

What is claimed is:

1. At least one recombinant polynucleotide encoding at least one synthetic antigen receptor (SAR) polypeptide, the at least one SAR polypeptide comprising:
 - a) a first module comprising one or more autonomous antigen binding domains (AABDs) selected from the group of:
 - a single vH domain (SVH);
 - a single vL domain (SVL); a vHH domain; a single domain antibody; a single variable domain of a TCR (svd-TCR);
 - a non-immunoglobulin antigen binding scaffold optionally selected from a DARPIN, an affibody, an adnectin, an affitin, an repebody, an fynomer, an alphabody, an avimer, an atrimer, an centyrin, a pronectin, an anticalins, an kunitz domain, an Armadillo repeat protein and a D domain;
 - a ligand-binding domain of a receptor; a receptor-binding domain of a ligand; an autoantigen; an adaptor binding domain; and an Fc binding domain;
 - b) a second module comprising vL (V_L), vH (V_H), Va/V α , Vb1 (V β 1), Vb2 (V β 2), Vg (V γ), Vd (V δ), scFv, scTCR, Ig linker domain or a combination thereof;
 - c) an optional third module comprising an extracellular domain, a connecting peptide or a hinge domain;
 - d) a fourth module that comprises a transmembrane domain; and
 - e) an optional fifth module comprising one or more intracellular signaling domains;wherein the one or more AABDs of the first module are operably linked, optionally via a linker, to the N-terminus or near the N-terminus of a vL, vH, Va, Vb, Vg, Vd or Ig linker domain of the second module.
2. At least one recombinant polynucleotide encoding at least one synthetic antigen receptor (SAR) polypeptide, wherein the at least one SAR polypeptide comprises a heterodimer of a first polypeptide chain and a second polypeptide chain;
wherein the first polypeptide chain and/or the second polypeptide chain comprises a first module comprising one or more autonomous antigen binding domains (AABDs) selected from the group of:
 - a single vH domain (SVH); a single vL domain (SVL); a vHH domain; a single domain antibody; a single variable domain of a TCR (svd-TCR);

a non-immunoglobulin antigen binding scaffold optionally selected from a DARPIN, an affibody, an adnectin, an affitin, an repebody, an fynomer, an alphabody, an avimer, an atrimer, an centyrin, a pronectin, an anticalins, an kunitz domain, an Armadillo repeat protein and a D domain;

a ligand-binding domain of a receptor; a receptor-binding domain of a ligand; an autoantigen; an adaptor binding domain; and an Fc binding domain;

and wherein each of the first polypeptide chain and the second polypeptide chain comprises:

(a) a second module comprising vL (VL), vH (VH), Va/V α , Vb1 (V β 1), Vb2 (V β 2), Vg (Vy), Vd (V δ), scTCR, or an Ig linker domain;

(b) an optional third module comprising an extracellular domain, a connecting peptide or a hinge domain;

(c) a fourth module that comprises a transmembrane domain; and

(d) an optional fifth module comprising one or more intracellular signaling domains;

wherein the one or more AABDs of the first module are operably linked, optionally via a linker, to the N-terminus or near the N-terminus of a vL, vH, Va, Vb, Vg, Vd or Ig linker domain of the second module of the first polypeptide chain, the second polypeptide chain, or both; and

wherein the variable domains of the second module of the first polypeptide chain and the second module of the second polypeptide chain, when present, form a cognate pair selected from the group consisting of a vH paired with a vL, a V α paired with a V β 1 or a V β 2, and a Vy paired with a V δ .

3. The recombinant polynucleotide of claim 2, wherein the polynucleotide encodes a SAR polypeptide whose first SAR chain amino acid sequence and second SAR chain amino acid sequence are contained within an amino acid sequence selected from the group consisting of SEQ ID NO: 16951, 12539-14188, 14778-14799, 14811-14835, 14853-14899, 14905-14926, 14938-14962, 14978-15026, 15032-15053, 15065-15090, 15105-15153, 15159-15180, 15192-15216, 15234-15280, 15286-15307, 15319-15343, 15361-15407, 15413-15434, 15446-15470, 15488-15534, 15540-15561, 15573-15597, 15615-15661, 15669-15693, 15708-15729, 15738-15759, 15763-15787, 15801-15842, 15846-15867, 15876-15911, 15917-15941, 15956-15977, 15986-16007, 16011-16035, 16049-16091, 16094-16115, 16124-16159, 16165-16189, 16204-16225, 16234-16255, 16259-16283, 16297-16338, 16342-16363, 16372-16407, 16413-16437, 16452-16473, 16507-

16531, 16545-16586, 16590-16611, 16661-16685, 16700-16721, 16730-16751, 16755-16779, 16793-16834, 16838-16859, 16909-16933, 16948-16950, 16952-16969, 16978-16999, 17003-17027, 17041-17083, 17086-17107, 17116-17151, 17160-17184, 17234-17257, 17306-17330, 17379-17403, 17452-17476, 17525-17549, and 22445-22460, or sequences having at least 75% identity to said first SAR chain amino acid sequence and said second SAR chain amino acid sequence, respectively, wherein, for the purpose of determining said sequence identity, any leader sequence, 2A self-cleaving peptide, Furin cleavage site, accessory module, selection marker, linker, and epitope tag present in the listed SEQ ID NO is excluded from the comparison.

4. The recombinant polynucleotide of claim 2, wherein the encoded first polypeptide chain and second polypeptide chain of the SAR comprise, respectively, the first SAR chain amino acid sequence and the second SAR chain amino acid sequence contained within an amino acid sequence selected from the group consisting of SEQ ID NO: 16951, 12539-14188, 14778-14799, 14811-14835, 14853-14899, 14905-14926, 14938-14962, 14978-15026, 15032-15053, 15065-15090, 15105-15153, 15159-15180, 15192-15216, 15234-15280, 15286-15307, 15319-15343, 15361-15407, 15413-15434, 15446-15470, 15488-15534, 15540-15561, 15573-15597, 15615-15661, 15669-15693, 15708-15729, 15738-15759, 15763-15787, 15801-15842, 15846-15867, 15876-15911, 15917-15941, 15956-15977, 15986-16007, 16011-16035, 16049-16091, 16094-16115, 16124-16159, 16165-16189, 16204-16225, 16234-16255, 16259-16283, 16297-16338, 16342-16363, 16372-16407, 16413-16437, 16452-16473, 16507-16531, 16545-16586, 16590-16611, 16661-16685, 16700-16721, 16730-16751, 16755-16779, 16793-16834, 16838-16859, 16909-16933, 16948-16950, 16952-16969, 16978-16999, 17003-17027, 17041-17083, 17086-17107, 17116-17151, 17160-17184, 17234-17257, 17306-17330, 17379-17403, 17452-17476, 17525-17549, and 22445-22460, or sequences having at least 95% sequence identity to said first SAR chain amino acid sequence and said second SAR chain amino acid sequence, respectively, wherein, for the purpose of determining said sequence identity, any leader sequence, 2A self-cleaving peptide, Furin cleavage site, accessory module, selection marker, linker, and epitope tag present in the listed SEQ ID NO is excluded from the comparison, and the first SAR chain amino acid sequence and the second SAR chain amino acid sequence are identified as the portions of the listed SEQ ID NO encoded between such leader sequence, 2A self-cleaving peptide, or Furin cleavage site boundaries.

5. The recombinant polynucleotide of claim 2, wherein the encoded SAR polypeptide comprises, in the first module of the first polypeptide chain, the first module of the second polypeptide chain, or the first modules of both polypeptide chains, one or more adaptor binding domains selected from the group consisting of an RZIP, an EZIP, an E4, a K4, a SYNZIP, a NKG2D-AF, a NKG2D-YA, a NKG2D-AF dimer, a NKG2D-YA dimer, a D domain, a Streptag binding moiety, an anti-FITC moiety, an anti-GCN4 moiety, a PDZ domain, a streptavidin domain, a streptavidin binding protein (SBP) domain, a PYL domain, an ABI domain, a zinc finger domain, an Fc-binding domain of CD16, an Fc-binding domain of CD16A-V158, an Fc-binding domain of CD32, and an Fc-binding domain of CD64; and wherein the encoded SAR polypeptide functions as an ON switch in the presence of a cognate SAR adaptor that binds to said one or more adaptor binding domains.
6. The recombinant polynucleotide of claim 1 or 2, wherein the SAR is bispecific, biparatopic, or multispecific and binds to two or more antigens, two or more different epitopes of the same antigen, or two or more different epitopes of two or more antigens.
7. The recombinant polynucleotide of claim 6, wherein at least one antigen targeted by the SAR is preferentially or exclusively expressed on hematopoietic lineage cells and at least one antigen targeted by the SAR is expressed on non-hematopoietic lineage cells, optionally wherein the antigen preferentially or exclusively expressed on hematopoietic lineage cells is selected from the group consisting of CD19, CD20, CD22, BCMA, CS1, CD30, CD33, MPL, CD138, CD38, CD79b, BAFF-R, and CD123, and the antigen expressed on non-hematopoietic lineage cells is selected from the group consisting of Mesothelin (MSLN), Her2, EGFR, EGFRviii, MUC16, PSMA, and IL-13Ra2.
8. The recombinant polynucleotide of claim 1 or 2, wherein the SAR comprises one or more protease-cleavable linkers, optionally wherein the protease-cleavable linker is cleavable by a matrix metalloproteinase (MMP) selected from the group consisting of MMP14, MMP2, MMP9, MMP1, and MMP8, and optionally wherein the protease-cleavable linker comprises an amino acid sequence selected from the group consisting of SEQ ID NO: 11908, 11909, 11910, 11911, 11912, and 11913, or a polynucleotide encoding said amino acid sequence.
9. A recombinant polynucleotide encoding a SAR polypeptide of claim 1, where the one or more AABDs are attached via an optional linker to the N-terminus or near the N-terminus of

1) a first polypeptide chain comprising a vH, Va, Vg or an Ig linker domain fragment operably linked via an optional linker to a first T cell receptor constant chain fragment comprising a first connecting peptide operably linked to a first transmembrane domain of a first TCR subunit; and

2) a second polypeptide chain comprising a vL, Vb, Vd or an Ig linker domain operably linked via an optional linker to a second T cell receptor constant chain fragment comprising a second connecting peptide operably linked to a second transmembrane domain of a second TCR subunit;

wherein the first TCR constant chain fragment and the second TCR constant chain fragment form a T cell receptor module (TCRM) that is capable of recruiting at least one TCR-associated signaling module when expressed in a T cell; and wherein the assignment of variable domains to the first and second polypeptide chains is interchangeable, such that the first polypeptide chain may instead comprise the vL, Vb or Vd and the second polypeptide chain may comprise the complementary vH, Va or Vg.

10. The at least one recombinant polynucleotide encoding at least one SAR polypeptide of claim 9, wherein the encoded vH, Va or Vg of one polypeptide chain and the complementary vL, Vb or Vd of the other polypeptide chain form an antigen-binding module that specifically binds to a target antigen.
11. The at least one recombinant polynucleotide encoding at least one SAR polypeptide of claim 1, 2 or 9, wherein the AABD, vL, vH, Va, Vb, Vg, Vd and/or Ig linker domain is a fully human, humanized, chimeric or a non-human domain.
12. The recombinant polynucleotide of claim 1 or 2, wherein: (I) the first polypeptide chain comprises: a) a light chain variable (vL) domain; b) an Ig-like linker domain derived from an antibody or a T cell receptor (TCR), optionally wherein the Ig-like linker domain has the amino acid sequence of any one of SEQ ID NOs: 11832-11865 or a functional mutant or variant thereof; and c) the connecting peptide, the transmembrane domain, and the cytosolic domain of a first TCR subunit, said first TCR subunit selected from TCR α (C α), TCR β 1 (C β 1), TCR β 2 (C β 2), TCR γ (C γ), TCR δ (C δ), and pre-TCR α (pre-C α), or a functional mutant or variant thereof; and (II) the second polypeptide chain comprises: a) a heavy chain variable (vH) domain; b) an Ig-like linker domain derived from an antibody or a TCR, optionally wherein the Ig-like linker domain has the amino acid sequence of any one of SEQ ID NOs: 11832-11865 or a functional mutant or variant thereof; and c) the connecting peptide, the transmembrane domain, and the cytosolic domain of a second

TCR subunit, said second TCR subunit selected from TCR α (C α), TCR β 1 (C β 1), TCR β 2 (C β 2), TCR γ (C γ), TCR δ (C δ), and pre-TCR α (pre-C α), or a functional mutant or variant thereof; or (III) the first polypeptide chain comprises elements (a)-(c) of section (II), and the second polypeptide chain comprises elements (a)-(c) of section (I); wherein the first TCR subunit and the second TCR subunit are capable of pairing to form a TCR heterodimer.

13. The recombinant polynucleotide of claim 1 or 2, wherein: (I) the first polypeptide chain comprises: a) a light chain variable (vL) domain; b) an Ig-like linker domain derived from an antibody or a T cell receptor (TCR), optionally wherein the Ig-like linker domain has the amino acid sequence of any one of SEQ ID NOs: 11832-11865 or a functional mutant or variant thereof; and c) a hinge domain, a transmembrane domain of CD3z, and optionally an intracellular domain of CD3z, or a functional mutant or variant of any one of the foregoing; and (II) the second polypeptide chain comprises: a) a heavy chain variable (vH) domain; b) an Ig-like linker domain derived from an antibody or a TCR, optionally wherein the Ig-like linker domain has the amino acid sequence of any one of SEQ ID NOs: 11832-11865 or a functional mutant or variant thereof; and c) a hinge domain, a transmembrane domain of CD3z, and optionally an intracellular domain of CD3z, or a functional mutant or variant of any one of the foregoing; or (III) the first polypeptide chain comprises elements (a)-(c) of section (II), and the second polypeptide chain comprises elements (a)-(c) of section (I); wherein one or both polypeptide chains further comprise one or more co-stimulatory domains located C-terminal to the transmembrane domain of CD3z.
14. The recombinant polynucleotide of claim 1 or 2, wherein the one or more AABDs are attached to the N-terminus or near the N-terminus of: the second module of the first polypeptide chain comprising a vH, vL or an Ig linker domain, which is in turn operably linked to a first T cell receptor constant chain fragment or a CD3 chain fragment comprising a first connecting peptide operably linked to a first transmembrane domain; and/or the second module of the second polypeptide chain comprising a vL, vH or an Ig linker domain, which is in turn operably linked to a second T cell receptor constant chain fragment or a CD3 chain fragment comprising a second connecting peptide operably linked to a second transmembrane domain.
15. The recombinant polynucleotide of claim 1 or 2, wherein the encoded SAR comprises one or more of the following features: (a) the vL domain and the vH domain are present on separate polypeptide chains; (b) the first and/or the second polypeptide chain comprises a fifth module comprising one or more intracellular signaling domains; (c) the first, second,

third, and fourth modules are operably linked by one or more linker sequences; (d) the AABD, the vL domain, the vH domain, and/or the Ig linker domain is fully human, humanized, chimeric, or non-human; (e) the SAR comprises a non-immunoglobulin antigen-binding scaffold selected from the group consisting of a DARPIN, affibody, adnectin, affitin, repebody, fynomer, alphabody, avimer, atrimer, centyrin, pronectin, anticalin, Kunitz domain, Armadillo repeat protein, and D domain; (f) the SAR has a backbone selected from a one-and-a-half chain Synthetic Immune Receptor (SIR), a double chain SIR, a CD3z-Synthetic Immune Receptor (zSIR), a one-and-a-half chain chimeric T cell receptor (cTCR), a double chain cTCR, an antibody-TCR (Ab-TCR), an AABD-T cell receptor (AABD-TCR), or an HLA-independent TCR; (g) the SAR specifically binds to one antigen or more than one antigen; (h) the SAR targets a first antigen expressed on blood lineage cells and a second antigen expressed on solid tumor cells; (i) the SAR comprises one or more epitope tags or mimotopes; (j) the first and/or the second polypeptide chains of the SAR comprise an extracellular domain, a connecting peptide, and a transmembrane domain; (k) the first and/or the second polypeptide chains of the SAR comprise an extracellular domain, a connecting peptide, a transmembrane domain, and one or more intracellular signaling domains, optionally wherein the extracellular domain comprises an extracellular linker domain, an Ig domain, or an Ig-like domain; (l) the first and/or the second polypeptide chains of the SAR comprise an extracellular domain, a hinge domain, and a transmembrane domain; (m) the first and/or the second polypeptide chains of the SAR comprise an extracellular domain, a hinge domain, a transmembrane domain, and one or more intracellular signaling domains; (n) the first and/or the second polypeptide chains of the SAR comprise one or more costimulatory domains; and/or (o) the extracellular domain of the first and/or the second polypeptide chains of the SAR comprises an extracellular linker domain, an Ig domain, or an Ig-like domain, optionally wherein the extracellular linker domain, the Ig domain, or the Ig-like domain is derived from an immunoglobulin or T cell receptor constant chain.

16. The at least one recombinant polynucleotide encoding at least one SAR polypeptide of claim 1, 2, or 9, wherein the encoded SAR polypeptide comprises one or more of: (a) an Ig linker domain comprising a polypeptide with SEQ ID NO: 11832-11865 or a fragment or variant thereof with at least 70% sequence homology to a polypeptide having the sequence of SEQ ID NO: 11832-11865; (b) an optional linker domain comprising a polypeptide with SEQ ID NO: 11832-11865, 11714-11730 or a fragment or a variant thereof with at least 70% sequence homology to a polypeptide having the sequence of

- SEQ ID NO: 11832-11865, 11714-11730 or a domain that is between 25 to 500 amino acids in length; (c) a T cell receptor constant chain fragment comprising a polypeptide or a fragment thereof having at least 70% sequence homology to a polypeptide having the sequence of any one of SEQ ID NO: 11732-11830; (d) a connecting peptide of a T cell receptor constant chain, or a fragment thereof, having at least 70% sequence homology to a connecting peptide having the sequence of any one of SEQ ID NO: 11867-11875; (e) a transmembrane domain, or a fragment thereof, having at least 70% sequence homology to a transmembrane domain having a sequence of any one of SEQ ID NO: 11877-11881 or 23332-23334; and (f) a cytosolic domain, or a fragment thereof, having at least 70% sequence homology to a polypeptide having the sequence of any one of SEQ ID NO: 11883-11886, 11785, or 23335-23337.
17. The at least one recombinant polynucleotide encoding at least one SAR polypeptide of claim 1 or 2, comprising one or more of: (a) a partial or entire extracellular, transmembrane and intracellular domain contains a cytosolic domain or a fragment thereof with at least 70% sequence homology to a polypeptide having the sequence of any one of SEQ ID NO: 11903 to 11906.
 18. The at least one recombinant polynucleotide encoding at least one SAR polypeptide of claim 1 or 2 which has the backbone of a first generation CAR, a second generation CAR, a third generation CAR, a single chain synthetic immune receptor (SIR), a one and a half chain SIR, a double chain SIR, a zSIR, a single chain chimeric T cell receptor (cTCR), a one and a half chain cTCR, a double chain cTCR, an antibody T cell receptor (Ab-TCR), an AABD-TCR, a T cell receptor fusion protein (TFP) ϵ , a TFP γ , a TFP δ , a TFP $\alpha\beta$, a TFP $\gamma\delta$, a Tri-TAC, a single chain TCR, a double chain TCR or an HLA-independent TCR.
 19. The at least one recombinant polynucleotide encoding at least one SAR polypeptide of claim 1, 2 or 9, wherein one or more of: (a) the SAR can bind to at least one antigen, and/or at least one epitope of one or more antigen(s); and (b) the encoded two or more AABDs bind to at least one antigen, and/or at least one epitope of one or more antigen(s).
 20. The at least one recombinant polynucleotide encoding at least one SAR polypeptide of claim 1, 2, or 9 wherein the encoded one or more antigen binding domains bind to at least one antigen selected from the group of CD5; CD19; CD123; CD22; CD30; CD171; CS1 (also referred to as CD2 subset 1, CRACC, SLAMF7, CD319, and 19A24); C-type lectin-like molecule-1 (CLL-1 or CLECL1); CD33; epidermal growth factor receptor variant III (EGFRviii); ganglioside G2 (GD2); ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(I-4)bDGlc(I-I)Cer); TNF receptor family member B cell maturation (BCMA); Tn

antigen ((Tn Ag) or (GalNAc α -Ser/Thr)); prostate-specific membrane antigen (PSMA); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Fms Like Tyrosine Kinase 3 (FLT3); Tumor-associated glycoprotein 72 (TAG72); CD38; CD44v6; a glycosylated CD43 epitope expressed on acute leukemia or lymphoma but not on hematopoietic progenitors, a glycosylated CD43 epitope expressed on non-hematopoietic cancers, Carcinoembryonic antigen (CEA); Epithelial cell adhesion molecule (EPCAM); B7H3 (CD276); KIT (CD117); Interleukin-13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Mesothelin; Interleukin 11 receptor alpha (IL-11Ra); prostate stem cell antigen (PSCA); Protease Serine 21 (Testisin or PRSS21); vascular endothelial growth factor receptor 2 (VEGFR2); Lewis(Y) antigen; CD24; Platelet-derived growth factor receptor beta (PDGFR-beta); Stage-specific embryonic antigen-4 (SSEA-4); CD20; Folate receptor alpha (FRa or FR1); Folate receptor beta (FRb); Receptor tyrosine-protein kinase ERBB2 (Her2/neu); Mucin 1, cell surface associated (MUC1); epidermal growth factor receptor (EGFR); neural cell adhesion molecule (NCAM); Prostase; prostatic acid phosphatase (PAP); elongation factor 2 mutated (ELF2M); Ephrin B2; fibroblast activation protein alpha (FAP); insulin-like growth factor 1 receptor (IGF-I receptor); carbonic anhydrase IX (CAIX); Proteasome (Prosome, Macropain) Subunit, Beta Type, 9 (LMP2); glycoprotein 100 (gp100); oncogene fusion protein consisting of breakpoint cluster region (BCR); Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); tyrosinase; ephrin type-A receptor 2 (EphA2); sialyl Lewis adhesion molecule (sLe); ganglioside GM3 (aNeu5Ac(2-3)bDCIalp(I- 4)bDGlc(p(I-1)Cer); transglutaminase 5 (TGS5); high molecular weight-melanoma associated antigen (HMWMAA); o-acetyl-GD2 ganglioside (OAcGD2); tumor endothelial marker 1 (TEM1/CD248); tumor endothelial marker 7-related (TEM7R); claudin 6 (CLDN6); thyroid stimulating hormone receptor (TSHR); G protein coupled receptor class C group 5, member D (GPRC5D); chromosome X open reading frame 61 (CXORF61); CD97; CD179a; anaplastic lymphoma kinase (ALK); Polysialic acid; placenta-specific 1 (PLAC1); hexasaccharide portion of globoH glycosphingolipid (GloboH); mammary gland differentiation antigen (NY-BR-1); uroplakin 2 (UPK2); Hepatitis A virus cellular receptor 1 (HAVCR1); adrenoceptor beta 3 (ADRB3); pannexin 3 (PANX3); G protein-coupled receptor 20 (GPR20); lymphocyte antigen 6 complex, locus K 9 (LY6K); Olfactory receptor 51E2 (OR51E2); TCR Gamma Alternate Reading Frame Protein (TARP); Wilms tumor protein (WT1); Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-1a); Melanoma-associated antigen 1 (MAGE-A1); ETS translocation-variant gene 6, located on chromosome 12p (ETV6-AML); sperm protein 17 (SPA17); X

Antigen Family, Member 1A (XAGE1); angiopoietin-binding cell surface receptor 2 (Tie 2); melanoma cancer testis antigen-1 (MAD-CT-1); melanoma cancer testis antigen-2 (MAD-CT-2); Fos-related antigen 1; tumor protein p53 (p53); p53 mutant; prostein; survivin; telomerase; prostate carcinoma tumor antigen-1 (PCT A-1 or Galectin 8), melanoma antigen recognized by T cells 1 (MelanA or MART1); Rat sarcoma (Ras) mutant; human Telomerase reverse transcriptase (hTERT); sarcoma translocation breakpoints; melanoma inhibitor of apoptosis (ML-IAP); ERG (transmembrane protease, serine 2 (TMPRSS2) ETS fusion gene); N-Acetyl glucosaminyl-transferase V (NA17); paired box protein Pax-3 (PAX3); Androgen receptor; Cyclin B1; v-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Ras Homolog Family Member C (RhoC); Tyrosinase-related protein 2 (TRP-2); Cytochrome P450 1B 1 (CYP1B 1); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites), Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Paired box protein Pax-5 (PAX5); proacrosin binding protein sp32 (OY-TESI); lymphocyte-specific protein tyrosine kinase (LCK); A kinase anchor protein 4 (AKAP-4); synovial sarcoma, X breakpoint 2 (SSX2); Receptor for Advanced Glycation Endproducts (RAGE-1); renal ubiquitous 1 (RUI); renal ubiquitous 2 (RU2); legumain; human papilloma virus E6 (HPV E6); human papilloma virus E7 (HPV E7); intestinal carboxyl esterase; heat shock protein 70-2 mutated (mut hsp70-2); CD79a; CD79b; CD72; Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Fc fragment of IgA receptor (FCAR or CD89); Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); CD300 molecule-like family member f (CD300LF); C-type lectin domain family 12 member A (CLEC12A); bone marrow stromal cell antigen 2 (BST2); EGF-like module-containing mucin-like hormone receptor-like 2 (EMR2); lymphocyte antigen 75 (LY75); Glypican-3 (GPC3); Fc receptor-like 5 (FCRL5); immunoglobulin lambda-like polypeptide 1 (IGLL1); MPL; Biotin; c-MYC epitope Tag; CD34; LAMP1 TROP2; GFRalpha4; CDH17; CDH6; NYBR1; CDH19; CD200R; Slea (CA19.9; Sialyl Lewis Antigen); Fucosyl-GM1; PTK7; gpNMB; CDH1-CD324; DLL3; CD276/B7H3; IL11Ra; IL13Ra2; CD179b-IGLI1; TCRgamma-delta; NKG2D; CD32 (FCGR2A); Tn ag; Tim1-/HVCR1; CSF2RA (GM-CSFR-alpha); TGFbetaR2; Lews Ag; TCR-beta1 chain; TCR-beta2 chain; TCR-gamma chain; TCR-delta chain; FITC; Leutenizing hormone receptor (LHR); Follicle stimulating hormone receptor (FSHR); Gonadotropin Hormone receptor (CGHR or GR); CCR4; GD3; SLAMF6; SLAMF4; HIV1 envelope glycoprotein; HTLV1-Tax; CMV pp65; EBV-EBNA3c; KSHV K8.1; KSHV-gH; influenza A hemagglutinin (HA); GAD; PDL1; Guanylyl cyclase C

(GCC); auto antibody to desmoglein 3 (Dsg3); auto antibody to desmoglein 1 (Dsg1); HLA; HLA-A; HLA-A2; HLA-B; HLA-C; HLA-DP; HLA-DM; HLA-DOA; HLA-DOB; HLA-DQ; HLA-DR; HLA-G; IgE, CD99; Ras G12V; Tissue Factor 1 (TF1); AFP; GPRC5D; Claudin18.2 (CLD18A2 or CLDN18A.2); P-glycoprotein; STEAP1; Liv1; Nectin-4; Cripto; gpA33; BST1/CD157; low conductance chloride channel (LCCC); TAJ/TROY; MPL (TPO-R); KIR3DL2; CD32b; CD229; Toso; GPC3; BAFF-R; MR1; CMV-pp65/MHC complex; and NYESO-1/MHC complex.

21. The at least one recombinant polynucleotide encoding at least one SAR polypeptide of claim 1, 2 or 9, wherein the encoded SAR polypeptide comprises one or more antigen binding domains selected from the group consisting of: (i) a heavy chain variable region (vH) comprising a sequence as set forth in any of SEQ ID NO: 10978-11214, 23148-23161 or a sequence that contains the three complementarity determining regions (CDRs) of the foregoing, and a light chain variable region (vL) comprising a sequence as set forth in any one of SEQ ID NO: 10736-10972 and 23136-23147 or a sequence that contains the three CDRs of the foregoing; (ii) a camelid VHH domain comprising a sequence as set forth in any one of SEQ ID NO: 11524-11525, 11530-11531, 11549-11575, 11576-11592 and 23163-23173 or a sequence that contains the three CDRs of the foregoing; (iii) a non-immunoglobulin scaffold encoded by a polynucleotide of any one of SEQ ID NO: 11662-11673 or sequences with at least 95% identity thereto, or sequences that bind to the same target antigens or the same epitopes on the target antigens; (iv) a ligand-binding domain of a receptor comprising a sequence as set forth in any one of SEQ ID NO: 11674-11691 or sequences with at least 95% identity thereto and which encodes a polypeptide that binds to its cognate receptor; (v) a receptor-binding domain of a ligand comprising a sequence as set forth in any one of SEQ ID NO: 11692-11702, 22391-22392, 22402-22404 or sequences with at least 95% identity thereto and which encodes a polypeptide that binds to its cognate receptor; (vi) a single vH domain comprising a sequence as set forth in any one of SEQ ID NO: 11519-11523, 11526-11529, 11532-11548, 11644-11645 and 23174 or a sequence that contains the three CDRs of the foregoing; (vii) an adaptor binding domain comprising a sequence as set forth in any one of SEQ ID NO: 11704-11712, or 22383, or sequences with at least 95% identity thereto and which encodes a polypeptide that binds to its adaptor; (viii) an autoantigen comprising a sequence as set forth in any one of SEQ ID NO: 11687 or 22406-22407, or sequences with at least 95% identity thereto and which encodes a polypeptide that binds to its autoantibody or autoantibody-producing cells; and/or (ix) a single variable TCR domain (svd-TCR)

comprising a sequence as set forth in any of SEQ ID NO: 22399-22400 or a sequence that contains the three CDRs of the foregoing.

22. The at least one recombinant polynucleotide encoding at least one SAR polypeptide of claim 1 or 2, wherein the SAR binds two or more target antigens, and wherein at least one of the target antigens is expressed on blood lineage cells while at least one of the target antigens is expressed on solid tumor cells.
23. A recombinant expression system comprising the recombinant polynucleotide of claim 1 which is co-expressed with a therapeutic control, wherein the therapeutic control is selected from the group consisting of a truncated epidermal growth factor receptor (tEGFR), truncated epidermal growth factor receptor viii (tEGFRviii), truncated CD30 (tCD30), truncated BCMA (tBCMA), truncated CD19 (tCD19), CD34, thymidine kinase, cytosine deaminase, nitroreductase, xanthine-guanine phosphoribosyl transferase, human caspase 8, human caspase 9, inducible caspase 9 (icaspase9), purine nucleoside phosphorylase, linamarase/linamarin/glucose oxidase, deoxyribonucleoside kinase, horseradish peroxidase (HRP)/indole-3-acetic (IAA), Gamma-glutamylcysteine synthetase, CD20/alphaCD20, CD34/thymidine kinase chimera, dox-dependent caspase-2, mutant thymidine kinase (HSV-TKSR39), AP1903/Fas system, a chimeric cytokine receptor (CCR), 41BBL, CD40L, K13, MC159, cFLIP-L/MRIT α , cFLIP-p22, HTLV1 Tax, HTLV2 Tax, HTLV2 Tax-RS mutant, FKBPx2-K13, FKBPx2-HTLV2-Tax, FKBPx2-HTLV2-Tax-RS, IL6R-304-vHH-Alb8-vHH, IL12f, PD1-4H1 scFV, PD1-5C4 scFV, PD1-4H1-Alb8-vHH, PD1-5C4-Alb8-vHH, CTLA4-Ipilimumab-scFv, CTLA4-Ipilimumab-Alb8-vHH, IL6-19A-scFV, IL6-19A-scFV-Alb8-vHH, sHVEM, sHVEM-Alb8-vHH, hTERT, Fx06, CD3z, CD3z-GGGS-41BB, CD3-BBz, CD3-CD28z, CD3-CD28-Lck fusion protein, shRNA targeting Brd4, chimeric antigen receptor (CAR), hTERT, heparinase, a CAR, an inhibitory CAR and combination thereof and combinations thereof.
24. At least one vector comprising the recombinant polynucleotide of claim 1, wherein the vector is selected from the group consisting of a DNA vector, an RNA vector, a plasmid, a lentivirus vector, an adenoviral vector, a retrovirus vector, a baculovirus vector, a sleeping beauty transposon vector, and a piggybac transposon vector.
25. At least one SAR polypeptide encoded by the at least one recombinant polynucleotide of claim 1.
26. A recombinant cell or a cell population that expresses the at least one recombinant polynucleotide of claim 1.

27. The cell or cell population of claim 26, wherein one or more of: (a) the cell is an immune effector cell or a stem cell that can give rise to an immune effector cell, or an induced pluripotent stem cell (iPSC) that can give rise to an immune effector cell; and (b) the cell is an autologous cell or an allogeneic cell.
28. The cell or cell population of any one of claims 26 to 27, wherein the cell has one or more of the following characteristics: (a) lacks the expression of a functional endogenous TCR on its surface; (b) decreased expression of a functional endogenous TCR on its surface; (c) lacks the expression of or has decreased expression of one or more subunits that comprise a functional endogenous TCR; (d) lacks the expression of or has decreased expression of one or more TCR chains selected from the group consisting of TCR α , TCR β 1, TCR β 2, TCR γ , TCR δ , and pre-TCR α ; (e) expresses a substantially impaired endogenous TCR; (f) is deficient in the expression of one or more target antigens of the SAR; (g) has a deletion or mutation in one or more target antigens of the SAR to a form that is no longer recognized by the SAR; (h) lacks the expression of or has low expression of a functional HLA; (i) lacks the expression of β 2 microglobulin; (j) lacks the expression of diacylglycerol kinase (DGK) or Ikaros; (k) expresses an agent that enhances the activity of the SAR-expressing cell; (l) expresses an agent that inhibits an inhibitory molecule; (m) expresses an agent that inhibits the expression of one or more target antigens of the SAR; (n) expresses an agent that provides co-stimulation to a SAR-expressing cell; (o) expresses a cytokine or a chemokine; (p) expresses an agent that promotes the proliferation, persistence, expansion, and activation of a SAR-expressing cell; (q) expresses a soluble receptor; (r) expresses a second SAR; (s) expresses a Chimeric Antigen Receptor (CAR); (t) expresses an inhibitory CAR comprising an antigen binding domain, a transmembrane domain, and an intracellular domain of an inhibitory molecule; (u) expresses a CAR comprising an antigen binding domain, a transmembrane domain, and a primary signaling domain; (v) expresses a CAR comprising an antigen binding domain, a transmembrane domain, a costimulatory signaling domain, but no primary signaling domain; (w) expresses a CAR comprising an antigen binding domain, a transmembrane domain, a primary signaling domain, and a costimulatory domain; (x) expresses an accessory module selected from the group consisting of PDL1, PDL2, CD80, CD86, crmA, p35, hNEMO-K277A, hNEMO-K277A-delta-V249-K555, mNEMO-K270A, K13-opt, IKK2-S177E-S181E, IKK1-S176E-S180E, MyD88-L265P, TCL-1a, MTCP-1, CMV-141, 41BBL, CD40L, K13, MC159, cFLIP-L/MRIT α , cFLIP-p22, HTLV1 Tax, HTLV2 Tax, HTLV2 Tax-RS mutant, FKBPx2-K13, FKBPx2-HTLV2-Tax, FKBPx2-

HTLV2-Tax-RS, IL6R-304-vHH-Alb8-vHH, IL12f, PD1-4H1 scFv, PD1-5C4 scFv, PD1-4H1-Alb8-vHH, PD1-5C4-Alb8-vHH, CTLA4-Ipilimumab-scFv, CTLA4-Ipilimumab-Alb8-vHH, IL6-19A-scFv, IL6-19A-scFv-Alb8-vHH, sHVEM, sHVEM-Alb8-vHH, hTERT, Fx06, CD3z, CD3z-GGGS-41BB, CD3-BBz, CD3-CD28z, CD3-CD28-Lck fusion protein, shRNA targeting Brd4, IgSP-[hTRAC-opt2], IgSP-[hTRBC-opt2], heparinase, IL-2, IL-7, IL-15, IL-21, and combinations thereof; and/or (y) expresses a therapeutic control selected from the group consisting of a truncated epidermal growth factor receptor (tEGFR), truncated epidermal growth factor receptor viii (tEGFRviii), truncated CD30 (tCD30), truncated BCMA (tBCMA), truncated CD19 (tCD19), CD34, thymidine kinase, cytosine deaminase, nitroreductase, xanthine-guanine phosphoribosyl transferase, human caspase 8, human caspase 9, inducible caspase 9 (icaspase9), purine nucleoside phosphorylase, linamarase/linamarin/glucose oxidase, deoxyribonucleoside kinase, horseradish peroxidase (HRP)/indole-3-acetic acid (IAA), Gamma-glutamylcysteine synthetase, CD20/alphaCD20, CD34/thymidine kinase chimera, dox-dependent caspase-2, mutant thymidine kinase (HSV-TKSR39), AP1903/Fas system, and combinations thereof.

29. The cell or cell population of claim 26 with impaired or abolished functional expression of an endogenous TCR and with functional expression of a SAR polypeptide.
30. The cell or cell population of claim 26, wherein one or more of: (a) the SAR polypeptide is expressed from an expression cassette placed in the locus of an endogenous T cell gene; and (b) the at least one polynucleotide is under the control of the promoter and/or regulatory elements for an endogenous T cell gene; and optionally wherein the endogenous T cell gene locus is the TRAC locus, the TRBC locus, the TRGC locus and/or the TRDC locus.
31. The cell or cell population of claim 30, wherein one or more of: (a) the placement of the SAR polynucleotide disrupts or abolishes the endogenous expression of a TCR comprising an endogenous TCR α chain and/or an endogenous TCR β chain, or an endogenous TCR γ chain and/or endogenous TCR δ chain in the T cell; and (b) the disruption or abolished expression of an endogenous TCR results in enhanced expression and/or activity of the SAR polypeptide as compared to its expression and/or activity in T cells with wild-type endogenous TCR.
32. The cell or cell population of claim 31, wherein the SAR has the backbone of one or more of a SIR, a cTCR and/or an Ab-TCR.

33. The cell or cell population of any one of claims 26 to 27, wherein the cell is obtained from an autologous or an allogeneic donor who has been administered one or more mobilizing agents prior to collection of immune cells, optionally wherein the one or more mobilizing agents are selected from the group consisting of a CXCR4 antagonist, a cytokine, a beta-2 agonist, a tyrosine kinase inhibitor, a chemotherapy drug, and combinations thereof, and optionally wherein the one or more mobilizing agents are selected from the group consisting of plerixafor, G-CSF, GM-CSF, sargramostim, pegfilgrastim, epinephrine, dasatinib, cyclophosphamide, doxorubicin, and combinations thereof.
34. The cell or cell population of claim 29 or 31, wherein the SAR polypeptide has the backbone of a TFP and the cell or cell population further expresses a sequence encoding a TCR constant chain, wherein the TCR constant chain is
- a TCR alpha constant chain or fragment thereof, or
 - a TCR beta constant chain or a fragment thereof, or
 - a TCR gamma constant chain or fragment thereof, or
 - a TCR delta constant chain or a fragment thereof, or
 - a combination of i) and ii) or iii) and iv).
35. A method of making a SAR-expressing immune effector cell, comprising introducing at least one vector of claim 24 or at least one recombinant polynucleotide of claim 1 into an immune effector cell or a hematopoietic stem cell or progenitor cell that can give rise to an immune effector cell, under conditions such that the SAR polypeptide is expressed.
36. A method of expanding the SAR-expressing immune effector cells of claim 27 in a gas permeable flask under normoxic or hypoxic conditions, optionally wherein the SAR-expressing immune effector cells are expanded in the presence of a SMAC mimetic or a NIK agonist compound.
37. Use of an immune effector cell or a stem cell that can give rise to an immune effector cell of any one of claims 27 to 34 in the manufacture of a medicament for providing anti-disease immunity in a subject, wherein the cell is an autologous T cell or an allogeneic T cell, or an autologous NKT cell or an allogeneic NKT cell or an autologous or an allogeneic hematopoietic stem cell or an autologous or an allogeneic iPSC that can give rise to an immune effector cell, and wherein the SAR polypeptide comprises one or more intracellular signaling domains and binds to a disease-associated antigen.
38. Use of an immune effector cell comprising a synthetic antigen receptor (SAR) polypeptide as defined in claim 1, in the manufacture of a medicament for treating a disease in which

cells express a disease-associated antigen in a subject, wherein the SAR polypeptide comprises one or more intracellular signaling domains and binds to one or more disease-associated antigens selected from a group consisting of: CD5, CD19; CD123; CD22; CD23, CD30; CD171; CS-1 (also referred to as CD2 subset 1, CRACC, SLAMF7, CD319, and 19A24); C-type lectin-like molecule-1 (CLL-1 or CLECL1); CD33; epidermal growth factor receptor variant III (EGFRviii); ganglioside G2 (GD2); ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(I-4)bDGlcp(I-I)Cer); TNF receptor family member B cell maturation (BCMA); Tn antigen (Tn Ag) or (GalNAc α -Ser/Thr)); prostate-specific membrane antigen (PSMA); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Fms Like Tyrosine Kinase 3 (FLT3); Tumor-associated glycoprotein 72 (TAG72); CD38; CD44v6; a glycosylated CD43 epitope expressed on acute leukemia or lymphoma but not on hematopoietic progenitors, a glycosylated CD43 epitope expressed on non-hematopoietic cancers, Carcinoembryonic antigen (CEA); Epithelial cell adhesion molecule (EPCAM); B7H3 (CD276); KIT (CD117); Interleukin-13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Mesothelin; Interleukin 11 receptor alpha (IL-11Ra); prostate stem cell antigen (PSCA); Protease Serine 21 (Testisin or PRSS21); vascular endothelial growth factor receptor 2 (VEGFR2); Lewis(Y) antigen; CD24; Platelet-derived growth factor receptor beta (PDGFR-beta); Stage-specific embryonic antigen-4 (SSEA-4); CD20; Folate receptor alpha (FRa or FR1); Folate receptor beta (FRb); Receptor tyrosine-protein kinase ERBB2 (Her2/neu); Mucin 1, cell surface associated (MUC1); epidermal growth factor receptor (EGFR); neural cell adhesion molecule (NCAM); Prostase; prostatic acid phosphatase (PAP); elongation factor 2 mutated (ELF2M); Ephrin B2; fibroblast activation protein alpha (FAP); insulin-like growth factor 1 receptor (IGF-I receptor), carbonic anhydrase IX (CAIX); Proteasome (Prosome, Macropain) Subunit, Beta Type, 9 (LMP2); glycoprotein 100 (gp100); oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); tyrosinase; ephrin type-A receptor 2 (EphA2); Fucosyl GM1; sialyl Lewis adhesion molecule (sLe); ganglioside GM3 (aNeu5Ac(2-3)bDCIalp(I- 4)bDGlcp(I-1)Cer); transglutaminase 5 (TGS5); high molecular weight-melanoma associated antigen (HMWMAA); o-acetyl-GD2 ganglioside (OAcGD2); \tumor endothelial marker 1 (TEM1/CD248); tumor endothelial marker 7-related (TEM7R); claudin 6 (CLDN6); thyroid stimulating hormone receptor (TSHR); G protein coupled receptor class C group 5, member D (GPRC5D); chromosome X open reading frame 61 (CXORF61); CD97; CD179a; anaplastic lymphoma kinase (ALK); Polysialic acid; placenta-specific 1 (PLAC1); hexasaccharide portion of globoH

glycoceramide (GloboH); mammary gland differentiation antigen (NY-BR-1); uroplakin 2 (UPK2); Hepatitis A virus cellular receptor 1 (HAVCR1); adrenoceptor beta 3 (ADRB3); pannexin 3 (PANX3); G protein-coupled receptor 20 (GPR20); lymphocyte antigen 6 complex, locus K 9 (LY6K); Olfactory receptor 51E2 (OR51E2); TCR Gamma Alternate Reading Frame Protein (TARP); Wilms tumor protein (WT1); Cancer/testis antigen 1 (NY-ES0-1); Cancer/testis antigen 2 (LAGE-1a); Melanoma-associated antigen 1 (MAGE-A1); ETS translocation-variant gene 6, located on chromosome 12p (ETV6-AML); sperm protein 17 (SPA17); X Antigen Family, Member IA (XAGEI); angiopoietin-binding cell surface receptor 2 (Tie 2); melanoma cancer testis antigen-1 (MAD-CT-1); melanoma cancer testis antigen-2 (MAD-CT-2); Fos-related antigen 1; tumor protein p53 (p53); p53 mutant; prostatein; surviving; telomerase; prostate carcinoma tumor antigen-1 (PCT A-1 or Galectin 8), melanoma antigen recognized by T cells 1 (MelanA or MARTI); Rat sarcoma (Ras) mutant; human Telomerase reverse transcriptase (hTERT); sarcoma translocation breakpoints; melanoma inhibitor of apoptosis (ML-IAP); ERG (transmembrane protease, serine 2 (TMPRSS2) ETS fusion gene); N-Acetyl glucosaminyl-transferase V (NA17); paired box protein Pax-3 (PAX3); Androgen receptor; Cyclin B1; v-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Ras Homolog Family Member C (RhoC); Tyrosinase-related protein 2 (TRP-2); Cytochrome P450 IB 1 (CYPIB 1); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites), Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Paired box protein Pax-5 (PAX5); proacrosin binding protein sp32 (OY-TESI); lymphocyte-specific protein tyrosine kinase (LCK); A kinase anchor protein 4 (AKAP-4); synovial sarcoma, X breakpoint 2 (SSX2); Receptor for Advanced Glycation End products (RAGE-1); renal ubiquitous 1 (RUI); renal ubiquitous 2 (RU2); legumain; human papilloma virus E6 (HPV E6); human papilloma virus E7 (HPV E7); intestinal carboxyl esterase; heat shock protein 70-2 mutated (mut hsp70-2); CD79a; CD79b; CD72; Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Fc fragment of IgA receptor (FCAR or CD89); Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); CD300 molecule-like family member f (CD300LF); C-type lectin domain family 12 member A (CLEC12A); bone marrow stromal cell antigen 2 (BST2); EGF-like module-containing mucin-like hormone receptor-like 2 (EMR2); lymphocyte antigen 75 (LY75); Glypican-3 (GPC3); Fc receptor-like 5 (FCRL5); and immunoglobulin lambda-like polypeptide 1 (IGLL1), MPL, Biotin, c-MYC epitope Tag, CD34, LAMP1 TROP2, GFRalpha4, CDH17, CDH6, NYBR1, CDH19, CD200R, Slea (CA19.9; Sialyl Lewis Antigen); Fucosyl-GM1,

PTK7, gpNMB, CDH1-CD324, DLL3, CD276/B7H3, IL11Ra, IL13Ra2, CD179b-IGLI1, TCRgamma-delta, NKG2D, CD32 (FCGR2A), Tim1-/HVCR1, CSF2RA (GM-CSFR-alpha), TGFbetaR2, , Lews Ag, TCR-beta1 chain, TCR-beta2 chain, TCR-gamma chain, TCR-delta chain, FITC, Leutenizing hormone receptor (LHR), Follicle stimulating hormone receptor (FSHR), Chorionic Gonadotropin Hormone receptor (CGHR), CCR4, SLAMF6, SLAMF4, HIV1 envelope glycoprotein, HTLV1-Tax, CMV pp65, EBV-EBNA3c, KSHV K8.1, KSHV-gH, influenza A hemagglutinin (HA), GAD, PDL1, Guanylyl cyclase C (GCC), auto antibody to desmoglein 3 (Dsg3) and desmoglein 1 (Dsg1), HLA, HLA-A, HLA-A2, HLA-B, HLA-C, HLA-DP, HLA-DM, HLA-DOA, HLA-DOB, HLA-DQ, HLA-DR, HLA-G, IGE, CD99, RAS G12V, Tissue Factor 1 (TF1), AFP, GPRC5D, claudin18.2 (CLD18A2 OR CLDN18A.2)), P-glycoprotein, STEAP1, LIV1, NECTIN-4, CRIPTO, GPA33, BST1/CD157, low conductance chloride channel, TAJ/TROY, MPL (TPO-R), KIR3DL2, CD32b, CD229, Toso, GPC3, MR1, NYESO-1/MHC complex, CMVpp65/MHC complex, and optionally wherein the disease in which cells express the disease-associated antigen is selected from the group consisting of a proliferative disease, a precancerous condition, a cancer, and a non-cancer related indication in which cells express the disease-associated antigen.

- 39.** A recombinant polynucleotide encoding a SAR polypeptide, the polynucleotide comprising a sequence selected from the group consisting of SEQ ID NO: 1849-10720, 21609-21625, 21626-21659, 21662-21792, 21808, 21813-21840, 21843-21879, 21882- 21892, 21894-21899, 21901-21947, 21949-21963, 21967-21972, 21985-22085, 22087-22099, 22104-22207, 22209-22250, 22252-22254, 22256-22262, 22264-22273, 22275-22284, 22286-22296 and 22307-22312 or a sequence with at least 75% identity to the nucleotide sequence of the above that encodes a SAR polypeptide retaining the ability to specifically bind the target antigen(s) of the recited sequence, wherein, for the purpose of determining said sequence identity, any leader sequence, 2A self-cleaving peptide, Furin cleavage site, accessory module, selection marker, linker, and epitope tag present in the listed SEQ ID NO is excluded from the comparison.
- 40.** An amino acid sequence encoding a synthetic antigen receptor (SAR) polypeptide selected from the group consisting of SEQ ID NO: 12539-21410, 22445-22460, 22462-22495, 22498-22614, 22624, 22626-22655, 22658-22685, 22687-22694, 22697-22707, 22709-22714, 22716-22762, 22764-22778, 22782-22787, 22800-22900, 22902-22914, 22919-23022, 23024-23065, 23067-23069, 23071-23077, 23090-23099, 23101-23111 and 23122-23127 or a sequence with at least 75% identity to an amino acid sequence of

the foregoing that retains the ability to specifically bind the target antigen(s) of the recited sequence, wherein, for the purpose of determining said sequence identity, any leader sequence, 2A self-cleaving peptide, Furin cleavage site, accessory module, selection marker, linker, and epitope tag present in the listed SEQ ID NO is excluded from the comparison.

- 41.** A composition comprising at least one polynucleotide of claim 1 or 39, a SAR polypeptide molecule of claim 25 or 40, a vector of claim 24 or the cell of any one of claims 26 to 34 and a pharmaceutically acceptable excipient.
- 42.** The composition of claim 41, further comprising one or more agents, optionally selected from the group consisting of a bispecific antibody, a bispecific T-cell engager, an immunomodulatory drug, a γ -secretase inhibitor, a Src kinase inhibitor, an Lck kinase inhibitor, a Bruton's tyrosine kinase (BTK) inhibitor, an IL-6R antagonist, a calcineurin inhibitor, a chemotherapy drug, a steroid, alemtuzumab, an immune checkpoint inhibitor, and an anti-cancer therapeutic agent, and optionally wherein the one or more agents are selected from the group consisting of lenalidomide, dasatinib, ibrutinib, tocilizumab, tacrolimus, cyclosporine A, cyclophosphamide, fludarabine, methotrexate, melphalan, etoposide, vincristine, doxorubicin, temozolomide, prednisone, dexamethasone, alemtuzumab, and an anti-PD-1, anti-PD-L1, or anti-CTLA-4 antibody.
- 43.** A multi-component synthetic antigen receptor (SAR) system comprising: (a) the SAR polypeptide of claim 25; and (b) one or more SAR adaptors, each SAR adaptor comprising: (i) an antigen binding moiety selected from the group consisting of an scFv, an Fv, a vHH, a single domain antibody, an FHVH, a non-immunoglobulin antigen binding scaffold, an antibody, an antibody fragment, and an Fc-containing antibody or antibody fragment; and (ii) an adaptor selected from the group consisting of an RZIP, an EZIP, an E4, a K4, a SYNZIP, a ULBP2R, a ULBP2-S3, a D domain, a Streptag, FITC, GCN4, a PDZ-binding domain, a streptavidin domain, a streptavidin binding protein (SBP) domain, a PYL domain, an ABI domain, and an Fc region of an immunoglobulin, wherein the adaptor of the SAR adaptor specifically binds to a cognate adaptor binding domain of the SAR polypeptide such that the antigen binding moiety of the SAR adaptor redirects the SAR polypeptide to a target antigen, and optionally wherein the adaptor of the SAR adaptor and the cognate adaptor binding domain of the SAR polypeptide form an orthogonal pair selected from the group consisting of: (i) RZIP and EZIP, in either orientation; (ii) E4 and K4, in either orientation; (iii) NKG2D-AF or a NKG2D-AF dimer paired with ULBP2R; (iv) NKG2D-YA or a NKG2D-YA dimer paired with ULBP2-S3; (v) two D domains; (vi) Streptag

and a Streptag-binding moiety; (vii) FITC and an anti-FITC moiety; (viii) GCN4 and an anti-GCN4 moiety; and (ix) an Fc region of an immunoglobulin and an Fc-binding domain of CD16, CD16A-V158, CD32, or CD64.

44. A kit comprising at least one polynucleotide of claim 1 or 39, a SAR polypeptide of claim 25 or 40, a vector of claim 24 or the cell of any one of claims 26 to 34.