

COMPOSITIONS FOR MODIFYING CELLS

CROSS REFERENCE TO RELATED APPLICATIONS

This application claims the benefit under 35 U.S. C. § 119(e) of U.S. Provisional Application No. 63/532,093, filed August 11, 2023, and U.S. Provisional Application No. 63/540,344, filed September 25, 2023, and each of which is incorporated by reference herein in its entirety.

STATEMENT REGARDING SEQUENCE LISTING

The Sequence Listing associated with this application is provided in XML format in lieu of a paper copy and is hereby incorporated by reference into the specification. The name of the XML file containing the Sequence Listing is KELO-010-WO1_ST26.xml. The XML file is 744 KB, was created on July 25, 2024, and is being submitted electronically via Patent Center, concurrent with the filing of the specification.

Technical Field

The present disclosure relates to recombinant particles engineered to deliver one or more engineered receptors to a cell. More particularly, the disclosure relates to recombinant particles engineered to deliver one or more engineered receptors to cells *in vivo*.

Description of the Related Art

Ex vivo gene therapies are potentially one-time therapeutic modalities that generally involve harvesting cells from a subject, modifying the cells by culturing them with a gene therapy vector, and delivering the modified cells back to the subject. Because *ex vivo* gene therapies are manufactured in a controlled environment, they do not generally require specialized targeting moieties and instead, targeting moieties with a broad tropism and that are highly efficient in delivering a gene therapy to most cell types are used.

In contrast, *in vivo* gene therapies are manufactured in the patient, in an uncontrolled environment. Accordingly, *in vivo* delivery of gene therapy vectors to specific cell types is

orders of magnitude more complex than *ex vivo* delivery. *In vivo* gene therapy vectors encounter many non-target or off-target cells and may require a narrower or more specific tropism to deliver therapeutic payloads to a particular cell type. The potential of *in vivo* gene therapies has yet to be realized primarily due to inefficient delivery to desired cell types in combination with substantial off-target delivery. Use of specialized targeting moieties to deliver gene therapies *in vivo* has proven difficult in abrogating the off-target delivery to undesired cell types. In addition, on-target delivery of *in vivo* gene therapies using such specialized targeting moieties is often inefficient.

BRIEF SUMMARY

The present disclosure generally relates, in part, to a recombinant particle comprising a fusogen and one or more tropism polypeptides that are suitable for delivering a payload to one or more desired cell types *in vivo*. The present disclosure more particularly relates to recombinant viral, *e.g.*, retroviral or lentiviral particles comprising a detargeted viral-based fusogen, one or more non-viral membrane bound tropism polypeptides and a vector, *e.g.*, a viral, retroviral, or lentiviral vector encoding an expressible polynucleotide encoding an engineered receptor.

In various embodiments, a recombinant particle is contemplated, comprising: (a) a surface comprising (i) one or more mutated viral envelope glycoproteins that retain fusogenic activity and that lack cognate receptor binding activity and (ii) a non-viral membrane-bound tropism polypeptide comprising an antibody or antigen binding fragment thereof that binds an antigen expressed on an immune effector cell, a spacer polypeptide, and a GPI anchor domain or a transmembrane domain, and optionally, an intracellular domain comprising no more than 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids; and (b) a therapeutic payload.

In particular embodiments, the particle is a fusosome; an extracellular vesicle, including a microvesicle, an apoptotic body, and an exosome; a lipid nanoparticle; a virus-like particle (VLPs); or a recombinant viral particle.

In certain embodiments, the surface comprises a single layer of phospholipid, a phospholipid bilayer, a cell membrane, a capsid, or a viral envelope.

In some embodiments, the payload comprises one or more polynucleotides and/or polypeptides.

In particular embodiments, the payload comprises a vector that encodes a therapeutic polynucleotide or polypeptide.

In particular embodiments, the payload comprises a vector that encodes one or more engineered receptors.

5 In further embodiments, the payload comprises a vector that encodes a promoter operably linked to a polynucleotide encoding one or more engineered receptors.

In various embodiments, a recombinant lentiviral particle is contemplated, comprising: (a) a viral envelope comprising (i) one or more mutated viral envelope glycoproteins that retain fusogenic activity and that lack cognate receptor binding activity
10 and (ii) a non-viral membrane-bound tropism polypeptide comprising an antibody or antigen binding fragment thereof that binds an antigen expressed on an immune effector cell, a spacer polypeptide, a GPI domain or transmembrane domain and optionally, an intracellular domain comprising no more than 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids; and (b) a recombinant lentiviral vector comprising a polynucleotide encoding a promoter operably linked to a
15 polynucleotide encoding one or more engineered receptors.

In some embodiments, the one or more mutated viral envelope glycoproteins comprise a rhabdovirus envelope glycoprotein, or one or more paramyxovirus envelope glycoproteins.

In certain embodiments, the one or more mutated viral envelope glycoproteins
20 comprise a vesiculovirus envelope glycoprotein, one or more morbillivirus envelope glycoproteins or one or more henipavirus envelope glycoproteins.

In particular embodiments, the vesiculovirus is selected from the group consisting of: vesicular stomatitis Alagoas virus (VSAV; Alagoas vesiculovirus), Carajás virus (CJSV; Carajas vesiculovirus), Chandipura virus (CHPV; Chandipura vesiculovirus), Cocal virus
25 (COCV; Cocal vesiculovirus), vesicular stomatitis Indiana virus (VSIV; Indiana vesiculovirus), Isfahan virus (ISFV; Isfahan vesiculovirus), Maraba virus (MARAV; Maraba vesiculovirus), Morreton virus (MORV; Morreton vesiculovirus), vesicular stomatitis New Jersey virus (VSNJV; New Jersey vesiculovirus), and Piry virus (PIRYV; Piry vesiculovirus).

30 In additional embodiments, the vesiculovirus envelope glycoprotein is a vesiculovirus G protein.

In additional embodiments, the vesiculovirus G protein is a COCV G glycoprotein (COCV-G) or a VSIV G glycoprotein (VSIV-G).

In certain embodiments, the VSIV-G envelope protein comprises one or more of: (a) one or more amino acid substitutions at H8, N9, Q10, K47, K50, A51, S183, S179, N180, I182, M184, Y209, I347, T350, T352, E353, and R354; (b) an insertion of TT between N9 and Q10, an insertion of GGS between H8 and N9, an insertion of GGS between N9 and Q10, an insertion of TT between N208 and Y209, an insertion of GGS between P46 and K47, and an insertion of GGS between N208 and Y209; or (c) amino acid substitutions at K47 and/or R354; or (d) a deletion of residues 1-8.

In particular embodiments, the VSIV-G envelope protein comprises one or more amino acid substitutions at H8, K47, Y209, and R354.

In particular embodiments, the VSIV-G polypeptide comprises one or more amino acid substitutions at K47, I182, and/or R354 (substitution with any amino acid; a conservation substitution; a disruptive substitution; substitution with D, E, A, G, F, or Q; or substitution with A, G, F, or Q). In particular embodiments, the VSIV-G polypeptide comprises amino acid substitutions at K47, I182, or R354; K47 and I182; K47 and R354; I182 and R354; or at K47, I182, and R354 of an amino acid sequence at least 95% identical to, at least 96% identical to, at least 97% identical to, and least 98% identical to, at least 99% identical to, or identical to, SEQ ID NO: 1.

In particular embodiments, the VSIV-G polypeptide comprises one or more of the following amino acid substitutions: K47A, K47Q, I182E, I182D, R354A, and/or R354Q.

In particular embodiments, the VSIV-G polypeptide comprises the following amino acid substitutions: K47A and I182E; K47A and I182D; K47Q and I182E; K47Q and I182D; I182E and R354A; I182E and R354Q; I182D and R354A; I182D and R354Q; K47A and R354A; K47A and R354Q; K47Q and R354A; K47Q and R354Q; K47A, I182E, and R354A; K47A, I182D, and R354A; K47Q, I182E, and R354A; K47Q, I182D, and R354A; K47A, I182E, and R354Q; K47A, I182D, and R354Q; K47Q, I182E, and R354Q; or K47Q, I182D, and R354Q of an amino acid sequence at least 95% identical to, at least 96% identical to, at least 97% identical to, and least 98% identical to, at least 99% identical to, or identical to, SEQ ID NO: 1.

In particular embodiments, the VSIV-G envelope protein comprises amino acid substitutions selected from the group consisting of: K47A and R354A; K47A and R354G; K47A and R354F; K47A and R354Q; K47G and R354A; K47G and R354G; K47G and R354F; K47G and R354Q; K47F and R354A; K47F and R354G; K47F and R354F; K47F

and R354Q; K47Q and R354A; K47Q and R354G; K47Q and R354F; and K47Q and R354Q.

In certain embodiments, the VSIV-G envelope protein comprises the amino acid sequence set forth in SEQ ID NO: 2 or an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical thereto, wherein $X_1 = I$, $X_2 = A$, $X_3 = Q$, and $X_4 = A$; $X_1 = I$, $X_2 = A$, $X_3 = Q$, and $X_4 = G$; $X_1 = I$, $X_2 = A$, $X_3 = Q$, and $X_4 = F$; $X_1 = I$, $X_2 = A$, $X_3 = Q$, and $X_4 = Q$; $X_1 = L$, $X_2 = A$, $X_3 = Q$, and $X_4 = A$; $X_1 = L$, $X_2 = A$, $X_3 = Q$, and $X_4 = G$; $X_1 = L$, $X_2 = A$, $X_3 = Q$, and $X_4 = F$; $X_1 = L$, $X_2 = A$, $X_3 = Q$, and $X_4 = Q$; $X_1 = I$, $X_2 = A$, $X_3 = H$, and $X_4 = A$; $X_1 = I$, $X_2 = A$, $X_3 = H$, and $X_4 = G$; $X_1 = I$, $X_2 = A$, $X_3 = H$, and $X_4 = F$; $X_1 = I$, $X_2 = A$, $X_3 = H$, and $X_4 = Q$; $X_1 = L$, $X_2 = A$, $X_3 = H$, and $X_4 = A$; $X_1 = L$, $X_2 = A$, $X_3 = H$, and $X_4 = G$; $X_1 = L$, $X_2 = A$, $X_3 = H$, and $X_4 = F$; $X_1 = L$, $X_2 = A$, $X_3 = H$, and $X_4 = Q$; $X_1 = I$, $X_2 = G$, $X_3 = Q$, and $X_4 = A$; $X_1 = I$, $X_2 = G$, $X_3 = Q$, and $X_4 = G$; $X_1 = I$, $X_2 = G$, $X_3 = Q$, and $X_4 = F$; $X_1 = I$, $X_2 = G$, $X_3 = Q$, and $X_4 = Q$; $X_1 = L$, $X_2 = G$, $X_3 = Q$, and $X_4 = A$; $X_1 = L$, $X_2 = G$, $X_3 = Q$, and $X_4 = G$; $X_1 = L$, $X_2 = G$, $X_3 = Q$, and $X_4 = F$; $X_1 = L$, $X_2 = G$, $X_3 = Q$, and $X_4 = Q$; $X_1 = I$, $X_2 = G$, $X_3 = H$, and $X_4 = A$; $X_1 = I$, $X_2 = G$, $X_3 = H$, and $X_4 = G$; $X_1 = I$, $X_2 = G$, $X_3 = H$, and $X_4 = F$; $X_1 = I$, $X_2 = G$, $X_3 = H$, and $X_4 = Q$; $X_1 = L$, $X_2 = G$, $X_3 = H$, and $X_4 = A$; $X_1 = L$, $X_2 = G$, $X_3 = H$, and $X_4 = G$; $X_1 = L$, $X_2 = G$, $X_3 = H$, and $X_4 = F$; $X_1 = L$, $X_2 = G$, $X_3 = H$, and $X_4 = Q$; $X_1 = I$, $X_2 = F$, $X_3 = Q$, and $X_4 = A$; $X_1 = I$, $X_2 = F$, $X_3 = Q$, and $X_4 = G$; $X_1 = I$, $X_2 = F$, $X_3 = Q$, and $X_4 = F$; $X_1 = I$, $X_2 = F$, $X_3 = Q$, and $X_4 = Q$; $X_1 = L$, $X_2 = F$, $X_3 = Q$, and $X_4 = A$; $X_1 = L$, $X_2 = F$, $X_3 = Q$, and $X_4 = G$; $X_1 = L$, $X_2 = F$, $X_3 = Q$, and $X_4 = F$; $X_1 = L$, $X_2 = F$, $X_3 = Q$, and $X_4 = Q$; $X_1 = I$, $X_2 = F$, $X_3 = H$, and $X_4 = A$; $X_1 = I$, $X_2 = F$, $X_3 = H$, and $X_4 = G$; $X_1 = I$, $X_2 = F$, $X_3 = H$, and $X_4 = F$; $X_1 = I$, $X_2 = F$, $X_3 = H$, and $X_4 = Q$; $X_1 = L$, $X_2 = F$, $X_3 = H$, and $X_4 = A$; $X_1 = L$, $X_2 = F$, $X_3 = H$, and $X_4 = G$; $X_1 = L$, $X_2 = F$, $X_3 = H$, and $X_4 = F$; $X_1 = L$, $X_2 = F$, $X_3 = H$, and $X_4 = Q$; $X_1 = I$, $X_2 = Q$, $X_3 = Q$, and $X_4 = A$; $X_1 = I$, $X_2 = Q$, $X_3 = Q$, and $X_4 = G$; $X_1 = I$, $X_2 = Q$, $X_3 = Q$, and $X_4 = F$; $X_1 = I$, $X_2 = Q$, $X_3 = Q$, and $X_4 = Q$; $X_1 = L$, $X_2 = Q$, $X_3 = Q$, and $X_4 = A$; $X_1 = L$, $X_2 = Q$, $X_3 = Q$, and $X_4 = G$; $X_1 = L$, $X_2 = Q$, $X_3 = Q$, and $X_4 = F$; $X_1 = L$, $X_2 = Q$, $X_3 = Q$, and $X_4 = Q$; $X_1 = I$, $X_2 = Q$, $X_3 = H$, and $X_4 = A$; $X_1 = I$, $X_2 = Q$, $X_3 = H$, and $X_4 = G$; $X_1 = I$, $X_2 = Q$, $X_3 = H$, and $X_4 = F$; $X_1 = I$, $X_2 = Q$, $X_3 = H$, and $X_4 = Q$; $X_1 = L$, $X_2 = Q$, $X_3 = H$, and $X_4 = A$; $X_1 = L$, $X_2 = Q$, $X_3 = H$, and $X_4 = G$; $X_1 = L$, $X_2 = Q$, $X_3 = H$, and $X_4 = F$; and $X_1 = L$, $X_2 = Q$, $X_3 = H$, and $X_4 = Q$.

In some embodiments, the VSIV-G envelope protein comprises the amino acid sequence set forth in any one of SEQ ID NOs: 582-645 or an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical thereto.

In particular embodiments, the VSIV-G envelope protein comprises the amino acid sequence set forth in any one of SEQ ID NOs: 630, 634, 638, and 642 or an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical thereto. In a particular preferred embodiment, the VSIV-G envelope protein comprises the amino acid sequence set forth in SEQ ID NO: 642 or an amino acid sequence at least 95%,
 5 at least 96%, at least 97%, at least 98%, or at least 99% identical thereto.

In additional embodiments, the vesiculovirus G protein is COCV-G.

In some embodiments, the COCV-G envelope protein comprises one or more amino acid substitutions at K47 and/or R354.

10 In certain embodiments, the COCV-G envelope protein comprises amino acid substitutions selected from the group consisting of: K47A and R354A; K47A and R354G; K47A and R354F; K47A and R354Q; K47G and R354A; K47G and R354G; K47G and R354F; K47G and R354Q; K47F and R354A; K47F and R354G; K47F and R354F; K47F and R354Q; K47Q and R354A; K47Q and R354G; K47Q and R354F; and K47Q and
 15 R354Q.

In further embodiments, the COCV-G envelope protein comprises the amino acid sequence set forth in SEQ ID NO: 4 or an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical thereto, wherein $X_1 = A$ and $X_2 = A$; $X_1 = A$ and $X_2 = G$; $X_1 = A$ and $X_2 = F$; $X_1 = A$ and $X_2 = Q$; $X_1 = G$ and $X_2 = A$; $X_1 = G$ and $X_2 = G$;
 20 $X_1 = G$ and $X_2 = F$; $X_1 = G$ and $X_2 = Q$; $X_1 = F$ and $X_2 = A$; $X_1 = F$ and $X_2 = G$; $X_1 = F$ and $X_2 = F$; $X_1 = F$ and $X_2 = Q$; $X_1 = Q$ and $X_2 = A$; $X_1 = Q$ and $X_2 = G$; $X_1 = Q$ and $X_2 = F$; or $X_1 = A$ and $X_2 = Q$.

In particular embodiments, the COCV-G envelope protein comprises the amino acid sequence set forth in any one of SEQ ID NOs: 646-661 or an amino acid sequence at least
 25 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical thereto.

In certain embodiments, the one or more morbillivirus envelope glycoproteins are measles virus F (MV-F) and measles virus H (MV-H).

In some embodiments, the MV-H protein comprises one or more amino acid substitutions at Y463, R515, S530, and F531.

30 In additional embodiments, the MV-H protein comprises one or more amino acid substitutions selected from the group consisting of: Y463A, R515A, S530, and F531.

In some embodiments, the MV-H protein comprises the amino acid sequence set forth in SEQ ID NO: 7.

In certain embodiments, the one or more henipavirus envelope glycoproteins are nipah virus F (NiV-F) and nipah virus G (NiV-G).

In particular embodiments, the NiV-G protein comprises one or more amino acid substitutions at E468, W471, Q497, and E500.

5 In additional embodiments, the NiV-G protein comprises one or more amino acid substitutions selected from the group consisting of: E468A, W471A, Q497A, and E500A.

In particular embodiments, the NiV-G protein comprises the amino acid sequence set forth in SEQ ID NO: 10.

10 In further embodiments, the antibody or antigen binding fragment thereof is selected from the group consisting of: a Camel Ig, a Llama Ig, an Alpaca Ig, Ig NAR, a Fab' fragment, a F(ab')₂ fragment, a bispecific Fab dimer (Fab₂), a trispecific Fab trimer (Fab₃), an Fv, a single chain Fv protein (scFv), a bis-scFv, (scFv)₂, a minibody, a diabody, a triabody, a tetrabody, a disulfide stabilized Fv protein ("dsFv"), a Fibronectin type III (FN3) domain antibody, a single-domain antibody (sdAb, a camelid VHH, Nanobody), and a centyrin.

15 In certain embodiments, the antibody or antigen binding fragment thereof binds an antigen expressed on an immune effector cell selected from the group consisting of: the alpha, beta, gamma, or delta chain of the T cell receptor, CD2, CD3δ, CD3ε, CD3γ, CD4, CD8α, and CD8β.

20 In particular embodiments, the antibody or antigen binding fragment thereof comprises (a) a heavy chain variable region (VH) comprising a CDRH1, a CDRH2, and a CDRH3 of an antibody or antigen binding fragment thereof set forth in Table 5; (b) a polypeptide linker; and (c) a light chain variable region (VL) comprising a CDRL1, a CDRL2, and a CDRL3 of an antibody or antigen binding fragment thereof set forth in Table 5.

25 In additional embodiments, the antibody or antigen binding fragment thereof comprises (a) a heavy chain variable region (VH) of an antibody or antigen binding fragment thereof set forth in Table 5; (b) a polypeptide linker; and (c) a light chain variable region (VL) of an antibody or antigen binding fragment thereof set forth in Table 5.

30 In some embodiments, the antibody or antigen binding fragment thereof comprises: (a) a heavy chain variable region (VH) of an antibody or antigen binding fragment thereof set forth in Table 5; (b) a polypeptide linker selected from the group consisting of: (GGGGS)_n wherein n = 1, 2, 3, 4 or 5; S(GGGGS)_n wherein n = 1, 2, 3, 4 or 5; GEGTSTGSGSGSGSGGAD, GSTSGSGKPGSGEGSTKG and variants thereof

comprising an amino acid sequence 95% identical thereto; and (c) the corresponding light chain variable region (VL) of the antibody or antigen binding fragment thereof set forth in Table 5.

5 In particular embodiments, the antibody or antigen binding fragment thereof comprises the amino acid sequence set forth in any one of SEQ ID NOs: 19, 20, 29, 30, 39, 40, 49, 50, 59, 60, 69, 70, 79, 80, 89, 90, 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, 170, 179, 180, 189, 190, 199, 200, 209, 210, 219, 220, 229, 230, 239, 240, 249, 250, 259, 260, 269, 270, 279, 280, 289, 290, 299, 300, 309, 310, 319, 320, 329, 330, 339, 340, 349, 350, 359, 360, 369, 370, 379, 380, 389, 390, 399, 400, 409, and 410.

10 In particular embodiments, the antibody or antigen binding fragment thereof comprises the amino acid sequence set forth in any one of SEQ ID NOs: 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, and 170.

In further embodiments, the antibody or antigen binding fragment thereof comprises the amino acid sequence set forth in any one of SEQ ID NOs: 99 or 100, 109 or 110, 119 or 120, 129 or 130, 139 or 140, 149 or 150, 159 or 160, and 169 or 170. In a preferred embodiment, the antibody or antigen binding fragment thereof comprises the amino acid sequence set forth in SEQ ID NOs: 99.

20 In some embodiments, the spacer comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 411-434.

In certain embodiments, the spacer comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 411-413, SEQ ID NOs: 414-423, SEQ ID NOs: 424-427, or SEQ ID NOs: 428-434.

25 In particular embodiments, the transmembrane domain comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 435, 436, 437, 438, 439, 440 or 441.

In some embodiments, the intracellular domain comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical

to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 442, 443, 444, 445, 446, 447 or 448.

5 In particular embodiments, the non-viral membrane-bound tropism polypeptide comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 455-576. In particular embodiments, the tropism polypeptide comprises an amino acid sequence set forth in any one of SEQ ID NOs: 461.

10 In additional embodiments, the non-viral membrane-bound tropism polypeptide comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 471-486. In particular embodiments, the tropism polypeptide comprises an amino acid sequence set forth in any one of SEQ ID NOs: 471 or 483.

15 In certain embodiments, the non-viral membrane-bound tropism polypeptide comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 535-554. In particular embodiments, the tropism polypeptide comprises an amino acid sequence set forth in any one of SEQ ID NOs: 537 or 553.

20 In particular embodiments, the non-viral membrane-bound tropism polypeptide comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 555-562.

25 In additional embodiments, the non-viral membrane-bound tropism polypeptide comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 563 or 564.

In additional embodiments, the non-viral membrane-bound tropism polypeptide comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least

95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 565-576.

5 In additional embodiments, the non-viral membrane-bound tropism polypeptide comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in SEQ ID NO: 471 or SEQ ID NO: 553.

10 In certain embodiments, the particle further comprises one or more secondary non-viral membrane bound tropism polypeptides.

In further embodiments, the one or more secondary non-viral membrane bound tropism polypeptides comprise one or more of CD80, CD86, CD137L, OX40L, and ICOSL or variants thereof.

15 In particular embodiments, the particle further comprises one or more secondary non-viral membrane-bound tropism polypeptides at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 577-581. In particular embodiments, the one or more secondary non-viral membrane-bound tropism polypeptide comprises an amino acid sequence set forth in
20 any one of SEQ ID NOs: 577.

In some embodiments, the recombinant lentiviral vector is engineered or derived from a lentiviral genome of a lentivirus selected from the group consisting of: human immunodeficiency virus 1 (HIV-1); human immunodeficiency virus 2 (HIV-2); visna-maedi virus (VMV); caprine arthritis-encephalitis virus (CAEV); equine infectious anemia virus (EIAV); feline immunodeficiency virus (FIV); bovine immune deficiency virus (BIV); and
25 simian immunodeficiency virus (SIV).

In additional embodiments, the recombinant lentiviral vector further comprises one or more polynucleotides encoding one or more of the following: a signal peptide, a post-transcriptional regulatory element, an insulator element, a selectable marker, and a cell
30 suicide gene.

In certain embodiments, the post-transcriptional regulatory element is a woodchuck hepatitis virus post-transcriptional regulatory element (WPRE) or a hepatitis B virus post-transcriptional regulatory element (HPRE).

In particular embodiments, the promoter is selected from the group consisting of: a β -actin promoter, a cytomegalovirus (CMV) immediate early promoter, a simian virus 40 (SV40) (*e.g.*, early or late) promoter, a Moloney murine leukemia virus (MoMLV) promoter, a Rous sarcoma virus (RSV) promoter, a herpes simplex virus (HSV) (thymidine kinase) promoter, an SV40/CD43 promoter, a spleen focus forming virus (SFFV) promoter, an elongation factor 1-alpha (EFl α) short promoter (intronless), an EFl α long promoter containing an intron, a Ubiquitin C (UBC) promoter, a phosphoglycerate kinase-1 (PGK) promoter, a cytomegalovirus enhancer/chicken β -actin (CAG) promoter, and a myeloproliferative sarcoma virus enhancer, negative control region deleted, dl587rev primer-binding site substituted (MND) U3 promoter.

In further embodiments, the one or more engineered receptors are selected from the group consisting of: a chimeric antigen receptor (CAR), a chimeric costimulatory receptor (CCR), an alpha-beta T cell receptor ($\alpha\beta$ TCR), a gamma delta T cell receptor ($\gamma\delta$ TCR), a dimerizing agent regulated immunoreceptor complex (DARIC), a chimeric TGF- β receptor (CTBR), and a zetakine receptor.

In certain embodiments, the one or more engineered receptors bind an antigen selected from the group consisting of: alpha folate receptor (FR α), $\alpha\beta$ 6 integrin, BAFFR, B cell maturation antigen (BCMA), B7-H3 (CD276), B7-H6, carbonic anhydrase IX (CAIX), CD16, CD19, CD20, CD22, CD30, CD33, CD37, CD38, CD44, CD44v6, CD44v7/8, CD70, CD79A, CD79B, CD123, CD133, CD138, CD171, carcinoembryonic antigen (CEA), claudin 6, (CLDN6), claudin 18 isoform 2 (CLDN18.2), C-type lectin-like molecule-1 (CLL-1), CD2 subset 1 (CS-1), chondroitin sulfate proteoglycan 4 (CSPG4), cutaneous T cell lymphoma-associated antigen 1 (CTAGE1), delta like canonical Notch ligand 3 (DLL3), epidermal growth factor receptor (EGFR), epidermal growth factor receptor variant III (EGFRvIII), epithelial glycoprotein 2 (EGP2), epithelial glycoprotein 40 (EGP40), epithelial cell adhesion molecule (EPCAM), ephrin type-A receptor 2 (EPHA2), erb-b2 receptor tyrosine kinase 4 (ERBB4), fibroblast activation protein (FAP), Fc Receptor Like 5 (FCRL5), fetal acetylcholinesterase receptor (AChR), ganglioside G2 (GD2), ganglioside G3 (GD3), Glypican-3 (GPC3), G Protein-Coupled Receptor Class C Group 5 Member D (GPCR5D), EGFR family including ErbB2 (HER2), HER2 p95, IL-10R α , IL-13R α 2, Kappa, cancer/testis antigen 2 (LAGE-1A), Lambda, Lewis-Y (LeY), L1 cell adhesion molecule (L1-CAM), melanoma antigen gene (MAGE)-A1, MAGE-A3, MAGE-A4, MAGE-A6, MAGEA10, melanoma antigen recognized by T cells 1 (MelanA or MART1),

Mesothelin (MSLN), MUC1, MUC16, MHC class I chain related proteins A (MICA), MHC class I chain related proteins B (MICB), neural cell adhesion molecule (NCAM), cancer/testis antigen 1 (NY-ESO-1), placenta-specific 1 (PLAC1), preferentially expressed antigen in melanoma (PRAME), prostate stem cell antigen (PSCA), prostate-specific membrane antigen (PSMA), receptor tyrosine kinase-like orphan receptor 1 (ROR1), SLAMF7, synovial sarcoma, X breakpoint 2 (SSX2), Survivin, TACI, tumor associated glycoprotein 72 (TAG72), tumor endothelial marker 1 (TEM1/CD248), tumor endothelial marker 7-related (TEM7R), transforming growth factor beta 1 (TGFβ1), trophoblast glycoprotein (TPBG), UL16-binding protein (ULBP) 1, ULBP2, ULBP3, ULBP4, ULBP5, ULBP6, vascular endothelial growth factor receptor 2 (VEGFR2), and Wilms tumor 1 (WT-1).

In some embodiments, the one or more engineered receptors bind an antigen selected from the group consisting of: BCMA, CD19, CD20, CD22, CD33, CD38, CD79A, CD79B, GPCR5D, MAGE-A4, MSLN, MUC16, NY-ESO-1, PSCA, PSMA and ROR1.

In particular embodiments, the one or more engineered receptors bind an antigen selected from the group consisting of: BCMA, CD19, CD20, CD22, CD38, CD79A, CD79B, and GPCR5D.

In additional embodiments, the one or more engineered receptors bind an antigen selected from the group consisting of: BCMA, CD38, and GPCR5D.

In particular embodiments, the one or more engineered receptors bind an antigen selected from the group consisting of: CD19, CD20, CD22, CD79A, and CD79B.

In certain embodiments, the one or more engineered receptors comprises an extracellular antigen binding domain, a hinge domain, a transmembrane domain, and one or more intracellular signaling domains.

In some embodiments, the one or more engineered antigen receptors comprises an extracellular antigen binding domain selected from the group consisting of: a receptor ectodomain, a ligand, or an antibody or antigen binding fragment thereof selected from the group consisting of: a Camel Ig, a Llama Ig, an Alpaca Ig, Ig NAR, a Fab' fragment, a F(ab')₂ fragment, a bispecific Fab dimer (Fab2), a trispecific Fab trimer (Fab3), an Fv, a single chain Fv protein (scFv), a bis-scFv, (scFv)₂, a minibody, a diabody, a triabody, a tetrabody, a disulfide stabilized Fv protein ("dsFv"), a Fibronectin type III (FN3) domain antibody, a single-domain antibody (sdAb, a camelid VHH, Nanobody), and a centyrin.

In further embodiments, the CAR comprises a hinge domain isolated or derived from a polypeptide selected from the group consisting of: CD4, CD8 β , CD8 α , CD28, CD134, CD137, CD152, CD278, IgG1, IgG2, IgG3, and IgG4.

In certain embodiments, the CAR comprises a transmembrane domain isolated or
5 derived from a polypeptide selected from the group consisting of: alpha, beta, gamma, or delta chain of the T-cell receptor, CD3 δ , CD3 ϵ , CD3 γ , CD3 ζ , CD4, CD5, CD8 α , CD9, CD16, CD22, CD27, CD28, CD33, CD37, CD45, CD64, CD80, CD86, CD134, CD137, CD152, CD154, CD278, amnionless (AMN), and programmed cell death 1 (PDCD1).

In particular embodiments, the CAR comprises a primary signaling domain isolated
10 or derived from a polypeptide selected from the group consisting of: FcR γ , FcR β , CD3 γ , CD3 δ , CD3 ϵ , CD3 ζ , CD22, CD79A, CD79B, and CD66d.

In some embodiments, the CAR comprises one or more costimulatory domains isolated or derived from a polypeptide selected from the group consisting of: Toll-like receptor 1 (TLR1), TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLR10,
15 caspase recruitment domain family member 11 (CARD11), CD2, CD7, CD27, CD28, CD30, CD40, CD54 (ICAM), CD83, CD94, CD134 (OX40), CD137 (4-1BB), CD278 (ICOS), DNAX-Activation Protein 10 (DAP10), Linker for activation of T-cells family member 1 (LAT), SH2 Domain-Containing Leukocyte Protein Of 76 kD (SLP76), T cell receptor associated transmembrane adaptor 1 (TRAT1), TNFR2, TNFRS14, TNFRS18, TNFRS25,
20 and zeta chain of T cell receptor associated protein kinase 70 (ZAP70).

In particular embodiments, the CAR comprises an amino acid sequence set forth in any one of SEQ ID NOs: 662, 663, 664, 665, or 666.

In certain embodiments, the one or more engineered receptors further comprises a CCR comprising an extracellular antigen binding domain that binds an antigen different than
25 the antigen bound by the CAR, a hinge domain, a transmembrane domain, and one or more intracellular signaling domains.

In particular embodiments, the one or more engineered receptors comprises a DARIC comprising a DARIC signaling component comprising a multimerization domain, a transmembrane domain and one or more intracellular signaling domains; and a DARIC
30 binding component comprising an extracellular antigen binding domain, an extracellular antigen binding domain, a transmembrane domain, and optionally one or more intracellular signaling domains.

In further embodiments, the one or more engineered receptors comprises a CTBR comprising (a) a first polypeptide comprising an extracellular TGF β 1-binding domain of TGF β R2, a transmembrane domain, and a first interleukin receptor intracellular signaling domain; (b) a polypeptide cleavage signal; and (c) a second polypeptide comprising an
5 extracellular TGF β 1-binding domain of TGF β R1, a transmembrane domain, and a second interleukin receptor intracellular signaling domain.

In various embodiments, a recombinant particle is contemplated, comprising: (a) a surface comprising (i) one or more mutated viral envelope glycoproteins that retain fusogenic activity and that lack cognate receptor binding activity, wherein the one or more mutated
10 viral envelope glycoproteins comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to any one of SEQ ID NOs: 630, 634, 638, and 642 and (ii) a non-viral membrane-bound tropism polypeptide comprising an antibody or antigen binding fragment thereof comprising an amino acid sequence set forth in any one of SEQ ID NOs: 91 and 95, and 99 or 100, that binds an antigen expressed on an
15 immune effector cell, a spacer polypeptide, and a GPI anchor domain or a transmembrane domain, and optionally, an intracellular domain comprising no more than 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids; and (b) a therapeutic payload encoding an engineered antigen receptor.

In various embodiments, a recombinant particle is contemplated, comprising: (a) a
20 surface comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642 and (ii) a non-viral membrane-bound tropism polypeptide comprising an antibody or antigen binding fragment thereof comprising an amino acid sequence set forth in SEQ ID NO: 99 or 100, that binds an antigen expressed on an immune
25 effector cell, a spacer polypeptide, and a GPI anchor domain or a transmembrane domain, and optionally, an intracellular domain comprising no more than 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids; and (b) a lentiviral vector encoding an engineered antigen receptor.

In various embodiments, a recombinant lentiviral particle is contemplated, comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that
30 comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642 and (ii) a non-viral membrane-bound tropism polypeptide comprising an amino acid sequence set forth in any one of SEQ ID NOs: 99 or 100, that binds an antigen expressed on an immune effector cell, a spacer polypeptide,

and a GPI anchor domain or a transmembrane domain, and optionally, an intracellular domain comprising no more than 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids; and (b) a therapeutic payload encoding an engineered antigen receptor.

In various embodiments, a recombinant lentiviral particle is contemplated,
5 comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide comprising an amino acid sequence set forth in any one of SEQ ID NOs: 461, 471, 483, 537, and 553; and optionally (iii) a secondary non-viral membrane-
10 bound tropism polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 577; and (b) a lentiviral vector encoding a chimeric antigen receptor.

In various embodiments, a recombinant lentiviral particle is contemplated,
comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least
15 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 471; and optionally (iii) a secondary non-viral membrane-bound tropism polypeptide that
comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at
20 least 99% identical to or identical to SEQ ID NO: 577; and (b) a lentiviral vector encoding a chimeric antigen receptor comprising an amino acid sequence set forth in any one of SEQ ID NOs: 662-666.

In various embodiments, a recombinant lentiviral particle is contemplated,
comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that
25 comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 471; and optionally (iii) a secondary non-viral membrane-bound tropism polypeptide that comprises
30 an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 577; and (b) a lentiviral vector encoding a chimeric antigen receptor that binds a polypeptide selected from any one of BCMA, CD19, CD20, CD22, CD38, CD79A, CD79B, and GPCR5D.

In various embodiments, a recombinant lentiviral particle is contemplated, comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 471; and optionally (iii) a secondary non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 577; and (b) a lentiviral vector encoding a chimeric antigen receptor that binds BCMA.

In various embodiments, a recombinant lentiviral particle is contemplated, comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 471; and optionally (iii) a secondary non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 577; and (b) a lentiviral vector encoding a chimeric antigen receptor that binds GPCR5D.

In various embodiments, a recombinant lentiviral particle is contemplated, comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 471; and optionally (iii) a secondary non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 577; and (b) a lentiviral vector encoding a chimeric antigen receptor that binds CD19.

In additional embodiments, a cell transduced with a particle contemplated herein.

In particular embodiments, the cell is an immune effector cell.

In some embodiments, the cell is a T cell, a natural killer (NK) cell, or a natural killer T (NKT) cell.

In certain embodiments, a composition comprising a particle or a cell contemplated herein.

5 In particular embodiments, a pharmaceutical composition comprises a pharmaceutically acceptable carrier and a particle, a cell, or a composition contemplated herein.

In some embodiments, a method of treating, preventing, or ameliorating at least one symptom of a disease, disorder or condition associated therewith in a subject comprises
10 administering to the subject an effective amount of a particle, a cell, a composition, or a pharmaceutical composition contemplated herein.

In further embodiments, the disease, disorder, or condition is a cancer.

In particular embodiments, the cancer is leukemia selected from the group consisting of: acute lymphocytic leukemia (ALL), an acute myeloid leukemia (AML), a
15 myelodysplastic syndrome (MDS), a plasma cell leukemia (PCL), erythroleukemia, a hairy cell leukemia (HCL), chronic lymphocytic leukemia (CLL), chronic myeloid leukemia (CML), chronic myelomonocytic leukemia (CMML) and polycythemia vera.

In additional embodiments, the cancer is non-NHL or NHL selected from the group consisting of: diffuse large B cell lymphoma (DLBCL), follicular lymphoma (FL), mantle-
20 cell lymphoma (MCL), small lymphocytic lymphoma (SLL), primary mediastinal large B-cell lymphoma, a marginal zone B cell lymphoma (MZL), mucosa-associated lymphatic tissue lymphoma (MALT), Burkitt's lymphoma (BL), immunoblastic large cell lymphoma, centroblastic large cell lymphoma, anaplastic B-cell lymphoma, mycosis fungoides, Sezary syndrome, T-lymphoblastic lymphoma, and anaplastic large-cell lymphoma (ALCL).

25 In certain embodiments, the cancer is MM selected from the group consisting of: active multiple myeloma, smoldering multiple myeloma, light chain myeloma, non-secretory myeloma, IgD myeloma, IgE myeloma, osteosclerotic myeloma, solitary plasmacytoma of bone, and extramedullary plasmacytoma.

In some embodiments, the cancer is relapsed and/or refractory.

30 In additional embodiments, the disease, disorder, or condition is an autoimmune disease.

In certain embodiments, the autoimmune disease is systemic lupus erythematosus, rheumatoid arthritis, idiopathic thrombocytopenic purpura, myasthenia gravis, or autoimmune hemolytic anemia.

In some embodiments, a method of transducing an immune effector cell *in vivo*,
5 comprises administering to a subject a pharmaceutical composition comprising a pharmaceutically acceptable carrier and an effective amount of a particle contemplated herein.

In particular embodiments, a method of making the recombinant lentivirus comprises
10 (a) transfecting a host cell with four polynucleotides: a first polynucleotide that encodes lentiviral gag-pol, a second polynucleotide that encodes lentiviral rev, a third polynucleotide that encodes one or more mutated viral envelope glycoproteins that retain fusogenic activity and lack cognate receptor binding activity and one or more non-viral membrane-bound tropism polypeptides, and a fourth polynucleotide that is a transfer plasmid encoding a recombinant lentiviral vector of any one of the preceding embodiments; and b) culturing the
15 transduced cell for about 1 to 3 days to produce the recombinant lentivirus.

In certain embodiments, a kit comprises a particle contemplated herein, a pharmaceutically acceptable carrier, and instructions for use.

BRIEF DESCRIPTION OF SEVERAL VIEWS OF THE DRAWINGS

Figure 1A shows GFP expression (transduction) and CD69 expression (activation)
20 in Jurkat cells targeted with lentiviral particles that have a viral envelope expressing tropism molecules that have T cell specific binding domains and a mutant fusogen.

Figure 1B shows flow cytometry analysis of GFP expression (transduction) and CD69 expression (activation) in PBMCs cells targeted with lentiviral particles that have a viral envelope expressing tropism molecules that have T cell specific binding domains and a
25 mutant fusogen.

Figure 2 shows flow cytometry analysis of GFP expression or CAR expression in HEK293T used to produce lentiviral particles that have a viral envelope expressing (i) tropism molecules that have T cell specific binding domains, a monomeric or dimeric CD8 α stalk and a CD8 α TM domain and an intracellular domain (ii) a mutant fusogen.

Figure 3A shows a diagram of various tropism molecule stalk architectures
30 experimentally examined in the Examples.

Figure 3B shows tropism molecule expression (measured by anti-CD3 scFv expression) in HEK293T cells used to produce lentiviral particles that have a viral envelope expressing (i) anti-CD3-based tropism molecules and (ii) a mutant fusogen.

Figure 3C shows the transducing units (TU) per nanogram of P24 for lentiviral particles that have anti-CD3-based tropism molecules with various stalk architectures and a mutated fusogen used to transduce Jurkat cells.

Figure 3D shows the transduction specificity for lentiviral particles that express anti-CD3-based tropism molecules with various stalk architectures and a mutated fusogen. Left panel compares on-target transduction in PBMCs to off-target transduction in A549 cells. Right panel compares on-target transduction in Jurkat cells to off-target transduction in A549 cells.

Figure 4 shows the effects of anti-CD3-based tropism molecule stalk architecture on titer and specificity. Left panel shows the effect of estimated tropism molecule stalk length on titer (TU/ng P24). Right panel shows the effect of estimated tropism molecule stalk length on transduction specificity.

Figure 5A shows the GFP expression (transduction, top panel) and cell count (activation, bottom panel) in PBMCs transduced with lentiviral particles that express anti-CD3-based tropism molecules that have a variety of stalk architectures and a mutant fusogen.

Figure 5B shows the GFP expression (transduction, left panel) in PBMCs transduced with 0.5 ng P24 or 2 ng P24 of lentiviral particles that express anti-CD3-based tropism molecules that have a variety of stalk architectures and a mutant fusogen. Right panel shows the effect of tropism molecule stalk architecture on PBMC transduction compared to Jurkat cell transduction.

Figure 6 shows transduction (top panel) and activation (bottom panel) human T cells in an *in vivo* mouse model. Mice were administered lentiviral particles expressing T cell targeting tropism molecules, a mutant fusogen and a lentiviral vector encoding GFP.

Figure 7A shows the number (left panel) and percentage (right panel) of GFP positive T cells in the blood of mice administered 1×10^7 TU, 2.5×10^7 TU, 1×10^8 TU, or 2.5×10^8 TU of lentiviral particles that express (i) T cell targeting tropism molecules (LV 2) or lack T cell targeting tropism molecules (LV 26), (ii) a mutant fusogen and (iii) a lentiviral vector encoding GFP.

Figure 7B shows immunohistochemistry staining in the heart, brain, ovaries, and small intestines of mice administered 1×10^7 TU, 2.5×10^7 TU, 1×10^8 TU, or 2.5×10^8 TU

of lentiviral particles that express (i) T cell targeting tropism molecules (LV 2) or lack T cell targeting tropism molecules (LV 26), (ii) a mutant fusogen and (iii) a lentiviral vector encoding GFP. The rightmost column shows flow cytometry data of GFP positive T cells in the spleen of these mice at each dose level.

5 **Figure 8** shows that lentiviral particles expressing an anti-CD3-based tropism molecule, a mutant fusogen, and a lentiviral vector encoding an anti-BCMA CAR reduce tumor growth comparable to *ex vivo* manufactured anti-BCMA CAR T cells in an RPMI multiple myeloma mouse model.

10 **Figure 9** shows that lentiviral particles expressing either of two different anti-CD3-based tropism molecules, and a mutant fusogen and a lentiviral vector encoding an anti-BCMA CAR reduce tumor growth comparable to *ex vivo* manufactured anti-BCMA CAR T cells in an Daudi multiple myeloma mouse model.

BRIEF DESCRIPTION OF THE SEQUENCE IDENTIFIERS

SEQ ID NOs: 1-10 set forth amino acid sequences of fusogens.

15 SEQ ID NOs: 11-410 set forth amino acid sequences of antibodies.

SEQ ID NOs: 411-434 set forth amino acid sequences of spacer domains.

SEQ ID NOs: 435-441 set forth amino acid sequences of transmembrane domains.

SEQ ID NOs: 442-448 set forth amino acid sequences of intracellular domains.

SEQ ID NOs: 449-454 set forth amino acid sequences of signal peptides.

20 SEQ ID NOs: 455-576 set forth amino acid sequences of non-viral membrane bound tropism polypeptides.

SEQ ID NOs: 577-581 set forth amino acid sequences of secondary tropism polypeptides.

SEQ ID NOs: 582-661 set forth amino acid sequences of fusogens.

25 SEQ ID NOs: 662-666 set forth amino acid sequences of engineered receptors.

SEQ ID NOs: 667-672 set forth nucleic acid sequences of promoters.

SEQ ID NOs: 673-693 set forth amino acid sequences of polypeptide linkers.

SEQ ID NOs: 694-713 set forth amino acid sequences of viral self-cleaving peptides.

SEQ ID NO: 714 sets forth an amino acid sequence of a lentivirus protease cleavage

30 site.

In the foregoing sequences, X, if present, refers to any amino acid, a specified group of amino acids or the absence of an amino acid.

Throughout the disclosure, the amino acid positions of a fusogen is with reference to the fusogen lacking a signal sequence (*i.e.*, the amino acid sequence after the signal peptide
5 has been cleaved).

DETAILED DESCRIPTION

A. OVERVIEW

The field of *ex vivo* gene therapy is not new and has been evolving for decades. Despite huge potential, *ex vivo* gene therapy has been met with limited success. Moreover,
10 substantial obstacles still plague the field of *ex vivo* gene therapy, obstacles including limited precision and lack of commercial viability are likely among the reasons that it has yet to see widespread adoption in a clinical setting. *In vivo* gene therapy however, is new and offers the potential to deliver life-altering therapies on an unprecedented scale. *In vivo* gene therapy solves the commercial viability issues associated with the astronomical costs associated with
15 manufacturing *ex vivo* gene therapies. But *in vivo* gene therapy comes with its own set of challenges, including potential off-target toxicity, low efficacy, and immunogenicity.

The present disclosure offers solutions to foregoing challenges and others that exist in the field of *in vivo* gene therapy.

The present disclosure generally relates to, in part, to an engineered cell-targeting
20 particle (*e.g.*, a fusosome; an extracellular vesicle, including a microvesicle, an apoptotic body, and an exosome; a lipid nanoparticle; a virus-like particle (VLPs); or a viral particle) that has improved specificity for a desired cell type, *e.g.*, an immune effector cell. Without wishing to be bound by any particular theory, it is contemplated that an engineered cell-targeting particle comprising an efficient fusogen and one or more cell-targeting polypeptides
25 (*i.e.*, tropism polypeptides) increase the on-target delivery of a cargo or payload to a desired cell type and decrease the off-target delivery to undesired cell types. It is further contemplated that particles comprising one or more non-viral tropism polypeptides and a viral envelope glycoprotein that is capable of cell fusion but not cell attachment or cell binding yields an engineered cell-targeting particle that has increased delivery specificity and
30 that efficiently delivers one or more nucleic acids or proteins to a desired cell type.

The disclosure contemplates, in part, recombinant particles with increased specificity for cellular vehicles to enable gene therapy or genome editing applications. Recombinant particles contemplated herein include but are not limited to, a fusosome, an extracellular vesicle, a microvesicle, an apoptotic body, an exosome, a lipid nanoparticle, a virus-like particle (VLPs), or a recombinant viral particle that has a single layer of phospholipid, a phospholipid bilayer, a cell membrane, a capsid, or a viral envelope comprising one or more membrane-bound viral glycoproteins modified to retain fusogenic activity and decrease, reduce, substantially ablate, ablate, abolish or eliminate cell binding or attachment activity; one or more non-viral membrane-bound tropism polypeptides; and a cargo or payload comprising one or more polynucleotides and/or polypeptides. The recombinant particles may be used for *ex vivo* gene therapy and genome editing but provide substantial advantages for use in *in vivo* gene therapy and genome editing.

The disclosure further contemplates, in part, gene therapy and genome editing compositions comprising a fusosome, an extracellular vesicle, a microvesicle, an apoptotic body, an exosome, a lipid nanoparticle, a virus-like particle (VLPs), or a recombinant viral particle that has a single layer of phospholipid, a phospholipid bilayer, a cell membrane, a capsid, or a viral envelope comprising one or more membrane-bound viral glycoproteins modified to retain fusogenic activity and that lack or substantially lack cell binding or attachment activity and/or cognate receptor binding activity; one or more non-viral membrane-bound tropism polypeptides; and a cargo or payload comprising one or more polynucleotides and/or polypeptides.

The disclosure further contemplates, in part, methods of making the recombinant particles contemplated herein, along with methods of using the particles.

In preferred embodiments, the recombinant particle is a recombinant viral particle, preferably a recombinant retroviral particle, more preferably a recombinant lentiviral particle, and even more preferably, a recombinant HIV-1 based lentiviral particle. In further preferred embodiments, the recombinant particle comprises a polynucleotide payload, preferably a vector, more preferably a viral vector, and even more preferably a retroviral or lentiviral vector.

In particular embodiments, the disclosure contemplates, methods of using a recombinant particle contemplated herein to decrease off-target delivery and increase targeted delivery to an immune effector cell *in vivo*, to increase the specificity of an *in vivo* gene therapy or genome editing composition, to deliver a cargo or payload of one or more

polynucleotides and/or polypeptides to an immune effector cell, to treat a wide variety of disorders, diseases and conditions or symptoms associated therewith, including but not limited to cancers, infectious diseases, autoimmune diseases, inflammatory diseases, immunodeficiencies, and monogeneic diseases.

5 Compositions, pharmaceutical compositions, and kits comprising one or more recombinant particles contemplated herein and methods of making and using the same are also provided in particular embodiments.

Techniques for recombinant (*i.e.*, engineered) DNA, peptide and oligonucleotide synthesis, immunoassays, tissue culture, transformation (*e.g.*, electroporation, lipofection),
 10 enzymatic reactions, purification and related techniques and procedures may be generally performed as described in various general and more specific references in microbiology, molecular biology, biochemistry, molecular genetics, cell biology, virology and immunology as cited and discussed throughout the present specification. See, *e.g.*, Sambrook *et al.*, *Molecular Cloning: A Laboratory Manual*, 4th ed., Cold Spring Harbor Laboratory Press,
 15 Cold Spring Harbor, N.Y.; *Current Protocols in Molecular Biology* (John Wiley and Sons, updated July 2008); *Short Protocols in Molecular Biology: A Compendium of Methods from Current Protocols in Molecular Biology*, Greene Pub. Associates and Wiley-Interscience (2002); Glover, *DNA Cloning: A Practical Approach*, vol. I & II (IRL Press, Oxford Univ. Press USA, 1985); *Current Protocols in Immunology* (Edited by: John E. Coligan, Ada M.
 20 Kruisbeek, David H. Margulies, Ethan M. Shevach, Warren Strober 2001 John Wiley & Sons, NY, NY); *Real-Time PCR: Current Technology and Applications*, Edited by Julie Logan, Kirstin Edwards and Nick Saunders, 2009, Caister Academic Press, Norfolk, UK; Anand, *Techniques for the Analysis of Complex Genomes*, (Academic Press, New York, 1992); Guthrie and Fink, *Guide to Yeast Genetics and Molecular Biology* (Academic Press,
 25 New York, 1991); *Oligonucleotide Synthesis* (N. Gait, Ed., 1984); *Nucleic Acid the Hybridization* (B. Hames & S. Higgins, Eds., 1985); *Transcription and Translation* (B. Hames & S. Higgins, Eds., 1984); *Animal Cell Culture* (R. Freshney, Ed., 1986); Perbal, *A Practical Guide to Molecular Cloning* (1984); *Next-Generation Genome Sequencing* (Janitz, 2008 Wiley-VCH); *PCR Protocols* (Methods in Molecular Biology) (Park, Ed., 3rd Edition,
 30 2010 Humana Press); *Immobilized Cells and Enzymes* (IRL Press, 1986); the treatise, *Methods in Enzymology* (Academic Press, Inc., N.Y.); *Gene Transfer Vectors for Mammalian Cells* (J. H. Miller and M. P. Calos eds., 1987, Cold Spring Harbor Laboratory); Harlow and Lane, *Antibodies*, (Cold Spring Harbor Laboratory Press, Cold Spring Harbor,

- N.Y., 1998); *Immunochemical Methods in Cell and Molecular Biology* (Mayer and Walker, eds., Academic Press, London, 1987); *Handbook of Experimental Immunology*, Volumes I-IV (D. M. Weir and CC Blackwell, eds., 1986); Roitt, *Essential Immunology*, 6th Edition, (Blackwell Scientific Publications, Oxford, 1988); *Current Protocols in Immunology* (Q. E. Coligan, A. M. Kruisbeek, D. H. Margulies, E. M. Shevach and W. Strober, eds., 1991); *Annual Review of Immunology*; as well as monographs in journals such as *Advances in Immunology*.

B. DEFINITIONS

Prior to setting forth this disclosure in more detail, it may be helpful to an understanding thereof to provide definitions of certain terms to be used herein.

Unless defined otherwise, all technical and scientific terms used herein have the same meaning as commonly understood by those of ordinary skill in the art to which the invention belongs. Although any methods and materials similar or equivalent to those described herein can be used in the practice or testing of particular embodiments, preferred embodiments of compositions, methods and materials are described herein. For the purposes of the present disclosure, the following terms are defined below.

The articles “a,” “an,” and “the” are used herein to refer to one or to more than one (*i.e.*, to at least one, or to one or more) of the grammatical object of the article. By way of example, “an element” means one element or one or more elements.

The use of the alternative (*e.g.*, “or”) should be understood to mean either one, both, or any combination of the recited alternatives.

The term “and/or” should be understood to mean either one of, or both of, the alternatives.

As used herein, the term “about” or “approximately” refers to a quantity, level, value, number, frequency, percentage, dimension, size, amount, weight or length that varies by as much as 15%, 10%, 9%, 8%, 7%, 6%, 5%, 4%, 3%, 2% or 1% to a reference quantity, level, value, number, frequency, percentage, dimension, size, amount, weight or length. In one embodiment, the term “about” or “approximately” refers a range of quantity, level, value, number, frequency, percentage, dimension, size, amount, weight or length $\pm 15\%$, $\pm 10\%$, $\pm 9\%$, $\pm 8\%$, $\pm 7\%$, $\pm 6\%$, $\pm 5\%$, $\pm 4\%$, $\pm 3\%$, $\pm 2\%$, or $\pm 1\%$ of a reference quantity, level, value, number, frequency, percentage, dimension, size, amount, weight or length.

In one embodiment, a range, *e.g.*, 1 to 5, about 1 to 5, or about 1 to about 5, refers to each numerical value encompassed by the range. For example, in one non-limiting and merely illustrative embodiment, the range “1 to 5” is equivalent to the expression 1, 2, 3, 4, 5; or 1.0, 1.5, 2.0, 2.5, 3.0, 3.5, 4.0, 4.5, or 5.0; or 1.0, 1.1, 1.2, 1.3, 1.4, 1.5, 1.6, 1.7, 1.8, 1.9, 2.0, 2.1, 2.2, 2.3, 2.4, 2.5, 2.6, 2.7, 2.8, 2.9, 3.0, 3.1, 3.2, 3.3, 3.4, 3.5, 3.6, 3.7, 3.8, 3.9, 4.0, 4.1, 4.2, 4.3, 4.4, 4.5, 4.6, 4.7, 4.8, 4.9, or 5.0.

As used herein, the term “substantially” refers to a quantity, level, value, number, frequency, percentage, dimension, size, amount, weight or length that is 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or higher compared to a reference quantity, level, value, number, frequency, percentage, dimension, size, amount, weight or length. In one embodiment, “substantially the same” refers to a quantity, level, value, number, frequency, percentage, dimension, size, amount, weight or length that produces an effect, *e.g.*, a physiological effect, that is approximately the same as a reference quantity, level, value, number, frequency, percentage, dimension, size, amount, weight or length. In particular embodiments, “substantially lacks cell binding or cell attachment activity and/or cognate receptor binding activity” or “substantially abates cell binding or cell attachment activity and/or cognate receptor binding activity” refers to the negligible or undetectable or absent cell binding activity or cell attachment activity of a modified membrane-bound viral glycoprotein contemplated herein to bind or attach to its cognate receptor on the surface of a cell compared to the cell binding activity or cell attachment activity of the unmodified membrane-bound viral glycoprotein to bind or attach to its cognate receptor on the surface of the cell.

Throughout this specification, unless the context requires otherwise, the words “comprise”, “comprises” and “comprising” will be understood to imply the inclusion of a stated step or element or group of steps or elements but not the exclusion of any other step or element or group of steps or elements. By “consisting of” is meant including, and limited to, whatever follows the phrase “consisting of.” Thus, the phrase “consisting of” indicates that the listed elements are required or mandatory and that no other elements may be present. The phrase “consisting essentially of” means including any elements listed after the phrase and other elements that do not interfere with or contribute to the activity or action specified in the disclosure for the listed elements. Thus, the phrase “consisting essentially of” indicates that the listed elements are required or mandatory but that no other elements are present that materially affect the activity or action of the listed elements.

Reference throughout this specification to “one embodiment,” “an embodiment,” “a particular embodiment,” “a related embodiment,” “a certain embodiment,” “an additional embodiment,” or “a further embodiment” or combinations thereof means that a particular feature, structure or characteristic described in connection with the embodiment is included in at least one embodiment. Thus, the appearances of the foregoing phrases in various places throughout this specification are not necessarily all referring to the same embodiment. Furthermore, the particular features, structures, or characteristics may be combined in any suitable manner in one or more embodiments. It is also understood that the positive recitation of a feature in one embodiment, serves as a basis for excluding the feature in a particular embodiment.

The terms, “binding domain,” “extracellular binding domain,” and “extracellular antigen binding domain” are used interchangeably and refers to a domain that enables an engineered receptor, *e.g.*, a chimeric antigen receptor (CAR), a chimeric costimulatory receptor (CCR), an alpha-beta T cell receptor ($\alpha\beta$ TCR), a gamma delta T cell receptor ($\gamma\delta$ TCR), a dimerizing agent regulated immunoreceptor complex (DARIC), a chimeric TGF- β receptor (CTBR), or a zetakine receptor to specifically bind to a target antigen. The binding domain may be derived either from a natural, synthetic, semi-synthetic, or recombinant source.

An “antibody” refers to a polypeptide that comprises at least a light chain immunoglobulin variable region and/or a heavy chain immunoglobulin variable region, which specifically recognizes and binds one or more epitopes of an antigen.

Antibodies include polyclonal and monoclonal antibodies and antigen binding fragments thereof; murine antibodies, camelid antibodies, and human antibodies, and antigen binding fragments thereof; and chimeric antibodies, an antibody that comprises variable regions from a non-human species and human constant regions, heteroconjugate antibodies, and humanized antibodies, an antibody that comprises complementarity determining regions (CDRs) from a non-human species and human framework and constant regions, and antigen binding fragments thereof.

Murine, chimeric, humanized, and human antibodies comprise two heavy chains and two light chains. Each heavy chain consists of a variable region (VH) and three constant regions (CH1, CH2, CH3), while each light chain consists of a variable region (VL) and a constant region (CL). Mammalian immunoglobulin heavy chains are classified as

immunoglobulin (Ig)A, IgD, IgE, IgG, and IgM. Mammalian immunoglobulin light chains are classified as λ or κ .

Light and heavy chain variable regions contain a “framework” region interrupted by three hypervariable regions, also called “complementarity-determining regions” or “CDRs.”

5 The sequences of the framework regions of different light or heavy chains are relatively conserved within a species, such as humans. The framework regions serve to position and align the CDRs in three-dimensional space to bind to an epitope. The CDRs of each chain are numbered sequentially starting from the N-terminus and are also typically identified by the chain in which the particular CDR is located. Heavy chain CDRs are referred to as CDRH1, CDRH2, and CDRH3, and light chain CDRs are referred to as CDRL1, CDRL2, and CDRL3. Although CDRs vary from antibody to antibody, the limited number of amino acid positions within the CDRs directly involved in antigen binding are called specificity determining residues (SDRs).

CDRs can be defined or identified by conventional methods, such as by sequence according to Wu and Kabat, *J Exp Med.* 132(2):211-50 (1970) and Kabat and Wu, *Ann New York Acad Sci.* 190:382-93 (1971), or by structure according to Chothia and Lesk, *J Mol. Biol.* 196(4): 901-917 (1987) and Chothia *et al.*, *Nature.* 342:877-83(1989). Other boundaries defining CDRs overlapping with the Kabat CDRs have been described by Padlan *et al.*, *FASEB J.* 9:133-9 (1995) and MacCallum *et al.*, *J Mol Biol.* 262:732-745 (1996). Additional methods of determining CDRs include the Gelfand numbering system described in Gelfand and Kister, *PNAS USA.* 92:10884-8(1995), Gelfand *et al.*, *Protein Eng.* 11:1015-25 (1998), and Gelfand *et al.*, *PNAS USA.* 93:3675-8 (1996); the Honneger number system described in Honneger and Plückthun, *J Mol Biol.* 309:657-70 (2001); the AbM numbering system described by Abhinandan and Martin, *Mol Immunol.* 45:3832-9 (2008); and the IMGT numbering system described in Giudicelli *et al.*, *Nucleic Acids Res.* 25:206-11 (1997), Lefranc, *Immunol Today* 18:509 (1997), and Lefranc *et al.*, *Dev Comp Immunol.* 27:55-77 (2003). Proprietary and publicly programs that identify CDRs are available, *e.g.*, abYsis (abysis.org/abysis/) and IMGT/V-QUEST (imgt.org/IMGT_vquest).

“VL” or “V_L” refers to the variable region of an immunoglobulin light chain, including that of an antibody, Fv, scFv, dsFv, Fab, or other antigen binding fragment thereof. “VH” or “V_H” refer to the variable region of an immunoglobulin heavy chain, including that of an antibody, Fv, scFv, dsFv, Fab, heavy chain only antibody (hcAb) or other antigen binding fragment thereof.

An “antigen binding fragment” or “antigen binding portion” refers to one or more fragments of an antibody that retain the ability to specifically bind to an antigen. An “isolated antibody or antigen binding fragment thereof” refers to an antibody or antigen binding fragment thereof that has been separated from its natural environment and/or that is derived from a natural, synthetic, semi-synthetic, or recombinant source. Illustrative examples of antigen binding fragments suitable for incorporation into engineered receptors contemplated in particular embodiments herein include, but are not limited to, a Camel Ig, a Llama Ig, an Alpaca Ig, Ig NAR, a Fab' fragment, a F(ab')₂ fragment, a bispecific Fab dimer (Fab₂), a trispecific Fab trimer (Fab₃), an Fv, a single chain Fv protein (“scFv”), a bis-scFv, (scFv)₂, a minibody, a diabody, a triabody, a tetrabody, a disulfide stabilized Fv protein (“dsFv”), a Fibronectin type III (FN3) domain antibody, a single-domain antibody (sdAb or nanobody, *e.g.*, a camelid VHH or shark VNAR), a centyrin, and other portions of full length antibodies sufficient for antigen binding, and combinations thereof.

A “heavy chain antibody” or “hcAb” refers to an antibody that contains two heavy chain variable domains and no light chains. A “camelid antibody” or “camelid Ig” refers to an hcAb isolated from a Camel, Alpaca, or Llama that consists of a homodimer of a heavy chain variable domain (VHH) and CH₂ and CH₃ constant domains. An “IgNAR” or “immunoglobulin new antigen receptor” refers to an hcAb isolated from the shark immune repertoire that consists of a homodimer of a variable new antigen receptor (VNAR) domain and five constant new antigen receptor (CNAR) domains.

A “single domain antibody,” “sdAb,” or “nanobody” as used herein refers to an antibody fragment that contains the smallest known antigen binding unit of the variable region of a heavy chain antibody, *e.g.*, a camelid VHH or shark VNAR. A “humanized VHH” refers to a single domain non-human VHH that has undergone humanization to reduce potential immunogenicity of the antibody in human recipients. A “humanized VNAR” refers to a single domain non-human VNAR that has undergone humanization to reduce potential immunogenicity of the antibody in human recipients.

A “single-chain Fv” or “scFv” antibody fragment comprises the VH and VL domains of an antibody, wherein these domains are present in a single polypeptide chain and in either orientation (*e.g.*, VL-VH or VH-VL). Generally, the scFv polypeptide further comprises a polypeptide linker between the VH and VL domains which enables the scFv to form the desired structure for antigen binding.

The terms “spacer,” “spacer domain,” or “spacer polypeptide” are used interchangeably and refer to a polypeptide domain or sequence of amino acids in a non-viral membrane-bound tropism polypeptide disposed between an extracellular antigen targeting domain and a transmembrane domain or an ω amino acid, *i.e.*, the amino acid serving as the attachment site of the GPI anchor. A spacer positions the extracellular antigen targeting domain away from the particle surface to enable proper particle/target cell contact, attachment, or binding. A spacer may be derived either from a natural, synthetic, semi-synthetic, or recombinant source. Illustrative examples of spacer domains include but are not limited to hinge or stalk domains derived, obtained, or isolated from IgG1, IgG2, IgG4, CD2, CD3, CD4, CD8 α , CD8 β , CD28, CD45ABC, CD45RO, CD45RAB, CD45RAC, CD45RBC, CD45RA, CD45RB, CD45RC, CD45del-d3, CD45del-d2-d3 (*e.g.*, SEQ ID NOs: 411-423), CADHERIN 1 and variants thereof (*e.g.*, SEQ ID NOs: 424-427), CEACAM 5 and variants thereof (*e.g.*, SEQ ID NOs: 428-433), and polypeptide linkers of similar amino acid composition, rigidity, flexibility and/or length.

A “hinge domain,” is a polypeptide domain or sequence of amino acids that plays a role in positioning the antigen binding domain away from the effector cell surface to enable proper cell/cell contact, antigen binding and activation. A hinge domain is placed between a binding domain and a transmembrane domain (TM). A hinge domain may be derived either from a natural, synthetic, semi-synthetic, or recombinant source. A hinge domain may be altered by substituting one or more cysteine and/or proline residues in a naturally occurring immunoglobulin hinge domain with one or more other amino acid residues (*e.g.*, one or more serine residues).

A “transmembrane domain” or “TM domain” refers to a hydrophobic portion of polypeptide that anchors the polypeptide to the plasma membrane of the cell. The TM domain may be derived either from a natural, synthetic, semi-synthetic, or recombinant source.

A “glycosylphosphatidylinositol anchor” or “GPI anchor” refers to a moiety comprising a hydrophilic oligosaccharide and a lipophilic fatty acid that attaches a protein to the endoplasmic reticulum (ER) membrane by a transamidase enzyme complex, the protein subsequently delivered to the outer leaflet of the plasma membrane.

An “intracellular signaling domain” refers to a portion of a polypeptide that participates in transducing the message of effective binding of a target antigen by a receptor expressed on an immune effector cell to the immune effector cell’s interior to elicit one or

more effector functions (an “effector function” refers to a specialized function of an immune effector cell), *e.g.*, activation, cytokine production, proliferation and cytotoxic activity, including the release of cytotoxic factors, or other cellular responses elicited with antigen binding to the receptor expressed on the immune effector cell. “Intracellular signaling domains” include a polypeptide domain or functional fragment thereof, which transduces an effector function signal and that directs a cell to perform a specialized function. The term intracellular signaling domain is meant to include any truncated portion of an intracellular signaling domain sufficient to transducing effector function signal.

T cell activation can be said to be mediated by two distinct classes of intracellular signaling domains: primary signaling domains that initiate antigen-dependent primary activation through the TCR (*e.g.*, a TCR/CD3 complex) and costimulatory signaling domains that act in an antigen-independent manner to provide a secondary or costimulatory signal.

A “primary signaling domain” refers to a signaling domain that regulates the primary activation of a TCR complex either in a stimulatory way, or in an inhibitory way. Primary signaling domains that act in a stimulatory manner may contain one or more signaling motifs which are known as immunoreceptor tyrosine-based activation motifs or ITAMs.

A “costimulatory signaling domain” or “costimulatory domain” refers to an intracellular signaling domain of a costimulatory molecule. Costimulatory molecules are cell surface molecules other than antigen receptors or Fc receptors that provide a second signal required for efficient activation and function of T lymphocytes upon binding to antigen.

The terms “individual” and “subject” are often used interchangeably and refer to any animal that exhibits a symptom of a disease, disorder, or condition, *e.g.*, cancer, that can be treated with the recombinant particles, *e.g.*, recombinant retroviral particles or lentiviral particles, gene therapy vectors, compositions, and methods contemplated elsewhere herein. Suitable subjects (*e.g.*, patients) include laboratory animals (*e.g.*, mouse, rat, rabbit, or guinea pig), farm animals, and domestic animals or pets (*e.g.*, cat or dog). Non-human primates and, preferably, human patients, are preferred subjects.

A “patient” refers to a subject that has been diagnosed with a particular disease, disorder, or condition that can be treated with the recombinant particles, *e.g.*, recombinant retroviral particles or lentiviral particles, gene therapy vectors, compositions and methods disclosed elsewhere herein.

“Treatment” or “treating,” as used herein includes any beneficial or desirable effect on the symptoms or pathology of a disease or pathological condition and may include even

minimal reductions in one or more measurable markers of the disease or condition being treated. Optionally, treatment can include reducing the disease burden or delaying disease progression. "Treatment" may, but does not necessarily, indicate complete eradication or cure of the disease or condition, or associated symptoms thereof.

5 "Prevent," "prevention," "preventing" and the like, as used herein, indicate an approach for preventing, inhibiting, or reducing the likelihood of occurrence or recurrence of a disease or condition. It also refers to delaying the onset or recurrence of a disease or condition or delaying the occurrence or recurrence of the symptoms of a disease or condition. Prevention includes reducing the intensity, effect, symptoms and/or burden of a disease or
10 condition prior to onset or recurrence of the disease or condition.

 "Ameliorating at least one symptom of" as used herein, refers to decreasing one or more symptoms of the disease or condition for which a subject is being treated. In particular embodiments, the disease or condition being treated is a cancer, and the one or more symptoms ameliorated include, but are not limited to, weakness, fatigue, shortness of breath,
15 easy bruising and bleeding, frequent infections, enlarged lymph nodes, distended or painful abdomen (due to enlarged abdominal organs), bone or joint pain, fractures, unplanned weight loss, poor appetite, night sweats, persistent mild fever, and decreased urination (due to impaired kidney function).

 Additional definitions are set forth throughout this disclosure.

20 **C. RECOMBINANT PARTICLES**

 Various particles have been proposed as gene delivery vehicles. The present disclosure contemplates, in part, a recombinant particle engineered to bind to a desired or target cell type and deliver a payload. Recombinant particles comprise a surface and a payload: the surface comprising one or more mutated viral envelope glycoproteins that retain
25 fusogenic activity and substantially lack or lack cognate receptor binding activity and one or more non-viral membrane-bound tropism polypeptides engineered to bind a cell, *e.g.*, an immune effector cell; and the payload comprising one or more polynucleotide and/or polypeptides. Suitable recombinant particles for use in particular embodiments contemplated herein include but are not limited to a fusosome; an extracellular vesicle, including a
30 microvesicle, an apoptotic body, and an exosome; a lipid nanoparticle; a virus-like particle (VLPs); or a recombinant viral particle.

In preferred embodiments, a recombinant particle is a recombinant viral particle or recombinant virus. The terms “recombinant viral particle” and “recombinant virus” are used interchangeably.

Recombinant viral particles have been used as a gene delivery platform for treatments of severe genetic diseases and cancer. Illustrative examples of recombinant viral particles suitable for use in particular embodiments contemplated herein are derived from an adenovirus (Ad), an adeno-associated virus (AAV), a rhabdovirus (*e.g.*, lyssavirus, vesiculovirus), a paramyxovirus (*e.g.*, henipavirus, morbillivirus, respirovirus, rubelavirus), a herpes simplex virus (*e.g.*, HSV-1, HSV-2), vaccinia virus, or a retrovirus (*e.g.*, gammaretrovirus, lentivirus).

Retroviruses are a commonly used tool for gene delivery (Miller, 2000, *Nature*. 357: 455-460). The term “retrovirus” refers to an enveloped RNA virus that reverse transcribes its genomic RNA into a linear double-stranded DNA copy and subsequently covalently integrates its genomic DNA into a host genome. A recombinant retroviral particle comprises a viral envelope, one or more retroviral proteins, *e.g.*, matrix protein (MA), capsid protein (CA), nucleocapsid protein (NC), reverse transcriptase (RT), and integrase (IN), and a retroviral vector derived or engineered from a retrovirus genome.

Illustrative retroviruses suitable for deriving or engineering recombinant retroviral particles contemplated in particular embodiments herein include but are not limited to an alpharetrovirus, a betaretrovirus, a gammaretrovirus, a deltaretrovirus, an epsilonretrovirus, a spumavirus, and a lentivirus.

Alpharetroviruses include but are not limited to avian leukosis virus, avian carcinoma Mill Hill virus 2, avian myeloblastosis virus, avian myelocytomatosis virus 29, avian sarcoma virus CT10, fujinami sarcoma virus, rous sarcoma virus, UR2 sarcoma virus and Y73 sarcoma virus.

Betaretroviruses include but are not limited to mouse mammary tumor virus, Jaagsiekte sheep retrovirus, langur virus, Mason-Pfizer monkey virus, and squirrel monkey retrovirus (SMRV).

Deltaretroviruses include but are not limited to bovine leukemia virus, primate T-lymphotropic virus 1, primate T-lymphotropic virus 2, primate T-lymphotropic virus 3, and primate T-lymphotropic virus 4.

Epsilonretroviruses include but are not limited to walleye dermal sarcoma virus, walleye epidermal hyperplasia virus 1, and walleye epidermal hyperplasia virus 2.

Gammaretroviruses include but are not limited to baboon endogenous virus (BaEV), chick syncytial virus, feline endogenous virus (*e.g.*, RD114), feline leukemia virus (FeLV), Finkel-Biskis-Jenkins murine sarcoma virus, Gardner-Arnstein feline sarcoma virus, gibbon ape leukemia virus (GALV), guinea pig type-C oncovirus, Hardy-Zuckerman feline sarcoma virus, Harvey murine sarcoma virus, Kirsten murine sarcoma virus, koala retrovirus, murine leukemia virus (MLV), Moloney murine leukemia virus (MoMLV), Moloney murine sarcoma virus, porcine endogenous virus (PERV), Porcine type-C oncovirus, reticuloendotheliosis virus (REV), Snyder-Theilen feline sarcoma virus, Trager duck spleen necrosis virus, viper retrovirus, xenotropic murine leukemia virus-related virus (XMRV), and woolly monkey sarcoma virus.

Spumaviruses include but are not limited to simian foamy virus, bovine foamy virus, equine foamy virus, feline foamy virus, human foamy virus (HFV), and brown greater galago prosimian foamy virus.

In particular embodiments, a recombinant retroviral particle is derived or engineered from a retrovirus selected from the group consisting of: SMRV, BaEV, RD114, FeLV, GALV, MLV, MoMLV, PERV, REV, XMRV, and HFV.

A “lentivirus” refers to a complex retrovirus. Among retroviruses, lentiviruses are the most efficient at transducing resting or growth-arrested cells. In preferred embodiments, a recombinant retroviral particle is a recombinant lentiviral particle or recombinant lentivirus.

Lentiviruses suitable for deriving or engineering recombinant lentiviruses contemplated in particular embodiments herein include but are not limited to human immunodeficiency virus (HIV), including HIV type 1 (HIV-1) and HIV type 2 (HIV-2); visna-maedi virus (VMV); caprine arthritis-encephalitis virus (CAEV); equine infectious anemia virus (EIAV); feline immunodeficiency virus (FIV); bovine immune deficiency virus (BIV); and simian immunodeficiency virus (SIV).

In particular embodiments, a recombinant lentiviral particle is derived or engineered from an HIV-1 or HIV-2 lentivirus.

D. PARTICLE SURFACE

Recombinant particles engineered to bind to a particular cell type and deliver a payload comprise an outer surface that comprises, expresses, or displays (i) one or more polypeptides that direct the particle to, and allow it to bind or attach to, a desired cell type and (ii) one or more polypeptides that mediate fusion with the cell. In particular

embodiments, a recombinant particle selected from the group consisting of a fusosome; a microvesicle, an apoptotic body, and an exosome; a lipid nanoparticle; a virus-like particle (VLPs); or a recombinant viral particle, comprises an outer surface selected from the group consisting of a single layer of phospholipid, a phospholipid bilayer, a cell membrane, a capsid, or a viral envelope.

In particular embodiments, the outer surface of the particle is engineered to express or display one or more mutated viral envelope glycoproteins that retain fusogenic activity and that substantially lack or lack cognate receptor binding activity and one or more non-viral membrane-bound tropism polypeptides engineered to bind a specific cell type, *e.g.*, an immune effector cell. Without wishing to be bound by any particular theory, it is contemplated that the viral envelope glycoproteins herein do not contribute to particle tropism. The viral envelope glycoproteins contemplated herein comprise one or more mutations (*e.g.*, amino acid substitution) that substantially reduce or eliminate their native antigen binding activities and/or blind the viral envelope glycoprotein from recognizing and binding or attaching to its cognate receptor expressed on a cell while still retaining the ability to mediate fusion with the cell. In this way, the native tropism activities of viral envelope glycoproteins contemplated herein are substantially extinguished or ablated while the fusion activity is retained or preserved.

Recombinant retroviral or lentiviral particles comprise an outer surface selected from the group consisting of a lipid bilayer, a cell membrane, or a viral envelope comprising polypeptides that mediate virus – cell attachment and fusion; and one or more polynucleotide and/or polypeptide payloads. The outer surface of the retroviral or lentiviral particle is engineered to uncouple or separate particle fusion and tropism activities.

In particular embodiments, the outer surface of the retroviral or lentiviral particle is engineered to express or display one or more non-viral membrane-bound tropism polypeptides that enable selective and/or specific binding of the virus to a desired cell type. The outer surface is also engineered to express or display a viral envelope glycoprotein that mediates virus – cell fusion but that substantially lacks or lacks the ability to bind its cognate receptor. In other words, the viral envelope glycoprotein provides the fusion activity of the recombinant particle and does not provide or contribute to the tropism activity of the particle. Likewise, the non-viral membrane-bound tropism polypeptides provide the tropism activity of the recombinant particle and do not provide or contribute to the fusion activity of the particle. The foregoing engineering strategy enables highly efficient on-target delivery of

therapeutic payloads to the desired cell types while minimizing, reducing and/or eliminating delivery to undesired cell types.

In particular embodiments, a recombinant retroviral particle comprises a lipid bilayer, cell membrane, or viral envelope comprising one or more mutated viral envelope glycoproteins that mediate fusion of the viral particle with a cell, but that do not substantially bind or bind its cognate receptor, and one or more non-viral membrane-bound tropism polypeptides.

In particular embodiments, one or more mutated viral envelope glycoproteins comprise one or more rhabdovirus (*e.g.*, vesiculovirus) envelope glycoproteins or one or more paramyxovirus (*e.g.*, morbillivirus or henipavirus) envelope glycoproteins. In particular embodiments, a mutated viral envelope glycoprotein comprises a heterologous signal peptide.

In particular embodiments, one or more mutated viral envelope glycoproteins comprise one or more rhabdovirus (*e.g.*, vesiculovirus) envelope glycoproteins or one or more paramyxovirus (*e.g.*, morbillivirus or henipavirus) envelope glycoproteins.

In particular embodiments, one or more mutated viral envelope glycoproteins comprise one or more rhabdovirus (*e.g.*, vesiculovirus) envelope glycoproteins and a native or heterologous signal peptide, which is subsequently cleaved.

In particular embodiments, one or more mutated viral envelope glycoproteins comprise one or more paramyxovirus (*e.g.*, morbillivirus or henipavirus) envelope glycoproteins and a native or heterologous signal peptide, which is subsequently cleaved.

Illustrative examples of heterologous signal peptides are set forth in SEQ ID NOs: 449-454.

I. RABDOVIRUS ENVELOPE GLYCOPROTEINS

The *Rhabdoviridae* family of viruses are negative-sense, single-stranded RNA viruses with a genome of about 10.8–16.1 kb. The prototypic mammalian rhabdoviruses include the rabies virus (RABV) and vesiculoviruses, which cause severe human and animal disease. In particular embodiments, a recombinant particle comprises one or more rhabdovirus envelope glycoproteins modified to substantially ablate or ablate the glycoprotein's ability bind its cognate receptor expressed on a cell while retaining fusogenic activity. The *Rhabdoviridae* family includes cytorhabdoviruses, dichorhavirus, ephemeroviruses, lyssaviruses, novirhabdoviruses, nucleorhabdoviruses, perhabdoviruses,

sigmaviruses, spriviviruses, tibroviruses, tupaviruses, varicosaviruses, and vesiculoviruses, among others.

a. Vesiculovirus Envelope Glycoproteins

Vesiculoviruses use a single glycoprotein to enter a cell: glycoprotein G mediates both cell attachment (tropism) and cell fusion. Glycoprotein G is normally responsible for virus attachment to specific receptors (*e.g.*, low-density lipoprotein receptor (LDL-R) and other members of this receptor family) and fusion between the viral and endosomal membranes. In particular embodiments, a modified vesiculovirus G envelope protein comprises one or more amino acid substitutions that enable the polypeptide to mediate fusion of the viral particle and a cell but that substantially ablate or ablate the polypeptide's ability to bind its cognate receptor expressed on a cell, *e.g.*, LDL-R.

Illustrative examples of vesiculoviruses suitable for use in particular embodiments from which G glycoproteins can be isolated include, but are not limited to vesicular stomatitis Alagoas virus (VSAV; Alagoas vesiculovirus), Carajás virus (CJSV; Carajas vesiculovirus), Chandipura virus (CHPV; Chandipura vesiculovirus), Cocal virus (COCV; Cocal vesiculovirus), vesicular stomatitis Indiana virus (VSIV, f.k.a. VSV; Indiana vesiculovirus), Isfahan virus (ISFV; Isfahan vesiculovirus), Maraba virus (MARAV; Maraba vesiculovirus), Morreton virus (MORV; Morreton vesiculovirus), vesicular stomatitis New Jersey virus (VSNJV; New Jersey vesiculovirus), and Piry virus (PIRYV; Piry vesiculovirus).

In particular embodiments, a vesiculovirus G envelope protein comprises an amino acid sequence set forth in any one of SEQ ID NOs: 15-322 disclosed in U.S. Patent Application No. 20200216502, each said sequence incorporated by reference herein in its entirety, or an amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical thereto that enables the polypeptide to mediate fusion of the viral particle with a cell but that substantially ablates or ablates the polypeptide's ability to bind its cognate receptor expressed on a cell, *e.g.*, LDL-R.

In particular embodiments, a vesiculovirus is vesicular stomatitis Indiana virus (VSIV). In particular embodiments, a mutated viral envelope glycoprotein is derived from a VSIV envelope glycoprotein (VSIV-G; *e.g.*, SEQ ID NO: 1: KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQA DGWMCHASKWVTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPG

FPPQSCGYATVTDAAEAVIVQVTPHHVLVDEYTGGEWVDSQFINGKCSNYICPTVHN
 STTWHSYKVKGLCDNLISMDITFFSEDGELSSLGKEGTGFRSNEYFAYETGGKA
 CKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLI
 QDVERILDYSLCQETWSKIRAGLPISPVDSLAPKNPGTGPAFTIINGTLKYFETR
 5 YIRVDIAAPILSRMVGMISSGTTTERELWDDWAPYEDVEIGPNGVLRRTSSGYKFPLY
 MIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNPIELVEG
 WFSSWKSSIASFFFIIGLIIGLFLVLRVGIHLCKIKHTKKRQIYTDIEMNRLGK) or an
 amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical thereto comprising one
 or more modifications that enable the polypeptide to mediate fusion of the viral particle and
 10 a cell but that substantially ablate or ablate the polypeptide's ability to bind its cognate
 receptor expressed on a cell, *e.g.*, LDL-R. In particular embodiments, a mutated viral
 envelope glycoprotein is derived from a VSIV-G polypeptide set forth in SEQ ID NO: 1
 comprising L47I and/or H80Q amino acid substitutions, such substitutions being present in
 naturally occurring variants of VSIV.

15 In particular embodiments, a mutated VSIV-G envelope protein comprises one or
 more of: one or more amino acid substitutions at H8, N9, Q10, K47, K50, A51, S183, S179,
 N180, I182, M184, Y209, I347, T350, T352, E353, and R354 (substitution with any amino
 acid; a conservation substitution; a disruptive substitution; substitution with D, E, A, G, F, or
 Q; or substitution with A, G, F, or Q); an insertion of TT between N9 and Q10, an insertion
 20 of GGS between H8 and N9, an insertion of GGS between N9 and Q10, an insertion of TT
 between N208 and Y209, an insertion of GGS between P46 and K47, and an insertion of
 GGS between N208 and Y209; or a deletion of residues 1-8. In particular embodiments, a
 VSIV-G envelope protein comprises one or more amino acid substitutions at H8, K47, Y209,
 and R354. In particular embodiments, a VSIV-G envelope protein comprises one or more
 25 amino acid substitutions at H8, K47, Y209, and R354, wherein each substitution can be with
 A, G, F, or Q. Amino acid positions are with reference to a VSIV-G envelope protein that
 lacks a signal peptide, *e.g.*, SEQ ID NO: 1. In particular embodiments, a mutated viral
 envelope glycoprotein is derived from a VSIV-G polypeptide set forth in SEQ ID NO: 1
 comprising L47I and/or H80Q amino acid substitutions, such substitutions present in
 30 naturally occurring variants of VSIV.

In particular embodiments, a mutated VSIV-G polypeptide comprises one or more
 amino acid substitutions at K47, I182, and/or R354 (substitution with any amino acid; a
 conservation substitution; a disruptive substitution; substitution with D, E, A, G, F, or Q; or

substitution with A, G, F, or Q). In particular embodiments, a mutated VSIV-G polypeptide comprises amino acid substitutions at K47, I182, or R354; K47 and I182; K47 and R354; I182 and R354; or at K47, I182, and R354 of SEQ ID NO: 1.

In particular embodiments, a mutated VSIV-G polypeptide comprises one or more
 5 of the following amino acid substitutions: K47A, K47Q, I182E, I182D, R354A, and/or R354Q. In particular embodiments, a mutated VSIV-G polypeptide comprises the following amino acid substitutions: K47A, K47Q, I182E, I182D, R354A, or R354Q; K47A and I182E; K47A and I182D; K47Q and I182E; K47Q and I182D; I182E and R354A; I182E and R354Q; I182D and R354A; I182D and R354Q; K47A and R354A; K47A and R354Q; K47Q
 10 and R354A; K47Q and R354Q; K47A, I182E, and R354A; K47A, I182D, and R354A; K47Q, I182E, and R354A; K47Q, I182D, and R354A; K47A, I182E, and R354Q; K47A, I182D, and R354Q; K47Q, I182E, and R354Q; or K47Q, I182D, and R354Q of SEQ ID NO: 1.

In particular embodiments, a VSIV-G envelope protein comprises one or more amino
 15 acid substitutions at K47 and R354 (with reference to a VSIV-G envelope protein that lacks a signal peptide, *e.g.*, SEQ ID NO: 1). In particular embodiments, a VSIV-G envelope protein comprises one or more amino acid substitutions selected from the group consisting of: K47A and R354A; K47A and R354G; K47A and R354F; K47A and R354Q; K47G and R354A; K47G and R354G; K47G and R354F; K47G and R354Q; K47F and R354A; K47F
 20 and R354G; K47F and R354F; K47F and R354Q; K47Q and R354A; K47Q and R354G; K47Q and R354F; and K47Q and R354Q. In a preferred embodiment, a VSIV-G envelope protein comprises the amino acid substitutions K47Q and R354A.

In particular embodiments, a mutated VSIV-G envelope protein comprises an amino acid sequence set forth in SEQ ID NO: 2 (wherein X₁= I, X₂= A, X₃= Q, and X₄= A; X₁=
 25 I, X₂= A, X₃= Q, and X₄= G; X₁= I, X₂= A, X₃= Q, and X₄= F; X₁= I, X₂= A, X₃= Q, and X₄= Q; X₁= L, X₂= A, X₃= Q, and X₄= A; X₁= L, X₂= A, X₃= Q, and X₄= G; X₁= L, X₂= A, X₃= Q, and X₄= F; X₁= L, X₂= A, X₃= Q, and X₄= Q; X₁= I, X₂= A, X₃= H, and X₄= A; X₁= I, X₂= A, X₃= H, and X₄= G; X₁= I, X₂= A, X₃= H, and X₄= F; X₁= I, X₂= A, X₃= H, and X₄= Q; X₁= L, X₂= A, X₃= H, and X₄= A; X₁= L, X₂= A, X₃= H,
 30 and X₄= G; X₁= L, X₂= A, X₃= H, and X₄= F; X₁= L, X₂= A, X₃= H, and X₄= Q; X₁= I, X₂= G, X₃= Q, and X₄= A; X₁= I, X₂= G, X₃= Q, and X₄= G; X₁= I, X₂= G, X₃= Q, and X₄= F; X₁= I, X₂= G, X₃= Q, and X₄= Q; X₁= L, X₂= G, X₃= Q, and X₄= A; X₁= L, X₂= G, X₃= Q, and X₄= G; X₁= L, X₂= G, X₃= Q, and X₄= F; X₁= L, X₂= G, X₃= Q, and X₄= Q; and

X₄ = Q; X₁ = I, X₂ = G, X₃ = H, and X₄ = A; X₁ = I, X₂ = G, X₃ = H, and X₄ = G; X₁ = I, X₂ = G, X₃ = H, and X₄ = F; X₁ = I, X₂ = G, X₃ = H, and X₄ = Q; X₁ = L, X₂ = G, X₃ = H, and X₄ = A; X₁ = L, X₂ = G, X₃ = H, and X₄ = G; X₁ = L, X₂ = G, X₃ = H, and X₄ = F; X₁ = L, X₂ = G, X₃ = H, and X₄ = Q; X₁ = I, X₂ = F, X₃ = Q, and X₄ = A; X₁ = I, X₂ = F, X₃ = Q, and X₄ = G; X₁ = I, X₂ = F, X₃ = Q, and X₄ = F; X₁ = I, X₂ = F, X₃ = Q, and X₄ = Q; X₁ = L, X₂ = F, X₃ = Q, and X₄ = A; X₁ = L, X₂ = F, X₃ = Q, and X₄ = G; X₁ = L, X₂ = F, X₃ = Q, and X₄ = F; X₁ = L, X₂ = F, X₃ = Q, and X₄ = Q; X₁ = I, X₂ = F, X₃ = H, and X₄ = A; X₁ = I, X₂ = F, X₃ = H, and X₄ = G; X₁ = I, X₂ = F, X₃ = H, and X₄ = F; X₁ = I, X₂ = F, X₃ = H, and X₄ = Q; X₁ = L, X₂ = F, X₃ = H, and X₄ = A; X₁ = L, X₂ = F, X₃ = H, and X₄ = G; X₁ = L, X₂ = F, X₃ = H, and X₄ = F; X₁ = L, X₂ = F, X₃ = H, and X₄ = Q; X₁ = I, X₂ = Q, X₃ = Q, and X₄ = A; X₁ = I, X₂ = Q, X₃ = Q, and X₄ = G; X₁ = I, X₂ = Q, X₃ = Q, and X₄ = F; X₁ = I, X₂ = Q, X₃ = Q, and X₄ = Q; X₁ = L, X₂ = Q, X₃ = Q, and X₄ = A; X₁ = L, X₂ = Q, X₃ = Q, and X₄ = G; X₁ = L, X₂ = Q, X₃ = Q, and X₄ = F; X₁ = L, X₂ = Q, X₃ = Q, and X₄ = Q; X₁ = I, X₂ = Q, X₃ = H, and X₄ = A; X₁ = I, X₂ = Q, X₃ = H, and X₄ = G; X₁ = I, X₂ = Q, X₃ = H, and X₄ = F; X₁ = I, X₂ = Q, X₃ = H, and X₄ = Q; X₁ = L, X₂ = Q, X₃ = H, and X₄ = A; X₁ = L, X₂ = Q, X₃ = H, and X₄ = G; X₁ = L, X₂ = Q, X₃ = H, and X₄ = F; and X₁ = L, X₂ = Q, X₃ = H, and X₄ = Q) or an amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical thereto that mediates fusion of the viral particle and a cell but that substantially ablates or ablates the polypeptide's ability to bind its cognate receptor expressed on a cell, *e.g.*, LDL-R.

Table 1

SEQ ID NO:	AMINO ACID SEQUENCE
2	KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTAX ₁ QVKMPX ₂ SHKAIQADGWMCHASKWVTTCDFRWYGPKYITX ₃ SIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQVTPHHVLVDEYTGGEVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDSLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMISGTTTEX ₄ ELWDDWAPYEDVEIGPNGVLRITSSGYKFPPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGWFFSSWKSSIASFFFIIGLIIGLFLVLRVGIHLCKIKLHTTKRQIYTDIEMNRLGK

In particular embodiments, a mutated VSIV-G envelope protein comprises an amino acid sequence set forth in any one of SEQ ID NOs: 582-645 or an amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical thereto that mediates fusion of the viral particle and a cell but that substantially ablates or ablates the polypeptide's ability to bind its cognate receptor expressed on a cell, *e.g.*, LDL-R. In particular embodiments, a mutated VSIV-G envelope protein comprises an amino acid sequence set forth in any one of SEQ ID NOs:

630-645 or an amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical thereto that mediates fusion of the viral particle and a cell but that substantially ablates or ablates the polypeptide's ability to bind its cognate receptor expressed on a cell, *e.g.*, LDL-R. In particular embodiments, a mutated VSIV-G envelope protein comprises an amino acid
5 sequence set forth in any one of SEQ ID NOs: 630, 634, 638, and 642 or an amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical thereto that mediates fusion of the viral particle and a cell but that substantially ablates or ablates the polypeptide's ability to bind its cognate receptor expressed on a cell, *e.g.*, LDL-R.

Table 2

SEQ ID NO:	AMINO ACID SEQUENCE
582	KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPASHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGGEWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEAELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIGLIIGLFLVLRVGIHLCKIKHHTKKRQIYTDIEMNRLGK
583	KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPASHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGGEWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEGELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIGLIIGLFLVLRVGIHLCKIKHHTKKRQIYTDIEMNRLGK
584	KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPASHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGGEWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEFELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIGLIIGLFLVLRVGIHLCKIKHHTKKRQIYTDIEMNRLGK
585	KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPASHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGGEWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEQELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIGLIIGLFLVLRVGIHLCKIKHHTKKRQIYTDIEMNRLGK
586	KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPASHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGGEWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEAELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIGLIIGLFLVLRVGIHLCKIKHHTKKRQIYTDIEMNRLGK

587	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPASHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNFYAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEGELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
588	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPASHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNFYAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEFELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
589	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPASHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNFYAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEQELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
590	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPASHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNFYAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEAELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
591	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPASHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNFYAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEGELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
592	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPASHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNFYAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEFELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
593	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPASHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNFYAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEQELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
594	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPASHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED

	GELSSLGKEGTGFRSNYFAYETGGKACKMÖYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEAELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
595	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWNHNDLIGTALQVKMPASHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHS DYKVKGLCD SNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMÖYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEGELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
596	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWNHNDLIGTALQVKMPASHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHS DYKVKGLCD SNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMÖYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEFELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
597	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWNHNDLIGTALQVKMPASHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHS DYKVKGLCD SNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMÖYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEQELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
598	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWNHNDLIGTALQVKMPGSHKAIQADGWMCHASKW VTTCDFRWYGPKYITQ SIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHS DYKVKGLCD SNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMÖYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEAELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
599	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWNHNDLIGTALQVKMPGSHKAIQADGWMCHASKW VTTCDFRWYGPKYITQ SIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHS DYKVKGLCD SNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMÖYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEGELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
600	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWNHNDLIGTALQVKMPGSHKAIQADGWMCHASKW VTTCDFRWYGPKYITQ SIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHS DYKVKGLCD SNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMÖYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEFELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
601	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWNHNDLIGTALQVKMPGSHKAIQADGWMCHASKW VTTCDFRWYGPKYITQ SIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHS DYKVKGLCD SNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMÖYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEQELWDDWAPYEDVEIGPNGVLR TSSGYKFPL

	YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNPIELVEGWFSWSSKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
602	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPGSHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMISSGTTTEAELWDDWAPYEDVEIGPNGVLRRTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNPIELVEGWFSWSSKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
603	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPGSHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMISSGTTTEGELWDDWAPYEDVEIGPNGVLRRTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNPIELVEGWFSWSSKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
604	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPGSHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMISSGTTTEFELWDDWAPYEDVEIGPNGVLRRTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNPIELVEGWFSWSSKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
605	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPGSHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMISSGTTTEQELWDDWAPYEDVEIGPNGVLRRTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNPIELVEGWFSWSSKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
606	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPGSHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMISSGTTTEAELWDDWAPYEDVEIGPNGVLRRTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNPIELVEGWFSWSSKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
607	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPGSHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMISSGTTTEGELWDDWAPYEDVEIGPNGVLRRTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNPIELVEGWFSWSSKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
608	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPGSHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMISSGTTTEFELWDDWAPYEDVEIGPNGVLRRTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNPIELVEGWFSWSSKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
609	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPGSHKAIQADGWMCHASKW

	VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMIISGTTTEQELWDDWAPYEDVEIGPNGVLRVTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNPIELVEGWFFSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
610	KFTIVFPHNQGNWKNVPSNYHYCPSSDDLWNHNDLIGTALQVKMPGSHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMIISGTTTEAELWDDWAPYEDVEIGPNGVLRVTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNPIELVEGWFFSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
611	KFTIVFPHNQGNWKNVPSNYHYCPSSDDLWNHNDLIGTALQVKMPGSHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMIISGTTTEGELWDDWAPYEDVEIGPNGVLRVTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNPIELVEGWFFSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
612	KFTIVFPHNQGNWKNVPSNYHYCPSSDDLWNHNDLIGTALQVKMPGSHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMIISGTTTEFELWDDWAPYEDVEIGPNGVLRVTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNPIELVEGWFFSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
613	KFTIVFPHNQGNWKNVPSNYHYCPSSDDLWNHNDLIGTALQVKMPGSHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMIISGTTTEQELWDDWAPYEDVEIGPNGVLRVTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNPIELVEGWFFSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
614	KFTIVFPHNQGNWKNVPSNYHYCPSSDDLWNHNDLIGTALQVKMPF SHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMIISGTTTEAELWDDWAPYEDVEIGPNGVLRVTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNPIELVEGWFFSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
615	KFTIVFPHNQGNWKNVPSNYHYCPSSDDLWNHNDLIGTALQVKMPF SHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMIISGTTTEGELWDDWAPYEDVEIGPNGVLRVTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNPIELVEGWFFSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
616	KFTIVFPHNQGNWKNVPSNYHYCPSSDDLWNHNDLIGTALQVKMPF SHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG

	SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMISSGTTTEFELWDDWAPYEDVEIGPNGVLRRTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNP IELVEGWFSWSSKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
617	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWNHNDLIGTAIQVKMPF SHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKM QYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMISSGTTTEQELWDDWAPYEDVEIGPNGVLRRTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNP IELVEGWFSWSSKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
618	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWNHNDLIGTAIQVKMPF SHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKM QYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMISSGTTTEAELWDDWAPYEDVEIGPNGVLRRTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNP IELVEGWFSWSSKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
619	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWNHNDLIGTAIQVKMPF SHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKM QYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMISSGTTTEGELWDDWAPYEDVEIGPNGVLRRTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNP IELVEGWFSWSSKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
620	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWNHNDLIGTAIQVKMPF SHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKM QYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMISSGTTTEFELWDDWAPYEDVEIGPNGVLRRTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNP IELVEGWFSWSSKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
621	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWNHNDLIGTAIQVKMPF SHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKM QYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMISSGTTTEQELWDDWAPYEDVEIGPNGVLRRTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNP IELVEGWFSWSSKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
622	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWNHNDLIGTAIQVKMPF SHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKM QYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMISSGTTTEAELWDDWAPYEDVEIGPNGVLRRTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNP IELVEGWFSWSSKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
623	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWNHNDLIGTAIQVKMPF SHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKM QYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMISSGTTTEGELWDDWAPYEDVEIGPNGVLRRTSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLEFFGDTGLSKNP IELVEGWFSWSSKSS

	IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
624	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPF SHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEFELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
625	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPF SHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEQELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
626	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPF SHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEAELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
627	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPF SHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEGELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
628	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPF SHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEFELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
629	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPF SHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEQELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
630	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMP SHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ VTPHHVLVDEYTGWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEAELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNP IELVEGW FSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
631	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMP SHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQ

	VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSSLGKEGTGFRSNYFAYETGGKACKMÖYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEGELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGW FSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
632	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPQSHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSSLGKEGTGFRSNYFAYETGGKACKMÖYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEFELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGW FSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
633	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPQSHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSSLGKEGTGFRSNYFAYETGGKACKMÖYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEQELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGW FSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
634	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPQSHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSSLGKEGTGFRSNYFAYETGGKACKMÖYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEAELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGW FSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
635	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPQSHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSSLGKEGTGFRSNYFAYETGGKACKMÖYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEGELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGW FSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
636	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPQSHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSSLGKEGTGFRSNYFAYETGGKACKMÖYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEFELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGW FSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
637	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPQSHKAIQADGWMCHASKW VTTCDFRWYGPKYITQSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSSLGKEGTGFRSNYFAYETGGKACKMÖYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEQELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGW FSSWKSS IASFFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
638	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPQSHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTGWEVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLISMDITFFSED GELSSSLGKEGTGFRSNYFAYETGGKACKMÖYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN

	GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEAELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
639	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPQSHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHS DYKVKGLCD SNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEGELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
640	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPQSHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHS DYKVKGLCD SNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEFELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
641	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTAIQVKMPQSHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHS DYKVKGLCD SNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEQELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
642	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPQSHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHS DYKVKGLCD SNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEAELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
643	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPQSHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHS DYKVKGLCD SNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEGELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
644	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPQSHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHS DYKVKGLCD SNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEFELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK
645	KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPQSHKAIQADGWMCHASKW VTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTD AEAIVIQ VTPHHVLVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHS DYKVKGLCD SNLISMDITFFSED GELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEG SSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRVDIAAPILSRMVGMI SGTTEQELWDDWAPYEDVEIGPNGVLR TSSGYKFPL YMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGW FSSWKSS IASFFFIIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK

In particular embodiments, a vesiculovirus is cocal virus (COCV). In particular embodiments, a mutated viral envelope glycoprotein is derived from a COCV envelope glycoprotein (COCV-G; *e.g.*, SEQ ID NO: 3: KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHNDLLGITMKVKMPKTHKAIQA
5 DGWMCHAAKWITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGF
PPQNCGYATVTDSVAVVVQATPHHVLVDEYTG EWIDSQFPNGKCETEECETVHN
STVWYS DYKVTGLCDATLVDTEITFFSEDGKKESIGKPNTGYRSNYFAYEKGD KV
CKMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVGATISAPTQTSVDVSLI
LDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIINGTLKYFETR
10 YIRIDIDNPIISKMVGKISGSQTERELWTEWFPYEGVEIGPNGILKTPTGYKFPLFMI
GHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWFS
SWKSTVVTFFFAIGVFILLYVVARIVIAVRYRYQGSNNKRIYNDIEMSRFRK) or an
amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical thereto comprising one
or more modifications that enable the polypeptide to mediate fusion of the viral particle and
15 a cell but that substantially ablate or ablate the polypeptide's ability to bind its cognate
receptor expressed on a cell, *e.g.*, LDL-R. In particular embodiments, a COCV-G envelope
protein comprises one or more amino acid substitutions at K47 and/or R354. In particular
embodiments, a COCV-G envelope protein comprises one or more amino acid substitutions
at K47 and/or R354, wherein each amino acid can be substituted with A, G, F, or Q. In
20 particular embodiments, a COCV-G envelope protein comprises one or more amino acid
substitutions at K47 and/or R354 (with reference to a COCV-G envelope protein that lacks a
signal peptide, *e.g.*, SEQ ID NO: 3). In particular embodiments, a COCV-G envelope protein
comprises one or more amino acid substitutions selected from the group consisting of: K47A
and R354A; K47A and R354G; K47A and R354F; K47A and R354Q; K47G and R354A;
25 K47G and R354G; K47G and R354F; K47G and R354Q; K47F and R354A; K47F and
R354G; K47F and R354F; K47F and R354Q; K47Q and R354A; K47Q and R354G; K47Q
and R354F; and K47Q and R354Q. In particular embodiments, a COCV-G envelope protein
comprises an amino acid sequence set forth in SEQ ID NO: 4 (wherein X₁ = A and X₂ = A;
X₁ = A and X₂ = G; X₁ = A and X₂ = F; X₁ = A and X₂ = Q; X₁ = G and X₂ = A; X₁ = G and X₂
30 = G; X₁ = G and X₂ = F; X₁ = G and X₂ = Q; X₁ = F and X₂ = A; X₁ = F and X₂ = G; X₁ = F and
X₂ = F; X₁ = F and X₂ = Q; X₁ = Q and X₂ = A; X₁ = Q and X₂ = G; X₁ = Q and X₂ = F; or X₁ =
A and X₂ = Q) or an amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical
thereto that mediates fusion of the viral particle and a cell but that substantially ablates or

ablates the polypeptide's ability to bind its cognate receptor expressed on a cell, *e.g.*, LDL-R.

Table 3

SEQ ID NO	AMINO ACID SEQUENCE
4	KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHDLLGITMKVKMPX ₁ THKAIQADGWMCHAAKW ITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTD ₁ SVAVVVQA TPHHVLVDEYTGWIDSQFPNGKCETEECETVHNSTVWYSDYKVTGLCDATLVDTEITFFSEDGK KESIGKPNTGYRSNYFAYEKGDKVCKMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVGATI SAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIINGTLK YFETRYIRIDIDNPIISKMVGKISGSQTEX ₂ ELWTEWFPYEGVEIGPNGLKTP ₁ GYKFPLFMIG HGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWFSSWKSTVVTFF FAIGVFILLYVVARIVIAVRYRYQGSNNKRIYNDIEMSRFRK

In particular embodiments, a mutated COCV-G envelope protein comprises an amino acid sequence set forth in any one of SEQ ID NOs: 646-661 or an amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical thereto that mediates fusion of the viral particle and a cell but that substantially ablates or ablates the polypeptide's ability to bind its cognate receptor expressed on a cell, *e.g.*, LDL-R. In particular embodiments, a mutated COCV-G envelope protein comprises an amino acid sequence set forth in any one of SEQ ID NOs: 658-661 or an amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical thereto that mediates fusion of the viral particle and a cell but that substantially ablates or ablates the polypeptide's ability to bind its cognate receptor expressed on a cell, *e.g.*, LDL-R. In particular embodiments, a mutated VSIV-G envelope protein comprises an amino acid sequence set forth in SEQ ID NOs: 658 or 661 or an amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical thereto that mediates fusion of the viral particle and a cell but that substantially ablates or ablates the polypeptide's ability to bind its cognate receptor expressed on a cell, *e.g.*, LDL-R.

Table 4

SEQ ID NO:	AMINO ACID SEQUENCE
646	KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHDLLGITMKVKMPATHKAIQADGWMCHAAKW ITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTD ₁ SVAVVVQ ATPHHVLVDEYTGWIDSQFPNGKCETEECETVHNSTVWYSDYKVTGLCDATLVDTEITFFSED GKESIGKPNTGYRSNYFAYEKGDKVCKMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVG ATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRIDIDNPIISKMVGKISGSQTEAELWTEWFPYEGVEIGPNGLKTP ₁ GYKFPL FMIGHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWFSSWKST VVTFFFAIGVFILLYVVARIVIAVRYRYQGSNNKRIYNDIEMSRFRK
647	KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHDLLGITMKVKMPATHKAIQADGWMCHAAKW ITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTD ₁ SVAVVVQ ATPHHVLVDEYTGWIDSQFPNGKCETEECETVHNSTVWYSDYKVTGLCDATLVDTEITFFSED GKESIGKPNTGYRSNYFAYEKGDKVCKMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVG

	ATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRIDIDNPIISKMVGKISGSQTEGELWTEWFFPYEGVEIGPNGILKPTPGYKFPL FMIGHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWFSWKST VVTFFFAIGVFILLYVVARIVIAVRVRYQGSNNKRIYNDIEMSRFRK
648	KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHDLLGITMKVKMPATHKAIQADGWMCHAAKW ITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQ ATPHHVLVDEYTGWIDSQFPNGKCETEECETVHNSTVWYSYKVTGLCDATLVDTEITFFSED GKKESIGKPNBTGYRSNYFAYEKGDVKCMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVG ATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRIDIDNPIISKMVGKISGSQTEFELWTEWFFPYEGVEIGPNGILKPTPGYKFPL FMIGHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWFSWKST VVTFFFAIGVFILLYVVARIVIAVRVRYQGSNNKRIYNDIEMSRFRK
649	KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHDLLGITMKVKMPATHKAIQADGWMCHAAKW ITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQ ATPHHVLVDEYTGWIDSQFPNGKCETEECETVHNSTVWYSYKVTGLCDATLVDTEITFFSED GKKESIGKPNBTGYRSNYFAYEKGDVKCMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVG ATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRIDIDNPIISKMVGKISGSQTEQELWTEWFFPYEGVEIGPNGILKPTPGYKFPL FMIGHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWFSWKST VVTFFFAIGVFILLYVVARIVIAVRVRYQGSNNKRIYNDIEMSRFRK
650	KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHDLLGITMKVKMPGTHKAIQADGWMCHAAKW ITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQ ATPHHVLVDEYTGWIDSQFPNGKCETEECETVHNSTVWYSYKVTGLCDATLVDTEITFFSED GKKESIGKPNBTGYRSNYFAYEKGDVKCMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVG ATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRIDIDNPIISKMVGKISGSQTEAELWTEWFFPYEGVEIGPNGILKPTPGYKFPL FMIGHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWFSWKST VVTFFFAIGVFILLYVVARIVIAVRVRYQGSNNKRIYNDIEMSRFRK
651	KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHDLLGITMKVKMPGTHKAIQADGWMCHAAKW ITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQ ATPHHVLVDEYTGWIDSQFPNGKCETEECETVHNSTVWYSYKVTGLCDATLVDTEITFFSED GKKESIGKPNBTGYRSNYFAYEKGDVKCMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVG ATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRIDIDNPIISKMVGKISGSQTEGELWTEWFFPYEGVEIGPNGILKPTPGYKFPL FMIGHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWFSWKST VVTFFFAIGVFILLYVVARIVIAVRVRYQGSNNKRIYNDIEMSRFRK
652	KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHDLLGITMKVKMPGTHKAIQADGWMCHAAKW ITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQ ATPHHVLVDEYTGWIDSQFPNGKCETEECETVHNSTVWYSYKVTGLCDATLVDTEITFFSED GKKESIGKPNBTGYRSNYFAYEKGDVKCMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVG ATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRIDIDNPIISKMVGKISGSQTEFELWTEWFFPYEGVEIGPNGILKPTPGYKFPL FMIGHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWFSWKST VVTFFFAIGVFILLYVVARIVIAVRVRYQGSNNKRIYNDIEMSRFRK
653	KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHDLLGITMKVKMPGTHKAIQADGWMCHAAKW ITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQ ATPHHVLVDEYTGWIDSQFPNGKCETEECETVHNSTVWYSYKVTGLCDATLVDTEITFFSED GKKESIGKPNBTGYRSNYFAYEKGDVKCMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVG ATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRIDIDNPIISKMVGKISGSQTEQELWTEWFFPYEGVEIGPNGILKPTPGYKFPL FMIGHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWFSWKST VVTFFFAIGVFILLYVVARIVIAVRVRYQGSNNKRIYNDIEMSRFRK
654	KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHDLLGITMKVKMPFTHKAIQADGWMCHAAKW ITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQ ATPHHVLVDEYTGWIDSQFPNGKCETEECETVHNSTVWYSYKVTGLCDATLVDTEITFFSED GKKESIGKPNBTGYRSNYFAYEKGDVKCMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVG ATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRIDIDNPIISKMVGKISGSQTEAELWTEWFFPYEGVEIGPNGILKPTPGYKFPL FMIGHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWFSWKST

	VVTTTTFAIGVFILLYVVARIVIAVRVRYQGSNNKRIYNDIEMSRFRK
655	KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHDLLGITMKVKMPFTHKAIQADGWMCHAAKW ITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQ ATPHHVLVDEYTGWIDSQFPNGKCETEECETVHNSTVWYSDYKVTGLCDATLVDTEITFFSED GKKESIGKPNBTGYRSNYFAYEKGDKVCKMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVG ATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRIDIDNP IISKMGKISGSQTEGELWTEWFPYEGVEIGPNGILKTPTGYKFPL FMIGHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWSSWKST VVTTTTFAIGVFILLYVVARIVIAVRVRYQGSNNKRIYNDIEMSRFRK
656	KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHDLLGITMKVKMPFTHKAIQADGWMCHAAKW ITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQ ATPHHVLVDEYTGWIDSQFPNGKCETEECETVHNSTVWYSDYKVTGLCDATLVDTEITFFSED GKKESIGKPNBTGYRSNYFAYEKGDKVCKMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVG ATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRIDIDNP IISKMGKISGSQTEFELWTEWFPYEGVEIGPNGILKTPTGYKFPL FMIGHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWSSWKST VVTTTTFAIGVFILLYVVARIVIAVRVRYQGSNNKRIYNDIEMSRFRK
657	KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHDLLGITMKVKMPFTHKAIQADGWMCHAAKW ITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQ ATPHHVLVDEYTGWIDSQFPNGKCETEECETVHNSTVWYSDYKVTGLCDATLVDTEITFFSED GKKESIGKPNBTGYRSNYFAYEKGDKVCKMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVG ATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRIDIDNP IISKMGKISGSQTEQELWTEWFPYEGVEIGPNGILKTPTGYKFPL FMIGHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWSSWKST VVTTTTFAIGVFILLYVVARIVIAVRVRYQGSNNKRIYNDIEMSRFRK
658	KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHDLLGITMKVKMPQTHKAIQADGWMCHAAKW ITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQ ATPHHVLVDEYTGWIDSQFPNGKCETEECETVHNSTVWYSDYKVTGLCDATLVDTEITFFSED GKKESIGKPNBTGYRSNYFAYEKGDKVCKMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVG ATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRIDIDNP IISKMGKISGSQTEAELWTEWFPYEGVEIGPNGILKTPTGYKFPL FMIGHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWSSWKST VVTTTTFAIGVFILLYVVARIVIAVRVRYQGSNNKRIYNDIEMSRFRK
659	KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHDLLGITMKVKMPQTHKAIQADGWMCHAAKW ITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQ ATPHHVLVDEYTGWIDSQFPNGKCETEECETVHNSTVWYSDYKVTGLCDATLVDTEITFFSED GKKESIGKPNBTGYRSNYFAYEKGDKVCKMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVG ATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRIDIDNP IISKMGKISGSQTEGELWTEWFPYEGVEIGPNGILKTPTGYKFPL FMIGHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWSSWKST VVTTTTFAIGVFILLYVVARIVIAVRVRYQGSNNKRIYNDIEMSRFRK
660	KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHDLLGITMKVKMPQTHKAIQADGWMCHAAKW ITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQ ATPHHVLVDEYTGWIDSQFPNGKCETEECETVHNSTVWYSDYKVTGLCDATLVDTEITFFSED GKKESIGKPNBTGYRSNYFAYEKGDKVCKMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVG ATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRIDIDNP IISKMGKISGSQTEFELWTEWFPYEGVEIGPNGILKTPTGYKFPL FMIGHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWSSWKST VVTTTTFAIGVFILLYVVARIVIAVRVRYQGSNNKRIYNDIEMSRFRK
661	KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHDLLGITMKVKMPQTHKAIQADGWMCHAAKW ITTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQ ATPHHVLVDEYTGWIDSQFPNGKCETEECETVHNSTVWYSDYKVTGLCDATLVDTEITFFSED GKKESIGKPNBTGYRSNYFAYEKGDKVCKMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVG ATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPVDLSYLAPKNPGTGPAFTIIN GTLKYFETRYIRIDIDNP IISKMGKISGSQTEQELWTEWFPYEGVEIGPNGILKTPTGYKFPL FMIGHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWSSWKST VVTTTTFAIGVFILLYVVARIVIAVRVRYQGSNNKRIYNDIEMSRFRK

2. *PARAMYXOVIRUS ENVELOPE GLYCOPROTEINS*

The Paramyxoviridae family of negative-sense single-stranded RNA viruses is known to cause different types of infections in vertebrates. Examples of these infections in humans include the measles virus, encephalitis, mumps virus, parainfluenza virus, and
5 respiratory syncytial virus. In particular embodiments, a recombinant particle comprises one or more paramyxovirus envelope glycoproteins modified to substantially ablate or ablate the glycoprotein's ability bind its cognate receptor expressed on a cell while retaining fusogenic activity. The Paramyxoviridae family includes morbilliviruses and henipaviruses, among others.

10 a. **Morbillivirus Envelope Glycoproteins**

Morbilliviruses use two types of glycoproteins to enter a cell: glycoprotein F (a fusion polypeptide) and glycoprotein H (an attachment protein). Although glycoprotein F mediates fusion and glycoprotein H mediates binding, both H and F glycoproteins are required for viral particle fusion with a cell, glycoprotein H supports glycoprotein F in its membrane
15 fusion function.

Efficient pseudotyping with morbillivirus envelope proteins may be accomplished using glycoprotein F comprising a truncated cytoplasmic portion comprising at least 1 positively charged amino acid residue and no more than 9 consecutive amino acid residues as counted from the N-terminal end of the cytoplasmic portion and glycoprotein H
20 comprising a truncated cytoplasmic portion comprising at least 9 and no more than 19 consecutive amino acid residues as counted from the C-terminal end of the cytoplasmic portion plus an additional methionine at the N-terminus. Moreover, glycoprotein H can be modified to ablate its antigen binding activity.

In particular embodiments, the vector comprises modified morbillivirus F and H viral
25 envelope glycoproteins, wherein glycoprotein H is modified to ablate cell binding activity and both H and F glycoproteins retain the ability to cooperatively mediate cell fusion.

Illustrative examples of morbilliviruses suitable for use in particular embodiments from which F and H glycoproteins can independently be isolated from include but are not limited to canine distemper virus (CDV), cetacean morbillivirus (CeMV), feline
30 morbillivirus (FeMV), measles virus (MV), peste-des-petits-ruminants virus (PPRV), phocine distemper virus (PDV), rinderpest virus (RPV).

- In particular embodiments, one or more mutated morbillivirus envelope glycoproteins are derived from measles virus F (MV-F) and measles virus H (MV-H). In particular embodiments, a recombinant particle comprises one or more measles virus viral envelope glycoproteins modified to lack cell binding activity and retain fusogenic activity.
- 5 In some embodiments, a recombinant particle comprises a modified MV-F glycoprotein and an MV-H glycoprotein modified to lack cell binding activity and retain fusogenic activity.

- In particular embodiments, one or more mutated morbillivirus envelope glycoproteins are derived from measles virus F (MV-F) polypeptide (*e.g.*, SEQ ID NO: 5: QIHWGNLSKIGVVGIGSASYKVMTRSSHQSLVIKLMPNITLLNCTRVEIAEYRRL
- 10 LRTVLEPIRDALNAMTQNIRPVQSVASSRRHKRFAGVVLAGAALGVATAAQITA GIALHQSMNLNSQAIDNLRASLETTNQAIEAIRQAGQEMILAVQGVQDYINNELIPS MNQLSCDLIGQKLGLKLLRYYTEILSLFGPSLRDPISAEISIQALSALGGDINKVLE KLGYSGGDLLGILESIRGIKARITHVDTESYFIVLSIAYPTLSEIKGVIVHRLEGVSYN IGSQEWYTTVPKYVATQGYLISNFEDESSCTFMPEGTVCSQNALYPMSPLLQECLR
- 15 GSTKSCARTLVSGSFGNRFILSQGNLIANCASILCKCYTTGTIINQDPDKILTYIAAD HCPVVEVNGVTIQVGSRRYPDAVYLHRIDLGPPISLERLDVGTNLGNIAKLEDA KELLESSDQILRSMKGLSSTSIVYILIAVCLGGLIGIPALICCCRGR) or an amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical thereto and a measles virus H (MV-H) polypeptide (*e.g.*, SEQ ID NO: 6:
- 20 MGSRIVINREHLMIDRPYVLLAVLFVFMFLSLIGLLAIAGIRLHRAAIYTAIEIHKSLST NLDVTNSIEHQVKDVLTPLFKIIGDEVGLRTPQRFTDLVKFISDKIKFLNPDREYDF RDLTWCINPPERIKLDYDQYCADVAAEELMNALVNSTLLETTRTTNQFLAVSKGN CSGPTTIRGQFSNMSLSLLDLYLGRGYNVSSIVTMTSQQMGYGGTYLVEKPNLSSK RSELSQLSMYRVFEVGVIRNPGLGAPVFHMTNYLEQPVSNDLNLCMVVALGELKL
- 25 AALCHGEDSITIPYQSGSGKGVSFQLVKLGVWKSPTDMQSWVPLSTDDPVIDRLYL SSHRGVIADNQAKWAVPTTRTDDKLRMETCFQQACKGKIQALCENPEWAPLKD NRIPSYGVLSVDLSLTVELKIKIASGFGPLITHGSGMDLYKSNHNNVYWLTIIPPMK NLALGVINTLEWIPRFKVSPYLFTVPIKEAGGDCHAPTYLPAEVDGDVKLSSNLVI LPGQDLQYVLATYDTSRVEHAVVYVYSPSRFSFYFPFRLPIKGVPIELQVECFT
- 30 WDQKLWCRHFCVLADSESGGHITHSGMVGMGVSCTVTREDGTN) or an amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical thereto, wherein the MV-H protein lacks cell binding activity and retains fusogenic activity. In particular embodiments,

the MV-H polypeptide comprises one or more amino acid substitutions at positions Y463, R515, S530, and F531 of a MV-H polypeptide (*e.g.*, SEQ ID NO 6). In particular embodiments, the MV-H polypeptide comprises one or more of the amino acid substitutions Y463A, R515A, S530L, and F531S in an MV-H polypeptide (*e.g.*, SEQ ID NO: 7:

5 MGSRIVINREHLMIDRPYVLLAVLFVMFLSLIGLLAIAGIRLHRAAIYTAIEHKSLST
 NLDVTNSIEHQVKDVLTPFKIIGDEVGLRTPQRFTDLVKFISDKIKFLNPDREYDF
 RDLTWCINPPERIKLDYDQYCADVAAEELMNALVNSTLLETTRTTNQFLAVSKGN
 CSGPTTIRGQFSNMSLSLLDLYLGRGYNVSSIVTMTSQGMYYGGTYLVEKPNLSSK
 RSELSQLSMYRVFEVGVIRNPGLGAPVFHMTNYLEQPVSNDSLNCMVALGELKL
 10 AALCHGEDSITIPYQSGSGKGVSFQLVKLGWKSPTDMQSWVPLSTDDPVIDRLYL
 SSHRGVIADNQAQWAVPTTRTDDKLRMETCFQQACKGKIQALCENPEWAPLKD
 NRIPSYGVLSVDLSLTVELKIKIASGFGPLITHGSGMDLYKSNHNNVYWLTIIPMK
 NLALGVINTLEWIPRFKVSPALFNVPIKEAGGDCHAPTYLPAEVDGDVKLSSNLVI
 LPGQDLQYVLATYDTSAVEHAVVYYVYSPSRLSSYFYPFRLPIKGVPIELQVECFT
 15 WDQKLWCRHFCVLADSESGGHITHSGMVGGMVSVCTVTREDGTN) or an amino
 acid sequence at least 95%, 96%, 97%, 98%, or 99% identical thereto, wherein the MV-H
 protein lacks cell binding activity and retains fusogenic activity.

a. Henipavirus Envelope Glycoproteins

Henipaviruses use two types of glycoproteins to enter a cell: glycoprotein F (a fusion
 20 polypeptide) and glycoprotein G (an attachment protein). Although glycoprotein F mediates
 fusion and glycoprotein G mediates binding, both F and G glycoproteins are required for
 viral particle fusion with a target cell, glycoprotein G supports glycoprotein F in its membrane
 fusion function.

Efficient pseudotyping with henipavirus envelope proteins may be accomplished
 25 using glycoprotein F comprising a truncated cytoplasmic portion comprising at least 6
 consecutive amino acid residues as counted from the N-terminal end of the cytoplasmic
 portion and glycoprotein G comprising a truncated cytoplasmic portion comprising at least
 11 to at least 15 consecutive amino acid residues as counted from the C-terminal end of the
 cytoplasmic portion plus an additional methionine at the N-terminus. Moreover,
 30 glycoprotein G can be modified to ablate its antigen binding activity.

In particular embodiments, a recombinant particle comprises henipaviruses F and G viral envelope glycoproteins, wherein glycoprotein G is modified to ablate cell binding activity and both G and F glycoproteins retain the ability to cooperatively mediate cell fusion.

Illustrative examples of henipaviruses suitable for use in particular embodiments from which F and H glycoproteins can independently be isolated from include but are not limited to Cedar virus (CedV; Cedar henipavirus), Kumasi virus (KV; Ghanaian bat henipavirus), Hendra virus (HeV), (MojV; Mojiang henipavirus), and Nipah virus (NiV).

In particular embodiments, one or more mutated henipaviruses envelope glycoproteins are derived from nipah virus F (NiV-F) and nipah virus G (NiV-G). In particular embodiments, a recombinant particle comprises one or more nipah virus viral envelope glycoproteins modified to lack cell binding activity and retain fusogenic activity. In some embodiments, a recombinant particle comprises a modified NiV-F glycoprotein and a NiV-G glycoprotein modified to lack cell binding activity and retain fusogenic activity.

In particular embodiments, one or more mutated henipavirus envelope glycoproteins are derived from a nipah virus F (NiV-F) polypeptide (*e.g.*, SEQ ID NO: 8: LHYEKLKIGLVKGVTRKYKIKSNPLTKDIVIKMIPNVSNMSQCTGSVMENYKTR LNGILTPIKGALEIYKNNTHDLVGDVRLAGVIMAGVAIGIATAAQITAGVALYEA MKNADNINKLKSSIESTNEAVVKLQETAECTVYVLTALQDYINTNLVPTIDKISCK QTELSLDLALSKYLSDLLFVFGPNLQDPVSNSMTIQAISQAFGGNYETLLRTLGYA TEDFDDLLESDSITGQIYVDLSSYYIIVRVYFPILTEIQQAYIQELLPVSFNNDNSEW ISIVPNFILVRNTLISNIEIGFCLITKRSVICNQDYATPMTNNMRECLTGSTEKCPREL VVSSHVPRFALSNGVLFANCISVTCQCQTGRAISQSGEQTLLMIDNTTCPTAVLG NVIISLGKYLGSVNYNSEGIAIGPPVFTDKVDISSQISSMNQSLQQSKDYIKEAQRLLDTVNPSLISMLSMILYVLSIASLCIGLITFISFIIVEKKRNT) or an amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical thereto and a nipah virus G (NiV-G) polypeptide (*e.g.*, SEQ ID NO: 9: MKKINEGLLDKILSAFNTVIALLGSIIVMNIMIIQNYTRSTDNQAVIDALQGIQ QQIKGLADKIGTEIGPKVSLIDTSSTITIPANIGLLGSKISQSTASINENVNEKCKFTL PPLKIHENISCPNPLPFREYRPQTEGVSNLVGLPNNICLQKTSNQILKPKLISYTLF VVGQSGTCITDPLLAMDEGYFAYSHLERIGSCSRGVSKQRIIGVGEVLDRGDEVPS LFMTNVWTPPNPNTVYHCSAVYNNEFYVLCVSTVGPILNSTYWSGLMMT RLAVKPKSNGGGYNQHQLALRSIEKGRYDKVMPYGPSGIKQGDYLYFPAVGFLV RTEFKYNDNSNCPITKCQYSKPENCRLSMGIRPNSHYILRSGLLKYNLSDGENPKVV

FIEISDQRLSIGSPSKIYDSLGGQPVFYQASFSWDTMIKFGDVLTVNPLVVNWRNNT
 VISRPGQSQCPRFNTCPEICWEGVYNDAFLIDRINWISAGVFLDSNQTAE NPVFTV
 FKDNEILYRAQLASEDTNAQKTITNCFLLNKIWCISLVEIYDTGDNVIRPKLFAV
 KIQEQCT) or an amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical
 5 thereto, wherein the NiV-G polypeptide lacks cell binding activity and retains fusogenic
 activity. In particular embodiments, the NiV-G polypeptide comprises one or more amino
 acid substitutions at positions E468, W471, Q497, and E500 of an NiV-G polypeptide (*e.g.*,
 SEQ ID NO: 9). In particular embodiments, the NiV-G polypeptide comprises one or more
 of the amino acid substitutions E468A, W471A, Q497A, and E500A in an NiV-G
 10 polypeptide (*e.g.*, SEQ ID NO: 10:
 MKKINEGLLD SKILSAFNTVIALLGSIIVMNIMIIQNYTRSTDNQA VIKDALQGIQ
 QQIKGLADKIGTEIGPKVSLIDTSSTITIPANIGLLGSKISQSTASINENVNEKCKFTL
 PPLKIH ECNISC PNLPFREYRPQTEGVSNLVGLPNNICLQKTSNQILKPKLISYTLP
 VVGQSGTCITDPLLAMDEGYFAYSHLERIGSCSRGVSKQRIIGVGEVLDRGDEVPS
 15 LFMTNVWTPPNPNTVYHCSAVYNNEFYVLC AVSTVGDPI LNSTYWSGSLMMT
 RLAVKPKSNGGGYNQHQLALRSIEKGRYDKVMPYGPSGIKQGDTLYFPAVGFLV
 RTEFKYND SNCPITKCQYSKPENCRLSMGIRPN SHYILRSGLLKYNLSDGENPKVV
 FIEISDQRLSIGSPSKIYDSLGGQPVFYQASFSWDTMIKFGDVLTVNPLVVNWRNNT
 VISRPGQSQCPRFNTCPAICAEGVYNDAFLIDRINWISAGVFLDSNATAANPVFTV
 20 FKDNEILYRAQLASEDTNAQKTITNCFLLNKIWCISLVEIYDTGDNVIRPKLFAV
 KIQEQCT) or an amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical
 thereto, wherein the NiV-G polypeptide lacks cell binding activity and retains fusogenic
 activity.

3. *TROPISM POLYPEPTIDES*

25 Recombinant particles contemplated herein comprise one or more tropism
 polypeptides that govern particle targeting. Without wishing to be bound by any particular
 theory, it is contemplated that decoupling particle fusion and tropism solves specificity and
 delivery issues associated with *in vivo* gene therapy and gene editing. In particular
 embodiments, recombinant particles comprise one or more viral envelope glycoproteins
 30 modified to retain cell fusion activity and substantially ablate or ablate native tropism activity
 and further comprise one or more non-viral membrane-bound tropism polypeptides to
 support particle targeting. Decoupling particle fusion and tropism activities enables particle

on-target delivery to the intended cells and decreases off-target delivery to other cells thereby increasing the safety and efficacy of the therapy.

In particular embodiments, a recombinant particle contemplated herein comprises an outer surface comprising, expressing, or displaying one or more non-viral membrane bound tropism polypeptides. A “tropism polypeptide” is a polypeptide that binds one or more antigens on a desired cell type. A “non-viral membrane bound tropism polypeptide” is a polypeptide that binds one or more antigens on a desired cell type; that is not native to, or derived from, either in whole or in part, a virus.

In particular embodiments, a recombinant particle comprises an outer surface comprising one or more mutated viral envelope glycoproteins that mediate fusion of the particle with a cell but that do not bind its cognate receptor expressed on a cell, and one or more non-viral membrane-bound tropism polypeptides that direct the particle to bind a specific antigen expressed on a cell, *e.g.*, an immune effector cell. In particular embodiments, a recombinant particle contemplated herein comprises an outer surface comprising, expressing or displaying a primary non-viral membrane bound tropism polypeptide and optionally, a secondary non-viral membrane bound tropism polypeptide.

In particular embodiments, a recombinant particle, *e.g.*, retroviral or lentiviral particle, comprises a lipid bilayer, cell membrane, or viral envelope comprising one or more mutated viral envelope glycoproteins that mediate fusion of the viral particle with a cell but that do not bind its cognate receptor expressed on a cell, and one or more non-viral membrane-bound tropism polypeptides, *e.g.*, a primary and optionally a secondary non-viral membrane bound tropism polypeptide, that direct the particle to bind one or more specific antigens expressed on a cell, *e.g.*, an immune effector cell.

In particular embodiments, a non-viral membrane bound tropism polypeptide comprises an extracellular antigen targeting domain, a spacer polypeptide, a transmembrane domain or GPI anchor, and optionally an intracellular domain. In particular embodiments, a non-viral membrane bound tropism polypeptide comprises an intracellular domain of no more than one, two, three, four, five, six, seven, eight, nine, or ten amino acids.

In particular embodiments, a non-viral membrane bound tropism polypeptide comprises an amino acid sequence set forth in any one of SEQ ID NOs: 455-576.

In particular embodiments, a non-viral membrane bound tropism polypeptide comprises an amino acid sequence set forth in any one of SEQ ID NOs: 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, and 486.

In particular embodiments, a non-viral membrane bound tropism polypeptide comprises an amino acid sequence set forth in any one of SEQ ID NOs: 535, 536, 537, 538, 539, 540, 541, 542, 543, 544, 545, 546, 547, 548, 549, 550, 551, 552, 553, and 554.

In particular embodiments, a non-viral membrane bound tropism polypeptide
5 comprises an amino acid sequence set forth in any one of SEQ ID NOs: 555, 556, 557, 558, 559, 560, 561, and 562.

In particular embodiments, a non-viral membrane bound tropism polypeptide comprises an amino acid sequence set forth in any one of SEQ ID NOs: 563, 564, 565, 566, 567, 568, 569, 570, 571, 572, 573, 574, 575, and 576.

10 In particular embodiments, a non-viral membrane bound tropism polypeptide comprises an amino acid sequence set forth in SEQ ID NO: 471 and SEQ ID NO: 472.

In particular embodiments, a non-viral membrane bound tropism polypeptide comprises an amino acid sequence set forth in SEQ ID NO: 553 and SEQ ID NO: 554.

In particular embodiments, a non-viral membrane bound tropism polypeptide
15 comprises an amino acid sequence set forth in SEQ ID NO: 563 and SEQ ID NO: 564.

a. Extracellular Antigen Targeting Domain

Recombinant particles contemplated in particular embodiments comprise a detargeted fusogen and one or more non-viral membrane bound tropism polypeptides that comprise an extracellular antigen targeting domain that binds one or more antigens
20 specifically or selectively expressed on a particular cell type, *e.g.*, an immune effector cell. As used herein, an “extracellular antigen targeting domain” (also referred to as an “extracellular targeting domain,” “antigen targeting domain,” or “targeting domain”) refers to any naturally occurring, synthetic, semi-synthetic, or recombinantly produced binding partner that binds a biological molecule or target antigen expressed or displayed on the
25 surface of a cell. In particular embodiments, an extracellular antigen targeting domain binds an antigen expressed on a desired or specified cell type. In some embodiments, expression of the antigen is specific to the cell. In preferred embodiments, an extracellular antigen targeting domain binds an antigen expressed on an immune effector cell.

In various embodiments, a non-viral membrane bound tropism polypeptide
30 comprises one or more extracellular targeting domains selected from the group consisting of:

an antibody, a ligand (*e.g.*, cytokines, chemokines, or cell surface associated ligands), a receptor ectodomain (*e.g.*, c-Met, EGFR), or an aptamer.

In particular embodiments, an extracellular antigen targeting domain comprises an antibody or antigen binding fragment thereof that binds an antigen expressed on the surface of a cell, *e.g.*, an immune effector cell. In certain embodiments, an extracellular antigen targeting domain comprises an antibody or antigen binding fragment thereof selected from the group consisting of: a Camel Ig, a Llama Ig, an Alpaca Ig, Ig NAR, a Fab' fragment, a F(ab')₂ fragment, a bispecific Fab dimer (Fab₂), a trispecific Fab trimer (Fab₃), an Fv, a single chain Fv protein (scFv), a bis-scFv, (scFv)₂, a minibody, a diabody, a triabody, a tetrabody, a disulfide stabilized Fv protein (dsFv), a Fibronectin type III (FN3) domain antibody, a single-domain antibody (sdAb or nanobody, *e.g.*, a camelid VHH or shark VNAR), and a centyrin; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain that binds an antigen expressed on an immune effector cell selected from the group consisting of: alpha, beta, gamma, or delta chain of the T-cell receptor, CD1a, CD1b, CD1c, CD2, CD3δ, CD3ε, CD3γ, CD4, CD5, CD6, CD7, CD8α, CD8β, CD11a, CD11b, CD11c, CD25, CD26, CD27, CD28, CD30, CD35, CD37, CD38, CD39, CD43, CD45RO, CD45RA, CD45RB, CD45RAB, CD45RBC, CD45ABC, CD49a, CD49f, CD49d, CD56, CD57, CD62L, CD69, CD70, CD73, CD74, CDw75, CDw76, CD80 (B7-1), CD83, CDw84, CD86 (B7-2), CD89, CD94, CD95, CD96, CD98, CD99, CD100, CDw101, CD102, CD103, CD104, CDw108, CDw121a (IL-1RI), CD122 (IL-2Rβ), CDw124 (IL-4R), CDw127 (IL-7R), CDw128 (IL-8R), CD134, CD137, CD152 (CTLA-4), CD154 (CD40L), CD161, CD183, CD184, CD185, CD193, CD194, CD195, CD196, CD197, CD223 (LAG-3), CD244 (SlamF4), CD270 (TNFRSF14; HVEM), CD272 (BTLA-4), CD273 (PD-L2), CD274 (PD-L1), CD278 (ICOS), CD279, CD300, CD357 (TNFRSF18; GITR), CMRF35, CCR10, IL-2Rγ, IL-10R, IL-12R, IL-13Rα1, P2RX7, Sca-1, SlamF6, TIGIT, TIM-3, TNRF2, and TNFRSF25; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain that binds an antigen expressed on an immune effector cell selected from the group consisting of: the alpha, beta, gamma, or delta

chain of the T cell receptor, CD2, CD3 δ , CD3 ϵ CD3 γ , CD4, CD7, CD8 α , and CD8 β ; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an scFv, a murine scFv, a
 5 humanized scFv, a human scFv, or one or more VHH or VNAR single domain antibodies that binds an antigen expressed on an immune effector cell selected from the group consisting of: the alpha, beta, gamma, or delta chain of the T cell receptor, CD2, CD3 δ , CD3 ϵ CD3 γ , CD4, CD7, CD8 α , and CD8 β ; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

10 In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof. Illustrative examples of anti-CD3 ϵ antibodies or antigen binding fragments thereof suitable for use in particular embodiments contemplated herein include but are not limited to scFvs or other antigen binding fragments isolated from OKT3,
 15 UCHT1, YTH12.5, and TR66, and variants thereof, having at least 75%, at least 80%, at least 85%, at least 90%, at least 95%, or at least 99% identity thereto.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising a CDRH1, a CDRH2, and a CDRH3 and a
 20 CDRL1, a CDRL2, and a CDRL3 of an antibody or antigen binding fragment thereof set forth in Table 5; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or
 25 antigen binding fragment thereof comprising: CDRH1, CDRH2, and CDRH3 amino acid sequences set forth in SEQ ID NOs: 12-14, and CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in SEQ ID NOs: 16-18; CDRH1, CDRH2, and CDRH3 amino acid sequences set forth in SEQ ID NOs: 22-24, and CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in SEQ ID NOs: 26-28; CDRH1, CDRH2, and CDRH3 amino acid
 30 sequences set forth in SEQ ID NOs: 32-34, and CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in SEQ ID NOs: 36-38; CDRH1, CDRH2, and CDRH3 amino acid sequences set forth in SEQ ID NOs: 42-44, and CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in SEQ ID NOs: 46-48; CDRH1, CDRH2, and CDRH3 amino acid

sequences set forth in SEQ ID NOs: 52-54, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 56-58; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 62-64, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 66-68; CDRH1, CDRH2, and CDRH3 amino acid
5 sequences set forth in SEQ ID NOs: 72-74, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 76-78; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 82-84, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 86-88; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 92-94, and CDRL1, CDRL2, and CDRL3 amino acid
10 sequences set forth in SEQ ID NOs: 96-98; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 102-104, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 106-108; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 112-114, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 116-118; CDRH1, CDRH2, and CDRH3 amino acid
15 sequences set forth in SEQ ID NOs: 122-124, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 126-128; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 132-134, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 136-138; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 142-144, and CDRL1, CDRL2, and CDRL3 amino acid
20 sequences set forth in SEQ ID NOs: 146-148; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 152-154, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 156-158; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 162-164, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 166-168; CDRH1, CDRH2, and CDRH3 amino acid
25 sequences set forth in SEQ ID NOs: 172-174, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 176-178; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 182-184, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 186-188; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 192-194, and CDRL1, CDRL2, and CDRL3 amino acid
30 sequences set forth in SEQ ID NOs: 196-198; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 202-204, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 206-208; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 212-214, and CDRL1, CDRL2, and CDRL3 amino acid

sequences set forth in SEQ ID NOs: 216-218; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 222-224, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 226-228; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 232-234, and CDRL1, CDRL2, and CDRL3 amino acid
5 sequences set forth in SEQ ID NOs: 236-238; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 242-244, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 246-248; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 252-254, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 256-258; CDRH1, CDRH2, and CDRH3 amino acid
10 sequences set forth in SEQ ID NOs: 262-264, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 266-268; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 272-274, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 276-278; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 282-284, and CDRL1, CDRL2, and CDRL3 amino acid
15 sequences set forth in SEQ ID NOs: 286-288; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 292-294, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 296-298; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 302-304, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 306-308; CDRH1, CDRH2, and CDRH3 amino acid
20 sequences set forth in SEQ ID NOs: 312-314, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 316-318; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 322-324, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 326-328; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 332-334, and CDRL1, CDRL2, and CDRL3 amino acid
25 sequences set forth in SEQ ID NOs: 336-338; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 342-344, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 346-348; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 352-354, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 356-358; CDRH1, CDRH2, and CDRH3 amino acid
30 sequences set forth in SEQ ID NOs: 362-364, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 366-368; CDRH1, CDRH2, and CDRH3 amino acid
sequences set forth in SEQ ID NOs: 372-374, and CDRL1, CDRL2, and CDRL3 amino acid
sequences set forth in SEQ ID NOs: 376-378; CDRH1, CDRH2, and CDRH3 amino acid

sequences set forth in SEQ ID NOs: 382-384, and CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in SEQ ID NOs: 386-388; CDRH1, CDRH2, and CDRH3 amino acid sequences set forth in SEQ ID NOs: 392-394, and CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in SEQ ID NOs: 396-398; or CDRH1, CDRH2, and CDRH3 amino acid sequences set forth in SEQ ID NOs: 402-404, and CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in SEQ ID NOs: 406-408; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising CDRH1, CDRH2, and CDRH3 amino acid sequences set forth in SEQ ID NOs: 92-94, and CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in SEQ ID NOs: 96-98; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising CDRH1, CDRH2, and CDRH3 amino acid sequences set forth in SEQ ID NOs: 102-104, and CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in SEQ ID NOs: 106-108; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising CDRH1, CDRH2, and CDRH3 amino acid sequences set forth in SEQ ID NOs: 112-114, and CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in SEQ ID NOs: 116-118; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising CDRH1, CDRH2, and CDRH3 amino acid sequences set forth in SEQ ID NOs: 122-124, and CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in SEQ ID NOs: 126-128; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or

antigen binding fragment thereof comprising CDRH1, CDRH2, and CDRH3 amino acid sequences set forth in SEQ ID NOs: 132-134, and CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in SEQ ID NOs: 136-138; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

5 In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising CDRH1, CDRH2, and CDRH3 amino acid sequences set forth in SEQ ID NOs: 142-144, and CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in SEQ ID NOs: 146-148; a spacer polypeptide; a transmembrane domain
10 or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising CDRH1, CDRH2, and CDRH3 amino acid sequences set forth in SEQ ID NOs: 152-154, and CDRL1, CDRL2, and CDRL3 amino acid
15 sequences set forth in SEQ ID NOs: 156-158; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising CDRH1, CDRH2, and CDRH3 amino acid
20 sequences set forth in SEQ ID NOs: 162-164, and CDRL1, CDRL2, and CDRL3 amino acid sequences set forth in SEQ ID NOs: 166-168; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or
25 antigen binding fragment thereof comprising a heavy chain variable (VH) domain and a light chain variable (VL) domain of an antibody or antigen binding fragment thereof set forth in Table 5; a polypeptide linker disposed between the VH domain and the VL domain; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain. In particular embodiments the polypeptide linker is selected from the group consisting of:
30 (GGGGS)_n wherein n = 1, 2, 3, 4 or 5; S(GGGGS)_n wherein n = 1, 2, 3, 4 or 5; GEGTSTGSGGSGGSGGAD, GSTSGSGKPGSGEGSTKG and variants thereof comprising an amino acid sequence at least 90% identical thereto.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising: a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 11 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 15; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 21 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 25; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 31 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 35; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 41 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 45; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 51 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 55; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 61 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 65; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 71 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 75; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 81 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 85; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 91 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 95; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 101 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 105; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 111 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 115; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 121 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 125; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 131 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 135; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 141 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 145; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 151 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 155; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 161 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 165; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 171 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 175; a VH domain comprising

[illegible]

and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 365; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 371 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 375; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 381 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 385; a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 391 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 395; or a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 401 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 405; a polypeptide linker disposed between the VH domain and the VL domain; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain. In particular embodiments the polypeptide linker is selected from the group consisting of: (GGGGS)_n wherein n = 1, 2, 3, 4 or 5; S(GGGGS)_n wherein n = 1, 2, 3, 4 or 5; GEGTSTGSGSGSGSGAD, GSTSGSGKPGSGEGSTKG and variants thereof comprising an amino acid sequence at least 90% identical thereto.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising: a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 91 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 95; a polypeptide linker disposed between the VH domain and the VL domain; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising: a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 101 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 105; a polypeptide linker disposed between the VH domain and the VL domain; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising: a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 111 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 115; a polypeptide linker disposed between the VH domain and the

VL domain; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising: a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 121 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 125; a polypeptide linker disposed between the VH domain and the VL domain; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

10 In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising: a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 131 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 135; a polypeptide linker disposed between the VH domain and the VL domain; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising: a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 141 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 145; a polypeptide linker disposed between the VH domain and the VL domain; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

25 In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising: a VH domain comprising an amino acid sequence set forth in SEQ ID NO: 151 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 155; a polypeptide linker disposed between the VH domain and the VL domain; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising: or a VH domain comprising an amino acid

sequence set forth in SEQ ID NO: 161 and a VL domain comprising an amino acid sequence set forth in SEQ ID NO: 165; a polypeptide linker disposed between the VH domain and the VL domain; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

5 In particular embodiments the polypeptide linker is selected from the group consisting of: (GGGGS)_n wherein n = 1, 2, 3, 4 or 5; S(GGGGS)_n wherein n = 1, 2, 3, 4 or 5; GEGTSTGSGGSGGSGGAD, GSTSGSGKPGSGEGSTKG and variants thereof comprising an amino acid sequence at least 90% identical thereto.

10 In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof set forth in Table 5; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising the amino acid sequence set forth in any one of
15 SEQ ID NOs: 19, 20, 29, 30, 39, 40, 49, 50, 59, 60, 69, 70, 79, 80, 89, 90, 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, 170, 179, 180, 189, 190, 199, 200, 209, 210, 219, 220, 229, 230, 239, 240, 249, 250, 259, 260, 269, 270, 279, 280, 289, 290, 299, 300, 309, 310, 319, 320, 329, 330, 339, 340, 349, 350, 359, 360, 369, 370, 379, 380,
20 389, 390, 399, 400, 409, and 410; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 79. In particular embodiments, a non-viral membrane-bound tropism
25 polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 80. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 89. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain
30 comprising the amino acid sequence set forth in SEQ ID NO: 90. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 99. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an

extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 100. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 109. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 110. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 119. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 120. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 129. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 130. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 139. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 140. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 149. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 150. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 159. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 160. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 169. In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising the amino acid sequence set forth in SEQ ID NO: 170.

Table 5

Ab ID	SEQ ID NO	ID	AMINO ACID SEQUENCE
CD3.1	11	VH	QVQLLESQAEELARPGASVKMSCKASGYTFTRYTMHWVKQRPQGQ LEWIGYINPSRGYTNYNQKFKDKATLTDDKSSSTAYMQLSSLTS EDSAVYYCAGYYDDHYCLDYWGQGTTLTVSS
	12	CDRH1	RYTMH
	13	CDRH2	YINPSRGYTNYNQKFKD
	14	CDRH3	YYDDHYCLDY
	15	VL	DIVMTQSPAIMASASPGEKVTMTCSASSSVSYMNWYQQKSGTSPK RWIYDTSKLAGVPAHFRGSGSGTSYSLTISGMEAEADAATYYCQ QWSSNPFTFGSGGTKLEIK
	16	CDRL1	SASSSVSYMN
	17	CDRL2	DTSKLAG
	18	CDRL3	QQWSSNPFT
	19	scFv	QVQLLESQAEELARPGASVKMSCKASGYTFTRYTMHWVKQRPQGQ LEWIGYINPSRGYTNYNQKFKDKATLTDDKSSSTAYMQLSSLTS EDSAVYYCAGYYDDHYCLDYWGQGTTLTVSSGGGGSGGGSGGG GSDIVMTQSPAIMASASPGEKVTMTCSASSSVSYMNWYQQKSGTS PKRWIYDTSKLAGVPAHFRGSGSGTSYSLTISGMEAEADAATYY CQQWSSNPFTFGSGGTKLEIKS
	20	scFv	DIVMTQSPAIMASASPGEKVTMTCSASSSVSYMNWYQQKSGTSPK RWIYDTSKLAGVPAHFRGSGSGTSYSLTISGMEAEADAATYYCQ QWSSNPFTFGSGGTKLEIKGGGGSGGGSGGGSGGGSGVQLLESQAE ELARPGASVKMSCKASGYTFTRYTMHWVKQRPQGQLEWIGYINPSR GYTNYNQKFKDKATLTDDKSSSTAYMQLSSLTSEDSAVYYCAGY YDDHYCLDYWGQGTTLTVSS
CD3.2	21	VH	QVQLQQSGAEELARPGASVKMSCKASGYTFTRYTMHWVKQRPQGQ LEWIGYINPSRGYTNYNQKFKDKATLTDDKSSSTAYMQLSSLTS EDSAVYYCARYYDDHYCLDYWGQGTTLTVSSS
	22	CDRH1	RYTMH
	23	CDRH2	YINPSRGYTNYNQKFKD
	24	CDRH3	YYDDHYCLDY
	25	VL	QIVLTQSPAIMASASPGEKVTMTCSASSSVSYMNWYQQKSGTSPK RWIYDTSKLAGVPAHFRGSGSGTSYSLTISGMEAEADAATYYCQ QWSSNPFTFGSGGTKLEIN
	26	CDRL1	SASSSVSYMN
	27	CDRL2	DTSKLAG
	28	CDRL3	QQWSSNPFT
	29	scFv	QVQLQQSGAEELARPGASVKMSCKASGYTFTRYTMHWVKQRPQGQ LEWIGYINPSRGYTNYNQKFKDKATLTDDKSSSTAYMQLSSLTS EDSAVYYCARYYDDHYCLDYWGQGTTLTVSSSGGGSGGGSGGG GGSQIVLTQSPAIMASASPGEKVTMTCSASSSVSYMNWYQQKSGT SPKRWIYDTSKLAGVPAHFRGSGSGTSYSLTISGMEAEADAATY YCQQWSSNPFTFGSGGTKLEIN
	30	scFv	QIVLTQSPAIMASASPGEKVTMTCSASSSVSYMNWYQQKSGTSPK RWIYDTSKLAGVPAHFRGSGSGTSYSLTISGMEAEADAATYYCQ QWSSNPFTFGSGGTKLEINGGGSGGGSGGGSGGGSGVQLQQSGAE ELARPGASVKMSCKASGYTFTRYTMHWVKQRPQGQLEWIGYINPSR GYTNYNQKFKDKATLTDDKSSSTAYMQLSSLTSEDSAVYYCARY YDDHYCLDYWGQGTTLTVSSS
CD3.3	31	VH	QVQLQQSGAEELARPGASVKMSCKASGYTFTSYTMHWVKQRPQGQ LEWIGYINPSSGYTKYNQKFKDKATLTADKSSSTAYMQLSSLTS EDSAVYYCARWQDYDVYFDYWGQGTTLTVSS
	32	CDRH1	SYTMH
	33	CDRH2	YINPSSGYTKYNQKFKD
	34	CDRH3	WQDYDVYFDY
	35	VL	QIVLSQSPAILASASPGEKVTMTCRASSSVSYMHWYQQKPGSSPK PWIYATSNLAGVPAHFRGSGSGTSYSLTISRVEAEADAATYYCQ

			QWSSNPPTFGGGTKLETK
	36	CDRL1	RASSSVSYMH
	37	CDRL2	ATSNLAS
	38	CDRL3	QQWSSNPPT
	39	scFv	QVQLQQSGAELARPGASVKMSCKASGYTFTSYTMHWVKQRPGQG LEWIGYINPSSGYTKYNQKFKDKATLTADKSSSTAYMQLSSLTS EDSAVYYCARWQDYDVFYDWGQGTTLTVSSGGGGSGGGSGGG GSQIVLSQSPAILSASPGEKVTMTCRASSSVSYMHWYQQKPGSS PKPWIYATSNLASGVPARFSGSGSGTSYSLTISRVEAEDAATYY CQQWSSNPPTFGGGTKLETK
	40	scFv	QIVLSQSPAILSASPGEKVTMTCRASSSVSYMHWYQQKPGSSPK PWIYATSNLASGVPARFSGSGSGTSYSLTISRVEAEDAATYYCQ QWSSNPPTFGGGTKLETKGGGGSGGGSGGGGSQVQLQQSGAELA RPGASVKMSCKASGYTFTSYTMHWVKQRPGQGLEWIGYINPSSG YTKYNQKFKDKATLTADKSSSTAYMQLSSLTSEDSAVYYCARWQ DYDVFYDWGQGTTLTVSS
CD3.4	41	VH	EVQLQQSGPELVKPGASMKISCKASGYSTGYTMNWVKQSHGKN LEWMGLINPYKGVSTYNQKFKDKATLTVDKSSSTAYMELLSSLTS EDSAVYYCARSGYYGDSWYFDVWGAGTTVTVSS
	42	CDRH1	GYTMN
	43	CDRH2	LINPYKGVSTYNQKFKD
	44	CDRH3	SGYYGDSWYFDV
	45	VL	DIQMTQTSSLSASLGDRVTISCRASQDIRNYLNWYQQKPDGTV KLLIYYTSRLHSGVPSKFSGSGSGTDYSLTISNLEQEDIATYFC QQGNTLPWTFAGGTKLEIK
	46	CDRL1	RASQDIRNYLN
	47	CDRL2	YTSRLHS
	48	CDRL3	QQGNTLPWT
	49	scFv	EVQLQQSGPELVKPGASMKISCKASGYSTGYTMNWVKQSHGKN LEWMGLINPYKGVSTYNQKFKDKATLTVDKSSSTAYMELLSSLTS EDSAVYYCARSGYYGDSWYFDVWGAGTTVTVSSGGGGSGGGGS GGGSDIQMTQTSSLSASLGDRVTISCRASQDIRNYLNWYQQK PDGTVKLLIYYTSRLHSGVPSKFSGSGSGTDYSLTISNLEQEDI ATYFCQQGNTLPWTFAGGTKLEIK
	50	scFv	DIQMTQTSSLSASLGDRVTISCRASQDIRNYLNWYQQKPDGTV KLLIYYTSRLHSGVPSKFSGSGSGTDYSLTISNLEQEDIATYFC QQGNTLPWTFAGGTKLEIKGGGGSGGGSGGGGSEVQLQQSGPE LVKPGASMKISCKASGYSTGYTMNWVKQSHGKNLEWMGLINPY KGVSTYNQKFKDKATLTVDKSSSTAYMELLSSLTSEDSAVYYCAR SGYYGDSWYFDVWGAGTTVTVSS
CD3.5	51	VH	QVQLQQSAAELARPGASVKMSCKASGYTFTTRYTMQWVKQRPGQG LEWIGYINPSSGYIGYSQKFKDKTTLTADKSSSTAYMQLSSLTS EDSAVYYCARSKVYYDYDVYSMDYWGQGTSTVTVSS
	52	CDRH1	RYTMQ
	53	CDRH2	YINPSSGYIGYSQKFKD
	54	CDRH3	SKVYYDYDVYSMDY
	55	VL	QIILTQSPAIMASASPGEKVTMTCSASSSVSYMHWYQQKSGTSPK RWIYDTSKLASGVPARFSGSGSGTSYSLTISSMEAEDAATYYCQ QWSSNPPLTFGAGTKLELK
	56	CDRL1	SASSSVSYMH
	57	CDRL2	DTSKLA
	58	CDRL3	QQWSSNPPLT
	59	scFv	QVQLQQSAAELARPGASVKMSCKASGYTFTTRYTMQWVKQRPGQG LEWIGYINPSSGYIGYSQKFKDKTTLTADKSSSTAYMQLSSLTS EDSAVYYCARSKVYYDYDVYSMDYWGQGTSTVTVSSGGGGSGGGG SGGGGSIILTQSPAIMASASPGEKVTMTCSASSSVSYMHWYQQK SGTSPKRWIYDTSKLASGVPARFSGSGSGTSYSLTISSMEAEDA ATYYCQQWSSNPPLTFGAGTKLELK

	60	scFv	QIILTQSPAIMASASPGEKVTMTCSASSSVSYMHWYQQKSGTSPK RWIYDTSKLAGVVPARFSGSGSGTSYSLTISSMEAEDAATYYCQ QWSSNPLTFGAGTKLELKGGGSGGGGSGGGGSGVQLQQSAAEL ARPGASVKMSCKASGYTFTRYTMQWVKQRPQGQLEWIGYINPSS GYIGYSQKFQDKTTLTADKSSSTAYMQLSSLTSEDSAVYYCARS KVVYDYDVSMDYWGQGTSTVTVSS
CD3.6	61	VH	QVQLQQSGAELARPGASVKMSCKASGYTFISYTMHWVKQRPQGQ LEWIGYINPRSGYTHYNQKLKDKATLTADKSSSSAYMQLSSLTS EDSAVYYCARSAYYDYGFAIWGQGTTLVTVSA
	62	CDRH1	SYTMH
	63	CDRH2	YINPRSGYTHYNQKLKD
	64	CDRH3	SAYYDYDGFAY
	65	VL	QIVLTQSPAIMASASPGEKVTMTCSASSSVSYMNWYKQKSGTSPK RWTYDTSKLAGVVPARFSGSGSGTSYSLTISSMEAEDAATYYCQ QWSSNPPTFGSGTKLEIK
	66	CDRL1	SASSSVSYMN
	67	CDRL2	DTSKLAS
	68	CDRL3	QQWSSNPPT
	69	scFv	QVQLQQSGAELARPGASVKMSCKASGYTFISYTMHWVKQRPQGQ LEWIGYINPRSGYTHYNQKLKDKATLTADKSSSSAYMQLSSLTS EDSAVYYCARSAYYDYGFAIWGQGTTLVTVSAGGGGSGGGGSGG GGSQIVLTQSPAIMASASPGEKVTMTCSASSSVSYMNWYKQKSGT SPKRWTYDTSKLAGVVPARFSGSGSGTSYSLTISSMEAEDAATY YCQQWSSNPPTFGSGTKLEIK
	70	scFv	QIVLTQSPAIMASASPGEKVTMTCSASSSVSYMNWYKQKSGTSPK RWTYDTSKLAGVVPARFSGSGSGTSYSLTISSMEAEDAATYYCQ QWSSNPPTFGSGTKLEIKGGGSGGGGSGGGGSGVQLQQSGAEL ARPGASVKMSCKASGYTFISYTMHWVKQRPQGQLEWIGYINPRS GYTHYNQKLKDKATLTADKSSSSAYMQLSSLTSEDSAVYYCARS AYYDYDGFAYWGQGTTLVTVSA
CD3.7	71	VH	QVQLVQSGAEVKKPGASVKVCKASGYTFISYTMHWVRQAPGQG LEWMGYINPRSGYTHYNQKLKDKATLTADKSASTAYMELSSLRS EDTAVYYCARSAYYDYGFAIWGQGTTLVTVSS
	72	CDRH1	SYTMH
	73	CDRH2	YINPRSGYTHYNQKLKD
	74	CDRH3	SAYYDYDGFAY
	75	VL	DIQMTQSPSSLSASVGDRTITCSASSSVSYMNWYQQKPKGAPK RLIYDTSKLAGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQ QWSSNPPTFGGGTKVEIK
	76	CDRL1	SASSSVSYMN
	77	CDRL2	DTSKLAS
	78	CDRL3	QQWSSNPPT
	79	scFv	QVQLVQSGAEVKKPGASVKVCKASGYTFISYTMHWVRQAPGQG LEWMGYINPRSGYTHYNQKLKDKATLTADKSASTAYMELSSLRS EDTAVYYCARSAYYDYGFAIWGQGTTLVTVSSGGGGSGGGGSGG GGSDIQMTQSPSSLSASVGDRTITCSASSSVSYMNWYQQKPKG APKRLIYDTSKLAGVPSRFSGSGSGTDFTLTISLQPEDFATY YCQQWSSNPPTFGGGTKVEIK
	80	scFv	DIQMTQSPSSLSASVGDRTITCSASSSVSYMNWYQQKPKGAPK RLIYDTSKLAGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQ QWSSNPPTFGGGTKVEIKGGGSGGGGSGGGGSGVQLVQSGAEV KKPGASVKVCKASGYTFISYTMHWVRQAPGQGLEWMGYINPRS GYTHYNQKLKDKATLTADKSASTAYMELSSLRSEDATVYYCARS AYYDYDGFAYWGQGTTLVTVSS
CD3.8	81	VH	EVQLVESGGGLVQPKGSLKLSCAASGFTFTNTYAMNWVRQAPGKG LEWVARIRSKYNNYATYYADSVKDRFTISRDDSQSILYLQMNLL KTEDTAMYYCVRHGNFGNSYVSWFAYWGQGTTLVTVSS
	82	CDRH1	TYAMN

	83	CDRH2	RIRSKYNNYATYYADSVKD
	84	CDRH3	HGNFGNSYVSWFAY
	85	VL	QAVVTQESALTTSPGETVTLTCRSSTGAVTTSNYANWVQEKPDH LFTGLIGGTNKRAPGVPARFSGSLIGDKAALTITGAQTEDEAIY FCALWYSNLWVFGGGTKLTVL
	86	CDRL1	RSSTGAVTTSNYAN
	87	CDRL2	GTNKRAP
	88	CDRL3	ALWYSNLWV
	89	scFv	EVQLVESGGGLVQPKGSLKLSCAASGFTFNTYAMNWVRQAPGKG LEWVARIRSKYNNYATYYADSVKDRFTISRDDSQSILYLQMNNL KTEDTAMYCYVRHGNFGNSYVSWFAYWGQGTTLTVSS GGGGSGGGSGGGGSQAVVTQESALTTSPGETVTLTCRSSTGAV TTSNYANWVQEKPDHFTGLIGGTNKRAPGVPARFSGSLIGDKA ALTITGAQTEDEAIYFCALWYSNLWVFGGGTKLTVL
	90	scFv	QAVVTQESALTTSPGETVTLTCRSSTGAVTTSNYANWVQEKPDH LFTGLIGGTNKRAPGVPARFSGSLIGDKAALTITGAQTEDEAIY FCALWYSNLWVFGGGTKLTVLGGGGSGGGSGGGGSEVQLVESG GGLVQPKGSLKLSCAASGFTFNTYAMNWVRQAPGKGLEWVARIR SKYNNYATYYADSVKDRFTISRDDSQSILYLQMNNLKTEDTAMY YCYVRHGNFGNSYVSWFAYWGQGTTLTVSS
	91	VH	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQG LEWIGYINPSRGYTNADSVKGRFTITTDKSTSTAYMELSSLRS EDTATYYCARYYDDHYCLDYWGQGTTLTVSS
	92	CDRH1	RYTMH
CD3.9	93	CDRH2	YINPSRGYTNADSVKG
	94	CDRH3	YYDDHYCLDY
	95	VL	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPKAPK RWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQ QWSSNPLTFGGGKVEIK
	96	CDRL1	RASQSVSYMN
	97	CDRL2	DTSKVAS
	98	CDRL3	QQWSSNPLT
	99	scFv	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQG LEWIGYINPSRGYTNADSVKGRFTITTDKSTSTAYMELSSLRS EDTATYYCARYYDDHYCLDYWGQGTTLTVSSSGGGSGGGSGGG GGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPKG APKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATY YCQWSSNPLTFGGGKVEIK
	100	scFv	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPKAPK RWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQ QWSSNPLTFGGGKVEIKSGGGSGGGSGGGGSDVQLVQSGAE VKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPS RGYTNADSVKGRFTITTDKSTSTAYMELSSLRSEDATYYCAR YYDDHYCLDYWGQGTTLTVSS
	101	VH	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQG LEWIGYINPSRGYTNADSVKGRFTITTDKSTSTAYMELSSLRS EDTATYYCARYYDDPYCLDYWGQGTTLTVSS
	102	CDRH1	RYTMH
CD3.10	103	CDRH2	YINPSRGYTNADSVKG
	104	CDRH3	YYDDPYCLDY
	105	VL	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPKAPK RWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQ QWSSNPLTFGGGKVEIK
	106	CDRL1	RASQSVSYMN
	107	CDRL2	DTSKVAS
	108	CDRL3	QQWSSNPLT
	109	scFv	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQG LEWIGYINPSRGYTNADSVKGRFTITTDKSTSTAYMELSSLRS

			EDTATYYCARYYDDPYCLDYWGQGTTVTVSSSSGGGGSGGGSGG GGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGK APKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATY YCQQWSSNPLTFGGGKVEIK
	110	scFv	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPK RWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQ QWSSNPLTFGGGKVEIKSGGGSGGGSGGGSDVQLVQSGAE VKKPGASVKVCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPS RGYTNYADSVKGRFTITTDKSTSTAYMELSSLRSEDATYYCAR YYDDPYCLDYWGQGTTVTVSS
CD3.11	111	VH	DVQLVQSGAEVKKPGASVKVCKASGYTFTRYTMHWVRQAPGQG LEWIGYINPSRGYTNYADSVKGRFTITTDKSTSTAYMELSSLR EDTATYYCARYYNDQYCLDYWGQGTTVTVSS
	112	CDRH1	RYTMH
	113	CDRH2	YINPSRGYTNYADSVKG
	114	CDRH3	YYNDQYCLDY
	115	VL	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPK RWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQ QWSSNPLTFGGGKVEIK
	116	CDRL1	RASQSVSYMN
	117	CDRL2	DTSKVAS
	118	CDRL3	QQWSSNPLT
	119	scFv	DVQLVQSGAEVKKPGASVKVCKASGYTFTRYTMHWVRQAPGQG LEWIGYINPSRGYTNYADSVKGRFTITTDKSTSTAYMELSSLR EDTATYYCARYYNDQYCLDYWGQGTTVTVSSSSGGGGSGGGSGG GGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPG KAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAAT YYCQQWSSNPLTFGGGKVEIK
	120	scFv	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPK RWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQ QWSSNPLTFGGGKVEIKSGGGSGGGSGGGSDVQLVQSGAE VKKPGASVKVCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPS RGYTNYADSVKGRFTITTDKSTSTAYMELSSLRSEDATYYCAR YYNDQYCLDYWGQGTTVTVSS
CD3.12	121	VH	DVQLVQSGAEVKKPGASVKVCKASGYTFTRYTMHWVRQAPGQG LEWIGYINPSRGYTNYADSVKGRFTITTDKSTSTAYMELSSLR EDTATYYCARYYDAHNCLDYWGQGTTVTVSS
	122	CDRH1	RYTMH
	123	CDRH2	YINPSRGYTNYADSVKG
	124	CDRH3	YYDAHNCLDY
	125	VL	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPK RWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQ QWSSNPLTFGGGKVEIK
	126	CDRL1	RASQSVSYMN
	127	CDRL2	DTSKVAS
	128	CDRL3	QQWSSNPLT
	129	scFv	DVQLVQSGAEVKKPGASVKVCKASGYTFTRYTMHWVRQAPGQG LEWIGYINPSRGYTNYADSVKGRFTITTDKSTSTAYMELSSLR EDTATYYCARYYDAHNCLDYWGQGTTVTVSSSSGGGGSGGGSGG GGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGK APKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATY YCQQWSSNPLTFGGGKVEIK
	130	scFv	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPK RWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQ QWSSNPLTFGGGKVEIKSGGGSGGGSGGGSDVQLVQSGAE VKKPGASVKVCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPS RGYTNYADSVKGRFTITTDKSTSTAYMELSSLRSEDATYYCAR YYDAHNCLDYWGQGTTVTVSS

CD3.13	131	VH	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQG LEWIGYINPSRGYTNADSVKGRFTITTDKSTSTAYMELSSLRS EDTATYYCARYSDDHYCLDYWGQGT'TVTVSS
	132	CDRH1	RYTMH
	133	CDRH2	YINPSRGYTNADSVKG
	134	CDRH3	YSDDHYCLDY
	135	VL	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPKAPK RWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQ QWSSNPLTFGGGKVEIK
	136	CDRL1	RASQSVSYMN
	137	CDRL2	DTSKVAS
	138	CDRL3	QQWSSNPLT
	139	scFv	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQG LEWIGYINPSRGYTNADSVKGRFTITTDKSTSTAYMELSSLRS EDTATYYCARYSDDHYCLDYWGQGT'TVTVSSSSGGGGSGGGSGG GGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPKG APKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATY YCQQWSSNPLTFGGGKVEIK
CD3.14	140	scFv	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPKAPK RWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQ QWSSNPLTFGGGKVEIKSGGGSGGGSGGGSDVQLVQSGAE VKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPS RGYTNADSVKGRFTITTDKSTSTAYMELSSLRSEDATYYCAR YSDDHYCLDYWGQGT'TVTVSS
	141	VH	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQG LEWIGYINPSRGYTNADSVKGRFTITTDKSTSTAYMELSSLRS EDTATYYCARYSDDRYCLDYWGQGT'TVTVSS
	142	CDRH1	RYTMH
	143	CDRH2	YINPSRGYTNADSVKG
	144	CDRH3	YSDDRYCLDY
	145	VL	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPKAPK RWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQ QWSSNPLTFGGGKVEIK
	146	CDRL1	RASQSVSYMN
	147	CDRL2	DTSKVAS
	148	CDRL3	QQWSSNPLT
CD3.15	149	scFv	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQG LEWIGYINPSRGYTNADSVKGRFTITTDKSTSTAYMELSSLRS EDTATYYCARYSDDRYCLDYWGQGT'TVTVSSSSGGGGSGGGSGG GGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPKG APKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATY YCQQWSSNPLTFGGGKVEIK
	150	scFv	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPKAPK RWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQ QWSSNPLTFGGGKVEIKSGGGSGGGSGGGSDVQLVQSGAE VKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPS RGYTNADSVKGRFTITTDKSTSTAYMELSSLRSEDATYYCAR YSDDRYCLDYWGQGT'TVTVSS
	151	VH	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQG LEWIGYINPSRGYTNADSVKGRFTITTDKSTSTAYMELSSLRS EDTATYYCARYDDNYCLDYWGQGT'TVTVSSS
	152	CDRH1	RYTMH
	153	CDRH2	YINPSRGYTNADSVKG
	154	CDRH3	YYDDNYCLDY
	155	VL	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPKAPK RWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQ QWSSNPLTFGGGKVEIK
	156	CDRL1	RASQSVSYMN

	157	CDRL2	DTSKVAS
	158	CDRL3	QQWSSNPLT
	159	scFv	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQG LEWIGYINPSRGYTNADSVKGRFTITTDKSTSTAYMELSSLRS EDTATYYCARYYDDNYCLDYWGQGTFTVTVSSSSGGGGSGGGSGG GGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPG KAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAAT YYCQQWSSNPLTFGGGKVEIK
	160	scFv	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPK RWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQ QWSSNPLTFGGGKVEIKSGGGSGGGSGGGSGGGSDVQLVQSGAE VKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPS RGYTNADSVKGRFTITTDKSTSTAYMELSSLRSEDATYYCAR YYDDNYCLDYWGQGTFTVTVSS
	161	VH	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQG LEWIGYINPSRGYTNADSVKGRFTITTDKSTSTAYMELSSLRS EDTATYYCARYYDDQYCLDYWGQGTFTVTVSS
	162	CDRH1	RYTMH
	163	CDRH2	YINPSRGYTNADSVKG
	164	CDRH3	YYDDQYCLDY
	165	VL	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPK RWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQ QWSSNPLTFGGGKVEIK
	166	CDRL1	RASQSVSYMN
CD3.16	167	CDRL2	DTSKVAS
	168	CDRL3	QQWSSNPLT
	169	scFv	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQG LEWIGYINPSRGYTNADSVKGRFTITTDKSTSTAYMELSSLRS EDTATYYCARYYDDQYCLDYWGQGTFTVTVSSSSGGGGSGGGSGG GGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGK APKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATY YCQQWSSNPLTFGGGKVEIK
	170	scFv	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPK RWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQ QWSSNPLTFGGGKVEIKSGGGSGGGSGGGSGGGSDVQLVQSGAE VKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPS RGYTNADSVKGRFTITTDKSTSTAYMELSSLRSEDATYYCAR YYDDQYCLDYWGQGTFTVTVSS
	171	VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSFPMWVRQAPGKG LEWVSTISTSGGRYYRDSVKGRFTISRDN SKNTLYLQMNSLRA EDTAVYYCAKFRQYSGGFDYWGQGTTLTVSS
	172	CDRH1	SFPMA
	173	CDRH2	TISTSGGRYYRDSVKG
	174	CDRH3	FRQYSGGFDY
	175	VL	DIQLTQPNVSVTSLGSTVKLSCTLSSGNIENNYVHWYQLYEGRS PTTMIYDDDKRPDGVDPDRFSGSIDRSSNSAFLTIHNVAIEDEAI YFCHSYVSSFNVFGGKTLTVL
	176	CDRL1	TLSSGNIENNYVH
CD3.17	177	CDRL2	DDDKRPD
	178	CDRL3	HSYVSSFNV
	179	scFv	EVQLLESGGGLVQPGGSLRLSCAASGFTFSFPMWVRQAPGKG LEWVSTISTSGGRYYRDSVKGRFTISRDN SKNTLYLQMNSLRA EDTAVYYCAKFRQYSGGFDYWGQGTTLTVTVSSGGGGSGGGSGGG GSDIQLTQPNVSVTSLGSTVKLSCTLSSGNIENNYVHWYQLYEG RSPTTMIYDDDKRPDGVDPDRFSGSIDRSSNSAFLTIHNVAIEDE AIYFCHSYVSSFNVFGGKTLTVL
	180	scFv	DIQLTQPNVSVTSLGSTVKLSCTLSSGNIENNYVHWYQLYEGRS PTTMIYDDDKRPDGVDPDRFSGSIDRSSNSAFLTIHNVAIEDEAI

			YFCHSYVSSFNVFGGGTKLTVLGGGGSGGGSGGGGSEVQLLES GGGLVQPGGSLRLSCAASGFTTFSSFPMAWVRQAPGKGLEWVSTI STSGGRYYRDSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYY CAKFRQYSGGFDYWGGQGTTLTVSS
CD3.18	181	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTTFSTYAMNWVRQAPGKG LEWVSRIRSKYNNYATYYADSVKDRFTISRDDSKNTLYLQMNSL RAEDTAVYYCARHGNFGNSYVSWFAYWGQGTMTVTVSS
	182	CDRH1	TYAMN
	183	CDRH2	RIRSKYNNYATYYADSVKD
	184	CDRH3	HGNFGNSYVSWFAY
	185	VL	QAVVTQEPSTLVSPGGTVTLTCSRSTGAVTTSNYANWVQOKPGQ APRGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGVQPEDEAEY YCALWYSNLWVFGGGTKLTVL
	186	CDRL1	RSSTGAVTTSNYAN
	187	CDRL2	GTNKRAP
	188	CDRL3	ALWYSNLWV
	189	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTTFSTYAMNWVRQAPGKG LEWVSRIRSKYNNYATYYADSVKDRFTISRDDSKNTLYLQMNSL RAEDTAVYYCARHGNFGNSYVSWFAYWGQGTMTVTVSSGGGGSGG GGSGGGGQAVVTQEPSTLVSPGGTVTLTCSRSTGAVTTSNYAN WVQOKPGQAPRGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGV QPEDEAEYYCALWYSNLWVFGGGTKLTVL
	190	scFv	QAVVTQEPSTLVSPGGTVTLTCSRSTGAVTTSNYANWVQOKPGQ APRGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGVQPEDEAEY YCALWYSNLWVFGGGTKLTVLGGGGSGGGSGGGGSEVQLVESG GGLVQPGGSLRLSCAASGFTTFSTYAMNWVRQAPGKGLEWVSRIR SKYNNYATYYADSVKDRFTISRDDSKNTLYLQMNSLRAEDTAVY YCARHGNFGNSYVSWFAYWGQGTMTVTVSS
CD3.19	191	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKG LEWVSRIRSKYNNYATYYADSVKDRFTISRDDSKNTLYLQMNSL RAEDTAVYYCARHGNFGNSYVSWFAYWGQGTMTVTVSS
	192	CDRH1	TYAMN
	193	CDRH2	RIRSKYNNYATYYADSVKD
	194	CDRH3	HGNFGNSYVSWFAY
	195	VL	QAVVTQEPSTLVSPGGTVTLTCSRSTGAVTTSNYANWFQOKPGQ APRGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGVQPEDEAEY YCALWYSNLWVFGGGTKLTVL
	196	CDRL1	RSSTGAVTTSNYAN
	197	CDRL2	GTNKRAP
	198	CDRL3	ALWYSNLWV
	199	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKG LEWVSRIRSKYNNYATYYADSVKDRFTISRDDSKNTLYLQMNSL RAEDTAVYYCARHGNFGNSYVSWFAYWGQGTMTVTVSSGGGGSGG GGSGGGGQAVVTQEPSTLVSPGGTVTLTCSRSTGAVTTSNYAN WFQOKPGQAPRGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGV QPEDEAEYYCALWYSNLWVFGGGTKLTVL
	200	scFv	QAVVTQEPSTLVSPGGTVTLTCSRSTGAVTTSNYANWFQOKPGQ APRGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGVQPEDEAEY YCALWYSNLWVFGGGTKLTVLGGGGSGGGSGGGGSEVQLVESG GGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVSRIR SKYNNYATYYADSVKDRFTISRDDSKNTLYLQMNSLRAEDTAVY YCARHGNFGNSYVSWFAYWGQGTMTVTVSS
CD3.20	201	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTTFSTYAMNWVRQAPGKG LEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTLYLQMNSL RAEDTAVYYCARHGNFGNSYVSWFAYWGQGTMTVTVSS
	202	CDRH1	TYAMN
	203	CDRH2	RIRSKYNNYATYYADSVKD
	204	CDRH3	HGNFGNSYVSWFAY

	205	VL	QAVVTQEPSTLVSPGGTVTLTCSRSTGAVTTSNYANWVQOKPGQ APRGLIGGTNKRAPWTPARFSGSLLGGKAALTLSGVQPEDEAEY YCALWYSNLWVFGGGTKLTVL
	206	CDRL1	RSSTGAVTTSNYAN
	207	CDRL2	GTNKRAP
	208	CDRL3	ALWYSNLWV
	209	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTTFSTYAMNWVRQAPGKG LEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTLYLQMNSL RAEDTAVYYCARHGNFGNSYVSWFAYWGQGTMTVTVSSGGGGGGGG GGSGGGGSQAVVTQEPSTLVSPGGTVTLTCSRSTGAVTTSNYAN WVQOKPGQAPRGLIGGTNKRAPWTPARFSGSLLGGKAALTLSGV QPEDEAEYCALWYSNLWVFGGGTKLTVL
	210	scFv	QAVVTQEPSTLVSPGGTVTLTCSRSTGAVTTSNYANWVQOKPGQ APRGLIGGTNKRAPWTPARFSGSLLGGKAALTLSGVQPEDEAEY YCALWYSNLWVFGGGTKLTVLGGGGSGGGSGGGGSEVQLVESG GGLVQPGGSLRLSCAASGFTTFSTYAMNWVRQAPGKLEWVARIR SKYNNYATYYADSVKDRFTISRDDSKNTLYLQMNSLRAEDTAVY YCARHGNFGNSYVSWFAYWGQGTMTVTVSS
	211	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTTFSTYAMNWVRQAPGKG LEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTLYLQMNSL RAEDTAVYYCVRHGNFGNSYVSWFAYWGQGTMTVTVSS
	212	CDRH1	TYAMN
	213	CDRH2	RIRSKYNNYATYYADSVKD
	214	CDRH3	HGNFGNSYVSW
CD3 . 21	215	VL	QAVVTQEPSTLVSPGGTVTLTCSRSTGAVTTSNYANWFQOKPGQ APRGLIGGTNKRAPWTPARFSGSLLGGKAALTLSGVQPEDEAEY YCALWYSNLWVFGGGTKLTVL
	216	CDRL1	RSSTGAVTTSNYAN
	217	CDRL2	GTNKRAP
	218	CDRL3	ALWYSNLWV
	219	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTTFSTYAMNWVRQAPGKG LEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTLYLQMNSL RAEDTAVYYCVRHGNFGNSYVSWFAYWGQGTMTVTVSSGGGGGGGG GGSGGGGSQAVVTQEPSTLVSPGGTVTLTCSRSTGAVTTSNYAN WFQOKPGQAPRGLIGGTNKRAPWTPARFSGSLLGGKAALTLSGV QPEDEAEYCALWYSNLWVFGGGTKLTVL
	220	scFv	QAVVTQEPSTLVSPGGTVTLTCSRSTGAVTTSNYANWFQOKPGQ APRGLIGGTNKRAPWTPARFSGSLLGGKAALTLSGVQPEDEAEY YCALWYSNLWVFGGGTKLTVLGGGGSGGGSGGGGSEVQLVESG GGLVQPGGSLRLSCAASGFTTFSTYAMNWVRQAPGKLEWVARIR SKYNNYATYYADSVKDRFTISRDDSKNTLYLQMNSLRAEDTAVY YCVRHGNFGNSYVSWFAYWGQGTMTVTVSS
	221	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTTFNTYAMNWVRQAPGKG LEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTLYLQMNSL RAEDTAVYYCVRHGNFGNSYVSWFAYWGQGTMTVTVSS
	222	CDRH1	TYAMN
	223	CDRH2	RIRSKYNNYATYYADSVKD
	224	CDRH3	HGNFGNSYVSWFAY
CD3 . 22	225	VL	QAVVTQEPSTLVSPGGTVTLTCSRSTGAVTTSNYANWYQOKPGQ APRGLIGGTNKRAPWTPARFSGSLLGGKAALTLSGVQPEDEAEY YCALWYSNLWVFGGGTKLTVL
	226	CDRL1	RSSTGAVTTSNYAN
	227	CDRL2	GTNKRAP
	228	CDRL3	ALWYSNLWV
	229	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTTFNTYAMNWVRQAPGKG LEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTLYLQMNSL RAEDTAVYYCVRHGNFGNSYVSWFAYWGQGTMTVTVSSGGGGGGGG GGSGGGGSQAVVTQEPSTLVSPGGTVTLTCSRSTGAVTTSNYAN

			WYQOKPGQAPRGLIGGTNKRAPWTPARFSGSLLGGKAALTLSGV QPEDEAEYYCALWYSNLWVFGGGTKLTVL
	230	scFv	QAVVTQEPSTVSPGGTVTLTCRSSTGAVTTSNYANWYQOKPGQ APRGLIGGTNKRAPWTPARFSGSLLGGKAALTLSGVQPEDEAEY YCALWYSNLWVFGGGTKLTVLGGGGSGGGSGGGGSEVQLVESG GGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVARIR SKYNNYATYYADSVKDRFTISRDDSKNTLYLQMNLSRAEDTAVY YCVRHGNGFNSYVSWFAYWGQTMVTVSS
CD3.23	231	VH	QVQLVESGGGVVQPGRSRLRLSCAASGFKFSGYGMHWVRQAPGKG LEWVAVIWDGSKKYYVDSVKGRFTISRDN SKNTLYLQMNLSRA EDTAVYYCARQMGYWHFDLWGRGTLTVTVSS
	232	CDRH1	GYGMH
	233	CDRH2	VIWYDGSKKYYVDSVKG
	234	CDRH3	QMGYWHFDL
	235	VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQOKPGQAP RLLIYDASN RATGIPARFSGSGSGTDFTLTISSELEPEDFAVYYC QQRSNWPPLTFGGGKTKVEIKR
	236	CDRL1	RASQSVSSYLA
	237	CDRL2	DASN RAT
	238	CDRL3	QQRSNWPPLT
	239	scFv	QVQLVESGGGVVQPGRSRLRLSCAASGFKFSGYGMHWVRQAPGKG LEWVAVIWDGSKKYYVDSVKGRFTISRDN SKNTLYLQMNLSRA EDTAVYYCARQMGYWHFDLWGRGTLTVTVSSGGGGSGGGSGGGG SEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQOKPGQAP PRLLIYDASN RATGIPARFSGSGSGTDFTLTISSELEPEDFAVYY CQQRSNWPPLTFGGGKTKVEIKR
	240	scFv	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQOKPGQAP RLLIYDASN RATGIPARFSGSGSGTDFTLTISSELEPEDFAVYYC QQRSNWPPLTFGGGKTKVEIKRGGGGSGGGSGGGGQVQLVESG GGVVQPGRSRLRLSCAASGFKFSGYGMHWVRQAPGKGLEWVAVI WDGSKKYYVDSVKGRFTISRDN SKNTLYLQMNLSRAEDTAVYYC ARQMGYWHFDLWGRGTLTVTVSS
CD3.24	241	VH	QVQLVQSGGGVVQPGRSRLRLSCKASGYTFTRYTMHWVRQAPGKG LEWIGYINPSRGYTNYNQVKDRFTISRDN SKNTAF LQMDSLRP EDTGVYFCARYYDDHYCLDYWGQGTPTVTVSS
	242	CDRH1	RYTMH
	243	CDRH2	YINPSRGYTNYNQVKD
	244	CDRH3	YYDDHYCLDY
	245	VL	DIQMTQSPSSLSASVGDRTTITCSASSSVSYMNWYQQTGKAPK RWIYDTSKLASGVPSRFSGSGSDTYFTTISSLQPED IATYYCQ QWSSNPFTFGQGT KLQIT
	246	CDRL1	SASSSVSYMN
	247	CDRL2	DTSKLAS
	248	CDRL3	QQWSSNPFT
	249	scFv	QVQLVQSGGGVVQPGRSRLRLSCKASGYTFTRYTMHWVRQAPGKG LEWIGYINPSRGYTNYNQVKDRFTISRDN SKNTAF LQMDSLRP EDTGVYFCARYYDDHYCLDYWGQGTPTVTVSSGGGGSGGGSGGGG GSDIQMTQSPSSLSASVGDRTTITCSASSSVSYMNWYQQTGKA PKRWIYDTSKLASGVPSRFSGSGSDTYFTTISSLQPED IATYY CQQWSSNPFTFGQGT KLQIT
	250	scFv	DIQMTQSPSSLSASVGDRTTITCSASSSVSYMNWYQQTGKAPK RWIYDTSKLASGVPSRFSGSGSDTYFTTISSLQPED IATYYCQ QWSSNPFTFGQGT KLQITGGGGSGGGSGGGGQVQLVQSGGGV VQPGRSRLRLSCKASGYTFTRYTMHWVRQAPGKGLEWIGYINPSR GYTNYNQVKDRFTISRDN SKNTAF LQMDSLRPEDTGVYFCARY YDDHYCLDYWGQGTPTVTVSS
CD3.25	251	VH	EVQLLEQSGAELVRPGTSVKISCKASGYAFTNYWLGWVKQRP GH GLEWIGDIFPGSGNIHYNEKFKGKATLTADKSSSTAYMQLSSLT

			FEDSAVYFCARLRNWDPEMDYWGQGTTVTVSS
	252	CDRH1	NYWLG
	253	CDRH2	DIFPGSGNIHYNEKFKG
	254	CDRH3	LRNWDPEMDY
	255	VL	ELVMTQSPSSSLTVTAGEKVTMSCKSSQSLNLSGNQKNYLTWYQQ KPGQPPKLLIYWASTRESGVPDRFTGSGSGTDFTLTISSVQAE LAVYYCQNDYSYPLTFGAGTKLEIK
	256	CDRL1	KSSQSLNLSGNQKNYLT
	257	CDRL2	WASTRES
	258	CDRL3	QNDYSYPLT
	259	scFv	EVQLLEQSGAELVRPGTSVKISCKASGYAFTNYWLGWVKQRP GHGLEWIGDIFPGSGNIHYNEKFKGKATLTADKSSSTAYMQLSSLT FEDSAVYFCARLRNWDPEMDYWGQGTTVTVSSGGGGSGGGSGG GGSELVMTQSPSSSLTVTAGEKVTMSCKSSQSLNLSGNQKNYLTW YQQKPGQPPKLLIYWASTRESGVPDRFTGSGSGTDFTLTISSVQ AEDLAVYYCQNDYSYPLTFGAGTKLEIK
	260	scFv	ELVMTQSPSSSLTVTAGEKVTMSCKSSQSLNLSGNQKNYLTWYQQ KPGQPPKLLIYWASTRESGVPDRFTGSGSGTDFTLTISSVQAE LAVYYCQNDYSYPLTFGAGTKLEIKGGGGSGGGSGGGGSEVQL LEQSGAELVRPGTSVKISCKASGYAFTNYWLGWVKQRP GHGLEWIGDIFPGSGNIHYNEKFKGKATLTADKSSSTAYMQLSSLT FEDSAVYFCARLRNWDPEMDYWGQGTTVTVSS
CD3 . 26	261	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFTNTYAMNWVRQAPGK GLEWVARIRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMN SLKTEDTAVYYCARHGNFGNSYVSWFAYWGQGTTLTVTVSS
	262	CDRH1	TYAMN
	263	CDRH2	RIRSKYNNYATYYAASVKG
	264	CDRH3	HGNFGNSYVSWFAY
	265	VL	QTVVTQEPSTLVSPGGTVTLTCRSSTGAVTTSNYANWVQKPGQ APRGLIGGTNKRAPGTPARFSGSLLGGAALTLSGVQPEDEAEY YCALWYSNLWVFGGGTKLTVL
	266	CDRL1	RSSTGAVTTSNYAN
	267	CDRL2	GTNKRAP
	268	CDRL3	ALWYSNLWV
	269	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTFTNTYAMNWVRQAPGK GLEWVARIRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMN SLKTEDTAVYYCARHGNFGNSYVSWFAYWGQGTTLTVTVSSGGGG SGGGSGGSGTQTVVTQEPSTLVSPGGTVTLTCRSSTGAVTTSNY ANWVQKPGQAPRGLIGGTNKRAPGTPARFSGSLLGGAALTLSGV QPEDEAEYCALWYSNLWVFGGGTKLTVL
	270	scFv	QTVVTQEPSTLVSPGGTVTLTCRSSTGAVTTSNYANWVQKPGQ APRGLIGGTNKRAPGTPARFSGSLLGGAALTLSGVQPEDEAEY YCALWYSNLWVFGGGTKLTVLGGGGSGGGSGGGGSEVQLVESG GGGLVQPGGSLRLSCAASGFTFTNTYAMNWVRQAPGKGLEWVAR IRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMN SLKTEDTAVYYCARHGNFGNSYVSWFAYWGQGTTLTVTVSS
CD3 . 27	271	VH	EVQLLESVGGGLVQPGGSLRLSCAASGFTFTNTYAMNWVRQAPGK GLEWVARIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMN SLRAEDTAVYYCVRHGNFGNSYVSWFAYWGQGTTLTVTVSS
	272	CDRH1	TYAMN
	273	CDRH2	RIRSKYNNYATYYADSVKG
	274	CDRH3	HGNFGNSYVSWFAY
	275	VL	QAVVTQEPSTLVSPGGTVTLTCGSSTGAVTTSNYANWVQKPGQ AFRGLIGGTNKRAPGTPARFSGSLLGGAALTLSGAQP EDEAEY YCALWYSNLWVFGGGTKLTVL
	276	CDRL1	GSSTGAVTTSNYAN
	277	CDRL2	GTNKRAP
	278	CDRL3	ALWYSNLWV

	279	scFv	EVQLLESGGGLVQPGGSLRLSCAASGFTTFSTYAMNWVRQAPGKG LEWVSRIISKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSL RAEDTAVYYCVRHGNFGNSYVSWFAYWGQGTTLVTVSSGGGGSGG GGSGGGGSQAVVTQEPSTLVSPGGTVTLTCGSSTGAVTTSNYAN WVQEKPGQAFRGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGA QPEDEAEYYCALWYSNLWVFGGGTKLTVL
	280	scFv	QAVVTQEPSTLVSPGGTVTLTCGSSTGAVTTSNYANWVQEKPGQ AFRGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGAQPEDEAEY YCALWYSNLWVFGGGTKLTVLGGGGSGGGSGGGGSEVQLLESG GGLVQPGGSLRLSCAASGFTTFSTYAMNWVRQAPGKLEWVSRI SKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVY YCVRHGNFGNSYVSWFAYWGQGTTLTVSS
CD3.28	281	VH	EVQLLESGGGLVQPGGSLRLSCAASGFQFSSYAMNWVRQAPGKG LEWVSRIISKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSL RAEDTAVYYCVRHTTFPSSYVSYGYWGQGTTLTVSS
	282	CDRH1	SYAMN
	283	CDRH2	RIRSKYNNYATYYADSVKG
	284	CDRH3	HTTFPSSYVSYGY
	285	VL	QAVVTQEPSTLVSPGGTVTLTCGSSTGAVTTSNYANWVQEKPGQ AFRGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGAQPEDEAEY YCALWYSNLWVFGGGTKLTVL
	286	CDRL1	GSSTGAVTTSNYAN
	287	CDRL2	GTNKRAP
	288	CDRL3	ALWYSNLWV
	289	scFv	EVQLLESGGGLVQPGGSLRLSCAASGFQFSSYAMNWVRQAPGKG LEWVSRIISKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSL RAEDTAVYYCVRHTTFPSSYVSYGYWGQGTTLTVSSGGGGSGG GGSGGGGSQAVVTQEPSTLVSPGGTVTLTCGSSTGAVTTSNYAN WVQEKPGQAFRGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGA QPEDEAEYYCALWYSNLWVFGGGTKLTVL
	290	scFv	QAVVTQEPSTLVSPGGTVTLTCGSSTGAVTTSNYANWVQEKPGQ AFRGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGAQPEDEAEY YCALWYSNLWVFGGGTKLTVLGGGGSGGGSGGGGSEVQLLESG GGLVQPGGSLRLSCAASGFQFSSYAMNWVRQAPGKLEWVSRI SKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRAEDTAVY YCVRHHTTFPSSYVSYGYWGQGTTLTVSS
CD3.29	291	VH	QVQLVQSGAEVKKPGASVKVCKASGYSTGYTMNWVRQAPGQG LEWMGLINPYNSTNYAQKLQGRVTMTDTSTSTAYMELRSLRS DDTAVYYCARVALRVALDYWGQGTTLTVSS
	292	CDRH1	GYTMN
	293	CDRH2	LINPYNSTNYAQKLQG
	294	CDRH3	VALRVALDY
	295	VL	DIQMTQSPSSLSASVGDRVTITCKASQNVATHVGWYQQKPGKAP KRLIYSASYRYSQVPSRFSGSGSGTEFTLTISNLPEDFATYYC QQYNRYPYTFGQGTKLEIK
	296	CDRL1	KASQNVATHVG
	297	CDRL2	SASYRYS
	298	CDRL3	QQYNRYPYT
	299	scFv	QVQLVQSGAEVKKPGASVKVCKASGYSTGYTMNWVRQAPGQG LEWMGLINPYNSTNYAQKLQGRVTMTDTSTSTAYMELRSLRS DDTAVYYCARVALRVALDYWGQGTTLTVSSGGGGSGGGSGGGG SDIQMTQSPSSLSASVGDRVTITCKASQNVATHVGWYQQKPGKA PKRLIYSASYRYSQVPSRFSGSGSGTEFTLTISNLPEDFATYY CQQYNRYPYTFGQGTKLEIK
	300	scFv	DIQMTQSPSSLSASVGDRVTITCKASQNVATHVGWYQQKPGKAP KRLIYSASYRYSQVPSRFSGSGSGTEFTLTISNLPEDFATYYC QQYNRYPYTFGQGTKLEIKGGGGSGGGSGGGGSQVQLVQSGAE VKKPGASVKVCKASGYSTGYTMNWVRQAPGQGLEWMGLINP YNSTNYAQKLQGRVTMTDTSTSTAYMELRSLRSDDTAVYYCAR

			VALRVALDYWGQGLTVTVSS
CD3 . 30	301	VH	EVQLVESGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKG LEWVSGISWNSGSGIGYADSVKGRFTISRDNAKNSLYLQMNSLRA EDTALYYCAKDSRGYGDYRLGGAYWGQGLTVTVSS
	302	CDRH1	DYAMH
	303	CDRH2	GISWNSGSGIGYADSVKG
	304	CDRH3	DSRGYGDYRLGGAY
	305	VL	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAP RLLIYGASTRATGIPARFSGSGSGTEFTLTISLSQSEDFAVYYC QQYNNWPWTFGQGTKVEIK
	306	CDRL1	RASQSVSSNLA
	307	CDRL2	GASTRAT
	308	CDRL3	QQYNNWPWT
	309	scFv	EVQLVESGGGLVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKG LEWVSGISWNSGSGIGYADSVKGRFTISRDNAKNSLYLQMNSLRA EDTALYYCAKDSRGYGDYRLGGAYWGQGLTVTVSSGGGGSGGGG SGGGGSEIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQ KPGQAPRLLIYGASTRATGIPARFSGSGSGTEFTLTISLSQSEDF FAVYYCQQYNNWPWTFGQGTKVEIK
	310	scFv	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAP RLLIYGASTRATGIPARFSGSGSGTEFTLTISLSQSEDFAVYYC QQYNNWPWTFGQGTKVEIKGGGGSGGGGSGGGGSEVQLVESGGG LVQPGRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVSGISWN SGSIGYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTALYYCAK DSRGYGDYRLGGAYWGQGLTVTVSS
CD3 . 31	311	VH	EVQLVQSGAEVKKPGASVKVCKASGFSFTNYYVHWMRQAPGQG LEWMGWISPGSDNTKYNEKFKGRVTMTRDTSISTAYMELSLRLS DDTAVYYCARDYGNYYFDYWGQGTITVTVSS
	312	CDRH1	NYYVH
	313	CDRH2	WISPGSDNTKYNEKFKG
	314	CDRH3	DDYGNYYFDY
	315	VL	DIVMTQSPDSLAVSLGERATINCKSSQSLNSRTRKKNYLAWYQQ KPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISLSQAED VAVYYCKQSYILRTFGGGTKVEIK
	316	CDRL1	KSSQSLNSRTRKKNYLA
	317	CDRL2	WASTRES
	318	CDRL3	KQSYILRT
	319	scFv	EVQLVQSGAEVKKPGASVKVCKASGFSFTNYYVHWMRQAPGQG LEWMGWISPGSDNTKYNEKFKGRVTMTRDTSISTAYMELSLRLS DDTAVYYCARDYGNYYFDYWGQGTITVTVSSGGGGSGGGGSGGG GSDIVMTQSPDSLAVSLGERATINCKSSQSLNSRTRKKNYLAWY QQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISLSQA EDVAVYYCKQSYILRTFGGGTKVEIK
	320	scFv	DIVMTQSPDSLAVSLGERATINCKSSQSLNSRTRKKNYLAWYQQ KPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISLSQAED VAVYYCKQSYILRTFGGGTKVEIKGGGGSGGGGSGGGGSEVQLV QSGAEVKKPGASVKVCKASGFSFTNYYVHWMRQAPGQGLEWMG WISPGSDNTKYNEKFKGRVTMTRDTSISTAYMELSLRLSDDTAV YYCARDYGNYYFDYWGQGTITVTVSS
CD3 . 32	321	VH	EVQLVESGGGLVQPGRSLRLSCAASGFTFDDYSMHWRQAPGKG LEWVSGISWNSGSGKYADSVKGRFTISRDNAKNSLYLQMNSLRA EDTALYYCAKYGSGYGFYHYGLDVWGQGTITVTVSS
	322	CDRH1	DYSMH
	323	CDRH2	GISWNSGSGKYADSVKG
	324	CDRH3	YSGYGFYHYGLDV
	325	VL	DIQMTQSPSSLSASVGRVTITCRASQSISSYLNWYQQKPGKAP KLLIYAASSLQSGVPSRFSGSGSGTDFTLTISLSQPEDFATYYC QQSYSTPPITFGQGTREIK

	326	CDRL1	RASQSISSYLN
	327	CDRL2	AASSLQS
	328	CDRL3	QQSYSTPPIT
	329	scFv	EVQLVESGGGLVQPGRSLRLSCAASGFTFDDYSMHWVRQAPGKG LEWVSGISWNSGSKGYADSVKGRFTISRDNAKNSLYLQMNSLRA EDTALYYCAKYGSGYGKFFHYGLDVWGQGTITVTVSSGGGGSGGG GSGGGGSDIQMTQSPSSLSASVGDRVITITCRASQSISSYLNWYQ QKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLOPE DFATYYCQQSYSTPPITFGQGRLEIK
	330	scFv	DIQMTQSPSSLSASVGDRVITITCRASQSISSYLNWYQQKPGKAP KLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLOPEDFATYYC QQSYSTPPITFGQGRLEIKGGGGSGGGSGGGGSEVQLVESGG GLVQPGRSLRLSCAASGFTFDDYSMHWVRQAPGKGLEWVSGISW NSGSKGYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTALYYCA KYGSGYGKFFHYGLDVWGQGTITVTVSS
	331	VH	EVQLVESGGGLVQPGRSLRLSCAASGFTFDDYSMHWVRQAPGKG LEWVSGISWNSGSIYADSVKGRFTISRDNAKNSLYLQMNSLRA EDTALYYCAKYGSGYGKFFYYGMDVWGQGTITVTVSS
CD3 . 33	332	CDRH1	DYSMH
	333	CDRH2	GISWNSGSIYADSVKG
	334	CDRH3	YGSGYGKFFYYGMDV
	335	VL	DIQMTQSPSSLSASVGDRVITITCRASQSISSYLNWYQQKPGKAP KLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLOPEDFATYYC QQSYSTPPITFGQGRLEIK
	336	CDRL1	RASQSISSYLN
	337	CDRL2	AASSLQS
	338	CDRL3	QQSYSTPPIT
	339	scFv	EVQLVESGGGLVQPGRSLRLSCAASGFTFDDYSMHWVRQAPGKG LEWVSGISWNSGSIYADSVKGRFTISRDNAKNSLYLQMNSLRA EDTALYYCAKYGSGYGKFFYYGMDVWGQGTITVTVSSGGGGSGGG GSGGGGSDIQMTQSPSSLSASVGDRVITITCRASQSISSYLNWYQ QKPGKAPKLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLOPE DFATYYCQQSYSTPPITFGQGRLEIK
	340	scFv	DIQMTQSPSSLSASVGDRVITITCRASQSISSYLNWYQQKPGKAP KLLIYAASSLQSGVPSRFSGSGSGTDFTLTISSLOPEDFATYYC QQSYSTPPITFGQGRLEIKGGGGSGGGSGGGGSEVQLVESGG GLVQPGRSLRLSCAASGFTFDDYSMHWVRQAPGKGLEWVSGISW NSGSIYADSVKGRFTISRDNAKNSLYLQMNSLRAEDTALYYCA KYGSGYGKFFYYGMDVWGQGTITVTVSS
	341	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKG LEWVARIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSL RAEDTAVYYCVRHGNFGNSYVSFYFAYWGQGTITVTVSS
CD3 . 34	342	CDRH1	TYAMN
	343	CDRH2	RIRSKYNNYATYYADSVKG
	344	CDRH3	HGNFGNSYVSFYFAY
	345	VL	EIVVTQSPATLSVSPGERATLSCRSTGAVTESNYANWVQEKPG QAFRGLIGGANKRAPGVPARFSGSLSGDEATLTISSLOSEDFAV YYCALFYNTWVFGQGTKLEIK
	346	CDRL1	RSSTGAVTESNYAN
	347	CDRL2	GANKRAP
	348	CDRL3	ALFYNTWV
	349	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKG LEWVARIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSL RAEDTAVYYCVRHGNFGNSYVSFYFAYWGQGTITVTVSSGGGGSGG GGSGGGGSEIVVTQSPATLSVSPGERATLSCRSTGAVTESNYA NWVQEKPGQAFRGLIGGANKRAPGVPARFSGSLSGDEATLTISS LQSEDFAVYYCALFYNTWVFGQGTKLEIK
	350	scFv	EIVVTQSPATLSVSPGERATLSCRSTGAVTESNYANWVQEKPG

			QAFRGLIGGANKRAPGVPARFSGSLSGDEATLTISSLQSEDFAV YYCALFYSNTWVFGQGTKLEIKGGGGSGGGSGGGGSEVQLVES GGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVARI RSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNLSRAEDTAV YYCVRHGNFGNSYVSYFAYWGQGTTVTVSS
CD3.35	351	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFNKYAMNWVRQAPGKG LEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNL KTEDTAVYYCVRHGNFGNSYISYWAYWGQGTTLTVTVSS
	352	CDRH1	KYAMN
	353	CDRH2	RIRSKYNNYATYYADSVKD
	354	CDRH3	HGNFGNSYISYWAY
	355	VL	QTVVTQEPSTVSPGGTVTLTCGSSTGAVTSGNYPNWVQOKPGQ APRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEY YCVLWYSNRWVFGGGTKLTVL
	356	CDRL1	GSSTGAVTSGNYPN
	357	CDRL2	GTKFLAP
	358	CDRL3	VLWYSNRWV
	359	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTFNKYAMNWVRQAPGKG LEWVARIRSKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNL KTEDTAVYYCVRHGNFGNSYISYWAYWGQGTTLTVTVSSGGGGSGG GGSGGGGQTVVTQEPSTVSPGGTVTLTCGSSTGAVTSGNYPN WVQOKPGQAPRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGV QPEDEAEYCVLWYSNRWVFGGGTKLTVL
	360	scFv	QTVVTQEPSTVSPGGTVTLTCGSSTGAVTSGNYPNWVQOKPGQ APRGLIGGTKFLAPGTPARFSGSLLGGKAALTLSGVQPEDEAEY YCVLWYSNRWVFGGGTKLTVLGGGGSGGGSGGGGSEVQLVESG GGGLVQPGGSLRLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIR SKYNNYATYYADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVY YCVRHGNFGNSYISYWAYWGQGTTLTVTVSS
CD3.36	361	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYYMTWVRQAPGKG LEWVAFIRNRARGYTS DHNPSVKGRFTISRDNKNSLYLQMNLSL RAEDTAVYYCARDRPSYYVLDYWGQGTTVTVTVSS
	362	CDRH1	DYYMT
	363	CDRH2	FIRNRARGYTS DHNPSVKG
	364	CDRH3	DRPSYYVLDY
	365	VL	DIVMTQSPDSLAVSLGERATINCKSSQSLFNVRSRKNYLAWYQQ KPGQPPKLLISWASTRESGVPDRFSGSGSGTDFTLTITSSLQAE DAEDVAVYYCKQSYDLFTFGSGTKLEIK
	366	CDRL1	KSSQSLFNVRSRKNYLA
	367	CDRL2	WASTRES
	368	CDRL3	KQSYDLFT
	369	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYYMTWVRQAPGKG LEWVAFIRNRARGYTS DHNPSVKGRFTISRDNKNSLYLQMNLSL RAEDTAVYYCARDRPSYYVLDYWGQGTTVTVTVSSGGGGSGGGGSG GGGSDIVMTQSPDSLAVSLGERATINCKSSQSLFNVRSRKNYLA WYQOKPGQPPKLLISWASTRESGVPDRFSGSGSGTDFTLTITSSL QAEADVAVYYCKQSYDLFTFGSGTKLEIK
	370	scFv	DIVMTQSPDSLAVSLGERATINCKSSQSLFNVRSRKNYLAWYQQ KPGQPPKLLISWASTRESGVPDRFSGSGSGTDFTLTITSSLQAE DAEDVAVYYCKQSYDLFTFGSGTKLEIKGGGGSGGGGSGGGGSEVQLV ESGGGLVQPGGSLRLSCAASGFTFSDYYMTWVRQAPGKGLEWVA FIRNRARGYTS DHNPSVKGRFTISRDNKNSLYLQMNLSRAEDT AVYYCARDRPSYYVLDYWGQGTTVTVTVSS
CD3.37	371	VH	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKG LEWVARIRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMNLSL KTEDTAVYYCARHGNFGNSYVSWFAYWGQGTTLTVTVSS
	372	CDRH1	TYAMN
	373	CDRH2	RIRSKYNNYATYYAASVKG

	374	CDRH3	HGNFGNSYVSWFAY
	375	VL	QTVVTQEPSTLVSPGGTVTLTCRSSTGAVTTSNYANWVQKPGQ APRGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGVQPEDEAEY YCALWYSNLWVFGGGTKLTVL
	376	CDRL1	RSSTGAVTTSNYAN
	377	CDRL2	GTNKRAP
	378	CDRL3	ALWYSNLWV
	379	scFv	EVQLVESGGGLVQPGGSLRLSCAASGFTTFNTYAMNWVRQAPGKG LEWVARIRSKYNNYATYYAASVKGRFTISRDDSKNSLYLQMNSL KTEDTAVYYCARHGNFGNSYVSWFAYWGQGTTLVTVSSGGGGSGG GGSGGGGSQTVVTQEPSTLVSPGGTVTLTCRSSTGAVTTSNYAN WVQKPGQAPRGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGV QPEDEAEYCALWYSNLWVFGGGTKLTVL
	380	scFv	QTVVTQEPSTLVSPGGTVTLTCRSSTGAVTTSNYANWVQKPGQ APRGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGVQPEDEAEY YCALWYSNLWVFGGGTKLTVLGGGGSGGGSGGGGSEVQLVESG GGLVQPGGSLRLSCAASGFTTFNTYAMNWVRQAPGKLEWVARIR SKYNNYATYYAASVKGRFTISRDDSKNSLYLQMNSLKTEDTAVY YCARHGNFGNSYVSWFAYWGQGTTLVTVSS
CD3.38	381	VH	QVQLVQSGAEVKKPGASVKVCKASGFNIKDYMHVVRQAPGQR LEWMGWIDLENANTIYDAKFQGRVTITRDTSASTAYMELSSLRS EDTAVYYCARDAYGRYFYDVWGQGTTLVTVSS
	382	CDRH1	DYYMH
	383	CDRH2	WIDLENANTIYDAKFQ
	384	CDRH3	DAYGRYFYDV
	385	VL	DIVMTQSPDSLAVSLGERATINCKSSQSLLNARTGKNYLAWYQQ KPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAE VAVYYCKQSYSRRTFGGGTKVEIK
	386	CDRL1	KSSQSLLNARTGKNYLA
	387	CDRL2	WASTRES
	388	CDRL3	KQSYSRRT
	389	scFv	QVQLVQSGAEVKKPGASVKVCKASGFNIKDYMHVVRQAPGQR LEWMGWIDLENANTIYDAKFQGRVTITRDTSASTAYMELSSLRS EDTAVYYCARDAYGRYFYDVWGQGTTLVTVSSGGGGSGGGSGGG GSDIVMTQSPDSLAVSLGERATINCKSSQSLLNARTGKNYLAWY QQKPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAE EDVAVYYCKQSYSRRTFGGGTKVEIK
	390	scFv	DIVMTQSPDSLAVSLGERATINCKSSQSLLNARTGKNYLAWYQQ KPGQPPKLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAE VAVYYCKQSYSRRTFGGGTKVEIKGGGGSGGGSGGGGSQVQLV QSGAEVKKPGASVKVCKASGFNIKDYMHVVRQAPGQRLWEMG WIDLENANTIYDAKFQGRVTITRDTSASTAYMELSSLRSED TAVYYCARDAYGRYFYDVWGQGTTLVTVSS
	391	VH	QVQLVQSGGGVVPGRSLRLSCKASGYTFTRYTMHVRQAPGKG LEWIGYINPSRGYTNYNQVKDRFTISRDNKNTAFQMDSLRLP EDTGVYFCARYYDDHYCLDYWGQGTPTVTVSS
CD3.39	392	CDRH1	RYTMH
	393	CDRH2	YINPSRGYTNYNQVKD
	394	CDRH3	YYDDHYCLDY
	395	VL	DIQMTQSPSSLSASVGDRVTITCSASSSVSYMNWYQQTPGKAPK RWIYDTSKLASGVPSRFSGSGSGTDYFTFTISSLQPEDIAITYYCQ QWSSNPFTFGQGTKLQIT
	396	CDRL1	SASSSVSYMN
	397	CDRL2	DTSKLAS
	398	CDRL3	QQWSSNPFT
	399	scFv	QVQLVQSGGGVVPGRSLRLSCKASGYTFTRYTMHVRQAPGKG LEWIGYINPSRGYTNYNQVKDRFTISRDNKNTAFQMDSLRLP EDTGVYFCARYYDDHYCLDYWGQGTPTVTVSSGGGGSGGGSGGG

			GSDIQMTQSPSSLSASVGDRTITCSASSSVSYMNWYQQTPGKAPKRWIYDTSKLAGVPSRFSGSGSGTDYFTTISLQPEDATYYCQQWSSNPFTFGQGTKLQIT
	400	scFv	DIQMTQSPSSLSASVGDRTITCSASSSVSYMNWYQQTPGKAPKRWIYDTSKLAGVPSRFSGSGSGTDYFTTISLQPEDATYYCQQWSSNPFTFGQGTKLQITGGGSGGGSGGGGSQVQLVQSGGVSQVQGRSLRLSCKASGYTFTRYTMHWVRQAPGKLEWIGYINPSRGYTNYNQVKDRFTISRDNKNTAFLOMDSLRLPEDTGVIYCARYDDHYCLDYWGQGTPTVTVSS
CD3.40	401	VH	QVQLVQSGPEVKKPGSSVKVSCASGYTFSRSTMHWVRQAPGQGLEWIGYINPSSAYTNYNQKFKDRVTITADKSTSTAYMELSSLRSEDTAVYYCARPQVHYDNGFPYWGQGTPLTVTVSS
	402	CDRH1	RSTMH
	403	CDRH2	YINPSSAYTNYNQKFKD
	404	CDRH3	PQVHYDNGFPY
	405	VL	DIQMTQSPSTLSASVGDRTMTCSASSSVSYMNWYQQKPGKAPKRWIYDSSKLAGVPSRFSGSGSGTEYTLTISLQPDFFATYYCQQWSRNPFTFGGGTKVEIKR
	406	CDRL1	SASSSVSYMN
	407	CDRL2	DSSKLAG
	408	CDRL3	QQWSRNPPT
	409	scFv	QVQLVQSGPEVKKPGSSVKVSCASGYTFSRSTMHWVRQAPGQGLEWIGYINPSSAYTNYNQKFKDRVTITADKSTSTAYMELSSLRSEDTAVYYCARPQVHYDNGFPYWGQGTPLTVTVSSGGGSGGGSGGGSDIQMTQSPSTLSASVGDRTMTCSASSSVSYMNWYQQKPGKAPKRWIYDSSKLAGVPSRFSGSGSGTEYTLTISLQPDFFATYYCQQWSRNPFTFGGGTKVEIKR
	410	scFv	DIQMTQSPSTLSASVGDRTMTCSASSSVSYMNWYQQKPGKAPKRWIYDSSKLAGVPSRFSGSGSGTEYTLTISLQPDFFATYYCQQWSRNPFTFGGGTKVEIKRGGGSGGGSGGGGSQVQLVQSGPEVKKPGSSVKVSCASGYTFSRSTMHWVRQAPGQGLEWIGYINPSAYTNYNQKFKDRVTITADKSTSTAYMELSSLRSEDTAVYYCARPQVHYDNGFPYWGQGTPLTVTVSS

b. Spacer

Non-viral membrane-bound tropism polypeptides contemplated in particular embodiments comprise a spacer domain. In particular embodiments, a spacer domain impacts the manufacturability of the particle, the expression of the tropism polypeptide and the on-target/off-target cell binding profile of the tropism polypeptide. Without wishing to be bound to any particular theory, it is contemplated that in particular embodiments, disposing the extracellular targeting domains of the one or more non-viral membrane bound tropism polypeptides a particular distance from a particle surface (*e.g.*, lipid bilayer, cell membrane, or envelope) out-competes the host cell derived membrane proteins and leads to increased targeting specificity of the vector. Increased vector specificity should correspond to efficacy at lower vector doses, which corresponds to increased safety. Lower doses also lead to manufacturing cost advantages and efficiencies, which has been an insurmountable obstacle for current *ex vivo* gene therapies.

In particular embodiments, a particle comprises a non-viral membrane bound tropism polypeptide that comprises a spacer domain of about 12 nm in length, about 13 nm in length, about 14 nm in length, about 15 nm in length, about 16 nm in length, about 17 nm in length, about 18 nm in length, about 19 nm in length, about 20 nm in length, about 21 nm in length, 5 about 22 nm in length, about 23 nm in length, about 24 nm in length, about 25 nm in length, about 26 nm in length, about 27 nm in length, about 28 nm in length, about 29 nm in length, about 30 nm in length, about 31 nm in length, about 32 nm in length, about 33 nm in length, about 34 nm in length, about 35 nm in length, about 36 nm in length, about 37 nm in length, about 38 nm in length, about 39 nm in length, about 40 nm in length, about 41 nm in length, 10 about 42 nm in length, about 43 nm in length, about 44 nm in length, about 45 nm in length, about 46 nm in length, about 47 nm in length, about 48 nm in length, about 49 nm in length, about 50 nm in length, about 51 nm in length, about 52 nm in length, about 53 nm in length, about 54 nm in length, or about 55 nm in length, wherein the targeting domain is disposed about 12 nm to about 25 nm, about 13 nm to about 20 nm, or about 12 nm, about 13, nm, 15 about 14 nm, about 15 nm, about 16 nm, about 17 nm, about 18 nm, about 19 nm, or about 20 nm from the vector surface.

In particular embodiments, a particle comprises a non-viral membrane bound tropism polypeptide that comprises a spacer domain about 12 nm in length to about 20 nm in length, wherein the extracellular antigen targeting domain is disposed at least about 12 nm, about 13, 20 nm, about 14 nm, about 15 nm, about 16 nm, about 17 nm, about 18 nm, about 19 nm, or about 20 nm from the particle surface.

In particular embodiments, a particle comprises a tropism polypeptide that comprises a spacer comprising a hinge or stalk polypeptide about 12 nm in length, about 13 nm in length, about 14 nm in length, about 15 nm in length, about 16 nm in length, about 17 nm in 25 length, about 18 nm in length, about 19 nm in length, or about 20 nm in length, wherein the targeting domain is disposed about 12 nm to about 20 nm from the particle surface.

In particular embodiments, a spacer comprises one, two, three, four, five, six, seven, eight, nine, ten or more domains are linked together to achieve the desired length and distance to dispose the extracellular targeting domain from the particle surface. The following table 30 lists exemplary spacers domains based on hinge or stalk polypeptides and their predicted lengths.

Table 6

Spacer	Est. Length	SEQUENCE
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SEQ ID NO	(nm)	
411	13	CD8 α
423	17	CD45RO del.d2-d3
422	21	CD45RO del.d3
415	25	CD45RO
419	30	CD45RA
416	35	CD45RAB
424	5	ECAD.5
425	10	ECAD.4-5
426	15	ECAD.3-5
427	20	ECAD.2-5
431	8	CEACAM.A3
430	16	CEACAM.A2
428	24	CEACAM.A1
434	4	CEACAM.B3
433	12	CEACAM.B2
432	20	CEACAM.B1

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain; a spacer comprising a hinge or stalk domain derived, obtained, or isolated from PDGFR, IgG1, IgG2, IgG4, CD2, CD3, CD4, CD8 α , CD8 β , CD28, CD45ABC, CD45RO, CD45RAB, CD45RAC, CD45RBC, CD45RA, CD45RB, CD45RC, CD45del-d3, CD45del-d2-d3, CADHERIN 1 (E-CADHERIN; ECAD), CEACAM 5, variants thereof, an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, or at least 99% identical thereto, and polypeptide linkers of similar amino acid composition and lengths; a transmembrane domain or GPI anchor, and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising a CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3; a VH and VL; and/or an scFv set forth in Table 5; a spacer comprising a hinge or stalk domain derived, obtained, or isolated from PDGFR, IgG1, IgG2, IgG4, CD2, CD3, CD4, CD8 α , CD8 β , CD28, CD45ABC, CD45RO, CD45RAB, CD45RAC, CD45RBC, CD45RA, CD45RB, CD45RC, CD45del-d3, CD45del-d2-d3, CADHERIN 1, CEACAM 5, or variants thereof; a transmembrane domain or GPI anchor, and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising the amino acid sequence set forth in any one of SEQ ID NOS: 19, 20, 29, 30, 39, 40, 49, 50, 59, 60, 69, 70, 79, 80, 89, 90, 99, 100, 109, 110,

119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, 170, 179, 180, 189, 190, 199, 200, 209, 210, 219, 220, 229, 230, 239, 240, 249, 250, 259, 260, 269, 270, 279, 280, 289, 290, 299, 300, 309, 310, 319, 320, 329, 330, 339, 340, 349, 350, 359, 360, 369, 370, 379, 380, 389, 390, 399, 400, 409, and 410; a spacer comprising a hinge or stalk domain derived, 5 obtained, or isolated from PDGFR, IgG1, IgG2, IgG4, CD2, CD3, CD4, CD8 α , CD8 β , CD28, CD45ABC, CD45RO, CD45RAB, CD45RAC, CD45RBC, CD45RA, CD45RB, CD45RC, CD45del-d3, CD45del-d2-d3, CADHERIN 1, CEACAM 5, or variants thereof; a transmembrane domain or GPI anchor, and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide 10 comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising the amino acid sequence set forth in any one of SEQ ID NOs: 19, 20, 29, 30, 39, 40, 49, 50, 59, 60, 69, 70, 79, 80, 89, 90, 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, 170, 179, 180, 189, 190, 199, 200, 209, 210, 219, 220, 229, 230, 239, 240, 249, 250, 259, 260, 269, 270, 279, 280, 289, 290, 15 299, 300, 309, 310, 319, 320, 329, 330, 339, 340, 349, 350, 359, 360, 369, 370, 379, 380, 389, 390, 399, 400, 409, and 410; a spacer comprising a hinge or stalk domain derived, obtained, or isolated from PDGFR, IgG1, IgG2, IgG4, CD2, CD3, CD4, CD8 α , CD8 β , CD28, CD45ABC, CD45RO, CD45RAB, CD45RAC, CD45RBC, CD45RA, CD45RB, CD45RC, CD45del-d3, CD45del-d2-d3, CADHERIN 1, CEACAM 5, or variants thereof; a 20 transmembrane domain or GPI anchor, and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising the amino acid sequence set forth in any one of SEQ ID NOs: 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, and 25 170; a spacer comprising a hinge or stalk domain derived, obtained, or isolated from PDGFR, IgG1, IgG2, IgG4, CD2, CD3, CD4, CD8 α , CD8 β , CD28, CD45ABC, CD45RO, CD45RAB, CD45RAC, CD45RBC, CD45RA, CD45RB, CD45RC, CD45del-d3, CD45del-d2-d3, CADHERIN 1, CEACAM 5, or variants thereof; a transmembrane domain or GPI anchor, and optionally an intracellular domain.

30 In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain; a spacer comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 411-413, SEQ ID NOs: 414-

423, SEQ ID NOs: 424-427, and SEQ ID NOs: 428-434; a transmembrane domain or GPI anchor, and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising a CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, a VH and VL, and/or an scFv set forth in Table 5; a spacer comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 411, 412, and 413, SEQ ID NOs: 414, 415, 416, 417, 418, 419, 420, 421, 422, and 423, SEQ ID NOs: 424, 425, 426, and 427, and SEQ ID NOs: 428, 429, 430, 431, 432, 433, and 434; a transmembrane domain or GPI anchor, and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising a CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3; a VH and VL; and/or an scFv set forth in Table 5; a spacer comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 411, 423, and 428; a transmembrane domain or GPI anchor, and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising the amino acid sequence set forth in any one of SEQ ID NOs: 19, 20, 29, 30, 39, 40, 49, 50, 59, 60, 69, 70, 79, 80, 89, 90, 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, 170, 179, 180, 189, 190, 199, 200, 209, 210, 219, 220, 229, 230, 239, 240, 249, 250, 259, 260, 269, 270, 279, 280, 289, 290, 299, 300, 309, 310, 319, 320, 329, 330, 339, 340, 349, 350, 359, 360, 369, 370, 379, 380, 389, 390, 399, 400, 409, and 410; a spacer comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 411, 412, and 413, SEQ ID NOs: 414, 415, 416, 417, 418, 419, 420, 421, 422, and 423, SEQ ID NOs: 424, 425, 426, and 427, and SEQ ID NOs: 428, 429, 430, 431, 432, 433, and 434; a transmembrane domain or GPI anchor, and optionally an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising the amino acid sequence set forth in any one of SEQ ID NOs: 19, 20, 29, 30, 39, 40, 49, 50, 59, 60, 69, 70, 79, 80, 89, 90, 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, 170, 179, 180, 189, 190, 199, 200,

209, 210, 219, 220, 229, 230, 239, 240, 249, 250, 259, 260, 269, 270, 279, 280, 289, 290, 299, 300, 309, 310, 319, 320, 329, 330, 339, 340, 349, 350, 359, 360, 369, 370, 379, 380, 389, 390, 399, 400, 409, and 410; a spacer comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 411, 412, and 413, SEQ ID NOs: 414, 415, 416, 417, 5 418, 419, 420, 421, 422, and 423, SEQ ID NOs: 424, 425, 426, and 427, SEQ ID NOs: 428, 429, 430, 431, 432, 433, and 434, and amino acid sequences at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, or at least 99% identical thereto; a transmembrane domain or GPI anchor, and optionally an intracellular domain.

10 In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising the amino acid sequence set forth in any one of SEQ ID NOs: 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, and 170; a spacer comprising an amino acid sequence selected from the group consisting of SEQ 15 ID NOs: 411, 412, and 413, SEQ ID NOs: 414, 415, 416, 417, 418, 419, 420, 421, 422, and 423, SEQ ID NOs: 424, 425, 426, and 427, SEQ ID NOs: 428, 429, 430, 431, 432, 433, and 434, and amino acid sequences at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, or at least 99% identical thereto; a transmembrane domain or GPI anchor, and optionally an 20 intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising the amino acid sequence set forth in any one of SEQ ID NOs: 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, and 25 170; a spacer comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 411, 423, 428, and amino acid sequences at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, or at least 99% identical thereto; a transmembrane domain or GPI anchor, and optionally an intracellular domain.

30 **Table 7**

SEQ ID NO:	AMINO ACID SEQUENCE
411	TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD
412	TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFAAD

413	TTTTAPRPPTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFAKD
414	SPTPSPTGLTTAKMPVSVPLSSDPLPHTHTAFSPASTFERENDFSETTTSLSPDNTSTQVSPDSL DNASAFNTTGVSSVQTPHLPHTADSQTPSAGTDTQTFSGSAANAKLNPTPGSNAISDVPGERST ASTFPTDPVSPPLTTTSLAHSSAALPARTSNTTITANTSDAYLNASETTTLSPPSGSAVISTTT IATTPSKPTCDEKYANITVDYLYNKETKLF TAKLNVNENVECGNNTCTNNEVHNLTECKNASVS ISHNSCTAPDKTLILDVPPGVEKFQLHDCTQVEKADTTICLKWKNIETFTCDTQNTYRFQCGN MIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSPGEPQIIFCRSEAAHQGVI TWNPPQRSFHNFTLCYIKETEKDCLNLDKNLIKDYDLQNLKPYTKYVLSLHAYIIIAKVQRNGSAA MCHFTTKSAPPSQVWNMTVSMSTSDNSMHVKCRPPRDRNGPHERYHLEVEAGNTLVRNESHKNC FRVKDLQYSTDYTFKAYFHNGDYPGEPFILHSTSYNSK
415	SPTPSPTDAYLNASETTTLSPPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLF TAK LNVNENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKFQLHDCTQVE KADTTICLKWKNIETFTCDTQNTYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFT NASKIIKTDFGSPGEPQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLNLDKNLIK YDLQNLKPYTKYVLSLHAYIIIAKVQRNGSAAAMCHFTTKSAPPSQVWNMTVSMSTSDNSMHVKCRP PRDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHHS TSYNSK
416	SPTPSPTGLTTAKMPVSVPLSSDPLPHTHTAFSPASTFERENDFSETTTSLSPDNTSTQVSPDSL DNASAFNTTGVSSVQTPHLPHTADSQTPSAGTDTQTFSGSAANAKLNPTPGSNAISDAYLNA SETTTLSPPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLF TAKLNVNENVECGNNTCT NNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKFQLHDCTQVEKADTTICLKWKNIET FTCDTQNTYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSPGE PQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLNLDKNLIKDYDLQNLKPYTKYVLS LHAYIIIAKVQRNGSAAAMCHFTTKSAPPSQVWNMTVSMSTSDNSMHVKCRPPRDRNGPHERYHLE VEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHSTSYNSK
417	SPTPSPTGLTTAKMPVSVPLSSDPLPHTHTAFSPASTFERENDFSETTTSLSPDNTSTQVSPDSL DNASAFNTTGVSSVQTPHLPHTADSQTPSAGTDTQTFSGSAANAKLNPTPGSNAISDAYLNA SETTTLSPPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLF TAKLNVNENVECGNNTCT NNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKFQLHDCTQVEKADTTICLKWKNIET FTCDTQNTYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSPGE PQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLNLDKNLIKDYDLQNLKPYTKYVLS LHAYIIIAKVQRNGSAAAMCHFTTKSAPPSQVWNMTVSMSTSDNSMHVKCRPPRDRNGPHERYHLE VEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHSTSYNSK
418	SPTPSPTGVSSVQTPHLPHTADSQTPSAGTDTQTFSGSAANAKLNPTPGSNAISDVPGERSTAS TFPTDPVSPPLTTTSLAHSSAALPARTSNTTITANTSDAYLNASETTTLSPPSGSAVISTTTIA TTPSKPTCDEKYANITVDYLYNKETKLF TAKLNVNENVECGNNTCTNNEVHNLTECKNASVSIS HNSCTAPDKTLILDVPPGVEKFQLHDCTQVEKADTTICLKWKNIETFTCDTQNTYRFQCGNMI FDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSPGEPQIIFCRSEAAHQGVITW NPPQRSFHNFTLCYIKETEKDCLNLDKNLIKDYDLQNLKPYTKYVLSLHAYIIIAKVQRNGSAAAMC HFTTKSAPPSQVWNMTVSMSTSDNSMHVKCRPPRDRNGPHERYHLEVEAGNTLVRNESHKNCDFR VKDLQYSTDYTFKAYFHNGDYPGEPFILHSTSYNSK
419	SPTPSPTGLTTAKMPVSVPLSSDPLPHTHTAFSPASTFERENDFSETTTSLSPDNTSTQVSPDSL DNASAFNTTDAYLNASETTTLSPPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLF AKLNVNENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKFQLHDCTQ VEKADTTICLKWKNIETFTCDTQNTYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHK FTNASKIIKTDFGSPGEPQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLNLDKNL IKYDLQNLKPYTKYVLSLHAYIIIAKVQRNGSAAAMCHFTTKSAPPSQVWNMTVSMSTSDNSMHVK RPPRDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILH HSTSYNSK
420	SPTPSPTGVSSVQTPHLPHTADSQTPSAGTDTQTFSGSAANAKLNPTPGSNAISDAYLNASETT TLSPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLF TAKLNVNENVECGNNTCTNN EVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKFQLHDCTQVEKADTTICLKWKNIETFT CDTQNTYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSPGEPQ IIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLNLDKNLIKDYDLQNLKPYTKYVLSLH AYIIIAKVQRNGSAAAMCHFTTKSAPPSQVWNMTVSMSTSDNSMHVKCRPPRDRNGPHERYHLEVEA GNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHSTSYNSK
421	SPTPSPTDVPGERSTASTFPTDPVSPPLTTTSLAHSSAALPARTSNTTITANTSDAYLNASET TTLSPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLF TAKLNVNENVECGNNTCTN NEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKFQLHDCTQVEKADTTICLKWKNIETFT

	TCDTQNIYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSPGEP QIIFCRSEAAHQGVITWNPPQORSFHNFTLCYIKETEKDCLNLDKNLIKDYDLQNLKPYTKYVLSL HAYIIAKVQRNGSAAMCHFTTKSAPPSQVWNMTVSMSTDNSMHVKCRPPDRNGPHERYHLEVE AGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHSTSYNSK
422	SPTPSPTDAYLNASETTTLSPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLF LNVNENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKFQLHDCTQVE KADTTICLKWKNIETFTCDTQNIYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFT NASKIIKTDFGSPPSQVWNMTVSMSTDNSMHVKCRPPDRNGPHERYHLEVEAGNTLVRNESHK NCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHSTSYNSK
423	SPTPSPTDAYLNASETTTLSPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLF LNVNENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPSQQVWNMTVSMSTDN SMHVKCRPPDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPG EPFILHSTSYNSK
424	APIPEPRTIFFCERNPKPQVINIIDADLPNTSPFTAELTHGASANWTIQYNDPTQESIILKPK MALEVGDYKINLKLMDNQNKDQVTTLEVSVCDCGAAGVCRKAQPV EAGLQIPA
425	APIFVPPEKRVSEDFGVGQEITSYTAQEPDTFMEQKITYRIWRDTANWLEINPDTGAISTRA ELDREDFEHVKNSTYTALIIATDNGSPVATGTGTLILLILSDVNDNAPIPEPRTIFFCERNPKPQ VINIIDADLPNTSPFTAELTHGASANWTIQYNDPTQESIILKPKMALEVGDYKINLKLMDNQN KDQVTTLEVSVCDCGAAGVCRKAQPV EAGLQIPA
426	NPPIFNPTYKQVPEANEANVITTLKVTADAPNTPAWEAVYTIILNDDGGQFVVTNPNVNDG ILKTAKGLDFEAKQQYILHVAVTNVVPEFVSLTTSTATVTVDVLDVNEAPIFVPPEKRVSEDF FGVGQEITSYTAQEPDTFMEQKITYRIWRDTANWLEINPDTGAISTRAELDREDFEHVKNSTYT ALIIATDNGSPVATGTGTLILLILSDVNDNAPIPEPRTIFFCERNPKPQVINIIDADLPNTSPF TAELTHGASANWTIQYNDPTQESIILKPKMALEVGDYKINLKLMDNQNKDQVTTLEVSVCDCG AAGVCRKAQPV EAGLQIPA
427	PEFTQEVFKGSVMGALPGTSVMEVTATDADDDVNTYNAAIAYTILSQDPELPDKNMTINRNT GVISVVTGLDRESFPTYTLVVQAADLQGEGLSTTATAVITVTDNDNPPIFNPTYKQVPEAN EANVITTLKVTADAPNTPAWEAVYTIILNDDGGQFVVTNPNVNDGILKTAKGLDFEAKQQYI LHVAVTNVVPEFVSLTTSTATVTVDVLDVNEAPIFVPPEKRVSEDFGVGQEITSYTAQEPDT FMEQKITYRIWRDTANWLEINPDTGAISTRAELDREDFEHVKNSTYTALIIATDNGSPVATGTG TLLILSDVNDNAPIPEPRTIFFCERNPKPQVINIIDADLPNTSPFTAELTHGASANWTIQYN DPTQESIILKPKMALEVGDYKINLKLMDNQNKDQVTTLEVSVCDCGAAGVCRKAQPV EAGLQI PA
428	ELPKPSSISNNKPVEDKDAVAFTCEPETQDATYLWWVNNQSLPVPRLQLSNGNRTLTLFNVT RNDTASYKCETQNPVSARRSDSVILNVLYGPDAPTISPLNTSYRSGENLNLSCHAASNPPAQYS WFWNGTFQQSTQELFIPNITVNNSGSYTCQAHNSDTGLNRTTVTTITVYAEPPKPFITSNNSNP VEDEDAVALTCEPEIQNTTYLWWVNNQSLPVPRLQLSNDNRTLTLSSVTRNDVGPYECGIONE LSVDHSDPVILNVLYGPDPTISPSTYTYRPGVNLSSLSCHAASNPPAQYSWLIDGNIQOHTQEL FISNITEKNSGLYTCQANNSASGHSRTTVKTTITVSAELPKPSSISNNKPVEDKDAVAFTCEPE AQNTTYLWWVNGQSLPVPRLQLSNGNRTLTLFNVTNRNDARAYVCGIQNSVSANRSDPVTLDVL YGPDPPTIISPDDSSYLSGANLNLSCHSASNPSPQYSWRINGIPQOHTQVLFIAKITPNNGTYA CFVSNLATGRNNSIVKSITVS
429	ELPKPSSISNNKPVEDKDAVAFTCEPETQDATYLWWVNNQSLPVPRLQLSNGNRTLTLFNVT RNDTASYKCETQNPVSARRSDSVILNVLYGPDAPTISPLNTSYRSGENLNLSCHAASNPPAQYS WFWNGTFQQSTQELFIPNITVNNSGSYTCQAHNSDTGLNRTTVTTITVYAEPPKPFITSNNSNP VEDEDAVALTCEPEIQNTTYLWWVNNQSLPVPRLQLSNDNRTLTLSSVTRNDVGPYECGIONE LSVDHSDPVILNVLYGPDPTISPSTYTYRPGVNLSSLSCHAASNPPAQYSWLIDGNIQOHTQEL FISNITEKNSGLYTCQANNSASGHSRTTVKTTITVSAELPKPSSISNNKPVEDKDAVAFTCEPE AQNTTYLWWVNGQSLPVPRLQLSNGNRTLTLFNVTNRNDARAYVCGIQNSVSANRSDPVTLDVL YGPDPPTIISPDDSSYLSGANLNLSCHSASNPSPQYSWRINGIPQOHTQVLFIAKITPNNGTYA CFVSNLATGRNNSIVKSITVSA
430	PKPFITSNNSNPVEDEDAVALTCEPEIQNTTYLWWVNNQSLPVPRLQLSNDNRTLTLSSVTRN DVGPYECGIONELSDHSDPVILNVLYGPDPTISPSTYTYRPGVNLSSLSCHAASNPPAQYSWL IDGNIQOHTQELFISNITEKNSGLYTCQANNSASGHSRTTVKTTITVSAELPKPSSISNNKPV DKDAVAFTCEPEAQNTTYLWWVNGQSLPVPRLQLSNGNRTLTLFNVTNRNDARAYVCGIQNSVS ANRSDPVTLDVLYGPDPTIISPDDSSYLSGANLNLSCHSASNPSPQYSWRINGIPQOHTQVLF IAKITPNNGTYACFVSNLATGRNNSIVKSITVSA
431	AELPKPSSISNNKPVEDKDAVAFTCEPEAQNTTYLWWVNGQSLPVPRLQLSNGNRTLTLFN TRNDARAYVCGIQNSVSANRSDPVTLDVLYGPDPTIISPDDSSYLSGANLNLSCHSASNPSPQY

	SWRINGIPQQHTQVLFIAKITPNNNGTYACFVSNLATGRNNSIVKSITVSA
432	PDAPTISPNTSYRSGENLNLSCHAASNPPAQYSWFVNGTFQQSTQELFIPNITVNNSGSYTCQ AHNSDTGLNRTTITVYAEPPKPFITSNNSNPVEDEDAVALTCEPEIQNTTYLWWVNNQSLP VSPRLQLSNDNRTLTLTLLSVTRNDVGPYECGIQNELSVDHSDPVIILNVLYGPDPTISPSTYYR PGVNLNLSCHAASNPPAQYSWLIDGNIQQHTQELFISNITEKNSGLYTCQANNSASGHSRTTVK TITVSAELPKPSISSNNSKPVEDKDAVAFTCEPEAQNTTYLWWVNGQSLPVSPRLQLSNGNRTL TLFNVTRNDARAYVCGIQNSVSANRSDPVTLDVLYGPDTPIIISPPDSSYLSGANLNLSCHSASN PSPQYSWRINGIPQQHTQVLFIAKITPNNNGTYACFVSNLATGRNNSIVKSITVSA
433	PDDPTISPSTYYRPGVNLNLSCHAASNPPAQYSWLIDGNIQQHTQELFISNITEKNSGLYTCQ ANNSASGHSRTTVKTTITVSAELPKPSISSNNSKPVEDKDAVAFTCEPEAQNTTYLWWVNGQSLP VSPRLQLSNGNRTLTLFNVTRNDARAYVCGIQNSVSANRSDPVTLDVLYGPDTPIIISPPDSSYL SGANLNLSCHSASNPSPOYSWRINGIPQQHTQVLFIAKITPNNNGTYACFVSNLATGRNNSIVK SITVSA
434	PDTPIISPPDSSYLSGANLNLSCHSASNPSPOYSWRINGIPQQHTQVLFIAKITPNNNGTYACF VSNLATGRNNSIVKSITVSA

c. Transmembrane Domain

Non-viral membrane-bound tropism polypeptides contemplated in particular embodiments comprise an extracellular antigen targeting domain that binds an antigen expressed on an immune effector cell; a spacer polypeptide; a transmembrane domain and optionally, an intracellular domain.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain that binds an antigen expressed on an immune effector cell; a spacer polypeptide; a transmembrane domain derived, obtained, or isolated from a polypeptide selected from the group consisting of: alpha, beta, gamma, or delta chain of the T-cell receptor, CD2, CD3δ, CD3ε CD3γ, CD4, CD5, CD7, CD8α, CD9, CD16, CD22, CD27, CD28, CD33, CD37, CD40, CD45, CD64, CD80, CD86, CD95, CD134, CD137, CD152, CD154, CD200R, CD223, CD235a, CD244, CD270, CD272, CD273, CD274, CD278, CD279, CD300, CD357, TNRF2, TNFRS14, TNFRS25, TLR2, TLR4, TLR5, TIM1, SlamF1, SlamF5, SlamF6, and an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, or at least 99% identical thereto; and optionally, an intracellular domain of no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain; a spacer comprising a hinge or stalk domain derived, obtained, or isolated from PDGFR, IgG1, IgG2, IgG4, CD2, CD3, CD4, CD8α, CD8β, CD28, CD45ABC, CD45RO, CD45RAB, CD45RAC, CD45RBC, CD45RA, CD45RB, CD45RC, CD45del-d3, CD45del-d2-d3, CADHERIN 1, CEACAM 5, variants thereof, and polypeptide linkers of similar amino acid composition and lengths; a

transmembrane domain derived, obtained, or isolated from a polypeptide selected from the group consisting of: alpha, beta, gamma, or delta chain of the T-cell receptor, CD2, CD3 δ , CD3 ϵ CD3 γ , CD4, CD5, CD7, CD8 α , CD9, CD16, CD22, CD27, CD28, CD33, CD37, CD40, CD45, CD64, CD80, CD86, CD95, CD 134, CD137, CD152, CD154, CD200R, 5 CD223, CD235a, CD244, CD270, CD272, CD273, CD274, CD278, CD279, CD300, CD357, PDGFR, TNRF2, TNFRS14, TNFRS25, TLR2, TLR4, TLR5, TIM1, SlamF1, SlamF5, SlamF6, and an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, or at least 99% identical thereto; and optionally, an intracellular domain of no 10 more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising a CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, a VH and VL, and/or an scFv set forth in Table 5; a spacer comprising 15 a hinge or stalk domain derived, obtained, or isolated from PDGFR, IgG1, IgG2, IgG4, CD2, CD3, CD4, CD8 α , CD8 β , CD28, CD45ABC, CD45RO, CD45RAB, CD45RAC, CD45RBC, CD45RA, CD45RB, CD45RC, CD45del-d3, CD45del-d2-d3, CADHERIN 1, CEACAM 5, or variants thereof; a transmembrane domain derived, obtained, or isolated from a polypeptide selected from the group consisting of: alpha, beta, gamma, or delta chain 20 of the T-cell receptor, CD2, CD3 δ , CD3 ϵ CD3 γ , CD4, CD5, CD7, CD8 α , CD9, CD16, CD22, CD27, CD28, CD33, CD37, CD40, CD45, CD64, CD80, CD86, CD95, CD 134, CD137, CD152, CD154, CD200R, CD223, CD235a, CD244, CD270, CD272, CD273, CD274, CD278, CD279, CD300, CD357, PDGFR, TNRF2, TNFRS14, TNFRS25, TLR2, TLR4, TLR5, TIM1, SlamF1, SlamF5, SlamF6, and an amino acid sequence at least 85% 25 identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, or at least 99% identical thereto; and optionally, an intracellular domain of no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or 30 antigen binding fragment thereof comprising the amino acid sequence set forth in any one of SEQ ID NOs: 19, 20, 29, 30, 39, 40, 49, 50, 59, 60, 69, 70, 79, 80, 89, 90, 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, 170, 179, 180, 189, 190, 199, 200, 209, 210, 219, 220, 229, 230, 239, 240, 249, 250, 259, 260, 269, 270, 279, 280, 289, 290,

299, 300, 309, 310, 319, 320, 329, 330, 339, 340, 349, 350, 359, 360, 369, 370, 379, 380, 389, 390, 399, 400, 409, and 410; a spacer comprising a hinge or stalk domain derived, obtained, or isolated from PDGFR, IgG1, IgG2, IgG4, CD2, CD3, CD4, CD8 α , CD8 β , CD28, CD45ABC, CD45RO, CD45RAB, CD45RAC, CD45RBC, CD45RA, CD45RB, CD45RC, CD45del-d3, CD45del-d2-d3, CADHERIN 1, CEACAM 5, or variants thereof; a transmembrane domain derived, obtained, or isolated from a polypeptide selected from the group consisting of: alpha, beta, gamma, or delta chain of the T-cell receptor, CD2, CD3 δ , CD3 ϵ CD3 γ , CD4, CD5, CD7, CD8 α , CD9, CD16, CD22, CD27, CD28, CD33, CD37, CD40, CD45, CD64, CD80, CD86, CD95, CD 134, CD137, CD152, CD154, CD200R, CD223, CD235a, CD244, CD270, CD272, CD273, CD274, CD278, CD279, CD300, CD357, PDGFR, TNRF2, TNFRS14, TNFRS25, TLR2, TLR4, TLR5, TIM1, SlamF1, SlamF5, SlamF6, and an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, or at least 99% identical thereto; and optionally, an intracellular domain of no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising the amino acid sequence set forth in any one of SEQ ID NOS: 19, 20, 29, 30, 39, 40, 49, 50, 59, 60, 69, 70, 79, 80, 89, 90, 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, 170, 179, 180, 189, 190, 199, 200, 209, 210, 219, 220, 229, 230, 239, 240, 249, 250, 259, 260, 269, 270, 279, 280, 289, 290, 299, 300, 309, 310, 319, 320, 329, 330, 339, 340, 349, 350, 359, 360, 369, 370, 379, 380, 389, 390, 399, 400, 409, and 410; a spacer comprising a hinge or stalk domain derived, obtained, or isolated from PDGFR, IgG1, IgG2, IgG4, CD2, CD3, CD4, CD8 α , CD8 β , CD28, CD45ABC, CD45RO, CD45RAB, CD45RAC, CD45RBC, CD45RA, CD45RB, CD45RC, CD45del-d3, CD45del-d2-d3, CADHERIN 1, CEACAM 5, or variants thereof; a transmembrane domain comprising an amino acid sequence set forth in any one of SEQ ID NOS: 435, 436, 437, 438, 439, 440, and 441 and an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, or at least 99% identical thereto; and optionally, an intracellular domain of no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or

antigen binding fragment thereof comprising the amino acid sequence set forth in any one of SEQ ID NOs: 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, and 170; a spacer comprising a hinge or stalk domain derived, obtained, or isolated from PDGFR, IgG1, IgG2, IgG4, CD2, CD3, CD4, CD8 α , CD8 β , CD28, CD45ABC, CD45RO, CD45RAB, CD45RAC, CD45RBC, CD45RA, CD45RB, CD45RC, CD45del-d3, CD45del-d2-d3, CADHERIN 1, CEACAM 5, or variants thereof; a transmembrane domain comprising an amino acid sequence set forth in any one of SEQ ID NOs: 435, 436, 437, 438, 439, 440, and 441, and an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, or at least 99% identical thereto; and optionally, an intracellular domain of no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain; a spacer comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 411-413, SEQ ID NOs: 414-423, SEQ ID NOs: 424-427, and SEQ ID NOs: 428-434; a transmembrane domain comprising an amino acid sequence set forth in any one of SEQ ID NOs: 435, 436, 437, 438, 439, 440, and 441; and optionally, an intracellular domain of no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising a CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, a VH and VL, and/or an scFv set forth in Table 5; a spacer comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 411, 412, and 413, SEQ ID NOs: 414, 415, 416, 417, 418, 419, 420, 421, 422, and 423, SEQ ID NOs: 424, 425, 426, and 427, and SEQ ID NOs: 428, 429, 430, 431, 432, 433, and 434; a transmembrane domain comprising an amino acid sequence set forth in any one of SEQ ID NOs: 435, 436, 437, 438, 439, 440, and 441; and optionally, an intracellular domain of no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids.

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising the amino acid sequence set forth in any one of SEQ ID NOs: 19, 20, 29, 30, 39, 40, 49, 50, 59, 60, 69, 70, 79, 80, 89, 90, 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, 170, 179, 180, 189, 190, 199, 200,

209, 210, 219, 220, 229, 230, 239, 240, 249, 250, 259, 260, 269, 270, 279, 280, 289, 290, 299, 300, 309, 310, 319, 320, 329, 330, 339, 340, 349, 350, 359, 360, 369, 370, 379, 380, 389, 390, 399, 400, 409, and 410; a spacer comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 411, 412, and 413, SEQ ID NOs: 414, 415, 416, 417, 5 418, 419, 420, 421, 422, and 423, SEQ ID NOs: 424, 425, 426, and 427, and SEQ ID NOs: 428, 429, 430, 431, 432, 433, and 434; a transmembrane domain comprising an amino acid sequence set forth in any one of SEQ ID NOs: 435, 436, 437, 438, 439, 440, and 441; and optionally, an intracellular domain of no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids.

In particular embodiments, a non-viral membrane-bound tropism polypeptide 10 comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising the amino acid sequence set forth in any one of SEQ ID NOs: 19, 20, 29, 30, 39, 40, 49, 50, 59, 60, 69, 70, 79, 80, 89, 90, 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, 170, 179, 180, 189, 190, 199, 200, 209, 210, 219, 220, 229, 230, 239, 240, 249, 250, 259, 260, 269, 270, 279, 280, 289, 290, 15 299, 300, 309, 310, 319, 320, 329, 330, 339, 340, 349, 350, 359, 360, 369, 370, 379, 380, 389, 390, 399, 400, 409, and 410; a spacer comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 411, 412, and 413, SEQ ID NOs: 414, 415, 416, 417, 418, 419, 420, 421, 422, and 423, SEQ ID NOs: 424, 425, 426, and 427, and SEQ ID NOs: 428, 429, 430, 431, 432, 433, and 434; a transmembrane domain comprising an amino acid 20 sequence set forth in any one of SEQ ID NOs: 435, 436, 437, 438, 439, 440, and 441, and an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, or at least 99% identical thereto; and optionally, an intracellular domain of no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids.

25 In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain comprising an anti-CD3ε antibody or antigen binding fragment thereof comprising the amino acid sequence set forth in any one of SEQ ID NOs: 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, and 170; a spacer comprising an amino acid sequence selected from the group consisting of SEQ 30 ID NOs: 411, 423, and 428; a transmembrane domain comprising an amino acid sequence set forth in any one of SEQ ID NOs: 437 and 439; and optionally, an intracellular domain of no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids.

Table 8

SEQ ID NO:	AMINO ACID SEQUENCE
435	VMSVATIVIVDICITGGLLLLVIYWS
436	MALIVLGGVAGLLFIGLGIFF
437	IYIWAPLAGTCGVLLLSLVITLYC
438	FWVLVVVGGVLACYSLLVTVAFIIFWV
439	ALIAFLAFLIIVTSIALLVVL
440	ILGILGGILALLILLLLLLF
441	IISFFLALTSTALLFLFFLTIRFSVV

In particular embodiments, a non-viral membrane-bound tropism polypeptide comprises a transmembrane domain and optionally, an intracellular domain of no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids. In preferred embodiments, an intracellular domain comprises, consists essentially of, or consists of one, two, three, four, five, or six of the amino acids set forth in any one of SEQ ID NOs: 442, 443, 444, 445, 446, 447, and 448.

Table 9

SEQ ID NO:	AMINO ACID SEQUENCE
442	KNRKA
443	CVRC
444	NHRNR
445	RSKRS
446	YKIYD
447	LRRRA
448	KRGRK

In particular embodiments, a non-viral membrane bound tropism polypeptide comprises an extracellular antigen targeting domain, a spacer polypeptide, and a GPI anchor. A “GPI anchor” or “glycosylphosphatidylinositol anchor” refers to a posttranslational modification that anchors a non-viral membrane bound tropism polypeptide in the outer leaflet of a lipid bilayer, a cell membrane, or a viral envelope of a recombinant particle contemplated herein. A GPI anchor is a complex structure comprising a phosphoethanolamine linker, glycan core, and phospholipid tail. In particular embodiments, a nascently translated non-viral membrane-bound tropism polypeptide comprises a GPI attachment signal peptide at its C-terminus. The signal peptide is recognized by GPI transamidase, which cleaves and replaces it with a preassembled GPI by transamidation at an amino acid termed the ω site amino acid thereby generating a GPI anchored non-viral membrane-bound tropism polypeptide.

In particular embodiments, a non-viral membrane bound tropism polypeptide comprises an amino acid sequence set forth in any one of SEQ ID NOs: 455-576. In

particular preferred embodiments, a non-viral membrane bound tropism polypeptide comprises an amino acid sequence set forth in any one of SEQ ID NOs: 461, 471, 483, 537, and 553.

5 Table 10

SEQ ID NO:	AMINO ACID SEQUENCE
455	QVQLLESGAELARPGASVKMSCKASGYTFTRYTMHWVKQRPQGQLEWIGYINPSRGYTNYNQ KFKDKATLTDDKSSSTAYMQLSSLTSEDSAVYYCAGYYDDHYCLDYWGQGTTLTVSSGGGGS GGGGSGGGSDIVMTQSPAIMASAPGEKVTMTCSASSSVSYMNWYQQKSGTSPKRWIYDTSK LASGVPAHFRRSGSGTSYSLTISGMEAEADAATYYCQQWSSNPFTHGSGTKLEIKSTTTTPAPR PPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
456	DIVMTQSPAIMASAPGEKVTMTCSASSSVSYMNWYQQKSGTSPKRWIYDTSKLASGVPAHFRR SGSGTSYSLTISGMEAEADAATYYCQQWSSNPFTHGSGTKLEIKSGGGSGGGSGGGGSQV QLLESGAELARPGASVKMSCKASGYTFTRYTMHWVKQRPQGQLEWIGYINPSRGYTNYNQKFK KDKATLTDDKSSSTAYMQLSSLTSEDSAVYYCAGYYDDHYCLDYWGQGTTLTVSTTTTPAPRP PPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
457	QVQLQQSGAELARPGASVKMSCKASGYTFTRYTMHWVKQRPQGQLEWIGYINPSRGYTNYNQ KFKDKATLTDDKSSSTAYMQLSSLTSEDSAVYYCARYYDDHYCLDYWGQGTTLTVSSSGGGG SGGGSGGGGSQIVLTQSPAIMASAPGEKVTMTCSASSSVSYMNWYQQKSGTSPKRWIYDTS KLASGVPAHFRRSGSGTSYSLTISGMEAEADAATYYCQQWSSNPFTHGSGTKLEINTTTTPAPR PPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
458	QIVLTQSPAIMASAPGEKVTMTCSASSSVSYMNWYQQKSGTSPKRWIYDTSKLASGVPAHFRR SGSGTSYSLTISGMEAEADAATYYCQQWSSNPFTHGSGTKLEINGGGSGGGSGGGGSQVQ LQQSGAELARPGASVKMSCKASGYTFTRYTMHWVKQRPQGQLEWIGYINPSRGYTNYNQKFK DKATLTDDKSSSTAYMQLSSLTSEDSAVYYCARYYDDHYCLDYWGQGTTLTVSSSTTTTPAPR PPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
459	QVQLQQSGAELARPGASVKMSCKASGYTFTSYTMHWVKQRPQGQLEWIGYINPSSGYTKYNQ KFKDKATLTADKSSSTAYMQLSSLTSEDSAVYYCARWQDYDVFYDYWGQGTTLTVSSGGGGS GGGGSGGGGSQIVLSQSPAILASAPGEKVTMTCRASSSVSYMHWYQQKPGSSPKPWIYATSN LASGVPARFSGSGSGTSYSLTISRVEAEADAATYYCQQWSSNPFTHGGGKLETKTTTPAPRP PPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
460	QIVLSQSPAILASAPGEKVTMTCRASSSVSYMHWYQQKPGSSPKPWIYATSNLASGVPARF SGSGTSYSLTISRVEAEADAATYYCQQWSSNPFTHGGGKLETTGGGGSGGGSGGGGSQVQL QQSGAELARPGASVKMSCKASGYTFTSYTMHWVKQRPQGQLEWIGYINPSSGYTKYNQKFKD KATLTADKSSSTAYMQLSSLTSEDSAVYYCARWQDYDVFYDYWGQGTTLTVSSSTTTTPAPRP TPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
461	EVQLQQSGPELVKPGASMKISCKASGYSTGYTMNWVKQSHGKNLEWMGLINPYKGVSTYNYQ KFKDKATLTVDKSSSTAYMQLSSLTSEDSAVYYCARSGYYGDSWYFDVWGAGTTTVTVSSGG GGSGGGSGGGSDIQMTQTSSLSASLGDRVTISCRASQDIRNYLNWYQQKPDGTVKLLIY YTSRLHSGVPSKFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPWTFAGGKLEIKTTTP APRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVIT LYC
462	DIQMTQTSSLSASLGDRVTISCRASQDIRNYLNWYQQKPDGTVKLLIYTSRLHSGVPSKF SGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPWTFAGGKLEIKGGGGSGGGSGGGGSSEV QLQQSGPELVKPGASMKISCKASGYSTGYTMNWVKQSHGKNLEWMGLINPYKGVSTYNYQKFK KDKATLTVDKSSSTAYMQLSSLTSEDSAVYYCARSGYYGDSWYFDVWGAGTTTVTVSSSTTP APRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVIT LYC
463	QVQLQQSAAELARPGASVKMSCKASGYTFTRYTMQWVKQRPQGQLEWIGYINPSSGYIGYSQ KFKDKTTLTADKSSSTAYMQLSSLTSEDSAVYYCARSKVYDYDVYSMDYWGQGTSTVTSSG GGGGSGGGSGGGGSQIILTQSPAIMASAPGEKVTMTCSASSSVSYMHWYQQKSGTSPKRWIY DTSKLASGVPARFSGSGSGTSYSLTISMEAEADAATYYCQQWSSNPLTFAGGKLELKTTTP APRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVIT LYC

464	QIILTQSPAIMASASPGEKVTMTCSASSSVSYMHWYQQKSGTSPKRWIYDTSKLASGVPARFS SGSGSTSYSLTISSMEAEDAATYYCQOWSSNPLTFGAGTKLELKGGGSGGGGSGGGGSGVQ LQQSAAELARPGASVKMSCKASGYTFTRYTMQWVKQRPQGQLEWIGYINPSSGYIGYSQKFK DKTTLTADKSSSTAYMQLSSLTSEDSAVYYCARSKVYDYDVSMDYWGQGTSTVTSSTTTP APRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVIT LYC
465	QVQLQQSGAELARPGASVKMSCKASGYTFISYTMHWVKQRPQGQLEWIGYINPRSGYTHYNQ KLKDKATLTADKSSSSAYMQLSSLTSEDSAVYYCARSAYDYDGFAYWGQGTTLTVTSAGGGG SGGGGSGGGGSDIVLTQSPAIMASASPGEKVTMTCSASSSVSYMNWYQKSGTSPKRWTYDTS KLASGVPARFSGSGSTSYSLTISSMEAEDAATYYCQOWSSNPTTFGSGTKLEIKTTTTPAPR PPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
466	QIVLTQSPAIMASASPGEKVTMTCSASSSVSYMNWYQKSGTSPKRWTYDTSKLASGVPARFS GSGSTSYSLTISSMEAEDAATYYCQOWSSNPTTFGSGTKLEIKGGGSGGGGSGGGGSGVQ LQQSGAELARPGASVKMSCKASGYTFISYTMHWVKQRPQGQLEWIGYINPRSGYTHYNQKLK DKATLTADKSSSSAYMQLSSLTSEDSAVYYCARSAYDYDGFAYWGQGTTLTVTSATTTTPAPR PPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
467	QVQLVQSGAEVKKPGASVKVSCASGYTFISYTMHWVRQAPGQGLEWMGYINPRSGYTHYNQ KLKDKATLTADKSASTAYMELSSLRSEDTAVYYCARSAYDYDGFAYWGQGTTLTVSSGGGG SGGGGSGGGGSDIQMTQSPSSLSASVGDRTITCSASSSVSYMNWYQKPKGKAPKRLIYDTS KLASGVPARFSGSGSGTDFTLTISLQPEDFATYYCQOWSSNPTTFGGGKVEIKTTTTPAPR PPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
468	DIQMTQSPSSLSASVGDRTITCSASSSVSYMNWYQKPKGKAPKRLIYDTSKLASGVPARF SGSGTDFTLTISLQPEDFATYYCQOWSSNPTTFGGGKVEIKGGGSGGGGSGGGGSGVQ LVQSGAEVKKPGASVKVSCASGYTFISYTMHWVRQAPGQGLEWMGYINPRSGYTHYNQKLK DKATLTADKSASTAYMELSSLRSEDTAVYYCARSAYDYDGFAYWGQGTTLTVSSSTTTTPAPR PPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
469	EVQLVESGGGLVQPKGSLKLSCAASGFTFNTYAMNWVRQAPGKLEWVARIRSKYNNYATYY ADSVKDRFTISRDDQSILYLQMNLLKTEDTAMYYCVRHGNFGNSYVSWFAYWGQGTTLTVTS SGGGGSGGGGSGGGGSAVVTTQESALTTSPGETVTILTCRSSTGAVTTSNYANWVQEKPDHLE TGLIGGINKRAPGVPARFSGSLIGDKAALTITGAQTEDEAIYFCALWYSNLWVFGGGTKLTV LTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLS SLVITLYC
470	QAVVTQESALTTSPGETVTILTCRSSTGAVTTSNYANWVQEKPDHLEFTGLIGGINKRAPGVPA RFSGLIGDKAALTITGAQTEDEAIYFCALWYSNLWVFGGGTKLTVLGGGSGGGGSGGGGSGVQ EVQLVESGGGLVQPKGSLKLSCAASGFTFNTYAMNWVRQAPGKLEWVARIRSKYNNYATYY ADSVKDRFTISRDDQSILYLQMNLLKTEDTAMYYCVRHGNFGNSYVSWFAYWGQGTTLTVTS STTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLS SLVITLYC
471	DVQLVQSGAEVKKPGASVKVSCASGYTFTRYTMHWVRQAPGQGLEWIGYINPRSGYTNAD SVKGRFTITTDKSTSTAYMELSSLRSEDTATYYCARYYDDHYCLDYWGQGTTVTVSSSGGGG SGGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPKGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGGKVEIKTTTTPAPR PPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
472	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPKGKAPKRWIYDTSKVASGVPARFS SGSGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGGKVEIKSGGGSGGGGSGGGGSDV QLVQSGAEVKKPGASVKVSCASGYTFTRYTMHWVRQAPGQGLEWIGYINPRSGYTNADSV KGRFTITTDKSTSTAYMELSSLRSEDTATYYCARYYDDHYCLDYWGQGTTVTVSSSTTTTPAPR PPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
473	DVQLVQSGAEVKKPGASVKVSCASGYTFTRYTMHWVRQAPGQGLEWIGYINPRSGYTNAD SVKGRFTITTDKSTSTAYMELSSLRSEDTATYYCARYYDDPYCLDYWGQGTTVTVSSSGGGG SGGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPKGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGGKVEIKTTTTPAPR PPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
474	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPKGKAPKRWIYDTSKVASGVPARFS SGSGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGGKVEIKSGGGSGGGGSGGGGSDV QLVQSGAEVKKPGASVKVSCASGYTFTRYTMHWVRQAPGQGLEWIGYINPRSGYTNADSV KGRFTITTDKSTSTAYMELSSLRSEDTATYYCARYYDDPYCLDYWGQGTTVTVSSSTTTTPAPR PPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
475	DVQLVQSGAEVKKPGASVKVSCASGYTFTRYTMHWVRQAPGQGLEWIGYINPRSGYTNAD

	SVKGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYYNDQYCLDYWGQGTTFVTVSSSSGGG SGSGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDT SKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGGKVEIKTTTTPAP RPPTPAPTIA SQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLY C
476	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDTSKVASGVPARFS SGSGGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGGKVEIKSGGGSGGGSGGGGSDV QLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYYNDQYCLDYWGQGTTFVTVSSSTTTPAP RPPTPAPTIA SQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLY C
477	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYYDAHNCLDYWGQGTTFVTVSSSGGGG SGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGGKVEIKTTTTPAPR PPTPAPTIA SQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
478	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDTSKVASGVPARFS SGSGGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGGKVEIKSGGGSGGGSGGGGSDV QLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYYDAHNCLDYWGQGTTFVTVSSSTTTPAPR PPTPAPTIA SQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
479	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYSDDHYCLDYWGQGTTFVTVSSSGGGG SGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGGKVEIKTTTTPAPR PPTPAPTIA SQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
480	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDTSKVASGVPARFS SGSGGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGGKVEIKSGGGSGGGSGGGGSDV QLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYSDDHYCLDYWGQGTTFVTVSSSTTTPAPR PPTPAPTIA SQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
481	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYSDDRYCLDYWGQGTTFVTVSSSGGGG SGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGGKVEIKTTTTPAPR PPTPAPTIA SQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
482	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDTSKVASGVPARFS SGSGGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGGKVEIKSGGGSGGGSGGGGSDV QLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYSDDRYCLDYWGQGTTFVTVSSSTTTPAPR PPTPAPTIA SQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
483	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYYDDNYCLDYWGQGTTFVTVSSSGGGG SGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDT SKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGGKVEIKTTTTPAP RPPTPAPTIA SQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLY C
484	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDTSKVASGVPARFS SGSGGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGGKVEIKSGGGSGGGSGGGGSDV QLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYYDDNYCLDYWGQGTTFVTVSSSTTTPAP RPPTPAPTIA SQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLY C
485	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYYDDQYCLDYWGQGTTFVTVSSSGGGG SGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGGKVEIKTTTTPAPR PPTPAPTIA SQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
486	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDTSKVASGVPARFS

	GSGSGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGGKVEIKSGGGSGGGSGGGSDV QLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATYYCARYDDQYCLDYWGQGTITVTVSSTTTTPAPR PPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
487	EVQLLESGGGLVQPGGSLRLSCAASGFTFSFPMWVRQAPGKGLEWVSTISTSGGRYYRD SVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAKFRQYSGGFDYWGQGTITVTVSSGGGGS GGGSGGGSDIQLTQPNVSTSLGSTVKLSCTLSSGNIENNYVHWYQLYEGRSPTTMIYDD DKRPDGVDPDRFSGSIDRSSNSAFLTIHNVAIEDEAIYFCHSYVSSFNVFGGGKLTTLVLTTP APRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVIT LYC
488	DIQLTQPNVSTSLGSTVKLSCTLSSGNIENNYVHWYQLYEGRSPTTMIYDDDKRPDGVDPDR FSGSIDRSSNSAFLTIHNVAIEDEAIYFCHSYVSSFNVFGGGKLTTLVGGGSGGGSGGGG SEVQLLESGGGLVQPGGSLRLSCAASGFTFSFPMWVRQAPGKGLEWVSTISTSGGRYYR DSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCAKFRQYSGGFDYWGQGTITVTVSSTTP APRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVIT LYC
489	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVSRIIRSKYNNYATYY ADSVKDRFTISRDDSKNTLYLQMNSLRAEDTAVYYCARHGNFGNSYVSWFAYWGQGTMTVTVS SGGGSGGGSGGGGSAVVTQEPSTVSPGGTVTLTCSRSTGAVTTSNYANWVQKPGQAP RGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYCALWYSNLWVFGGGTKLTV LTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL SLVITLYC
490	QAVVTQEPSTVSPGGTVTLTCSRSTGAVTTSNYANWVQKPGQAPRGLIGGTNKRAPGTPA RFSGSLLGGKAALTLSGVQPEDEAEYCALWYSNLWVFGGGTKLTVLGGGSGGGSGGGGGS EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVSRIIRSKYNNYATYY ADSVKDRFTISRDDSKNTLYLQMNSLRAEDTAVYYCARHGNFGNSYVSWFAYWGQGTMTVTVS STTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL SLVITLYC
491	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVSRIIRSKYNNYATYY ADSVKDRFTISRDDSKNTLYLQMNSLRAEDTAVYYCARHGNFGNSYVSWFAYWGQGTMTVTVS SGGGSGGGSGGGGSAVVTQEPSTVSPGGTVTLTCSRSTGAVTTSNYANWVQKPGQAP RGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYCALWYSNLWVFGGGTKLTV LTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL SLVITLYC
492	QAVVTQEPSTVSPGGTVTLTCSRSTGAVTTSNYANWVQKPGQAPRGLIGGTNKRAPGTPA RFSGSLLGGKAALTLSGVQPEDEAEYCALWYSNLWVFGGGTKLTVLGGGSGGGSGGGGGS EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVSRIIRSKYNNYATYY ADSVKDRFTISRDDSKNTLYLQMNSLRAEDTAVYYCARHGNFGNSYVSWFAYWGQGTMTVTVS STTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL SLVITLYC
493	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVARIRSKYNNYATYY ADSVKDRFTISRDDSKNTLYLQMNSLRAEDTAVYYCARHGNFGNSYVSWFAYWGQGTMTVTVS SGGGSGGGSGGGGSAVVTQEPSTVSPGGTVTLTCSRSTGAVTTSNYANWVQKPGQAP RGLIGGTNKRAPWTPARFSGSLLGGKAALTLSGVQPEDEAEYCALWYSNLWVFGGGTKLTV LTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL SLVITLYC
494	QAVVTQEPSTVSPGGTVTLTCSRSTGAVTTSNYANWVQKPGQAPRGLIGGTNKRAPWTPA RFSGSLLGGKAALTLSGVQPEDEAEYCALWYSNLWVFGGGTKLTVLGGGSGGGSGGGGGS EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVARIRSKYNNYATYY ADSVKDRFTISRDDSKNTLYLQMNSLRAEDTAVYYCARHGNFGNSYVSWFAYWGQGTMTVTVS STTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL SLVITLYC
495	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVARIRSKYNNYATYY ADSVKDRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGNSYVSWFAYWGQGTMTVTVS SGGGSGGGSGGGGSAVVTQEPSTVSPGGTVTLTCSRSTGAVTTSNYANWVQKPGQAP RGLIGGTNKRAPWTPARFSGSLLGGKAALTLSGVQPEDEAEYCALWYSNLWVFGGGTKLTV LTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL SLVITLYC
496	QAVVTQEPSTVSPGGTVTLTCSRSTGAVTTSNYANWVQKPGQAPRGLIGGTNKRAPWTPA

	RFSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNLWVFGGGTKLTVLGGGSGGGGSGGGGS EVQLVESGGGLVQPGGSLRLSCAASGFTTFSTYAMNWVRQAPGKGLEWVARIRSKYNNYATYY ADSVKDRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGNSYVSWFAYWGQGTMTVTS STTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLL SLVITLYC
497	EVQLVESGGGLVQPGGSLRLSCAASGFTTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATYY ADSVKDRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGNSYVSWFAYWGQGTMTVTS SGGGSGGGGSGGGGSAVVVTQEPSTVSPGGTVTLTCSRSTGAVTTSNYANWYQKPGQAP RGLIGGTNKRAPWTPARFSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNLWVFGGGTKLTV LTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLL SLVITLYC
498	QAVVTQEPSTVSPGGTVTLTCSRSTGAVTTSNYANWYQKPGQAPRGLIGGTNKRAPWTPA RFSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNLWVFGGGTKLTVLGGGSGGGGSGGGGS EVQLVESGGGLVQPGGSLRLSCAASGFTTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATYY ADSVKDRFTISRDDSKNTLYLQMNSLRAEDTAVYYCVRHGNFGNSYVSWFAYWGQGTMTVTS STTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLL SLVITLYC
499	QVQLVESGGGVVQPGRSRLRLSCAASGFKFSGYGMHWVRQAPGKGLEWVAVIWDGSKKYYVD SVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCARQMGYWHFDLWGRGTLTVSSGGGSGG GGGSGGGGSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQKPGQAPRLLIYDASN RATGIPARFSGSGSGTDFTLTITSSLEPEDFAVYYCQQRSNWPPLTFGGGTKVEIKRTTTPAP RPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLY C
500	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQKPGQAPRLLIYDASN RATGIPARF SGSGSGTDFTLTITSSLEPEDFAVYYCQQRSNWPPLTFGGGTKVEIKRGGGSGGGGSGGGGS QVQLVESGGGVVQPGRSRLRLSCAASGFKFSGYGMHWVRQAPGKGLEWVAVIWDGSKKYYVD SVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCARQMGYWHFDLWGRGTLTVSSTTTPAP RPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLY C
501	QVQLVQSGGGVVQPGRSRLRLSCKASGYTFTRYTMHWVRQAPGKGLEWIGYINPSRGYTNYNQ KVKDRFTISRDNKNTAFLQMDSLRPEDTGVIYFCARYYDDHYCLDYWGQGTPTVTVSSGGGGS GGGSGGGGSDIQMTQSPSSLSASVGDRTVITCSASSSVSYMNWYQQTGPKAPKRWIYDTSK LASGVP SRFSGSGSGTDYFTTITSSLPEDIATYYCQWSSNPF TFQGT KLQITTTTPAPRP PTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
502	DIQMTQSPSSLSASVGDRTVITCSASSSVSYMNWYQQTGPKAPKRWIYDTSKLASGVP SRFS GSGSGTDYFTTITSSLPEDIATYYCQWSSNPF TFQGT KLQITGGGSGGGGSGGGGSGQVQ LVQSGGGVVQPGRSRLRLSCKASGYTFTRYTMHWVRQAPGKGLEWIGYINPSRGYTNYNQVK DRFTISRDNKNTAFLQMDSLRPEDTGVIYFCARYYDDHYCLDYWGQGTPTVTVSSTTTPAPRP PTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
503	EVQLLEQSGAELVRPGTSVKISCKASGYAFTNYWLGWVKQRP GHGLEWIGDIFPGSGNIHYN EKFKGKATLTADKSSSTAYMQLSSSLTFEDSAVYFCARLRNWDEPMDYWGQGT TVTVSSGGGG SGGGSGGGGSELVMTQSPSSSLTVTAGEKVTMSCKSSQSLNLSGNQKNYLTWYQKPGQPPK LLIYWASTRESGVPDRFTGSGSGTDFTLTITSSVQAE DLAVYYCQNDYSYPLTFGAGTKLEIK TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLS LVITLYC
504	ELVMTQSPSSSLTVTAGEKVTMSCKSSQSLNLSGNQKNYLTWYQKPGQPPKLLIYWASTRES GVPDRFTGSGSGTDFTLTITSSVQAE DLAVYYCQNDYSYPLTFGAGTKLEIKGGGSGGGGSG GGGSEVQLLEQSGAELVRPGTSVKISCKASGYAFTNYWLGWVKQRP GHGLEWIGDIFPGSGN IHYN EKFKGKATLTADKSSSTAYMQLSSSLTFEDSAVYFCARLRNWDEPMDYWGQGT TVTVSS TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLS LVITLYC
505	EVQLVESGGGLVQPGGSLRLSCAASGFTTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNLSLKTEDTAVYYCARHGNFGNSYVSWFAYWGQGT TVTVS SGGGSGGGGSGGGGSGTVVVTQEPSTVSPGGTVTLTCSRSTGAVTTSNYANWYQKPGQAP RGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNLWVFGGGTKLTV LTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLL SLVITLYC
506	QTVVTQEPSTVSPGGTVTLTCSRSTGAVTTSNYANWYQKPGQAPRGLIGGTNKRAPGTPA RFSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNLWVFGGGTKLTVLGGGSGGGGSGGGGS

	EVQLVESGGGLVQPGGSLRLSCAASGFTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATYY AASVKGRFTISRDDSKNTLYLQMNLSLKTEDTAVYYCARHGNFGNSYVSWFAYWGQGLVTVS STTTTPAPRPPTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLL SLVITLYC
507	EVQLLESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVSRIIRSKYNNYATYY ADSVKGRFTISRDDSKNTLYLQMNLSRAEDTAVYYCVRHGNFGNSYVSWFAYWGQGLVTVS SGGGSGGGSGGGSGGQAVVTQEPSTLVSPGGTVTLTCSSTGAVTTSNYANWVQEKPGQAF RGLIGGTNKRAPGTPARFSGSLLGGKAALTLGAQPEDEAEYCALWYSNLWVFGGGTKLTV LTTTPAPRPPTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLL SLVITLYC
508	QAVVTQEPSTLVSPGGTVTLTCSSTGAVTTSNYANWVQEKPGQAFRGLIGGTNKRAPGTPA RFGSLLGGKAALTLGAQPEDEAEYCALWYSNLWVFGGGTKLTVLGGGGSGGGSGGGGS EVQLLESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGLEWVSRIIRSKYNNYATYY ADSVKGRFTISRDDSKNTLYLQMNLSRAEDTAVYYCVRHGNFGNSYVSWFAYWGQGLVTVS STTTTPAPRPPTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLL SLVITLYC
509	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMNWVRQAPGKGLEWVSRIIRSKYNNYATYY ADSVKGRFTISRDDSKNTLYLQMNLSRAEDTAVYYCVRHTTTPSSYVSYGYWGQGLVTVS SGGGSGGGSGGGSGGQAVVTQEPSTLVSPGGTVTLTCSSTGAVTTSNYANWVQEKPGQAF RGLIGGTNKRAPGTPARFSGSLLGGKAALTLGAQPEDEAEYCALWYSNLWVFGGGTKLTV LTTTPAPRPPTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLL SLVITLYC
510	QAVVTQEPSTLVSPGGTVTLTCSSTGAVTTSNYANWVQEKPGQAFRGLIGGTNKRAPGTPA RFGSLLGGKAALTLGAQPEDEAEYCALWYSNLWVFGGGTKLTVLGGGGSGGGSGGGGS EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMNWVRQAPGKGLEWVSRIIRSKYNNYATYY ADSVKGRFTISRDDSKNTLYLQMNLSRAEDTAVYYCVRHTTTPSSYVSYGYWGQGLVTVS STTTTPAPRPPTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLL SLVITLYC
511	QVQLVQSGAEVKKPGASVKVSCKASGYSTGYTMNWVRQAPGQGLEWMGLINPYNSTNYAQ KLQGRVTMTDTSTSTAYMELRSLRSDDTAVYYCARVALRVALDYWGQGLVTVSSGGGGSG GGSGGGGSDIQMTQSPSSLSASVGDRTVITCKASQNVATHVGYQQKPKGKAPKRLIYSASY RYSQVPSRFSGSGSGTEFTLTISNLPQEDFATYYCQQYNRYPYTFGQGTKEIKTTTPAPRP PTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
512	DIQMTQSPSSLSASVGDRTVITCKASQNVATHVGYQQKPKGKAPKRLIYSASYRYSQVPSRF SGSGSGTEFTLTISNLPQEDFATYYCQQYNRYPYTFGQGTKEIKGGGGSGGGSGGGGSQV QLVQSGAEVKKPGASVKVSCKASGYSTGYTMNWVRQAPGQGLEWMGLINPYNSTNYAQKL QGRVTMTDTSTSTAYMELRSLRSDDTAVYYCARVALRVALDYWGQGLVTVSSTTTTPAPRP PTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
513	EVQLVESGGGLVQPGSRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVSGISWNSGSGIGYAD SVKGRFTISRDNKNSLYLQMNLSRAEDTALYYCAKDSRGYGDYRLGGAYWGQGLVTVSSG GGSGGGGGSGGGGSEIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLI YGASTRATGIPARFSGSGSGTEFTLTISLQSEDFAVYYCQQYNWNPWTFGQGTKEIKTTT PAPRPPTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVI TLYC
514	EIVMTQSPATLSVSPGERATLSCRASQSVSSNLAWYQQKPGQAPRLLIYGASTRATGIPARF SGSGSGTEFTLTISLQSEDFAVYYCQQYNWNPWTFGQGTKEIKGGGGSGGGSGGGGSEV QLVESGGGLVQPGSRSLRLSCAASGFTFDDYAMHWVRQAPGKGLEWVSGISWNSGSGIGYADSV KGRFTISRDNKNSLYLQMNLSRAEDTALYYCAKDSRGYGDYRLGGAYWGQGLVTVSSTTT PAPRPPTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVI TLYC
515	EVQLVQSGAEVKKPGASVKVSCKASGFSFTNYYVHWMRQAPGQGLEWMGWISPGSDNTKYNE KFKGRVTMTDRDTSISTAYMELSLRSDDTAVYYCARDYGNYYFDYWGQGTTVTVSSGGGGSG GGGGSGGGGSDIVMTQSPDSLAVSLGERATINCKSSQSLLSNRTRKKNYLAWYQQKPGQPPKL LIYWASTRESGVPDRFSGSGSGTDFTLTISLQAEADVAVYYCKQSYILRTFGGGTKVEIKTT TPAPRPPTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLV ITLYC
516	DIVMTQSPDSLAVSLGERATINCKSSQSLLSNRTRKKNYLAWYQQKPGQPPKLLIYWASTRES GVPDRFSGSGSGTDFTLTISLQAEADVAVYYCKQSYILRTFGGGTKVEIKGGGGSGGGSGG GGSEVQLVQSGAEVKKPGASVKVSCKASGFSFTNYYVHWMRQAPGQGLEWMGWISPGSDNTK

	YNEKFKGRVTMTRDTSISTAYMELSLRLSDDTAVYYCARDGYGNYFDYWGQGTTVTVSSTT TPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLV ITLYC
517	EVQLVESGGGLVQPGRSLRLSCAASGFTFDDYSMHWVRQAPGKGLEWVSGISWNSGSKGYAD SVKGRFTISRDNANKNSLYLQMNLSRAEDTALYYCAKYGSGYGFYHYGLDVWGQGTTVTVSS GGGGSGGGSGGGSDIQMTQSPSSLSASVGDRTITCRASQSISSYLNWYQQKPKGAPKLL IYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQSYSTPPITFGQGTREIKT TTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSL VITLYC
518	DIQMTQSPSSLSASVGDRTITCRASQSISSYLNWYQQKPKGAPKLLIYAASSLQSGVPSRF SGSGSGTDFTLTISLQPEDFATYYCQQSYSTPPITFGQGTREIKGGGGSGGGSGGGGSE VQLVESGGGLVQPGRSLRLSCAASGFTFDDYSMHWVRQAPGKGLEWVSGISWNSGSKGYAD VKGRFTISRDNANKNSLYLQMNLSRAEDTALYYCAKYGSGYGFYHYGLDVWGQGTTVTVSS TTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSL VITLYC
519	EVQLVESGGGLVQPGRSLRLSCAASGFTFDDYSMHWVRQAPGKGLEWVSGISWNSGSIYAD SVKGRFTISRDNANKNSLYLQMNLSRAEDTALYYCAKYGSGYGFYYYGMDVWGQGTTVTVSS GGGGSGGGSGGGSDIQMTQSPSSLSASVGDRTITCRASQSISSYLNWYQQKPKGAPKLL IYAASSLQSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQSYSTPPITFGQGTREIKT TTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSL VITLYC
520	DIQMTQSPSSLSASVGDRTITCRASQSISSYLNWYQQKPKGAPKLLIYAASSLQSGVPSRF SGSGSGTDFTLTISLQPEDFATYYCQQSYSTPPITFGQGTREIKGGGGSGGGSGGGGSE VQLVESGGGLVQPGRSLRLSCAASGFTFDDYSMHWVRQAPGKGLEWVSGISWNSGSIYADS VKGRFTISRDNANKNSLYLQMNLSRAEDTALYYCAKYGSGYGFYYYGMDVWGQGTTVTVSS TTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSL VITLYC
521	EVQLVESGGGLVQPGGSLRLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYY ADSVKGRFTISRDDSKNTLYLQMNLSRAEDTAVYYCVRHGNFGNSYVSFYAYWGQGTTVTVS SGGGSGGGSGGGSEIVVTQSPATLSVSPGERATLSCRSTGAVTESNYANWVQEKPGQA FRGLIGGANKRAPGVPARFSGSLSGDEATLTISLQSEDFAVYYCALFYSNWVFGQGTKE IKTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL LSLVITLYC
522	EIVVTQSPATLSVSPGERATLSCRSTGAVTESNYANWVQEKPGQAFRGLIGGANKRAPGVP ARFSGSLSGDEATLTISLQSEDFAVYYCALFYSNWVFGQGTKEIKGGGGSGGGSGGGG SEVQLVESGGGLVQPGGSLRLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATY YADSVKGRFTISRDDSKNTLYLQMNLSRAEDTAVYYCVRHGNFGNSYVSFYAYWGQGTTVTV SSTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL LSLVITLYC
523	EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYY ADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTTLTVS SGGGSGGGSGGGSGQTVVTQEPSTVSPGGTVTLTCGSSTGAVTSGNYPNWVQKPGQAP RGLIGGTFKFLAPGTPARFSGSLGGAALTLTSGVQPEDEAEYYCVLWYSNRWVFGGQTKLTV LTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL SLVITLYC
524	QTVVTQEPSTVSPGGTVTLTCGSSTGAVTSGNYPNWVQKPGQAPRGLIGGTFKFLAPGTPA RFSGSLGGAALTLTSGVQPEDEAEYYCVLWYSNRWVFGGQTKLTVLGGGGSGGGSGGGG EVQLVESGGGLVQPGGSLKLSCAASGFTFNKYAMNWVRQAPGKGLEWVARIRSKYNNYATYY ADSVKDRFTISRDDSKNTAYLQMNNLKTEDTAVYYCVRHGNFGNSYISYWAYWGQGTTLTVS STTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLL SLVITLYC
525	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDYYMTWVRQAPGKGLEWVAFIRNRARGYTS NPSVKGRFTISRDNANKNSLYLQMNLSRAEDTAVYYCARDRPSYVLDYWGQGTTVTVSSGGG SGGGSGGGSGGGSDIVMTQSPDSLAVSLGERATINCKSSQSLFNVRSRKNYLAWYQQKPGQPP KLLISWASTRESGVPDRFSGSGSGTDFTLTISLQAEADVAVYYCKQSYDLFTFGSGTKLEIK TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLS LVITLYC
526	DIVMTQSPDSLAVSLGERATINCKSSQSLFNVRSRKNYLAWYQQKPGQPPKLLISWASTRES GVPDRFSGSGSGTDFTLTISLQAEADVAVYYCKQSYDLFTFGSGTKLEIKGGGGSGGGSGG

	GGSEVQLVESGGGLVQPGGSLRLSCAASGFTTFSDYYMTWVRQAPGKGLEWVAFIRNRARGYT SDHNPVSKGRFTISRDNAKNSLYLQMNLSRAEDTAVYYCARDRPSYYVLDYWGQGTITVTVSS TTTTAPRPPTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLS LVITLYC
527	EVQLVESGGGLVQPGGSLRLSCAASGFTTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNLSKTEDTAVYYCARHGNFNSYVSWFAYWGQGTITVTVS SGGGSGGGSGGGSGGGSTVVTQEPSTLVSPGGTVTLTCSRSTGAVTTSNYANWVQKPGQAP RGLIGGTNKRAPGTPARFSGSLLGGKAALTLSGVQPEDEAEYYCALWYSNLWVFGGGTKLTV LTTTTAPRPPTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLL SLVITLYC
528	QTVVTQEPSTLVSPGGTVTLTCSRSTGAVTTSNYANWVQKPGQAPRGLIGGTNKRAPGTPA RFGSLLGGKAALTLSGVQPEDEAEYYCALWYSNLWVFGGGTKLTVLGGGGSGGGSGGGGS EVQLVESGGGLVQPGGSLRLSCAASGFTTFNTYAMNWVRQAPGKGLEWVARIRSKYNNYATYY AASVKGRFTISRDDSKNSLYLQMNLSKTEDTAVYYCARHGNFNSYVSWFAYWGQGTITVTVS STTTAPRPPTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLL SLVITLYC
529	QVQLVQSGAEVKKPGASVKVSKASGFNIKDYMHVVRQAPGQRLWGMWIDLENANTIYDA KFQGRVTITRDTSASTAYMELSSLRSEDVAVYYCARDAYGRFYDVWGQGTITVTVSSGGGS GGGGSGGGSDIVMTQSPDSLAVSLGERATINCKSSQSLLNARTGKNYLAWYQKPGQPPKL LIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEADVAVYYCKQSYSRRTFGGGTKVEIKTT TPAPRPPTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLV ITLYC
530	DIVMTQSPDSLAVSLGERATINCKSSQSLLNARTGKNYLAWYQKPGQPPKLLIYWASTRES GVPDRFSGSGSGTDFTLTISSLQAEADVAVYYCKQSYSRRTFGGGTKVEIKGGGGSGGGSGG GGSQVQLVQSGAEVKKPGASVKVSKASGFNIKDYMHVVRQAPGQRLWGMWIDLENANTI YDAKFQGRVTITRDTSASTAYMELSSLRSEDVAVYYCARDAYGRFYDVWGQGTITVTVSSTT TPAPRPPTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLV ITLYC
531	QVQLVQSGGGVVPGRSLRLSCKASGYTFTRYTMHWVRQAPGKGLEWIGYINPSRGYTNYNQ KVKDRFTISRDNKNATFLQMDSLRPEDTGVYFCARYYDDHYCLDYWGQGTPTVTVSSGGGS GGGGSGGGSDIQMTQSPSSLSASVGDRTVITCSASSSVSYMNWYQQTGKAPKRWIYDTSK LASGVP SRFSGSGSGTDYFTTISSLQPEDIATYYCQWSSNPFTFGQGTKLQITTTTPAPRP PTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
532	DIQMTQSPSSLSASVGDRTVITCSASSSVSYMNWYQQTGKAPKRWIYDTSKLASGVP SRFS GSGSGTDYFTTISSLQPEDIATYYCQWSSNPFTFGQGTKLQITGGGGSGGGSGGGGSQVQ LVQSGGGVVPGRSLRLSCKASGYTFTRYTMHWVRQAPGKGLEWIGYINPSRGYTNYNQVK DRFTISRDNKNATFLQMDSLRPEDTGVYFCARYYDDHYCLDYWGQGTPTVTVSSSTTTAPRP PTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
533	QVQLVQSGPEVKKPGSSVKVSKASGYTFSRSTMHWVRQAPGQGLEWIGYINPSSAYTNYNQ KFKDRVTITADKSTSTAYMELSSLRSEDVAVYYCARPVHYDYNFGFPYWGQGTITVTVSSGGG SGGGSGGGSDIQMTQSPSTLSASVGDRTVMTCSASSSVSYMNWYQKPGKAPKRWIYDS SKLASGVP SRFSGSGSGTEYTLTISSLQPDDEFATYYCQWSSNPFTFGGGTKVEIKRTTTPA PRPPTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITL YC
534	DIQMTQSPSTLSASVGDRTVMTCSASSSVSYMNWYQKPGKAPKRWIYDSSKLASGVP SRFS GSGSGTEYTLTISSLQPDDEFATYYCQWSSNPFTFGGGTKVEIKRGGGGSGGGSGGGGSQV QLVQSGPEVKKPGSSVKVSKASGYTFSRSTMHWVRQAPGQGLEWIGYINPSSAYTNYNQKF KDRVTITADKSTSTAYMELSSLRSEDVAVYYCARPVHYDYNFGFPYWGQGTITVTVSSSTTTA PRPPTPAPTIIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITL YC
535	DVQLVQSGAEVKKPGASVKVSKASGYTFSRSTMHWVRQAPGQGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTITVTVSSSGGG SGGGSGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPFTFGGGTKVEIKASSPTPS PTGLTTAKMPSVPLSSDPLPHTTAFSPASTFERENDFSETTTLSPDNTSTQVSPDSLNDNA SAFNTTGVSSTQTPHLPHTHADSQTPSAGTDTQTFSGSAANAKLNPTPGSNATSDVPPERSTA STFPTDPVSPPLTTTSLAHHSSAALPARTSNTTITANTSDAYLNASETTTLSPSGSAVISTT TIATTPSKPTCDEKYANITVDYLYNKETKLF TAKLVNENVECGNNTCTNNEVHNLTCKNA SVSISHNSCTAPDKTLILDVPPGVEKFLQHDCTQVEKADTTICLKWKNIETFTCDTQNTITYR

	FQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSPGEPQIIFCRSE AAHQGVITWNPPQRSFHNFTLCYIKETEKDCLNLDKNLIKDYDLQNLKPYTKYVLSLHAYIIA KVQRNGSAAMCHFTTKSAPPSQVWNMTVSMTSDNSMHVKCRPPDRNGPHERYHLEVEAGNT LVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHHSTSYNSKALIAFLAFLIIV TSIALLVVLYKIYD
536	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFS SGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKSGGGSGGGSGGGGSDV QLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTITVTVSSASSPTPS PTGLTTAKMPSVPLSSDPLPHTTAFSPASTFERENDFSETTTSLSPDNTSTQVSPDSLDA SAFNTTGVSSVQTPHLPHTADSQTPSAGTDTQTFSGSAANAKLNPTPGSNAISDVPGERSTA STFPTDVPSPPLTTTSLAHSSAALPARTSNTTITANTSDAYLNASETTTSLSPSGSAVISTT TIATTPSKPTCDEKYANITVDYLYNKETKLF TAKLNVNENVECGNNTCTNNEVHNLTECKNA SVSISHNSCTAPDKTLILDVPPGVEKQQLHDCQVEKADTTICLKWKNIETFTCDTQONITYR FQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSPGEPQIIFCRSE AAHQGVITWNPPQRSFHNFTLCYIKETEKDCLNLDKNLIKDYDLQNLKPYTKYVLSLHAYIIA KVQRNGSAAMCHFTTKSAPPSQVWNMTVSMTSDNSMHVKCRPPDRNGPHERYHLEVEAGNT LVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHHSTSYNSKALIAFLAFLIIV TSIALLVVLYKIYD
537	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTITVTVSSSGGGG SGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKASSPTPS PTDAYLNASETTTSLSPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLF TAKLNV NENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKQQLHDCQVEK ADTTICLKWKNIETFTCDTQONITYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKF TNASKIIKTDFGSPGEPQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLNLDKN LIKDYDLQNLKPYTKYVLSLHAYIIAKVQRNGSAAMCHFTTKSAPPSQVWNMTVSMTSDNSMH VKCRPPDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGE PFILHHSTSYNSKALIAFLAFLIIVTSIALLVVLYKIYD
538	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFS SGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKSGGGSGGGSGGGGSDV QLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTITVTVSSASSPTPS PTDAYLNASETTTSLSPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLF TAKLNV NENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKQQLHDCQVEK ADTTICLKWKNIETFTCDTQONITYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKF TNASKIIKTDFGSPGEPQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLNLDKN LIKDYDLQNLKPYTKYVLSLHAYIIAKVQRNGSAAMCHFTTKSAPPSQVWNMTVSMTSDNSMH VKCRPPDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGE PFILHHSTSYNSKALIAFLAFLIIVTSIALLVVLYKIYD
539	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTITVTVSSSGGGG SGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKASSPTPS PTGLTTAKMPSVPLSSDPLPHTTAFSPASTFERENDFSETTTSLSPDNTSTQVSPDSLDA SAFNTTGVSSVQTPHLPHTADSQTPSAGTDTQTFSGSAANAKLNPTPGSNAISDAYLNASET TTLSPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLF TAKLNVNENVECGNNTC TNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKQQLHDCQVEKADTTICLKWKNI IETFTCDTQONITYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDF GSPGEPQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLNLDKNLIKDYDLQNLKP YTKYVLSLHAYIIAKVQRNGSAAMCHFTTKSAPPSQVWNMTVSMTSDNSMHVKCRPPDRNG PHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHHSTSYN SKALIAFLAFLIIVTSIALLVVLYKIYD
540	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFS SGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKSGGGSGGGSGGGGSDV QLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTITVTVSSASSPTPS PTGLTTAKMPSVPLSSDPLPHTTAFSPASTFERENDFSETTTSLSPDNTSTQVSPDSLDA

	SAFNTTGVSSVQTPHLPHTHADSQTPSAGTDTQTTFSGSAANAKLNPTPGSNAISDAYLNASET TTLSPPSGSAVISTTTTIATTPSKPTCDEKYANITVDYLYNKETKLF TAKLNVNENVECGNNTC TNNEVHNLTECKNASVSI SHNSCTAPDKTLILDVPPGVEKFQ LHDCTQVEKADTTICLKWK IETFTCDTQONITYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDF GSPGEPQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCNLNDKNLIKDYDLQNLKP YTKYVLSLHAYIIIAKVQRNGSAAMCHFTTKSAPPSQVWNMTVSM TSDNSMHVKCRPPDRNG PHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHSTSYN SKALIAFLAFLIIIVTSIALLVVLYKIYD
541	DVQLVQSGAEVKKPGASVKVCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGT TTVTVSSSGGGG SGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQ QKPGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGG TKVEIKASSPTPS PTGLTTAKMPSVPLSSDPLPHTHTTAFSPASTFERENDFSETTTSLSPDNTSTQVSPDSL DNA SAFNTTDPVGERSTASTFP TDPVSP LTTTSLAHSSAALPARTSNTTITANTSDAYLNASE TTTSLSPSGSAVISTTTTIATTPSKPTCDEKYANITVDYLYNKETKLF TAKLNVNENVECGNNT CTNNEVHNLTECKNASVSI SHNSCTAPDKTLILDVPPGVEKFQ LHDCTQVEKADTTICLKWK NIETFTCDTQONITYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDF FGSPGEPQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCNLNDKNLIKDYDLQNLK PYTKYVLSLHAYIIIAKVQRNGSAAMCHFTTKSAPPSQVWNMTVSM TSDNSMHVKCRPPDRN GPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHSTSY NSKALIAFLAFLIIIVTSIALLVVLYKIYD
542	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQ QKPGKAPKRWIYDTSKVASGVPARF S GSGSGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGG TKVEIKSGGGSGGGSGGGGSDV QLVQSGAEVKKPGASVKVCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGT TTVTVSSASSPTPS PTGLTTAKMPSVPLSSDPLPHTHTTAFSPASTFERENDFSETTTSLSPDNTSTQVSPDSL DNA SAFNTTDPVGERSTASTFP TDPVSP LTTTSLAHSSAALPARTSNTTITANTSDAYLNASE TTTSLSPSGSAVISTTTTIATTPSKPTCDEKYANITVDYLYNKETKLF TAKLNVNENVECGNNT CTNNEVHNLTECKNASVSI SHNSCTAPDKTLILDVPPGVEKFQ LHDCTQVEKADTTICLKWK NIETFTCDTQONITYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDF FGSPGEPQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCNLNDKNLIKDYDLQNLK PYTKYVLSLHAYIIIAKVQRNGSAAMCHFTTKSAPPSQVWNMTVSM TSDNSMHVKCRPPDRN GPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHSTSY NSKALIAFLAFLIIIVTSIALLVVLYKIYD
543	DVQLVQSGAEVKKPGASVKVCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGT TTVTVSSSGGGG SGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQ QKPGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGG TKVEIKASSPTPS PTGVSSVQTPHLPHTHADSQTPSAGTDTQTTFSGSAANAKLNPTPGSNAISDVPGERSTASTFP TDPVSP LTTTSLAHSSAALPARTSNTTITANTSDAYLNASETTTSLSPSGSAVISTTTTIAT TPSKPTCDEKYANITVDYLYNKETKLF TAKLNVNENVECGNNTCTNNEVHNLTECKNASVSI SHNSCTAPDKTLILDVPPGVEKFQ LHDCTQVEKADTTICLKWKNIETFTCDTQONITYRFQCG NMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSPGEPQIIFCRSEAAHQ GVITWNPPQRSFHNFTLCYIKETEKDCNLNDKNLIKDYDLQNLKP YTKYVLSLHAYIIIAKVQ RNGSAAMCHFTTKSAPPSQVWNMTVSM TSDNSMHVKCRPPDRNGPHERYHLEVEAGNTLVRN ESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHSTSYNSKALIAFLAFLIIIVTSIA LLVVLYKIYD
544	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQ QKPGKAPKRWIYDTSKVASGVPARF S GSGSGTDYSLTINSLEAEDAATYYCQOWSSNPLTFGGG TKVEIKSGGGSGGGSGGGGSDV QLVQSGAEVKKPGASVKVCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGT TTVTVSSASSPTPS PTGVSSVQTPHLPHTHADSQTPSAGTDTQTTFSGSAANAKLNPTPGSNAISDVPGERSTASTFP TDPVSP LTTTSLAHSSAALPARTSNTTITANTSDAYLNASETTTSLSPSGSAVISTTTTIAT TPSKPTCDEKYANITVDYLYNKETKLF TAKLNVNENVECGNNTCTNNEVHNLTECKNASVSI SHNSCTAPDKTLILDVPPGVEKFQ LHDCTQVEKADTTICLKWKNIETFTCDTQONITYRFQCG NMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSPGEPQIIFCRSEAAHQ GVITWNPPQRSFHNFTLCYIKETEKDCNLNDKNLIKDYDLQNLKP YTKYVLSLHAYIIIAKVQ RNGSAAMCHFTTKSAPPSQVWNMTVSM TSDNSMHVKCRPPDRNGPHERYHLEVEAGNTLVRN ESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHSTSYNSKALIAFLAFLIIIVTSIA

	LLVVLYKIYD
545	DVQLVQSGAEVKKPGASVKVSCASGYTFTRYTMHWVRQAPGGQLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTTVTVSSSSGGGG SGGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGTKEIKASSPTPS PTGLTTAKMPSVPLSDPLPHTHTAFSPASTFERENDFSETTSLSPDNTSTQVSPDSLNDNA SAFNTTDAYLNASETTTLSPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLF KLVNENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKQQLHDC TQVEKADTTICLKWKNIETFTCDTQNTYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYN NHKFTNASKIIKTDFGSPGEPQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLN LDKNLIKDYDLQNLKPYTKYVLSLHAYIIAKVQRNGSAAMCHFTTKSAPPSQVWNMTVSM TSDNSMHVKCRPPDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFH NGDYPGEPFILHHSTSYNSKALIAFLAFLIIVTSIALLVVLYKIYD
546	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARF SGSGGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGTKEIKSGGGGSGGGGSGGGGSDV QLVQSGAEVKKPGASVKVSCASGYTFTRYTMHWVRQAPGGQLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTTVTVSSASSPTPS PTGLTTAKMPSVPLSDPLPHTHTAFSPASTFERENDFSETTSLSPDNTSTQVSPDSLNDNA SAFNTTDAYLNASETTTLSPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLF KLVNENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKQQLHDC TQVEKADTTICLKWKNIETFTCDTQNTYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYN NHKFTNASKIIKTDFGSPGEPQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLN LDKNLIKDYDLQNLKPYTKYVLSLHAYIIAKVQRNGSAAMCHFTTKSAPPSQVWNMTVSM TSDNSMHVKCRPPDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFH NGDYPGEPFILHHSTSYNSKALIAFLAFLIIVTSIALLVVLYKIYD
547	DVQLVQSGAEVKKPGASVKVSCASGYTFTRYTMHWVRQAPGGQLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTTVTVSSSSGGGG SGGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGTKEIKASSPTPS PTGVSSVQTPHLPHTHDSQTPSAGTDQTFSGSAANAKLNPTPGSNAISDAYLNASETTTL SPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLF TAKLVNENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKQQLHDC TQVEKADTTICLKWKNIETFTCDTQNTYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYN NHKFTNASKIIKTDFGSPGEPQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLN LDKNLIKDYDLQNLKPYTKYVLSLHAYIIAKVQRNGSAAMCHFTTKSAPPSQVWNMTVSM TSDNSMHVKCRPPDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFH NGDYPGEPFILHHSTSYNSKALIAFLAFLIIVTSIALLVVLYKIYD
548	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARF SGSGGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGTKEIKSGGGGSGGGGSGGGGSDV QLVQSGAEVKKPGASVKVSCASGYTFTRYTMHWVRQAPGGQLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTTVTVSSASSPTPS PTGVSSVQTPHLPHTHDSQTPSAGTDQTFSGSAANAKLNPTPGSNAISDAYLNASETTTL SPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLF TAKLVNENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKQQLHDC TQVEKADTTICLKWKNIETFTCDTQNTYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYN NHKFTNASKIIKTDFGSPGEPQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLN LDKNLIKDYDLQNLKPYTKYVLSLHAYIIAKVQRNGSAAMCHFTTKSAPPSQVWNMTVSM TSDNSMHVKCRPPDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFH NGDYPGEPFILHHSTSYNSKALIAFLAFLIIVTSIALLVVLYKIYD
549	DVQLVQSGAEVKKPGASVKVSCASGYTFTRYTMHWVRQAPGGQLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTTVTVSSSSGGGG SGGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGTKEIKASSPTPS PTDVPGERSTASTFPTDPVSPLTTTSLAHSSAALPARTSNTTITANTSDAYLNASETTTL SPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLF TAKLVNENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKQQLHDC TQVEKADTTICLKWKNIETFTCDTQNTYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYN NHKFTNASKIIKTDFGSPGEPQIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLN LDKNLIKDYDLQNLKPYTKYVLSLHAYIIAKVQRNGSAAMCHFTTKSAPPSQVWNMTVSM TSDNSMHVKCRPPDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFH NGDYPGEPFILHHSTSYNSKALIAFLAFLIIVTSIALLVVLYKIYD

	RYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHHSTSYNSKALIAFLAFLIIIVTSIALLVVLYKIYD
550	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKSGGGSGGGSGGGGSDVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTITVTVSSASSPTPSPTDVPGERSTASTFPTDPVSPLTTTSLAHSSAALPARTSNTTITANTSDAYLNASETTTLSPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLTAKLNVNENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKFLHDCTQVEKADTTICLKWKNIETFTCDTQNTITYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSGPGEPIIFCRSEAAHQGVITWNPPQRSFHNFTLCYIKETEKDCLNLDKNLIKDYDLQNLKPYTKYVLSLHAYIIAKVQRNGSAAMCHFTTKSAPPSQVWNMTVSMSTSDNSMHVKCRPPDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHHSTSYNSKALIAFLAFLIIIVTSIALLVVLYKIYD
551	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTITVTVSSSGGGSGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKASSPTPSPTDAYLNASETTTLSPPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLTAKLNVNENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPGVEKFLHDCTQVEKADTTICLKWKNIETFTCDTQNTITYRFQCGNMIFDNKEIKLENLEPEHEYKCDSEILYNNHKFTNASKIIKTDFGSPSQVWNMTVSMSTSDNSMHVKCRPPDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHHSTSYNSKALIAFLAFLIIIVTSIALLVVLYKIYD
552	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKSGGGSGGGSGGGGSDVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTITVTVSSASSPTPSPTDAYLNASETTTLSPPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLTAKLNVNENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPSQVWNMTVSMSTSDNSMHVKCRPPDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHHSTSYNSKALIAFLAFLIIIVTSIALLVVLYKIYD
553	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTITVTVSSSGGGSGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKASSPTPSPTDAYLNASETTTLSPPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLTAKLNVNENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPSQVWNMTVSMSTSDNSMHVKCRPPDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHHSTSYNSKALIAFLAFLIIIVTSIALLVVLYKIYD
554	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKSGGGSGGGSGGGGSDVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTITVTVSSASSPTPSPTDAYLNASETTTLSPPSGSAVISTTTIATTPSKPTCDEKYANITVDYLYNKETKLTAKLNVNENVECGNNTCTNNEVHNLTECKNASVSISHNSCTAPDKTLILDVPPSQVWNMTVSMSTSDNSMHVKCRPPDRNGPHERYHLEVEAGNTLVRNESHKNCDFRVKDLQYSTDYTFKAYFHNGDYPGEPFILHHSTSYNSKALIAFLAFLIIIVTSIALLVVLYKIYD
555	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTITVTVSSSGGGSGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKASAPIEPRTIFFCERNPKPVINIIDADLPNTSPFTAELTHGASANWTIQYNDPTQESIILKPKMALVGVGDIKINLKLMDNQNKDQVTTLEVSVCDEGAAGVCRKAQPVAGLQIPAILGILGGILALLILILLLLLLFLRRRA
556	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKSGGGSGGGSGGGGSDV

	QLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGGGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATYYCARYDDHYCLDYWGQGTTVTVSSASAPIPE PRTIFFCERNPKPQVINI IDADLPNTSPFTAELTHGASANWTIQYNDPTQESIILKPKMAL EVGDYKINLKLMDNQNKDQVTTLEVSVCDCEGAAGVCRKAQPVEAGLQIPAILGILGGILAL LILILLLLLLFLRRRA
557	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGGGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYDDHYCLDYWGQGTTVTVSSSGGGG SGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKASAPIFV PPEKRVESSEDFGVGQEIITSYTAQEPDTFMEQKITRYRIWRDTANWLEINPDTGAISTRAELD REDFEHVKNSTY TALIIATDNGSPVATGTGTLILLILSDVNDNAPIPEPRTIFFCERNPKPQV INI IDADLPNTSPFTAELTHGASANWTIQYNDPTQESIILKPKMALEVGDYKINLKLMDNQ NKDQVTTLEVSVCDCEGAAGVCRKAQPVEAGLQIPAILGILGGILALLILILLLLLLFLRRRA
558	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDTSKVASGVPARF SGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKSGGGSGGGSGGGGSDV QLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGGGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATYYCARYDDHYCLDYWGQGTTVTVSSASAPIFV PPEKRVESSEDFGVGQEIITSYTAQEPDTFMEQKITRYRIWRDTANWLEINPDTGAISTRAELD REDFEHVKNSTY TALIIATDNGSPVATGTGTLILLILSDVNDNAPIPEPRTIFFCERNPKPQV INI IDADLPNTSPFTAELTHGASANWTIQYNDPTQESIILKPKMALEVGDYKINLKLMDNQ NKDQVTTLEVSVCDCEGAAGVCRKAQPVEAGLQIPAILGILGGILALLILILLLLLLFLRRRA
559	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGGGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYDDHYCLDYWGQGTTVTVSSSGGGG SGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKASNPPIF NPTTYKGQVPENEANVVITTLKVTADAPNTPAWEAVYTILNDDGGQFVVTNPNVNDGILK TAKGLDFAKQQYILHVAVTNVVPEVSLTTSTATVTVDVLDVNEAPIFVPPPEKRVESSEDF GVGQEIITSYTAQEPDTFMEQKITRYRIWRDTANWLEINPDTGAISTRAELDREDFEHVKNSTY TALIIATDNGSPVATGTGTLILLILSDVNDNAPIPEPRTIFFCERNPKPQVINI IDADLPNT SPFTAELTHGASANWTIQYNDPTQESIILKPKMALEVGDYKINLKLMDNQNKDQVTTLEVS VCDCEGAAGVCRKAQPVEAGLQIPAILGILGGILALLILILLLLLLFLRRRA
560	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDTSKVASGVPARF SGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKSGGGSGGGSGGGGSDV QLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGGGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATYYCARYDDHYCLDYWGQGTTVTVSSASNPPIF NPTTYKGQVPENEANVVITTLKVTADAPNTPAWEAVYTILNDDGGQFVVTNPNVNDGILK TAKGLDFAKQQYILHVAVTNVVPEVSLTTSTATVTVDVLDVNEAPIFVPPPEKRVESSEDF GVGQEIITSYTAQEPDTFMEQKITRYRIWRDTANWLEINPDTGAISTRAELDREDFEHVKNSTY TALIIATDNGSPVATGTGTLILLILSDVNDNAPIPEPRTIFFCERNPKPQVINI IDADLPNT SPFTAELTHGASANWTIQYNDPTQESIILKPKMALEVGDYKINLKLMDNQNKDQVTTLEVS VCDCEGAAGVCRKAQPVEAGLQIPAILGILGGILALLILILLLLLLFLRRRA
561	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGGGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYDDHYCLDYWGQGTTVTVSSSGGGG SGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKASPEFTQ EVFKGSVMGALPGTSVMEVTATDADDVNTYNAAIAYTILSQDPELPDKNMFITINRNTGVI SVVTTGLDRESFPTYTLVVQAADLQGEGLSTTATAVITVTDNDNPPIFNPTTYKGQVPENE ANVITTLKVTADAPNTPAWEAVYTILNDDGGQFVVTNPNVNDGILKTAKGLDFAKQQY ILHVAVTNVVPEVSLTTSTATVTVDVLDVNEAPIFVPPPEKRVESSEDFGVGQEIITSYTAQ PDTFMEQKITRYRIWRDTANWLEINPDTGAISTRAELDREDFEHVKNSTY TALIIATDNGSPV ATGTGTLILLILSDVNDNAPIPEPRTIFFCERNPKPQVINI IDADLPNTSPFTAELTHGASA NWTIQYNDPTQESIILKPKMALEVGDYKINLKLMDNQNKDQVTTLEVSVCDCEGAAGVCRKA QPVEAGLQIPAILGILGGILALLILILLLLLLFLRRRA
562	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPGKAPKRWIYDTSKVASGVPARF SGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKSGGGSGGGSGGGGSDV QLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGGGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATYYCARYDDHYCLDYWGQGTTVTVSSASPEFTQ EVFKGSVMGALPGTSVMEVTATDADDVNTYNAAIAYTILSQDPELPDKNMFITINRNTGVI SVVTTGLDRESFPTYTLVVQAADLQGEGLSTTATAVITVTDNDNPPIFNPTTYKGQVPENE

	ANVVITTLKVTADADAPNTPAWEAVYTIILNDDGGQFVVTNPNVNDGILKTAKGLDFEAKQQY ILHVAVTNVVPPFEVSLTTSTATVTVDVLDVNEAIFVPPPEKRVEVSEDFGVGQEITSYTAQE PDTFMEQKITYRIWRDTANWLEINPDTGAISTRAELDREDFEHVKNSTYTALIIATDNGSPV ATGTGTLILLILSDVNDNAPIPEPRTIFFCERNPKPQVINIIDADLPNTSPFTAELTHGASA NWTIQYNDPTQESIILKPKMALEVGDYKINLKLMDNQNKDQVTTLEVSVCDEGAAGVCRKA QPVEAGLQIPAILGILGGILALLILILLILLFLRRRA
563	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTITVTVSSSGGGG SGGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPKGAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKTVEIKASPELPK PSISSNNSKPVEDKDAVAFTCEPETQDATYLWVNNQSLPVSRLQLSNGNRTLTLFNVTRN DTASYKCETQNPVSARRSDSVILNVLYGPDAPTISPLNTSYRSGENLNLSCHAAASNPPAQYS WVFNQGTQQSTQELFIPNITVNNSGSYTCQAHNSDTGLNRTTITVYAEPPKPFITSNNS NPVEDEDAVALTCEPEIQNTTYLWVNNQSLPVSRLQLSNDNRTLTLTLLSVTRNDVGPYECG IQNELSVDHSDPVILNVLYGPDPTISPSYTYRPGVNLNLSCHAAASNPPAQYSWLIDGNIQ QHTQELFISNITEKNSGLYTCQANNSASGHSRTTVKTIITVSAELPKPSISSNNSKPVEDKDA VAFTCEPEAQNTTYLWVNNQSLPVSRLQLSNGNRTLTLFNVTRNDARAYVCGIQNSVSAN RSDPVTLDVLYGPDPTIISPPDSSYLSGANLNLSCHSASNPSQYSWRINGIPQHTQVLF AKITPNNNGTYACFVSNLATGRNNSIVKSITVSKALIAFLAFLIIVTSIALLVVLYKIYD
564	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPKGAPKRWIYDTSKVASGVPARF SGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKTVEIKSGGGGSGGGGSGGGGSDV QLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTITVTVSSASPELPK PSISSNNSKPVEDKDAVAFTCEPETQDATYLWVNNQSLPVSRLQLSNGNRTLTLFNVTRN DTASYKCETQNPVSARRSDSVILNVLYGPDAPTISPLNTSYRSGENLNLSCHAAASNPPAQYS WVFNQGTQQSTQELFIPNITVNNSGSYTCQAHNSDTGLNRTTITVYAEPPKPFITSNNS NPVEDEDAVALTCEPEIQNTTYLWVNNQSLPVSRLQLSNDNRTLTLTLLSVTRNDVGPYECG IQNELSVDHSDPVILNVLYGPDPTISPSYTYRPGVNLNLSCHAAASNPPAQYSWLIDGNIQ QHTQELFISNITEKNSGLYTCQANNSASGHSRTTVKTIITVSAELPKPSISSNNSKPVEDKDA VAFTCEPEAQNTTYLWVNNQSLPVSRLQLSNGNRTLTLFNVTRNDARAYVCGIQNSVSAN RSDPVTLDVLYGPDPTIISPPDSSYLSGANLNLSCHSASNPSQYSWRINGIPQHTQVLF AKITPNNNGTYACFVSNLATGRNNSIVKSITVSKALIAFLAFLIIVTSIALLVVLYKIYD
565	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTITVTVSSSGGGG SGGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPKGAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKTVEIKASPELPK PSISSNNSKPVEDKDAVAFTCEPETQDATYLWVNNQSLPVSRLQLSNGNRTLTLFNVTRN DTASYKCETQNPVSARRSDSVILNVLYGPDAPTISPLNTSYRSGENLNLSCHAAASNPPAQYS WVFNQGTQQSTQELFIPNITVNNSGSYTCQAHNSDTGLNRTTITVYAEPPKPFITSNNS NPVEDEDAVALTCEPEIQNTTYLWVNNQSLPVSRLQLSNDNRTLTLTLLSVTRNDVGPYECG IQNELSVDHSDPVILNVLYGPDPTISPSYTYRPGVNLNLSCHAAASNPPAQYSWLIDGNIQ QHTQELFISNITEKNSGLYTCQANNSASGHSRTTVKTIITVSAELPKPSISSNNSKPVEDKDA VAFTCEPEAQNTTYLWVNNQSLPVSRLQLSNGNRTLTLFNVTRNDARAYVCGIQNSVSAN RSDPVTLDVLYGPDPTIISPPDSSYLSGANLNLSCHSASNPSQYSWRINGIPQHTQVLF AKITPNNNGTYACFVSNLATGRNNSIVKSITVSA
566	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPKGAPKRWIYDTSKVASGVPARF SGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKTVEIKSGGGGSGGGGSGGGGSDV QLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATYYCARYYDDHYCLDYWGQGTITVTVSSASPELPK PSISSNNSKPVEDKDAVAFTCEPETQDATYLWVNNQSLPVSRLQLSNGNRTLTLFNVTRN DTASYKCETQNPVSARRSDSVILNVLYGPDAPTISPLNTSYRSGENLNLSCHAAASNPPAQYS WVFNQGTQQSTQELFIPNITVNNSGSYTCQAHNSDTGLNRTTITVYAEPPKPFITSNNS NPVEDEDAVALTCEPEIQNTTYLWVNNQSLPVSRLQLSNDNRTLTLTLLSVTRNDVGPYECG IQNELSVDHSDPVILNVLYGPDPTISPSYTYRPGVNLNLSCHAAASNPPAQYSWLIDGNIQ QHTQELFISNITEKNSGLYTCQANNSASGHSRTTVKTIITVSAELPKPSISSNNSKPVEDKDA VAFTCEPEAQNTTYLWVNNQSLPVSRLQLSNGNRTLTLFNVTRNDARAYVCGIQNSVSAN RSDPVTLDVLYGPDPTIISPPDSSYLSGANLNLSCHSASNPSQYSWRINGIPQHTQVLF AKITPNNNGTYACFVSNLATGRNNSIVKSITVSA
567	DVQLVQSGAEVKKPGASVKVSKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAD

	SVKGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYYDDHYCLDYWGQGTTVTVSSSGGGG SGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPKGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKTVEIKASPPKPF ITSNNSNPVEDEDAVALTCEPEIQNTTYLWWVNNQSLPVSRLQLSNDNRTLTLLSVTRNDV GPYECGIQNELSVDHSDPVLNVLYGPDPTISPSTYYRPGVNLSSLCHAASNPPAQYSWL IDGNIQOHTQELFISNITEKNSGLYTCQANNSASGHSRTTVKTTITVSAELPKPSISSNNSKP VEDKDAVAFTCEPEAQNTTYLWWVNGQSLPVSRLQLSNGNRTLTLFNVTRNDARAYVCGIQ NSVSANRSDPVTLDVLYGPDTPIIISPDDSSYLSGANLNLCHSASNPSPQYSWRINGIPQOQ TQVLFIAKITPNNNGTYACFVSNLATGRNNSIVKSITVSA
568	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPKGKAPKRWIYDTSKVASGVPARF SGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKTVEIKSGGGSGGGSGGGGSDV QLVQSGAEVKKPGASVKVCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYYDDHYCLDYWGQGTTVTVSSASPPKPF ITSNNSNPVEDEDAVALTCEPEIQNTTYLWWVNNQSLPVSRLQLSNDNRTLTLLSVTRNDV GPYECGIQNELSVDHSDPVLNVLYGPDPTISPSTYYRPGVNLSSLCHAASNPPAQYSWL IDGNIQOHTQELFISNITEKNSGLYTCQANNSASGHSRTTVKTTITVSAELPKPSISSNNSKP VEDKDAVAFTCEPEAQNTTYLWWVNGQSLPVSRLQLSNGNRTLTLFNVTRNDARAYVCGIQ NSVSANRSDPVTLDVLYGPDTPIIISPDDSSYLSGANLNLCHSASNPSPQYSWRINGIPQOQ TQVLFIAKITPNNNGTYACFVSNLATGRNNSIVKSITVSA
569	DVQLVQSGAEVKKPGASVKVCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYYDDHYCLDYWGQGTTVTVSSSGGGG SGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPKGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKTVEIKASAEALPK PSISSNNSKPVEDKDAVAFTCEPEAQNTTYLWWVNGQSLPVSRLQLSNGNRTLTLFNVTRN DARAYVCGIQNSVSANRSDPVTLDVLYGPDTPIIISPDDSSYLSGANLNLCHSASNPSPQYS WRINGIPQOHTQVLFIAKITPNNNGTYACFVSNLATGRNNSIVKSITVSA
570	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPKGKAPKRWIYDTSKVASGVPARF SGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKTVEIKSGGGSGGGSGGGGSDV QLVQSGAEVKKPGASVKVCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYYDDHYCLDYWGQGTTVTVSSASAEALPK PSISSNNSKPVEDKDAVAFTCEPEAQNTTYLWWVNGQSLPVSRLQLSNGNRTLTLFNVTRN DARAYVCGIQNSVSANRSDPVTLDVLYGPDTPIIISPDDSSYLSGANLNLCHSASNPSPQYS WRINGIPQOHTQVLFIAKITPNNNGTYACFVSNLATGRNNSIVKSITVSA
571	DVQLVQSGAEVKKPGASVKVCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYYDDHYCLDYWGQGTTVTVSSSGGGG SGGGSGGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPKGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKTVEIKASPDAPT ISPLNTSYRSGENLNLCHAASNPPAQYSWVFNQTFQOSTQELFIPNITVNNSGSYTCQAHN SDTGLNRTTVTTITVYAEPPKPFITSNNSNPVEDEDAVALTCEPEIQNTTYLWWVNNQSLPV SPRLQLSNDNRTLTLLSVTRNDVGPYECGIQNELSVDHSDPVLNVLYGPDPTISPSTYY RPGVNLSSLCHAASNPPAQYSWLIDGNIQOHTQELFISNITEKNSGLYTCQANNSASGHSRT TVKTTITVSAELPKPSISSNNSKPVEDKDAVAFTCEPEAQNTTYLWWVNGQSLPVSRLQLSN GNRTLTLFNVTRNDARAYVCGIQNSVSANRSDPVTLDVLYGPDTPIIISPDDSSYLSGANLNL SCHSASNPSPQYSWRINGIPQOHTQVLFIAKITPNNNGTYACFVSNLATGRNNSIVKSITVS A
572	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQKPKGKAPKRWIYDTSKVASGVPARF SGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKTVEIKSGGGSGGGSGGGGSDV QLVQSGAEVKKPGASVKVCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYADSV KGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYYDDHYCLDYWGQGTTVTVSSASPDAPT ISPLNTSYRSGENLNLCHAASNPPAQYSWVFNQTFQOSTQELFIPNITVNNSGSYTCQAHN SDTGLNRTTVTTITVYAEPPKPFITSNNSNPVEDEDAVALTCEPEIQNTTYLWWVNNQSLPV SPRLQLSNDNRTLTLLSVTRNDVGPYECGIQNELSVDHSDPVLNVLYGPDPTISPSTYY RPGVNLSSLCHAASNPPAQYSWLIDGNIQOHTQELFISNITEKNSGLYTCQANNSASGHSRT TVKTTITVSAELPKPSISSNNSKPVEDKDAVAFTCEPEAQNTTYLWWVNGQSLPVSRLQLSN GNRTLTLFNVTRNDARAYVCGIQNSVSANRSDPVTLDVLYGPDTPIIISPDDSSYLSGANLNL SCHSASNPSPQYSWRINGIPQOHTQVLFIAKITPNNNGTYACFVSNLATGRNNSIVKSITVS A
573	DVQLVQSGAEVKKPGASVKVCKASGYTFTRYTMHWVRQAPGQGLEWIGYINPSRGYTNYAD SVKGRFTITTDKSTSTAYMELSSLRSEDATATYYCARYYDDHYCLDYWGQGTTVTVSSSGGGG

	SGGGSGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKASPDPT ISPSYTYRPGVNLSSLCHAASNPPAQYSLIDGNIQQHTQELFISNITEKNSGLYTQANN SASGHSRTTVKTTITVSAELPKPSISSNNSKPVEDKDAVAFTCEPEAQNTTYLWWVNGQSLPV SPRLQLSNGNRTLTLFNVTRNDARAYVCGIQNSVSANRSDPVTLDVLYGPDTPIIISPDDSSY LSGANLNLSCHSASNPPQYSWRINGIPQQHTQVLFIAKITPNNNGTYACFVSNLATGRNNS IVKSITVSA
574	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFS GSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKSGGGSGGGSGGGSDV QLVQSGAEVKKPGASVKVCKASGYTFTRYTMHWVRQAPGGGLEWIGYINPSRGYTNADSV KGRFTITTDKSTSTAYMELSSLRSEDATYYCARYDDHYCLDYWGQGTITVTVSSASPDPT ISPSYTYRPGVNLSSLCHAASNPPAQYSLIDGNIQQHTQELFISNITEKNSGLYTQANN SASGHSRTTVKTTITVSAELPKPSISSNNSKPVEDKDAVAFTCEPEAQNTTYLWWVNGQSLPV SPRLQLSNGNRTLTLFNVTRNDARAYVCGIQNSVSANRSDPVTLDVLYGPDTPIIISPDDSSY LSGANLNLSCHSASNPPQYSWRINGIPQQHTQVLFIAKITPNNNGTYACFVSNLATGRNNS IVKSITVSA
575	DVQLVQSGAEVKKPGASVKVCKASGYTFTRYTMHWVRQAPGGGLEWIGYINPSRGYTNAD SVKGRFTITTDKSTSTAYMELSSLRSEDATYYCARYDDHYCLDYWGQGTITVTVSSSGGG SGGGSGGGSDIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTS KVASGVPARFSGSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKASPDPT ISPDDSSYLSGANLNLSCHSASNPPQYSWRINGIPQQHTQVLFIAKITPNNNGTYACFVSN LATGRNNSIVKSITVSA
576	DIVLTQSPATLSLSPGERATLSCRASQSVSYMNWYQQKPGKAPKRWIYDTSKVASGVPARFS GSGSGTDYSLTINSLEAEDAATYYCQWSSNPLTFGGGKVEIKSGGGSGGGSGGGSDV QLVQSGAEVKKPGASVKVCKASGYTFTRYTMHWVRQAPGGGLEWIGYINPSRGYTNADSV KGRFTITTDKSTSTAYMELSSLRSEDATYYCARYDDHYCLDYWGQGTITVTVSSASPDPT ISPDDSSYLSGANLNLSCHSASNPPQYSWRINGIPQQHTQVLFIAKITPNNNGTYACFVSN LATGRNNSIVKSITVSA

d. Additional Tropism Polypeptides

Recombinant particles contemplated herein comprise at least one non-viral membrane-bound tropism polypeptide. In particular embodiments, it may be preferred, and in some cases necessary or advantageous, to engineer a recombinant particle that comprises

5 at least one additional non-viral membrane-bound tropism polypeptide. In some embodiments, a recombinant particle comprises two non-viral membrane-bound tropism polypeptides. In some embodiments, a recombinant particle comprises three non-viral membrane-bound tropism polypeptides.

In particular embodiments, a recombinant particle comprises a lipid bilayer, cell

10 membrane, or viral envelope comprising one or more mutated viral envelope glycoproteins that mediate fusion of the viral particle with a cell but that do not bind its cognate receptor expressed on a cell, and at least two non-viral membrane-bound tropism polypeptides, *e.g.*, a primary and/or secondary non-viral membrane bound tropism polypeptide, that direct the particle to bind one or more specific antigens expressed on a desired cell type, *e.g.*, an

15 immune effector cell. In preferred embodiments, the recombinant particle is a recombinant viral particle, *e.g.*, a retroviral or lentiviral particle.

In particular embodiments, wherein a recombinant particle comprises at least two non-viral membrane-bound tropism polypeptides, each non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain that binds an antigen expressed on an immune effector cell; a spacer polypeptide, a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a recombinant particle comprises at least two non-viral membrane-bound tropism polypeptides, one non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain that binds an antigen expressed on an immune effector cell including but not limited to the alpha, beta, gamma, or delta chain of the T cell receptor, CD2, CD3 δ , CD3 ϵ CD3 γ , CD4, CD8 α , and CD8 β ; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain; and another non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain that an antigen expressed on an immune effector cell including but not limited to the alpha or beta chain of a TCR, CD28, CD134 (OX40), CD137 (4-1BB), and CD278 (ICOS); a spacer polypeptide, a transmembrane domain or GPI anchor; and optionally an intracellular domain.

In particular embodiments, a recombinant particle comprises at least two non-viral membrane-bound tropism polypeptides, one non-viral membrane-bound tropism polypeptide comprises an extracellular antigen targeting domain that binds an antigen expressed on an immune effector cell including but not limited to the alpha, beta, gamma, or delta chain of the T cell receptor, CD2, CD3 δ , CD3 ϵ CD3 γ , CD4, CD8 α , and CD8 β ; a spacer polypeptide; a transmembrane domain or GPI anchor; and optionally an intracellular domain; and another non-viral membrane bound tropism polypeptide comprises all or part of a costimulatory molecule including but not limited to CD80, CD86, OX40L, 4-1BBL, and ICOSL or a functional fragment thereof. In particular embodiments, the functional fragment is a CD80, CD86, OX40L, 4-1BBL, and ICOSL comprising a C-terminal truncation that results in a cytoplasmic domain of about 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids or more). In particular embodiments, the functional fragment comprises, consists essentially of, or consists of the amino acid sequence set forth in any one of SEQ ID NOs: 577, 578, 579, 580, and 581.

In particular embodiments, a recombinant particle comprises a first non-viral membrane-bound tropism polypeptide comprising an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising a

CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, a VH and VL, and/or an scFv set forth in Table 5; a spacer comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 411, 412, and 413, SEQ ID NOs: 414, 415, 416, 417, 418, 419, 420, 421, 422, and 423, SEQ ID NOs: 424, 425, 426, and 427, and SEQ ID NOs: 428, 429, 430, 431, 432, 433, and 434; a transmembrane domain comprising an amino acid sequence set forth in any one of SEQ ID NOs: 435, 436, 437, 438, 439, 440, and 441; and optionally, an intracellular domain of no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids; and a second non-viral membrane bound tropism polypeptide comprising, consisting essentially of, or consisting of the amino acid sequence set forth in any one of SEQ ID NOs: 577, 578, 579, 580, and 581.

In particular embodiments, a recombinant particle comprising a first non-viral membrane-bound tropism polypeptide comprising an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising the amino acid sequence set forth in any one of SEQ ID NOs: 19, 20, 29, 30, 39, 40, 49, 50, 59, 60, 69, 70, 79, 80, 89, 90, 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, 170, 179, 180, 189, 190, 199, 200, 209, 210, 219, 220, 229, 230, 239, 240, 249, 250, 259, 260, 269, 270, 279, 280, 289, 290, 299, 300, 309, 310, 319, 320, 329, 330, 339, 340, 349, 350, 359, 360, 369, 370, 379, 380, 389, 390, 399, 400, 409, and 410; a spacer comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 411, 412, and 413, SEQ ID NOs: 414, 415, 416, 417, 418, 419, 420, 421, 422, and 423, SEQ ID NOs: 424, 425, 426, and 427, and SEQ ID NOs: 428, 429, 430, 431, 432, 433, and 434; a transmembrane domain comprising an amino acid sequence set forth in any one of SEQ ID NOs: 435, 436, 437, 438, 439, 440, and 441; and optionally, an intracellular domain of no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids; and a second non-viral membrane bound tropism polypeptide comprising, consisting essentially of, or consisting of the amino acid sequence set forth in any one of SEQ ID NOs: 577, 578, 579, 580, and 581.

In particular embodiments, a recombinant particle comprising a non-viral membrane-bound tropism polypeptide comprising an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising the amino acid sequence set forth in any one of SEQ ID NOs: 19, 20, 29, 30, 39, 40, 49, 50, 59, 60, 69, 70, 79, 80, 89, 90, 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, 170, 179, 180, 189, 190, 199, 200, 209, 210, 219, 220, 229, 230, 239, 240, 249, 250, 259, 260, 269, 270, 279, 280, 289, 290, 299, 300, 309, 310, 319, 320, 329, 330, 339, 340, 349, 350,

359, 360, 369, 370, 379, 380, 389, 390, 399, 400, 409, and 410; a spacer polypeptide comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 411, 412, and 413, SEQ ID NOs: 414, 415, 416, 417, 418, 419, 420, 421, 422, and 423, SEQ ID NOs: 424, 425, 426, and 427, and SEQ ID NOs: 428, 429, 430, 431, 432, 433, and 434; a
5 transmembrane domain comprising an amino acid sequence set forth in any one of SEQ ID NOs: 435, 436, 437, 438, 439, 440, and 441; and optionally, an intracellular domain of no more than 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10 amino acids; and a second non-viral membrane bound tropism polypeptide comprising, consisting essentially of, or consisting of the amino acid sequence set forth in any one of SEQ ID NOs: 577, 578, 579, 580, and 581.

10 In particular embodiments, a recombinant particle comprising a non-viral membrane-bound tropism polypeptide comprising an extracellular antigen targeting domain comprising an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising the amino acid sequence set forth in any one of SEQ ID NOs: 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, and 170; a spacer comprising an amino acid sequence selected
15 from the group consisting of SEQ ID NOs: 411, 412, and 413, SEQ ID NOs: 414, 415, 416, 417, 418, 419, 420, 421, 422, and 423, SEQ ID NOs: 424, 425, 426, and 427, and SEQ ID NOs: 428, 429, 430, 431, 432, 433, and 434; a transmembrane domain comprising an amino acid sequence set forth in any one of SEQ ID NOs: 435, 436, 437, 438, 439, 440, and 441; and optionally, an intracellular domain comprising, consisting essentially of, or consisting of
20 one, two, three, four, five, or six of the amino acids set forth in any one of SEQ ID NOs: 442, 443, 444, 445, 446, 447 and 448; and a second non-viral membrane bound tropism polypeptide comprising, consisting essentially of, or consisting of the amino acid sequence set forth in any one of SEQ ID NOs: 577, 578, 579, 580, and 581.

In particular embodiments, a recombinant particle comprising a non-viral membrane-bound tropism polypeptide comprising an extracellular antigen targeting domain comprising
25 an anti-CD3 ϵ antibody or antigen binding fragment thereof comprising the amino acid sequence set forth in any one of SEQ ID NOs: 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, and 170; a spacer comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 411, 423, and 428; a transmembrane domain
30 comprising an amino acid sequence set forth in any one of SEQ ID NOs: 437 and 439; and optionally, an intracellular domain comprising, consisting essentially of, or consisting of one, two, three, four, five, or six of the amino acids set forth in any one of SEQ ID NOs 444 and 446; and a second non-viral membrane bound tropism polypeptide comprising, consisting

essentially of, or consisting of the amino acid sequence set forth in any one of SEQ ID NOs: 577, 578, 579, 580, and 581.

In particular embodiments, a recombinant particle comprising a non-viral membrane-bound tropism polypeptide comprising an amino acid sequence set forth in any one of SEQ ID NOs: 461, 471, 483, 537, and 553; and a second non-viral membrane bound tropism polypeptide comprising, consisting essentially of, or consisting of the amino acid sequence set forth in any one of SEQ ID NOs: 577, 578, 579, 580, and 581. In particular embodiments, a recombinant particle comprising a non-viral membrane-bound tropism polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 461; and a second non-viral membrane bound tropism polypeptide comprising, consisting essentially of, or consisting of the amino acid sequence set forth in any one of SEQ ID NOs: 577, 578, 579, 580, and 581. In particular embodiments, a recombinant particle comprising a non-viral membrane-bound tropism polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 471; and a second non-viral membrane bound tropism polypeptide comprising, consisting essentially of, or consisting of the amino acid sequence set forth in any one of SEQ ID NOs: 577, 578, 579, 580, and 581. In particular embodiments, a recombinant particle comprising a non-viral membrane-bound tropism polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 483; and a second non-viral membrane bound tropism polypeptide comprising, consisting essentially of, or consisting of the amino acid sequence set forth in any one of SEQ ID NOs: 577, 578, 579, 580, and 581. In particular embodiments, a recombinant particle comprising a non-viral membrane-bound tropism polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 537; and a second non-viral membrane bound tropism polypeptide comprising, consisting essentially of, or consisting of the amino acid sequence set forth in any one of SEQ ID NOs: 577, 578, 579, 580, and 581. In particular embodiments, a recombinant particle comprising a non-viral membrane-bound tropism polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 553; and a second non-viral membrane bound tropism polypeptide comprising, consisting essentially of, or consisting of the amino acid sequence set forth in any one of SEQ ID NOs: 577, 578, 579, 580, and 581.

Table 11

SEQ ID NO:	AMINO ACID SEQUENCE
577	VIHVTKEVKEVATLSCGHNVSV EELAQTRIYWQKEKKMVLTMMSGDMNIWPEYKNRTIFDITNNLSIVILALRPSDEGTYECVVLKYEKDAFKREHLAEVTL SVKADFPTPSISDFEIP TSNIRRIICSTSGGFPEPHLSWLENGEELNAINTTVSQDPETELYAVSSKLDFNMTNHSFMCLIKYGH LRVN

	QTFNWNNTTKQEHFPDNLPSWAITLISVNGIFVICCLTYCFAPRCRE
578	APLKIQAYFNETADLPCQFANSQNSLSSELVVFWDQENLVLNEVYLGKEKFDSVHSKYMGRTS FSDSDSWTLRLHNLQIKDKGLYQCIHHKKPTGMIRIHQMNSELSVLANSQPEIVPISNITENV YINLTCSIIHGYPEPKKMSVLLRTKNSTIEYDGVMOQSQDNVTELYDVSISLSVSFPDVTSNMT IFCILETDKTRLLSSPFSIELEDPQPPPDHIPWITAVLPTVIICVMVFCLILWKWKKKKR
579	RVLFPWALVAGLLLLLLLLAAACAVFLACPWAVSGARASPGSAASPRLREGPELSPDDFAGLLDLR QGMFAQLVQNVLLIDGPLSWYSDPGLAGVSLTGGLSYKEDTKELVVAKAGVYYVFFQLELRRV VAGEGSGSVSLALHLQPLRSAAGAAALATVDLPPASSEARNSAFGFQGRLLHLSAGQRLGVHL HTEARARHAWQLTQGATVLGLFRVTPEIPAGLPSPRSE
580	ERNKLLLVASVIQGLGLLLCFTYICLHFSALQVSHRYPRIQSIKVQFTEYKKEKGFIILTSQKED EIMKVQNNSVIINCDGFYILSLKGYFSQEVNISLHYQKDEEPLFQLKKVRSVNSLMVASLTYKD KVYLNVTDDNTSLDDFHVNGGELILIHQNPGEFCVL
581	DTQKEVRAMVGSDELSCAPEGSRFDLNDVYVYQWTSSEKTVVTYHIPQNSSLENVDSRYRN RALMSPAGMLRGDFSLRLFNVTPODEQKFHCLVLSQSLGFQEVLSVEVTLHVAANFVVPVVSAP HSPSQDELFTCTTSINGYPRPNVYWINKTDNSLLDQALQNDTVFLNMRGLYDVVSVLRIARTPS VNIGCCIEENVLLQQNLTVGSQTGNDIGERDKITENPVSTGEKNAATWSILAVLCLLVVVAIGA WVCRDRCL

E. PAYLOAD

Recombinant particles contemplated herein are engineered to efficiently deliver a payload comprising one or more polynucleotides, polypeptides, and/or small molecules to a specific cell type recognized by one or more tropism molecules expressed or displayed on the surface of the particle. A payload may comprise one or more polynucleotides, polypeptides, and/or small molecules sufficient to enable gene therapy, gene editing, or cell therapy. In particular embodiments, the payload is a therapeutic payload. Without wishing to be bound to any particular theory it is further contemplated in particular embodiments that once the particle binds to and fuses with a specific cell, the payload is introduced into the cell and either genetically modifies the cell or is maintained episomally in the cell. In particular embodiments, a recombinant particle delivers a payload comprising one or more gene therapy vectors, therapeutic proteins, and/or genome editing compositions to a specified cell-type in a subject *in vivo*.

Recombinant particles contemplated in particular embodiments comprise a surface and a payload: the surface comprising one or more mutated viral envelope glycoproteins that retain fusogenic activity and substantially lack or lack cognate receptor binding activity and one or more non-viral membrane-bound tropism polypeptides engineered to bind a desired cell type, *e.g.*, an immune effector cell; and the payload comprising one or more polynucleotide and/or polypeptides. Suitable recombinant particles include but are not limited to a fusosome; an extracellular vesicle, including a microvesicle, an apoptotic body, and an exosome; a lipid nanoparticle; a virus-like particle (VLPs); or a recombinant viral particle.

In particular embodiments, a recombinant particle comprises (i) a surface comprising one or more mutated viral envelope glycoproteins that retain fusogenic activity and lack cognate receptor binding activity and one or more non-viral membrane-bound tropism polypeptides that bind an antigen expressed on a cell and (ii) a payload comprising one or
5 more vectors.

In particular embodiments, a recombinant particle comprises (i) a surface comprising one or more mutated viral envelope glycoproteins that retain fusogenic activity and lack cognate receptor binding activity and one or more non-viral membrane-bound tropism polypeptides that bind an antigen expressed on a cell and (ii) a payload comprising a genome
10 editing composition.

I. VECTOR PAYLOADS

Recombinant particles contemplated in particular embodiments comprise (i) a surface comprising one or more mutated viral envelope glycoproteins that retain fusogenic activity and lack cognate receptor binding activity and one or more non-viral membrane-bound tropism polypeptides that bind an antigen expressed on a cell and (ii) a payload
15 comprising one or more polynucleotides.

In particular embodiments, a payload comprises one or more polynucleotides. Illustrative examples of polynucleotide payloads include but are not limited to: RNAs including but not limited to circRNAs, miRNAs, siRNAs, sgRNAs, shRNAs, or ribozymes; RNAs including therapeutic polypeptides; RNAs including genome editing enzymes and/or
20 donor templates; non-viral vectors and viral vectors.

Illustrative examples non-viral vectors include but are not limited to: plasmids, phagemids, cosmids, artificial chromosomes such as yeast artificial chromosomes (YAC), bacterial artificial chromosomes (BAC), or P1-derived artificial chromosomes (PAC), and
25 bacteriophages such as lambda phage or M13 phage.

Illustrative examples viral vectors include but are not limited to: Adenoviral (Ad) vectors, adeno-associated virus (AAV) vectors, rhabdovirus (*e.g.*, lyssavirus, vesiculovirus) vectors, paramyxovirus (*e.g.*, henipavirus, morbillivirus, respirovirus, rubelavirus) vectors, herpes simplex virus (*e.g.*, HSV-1, HSV-2) vectors, vaccinia virus vectors, and retroviral
30 vectors, preferably lentiviral vectors (LVV). A “viral vector” is a nucleic acid molecule derived from a viral genome that is used to transfer or deliver another nucleic acid to a cell. A viral vector is based on, and derived from, a virus genome that has been engineered to

remove viral accessory proteins but leave elements intact for packaging, reverse transcription and integration. In preferred embodiments, viral vectors contemplated herein comprise a polynucleotide encoding a promoter operably linked to a polynucleotide encoding an engineered receptor, *e.g.*, a chimeric antigen receptor (CAR), a chimeric costimulatory receptor (CCR), an alpha-beta T cell receptor ($\alpha\beta$ TCR), a gamma delta T cell receptor ($\gamma\delta$ TCR), a dimerizing agent regulated immunoreceptor complex (DARIC), a chimeric TGF- β receptor (CTBR), or a zetakine receptor.

In particular embodiments, a recombinant particle comprises (i) a surface comprising one or more mutated viral envelope glycoproteins that retain fusogenic activity and lack cognate receptor binding activity and one or more non-viral membrane-bound tropism polypeptides that bind an antigen expressed on a cell and (ii) a payload comprising an adenoviral vector. High-capacity adenoviral vectors (HC-Ads) (third generation) only retain short non-coding regions from the Ad genome (ITRs and ψ signal), which enables the vector to carry large polynucleotide payloads (~37kb).

In particular embodiments, a recombinant particle comprises (i) a surface comprising one or more mutated viral envelope glycoproteins that retain fusogenic activity and lack cognate receptor binding activity and one or more non-viral membrane-bound tropism polypeptides that bind an antigen expressed on a cell and (ii) a payload comprising an AAV vector. Recombinant AAV (rAAV) vectors are primarily episomally maintained and have a polynucleotide payload capacity of about 4.7kb. rAAV vectors are typically composed of, at a minimum, a transgene and its regulatory sequences, and 5' and 3' AAV inverted terminal repeats (ITRs). rAAV vectors may comprise ITRs from any one of AAV1, AAV2, AAV3, AAV4, AAV5, AAV6, AAV7, AAV8, AAV9, or AAV10. Construction of rAAV vectors, and production, and purification of AAV have been disclosed, *e.g.*, in U.S. Patent Nos. 9,169,494; 9,169,492; 9,012,224; 8,889,641; 8,809,058; and 8,784,799, each of which is incorporated by reference herein, in its entirety.

In particular embodiments, a recombinant particle comprises (i) a surface comprising one or more mutated viral envelope glycoproteins that retain fusogenic activity and lack cognate receptor binding activity and one or more non-viral membrane-bound tropism polypeptides that bind an antigen expressed on a cell and (ii) a payload comprising an HSV vector. HSV vectors are relatively large, *e.g.*, up to 152 kb. Typically, HSV vectors are rendered replication deficient; moreover, one or more essential or non-essential HSV genes are removed from the vector backbone to make room for polynucleotide payloads. Most

replication deficient HSV vectors contain a deletion to remove one or more intermediate-early, early, or late HSV genes to prevent replication. Advantages of the HSV vector are its ability to enter a latent stage that can result in long-term DNA expression and its large viral DNA genome that can accommodate exogenous DNA inserts of up to 25 kb. HSV-based
5 vectors are described in, for example, U.S. Pat. Nos. 5,837,532, 5,846,782, and 5,804,413, and International Patent Applications WO 91/02788, WO 96/04394, WO 98/15637, and WO 99/06583, each of which are incorporated by reference herein in its entirety.

In particular embodiments, a recombinant particle comprises (i) a surface comprising one or more mutated viral envelope glycoproteins that retain fusogenic activity and lack
10 cognate receptor binding activity and one or more non-viral membrane-bound tropism polypeptides that bind an antigen expressed on a cell and (ii) a payload comprising a retroviral vector or a lentiviral vector. In particular embodiments, a recombinant particle comprises two copies of a vector, a genomic RNA comprising backbone sequences derived from a retrovirus genome, *e.g.*, a lentivirus genome.

15 In various embodiments, a retroviral vector is engineered or derived from a retrovirus genome selected from the group consisting of: an alpharetrovirus genome, a betaretrovirus genome, a gammaretrovirus genome, a deltaretrovirus genome, or a spumavirus genome (*e.g.*, an epsilon-retrovirus genome, a simiispumavirus genome, a bovispumavirus genome, an equispumavirus genome, a felispumavirus genome, and a prosimiispumavirus genome).

20 In particular embodiments, a retroviral vector comprises a 5' LTR and a 3' LTR each isolated, obtained, or derived from a retrovirus genome selected from the group consisting of: an alpharetrovirus genome, a betaretrovirus genome, a gammaretrovirus genome, a deltaretrovirus genome, an epsilon-retrovirus genome, and a spumavirus genome.

25 Illustrative examples of alpharetroviruses from which a retroviral vector may be isolated, obtained, or derived from include but are not limited to avian leukosis virus, avian carcinoma Mill Hill virus 2, avian myeloblastosis virus, avian myelocytomatosis virus 29, avian sarcoma virus CT10, fujinami sarcoma virus, rous sarcoma virus, UR2 sarcoma virus and Y73 sarcoma virus.

30 Illustrative examples of betaretroviruses from which a retroviral vector may be isolated, obtained, or derived from include but are not limited to mouse mammary tumor virus, Jaagsiekte sheep retrovirus, langur virus, Mason-Pfizer monkey virus, and squirrel monkey retrovirus (SMRV).

Illustrative examples of deltaretroviruses from which a retroviral vector may be isolated, obtained, or derived from include but are not limited to bovine leukemia virus, primate T-lymphotropic virus 1, primate T-lymphotropic virus 2, primate T-lymphotropic virus 3, and primate T-lymphotropic virus 4.

- 5 Illustrative examples of epsilonretroviruses from which a retroviral vector may be isolated, obtained, or derived from include but are not limited to walleye dermal sarcoma virus, walleye epidermal hyperplasia virus 1, and walleye epidermal hyperplasia virus 2.

- Illustrative examples of gammaretrovirus from which a retroviral vector may be isolated, obtained, or derived from include but are not limited to baboon endogenous virus
 10 (BaEV), chick syncytial virus, feline endogenous virus (*e.g.*, RD114), feline leukemia virus (FeLV), Finkel-Biskis-Jenkins murine sarcoma virus, Gardner-Amstein feline sarcoma virus, gibbon ape leukemia virus (GALV), guinea pig type-C oncovirus, Hardy-Zuckerman feline sarcoma virus, Harvey murine sarcoma virus, Kirsten murine sarcoma virus, koala retrovirus, murine leukemia virus (MLV), Moloney murine leukemia virus (MoMLV), Moloney murine
 15 sarcoma virus, porcine endogenous virus (PERV), Porcine type-C oncovirus, reticuloendotheliosis virus (REV), Snyder-Theilen feline sarcoma virus, Trager duck spleen necrosis virus, viper retrovirus, xenotropic murine leukemia virus-related virus (XMRV), and woolly monkey sarcoma virus.

- Illustrative examples of spumaviruses from which a retroviral vector may be isolated,
 20 obtained, or derived from include but are not limited to simian foamy virus, bovine foamy virus, equine foamy virus, feline foamy virus, human foamy virus (HFV), and brown greater galago prosimian foamy virus.

- In particular embodiments, a recombinant particle comprises a recombinant retroviral vector engineered or derived from a retrovirus genome selected from the group consisting of:
 25 SMRV, BaEV, RD114, FeLV, GALV, MLV, MoMLV, PERV, REV, XMRV, and HFV; gag and pol from an alpharetrovirus, a betaretrovirus, a gammaretrovirus, a deltaretrovirus, an epsilonretrovirus, or a spumavirus; and a 5' LTR and a 3' LTR each isolated, obtained, or derived from a retrovirus genome selected from the group consisting of: an alpharetrovirus genome, a betaretrovirus genome, a gammaretrovirus genome, a deltaretrovirus genome, an
 30 epsilonretrovirus genome, and a spumavirus genome.

In particular embodiments, a recombinant particle comprises a recombinant lentiviral vector engineered or derived from a lentivirus genome. Illustrative lentiviruses include, but are not limited to, HIV (human immunodeficiency virus; including HIV type 1, and HIV type

2); visna-maedi virus (VMV); caprine arthritis-encephalitis virus (CAEV); equine infectious anemia virus (EIAV); feline immunodeficiency virus (FIV); bovine immune deficiency virus (BIV); and simian immunodeficiency virus (SIV). In particular embodiments, lentiviral vectors are derived from HIV-1 viral genomes, preferably HIV-1 or HIV-2 viral genomes and more preferably, HIV-1 viral genomes (*i.e.*, HIV-1 cis-acting sequence elements are preferred).

In various embodiments, a lentiviral vector payload contemplated herein comprises two copies of a lentiviral vector-based RNA genome comprising a 5' long terminal repeat (LTR) comprising R and U5 regions, a Psi (Ψ) packaging signal, a cPPT/FLAP, an export element, a polynucleotide comprising a promoter operably linked to a therapeutic polynucleotide or a polynucleotide encoding a therapeutic polypeptide, a 3' LTR comprising U3 and R regions, a polyadenylation signal, a poly(A) tail; and optionally one or more of a WPRE or HPRE, one or more microRNA (miRNA) target sequences, an insulator element, a selectable marker, and a cell suicide gene.

The term "long terminal repeat (LTR)," as used herein, refers to elements located at the ends of retroviral polynucleotides which, in their natural sequence context, are direct repeats and contain U3, R and U5 regions. LTRs generally provide functions fundamental to the expression of retroviral genes (*e.g.*, promotion, initiation and polyadenylation of gene transcripts) and to viral replication. The LTR contains numerous regulatory signals including transcriptional control elements, polyadenylation signals and sequences needed for replication and integration of the viral genome. The viral LTR is divided into three regions called U3, R and U5. The U3 region contains the enhancer and promoter elements. The U5 region is the sequence between the primer binding site and the R region and contains the polyadenylation signal. The R (repeat) region is flanked by the U3 and U5 regions. A transfer plasmid, which is used as the vector genome template comprises a 5' LTR comprising U3, R and/or U5 regions and a 3' LTR comprising U3, R and/or U5 regions. Adjacent to the 5' LTR are sequences necessary for reverse transcription of the genome (the tRNA primer binding site) and for efficient packaging of viral RNA into particles (the Psi "Ψ" site). A retroviral vector-based genome packaged in a particle comprises a 5' LTR comprising R and U5 regions and a 3' LTR comprising U3 and R regions. The retroviral vector-based genome is reverse transcribed and integrated into the host cell genome as a provector. Through reverse transcription and second strand synthesis of the retroviral vector

genome, provectors comprise two copies of the 3' LTR, one copy that replaces the 5' LTR and the 3' LTR.

A "TAR" element as used herein, refers to the "trans-activation response" genetic element located in the R region of lentiviral vector LTRs. This element interacts with the
5 lentiviral trans-activator (tat) genetic element to enhance lentiviral vector genome replication. In third generation lentiviral vectors, this element is not usually present because lentiviral vector transfer vectors comprise a 5' LTR U3 region replaced by a heterologous promoter.

An "R region," as used herein, refers to the region within LTRs beginning at the start of the capping group (*i.e.*, the start of transcription) and ending immediately prior to the start
10 of the polyA tract. The R region is also defined as being flanked by the U3 and U5 regions. The R region plays a role during reverse transcription in permitting the transfer of nascent DNA from one end of the genome to the other.

As used herein, a "packaging signal" or "packaging sequence" refers to sequences located within the retroviral genome which are required for insertion of the viral RNA into
15 the viral capsid or particle, see *e.g.*, Clever *et al.*, 1995. J. of Virology, Vol. 69, No. 4; pp. 2101-2109. Several retroviral vectors use the minimal packaging signal (also referred to as the psi [Ψ] or [Ψ +] sequence) needed for encapsidation of the viral genome. Thus, as used herein, the terms "packaging sequence," "packaging signal," "psi" and the symbol " Ψ ," are used in reference to the non-coding sequence required for encapsidation of retroviral RNA
20 strands during viral particle formation.

A "FLAP element" or "cPPT/FLAP," as used herein refers to a nucleic acid whose sequence includes the central polypurine tract and central termination sequences (cPPT and CTS) of a lentivirus, *e.g.*, HIV-1 or HIV-2. "FLAP element" and "cPPT/FLAP" may used interchangeably to refer to the foregoing FLAP element. Suitable FLAP elements are
25 described in U.S. Pat. No. 6,682,907 and in Zennou, *et al.*, 2000, Cell, 101:173. During HIV-1 reverse transcription, central initiation of the plus-strand DNA at the central polypurine tract (cPPT) and central termination at the central termination sequence (CTS) lead to the formation of a three-stranded DNA structure: the HIV-1 central DNA flap. While not wishing to be bound by any particular theory, the DNA flap may act as a cis-active
30 determinant of lentiviral genome nuclear import and/or may increase virus titer.

As used herein, an "export element" refers to a cis-acting post-transcriptional regulatory element which regulates the transport of an RNA transcript from the nucleus to the cytoplasm of a cell. Examples of RNA export elements include, but are not limited to,

the human immunodeficiency virus (HIV) rev response element (RRE) (see *e.g.*, Cullen *et al.*, 1991. J. Virol. 65: 1053; and Cullen *et al.*, 1991. Cell 58: 423), the woodchuck hepatitis virus posttranscriptional regulatory element (WPRE), and the hepatitis B virus post-transcriptional regulatory element (HPRE).

5 Expression of heterologous sequences in viral vectors may be increased by incorporating posttranscriptional regulatory elements, efficient polyadenylation signals, and optionally, transcription termination signals into the vectors. A variety of posttranscriptional regulatory elements can increase expression of a heterologous nucleic acid at the protein, *e.g.*, WPRE, HPRE.

10 Lentiviral vectors may contain one or more safety enhancements to reduce the risk of replication, insertional mutagenesis, and off-target transduction and/or expression. In particular embodiments, a lentiviral vector comprises one or more of the following safety enhancements: one or more modifications of the 5' and 3' LTRs, and cell or tissue specific expression control sequences, *e.g.*, promoters, enhancers, miRNA target sequences. A
15 “modified LTR,” as used herein, refers to one or more nucleotide additions, deletions or substitutions in the native HIV-1 5' LTR and/or 3' LTR. The skilled artisan would be able to determine whether an LTR is modified by comparison to a reference LTR.

 “Self-inactivating” (SIN) vectors, as used herein, refer to replication-defective vectors, *e.g.*, retroviral or lentiviral vectors, in which the right (3') LTR enhancer-promoter
20 region, known as the U3 region, has been modified (*e.g.*, by deletion or substitution) to prevent viral transcription beyond the first round of viral replication. Self-inactivation is achieved through a deletion in the U3 region of the 3' LTR of the lentiviral vector transfer plasmid that removes the LTR TATA box (*e.g.*, deletions from -418 to -18), without significant reductions in titers.

25 An additional safety enhancement is provided by replacing the U3 region of the 5' LTR with a heterologous promoter to drive transcription of the viral genome during production of recombinant viral particles. Examples of heterologous promoters which can be used include, for example, viral simian virus 40 (SV40) (*e.g.*, early or late), cytomegalovirus (CMV) (*e.g.*, immediate early), Moloney murine leukemia virus
30 (MoMLV), Rous sarcoma virus (RSV), and herpes simplex virus (HSV) (thymidine kinase) promoters.

 In particular embodiments, a lentiviral vector integrates into the host cell genome.

In certain embodiments, a lentiviral vector is integration defective, episomal, and does not integrate in the cell genome. As used herein, the term “integration defective lentivirus” or “IDLV” refers to a lentivirus having an integrase that lacks the capacity to integrate the viral vector into the host cell genome. Integration-incompetent viral vectors have been described in patent application WO 2006/010834, which is herein incorporated by reference in its entirety. Illustrative mutations in HIV-1 integrase suitable to reduce integrase activity include, but are not limited to: H12N, H12C, H16C, H16V, S81R, D41A, K42A, H51A, Q53C, D55V, D64E, D64V, E69A, K71A, E85A, E87A, D116N, D116I, D116A, N120G, N120I, N120E, E152G, E152A, K156E, K156A, E157A, K159E, K159A, K160A, R166A, D167A, E170A, H171A, K173A, K186Q, K186T, K188T, E198A, R199C, R199T, R199A, D202A, K211A, Q214L, Q216L, Q221L, W235F, W235E, K236S, K236A, K246A, G247W, D253A, R262A, R263A and K264H. In particular embodiments, an HIV-1 integration deficient integrase comprises a D64V, D161I, D116A, E152G, or E152A mutation; D64V, D116A, and E152G mutations; D64V, D116A, and E152A mutations; or a D64V mutation.

In preferred embodiments, a recombinant particle, *e.g.*, a lentiviral particle, comprises a lentiviral vector comprising a polynucleotide encoding a promoter operably linked to a polynucleotide encoding an engineered receptor, *e.g.*, a chimeric antigen receptor (CAR), a chimeric costimulatory receptor (CCR), an alpha-beta T cell receptor ($\alpha\beta$ TCR), a gamma delta T cell receptor ($\gamma\delta$ TCR), a dimerizing agent regulated immunoreceptor complex (DARIC), a chimeric TGF- β receptor (CTBR), or a zetakine receptor.

In particular embodiments, a recombinant particle, *e.g.*, a lentiviral particle, comprises a lentiviral vector comprising a polynucleotide encoding a promoter operably linked to a polynucleotide encoding an engineered receptor that binds an antigen selected from the group consisting of alpha folate receptor (FR α), $\alpha v\beta 6$ integrin, BAFFR, B cell maturation antigen (BCMA), B7-H3 (CD276), B7-H6, carbonic anhydrase IX (CAIX), CD16, CD19, CD20, CD22, CD30, CD33, CD37, CD38, CD44, CD44v6, CD44v7/8, CD70, CD79a, CD79b, CD123, CD133, CD138, CD171, carcinoembryonic antigen (CEA), claudin 6, (CLDN6), claudin 18 isoform 2 (CLDN18.2), C-type lectin-like molecule-1 (CLL-1), CD2 subset 1 (CS-1), chondroitin sulfate proteoglycan 4 (CSPG4), cutaneous T cell lymphoma-associated antigen 1 (CTAGE1), delta like canonical Notch ligand 3 (DLL3), epidermal growth factor receptor (EGFR), epidermal growth factor receptor variant III (EGFRvIII), epithelial glycoprotein 2 (EGP2), epithelial glycoprotein 40 (EGP40), epithelial cell adhesion

molecule (EPCAM), ephrin type-A receptor 2 (EPHA2), erb-b2 receptor tyrosine kinase 4 (ERBB4), fibroblast activation protein (FAP), Fc Receptor Like 5 (FCRL5), fetal acetylcholinesterase receptor (AchR), ganglioside G2 (GD2), ganglioside G3 (GD3), Glypican-3 (GPC3), G Protein-Coupled Receptor Class C Group 5 Member D (GPCR5D),

5 EGFR family including ErbB2 (HER2), HER2 p95, IL-10R α , IL-13R α 2, Kappa, cancer/testis antigen 2 (LAGE-1A), Lambda, Lewis-Y (LeY), L1 cell adhesion molecule (L1-CAM), melanoma antigen gene (MAGE)-A1, MAGE-A3, MAGE-A4, MAGE-A6, MAGEA10, melanoma antigen recognized by T cells 1 (MelanA or MART1), Mesothelin (MSLN), MUC1, MUC16, MHC class I chain related proteins A (MICA), MHC class I chain

10 related proteins B (MICB), neural cell adhesion molecule (NCAM), cancer/testis antigen 1 (NY-ESO-1); placenta-specific 1 (PLAC1), preferentially expressed antigen in melanoma (PRAME), prostate stem cell antigen (PSCA), prostate-specific membrane antigen (PSMA), receptor tyrosine kinase-like orphan receptor 1 (ROR1), SLAMF7, synovial sarcoma, X breakpoint 2 (SSX2), Survivin, TACI, tumor associated glycoprotein 72 (TAG72), tumor

15 endothelial marker 1 (TEM1/CD248), tumor endothelial marker 7-related (TEM7R), trophoblast glycoprotein (TPBG), UL16-binding protein (ULBP) 1, ULBP2, ULBP3, ULBP4, ULBP5, ULBP6, vascular endothelial growth factor receptor 2 (VEGFR2), and Wilms tumor 1 (WT-1)

a. Chimeric antigen receptor (CAR)

20 A CAR is a molecule that combines antibody-based specificity for a target antigen with one or more intracellular T cell signaling domains to generate a chimeric protein that exhibits a specific anti-tumor cellular immune activity. In particular embodiments, a recombinant particle, *e.g.*, a retroviral or lentiviral particles, comprises (a) a phospholipid bilayer, a cellular membrane, or a viral envelope comprising (i) one or more mutated viral

25 envelope glycoproteins that retain fusogenic activity and lack cognate receptor binding activity and (ii) a non-viral membrane-bound tropism polypeptide comprising an antibody or antigen binding fragment thereof that binds an antigen expressed on an immune effector cell, a spacer polypeptide, a transmembrane domain, and optionally, an intracellular domain comprising no more than 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids; and (b) a recombinant

30 retroviral or lentiviral vector comprising a polynucleotide encoding a promoter operably linked to a polynucleotide encoding a CAR.

In particular embodiments, a retroviral or lentiviral vector comprises a polynucleotide comprising or encoding a promoter operably linked to a polynucleotide encoding a CAR comprising a signal peptide, an extracellular antigen binding domain that specifically binds to a target polypeptide expressed on the surface of a cell, a hinge domain, a transmembrane domain, and one or more intracellular signaling domains, and optionally a polynucleotide encoding a posttranscriptional regulatory element, *e.g.*, a WPRE or HPRE.

In particular embodiments, a CAR comprises an extracellular antigen binding domain that comprises an antibody or antigen binding fragment thereof.

In particular embodiments, a CAR comprises an extracellular antigen binding domain that comprises an antibody or antigen binding fragment thereof selected from the group consisting of: a Camel Ig, a Llama Ig, an Alpaca Ig, Ig NAR, a Fab' fragment, a F(ab')₂ fragment, a bispecific Fab dimer (Fab₂), a trispecific Fab trimer (Fab₃), an Fv, a single chain Fv protein ("scFv"), a bis-scFv, (scFv)₂, a minibody, a diabody, a triabody, a tetrabody, a disulfide stabilized Fv protein ("dsFv"), a Fibronectin type III (FN3) domain antibody, a single-domain antibody (sdAb or nanobody, *e.g.*, a camelid VHH or shark VNAR) and a centyrin that binds an antigen selected from the group consisting of FR α , α v β 6 integrin, BAFFR, BCMA, CD276, B7-H6, CAIX, CD16, CD19, CD20, CD22, CD30, CD33, CD37, CD38, CD44, CD44v6, CD44v7/8, CD70, CD79a, CD79b, CD123, CD133, CD138, CD171, CEA, CLDN6, CLDN18.2, CLL-1, CS-1, CSPG4, CTAGE1, DLL3, EGFR, EGFRvIII, EGP2, EGP40, EPCAM, EPHA2, ERBB4, FAP, FCRL5, AchR, GD2, GD3, GPC3, GPCR5D, HER2, HER2 p95, IL-10R α , IL-13R α 2, Kappa, LAGE-1A, Lambda, LeY, L1-CAM, MAGE-A1, MAGE-A3, MAGE-A4, MAGE-A6, MAGEA10, MART1, MSLN, MUC1, MUC16, MICA, MICB, NCAM, NY-ESO-1, PLAC1, PRAME, PSCA, PSMA, ROR1, SLAMF7, SSX2, Survivin, TACI, TAG72, TEM1/CD248, TEM7R, TPBG, ULBP1, ULBP2, ULBP3, ULBP4, ULBP5, ULBP6, VEGFR2, and WT-1; a hinge domain selected from the group consisting of a CD4 hinge, a CD8 β hinge, a CD8 α hinge, a CD28 hinge, a CD134 hinge, a CD137 hinge, a CD152 hinge, a CD278 hinge, an IgG1 hinge, an IgG2 hinge, an IgG3 hinge, an IgG4 hinge; a transmembrane domain isolated or derived from a polypeptide selected from the group consisting of an alpha, beta, gamma, or delta chain of the T-cell receptor, CD3 δ , CD3 ϵ , CD3 γ , CD3 ζ , CD4, CD5, CD8 α , CD9, CD16, CD22, CD27, CD28, CD33, CD37, CD45, CD64, CD80, CD86, CD134, CD137, CD152, CD154, CD278, amnionless (AMN), and programmed cell death 1 (PDCD1); a primary signaling domain isolated or derived from a polypeptide selected from the group consisting of FcR γ ,

FcR β , CD3 γ , CD3 δ , CD3 ϵ , CD3 ζ , CD22, CD79a, CD79b, and CD66d; and optionally, one or more costimulatory signaling domains isolated or derived from a polypeptide selected from the group consisting of TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLR10, CARD11, CD2, CD7, CD27, CD28, CD30, CD40, ICAM, CD83, CD94, CD134 (OX40), CD137 (4-1BB), CD278 (ICOS), DAP10, LAT, SLP76, TRAT1, TNFR2, TNFRS14, TNFRS18, TNFRS25, and ZAP70.

In particular embodiments, a retroviral or lentiviral vector comprises a polynucleotide comprising or encoding a promoter operably linked to a polynucleotide encoding a CAR having an amino acid sequence set forth in any one of SEQ ID NOs: 662-666.

10 Table 12

SEQ ID NO:	AMINO ACID SEQUENCE
662	DIVLTQSPPSLAMSLGKRATISCRASESVTILGSHLIHWYQQKPGQPPTLLIQLASNVQTVGPA RFSGSGSRDFTLTIDPVEEDDVAVYYCLQSRTIPRTFGGGTKLEIKGSTSGSGKPGSGEGSTK GQIQLVQSGPELKKPGETVKISKASGYTFTDYSINWVKRAPGKGLKWMGWINTETREPAYAYD FRGRFAFSLETSASTAYLQINNLYEDTATYFCALDYSYAMDYWGQTSVTVSAAATTPAPR PPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKR GRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYQQGQNLYNEL NLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDG LYQGLSTATKDTYDALHMQALPPR
663	DIQMTQTSSLSASLGDRVTISCRASQDISKYLNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSG SGSGTDYSLTISNLEQEDIATYFCQQGNTLPYTFGGGTKEITGSTSGSGKPGSGEGSTKGEVK LQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQPPRKGLEWLGVIWGSETTYNSALKSRL TIKDNKSQVFLKMNSLQTDITAIYYCAKHYGGSYAMDYWGQTSVTVSSESKYGPCCPPC PMFWVLVVGGLVACYSLLVTVAFIIFWVKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFEE EGGCELRVKFSRSADAPAYQQGQNLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEG LYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
664	QVKLEESGGGLVQAGSLRLSCAASEHTFSSVHMGWFRQAPGKERESVAVIGWRDISTSYADSV KGRFTISRDNAKKTLYLQMNSLKPEDTAVYYCAARRIDAADFDSWGQGTQVTVSSGGGSEVQL VESGGGLVQAGGSLRLSCAASGRTFTMGWFRQAPGKEREFVAIISLPTLAYAESVKGRFTIS RDNAKNTVVLQMNSLKPEDTALYYCAADRKSVMISIRPDYWGQGTQVTVSSSTTTTPAPRPTPA PTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKL LYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYQQGQNLYNELNLGR EEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGL STATKDTYDALHMQALPPR
665	DIQMTQTSSLSASLGDRVTISCRASQDISKYLNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSG SGSGTDYSLTISNLEQEDIATYFCQQGNTLPYTFGGGTKEITGGGSGGGSGGGGSEVKLQE SGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQPPRKGLEWLGVIWGSETTYNSALKSRLTII KDNKSQVFLKMNSLQTDITAIYYCAKHYGGSYAMDYWGQTSVTVSSTTTTPAPRPTPAPT IASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCKRGRKKLLY IFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYKQGGQNLYNELNLGR EYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGL ATKDTYDALHMQALPPR
666	DIQMTQTSSLSASLGDRVTISCRASQDISKYLNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSG SGSGTDYSLTISNLEQEDIATYFCQQGNTLPYTFGGGTKEITGGGSGGGSGGGGSEVKLQE SGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQPPRKGLEWLGVIWGSETTYNSALKSRLTII KDNKSQVFLKMNSLQTDITAIYYCAKHYGGSYAMDYWGQTSVTVSSTTTTPAPRPTPAPT KSNGTIIHVKGKHLCPSPFLFPGPSKPFVVLVVGGLVACYSLLVTVAFIIFWVRSKRSLHSD YMNMTPRRPGPTRKHYPYAPPRDFAAYRSRVKFSRSADAPAYQQGQNLYNELNLGRREEYD VLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATK

	DTYDALHMQALPPR
--	----------------

b. Chimeric costimulatory receptor (CCR)

A chimeric costimulatory receptor (CCR) is a molecule that combines antibody-based specificity to a desired antigen with a costimulatory domain but that lacks a primary signaling domain. CCRs redirect immune effector cell specificity in an MHC independent manner and enhance the immune effector cell response in the presence of a CAR. In particular embodiments, a CAR comprises a first costimulatory domain and a primary signaling domain and a CCR comprises a second costimulatory domain, wherein the first and second costimulatory domains are different from each other and synergize to immune effector cell proliferation, persistence, cytokine production, and/or phagocytosis or production of molecules that can mediate cell death of the target antigen expressing cell.

In particular embodiments, a retroviral or lentiviral vector comprises a polynucleotide comprising or encoding a promoter operably linked to a polynucleotide encoding a CAR comprising a signal peptide, an extracellular antigen binding domain that specifically binds to a target polypeptide expressed on the surface of a cell, a hinge domain, a transmembrane domain, and one or more intracellular signaling domains; a polypeptide cleavage signal; a CCR that comprises a signal peptide, an extracellular antigen binding domain, a hinge domain, a transmembrane domain, and a costimulatory signaling domain; and optionally a polynucleotide encoding a posttranscriptional regulatory element, *e.g.*, a WPRE or HPRE.

In particular embodiments, the signal peptide of the CAR is the same as, or different from, the signal peptide of the CCR; the extracellular antigen binding domain of the CAR is different than the extracellular antigen binding domain of the CCR; the hinge domain of the CAR is the same as, or different from, the hinge domain of the CCR; the transmembrane domain of the CAR is the same as, or different from, the transmembrane domain of the CCR; the costimulatory domain of the CAR is the same as, or different from, the costimulatory domain of the CCR; and the CAR comprises a primary signaling domain.

In particular embodiments, a retroviral or lentiviral vector comprises a polynucleotide comprising or encoding a promoter operably linked to (a) a polynucleotide encoding a CAR comprising an extracellular antigen binding domain that comprises an antibody or antigen binding fragment thereof selected from the group consisting of: a Camel Ig, a Llama Ig, an Alpaca Ig, Ig NAR, a Fab' fragment, a F(ab')₂ fragment, a bispecific Fab dimer (Fab₂), a trispecific Fab trimer (Fab₃), an Fv, a single chain Fv protein ("scFv"), a bis-scFv, (scFv)₂,

a minibody, a diabody, a triabody, a tetrabody, a disulfide stabilized Fv protein ("dsFv"), a Fibronectin type III (FN3) domain antibody, a single-domain antibody (sdAb or nanobody, *e.g.*, a camelid VHH or shark VNAR) and a centyrin that binds an antigen selected from the group consisting of FR α , α v β 6 integrin, BAFFR, BCMA, CD276, B7-H6, CAIX, CD16, CD19, CD20, CD22, CD30, CD33, CD37, CD38, CD44, CD44v6, CD44v7/8, CD70, CD79a, CD79b, CD123, CD133, CD138, CD171, CEA, CLDN6, CLDN18.2, CLL-1, CS-1, CSPG4, CTAGE1, DLL3, EGFR, EGFRvIII, EGP2, EGP40, EPCAM, EPHA2, ERBB4, FAP, FCRL5, AchR, GD2, GD3, GPC3, GPCR5D, HER2, HER2 p95, IL-10R α , IL-13R α 2, Kappa, LAGE-1A, Lambda, LeY, L1-CAM, MAGE-A1, MAGE-A3, MAGE-A4, MAGE-A6, MAGEA10, MART1, MSLN, MUC1, MUC16, MICA, MICB, NCAM, NY-ESO-1, PLAC1, PRAME, PSCA, PSMA, ROR1, SLAMF7, SSX2, Survivin, TACI, TAG72, TEM1/CD248, TEM7R, TPBG, ULBP1, ULBP2, ULBP3, ULBP4, ULBP5, ULBP6, VEGFR2, and WT-1; a hinge domain selected from the group consisting of a CD4 hinge, a CD8 β hinge, a CD8 α hinge, a CD28 hinge, a CD134 hinge, a CD137 hinge, a CD152 hinge, a CD278 hinge, an IgG1 hinge, an IgG2 hinge, an IgG3 hinge, an IgG4 hinge; a transmembrane domain isolated or derived from a polypeptide selected from the group consisting of an alpha, beta, gamma, or delta chain of the T-cell receptor, CD3 δ , CD3 ϵ , CD3 γ , CD3 ζ , CD4, CD5, CD8 α , CD9, CD16, CD22, CD27, CD28, CD33, CD37, CD45, CD64, CD80, CD86, CD134, CD137, CD152, CD154, CD278, amnionless (AMN), and programmed cell death 1 (PDCD1); a primary signaling domain isolated or derived from a polypeptide selected from the group consisting of FcR γ , FcR β , CD3 γ , CD3 δ , CD3 ϵ , CD3 ζ , CD22, CD79a, CD79b, and CD66d; and optionally, one or more costimulatory signaling domains isolated or derived from a polypeptide selected from the group consisting of TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLR10, CARD11, CD2, CD7, CD27, CD28, CD30, CD40, ICAM, CD83, CD94, CD134 (OX40), CD137 (4-1BB), CD278 (ICOS), DAP10, LAT, SLP76, TRAT1, TNFR2, TNFRS14, TNFRS18, TNFRS25, and ZAP70; (b) a self-cleaving viral polypeptide or ribosomal skipping polypeptide; (c) a polynucleotide encoding a CCR that comprises an antibody or antigen binding fragment thereof selected from the group consisting of: a Camel Ig, a Llama Ig, an Alpaca Ig, Ig NAR, a Fab' fragment, a F(ab')₂ fragment, a bispecific Fab dimer (Fab₂), a trispecific Fab trimer (Fab₃), an Fv, a single chain Fv protein ("scFv"), a bis-scFv, (scFv)₂, a minibody, a diabody, a triabody, a tetrabody, a disulfide stabilized Fv protein ("dsFv"), a Fibronectin type III (FN3) domain antibody, a single-domain antibody (sdAb or nanobody, *e.g.*, a camelid VHH or

shark VNAR) and a centyrin that binds an antigen selected from the group consisting of FR α , α v β 6 integrin, BAFRR, BCMA, CD276, B7-H6, CAIX, CD16, CD19, CD20, CD22, CD30, CD33, CD37, CD38, CD44, CD44v6, CD44v7/8, CD70, CD79a, CD79b, CD123, CD133, CD138, CD171, CEA, CLDN6, CLDN18.2, CLL-1, CS-1, CSPG4, CTAGE1, DLL3, EGFR, EGFRvIII, EGP2, EGP40, EPCAM, EPHA2, ERBB4, FAP, FCRL5, AchR, GD2, GD3, GPC3, GPCR5D, HER2, HER2 p95, IL-10R α , IL-13R α 2, Kappa, LAGE-1A, Lambda, LeY, L1-CAM, MAGE-A1, MAGE-A3, MAGE-A4, MAGE-A6, MAGEA10, MART1, MSLN, MUC1, MUC16, MICA, MICB, NCAM, NY-ESO-1, PLAC1, PRAME, PSCA, PSMA, ROR1, SLAMF7, SSX2, Survivin, TACI, TAG72, TEM1/CD248, TEM7R, TPBG, ULBP1, ULBP2, ULBP3, ULBP4, ULBP5, ULBP6, VEGFR2, and WT-1 that is different than the antigen bound by the CAR; a hinge domain selected from the group consisting of a CD4 hinge, a CD8 β hinge, a CD8 α hinge, a CD28 hinge, a CD134 hinge, a CD137 hinge, a CD152 hinge, a CD278 hinge, an IgG1 hinge, an IgG2 hinge, an IgG3 hinge, an IgG4 hinge, optionally that comprises one or more amino acid substitutions that reduces antigen independent signaling of the CCR compared to the unmodified hinge domain; a transmembrane domain isolated or derived from a polypeptide selected from the group consisting of an alpha, beta, gamma, or delta chain of the T-cell receptor, CD3 δ , CD3 ϵ , CD3 γ , CD3 ζ , CD4, CD5, CD8 α , CD9, CD16, CD22, CD27, CD28, CD33, CD37, CD45, CD64, CD80, CD86, CD134, CD137, CD152, CD154, CD278, amnionless (AMN), and programmed cell death 1 (PDCD1); and one or more costimulatory signaling domains isolated or derived from a polypeptide selected from the group consisting of TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLR10, CARD11, CD2, CD7, CD27, CD28, CD30, CD40, ICAM, CD83, CD94, CD134 (OX40), CD137 (4-1BB), CD278 (ICOS), DAP10, LAT, SLP76, TRAT1, TNFR2, TNFRS14, TNFRS18, TNFRS25, and ZAP70 that are different than the costimulatory domain of the CAR.

c. Engineered T Cell Receptors (TCR)

Naturally occurring T cell receptors have two chains: an $\alpha\beta$ TCR comprises an alpha chain and a beta chain and a $\gamma\delta$ TCR comprises a gamma chain and a delta chain. Each TCR is a unique protein produced by a recombination event in each T cell's genome. Libraries of TCRs may be screened for their selectivity to particular target antigens and natural TCRs

with high-avidity and reactivity toward target antigens may be selected, cloned, and incorporated into a payload to deliver to an immune effector cell.

In particular embodiments, a recombinant particle, *e.g.*, a retroviral or lentiviral particles, comprises (a) a phospholipid bilayer, a cellular membrane, or a viral envelope comprising (i) one or more mutated viral envelope glycoproteins that retain fusogenic activity and lack cognate receptor binding activity and (ii) a non-viral membrane-bound tropism polypeptide comprising an antibody or antigen binding fragment thereof that binds an antigen expressed on an immune effector cell, a spacer polypeptide, a transmembrane domain, and optionally, an intracellular domain comprising no more than 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids; and (b) a recombinant retroviral or lentiviral vector comprising a polynucleotide encoding a promoter operably linked to a polynucleotide encoding an alpha chain and/or a beta chain of an $\alpha\beta$ TCR or a gamma chain and/or a delta chain of a $\gamma\delta$ TCR.

In particular embodiments, a retroviral or lentiviral vector comprises a polynucleotide comprising or encoding a promoter operably linked to a polynucleotide encoding an alpha chain and/or a beta chain of an $\alpha\beta$ TCR or a gamma chain and/or a delta chain of a $\gamma\delta$ TCR, and optionally a polynucleotide encoding a posttranscriptional regulatory element, *e.g.*, a WPRE or HPRE. In particular embodiments, the vector comprises a polynucleotide encoding a self-cleaving viral polypeptide or ribosomal skipping polypeptide disposed between the chains of the $\alpha\beta$ TCR or $\gamma\delta$ TCR.

In particular embodiments, an engineered TCR comprises an extracellular antigen binding domain that binds an antigen selected from the group consisting of FR α , $\alpha\beta$ 6 integrin, BAFFR, BCMA, CD276, B7-H6, CAIX, CD16, CD19, CD20, CD22, CD30, CD33, CD37, CD38, CD44, CD44v6, CD44v7/8, CD70, CD79a, CD79b, CD123, CD133, CD138, CD171, CEA, CLDN6, CLDN18.2, CLL-1, CS-1, CSPG4, CTAGE1, DLL3, EGFR, EGFRvIII, EGP2, EGP40, EPCAM, EPHA2, ERBB4, FAP, FCRL5, AchR, GD2, GD3, GPC3, GPCR5D, HER2, HER2 p95, IL-10R α , IL-13R α 2, Kappa, LAGE-1A, Lambda, LeY, L1-CAM, MAGE-A1, MAGE-A3, MAGE-A4, MAGE-A6, MAGEA10, MART1, MSLN, MUC1, MUC16, MICA, MICB, NCAM, NY-ESO-1, PLAC1, PRAME, PSCA, PSMA, ROR1, SLAMF7, SSX2, Survivin, TACI, TAG72, TEM1/CD248, TEM7R, TPBG, ULBP1, ULBP2, ULBP3, ULBP4, ULBP5, ULBP6, VEGFR2, and WT-1.

d. Dimerizing agent regulated immunoreceptor complex (DARIC)

A DARIC is a multi-component signaling receptor comprising one or more non-naturally occurring polypeptides that transduces an immunostimulatory signal in an immune effector cell upon exposure to a multimerizing agent or bridging factor, *e.g.*, stimulating immune effector cell activity and function, increasing production and/or secretion of proinflammatory cytokines.

In particular embodiments, a recombinant particle, *e.g.*, a retroviral or lentiviral particles, comprises (a) a phospholipid bilayer, a cellular membrane, or a viral envelope comprising (i) one or more mutated viral envelope glycoproteins that retain fusogenic activity and lack cognate receptor binding activity and (ii) a non-viral membrane-bound tropism polypeptide comprising an antibody or antigen binding fragment thereof that binds an antigen expressed on an immune effector cell, a spacer polypeptide, a transmembrane domain, and optionally, an intracellular domain comprising no more than 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids; and (b) a recombinant retroviral or lentiviral vector comprising a polynucleotide encoding a promoter operably linked to a polynucleotide encoding a DARIC signaling component and a DARIC binding component.

In particular embodiments, a retroviral or lentiviral vector comprises a polynucleotide comprising or encoding a promoter operably linked to a polynucleotide encoding a DARIC signaling component comprising a signal peptide, a multimerization domain, a transmembrane domain, a costimulatory domain and/or a primary signaling domain; a self-cleaving viral polypeptide or ribosomal skipping polypeptide; and a DARIC binding component comprising a signal peptide, an extracellular antigen binding domain, a multimerization domain, a transmembrane domain, and optionally, a costimulatory domain, and optionally a polynucleotide encoding a posttranscriptional regulatory element, *e.g.*, a WPRE or HPRE; wherein a bridging factor regulates association of the DARIC binding component and DARIC signaling component by interacting with the multimerization domains.

In particular embodiments, a DARIC signaling component comprises a multimerization domain selected from the group consisting of an FK506 binding protein (FKBP) polypeptide or variants thereof (*e.g.*, FKBP12), or an FKBP-rapamycin binding (FRB) polypeptide or variants thereof (*e.g.*, T2098L); a transmembrane domain isolated or

derived from a polypeptide selected from the group consisting of an alpha, beta, gamma, or delta chain of the T-cell receptor, CD3 δ , CD3 ϵ , CD3 γ , CD3 ζ , CD4, CD5, CD8 α , CD9, CD16, CD22, CD27, CD28, CD33, CD37, CD45, CD64, CD80, CD86, CD134, CD137, CD152, CD154, CD278, amnionless (AMN), and programmed cell death 1 (PDCD1); one
 5 or more costimulatory signaling domains isolated or derived from a polypeptide selected from the group consisting of TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLR10, CARD11, CD2, CD7, CD27, CD28, CD30, CD40, ICAM, CD83, CD94, CD134 (OX40), CD137 (4-1BB), CD278 (ICOS), DAP10, LAT, SLP76, TRAT1, TNFR2, TNFRS14, TNFRS18, TNFRS25, and ZAP70; and a primary signaling domain isolated or
 10 derived from a polypeptide selected from the group consisting of FcR γ , FcR β , CD3 γ , CD3 δ , CD3 ϵ , CD3 ζ , CD22, CD79a, CD79b, and CD66d.

In particular embodiments, a DARIC binding component comprises an extracellular antigen binding domain comprising an antibody or antigen binding fragment thereof selected from the group consisting of a Camel Ig, a Llama Ig, an Alpaca Ig, Ig NAR, a Fab' fragment,
 15 a F(ab')₂ fragment, a bispecific Fab dimer (Fab2), a trispecific Fab trimer (Fab3), an Fv, a single chain Fv protein ("scFv"), a bis-scFv, (scFv)₂, a minibody, a diabody, a triabody, a tetrabody, a disulfide stabilized Fv protein ("dsFv"), a Fibronectin type III (FN3) domain antibody, and a single-domain antibody (sdAb or nanobody, *e.g.*, a camelid VHH or shark VNAR) that binds an antigen selected from the group consisting of FR α , α v β 6 integrin,
 20 BAFFR, BCMA, CD276, B7-H6, CAIX, CD16, CD19, CD20, CD22, CD30, CD33, CD37, CD38, CD44, CD44v6, CD44v7/8, CD70, CD79a, CD79b, CD123, CD133, CD138, CD171, CEA, CLDN6, CLDN18.2, CLL-1, CS-1, CSPG4, CTAGE1, DLL3, EGFR, EGFRvIII, EGP2, EGP40, EPCAM, EPHA2, ERBB4, FAP, FCRL5, AchR, GD2, GD3, GPC3, GPCR5D, HER2, HER2 p95, IL-10R α , IL-13R α 2, Kappa, LAGE-1A, Lambda, LeY,
 25 L1-CAM, MAGE-A1, MAGE-A3, MAGE-A4, MAGE-A6, MAGEA10, MART1, MSLN, MUC1, MUC16, MICA, MICB, NCAM, NY-ESO-1, PLAC1, PRAME, PSCA, PSMA, ROR1, SLAMF7, SSX2, Survivin, TACI, TAG72, TEM1/CD248, TEM7R, TPBG, ULBP1, ULBP2, ULBP3, ULBP4, ULBP5, ULBP6, VEGFR2, and WT-1; a multimerization domain selected from the group consisting of an FK506 binding protein (FKBP) polypeptide or
 30 variants thereof (*e.g.*, FKBP12), or an FKBP-rapamycin binding (FRB) polypeptide or variants thereof (*e.g.*, T2098L); a transmembrane domain isolated or derived from a polypeptide selected from the group consisting of an alpha, beta, gamma, or delta chain of the T-cell receptor, CD3 δ , CD3 ϵ , CD3 γ , CD3 ζ , CD4, CD5, CD8 α , CD9, CD16, CD22,

CD27, CD28, CD33, CD37, CD45, CD64, CD80, CD86, CD134, CD137, CD152, CD154, CD278, amnionless (AMN), and programmed cell death 1 (PDCD1); and optionally one or more costimulatory signaling domains isolated or derived from a polypeptide selected from the group consisting of TLR1, TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, 5 TLR10, CARD11, CD2, CD7, CD27, CD28, CD30, CD40, ICAM, CD83, CD94, CD134 (OX40), CD137 (4-1BB), CD278 (ICOS), DAPI0, LAT, SLP76, TRAT1, TNFR2, TNFRS14, TNFRS18, TNFRS25, and ZAP70.

Illustrative examples of bridging factors suitable for use in particular embodiments comprising a DARIC receptor contemplated herein include, but are not limited to, AP1903, 10 AP20187, AP21967 (also known as C-16-(S)-7-methylindolerapamycin), everolimus, novolimus, pimecrolimus, ridaforolimus, tacrolimus, temsirolimus, umirolimus, and zotarolimus.

e. Chimeric TGF- β receptor (CTBR)

A chimeric TGF- β receptor (CTBR) is a fusion polypeptide that when expressed on 15 an immune effector cell, transduces an immunostimulatory signal to the immune effector cell in the presence of immunosuppressive cytokines (*e.g.*, TGF β) produced by tumor cells and tumor-infiltrating lymphocytes in the tumor microenvironment (TME).

In particular embodiments, a retroviral or lentiviral vector comprises a polynucleotide comprising or encoding a promoter operably linked to a polynucleotide encoding a CAR, $\alpha\beta$ 20 TCR, $\gamma\delta$ TCR, DARIC, or zetakine; a self-cleaving viral polypeptide or ribosomal skipping polypeptide; a CTBR; and optionally a polynucleotide encoding a posttranscriptional regulatory element, *e.g.*, a WPRE or HPRE.

In particular embodiments, a CTBR comprises (a) a first polypeptide comprising an extracellular TGF β 1-binding domain of TGF β R2, a transmembrane domain, and a first 25 interleukin receptor intracellular signaling domain; (b) a polypeptide cleavage signal; and (c) a second polypeptide comprising an extracellular TGF β 1-binding domain of TGF β R1, a transmembrane domain, and a second interleukin receptor intracellular signaling domain.

Illustrative examples of first and second interleukin receptor intracellular signaling domains suitable for use in a CTBR include but are not limited to IL-12R β 1 and IL-12R β 2 30 (IL-12 receptor); IL-7R α and IL-2R γ (IL-7 receptor); IL-2R γ and IL-2R γ (IL-2 receptor); IL-

21R and IL-2R γ (IL-21 receptor); IL-18R1 and IL-18RAP (IL-18 receptor); and IL-1R1 and IL-1RAP (IL-1 receptor).

In particular embodiments, a retroviral or lentiviral vector comprises a polynucleotide comprising or encoding a promoter operably linked to (a) a CAR, $\alpha\beta$ TCR, $\gamma\delta$ TCR, DARIC, or zetakine; (b) a self-cleaving viral polypeptide or ribosomal skipping polypeptide; and (c) a polynucleotide encoding a CTBR comprising (i) a first polypeptide comprising an extracellular TGF β 1-binding domain of TGF β R2, a TGF β R2 or an IL-12R β 2 transmembrane domain and an IL-12R β 2 intracellular signaling domain; (ii) a self-cleaving viral peptide or ribosomal skipping polypeptide and (iii) a second polypeptide comprising an extracellular TGF β 1-binding domain of TGF β R1; a TGF β R1 or an IL-12R β 1 transmembrane domain, and an IL-12R β 1 intracellular signaling domain.

In particular embodiments, a retroviral or lentiviral vector comprises a polynucleotide comprising or encoding a promoter operably linked to (a) a CAR, $\alpha\beta$ TCR, $\gamma\delta$ TCR, DARIC, or zetakine; (b) a self-cleaving viral polypeptide or ribosomal skipping polypeptide; and (c) a polynucleotide encoding a CTBR comprising (i) a first polypeptide comprising an extracellular TGF β 1-binding domain of TGF β R2, a TGF β R2 or an IL-7R α transmembrane domain and an IL-7R α intracellular signaling domain; (ii) a self-cleaving viral peptide or ribosomal skipping polypeptide; and (iii) a second polypeptide comprising an extracellular TGF β 1-binding domain of TGF β R1; a TGF β R1 or an IL-2R γ transmembrane domain, and an IL-2R γ intracellular signaling domain.

In particular embodiments, a retroviral or lentiviral vector comprises a polynucleotide comprising or encoding a promoter operably linked to (a) a CAR, $\alpha\beta$ TCR, $\gamma\delta$ TCR, DARIC, or zetakine; (b) a self-cleaving viral polypeptide or ribosomal skipping polypeptide; and (c) a polynucleotide encoding a CTBR comprising (i) a first polypeptide comprising an extracellular TGF β 1-binding domain of TGF β R2, a TGF β R2 or an IL-2R β transmembrane domain and an IL-2R β intracellular signaling domain; (ii) a self-cleaving viral peptide or ribosomal skipping polypeptide; and (iii) a second polypeptide comprising an extracellular TGF β 1-binding domain of TGF β R1; a TGF β R1 or an IL-2R γ transmembrane domain, and an IL-2R γ intracellular signaling domain.

In particular embodiments, a retroviral or lentiviral vector comprises a polynucleotide comprising or encoding a promoter operably linked to (a) a CAR, $\alpha\beta$ TCR, $\gamma\delta$ TCR, DARIC, or zetakine; (b) a self-cleaving viral polypeptide or ribosomal skipping polypeptide; and (c) a polynucleotide encoding a CTBR comprising (i) a first polypeptide comprising an

extracellular TGFβ1-binding domain of TGFβR2, a TGFβR2 or an IL-21R transmembrane domain and an IL-21R intracellular signaling domain; (ii) a self-cleaving viral peptide or ribosomal skipping polypeptide; and (iii) a second polypeptide comprising an extracellular TGFβ1-binding domain of TGFβR1; a TGFβR1 or an IL-2Rγ transmembrane domain, and
 5 an IL-2Rγ intracellular signaling domain.

2. GENE EDITING PAYLOADS

Recombinant particles contemplated in particular embodiments comprise (i) a surface comprising one or more mutated viral envelope glycoproteins that retain fusogenic activity and lack cognate receptor binding activity and one or more non-viral membrane-bound tropism polypeptides that bind an antigen expressed on a cell and (ii) a payload
 10 comprising a genome editing composition comprising one or more polynucleotides and/or polypeptides. Without wishing to be bound to any particular theory it is believed that genome editing compositions can be delivered using the recombinant particles contemplated herein to modify the target cell genome and introduce one or more exogenous genes or modulate
 15 expression of one or more endogenous genes in the cell.

In a particular embodiment, a genome editing payload comprises a template and a nuclease both formatted as circRNAs, mRNAs or DNAs.

In a particular embodiment, a genome editing payload comprises a template formatted as RNA or DNA and a nuclease formatted as a polypeptide.

20 In a particular embodiment, a genome editing payload comprises a nucleic acid-polypeptide complex comprising a template formatted as RNA or DNA and a nuclease formatted as a polypeptide.

In a particular embodiment, a genome editing payload comprises a nuclease formatted as circRNA, mRNA, DNA, or polypeptide.

25 In particular embodiments, a genome editing payload comprises a fusion protein comprising a viral accessory protein and a nuclease and optionally, a DNA repair template.

In particular embodiments, a genome editing payload comprises a fusion protein comprising a lentiviral accessory protein, a lentivirus protease cleavage site (*e.g.*, SQNYPIVQ (SEQ ID NO: 714)) and a nuclease and optionally, a DNA repair template.

30 In particular embodiments, the viral accessory protein is a gag or vpr polypeptide, and in preferred embodiments, a lentiviral (*e.g.*, HIV-1) gag or vpr polypeptide. In particular embodiments, the lentivirus protease cleavage site is an HIV-1 protease cleavage site.

Illustrative examples of genome editing compositions suitable for use in particular embodiments contemplated herein include, but are not limited to base editors (*e.g.*, cytosine base editors (Cas9-cytosine deaminase fusion proteins; CBEs), adenosine base editors (Cas9-deoxyadenosine deaminase fusion proteins; ABEs), sgRNA), prime editors (Cas9-reverse transcriptase fusion proteins; pegRNAs), clustered regularly-interspaced short palindromic repeats (CRISPR)/Cas nuclease systems (Cas9, sgRNA), retrotransposons, homing endonucleases (meganucleases), megaTALs, transcription activator-like effector nucleases (TALENs), zinc finger nucleases (ZFNs), and ARCUS nucleases.

F. POLYNUCLEOTIDES

Polynucleotides comprising vectors, vector-based genomes, transfer vectors, packaging plasmids, expression control sequences, therapeutic polynucleotides, nucleases, DNA repair templates and polynucleotides encoding polypeptides, fusion polypeptides, viral envelope glycoproteins, non-viral membrane-bound tropism polypeptides, CARs, CCRs, TCRs, DARICs, CTBRs, nucleases, and therapeutic polypeptides and variants thereof are contemplated herein.

As used herein, the terms “polynucleotide” or “nucleic acid” refer to deoxyribonucleic acid (DNA), ribonucleic acid (RNA) and DNA/RNA hybrids. Polynucleotides may be single-stranded or double-stranded and either recombinant, synthetic, or isolated. Polynucleotides include but are not limited to: pre-messenger RNA (pre-mRNA), messenger RNA (mRNA), RNA, circular RNA (circRNA), synthetic RNA, short interfering RNA (siRNA), short hairpin RNA (shRNA), microRNA (miRNA), ribozymes, genomic RNA (gRNA), viral genomic RNA, plus strand RNA (RNA(+)), minus strand RNA (RNA(-)), tracrRNA, crRNA, single guide RNA (sgRNA), PCR amplified DNA, complementary DNA (cDNA), synthetic DNA, or recombinant DNA. Polynucleotides refer to a polymeric form of nucleotides of at least 5, at least 10, at least 15, at least 20, at least 25, at least 30, at least 40, at least 50, at least 100, at least 200, at least 300, at least 400, at least 500, at least 1000, at least 5000, at least 10000, or at least 15000 or more nucleotides in length, either ribonucleotides or deoxyribonucleotides or a modified form of either type of nucleotide, as well as all intermediate lengths. It will be readily understood that “intermediate lengths,” in this context, means any length between the quoted values, such as 6, 7, 8, 9, *etc.*, 101, 102, 103, *etc.*, 151, 152, 153, *etc.*, 201, 202, 203, *etc.*

In particular embodiments, polynucleotides contemplated herein are polynucleotide variants. As used herein, the terms “polynucleotide variant” and “variant” and the like refer to polynucleotides displaying substantial sequence identity with a reference polynucleotide sequence or polynucleotides that hybridize with a reference sequence under stringent
5 conditions that are defined hereinafter. These terms also encompass polynucleotides that are distinguished from a reference polynucleotide by the addition, deletion, substitution, or modification of one or more nucleotides. Accordingly, the terms “polynucleotide variant” and “variant” include polynucleotides in which one or more nucleotides have been added or deleted, or modified, or replaced with different nucleotides. In this regard, it is well
10 understood in the art that certain alterations inclusive of mutations, additions, deletions and substitutions can be made to a reference polynucleotide whereby the altered polynucleotide retains the biological function or activity of the reference polynucleotide or wherein the function or activity of the altered polynucleotide is modulated.

In particular embodiments, polynucleotides or polynucleotide variants have at least
15 or about 50%, 55%, 60%, 65%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% sequence identity to a reference sequence.

As used herein, “isolated polynucleotide” refers to a polynucleotide that has been isolated from or purified from the sequences which flank it in a naturally-occurring state. In
20 particular embodiments, an isolated polynucleotide is a synthetic polynucleotide, a semi-synthetic polynucleotide, or a polynucleotide obtained or derived from a recombinant source, or other polynucleotide that does not exist in nature and that has been made by the hand of man.

In various embodiments, a polynucleotide comprises a vector, optionally a retroviral
25 vector, optionally a lentiviral vector.

In various embodiments, a polynucleotide comprises a retroviral vector-based RNA genome, optionally a lentiviral vector-based RNA genome.

Illustrative examples of polynucleotides include, but are not limited to, polynucleotide sequences set forth in any one of SEQ ID NOs: 667-672 and polynucleotides
30 encoding polypeptides set forth in SEQ ID NOs: 1-666 and 673-714.

In particular embodiments, polynucleotides may be codon-optimized. As used herein, the term “codon-optimized” refers to substituting codons in a polynucleotide encoding a polypeptide in order to modulate polypeptide expression, stability and/or activity.

Factors that influence codon optimization include, but are not limited to one or more of: (i) variation of codon biases between two or more organisms or genes or synthetically constructed bias tables, (ii) variation in the degree of codon bias within an organism, gene, or set of genes, (iii) systematic variation of codons including context, (iv) variation of codons according to their decoding tRNAs, (v) variation of codons according to GC %, either overall or in one position of the triplet, (vi) variation in degree of similarity to a reference sequence for example a naturally occurring sequence, (vii) variation in the codon frequency cutoff, (viii) structural properties of mRNAs transcribed from the DNA sequence, (ix) prior knowledge about the function of the DNA sequences upon which design of the codon substitution set is to be based, (x) systematic variation of codon sets for each amino acid, and/or (xi) isolated removal of spurious translation initiation sites.

Polynucleotides contemplated in particular embodiments, regardless of the length of the coding sequence itself, may be combined with other polynucleotide sequences, such as expression control sequences, promoters and/or enhancers, untranslated regions (UTRs), polynucleotides encoding signal peptides, Kozak sequences, polyadenylation signals, restriction enzyme sites, multiple cloning sites, internal ribosomal entry sites (IRES), recombinase recognition sites (*e.g.*, LoxP, FRT, and Att sites), termination codons, transcriptional termination signals, and polynucleotides encoding self-cleaving polypeptides or epitope tags, as disclosed elsewhere herein or as known in the art.

In particular embodiments, a polynucleotide encodes a fusion polypeptide, viral envelope glycoprotein, non-viral membrane-bound tropism polypeptide, CAR, CCR, $\alpha\beta$ TCR, $\gamma\delta$ TCR, DARIC, CTBR, nuclease, or therapeutic polypeptide comprising signal peptide, *e.g.*, a polynucleotide encoding any one of SEQ ID NOs: 449-454.

Signal peptides are short 16 to 30 amino acid N-terminal sequences of nascently synthesized polypeptide chains that mediate protein targeting to the membrane of the endoplasmic reticulum (ER). Typically, signal peptides are cleaved cotranslationally by signal peptidase, a heterooligomeric polypeptide complex. In particular embodiments, a polypeptide comprises a signal peptide. In preferred embodiments, a polynucleotide encoding a polypeptide comprises a polynucleotide encoding a signal polypeptide; and the translated polypeptide does not comprise a signal peptide.

In particular embodiments, a vector comprises a polynucleotide comprising or encoding one or more exogenous, endogenous, or heterologous expression control sequences

operably linked to a polynucleotide encoding one or more polynucleotides and/or polypeptides contemplated herein.

“Expression control sequences,” “control elements,” or “regulatory sequences” contemplated in particular embodiments include but not limited to promoters, enhancers, translation initiation signals (Shine Dalgarno sequence or Kozak sequence), introns, polyadenylation signals, 5′ and 3′ untranslated regions, all of which may interact with host cell proteins to carry out transcription and translation.

The term “promoter” as used herein refers to a recognition site of a polynucleotide (DNA or RNA) to which an RNA polymerase binds. An RNA polymerase initiates and transcribes polynucleotides operably linked to the promoter. In particular embodiments, promoters operative in mammalian cells comprise an AT-rich region located approximately 25 to 30 bases upstream from the site where transcription is initiated and/or another sequence found 70 to 80 bases upstream from the start of transcription, a CNCAAT region where N may be any nucleotide. The term “enhancer” refers to a segment of DNA which contains sequences capable of providing enhanced transcription and in some instances can function independent of their orientation relative to another control sequence. An enhancer can function cooperatively or additively with promoters and/or other enhancer elements. The term “promoter/enhancer” refers to a segment of DNA which contains sequences capable of providing both promoter and enhancer functions.

The term “operably linked”, refers to a juxtaposition wherein the components described are in a relationship permitting them to function in their intended manner. In one embodiment, the term refers to a functional linkage between an expression control sequence (such as a promoter, and/or enhancer) and a second polynucleotide sequence encoding a polypeptide, wherein the expression control sequence directs transcription of the nucleic acid corresponding to the second sequence.

Illustrative expression control sequences suitable for use in particular embodiments include, but are not limited to, a β -actin promoter, a cytomegalovirus (CMV) immediate early promoter, a simian virus 40 (SV40) (*e.g.*, early or late) promoter, a Moloney murine leukemia virus (MoMLV) promoter, a Rous sarcoma virus (RSV) promoter, a herpes simplex virus (HSV) (thymidine kinase) promoter, an SV40/CD43 promoter, a spleen focus forming virus (SFFV) promoter, an elongation factor 1-alpha (EF1 α) short promoter (intronless), an EF1 α long promoter containing an intron, a Ubiquitin C (UBC) promoter, a phosphoglycerate kinase-1 (PGK) promoter, a cytomegalovirus enhancer/chicken β -actin (CAG) promoter, and

a myeloproliferative sarcoma virus enhancer, negative control region deleted, dl587rev primer-binding site substituted (MND) U3 promoter (Haas *et al.*, Journal of Virology. 2003;77(17): 9439-9450).

5 In particular embodiments, a polynucleotide comprises one or more cell type- or tissue-specific expression control sequences. In particular embodiments a cell type-specific expression control sequence is specific for immune effector cells. In particular embodiments a cell type-specific expression control sequence is a T cell specific promoter, an NK cell specific promoter, an NKT cell specific promoter, or a mucosal-associated invariant T (MAIT) cell promoter.

10 In particular embodiments, a cell type-specific expression control sequence is selected from the group consisting of a distal lymphocyte protein tyrosine kinase (LCK) promoter (Brenner *et al.*, Proc. Natl. Acad. Sci. USA 99:2936-2941 (2002)), a CD3δ promoter (Ji *et al.*, J Biol Chem. 277(49):47898-906 (2002)), a CD4 gene promoter (Salmon *et al.*, Proc. Natl. Acad. Sci. USA 90:7739 (1993), a CD2 promoter (Greaves *et al.*, Cell
15 56:979-86 (1989)), and a TCF7 promoter (van de Wetering *et al.* J. of Bio. Chem. 267: 8530-8536 (1992)).

Efficient expression of polynucleotides can be increased in some embodiments, by using sequences that increase translational efficiency, *e.g.*, through an increase in mRNA ribosomal binding or an increase in mRNA stability. In certain embodiments,
20 polynucleotides encoding a polypeptide of the invention comprise a short recognition sequence, *i.e.*, a Kozak sequence, that greatly facilitates the initial binding of mRNA to the small subunit of the ribosome and increases translation. The consensus Kozak sequence is (GCC)RCCATGG, where R is a purine (A or G) (Kozak, Cell. 44:283-92 (1986), and Kozak, Nucleic Acids Res. 15:8125-48 (1987)).

25 Elements directing the efficient termination and polyadenylation of heterologous nucleic acid transcripts increases heterologous gene expression. Transcription termination signals are generally found downstream of the polyadenylation signal. In particular embodiments, vectors comprise a polyadenylation sequence 3' to a sequence to be transcribed and/or expressed. The term "polyadenylation (or poly(A)) signal" refers to a
30 DNA sequence which directs both the termination and polyadenylation of the nascent RNA transcript by RNA polymerase II. Polyadenylation signals can promote mRNA stability by addition of a poly(A) tail to the 3' end of the coding sequence and thus, contribute to increased translational efficiency. Cleavage and polyadenylation are directed by a poly(A) signal in

the RNA. The core poly(A) signal for mammalian pre-mRNAs has two recognition elements flanking a cleavage-polyadenylation site. Typically, an almost invariant AAUAAA hexamer lies 20-50 nucleotides upstream of a more variable element rich in U or GU residues. Cleavage of the nascent transcript occurs between these two elements and is coupled to the addition of up to 250 adenosines to the 5' cleavage product. In particular embodiments, the core poly(A) signal is an ideal poly(A) signal (*e.g.*, AATAAA, ATTAAA, AGTAAA). In particular embodiments, the poly(A) signal is an SV40 poly(A) signal, a bovine growth hormone poly(A) signal (BGHpA), a rabbit β -globin poly(A) signal (r β gpA), variants thereof, or another suitable heterologous or endogenous poly(A) signal known in the art. In particular embodiments, the poly(A) signal is synthetic.

In particular embodiments, a polynucleotide, *e.g.*, a vector, a viral vector, a retroviral vector, or lentiviral vector, comprises one or more off-target (*e.g.*, brain, heart, liver, lung) miR target sequences inserted into a 5' UTR, intron, and/or 3' UTR.

In some embodiments, a polynucleotide comprises an inducible suicide gene to reduce the risk of direct toxicity and/or uncontrolled proliferation. In some embodiment, the suicide gene is caspase-8 or caspase-9. Caspase-9 can be activated using a specific chemical inducer of dimerization (CID).

In some embodiments, a polynucleotide comprises a gene or gene segment that when introduced into a cell, renders the cell susceptible to negative selection. Negative selection suitable for use in particular embodiments include but are not limited to the HSV-TK gene which confers ganciclovir sensitivity; the cellular hypoxanthine phosphoribosyltransferase (HPRT) gene, the cellular adenine phosphoribosyltransferase (APRT) gene, and bacterial cytosine deaminase.

In some embodiments, a polynucleotide comprises a gene or gene segment that when introduced into a cell, renders the cell susceptible to positive selection. Positive selection genes suitable for use in particular embodiments contemplated herein include but are not limited to hygromycin-B phosphotransferase gene (hph) which confers resistance to hygromycin B, the amino glycoside phosphotransferase gene (neo or aph) from Tn5 which codes for resistance to the antibiotic G418, the dihydrofolate reductase (DHFR) gene, the adenosine deaminase gene (ADA), and the multi-drug resistance (MDR) gene.

In particular embodiments, a polynucleotide is a vector comprising or encoding a promoter operably linked to a polynucleotide encoding one or more engineered receptors, *e.g.*, CAR, CCR, $\alpha\beta$ TCR, $\gamma\delta$ TCR, DARIC, and/or CTBR, or components thereof.

In particular embodiments, a polynucleotide is a retroviral or lentiviral vector comprising or encoding a promoter active in immune effector cells operably linked to a polynucleotide encoding one or more engineered receptors, *e.g.*, CAR, CCR, $\alpha\beta$ TCR, $\gamma\delta$ TCR, DARIC, and/or CTBR, or components thereof.

5 In particular embodiments, a polynucleotide is a retroviral or lentiviral vector comprising or encoding a promoter active in immune effector cells operably linked to a polynucleotide encoding an engineered receptor comprising an extracellular antigen binding domain that binds BCMA, CD19, CD20, CD22, CD38, CD79A, CD79B, GPCR5D, MAGE-A4, MSLN, MUC16, NY-ESO-1, PSCA, PSMA and ROR1.

10 In particular embodiments, a polynucleotide is a retroviral or lentiviral vector comprising or encoding a promoter selected from the group consisting of a CMV promoter, an SFFV promoter, an EFl α short promoter, a UBC promoter, a PGK promoter, a CAG promoter, and an MNDU3 promoter operably linked to a polynucleotide encoding an engineered receptor comprising an extracellular antigen binding domain that binds BCMA,
15 CD19, CD20, CD22, CD38, CD79A, CD79B, GPCR5D, MAGE-A4, MSLN, MUC16, NY-ESO-1, PSCA, PSMA and ROR1.

In particular embodiments, a polynucleotide is a retroviral or lentiviral vector comprising or encoding an SFFV promoter, operably linked to a polynucleotide encoding an engineered receptor comprising an extracellular antigen binding domain that binds BCMA,
20 CD19, CD20, CD22, CD38, CD79A, CD79B, GPCR5D, MAGE-A4, MSLN, MUC16, NY-ESO-1, PSCA, PSMA and ROR1.

In particular embodiments, a polynucleotide is a retroviral or lentiviral vector comprising or encoding an EFl α short promoter operably linked to a polynucleotide encoding an engineered receptor comprising an extracellular antigen binding domain that binds
25 BCMA, CD19, CD20, CD22, CD38, CD79A, CD79B, GPCR5D, MAGE-A4, MSLN, MUC16, NY-ESO-1, PSCA, PSMA and ROR1.

In particular embodiments, a polynucleotide is a retroviral or lentiviral vector comprising or encoding a UBC promoter operably linked to a polynucleotide encoding an engineered receptor comprising an extracellular antigen binding domain that binds BCMA,
30 CD19, CD20, CD22, CD38, CD79A, CD79B, GPCR5D, MAGE-A4, MSLN, MUC16, NY-ESO-1, PSCA, PSMA and ROR1.

In particular embodiments, a polynucleotide is a retroviral or lentiviral vector comprising or encoding a CAG promoter operably linked to a polynucleotide encoding an

engineered receptor comprising an extracellular antigen binding domain that binds BCMA, CD19, CD20, CD22, CD38, CD79A, CD79B, GPCR5D, MAGE-A4, MSLN, MUC16, NY-ESO-1, PSCA, PSMA and ROR1.

In particular embodiments, a polynucleotide is a retroviral or lentiviral vector
5 comprising or encoding an MND promoter operably linked to a polynucleotide encoding an
engineered receptor comprising an extracellular antigen binding domain that binds BCMA,
CD19, CD20, CD22, CD38, CD79A, CD79B, GPCR5D, MAGE-A4, MSLN, MUC16, NY-
ESO-1, PSCA, PSMA and ROR1.

In particular embodiments, a polynucleotide is a retroviral or lentiviral vector
10 comprising or encoding a promoter comprising a polynucleotide sequence set forth in any
one of SEQ ID NOs: 667-672 operably linked to a polynucleotide encoding an engineered
receptor comprising an amino acid sequence set forth in any one of SEQ ID NOs: 662-666.

Table 13: Exemplary Promoters

SEQ ID NO:	NUCLEIC ACID SEQUENCE
667	GCGTTACATAACTTACGGTAAATGGCCCCCTGGCTGACCGCCCAACGACCCCCGCCCATTTGAC GTCAATAATGACGTATGTTCCCATAGTAAACGCCAATAGGGACTTTCCATTGACAGTCAATGGGTG GAGTATTTACGGTAACTGCCACTTGGCAGTACATCAAGTGTATCATATGCCAAGTACGCCCC CTATTGACGTC AATGACGGTAAATGGCCCCGCTGGCATTATGCCAGTACATGACCTTATGGGA CTTTCTACTTGGCAGTACATCTACGTATTAGTCATCGCTATTACCATGGTTCGAGGTGAGCCCC ACGTTCTGCTTCACTCTCCCATCTCCCCCCCCTCCCCACCCCAATTTTGTATTTATTTATTT TTTAATTATTTTTGTGCAGCGATGGGGGCGGGGGGGGGGGGGGGCGCGCCGAGGCGGGGCGGG GCGGGCGGAGGGGCGGGGCGGGGCGAGGCGGAGAGGTGCGGCGGCAGCCAATCAGAGCGGCGCG CTCCGAAAGTTTCTTTTATGGCGAGGCGGCGCGCGCGGCCCTATAAAAAGCGAAGCGCGC GGCGGGCG
668	CGTGAGGCTCCGGTGCCCGTCAGTGGGCAGAGCGCACATCGCCACAGTCCCCGAGAAGTTGGG GGGAGGGGTCGGCAATTGAACCGGTGCCTAGAGAAGGTGGCGCGGGGTAACTGGGAAAGTGAT GTCGTGTACTGGCTCCGCCTTTTTTCCCGAGGGTGGGGGAGAACCGTATATATAAGTGCAAGTAGTCG CCGTGAACGTTCTTTTTCGCAACGGGTTTGGCCGCCAGAACACAGGTAAGTGCCTGTGTGGTTT CCGCGCCGCTGGCCCTCTTTACGGGTTATGGCCCTTGCCTGCTTGAATTAATTTCCACTTGGCTG CAGTACGTGATTCTTGATCCCGAGCTTCGGGTTGGAAGTGGGTGGGAGAGTTTCGAGGCCTTGCG CTTAAGGAGCCCCCTTCGCCTCGTGCTTGAGTTGAGGCCGCGCCTGGGCGCTGGGGCCGCCGCGT GCGAATCTGGTGGCACCTTCGCGCCTGTCTCGCTGCTTTTGATAAGTCTCTAGCCATTAAAAAT TTTTGATGACCTGCTGCGACGCTTTTTTTCTGGCAAGATAGTCTTTGTAATGCGGGCCAAGATC TGCACACTGGTATTTCGGTTTTTGGGGCCGGGGCGGCGACGGGGCCCGTGCCTCCAGCGCAC ATGTTCCGCGAGGCGGGGCTTCGAGCGCGGCCACCGAGAATCGGACGGGGGTAGTCTCAAGCT GGCCGCGCTGCTCTGGTGCTTGCCCTCGCGCCGCCGCTGTATCGCCCCGCCCTGGGCGGCAAGGC TGGCCCCGTCGGCACCAAGTTGCGTGAGCGGAAAGATGGCCGCTTCCCGGCCCTGCTGCAGGGAG CTCAAAATGGAGGACGCGGCGCTCGGGAGAGCGGGCGGGTGAGTCAACCACACAAAGGAAAAGG GCCTTTCCGTCCTCAGCCGTCGCTTCATGTGACTCCACGGAGTACCGGGCGCGCTCCAGGCACC TCGATTAGTTCTCGAGCTTTTGGAGTACGTCGCTTTAGGTTGGGGGAGGGGTTTTATGCGAT GGAGTTTTCCCACTAGTGGTGGGAGACTGAAGTTATGCCAGCTTGGCAGTTGATGTAATTC TCCTTGAATTTGCCCTTTTTGAGTTTGATCTTGTTTCAATCTCAAGCCTCAGACAGTGGTTC AAAGTTTTTTCTTCCATTTCAAGTGTGCTGA
669	AATGAAAGACCCCACTGTAGGTTTGGCAAGCTAGGATCAAGGTTAGGAACAGAGAGACAGCAG AATATGGGCCAAACAGGATATCTGTGGTAAGCAGTTCCTGCCCGGGCTCAGGGCCAAGAACAGT TGAACACAGCAGAATGGGCCAAACAGGATATCTGTGGTAAGCAGATTCCTGCCCGGCTCAGGG CCAAAGAACAGATGGTCCCCAGATCGGGTCCCCGCCCTCAGCAGTTTCTGAGAAACCATCAGATG

	TTCCAGGGTGCCCCAAGGACCTGAAATGACCCTGTGCCTTATTTGAACTAACCAATCAGTTTCGCTTCTCGCTTCTGTTTCGCGCGCTTCTGCTCCCCGAGCTCAATAAAAGAGCCACAAACCCCTCACTCGGC
670	GGGTAGGGGAGGCGCTTTTCCCAAGGCAGTCTGGAGCATGCGCTTTAGCAGCCCCGCTGGGCAC TTGGCGCTACACAAGTGGCCTCTGGCCTCGCACACATTCCACATCCACCGGTAGGCGCCAACCG GCTCCGTTCTTTGGTGGCCCCCTTCGCGCCACCTTCTACTCCTCCCTAGTCAGGAAGTTCCCC CCGCCCCGAGCTCGCGTCGTGCAGGACGTGACAAATGGAAGTAGCACGTCTCACTAGTCTCGT GCAGATGGACAGCACCGCTGAGCAATGGAAGCGGGTAGGCCTTTGGGGCAGCGGCCAATAGCAG CTTTGCTCCTTCGCTTTCTGGGCTCAGAGGCTGGGAAGGGGTGGGTCCGGGGGCGGGCTCAGGG GCGGGCTCAGGGGCGGGGCGGGCGCCGAAGGTCTCCGGAGGCGCGGCATTCTGCACGCTTCA AAAGCGCACGTCTGCCGCGCTGTTCTCCTCTTCTCATCTCCGGGCCTTTTCG
671	TGAAAGACCCACCTGTAGGTTTGGCAAGATAGCTGCAGTAACGCCATTTTGAAGGCATGGAA AAATACCAAACCAAGAATAGAGAAGTTCAGATCAAGGGCGGGTACATGAAAATAGCTAACGTTG GGCCAAACAGGATATCTGCGGTGAGCAGTTTCGGCCCCGCGCCGGGGCCAAGAACAGATGGTCA CCGCAGTTTCGGCCCCGCGCCGAGGCCAAGAACAGATGGTCCCAGATATGGCCCAACCCCTCAG CAGTTTCTTAAGACCCATCAGATGTTTCCAGGCTCCCCCAAGGACCTGAAATGACCCTGCGCCT TATTTGAATTAACCAATCAGCCTGCTTCTCGCTTCTGTTTCGCGCGCTTCTGCTTCCGAGCTCT AAGAAGAGCTCACAACCCCTCACTCGCGCGCCAGTCTCCGATTGACTGAGTCGCCC
672	GGCCTCCGCGCCGGGTTTGGCGCCTCCCGCGGGCGCCCCCTCCTCAGCGCGAGCGCTGCCAC GTCAGACGAAGGGCGCAGCGAGCGTCTGATCCTTCCGCCCCGACGCTCAGGACAGCGGCCCCGC TGCTCATAAGACTCGGCCTTAGAACCCAGTATCAGCAGAAGGACATTTTAGGACGGGACTTGG GTGACTCTAGGGCACTGGTTTTCTTTCCAGAGAGCGGAACAGGCGAGGAAAAGTAGTCCCTTCT CCGCGATTCTGCGGAGGGATCTCCGTGGGGCGGTGAACGCCGATGATTATATAAGGACGCGCCG GGTGTGGCACAGCTAGTTCCGTGCGAGCCGGGATTGGGTGCGGTTCTTTGTTGTGGATCGCT GTGATCGTCACTTGGTGAGTAGCGGGCTGCTGGGCTGGCCGGGGCTTTCTGTCGCGCGCGCCG CTGCGTGGGACGGAAGCGTGTGGAGAGACGCCAAGGGCTGTAGTCTGGGTCCGCGAGCAAGGT TGCCCTGAACTGGGGGTGGGGGGAGCGCAGCAAAATGGCGGCTGTTCCCGAGTCTTGAATGGA AGACGCTTGTGAGGCGGGCTGTGAGGTCGTTGAAACAAGGTGGGGGGCATGGTGGGCGGCAAGA ACCCAAGGTCTTGAGGCCTTCGCTAATGCGGGAAGCTCTTATTCGGGTGAGATGGGCTGGGGC ACCATCTGGGGACCTGACGTGAAGTTTGTCACTGACTGGAGAACTCGGTTTGTGCTCTGTTGC GGGGGCGGCAGTTATGGCGGTGCCGTTGGGCAGTGCACCCGTACCTTTGGGAGCGCGCGCCCTC GTCGTGTCGTGACGTACCCGTTCTGTTGGCTTATAATGCAGGGTGGGGCCACCTGCCGGTAGG TGTGCGGTAGGCTTTTTCTCCGTGCGCAGGACGCAGGGTTTCGGGCTAGGGTAGGCTCTCCTGAAT CGACAGGCGCCGACCTCTGGTGAGGGGAGGGATAAGTGAGGCGTCAGTTTCTTTGGTGGTTTT TATGTACCTATCTTCTTAAGTAGCTGAAGCTCCGGTTTTGAACTATGCGCTCGGGGTGGCGAG TGTGTTTTGTGAAGTTTTTTAGGCACCTTTTGAATGTAATCATTTGGGTCAATATGTAATTTT CAGTGTTAGACTAGTAAATTGTCCGCTAAATTCTGGCCGTTTTTTGGCTTTTTTTGTTAGAC

G. POLYPEPTIDES

Polypeptides, fusion polypeptides, and polypeptide variants are contemplated herein. Exemplary polypeptides contemplated herein include but not limited to, fusion polypeptides, viral envelope glycoproteins, non-viral membrane-bound tropism polypeptides, CARs, CCRs, TCRs, DARICs, CTBRs, nucleases, and therapeutic polypeptides, and variants and/or fragments thereof, *e.g.*, SEQ ID NOs: 1-666 and 673-714.

Polypeptide,” “polypeptide,” “peptide,” and “protein” are used interchangeably, unless specified to the contrary, and according to conventional meaning, *i.e.*, as a sequence of amino acids. In particular embodiments, a “polypeptide” is a fusion polypeptide or polypeptide variant. Polypeptides can be prepared using any of a variety of well-known recombinant and/or synthetic techniques. Polypeptides are not limited to a specific length,

e.g., they may comprise a full-length protein sequence, a fragment of a full-length protein, or a fusion protein, and may include post-translational modifications, *e.g.*, glycosylations, acetylations, phosphorylations and the like, as well as other modifications known in the art, both naturally occurring and non-naturally occurring.

5 An “isolated peptide,” “isolated protein” or an “isolated polypeptide” as used herein, refers to isolation, separation, and/or purification of a polypeptide molecule from a cellular environment, and from association with other components of the cell, *i.e.*, it is not significantly associated with *in vivo* substances.

10 Polypeptides include “polypeptide variants.” In particular embodiments, a polypeptide variant is referred to as a “modified polypeptide.” Polypeptide variants may differ from a naturally occurring polypeptide in one or more amino acid substitutions, deletions, additions and/or insertions. For example, in particular embodiments, it may be desirable to modulate one or more biological activities of a viral envelope glycoprotein, non-viral membrane-bound tropism polypeptide, or engineered receptor by introducing one or
15 more amino acid substitutions, deletions, additions and/or insertions into the polypeptide. Such variants may be naturally occurring or may be synthetically generated. In particular embodiments, polypeptides include polypeptide variants having at least about 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 86%, 97%, 98%,
20 or 99% amino acid identity to any reference sequence contemplated herein, typically where the variant maintains at least one biological activity of the reference sequence.

 In particular embodiments, a polypeptide variant is a viral envelope glycoprotein that has been modified to preserve its fusogenic activity and remove, disable, decrease, eliminate, or abate its binding activity to its cognate receptor on a cell. In particular embodiments, a
25 polypeptide variant is a viral envelope glycoprotein that has at least about 65%, 66%, 67%, 68%, 69%, 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 86%, 97%, 98%, or 99% amino acid identity to any one of SEQ ID NOs: 582-645 or 646-661, wherein the variant comprises fusogenic activity and but is unable to bind or substantially bind to its cognate
30 receptor on a cell.

 Polypeptides variants include biologically active “polypeptide fragments.”

 Illustrative examples of biologically active polypeptide fragments include but are not limited to binding domains, hinges, transmembrane domains, intracellular domains, and the

like. As used herein, the term “biologically active fragment” or “minimal biologically active fragment” refers to a polypeptide fragment that retains at least 100%, at least 95%, at least 90%, at least 85%, at least 80%, at least 75%, at least 70%, at least 65%, at least 60%, at least 55%, or at least 50% of the naturally occurring polypeptide activity. In particular
5 embodiments, a biologically active fragment is a polypeptide comprising an N-terminal and/or C-terminal truncation of 1, 2, 3, 4, 5, 6, 7, 8, 9, 10 or more amino acids. In particular
embodiments, a mutated viral envelope glycoprotein or non-viral membrane-bound tropism
polypeptide comprises a truncation of the cytoplasmic domain that results in a cytoplasmic
tail or stub comprising, consisting essentially of, or consisting of 1, 2, 3, 4, 5, 6, 7, 8, 9, or 10
10 amino acids.

In particular embodiments, polypeptides contemplated herein may comprise one or more amino acids denoted as “X” or “X_n” wherein n is an integer that denotes the particular X amino acid. “X” if present in an amino acid SEQ ID NO, refers to any one or more amino acids or particular amino acids if disclosed.

15 As noted above, polypeptides may be altered in various ways including amino acid substitutions, deletions, truncations, and insertions. Methods for such manipulations are generally known in the art. For example, amino acid sequence variants of a reference polypeptide can be prepared by mutations in the DNA. Methods for mutagenesis and nucleotide sequence alterations are well known in the art. See, for example, Kunkel (Proc.
20 Natl. Acad. Sci. USA. 82: 488-492. (1985)), Kunkel *et al.*, (Methods in Enzymol, 154: 367-382. (1987)), U.S. Pat. No. 4,873,192, Watson, J. D. *et al.*, (Molecular Biology of the Gene , Fourth Edition, Benjamin/Cummings, Menlo Park, Calif. (1987)) and the references cited therein. Guidance as to appropriate amino acid substitutions that do not affect biological activity of the protein of interest may be found in the model of Dayhoff *et al.*, Atlas of Protein
25 Sequence and Structure (Natl. Biomed. Res. Found., Washington, D.C. (1978)).

In certain embodiments, a polypeptide variant comprises one or more conservative substitutions or disruptive substitutions. A “conservative substitution” is one in which an amino acid is substituted for another amino acid that has similar properties. In particular
embodiments, polypeptide variants contemplated herein comprise one or more conservative
30 amino acid changes compared to a reference polypeptide. In particular embodiments, a conservative amino acid substitution involves substituting an amino acid with an amino acid having a related side chain. A “disruptive substitution” is one in which an amino acid is substituted for another amino acid that has different properties, *e.g.*, polar vs. non-polar,

bulky vs. non-bulky, charged vs. uncharged, acidic vs. basic. In particular embodiments, polypeptide variants contemplated herein comprise one or more disruptive amino acid changes compared to a reference polypeptide. In particular embodiments, a disruptive amino acid substitution involves substituting an amino acid with an amino acid having an unrelated
5 side chain or side change with a different chemical property. Guidance in determining which amino acid residues can be substituted, inserted, or deleted can be found using computer programs well known in the art, such as DNASTAR, DNA Strider, Geneious, Mac Vector, or Vector NTI software.

Naturally occurring amino acids are generally divided into four groups or families:
10 acidic (aspartate, glutamate), basic (lysine, arginine, histidine), non-polar (alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan), and uncharged polar (glycine, asparagine, glutamine, cysteine, serine, threonine, tyrosine) amino acids. Phenylalanine, tryptophan, and tyrosine are sometimes classified jointly as aromatic amino acids. In particular embodiments, a conservative amino acid substitution refers to
15 substituting amino acids within the same group or family.

Those of skill in this art recognize that, in general, conservative single amino acid substitutions in non-essential regions of a polypeptide do not substantially alter biological activity (see, *e.g.*, Watson *et al.* Molecular Biology of the Gene, 4th Edition, 1987, The Benjamin/Cummings Pub. Co., p.224), whereas disruptive single amino acid substitutions
20 may.

In particular embodiments, a conservative amino acid substitution refers to substituting amino acids having a similar hydropathic index or score. The importance of the hydropathic amino acid index in conferring interactive biologic function on a protein is generally understood in the art (Kyte and Doolittle, 1982, incorporated herein by reference).
25 Each amino acid has been assigned a hydropathic index on the basis of its hydrophobicity and charge characteristics (Kyte and Doolittle, 1982). These values are: isoleucine (+4.5); valine (+4.2); leucine (+3.8); phenylalanine (+2.8); cysteine/cysteine (+2.5); methionine (+1.9); alanine (+1.8); glycine (-0.4); threonine (-0.7); serine (-0.8); tryptophan (-0.9); tyrosine (-1.3); proline (-1.6); histidine (-3.2); glutamate (-3.5); glutamine (-3.5); aspartate (-3.5); asparagine (-3.5); lysine (-3.9); and arginine (-4.5). In particular embodiments, a conservative amino acid substitution refers to substituting amino acids having a similar hydropathic index or score. In particular embodiments, substitution of amino acids whose hydropathic indices are within ± 2 is preferred, those within ± 1 are particularly preferred, and

those within ± 0.5 are even more particularly preferred. It is also understood in the art that the substitution of like amino acids can be made effectively on the basis of hydrophilicity.

In particular embodiments, a conservative amino acid substitution refers to substituting amino acids having a similar hydrophilic index or score. As detailed in U.S. Patent No. 4,554,101, the following hydrophilicity values have been assigned to amino acid residues: arginine (+3.0); lysine (+3.0); aspartate (+3.0 $\pm$ 1); glutamate (+3.0 $\pm$ 1); serine (+0.3); asparagine (+0.2); glutamine (+0.2); glycine (0); threonine (-0.4); proline (-0.5 $\pm$ 1); alanine (-0.5); histidine (-0.5); cysteine (-1.0); methionine (-1.3); valine (-1.5); leucine (-1.8); isoleucine (-1.8); tyrosine (-2.3); phenylalanine (-2.5); tryptophan (-3.4). In particular
10 embodiments, a conservative amino acid substitution refers to substituting amino acids having a similar hydrophilic index or score. In particular embodiments, substitution of amino acids whose hydrophilic indices are substitution of amino acids whose hydrophilicity values are within ± 2 is preferred, those within ± 1 are particularly preferred, and those within ± 0.5 are even more particularly preferred.

15 In particular embodiments, a conservative amino acid substitution may be based on the relative similarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size, and the like. In particular embodiments, a disruptive amino acid substitution may be based on the relative dissimilarity of the amino acid side-chain substituents, for example, their hydrophobicity, hydrophilicity, charge, size,
20 and the like.

In particular embodiments, a vector comprises one or more polynucleotides encoding two or more polypeptides. In particular embodiments, a polynucleotide encoding a polypeptide cleavage signal is disposed between the polynucleotide sequences encoding the two or more polypeptides to enable efficient translation and subsequent cleavage of a fusion
25 polypeptide.

Polypeptides contemplated in particular embodiments include fusion polypeptides. In particular embodiments, fusion polypeptides and polynucleotides encoding fusion polypeptides are provided. Fusion polypeptides can include one or more polypeptide domains or segments including signal peptides, cell permeable peptide domains (CPP),
30 binding domains, signaling domains, *etc.*, epitope tags (*e.g.*, maltose binding protein ("MBP"), glutathione S transferase (GST), HIS6, MYC, FLAG, V5, VSV-G, and HA), polypeptide linkers, and polypeptide cleavage signals. Fusion proteins and polypeptides are typically linked C-terminus to N-terminus, although they can also be linked C-terminus to C-

terminus, N-terminus to N-terminus, or N-terminus to C-terminus. Fusion polypeptides and fusion proteins refer to a polypeptide having at least two, three, four, five, six, seven, eight, nine, or ten polypeptide segments.

In particular embodiments, a fusion polypeptide, viral envelope glycoprotein, non-viral membrane-bound tropism polypeptide, CAR, CCR, $\alpha\beta$ TCR, $\gamma\delta$ TCR, DARIC, CTBR, nuclease, or therapeutic polypeptide comprises signal peptide set forth in any one of SEQ ID NOs: 449-454 that is subsequently cleaved from the fusion polypeptide, viral envelope glycoprotein, non-viral membrane-bound tropism polypeptide, CAR, CCR, $\alpha\beta$ TCR, $\gamma\delta$ TCR, DARIC, CTBR, nuclease, or therapeutic polypeptide.

Table 14: Exemplary Signal Peptides

SEQ ID NO	AMINO ACID SEQUENCE
449	MALPVTALLLP LALLLHAARP
450	METDTLLLWVLLLWVPGSTG
451	MGVKVLFALICIAVAEA
452	MLLLVTSLLLCELPHPAFLLIP
453	MSRSVALAVLALLSLSGLEA
454	MGHTRRQGTSPSKCPYLNFFQLLVLAGLSHFCSG

Fusion polypeptides may optionally comprise a polypeptide linker contemplated elsewhere herein that can be used to link one or more polypeptides or domains within a polypeptide. “Linker,” “peptide linker,” and “polypeptide linker” are used interchangeably and refer to a plurality of amino acid residues between various polypeptide domains added for appropriate spacing, conformation, and function. A polypeptide linker sequence may be employed to separate any two or more polypeptide components by a distance sufficient to ensure that each polypeptide folds into its appropriate secondary and tertiary structures so as to allow the polypeptide domains to exert their desired functions. Linkers include a “variable domain linking sequence,” an amino acid sequence that connects two or more domains of an antibody or antigen binding fragments thereof and provides a spacer function compatible with interaction of the two sub-binding domains so that the resulting polypeptide retains a specific binding affinity to the same target molecule as an antibody that comprises the same light and/or heavy chain variable domains. A linker may be 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 24, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, or 50 or more amino acids long.

Illustrative examples of linkers include, but are not limited to the following amino acid sequences: AS, ASP, GGG; DGGS (SEQ ID NO: 673); TGEKP (SEQ ID NO: 674); GGRR (SEQ ID NO: 675); (GGGS)_n wherein n = 1, 2, 3, 4 or 5 (SEQ ID NO: 676-680); S(GGGS)_n wherein n = 1, 2, 3, 4 or 5 (SEQ ID NO: 681-685); EGKSSGSGSESKVD (SEQ ID NO: 686); KESGSVSSEQLAQFRSLD (SEQ ID NO: 687); GGRRGGGS (SEQ ID NO: 688); LRQRDGERP (SEQ ID NO: 689); LRQKDGGGSRP (SEQ ID NO: 690); LRQKDGGSGGGSRP (SEQ ID NO: 691), GEGTSTGSGGSGGGAD (SEQ ID NO: 692), and GSTSGSGKPGSGEGSTKG (SEQ ID NO: 693).

In particular embodiments, two or more polypeptides can be expressed as a fusion polypeptides that comprises one or more polypeptide cleavage signals disposed between the two or more polypeptides.

In particular embodiments, a fusion polypeptide comprises a CAR, a polypeptide cleavage signal and a CCR. In particular embodiments, a fusion polypeptide comprises a DARIC binding component, a polypeptide cleavage signal and a DARIC signaling component. In particular embodiments, a fusion polypeptide comprises a CAR, $\alpha\beta$ TCR, $\gamma\delta$ TCR, or DARIC, a polypeptide cleavage signal, and a CTBR.

Exemplary polypeptide cleavage signals include, but are not limited to, protease cleavage sites, nuclease cleavage sites and ribosomal skipping polypeptide or self-cleaving viral polypeptides (see, *e.g.*, in Ryan *et al.*, 1997. J. Gener. Virol. 78, 699-722; deFelipe and Ryan, 2004. Traffic, 5(8); 616-26; and Scymczak *et al.* (2004) Nature Biotech. 5, 589-594).

Exemplary protease cleavage sites include, but are not limited to the cleavage sites of potyvirus NIa proteases (*e.g.* tobacco etch virus protease), poty virus HC proteases, potyvirus PI (P35) proteases, byovirus NIa proteases, byovirus RNA-2-encoded proteases, aphthovirus L proteases, enterovirus 2A proteases, rhinovirus 2 A proteases, picoma 3C proteases, comovirus 24K proteases, nepovirus 24K proteases, RTSV (rice tungro spherical virus) 3C-like protease, PYVF (parsnip yellow fleck virus) 3C-like protease, heparin, thrombin, factor Xa and enterokinase.

Illustrative examples of ribosomal skipping polypeptides include but are not limited to: a viral 2A peptide or sequence (Donnelly *et al.*, 2001. J. Gen. Virol. 82: 1027-1041). In a particular embodiment, the viral 2A peptide is an aphthovirus 2A peptide, a potyvirus 2A peptide, or a cardiovirus 2A peptide.

In one embodiment, the viral 2A peptide is selected from the group consisting of: a foot-and-mouth disease virus (FMDV) 2A peptide, an equine rhinitis A virus (ERAV) 2A

peptide, a *Thosea asigna* virus (TaV) 2A peptide, a porcine teschovirus-1 (PTV-1) 2A peptide, a Theilovirus 2A peptide, and an encephalomyocarditis virus 2A peptide.

Illustrative examples of viral 2A sequences include, but are not limited to:
 GSGATNFSLLKQAGDVEENPGP (SEQ ID NO: 694); ATNFSLLKQAGDVEENPGP
 5 (SEQ ID NO: 695); LLKQAGDVEENPGP (SEQ ID NO: 696);
 GSGEGRGSLLTCGDVEENPGP (SEQ ID NO: 697); EGRGSLLTCGDVEENPGP (SEQ
 ID NO: 698); LLTCGDVEENPGP (SEQ ID NO: 699);
 GSGQCTNYALLKLAGDVESNPGP (SEQ ID NO: 700);
 QCTNYALLKLAGDVESNPGP (SEQ ID NO: 701); LLKLAGDVESNPGP (SEQ ID NO:
 10 702); GSGVKQTLNFDLLKLAGDVESNPGP (SEQ ID NO: 703);
 VKQTLNFDLLKLAGDVESNPGP (SEQ ID NO: 704); LLNFDLLKLAGDVESNPGP
 (SEQ ID NO: 705); TLNFDLLKLAGDVESNPGP (SEQ ID NO: 706);
 NFDLLKLAGDVESNPGP (SEQ ID NO: 707); QLLNFDLLKLAGDVESNPGP (SEQ ID
 NO: 708); APVKQTLNFDLLKLAGDVESNPGP (SEQ ID NO: 709);
 15 VTELLYRMKRAETYCPRLAIHPTEARHKQKIVAPVKQT (SEQ ID NO: 710);
 LNFDLLKLAGDVESNPGP (SEQ ID NO: 711);
 LLAIHPTEARHKQKIVAPVKQTLNFDLLKLAGDVESNPGP (SEQ ID NO: 712); and
 EARHKQKIVAPVKQTLNFDLLKLAGDVESNPGP (SEQ ID NO: 713).

H. CELLS

20 Recombinant particles contemplated herein are engineered to bind and transduce a cell. In particular embodiments, a recombinant particle contemplated herein is engineered to bind and transduce an immune effector cell. In particular embodiments, a cell transduced with a recombinant particle comprising a payload is modified to modulate the expression of one or more endogenous genes, and/or express one or more therapeutic polynucleotides
 25 and/or therapeutic polypeptides (*e.g.*, an engineered receptor) contemplated herein.

In particular embodiments, a recombinant particle, *e.g.*, a recombinant retroviral or lentiviral particle comprises a viral envelope comprising one or more mutated viral envelope glycoproteins that mediate virus-target cell fusion and one or more non-viral membrane-bound tropism polypeptides that bind an antigen expressed on a cell, *e.g.*, an immune effector
 30 cell.

An “immune effector cell” is any cell of the immune system that has one or more effector functions (*e.g.*, cytotoxic cell killing activity, secretion of cytokines, induction of

ADCC and/or CDC). Illustrative types of immune effector cells contemplated in particular embodiments include, without limitation, T lymphocytes, dendritic cells (DC), Treg cells, natural killer (NK) cells, natural killer T (NKT) cells, and macrophages. The terms “T cell” or “T lymphocyte” are art-recognized and are intended, in particular embodiments, to include
5 thymocytes, immature T lymphocytes, mature T lymphocytes, resting T lymphocytes, and/or activated T lymphocytes. Illustrative examples of T lymphocytes suitable for use in particular embodiments, include but not limited to cytotoxic T cells (CTLs; CD8⁺ T cells), TILs, helper T cells (HTLs; CD4⁺ T cells), CD4⁺CD8⁺ T cells, CD4⁻ CD8⁻ T cells, or any other subset of T cells that has an effector function. In a particular embodiment, the cells
10 comprise αβ T cells. In a particular embodiment, the cells comprise γδ T cells.

In particular embodiments, a recombinant particle, *e.g.*, a recombinant retroviral or lentiviral particle comprises a viral envelope comprising one or more mutated viral envelope glycoproteins that mediate virus-target cell fusion and one or more non-viral membrane-bound tropism polypeptides that bind an antigen on an immune effector cell, wherein the
15 antigen is selected from the group consisting of: alpha, beta, gamma, or delta chain of the T cell receptor, CD2, CD3δ, CD3ε CD3γ, CD4, CD8α, CD8β, CD28, CD134 (OX40), CD137 (4-1BB), and CD278 (ICOS).

In particular embodiments, immune effector cells include natural killer (NK) cells. NK cells do not express T cell antigen receptors (TCR), CD3 or surface immunoglobulins
20 (Ig) B cell receptor, but usually express the surface markers CD16 (FcγRIII) and CD56 in humans. In particular embodiments, a recombinant particle, *e.g.*, a recombinant retroviral or lentiviral particle comprises a viral envelope comprising one or more mutated viral envelope glycoproteins that mediate virus-target cell fusion and one or more non-viral membrane-bound tropism polypeptides that bind an antigen on an immune effector cell, wherein the
25 antigen is CD 16 (FcγRIII) and/or CD56.

In particular embodiments, immune effector cells include natural killer T (NKT) cells.

In particular embodiments, a progenitor of an immune effector cell is transduced with a recombinant particle contemplated herein and is subsequently induced to differentiate, or
30 differentiates, into one or more immune effector cells. In particular embodiments, progenitors of immune effectors cells include hematopoietic stem cells (HSCs) contained within the CD34⁺ population of cells derived from cord blood, bone marrow or mobilized peripheral blood which naturally differentiate into mature immune effector cells, or which

can be induced to differentiate into mature immune effector cells. In particular embodiments, a recombinant particle, *e.g.*, a recombinant retroviral or lentiviral particle comprises a viral envelope comprising one or more mutated viral envelope glycoproteins that mediate virus-target cell fusion and one or more non-viral membrane-bound tropism polypeptides that bind
5 an antigen on a hematopoietic stem cell, wherein the antigen is selected from the group consisting of: CD7, CD33, CD34, CD45, CD49f, CD90, CD98, CD110, CD117, CD123, CD133, CD184, CD201, FMS-like tyrosine kinase 3 (FLT3), and thrombopoietin receptor.

I. COMPOSITIONS AND FORMULATIONS

Formulations and compositions contemplated herein comprise one or more
10 polypeptides, polynucleotides, vectors, genome editing components, recombinant particles and/or immune effector cells modified *ex vivo* formulated in pharmaceutically acceptable or physiologically-acceptable compositions for administration to a cell, tissue, organ, or an animal, either alone, or in combination with one or more other modalities of therapy.

15 In particular embodiments, a composition comprises a recombinant particle, *e.g.*, a recombinant retroviral or lentiviral particle comprises a viral envelope comprising one or more mutated viral envelope glycoproteins that mediate virus-target cell fusion and one or more non-viral membrane-bound tropism polypeptides, and a payload comprising one or more polynucleotides and/or polypeptides.

20 In particular embodiments, a composition comprises a recombinant particle, *e.g.*, a recombinant retroviral or lentiviral particle comprises a viral envelope comprising one or more mutated viral envelope glycoproteins that mediate virus-target cell fusion and one or more non-viral membrane-bound tropism polypeptides, and a payload comprising a vector comprising a polynucleotide comprising or encoding a promoter operably
25 linked to one or more polynucleotide encoding one or more engineered receptors.

In particular embodiments, a composition comprises a recombinant particle, *e.g.*, a recombinant retroviral or lentiviral particle comprises a viral envelope comprising one or more mutated viral envelope glycoproteins that mediate virus-target cell fusion and one or more non-viral membrane-bound tropism polypeptides, and a payload comprising
30 a genome editing composition comprising one or more polynucleotides encoding a nuclease, a nuclease, or one or more polynucleotides encoding a DNA repair template and a nuclease.

In particular embodiments, the composition is a pharmaceutical composition. A “pharmaceutical composition” refers to a composition formulated in a pharmaceutically-acceptable or physiologically-acceptable solution for administration to a cell or a subject, either alone, or in combination with one or more other modalities of therapy.

5 “Pharmaceutically acceptable” refers to molecular entities and compositions that do not produce excessive toxicity, irritation, allergic response, or other problems or complications, commensurate with a reasonable benefit/risk ratio when administered to a human.

In particular embodiments, a composition comprises a pharmaceutically acceptable
10 carrier and a recombinant particle contemplated herein. The term “pharmaceutically acceptable carrier” refers to a diluent, adjuvant, excipient, vehicle and the like with which a recombinant particle, *e.g.*, a recombinant retroviral or lentiviral particle, is physiologically compatible with administration to a human, including but not limited to pharmaceutically acceptable cell culture media, Dulbecco's phosphate buffered saline (PBS), Ringer's solution,
15 5% dextrose in water (D5W), and normal/physiologic saline (0.9% NaCl).

In particular embodiments, a composition comprises a recombinant particle and a pharmaceutically acceptable carrier suitable for enteral or parenteral, *e.g.*, intravascular (intravenous or intraarterial), intraosseous, intraperitoneal, intraventricular, intracerebral, intracranial, intraspinal, intrathecal, intramuscular, and intramedullary, administration and
20 formulation.

In particular embodiments, a composition is substantially free of mycoplasma, endotoxin, and microbial contamination. By “substantially free” with respect to endotoxin is meant that there is less endotoxin per dose of cells than is allowed by the FDA for a biologic, which is a total endotoxin of 5 EU/kg body weight per day, which for an average
25 70 kg person is 350 EU per total dose of cells. In particular embodiments, compositions contemplated herein contain about 0.5 EU/mL to about 5.0 EU/mL, or about 0.5 EU/mL, 1.0 EU/mL, 1.5 EU/mL, 2.0 EU/mL, 2.5 EU/mL, 3.0 EU/mL, 3.5 EU/mL, 4.0 EU/mL, 4.5 EU/mL, or 5.0 EU/mL.

In particular embodiments, compositions contemplated herein are used in the
30 treatment of a cancer, GVHD, an infectious disease, an autoimmune disease, an inflammatory disease, or an immunodeficiency. In particular embodiments, a composition comprises a recombinant particle contemplated herein and one or more cytokines, growth factors, steroids, NSAIDs, DMARDs, anti-inflammatories, chemotherapeutics,

radiotherapeutics, therapeutic antibodies, or other active and ancillary agents, either alone or in combination.

It would be understood by the skilled artisan that particular embodiments contemplated herein may comprise other formulations, such as those that are well known
5 in the pharmaceutical art, and are described, for example, in *Remington: The Science and Practice of Pharmacy*, Volume I and Volume II. 23rd Edition. Edited by Adeboye Adejare. Academic Press, 2020, which is incorporated by reference herein, in its entirety.

J. METHODS OF MAKING

10 The manufacturing processes contemplated herein comprise an upstream process that produces a recombinant particle and a downstream process that purifies the recombinant particle. In preferred embodiments, a method of manufacturing a recombinant retroviral particle or recombinant lentiviral particle comprises an upstream process that produces the recombinant viral particle and a downstream process that purifies the recombinant viral
15 particle. Methods of manufacturing lentiviral particles are described in WO2023/003844, which is hereby incorporated by reference in its entirety. See, also Kutner *et al.*, BMC Biotechnol. 2009;9:10. doi: 10.1186/1472-6750-9-10 and Kutner *et al.* Nat. Protoc. 2009;4(4):495-505. doi: 10.1038/nprot.2009.22.

In particular embodiments, a method of manufacturing recombinant retroviral
20 particles or recombinant lentiviral particles comprises transfecting a host cell culture with packaging plasmids and a transfer plasmid, culturing transfected host cells to produce viral particles; and collecting and processing the culture supernatant that contains the crude viral particles to remove impurities and concentrate and formulate the particles for clinical use.

In particular embodiments, retroviral particles are manufactured by transfecting host
25 cells with a multi-plasmid system comprising (i) an envelope plasmid encoding one or more mutated viral envelope glycoproteins that retain fusogenic activity and substantially lack or lack cognate receptor binding activity and one or more non-viral membrane-bound tropism polypeptides, (ii) a packaging plasmid encoding gag-pol and (iii) a transfer plasmid or vector.

In particular embodiments, lentiviral particles are manufactured by transfecting host
30 cells with a third-generation lentiviral vector plasmid system comprising (i) an envelope plasmid encoding one or more mutated viral envelope glycoproteins that retain fusogenic activity and substantially lack or lack cognate receptor binding activity and one or more non-

viral membrane-bound tropism polypeptides, (ii) a packaging plasmid encoding gag-pol, (iii) a packaging plasmid encoding rev, and (iv) a transfer plasmid or vector.

A “transfer plasmid” or “transfer vector” encodes a viral genomic RNA modified to package a viral vector that comprises a polynucleotide sequence delivered by recombinant viral particle to a cell. In particular embodiments, a transfer plasmid comprises one or more polynucleotide sequences of interest flanked by long terminal repeat (LTR) sequences, which facilitate packaging, reverse transcription and integration of the viral vector and associated polynucleotide sequences into the host genome. Viral vectors contemplated herein are replication incompetent, *i.e.*, lack the genetic elements necessary for generation of infective particles in the host cell. For example, the viral vector may be designed with a deletion of the 3' LTR, rendering the virus “self-inactivating” (SIN).

Illustrative examples of host cells suitable for transfection with the aforementioned plasmid systems include but are not limited to HEK293 cells, HEK293S cells, HEK293T cells, HEK293T cells adapted for suspension culture (HEK293Ts), HEK293F cells, HEK293FT cells, HEK293FTM cells, and HEK293E cells.

Once host cells are transfected and produce viral particles, the cell culture is subjected to a downstream process that yields particles sufficient for clinical use. In particular embodiments, a downstream process comprises treating the contents of the bioreactor with a DNA endonuclease, *.e.g.*, benzonase; harvesting and clarifying the suspension culture supernatant by filtration; capturing and concentrating the viral particles in the resultant filtrate using affinity chromatography or cation exchange chromatography; filtering the eluate comprising the viral particles; ultrafiltering and diafiltering the viral particles using tangential flow filtration (TFF); and formulating the viral particles in a culture medium to produce a formulated bulk viral particles. In one embodiment, the formulated bulk lentiviral particles are sterile filtered, filled, and frozen; and subsequently thawed, sterile filtered, subjected to a final fill finish, and frozen. In another embodiment, the bulk lentiviral particles are sterile filtered, subjected to a final fill finish, and frozen.

K. METHODS OF USE

Recombinant particles contemplated herein are engineered to modify a cell *in vivo* to express one or more engineered receptors that bind one or more target antigens and redirect the cell to a target cell expressing the target antigen, thereby preventing, treating, or

ameliorating at least one symptom associated with, a cancer, GVHD, an infectious disease, an autoimmune disease, an inflammatory disease, or an immunodeficiency in a subject.

In particular embodiments, a method of preventing, treating, or ameliorating at least one symptom of a cancer, GVHD, an infectious disease, an autoimmune disease, an inflammatory disease, or an immunodeficiency comprises administering the subject an amount of recombinant particle contemplated herein. The term “amount” as used herein, refers to “an amount effective” or “an effective amount” of a recombinant particle contemplated herein comprising a payload contemplated herein, *etc.*, to achieve a beneficial or desired prophylactic or therapeutic result, including clinical results. A “prophylactically effective amount” refers to an amount of recombinant particle contemplated herein comprising payload contemplated herein, effective to achieve the desired prophylactic result. A “therapeutically effective amount” refers to an amount of recombinant particle contemplated herein comprising a payload contemplated herein, that is effective to “treat” a subject (*e.g.*, a patient). When a therapeutic amount is indicated, the precise amount of the compositions to be administered can be determined by a physician with consideration of individual differences in age, weight, tumor size, extent of infection or metastasis, and condition of the patient (subject).

In particular embodiments, a recombinant retroviral or lentiviral particle is engineered to modify an immune effector cell *in vivo* to express one or more engineered receptors that bind one or more target antigens to redirect the immune effector cell to a target cell expressing the target antigens, thereby preventing, treating, or ameliorating at least one symptom associated with, a cancer, GVHD, an infectious disease, an autoimmune disease, an inflammatory disease, or an immunodeficiency in a subject.

In particular embodiments, a recombinant particle contemplated herein is administered to a subject to treat, prevent, or ameliorate at least one symptom of a solid tumor in the subject.

In particular embodiments, a recombinant particle contemplated herein is administered to a subject to treat, prevent, or ameliorate at least one symptom of a solid tumor selected from the group consisting of prostate cancer, lung cancer, non-small cell lung cancer (NSCLC), liver cancer, cervical cancer, colon cancer, breast cancer, ovarian cancer, endometrial cancer, pancreatic cancer, melanoma, esophageal cancer, gastric cancer, stomach cancer, renal carcinoma, bladder cancer, hepatocellular carcinoma, renal cell

carcinoma, urothelial carcinoma, head and neck cancer, glioma, glioblastoma, colorectal cancer, thyroid cancer, epithelial cancers, or adenocarcinomas.

In particular embodiments, a recombinant particle contemplated herein is administered to a subject to treat, prevent, or ameliorate at least one symptom of a liquid or
5 hematological cancer in the subject.

In particular embodiments, a recombinant particle contemplated herein is administered to a subject to treat, prevent, or ameliorate at least one symptom of a liquid or hematological cancer selected from the group consisting of leukemias, lymphomas, and multiple myeloma. In particular embodiments, a recombinant particle contemplated herein
10 is administered to a subject to treat, prevent, or ameliorate at least one symptom of a relapsed and/or refractory leukemia, a relapsed and/or refractory lymphoma, or a relapsed and/or refractory multiple myeloma.

In particular embodiments, a recombinant particle contemplated herein is administered to a subject to treat, prevent, or ameliorate at least one symptom of a leukemia
15 or precursor thereof selected from the group consisting of: an acute lymphocytic leukemia (ALL), an acute myeloid leukemia (AML), a myelodysplastic syndrome (MDS), a plasma cell leukemia (PCL), erythroleukemia, a hairy cell leukemia (HCL), chronic lymphocytic leukemia (CLL), chronic myeloid leukemia (CML), chronic myelomonocytic leukemia (CMML) and polycythemia vera.

In particular embodiments, a recombinant particle contemplated herein is administered to a subject to treat, prevent, or ameliorate at least one symptom of a lymphoma or precursor thereof selected from the group consisting of: a Hodgkin's lymphoma or a non-Hodgkin's lymphoma, *e.g.*, diffuse large B cell lymphoma (DLBCL), follicular lymphoma (FL), mantle-cell lymphoma (MCL), small lymphocytic lymphoma (SLL), primary
25 mediastinal large B-cell lymphoma, a marginal zone B cell lymphoma (MZL), mucosa-associated lymphatic tissue lymphoma (MALT), Waldenstrom's macroglobulinemia, Burkitt's lymphoma (BL), immunoblastic large cell lymphoma, centroblastic large cell lymphoma, anaplastic B-cell lymphoma, mycosis fungoides, Sezary syndrome, T-lymphoblastic lymphoma, and anaplastic large-cell lymphoma (ALCL).

In particular embodiments, a recombinant particle contemplated herein is administered to a subject to treat, prevent, or ameliorate at least one symptom of a multiple myeloma or precursor thereof selected from the group consisting of: monoclonal gammopathy of undetermined significance (MGUS), active multiple myeloma, smoldering

multiple myeloma, light chain myeloma, non-secretory myeloma, IgD myeloma, IgE myeloma, osteosclerotic myeloma, solitary plasmacytoma of bone, and extramedullary plasmacytoma.

In particular embodiments, a recombinant particle is administered to a subject in combination with one or more anti-cancer therapies including, but not limited to, an autologous stem cell transplant (ASCT), radiation, surgery, a chemotherapeutic agent, an immunomodulatory agent and a targeted cancer therapy.

In particular embodiments, the one or more anti-cancer therapies is selected from the group consisting of 6-mercaptopurine, abiraterone, alemtuzumab, all-trans retinoic acid, anastrozole, aprepitant, arsenic trioxide, atezolizumab, avelumab, azacytidine, bafetinib, bavituximab, bevacizumab, bivatuzumab, bleomycin, blinatumomab, bortezomib, bosutinib, cabazitaxel, capecitabine, carboplatin, carfilzomib, cetuximab, cisplatin, cladribine, conatumumab, corticosteroid, crizotinib, cyclophosphamide, cytarabine, dacetuzumab, dalotuzumab, daratumumab, dasatinib, daunorubicin, danusertib, decitabine, denosumab, dexamethasone, docetaxel, doxorubicin, duligotumab, durvalumab, elotozumab, eribulin, erlotinib, etoposide, everolimus, exemestane, filgrastim, fludarabine, fluorouracil, fulvestrant, gemcitabine, gemtuzumab, hydroxyurea, ibritumomab, idarubicin, imatinib, imiquimod, indatuximab, inotuzumab, ipilimumab, ixabepilone, ixazomib, lapatinib, lenalidomide, letrozole, leuprolide, lorvotuzumab, lucatumumab, melphalan, methotrexate, milatuzumab, mitoxantrone, moxetumomab, nilotinib, nivolumab, ocaratuzumab, ofatumumab, oxaliplatin, paclitaxel, palonosetron, pembrolizumab, pemetrexed, pomalidomide, ponatinib, prednisone, radium-223, rituximab, saracatinib, siltuximab, sipuleucel-T, sorafenib, sunitinib, tamoxifen, temozolomide, temsirolimus, teprotumumab, thalidomide, tinorelbine, topotecan, tozasertib, trastuzumab, ublituximab, vincristine, and zoledronic acid.

In particular embodiments, a recombinant particle comprising one or more mutated viral envelope glycoproteins that mediate virus-target cell fusion, one or more non-viral membrane-bound tropism polypeptides, and a vector encoding a CAR, CCR, $\alpha\beta$ TCR, $\gamma\delta$ TCR, and/or a DARIC that binds BCMA, GPCR5D and/or CD38, and optionally a CTBR is administered to a subject to treat, prevent, or ameliorate at least one symptom of a multiple myeloma in the subject. In preferred embodiments, the recombinant particle is a recombinant retroviral particle or more preferably, a recombinant lentiviral particle.

In particular embodiments, a recombinant lentiviral particle comprising a viral envelope comprising a mutated VSIV-G envelope protein (*e.g.*, SEQ ID NOs: 582-645, or an amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical thereto) that mediates fusion of the viral particle and a cell but that substantially ablates or ablates the protein's ability to bind its cognate receptor expressed on a cell; one or more non-viral membrane-bound tropism polypeptides comprising an amino acid sequence set forth in any one of SEQ ID NOs: 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, and 486; and a lentiviral vector comprising or encoding a promoter operably linked to a polynucleotide encoding a CAR, CCR, $\alpha\beta$ TCR, $\gamma\delta$ TCR, and/or a DARIC that binds BCMA (*e.g.*, SEQ ID NOs: 662, 664), GPCR5D and/or CD38, and optionally a CTBR is administered to a subject to treat, prevent, or ameliorate at least one symptom of a multiple myeloma in the subject.

In particular embodiments, a recombinant lentiviral particle comprising a viral envelope comprising a mutated VSIV-G envelope protein (*e.g.*, SEQ ID NOs: 582-645, or an amino acid sequence at least 95%, 96%, 97%, 98%, or 99% identical thereto) that mediates fusion of the viral particle and a cell but that substantially ablates or ablates the protein's ability to bind its cognate receptor expressed on a cell; one or more non-viral membrane-bound tropism polypeptides comprising an amino acid sequence set forth in any one of SEQ ID NOs: 471, 472, 473, 474, 475, 476, 477, 478, 479, 480, 481, 482, 483, 484, 485, and 486; and a lentiviral vector comprising or encoding a promoter operably linked to a polynucleotide encoding a CAR, CCR, $\alpha\beta$ TCR, $\gamma\delta$ TCR, and/or a DARIC that binds CD19 (*e.g.*, SEQ ID NOs: 663, 665, 666), CD79A, or CD79B and a CCR that binds CD20 or CD22 is administered to a subject to treat, prevent, or ameliorate at least one symptom of a non-Hodgkin's lymphoma in the subject.

L. ENUMERATED EMBODIMENTS

Embodiment 1: A recombinant particle comprising: (a) a surface comprising (i) one or more mutated viral envelope glycoproteins that retain fusogenic activity and that lack cognate receptor binding activity and (ii) a non-viral membrane-bound tropism polypeptide comprising an antibody or antigen binding fragment thereof that binds an antigen expressed on an immune effector cell, a spacer polypeptide, a transmembrane domain, and optionally, an intracellular domain comprising no more than 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids; and (b) a therapeutic payload.

Embodiment 2: The particle of embodiment 1, wherein the particle is a fusosome; an extracellular vesicle, including a microvesicle, an apoptotic body, and an exosome; a lipid nanoparticle; a virus-like particle (VLPs); or a recombinant viral particle.

Embodiment 3: The particle of embodiment 1 or embodiment 2, wherein the surface
5 comprises a single layer of phospholipid, a phospholipid bilayer, a cell membrane, a capsid, or a viral envelope.

Embodiment 4: The particle of any one of embodiments 1 to 3, wherein the payload comprises one or more polynucleotides and/or polypeptides.

Embodiment 5: The particle of any one of embodiments 1 to 4, wherein the payload
10 comprises a vector that encodes a therapeutic polynucleotide or polypeptide.

Embodiment 6: The particle of any one of embodiments 1 to 5, wherein the payload comprises a vector that encodes one or more engineered receptors.

Embodiment 7: The particle of any one of embodiments 1 to 6, wherein the payload
15 comprises a vector that encodes a promoter operably linked to a polynucleotide encoding one or more engineered receptors.

Embodiment 8: A recombinant lentiviral particle comprising: (a) a viral envelope comprising (i) one or more mutated viral envelope glycoproteins that retain fusogenic activity and that lack cognate receptor binding activity and (ii) a non-viral membrane-bound tropism polypeptide comprising an antibody or antigen binding fragment thereof that binds an antigen
20 expressed on an immune effector cell, a spacer polypeptide, a transmembrane domain, and optionally, an intracellular domain comprising no more than 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids; and (b) a recombinant lentiviral vector comprising a polynucleotide encoding a promoter operably linked to a polynucleotide encoding one or more engineered receptors.

Embodiment 9: The particle of any one of embodiments 1 to 8, wherein the one or
25 more mutated viral envelope glycoproteins comprise a rhabdovirus envelope glycoprotein, or one or more paramyxovirus envelope glycoproteins.

Embodiment 10: The particle of any one of embodiments 1 to 8, wherein the one or more mutated viral envelope glycoproteins comprise a vesiculovirus envelope glycoprotein, one or more morbillivirus envelope glycoproteins or one or more henipavirus envelope
30 glycoproteins.

Embodiment 11: The particle of embodiment 10, wherein the vesiculovirus is selected from the group consisting of: vesicular stomatitis Alagoas virus (VSAV; Alagoas vesiculovirus), Carajás virus (CJSV; Carajas vesiculovirus), Chandipura virus (CHPV;

Chandipura vesiculovirus), Cocal virus (COCV; Cocal vesiculovirus), vesicular stomatitis Indiana virus (VSIV; Indiana vesiculovirus), Isfahan virus (ISFV; Isfahan vesiculovirus), Maraba virus (MARAV; Maraba vesiculovirus), Morreton virus (MORV; Morreton vesiculovirus), vesicular stomatitis New Jersey virus (VSNJV; New Jersey vesiculovirus),
 5 and Piry virus (PIRYV; Piry vesiculovirus).

Embodiment 12: The particle of embodiment 10 or embodiment 11, wherein vesiculovirus envelope glycoprotein is a vesiculovirus G protein.

Embodiment 13: The particle of any one of embodiments 10 to 12, wherein the vesiculovirus G protein is a COCV G glycoprotein (COCV-G) or a VSIV G glycoprotein
 10 (VSIV-G).

Embodiment 14: The particle of any one of embodiments 10 to 13, wherein the VSIV-G envelope protein comprises one or more of: (a) one or more amino acid substitutions at H8, N9, Q10, K47, K50, A51, S183, S179, N180, I182, M184, Y209, I347, T350, T352, E353, and R354; (b) an insertion of TT between N9 and Q10, an insertion of GGS between
 15 H8 and N9, an insertion of GGS between N9 and Q10, an insertion of TT between N208 and Y209, an insertion of GGS between P46 and K47, and an insertion of GGS between N208 and Y209; or (c) amino acid substitutions at K47 and/or R354; or (d) a deletion of residues 1-8.

Embodiment 15: The particle of any one of embodiments 10 to 14, wherein the
 20 VSIV-G envelope protein comprises one or more amino acid substitutions at H8, K47, Y209, and R354.

Embodiment 16: The particle of any one of embodiments 10 to 15, wherein the VSIV-G envelope protein comprises amino acid substitutions selected from the group consisting of: K47A and R354A; K47A and R354G; K47A and R354F; K47A and R354Q;
 25 K47G and R354A; K47G and R354G; K47G and R354F; K47G and R354Q; K47F and R354A; K47F and R354G; K47F and R354F; K47F and R354Q; K47Q and R354A; K47Q and R354G; K47Q and R354F; and K47Q and R354Q.

Embodiment 17: The particle of any one of embodiments 10 to 16, wherein the VSIV-G envelope protein comprises the amino acid sequence set forth in SEQ ID NO: 2 or
 30 an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical thereto, wherein X1= I, X2 = A, X3 = Q, and X4 = A; X1= I, X2 = A, X3 = Q, and X4 = G; X1= I, X2 = A, X3 = Q, and X4 = F; X1= I, X2 = A, X3 = Q, and X4 = Q; X1= L, X2 = A, X3 = Q, and X4 = A; X1= L, X2 = A, X3 = Q, and X4 = G; X1= L, X2 = A, X3 =

Q, and X4 = F; X1 = L, X2 = A, X3 = Q, and X4 = Q; X1 = I, X2 = A, X3 = H, and X4 = A; X1 = I, X2 = A, X3 = H, and X4 = G; X1 = I, X2 = A, X3 = H, and X4 = F; X1 = I, X2 = A, X3 = H, and X4 = Q; X1 = L, X2 = A, X3 = H, and X4 = A; X1 = L, X2 = A, X3 = H, and X4 = G; X1 = L, X2 = A, X3 = H, and X4 = F; X1 = L, X2 = A, X3 = H, and X4 = Q; X1 = I, X2 = G, X3 = Q, and X4 = A; X1 = I, X2 = G, X3 = Q, and X4 = G; X1 = I, X2 = G, X3 = Q, and X4 = F; X1 = I, X2 = G, X3 = Q, and X4 = Q; X1 = L, X2 = G, X3 = Q, and X4 = A; X1 = L, X2 = G, X3 = Q, and X4 = G; X1 = L, X2 = G, X3 = Q, and X4 = F; X1 = L, X2 = G, X3 = Q, and X4 = Q; X1 = I, X2 = G, X3 = H, and X4 = A; X1 = I, X2 = G, X3 = H, and X4 = G; X1 = I, X2 = G, X3 = H, and X4 = F; X1 = I, X2 = G, X3 = H, and X4 = Q; X1 = L, X2 = G, X3 = H, and X4 = A; X1 = L, X2 = G, X3 = H, and X4 = G; X1 = L, X2 = G, X3 = H, and X4 = F; X1 = L, X2 = G, X3 = H, and X4 = Q; X1 = I, X2 = F, X3 = Q, and X4 = A; X1 = I, X2 = F, X3 = Q, and X4 = G; X1 = I, X2 = F, X3 = Q, and X4 = F; X1 = I, X2 = F, X3 = Q, and X4 = Q; X1 = L, X2 = F, X3 = Q, and X4 = A; X1 = L, X2 = F, X3 = Q, and X4 = G; X1 = L, X2 = F, X3 = Q, and X4 = F; X1 = L, X2 = F, X3 = Q, and X4 = Q; X1 = I, X2 = F, X3 = H, and X4 = A; X1 = I, X2 = F, X3 = H, and X4 = G; X1 = I, X2 = F, X3 = H, and X4 = F; X1 = I, X2 = F, X3 = H, and X4 = Q; X1 = L, X2 = F, X3 = H, and X4 = A; X1 = L, X2 = F, X3 = H, and X4 = G; X1 = L, X2 = F, X3 = H, and X4 = F; X1 = L, X2 = F, X3 = H, and X4 = Q; X1 = I, X2 = Q, X3 = Q, and X4 = A; X1 = I, X2 = Q, X3 = Q, and X4 = G; X1 = I, X2 = Q, X3 = Q, and X4 = F; X1 = I, X2 = Q, X3 = Q, and X4 = Q; X1 = L, X2 = Q, X3 = Q, and X4 = A; X1 = L, X2 = Q, X3 = Q, and X4 = G; X1 = L, X2 = Q, X3 = Q, and X4 = F; X1 = L, X2 = Q, X3 = Q, and X4 = Q; X1 = I, X2 = Q, X3 = H, and X4 = A; X1 = I, X2 = Q, X3 = H, and X4 = G; X1 = I, X2 = Q, X3 = H, and X4 = F; X1 = I, X2 = Q, X3 = H, and X4 = Q; X1 = L, X2 = Q, X3 = H, and X4 = A; X1 = L, X2 = Q, X3 = H, and X4 = G; X1 = L, X2 = Q, X3 = H, and X4 = F; and X1 = L, X2 = Q, X3 = H, and X4 = Q.

Embodiment 18: The particle of any one of embodiments 10 to 17, wherein the VSIV-G envelope protein comprises the amino acid sequence set forth in any one of SEQ ID NOs: 582-645 or an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical thereto.

Embodiment 19: The particle of any one of embodiments 10 to 18, wherein the VSIV-G envelope protein comprises the amino acid sequence set forth in any one of SEQ ID NOs: 630, 634, 638, and 642 or an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical thereto.

Embodiment 20: The particle of any one of embodiments 10 to 13, wherein the vesiculovirus G protein is COCV-G.

Embodiment 21: The recombinant lentivirus of embodiment 11, wherein the COCV-G envelope protein comprises one or more amino acid substitutions at K47 and/or R354.

5 Embodiment 22: The recombinant lentivirus of embodiment 11 or embodiment 12, wherein the COCV-G envelope protein comprises amino acid substitutions selected from the group consisting of: K47A and R354A; K47A and R354G; K47A and R354F; K47A and R354Q; K47G and R354A; K47G and R354G; K47G and R354F; K47G and R354Q; K47F and R354A; K47F and R354G; K47F and R354F; K47F and R354Q; K47Q and R354A; K47Q and R354G; K47Q and R354F; and K47Q and R354Q.

Embodiment 23: The recombinant lentivirus of any one of embodiments 11 to 13, wherein the COCV-G envelope protein comprises the amino acid sequence set forth in SEQ ID NO: 4 or an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical thereto, wherein X1 = A and X2 = A; X1 = A and X2 = G; X1 = A and X2 = F; X1 = A and X2 = Q; X1 = G and X2 = A; X1 = G and X2 = G; X1 = G and X2 = F; X1 = G and X2 = Q; X1 = F and X2 = A; X1 = F and X2 = G; X1 = F and X2 = F; X1 = F and X2 = Q; X1 = Q and X2 = A; X1 = Q and X2 = G; X1 = Q and X2 = F; or X1 = Q and X2 = Q.

Embodiment 24: The recombinant lentivirus of any one of embodiments 11 to 14, wherein the COCV-G envelope protein comprises the amino acid sequence set forth in any one of SEQ ID NOs: 646-661 or an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical thereto.

Embodiment 25: The particle of embodiment 10, wherein the one or more morbillivirus envelope glycoproteins are measles virus F (MV-F) and measles virus H (MV-H).

Embodiment 26: The particle of embodiment 25, wherein the MV-H protein comprises one or more amino acid substitutions at Y463, R515, S530, and F531.

Embodiment 27: The particle of embodiment 16 or embodiment 17, wherein the MV-H protein comprises one or more amino acid substitutions selected from the group consisting of: Y463A, R515A, S530, and F531.

Embodiment 28: The particle of any one of embodiments 25 to 27, wherein the MV-H protein comprises the amino acid sequence set forth in SEQ ID NO: 7.

Embodiment 29: The particle of embodiment 10, wherein the one or more henipavirus envelope glycoproteins are nipah virus F (NiV-F) and nipah virus G (NiV-G).

Embodiment 30: The particle of embodiment 29, wherein the NiV-G protein comprises one or more amino acid substitutions at E468, W471, Q497, and E500.

5 Embodiment 31: The particle of embodiment 29 or embodiment 30, wherein the NiV-G protein comprises one or more amino acid substitutions selected from the group consisting of: E468A, W471A, Q497A, and E500A.

Embodiment 32: The particle of any one of embodiments 29 to 31, wherein the NiV-G protein comprises the amino acid sequence set forth in SEQ ID NO: 10.

10 Embodiment 33: The particle of any one of embodiments 1 to 32, wherein the antibody or antigen binding fragment thereof is selected from the group consisting of: a Camel Ig, a Llama Ig, an Alpaca Ig, Ig NAR, a Fab' fragment, a F(ab')₂ fragment, a bispecific Fab dimer (Fab₂), a trispecific Fab trimer (Fab₃), an Fv, a single chain Fv protein (scFv), a bis-scFv, (scFv)₂, a minibody, a diabody, a triabody, a tetrabody, a disulfide stabilized Fv protein ("dsFv"), a Fibronectin type III (FN3) domain antibody, and a single-domain antibody (sdAb, a camelid VHH, Nanobody).

Embodiment 34: The particle of any one of embodiments 1 to 33, wherein the antibody or antigen binding fragment thereof binds an antigen expressed on an immune effector cell selected from the group consisting of: the alpha, beta, gamma, or delta chain of
20 the T cell receptor, CD2, CD3δ, CD3ε CD3γ, CD4, CD8α, and CD8β.

Embodiment 35: The particle of any one of embodiments 1 to 34, wherein the antibody or antigen binding fragment thereof comprises (a) a heavy chain variable region (VH) comprising a CDRH1, a CDRH2, and a CDRH3 of an antibody or antigen binding fragment thereof set forth in Table 5; (b) a polypeptide linker; and (c) a light chain variable
25 region (VL) comprising a CDRL1, a CDRL2, and a CDRL3 of an antibody or antigen binding fragment thereof set forth in Table 5.

Embodiment 36: The particle of any one of embodiments 1 to 35, wherein the antibody or antigen binding fragment thereof comprises (a) a heavy chain variable region (VH) of an antibody or antigen binding fragment thereof set forth in Table 5; (b) a
30 polypeptide linker; and (c) a light chain variable region (VL) of an antibody or antigen binding fragment thereof set forth in Table 5.

Embodiment 37: The particle of any one of embodiments 1 to 36, wherein the antibody or antigen binding fragment thereof comprises: (a) a heavy chain variable region

(VH) of an antibody or antigen binding fragment thereof set forth in Table 5; (b) a polypeptide linker selected from the group consisting of: (GGGGS)_n wherein n = 1, 2, 3, 4 or 5; S(GGGGS)_n wherein n = 1, 2, 3, 4 or 5; GEGTSTGSGGSGGSGGAD, GSTSGSGKPGSGEGSTKG and variants thereof comprising an amino acid sequence 95% identical thereto; and (c) the corresponding light chain variable region (VL) of the antibody or antigen binding fragment thereof set forth in Table 5.

Embodiment 38: The particle of any one of embodiments 1 to 37, wherein the antibody or antigen binding fragment thereof comprises the amino acid sequence set forth in any one of SEQ ID NOs: 19, 20, 29, 30, 39, 40, 49, 50, 59, 60, 69, 70, 79, 80, 89, 90, 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, 170, 179, 180, 189, 190, 199, 200, 209, 210, 219, 220, 229, 230, 239, 240, 249, 250, 259, 260, 269, 270, 279, 280, 289, 290, 299, 300, 309, 310, 319, 320, 329, 330, 339, 340, 349, 350, 359, 360, 369, 370, 379, 380, 389, 390, 399, 400, 409, and 410.

Embodiment 39: The particle of any one of embodiments 1 to 38, wherein the antibody or antigen binding fragment thereof comprises the amino acid sequence set forth in any one of SEQ ID NOs: 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, and 170.

Embodiment 40: The particle of any one of embodiments 1 to 39, wherein the antibody or antigen binding fragment thereof comprises the amino acid sequence set forth in any one of SEQ ID NOs: 99 or 100, 109 or 110, 119 or 120, 129 or 130, 139 or 140, 149 or 150, 159 or 160, and 169 or 170.

Embodiment 41: The particle of any one of embodiments 1 to 40, wherein the spacer comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 411-434.

Embodiment 42: The particle of any one of embodiments 1 to 41, wherein the spacer comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 411-413, SEQ ID NOs: 414-423, SEQ ID NOs: 424-427, or SEQ ID NOs: 428-434.

Embodiment 43: The particle of any one of embodiments 1 to 42, wherein the transmembrane domain comprises an amino acid sequence at least 85% identical to, at least

90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 435, 436, 437, 438, 439, 440 and 441.

5 Embodiment 44: The particle of any one of embodiments 1 to 43, wherein the intracellular domain comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 442, 443, 444, 445, 446, 447 and 448.

10 Embodiment 45: The particle of any one of embodiments 1 to 44, wherein the tropism polypeptide comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 455-576.

15 Embodiment 46: The particle of any one of embodiments 1 to 45, wherein the tropism polypeptide comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 471-486.

20 Embodiment 47: The particle of any one of embodiments 1 to 45, wherein the tropism polypeptide comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 535-554.

25 Embodiment 48: The particle of any one of embodiments 1 to 45, wherein the tropism polypeptide comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 555-562.

30 Embodiment 49: The particle of any one of embodiments 1 to 45, wherein the tropism polypeptide comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 563 or 564 or SEQ ID NO: 471 or SEQ ID NO: 553.

Embodiment 50: The particle of any one of embodiments 1 to 49, further comprising one or more secondary non-viral membrane bound tropism polypeptides.

Embodiment 51: The particle of embodiment 50, wherein the one or more secondary non-viral membrane bound tropism polypeptides comprise one or more of CD80, CD86,
5 CD137L, OX40L, and ICOSL or variants thereof.

Embodiment 52: The particle of any one of embodiments 1 to 51, further comprising one or more secondary non-viral membrane-bound tropism polypeptides at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the
10 amino acid sequence set forth in any one of SEQ ID NOs: 577-581.

Embodiment 53: The particle of any one of embodiments 8 to 52, wherein the recombinant lentiviral vector is engineered or derived from a lentiviral genome of a lentivirus selected from the group consisting of: human immunodeficiency virus 1 (HIV-1); human immunodeficiency virus 2 (HIV-2); visna-maedi virus (VMV); caprine arthritis-encephalitis
15 virus (CAEV); equine infectious anemia virus (EIAV); feline immunodeficiency virus (FIV); bovine immune deficiency virus (BIV); and simian immunodeficiency virus (SIV).

Embodiment 54: The particle of any one of embodiments 8 to 53, wherein the recombinant lentiviral vector further comprises one or more polynucleotides encoding one or more of the following: a signal peptide, a post-transcriptional regulatory element, an
20 insulator element, a selectable marker, and a cell suicide gene.

Embodiment 55: The particle of embodiment 54, wherein the post-transcriptional regulatory element is a woodchuck hepatitis virus post-transcriptional regulatory element (WPRE) or a hepatitis B virus post-transcriptional regulatory element (HPRE).

Embodiment 56: The particle of any one of embodiments 7 to 55, wherein the
25 promoter is selected from the group consisting of: a β -actin promoter, a cytomegalovirus (CMV) immediate early promoter, a simian virus 40 (SV40) (*e.g.*, early or late) promoter, a Moloney murine leukemia virus (MoMLV) promoter, a Rous sarcoma virus (RSV) promoter, a herpes simplex virus (HSV) (thymidine kinase) promoter, an SV40/CD43 promoter, a spleen focus forming virus (SFFV) promoter, an elongation factor 1-alpha (EF1 α)
30 short promoter (intronless), an EF1 α long promoter containing an intron, a Ubiquitin C (UBC) promoter, a phosphoglycerate kinase-1 (PGK) promoter, a cytomegalovirus enhancer/chicken β -actin (CAG) promoter, and a myeloproliferative sarcoma virus enhancer,

negative control region deleted, dl587rev primer-binding site substituted (MND) U3 promoter.

Embodiment 57: The particle of any one of embodiments 6 to 56, wherein the one or more engineered receptors are selected from the group consisting of: a chimeric antigen
5 receptor (CAR), a chimeric costimulatory receptor (CCR), an alpha-beta T cell receptor ($\alpha\beta$ TCR), a gamma delta T cell receptor ($\gamma\delta$ TCR), a dimerizing agent regulated immunoreceptor complex (DARIC), a chimeric TGF- β receptor (CTBR), and a zetakine receptor.

Embodiment 58: The particle of any one of embodiments 6 to 57, wherein the one or more engineered receptors bind an antigen selected from the group consisting of: alpha
10 folate receptor (FR α), $\alpha\beta$ 6 integrin, BAFFR, B cell maturation antigen (BCMA), B7-H3 (CD276), B7-H6, carbonic anhydrase IX (CAIX), CD16, CD19, CD20, CD22, CD30, CD33, CD37, CD38, CD44, CD44v6, CD44v7/8, CD70, CD79A, CD79B, CD123, CD133, CD138, CD171, carcinoembryonic antigen (CEA), claudin 6, (CLDN6), claudin 18 isoform 2 (CLDN18.2), C-type lectin-like molecule-1 (CLL-1), CD2 subset 1 (CS-1), chondroitin
15 sulfate proteoglycan 4 (CSPG4), cutaneous T cell lymphoma-associated antigen 1 (CTAGE1), delta like canonical Notch ligand 3 (DLL3), epidermal growth factor receptor (EGFR), epidermal growth factor receptor variant III (EGFRvIII), epithelial glycoprotein 2 (EGP2), epithelial glycoprotein 40 (EGP40), epithelial cell adhesion molecule (EPCAM), ephrin type-A receptor 2 (EPHA2), erb-b2 receptor tyrosine kinase 4 (ERBB4), fibroblast
20 activation protein (FAP), Fc Receptor Like 5 (FCRL5), fetal acetylcholinesterase receptor (AChR), ganglioside G2 (GD2), ganglioside G3 (GD3), Glypican-3 (GPC3), G Protein-Coupled Receptor Class C Group 5 Member D (GPCR5D), EGFR family including ErbB2 (HER2), HER2 p95, IL-10R α , IL-13R α 2, Kappa, cancer/testis antigen 2 (LAGE-1A), Lambda, Lewis-Y (LeY), L1 cell adhesion molecule (L1-CAM), melanoma antigen gene
25 (MAGE)-A1, MAGE-A3, MAGE-A4, MAGE-A6, MAGEA10, melanoma antigen recognized by T cells 1 (MelanA or MART1), Mesothelin (MSLN), MUC1, MUC16, MHC class I chain related proteins A (MICA), MHC class I chain related proteins B (MICB), neural cell adhesion molecule (NCAM), cancer/testis antigen 1 (NY-ESO-1), placenta-specific 1 (PLAC1), preferentially expressed antigen in melanoma (PRAME), prostate stem cell
30 antigen (PSCA), prostate-specific membrane antigen (PSMA), receptor tyrosine kinase-like orphan receptor 1 (ROR1), SLAMF7, synovial sarcoma, X breakpoint 2 (SSX2), Survivin, TACI, tumor associated glycoprotein 72 (TAG72), tumor endothelial marker 1 (TEM1/CD248), tumor endothelial marker 7-related (TEM7R), transforming growth factor

beta 1 (TFGβ1), trophoblast glycoprotein (TPBG), UL16-binding protein (ULBP) 1, ULBP2, ULBP3, ULBP4, ULBP5, ULBP6, vascular endothelial growth factor receptor 2 (VEGFR2), and Wilms tumor 1 (WT-1).

Embodiment 59: The particle of any one of embodiments 6 to 58, wherein the one
5 or more engineered receptors bind an antigen selected from the group consisting of: BCMA, CD19, CD20, CD22, CD33, CD38, CD79A, CD79B, GPCR5D, MAGE-A4, MSLN, MUC16, NY-ESO-1, PSCA, PSMA and ROR1.

Embodiment 60: The particle of any one of embodiments 6 to 58, wherein the one
10 or more engineered receptors bind an antigen selected from the group consisting of: BCMA, CD19, CD20, CD22, CD38, CD79A, CD79B, and GPCR5D.

Embodiment 61: The particle of any one of embodiments 6 to 60, wherein the one
or more engineered receptors bind an antigen selected from the group consisting of: BCMA, CD38, and GPCR5D.

Embodiment 62: The particle of any one of embodiments 6 to 60, wherein the one
15 or more engineered receptors bind an antigen selected from the group consisting of: CD19, CD20, CD22, CD79A, and CD79B.

Embodiment 63: The particle of any one of embodiments 6 to 62, wherein the one
or more engineered receptors comprises an extracellular antigen binding domain, a hinge domain, a transmembrane domain, and one or more intracellular signaling domains.

Embodiment 64: The particle of any one of embodiments 6 to 63, wherein the one
20 or more engineered antigen receptors comprises an extracellular antigen binding domain selected from the group consisting of: a receptor ectodomain, a ligand, or an antibody or antigen binding fragment thereof selected from the group consisting of: a Camel Ig, a Llama Ig, an Alpaca Ig, Ig NAR, a Fab' fragment, a F(ab')₂ fragment, a bispecific Fab dimer (Fab₂),
25 a trispecific Fab trimer (Fab₃), an Fv, a single chain Fv protein (scFv), a bis-scFv, (scFv)₂, a minibody, a diabody, a triabody, a tetrabody, a disulfide stabilized Fv protein ("dsFv"), a Fibronectin type III (FN3) domain antibody, a single-domain antibody (sdAb, a camelid VHH, Nanobody), and a centyrin.

Embodiment 65: The particle of any one of embodiments 57 to 64, wherein the CAR
30 comprises a hinge domain isolated or derived from a polypeptide selected from the group consisting of: CD4, CD8β, CD8α, CD28, CD134, CD137, CD152, CD278, IgG1, IgG2, IgG3, and IgG4.

Embodiment 66: The particle of any one of embodiments 57 to 65, wherein the CAR comprises a transmembrane domain isolated or derived from a polypeptide selected from the group consisting of: alpha, beta, gamma, or delta chain of the T-cell receptor, CD3 δ , CD3 ϵ , CD3 γ , CD3 ζ , CD4, CD5, CD8 α , CD9, CD16, CD22, CD27, CD28, CD33, CD37, CD45, 5 CD64, CD80, CD86, CD134, CD137, CD152, CD154, CD278, amnionless (AMN), and programmed cell death 1 (PDCD1).

Embodiment 67: The particle of any one of embodiments 57 to 66, wherein CAR comprises a primary signaling domain isolated or derived from a polypeptide selected from the group consisting of: FcR γ , FcR β , CD3 γ , CD3 δ , CD3 ϵ , CD3 ζ , CD22, CD79A, CD79B, 10 and CD66d.

Embodiment 68: The particle of any one of embodiments 57 to 67, wherein the CAR comprises one or more costimulatory domains isolated or derived from a polypeptide selected from the group consisting of: Toll-like receptor 1 (TLR1), TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLR10, caspase recruitment domain family member 11 15 (CARD11), CD2, CD7, CD27, CD28, CD30, CD40, CD54 (ICAM), CD83, CD94, CD134 (OX40), CD137 (4-1BB), CD278 (ICOS), DNAX-Activation Protein 10 (DAP10), Linker for activation of T-cells family member 1 (LAT), SH2 Domain-Containing Leukocyte Protein Of 76 kD (SLP76), T cell receptor associated transmembrane adaptor 1 (TRAT1), TNFR2, TNFRS14, TNFRS18, TNFRS25, and zeta chain of T cell receptor associated 20 protein kinase 70 (ZAP70).

Embodiment 69: The particle of any one of embodiments 6 to 68, wherein the one or more engineered receptors further comprises a CCR comprising an extracellular antigen binding domain that binds an antigen different than the antigen bound by the CAR, a hinge domain, a transmembrane domain, and one or more intracellular signaling domains.

Embodiment 70: The particle of any one of embodiments 6 to 57, wherein the one or more engineered receptors comprises a DARIC comprising a DARIC signaling component comprising a multimerization domain, a transmembrane domain and one or more intracellular signaling domains; and a DARIC binding component comprising an extracellular antigen binding domain, an extracellular antigen binding domain, a 25 transmembrane domain, and optionally one or more intracellular signaling domains.

Embodiment 71: The particle of any one of embodiments 6 to 70, wherein the one or more engineered receptors comprises a CTBR comprising (a) a first polypeptide comprising an extracellular TGF β 1-binding domain of TGF β R2, a transmembrane domain,

and a first interleukin receptor intracellular signaling domain; (b) a polypeptide cleavage signal; and (c) a second polypeptide comprising an extracellular TGF β 1-binding domain of TGF β R1, a transmembrane domain, and a second interleukin receptor intracellular signaling domain.

5 Embodiment 72: A recombinant lentiviral particle comprising: (a) a surface comprising (i) one or more mutated viral envelope glycoproteins that retain fusogenic activity and that lack cognate receptor binding activity, wherein the one or more mutated viral envelope glycoproteins comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to any one of SEQ ID NOs: 630,
10 634, 638, and 642 and (ii) a non-viral membrane-bound tropism polypeptide comprising an antibody or antigen binding fragment thereof comprising an amino acid sequence set forth in any one of SEQ ID NOs: 91 and 95, and 99 or 100, that binds an antigen expressed on an immune effector cell, a spacer polypeptide, and a GPI anchor domain or a transmembrane domain, and optionally, an intracellular domain comprising no more than 1, 2, 3, 4, 5, 6, 7,
15 8, 9 or 10 amino acids; and (b) a therapeutic payload encoding an engineered antigen receptor.

 Embodiment 73: A recombinant lentiviral particle comprising: (a) a surface comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or
20 identical to SEQ ID NO: 642 and (ii) a non-viral membrane-bound tropism polypeptide comprising an antibody or antigen binding fragment thereof comprising an amino acid sequence set forth in SEQ ID NO: 99 or 100, that binds an antigen expressed on an immune effector cell, a spacer polypeptide, and a GPI anchor domain or a transmembrane domain, and optionally, an intracellular domain comprising no more than 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10
25 amino acids; and (b) a lentiviral vector encoding an engineered antigen receptor.

 Embodiment 74: A recombinant lentiviral particle comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or
30 identical to SEQ ID NO: 642 and (ii) a non-viral membrane-bound tropism polypeptide comprising an amino acid sequence set forth in any one of SEQ ID NOs: 99 or 100, that binds an antigen expressed on an immune effector cell, a spacer polypeptide, and a GPI anchor domain or a transmembrane domain, and optionally, an intracellular domain comprising no

more than 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids; and (b) a therapeutic payload encoding an engineered antigen receptor.

Embodiment 75: A recombinant lentiviral particle comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid
5 sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide comprising an amino acid sequence set forth in any one of SEQ ID NOs: 461, 471, 483, 537, and 553; and optionally (iii) a secondary non-viral membrane-bound tropism polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 577; and (b) a lentiviral vector
10 encoding a chimeric antigen receptor.

Embodiment 76: A recombinant lentiviral particle comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide that
15 comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 471; and optionally (iii) a secondary non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 577; and (b) a lentiviral vector encoding a chimeric antigen receptor comprising an
20 amino acid sequence set forth in any one of SEQ ID NOs: 662-666.

Embodiment 77: A recombinant lentiviral particle comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide that
25 comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 471; and optionally (iii) a secondary non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 577; and (b) a lentiviral vector encoding a chimeric antigen receptor that binds a
30 polypeptide selected from any one of BCMA, CD19, CD20, CD22, CD38, CD79A, CD79B, and GPCR5D.

Embodiment 78: A recombinant lentiviral particle comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid

sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 471; and optionally (iii) a secondary non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 577; and (b) a lentiviral vector encoding a chimeric antigen receptor that binds BCMA.

Embodiment 79: A recombinant lentiviral particle comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 471; and optionally (iii) a secondary non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 577; and (b) a lentiviral vector encoding a chimeric antigen receptor that binds GPCR5D.

Embodiment 80: A recombinant lentiviral particle comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 471; and optionally (iii) a secondary non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 577; and (b) a lentiviral vector encoding a chimeric antigen receptor that binds CD19.

Embodiment 81: A cell transduced with the particle of any one of embodiments 1 to 80.

Embodiment 82: The cell of embodiment 81, wherein the cell is an immune effector cell.

Embodiment 83: The cell of embodiment 81 or embodiment 82, wherein the cell is a T cell, a natural killer (NK) cell, or a natural killer T (NKT) cell.

Embodiment 84: A composition comprising the particle of any one of embodiments 1 to 80 or the cell of any one of embodiments 81 to 83.

5 Embodiment 85: A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the particle of any one of embodiments 1 to 80, the cell of any one of embodiments 81 to 83, or the composition of embodiment 84.

Embodiment 86: A method of treating, preventing, or ameliorating at least one symptom of a disease, disorder or condition associated therewith in a subject, comprising
10 administering to the subject an effective amount of the particle of any one of embodiments 1 to 80, the cell of any one of embodiments 81 to 83, the composition of embodiment 84, or the pharmaceutical composition of embodiment 85.

Embodiment 87: The method of embodiment 86, wherein the disease, disorder, or condition is a cancer.

15 Embodiment 88: The method of embodiment 86 or embodiment 87, wherein the cancer is leukemia selected from the group consisting of: acute lymphocytic leukemia (ALL), an acute myeloid leukemia (AML), a myelodysplastic syndrome (MDS), a plasma cell leukemia (PCL), erythroleukemia, a hairy cell leukemia (HCL), chronic lymphocytic leukemia (CLL), chronic myeloid leukemia (CML), chronic myelomonocytic leukemia
20 (CMML) and polycythemia vera.

Embodiment 89: The method of embodiment 86 or embodiment 87, wherein the cancer is non-NHL or NHL selected from the group consisting of: diffuse large B cell lymphoma (DLBCL), follicular lymphoma (FL), mantle-cell lymphoma (MCL), small lymphocytic lymphoma (SLL), primary mediastinal large B-cell lymphoma, a marginal
25 zone B cell lymphoma (MZL), mucosa-associated lymphatic tissue lymphoma (MALT), Burkitt's lymphoma (BL), immunoblastic large cell lymphoma, centroblastic large cell lymphoma, anaplastic B-cell lymphoma, mycosis fungoides, Sezary syndrome, T-lymphoblastic lymphoma, and anaplastic large-cell lymphoma (ALCL).

Embodiment 90: The method of embodiment 86 or embodiment 87, wherein the
30 cancer is MM selected from the group consisting of: active multiple myeloma, smoldering multiple myeloma, light chain myeloma, non-secretory myeloma, IgD myeloma, IgE myeloma, osteosclerotic myeloma, solitary plasmacytoma of bone, and extramedullary plasmacytoma.

Embodiment 91: The method of any one of embodiments 86 to 90, wherein the cancer is relapsed and/or refractory.

Embodiment 92: The method of embodiment 86, wherein the disease, disorder, or condition is an autoimmune disease.

5 Embodiment 93: The method of embodiment 92, wherein the autoimmune disease is systemic lupus erythematosus, rheumatoid arthritis, idiopathic thrombocytopenic purpura, myasthenia gravis, or autoimmune hemolytic anemia.

 Embodiment 94: A method of transducing an immune effector cell *in vivo*, comprising administering to a subject a pharmaceutical composition comprising a
10 pharmaceutically acceptable carrier and an effective amount of the particle of any one of embodiments 1 to 80.

 Embodiment 95: A method of making the particle of any one of embodiments 1 to 80 comprising (a) transfecting a host cell with four polynucleotides: a first polynucleotide that encodes lentiviral gag-pol, a second polynucleotide that encodes lentiviral rev, a third
15 polynucleotide that encodes the one or more mutated viral envelope glycoproteins that retain fusogenic activity and lack cognate receptor binding activity and the one or more non-viral membrane-bound tropism polypeptides, and a fourth polynucleotide that is a transfer plasmid encoding a recombinant lentiviral vector encoding an engineered antigen receptor; and b) culturing the transduced cell for about 1 to 3 days to produce the particle.

20 Embodiment 96: A kit comprising the particle of any one of embodiments 1 to 80, a pharmaceutically acceptable carrier, and instructions for use.

 All publications, patent applications, and issued patents cited in this specification are
25 herein incorporated by reference as if each individual publication, patent application, or issued patent were specifically and individually indicated to be incorporated by reference.

 Although the foregoing embodiments have been described in some detail by way of illustration and example for purposes of clarity of understanding, it will be readily apparent to one of ordinary skill in the art in light of the teachings contemplated herein that certain
30 changes and modifications may be made thereto without departing from the spirit or scope of the appended claims. The following examples are provided by way of illustration only and not by way of limitation. Those of skill in the art will readily recognize a variety of noncritical parameters that could be changed or modified to yield essentially similar results.

M. EXAMPLESEXAMPLE 1**T CELL SPECIFIC TROPISM MOLECULES TRANSDUCE AND ACTIVATE JURKAT CELLS AND PERIPHERAL BLOOD MONONUCLEAR CELLS (PBMCs)**

5 Transduction and activation of Jurkat cells and human PBMCs with recombinant lentivirus generated with an envelope expressing T cell specific tropism molecules, *e.g.*, CD3.2, CD3.3, CD3.4, CD3.5, CD3.6, CD3.8, CD3.9, CD3.11, and CD3.15, was determined. The tropism molecules comprised anti-CD3 scFvs in either or both heavy chain (HC) – light chain (LC) orientations, fused to a CD8 α stalk, transmembrane and intracellular
10 domains (*e.g.*, SEQ ID NOs: 457, 459, 460, 461, 462, 463, 464, 465, 469, 471, 475, and 483).

1 $\times 10^5$ Jurkat cells were plated in each well of a 96-well plate. Some wells were used as untransduced controls (UTD), controls harboring a wild-type fusogen (WT), or controls lacking a mutant fusogen (-) and/or tropism molecule (-). The remaining wells were treated with recombinant lentivirus comprising a lentiviral vector (LVV) encoding GFP, a
15 CD3-based tropism molecule (*e.g.*, SEQ ID NOs: 457, 459, 460, 461, 462, 463, 464, 465, 469, 471, 475, and 483), and a mutant fusogen (+; *e.g.*, SEQ ID NO: 642). Three days post-transduction, Jurkat cells were harvested and CD69 expression (activation) and GFP expression (transduction) analyzed by flow cytometry. Recombinant lentivirus expressing different tropism molecules independently led to different amounts of transduction and CD69
20 expression. For example, lentivirus expressing CD3.4 based tropism molecules transduced relatively fewer cells than CD3.3, CD3.6, CD3.9, CD3.11, or CD3.15 based tropism molecules whereas the level of activation among lentivirus expressing these tropism molecules was comparable. See Figure 1A.

1 $\times 10^6$ human PBMCs were plated in each well of a 24-well plate. Some wells were
25 used as untransduced controls (UTD), controls harboring a wild-type fusogen (VSIV-G WT) or controls lacking a mutant fusogen (CD3.4) and/or tropism molecule (mVSIV-G). The remaining wells were treated with recombinant lentivirus comprising a LVV encoding GFP, a CD3-based tropism molecule (*e.g.*, SEQ ID NOs: 457, 459, 460, 461, 462, 463, 464, 465, 469, 471, 475, and 483), and a mutant fusogen (*e.g.*, SEQ ID NO: 642). Three days post-
30 transduction, PBMCs were harvested and CD69 expression (activation) and GFP expression (transduction) analyzed by flow cytometry. Recombinant lentivirus expressing different

tropism molecules independently led to different amounts of transduction and CD69 expression. For example, lentivirus expressing CD3.4 based tropism molecules transduced relatively fewer cells than CD3.3, CD3.5, and CD3.9 based tropism molecules whereas the level of activation among lentivirus expressing these tropism molecules was comparable.

5 See Figure 1B.

Taken together, the data indicated that binder selection impacts target cell transduction and activation in a cell type specific manner.

EXAMPLE 2

TROPISM MOLECULES WITH MONOMERIC OR DIMERIC CD8A STALKS

10

SHOW COMPARABLE EXPRESSION

Tropism molecule expression (as determined by anti-CD3 surface expression) was examined on HEK293T cells transfected with plasmids encoding tropism molecules encoding anti-CD3 scFvs, *e.g.*, CD3.3, CD3.4, CD3.9, CD3.11, CD3.12, CD3.13, CD3.15, and CD3.16 (*e.g.*, SEQ ID NOs: 459, 461, 471, 475, 477, 479, 483, 485), fused to monomeric
15 or dimeric CD8 α stalk architectures (*e.g.*, SEQ ID NOs: 412, 411); mutant VSIV-G fusogen (*e.g.*, SEQ ID NOs: 642); lentiviral GAG/POL; lentiviral REV; and a transfer vector plasmid encoding GFP or an anti-BCMA CAR.

6 x 10⁵ HEK293T cells were plated in each well of a 6-well plate, and the next day transfected with tropism plasmids, lentiviral packaging plasmids, and one of two transfer
20 vector plasmids using standard techniques. After 3 days, producer cells were harvested for flow cytometry analysis of cell-surface anti-CD3 expression. Flow cytometry plots depict anti-CD3 molecule expression on HEK293T producer cells. Many of the anti-CD3 binders were highly expressed on the producer cell surface regardless of the monomeric or dimeric CD8 α stalk architecture. See Figure 2. In addition, CAR expression did not significantly
25 alter the relative expression levels among the tropism molecules assayed.

These data indicated that tropism molecules are sufficiently expressed on producer cells and that CD8 α stalk architecture had little to no detectable impact on tropism molecule expression in the presence or absence of CAR expression.

EXAMPLE 3TROPISM MOLECULE ARCHITECTURE AND TROPISM MOLECULE EXPRESSION,
FUNCTIONAL LENTIVIRAL TITER, AND SPECIFICITY*Tropism Molecule Architecture*

- 5 Tropism molecules were built using CD4, CD8 α , CD45, CEACAM, and CADHERIN 1 (ECAD) stalks of different predicted lengths and rigidity. See Figure 3A.

Tropism Molecule Expression

- Tropism molecule expression (as determined by anti-CD3 surface expression) was examined on HEK293T cells transfected with plasmids encoding tropism molecules identified in the following table; mutant VSIV-G fusogen (*e.g.*, SEQ ID NO: 642); lentiviral GAG/POL; lentiviral REV; and a transfer vector plasmid encoding GFP.

Table 15 lists the lentivirus ID, and the SEQ ID NOs for tropism molecule components as well as a representative SEQ ID NO of the complete tropism molecule. Note that lentivirus (LV) 1 also comprises a human CD80 molecule, *e.g.*, SEQ ID NO: 577.

15 **Table 15**

Lentivirus ID	Tropism Molecule Architecture					
	Binder	Stalk	Est. Stalk Length (nm)	TM domain	IC domain	Tropism
1	49	411	13	437	444	461
2	99	411	13	437	444	471
3	99	415	25	439	446	537
4	99	419	30	439	446	545
5	99	416	35	439	446	539
6	99	423	17	439	446	553
7	99	422	21	439	446	551
8	99		16			
9	99		not determined			
10	99		16			
11	99	427	20	440	447	561
12	99	426	15	440	447	559
13	99	425	10	440	447	557
14	99	424	5	440	447	555
15	99	428	24	NA	NA	565
16	99	429	24	439	446	563
17	99	430	16	NA	NA	567
18	99	431	8	NA	NA	569
19	99	432	20	NA	NA	571
20	99	433	12	NA	NA	573

21	99	434	4	NA	NA	575
22	99	412	13	437	444	-
23	99	414	40	439	446	535

6 x 10⁵ HEK293T producer cells were plated in each well of a 6-well plate, and the next day transfected with tropism plasmids, lentiviral packaging plasmids, and transfer vector plasmid using standard techniques. After 3 days, producer cells were harvested for flow cytometry analysis of cell-surface anti-CD3 expression. Flow cytometry plots depict anti-CD3 molecule expression on HEK293T producer cells. Anti-CD3 binders were expressed on producer cells, and expression appeared independent of stalk architecture, with a minimum log-fold difference in anti-CD3 geometric mean fluorescence intensity (gMFI) from untransfected controls. See Figure 3B.

These data indicated that tropism molecules comprising stalks and transmembrane domains or GPI anchors are sufficiently expressed and/or presented on producer cells and that stalk length and rigidity did not substantially alter the relative expression levels among most tropism molecules assayed.

Functional Lentiviral Titer

Recombinant lentiviral particles were generated as described in the *Tropism Molecule Expression* section and Table 15 of this Example and the transducing units per nanogram of P24 of each lentivirus was determined.

1 x 10⁵ Jurkat cells were plated in each well of a 96-well plate and treated with LV1-LV21. The number of transduced cells was determined three days after transduction using GFP expression analyzed by flow cytometry. The number of recombinant lentiviral particles per transduction was quantified using a P24 ELISA and the transducing units per nanogram P24 was determined. See Figure 3C.

These data indicated that tropism molecule stalk architecture may influence the functional titer of recombinant lentivirus and that some stalk architectures may enable more potent lentivirus than others, *e.g.*, compare LVs 2, 3, 7, 8 with LVs 11-14.

In vitro Specificity

Recombinant lentiviral particles were generated as described in the *Tropism Molecule Expression* section and Table 15 of this Example and specificity of LV comprising tropism molecules with different stalk architectures was determined *in vitro*.

5 5×10^5 human PBMCs ($CD3^+$) from three donors were each plated in a well of a 24-well plate and treated with P24-matched (9083 pg P24) of LV 2, LV 3, LV 22, or LV 23. After three days, the PBMCs in each well were transferred to a well of a 24-well GREX vessel and supplemented with growth media. On day 9, the cells were harvested and the number of transduced cells expressing GFP was determined using flow cytometry. 1×10^5 Jurkat cells ($CD3^+$) were plated in each well of a 96-well plate and treated with P24-matched (1816 pg P24) of LV1, LV 2, LV 3, LV6, LV7, LV 15, LV16, or LV19. After 3 days, the cells were harvested and the number of transduced cells expressing GFP was determined using flow cytometry. 1×10^5 A549 cells ($CD3^-$) were plated in each well of a 24-well plate and treated with P24-matched (1816 pg P24) of LV1, LV 2, LV 3, LV6, LV7, LV 15, LV16, LV19, LV 22, or LV 23. After 3 days, the cells were harvested and the number of transduced cells expressing GFP was determined using flow cytometry.

On-target PBMC transduction was plotted against off-target A549 transduction. These data indicated that tropism molecules comprising an anti-CD3 scFv with different stalk architectures can affect lentivirus specificity *in vitro*. See Figure 3D, left panel. On-target Jurkat cell transduction was plotted against off-target A549 transduction using LVs expressing different stalk architectures. These data indicated that stalk architectures can be engineered to substantially improve LV specificity *in vitro*. See Figure 3D, right panel.

EXAMPLE 4

20 TROPISM MOLECULE ARCHITECTURE VERSUS FUNCTIONAL LENTIVIRAL TITER AND SPECIFICITY

The relationship between stalk length, LV titer, and specificity was determined for recombinant lentiviral particles expressing tropism molecules with different stalk architectures. Recombinant lentiviruses were generated as described in the *Tropism Molecule Expression* section and Table 15 of Example 3.

1×10^5 Jurkat cells ($CD3^+$) were plated in each well of a 96-well plate and treated with P24-matched (1816 pg P24) of LV 1 - LV 21. After 3 days, the cells were harvested and the number of transduced cells expressing GFP was determined using flow cytometry. 1×10^5 A549 cells ($CD3^-$) were plated in each well of a 24-well plate and treated with P24-matched (1816 pg P24) of LV 1 – LV 21.

Tropism molecule stalk length did not positively correlate with LV functional titer when assessed in either Jurkat or A549 cells. See Figure 4, left panel. Tropism molecule stalk length showed a positive correlation with LV specificity, measured as the ratio of Jurkat cell (on-target) transduction to A549 cell (off-target) transduction. See Figure 4, right panel.

5 In addition to being a general trend among the data, the correlation between tropism molecule stalk length and LV specificity also depended on the specific protein from which the stalk was derived. These data indicated that stalk length is a variable that affects LV specificity.

EXAMPLE 5

10 TROPISM MOLECULE ARCHITECTURE AFFECTS LENTIVIRAL TRANSDUCTION AND ACTIVATION OF PBMCs

Transduction and activation of human PBMCs with recombinant lentivirus generated as described in the *Tropism Molecule Expression* section and Table 15 of Example 3 were determined.

5 x 10⁵ human PBMCs were plated in each well of a 24-well plate and treated with
15 untransduced control (UTD) cells activated with anti-CD3 and anti-CD28 coated beads or P24-matched (0.5 ng or 2 ng of P24) of LV 1 – LV 21. After three days, the PBMCs in each well were transferred to a well of a 24-well GREX vessel and supplemented with growth media. On days 9 and 10, cells were harvested and the number of transduced cells expressing GFP was determined using flow cytometry.

20 Recombinant lentivirus expressing anti-CD3-based tropism molecules with different stalks displayed different levels of PBMC transduction and activation at day 9. For example, LV 2, 3, 6, and 7 transduced relatively more cells than LV 14, 15, 17, and 18 whereas the level of activation among lentivirus expressing these tropism molecules was somewhat comparable. See Figure 5A, compare top and bottom panels.

25 Dose-dependent differences in PBMC transduction were also apparent in day 10 cells transduced with LV expressing anti-CD3-based tropism molecules with different stalks; PBMCs transduced with increased amounts of LV (2 ng P24) displayed increased GFP expression compared to PBMCs transduced with less LV (0.5 ng P24). See Figure 5B, left panel. P24 matched titers of LV 1 – LV 21 on both PBMCs and Jurkat cells were positively
30 correlated. Moreover, LV comprising anti-CD3-based tropism molecules with particular

stalks, *e.g.*, LV 3, 6, 7 favored on-target transduction in both cell types. See Figure 5B, right panel.

These data indicated that anti-CD3-based tropism molecule stalk length contributes to LV transduction and activation in primary cells and cell lines *in vitro*.

5

EXAMPLE 6

TROPISM MOLECULE ARCHITECTURE AFFECTS LENTIVIRAL TRANSDUCTION AND ACTIVATION OF CD3 POSITIVE CELLS *IN VIVO*

Transduction and activation of human T cells with recombinant lentivirus expressing different tropism molecules were determined in an *in vivo* NOD scid gamma (NSG) mouse model.

Recombinant lentivirus was produced by transient transfection of HEK293T cells with plasmids encoding tropism molecules identified in the following table; a wild type VSIV-G fusogen or mutant VSIV-G fusogen (*e.g.*, SEQ ID NO: 642); lentiviral GAG/POL; lentiviral REV; and a transfer vector plasmid encoding GFP.

Table 16 lists the lentivirus ID, and the SEQ ID NOs for tropism molecule components as well as a representative SEQ ID NO of the complete tropism molecule and the fusogen that was used. Note that lentivirus (LV) 1 also comprises a human CD80 molecule, *e.g.*, SEQ ID NO: 577.

Table 16

Lentivirus ID	Tropism Molecule Architecture						VSIV-G Fusogen
	Binder	Stalk	Est. Stalk Length (nm)	TM domain	IC domain	Tropism	
1	49	411	13	437	444	461	642
2	99	411	13	437	444	471	642
3	99	415	25	439	446	537	642
24	159	411	13	437	444	483	642
25	159	415	25	439	446	-	642
26	No tropism molecule						wild type

NSG mice were injected intravenously with 1×10^6 human PBMCs, one day later mice were intravenously with vehicle (DMEM; (-)) or 2.5×10^7 TU of LV 1-3 or 24-26. Mice received three doses of 2×10^5 IU recombinant human IL-2 at 6, 24, and 48h post LV administration. Seven days post LV administration, mice were sacrificed. LV transduction

and activation of GFP-expressing human PBMCs in mouse blood and spleens was analyzed using flow cytometry.

LV 2 and LV 24, which share the same stalk architecture, transduced human PBMCs as well as control LV 1, which expresses both an anti-CD3-based tropism molecule (same stalk as LV 2 and LV 24) and a CD80-based tropism molecule. In addition, LV 1, LV 2 and LV 24 demonstrably activated human PBMCs in both the blood and spleen. In contrast, LV 3 and LV 25, which share the same stalk architecture but a different stalk architecture than the anti-CD3-based tropism molecules in LV 1, 2 and 24, did not transduce or activate human PBMCs to the same extent. See Figure 6, top panel (transduction), bottom panel (activation). These data indicated that anti-CD3-based tropism molecule stalk architecture affects PBMC transduction and activation in mice.

EXAMPLE 7

TROPISM MOLECULE DEMONSTRATES EXQUISITE SPECIFICITY *IN VIVO*

The specificity of recombinant lentivirus comprising an envelope that expresses an anti-CD3-based tropism molecule and a mutant VSIV-G fusogen and a lentiviral vector encoding GFP was investigated in a mouse model.

8-week-old NOD scid gamma (NSG) mice were intravenously administered 1×10^6 human PBMCs. The next day, mice were intravenously administered vehicle (DMEM) or LV 2 or LV 26 (Example 6) at 1×10^7 TU, 2.5×10^7 TU, 1×10^8 TU, or 2.5×10^8 TU per mouse. 2.5×10^7 TU was previously identified as the therapeutic dose in a related model.

Seven days later, mice were euthanized and heart, brain, ovary, stomach, eye, skeletal muscle, skin, large intestine, small intestine, pancreas, kidney, lung, liver, bone marrow, blood, and spleen among others were collected and analyzed. Vector copy number (VCN), immunohistochemistry (IHC), and flow cytometry were used to assess the safety/biodistribution profile of LV 2.

Mice treated with LV 2 displayed dose dependent increases in GFP positive T cells in the blood (Figure 7A) and spleen (Figure 7B, rightmost column). No GFP positive T cells were seen in mice treated with vehicle or LV 26, which lacks a CD3-based tropism molecule.

At the therapeutic dose level (2.5×10^7 TU/mouse), flow cytometry detected LV 2 transduced cells in the spleen (13.1% GFP positive T cells). Importantly, GFP expression was only detected in resident immune cells and phagocytic cells in some non-target tissues.

GFP expression was not detected in the majority of tissues examined. At log-fold higher doses (2.5×10^8 TU/mouse), flow cytometry detected LV 2 transduced cells in the spleen (29.6% GFP positive T cells). Importantly, GFP expression was only detected in resident immune cells and phagocytic cells in some non-target tissues. GFP expression was not
5 detected in the majority of tissues examined at therapeutic dose levels.

Together these data showed the exquisite sensitivity mediated by the anti-CD3-based tropism molecule expressed on the envelope of LV 2 highlighted by the on-target transduction detected in CD3 expressing cells in the spleen; the lack of GFP expression detected in non-target tissues such as the brain and heart; and GFP expression restricted to
10 resident immune cells and phagocytic cells in some non-target tissues. See Figure 7B.

EXAMPLE 8

IN VIVO ADMINISTERED LENTIVIRUS DEMONSTRATES ANTI-TUMOR EFFICACY IN A MULTIPLE MYELOMA MOUSE MODEL

The anti-tumor efficacy of *in vivo* administered recombinant lentivirus comprising
15 an envelope that expresses an anti-CD3-based tropism molecule and a mutant VSIV-G fusogen and a lentiviral vector encoding an anti-BCMA CAR was investigated in a multiple myeloma mouse model.

Recombinant lentivirus for *in vivo* administration was produced by transient transfection of HEK293T cells with plasmids encoding an anti-CD3-based tropism molecule
20 (SEQ ID NO: 471); a mutant VSIV-G fusogen (*e.g.*, SEQ ID NO: 642); lentiviral GAG/POL; lentiviral REV; and a transfer vector plasmid encoding GFP (LV GFP) or an anti-BCMA CAR (LV anti-BCMA CAR).

Ex vivo anti-BCMA CAR T cells were also prepared. Briefly, HEK293T cells were transiently transfected with plasmids encoding a wild-type VSIV-G fusogen; lentiviral
25 GAG/POL; lentiviral REV; and a transfer vector plasmid encoding the same anti-BCMA CAR used in manufacturing the *in vivo* administered lentivirus. PBMCs were then transduced with the recombinant lentivirus and cultured for 7 days to generate anti-BCMA CAR T cells.

RPMI Model First Study

NOD scid gamma (NSG) mice were subcutaneously injected with 1×10^6 RPMI-8226 cells (a BMCA positive tumor cell line). Tumors were allowed to grow to a size of about 50mm^3 (about two weeks).

Three groups of mice were then intravenously administered 1×10^6 human PBMCs.
5 The next day: a fourth group of mice was administered 2×10^6 unmodified *ex vivo* cultured T cells; a fifth group of mice was administered 2×10^6 *ex vivo* anti-BCMA CAR T cells; mice that received the 1×10^6 human PBMCs the day before were administered vehicle control (DMEM) or 2.5×10^7 TU LV GFP or LV anti-BCMA CAR. All groups of mice then received three doses of 2×10^5 IU recombinant human IL-2 at 6, 24, and 48 hours post LV
10 administration. Tumor volume was measured externally using calipers and mice were euthanized at pre-determined humane endpoints based on tumor size and body condition.

Tumor size increased in mice treated with vehicle, unmodified *ex vivo* cultured T cells, and LV GFP. Mice treated with *ex vivo* anti-BCMA CAR T cells or *in vivo* with LV anti-BCMA CAR experienced complete and comparable tumor regression. Figure 8, left
15 panel.

RPMI Model Second Study

NSG mice were subcutaneously injected with 1×10^6 RPMI-8226 and tumors were allowed to grow to a size of about 50mm^3 (about two weeks).

Two groups of mice were then intravenously administered 1×10^6 human PBMCs.
20 The next day: a third group of mice was administered 2×10^6 *ex vivo* anti-BCMA CAR T cells; mice that received the 1×10^6 human PBMCs the day before were administered vehicle control (DMEM) or 2.5×10^7 TU LV anti-BCMA CAR. All groups of mice then received three doses of 2×10^5 IU recombinant human IL-2 at 6, 24, and 48 hours post LV administration. Tumor volume was measured externally using calipers and mice were
25 euthanized at pre-determined humane endpoints based on tumor size and body condition.

Tumor size increased in mice treated with vehicle. Mice treated with *ex vivo* anti-BCMA CAR T cells or *in vivo* with LV anti-BCMA CAR experienced complete and comparable tumor regression. Figure 8, right panel.

EXAMPLE 9

IN VIVO ADMINISTERED LENTIVIRUS DEMONSTRATES ANTI-TUMOR EFFICACY
IN A MULTIPLE MYELOMA MOUSE MODEL

The anti-tumor efficacy of *in vivo* administered recombinant lentivirus comprising
5 an envelope that expresses an anti-CD3-based tropism molecule and a mutant VSIV-G
fusogen and a lentiviral vector encoding an anti-BCMA CAR was investigated in a multiple
myeloma mouse model.

Recombinant lentivirus for *in vivo* administration was produced by transient
transfection of HEK293T cells with plasmids encoding an anti-CD3-based tropism molecule
10 (SEQ ID NO: 471 or SEQ ID NO: 553); a mutant VSIV-G fusogen (*e.g.*, SEQ ID NO: 642);
lentiviral GAG/POL; lentiviral REV; and a transfer vector plasmid encoding an anti-BCMA
CAR (LV anti-BCMA CAR).

Ex vivo anti-BCMA CAR T cells were also prepared. Briefly, HEK293T cells were
transiently transfected with plasmids encoding a wild-type VSIV-G fusogen; lentiviral
15 GAG/POL; lentiviral REV; and a transfer vector plasmid encoding the same anti-BCMA
CAR used in manufacturing the *in vivo* administered lentivirus. PBMCs were then
transduced with the recombinant lentivirus and cultured for 7 days to generate anti-BCMA
CAR T cells.

Daudi Model Study

20 NSG mice were intravenously injected with 2×10^6 Daudi cells labeled with firefly
luciferase. After four days, five out of six groups of mice were intravenously administered 1×10^6
human PBMCs. The next day mice that received the 1×10^6 human PBMCs were
administered vehicle control (DMEM); 1.25×10^7 or IU 1.25×10^8 IU of recombinant
lentivirus comprising a viral envelope expressing SEQ ID NO: 471 (LV 27) or SEQ ID NO:
25 553 (LV 28). Mice that were not administered PBMCs were administered 5×10^6 *ex vivo*
anti-BCMA CAR T cells. All groups of mice then received three doses of 2×10^5 IU
recombinant human IL-2 at 6, 24, and 48 hours post LV administration. Tumor volume was
measured by using a bioluminescence imaging system.

Tumor size increased in mice treated with vehicle. Mice treated with *ex vivo* anti-
30 BCMA CAR T cells demonstrated transient control of tumor growth. Mice treated with

recombinant lentivirus comprising a viral envelope expressing SEQ ID NO: 471 or SEQ ID NO: 553 experienced dose-dependent tumor regression. Figure 9.

- 5 In general, in the following claims, the terms used should not be construed to limit the claims to the specific embodiments disclosed in the specification and the claims, but should be construed to include all possible embodiments along with the full scope of equivalents to which such claims are entitled. Accordingly, the claims are not limited by the disclosure.

CLAIMS

What is claimed is:

1. A recombinant particle comprising:

(a) a surface comprising (i) one or more mutated viral envelope glycoproteins that retain fusogenic activity and that lack cognate receptor binding activity and (ii) a non-viral membrane-bound tropism polypeptide comprising an antibody or antigen binding fragment thereof that binds an antigen expressed on an immune effector cell, a spacer polypeptide, a transmembrane domain, and optionally, an intracellular domain comprising no more than 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids; and

(b) a therapeutic payload.

2. The particle of claim 1, wherein the particle is a fusosome; an extracellular vesicle, a microvesicle, an apoptotic body, or an exosome; a lipid nanoparticle; a virus-like particle (VLP); or a recombinant viral particle.

3. The particle of claim 1 or claim 2, wherein the surface comprises a single layer of phospholipid, a phospholipid bilayer, a cell membrane, a capsid, or a viral envelope.

4. The particle of any one of claims 1 to 3, wherein the payload comprises one or more polynucleotides and/or polypeptides.

5. The particle of any one of claims 1 to 4, wherein the payload comprises a vector that encodes a therapeutic polynucleotide or polypeptide.

6. The particle of any one of claims 1 to 5, wherein the payload comprises a vector that encodes one or more engineered receptors.

7. The particle of any one of claims 1 to 6, wherein the payload comprises a vector that encodes a promoter operably linked to a polynucleotide encoding one or more engineered receptors.

8. A recombinant lentiviral particle comprising:

(a) a viral envelope comprising (i) one or more mutated viral envelope glycoproteins that retain fusogenic activity and that lack cognate receptor binding activity and (ii) a non-viral membrane-bound tropism polypeptide comprising an antibody or antigen binding fragment thereof that binds an antigen expressed on an immune effector cell, a spacer polypeptide, a transmembrane domain, and optionally, an intracellular domain comprising no more than 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids; and

(b) a recombinant lentiviral vector comprising a polynucleotide encoding a promoter operably linked to a polynucleotide encoding one or more engineered receptors.

9. The particle of any one of claims 1 to 8, wherein the one or more mutated viral envelope glycoproteins comprise a rhabdovirus envelope glycoprotein, or one or more paramyxovirus envelope glycoproteins.

10. The particle of any one of claims 1 to 9, wherein the one or more mutated viral envelope glycoproteins comprise a vesiculovirus envelope glycoprotein, one or more morbillivirus envelope glycoproteins or one or more henipavirus envelope glycoproteins.

11. The particle of claim 10, wherein the vesiculovirus is selected from the group consisting of: vesicular stomatitis Alagoas virus (VSAV; Alagoas vesiculovirus), Carajás virus (CJSV; Carajas vesiculovirus), Chandipura virus (CHPV; Chandipura vesiculovirus), Cocal virus (COCV; Cocal vesiculovirus), vesicular stomatitis Indiana virus (VSIV; Indiana vesiculovirus), Isfahan virus (ISFV; Isfahan vesiculovirus), Maraba virus (MARAV; Maraba vesiculovirus), Morreton virus (MORV; Morreton vesiculovirus), vesicular stomatitis New Jersey virus (VSNJV; New Jersey vesiculovirus), and Piry virus (PIRYV; Piry vesiculovirus).

12. The particle of claim 10 or claim 11, wherein the vesiculovirus envelope glycoprotein is a vesiculovirus G protein.

13. The particle of any one of claims 10 to 12, wherein the vesiculovirus G protein is a COCV G glycoprotein (COCV-G) or a VSIV G glycoprotein (VSIV-G).

14. The particle of any one of claims 10 to 13, wherein the VSIV-G envelope protein comprises one or more of:

(a) one or more amino acid substitutions at H8, N9, Q10, K47, K50, A51, S183, S179, N180, I182, M184, Y209, I347, T350, T352, E353, and R354;

(b) an insertion of TT between N9 and Q10, an insertion of GGS between H8 and N9, an insertion of GGS between N9 and Q10, an insertion of TT between N208 and Y209, an insertion of GGS between P46 and K47, and an insertion of GGS between N208 and Y209; or

(c) amino acid substitutions at K47 and/or R354; or

(d) a deletion of residues 1-8.

15. The particle of any one of claims 10 to 14, wherein the VSIV-G envelope protein comprises one or more amino acid substitutions at H8, K47, Y209, and R354.

16. The particle of any one of claims 10 to 15, wherein the VSIV-G envelope protein comprises amino acid substitutions selected from the group consisting of: K47A and R354A; K47A and R354G; K47A and R354F; K47A and R354Q; K47G and R354A; K47G and R354G; K47G and R354F; K47G and R354Q; K47F and R354A; K47F and R354G; K47F and R354Q; K47Q and R354A; K47Q and R354G; K47Q and R354F; and K47Q and R354Q.

17. The particle of any one of claims 10 to 16, wherein the VSIV-G envelope protein comprises the amino acid sequence set forth in SEQ ID NO: 2 or an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical thereto, wherein $X_1 = I$, $X_2 = A$, $X_3 = Q$, and $X_4 = A$; $X_1 = I$, $X_2 = A$, $X_3 = Q$, and $X_4 = G$; $X_1 = I$, $X_2 = A$, $X_3 = Q$, and $X_4 = F$; $X_1 = I$, $X_2 = A$, $X_3 = Q$, and $X_4 = Q$; $X_1 = L$, $X_2 = A$, $X_3 = Q$, and $X_4 = A$; $X_1 = L$, $X_2 = A$, $X_3 = Q$, and $X_4 = G$; $X_1 = L$, $X_2 = A$, $X_3 = Q$, and $X_4 = F$; $X_1 = L$, $X_2 = A$, $X_3 = Q$, and $X_4 = Q$; $X_1 = I$, $X_2 = A$, $X_3 = H$, and $X_4 = A$; $X_1 = I$, $X_2 = A$, $X_3 = H$, and $X_4 = G$; $X_1 = I$, $X_2 = A$, $X_3 = H$, and $X_4 = F$; $X_1 = I$, $X_2 = A$, $X_3 = H$, and $X_4 = Q$; $X_1 = L$, $X_2 = A$, $X_3 = H$, and $X_4 = A$; $X_1 = L$, $X_2 = A$, $X_3 = H$, and $X_4 = G$; $X_1 = L$, $X_2 = A$, $X_3 = H$, and $X_4 = F$; $X_1 = L$, $X_2 = A$, $X_3 = H$, and $X_4 = Q$; $X_1 = I$, $X_2 = G$, $X_3 = Q$, and $X_4 = A$; $X_1 = I$, $X_2 = G$, $X_3 = Q$, and $X_4 = G$; $X_1 = I$, $X_2 = G$, $X_3 = Q$, and $X_4 = F$; $X_1 = I$, $X_2 = G$, $X_3 = Q$, and $X_4 = Q$; $X_1 = L$, $X_2 = G$, $X_3 = Q$, and $X_4 = A$; $X_1 = L$, $X_2 = G$, $X_3 = Q$, and $X_4 = G$; $X_1 = L$, $X_2 = G$, $X_3 = Q$, and $X_4 = F$; $X_1 = L$, $X_2 = G$, $X_3 = Q$, and $X_4 = Q$; $X_1 = I$, $X_2 = G$, $X_3 = H$, and $X_4 = A$; $X_1 = I$, $X_2 = G$, $X_3 = H$, and $X_4 = G$; $X_1 = I$, $X_2 = G$, $X_3 = H$, and $X_4 = F$; $X_1 = I$, $X_2 = G$, $X_3 = H$, and $X_4 = Q$; $X_1 = L$, $X_2 = G$, $X_3 = H$, and $X_4 = A$; $X_1 = L$, $X_2 = G$, $X_3 = H$, and $X_4 = G$; $X_1 = L$, $X_2 = G$, $X_3 = H$, and $X_4 = F$; $X_1 = L$, $X_2 = G$, $X_3 = H$, and $X_4 = Q$; $X_1 = I$, $X_2 = F$, $X_3 = Q$, and $X_4 = A$; $X_1 = I$, $X_2 = F$, $X_3 = Q$, and $X_4 = G$; $X_1 = I$, $X_2 = F$, $X_3 = Q$, and $X_4 = F$; $X_1 = I$, $X_2 = F$, $X_3 = Q$, and $X_4 = Q$; $X_1 = L$,

X₂ = F, X₃ = Q, and X₄ = A; X₁ = L, X₂ = F, X₃ = Q, and X₄ = G; X₁ = L, X₂ = F, X₃ = Q, and X₄ = F; X₁ = L, X₂ = F, X₃ = Q, and X₄ = Q; X₁ = I, X₂ = F, X₃ = H, and X₄ = A; X₁ = I, X₂ = F, X₃ = H, and X₄ = G; X₁ = I, X₂ = F, X₃ = H, and X₄ = F; X₁ = I, X₂ = F, X₃ = H, and X₄ = Q; X₁ = L, X₂ = F, X₃ = H, and X₄ = A; X₁ = L, X₂ = F, X₃ = H, and X₄ = G; X₁ = L, X₂ = F, X₃ = H, and X₄ = F; X₁ = L, X₂ = F, X₃ = H, and X₄ = Q; X₁ = I, X₂ = Q, X₃ = Q, and X₄ = A; X₁ = I, X₂ = Q, X₃ = Q, and X₄ = G; X₁ = I, X₂ = Q, X₃ = Q, and X₄ = F; X₁ = I, X₂ = Q, X₃ = Q, and X₄ = Q; X₁ = L, X₂ = Q, X₃ = Q, and X₄ = A; X₁ = L, X₂ = Q, X₃ = Q, and X₄ = G; X₁ = L, X₂ = Q, X₃ = Q, and X₄ = F; X₁ = L, X₂ = Q, X₃ = Q, and X₄ = Q; X₁ = I, X₂ = Q, X₃ = H, and X₄ = A; X₁ = I, X₂ = Q, X₃ = H, and X₄ = G; X₁ = I, X₂ = Q, X₃ = H, and X₄ = F; X₁ = I, X₂ = Q, X₃ = H, and X₄ = Q; X₁ = L, X₂ = Q, X₃ = H, and X₄ = A; X₁ = L, X₂ = Q, X₃ = H, and X₄ = G; X₁ = L, X₂ = Q, X₃ = H, and X₄ = F; and X₁ = L, X₂ = Q, X₃ = H, and X₄ = Q.

18. The particle of any one of claims 10 to 17, wherein the VSIV-G envelope protein comprises the amino acid sequence set forth in any one of SEQ ID NOs: 582-645 or an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical thereto.

19. The particle of any one of claims 10 to 18, wherein the VSIV-G envelope protein comprises the amino acid sequence set forth in any one of SEQ ID NOs: 630, 634, 638, and 642 or an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical thereto.

20. The particle of any one of claims 10 to 13, wherein the vesiculovirus G protein is COCV-G.

21. The recombinant lentivirus of claim 20, wherein the COCV-G envelope protein comprises one or more amino acid substitutions at K47 and/or R354.

22. The recombinant lentivirus of claim 20 or claim 21, wherein the COCV-G envelope protein comprises amino acid substitutions selected from the group consisting of: K47A and R354A; K47A and R354G; K47A and R354F; K47A and R354Q; K47G and R354A; K47G and R354G; K47G and R354F; K47G and R354Q; K47F and R354A; K47F and R354G; K47F and R354F; K47F and R354Q; K47Q and R354A; K47Q and R354G; K47Q and R354F; and K47Q and R354Q.

23. The recombinant lentivirus of any one of claims 20 to 22, wherein the COCV-G envelope protein comprises the amino acid sequence set forth in SEQ ID NO: 4 or an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical thereto, wherein $X_1 = A$ and $X_2 = A$; $X_1 = A$ and $X_2 = G$; $X_1 = A$ and $X_2 = F$; $X_1 = A$ and $X_2 = Q$; $X_1 = G$ and $X_2 = A$; $X_1 = G$ and $X_2 = G$; $X_1 = G$ and $X_2 = F$; $X_1 = G$ and $X_2 = Q$; $X_1 = F$ and $X_2 = A$; $X_1 = F$ and $X_2 = G$; $X_1 = F$ and $X_2 = F$; $X_1 = F$ and $X_2 = Q$; $X_1 = Q$ and $X_2 = A$; $X_1 = Q$ and $X_2 = G$; $X_1 = Q$ and $X_2 = F$; or $X_1 = Q$ and $X_2 = Q$.

24. The recombinant lentivirus of any one of claims 20 to 23, wherein the COCV-G envelope protein comprises the amino acid sequence set forth in any one of SEQ ID NOs: 646-661 or an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% identical thereto.

25. The particle of claim 10, wherein the one or more morbillivirus envelope glycoproteins are measles virus F (MV-F) and measles virus H (MV-H).

26. The particle of claim 25, wherein the MV-H protein comprises one or more amino acid substitutions at Y463, R515, S530, and F531.

27. The particle of claim 25 or claim 26, wherein the MV-H protein comprises one or more amino acid substitutions selected from the group consisting of: Y463A, R515A, S530, and F531.

28. The particle of any one of claims 25 to 27, wherein the MV-H protein comprises the amino acid sequence set forth in SEQ ID NO: 7.

29. The particle of claim 10, wherein the one or more henipavirus envelope glycoproteins are nipah virus F (NiV-F) and nipah virus G (NiV-G).

30. The particle of claim 29, wherein the NiV-G protein comprises one or more amino acid substitutions at E468, W471, Q497, and E500.

31. The particle of claim 29 or claim 30, wherein the NiV-G protein comprises one or more amino acid substitutions selected from the group consisting of: E468A, W471A, Q497A, and E500A.

32. The particle of any one of claims 29 to 31, wherein the NiV-G protein comprises the amino acid sequence set forth in SEQ ID NO: 10.

33. The particle of any one of claims 1 to 32, wherein the antibody or antigen binding fragment thereof is selected from the group consisting of: a Camel Ig, a Llama Ig, an Alpaca Ig, Ig NAR, a Fab' fragment, a F(ab')₂ fragment, a bispecific Fab dimer (Fab₂), a trispecific Fab trimer (Fab₃), an Fv, a single chain Fv protein (scFv), a bis-scFv, (scFv)₂, a minibody, a diabody, a triabody, a tetrabody, a disulfide stabilized Fv protein ("dsFv"), a Fibronectin type III (FN3) domain antibody, a single-domain antibody (sdAb, a camelid VHH, Nanobody), and a centyrin.

34. The particle of any one of claims 1 to 33, wherein the antibody or antigen binding fragment thereof binds an antigen expressed on an immune effector cell selected from the group consisting of: the alpha, beta, gamma, or delta chain of the T cell receptor, CD2, CD3δ, CD3ε CD3γ, CD4, CD8α, and CD8β.

35. The particle of any one of claims 1 to 34, wherein the antibody or antigen binding fragment thereof comprises (a) a heavy chain variable region (VH) comprising a CDRH1, a CDRH2, and a CDRH3 of an antibody or antigen binding fragment thereof set forth in Table 5; (b) a polypeptide linker; and (c) a light chain variable region (VL) comprising a CDRL1, a CDRL2, and a CDRL3 of an antibody or antigen binding fragment thereof set forth in Table 5.

36. The particle of any one of claims 1 to 35, wherein the antibody or antigen binding fragment thereof comprises (a) a heavy chain variable region (VH) of an antibody or antigen binding fragment thereof set forth in Table 5; (b) a polypeptide linker; and (c) a light chain variable region (VL) of an antibody or antigen binding fragment thereof set forth in Table 5.

37. The particle of any one of claims 1 to 36, wherein the antibody or antigen binding fragment thereof comprises:

(a) a heavy chain variable region (VH) of an antibody or antigen binding fragment thereof set forth in Table 5;

(b) a polypeptide linker selected from the group consisting of: (GGGGS)_n wherein n = 1, 2, 3, 4 or 5; S(GGGGS)_n wherein n = 1, 2, 3, 4 or 5; GEGTSTGSGGSGGSGGAD, GSTSGSGKPGSGEGSTKG and variants thereof comprising an amino acid sequence 95% identical thereto; and

(c) the corresponding light chain variable region (VL) of the antibody or antigen binding fragment thereof set forth in Table 5.

38. The particle of any one of claims 1 to 37, wherein the antibody or antigen binding fragment thereof comprises the amino acid sequence set forth in any one of SEQ ID NOs: 19, 20, 29, 30, 39, 40, 49, 50, 59, 60, 69, 70, 79, 80, 89, 90, 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, 170, 179, 180, 189, 190, 199, 200, 209, 210, 219, 220, 229, 230, 239, 240, 249, 250, 259, 260, 269, 270, 279, 280, 289, 290, 299, 300, 309, 310, 319, 320, 329, 330, 339, 340, 349, 350, 359, 360, 369, 370, 379, 380, 389, 390, 399, 400, 409, and 410.

39. The particle of any one of claims 1 to 38, wherein the antibody or antigen binding fragment thereof comprises the amino acid sequence set forth in any one of SEQ ID NOs: 99, 100, 109, 110, 119, 120, 129, 130, 139, 140, 149, 150, 159, 160, 169, and 170.

40. The particle of any one of claims 1 to 39, wherein the antibody or antigen binding fragment thereof comprises the amino acid sequence set forth in any one of SEQ ID NOs: 99 or 100, 109 or 110, 119 or 120, 129 or 130, 139 or 140, 149 or 150, 159 or 160, and 169 or 170.

41. The particle of any one of claims 1 to 40, wherein the spacer comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 411-434.

42. The particle of any one of claims 1 to 41, wherein the spacer comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical

to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 411-413, SEQ ID NOs: 414-423, SEQ ID NOs: 424-427, or SEQ ID NOs: 428-434.

43. The particle of any one of claims 1 to 42, wherein the transmembrane domain comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 435, 436, 437, 438, 439, 440 or 441.

44. The particle of any one of claims 1 to 43, wherein the intracellular domain comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 442, 443, 444, 445, 446, 447 or 448.

45. The particle of any one of claims 1 to 44, wherein the tropism polypeptide comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 455-576.

46. The particle of any one of claims 1 to 45, wherein the tropism polypeptide comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 471-486.

47. The particle of any one of claims 1 to 45, wherein the tropism polypeptide comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 535-554.

48. The particle of any one of claims 1 to 45, wherein the tropism polypeptide comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 555-562.

49. The particle of any one of claims 1 to 45, wherein the tropism polypeptide comprises an amino acid sequence at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 563 or 564.

50. The particle of any one of claims 1 to 49, further comprising one or more secondary non-viral membrane bound tropism polypeptides.

51. The particle of claim 50, wherein the one or more secondary non-viral membrane bound tropism polypeptides comprise one or more of CD80, CD86, CD137L, OX40L, and ICOSL or variants thereof.

52. The particle of any one of claims 1 to 51, further comprising one or more secondary non-viral membrane-bound tropism polypeptides at least 85% identical to, at least 90% identical to, at least 95% identical to, at least 96% identical to, at least 97% identical to, at least 98% identical to, at least 99% identical to, or identical to the amino acid sequence set forth in any one of SEQ ID NOs: 577-581.

53. The particle of any one of claims 8 to 52, wherein the recombinant lentiviral vector is engineered or derived from a lentiviral genome of a lentivirus selected from the group consisting of: human immunodeficiency virus 1 (HIV-1); human immunodeficiency virus 2 (HIV-2); visna-maedi virus (VMV); caprine arthritis-encephalitis virus (CAEV); equine infectious anemia virus (EIAV); feline immunodeficiency virus (FIV); bovine immune deficiency virus (BIV); and simian immunodeficiency virus (SIV).

54. The particle of any one of claims 8 to 53, wherein the recombinant lentiviral vector further comprises one or more polynucleotides encoding one or more of the following:

a signal peptide, a post-transcriptional regulatory element, an insulator element, a selectable marker, and a cell suicide gene.

55. The particle of claim 54, wherein the post-transcriptional regulatory element is a woodchuck hepatitis virus post-transcriptional regulatory element (WPRE) or a hepatitis B virus post-transcriptional regulatory element (HPRE).

56. The particle of any one of claims 7 to 55, wherein the promoter is selected from the group consisting of: a β -actin promoter, a cytomegalovirus (CMV) immediate early promoter, a simian virus 40 (SV40) (*e.g.*, early or late) promoter, a Moloney murine leukemia virus (MoMLV) promoter, a Rous sarcoma virus (RSV) promoter, a herpes simplex virus (HSV) (thymidine kinase) promoter, an SV40/CD43 promoter, a spleen focus forming virus (SFFV) promoter, an elongation factor 1-alpha (EF1 α) short promoter (intronless), an EF1 α long promoter containing an intron, a Ubiquitin C (UBC) promoter, a phosphoglycerate kinase-1 (PGK) promoter, a cytomegalovirus enhancer/chicken β -actin (CAG) promoter, and a myeloproliferative sarcoma virus enhancer, negative control region deleted, dl587rev primer-binding site substituted (MND) U3 promoter.

57. The particle of any one of claims 6 to 56, wherein the one or more engineered receptors are selected from the group consisting of: a chimeric antigen receptor (CAR), a chimeric costimulatory receptor (CCR), an alpha-beta T cell receptor ($\alpha\beta$ TCR), a gamma delta T cell receptor ($\gamma\delta$ TCR), a dimerizing agent regulated immunoreceptor complex (DARIC), a chimeric TGF- β receptor (CTBR), and a zetakine receptor.

58. The particle of any one of claims 6 to 57, wherein the one or more engineered receptors bind an antigen selected from the group consisting of: alpha folate receptor (FR α), $\alpha\beta$ 6 integrin, BAFFR, B cell maturation antigen (BCMA), B7-H3 (CD276), B7-H6, carbonic anhydrase IX (CAIX), CD16, CD19, CD20, CD22, CD30, CD33, CD37, CD38, CD44, CD44v6, CD44v7/8, CD70, CD79A, CD79B, CD123, CD133, CD138, CD171, carcinoembryonic antigen (CEA), claudin 6, (CLDN6), claudin 18 isoform 2 (CLDN18.2), C-type lectin-like molecule-1 (CLL-1), CD2 subset 1 (CS-1), chondroitin sulfate proteoglycan 4 (CSPG4), cutaneous T cell lymphoma-associated antigen 1 (CTAGE1), delta like canonical Notch ligand 3 (DLL3), epidermal growth factor receptor (EGFR), epidermal growth factor receptor variant III (EGFRvIII), epithelial glycoprotein 2 (EGP2), epithelial glycoprotein 40

(EGP40), epithelial cell adhesion molecule (EPCAM), ephrin type-A receptor 2 (EPHA2), erb-b2 receptor tyrosine kinase 4 (ERBB4), fibroblast activation protein (FAP), Fc Receptor Like 5 (FCRL5), fetal acetylcholinesterase receptor (AchR), ganglioside G2 (GD2), ganglioside G3 (GD3), Glypican-3 (GPC3), G Protein-Coupled Receptor Class C Group 5 Member D (GPCR5D), EGFR family including ErbB2 (HER2), HER2 p95, IL-10R α , IL-13R α 2, Kappa, cancer/testis antigen 2 (LAGE-1A), Lambda, Lewis-Y (LeY), L1 cell adhesion molecule (L1-CAM), melanoma antigen gene (MAGE)-A1, MAGE-A3, MAGE-A4, MAGE-A6, MAGEA10, melanoma antigen recognized by T cells 1 (MelanA or MART1), Mesothelin (MSLN), MUC1, MUC16, MHC class I chain related proteins A (MICA), MHC class I chain related proteins B (MICB), neural cell adhesion molecule (NCAM), cancer/testis antigen 1 (NY-ESO-1), placenta-specific 1 (PLAC1), preferentially expressed antigen in melanoma (PRAME), prostate stem cell antigen (PSCA), prostate-specific membrane antigen (PSMA), receptor tyrosine kinase-like orphan receptor 1 (ROR1), SLAMF7, synovial sarcoma, X breakpoint 2 (SSX2), Survivin, TACI, tumor associated glycoprotein 72 (TAG72), tumor endothelial marker 1 (TEM1/CD248), tumor endothelial marker 7-related (TEM7R), transforming growth factor beta 1 (TGF β 1), trophoblast glycoprotein (TPBG), UL16-binding protein (ULBP) 1, ULBP2, ULBP3, ULBP4, ULBP5, ULBP6, vascular endothelial growth factor receptor 2 (VEGFR2), and Wilms tumor 1 (WT-1).

59. The particle of any one of claims 6 to 58, wherein the one or more engineered receptors bind an antigen selected from the group consisting of: BCMA, CD19, CD20, CD22, CD33, CD38, CD79A, CD79B, GPCR5D, MAGE-A4, MSLN, MUC16, NY-ESO-1, PSCA, PSMA and ROR1.

60. The particle of any one of claims 6 to 58, wherein the one or more engineered receptors bind an antigen selected from the group consisting of: BCMA, CD19, CD20, CD22, CD38, CD79A, CD79B, and GPCR5D.

61. The particle of any one of claims 6 to 60, wherein the one or more engineered receptors bind an antigen selected from the group consisting of: BCMA, CD38, and GPCR5D.

62. The particle of any one of claims 6 to 60, wherein the one or more engineered receptors bind an antigen selected from the group consisting of: CD19, CD20, CD22, CD79A, and CD79B.

63. The particle of any one of claims 6 to 62, wherein the one or more engineered receptors comprises an extracellular antigen binding domain, a hinge domain, a transmembrane domain, and one or more intracellular signaling domains.

64. The particle of any one of claims 6 to 63, wherein the one or more engineered antigen receptors comprises an extracellular antigen binding domain selected from the group consisting of: a receptor ectodomain, a ligand, or an antibody or antigen binding fragment thereof selected from the group consisting of: a Camel Ig, a Llama Ig, an Alpaca Ig, Ig NAR, a Fab' fragment, a F(ab')₂ fragment, a bispecific Fab dimer (Fab₂), a trispecific Fab trimer (Fab₃), an Fv, a single chain Fv protein (scFv), a bis-scFv, (scFv)₂, a minibody, a diabody, a triabody, a tetrabody, a disulfide stabilized Fv protein ("dsFv"), a Fibronectin type III (FN3) domain antibody, and a single-domain antibody (sdAb, a camelid VHH, Nanobody).

65. The particle of any one of claims 57 to 64, wherein the CAR comprises a hinge domain isolated or derived from a polypeptide selected from the group consisting of: CD4, CD8 β , CD8 α , CD28, CD134, CD137, CD152, CD278, IgG1, IgG2, IgG3, and IgG4.

66. The particle of any one of claims 57 to 65, wherein the CAR comprises a transmembrane domain isolated or derived from a polypeptide selected from the group consisting of: alpha, beta, gamma, or delta chain of the T-cell receptor, CD3 δ , CD3 ϵ , CD3 γ , CD3 ζ , CD4, CD5, CD8 α , CD9, CD16, CD22, CD27, CD28, CD33, CD37, CD45, CD64, CD80, CD86, CD134, CD137, CD152, CD154, CD278, amnionless (AMN), and programmed cell death 1 (PDCD1).

67. The particle of any one of claims 57 to 66, wherein the CAR comprises a primary signaling domain isolated or derived from a polypeptide selected from the group consisting of: FcR γ , FcR β , CD3 γ , CD3 δ , CD3 ϵ , CD3 ζ , CD22, CD79A, CD79B, and CD66d.

68. The particle of any one of claims 57 to 67, wherein the CAR comprises one or more costimulatory domains isolated or derived from a polypeptide selected from the group consisting of: Toll-like receptor 1 (TLR1), TLR2, TLR3, TLR4, TLR5, TLR6, TLR7, TLR8, TLR9, TLR10, caspase recruitment domain family member 11 (CARD11), CD2, CD7, CD27, CD28, CD30, CD40, CD54 (ICAM), CD83, CD94, CD134 (OX40), CD137 (4-1BB), CD278 (ICOS), DNAX-Activation Protein 10 (DAP10), Linker for activation of T-cells family member 1 (LAT), SH2 Domain-Containing Leukocyte Protein Of 76 kD (SLP76), T cell

receptor associated transmembrane adaptor 1 (TRAT1), TNFR2, TNFRS14, TNFRS18, TNFRS25, and zeta chain of T cell receptor associated protein kinase 70 (ZAP70).

69. The particle of any one of claims 6 to 68, wherein the one or more engineered receptors further comprises a CCR comprising an extracellular antigen binding domain that binds an antigen different than the antigen bound by the CAR, a hinge domain, a transmembrane domain, and one or more intracellular signaling domains.

70. The particle of any one of claims 6 to 57, wherein the one or more engineered receptors comprises a DARIC comprising a DARIC signaling component comprising a multimerization domain, a transmembrane domain and one or more intracellular signaling domains; and a DARIC binding component comprising an extracellular antigen binding domain, an extracellular antigen binding domain, a transmembrane domain, and optionally one or more intracellular signaling domains.

71. The particle of any one of claims 6 to 70, wherein the one or more engineered receptors comprises a CTBR comprising (a) a first polypeptide comprising an extracellular TGF β 1-binding domain of TGF β R2, a transmembrane domain, and a first interleukin receptor intracellular signaling domain; (b) a polypeptide cleavage signal; and (c) a second polypeptide comprising an extracellular TGF β 1-binding domain of TGF β R1, a transmembrane domain, and a second interleukin receptor intracellular signaling domain.

72. A recombinant lentiviral particle comprising: (a) a surface comprising (i) one or more mutated viral envelope glycoproteins that retain fusogenic activity and that lack cognate receptor binding activity, wherein the one or more mutated viral envelope glycoproteins comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to any one of SEQ ID NOs: 630, 634, 638, and 642 and (ii) a non-viral membrane-bound tropism polypeptide comprising an antibody or antigen binding fragment thereof comprising an amino acid sequence set forth in any one of SEQ ID NOs: 91 and 95, and 99 or 100, that binds an antigen expressed on an immune effector cell, a spacer polypeptide, and a GPI anchor domain or a transmembrane domain, and optionally, an intracellular domain comprising no more than 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids; and (b) a therapeutic payload encoding an engineered antigen receptor.

73. A recombinant lentiviral particle comprising: (a) a surface comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642 and (ii) a non-viral membrane-bound tropism polypeptide comprising an antibody or antigen binding fragment thereof comprising an amino acid sequence set forth in SEQ ID NO: 99 or 100, that binds an antigen expressed on an immune effector cell, a spacer polypeptide, and a GPI anchor domain or a transmembrane domain, and optionally, an intracellular domain comprising no more than 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids; and (b) a lentiviral vector encoding an engineered antigen receptor.

74. A recombinant lentiviral particle comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642 and (ii) a non-viral membrane-bound tropism polypeptide comprising an amino acid sequence set forth in any one of SEQ ID NOs: 99 or 100, that binds an antigen expressed on an immune effector cell, a spacer polypeptide, and a GPI anchor domain or a transmembrane domain, and optionally, an intracellular domain comprising no more than 1, 2, 3, 4, 5, 6, 7, 8, 9 or 10 amino acids; and (b) a therapeutic payload encoding an engineered antigen receptor.

75. A recombinant lentiviral particle comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide comprising an amino acid sequence set forth in any one of SEQ ID NOs: 461, 471, 483, 537, and 553; and optionally (iii) a secondary non-viral membrane-bound tropism polypeptide comprising an amino acid sequence set forth in SEQ ID NO: 577; and (b) a lentiviral vector encoding a chimeric antigen receptor.

76. A recombinant lentiviral particle comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 471; and optionally (iii) a secondary non-viral membrane-bound

tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 577; and (b) a lentiviral vector encoding a chimeric antigen receptor comprising an amino acid sequence set forth in any one of SEQ ID NOs: 662-666.

77. A recombinant lentiviral particle comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 471; and optionally (iii) a secondary non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 577; and (b) a lentiviral vector encoding a chimeric antigen receptor that binds a polypeptide selected from any one of BCMA, CD19, CD20, CD22, CD38, CD79A, CD79B, and GPCR5D.

78. A recombinant lentiviral particle comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 471; and optionally (iii) a secondary non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 577; and (b) a lentiviral vector encoding a chimeric antigen receptor that binds BCMA.

79. A recombinant lentiviral particle comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 471; and optionally (iii) a secondary non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least

97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 577; and (b) a lentiviral vector encoding a chimeric antigen receptor that binds GPCR5D.

80. A recombinant lentiviral particle comprising: (a) a viral envelope comprising (i) a mutated VSIV-G envelope glycoprotein that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 642; (ii) a non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 471; and optionally (iii) a secondary non-viral membrane-bound tropism polypeptide that comprises an amino acid sequence at least 95%, at least 96%, at least 97%, at least 98%, at least 99% identical to or identical to SEQ ID NO: 577; and (b) a lentiviral vector encoding a chimeric antigen receptor that binds CD19.

81. A cell transduced with the particle of any one of claims 1 to 80.

82. The cell of claim 81, wherein the cell is an immune effector cell.

83. The cell of claim 81 or claim 82, wherein the cell is a T cell, a natural killer (NK) cell, or a natural killer T (NKT) cell.

84. A composition comprising the particle of any one of claims 1 to 80 or the cell of any one of claims 81 to 83.

85. A pharmaceutical composition comprising a pharmaceutically acceptable carrier and the particle of any one of claims 1 to 80, the cell of any one of claims 81 to 83, or the composition of claim 84.

86. A method of treating, preventing, or ameliorating at least one symptom of a disease, disorder or condition associated therewith in a subject, comprising administering to the subject an effective amount of the particle of any one of claims 1 to 80, the cell of any one of claims 81 to 83, the composition of claim 84, or the pharmaceutical composition of claim 85.

87. The method of claim 86, wherein the disease, disorder, or condition is a cancer.

88. The method of claim 86 or claim 87, wherein the cancer is leukemia selected from the group consisting of: acute lymphocytic leukemia (ALL), an acute myeloid leukemia (AML), a myelodysplastic syndrome (MDS), a plasma cell leukemia (PCL), erythroleukemia, a hairy cell leukemia (HCL), chronic lymphocytic leukemia (CLL), chronic myeloid leukemia (CML), chronic myelomonocytic leukemia (CMML) and polycythemia vera.

89. The method of claim 86 or claim 87, wherein the cancer is non-NHL or NHL selected from the group consisting of: diffuse large B cell lymphoma (DLBCL), follicular lymphoma (FL), mantle-cell lymphoma (MCL), small lymphocytic lymphoma (SLL), primary mediastinal large B-cell lymphoma, a marginal zone B cell lymphoma (MZL), mucosa-associated lymphatic tissue lymphoma (MALT), Burkitt's lymphoma (BL), immunoblastic large cell lymphoma, centroblastic large cell lymphoma, anaplastic B-cell lymphoma, mycosis fungoides, Sezary syndrome, T-lymphoblastic lymphoma, and anaplastic large-cell lymphoma (ALCL).

90. The method of claim 86 or claim 87, wherein the cancer is MM selected from the group consisting of: active multiple myeloma, smoldering multiple myeloma, light chain myeloma, non-secretory myeloma, IgD myeloma, IgE myeloma, osteosclerotic myeloma, solitary plasmacytoma of bone, and extramedullary plasmacytoma.

91. The method of any one of claims 86 to 90, wherein the cancer is relapsed and/or refractory.

92. The method of claim 86, wherein the disease, disorder, or condition is an autoimmune disease.

93. The method of claim 92, wherein the autoimmune disease is systemic lupus erythematosus, rheumatoid arthritis, idiopathic thrombocytopenic purpura, myasthenia gravis, or autoimmune hemolytic anemia.

94. A method of transducing an immune effector cell *in vivo*, comprising administering to a subject a pharmaceutical composition comprising a pharmaceutically acceptable carrier and an effective amount of the particle of any one of claims 1 to 80.

95. A method of making the particle of any one of claims 1 to 80 comprising (a) transfecting a host cell with four polynucleotides: a first polynucleotide that encodes lentiviral gag-pol, a second polynucleotide that encodes lentiviral rev, a third polynucleotide that encodes the one or more mutated viral envelope glycoproteins that retain fusogenic activity and lack cognate receptor binding activity and the one or more non-viral membrane-bound tropism polypeptides, and a fourth polynucleotide that is a transfer plasmid encoding a recombinant lentiviral vector encoding an engineered antigen receptor; and b) culturing the transduced cell for about 1 to 3 days to produce the particle.

96. A kit comprising the particle of any one of claims 1 to 80, a pharmaceutically acceptable carrier, and instructions for use.