1.89, anti-CD3 L1.47_H1.90, anti-CD3 L1.47_H1.33, and anti-CD3 L1.47_H1.31.

[00347] In particular 2+1 format embodiments, the α CLDN6 ABD is the Fab and has the VH_VL pair H1.24_L1.187, and the α CD3 ABD is a scFv selected from the group consisting of anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47, anti-CD3 H1.31_L1.47, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.32, anti-CD3 L1.47_H1.89, anti-CD3 L1.47_H1.90, anti-CD3 L1.47_H1.33, and anti-CD3 L1.47_H1.31.

[00348] In particular 2+1 format embodiments, the α CLDN6 ABD is the Fab and has the VH_VL pair H2.91_L1.187 and the α CD3 ABD is a scFv selected from the group consisting of anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47, anti-CD3 H1.31_L1.47, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.32, anti-CD3 L1.47_H1.89, anti-CD3 L1.47_H1.90, anti-CD3 L1.47_H1.33, and anti-CD3 L1.47_H1.31.

[00349] In particular 2+1 format embodiments, the α CLDN6 ABD is the Fab and has the VH_VL pair H1.9_L1.187. and the α CD3 ABD is a scFv selected from the group consisting of anti-CD3 H1.30_L1.47, anti-CD3 H1.32_L1.47, anti-CD3 H1.89_L1.47, anti-CD3 H1.90_L1.47, anti-CD3 H1.33_L1.47, anti-CD3 H1.31_L1.47, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.30, anti-CD3 L1.47_H1.32, anti-CD3 L1.47_H1.89, anti-CD3 L1.47_H1.90, anti-CD3 L1.47_H1.33, and anti-CD3 L1.47_H1.31.

V. Nucleic Acids of the Invention

[00350] The disclosure further provides nucleic acid compositions encoding the anti-CLDN6 antibodies provided herein, including, but not limited to, anti-CLDN6 x anti-CD3 bispecific antibodies and CLDN6 monospecific antibodies.

[00351] As will be appreciated by those in the art, the nucleic acid compositions will depend on the format and scaffold of the heterodimeric protein. Thus, for example, when the format requires three amino acid sequences, such as for the 1+1 Fab-scFv-Fc format (e.g. a first amino acid monomer comprising an Fc domain and a scFv, a second amino acid monomer comprising a heavy chain and a light chain), three nucleic acid sequences can be incorporated into one or more expression vectors for expression. Similarly, some formats (e.g. dual scFv formats such as disclosed in Figure 1) only two nucleic acids are needed; again, they can be put into one or two expression vectors.

[00352] As is known in the art, the nucleic acids encoding the components of the antibodies described herein can be incorporated into expression vectors as is known in the art, and depending on the host cells used to produce the heterodimeric antibodies described herein. Generally the nucleic acids are operably linked to any number of regulatory elements (promoters, origin of replication, selectable markers, ribosomal binding sites, inducers, etc.). The expression vectors can be extra-chromosomal or integrating vectors.

[00353] The nucleic acids and/or expression vectors of the antibodies described herein are then transformed into any number of different types of host cells as is well known in the art, including mammalian, bacterial, yeast, insect and/or fungal cells, with mammalian cells (e.g. CHO cells), finding use in many embodiments.

[00354] In some embodiments, nucleic acids encoding each monomer and the optional nucleic acid encoding a light chain, as applicable depending on the format, are each contained within a single expression vector, generally under different or the same promoter controls. In

embodiments of particular use in the antibodies described herein, each of these two or three nucleic acids are contained on a different expression vector. As shown herein and in 62/025,931, hereby incorporated by reference, different vector ratios can be used to drive heterodimer formation. That is, surprisingly, while the proteins comprise first monomer:second monomer:light chains (in the case of many of the embodiments herein that have three polypeptides comprising the heterodimeric antibody) in a 1:1:2 ratio, these are not the ratios that give the best results.

[00355] The heterodimeric antibodies described herein are made by culturing host cells comprising the expression vector(s) as is well known in the art. Once produced, traditional antibody purification steps are done, including an ion exchange chromatography step. As discussed herein, having the pIs of the two monomers differ by at least 0.5 can allow separation by ion exchange chromatography or isoelectric focusing, or other methods sensitive to isoelectric point. That is, the inclusion of pI substitutions that alter the isoelectric point (pI) of each monomer so that each monomer has a different pI and the heterodimer also has a distinct pI, thus facilitating isoelectric purification of the "1+1 Fab-scFv-Fc" and "2+1" heterodimers (e.g., anionic exchange columns, cationic exchange columns). These substitutions also aid in the determination and monitoring of any contaminating dual scFv-Fc and mAb homodimers post-purification (e.g., IEF gels, cIEF, and analytical IEX columns).

VI. Biological and Biochemical Functionality of the Heterodimeric Bispecific Antibodies

[00356] Generally the bispecific CLDN6 x CD3 antibodies described herein are administered to patients with cancer, and efficacy is assessed, in a number of ways as described herein. Thus, while standard assays of efficacy can be run, such as cancer load, size of tumor, evaluation of presence or extent of metastasis, etc., immuno-oncology treatments can be assessed on the basis of immune status evaluations as well. This can be done in a number of ways, including both in vitro and in vivo assays.

VII. Treatments

[00357] Once made, the compositions of the antibodies described herein find use in a number of applications. CLDN6 is highly expressed in renal cell carcinoma, accordingly, the

heterodimeric compositions of the antibodies described herein find use in the treatment of such CLDN6 positive cancers.

VIII. Antibody Compositions for In Vivo Administration

[00358] Formulations of the antibodies used in accordance with the antibodies described herein are prepared for storage by mixing an antibody having the desired degree of purity with optional pharmaceutically acceptable carriers, excipients or stabilizers (Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. [1980]), in the form of lyophilized formulations or aqueous solutions.

IX. Administrative modalities

[00359] The antibodies and chemotherapeutic agents described herein are administered to a subject, in accord with known methods, such as intravenous administration as a bolus or by continuous infusion over a period of time.

X. Treatment modalities

[00360] In the methods described herein, therapy is used to provide a positive therapeutic response with respect to a disease or condition. By "positive therapeutic response" is intended an improvement in the disease or condition, and/or an improvement in the symptoms associated with the disease or condition. For example, a positive therapeutic response would refer to one or more of the following improvements in the disease: (1) a reduction in the number of neoplastic cells; (2) an increase in neoplastic cell death; (3) inhibition of neoplastic cell survival; (5) inhibition (i.e., slowing to some extent, preferably halting) of tumor growth; (6) an increased patient survival rate; and (7) some relief from one or more symptoms associated with the disease or condition.

[00361] Positive therapeutic responses in any given disease or condition can be determined by standardized response criteria specific to that disease or condition. Tumor response can be assessed for changes in tumor morphology (i.e., overall tumor burden, tumor size, and the like) using screening techniques such as magnetic resonance imaging (MRI) scan, x-radiographic imaging, computed tomographic (CT) scan, bone scan imaging,

endoscopy, and tumor biopsy sampling including bone marrow aspiration (BMA) and counting of tumor cells in the circulation.

[00362] In addition to these positive therapeutic responses, the subject undergoing therapy may experience the beneficial effect of an improvement in the symptoms associated with the disease.

[00363] Treatment according to the disclosure includes a “therapeutically effective amount” of the medicaments used. A “therapeutically effective amount” refers to an amount effective, at dosages and for periods of time necessary, to achieve a desired therapeutic result.

[00364] A therapeutically effective amount may vary according to factors such as the disease state, age, sex, and weight of the individual, and the ability of the medicaments to elicit a desired response in the individual. A therapeutically effective amount is also one in which any toxic or detrimental effects of the antibody or antibody portion are outweighed by the therapeutically beneficial effects.

[00365] A “therapeutically effective amount” for tumor therapy may also be measured by its ability to stabilize the progression of disease. The ability of a compound to inhibit cancer may be evaluated in an animal model system predictive of efficacy in human tumors.

[00366] Alternatively, this property of a composition may be evaluated by examining the ability of the compound to inhibit cell growth or to induce apoptosis by in vitro assays known to the skilled practitioner. A therapeutically effective amount of a therapeutic compound may decrease tumor size, or otherwise ameliorate symptoms in a subject. One of ordinary skill in the art would be able to determine such amounts based on such factors as the subject’s size, the severity of the subject’s symptoms, and the particular composition or route of administration selected.

[00367] Dosage regimens are adjusted to provide the optimum desired response (e.g., a therapeutic response). For example, a single bolus may be administered, several divided doses may be administered over time or the dose may be proportionally reduced or increased as indicated by the exigencies of the therapeutic situation. Parenteral compositions may be formulated in dosage unit form for ease of administration and uniformity of dosage. Dosage unit form as used herein refers to physically discrete units suited as unitary dosages for the subjects to be treated; each unit contains a predetermined quantity of active compound calculated to produce the desired therapeutic effect in association with the required pharmaceutical carrier.

[00368] The specification for the dosage unit forms of the disclosure are dictated by and directly dependent on (a) the unique characteristics of the active compound and the particular therapeutic effect to be achieved, and (b) the limitations inherent in the art of compounding such an active compound for the treatment of sensitivity in individuals.

[00369] The efficient dosages and the dosage regimens for the bispecific antibodies described herein depend on the disease or condition to be treated and may be determined by the persons skilled in the art.

[00370] An exemplary, non-limiting range for a therapeutically effective amount of an bispecific antibody used in the antibodies described herein is about 0.1-100 mg/kg.

[00371] All cited references are herein expressly incorporated by reference in their entirety.

[00372] Whereas particular embodiments of the disclosure have been described above for purposes of illustration, it will be appreciated by those skilled in the art that numerous variations of the details may be made without departing from the invention as described in the appended claims.

EXAMPLES

A. Example 1: Engineering α CLDN6 x α CD3 Bispecific Antibodies

[00373] Sequences for CD3 binding domains having different CD3 binding affinities are depicted in Figure 10. Sequences for CLDN6 binding domains are depicted in Figures 14-15. A number of formats for α CLDN6 x α CD3 bispecific antibodies (bsAbs) were conceived, illustrative formats for which are outlined below and in Figure 17.

[00374] One such format is the 1 + 1 Fab-scFv-Fc format which comprises a single-chain Fv ("scFv") covalently attached to a first heterodimeric Fc domain, a heavy chain variable region (VH) covalently attached to a complementary second heterodimeric Fc domain, and a light chain (LC) transfected separately so that a Fab domain is formed with the variable heavy domain.

[00375] Another format is the 2 + 1 Fab2-scFv-Fc format which comprises a VH domain covalently attached to a CH1 domain covalently attached to an scFv covalently attached to a first heterodimeric Fc domain (VH-CH1-scFv-Fc), a VH domain covalently

attached to a complementary second heterodimeric Fc domain, and a LC transfected separately so that Fab domains are formed with the VH domains.

[00376] DNA encoding chains of the α CLDN6 x α CD3 bsAbs were generated by standard gene synthesis followed by isothermal cloning (Gibson assembly) or subcloning into a pTT5 expression vector containing fusion partners (e.g. domain linkers as depicted in Figure 6 and/or backbones as depicted in Figures 7-9). DNA was transfected into HEK293E cells for expression. Sequences for illustrative α CLDN6 x α CD3 bsAbs (based on binding domains as described above) in the 1 + 1 Fab-scFv-Fc format and in the 2 + 1 Fab2-scFv-Fc format are depicted respectively in Figures 19-22.

B. Example 2: Engineering CLDN6 Binding Domains for Enhanced Selectivity

[00377] The claudin family of proteins include numerous other claudins. Jukes-Cantor distance of various claudin sequences to CLDN6 were determined as follows: CLDN9 (0.32), CLDN4 (0.51), CLDN3 (0.52), CLDN5 (0.64), CLDN8 (0.8), and CLDN17 (0.82). In comparison to CLDN6, CLDN9 is more highly expressed in healthy tissues (e.g. the cervix and the esophagus), so cross-reactivity of CLDN6 therapeutic with CLDN9 could lead to off-target toxicity. However in addition to having Jukes-Cantor Distance off just 0.32 and 96% identity, CLDN6 and CLDN9 differ by only 3 residues in their extracellular loops (as depicted in Figure 12); therefore, it is a significant challenge to develop an antibody capable of binding CLDN6 selectively over CLDN9. Accordingly, this section describes identification and engineering of suitable CLDN6 binding domains (with minimal cross-reactivity) suitable for use in the α CLDN6 x α CD3 bsAbs of the invention. Additionally, a prior art CLDN6 binding domain described in US Patent No. 10,233,253 was used as a comparator (in a bivalent mAb format as in XENP26863 and in a 1 + 1 Fab-scFv-Fc bsAb with CD3 High scFv as in XENP26849; sequences depicted in Figure 18).

[00378] The following experiments used to screen CLDN6 binding domains were generally performed as follows. HEK293T or HEK293E cells were respectively stably or transiently transfected to express CLDN6, CLDN9, or other targets of interest. 48 hours post transfection, cells were harvested and incubated with dilutions of the indicated test articles for 1 hour at 40C. Next, cells were washed and stained with a secondary antibody (typically anti-human Fc AlexaFluor647) for 1 hour at 40C, followed by two more washes. Binding was then assessed via flow cytometry.

1. Identification of CLDN6 binding domains selective for CLDN6 over CLDN9

[00379] Six murine anti-CLDN6 mAbs were investigated for their binding to CLDN6 and CLDN9, as well to CLDN3 and CLDN4 which are also members of the claudin family. Figure 23 depicts binding of the mAbs to transfected cells. Specificity for targets was determined by comparing EC50 values and AUC (area under the binding curve). The data show that clones C6-10, C6-15, and C6-21 were not selective for CLDN6 over CLDN9. Additionally, clone C6-10 even showed some binding to CLDN4. Notably, clones C6-11, C6-24, and C6-30 demonstrated selectivity for CLDN6 over CLDN9 and little to no binding to CLDN3 and CLDN4.

2. Humanization of CLDN6 binding domains

[00380] The variable regions of C6-11, C6-24, and C6-30 were humanized using string content optimization (see, e.g., U.S. Patent No. 7,657,380, issued February 2, 2010). For each clone, two humanized variable heavy domains (i.e. H1 and H2) and two humanized variable light domains (i.e. L1 and L2) were engineered and paired (i.e. H1L1, H1L2, H2L1, H2L2). Sequences for humanized C6-30 variable domains and bivalent mAbs based on the domains are depicted respectively in Figures 14 and 16 (as XENP34218, XENP34219, XENP34220, and XENP34221). Binding of the humanized clones to CLDN3, CLDN4, CLDN6, and CLDN9 were investigated to determine whether humanization affected their binding profiles and are depicted in Figures 24-26. All humanized variants of clone C6-30 and C6-24 demonstrated binding profiles equivalent to their murine precursor. Unexpectedly, all humanized variants of clone C6-11 unfavorably demonstrated increased binding to CLDN4.

3. Engineering to remove degradation liable residues

[00381] The sequence for C6-30 was investigated for degradation liable residues. Heavy chain CDR2 included D52/P52a as an isomerization motif, N54/G55 as a deamidation motif, and Q64/G75 as a deamidation motif. Accordingly, a library was made with mutations at these residues to investigate whether the liability could be removed without impacting on CLDN6 binding and selectivity. Figure 27 depicts the variants investigated as well as their binding to CLDN6 and CLDN9 as generally described above. The data show that many of the

variants that maintained selectivity had decreased binding to CLDN6. Notably, G55A did maintain selectivity with minimal loss to CLDN6 binding.

4. Characterization of CLDN6 binding domains for cross-reactivity in the context of a bispecific antibody

[00382] Prototype α CLDN6 x α CD3 bispecific antibodies (bsAbs) in both the 1 + 1 Fab-scFv-Fc format and the 2 + 1 Fab2-scFv-Fc format were engineered and produced (as described in Example 1) using the humanized CLDN6 binding domains described above and the CD3 binding domains as described in Example 1.

[00383] For ease of clinical development (e.g. by investigating the therapeutics in model animals), it is useful for the binding domains to be cross-reactive for mouse and/or cynomolgus antigen. Therefore, the prototype α CLDN6 x α CD3 bsAbs were investigated for their binding to human CLDN6, cynomolgus CLDN6, and murine CLDN6. As shown in Figure 28, each of the prototype bsAbs were able to human, cynomolgus, and mouse CLDN6.

[00384] Next, the prototype bsAbs were investigated for their binding to confirm that formatting the CLDN6 binding domains as bispecific antibodies did not affect their selectivity for CLDN6 over CLDN9. Selectivity was determined according to CLDN9/CLDN6 EC50 ratio. As shown in Figure 29, each of the bispecific antibodies maintained selectivity for CLDN6 over CLDN9, although the ones based on C6-30 were more selective. Notably as well, while humanized C6-24 demonstrated similar selectivity in both the 1 + 1 Fab-scFv-Fc format and the 2 + 1 Fab2-scFv-Fc format, the humanized C6-30 variants demonstrated further enhanced selectivity in the 2 + 1 Fab2-scFv-Fc format.

[00385] Additionally, binding to CLDN6 I143V isotype was investigated, as this variant is found in ~30% of the population, and the data show that each of the variant was able to bind the I143V isotype.

5. Engineering for enhanced CLDN6 selectivity

[00386] Humanized C6-30 (both H1L1 and H2L1) which already demonstrated good selectivity, especially in the context of 2 + 1 Fab2-scFv-Fc, was engineered to enhance selectivity. In a first round of engineering, single point mutations were introduced into either the variable heavy or the variable light domain resulting in a library of ~300 variants

formatted as bivalent mAbs. Each mAb was screened for binding to CLDN6 and CLDN9 (on transfected cells) at a single concentration of 30 µg/ml. Most of point mutations had a similar impact on both CLDN6 and CLDN9 (e.g. improved binding to both or reduced binding to both). Nonetheless, there were several point mutations which were found to reduce binding to CLDN9 while maintaining or even improving binding to CLDN6 (as indicated by a skew toward higher CLDN6 MFI values and lower CLDN9 MFI values; circled in Figure 30). The binding of these variants to CLDN6 and CLDN9 were re-investigated at various concentrations in two separate experiments, data depicting EC50 and CLDN9/CLDN6 EC50 ratio for which are depicted in Figure 31. It should be noted that binding data from the experiments cannot be compared head-to-head as antigen density on the transfected cells vary between experiments. Nonetheless, several variants were enhanced in selectivity in comparison to the parental humanized clone (i.e. XENP34218_H1L1 and XENP34220_H2L1) and in comparison to comparator XENP26863. While some of the variants such as XENP35865 having H2_L1.60 were weaker CLDN6 binders in comparison to the parental humanized clones, they were also much weaker CLDN9 binders providing drastically enhanced selectivity for CLDN6 over CLDN9. Interestingly, several variants such as XENP35101 and XENP35102 respectively having H2.8_L1 and H2.9_L1 resulted in drastically enhanced selectivity for CLDN9 over CLDN6.

[00387] Next, favorite variant heavy domains (H1.9, H1.22, H1.24, H2.3, H2.9, H2.12, H2.90, H2.91, and H2.118) and favorite variant light domains (L1.187 and L1.189) from the first round of engineering that provided the best improvement in CLDN6 selectivity were combined to create a new library of 16 variants. The binding of these variants to CLDN6 and CLDN9 were investigated as described above, data for which are shown in Figure 32. The data in Figure 33 depicts the EC50 and AUC for each of the test articles as well as the CLDN9/CLDN6 EC50 ratio and CLDN6/CLDN9 AUC ratio as indicators of selectivity. Each of the 16 combination variants were enhanced in selectivity in comparison to the parental humanized clone (e.g. XENP36956 having H1.22_L1.87 and a CLDN9/CLDN6 EC50 ratio of 44.94 in comparison to XENP34218 having H1L1 and a CLDN9/CLDN6 EC50 ratio of 23.03). Notably, combining favorite variant heavy domains and favorite variant light domain did not always enhance selectivity in comparison to the parental variant (e.g. XENP36956 having H1.22_L1.187 and a CLDN9/CLDN6 EC50 ratio of 44.94 in comparison to XENP36972 having H1_L1.187 and a CLDN9/CLDN6 EC50 ratio of 52.64). Finally, 10 of the 16 combination variants demonstrated superior selectivity in comparison to

comparator XENP26863 based on CLDN9/CLDN6 EC50 ratio; and 16/16 combination variants demonstrated superiority based on CLDN6/CLDN9 AUC ratio. It should be noted that variants combining variable heavy domain mutations were also investigated, but these variants did not outperform the clones with only one mutation per variable heavy domain. It should also be noted that the ratios should not be the only determinant of enhanced selectivity. For example, although XENP36956 having H1.9_L1.187 and CLDN9/CLDN6 EC50 of 44.94 appears to be slightly less selective than control XENP26863, XENP36956 had a much higher EC50 for CLDN9 binding in comparison to XENP26863 (29584 ng/ml in comparison to 2146 ng/ml) while maintaining a reasonable EC50 for CLDN6 binding.

6. Investigating engineered CLDN6 binding domains in the context of bispecific antibodies

[00388] Finally, several of the preferred combination variants were incorporated into 2 + 1 Fab2-scFv-Fc CD3 bsAbs to investigate whether the bispecific format affected their selectivity. Surprisingly as depicted in Figure 34A, many of the 2 + 1 Fab2-scFv-Fc bispecific antibodies including XENP37231 having C6-30_H1.24_L1.187, XENP37227 having C6-30_H1.9_L1.187, and XENP37233 having C6-30_H2.91_L1.187 demonstrated enhanced CLDN6 binding in comparison to corresponding bivalent mAb having the same variant CLDN6 binding domain; however, the C6-30_H1.22_L1.89 variant actually demonstrated decreased binding in the bispecific format in comparison to the monospecific bivalent format while several other variants demonstrated similar binding in both the bispecific format and the monospecific bivalent format. Additionally surprising as depicted in Figure 34B, several of the 2 + 1 Fab2-scFv-Fc bispecific antibodies including XENP37227 comprising C6-30_H1.9_L1.187 variant and XENP37231 having C6-30_H1.24_L1.187 variant demonstrated reduced CLDN9 binding in comparison to corresponding bivalent mAb having the same variant CLDN6 binding domain.

7. Investigating additional off-target binding

[00389] To ascertain cross-reactivity to other proteins in the claudin family, binding of C6-24_H1L1, C6-30_H1L1, and C6-30_H2L1 to CLDN5, CLDN8, and CLDN17 was investigated as generally described above. Data as depicted in Figure 35 show that none of the clones were cross-reactive for the additional claudins investigated. Additionally, C6-30

variants were screened alongside XENP37217 (a CLDN6 x CD3 bispecific using a comparator CLDN6 binding domain, the sequence for which is depicted in Figure 60) for binding to CLDN3, CLDN4, CLDN8, and CLDN17. 293 cells were transiently transfected with CLDN3, CLDN4, CLDN8, or CLDN17. Cells were plated and each test article was added to each cell line at a 100 µg/ml dose. After 1 hour incubation at 4°C, cells were washed and a secondary AF647 antibody was added. Cells were incubated at 4°C for another hour, followed by additional washing and then analysis by flow cytometry. For each of these different claudin family members, the comparator molecule XENP37217 showed higher binding than the test articles utilizing the C6-30 binding domains. XENP37217 showed particularly strong binding for CLDN8 and CLDN17, producing an MFI more than an order of magnitude higher than the C6-30 variants, as depicted in Figure 61. This highlights the potential of CLDN6 binding domains having specificity for binding not only CLDN6 but also other claudin family members.

C. Example 3: Engineering αCLDN6 x αCD3 bsAbs to optimize redirected T cell cytotoxicity on CLDN6-expressing cells

[00390] αCLDN6 x αCD3 bsAbs were engineered with various tuned CLDN6 and CD3 binding domains and in different bispecific formats and produced as generally described in Example 1 to optimize redirected T cell cytotoxicity (RTCC), CLDN6 selectivity, and potential therapeutic index.

1. αCLDN6 x αCD3 bsAbs with bivalent CLDN6 binding are enhanced in redirected T cell cytotoxicity (RTCC) on CLDN6+ cells

[00391] αCLDN6 x αCD3 bsAbs were engineered using C6-24_H1L1, C6-30_H1L1, and C6-30_H2L1 in 1 + 1 Fab-scFv-Fc and 2 + 1 Fab2-scFv-Fc formats to investigate the impact of avidity (i.e. monovalent vs. bivalent binding of CLDN6 antigen). PA-1 cells (CLDN6hi; 1.1 X 10⁶ CLDN6 density) were incubated with T cells isolated from human PBMCs at a 10:1 effector:target ratio for 48 hours. Data showing RTCC activity (as indicated by percentage dead cells and T cell activation) are depicted in Figures 37-38. The 2 + 1 Fab2-scFv-Fc constructs showed 20-100 fold lower EC50 in comparison to 1 + 1 constructs. Additionally, potency shifts between the 2 + 1 vs. 1 + 1 construct were ~half-log more for C6-30_H2L1 in comparison to C6-30_H1L1. Collectively, the data indicate that bsAbs with bivalent CLDN6 binding are enhanced in RTCC on CLDN6+ target cells.

2. α CLDN6 x α CD3 bsAbs with bivalent CLDN6 binding and lower affinity CD3 binding are enhanced in selectivity for CLDN6 over CLDN9

[00392] Next, α CLDN6 x α CD3 bsAbs having C6-30_H2L1 and either high affinity CD3_High or lower affinity CD3_High-Int#1 and in either 1 + 1 Fab-scFv-Fc or 2 + 1 Fab2-scFv-Fc formats were investigated for their selectivity for CLDN6+ target cells. HUTU-80 cells (CLDN6+) or HEK293-TREX cells stably transfected to express CLDN9 were incubated with T cells purified from human PBMCs at a 10:1 effector:target ratio for 48 hours. Comparator bsAb XENP26849 was also used. Data showing RTCC activity (as indicated by percentage dead cells and T cell activation) are depicted in Figures 39-40. Surprisingly, induction of RTCC activity on HUTU-80 cells by bsAbs having high affinity CD3_High only differed slightly than by bsAbs having lower affinity CD3_High-Int#1. However, consistent with Example 3A, the 2 + 1 format enabled much more potent RTCC activity in comparison to the 1 + 1 format. Notably, 2 + 1 Fab2-scFv-Fc bsAb having the lower affinity CD3_High-Int#1 induced RTCC on off-target CLDN9+ cells less potently than 2 + 1 bsAbs having high affinity CD3_High, indicating that using lower affinity CD3 binding domains in the context of a 2 + 1 Fab2-scFv-Fc format favorably improves selectivity for CLDN6 over CLDN9 expressing cells. Further, each of the bsAbs based on C6-30 demonstrated much weaker induction of RTCC on CLDN9 expressing cells in comparison to comparator bsAb XENP26849.

3. α CLDN6 x α CD3 bsAb activity correlates with CLDN6 antigen density and CD3 binding affinity

[00393] Next, RTCC activity on cell lines having different CLDN6 densities was investigated. 30K PA-1 (1.1×10^6 CLDN6 density), OV-90 (195K CLDN6 density), NEC-8 (175K CLDN6 density), and COV-318 (11K CLDN6 density) cells were incubated with T cells purified from human PBMCs at a 10:1 E:T ratio for 48 hours. RTCC activity (as indicated by percentage dead cells and T cell activation) are depicted in Figures 41-44. The data show that cell killing activity and T cell activation correlates with CLDN6 antigen density and affinity of the CD3 binding domain. Selectivity for higher CLDN6 antigen density over lower CLDN6 antigen density suggests potential reduced off-target killing of healthy tissue expressing low levels of CLDN6 in a clinical setting and improved therapeutic index.

4. Tuning α CLDN6 x α CD3 bsAb activity and selectivity

[00394] α CLDN6 x α CD3 bsAbs were further tuned by incorporating the lead selectivity-tuned CLDN6 binding domains (as described in Example 2) into the 2 + 1 Fab2-scFv-Fc format with CD3_High-Int#1.

[00395] 30K HUTU-80 (CLDN6+) or HEK293TREX cells stably transfected to express CLDN9 were incubated with T cells purified from human PBMC and test articles for 48 hours. In a first experiment, 10:1 effector:target ratio was used, data for which are depicted in Figure 45. In a second experiment, 1:1 effector:target ratio was used, data for which are depicted in Figure 46. Consistent with the data in Example 2.6, the bsAbs having selectivity-engineered CLDN6 binding domains demonstrated modulated activity on CLDN6+ cells and/or modulated activity on CLDN9+ cells in comparison to bsAbs having the parental C6-30_H1L1 and C6-30_H2L1. In one instance, XENP37233 demonstrated similar activity on CLDN9+ cells but significantly enhanced activity on CLDN6+ cells in comparison to the parental clones. In another instance, XENP37227 demonstrated reduced activity on CLDN9+ cells and enhanced activity on CLDN6+ cells (in comparison to the parental clones. In yet another instance, XENP37231 demonstrated little to no activity on CLDN9+ cells but slightly reduced activity on CLDN6+ cells in comparison to the parental clones. Each of these bsAbs may be suitable depending on whether clinical development favors enhanced activity on CLDN6+ cells, reduced activity on CLDN9+ cells, or preferably a balance of the two. Additionally in the second experiment, activation of T cells as indicated by CD69 expression, CD107a expression, and cytokine (IFN γ , IL-2, and TNF α) secretion was also determined as depicted in Figures 47-51, and the observations are consistent with the cell killing data.

[00396] Figure 52 additionally depicts overlay of RTCC activity on HUTU-80 vs. on HEK293TREX expressing CLDN9 cells. The data show that each bsAb can be dosed at high concentrations to achieve efficacious killing of CLDN6+ cells while avoiding killing of CLDN9+ cells.

[00397] In another experiment, the RTCC activity of the bsAbs described above on PA-1 cells were compared to XENP37630 (sequences for which are depicted in Figure 59) having the same CLDN6 binding domain as XENP37227 (i.e. C6-30_H1.9_L1.187) and lower affinity CD3 scFv (i.e. CD3_High-Int#2). Cell kill and T cell activation (as indicated by CD25 and CD107a expression) are depicted in Figure 53 and show that each of the 4

bsAbs achieved efficacious target cell killing at high concentrations, with potencies ranked as XENP37223 (highest potency) > XENP37227 > XENP37630 > XENP37231 (lowest potency).

D. Example 4: Further Characterization of α CLDN6 x α CD3 bsAbs of the invention

[00398] Based on the above in vitro experiments, several bsAbs were selected for further analysis in vivo. These antibodies were further engineered with Xtend Fc (M428L/N434S) to enhanced serum half-life, illustrative sequences for which are depicted in Figures 22 and 59 as XENP37547 (Xtend analog to XENP37233), XENP37545 (Xtend analog to XENP37231), XENP37634 (Xtend analog to XENP37630), and XENP37541 (Xtend analog to XENP37227).

1. α CLDN6 x α CD3 bsAbs kill cells representative of CLDN6 in tumors

[00399] In order to confirm the ability of α CLDN6 x α CD3 bsAbs to effectively target cell lines expressing levels of CLDN6 antigen that are biologically relevant to tumor cells, , IHC was conducted on biopsy cores of ovarian cancers and were qualitatively scored on a scale of 0-3 with 0 representing little to no target antigen expression and 3 representing high target antigen expression (herein referred to as IHC score). While there was significant variation among different types of ovarian cancers, many had IHC scores in the 1-2 range, representing approximately 200k or fewer CLDN6 antigens per cell. For this reason, PA-1 cells were genetically engineered to express CLDN6 at a lower range of densities. Engineered PA-1 cell lines were established to express either 47k, 55k, 77k, 105k, 212k, or 228k CLDN6 antigens per cell approximately. A cell binding experiment was performed in which XENP37541 was incubated with each of the lower density PA-1 cell lines. Cell lines were then washed, stained with secondary antibody, and washed again before measuring binding by flow cytometry. As seen in Figure 54, the level of binding is dependent on the density of CLDN6 expression, but XENP37541 is still capable of binding to cells with lower levels of CLDN6 expression, even down to 47k CLDN6 antigens per cell.

[00400] Next, α CLDN6 x α CD3 bsAbs XENP37541, XENP37634, and XENP37545, along with XENP32140 (a negative control RSV x CD3 bsAb), were tested for their ability to induce RTCC on these lower CLDN6 density PA-1 cell lines. A 1:1 effector:target cell ratio

was used, along with the test articles at the range of concentrations indicated in Figure 55. After a 72 hour incubation, results were measured as depicted in Figure 55, and showed that XENP37541, XENP37634, and XENP37545 are all able to effectively induce RTCC in a CLDN6 density dependent manner even at a lower CLDN6 expression levels. The results showed that XENP37541 had the strongest potency and lowest EC50 values across all CLDN6 densities.

2. α CLDN6 x α CD3 bsAbs enhance allogeneic anti-tumor effect of T cells in vivo

[00401] NOD SCID gamma (NSG) mice (n = 10) were engrafted intradermally with 10×10^6 PA-1 cells (in Matrigel) on Day -7. On Day 0, mice were engrafted intraperitoneally with 5×10^6 human PBMCs. Mice were then treated on Days 0, 7, 14, and 21 with XENP37233, XENP37227, XENP37630, or XENP37231 at 0.3, 1.0, or 3.0 mg/kg or PBS control. Tumor volume was measured by caliper three times per week (data for which are shown in Figure 56) and blood was drawn to investigate lymphocyte expansion (data not shown). The data show that each of the 4 bsAbs were able to induce anti-tumor effect at all concentrations. By Day 14, each of the bispecific antibodies enhanced anti-tumor activity in comparison to PBS control. Notably, lower potency molecules XENP37630 and XENP37231 demonstrated some dose dependency in anti-tumor activity.

3. α CLDN6 x α CD3 bsAbs are well tolerated and demonstrate good pharmacokinetic profile in cynomolgus monkeys

[00402] Animals (n = 1) were dosed with XENP37547, XENP37545, XENP37634, and XENP37541 at 1X, 10X, 30X, and 60X dose on Day 0. Blood was drawn over time to determine concentration of drug in serum over time, data for which are depicted in Figures 57-58. The data show that the bsAbs have an in vivo half-life of ~2 weeks and was dose dependent. Additionally, the bsAbs were generally well-tolerated as indicated by clinical observations (e.g. of body weight; data not shown).

WHAT IS CLAIMED IS:

1. A composition comprising an CLDN6 antigen binding domain (ABD), wherein the CLDN6 antigen binding domain comprises a set of 6 CDRs (vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2 and vlCDR3) from a variable heavy domain (VH)/variable light domain (VL) pair selected from the group consisting: H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1, H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1, H2.12_L1, H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1, H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1, H1.9_L1.1, H1.19_L1.1, H1.22_L1.1, H1.24_L1.1, H2_L1.1, H2.1_L1.1, H2.2_L1.1, H2.3_L1.1, H2.4_L1.1, H2.5_L1.1, H2.6_L1.1, H2.7_L1.1, H2.8_L1.1, H2.9_L1.1, H2.11_L1.1, H2.12_L1.1, H2.71_L1.1, H2.75_L1.1, H2.90_L1.1, H2.91_L1.1, H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4, H1.2_L1.4, H1.3_L1.4, H1.4_L1.4, H1.5_L1.4, H1.6_L1.4, H1.7_L1.4, H1.8_L1.4, H1.9_L1.4, H1.19_L1.4, H1.22_L1.4, H1.24_L1.4, H2_L1.4, H2.1_L1.4, H2.2_L1.4, H2.3_L1.4, H2.4_L1.4, H2.5_L1.4, H2.6_L1.4, H2.7_L1.4, H2.8_L1.4, H2.9_L1.4, H2.11_L1.4, H2.12_L1.4, H2.71_L1.4, H2.75_L1.4, H2.90_L1.4, H2.91_L1.4, H2.118_L1.4, H2.119_L1.4, H1_L1.7, H1.1_L1.7, H1.2_L1.7, H1.3_L1.7, H1.4_L1.7, H1.5_L1.7, H1.6_L1.7, H1.7_L1.7, H1.8_L1.7, H1.9_L1.7, H1.19_L1.7, H1.22_L1.7, H1.24_L1.7, H2_L1.7, H2.1_L1.7, H2.2_L1.7, H2.3_L1.7, H2.4_L1.7, H2.5_L1.7, H2.6_L1.7, H2.7_L1.7, H2.8_L1.7, H2.9_L1.7, H2.11_L1.7, H2.12_L1.7, H2.71_L1.7, H2.75_L1.7, H2.90_L1.7, H2.91_L1.7, H2.118_L1.7, H2.119_L1.7, H1_L1.16, H1.1_L1.16, H1.2_L1.16, H1.3_L1.16, H1.4_L1.16, H1.5_L1.16, H1.6_L1.16, H1.7_L1.16, H1.8_L1.16, H1.9_L1.16, H1.19_L1.16, H1.22_L1.16, H1.24_L1.16, H2_L1.16, H2.1_L1.16, H2.2_L1.16, H2.3_L1.16, H2.4_L1.16, H2.5_L1.16, H2.6_L1.16, H2.7_L1.16, H2.8_L1.16, H2.9_L1.16, H2.11_L1.16, H2.12_L1.16, H2.71_L1.16, H2.75_L1.16, H2.90_L1.16, H2.91_L1.16, H2.118_L1.16, H2.119_L1.16, H1_L1.18, H1.1_L1.18, H1.2_L1.18, H1.3_L1.18, H1.4_L1.18, H1.5_L1.18, H1.6_L1.18, H1.7_L1.18, H1.8_L1.18, H1.9_L1.18, H1.19_L1.18, H1.22_L1.18, H1.24_L1.18, H2_L1.18, H2.1_L1.18, H2.2_L1.18, H2.3_L1.18, H2.4_L1.18, H2.5_L1.18, H2.6_L1.18, H2.7_L1.18, H2.8_L1.18, H2.9_L1.18, H2.11_L1.18, H2.12_L1.18, H2.71_L1.18, H2.75_L1.18, H2.90_L1.18, H2.91_L1.18, H2.118_L1.18, H2.119_L1.18, H1_L1.19, H1.1_L1.19, H1.2_L1.19, H1.3_L1.19,

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H2.91_L1.107, H2.118_L1.107, H2.119_L1.107, H1_L1.114, H1.1_L1.114, H1.2_L1.114, H1.3_L1.114, H1.4_L1.114, H1.5_L1.114, H1.6_L1.114, H1.7_L1.114, H1.8_L1.114, H1.9_L1.114, H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114, H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114, H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114, H2.90_L1.114, H2.91_L1.114, H2.118_L1.114, H2.119_L1.114, H1_L1.187, H1.1_L1.187, H1.2_L1.187, H1.3_L1.187, H1.4_L1.187, H1.5_L1.187, H1.6_L1.187, H1.7_L1.187, H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187, H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187, H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187, H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187, H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189, H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189, H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189, H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189, H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189, H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2, H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2.

2. A composition according to claim 1, wherein the ABD comprises a VH/VL pair selected from the group consisting of: H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1, H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1, H2.12_L1, H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1, H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1, H1.9_L1.1, H1.19_L1.1, H1.22_L1.1, H1.24_L1.1, H2_L1.1, H2.1_L1.1, H2.2_L1.1, H2.3_L1.1, H2.4_L1.1, H2.5_L1.1, H2.6_L1.1, H2.7_L1.1, H2.8_L1.1, H2.9_L1.1, H2.11_L1.1, H2.12_L1.1, H2.71_L1.1, H2.75_L1.1, H2.90_L1.1, H2.91_L1.1, H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4, H1.2_L1.4, H1.3_L1.4, H1.4_L1.4, H1.5_L1.4, H1.6_L1.4, H1.7_L1.4, H1.8_L1.4, H1.9_L1.4, H1.19_L1.4, H1.22_L1.4, H1.24_L1.4, H2_L1.4, H2.1_L1.4, H2.2_L1.4, H2.3_L1.4, H2.4_L1.4, H2.5_L1.4,

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 H1.1_L1.22, H1.2_L1.22, H1.3_L1.22, H1.4_L1.22, H1.5_L1.22, H1.6_L1.22, H1.7_L1.22,
 H1.8_L1.22, H1.9_L1.22, H1.19_L1.22, H1.22_L1.22, H1.24_L1.22, H2_L1.22,
 H2.1_L1.22, H2.2_L1.22, H2.3_L1.22, H2.4_L1.22, H2.5_L1.22, H2.6_L1.22, H2.7_L1.22,
 H2.8_L1.22, H2.9_L1.22, H2.11_L1.22, H2.12_L1.22, H2.71_L1.22, H2.75_L1.22,
 H2.90_L1.22, H2.91_L1.22, H2.118_L1.22, H2.119_L1.22, H1_L1.23, H1.1_L1.23,
 H1.2_L1.23, H1.3_L1.23, H1.4_L1.23, H1.5_L1.23, H1.6_L1.23, H1.7_L1.23, H1.8_L1.23,
 H1.9_L1.23, H1.19_L1.23, H1.22_L1.23, H1.24_L1.23, H2_L1.23, H2.1_L1.23,

H2.2_L1.23, H2.3_L1.23, H2.4_L1.23, H2.5_L1.23, H2.6_L1.23, H2.7_L1.23, H2.8_L1.23, H2.9_L1.23, H2.11_L1.23, H2.12_L1.23, H2.71_L1.23, H2.75_L1.23, H2.90_L1.23, H2.91_L1.23, H2.118_L1.23, H2.119_L1.23, H1_L1.27, H1.1_L1.27, H1.2_L1.27, H1.3_L1.27, H1.4_L1.27, H1.5_L1.27, H1.6_L1.27, H1.7_L1.27, H1.8_L1.27, H1.9_L1.27, H1.19_L1.27, H1.22_L1.27, H1.24_L1.27, H2_L1.27, H2.1_L1.27, H2.2_L1.27, H2.3_L1.27, H2.4_L1.27, H2.5_L1.27, H2.6_L1.27, H2.7_L1.27, H2.8_L1.27, H2.9_L1.27, H2.11_L1.27, H2.12_L1.27, H2.71_L1.27, H2.75_L1.27, H2.90_L1.27, H2.91_L1.27, H2.118_L1.27, H2.119_L1.27, H1_L1.60, H1.1_L1.60, H1.2_L1.60, H1.3_L1.60, H1.4_L1.60, H1.5_L1.60, H1.6_L1.60, H1.7_L1.60, H1.8_L1.60, H1.9_L1.60, H1.19_L1.60, H1.22_L1.60, H1.24_L1.60, H2_L1.60, H2.1_L1.60, H2.2_L1.60, H2.3_L1.60, H2.4_L1.60, H2.5_L1.60, H2.6_L1.60, H2.7_L1.60, H2.8_L1.60, H2.9_L1.60, H2.11_L1.60, H2.12_L1.60, H2.71_L1.60, H2.75_L1.60, H2.90_L1.60, H2.91_L1.60, H2.118_L1.60, H2.119_L1.60, H1_L1.107, H1.1_L1.107, H1.2_L1.107, H1.3_L1.107, H1.4_L1.107, H1.5_L1.107, H1.6_L1.107, H1.7_L1.107, H1.8_L1.107, H1.9_L1.107, H1.19_L1.107, H1.22_L1.107, H1.24_L1.107, H2_L1.107, H2.1_L1.107, H2.2_L1.107, H2.3_L1.107, H2.4_L1.107, H2.5_L1.107, H2.6_L1.107, H2.7_L1.107, H2.8_L1.107, H2.9_L1.107, H2.11_L1.107, H2.12_L1.107, H2.71_L1.107, H2.75_L1.107, H2.90_L1.107, H2.91_L1.107, H2.118_L1.107, H2.119_L1.107, H1_L1.114, H1.1_L1.114, H1.2_L1.114, H1.3_L1.114, H1.4_L1.114, H1.5_L1.114, H1.6_L1.114, H1.7_L1.114, H1.8_L1.114, H1.9_L1.114, H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114, H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114, H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114, H2.90_L1.114, H2.91_L1.114, H2.118_L1.114, H2.119_L1.114, H1_L1.187, H1.1_L1.187, H1.2_L1.187, H1.3_L1.187, H1.4_L1.187, H1.5_L1.187, H1.6_L1.187, H1.7_L1.187, H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187, H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187, H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187, H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187, H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189, H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189, H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189, H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189, H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189,

H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2, H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2.

3. A composition according to claim 2, wherein the VH/VL pair is selected from the group consisting of H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187.

4. A composition according to any of claims 1-3, wherein the composition is a monoclonal antibody.

5. A nucleic acid composition comprising:

a) a first nucleic acid encoding a VH domain; and

b) a second nucleic acid encoding a VL domain,

wherein the VH and the VL are a pair selected from the group consisting of: H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1, H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1, H2.12_L1, H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1, H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1, H1.9_L1.1, H1.19_L1.1, H1.22_L1.1, H1.24_L1.1, H2_L1.1, H2.1_L1.1, H2.2_L1.1, H2.3_L1.1, H2.4_L1.1, H2.5_L1.1, H2.6_L1.1, H2.7_L1.1, H2.8_L1.1, H2.9_L1.1, H2.11_L1.1, H2.12_L1.1, H2.71_L1.1, H2.75_L1.1, H2.90_L1.1, H2.91_L1.1, H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4, H1.2_L1.4, H1.3_L1.4, H1.4_L1.4, H1.5_L1.4, H1.6_L1.4, H1.7_L1.4, H1.8_L1.4, H1.9_L1.4, H1.19_L1.4, H1.22_L1.4, H1.24_L1.4, H2_L1.4, H2.1_L1.4, H2.2_L1.4, H2.3_L1.4, H2.4_L1.4, H2.5_L1.4, H2.6_L1.4, H2.7_L1.4, H2.8_L1.4, H2.9_L1.4, H2.11_L1.4, H2.12_L1.4, H2.71_L1.4, H2.75_L1.4, H2.90_L1.4, H2.91_L1.4, H2.118_L1.4, H2.119_L1.4, H1_L1.7, H1.1_L1.7, H1.2_L1.7, H1.3_L1.7, H1.4_L1.7, H1.5_L1.7, H1.6_L1.7, H1.7_L1.7, H1.8_L1.7, H1.9_L1.7, H1.19_L1.7, H1.22_L1.7, H1.24_L1.7, H2_L1.7, H2.1_L1.7, H2.2_L1.7, H2.3_L1.7, H2.4_L1.7, H2.5_L1.7, H2.6_L1.7, H2.7_L1.7, H2.8_L1.7, H2.9_L1.7, H2.11_L1.7, H2.12_L1.7, H2.71_L1.7, H2.75_L1.7, H2.90_L1.7, H2.91_L1.7, H2.118_L1.7, H2.119_L1.7, H1_L1.16, H1.1_L1.16, H1.2_L1.16, H1.3_L1.16, H1.4_L1.16, H1.5_L1.16,

L1.16, H1.6_L1.16, H1.7_L1.16, H1.8_L1.16, H1.9_L1.16, H1.19_L1.16, H1.22_L1.16, H1.24_L1.16, H2_L1.16, H2.1_L1.16, H2.2_L1.16, H2.3_L1.16, H2.4_L1.16, H2.5_L1.16, H2.6_L1.16, H2.7_L1.16, H2.8_L1.16, H2.9_L1.16, H2.11_L1.16, H2.12_L1.16, H2.71_L1.16, H2.75_L1.16, H2.90_L1.16, H2.91_L1.16, H2.118_L1.16, H2.119_L1.16, H1_L1.18, H1.1_L1.18, H1.2_L1.18, H1.3_L1.18, H1.4_L1.18, H1.5_L1.18, H1.6_L1.18, H1.7_L1.18, H1.8_L1.18, H1.9_L1.18, H1.19_L1.18, H1.22_L1.18, H1.24_L1.18, H2_L1.18, H2.1_L1.18, H2.2_L1.18, H2.3_L1.18, H2.4_L1.18, H2.5_L1.18, H2.6_L1.18, H2.7_L1.18, H2.8_L1.18, H2.9_L1.18, H2.11_L1.18, H2.12_L1.18, H2.71_L1.18, H2.75_L1.18, H2.90_L1.18, H2.91_L1.18, H2.118_L1.18, H2.119_L1.18, H1_L1.19, H1.1_L1.19, H1.2_L1.19, H1.3_L1.19, H1.4_L1.19, H1.5_L1.19, H1.6_L1.19, H1.7_L1.19, H1.8_L1.19, H1.9_L1.19, H1.19_L1.19, H1.22_L1.19, H1.24_L1.19, H2_L1.19, H2.1_L1.19, H2.2_L1.19, H2.3_L1.19, H2.4_L1.19, H2.5_L1.19, H2.6_L1.19, H2.7_L1.19, H2.8_L1.19, H2.9_L1.19, H2.11_L1.19, H2.12_L1.19, H2.71_L1.19, H2.75_L1.19, H2.90_L1.19, H2.91_L1.19, H2.118_L1.19, H2.119_L1.19, H1_L1.21, H1.1_L1.21, H1.2_L1.21, H1.3_L1.21, H1.4_L1.21, H1.5_L1.21, H1.6_L1.21, H1.7_L1.21, H1.8_L1.21, H1.9_L1.21, H1.19_L1.21, H1.22_L1.21, H1.24_L1.21, H2_L1.21, H2.1_L1.21, H2.2_L1.21, H2.3_L1.21, H2.4_L1.21, H2.5_L1.21, H2.6_L1.21, H2.7_L1.21, H2.8_L1.21, H2.9_L1.21, H2.11_L1.21, H2.12_L1.21, H2.71_L1.21, H2.75_L1.21, H2.90_L1.21, H2.91_L1.21, H2.118_L1.2, H2.119_L1.21, H1_L1.22, H1.1_L1.22, H1.2_L1.22, H1.3_L1.22, H1.4_L1.22, H1.5_L1.22, H1.6_L1.22, H1.7_L1.22, H1.8_L1.22, H1.9_L1.22, H1.19_L1.22, H1.22_L1.22, H1.24_L1.22, H2_L1.22, H2.1_L1.22, H2.2_L1.22, H2.3_L1.22, H2.4_L1.22, H2.5_L1.22, H2.6_L1.22, H2.7_L1.22, H2.8_L1.22, H2.9_L1.22, H2.11_L1.22, H2.12_L1.22, H2.71_L1.22, H2.75_L1.22, H2.90_L1.22, H2.91_L1.22, H2.118_L1.22, H2.119_L1.22, H1_L1.23, H1.1_L1.23, H1.2_L1.23, H1.3_L1.23, H1.4_L1.23, H1.5_L1.23, H1.6_L1.23, H1.7_L1.23, H1.8_L1.23, H1.9_L1.23, H1.19_L1.23, H1.22_L1.23, H1.24_L1.23, H2_L1.23, H2.1_L1.23, H2.2_L1.23, H2.3_L1.23, H2.4_L1.23, H2.5_L1.23, H2.6_L1.23, H2.7_L1.23, H2.8_L1.23, H2.9_L1.23, H2.11_L1.23, H2.12_L1.23, H2.71_L1.23, H2.75_L1.23, H2.90_L1.23, H2.91_L1.23, H2.118_L1.23, H2.119_L1.23, H1_L1.27, H1.1_L1.27, H1.2_L1.27, H1.3_L1.27, H1.4_L1.27, H1.5_L1.27, H1.6_L1.27, H1.7_L1.27, H1.8_L1.27, H1.9_L1.27, H1.19_L1.27, H1.22_L1.27, H1.24_L1.27, H2_L1.27, H2.1_L1.27, H2.2_L1.27, H2.3_L1.27, H2.4_L1.27, H2.5_L1.27, H2.6_L1.27, H2.7_L1.27, H2.8_L1.27, H2.9_L1.27, H2.11_L1.27, H2.12_L1.27, H2.71_L1.27, H2.75_L1.27, H2.90_L1.27, H2.91_L1.27, H2.118_L1.27,

H2.119_L1.27, H1_L1.60, H1.1_L1.60, H1.2_L1.60, H1.3_L1.60, H1.4_L1.60, H1.5_L1.60, H1.6_L1.60, H1.7_L1.60, H1.8_L1.60, H1.9_L1.60, H1.19_L1.60, H1.22_L1.60, H1.24_L1.60, H2_L1.60, H2.1_L1.60, H2.2_L1.60, H2.3_L1.60, H2.4_L1.60, H2.5_L1.60, H2.6_L1.60, H2.7_L1.60, H2.8_L1.60, H2.9_L1.60, H2.11_L1.60, H2.12_L1.60, H2.71_L1.60, H2.75_L1.60, H2.90_L1.60, H2.91_L1.60, H2.118_L1.60, H2.119_L1.60, H1_L1.107, H1.1_L1.107, H1.2_L1.107, H1.3_L1.107, H1.4_L1.107, H1.5_L1.107, H1.6_L1.107, H1.7_L1.107, H1.8_L1.107, H1.9_L1.107, H1.19_L1.107, H1.22_L1.107, H1.24_L1.107, H2_L1.107, H2.1_L1.107, H2.2_L1.107, H2.3_L1.107, H2.4_L1.107, H2.5_L1.107, H2.6_L1.107, H2.7_L1.107, H2.8_L1.107, H2.9_L1.107, H2.11_L1.107, H2.12_L1.107, H2.71_L1.107, H2.75_L1.107, H2.90_L1.107, H2.91_L1.107, H2.118_L1.107, H2.119_L1.107, H1_L1.114, H1.1_L1.114, H1.2_L1.114, H1.3_L1.114, H1.4_L1.114, H1.5_L1.114, H1.6_L1.114, H1.7_L1.114, H1.8_L1.114, H1.9_L1.114, H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114, H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114, H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114, H2.90_L1.114, H2.91_L1.114, H2.118_L1.114, H2.119_L1.114, H1_L1.187, H1.1_L1.187, H1.2_L1.187, H1.3_L1.187, H1.4_L1.187, H1.5_L1.187, H1.6_L1.187, H1.7_L1.187, H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187, H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187, H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187, H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187, H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189, H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189, H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189, H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189, H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189, H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2, H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2.

6. An expression vector composition comprising:

- a) a first expression vector comprising the first nucleic acid of claim 5; and

b) a second expression vector comprising the second nucleic acid of claim 5, respectively.

7. An expression vector comprising the first and the second nucleic acid of claim 5.

8. A host cell comprising the expression vector composition of claim 6 or the expression vector of claim 7.

9. A method of making a CLDN6 ABD comprising culturing the host cell of claim 8 under conditions wherein the ABD is expressed and recovering the ABD.

10. A heterodimeric antibody comprising:

a) a first monomer comprising:

i) an anti-CD3 scFv comprising a first variable light domain, an scFv linker and a first variable heavy domain; and

ii) a first Fc domain, wherein the scFv is covalently attached to the N-terminus of the first Fc domain using a domain linker;

b) a second monomer comprising a VH2-CH1-hinge-CH2-CH3 monomer, wherein VH is a second variable heavy domain and CH2-CH3 is a second Fc domain; and

c) a light chain comprising a second variable light domain,

wherein the second variable heavy domain and the second variable light domain form a CLDN6 antigen binding domain (ABD).

11. A heterodimeric antibody according to claim 10, wherein the CLDN6 binding domain comprises a set of 6 CDRs (vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2 and vlCDR3) from a variable heavy domain/variable light domain pair selected from the group consisting of: H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1, H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1, H2.12_L1, H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1, H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1, H1.9_L1.1, H1.19_L1.1, H1.22_L1.1, H1.24_L1.1, H2_L1.1, H2.1_L1.1, H2.2_L1.1, H2.3_L1.1, H2.4_L1.1, H2.5_L1.1, H2.6_L1.1, H2.7_L1.1, H2.8_L1.1, H2.9_L1.1,

H2.11_L1.1, H2.12_L1.1, H2.71_L1.1, H2.75_L1.1, H2.90_L1.1, H2.91_L1.1,
H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4, H1.2_L1.4, H1.3_L1.4, H1.4_L1.4,
H1.5_L1.4, H1.6_L1.4, H1.7_L1.4, H1.8_L1.4, H1.9_L1.4, H1.19_L1.4, H1.22_L1.4,
H1.24_L1.4, H2_L1.4, H2.1_L1.4, H2.2_L1.4, H2.3_L1.4, H2.4_L1.4, H2.5_L1.4,
H2.6_L1.4, H2.7_L1.4, H2.8_L1.4, H2.9_L1.4, H2.11_L1.4, H2.12_L1.4, H2.71_L1.4,
H2.75_L1.4, H2.90_L1.4, H2.91_L1.4, H2.118_L1.4, H2.119_L1.4, H1_L1.7, H1.1_L1.7,
H1.2_L1.7, H1.3_L1.7, H1.4_L1.7, H1.5_L1.7, H1.6_L1.7, H1.7_L1.7, H1.8_L1.7,
H1.9_L1.7, H1.19_L1.7, H1.22_L1.7, H1.24_L1.7, H2_L1.7, H2.1_L1.7, H2.2_L1.7,
H2.3_L1.7, H2.4_L1.7, H2.5_L1.7, H2.6_L1.7, H2.7_L1.7, H2.8_L1.7, H2.9_L1.7,
H2.11_L1.7, H2.12_L1.7, H2.71_L1.7, H2.75_L1.7, H2.90_L1.7, H2.91_L1.7,
H2.118_L1.7, H2.119_L1.7, H1_L1.16, H1.1_L1.16, H1.2_L1.16, H1.3_L1.16, H1.4_L1.16,
H1.5_L1.16, H1.6_L1.16, H1.7_L1.16, H1.8_L1.16, H1.9_L1.16, H1.19_L1.16,
H1.22_L1.16, H1.24_L1.16, H2_L1.16, H2.1_L1.16, H2.2_L1.16, H2.3_L1.16, H2.4_L1.16,
H2.5_L1.16, H2.6_L1.16, H2.7_L1.16, H2.8_L1.16, H2.9_L1.16, H2.11_L1.16,
H2.12_L1.16, H2.71_L1.16, H2.75_L1.16, H2.90_L1.16, H2.91_L1.16, H2.118_L1.16,
H2.119_L1.16, H1_L1.18, H1.1_L1.18, H1.2_L1.18, H1.3_L1.18, H1.4_L1.18, H1.5_L1.18,
H1.6_L1.18, H1.7_L1.18, H1.8_L1.18, H1.9_L1.18, H1.19_L1.18, H1.22_L1.18,
H1.24_L1.18, H2_L1.18, H2.1_L1.18, H2.2_L1.18, H2.3_L1.18, H2.4_L1.18, H2.5_L1.18,
H2.6_L1.18, H2.7_L1.18, H2.8_L1.18, H2.9_L1.18, H2.11_L1.18, H2.12_L1.18,
H2.71_L1.18, H2.75_L1.18, H2.90_L1.18, H2.91_L1.18, H2.118_L1.18, H2.119_L1.18,
H1_L1.19, H1.1_L1.19, H1.2_L1.19, H1.3_L1.19, H1.4_L1.19, H1.5_L1.19,
H1.6_L1.19, H1.7_L1.19, H1.8_L1.19, H1.9_L1.19, H1.19_L1.19, H1.22_L1.19,
H1.24_L1.19, H2_L1.19, H2.1_L1.19, H2.2_L1.19, H2.3_L1.19, H2.4_L1.19, H2.5_L1.19,
H2.6_L1.19, H2.7_L1.19, H2.8_L1.19, H2.9_L1.19, H2.11_L1.19, H2.12_L1.19,
H2.71_L1.19, H2.75_L1.19, H2.90_L1.19, H2.91_L1.19, H2.118_L1.19, H2.119_L1.19,
H1_L1.21, H1.1_L1.21, H1.2_L1.21, H1.3_L1.21, H1.4_L1.21, H1.5_L1.21, H1.6_L1.21,
H1.7_L1.21, H1.8_L1.21, H1.9_L1.21, H1.19_L1.21, H1.22_L1.21, H1.24_L1.21,
H2_L1.21, H2.1_L1.21, H2.2_L1.21, H2.3_L1.21, H2.4_L1.21, H2.5_L1.21, H2.6_L1.21,
H2.7_L1.21, H2.8_L1.21, H2.9_L1.21, H2.11_L1.21, H2.12_L1.21, H2.71_L1.21,
H2.75_L1.21, H2.90_L1.21, H2.91_L1.21, H2.118_L1.21, H2.119_L1.21, H1_L1.22,
H1.1_L1.22, H1.2_L1.22, H1.3_L1.22, H1.4_L1.22, H1.5_L1.22, H1.6_L1.22, H1.7_L1.22,
H1.8_L1.22, H1.9_L1.22, H1.19_L1.22, H1.22_L1.22, H1.24_L1.22, H2_L1.22,
H2.1_L1.22, H2.2_L1.22, H2.3_L1.22, H2.4_L1.22, H2.5_L1.22, H2.6_L1.22, H2.7_L1.22,

H2.8_L1.22, H2.9_L1.22, H2.11_L1.22, H2.12_L1.22, H2.71_L1.22, H2.75_L1.22,
H2.90_L1.22, H2.91_L1.22, H2.118_L1.22, H2.119_L1.22, H1_L1.23, H1.1_L1.23,
H1.2_L1.23, H1.3_L1.23, H1.4_L1.23, H1.5_L1.23, H1.6_L1.23, H1.7_L1.23, H1.8_L1.23,
H1.9_L1.23, H1.19_L1.23, H1.22_L1.23, H1.24_L1.23, H2_L1.23, H2.1_L1.23,
H2.2_L1.23, H2.3_L1.23, H2.4_L1.23, H2.5_L1.23, H2.6_L1.23, H2.7_L1.23, H2.8_L1.23,
H2.9_L1.23, H2.11_L1.23, H2.12_L1.23, H2.71_L1.23, H2.75_L1.23, H2.90_L1.23,
H2.91_L1.23, H2.118_L1.23, H2.119_L1.23, H1_L1.27, H1.1_L1.27, H1.2_L1.27,
H1.3_L1.27, H1.4_L1.27, H1.5_L1.27, H1.6_L1.27, H1.7_L1.27, H1.8_L1.27, H1.9_L1.27,
H1.19_L1.27, H1.22_L1.27, H1.24_L1.27, H2_L1.27, H2.1_L1.27, H2.2_L1.27,
H2.3_L1.27, H2.4_L1.27, H2.5_L1.27, H2.6_L1.27, H2.7_L1.27, H2.8_L1.27, H2.9_L1.27,
H2.11_L1.27, H2.12_L1.27, H2.71_L1.27, H2.75_L1.27, H2.90_L1.27, H2.91_L1.27,
H2.118_L1.27, H2.119_L1.27, H1_L1.60, H1.1_L1.60, H1.2_L1.60, H1.3_L1.60,
H1.4_L1.60, H1.5_L1.60, H1.6_L1.60, H1.7_L1.60, H1.8_L1.60, H1.9_L1.60, H1.19_L1.60,
H1.22_L1.60, H1.24_L1.60, H2_L1.60, H2.1_L1.60, H2.2_L1.60, H2.3_L1.60, H2.4_L1.60,
H2.5_L1.60, H2.6_L1.60, H2.7_L1.60, H2.8_L1.60, H2.9_L1.60, H2.11_L1.60,
H2.12_L1.60, H2.71_L1.60, H2.75_L1.60, H2.90_L1.60, H2.91_L1.60, H2.118_L1.60,
H2.119_L1.60, H1_L1.107, H1.1_L1.107, H1.2_L1.107, H1.3_L1.107, H1.4_L1.107,
H1.5_L1.107, H1.6_L1.107, H1.7_L1.107, H1.8_L1.107, H1.9_L1.107, H1.19_L1.107,
H1.22_L1.107, H1.24_L1.107, H2_L1.107, H2.1_L1.107, H2.2_L1.107, H2.3_L1.107,
H2.4_L1.107, H2.5_L1.107, H2.6_L1.107, H2.7_L1.107, H2.8_L1.107, H2.9_L1.107,
H2.11_L1.107, H2.12_L1.107, H2.71_L1.107, H2.75_L1.107, H2.90_L1.107,
H2.91_L1.107, H2.118_L1.107, H2.119_L1.107, H1_L1.114, H1.1_L1.114, H1.2_L1.114,
H1.3_L1.114, H1.4_L1.114, H1.5_L1.114, H1.6_L1.114, H1.7_L1.114, H1.8_L1.114,
H1.9_L1.114, H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114,
H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114,
H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114,
H2.90_L1.114, H2.91_L1.114, H2.118_L1.114, H2.119_L1.114, H1_L1.187, H1.1_L1.187,
H1.2_L1.187, H1.3_L1.187, H1.4_L1.187, H1.5_L1.187, H1.6_L1.187, H1.7_L1.187,
H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187,
H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187,
H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187,
H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187,
H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189,

H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189, H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189, H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189, H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189, H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2, H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2.

12. A heterodimeric antibody according to claim 10 or 11, wherein the CLDN6 binding domain comprises a VH/VL pair selected from the group consisting of: H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1, H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1, H2.12_L1, H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1, H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1, H1.9_L1.1, H1.19_L1.1, H1.22_L1.1, H1.24_L1.1, H2_L1.1, H2.1_L1.1, H2.2_L1.1, H2.3_L1.1, H2.4_L1.1, H2.5_L1.1, H2.6_L1.1, H2.7_L1.1, H2.8_L1.1, H2.9_L1.1, H2.11_L1.1, H2.12_L1.1, H2.71_L1.1, H2.75_L1.1, H2.90_L1.1, H2.91_L1.1, H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4, H1.2_L1.4, H1.3_L1.4, H1.4_L1.4, H1.5_L1.4, H1.6_L1.4, H1.7_L1.4, H1.8_L1.4, H1.9_L1.4, H1.19_L1.4, H1.22_L1.4, H1.24_L1.4, H2_L1.4, H2.1_L1.4, H2.2_L1.4, H2.3_L1.4, H2.4_L1.4, H2.5_L1.4, H2.6_L1.4, H2.7_L1.4, H2.8_L1.4, H2.9_L1.4, H2.11_L1.4, H2.12_L1.4, H2.71_L1.4, H2.75_L1.4, H2.90_L1.4, H2.91_L1.4, H2.118_L1.4, H2.119_L1.4, H1_L1.7, H1.1_L1.7, H1.2_L1.7, H1.3_L1.7, H1.4_L1.7, H1.5_L1.7, H1.6_L1.7, H1.7_L1.7, H1.8_L1.7, H1.9_L1.7, H1.19_L1.7, H1.22_L1.7, H1.24_L1.7, H2_L1.7, H2.1_L1.7, H2.2_L1.7, H2.3_L1.7, H2.4_L1.7, H2.5_L1.7, H2.6_L1.7, H2.7_L1.7, H2.8_L1.7, H2.9_L1.7, H2.11_L1.7, H2.12_L1.7, H2.71_L1.7, H2.75_L1.7, H2.90_L1.7, H2.91_L1.7, H2.118_L1.7, H2.119_L1.7, H1_L1.16, H1.1_L1.16, H1.2_L1.16, H1.3_L1.16, H1.4_L1.16, H1.5_L1.16, H1.6_L1.16, H1.7_L1.16, H1.8_L1.16, H1.9_L1.16, H1.19_L1.16, H1.22_L1.16, H1.24_L1.16, H2_L1.16, H2.1_L1.16, H2.2_L1.16, H2.3_L1.16, H2.4_L1.16, H2.5_L1.16, H2.6_L1.16, H2.7_L1.16, H2.8_L1.16, H2.9_L1.16, H2.11_L1.16, H2.12_L1.16, H2.71_L1.16, H2.75_L1.16, H2.90_L1.16, H2.91_L1.16, H2.118_L1.16, H2.119_L1.16, H1_L1.18, H1.1_L1.18,

H1.2_L1.18, H1.3_L1.18, H1.4_L1.18, H1.5_L1.18, H1.6_L1.18, H1.7_L1.18, H1.8_L1.18, H1.9_L1.18, H1.19_L1.18, H1.22_L1.18, H1.24_L1.18, H2_L1.18, H2.1_L1.18, H2.2_L1.18, H2.3_L1.18, H2.4_L1.18, H2.5_L1.18, H2.6_L1.18, H2.7_L1.18, H2.8_L1.18, H2.9_L1.18, H2.11_L1.18, H2.12_L1.18, H2.71_L1.18, H2.75_L1.18, H2.90_L1.18, H2.91_L1.18, H2.118_L1.18, H2.119_L1.18, H1_L1.19, H1.1_L1.19, H1.2_L1.19, H1.3_L1.19, H1.4_L1.19, H1.5_L1.19, H1.6_L1.19, H1.7_L1.19, H1.8_L1.19, H1.9_L1.19, H1.19_L1.19, H1.22_L1.19, H1.24_L1.19, H2_L1.19, H2.1_L1.19, H2.2_L1.19, H2.3_L1.19, H2.4_L1.19, H2.5_L1.19, H2.6_L1.19, H2.7_L1.19, H2.8_L1.19, H2.9_L1.19, H2.11_L1.19, H2.12_L1.19, H2.71_L1.19, H2.75_L1.19, H2.90_L1.19, H2.91_L1.19, H2.118_L1.19, H2.119_L1.19, H1_L1.21, H1.1_L1.21, H1.2_L1.21, H1.3_L1.21, H1.4_L1.21, H1.5_L1.21, H1.6_L1.21, H1.7_L1.21, H1.8_L1.21, H1.9_L1.21, H1.19_L1.21, H1.22_L1.21, H1.24_L1.21, H2_L1.21, H2.1_L1.21, H2.2_L1.21, H2.3_L1.21, H2.4_L1.21, H2.5_L1.21, H2.6_L1.21, H2.7_L1.21, H2.8_L1.21, H2.9_L1.21, H2.11_L1.21, H2.12_L1.21, H2.71_L1.21, H2.75_L1.21, H2.90_L1.21, H2.91_L1.21, H2.118_L1.2, H2.119_L1.21, H1_L1.22, H1.1_L1.22, H1.2_L1.22, H1.3_L1.22, H1.4_L1.22, H1.5_L1.22, H1.6_L1.22, H1.7_L1.22, H1.8_L1.22, H1.9_L1.22, H1.19_L1.22, H1.22_L1.22, H1.24_L1.22, H2_L1.22, H2.1_L1.22, H2.2_L1.22, H2.3_L1.22, H2.4_L1.22, H2.5_L1.22, H2.6_L1.22, H2.7_L1.22, H2.8_L1.22, H2.9_L1.22, H2.11_L1.22, H2.12_L1.22, H2.71_L1.22, H2.75_L1.22, H2.90_L1.22, H2.91_L1.22, H2.118_L1.22, H2.119_L1.22, H1_L1.23, H1.1_L1.23, H1.2_L1.23, H1.3_L1.23, H1.4_L1.23, H1.5_L1.23, H1.6_L1.23, H1.7_L1.23, H1.8_L1.23, H1.9_L1.23, H1.19_L1.23, H1.22_L1.23, H1.24_L1.23, H2_L1.23, H2.1_L1.23, H2.2_L1.23, H2.3_L1.23, H2.4_L1.23, H2.5_L1.23, H2.6_L1.23, H2.7_L1.23, H2.8_L1.23, H2.9_L1.23, H2.11_L1.23, H2.12_L1.23, H2.71_L1.23, H2.75_L1.23, H2.90_L1.23, H2.91_L1.23, H2.118_L1.23, H2.119_L1.23, H1_L1.27, H1.1_L1.27, H1.2_L1.27, H1.3_L1.27, H1.4_L1.27, H1.5_L1.27, H1.6_L1.27, H1.7_L1.27, H1.8_L1.27, H1.9_L1.27, H1.19_L1.27, H1.22_L1.27, H1.24_L1.27, H2_L1.27, H2.1_L1.27, H2.2_L1.27, H2.3_L1.27, H2.4_L1.27, H2.5_L1.27, H2.6_L1.27, H2.7_L1.27, H2.8_L1.27, H2.9_L1.27, H2.11_L1.27, H2.12_L1.27, H2.71_L1.27, H2.75_L1.27, H2.90_L1.27, H2.91_L1.27, H2.118_L1.27, H2.119_L1.27, H1_L1.60, H1.1_L1.60, H1.2_L1.60, H1.3_L1.60, H1.4_L1.60, H1.5_L1.60, H1.6_L1.60, H1.7_L1.60, H1.8_L1.60, H1.9_L1.60, H1.19_L1.60, H1.22_L1.60, H1.24_L1.60, H2_L1.60, H2.1_L1.60, H2.2_L1.60, H2.3_L1.60, H2.4_L1.60, H2.5_L1.60, H2.6_L1.60, H2.7_L1.60, H2.8_L1.60, H2.9_L1.60, H2.11_L1.60, H2.12_L1.60, H2.71_L1.60, H2.75_L1.60, H2.90_L1.60,

H2.91_L1.60, H2.118_L1.60, H2.119_L1.60, H1_L1.107, H1.1_L1.107, H1.2_L1.107, H1.3_L1.107, H1.4_L1.107, H1.5_L1.107, H1.6_L1.107, H1.7_L1.107, H1.8_L1.107, H1.9_L1.107, H1.19_L1.107, H1.22_L1.107, H1.24_L1.107, H2_L1.107, H2.1_L1.107, H2.2_L1.107, H2.3_L1.107, H2.4_L1.107, H2.5_L1.107, H2.6_L1.107, H2.7_L1.107, H2.8_L1.107, H2.9_L1.107, H2.11_L1.107, H2.12_L1.107, H2.71_L1.107, H2.75_L1.107, H2.90_L1.107, H2.91_L1.107, H2.118_L1.107, H2.119_L1.107, H1_L1.114, H1.1_L1.114, H1.2_L1.114, H1.3_L1.114, H1.4_L1.114, H1.5_L1.114, H1.6_L1.114, H1.7_L1.114, H1.8_L1.114, H1.9_L1.114, H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114, H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114, H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114, H2.90_L1.114, H2.91_L1.114, H2.118_L1.114, H2.119_L1.114, H1_L1.187, H1.1_L1.187, H1.2_L1.187, H1.3_L1.187, H1.4_L1.187, H1.5_L1.187, H1.6_L1.187, H1.7_L1.187, H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187, H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187, H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187, H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187, H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189, H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189, H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189, H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189, H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189, H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2, H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2.

13. A heterodimeric antibody according to claim 10 or 11 wherein the CLDN6 binding domain comprises a VH/VL pair selected from the group consisting of: H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187.

14. A heterodimeric antibody according to any of claims 10 to 13, wherein the anti-CD3 scFv comprises a VH/VL pair selected from the group consisting of H1.30_L1.47,

H1.32_L1.47, H1.89_L1.47, H1.90_L1.47, H1.33_L1.47, H1.31_L1.47, L1.47_H1.30, L1.47_H1.30, L1.47_H1.32, L1.47_H1.89, L1.47_H1.90, L1.47_H1.33, and L1.47_H1.31.

15. A heterodimeric antibody according to any one of claims 10 to 15, wherein the scFv linker is a charged scFv linker.

16. A heterodimeric antibody according to any one of claims 10 to 16, wherein the first and second Fc domains are variant Fc domains.

17. A heterodimeric antibody according to claim 16, wherein the first and second Fc domains comprise a set of heterodimerization variants selected from the group consisting of those depicted in Figures 1A-1E.

18. A heterodimeric antibody according to claim 17, wherein the set of heterodimerization variants selected is from the group consisting of S364K/E357Q : L368D/K370S; S364K : L368D/K370S; S364K : L368E/K370S; D401K: T411E/K360E/Q362E; and T366W : T366S/L368A/Y407V, wherein numbering is according to EU numbering.

19. A heterodimeric antibody according to claims 17 or 18, wherein the first and second monomers further comprise one or more ablation variants.

20. A heterodimeric antibody according to claim 19, wherein the one or more ablation variants are E233P/L234V/L235A/G236del/S267K, wherein numbering is according to EU numbering.

21. A heterodimeric antibody according to any of claims 10 to 20, wherein one of the first or second monomer comprises one or more pI variants.

22. A heterodimeric antibody according to claim 21, wherein the one or more pI variants are N208D/Q295E/N384D/Q418E/N421D, wherein numbering is according to EU numbering.

23. A heterodimeric antibody according to any of claims 10 to 22, wherein the first monomer comprises amino acid variants S364K/E357Q/ E233P/L234V/L235A/G236del/S267K,

wherein the second monomer comprises amino acid variants L368D/K370S/N208D/Q295E/N384D/Q418E/N421D/E233P/L234V/L235A/G236del/S267K, and wherein numbering is according to EU numbering.

24. A heterodimeric antibody according to claim 23, wherein the first and second monomers each further comprise amino acid variants 428/434S, wherein numbering is according to EU numbering.

25. A heterodimeric antibody comprising:

- a) a first monomer comprising, from N-terminal to C-terminal, a scFv-linker-CH2-CH3,
wherein scFv is an anti-CD3 scFv and CH2-CH3 is a first Fc domain;
- b) a second monomer comprising, from N-terminal to C-terminal, a VH-CH1-hinge-CH2-CH3, wherein CH2-CH3 is a second Fc domain; and
- c) a light chain comprising VL-CL;
wherein the first variant Fc domain comprises amino acid variants S364K/E357Q,
wherein the second variant Fc domain comprises amino acid variants L368D/K370S,
wherein the first and second variant Fc domains each comprises amino acid variants E233P/L234V/L235A/G236del/S267K,
wherein the CH1-hinge-CH2-CH3 of the second monomer comprises amino acid variants N208D/Q295E/N384D/Q418E/N421D,
wherein the VH and VL form an CLDN6 binding domain comprising the variable heavy domain and the variable light domain, respectively, of an CLDN6 binding domain selected from H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187;
wherein the anti-CD3 scFv comprises the variable heavy domain and the variable light domain of a CD3 binding domain selected from H1.30_L1.47, H1.32_L1.47, H1.89_L1.47, H1.90_L1.47, H1.33_L1.47, H1.31_L1.47, L1.47_H1.30, L1.47_H1.30, L1.47_H1.32, L1.47_H1.89, L1.47_H1.90, L1.47_H1.33, and L1.47_H1.31, and
wherein numbering is according to EU numbering.

26. A heterodimeric antibody according to 25, wherein the first and second variant Fc domains each further comprise amino acid variants 428/434S, wherein numbering is according to EU numbering.
27. A nucleic acid composition comprising:
- a) a first nucleic acid encoding the first monomer of any of claims 10 to 26;
 - b) a second nucleic acid encoding the second monomer of any of claims 10 to 26; and
 - c) a third nucleic acid encoding the light chain of any of claims 10 to 26, respectively.
28. An expression vector composition comprising:
- a) a first expression vector comprising the first nucleic acid of claim 27;
 - b) a second expression vector comprising the second nucleic acid of claim 27; and
 - c) a third expression vector comprising the third nucleic acid of claim 27.
29. A host cell transformed with the expression vector composition of claim 28.
30. A method of making a heterodimeric antibody comprising culturing the host cell of claim 29 under conditions wherein the antibody is expressed and recovering the antibody.
31. A heterodimeric antibody comprising:
- a) a first monomer comprising, from N-terminal to C-terminal, a VH1-CH1-linker 1-scFv-linker 2-CH2-CH3,
wherein VH1 is a first variable heavy domain, scFv is an anti-CD3 scFv, linker 1 and linker 2 are a first domain linker and second domain linker, respectively, and CH2-CH3 is a first Fc domain;
 - b) a second monomer comprising, from N-terminal to C-terminal, a VH2-CH1-hinge-CH2-CH3, wherein VH2 is a second variable heavy domain and CH2-CH3 is a second Fc domain; and
 - c) a common light chain comprising a variable light domain;
wherein the first variable heavy domain and the variable light domain form a first CLDN6 ABD, and the second variable heavy domain and the variable light domain form a second CLDN6 ABD.

32. A heterodimeric antibody according to claim 31, wherein the first and second CLDN6 binding domains each comprise a set of 6 CDRs (vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2 and vlCDR3) from a VH/VL pair selected from the group consisting of: H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1, H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1, H2.12_L1, H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1, H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1, H1.9_L1.1, H1.19_L1.1, H1.22_L1.1, H1.24_L1.1, H2_L1.1, H2.1_L1.1, H2.2_L1.1, H2.3_L1.1, H2.4_L1.1, H2.5_L1.1, H2.6_L1.1, H2.7_L1.1, H2.8_L1.1, H2.9_L1.1, H2.11_L1.1, H2.12_L1.1, H2.71_L1.1, H2.75_L1.1, H2.90_L1.1, H2.91_L1.1, H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4, H1.2_L1.4, H1.3_L1.4, H1.4_L1.4, H1.5_L1.4, H1.6_L1.4, H1.7_L1.4, H1.8_L1.4, H1.9_L1.4, H1.19_L1.4, H1.22_L1.4, H1.24_L1.4, H2_L1.4, H2.1_L1.4, H2.2_L1.4, H2.3_L1.4, H2.4_L1.4, H2.5_L1.4, H2.6_L1.4, H2.7_L1.4, H2.8_L1.4, H2.9_L1.4, H2.11_L1.4, H2.12_L1.4, H2.71_L1.4, H2.75_L1.4, H2.90_L1.4, H2.91_L1.4, H2.118_L1.4, H2.119_L1.4, H1_L1.7, H1.1_L1.7, H1.2_L1.7, H1.3_L1.7, H1.4_L1.7, H1.5_L1.7, H1.6_L1.7, H1.7_L1.7, H1.8_L1.7, H1.9_L1.7, H1.19_L1.7, H1.22_L1.7, H1.24_L1.7, H2_L1.7, H2.1_L1.7, H2.2_L1.7, H2.3_L1.7, H2.4_L1.7, H2.5_L1.7, H2.6_L1.7, H2.7_L1.7, H2.8_L1.7, H2.9_L1.7, H2.11_L1.7, H2.12_L1.7, H2.71_L1.7, H2.75_L1.7, H2.90_L1.7, H2.91_L1.7, H2.118_L1.7, H2.119_L1.7, H1_L1.16, H1.1_L1.16, H1.2_L1.16, H1.3_L1.16, H1.4_L1.16, H1.5_L1.16, H1.6_L1.16, H1.7_L1.16, H1.8_L1.16, H1.9_L1.16, H1.19_L1.16, H1.22_L1.16, H1.24_L1.16, H2_L1.16, H2.1_L1.16, H2.2_L1.16, H2.3_L1.16, H2.4_L1.16, H2.5_L1.16, H2.6_L1.16, H2.7_L1.16, H2.8_L1.16, H2.9_L1.16, H2.11_L1.16, H2.12_L1.16, H2.71_L1.16, H2.75_L1.16, H2.90_L1.16, H2.91_L1.16, H2.118_L1.16, H2.119_L1.16, H1_L1.18, H1.1_L1.18, H1.2_L1.18, H1.3_L1.18, H1.4_L1.18, H1.5_L1.18, H1.6_L1.18, H1.7_L1.18, H1.8_L1.18, H1.9_L1.18, H1.19_L1.18, H1.22_L1.18, H1.24_L1.18, H2_L1.18, H2.1_L1.18, H2.2_L1.18, H2.3_L1.18, H2.4_L1.18, H2.5_L1.18, H2.6_L1.18, H2.7_L1.18, H2.8_L1.18, H2.9_L1.18, H2.11_L1.18, H2.12_L1.18, H2.71_L1.18, H2.75_L1.18, H2.90_L1.18, H2.91_L1.18, H2.118_L1.18, H2.119_L1.18, H1_L1.19, H1.1_L1.19, H1.2_L1.19, H1.3_L1.19, H1.4_L1.19, H1.5_L1.19, H1.6_L1.19, H1.7_L1.19, H1.8_L1.19, H1.9_L1.19, H1.19_L1.19, H1.22_L1.19, H1.24_L1.19, H2_L1.19, H2.1_L1.19, H2.2_L1.19, H2.3_L1.19, H2.4_L1.19, H2.5_L1.19, H2.6_L1.19,

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H1.1_L1.21, H1.2_L1.21, H1.3_L1.21, H1.4_L1.21, H1.5_L1.21, H1.6_L1.21, H1.7_L1.21,
H1.8_L1.21, H1.9_L1.21, H1.19_L1.21, H1.22_L1.21, H1.24_L1.21, H2_L1.21,
H2.1_L1.21, H2.2_L1.21, H2.3_L1.21, H2.4_L1.21, H2.5_L1.21, H2.6_L1.21, H2.7_L1.21,
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H2.90_L1.21, H2.91_L1.21, H2.118_L1.2, H2.119_L1.21, H1_L1.22, H1.1_L1.22,
H1.2_L1.22, H1.3_L1.22, H1.4_L1.22, H1.5_L1.22, H1.6_L1.22, H1.7_L1.22, H1.8_L1.22,
H1.9_L1.22, H1.19_L1.22, H1.22_L1.22, H1.24_L1.22, H2_L1.22, H2.1_L1.22,
H2.2_L1.22, H2.3_L1.22, H2.4_L1.22, H2.5_L1.22, H2.6_L1.22, H2.7_L1.22, H2.8_L1.22,
H2.9_L1.22, H2.11_L1.22, H2.12_L1.22, H2.71_L1.22, H2.75_L1.22, H2.90_L1.22,
H2.91_L1.22, H2.118_L1.22, H2.119_L1.22, H1_L1.23, H1.1_L1.23, H1.2_L1.23,
H1.3_L1.23, H1.4_L1.23, H1.5_L1.23, H1.6_L1.23, H1.7_L1.23, H1.8_L1.23, H1.9_L1.23,
H1.19_L1.23, H1.22_L1.23, H1.24_L1.23, H2_L1.23, H2.1_L1.23, H2.2_L1.23,
H2.3_L1.23, H2.4_L1.23, H2.5_L1.23, H2.6_L1.23, H2.7_L1.23, H2.8_L1.23, H2.9_L1.23,
H2.11_L1.23, H2.12_L1.23, H2.71_L1.23, H2.75_L1.23, H2.90_L1.23, H2.91_L1.23,
H2.118_L1.23, H2.119_L1.23, H1_L1.27, H1.1_L1.27, H1.2_L1.27, H1.3_L1.27,
H1.4_L1.27, H1.5_L1.27, H1.6_L1.27, H1.7_L1.27, H1.8_L1.27, H1.9_L1.27, H1.19_L1.27,
H1.22_L1.27, H1.24_L1.27, H2_L1.27, H2.1_L1.27, H2.2_L1.27, H2.3_L1.27, H2.4_L1.27,
H2.5_L1.27, H2.6_L1.27, H2.7_L1.27, H2.8_L1.27, H2.9_L1.27, H2.11_L1.27,
H2.12_L1.27, H2.71_L1.27, H2.75_L1.27, H2.90_L1.27, H2.91_L1.27, H2.118_L1.27,
H2.119_L1.27, H1_L1.60, H1.1_L1.60, H1.2_L1.60, H1.3_L1.60, H1.4_L1.60, H1.5_L1.60,
H1.6_L1.60, H1.7_L1.60, H1.8_L1.60, H1.9_L1.60, H1.19_L1.60, H1.22_L1.60,
H1.24_L1.60, H2_L1.60, H2.1_L1.60, H2.2_L1.60, H2.3_L1.60, H2.4_L1.60, H2.5_L1.60,
H2.6_L1.60, H2.7_L1.60, H2.8_L1.60, H2.9_L1.60, H2.11_L1.60, H2.12_L1.60,
H2.71_L1.60, H2.75_L1.60, H2.90_L1.60, H2.91_L1.60, H2.118_L1.60, H2.119_L1.60,
H1_L1.107, H1.1_L1.107, H1.2_L1.107, H1.3_L1.107, H1.4_L1.107, H1.5_L1.107,
H1.6_L1.107, H1.7_L1.107, H1.8_L1.107, H1.9_L1.107, H1.19_L1.107, H1.22_L1.107,
H1.24_L1.107, H2_L1.107, H2.1_L1.107, H2.2_L1.107, H2.3_L1.107, H2.4_L1.107,
H2.5_L1.107, H2.6_L1.107, H2.7_L1.107, H2.8_L1.107, H2.9_L1.107, H2.11_L1.107,
H2.12_L1.107, H2.71_L1.107, H2.75_L1.107, H2.90_L1.107, H2.91_L1.107,
H2.118_L1.107, H2.119_L1.107, H1_L1.114, H1.1_L1.114, H1.2_L1.114, H1.3_L1.114,
H1.4_L1.114, H1.5_L1.114, H1.6_L1.114, H1.7_L1.114, H1.8_L1.114, H1.9_L1.114,

H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114, H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114, H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114, H2.90_L1.114, H2.91_L1.114, H2.118_L1.114, H2.119_L1.114, H1_L1.187, H1.1_L1.187, H1.2_L1.187, H1.3_L1.187, H1.4_L1.187, H1.5_L1.187, H1.6_L1.187, H1.7_L1.187, H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187, H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187, H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187, H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187, H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189, H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189, H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189, H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189, H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189, H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2, H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2.

33. A heterodimeric antibody according to claim 31 or 32, wherein each of the first and second CLDN6 binding domains comprises a VH/VL pair selected from the group consisting of: H1_L1, H1.1_L1, H1.2_L1, H1.3_L1, H1.4_L1, H1.5_L1, H1.6_L1, H1.7_L1, H1.8_L1, H1.9_L1, H1.19_L1, H1.22_L1, H1.24_L1, H2_L1, H2.1_L1, H2.2_L1, H2.3_L1, H2.4_L1, H2.5_L1, H2.6_L1, H2.7_L1, H2.8_L1, H2.9_L1, H2.11_L1, H2.12_L1, H2.71_L1, H2.75_L1, H2.90_L1, H2.91_L1, H2.118_L1, H2.119_L1, H1_L1.1, H1.1_L1.1, H1.2_L1.1, H1.3_L1.1, H1.4_L1.1, H1.5_L1.1, H1.6_L1.1, H1.7_L1.1, H1.8_L1.1, H1.9_L1.1, H1.19_L1.1, H1.22_L1.1, H1.24_L1.1, H2_L1.1, H2.1_L1.1, H2.2_L1.1, H2.3_L1.1, H2.4_L1.1, H2.5_L1.1, H2.6_L1.1, H2.7_L1.1, H2.8_L1.1, H2.9_L1.1, H2.11_L1.1, H2.12_L1.1, H2.71_L1.1, H2.75_L1.1, H2.90_L1.1, H2.91_L1.1, H2.118_L1.1, H2.119_L1.1, H1_L1.4, H1.1_L1.4, H1.2_L1.4, H1.3_L1.4, H1.4_L1.4, H1.5_L1.4, H1.6_L1.4, H1.7_L1.4, H1.8_L1.4, H1.9_L1.4, H1.19_L1.4, H1.22_L1.4, H1.24_L1.4, H2_L1.4, H2.1_L1.4, H2.2_L1.4, H2.3_L1.4, H2.4_L1.4, H2.5_L1.4, H2.6_L1.4, H2.7_L1.4, H2.8_L1.4, H2.9_L1.4, H2.11_L1.4, H2.12_L1.4, H2.71_L1.4,

H2.75_L1.4, H2.90_L1.4, H2.91_L1.4, H2.118_L1.4, H2.119_L1.4, H1_L1.7, H1.1_L1.7, H1.2_L1.7, H1.3_L1.7, H1.4_L1.7, H1.5_L1.7, H1.6_L1.7, H1.7_L1.7, H1.8_L1.7, H1.9_L1.7, H1.19_L1.7, H1.22_L1.7, H1.24_L1.7, H2_L1.7, H2.1_L1.7, H2.2_L1.7, H2.3_L1.7, H2.4_L1.7, H2.5_L1.7, H2.6_L1.7, H2.7_L1.7, H2.8_L1.7, H2.9_L1.7, H2.11_L1.7, H2.12_L1.7, H2.71_L1.7, H2.75_L1.7, H2.90_L1.7, H2.91_L1.7, H2.118_L1.7, H2.119_L1.7, H1_L1.16, H1.1_L1.16, H1.2_L1.16, H1.3_L1.16, H1.4_L1.16, H1.5_L1.16, H1.6_L1.16, H1.7_L1.16, H1.8_L1.16, H1.9_L1.16, H1.19_L1.16, H1.22_L1.16, H1.24_L1.16, H2_L1.16, H2.1_L1.16, H2.2_L1.16, H2.3_L1.16, H2.4_L1.16, H2.5_L1.16, H2.6_L1.16, H2.7_L1.16, H2.8_L1.16, H2.9_L1.16, H2.11_L1.16, H2.12_L1.16, H2.71_L1.16, H2.75_L1.16, H2.90_L1.16, H2.91_L1.16, H2.118_L1.16, H2.119_L1.16, H1_L1.18, H1.1_L1.18, H1.2_L1.18, H1.3_L1.18, H1.4_L1.18, H1.5_L1.18, H1.6_L1.18, H1.7_L1.18, H1.8_L1.18, H1.9_L1.18, H1.19_L1.18, H1.22_L1.18, H1.24_L1.18, H2_L1.18, H2.1_L1.18, H2.2_L1.18, H2.3_L1.18, H2.4_L1.18, H2.5_L1.18, H2.6_L1.18, H2.7_L1.18, H2.8_L1.18, H2.9_L1.18, H2.11_L1.18, H2.12_L1.18, H2.71_L1.18, H2.75_L1.18, H2.90_L1.18, H2.91_L1.18, H2.118_L1.18, H2.119_L1.18, H1_L1.19, H1.1_L1.19, H1.2_L1.19, H1.3_L1.19, H1.4_L1.19, H1.5_L1.19, H1.6_L1.19, H1.7_L1.19, H1.8_L1.19, H1.9_L1.19, H1.19_L1.19, H1.22_L1.19, H1.24_L1.19, H2_L1.19, H2.1_L1.19, H2.2_L1.19, H2.3_L1.19, H2.4_L1.19, H2.5_L1.19, H2.6_L1.19, H2.7_L1.19, H2.8_L1.19, H2.9_L1.19, H2.11_L1.19, H2.12_L1.19, H2.71_L1.19, H2.75_L1.19, H2.90_L1.19, H2.91_L1.19, H2.118_L1.19, H2.119_L1.19, H1_L1.21, H1.1_L1.21, H1.2_L1.21, H1.3_L1.21, H1.4_L1.21, H1.5_L1.21, H1.6_L1.21, H1.7_L1.21, H1.8_L1.21, H1.9_L1.21, H1.19_L1.21, H1.22_L1.21, H1.24_L1.21, H2_L1.21, H2.1_L1.21, H2.2_L1.21, H2.3_L1.21, H2.4_L1.21, H2.5_L1.21, H2.6_L1.21, H2.7_L1.21, H2.8_L1.21, H2.9_L1.21, H2.11_L1.21, H2.12_L1.21, H2.71_L1.21, H2.75_L1.21, H2.90_L1.21, H2.91_L1.21, H2.118_L1.2, H2.119_L1.21, H1_L1.22, H1.1_L1.22, H1.2_L1.22, H1.3_L1.22, H1.4_L1.22, H1.5_L1.22, H1.6_L1.22, H1.7_L1.22, H1.8_L1.22, H1.9_L1.22, H1.19_L1.22, H1.22_L1.22, H1.24_L1.22, H2_L1.22, H2.1_L1.22, H2.2_L1.22, H2.3_L1.22, H2.4_L1.22, H2.5_L1.22, H2.6_L1.22, H2.7_L1.22, H2.8_L1.22, H2.9_L1.22, H2.11_L1.22, H2.12_L1.22, H2.71_L1.22, H2.75_L1.22, H2.90_L1.22, H2.91_L1.22, H2.118_L1.22, H2.119_L1.22, H1_L1.23, H1.1_L1.23, H1.2_L1.23, H1.3_L1.23, H1.4_L1.23, H1.5_L1.23, H1.6_L1.23, H1.7_L1.23, H1.8_L1.23, H1.9_L1.23, H1.19_L1.23, H1.22_L1.23, H1.24_L1.23, H2_L1.23, H2.1_L1.23, H2.2_L1.23, H2.3_L1.23, H2.4_L1.23, H2.5_L1.23, H2.6_L1.23, H2.7_L1.23, H2.8_L1.23,

H2.9_L1.23, H2.11_L1.23, H2.12_L1.23, H2.71_L1.23, H2.75_L1.23, H2.90_L1.23,
H2.91_L1.23, H2.118_L1.23, H2.119_L1.23, H1_L1.27, H1.1_L1.27, H1.2_L1.27,
H1.3_L1.27, H1.4_L1.27, H1.5_L1.27, H1.6_L1.27, H1.7_L1.27, H1.8_L1.27, H1.9_L1.27,
H1.19_L1.27, H1.22_L1.27, H1.24_L1.27, H2_L1.27, H2.1_L1.27, H2.2_L1.27,
H2.3_L1.27, H2.4_L1.27, H2.5_L1.27, H2.6_L1.27, H2.7_L1.27, H2.8_L1.27, H2.9_L1.27,
H2.11_L1.27, H2.12_L1.27, H2.71_L1.27, H2.75_L1.27, H2.90_L1.27, H2.91_L1.27,
H2.118_L1.27, H2.119_L1.27, H1_L1.60, H1.1_L1.60, H1.2_L1.60, H1.3_L1.60,
H1.4_L1.60, H1.5_L1.60, H1.6_L1.60, H1.7_L1.60, H1.8_L1.60, H1.9_L1.60, H1.19_L1.60,
H1.22_L1.60, H1.24_L1.60, H2_L1.60, H2.1_L1.60, H2.2_L1.60, H2.3_L1.60, H2.4_L1.60,
H2.5_L1.60, H2.6_L1.60, H2.7_L1.60, H2.8_L1.60, H2.9_L1.60, H2.11_L1.60,
H2.12_L1.60, H2.71_L1.60, H2.75_L1.60, H2.90_L1.60, H2.91_L1.60, H2.118_L1.60,
H2.119_L1.60, H1_L1.107, H1.1_L1.107, H1.2_L1.107, H1.3_L1.107, H1.4_L1.107,
H1.5_L1.107, H1.6_L1.107, H1.7_L1.107, H1.8_L1.107, H1.9_L1.107, H1.19_L1.107,
H1.22_L1.107, H1.24_L1.107, H2_L1.107, H2.1_L1.107, H2.2_L1.107, H2.3_L1.107,
H2.4_L1.107, H2.5_L1.107, H2.6_L1.107, H2.7_L1.107, H2.8_L1.107, H2.9_L1.107,
H2.11_L1.107, H2.12_L1.107, H2.71_L1.107, H2.75_L1.107, H2.90_L1.107,
H2.91_L1.107, H2.118_L1.107, H2.119_L1.107, H1_L1.114, H1.1_L1.114, H1.2_L1.114,
H1.3_L1.114, H1.4_L1.114, H1.5_L1.114, H1.6_L1.114, H1.7_L1.114, H1.8_L1.114,
H1.9_L1.114, H1.19_L1.114, H1.22_L1.114, H1.24_L1.114, H2_L1.114, H2.1_L1.114,
H2.2_L1.114, H2.3_L1.114, H2.4_L1.114, H2.5_L1.114, H2.6_L1.114, H2.7_L1.114,
H2.8_L1.114, H2.9_L1.114, H2.11_L1.114, H2.12_L1.114, H2.71_L1.114, H2.75_L1.114,
H2.90_L1.114, H2.91_L1.114, H2.118_L1.114, H2.119_L1.114, H1_L1.187, H1.1_L1.187,
H1.2_L1.187, H1.3_L1.187, H1.4_L1.187, H1.5_L1.187, H1.6_L1.187, H1.7_L1.187,
H1.8_L1.187, H1.9_L1.187, H1.19_L1.187, H1.22_L1.187, H1.24_L1.187, H2_L1.187,
H2.1_L1.187, H2.2_L1.187, H2.3_L1.187, H2.4_L1.187, H2.5_L1.187, H2.6_L1.187,
H2.7_L1.187, H2.8_L1.187, H2.9_L1.187, H2.11_L1.187, H2.12_L1.187, H2.71_L1.187,
H2.75_L1.187, H2.90_L1.187, H2.91_L1.187, H2.118_L1.187, H2.119_L1.187,
H1_L1.189, H1.1_L1.189, H1.2_L1.189, H1.3_L1.189, H1.4_L1.189, H1.5_L1.189,
H1.6_L1.189, H1.7_L1.189, H1.8_L1.189, H1.9_L1.189, H1.19_L1.189, H1.22_L1.189,
H1.24_L1.189, H2_L1.189, H2.1_L1.189, H2.2_L1.189, H2.3_L1.189, H2.4_L1.189,
H2.5_L1.189, H2.6_L1.189, H2.7_L1.189, H2.8_L1.189, H2.9_L1.189, H2.11_L1.189,
H2.12_L1.189, H2.71_L1.189, H2.75_L1.189, H2.90_L1.189, H2.91_L1.189,
H2.118_L1.189, H2.119_L1.189, H1_L2, H1.1_L2, H1.2_L2, H1.3_L2, H1.4_L2, H1.5_L2,

H1.6_L2, H1.7_L2, H1.8_L2, H1.9_L2, H1.19_L2, H1.22_L2, H1.24_L2, H2_L2, H2.1_L2, H2.2_L2, H2.3_L2, H2.4_L2, H2.5_L2, H2.6_L2, H2.7_L2, H2.8_L2, H2.9_L2, H2.11_L2, H2.12_L2, H2.71_L2, H2.75_L2, H2.90_L2, H2.91_L2, H2.118_L2 and H2.119_L2.

34. A heterodimeric antibody according to any one of claims 31 to 33, wherein the VH/VL pairs are selected from the group consisting of H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and H1.9_L1.187.

35. A heterodimeric antibody according to any of claims 31 to 34, wherein the scFv comprises has a set of 6 CDRs (vhCDR1, vhCDR2, vhCDR3, vlCDR1, vlCDR2 and vlCDR3) from VH/VL pairs selected from the group consisting of: H1.30_L1.47, H1.32_L1.47, H1.89_L1.47, H1.90_L1.47, H1.33_L1.47, H1.31_L1.47, L1.47_H1.30, L1.47_H1.30, L1.47_H1.32, L1.47_H1.89, L1.47_H1.90, L1.47_H1.33, and L1.47_H1.31.

36. A heterodimeric antibody according to claim 35, wherein the scFv comprises the variable heavy domain and variable light domain of any of the following CD3 binding domains: H1.30_L1.47, H1.32_L1.47, H1.89_L1.47, H1.90_L1.47, H1.33_L1.47, H1.31_L1.47, L1.47_H1.30, L1.47_H1.30, L1.47_H1.32, L1.47_H1.89, L1.47_H1.90, L1.47_H1.33, and L1.47_H1.31.

37. A heterodimeric antibody according to any one of claims 31 to 36, wherein the first and second Fc domains are variant Fc domains.

38. A heterodimeric antibody according to any of claims 31 to 37, wherein the first and second Fc domains comprise a set of heterodimerization variants selected from the group consisting of those depicted in Figures 1A-1E.

39. A heterodimeric antibody according to claim 38, wherein the set of heterodimerization variants selected is from the group consisting of S364K/E357Q : L368D/K370S; S364K : L368D/K370S; S364K : L368E/K370S; D401K: T411E/K360E/Q362E; and T366W : T366S/L368A/Y407V, wherein numbering is according to EU numbering.

40. A heterodimeric antibody according to any of claims 31 to 39, wherein the first and second monomers further comprise one or more ablation variants.

41. A heterodimeric antibody according to claim 40, wherein one or more ablation variants are E233P/L234V/L235A/G236del/S267K, wherein numbering is according to EU numbering.
42. A heterodimeric antibody according to any of claims 31 to 41, wherein one of the first or second monomer further comprises one or more pI variants.
43. A heterodimeric antibody according to claim 42, wherein the pI variants are N208D/Q295E/N384D/Q418E/N421D, wherein numbering is according to EU numbering.
44. A heterodimeric antibody according to any one of claims 31 to 43, wherein the first variant Fc domain comprises amino acid variants S364K/E357Q/E233P/L234V/L235A/G236del/S267K,
wherein the second variant Fc domain comprises amino acid variants L368D/K370S/N208D/Q295E/N384D/Q418E/N421D/E233P/L234V/L235A/G236del/S267K, and wherein numbering is according to EU numbering.
45. A heterodimeric antibody according to claim 44, wherein the scFv linker is a charged scFv linker having the amino acid sequence (GKPGS)₄ (SEQ ID NO: 1).
46. A heterodimeric antibody according to 45, wherein the first and second variant Fc domains each further comprise amino acid variants 428/434S, wherein numbering is according to EU numbering.
47. A heterodimeric antibody comprising:
- a) a first monomer comprising, from N-terminal to C-terminal, a VH1-CH1-linker 1-scFv-linker 2-CH2-CH3,
wherein scFv is an anti-CD3 scFv and CH2-CH3 is a first Fc domain;
 - b) a second monomer comprising, from N-terminal to C-terminal, a VH1-CH1-hinge-CH2-CH3, wherein CH2-CH3 is a second Fc domain; and
 - c) a common light chain comprising VL-CL;
wherein the first variant Fc domain comprises amino acid variants S364K/E357Q,

wherein the second variant Fc domain comprises amino acid variants L368D/K370S,
wherein the first and second variant Fc domains each comprises amino acid variants
E233P/L234V/L235A/G236del/S267K,

wherein the CH1-hinge-CH2-CH3 of the second monomer comprises amino acid
variants N208D/Q295E/N384D/Q418E/N421D,

wherein the VH and VL comprise the variable heavy domain and the variable light
domain of a CLDN6 ABD selected from H1.9_L1.187, H1.24_L1.187, H2.91_L1.187 and
H1.9_L1.187;

wherein the anti-CD3 scFv comprises the variable heavy domain and the variable
light domain of a CD3 binding domain selected from H1.30_L1.47, H1.32_L1.47,
H1.89_L1.47, H1.90_L1.47, H1.33_L1.47, H1.31_L1.47, L1.47_H1.30, L1.47_H1.30,
L1.47_H1.32, L1.47_H1.89, L1.47_H1.90, L1.47_H1.33, and L1.47_H1.31, and

wherein numbering is according to EU numbering.

48. A heterodimeric antibody according to 47, wherein the first and second variant Fc
domains each further comprise amino acid variants 428/434S.

49. A nucleic acid composition comprising:

- a) a first nucleic acid encoding the first monomer of any of claims 31 to 48;
- b) a second nucleic acid encoding the second monomer of any of claims 31 to 48; and
- c) a third nucleic acid encoding the light chain of any of claims 31 to 48, respectively.

50. An expression vector composition comprising:

- a) a first expression vector comprising the first nucleic acid of claim 49;
- b) a second expression vector comprising the second nucleic acid of claim 49; and
- c) a third expression vector comprising the third nucleic acid of claim 49.

51. A host cell transformed with the expression vector composition of claim 50.

52. A method of making a heterodimeric antibody comprising culturing the host cell of claim
51 under conditions wherein the antibody is expressed and recovering the antibody.