

CLAIMS

What Is Claimed Is:

1. An anti-cluster of differentiation three (“CD3”) antibody or antigen-binding antibody fragment, wherein said anti-CD3 antibody or antigen-binding antibody fragment comprises:
 - a. a variable heavy (V_H) chain polypeptide comprising:
 - i. a V_H CDR1 (CDRH1) of FNIKDYYMH (SEQ ID NO: 13);
 - ii. a V_H CDR2 (CDRH2) of WIDLENANTVYDAKFQG (SEQ ID NO: 15);
 - iii. a V_H CDR3 (CDRH3) of ARDAYGRYFYDV (SEQ ID NO: 103); and/or
 - b. a variable light (V_L) chain polypeptide comprising:
 - i. a V_L CDR1 (CDRL1) of KSSQSLLNARTGKNYLA (SEQ ID NO: 8);
 - ii. a V_L CDR2 (CDRL2) of WASTRX₁S (SEQ ID NO: 133); and
 - iii. a V_L CDR3 (CDRL3) of X₂QSYFRRT (SEQ ID NO: 134);wherein X₁ and X₂ are each independently any amino acid.
2. The anti-CD3 antibody or antigen-binding antibody fragment of claim 1, wherein:
 - a. X₁ is E or S; and/or
 - b. X₂ is K or V.
3. The anti-CD3 antibody or antigen-binding antibody fragment of claim 1 or claim 2, wherein said antibody or antigen-binding antibody fragment comprises:
 - a. a CDRL2 of SEQ ID NO: 10 or SEQ ID NO: 11; and/or
 - b. a CDRL3 of SEQ ID NO: 5 or SEQ ID NO: 4.

4. The anti-CD3 antibody or antigen-binding antibody fragment of any one of the foregoing claims, wherein said anti-CD3 antibody or antigen-binding antibody fragment is selected from the group consisting of:
 - a. one which comprises a V_H chain CDR1 (CDRH1) of FNIKDYYMH (SEQ ID NO: 13), a V_H chain CDR2 (CDRH2) of WIDLENANTVYDAKFQG (SEQ ID NO: 15), and a V_H chain CDR3 (CDRH3) of ARDAYGRYFYDV (SEQ ID NO: 103); and/or a V_L chain CDR1 (CDRL1) of KSSQSLLNARTGKNYLA (SEQ ID NO: 8), a V_L chain CDR2 (CDRL2) of WASTRES (SEQ ID NO: 10), and a V_L chain CDR3 (CDRL3) of KQSYFRRT (SEQ ID NO: 5); and
 - b. one which comprises a V_H chain CDR1 (CDRH1) of FNIKDYYMH (SEQ ID NO: 13), a V_H chain CDR2 (CDRH2) of WIDLENANTVYDAKFQG (SEQ ID NO: 15), and a V_H chain CDR3 (CDRH3) of ARDAYGRYFYDV (SEQ ID NO: 103); and/or a V_L chain CDR1 (CDRL1) of KSSQSLLNARTGKNYLA (SEQ ID NO: 8), a V_L chain CDR2 (CDRL2) of WASTRSS (SEQ ID NO: 11), and a V_L chain CDR3 (CDRL3) of VQSYFRRT (SEQ ID NO: 4).
5. The anti-CD3 antibody or antigen-binding antibody fragment of any one of the foregoing claims, wherein said anti-CD3 antibody or antigen-binding antibody fragment comprises:
 - a. a V_L chain polypeptide comprising an amino acid sequence that possesses at least 90% sequence identity to SEQ ID NO: 18 or SEQ ID NO: 34;
 - b. a V_L chain polypeptide comprising an amino acid sequence that possesses at least 95% sequence identity to SEQ ID NO: 18 or SEQ ID NO: 34;
 - c. a V_L chain polypeptide comprising the amino acid sequence of SEQ ID NO: 18 or SEQ ID NO: 34;
 - d. a V_H chain polypeptide comprising an amino acid sequence that possesses at least 90% sequence identity to SEQ ID NO: 17;

- e. a V_H chain polypeptide comprising an amino acid sequence that possesses at least 95% sequence identity to SEQ ID NO: 17; and/or
 - f. a V_H chain comprising the amino acid sequence of SEQ ID NO: 17.
6. The anti-CD3 antibody or antigen-binding antibody fragment of any one of the foregoing claims, wherein said anti-CD3 antibody or antigen-binding antibody fragment comprises:
- a. a V_L chain polypeptide comprising an amino acid sequence that possesses at least 90% sequence identity to SEQ ID NO: 18 or SEQ ID NO: 34; and a V_H chain polypeptide comprising an amino acid sequence that possesses at least 90% sequence identity to SEQ ID NO: 17;
 - b. a V_L chain polypeptide comprising an amino acid sequence that possesses at least 95% sequence identity to SEQ ID NO: 18 or SEQ ID NO: 34; and a V_H chain polypeptide comprising an amino acid sequence that possesses at least 95% sequence identity to SEQ ID NO: 17;
 - c. a V_L chain polypeptide comprising the amino acid sequence of SEQ ID NO: 18 or SEQ ID NO: 34; and a V_H chain comprising the amino acid sequence of SEQ ID NO: 17;
 - d. a V_L chain polypeptide comprising the amino acid sequence of SEQ ID NO: 18; and a V_H chain comprising the amino acid sequence of SEQ ID NO: 17; and/or
 - e. a V_L chain polypeptide comprising the amino acid sequence of SEQ ID NO: 34; and a V_H chain comprising the amino acid sequence of SEQ ID NO: 17.
7. The anti-CD3 antibody or antigen-binding antibody fragment of any one of the foregoing claims, wherein said anti-CD3 antibody or antigen-binding antibody fragment binds to CD3 with a dissociation constant (K_D) of about 500 pM or less, about 450 pM or less, about 400 pM or less, about 350 pM or less, about 300 pM or less, about 250 pM or less, about 200 pM or less, about 150 pM or less, or about 100 pM or less, optionally wherein said CD3 is human and/or cynomolgus,

further optionally wherein said binding affinity is measured by surface plasmon resonance.

8. The anti-CD3 antibody or antigen-binding antibody fragment of claim 7, wherein said K_D is a monovalent K_D and/or wherein said K_D is measured using an scFv fragment of said anti-CD3 antibody or antibody fragment.
9. The anti-CD3 antibody or antigen-binding antibody fragment according to any one of the foregoing claims, wherein:
 - a. said antibody or antigen-binding antibody 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 antibody fragment comprises a multispecific antibody;
 - c. the antibody or antigen-binding antibody fragment comprises a bispecific antibody;
 - d. the antibody or antigen-binding antibody fragment comprises an scFv;
 - e. the antibody or antigen-binding antibody 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 antibody 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-PGF1 α , 8-iso-PGF2 α , 8-oxo-dG, AI 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-1-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(l-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-alpha1, GFR-alpha2, GFR-alpha3, GTR, 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/betal, integrin, alpha4/beta7, integrin alpha5 (alphaV), integrin alpha5/betal, integrin alpha5/beta3, integrin alpha6, integrin betal, 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, Lfo, 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, Muellierian- 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-betal, 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 RI Apo-2, DR4), TNFRSF10B (TRAIL R2 DR5, KILLER, TRICK-2A, TRICK-B), TNFRSF10C (TRAIL R3 DcRI, LIT, TRID), TNFRSF10D (TRAIL R4 DcR2, TRUNDD), TNFRSF11A (RANK ODF R, TRANCE R), TNFRSF11B (OPG OCIF, TR1),

TNFRSF12 (TWEAK R FN14), TNFRSF13B (TAC1), 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 RI 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 antibody 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), FcγRIIa (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 antibody 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 antibody fragment comprises an scFv2-Fc2 and/or scFv-IgG;
 - j. the antibody or antigen-binding antibody fragment comprises an IgG constant domain; and/or
 - k. the antibody or antigen-binding antibody fragment comprises at least a second antigen binding domain that specifically binds to an antigen, wherein said antibody or antigen-binding antibody fragment 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.
10. An isolated or recombinant nucleic acid sequence encoding an antibody or antigen-binding antibody fragment according to any one of the foregoing claims.

11. An expression vector comprising an isolated or recombinant nucleic acid sequence according to claim 10.
12. A host cell transfected, transformed, or transduced with a nucleic acid sequence according to claim 10, optionally a mammalian or yeast cell, or a vector containing said nucleic acid sequence.
13. A pharmaceutical composition comprising an antibody or antigen-binding antibody fragment according to any one of the foregoing claims; and a pharmaceutically acceptable carrier and/or excipient.
14. 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 one or more antibodies or antibody fragments according to any one of claims 1-9 or a host cell which expresses one of said antibodies or antibody fragments according to claim 12, optionally an immune cell, further optionally a T or NK cell.
15. The method according to claim 14, wherein the method further comprises administering to the mammal an additional therapeutic agent, optionally wherein the mammal is a human.
16. An anti-cluster of differentiation three ("CD3") antibody or antibody fragment, wherein said anti-CD3 antibody or antigen-binding antibody fragment comprises:
 - a. a variable light (V_L) chain polypeptide comprising a V_L CDR3 (CDRL3) of X_1 QSYFRRT (SEQ ID NO: 1), optionally wherein X_1 is K, A, T, or V;
 - b. a variable heavy (V_H) chain polypeptide comprising a V_H CDR3 (CDRH3) of X_3 RDAYGX4YFYDV (SEQ ID NO: 6), optionally wherein X_3 is A or V and X_4 is R or Q;

- c. a variable light (V_L) chain polypeptide comprising a V_L CDR1 (CDRL1) of KSSQSLLNARTX₅KNYLA (SEQ ID NO: 7), optionally wherein X₅ is G, M, N, or R;
 - d. a variable light (V_L) chain polypeptide comprising a V_L CDR2 (CDRL2) of WASTRES (SEQ ID NO: 10) or WASTRSS (SEQ ID NO: 11);
 - e. a variable heavy (V_H) chain polypeptide comprising a V_H CDR1 (CDRH1) of FNX₆KDYXX₇H (SEQ ID NO: 12), wherein X₆ is I, N or V and X₇ is M or I; and/or
 - f. a variable heavy (V_H) chain polypeptide comprising a V_H CDR2 (CDRH2) of WIDLX₈NANTVYDX₉KX₁₀QG (SEQ ID NO: 14), wherein X₈ is E or N, X₉ is A, H, or T, and X₁₀ is F or L.
17. The anti-CD3 antibody or antigen-binding antibody fragment of claim 16, wherein:
- a. X₁ is A, T or V;
 - b. the CDRL3 comprises an amino acid sequence of AQSIFYRRT (SEQ ID NO: 2); TQSIFYRRT (SEQ ID NO: 3); VQSIFYRRT (SEQ ID NO: 4); or KQSIFYRRT (SEQ ID NO: 5);
 - c. X₃ is A;
 - d. X₅ is G or R;
 - e. the CDRL1 comprises an amino acid sequence of KSSQSLLNARTGKNYLA (SEQ ID NO: 8) or KSSQSLLNARTRKNYLA (SEQ ID NO: 9);
 - f. the CDRL2 comprises an amino acid sequence of WASTRES (SEQ ID NO: 10);
 - g. the CDRL2 comprises an amino acid sequence of WASTRSS (SEQ ID NO: 11);
 - h. X₆ is I;

- i. X_7 is M;
 - j. the CDRH1 comprises an amino acid sequence of FNIKDYMH (SEQ ID NO: 13);
 - k. X_8 is E;
 - l. X_9 is A;
 - m. X_{10} is F;
 - n. the CDRH2 comprises an amino acid sequence of WIDLENANTVYDAKFQG (SEQ ID NO: 15); and/or
 - o. the CDRH2 comprises an amino acid sequence of WIDLENANTIYDAKFQG (SEQ ID NO: 16).
18. The anti-CD3 antibody or antigen-binding antibody fragment of claim 16 or claim 17, wherein:
- a. said anti-CD3 antibody or antigen-binding antibody fragment binds to CD3 with a dissociation constant (K_D) of about 500 pM or more, about 500 pM or less, about 450 pM or less, about 400 pM or less, about 350 pM or less, about 300 pM or less, about 250 pM or less, about 200 pM or less, about 150 pM or less, or about 100 pM or less, optionally wherein said CD3 is human and/or cynomolgus, further optionally wherein said binding affinity is measured by surface plasmon resonance;
 - b. said antibody or antigen-binding antibody 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;
 - c. the antibody or antigen-binding antibody fragment comprises a multispecific antibody;
 - d. the antibody or antigen-binding antibody fragment comprises a bispecific antibody;

- e. the antibody or antigen-binding antibody fragment comprises an scFv;
- f. the antibody or antigen-binding antibody 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;
- g. the antibody or antigen-binding antibody fragment comprises at least a second antigen binding domain that specifically binds to an antigen selected from the group consisting of: 17-1A, 4-1BB, 4Dc, 6- keto-PGF α , 8-iso-PGF 2α , 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-l-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-1A (ALK-3), BMPR-1B (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-alpha1, GFR-alpha2, GFR-alpha3, GTR, 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/betal, integrin, alpha4/beta7, integrin alpha5 (alphaV), integrin alpha5/betal, integrin alpha5/beta3, integrin alpha6, integrin betal, 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, Lfo, 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-betal, 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 RI Apo-2, DR4), TNFRSFIOB (TRAIL R2 DR5, KILLER, TRICK-2A, TRICK-B), TNFRSF10C (TRAIL R3 DcRI, 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 RI 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;

- h. the antibody or antigen-binding antibody 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), FcγRIIa (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;
- i. the antibody or antigen-binding antibody 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;
- j. the antibody or antigen-binding antibody fragment comprises an scFv2-Fc2 and/or scFv-IgG;

- k. the antibody or antigen-binding antibody fragment comprises an IgG constant domain; and/or
 - l. the antibody or antigen-binding antibody 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.
19. An anti-cluster of differentiation three ("CD3") antibody or antibody fragment, wherein said anti-CD3 antibody or antigen-binding antibody fragment comprises one or more CDRs of any one or more of Ab1-Ab50.
20. An anti-cluster of differentiation three ("CD3") antibody or antibody fragment, wherein said anti-CD3 antibody or antigen-binding antibody fragment comprises one or more V_H and/or V_L chains comprising an amino acid sequence selected from those in Table 4.
21. An isolated or recombinant nucleic acid sequence encoding an antibody or antigen-binding antibody fragment according to any one of claims 16-20.
22. An expression vector comprising an isolated or recombinant nucleic acid sequence according to claim 21.
23. A host cell transfected, transformed, or transduced with a nucleic acid sequence according to claim 21, optionally a mammalian or yeast cell, or a vector containing said nucleic acid sequence.
24. A pharmaceutical composition comprising an antibody or antigen-binding antibody fragment according to any one of the claims 16-20; and a pharmaceutically acceptable carrier and/or excipient.

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 one or more antibodies or antibody fragments according to any one of claims 16-20 or a host cell which expresses one of said antibodies or antibody fragments according to claim 23, optionally an immune cell, further optionally a T or NK cell.