

CLAIMS

~~What Is Claimed Is:~~

1. An anti-cluster of differentiation three (“CD3”) antibody and/or antigen-binding fragment comprising:
 - (a) a variable heavy (V_H) chain polypeptide comprising a V_H chain CDR3 (CDRH3) selected from the group consisting of:
 - i. AX₁DX₂X₃X₄X₅X₆X₇X₈DX₉, wherein X₁ is R or H, wherein X₂ is A, H, M, or Q, wherein X₃ is Y, H, S, G, A, T, V, or R; wherein X₄ is G, H, P, E, or R; wherein X₅ is H or R, wherein X₆ is Y, N, F, H, D, E, S, L, M, I, G, A, Q, or T; wherein X₇ is F or H; wherein X₈ is Y or H; wherein X₉ is V, H, or M; and, optionally, wherein at least one of X₁, X₂, X₃, X₄, X₅, X₆, X₇, X₈, and X₉ is H (SEQ ID NO: 58);
 - ii. ARDX₁X₂X₃X₄YFYDX₅, wherein X₁ is H or A, wherein X₂ is T, Y, or H, wherein X₃ is G or H, wherein X₄ is H, R, V, or I, wherein X₅ is V or H, and, optionally, wherein at least one of X₁, X₂, X₃, X₄, and X₅ is H (SEQ ID NO: 43); or
 - iii. AX₁DX₂YX₃HX₄FYDV, wherein X₁ is R or H, wherein X₂ is A or H, wherein X₃ is G, H, or P, wherein X₄ is Y, H, D, V, E, S, N, L, M, I, G, A, Q, or T, and, optionally, wherein at least one of X₁, X₂, X₃, and X₄ is H (SEQ ID NO: 1);
 - iv. ARDX₁YGX₂X₃X₄YDX₅ wherein X₁ is A or H, wherein X₂ is R or H, wherein X₃ is H or Y, wherein X₄ is F or H, wherein X₅ is H or V, and, optionally, wherein at least one of X₁, X₂, X₃, X₄, and X₅ is H (SEQ ID NO: 2);
 - v. ARDAHX₁X₂YX₃X₄DX₅, wherein X₁ is G, E, or R, wherein X₂ is R or H, wherein X₃ is F or H, wherein X₄ is Y or H, wherein X₅ is V or H, and, optionally, wherein at least one of X₁, X₂, X₃, X₄, and X₅ is H (SEQ ID NO: 3);
 - vi. ARDAX₁HRX₂FYDV, wherein X₁ is H, Y, S, G, A, T, V, or R, wherein X₂ is Y or H, and, optionally, wherein at least one of X₁ and X₂ is H (SEQ ID NO: 4);
 - vii. ARDX₁YHRYFYDX₂, wherein X₁ is H or A, wherein X₂ is H, V, or M, and, optionally, wherein at least one of X₁ and X₂ is H (SEQ ID NO: 5);

- viii. AX₁DAYX₂X₃X₄HX₅DV, wherein X₁ is R or H, wherein X₂ is G or H, wherein X₃ is H or R, wherein X₄ is N, F, or Y, wherein X₅ is Y or H, and, optionally, wherein at least one of X₁, X₂, X₃, X₄, and X₅ is H (SEQ ID NO: 6);
 - ix. ARDX₁X₂GRYFYDV, wherein X₁ is M, Q, or H, wherein X₂ is R or H, and, optionally, wherein at least one of X₁ and X₂ is H (SEQ ID NO: 7);
 - x. ARDX₁X₂X₃RYFYDX₄, wherein X₁ is H or A, wherein X₂ is T, Y, or H, wherein X₃ is G or H, wherein X₄ is V or H, and, optionally, wherein at least one of X₁, X₂, X₃, and X₄ is H (SEQ ID NO: 8);
 - xi. ARDAX₁X₂X₃X₄FYDX₅, wherein X₁ is T, H, or Y, wherein X₂ is G or H, wherein X₃ is H or R, wherein X₄ is V or Y, wherein X₅ is V or H, and wherein, optionally, at least one of X₁, X₂, X₃, and X₅ is H (SEQ ID NO: 593); and
 - xii. AX₁DX₂X₃X₄X₅X₆X₇YDX₈, wherein X₁ is R or H, wherein X₂ is H or A, wherein X₃ is H or Y, wherein X₄ is H, G, or P, wherein X₅ is R or H, wherein X₆ is Y, I, or V, wherein X₇ is F or H, wherein X₈ is V or H, and wherein, optionally, at least one of X₁, X₂, X₃, X₄, X₅, X₇, and X₈ is H (SEQ ID NO: 596).
- (b) a variable heavy (V_H) chain polypeptide comprising a V_H chain CDR2 (CDRH2) selected from the group consisting of:
- i. X₁IX₂X₃X₄X₅X₆X₇TX₈YSQKFQG, wherein X₁ is W, S, Y, F, G, or D, wherein X₂ is N, T, D, V, or H, wherein X₃ is A, P, or S, wherein X₄ is G, A, S, N, D, L, V, H, Q, T, I, or Y, wherein X₅ is D or T, wherein X₆ is A or G, wherein X₇ is A, N, T, S, L, D, F, Y, or E, wherein X₈ is V, K, T, D, Y, F, A, H, N, L, I, or E, and, optionally, wherein at least one of X₁, X₂, X₃, X₄, X₅, X₆, X₇, and X₈ is H (SEQ ID NO: 59);
 - ii. WIDLENANTIYDAKFQG (SEQ ID NO: 9);
 - iii. X₁INPX₂TGX₃TX₄YSQKFQG, wherein X₁ is W or Y, wherein X₂ is A, S, D, G, N, L, V, H, or Q, wherein X₃ is A, T, or S, and wherein X₄ is K, V, T, D, Y, F, or A (SEQ ID NO: 10);
 - iv. X₁IX₂AGTGX₃TX₄YSQKFQG, wherein X₁ is W, Y, or F, wherein X₂ is T, N,

- or D, wherein X_3 is A, T, or L, and wherein X_4 is A, K, V, H, T, or N (SEQ ID NO: 11);
- v. $X_1IDAGTGX_2TX_3YSQKFQG$, wherein X_1 is S or W, wherein X_2 is L, N, D, or F, and wherein X_3 is D, Y, or K (SEQ ID NO: 12);
 - vi. $X_1IX_2AGTGATX_3YSQKFQG$, wherein X_1 is G, D, or S, wherein X_2 is I or D, and wherein X_3 is K or D (SEQ ID NO: 13);
 - vii. $WINPX_1TGNTX_2YSQKFQG$, wherein X_1 is D, T, L, S, or A, and wherein X_2 is D, V, L, or N (SEQ ID NO: 14);
 - viii. $X_1INAGTGX_2TX_3YSQKFQG$, wherein X_1 is Y or W, wherein X_2 is N, D, or A, and wherein X_3 is I or V (SEQ ID NO: 15);
 - ix. $X_1INPX_2TGX_3TKYSQKFQG$, wherein X_1 is W or Y, wherein X_2 is D, I or Y, and wherein X_3 is D, Y, or E (SEQ ID NO: 16);
 - x. $SIX_1AGTGX_2TKYSQKFQG$, wherein X_1 is N or V, and wherein X_2 is A or I (SEQ ID NO: 17);
 - xi. $SINAGTGX_1TX_2YSQKFQG$, wherein X_1 is F or N, and wherein X_2 is Y or D (SEQ ID NO: 18);
 - xii. $X_1IX_2X_3GTGX_4TDYSQKFQG$, wherein X_1 is D or W, wherein X_2 is N or H, wherein X_3 is A or S, and wherein X_4 is A or N (SEQ ID NO: 19);
 - xiii. $WIDPX_1TGATX_2YSQKFQG$, wherein X_1 is N, H, or Y, and wherein X_2 is V or K (SEQ ID NO: 20);
 - xiv. $WIX_1PX_2TGNTKYSQKFQG$, wherein X_1 is D or N, and wherein X_2 is L, I, or V (SEQ ID NO: 21);
 - xv. $SINAGDANTKYSQKFQG$ (SEQ ID NO: 22);
 - xvi. $X_1IDPX_2TGATX_3YSQKFQG$, wherein X_1 is D or W, wherein X_2 is D or V, and wherein X_3 is E or D (SEQ ID NO: 23);
 - xvii. $WINAGDAATVYSQKFQG$ (SEQ ID NO: 24); and
 - xviii. $WIDAGTGX_1TX_2YSQKFQG$, wherein X_1 is L, F, N, or A and wherein X_2 is T or K (SEQ ID NO: 595).

- (c) a variable heavy (V_H) chain polypeptide comprising a V_H chain CDR1 (CDRH1) selected from the group consisting of:
- i. FNIKDYHMH (SEQ ID NO: 25);
 - ii. SNIKDYMH (SEQ ID NO: 26);
 - iii. SNIKDYHMH (SEQ ID NO: 27);
 - iv. YTFX₁X₂X₃X₄MH, wherein X₁ is A, K, D, Q, E, N, T, L, Y, S, P, G, H or V, wherein X₂ is T, S, or A, wherein X₃ is Y or I, and wherein X₄ is A, D, N, S, Y, T, I, V, L, E, P, R, or G (SEQ ID NO: 28);
 - v. YTFX₁X₂X₃X₄MH, wherein X₁ is T, D, A, N, or V, wherein X₂ is D, E, G, or Q, wherein X₃ is Y or D, and wherein X₄ is D, A, E, N, S, Y, or V (SEQ ID NO: 29);
 - vi. YTFTSX₁X₂MH, wherein X₁ is A, D, or T, and wherein X₂ is D, F, A, M, V, or Y (SEQ ID NO: 30);
 - vii. YTFX₁X₂YX₃MH, wherein X₁ is N or T, X₂ is Q or N, and X₃ is S, T, or A (SEQ ID NO: 31); and
 - viii. YTFX₁X₂YVMH, wherein X₁ is I or N, and wherein X₂ is K or R (SEQ ID NO: 32);
 - ix. FNIKDYMH (SEQ ID NO: 47); and
 - x. YTFX₁X₂YX₃MH, wherein X₁ is E, S, or T, wherein X₂ is S or D, and wherein X₃ is A or D (SEQ ID NO: 31).
- (d) a variable light (V_L) chain polypeptide comprising a V_L chain CDR3 (CDRL3) selected from the group consisting of:
- i. X₁X₂SX₃X₄X₅RX₆, wherein X₁ is H, K, or G, wherein X₂ is Q or H, wherein X₃ is Y or H, wherein X₄ is S, H, D, T, V, M, or L, wherein X₅ is R or H, wherein X₆ is T or H, and, optionally, wherein at least one of X₁, X₂, X₃, X₄, X₅, and X₆ is H (SEQ ID NO: 33);
 - ii. KQSYX₁X₂RT, wherein X₁ is H, V, K, W, R, L, G, Y, or Q, wherein X₂ is H, L, E, W, G, M, P, T, Q, or V, and, optionally, wherein at least one of X₁ and X₂ is H (SEQ ID NO: 34);

- iii. $X_1QSX_2HX_3RT$, wherein X_1 is K or H, wherein X_2 is H, Y, M, S, L, E, G, or W, wherein X_3 is R or K, and, optionally, wherein at least one of X_1 and X_2 is H (SEQ ID NO: 35);
 - iv. $KQSX_1X_2X_3RT$, wherein X_1 is Y or H, wherein X_2 is T, S, V, or K, wherein X_3 is R or H, and, optionally, wherein at least one of X_1 and X_3 is H (SEQ ID NO: 36);
 - v. $KQSX_1X_2X_3RT$, wherein X_1 is H or Y, wherein X_2 is T, S, or Q, wherein X_3 is R or H, and, optionally, wherein at least one of X_1 and X_3 is H (SEQ ID NO: 36); and
 - vi. $X_1QSX_2X_3X_4RT$, wherein X_1 is K or H, wherein X_2 is Y or H, wherein X_3 is S, H, L, V, or K, wherein X_4 is H, R, or E, and, optionally, wherein at least one of X_1 , X_2 , X_3 , and X_4 is H (SEQ ID NO: 598);
- (e) a variable light (V_L) chain polypeptide comprising a V_L chain CDR2 (CDRL2) of WASTRES (SEQ ID NO: 37); and/or
- (f) a variable light (V_L) chain polypeptide comprising a V_L chain CDR1 (CDRL1) selected from the group consisting of:
- i. $KSSQSLLX_1X_2X_3X_4GX_5NX_6LA$, wherein X_1 is N or H, wherein X_2 is A, R, or T, wherein X_3 is R or H, wherein X_4 is T, P, or E, wherein X_5 is H or K, wherein X_6 is H or Y, and, optionally, wherein at least one of X_1 , X_3 , X_5 , and X_6 is H (SEQ ID NO: 38);
 - ii. $KSSQSLLX_1AX_2THX_3NX_4LA$, wherein X_1 is N or H, wherein X_2 is R or H, wherein X_3 is K or H, wherein X_4 is Y or H, and, optionally, wherein at least one of X_1 , X_2 , X_3 , and X_4 is H (SEQ ID NO: 39);
 - iii. $KSSQSLLNASTAKNYLA$ (SEQ ID NO: 40);
 - iv. $KSSQSLLNARTRTNYLA$ (SEQ ID NO: 41);
 - v. $KSSQSLLNX_1X_2X_3GX_4NX_5LA$, wherein X_1 is S or A, wherein X_2 is R or H, wherein X_3 is E or T, wherein X_4 is H or K, wherein X_5 is H or Y, and, optionally, wherein at least one of X_2 , X_4 , and X_5 is H (SEQ ID NO: 42);
 - vi. $KSSQSLLNX_1X_2TGX_3NYLA$, wherein X_1 is A or S, wherein X_2 is R or H,

wherein X₃ is H or K, and, optionally, wherein at least one of X₂ and X₃ is H (SEQ ID NO: 594); and

vii. KSSQSLLX₁AX₂X₃X₄X₅NX₆LA, wherein X₁ is N or H, wherein X₂ is R or H, wherein X₃ is T or E, wherein X₄ is G or H, wherein X₅ is H or K, wherein X₆ is H or Y, and wherein, optionally, at least one of X₁, X₂, X₄, X₅, and X₆ is H (SEQ ID NO: 597); or

(g) an anti-CD3 antibody comprising the same CDRs or CD3 binding domain as:

i. ADI-48587, ADI-48576, ADI-48587, ADI-48592, ADI-48595, ADI-48635, ADI-48643, ADI-48645, ADI-48650, ADI-48652, and ADI-48666;

ii. ADI-48592, ADI-48595, ADI-48650, ADI-48652, ADI-48662, and ADI-48666;

iii. ADI-48587, ADI-48588, ADI-48577, ADI-48590, ADI-48581, ADI-48575, ADI-48593, ADI-48591, ADI-48647, ADI-48636, ADI-48586, ADI-48646, ADI-48638, ADI-48597, ADI-48601, ADI-48576, ADI-48643, ADI-48624, ADI-48632, ADI-48635, and ADI-48645;

iv. any of the anti-CD3 antibodies in Table 1 or an anti-CD3 antibody comprising the same CDRs as ADI-48587 or Ab36 in Table 1.

vii. —

2. The anti-CD3 antibody and/or antigen-binding fragment according to claim 1, comprising:
- (a) a CDRH3 comprising an amino acid sequence ARDX₁X₂X₃X₄YFYDX₅, wherein X₁ is H or A, wherein X₂ is T, Y, or H, wherein X₃ is G or H, X₄ is H, R, V, or I, wherein X₅ is V or H, and, optionally, wherein at least one of X₁, X₂, X₃, X₄, and X₅ is H (SEQ ID NO: 43);
 - (b) a CDRL3 comprising an amino acid sequence KQSX₁X₂X₃RT, wherein X₁ is Y or H, X₂ is T, S, V, or K, X₃ is R or H, and, optionally, wherein at least one of X₁ and X₃ is H (SEQ ID NO: 36); and/or
 - (c) a CDRL1 comprising an amino acid sequence KSSQSLLNX₁X₂X₃GX₄NX₅LA, wherein X₁ is S or A, wherein X₂ is R or H, wherein X₃ is E or T, wherein X₄ is H or

K, wherein X₅ is H or Y, and, optionally, wherein at least one of X₂, X₄, and X₅ is H (SEQ ID NO: 42).

3. The anti-CD3 antibody or antigen-binding fragment according to claim 1, comprising:
- (a) a CDRH3 comprising an amino acid sequence ARDAX₁X₂X₃X₄FYDX₅, wherein X₁ is T, H, or Y, wherein X₂ is G or H, wherein X₃ is H or R, wherein X₄ is V or Y, wherein X₅ is V or H, and wherein, optionally, at least one of X₁, X₂, X₃, and X₅ is H (SEQ ID NO: 593);
 - (b) a CDRH2 comprising an amino acid sequence WIDLENANTIYDAKFQG (SEQ ID NO: 9);
 - (c) a CDRH1 comprising an amino acid sequence FNIKDYMH (SEQ ID NO: 47);
 - (d) a CDRL3 comprising an amino acid sequence KQSX₁X₂X₃RT, wherein X₁ is H or Y, wherein X₂ is T, S, or Q, wherein X₃ is R or H, and, optionally, wherein at least one of X₁ and X₃ is H (SEQ ID NO: 36);
 - (e) a CDRL2 comprising an amino acid sequence WASTRES (SEQ ID NO: 37); and/or
 - (f) a CDRL1 comprising an amino acid sequence KSSQSLLNX₁X₂TGX₃NYLA, wherein X₁ is A or S, wherein X₂ is R or H, wherein X₃ is H or K, and, optionally, wherein at least one of X₂ and X₃ is H (SEQ ID NO: 594).
4. The anti-CD3 antibody or antigen-binding fragment according to claim 1, comprising:
- (a) a CDRH3 comprising an amino acid sequence AX₁DX₂X₃X₄X₅X₆X₇YDX₈, wherein X₁ is R or H, wherein X₂ is H or A, wherein X₃ is H or Y, wherein X₄ is H, G, or P, wherein X₅ is R or H, wherein X₆ is Y, I, or V, wherein X₇ is F or H, wherein X₈ is V or H, and wherein, optionally, at least one of X₁, X₂, X₃, X₄, X₅, X₇, and X₈ is H (SEQ ID NO: 596);
 - (b) a CDRH2 comprising an amino acid sequence selected from the group consisting of:
 - i. WIDLENANTIYDAKFQG (SEQ ID NO: 9); and
 - ii. WIDAGTGX₁TX₂YSQKFQG, wherein X₁ is L, F, N, or A and wherein X₂ is T or K (SEQ ID NO: 595);
 - (c) a CDRH1 comprising an amino acid sequence selected from the group consisting of:
 - i. FNIKDYMH (SEQ ID NO: 47); and
 - ii. YTFX₁X₂YX₃MH, wherein X₁ is E, S, or T, wherein X₂ is S or D, and wherein X₃ is A or D (SEQ ID NO: 31);

- (d) a CDRL3 comprising an amino acid sequence $X_1QSX_2X_3X_4RT$, wherein X_1 is K or H, wherein X_2 is Y or H, wherein X_3 is S, H, L, V, or K, wherein X_4 is H, R, or E, and, optionally, wherein at least one of X_1 , X_2 , X_3 , and X_4 is H (SEQ ID NO: 598);
 - (e) a CDRL2 comprising an amino acid sequence WASTRES (SEQ ID NO: 37); and/or
 - (f) a CDRL1 comprising an amino acid sequence $KSSQSLLX_1AX_2X_3X_4X_5NX_6LA$, wherein X_1 is N or H, wherein X_2 is R or H, wherein X_3 is T or E, wherein X_4 is G or H, wherein X_5 is H or K, wherein X_6 is H or Y, and wherein, optionally, at least one of X_1 , X_2 , X_4 , X_5 , and X_6 is H (SEQ ID NO: 597).
5. The anti-CD3 antibody or antigen-binding fragment according to any one of the foregoing claims, wherein:
- (a) said antibody or antigen-binding fragment elicits T cell activation or T cell killing while displaying a decreased propensity to elicit cytokine production to levels capable of inducing cytokine release syndrome;
 - (b) the antibody or antigen-binding fragment comprises a multispecific antibody;
 - (c) the antibody or antigen-binding fragment comprises a bispecific antibody;
 - (d) the antibody or antigen-binding fragment comprises an scFv;
 - (e) the antibody or antigen-binding fragment comprises at least a second antigen-binding domain that specifically binds to an oncology target; an immune-oncology target; a neurodegenerative disease targets; an autoimmune disorder target; an infectious disease target; a metabolic disease target; a cognitive disorder target; a blood-brain barrier target; or a blood disease target;
 - (f) the antibody or antigen-binding fragment comprises at least a second antigen-binding domain that specifically binds to an antigen selected from the group consisting of: 17-IA, 4-1BB, 4Dc, 6- keto-PGFla, 8-iso-PGF2a, 8-oxo-dG, A1 Adenosine Receptor, A33, ACE, ACE-2, Activin, Activin A, Activin AB, Activin B, Activin C, Activin RIA, Activin RIA ALK-2, Activin RIB ALK-4, Activin RIIA, Activin RUB, ADAM, ADAM10, ADAM12, ADAM 15, ADAM 17/T ACE, ADAM8, ADAM9, ADAMTS, ADAMTS4, ADAMTS5, Addressins, aFGF, ALCAM, ALK, ALK-1, ALK-7, alpha-I-antitrypsin, alpha-V/beta-1 antagonist, ANG, Ang, APAF-1, APE, APJ, APP, APRIL, AR, ARC, ART, Artemin, anti-Id, ASPARTIC, Atrial natriuretic factor, av/b3 integrin, Axl, b2M, B7-1, B7-2, B7-H, B-lymphocyte Stimulator (BlyS), BACE, BACE-1, Bad, BAFF, BAFF-R, Bag-1, BAK, Bax, BCA-1, BCAM, Bel, BCMA, BDNF, b-ECGF, bFGF, BID, Bik, BFM, BLC, BL-CAM, BLK, BMP,

BMP-2 BMP-2a, BMP-3 Osteogenin, BMP-4 BMP-2b, BMP-5, BMP-6 Vgr-1,
 BMP-7 (OP-1), BMP-8 (BMP-8a, OP-2), BMPR, BMPR-IA (ALK-3), BMPR-IB
 (ALK-6), BRK-2, RPK-1, BMPR-II (BRK-3), BMPs, b- NGF, BOK, Bombesin,
 Bone-derived neurotrophic factor, BPDE, BPDE-DNA, BTC, complement factor 3
 (C3), C3a, C4, C5, C5a, CIO, CA125, CAD-8, Calcitonin, cAMP, carcinoembryonic
 antigen (CEA), carcinoma-associated antigen, Cathepsin A, Cathepsin B, Cathepsin
 C/DPPI, Cathepsin D, Cathepsin E, Cathepsin H, Cathepsin L, Cathepsin O,
 Cathepsin S, Cathepsin V, Cathepsin X/Z/P, CBL, CCI, CCK2, CCL, CCL1, CCL11,
 CCL12, CCL13, CCL 14, CCL15, CCL16, CCL1 7, CCL18, CCL19, CCL2, CCL20,
 CCL21, CCL22, CCL23, CCL24, CCL25, CCL26, CCL27, CCL28, CCL3, CCL4,
 CCL5, CCL6, CCL7, CCL8, CCL9/10, CCR, CCR1, CCR10, CCR10, CCR2,
 CCR3, CCR4, CCR5, CCR6, CCR7, CCR8, CCR9, CD1, CD2, CD4, CD5, CD6,
 CD7, CD8, CD10, CD11a, CD11b, CD11c, CD13, CD14, CD15, CD16, CD18, CD19,
 CD20, CD21, CD22, CD23, CD25, CD27L, CD28, CD29, CD30, CD30L, CD32,
 CD33 (p67 proteins), CD34, CD38, CD40, CD40L, CD44, CD45, CD46, CD49a,
 CD52, CD54, CD55, CD56, CD61, CD64, CD66e, CD74, CD80 (B7-1), CD89,
 CD95, CD123, CD137, CD138, CD140a, CD146, CD147, CD148, CD152, CD164,
 CEACAM5, CFTR, cGMP, CINC, Clostridium botulinum toxin, Clostridium
 perfringens toxin, CKb8-l, CLC, CMV, CMV UL, CNTF, CNTN-1, COX, C-Ret,
 CRG-2, CT-1, CTACK, CTGF, CTLA-4, CX3CL1, CX3CR1, CXCL, CXCL1,
 CXCL2, CXCL3, CXCL4, CXCL5, CXCL6, CXCL7, CXCL8, CXCL9, CXCL10,
 CXCL11, CXCL12, CXCL13, CXCL14, CXCL15, CXCL16, CXCR, CXCR1,
 CXCR2, CXCR3, CXCR4, CXCR5, CXCR6, cytokeratin tumor-associated antigen,
 DAN, DCC, DcR3, DC-SIGN, Decay accelerating factor, des(1-3)-IGF-I (brain IGF-
 1), Dhh, digoxin, DNAM-1, Dnase, Dpp, DPPIV/CD26, Dtk, ECAD, EDA, EDA-
 A1, EDA-A2, EDAR, EGF, EGFR (ErbB-1), EMA, EMMPRIN, EN A, endothelin
 receptor, Enkephalinase, eNOS, Eot, eotaxinl, EpCAM, Ephrin B2/ EphB4, EPO,
 ERCC, E-selectin, ET-1, Factor IIa, Factor VII, Factor VIIIc, Factor IX, fibroblast
 activation protein (FAP), Fas, FcRI, FEN-1, Ferritin, FGF, FGF-19, FGF-2, FGF3,
 FGF-8, FGFR, FGFR-3, Fibrin, FL, FLIP, Flt-3, Flt-4, Follicle stimulating hormone,
 Fractalkine, FZD1, FZD2, FZD3, FZD4, FZD5, FZD6, FZD7, FZD8, FZD9, FZD10,
 G250, Gas 6, GCP-2, GCSF, GD2, GD3, GDF, GDF-1, GDF-3 (Vgr-2), GDF-5
 (BMP-14, CDMP- 1), GDF-6 (BMP-13, CDMP-2), GDF-7 (BMP-12, CDMP-3),
 GDF-8 (Myostatin), GDF-9, GDF- 15 (MIC-1), GDNF, GFAP, GFRa-1, GFR-

alphas, GFR-alpha2, GFR-alpha3, GPCR, Glucagon, Glut 4, glycoprotein IIb/IIIa (GP IIb/IIIa), GM-CSF, gp130, gp72, GRO, Growth hormone releasing factor, Hapten (NP-cap or NIP-cap), HB-EGF, HCC, HCMV gB envelope glycoprotein, HCMV gH envelope glycoprotein, HCMV UL, Hemopoietic growth factor (HGF), Hep B gp120, heparanase, Her2, Her2/neu (ErbB-2), Her3 (ErbB-3), Her4 (ErbB-4), herpes simplex virus (HSV) gB glycoprotein, HSV gD glycoprotein, HGFA, High molecular weight melanoma-associated antigen (HMW-MAA), HIV gp120, HIV IIIb gp 120 V3 loop, HLA, HLA-DR, HM1.24, HMFG PEM, HRG, Hrk, human cardiac myosin, human cytomegalovirus (HCMV), human growth hormone (HGH), HVEM, 1-309, IAP, ICAM, ICAM-1, ICAM-3, ICE, ICOS, IFNg, Ig, IgA receptor, IgE, IGF, IGF binding proteins, IGF-1R, IGFBP, IGF-I, IGF-II, IL, IL-1, IL-1R, IL-2, IL-2R, IL-4, IL-4R, IL-5, IL-5R, IL-6, IL-6R, IL-8, IL-9, IL-10, IL-12, IL-13, IL-15, IL-18, IL-18R, IL-23, interferon (INF)-alpha, INF-beta, INF-gamma, Inhibin, iNOS, Insulin A-chain, Insulin B-chain, Insulin-like growth factor 1, integrin alpha2, integrin alpha3, integrin alpha4, integrin alpha4/beta1, integrin alpha4/beta7, integrin alpha5 (alphaV), integrin alpha5/beta1, integrin alpha5/beta3, integrin alpha6, integrin beta1, integrin beta2, interferon gamma, IP-10, 1-TAC, JE, Kallikrein 2, Kallikrein 5, Kallikrein 6, Kallikrein 11, Kallikrein 12, Kallikrein 14, Kallikrein 15, Kallikrein LI, Kallikrein L2, Kallikrein L3, Kallikrein L4, KC, KDR, Keratinocyte Growth Factor (KGF), laminin 5, LAMP, LAP, LAP (TGF-1), Latent TGF-1, Latent TGF-1 bpl, LBP, LDGF, LECT2, Lefty, Lewis-Y antigen, Lewis-Y related antigen, LFA-1, LFA-3, Lf, LIF, LIGHT, lipoproteins, LIX, LKN, Lptn, L-Selectin, LT-a, LT-b, LTb4, LTBP-1, Lung surfactant, Luteinizing hormone, Lymphotoxin Beta Receptor, Mac-1, MAdCAM, MAG, MAP2, MARC, MCAM, MCAM, MCK-2, MCP, M-CSF, MDC, Mer, a metalloprotease, MGDF receptor, MGMT, MHC (HLA-DR), MIF, MIG, MIP, MIP-1-alpha, MK, MMAC1, MMP, MMP-1, MMP-10, MMP-11, MMP-12, MMP-13, MMP-14, MMP-15, MMP-2, MMP-24, MMP-3, MMP-7, MMP-8, MMP-9, MPIF, Mpo, MSK, MSP, mucin (Mucl), MUC18, Muellerian-inhibiting substance, Mug, MuSK, NAIP, NAP, NCAD, N-Cadherin, NCA 90, NCAM, NCAM, Neprilysin, Neurotrophin-3, -4, or -6, Neurturin, Neuronal growth factor (NGF), NGFR, NGF-beta, nNOS, NO, NOS, Npn, NRG-3, NT, NTN, OB, OGG1, OPG, OPN, OSM, OX40L, OX40R, pl50, p95, PADPr, Parathyroid hormone, PARC, PARP, PBR, PBSF, PCAD, P-Cadherin, PCNA, PDGF, PDGF, PDK-1, PECAM, PEM, PF4, PGE, PGF, PGI2, PGJ2, PIN, PLA2, placental alkaline

phosphatase (PLAP), PIGF, PLP, PP14, Proinsulin, Prorelaxin, Protein C, PS, PSA, PSCA, prostate specific membrane antigen (PSMA), PTEN, PTHrp, Ptk, PTN, R51, RANK, RANKL, RANTES, Relaxin A-chain, Relaxin B-chain, renin, respiratory syncytial virus (RSV) F, RSV Fgp, Ret, Rheumatoid factors, RLIP76, RPA2, RSK, S100, SCF/KL, SDF-1, SERINE, Serum albumin, sFRP-3, Shh, SIGIRR, SK-1, SLAM, SLPI, SMAC, SMDF, SMOH, SOD, SPARC, Stat, STEAP, STEAP-II, TACE, TACI, TAG-72 (tumor- associated glycoprotein-72), TARC, TCA-3, T-cell receptors (e.g., T-cell receptor alpha/beta), TdT, TECK, TEM1, TEM5, TEM7, TEM8, TERT, testicular PLAP-like alkaline phosphatase, Tfr, TGF, TGF-alpha, TGF-beta, TGF-beta Pan Specific, TGF-beta RI (ALK-5), TGF-beta RII, TGF-beta RIIb, TGF-beta RIII, TGF-beta1, TGF-beta2, TGF-beta3, TGF-beta4, TGF-beta5, Thrombin, Thymus Ck-1, Thyroid stimulating hormone, Tie, TIMP, TIQ, Tissue Factor, TMEFF2, Tmpo, TMPRSS2, TNF, TNF-alpha, TNF-alpha beta, TNF-beta2, TNFc, TNF-RI, TNF-RII, TNFRSF10A (TRAIL R1 Apo-2, DR4), TNFRSF10B (TRAIL R2 DR5, KILLER, TRICK-2A, TRICK-B), TNFRSF10C (TRAIL R3 DcR1, LIT, TRID), TNFRSF10D (TRAIL R4 DcR2, TRUND), TNFRSF11A (RANK ODF R, TRANCE R), TNFRSF11B (OPG OCIF, TR1), TNFRSF12 (TWEAK R FN14), TNFRSF13B (TACI), TNFRSF13C (BAFF R), TNFRSF14 (HVEM ATAR, HveA, LIGHT R, TR2), TNFRSF16 (NGFR p75NTR), TNFRSF17 (BCMA), TNFRSF 18 (GITR AITR), TNFRSF19 (TROY TAJ, TRADE), TNFRSF19L (RELT), TNFRSF1A (TNF RI CD120a, p55-60), TNFRSF1B (TNF RII CD120b, p75-80), TNFRSF26 (TNFRH3), TNFRSF3 (LTbR TNF RIII, TNFC R), TNFRSF4 (OX40 ACT35, TXGP1 R), TNFRSF 5 (CD40 p50), TNFRSF6 (Fas Apo-1, APT1, CD95), TNFRSF6B (DcR3 M68, TR6), TNFRSF7 (CD27), TNFRSF8 (CD30), TNFRSF9 (4-1BB CD137, ILA), TNFRSF21 (DR6), TNFRSF22 (DcTRAIL R2 TNFRH2), TNFRST23 (DcTRAIL R1 TNFRH1), TNFRSF25 (DR3 Apo-3, LARD, TR-3, TRAMP, WSL-1), TNFSF10 (TRAIL Apo-2 Ligand, TL2), TNFSF11 (TRANCE/RANK Ligand ODF, OPG Ligand), TNFSF12 (TWEAK Apo-3 Ligand, DR3 Ligand), TNFSF13 (APRIL TALL2), TNFSF13B (BAFF BLYS, TALL1, THANK, TNFSF20), TNFSF14 (LIGHT HVEM Ligand, LTg), TNFSF15 (TLIA/VEGI), TNFSF18 (GITR Ligand AITR Ligand, TL6), TNFSF1A (TNF-a Conectin, DIF, TNFSF2), TNFSF1B (TNF-b LTa, TNFSF1), TNFSF3 (LTb TNFC, p33), TNFSF4 (OX40 Ligand gp34, TXGP1), TNFSF5 (CD40 Ligand CD154, gp39, HIGM1, IMD3, TRAP), TNFSF6 (Fas Ligand Apo-1 Ligand, APT1 Ligand),

- TNFSF7 (CD27 Ligand CD70), TNFSF8 (CD30 Ligand CD153), TNFSF9 (4-1BB Ligand CD137 Ligand), TP-1, t-PA, Tpo, TRAIL, TRAIL R, TRAIL-R1, TRAIL-R2, TRANCE, transferring receptor, TRF, Trk, TROP-2, TSG, TSLP, tumor-associated antigen CA 125, tumor-associated antigen expressing Lewis Y related carbohydrate, TWEAK, TXB2, Ung, uPAR, uPAR-1, Urokinase, VCAM, VCAM-1, VECAD, VE-Cadherin, VE-cadherin-2, VEGFR-1 (flt-1), VEGF, VEGFR, VEGFR-3 (flt-4), VEGI, VFM, Viral antigens, VLA, VLA-1, VLA-4, VNR integrin, von Willebrands factor, WIF- 1, WNT1, WNT2, WNT2B/13, WNT3, WNT3A, WNT4, WNT5A, WNT5B, WNT6, WNT7A, WNT7B, WNT8A, WNT8B, WNT9A, WNT9A, WNT9B, WNT10A, WNT10B, WNT11, WNT16, XCL1, XCL2, XCR1, XCR1, XEDAR, XIAP, XPD, CTLA4 (cytotoxic T lymphocyte antigen-4), PD1 (programmed cell death protein 1), PD-L1 (programmed cell death ligand 1), LAG-3 (lymphocyte activation gene-3), TIM-3 (T cell immunoglobulin and mucin protein-3), hormone receptors and growth factors;
- (g) the antibody or antigen-binding fragment comprises at least a second antigen-binding domain that specifically binds to an antigen selected from the group consisting of: BCMA, CTLA4 (cytotoxic T lymphocyte antigen-4), PD1 (programmed cell death protein 1), PD-L1 (programmed cell death ligand 1), LAG-3 (lymphocyte activation gene-3), TIM-3, CD20, CD2, CD19, Her2, EGFR, EpCAM, FcγRIIIa (CD16), FcγRIIIa (CD32a), FcγRIIb (CD32b), FcγRI (CD64), Toll-like receptors (TLRs), TLR4, TLR9, cytokines, IL-2, IL-5, IL-13, IL-6, IL-17, IL-12, IL-23, TNFα, TGFβ, cytokine receptors, IL-2R, chemokines, chemokine receptors, growth factors, VEGF, and HGF;
 - (h) the antibody or antigen-binding fragment is comprised in a chimeric antigen receptor (CAR), which optionally comprises at least one transmembrane domain, and at least one intracellular domain from a T-cell receptor, optionally a CD3ζ subunit, and at least one co-stimulatory domain;
 - (i) the antibody or antigen-binding fragment comprises an scFv2-Fc2 and/or scFv-IgG;
 - (j) the antibody or antigen-binding fragment comprises an IgG constant domain; and/or
 - (k) the antibody or antigen-binding fragment comprises at least a second antigen-binding domain that specifically binds to an antigen, wherein said antibody comprises a multispecific format selected from the group consisting of: Fab-Fc-scFv, “bottle-opener”, Mab-scFv, Mab-Fv, Dual scFv, central Fv, central scFv, one-arm central

scFv, Fab-Fab, Fab-Fv, mAb-Fv, mAb-Fab, DART, BiTE, common light chain-IgG, TandAb, Cross-Mab, SEED, BEAT, TrioMab, and DuetMab.

6. The anti-CD3 antibody and/or antigen-binding fragment according to any of the foregoing claims, which binds to CD3 or CD3-expressing cells with a greater binding affinity at pH 6.0 than at pH 7.4.
7. An isolated or recombinant nucleic acid sequence encoding an antibody or antigen-binding fragment according to any one of the foregoing claims.
8. An expression vector comprising an isolated or recombinant nucleic acid sequence according to claim 7.
9. A host cell transfected, transformed, or transduced with a nucleic acid sequence according to claim 7, or an expression vector according to claim 8, wherein the host cell is optionally a mammalian cell or a yeast cell.
10. A pharmaceutical composition comprising an antibody or antigen-binding fragment according to any one of claims 1-6 or a host cell according to claim 9, and a pharmaceutically acceptable carrier and/or excipient.
11. ~~A method of treating a disorder in a mammal in need of such treatment, wherein the disorder comprises a proliferative disorder, an oncological disorder, an immuno-oncological disorder, a neurological disorder, a neurodegenerative disorder, or an autoimmune disorder, comprising administering an effective amount of at least~~ Use of at least one antibody or antigen-binding fragment according to any one of claims 1-6 or a host cell which expresses at least one of said antibody or antigen-binding fragment according to claim 9, optionally an immune cell, further optionally a T or NK cell in the manufacture of a medicament for the treatment of a proliferative disorder, an oncological disorder, an immuno-oncological disorder, a neurological disorder, a neurodegenerative disorder, or an autoimmune disorder in a mammal, wherein an effective amount of medicament is to be administered to the mammal.

12. ~~The method use~~ according to claim 11, wherein ~~the method further comprises administering to the mammal an additional therapeutic agent is to be administered with the medicament,~~ optionally wherein the mammal is a human.
- ~~12.~~13. The at least one antibody or antigen-binding fragment according to any one of claims 1-6 or a host cell which expresses at least one of said antibody or antigen-binding fragment according to claim 9, optionally an immune cell, further optionally a T or NK cell for use in the treatment of a proliferative disorder, an oncological disorder, an immuno-oncological disorder, a neurological disorder, a neurodegenerative disorder, or an autoimmune disorder in a mammal.