

ACTIVATION OF T-CELLS WITH MUTANT G-CSFR

RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application Ser. No. 63/508,055 filed June 14, 2023 and U.S. Provisional Application Ser. No. 63/510,745 filed June 28, 2023, each of which are hereby incorporated by referenced in their entirety.

REFERENCE TO SEQUENCE LISTING SUBMITTED ELECTRONICALLY

[0002] The instant application contains a Sequence Listing which has been submitted electronically in XML format and is hereby incorporated by reference in its entirety. Said XML copy, created on June 5, 2024, is named "INH-023WO_SL.xml" and is 146,320 bytes in size.

FIELD

[0003] Embodiments provided herein relate to mutant G-CSFR constructs and methods of using the same. Embodiments provided herein also relate to viral particles comprising a heterologous viral glycoprotein, a targeting moiety and a nucleic acid molecule encoding for a heterologous molecule of interest. In some embodiments, the nucleic acid molecule encodes for a chimeric antigen receptor and the mutant G-CSFR. Embodiments provided herein further relate to compositions comprising the viral particles provided for herein and methods of using the same.

BACKGROUND

[0004] Chimeric antigen receptor T (CAR-T) cell therapy has revolutionized antitumor treatments, especially against hematological malignancies. However, significant limitations such as high costs, long manufacturing periods, and safety concerns persist and hinder the broad applicability of this technology. *In vivo* CAR-T is based on the concept that the CAR molecules can be delivered *in vivo* to the target T cells with T cell-targeted vectors. Traditional CAR-T methods require the isolation and proliferation of individualized T cells prior to infusion back into the patient after CAR transduction. Therefore, one potential pitfall of *in vivo* CAR-T is a hypothesized lack of proliferation of CAR containing T cells which might limit the efficacy of the method. The present embodiments, fulfill these needs as well as others.

BRIEF SUMMARY

[0005] In some embodiments, a particle or composition is provided. In some embodiments, the particle or composition comprises one or more nucleic acid molecules encoding for a) a chimeric antigen receptor (CAR); and b) a polypeptide comprising: i) a ligand binding extracellular domain (ECD); ii) an immune cell activating intracellular domain (ICD); and iii) a transmembrane domain linking the ECD to the ICD.

[0006] In some embodiments, the immune cell activating ICD comprises the ICD of hGCSF-R (human granulocyte colony-stimulating factor receptor), or a mutant or fragment thereof. In some embodiments, the hGCSF-R ICD comprises a sequence of SEQ ID NO: 111, or an amino acid sequence having at least 50, 60, 70, 75, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to the same.

[0007] In some embodiments, the ECD is a GCSF-R ECD. In some embodiments, the GCSF-R ECD is a human GCSF-R ECD. In some embodiments, the human GCSF-R ECD comprises an amino acid sequence of SEQ ID NO: 107 or SEQ ID NO: 108.

[0008] In some embodiments, the ECD is a human growth hormone receptor (hGH-R) ECD, or a mutant or fragment thereof. In some embodiments, the hGH-R ECD comprises an amino acid sequence of SEQ ID NO: 114 or SEQ ID NO: 115, or an amino acid sequence having at least 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to the same.

[0009] In some embodiments, the polypeptide comprises: an ECD that is a GCSFR-ECD, or variant thereof (e.g. as set forth herein); a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof (e.g. as set forth herein), and an immune activating ICD that is a GCSF-R ICD, or variant thereof (e.g. as set forth herein).

[0010] In some embodiments, the polypeptide comprises: an ECD that is a hGH-R-ECD, or variant thereof (e.g. as set forth herein); a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof (e.g. as set forth herein), and immune activating ICD that is a GCSF-R ICD, or variant thereof (e.g. as set forth herein).

[0011] In some embodiments, the polypeptide comprises: an ECD that is a hGH-R-ECD, or variant thereof (e.g. as set forth herein); a transmembrane domain that is a gp130 transmembrane domain, or variant thereof (e.g. as set forth herein), and immune activating ICD that comprises a gp130 ICD, or variant thereof (e.g. as set forth herein) and a IL-2R β ICD, or variant thereof (e.g. as set forth herein).

[0012] In some embodiments, the polypeptide comprises: an ECD that is a hGH-R-ECD, or variant thereof (e.g. as set forth herein); a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof (e.g. as set forth herein), and immune activating ICD

that comprises a GCSF-R ICD, or variant thereof (e.g. as set forth herein) and a IL-7R α ICD, or variant thereof (e.g. as set forth herein).

[0013] In some embodiments, the polypeptide comprises an amino acid sequence of SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 120, or SEQ ID NO: 124, or a variant of any of the foregoing. In some embodiments, the variant comprises a polypeptide having at least 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%, or 99% identity to SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 120, or SEQ ID NO: 124.

[0014] In some embodiments, a nucleic acid molecule is provided, the nucleic acid molecule encoding a polypeptide comprising i) a ligand binding extracellular domain (ECD) as provided for herein; ii) an immune cell activating intracellular domain (ICD) as provided for herein; and iii) a transmembrane domain linking the ECD to the ICD as provided for herein.

[0015] In some embodiments, the nucleic acid molecule further encodes for a chimeric antigen receptor (CAR). In some embodiments, the CAR is as provided for herein. In some embodiments, the CAR is a CD20 CAR as provided for herein. In some embodiments, the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99. In some embodiments, the nucleic acid sequence encoding for the polypeptide and the nucleic acid sequence encoding for the CAR are separated by a nucleic acid sequence encoding for a cleavable peptide sequence, such as a 2A sequence.

[0016] In some embodiments, a polypeptide is provided. In some embodiments, the polypeptide comprises i) a ligand binding extracellular domain (ECD) as provided for herein; ii) an immune cell activating intracellular domain (ICD) as provided for herein; and iii) a transmembrane domain linking the ECD to the ICD as provided for herein.

[0017] In some embodiments, a particle is provided comprising a polypeptide as provided for herein. In some embodiments, the particle is a virus or a viral vector. In some embodiments, the viral vector is a lentiviral vector, AV vector, an AAV vector, and the like. In some embodiments, the viral vector is a pseudotyped viral vector.

[0018] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein, a targeting moiety, and one or more nucleic acid molecules encoding for one or more heterologous molecules of interest, wherein

the targeting moiety comprises a polypeptide having the formula T-S₁, wherein T is a target binding domain and S₁ is a stalk portion, and wherein the nucleic acid molecule encoding for a heterologous molecule of interest is a nucleic acid molecule as provided for herein.

[0019] In some embodiments, the stalk portion S₁ comprises variant Fc protein. In some embodiments, the variant Fc protein comprises a transmembrane domain, such as, but not limited to, a CD8 or CD28 transmembrane domain. In some embodiments, the variant Fc protein comprises an effector mutation, wherein the effector mutation inhibits the interaction between the Fc protein and a Fc interacting protein, such as FcγR, C1q, FcRβ, or FcRn.

[0020] In some embodiments, the variant Fc protein is a variant IgG1 Fc protein comprising one or more mutations selected from the group consisting of: L234A, L235A, N297A, P329G, I253A, H310A, and H435A.

[0021] In some embodiments, the variant IgG1 Fc protein comprises an amino acid sequence having at least 80% identity to SEQ ID NO: 104, at least 85% identity to SEQ ID NO: 104, at least 90% identity to SEQ ID NO: 104, at least 95% identity to SEQ ID NO: 104, at least 98% identity to SEQ ID NO: 104, or at least 100% identity to SEQ ID NO: 104.

[0022] In some embodiments, the variant Fc protein is a variant IgG2 Fc protein comprising one or more mutations selected from the group consisting of: N297A, P329G, I253A, H310A, and H435A.

[0023] In some embodiments, the variant Fc protein is a variant IgG4 Fc protein comprising one or more mutations selected from the group consisting of: S228P, L235E, N297A, P329G, I253A, H310A, and H435A.

[0024] In some embodiments, the targeting moiety having the formula T-S₁ comprises a stalk portion S₁ having a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker or absent, Fc is a variant Fc protein, L₂ is a linker or absent, and X₁ is a polypeptide comprising the transmembrane domain, wherein the targeting moiety having the formula T-S₁ has a formula of T-L₁-Fc-L₂-X₁.

[0025] In some embodiments, the polypeptide comprising the transmembrane domain (X₁) comprises a polypeptide having a formula of ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof, of a cell surface protein, or is absent; T_M is a transmembrane domain of a transmembrane protein; and ICD is an intracellular domain or a protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, or is absent; wherein the targeting moiety having the formula of T-L₁-Fc-L₂-X₁ has a formula of T-L₁-Fc-L₂-ECD-T_M-ICD.

[0026] In some embodiments, the stalk portion S_1 comprises a formula of L_3-X_1 , wherein L_3 is a flexible peptide linker, and X_1 is a polypeptide comprising a transmembrane domain; wherein the targeting moiety having the formula $T-S_1$ has a formula of $T-L_3-X_1$.

[0027] In some embodiments, the polypeptide comprising the transmembrane domain (X_1) comprises a polypeptide having a formula of $ECD-T_M-ICD$, wherein ECD is an extracellular domain, or a fragment thereof, of a cell surface protein, or is absent; T_M is a transmembrane domain of a transmembrane protein; and ICD is an intracellular domain or a protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, or is absent; wherein the targeting moiety having the formula of $T-L_3-X_1$ has a formula of $T-L_3-ECD-T_M-ICD$.

[0028] In some embodiments, the targeting moiety binds to CD7. In some embodiments, the targeting moiety comprises a polypeptide having a heavy chain variable region comprising a HCDR1 of SEQ ID NO: 30, a HCDR2 of SEQ ID NO: 31, and an HCDR3 of SEQ ID NO: 32, or variants of any of the foregoing. In some embodiments, the targeting moiety comprises a polypeptide having a light chain variable region comprising a LCDR1 of SEQ ID NO: 33, a LCDR2 of SEQ ID NO: 34, and an LCDR3 of SEQ ID NO: 35, or variants of any of the foregoing. In some embodiments, the heavy chain comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 36. In some embodiments, the light chain comprises a light chain variable region having at least 90% sequence identity to SEQ ID NO: 37. In some embodiments, the targeting moiety that binds to CD7 comprises a polypeptide having a sequence having at least 90% sequence identity to SEQ ID NO: 38. In some embodiments, the targeting moiety that binds to CD7 comprises a polypeptide having a sequence having at least 90% sequence identity to SEQ ID NO: 39.

[0029] In some embodiments, the targeting moiety binds to CD8. In some embodiments, the targeting moiety comprises a polypeptide having a heavy chain variable region comprising a HCDR1 of SEQ ID NO: 42, a HCDR2 of SEQ ID NO: 43, and an HCDR3 of SEQ ID NO: 44, or variants of any of the foregoing. In some embodiments, the targeting moiety comprises a polypeptide having a light chain variable region comprising a LCDR1 of SEQ ID NO: 45, a LCDR2 of SEQ ID NO: 46, and an LCDR3 of SEQ ID NO: 47, or variants of any of the foregoing. In some embodiments, the heavy chain comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 48. In some embodiments, the light chain comprises a light chain variable region having at least 90% sequence identity to SEQ ID NO: 49. In some embodiments, the targeting moiety that binds to CD8 comprises a polypeptide having a sequence having at least 90% sequence identity to SEQ ID NO: 50. In some embodiments, the

targeting moiety that binds to CD8 comprises a polypeptide having a sequence having at least 90% sequence identity to SEQ ID NO: 51.

[0030] In some embodiments, the heterologous viral glycoprotein is a SVCV-G polypeptide as provided for herein.

[0031] In some embodiments, the heterologous viral glycoprotein is a VSV-G polypeptide. In some embodiments, the VSV-G polypeptide comprises substitutions at positions I182, T214, and T352 of SEQ ID NO: 2. In some embodiments, the substitution at position 182 is I182D or I182E. In some embodiments, the substitution at position 214 is T214N. In some embodiments, the substitution at position 352 is T352A.

[0032] In some embodiments, the viral particle provided for herein further comprises a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments, the heterologous molecule of interest is as provided for herein. In some embodiments, the heterologous molecule of interest is a CAR. In some embodiments, the CAR comprises an antigen binding domain having a heavy chain variable region having at least 95% identity to SEQ ID NO: 89 and a light chain variable region having at least 95% identity to SEQ ID NO: 90. In some embodiments, the CAR comprises an antigen binding domain having a heavy chain variable region having at least 95% identity to SEQ ID NO: 94 and a light chain variable region having at least 95% identity to SEQ ID NO: 95.

[0033] In some embodiments, the CAR comprises an antigen binding domain having an amino acid sequence having at least 95% identity to SEQ ID NO: 92. In some embodiments, the CAR comprises an antigen binding domain having an amino acid sequence having at least 95% identity to SEQ ID NO: 93. In some embodiments, the CAR comprises an antigen binding domain having an amino acid sequence having at least 95% identity to SEQ ID NO: 96. In some embodiments, CAR comprises an antigen binding domain having an amino acid sequence having at least 95% identity to SEQ ID NO: 97.

[0034] In some embodiments, the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

[0035] In some embodiments, a method of infecting a cell is provided. In some embodiments the method comprises contacting the cell with a viral particle as provided for herein.

[0036] In some embodiments, a method of infecting a cell in a subject is provided. In some embodiments, the method comprises administering to the subject a pharmaceutical composition comprising a viral particle as provided for herein.

[0037] In some embodiments, a method of delivering a heterologous molecule of interest to a cell is provided. In some embodiments, the method comprises contacting the cell with a viral particle as provided for herein, wherein the viral particle comprises a nucleic acid molecule encoding the heterologous molecule of interest.

[0038] In some embodiments, a method of delivering a heterologous molecule of interest to a cell in a subject is provided. In some embodiments, the method comprises administering to the subject a viral particle as provided for herein, wherein the viral particle comprises a nucleic acid molecule encoding the heterologous molecule of interest.

[0039] In some embodiments, a method of treating a disease or disorder in a subject is provided. In some embodiments, the method comprises administering to the subject a viral particle as provided for herein, wherein the viral particle comprises a nucleic acid molecule encoding a heterologous molecule of interest to treat the disease or disorder.

[0040] In some embodiments, a method of delivering a heterologous molecule to a target cell is provided. In some embodiments, the method comprises contacting the cell with a viral particle as provided for herein, wherein the viral particle comprises a nucleic acid molecule encoding the heterologous molecule.

[0041] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein, a targeting moiety comprising a polypeptide having the formula T-S₁, and a nucleic acid molecule encoding for a heterologous molecule of interest, wherein T is a target binding domain and S₁ is a stalk portion. In some embodiments, the heterologous viral glycoprotein comprises a sequence selected from SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 52, or SEQ ID NO: 53. In some embodiments, the targeting binding domain comprises a sequence selected from SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50, or SEQ ID NO: 51. In some embodiments, the stalk portion S₁ comprises a variant Fc protein comprising a sequence that is a variant of SEQ ID NO: 26, SEQ ID NO: 27, or SEQ ID NO: 28. In some embodiments, the variant of SEQ ID NO: 26 comprises one or more mutations selected from the group consisting of L234A, L235A, N297A, P329G, I253A, H310A, and H435A. In some embodiments, the variant of SEQ ID NO: 27 comprises one or more mutations selected from the group consisting of N297A, P329G, I253A, H310A, and H435A. In some embodiments, the variant of SEQ ID NO: 28 comprises one or more mutations selected from the group consisting of S228P, L235E, N297A, P329G, I253A, H310A and H435A. In some embodiments, the variant Fc protein further comprises a transmembrane domain comprising a sequence selected from SEQ ID NO:

61 or SEQ ID NO: 62. In some embodiments, the nucleic acid molecule encoding for a heterologous molecule of interest is a nucleic acid molecule as provided for herein.

[0042] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein, a targeting moiety comprising a polypeptide having the formula T-S₁, and a nucleic acid molecule encoding for a heterologous molecule of interest, wherein T is a target binding domain and S₁ is a stalk portion. In some embodiments, the heterologous viral glycoprotein comprises a sequence selected from SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 52, or SEQ ID NO: 53. In some embodiments, the target binding domain comprises a sequence selected from SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50, or SEQ ID NO: 51. In some embodiments, the stalk portion S₁ comprises a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker comprising a sequence selected from SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, or SEQ ID NO: 76, or is absent; Fc is a variant Fc protein comprising a sequence that is a variant of SEQ ID NO: 26, SEQ ID NO: 27, or SEQ ID NO: 28, L₂ is a linker comprising a sequence selected from SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, or SEQ ID NO: 76, or is absent; and X₁ is a polypeptide comprising a transmembrane domain. In some embodiments, the variant of SEQ ID NO: 26 comprises one or more mutations selected from the group consisting of L234A, L235A, N297A, P329G, I253A, H310A, and H435A. In some embodiments, the variant of SEQ ID NO: 27 comprises one or more mutations selected from the group consisting of N297A, P329G, I253A, H310A, and H435A. In some embodiments, the variant of SEQ ID NO: 28 comprises one or more mutations selected from the group consisting of S228P, L235E, N297A, P329G, I253A, H310A and H435A. In some embodiments, the polypeptide comprising a transmembrane domain (X₁) has a formula of ECD-T_M-ICD, wherein ECD is an extracellular domain having a sequence selected from SEQ ID NO: 59 or SEQ ID NO: 60, or is a fragment thereof, or is absent; T_M is a transmembrane domain having a sequence of SEQ ID NO: 61 or SEQ ID NO: 62 or a fragment thereof; and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64, or the ICD is absent. In some embodiments, the nucleic acid molecule encoding for a heterologous molecule of interest is a nucleic acid molecule as provided for herein.

[0043] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein, a targeting moiety comprising a polypeptide having the formula T-S₁, and a nucleic acid molecule encoding for a heterologous molecule of interest, wherein T is a target binding domain and S₁ is a stalk portion. In some embodiments, the heterologous viral glycoprotein comprises a sequence selected from SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 52, or SEQ ID NO: 53. In some embodiments, the target binding domain comprises a sequence selected from SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50, or SEQ ID NO: 51. In some embodiments, the stalk portion S₁ comprises a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker comprising a sequence of SEQ ID NO: 55 or is absent; Fc is a variant Fc protein comprises a sequence that is a variant of SEQ ID NO: 26, SEQ ID NO: 27, or SEQ ID NO: 28, L₂ is a linker comprising a sequence of SEQ ID NO: 55 or is absent; and X₁ is a polypeptide comprising a transmembrane domain. In some embodiments, the variant of SEQ ID NO: 26 comprises one or more mutations selected from the group consisting of L234A, L235A, N297A, P329G, I253A, H310A, and H435A. In some embodiments, the variant of SEQ ID NO: 27 comprises one or more mutations selected from the group consisting of N297A, P329G, I253A, H310A, and H435A. In some embodiments, the variant of SEQ ID NO: 28 comprises one or more mutations selected from the group consisting of S228P, L235E, N297A, P329G, I253A, H310A and H435A. In some embodiments, the polypeptide comprising a transmembrane domain (X₁) has a formula of ECD-T_M-ICD, wherein ECD is an extracellular domain having a sequence of SEQ ID NO: 60, or a fragment thereof, or is absent; T_M is a transmembrane domain having a sequence of SEQ ID NO: 62 or a fragment thereof; and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64, or the ICD is absent. In some embodiments, the nucleic acid molecule encoding for a heterologous molecule of interest is a nucleic acid molecule as provided for herein.

[0044] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein, a targeting moiety comprising a polypeptide having the formula T-S₁, and a nucleic acid molecule encoding for a heterologous molecule of interest, wherein T is a target binding domain and S₁ is a stalk portion. In some embodiments, heterologous viral glycoprotein comprises a sequence selected from SEQ ID NO: 23 or SEQ ID NO: 25. In some embodiments, the target binding domain comprises a of SEQ ID NO: 39. In some embodiments, the stalk portion S₁ comprises a formula of L₁-Fc-L₂-

X₁, wherein L₁ is a linker comprising a sequence of SEQ ID NO: 55; Fc is a variant Fc protein comprising a sequence of SEQ ID NO: 104, L₂ is a linker and is absent; and X₁ is a polypeptide comprising a transmembrane domain. In some embodiments, the polypeptide comprising a transmembrane domain (X₁) has a formula of ECD-T_M-ICD, wherein ECD is an extracellular domain having a sequence of SEQ ID NO: 60; T_M is a transmembrane domain having a sequence of SEQ ID NO: 62; and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63. In some embodiments, the nucleic acid molecule encoding for a heterologous molecule of interest encodes for a chimeric antigen receptor as provided for herein and a polypeptide comprising i) a ligand binding extracellular domain (ECD) as provided for herein, ii) an immune cell activating intracellular domain (ICD) as provided for herein, and ii) a transmembrane domain linking the ECD to the ICD as provided for herein.

[0045] In some embodiments, a viral particle is provided, wherein the viral particle comprises a heterologous viral glycoprotein, a targeting moiety, and a nucleic acid molecule encoding for a heterologous molecule of interest. In some embodiments, the heterologous viral glycoprotein comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 23 or SEQ ID NO: 25, having at least 95% identity to SEQ ID NO: 23 or SEQ ID NO: 25, having at least 99% identity to SEQ ID NO: 23 or SEQ ID NO: 25, or having at least 100% identity to SEQ ID NO: 23 or SEQ ID NO: 25. In some embodiments, the targeting moiety comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 98, at least 95% identity to SEQ ID NO: 98, at least 99% identity to SEQ ID NO: 98, or at least 100% identity to SEQ ID NO: 98. In some embodiments, the nucleic acid molecule encoding for a heterologous molecule of interest encodes for a chimeric antigen receptor as provided for herein and a polypeptide comprising i) a ligand binding extracellular domain (ECD) as provided for herein, ii) an immune cell activating intracellular domain (ICD) as provided for herein, and ii) a transmembrane domain linking the ECD to the ICD as provided for herein.

[0046] In some embodiments, a viral particle is provided, wherein the viral particle comprises a heterologous viral glycoprotein, a targeting moiety, and a nucleic acid molecule encoding for a heterologous molecule of interest. In some embodiments, the heterologous viral glycoprotein comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 52 or SEQ ID NO: 53, having at least 95% identity to SEQ ID NO: 52 or SEQ ID NO: 53, having at least 99% identity to SEQ ID NO: 52 or SEQ ID NO: 53, or having at least 100% identity to SEQ ID NO: 52 or SEQ ID NO: 53. In some embodiments, the targeting moiety

comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 98, at least 95% identity to SEQ ID NO: 98, at least 99% identity to SEQ ID NO: 98, or at least 100% identity to SEQ ID NO: 98. In some embodiments, the nucleic acid molecule encoding for a heterologous molecule of interest encodes for a chimeric antigen receptor as provided for herein and a polypeptide comprising i) a ligand binding extracellular domain (ECD) as provided for herein, ii) an immune cell activating intracellular domain (ICD) as provided for herein, and iii) a transmembrane domain linking the ECD to the ICD as provided for herein.

[0047] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein, a targeting moiety comprising a polypeptide having the formula T-S₁, and a nucleic acid molecule encoding for a heterologous molecule of interest, wherein T is a target binding domain and S₁ is a stalk portion. In some embodiments, the target binding domain comprises an amino acid sequence of SEQ ID NO: 38 or SEQ ID NO: 39. In some embodiments, the stalk portion S₁ comprises a formula L₃-X₁, wherein L₃ is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, or SEQ ID NO: 58 and X₁ is a polypeptide linker comprising a transmembrane domain. In some embodiments, the polypeptide comprising a transmembrane domain (X₁) has a formula of ECD-T_M-ICD, wherein ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59 or SEQ ID NO: 60, or is a fragment thereof, or is absent, T_M is a transmembrane domain comprising an amino acid sequence of SEQ ID NO: 61 or SEQ ID NO: 62, and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64, or the ICD is absent. In some embodiments, the nucleic acid molecule encoding for a heterologous molecule of interest is a nucleic acid molecule as provided for herein.

[0048] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein, a targeting moiety comprising a polypeptide having the formula T-S₁, and a nucleic acid molecule encoding for a heterologous molecule of interest, wherein T is a target binding domain and S₁ is a stalk portion. In some embodiments, the target binding domain comprises an amino acid sequence of SEQ ID NO: 50 or SEQ ID NO: 51. In some embodiments, the stalk portion S₁ comprises a formula L₃-X₁, wherein L₃ is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, or SEQ ID NO: 58 and X₁ is a polypeptide linker comprising a transmembrane domain. In some embodiments, the polypeptide

comprising a transmembrane domain (X_1) has a formula of ECD- T_M -ICD, wherein ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59 or SEQ ID NO: 60, or is a fragment thereof, or is absent, T_M is a transmembrane domain comprising an amino acid sequence of SEQ ID NO: 61 or SEQ ID NO: 62, and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64, or the ICD is absent. In some embodiments, the nucleic acid molecule encoding for a heterologous molecule of interest is a nucleic acid molecule as provided for herein.

[0049] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein, a targeting moiety comprising a polypeptide having the formula $T-S_1$, and a nucleic acid molecule encoding for a heterologous molecule of interest, wherein T is a target binding domain and S_1 is a stalk portion. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 52, or SEQ ID NO: 53. In some embodiments, the target binding domain comprises an amino acid sequence of SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50, or SEQ ID NO: 51. In some embodiments, the stalk portion S_1 comprises a formula L_3-X_1 , wherein L_3 is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, or SEQ ID NO: 58 and X_1 is a polypeptide linker comprising a transmembrane domain. In some embodiments, the polypeptide comprising a transmembrane domain (X_1) has a formula of ECD- T_M -ICD, wherein ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59 or SEQ ID NO: 60, or is a fragment thereof, or is absent, T_M is a transmembrane domain comprising an amino acid sequence of SEQ ID NO: 61 or SEQ ID NO: 62, and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64, or the ICD is absent. In some embodiments, the nucleic acid molecule encoding for a heterologous molecule of interest is a nucleic acid molecule as provided for herein.

[0050] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein, a targeting moiety comprising a polypeptide having the formula $T-S_1$, and a nucleic acid molecule encoding for a heterologous molecule of interest, wherein T is a target binding domain and S_1 is a stalk portion. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 22,

SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 52, or SEQ ID NO: 53. In some embodiments, the target binding domain comprises an amino acid sequence of SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50, or SEQ ID NO: 51. In some embodiments, the stalk portion S_1 comprises a formula L_3 - X_1 , wherein L_3 is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 55, and X_1 is a polypeptide linker comprising a transmembrane domain. In some embodiments, the polypeptide comprising a transmembrane domain (X_1) has a formula of ECD- T_M -ICD, wherein ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59 or SEQ ID NO: 60, or is a fragment thereof, or is absent, T_M is a transmembrane domain comprising an amino acid sequence of SEQ ID NO: 61 or SEQ ID NO: 62, and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64, or the ICD is absent. In some embodiments, the nucleic acid molecule encoding for a heterologous molecule of interest is a nucleic acid molecule as provided for herein.

[0051] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein, a targeting moiety comprising a polypeptide having the formula T - S_1 , and a nucleic acid molecule encoding for a heterologous molecule of interest, wherein T is a target binding domain and S_1 is a stalk portion. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 23 or SEQ ID NO: 25. In some embodiments, the target binding domain comprises an amino acid sequence of SEQ ID NO: 39. In some embodiments, the stalk portion S_1 comprises a formula L_3 - X_1 , wherein L_3 is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 55, and X_1 is a polypeptide linker comprising a transmembrane domain. In some embodiments, the polypeptide comprising a transmembrane domain (X_1) has a formula of ECD- T_M -ICD, wherein ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59, T_M is a transmembrane domain comprising an amino acid sequence of SEQ ID NO: 61, and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64. In some embodiments, the nucleic acid molecule encoding for a heterologous molecule of interest is a nucleic acid molecule as provided for herein.

[0052] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein, a targeting moiety comprising a

polypeptide having the formula T-S₁, and a nucleic acid molecule encoding for a heterologous molecule of interest, wherein T is a target binding domain and S₁ is a stalk portion. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 52 or SEQ ID NO: 53. In some embodiments, the target binding domain comprises an amino acid sequence of SEQ ID NO: 39. In some embodiments, the stalk portion S₁ comprises a formula L₃-X₁, wherein L₃ is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 55, and X₁ is a polypeptide linker comprising a transmembrane domain. In some embodiments, the polypeptide comprising a transmembrane domain (X₁) has a formula of ECD-T_M-ICD, wherein ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59, T_M is a transmembrane domain comprising an amino acid sequence of SEQ ID NO: 61, and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64. In some embodiments, the nucleic acid molecule encoding for a heterologous molecule of interest encodes for a chimeric antigen receptor as provided for herein and a polypeptide comprising i) a ligand binding extracellular domain (ECD) as provided for herein, ii) an immune cell activating intracellular domain (ICD) as provided for herein, and ii) a transmembrane domain linking the ECD to the ICD as provided for herein.

[0053] In some embodiments, the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

BRIEF DESCRIPTION OF FIGURES

[0054] FIG. 1A and FIG. 1B illustrate exemplary chimeric GCSFR constructs provided for herein.

[0055] FIG. 2A and FIG. 2B illustrate crystal structures of VSV-G bound to LDL-R. FIG. 2A illustrates the crystal structure of VSV-G bound to CR3 of the LDL-R. FIG. 2B illustrates the crystal structure of VSV-G bound to CR2 of the LDL-R.

[0056] FIG. 3A and FIG. 3B illustrate the effect of adding negatively charged amino acids to the VSV-G:LDL-R binding interface on native tropism and fusogenicity. FIG. 3A illustrates the titration of VSV-G constructs on SupT1 cells. FIG. 3B illustrates functional titer of each construct calculated from the titration in FIG. 3A.

[0057] FIG. 4 illustrates an alignment of the ectodomains of different VSV-G proteins from different strains.

[0058] FIG. 5 illustrates the effect of various VSV-G mutations on the serum stability of viral constructs in combination with a CD7 binder.

[0059] FIG. 6 illustrates the effect of various VSV-G mutations on the serum stability of viral constructs in combination with a CD7 binder.

[0060] FIG. 7 illustrates the ability of various rhabdovirus G proteins to transduce SupT1 and PBMC cells alone or in combination with a CD7 binder.

[0061] FIG. 8A-L show flow cytometry data of human PBMCs transduced with exemplary vectors comprising CD7 binders as disclosed herein.

[0062] FIG. 8M shows flow cytometry data of human PBMCs transduced with exemplary vectors comprising CD7 binders as disclosed herein.

[0063] FIG. 9A-L shows flow cytometry data of non-human primate PBMCs transduced with exemplary vectors comprising CD7 binders as disclosed herein.

[0064] FIG. 9M shows flow cytometry data of non-human primate PBMCs transduced with exemplary vectors comprising CD7 binders as disclosed herein.

[0065] FIG. 10A shows flow cytometry data of human PBMCs transduced with exemplary vectors comprising CD8 binders as disclosed herein.

[0066] FIG. 10B shows flow cytometry data of non-human primate PBMCs transduced with exemplary vectors comprising CD8 binders as disclosed herein.

[0067] FIG. 11A illustrates the ability of VSV-G* pseudotyped lentiviral particles harboring a CD7 binder with a variant Fc stalk to transduce SupT1 cells as well as human and non-human primate PBMCs. FIG. 11B illustrates the transduction of cells in the absence of the CD7 binder. FIG. 11C illustrates the transduction of human and non-human primate PBMCs in terms of MOI calculated from SupT1 titration. VSV-G* denotes VSV-G (I182E, T214N, T352A).

[0068] FIG. 12A illustrates the ability of VSV-G* pseudotyped lentiviral particles harboring a CD7 binder with a flexible stalk to transduce SupT1 cells as well as human and non-human primate PBMCs. FIG. 12B illustrates the transduction of cells in the absence of the CD7 binder. FIG. 12C illustrates the transduction of human and non-human primate PBMCs in terms of MOI calculated from SupT1 titration. VSV-G* denotes VSV-G (I182E, T214N, T352A).

[0069] FIG. 13A illustrates the ability of viral particles harboring a CD7 binder with flexible stalks of varying length to transduce SupT1 cells in comparison to other IgG based binders. FIG. 13B illustrates the ability of viral particles harboring a CD7 binder with flexible stalks of varying length to transduce activated PBMC cells in comparison to other IgG based binders.

[0070] FIG. 14A illustrates the ability of SVCV-G pseudotyped lentiviral particles harboring a CD7 binder with a variant Fc stalk to transduce SupT1 cells as well as human and non-human primate PBMCs. FIG 14B illustrates the transduction of cells in the absence of the CD7 binder. FIG. 14C illustrates the transduction of human and non-human primate PBMCs in terms of MOI calculated from SupT1 titration.

[0071] FIG. 15A illustrates the ability of SVCV-G pseudotyped lentiviral particles harboring a CD7 binder with a flexible stalk to transduce SupT1 cells as well as human and non-human primate PBMCs. FIG. 15B illustrates the transduction of cells in the absence of the CD7 binder. FIG 15C illustrates the transduction of human and non-human primate PBMCs in terms of MOI calculated from SupT1 titration.

[0072] FIG. 16A-D is a comparison of the ability of VSV-G* pseudotyped lentiviral particles (panels A and B) and SVCV-G pseudotyped lentiviral particles (panels C and D) to transduce SupT1 cells as well as human and non-human primate PBMCs. VSV-G* denotes VSV-G (I182E, T214N, T352A).

[0073] FIG. 17A-D is a comparison of the ability of VSV-G* pseudotyped lentiviral particles (panels A and B) and SVCV-G pseudotyped lentiviral particles (panels C and D) to transduce SupT1 cells as well as human and non-human primate PBMCs. VSV-G* denotes VSV-G (I182E, T214N, T352A).

[0074] FIG. 18A and FIG. 18B is a comparison of the off target transduction of GFP in a panel of B-cell cell lines as compared to control SupT1 cells. FIG. 18A illustrates the data for VSV-G* pseudotyped lentiviral particles harboring a CD7 binder with a variant Fc stalk. VSV-G* denotes VSV-G (I182E, T214N, T352A). FIG. 18B illustrates the data for SVCV-G pseudotyped lentiviral particles harboring a CD7 binder with a variant Fc stalk.

[0075] FIG. 19A and FIG. 19B is a comparison of the off target transduction of a CAR20-T2A-GFP construct in a panel of B-cell cell lines as compared to control SupT1 cells. FIG. 19A illustrates the data for VSV-G* pseudotyped lentiviral particles harboring a CD7 binder with a variant Fc stalk. VSV-G* denotes VSV-G (I182E, T214N, T352A). FIG. 19B illustrates the data for SVCV-G pseudotyped lentiviral particles harboring a CD7 binder with a variant Fc stalk.

[0076] FIG. 20A and FIG. 20B is a comparison of the off target transduction of GFP in a panel of B-cell cell lines as compared to control SupT1. FIG. 20A illustrates the data for VSV-G* pseudotyped lentiviral particles harboring a CD7 binder with a flexible stalk. VSV-G* denotes VSV-G (I182E, T214N, T352A). FIG 20B illustrates the data for SVCV-G pseudotyped lentiviral particles harboring a CD7 binder with a flexible stalk.

[0077] FIG. 21A and FIG. 21B is a comparison of the off target transduction of a CAR20-T2A-GFP construct in a panel of B-cell cell lines as compared to control SupT1. FIG. 21A illustrates the data for VSV-G* pseudotyped lentiviral particles harboring a CD7 binder with a flexible stalk. VSV-G* denotes VSV-G (I182E, T214N, T352A). FIG 21B illustrates the data for SVCV-G pseudotyped lentiviral particles harboring a CD7 binder with a flexible stalk.

[0078] FIG. 22A and 22B illustrate the ability of VSV-G* pseudotyped lentiviral particles utilizing CD7 binders and a CD20-CAR transgene as provided for herein to kill Daudi lymphoma cells (FIG. 22A) or Raji lymphoma cells (FIG. 22B). CAR20 constructs utilized antigen binding domains comprising rituximab, or CD20AB1 SEQ ID NOs 92 or 93 as provided for herein.

[0079] FIG. 23A-F illustrates the toxicity of the ligand GCSF on PBMCs transduced with a CAR20-2A-chimeric GCSFR construct as provided for herein. FIG. 23A illustrates the results for no chimeric receptor control. FIG. 23B illustrates the results for GCSFR-d15. FIG. 23C illustrates the results for G7R1. FIG. 23D illustrates the results for G21/R1. FIG. 23E illustrates the results for G2R2. FIG. 23F illustrates the results for G27/2R1.

[0080] FIG. 24A-E illustrates the toxicity of the ligand hGH on PBMCs transduced with a CAR20-2A-chimeric GHR construct as provided for herein. FIG. 24A illustrates the results for GHR-GCSFRd715. FIG. 24B illustrates the results for GHR-G7R1. FIG. 24C illustrates the results for GHR-G21/7R1. FIG. 24D illustrates the results for GHR-G2R2. FIG. 24E illustrates the results for GHR-G27/2R1.

[0081] FIG. 25A-F illustrates the ability of the chimeric GCSFR receptors provided for herein to induce proliferation of transduced PBMCs. FIG. 25A illustrates the results for no chimeric receptor control. FIG. 25B illustrates the results for GCSFR-d15. FIG. 25C illustrates the results for G7R1. FIG. 25D illustrates the results for G21/R1. FIG. 25E illustrates the results for G2R2. FIG. 25F illustrates the results for G27/2R1.

[0082] FIG. 26A-E illustrates the ability of the chimeric GHR receptors provided for herein to induce proliferation of transduced PBMCs. FIG. 26A illustrates the results for GHR-GCSFRd715. FIG. 26B illustrates the results for GHR-G7R1. FIG. 26C illustrates the results for GHR-G21/7R1. FIG. 26D illustrates the results for GHR-G2R2. FIG. 26E illustrates the results for GHR-G27/2R1.

[0083] FIG. 27A-E illustrates the results of a follow up PBMC induced proliferation experiment with select chimeric receptor constructs. FIG. 27A illustrates the results for GCSFR FL. FIG. 27B illustrates the results for GCSFRd715. FIG. 27C illustrates the results

for GCSFR-G2R2. FIG. 27D illustrates the results for GHR-GCSFR. FIG. 27E illustrates the results for GHR-dFN-GCSFR. FIG. 27F illustrates the results for GHR-G2R2.

[0084] FIG. 28A and 28B illustrate the ability of VSV-G* pseudotyped lentiviral particles utilizing CD7 binders and a CD20-CAR transgene as provided for herein to deplete B-cells *in vivo* in huCD34 NSG mice. B-cells were detected via assessment for CD20 (FIG. 28A) or CD19 (FIG. 28B).

[0085] FIG. 29A and 29B illustrate the ability of VSV-G* pseudotyped lentiviral particles utilizing CD7 binders and a CD20-CAR transgene as provided for herein to prevent tumor formation *in vivo*. FIG. 29A depicts the experimental design. FIG. 29B illustrates that mice receiving i.v. lentiviral particles as provided for herein prior to Raji tumor infusion had significantly lower tumor burden than mice receiving control (GFP) vector or untreated mice. Tumor burden measured via IVIS imaging.

[0086] FIG. 30A and 30B illustrate the ability of VSV-G* pseudotyped lentiviral particles utilizing CD7 binders and a CD20-CAR transgene as provided for herein to eliminate established Raji tumors *in vivo*. FIG. 30A depicts the experimental design. FIG. 30B illustrates that mice receiving i.v. lentiviral particles as provided for herein after 6 days after Raji tumor infusion had their tumor burdens diminished below the limit of detection. Tumor burden measured via IVIS imaging.

[0087] FIG. 31A shows an example CAR – GCSF Receptor construct for tunable expansion of cells. FIG. 31B shows flow cytometry data demonstrating tunable CAR cell proliferation *in vitro*. FIG. 31C shows a dose response of CAR-T cells to an exogenous GCSF agonist. FIGs. 31D and 31E depict an example *in vivo* experimental design for evaluating the CAR-GSCFR construct. FIGs. 31F and 31G show significant proliferation of CAR20+ cells in the presence of GCSF agonist.

[0088] FIG. 32A – 32F illustrate the results of a cell count analysis of PBMCs transduced with combinations of a CAR20 construct, GCSFR construct, or GFP when treated with the indicated concentrations of GCSF or complete media. FIG. 32A illustrates the growth of PBMCs from PBMC donor 1 transduced with CAR20 alone. FIG. 32B illustrates the growth of PBMCs from PBMC donor 2 transduced with CAR20 alone. FIG. 32C illustrates the growth of PBMCs from PBMC donor 1 transduced with CAR20 and a GCSFR construct. FIG. 32D illustrates the growth of PBMCs from PBMC donor 2 transduced with CAR20 and a GCSFR construct. FIG. 32E illustrates the growth of PBMCs from PBMC donor 1 transduced with GFP and a GCSFR construct. FIG. 32F illustrates the growth of PBMCs from PBMC donor 2 transduced with GFP and a GCSFR construct.

[0089] FIG. 33A – 33F illustrate the results of a cell count analysis of PBMCs transduced with combinations of a CAR20 construct, GHR construct, or GFP when treated with the indicated concentrations of GH or complete media. FIG. 33A illustrates the growth of PBMCs from PBMC donor 1 transduced with CAR20 alone. FIG. 33B illustrates the growth of PBMCs from PBMC donor 2 transduced with CAR20 alone. FIG. 33C illustrates the growth of PBMCs from PBMC donor 1 transduced with CAR20 and a GHR construct. FIG. 33D illustrates the growth of PBMCs from PBMC donor 2 transduced with CAR20 and a GHR construct. FIG. 33E illustrates the growth of PBMCs from PBMC donor 1 transduced with GFP and a GHR construct. FIG. 33F illustrates the growth of PBMCs from PBMC donor 2 transduced with GFP and a GHR construct.

DETAILED DESCRIPTION

[0090] Provided for herein are particles or compositions comprising one or more nucleic acid molecules encoding for a chimeric antigen receptor (CAR) and a polypeptide comprising i) a ligand binding extracellular domain (ECD); ii) an immune cell activating intracellular domain (ICD); and iii) a transmembrane domain linking the ECD to the ICD. As provided for herein, the particle may be a viral particle. Accordingly, also provided for herein are viral particles comprising a heterologous viral glycoprotein, a targeting moiety, and one or more nucleic acid molecules encoding for one or more heterologous molecules of interest, wherein the targeting moiety comprises a polypeptide having the formula of T-S₁, wherein T is a target binding domain, and S₁ is a stalk portion, and wherein the one or more nucleic acid molecules encode for a chimeric antigen receptor (CAR) and a polypeptide comprising i) a ligand binding extracellular domain (ECD); ii) an immune cell activating intracellular domain (ICD); and iii) a transmembrane domain linking the ECD to the ICD. In some embodiments, S₁ comprises a mutant Fc polypeptide that can be, for example, linked to a transmembrane domain as provided for herein. In some embodiments, S₁ comprises flexible polypeptides as provided for herein. The mutant Fc polypeptides or the flexible polypeptides can be incorporated into a viral particle to help facilitate the targeting of the viral particle to a specific cell type.

[0091] Additionally, the viral particle can comprise VSV-G proteins that can be used, for example, to pseudotype a virus, such as a lentivirus. In some embodiments, the pseudotyped viral-like particles are pseudotyped using viral glycoproteins of a vesicular stomatitis New Jersey virus strain, a vesicular stomatitis Indiana virus strain, a vesicular stomatitis Alagoas virus strain, a vesicular stomatitis Maraba virus strain, or a vesicular stomatitis Carajas virus strain. Examples of such proteins are provided for herein.

[0092] The pseudotyped viruses comprising the mutant VSV-G proteins, such as those provided for herein, can be used in conjunction with a targeting moiety to facilitate the fusion of the pseudotyped virus with a specific cell or tissue based on the expression of the target on the cell or the tissue. As provided for herein, the targeting moiety can be linked to a Fc protein, which can be referred to a stalk protein that comprises a transmembrane domain to facilitate the attachment of the targeting moiety to the surface of the virus. In some embodiments, the Fc protein comprises a Fc effector mutation, such as those provided for herein.

[0093] Unless defined otherwise, all technical and scientific terms have the same meaning as is commonly understood by one of ordinary skill in the art to which the embodiments disclosed belongs.

[0094] As used herein, the terms “a” or “an” means that “at least one” or “one or more” unless the context clearly indicates otherwise.

[0095] As used herein, the term “about” means that the numerical value is approximate and small variations would not significantly affect the practice of the disclosed embodiments. Where a numerical limitation is used, unless indicated otherwise by the context, “about” means the numerical value can vary by $\pm 10\%$ and remain within the scope of the disclosed embodiments. Additionally, where a phrase recites “about x to y,” the term “about” modifies both x and y and can be used interchangeably with the phrase “about x to about y” unless context dictates differently.

[0096] As used herein, the term “individual” or “subject,” or “patient” used interchangeably, means any animal, including mammals, such as mice, rats, other rodents, rabbits, dogs, cats, swine, cattle, sheep, horses, or primates, such as humans.

[0097] As used herein, the terms “comprising” (and any form of comprising, such as “comprise”, “comprises”, and “comprised”), “having” (and any form of having, such as “have” and “has”), “including” (and any form of including, such as “includes” and “include”), or “containing” (and any form of containing, such as “contains” and “contain”), are inclusive or open-ended and do not exclude additional, unrecited elements or method steps. Any step or composition that uses the transitional phrase of “comprise” or “comprising” can also be said to describe the same with the transitional phrase of “consisting of” or “consists.”

[0098] As used herein, the term “contacting” means bringing together of two elements in an in vitro system or an in vivo system. For example, “contacting” virus or vector described herein with an individual or patient or cell includes the administration of the virus to an individual or patient, such as a human, as well as, for example, introducing a compound into a sample containing a cellular or purified preparation containing the cell.

[0099] As used herein, the term “fused” or “linked” when used in reference to a protein having different domains or heterologous sequences means that the protein domains are part of the same peptide chain that are connected to one another with either peptide bonds or other covalent bonding. The domains or section can be linked or fused directly to one another or another domain or peptide sequence can be between the two domains or sequences and such sequences would still be considered to be fused or linked to one another. In some embodiments, the various domains or proteins provided for herein are linked or fused directly to one another or a linker sequences, such as the glycine/serine sequences described herein link the two domains together.

[0100] A “disease” is a state of health of an animal wherein the animal cannot maintain homeostasis, and wherein if the disease is not ameliorated then the animal’s health continues to deteriorate. In contrast, a “disorder” in an animal is a state of health in which the animal is able to maintain homeostasis, but in which the animal’s state of health is less favorable than it would be in the absence of the disorder. Left untreated, a disorder does not necessarily cause a further decrease in the animal’s state of health.

[0101] “Effective amount” or “therapeutically effective amount” are used interchangeably herein, and refer to an amount of a compound, formulation, material, or composition, as described herein effective to achieve a particular biological result or provides a therapeutic or prophylactic benefit. Such results may include, but are not limited to an amount that when administered to a mammal, causes a detectable level of immune cell activation compared to the immune cell activation detected in the absence of the composition. The immune response can be readily assessed by a plethora of art-recognized methods. The skilled artisan would understand that the amount of the composition administered herein varies and can be readily determined based on a number of factors such as the disease or condition being treated, the age and health and physical condition of the mammal being treated, the severity of the disease, the particular compound being administered, and the like.

[0102] “Encoding” refers to the inherent property of specific sequences of nucleotides in a polynucleotide, such as a gene, a cDNA, or an mRNA, to serve as templates for synthesis of other polymers and macromolecules in biological processes having either a defined sequence of nucleotides (i.e., rRNA, tRNA and mRNA) or a defined sequence of amino acids and the biological properties resulting therefrom. Thus, a gene encodes a protein if transcription and translation of mRNA corresponding to that gene produces the protein in a cell or other biological system. Both the coding strand, the nucleotide sequence of which is identical to the mRNA sequence and is usually provided in sequence listings, and the non-coding strand, used

as the template for transcription of a gene or cDNA, can be referred to as encoding the protein or other product of that gene or cDNA.

[00103] “Expression vector” refers to a vector comprising a recombinant polynucleotide comprising expression control sequences operatively linked to a nucleotide sequence to be expressed. An expression vector comprises sufficient cis-acting elements for expression; other elements for expression can be supplied by the host cell or in an in vitro expression system. Expression vectors include all those known in the art, such as cosmids, plasmids (e.g., naked or contained in liposomes) and viruses (e.g., Sendai viruses, lentiviruses, retroviruses, adenoviruses, and adeno-associated viruses) that incorporate the recombinant polynucleotide.

[00104] As used herein, the phrase “ex vivo” in reference to a cell being transduced, transfected or transformed ex vivo, refers to a cell being transduced, transfected or transformed outside of the subject, that is with the cells being removed from the subject before such cells are transduced, transfected or transformed.

[00105] “Identity” as used herein refers to the subunit sequence identity between two polymeric molecules such as between two nucleic acid or amino acid molecules, such as, between two polynucleotide or polypeptide molecules. When two amino acid sequences have the same residues at the same positions; e.g., if a position in each of two polypeptide molecules is occupied by an Arginine, then they are identical at that position. The identity or extent to which two amino acid or two nucleic acid sequences have the same residues at the same positions in an alignment is often expressed as a percentage. The identity between two amino acid or two nucleic acid sequences is a direct function of the number of matching or identical positions; e.g., if half of the positions in two sequences are identical, the two sequences are 50% identical; if 90% of the positions (e.g., 9 of 10), are matched or identical, the two amino acids sequences are 90% identical.

[00106] By “substantially identical” is meant a polypeptide or nucleic acid molecule exhibiting at least 50% identity to a reference amino acid sequence (for example, any one of the amino acid sequences described herein) or nucleic acid sequence (for example, any one of the nucleic acid sequences described herein). In some embodiments, such a sequence is at least 60%, 80% or 85%, or 90%, 95% or even 99% identical at the amino acid level or nucleic acid to the sequence used for comparison. Other percentages of identity in reference to specific sequences are described herein.

[00107] Sequence identity can be measured/determined using sequence analysis software (for example, Sequence Analysis Software Package of the Genetics Computer Group, University of Wisconsin Biotechnology Center, 1710 University Avenue, Madison, Wis. 53705, BLAST,

BESTFIT, GAP, or PILEUP/PRETTYBOX programs). Such software matches identical or similar sequences by assigning degrees of homology to various substitutions, deletions, and/or other modifications. Conservative substitutions typically include substitutions within the following groups: glycine, alanine; valine, isoleucine, leucine; aspartic acid, glutamic acid, asparagine, glutamine; serine, threonine; lysine, arginine; and phenylalanine, tyrosine. In an exemplary approach to determining the degree of identity, a BLAST program may be used, with a probability score between e^{-3} and e^{-100} indicating a closely related sequence. In some embodiments, sequence identity is determined by using BLAST with the default settings.

[00108] To the extent embodiments provided for herein, includes composition comprising various proteins, these proteins may, in some instances, comprise amino acid sequences that have sequence identity to the amino acid sequences disclosed herein. Therefore, in certain embodiments, depending on the particular sequence, the degree of sequence identity is preferably greater than 50% (e.g. 60%, 70%, 75%, 80%, 85%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more) to the SEQ ID NOs disclosed herein. In addition to these percentages, other percentages of identity are provided for herein. Identity between polypeptides can be determined by the Smith-Waterman homology search algorithm as implemented in the MPSRCH program (Oxford Molecular), using an affine gap search with parameters gap open penalty = 12 and gap extension penalty = 1.

[00109] These proteins may, compared to the disclosed proteins, include one or more (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, etc.) conservative amino acid replacements i.e. replacements of one amino acid with another which has a related side chain. Genetically-encoded amino acids are generally divided into four families: (1) acidic i.e. aspartate, glutamate; (2) basic i.e. lysine, arginine, histidine; (3) non polar i.e. alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine, tryptophan; and (4) uncharged polar i.e. glycine, asparagine, glutamine, cysteine, serine, threonine, tyrosine. Phenylalanine, tryptophan, and tyrosine are sometimes classified jointly as aromatic amino acids. In general, Substitution of single amino acids within these families does not have a major effect on the biological activity. The proteins may have one or more (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, etc.) single amino acid deletions relative to the disclosed protein sequences. The proteins may also include one or more (e.g. 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, etc.) insertions (e.g. each of 1, 2, 3, 4 or 5 amino acids) relative to the disclosed protein sequences.

[00110] As used herein, the phrase “in vivo” in reference to a cell being transduced, transfected or transformed in vivo, refers to a cell being transduced, transfected or transformed

in the subject without the cells being removed from the subject before such cells are transduced, transfected or transformed.

[00111] “Isolated” means altered or removed from the natural state. For example, a nucleic acid or a peptide naturally present in a living animal is not “isolated,” but the same nucleic acid or peptide partially or completely separated from the coexisting materials of its natural state is “isolated.” An isolated nucleic acid or protein can exist in substantially purified form, or can exist in a non-native environment such as, for example, a host cell.

[00112] A “lentivirus” as used herein refers to a genus of the Retroviridae family that is able to infect non-dividing cells. Non-limiting examples of lentiviruses are HIV, SIV, and FIV. Vectors or viral-like particles derived from lentiviruses can be used to transduce cells and deliver genes or other molecules and have them expressed in a cell either in vitro (ex-vivo) or in vivo.

[00113] By the term “modified” as used herein, is meant a changed state or structure of a molecule or cell as provided herein. Molecules may be modified in many ways, including chemically, structurally, and functionally, such as mutations, substitutions, insertions, or deletions (e.g. internal deletions truncations). Cells may be modified through the introduction of nucleic acids or the expression of heterologous proteins.

[00114] By the term “modulating,” as used herein, is meant mediating an increase or decrease in the level of a response in a subject compared with the level of a response in the subject in the absence of a treatment or compound, and/or compared with the level of a response in an otherwise identical but untreated subject. The term encompasses perturbing and/or affecting a native signal or response thereby mediating a beneficial therapeutic response in a subject, such as, a human.

[00115] Unless otherwise specified, a “nucleotide sequence encoding an amino acid sequence” includes all nucleotide sequences that are degenerate versions of each other and that encode the same amino acid sequence. The phrase nucleotide sequence that encodes a protein or an RNA may also include introns to the extent that the nucleotide sequence encoding the protein may in some version contain an intron(s).

[00116] The term “oligonucleotide” typically refers to short polynucleotides. It will be understood that when a nucleotide sequence is represented by a DNA sequence (i.e., A, T, C, G), this also provides the corresponding RNA sequence (i.e., A, U, C, G) in which “U” replaces “T.”

[00117] “Parenteral” administration of a composition includes, e.g., subcutaneous (s.c.), intravenous (i.v.), intramuscular (i.m.), or intrasternal injection, or infusion techniques.

[00118] The term “polynucleotide” as used herein is defined as a chain of nucleotides. Furthermore, nucleic acids are polymers of nucleotides. Thus, the terms “nucleic acids” and “polynucleotides” as used herein are interchangeable. As used herein polynucleotides include, but are not limited to, all nucleic acid sequences which are obtained by any methods available in the art, including, without limitation, recombinant methods, i.e., the cloning of nucleic acid sequences from a recombinant library or a cell genome, using cloning technology and PCR, and the like, and by synthetic means.

[00119] As used herein, the terms “peptide,” “polypeptide,” and “protein” are used interchangeably, and refer to a compound comprised of a plurality of amino acid residues covalently linked by peptide bonds. As used herein, the term refers to both short chains, which also commonly are referred to in the art as peptides, oligopeptides and oligomers, for example, and to longer chains, which generally are referred to in the art as proteins, of which there are many types. “Polypeptides” include, for example, biologically active fragments, substantially homologous polypeptides, oligopeptides, homodimers, heterodimers, variants of polypeptides, modified polypeptides, derivatives, analogs, fusion proteins, among others. The polypeptides include natural peptides, recombinant peptides, synthetic peptides, or a combination thereof.

[00120] Unless explicitly stated otherwise, the terms “heterologous viral structural protein” and “heterologous viral glycoprotein” as used herein are used synonymously and interchangeably. Accordingly, unless explicitly stated otherwise, an embodiment referring to a “heterologous viral structural protein” is understood to be referring to a “heterologous viral glycoprotein” and vice versa.

[00121] The term “pseudotyped” or “pseudotyped viral particle”, as used herein, refers to a viral particle bearing glycoproteins derived from other viruses having envelopes or a viral vector encoding envelope glycoproteins from a virus that is different from the parental virus. The host range of the vector particles can thus be expanded or altered depending on the type of cell surface receptor used by the glycoprotein. For example, a virus can be pseudotyped with a VSV-G mutant protein as provided for herein.

[00122] By the term “specifically binds,” as used herein with respect to an antibody, is meant an antibody which recognizes a specific antigen, but does not substantially recognize or bind other molecules in a sample. For example, an antibody that specifically binds to an antigen from one species may also bind to that antigen from one or more species. But, such cross-species reactivity does not itself alter the classification of an antibody as specific. In another example, an antibody that specifically binds to an antigen may also bind to different allelic forms of the antigen. However, such cross reactivity does not itself alter the classification of

an antibody as specific. In some instances, the terms “specific binding” or “specifically binding,” can be used in reference to the interaction of an antibody, a protein, or a peptide with a second chemical species, to mean that the interaction is dependent upon the presence of a particular structure (e.g., an antigenic determinant or epitope) on the chemical species; for example, an antibody recognizes and binds to a specific protein structure rather than to proteins generally. If an antibody is specific for epitope “A”, the presence of a molecule containing epitope A (or free, unlabeled A), in a reaction containing labeled “A” and the antibody, will reduce the amount of labeled A bound to the antibody. In some embodiments, the targeting moieties described herein that can be used to target the viral particles comprising the mutant VSV-G protein, or other viral structural proteins used to pseudotype a virus, can specifically bind to their target.

[00123] The term “subject” includes living organisms, including those in which an immune response can be elicited (e.g., mammals). A “subject” or “patient,” as used therein, may be a human or non-human mammal. Non-human mammals include, for example, livestock and pets, such as ovine, bovine, porcine, canine, non-human primates, feline and murine mammals. In some embodiments, the subject is human.

[00124] The term “therapeutic” as used herein means a treatment and/or prophylaxis. A therapeutic effect is obtained by suppression, remission, or eradication of a disease state.

[00125] The term “transfected” or “transformed” or “transduced” as used herein refers to a process by which exogenous nucleic acid is transferred or introduced into a cell. A “transfected” or “transformed” or “transduced” cell is one which has been transfected, transformed or transduced with exogenous nucleic acid. The cell includes the primary subject cell and its progeny. In some embodiments, the transfection, transformation, or transduction is performed or occurs in vivo.

[00126] To “treat” a disease as the term is used herein, means to reduce the frequency or severity of at least one sign or symptom of a disease or disorder experienced by a subject.

[00127] A “vector” is a composition of matter which comprises an isolated nucleic acid encoding a protein or a peptide. Numerous vectors are known in the art including, but not limited to, linear polynucleotides, plasmids, DNA, and RNA. Examples of viral vectors include, but are not limited to, Sendai viral vectors, adenoviral vectors, adeno-associated virus vectors, retroviral vectors, lentiviral vectors, and the like.

[00128] A “carrier” or “delivery vehicle” includes viral particles, viruses, polylysine compounds, and liposomes, which facilitate transfer of nucleic acid into cells. A carrier or delivery vehicle can also be used to deliver a protein or peptide to a cell.

[00129] Ranges: throughout this disclosure, various aspects of the embodiments can be presented in a range format. It should be understood that the description in range format is merely for convenience and brevity and should not be construed as an inflexible limitation. Accordingly, the description of a range should be considered to have specifically disclosed all the possible subranges as well as individual numerical values within that range. For example, description of a range such as from 1 to 6 should be considered to have specifically disclosed subranges such as from 1 to 3, from 1 to 4, from 1 to 5, from 2 to 4, from 2 to 6, from 3 to 6 etc., as well as individual numbers within that range, for example, 1, 2, 2.7, 3, 4, 5, 5.3, and 6. This applies regardless of the breadth of the range. Unless otherwise explicitly stated to the contrary, a range that is disclosed also includes the endpoints of the range.

Heterologous Proteins

[00130] In some embodiments, polypeptides are provided that are recombinant fusion proteins that comprise a ligand binding extracellular domain (ECD); ii) an immune cell activating intracellular domain (ICD); and iii) a transmembrane domain linking the ECD to the ICD.

[00131] As used herein, the term, “an immune cell activating intracellular domain (ICD)” refers a domain that when activated can activate or enhance the number of immune cells. In some embodiments, the immune cell activating ICD comprises the ICD of hGCSF-R, or a mutant or fragment thereof. In some embodiments, the ICD of hGCSF-R comprise a substitution, an insertion or deletion. In some embodiments, the hGCSF-R ICD comprises a sequence of SEQ ID NO: 111), or an amino acid sequence having at least 50, 60, 70, 75, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to the same. In some embodiments, the hGCSF-R ICD does not comprise the sequence of SEQ ID NO: 110. In some embodiments, the hGCSF-R ICD comprises a sequence of SEQ ID NO: 111 and does not comprise amino acid residues 800-813, 775-813, 750-813, 725-813, or 716-813 of SEQ ID NO: 125, or a fragment thereof, positioned to the C-terminal residue of SEQ ID NO: 111.

[00132] In some embodiments, the hGCSF-R ICD comprises a sequence of SEQ ID NO: 111 and amino acid residues 716-812 of SEQ ID NO: 125, or a fragment thereof positioned to the C-terminal residue of SEQ ID NO: 111, provided that the ICD does not comprise the contiguous fragment of amino acid residues 716-813 of SEQ ID NO: 125.

[00133] As used herein, the term “ligand binding extracellular domain (ECD)” refers to a domain of a protein that can bind to ligand and can act to transmit a signal through the ICD. This signal can be a signal to enhance the activation of a cell or to increase the rate of cell division to increase the number of cells. This ligand can be naturally occurring or synthetic

or made recombinantly. For example, G-CSF (granulocyte-colony stimulating factor) or human growth hormone (HGH) can be used as a ligand that can bind to the ECD to transmit the signal. For example, somatropin can be used as a ligand that can bind to an ECD that can bind to HGH. Additionally, in some embodiments, or lenograstim (Granocyte), filgrastim (Neupogen, Zarzio, Nivestim, Accofil), long acting (pegylated) filgrastim (pegfilgrastim, Neulasta, Pelmeg, Ziextenco) or lipegfilgrastim (Lonquex) can be used to as a ligand that can bind to an G-CSF that can bind to HGH. Examples of ECD are provided for herein and include, but are not limited to, G-CSFR or hGHR. Without being bound to any particular theory, when these drugs are administered to a patient expressing these polypeptides, the T cells will expand (increase in number) and lead to a greater response against the tumor.

[00134] In some embodiments, the ECD is a GCSF-R ECD. In some embodiments, the GCSF-R ECD is a human GCSF-R ECD. In some embodiments, the human GCSF-R ECD comprises the amino acid sequence of SEQ ID NO: 107 or SEQ ID NO: 108.

[00135] In some embodiments, the ECD comprises the ECD of human growth hormone receptor (hGH-R), or a mutant or fragment thereof. In some embodiments, the ECD of human growth hormone receptor (hGH-comprises the amino acid sequence encoded by exons 1-7 of hGH-R, or a mutant or fragment thereof. In some embodiments, the ECD of the hGH-R comprises the mutation of C259R. In some embodiments, the ECD of the hGH-R comprises an amino acid sequence of SEQ ID NO: 114 or SEQ ID NO: 115, or an amino acid sequence having at least 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to the same. In some embodiments, the ECD of the hGH-R comprises an amino acid sequence of SEQ ID NO: 114 or SEQ ID NO: 115 that excludes a leader sequence, or an amino acid sequence having at least 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to the same.

[00136] In some embodiments, the ICD comprises an ICD of glycoprotein 130 ("gp130 ICD"), or a variant or fragment thereof. In some embodiments, the gp130 ICD comprises a fragment of the gp130 ICD. In some embodiments, the gp130 ICD fragment comprises a Jak1 binding site and/or a SHP-2/STAT3 binding site. A non-limiting example of this is the amino acid sequence of SEQ ID NO: 122. Another non-limiting example of a gp130 ICD, or fragment thereof, includes the amino acid sequence of the gp130 ICD of Construct G, described in further detail herein.

[00137] In some embodiments, the ICD comprises a fragment of the GCSF-R ICD. In some embodiments, the GCSF-R ICD fragment does not comprise the STAT3, SH3 and/or the SHC domains. In some embodiments, the GCSF-R ICD fragment comprises the Jak1 and/or the STAT3 binding site. In some embodiments, the ICD comprises a IL-2R β ICD, or a fragment

or variant thereof. In some embodiments, the IL-2R β ICD is a fragment of the IL-2R β ICD. In some embodiments, the IL-2R β ICD, or fragment thereof, comprises the SHC or STAT5 binding domains. In some embodiments, the ICD comprises a IL-7R α ICD, or a fragment or variant thereof. In some embodiments, the IL-7R α ICD is a fragment of the IL-7R α ICD. In some embodiments, the ICD comprises a IL-7R α ICD, or a fragment thereof, comprises a STAT5 and/or PI3K binding domain. In some embodiments, the ICD comprises a gp130 ICD, or a variant or fragment thereof, linked to an IL-2R β ICD, or fragment thereof. A non-limiting example of an IL-2R β ICD, or fragment thereof is the amino acid sequence of SEQ ID NO: 123. In some embodiments, the ICD comprises a hCCSF-R ICD, or a variant or fragment thereof, linked to an IL-7R α ICD, or fragment thereof. A non-limiting example of an IL-7R α ICD, or fragment thereof is the amino acid sequence of SEQ ID NO: 118. Another non-limiting example of an IL-7R α ICD, or fragment thereof includes the amino acid sequence of the IL-7R α ICD of Construct E, described in further detail herein.

[00138] In some embodiments, the transmembrane domain, comprises a GCSF-R, gp130, or hGH-R transmembrane domain. In some embodiments, the transmembrane domain comprises the hGCSF-R transmembrane domain, or a variant thereof. In some embodiments, the transmembrane domain comprises the gp130 transmembrane domain, or a variant thereof. Examples of gp130 transmembrane domains include, but are not limited to, an amino acid sequence of SEQ ID NO: 121. In some embodiments, transmembrane domain comprises the hGH-R transmembrane domain, or a variant thereof.

[00139] In some embodiments, the polypeptide comprises an ECD that is a GCSF-R-ECD, or variant thereof (e.g. as set forth herein and above); a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof (e.g. as set forth herein and above), and an immune activating ICD that is a GCSF-R ICD, or variant thereof (e.g. as set forth herein and above).

[00140] In some embodiments, the polypeptide comprises an ECD that is a hGH-R-ECD, or variant thereof (e.g. as set forth herein and above); a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof (e.g. as set forth herein and above), and immune activating ICD that is a GCSF-R ICD, or variant thereof (e.g. as set forth herein and above).

[00141] In some embodiments, the polypeptide comprises an ECD that is a hGH-R-ECD, or variant thereof (e.g. as set forth herein and above); a transmembrane domain that is a gp130 transmembrane domain, or variant thereof (e.g. as set forth herein and above), and immune activating ICD that comprises a gp130 ICD, or variant thereof (e.g. as set forth herein and above) and a IL-2R β ICD, or variant thereof (e.g. as set forth herein and above).

[00142] In some embodiments, the polypeptide comprises an ECD that is a hGH-R-ECD, or variant thereof (e.g. as set forth herein and above); a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof (e.g. as set forth herein and above), and immune activating ICD that comprises a GCSF-R ICD, or variant thereof (e.g. as set forth herein and above) and a IL-7R α ICD, or variant thereof (e.g. as set forth herein and above).

[00143] In some embodiments, the polypeptide comprises an amino acid sequence of SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 120, or SEQ ID NO: 124, or a variant of any of the foregoing. In some embodiments, the variant comprises a polypeptide having at least 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%, or 99% identity to SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 120, or SEQ ID NO: 124.

[00144] Examples of these domains or sequences are provided for herein in the present specification.

[00145] The polypeptides with the different domains described in this section are distinct from what is known as a chimeric antigen receptor. Chimeric antigen receptors can be present in the same cell as these polypeptides, but this polypeptide would not be considered a chimeric antigen receptor by one of skill in the art. Thus, in some embodiments, the polypeptide does not comprise an antigen binding domain. For example, in some embodiments, polypeptide does not comprise an antigen binding domain that is in an scFv, Fab, or single domain antibody format. Other antigen binding domains are provided for herein, and in some embodiments, the polypeptide does not comprise an antigen binding domain in any format. One of skill in the art would not consider the ligand ECD domain the same as an antigen binding domain. Examples of domains that the polypeptide may not comprises are also described in Guedan, et al., Engineering and Design of Chimeric Antigen Receptors, Molecular Therapy: Methods & Clinical Development Vol. 12 March 2019, pp. 145-156, which is hereby incorporated by reference in its entirety.

[00146] In some embodiments, these polypeptides do not comprises an ECD that comprises a binding domain that binds to a tumor antigen. In some embodiments, the polypeptide does not comprise a co-stimulatory domain. In some embodiments, the polypeptide does not comprise a CD3 ζ signaling domain. In some embodiments, the polypeptide does not comprise a CD28 ζ signaling domain. In some embodiments, the polypeptide does not comprise an immune receptor tyrosine-based activation motifs (ITAMs). In some embodiments, the polypeptide

does not comprise a costimulatory endodomain. In some embodiments, the polypeptide does not comprise a 4-1BB signaling or costimulatory endodomain. In some embodiments, the polypeptide does not comprise a CD28 signaling or costimulatory endodomain. In some embodiments, the polypeptide does not comprise an inducible T cell costimulator (ICOS) intracellular domain.

[00147] In some embodiments, the polypeptide does not comprise a CH2, CH3, CD28, or CD8 α hinge region.

[00148] In some embodiments, the polypeptide comprising the ECD of G-CSFR, or a variant thereof, such as those provided for herein, does not comprise an antigen binding domain.

[00149] These polypeptides can be incorporated into any of the particles provided for herein. According in some embodiments, a particle comprising the polypeptide is provided. In some embodiments, the particle is a vector (e.g., virus, a liposome, plasmid, and the like) or a cell. In some embodiments, the particle is a virus or viral vector. In some embodiments, the viral vector is a lentiviral vector, AV vector, an AAV vector, and the like. In some embodiments, the viral vector is a pseudotyped viral vector. Non-limiting examples of pseudotyped viral vector are provided for herein, but it can be pseudotyped with any viral structural protein. In some embodiments, the particle further comprises a chimeric antigen receptor, such as a chimeric antigen receptor comprising an antigen binding domain that binds to a tumor antigen.

[00150] Also provided herein are nucleic acid molecules encoding for a chimeric antigen receptor (CAR), the polypeptides, or a combination thereof. In some embodiments, the CAR is as provided for herein. In some embodiments, the CAR and the polypeptide are encoded by unique nucleic acid molecules. In some embodiments, the CAR and the polypeptide are encoded by the same nucleic acid molecule. Methods of encoding multiple proteins of interest from a single nucleic acid molecule are known in the art, and any such method is within the scope of the present disclosure. In some embodiments, the single nucleic acid molecule encodes the CAR and the polypeptide as a bicistronic molecule, wherein the CAR and the polypeptide are separated by a cleavable peptide linker. Cleavable peptide linkers are known in the art, and any such cleavable linker is within the scope of the present disclosure. In some embodiments, the cleavable peptide linker is a 2A peptide linker. In some embodiments, the nucleic acid molecule encodes for a bicistronic construct, wherein from 5' to 3' the nucleic acid molecule encodes for the CAR, the cleavable linker (e.g. a 2A linker), and the polypeptide. In some embodiments, the nucleic acid molecule encodes for a bicistronic construct, wherein

from 5' to 3' the nucleic acid molecule encodes for the polypeptide, the cleavable linker (e.g. a 2A linker), and the CAR. In some embodiments, a particle comprising the nucleic acid molecule is provided. In some embodiments, the particle is a vector (e.g., virus, a liposome, plasmid, and the like) or a cell. In some embodiments, the particle is a virus or viral vector. In some embodiments, the viral vector is a lentiviral vector, AV vector, an AAV vector, and the like. In some embodiments, the viral vector is a pseudotyped viral vector. Non-limiting examples of pseudotyped viral vector are provided for herein, but it can be pseudotyped with any viral structural protein.

Viral Particles Comprising Heterologous Viral Glycoprotein and Targeting Moiety

[00151] In some embodiments, viral particles are provided comprising a heterologous viral glycoprotein and a targeting moiety. In some embodiments, the targeting moiety comprises a polypeptide having the formula T-S₁, wherein T is a target binding domain, and S₁ is a stalk portion. In some embodiments, S₁ comprises a variant Fc protein, wherein the variant Fc protein comprises a transmembrane domain, such as, but not limited to a CD8 or CD28 transmembrane domain. Accordingly, in some embodiments, the stalk portion S₁ comprises an N-terminus to C-terminus orientation of variant Fc – transmembrane domain. In some embodiments, the variant Fc protein comprises an effector mutation, wherein the effector mutation inhibits the interaction between the Fc protein and a Fc interacting protein, such as FcγR, C1q, FcRβ, or FcRn.

[00152] In some embodiments, the S₁ stalk portion is attached to the surface of the viral particle through the transmembrane domain. In some embodiments, the variant Fc protein is a variant of an IgG1 Fc, IgG2 Fc or IgG4 Fc protein. In some embodiments, the variant Fc protein comprises a variant of a sequence of SEQ ID NO: 26 (IgG1 Fc), SEQ ID NO: 27 (IgG2 Fc), or SEQ ID NO: 28 (IgG4 Fc).

[00153] In some embodiments, the variant Fc protein is a variant IgG1 Fc protein (SEQ ID NO: 26). In some embodiments, the variant IgG1 Fc protein comprises one or more of the mutations that corresponds to those selected from the group consisting of: L234A, L235A, N297A, P329G, I253A, H310A, and H435A of SEQ ID NO: 26, numbered according to the EU numbering index of Kabat as described in Edelman, G M et al. "The covalent structure of an entire gammaG immunoglobulin molecule." *Proceedings of the National Academy of Sciences of the United States of America* vol. 63,1 (1969): 78-85. doi:10.1073/pnas.63.1.78, hereby incorporated by reference in its entirety. Any of the mutations L234A, L235A, N297A,

P329G, I253A, H310A, and H435A of SEQ ID NO: 26 may be present or absent and the mutations may be combined in any combination. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to L234A and L235A of SEQ ID NO: 26. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to N297A of SEQ ID NO: 26. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to P329G of SEQ ID NO: 26. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to L234A, L235A, N297A, and P329G of SEQ ID N: 26. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to I253A of SEQ ID NO: 26. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to H310A of SEQ ID NO: 26. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to H435A of SEQ ID NO: 26. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to I253A, H310A, and H435A of SEQ ID NO: 26. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to L234A, L235A, N297A, P329G, I253A, H310A, and H435A of SEQ ID NO: 26.

[00154] In some embodiments, the variant Fc protein comprising a variant IgG1 Fc protein comprises a truncation of the IgG1 Fc sequence. The truncation can comprise the deletion of any number of amino acids from the N-terminus, the C-terminus, or both of the IgG1 Fc sequence. In some embodiments, the variant Fc protein comprising a variant IgG1 Fc protein comprises a truncation of SEQ ID NO: 26. The truncation can comprises the deletion of any number of amino acids from the N-terminus, the C-terminus, or both of SEQ ID NO: 26. In some embodiments, the truncation comprises the deletion of amino acids from the N-terminus of SEQ ID NO: 26. In some embodiments, the truncation comprises the deletion of amino acids from the C-terminus of SEQ ID NO: 26. In some embodiments, the truncation comprises the deletion of amino acids from both the N-terminus and the C-terminus of SEQ ID NO: 26. In some embodiments, the truncation of SEQ ID NO: 26 comprises an amino acid sequence of SEQ ID NO: 103:

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EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKG
FYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVF
SCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 103)
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[00155] In some embodiments, the variant IgG1 Fc protein comprises one or more mutations relative to SEQ ID NO: 103 selected from the group consisting of: L19A, L20A, N82A, P114G, I38A, H95A, and H220A. It is to be understood that the positions L19, L20, N82, P114, I38,

H95, and H220 are in reference to SEQ ID NO: 103 only. The skilled artisan would readily recognize that positions L234, L235, N297, P329, I253, H310, and H435 numbered according to the EU numbering system of Kabat correspond to positions L19, L20, N82, P114, I38, H95, and H220, respectively, of SEQ ID NO: 103. Any of the mutations L19A, L20A, N82A, P114G, I38A, H95A, and H220A of SEQ ID NO: 103 may be present or absent and the mutations may be combined in any combination. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to L19A and L20A of SEQ ID NO: 103. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to N82A of SEQ ID NO: 103. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to P114G of SEQ ID NO: 103. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to L19A, L20A, N82A, and P114G of SEQ ID NO: 103. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to I38A of SEQ ID NO: 103. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to H95A of SEQ ID NO: 103. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to H220A of SEQ ID NO: 103. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to I38A, H95A, and H220A of SEQ ID NO: 103. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to L19A, L20A, N82A, P114G, I38A, H95A, and H220A of SEQ ID NO: 103. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to each of L18A, L19A, N82A, P114G, I38A, H95A, and H220A of SEQ ID NO: 103. An exemplary variant IgG1 protein that comprises each of L18A, L19A, N82A, P114G, I38A, H95A, and H220A is shown below in the amino acid sequence of SEQ ID NO: 104:

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EPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMASRTPEVTCVVDVS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLAQDNLNGKEY
KCKVSNKALGAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKG
FYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVF
SCSVMHEALHNAYTQKSLSLSPGK (SEQ ID NO: 104)
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[00156] In some embodiments, the variant Fc protein is a variant IgG2 Fc protein (SEQ ID NO: 27). In some embodiments, the variant IgG2 Fc protein comprises one or more mutations selected from the group consisting of: N297A, P329G, I253A, H310A, and H435A as those positions correspond to SEQ ID NO: 27, numbered according to the EU numbering index of Kabat. Any of the mutations N297A, P329G, I253A, H310A, and H435A of SEQ ID NO: 27 may be present or absent and the mutations may be combined in any combination. In some

embodiments, the variant IgG2 Fc protein comprises a mutation that corresponds to N297A of SEQ ID NO: 27. In some embodiments, the variant IgG2 Fc protein comprises a mutation that corresponds to P329G of SEQ ID NO: 27. In some embodiments, the variant IgG2 Fc protein comprises a mutation that corresponds to N297A and P329G of SEQ ID NO: 27. In some embodiments, the variant IgG2 Fc protein comprises a mutation that corresponds to I253A of SEQ ID NO: 27. In some embodiments, the variant IgG2 Fc protein comprises a mutation that corresponds to H310A of SEQ ID NO: 27. In some embodiments, the variant IgG2 Fc protein comprises a mutation that corresponds to H435A of SEQ ID NO: 27. In some embodiments, the variant IgG2 Fc protein comprises a mutation that corresponds to I253A, H310A, and H435A of SEQ ID NO: 27.

[00157] In some embodiments, the variant Fc protein comprising a variant IgG2 Fc protein comprises a truncation of the IgG2 Fc sequence. The truncation can comprise the deletion of any number of amino acids from the N-terminus, the C-terminus, or both of the IgG2 Fc sequence. In some embodiments, the variant Fc protein comprising a variant IgG2 Fc protein comprises a truncation of SEQ ID NO: 27. The truncation can comprises the deletion of any number of amino acids from the N-terminus, the C-terminus, or both of SEQ ID NO: 27. In some embodiments, the truncation comprises the deletion of amino acids from the N-terminus of SEQ ID NO: 27. In some embodiments, the truncation comprises the deletion of amino acids from the C-terminus of SEQ ID NO: 27. In some embodiments, the truncation comprises the deletion of amino acids from both the N-terminus and the C-terminus of SEQ ID NO: 27.

[00158] In some embodiments, the variant Fc protein is a variant IgG4 Fc protein (SEQ ID NO: 28). In some embodiments, the variant IgG4 Fc protein comprises one or more mutations selected from the group consisting of: S228P, L235E, N297A, P329G, I253A, H310A, and H435A as those positions correspond to SEQ ID NO: 28, numbered according to the EU numbering index of Kabat. Any of the mutations S228P, L235E, N297A, P329G, I253A, H310A, and H435A of SEQ ID NO: 28 may be present or absent and the mutations may be combined in any combination. In some embodiments, the variant IgG4 Fc protein comprises a mutation that corresponds to S228P of SEQ ID NO: 28. In some embodiments, the variant IgG4 Fc protein comprises a mutation that corresponds to L235E of SEQ ID NO: 28. In some embodiments, the variant IgG4 Fc protein comprises a mutation that corresponds to N297A of SEQ ID NO: 28. In some embodiments, the variant IgG4 Fc protein comprises a mutation that corresponds to P329G of SEQ ID NO: 28. In some embodiments, the variant IgG4 Fc protein comprises a mutation that corresponds to S228P, L235E, N297A, and P329G of SEQ ID NO: 28. In some embodiments, the variant IgG4 Fc protein comprises a mutation that corresponds

to I253A of SEQ ID NO: 28. In some embodiments, the variant IgG4 Fc protein comprises a mutation that corresponds to H310A of SEQ ID NO: 28. In some embodiments, the variant IgG4 Fc protein comprises a mutation that corresponds to H435A of SEQ ID NO: 28. In some embodiments, the variant IgG4 Fc protein comprises a mutation that corresponds to I253A, H310A, and H435A of SEQ ID NO: 28.

[00159] In some embodiments, the variant Fc protein comprising a variant IgG4 Fc protein comprises a truncation of the IgG4 Fc sequence. The truncation can comprise the deletion of any number of amino acids from the N-terminus, the C-terminus, or both of the IgG4 Fc sequence. In some embodiments, the variant Fc protein comprising a variant IgG4 Fc protein comprises a truncation of SEQ ID NO: 28. The truncation can comprises the deletion of any number of amino acids from the N-terminus, the C-terminus, or both of SEQ ID NO: 28. In some embodiments, the truncation comprises the deletion of amino acids from the N-terminus of SEQ ID NO: 28. In some embodiments, the truncation comprises the deletion of amino acids from the C-terminus of SEQ ID NO: 28. In some embodiments, the truncation comprises the deletion of amino acids from both the N-terminus and the C-terminus of SEQ ID NO: 28.

[00160] In some embodiments, the stalk portion S_1 comprising a variant Fc protein is given by the formula L_1 -Fc- L_2 - X_1 , wherein L_1 is a linker or absent; Fc is the variant Fc protein; L_2 is a linker or absent; and X_1 is a polypeptide comprising the transmembrane domain. Accordingly, the targeting moiety comprising the formula T- S_1 may also be given by the formula T- L_1 -Fc- L_2 - X_1 , wherein: T is a target binding domain; L_1 is a linker or absent; Fc is the variant Fc protein; L_2 is a linker or absent; and X_1 is a polypeptide comprising the transmembrane domain. Therefore, it is to be understood that, in some embodiments, the stalk portion S_1 may be given by the formula L_1 -Fc- L_2 - X_1 . In some embodiments, the target binding domain T is as provided for herein. In some embodiments, the variant Fc protein is as provided for herein.

[00161] In some embodiments, L_1 and L_2 are each, independently, a polypeptide linker. In some embodiments, the polypeptide linker comprises (GGGGA)_n (SEQ ID NO: 54), (GGGGS)_n (SEQ ID NO: 55), (EAAAK)_n (SEQ ID NO: 73), A(EAAAK)_nA (SEQ ID NO: 74), (XP)_n (SEQ ID NO: 75), wherein X is Ala, Lys, or Glu, GSAGSAAGSGEF (SEQ ID NO: 56), KESGSVSSEQLAQFRSLD (SEQ ID NO: 57), EGKSSGSGSESKST (SEQ ID NO: 58), AEAAAKEAAAKA (SEQ ID NO: 76), or a combination thereof, wherein each n is, independently, 1-5. In some embodiments, each n is, independently, 1. In some embodiments, each n is, independently, 2. In some embodiments, each n is, independently, 3. In some embodiments, each n is, independently, 4. In some embodiments, each n is, independently, 5.

In some embodiments, each n is, independently, greater than 5. In some embodiments, L_1 is absent. In some embodiments, L_1 is $(GGGGA)_n$ (SEQ ID NO: 54) or $(GGGGS)_n$ (SEQ ID NO: 55), wherein each n is, independently, 1-5. In some embodiments, L_1 is $(GGGGA)_n$ (SEQ ID NO: 54) or $(GGGGS)_n$ (SEQ ID NO: 55), wherein each n is, independently, 1. In some embodiments, L_1 is $(GGGGA)_n$ (SEQ ID NO: 54) or $(GGGGS)_n$ (SEQ ID NO: 55), wherein each n is, independently, 2. In some embodiments, L_1 is $(GGGGA)_n$ (SEQ ID NO: 54) or $(GGGGS)_n$ (SEQ ID NO: 55), wherein each n is, independently, 3. In some embodiments, L_1 is $(GGGGA)_n$ (SEQ ID NO: 54) or $(GGGGS)_n$ (SEQ ID NO: 55), wherein each n is, independently, 4. In some embodiments, L_1 is $(GGGGA)_n$ (SEQ ID NO: 54) or $(GGGGS)_n$ (SEQ ID NO: 55), wherein each n is, independently, 5. In some embodiments, L_1 is $(GGGGA)_n$ (SEQ ID NO: 54) or $(GGGGS)_n$ (SEQ ID NO: 55), wherein each n is, independently, greater than 5. In some embodiments, L_2 is absent. In some embodiments, L_2 is $(GGGGA)_n$ (SEQ ID NO: 54) or $(GGGGS)_n$ (SEQ ID NO: 55), wherein each n is, independently, 1-5. In some embodiments, L_2 is $(GGGGA)_n$ (SEQ ID NO: 54) or $(GGGGS)_n$ (SEQ ID NO: 55), wherein each n is, independently, 1. In some embodiments, L_2 is $(GGGGA)_n$ (SEQ ID NO: 54) or $(GGGGS)_n$ (SEQ ID NO: 55), wherein each n is, independently, 2. In some embodiments, L_2 is $(GGGGA)_n$ (SEQ ID NO: 54) or $(GGGGS)_n$ (SEQ ID NO: 55), wherein each n is, independently, 3. In some embodiments, L_2 is $(GGGGA)_n$ (SEQ ID NO: 54) or $(GGGGS)_n$ (SEQ ID NO: 55), wherein each n is, independently, 4. In some embodiments, L_2 is $(GGGGA)_n$ (SEQ ID NO: 54) or $(GGGGS)_n$ (SEQ ID NO: 55), wherein each n is, independently, 5. In some embodiments, L_2 is $(GGGGA)_n$ (SEQ ID NO: 54) or $(GGGGS)_n$ (SEQ ID NO: 55), wherein each n is, independently, greater than 5.

[00162] In some embodiments, X_1 comprises a polypeptide having a formula of ECD- T_M -ICD, wherein ECD is an extracellular domain, or a fragment thereof, of a cell surface protein, or is absent; T_M is a transmembrane domain of a transmembrane protein; and ICD is an intracellular domain of a protein or a protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, or is absent. Accordingly, in some embodiments, the targeting moiety comprising the formula T- S_1 that may also be given by the formula T- L_1 -Fc- L_2 - X_1 may also be given by the formula T- L_1 -Fc- L_2 -ECD- T_M -ICD, wherein T is a target binding domain; L_1 is a linker or absent; Fc is the variant Fc protein; L_2 is a linker or absent; ECD is an extracellular domain, or a fragment thereof, of a cell surface protein, or is absent; T_M is a transmembrane domain of a transmembrane protein; and ICD is an intracellular domain of a protein or a protein that facilitates the incorporation of the targeting moiety into the

envelope of the viral particle, or is absent. Therefore, it is to be understood that, in some embodiments, the stalk portion S_1 may be given by the formula L_1 -Fc- L_2 -ECD- T_M -ICD.

[00163] In some embodiments, the stalk portion S_1 does not comprise a variant Fc region. In some embodiments, the stalk portion S_1 is given by the formula L_3 - X_1 , wherein L_3 is a flexible peptide linker and X_1 is a polypeptide comprising a transmembrane domain as provided for herein. Accordingly, in some embodiments, the targeting moiety comprising the formula T- S_1 may also be given by the formula T- L_3 - X_1 , wherein T is a target binding domain, L_3 is a flexible peptide linker, and X_1 is a polypeptide comprising a transmembrane domain as provided for herein. Therefore, it is to be understood that, in some embodiments, the stalk portion S_1 may be given by the formula L_3 - X_1 . In some embodiments, the S_1 stalk portion is attached to the surface of the viral particle through the transmembrane domain.

[00164] In some embodiments, the flexible peptide linker L_3 may be any flexible peptide linker. In some embodiments, L_3 is selected from the group of flexible linkers including, but not limited to, (GGGGA)_n (SEQ ID NO: 54), (GGGGS)_n (SEQ ID NO: 55), GSAGSAAGSGEF (SEQ ID NO: 56), KESGSVSSEQLAQFRSLD (SEQ ID NO: 57), EGKSSGSGSESKST (SEQ ID NO: 58), or any combination thereof, wherein each n is, independently, an integer selected from 1-4. In some embodiments, each n is, independently, an integer selected from 1-4, 1-5, 1-6, 1-7, 1-8, 1-9, or 1-10. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, n is 5. In some embodiments, n is 6. In some embodiments, n is 7. In some embodiments, n is 8. In some embodiments, n is 9. In some embodiments, n is 10. In some embodiments, each n is, independently, greater than 10. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is 1. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is 2. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is 3. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is 4. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is 5. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is 6. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is 7. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is 8. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is 9. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is 10. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is greater than 10. In some embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is 1. In some embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is 2. In some embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is 3. In some embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is 4. In some embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is 5. In some

embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is 6. In some embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is 7. In some embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is 8. In some embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is 9. In some embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is 10. In some embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is greater than 10. In some embodiments, L_3 is GSAGSAAGSGEF (SEQ ID NO: 56). In some embodiments, L_3 is KESGSVSSEQLAQFRSLD (SEQ ID NO: 57). In some embodiments, L_3 is EGKSSGSGSESKST (SEQ ID NO: 58).

[00165] In some embodiments, the flexible peptide linker L_3 may be any flexible peptide linker. In some embodiments, L_3 is selected from the group of flexible linkers including, but not limited to, (GGGGA)_n (SEQ ID NO: 54), (GGGGS)_n (SEQ ID NO: 55), GSAGSAAGSGEF (SEQ ID NO: 56), KESGSVSSEQLAQFRSLD (SEQ ID NO: 57), EGKSSGSGSESKST (SEQ ID NO: 58), or any combination thereof, wherein each n is, independently, an integer selected from 1-4. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is 1. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is 2. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is 3. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is 4. In some embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is 1. In some embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is 2. In some embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is 3. In some embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is 4. In some embodiments, L_3 is GSAGSAAGSGEF (SEQ ID NO: 56). In some embodiments, L_3 is KESGSVSSEQLAQFRSLD (SEQ ID NO: 57). In some embodiments, L_3 is EGKSSGSGSESKST (SEQ ID NO: 58).

[00166] In some embodiments, L_3 is selected from the group of flexible linkers including, but not limited to, (GGGGA)_n (SEQ ID NO: 54), (GGGGS)_n (SEQ ID NO: 55), GSAGSAAGSGEF (SEQ ID NO: 56), KESGSVSSEQLAQFRSLD (SEQ ID NO: 57), EGKSSGSGSESKST (SEQ ID NO: 58), or any combination thereof, wherein each n is, independently, an integer selected from 1, 2, or 4. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 4. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is 1. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is 2. In some embodiments, L_3 is (GGGGA)_n (SEQ ID NO: 54) and n is 4. In some embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is 1. In some embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is 2. In some embodiments, L_3 is (GGGGS)_n (SEQ ID NO: 55) and n is 4.

55) and n is 4. In some embodiments, L₃ is GSAGSAAGSGEF (SEQ ID NO: 56). In some embodiments, L₃ is KESGSVSSEQLAQFRSLD (SEQ ID NO: 57). In some embodiments, L₃ is EGKSSGSGSESKST (SEQ ID NO: 58).

[00167] In some embodiments, X₁ comprises a polypeptide having a formula of ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof, of a cell surface protein, or is absent; T_M is a transmembrane domain of a transmembrane protein; and ICD is an intracellular domain of a protein or a protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, or is absent. Accordingly, in some embodiments, the targeting moiety comprising the formula T-S₁ that may also be given by the formula T-L₃-X₁, may also be given by the formula T-L₃-ECD-T_M-ICD, wherein T is a target binding domain, L₃ is a flexible peptide linker ECD is an extracellular domain, or a fragment thereof, of a cell surface protein, or is absent; T_M is a transmembrane domain of a transmembrane protein; and ICD is an intracellular domain of a protein or a protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, or is absent. Therefore, it is to be understood that, in some embodiments, the stalk portion S₁ may be given by the formula L₃-ECD-T_M-ICD.

[00168] In some embodiments, the ECD is absent. In some embodiments, the ECD can be any appropriate extracellular domain or fragment thereof. In some embodiments, the ECD is from a different protein as compared to the transmembrane domain. The ECD domain can be the entire ECD domain or a fragment thereof. In some embodiments, the ECD domain is a CD8 or CD28 ECD domain, or a fragment thereof. In some embodiments, the ECD domain is a CD8 ECD domain or fragment thereof. In some embodiments, the CD8 ECD domain comprises the polypeptide of FVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 59). In some embodiments, the CD8 ECD domain consists or consists essentially of the polypeptide of FVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 59). In some embodiments, the ECD domain comprises a polypeptide that is 25-45 amino acids in length. In some embodiments, the ECD comprises a polypeptide that is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of FVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 59). In some embodiments, the ECD domain is a CD28 ECD domain or fragment thereof. In some embodiments, the CD28 ECD domain comprises the polypeptide of KIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPFPGPSKP (SEQ ID NO: 60). In some

embodiments, the CD28 ECD domain consists or consists essentially of the polypeptide of KIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPFLFPGPSKP (SEQ ID NO: 60). In some embodiments, the ECD domain comprises a polypeptide that is 25-45 amino acids in length. In some embodiments, the ECD comprises a polypeptide that is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of KIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPFLFPGPSKP (SEQ ID NO: 60).

[00169] In some embodiments, the T_M can be any appropriate transmembrane domain or fragment thereof. In some embodiments, the T_M domain is a CD8 or CD28 T_M domain or a fragment thereof. In some embodiments, the T_M domain is a CD8 T_M domain or fragment thereof. In some embodiments, the CD8 T_M domain comprises the polypeptide of IYIWAPLAGTCGVLLLSLVITLYCNHRN (SEQ ID NO: 61). In some embodiments, the CD8 T_M domain consists or consists essentially of the polypeptide of IYIWAPLAGTCGVLLLSLVITLYCNHRN (SEQ ID NO: 61). In some embodiments, the T_M comprises a polypeptide that is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of IYIWAPLAGTCGVLLLSLVITLYCNHRN (SEQ ID NO: 61). In some embodiments, the T_M domain is a CD28 T_M domain or fragment thereof. In some embodiments, the CD28 T_M domain comprises the polypeptide of FWVLVVGGVLACYSLLVTVAFIIFWV (SEQ ID NO: 62). In some embodiments, the CD28 T_M domain consists or consists essentially of the polypeptide of FWVLVVGGVLACYSLLVTVAFIIFWV (SEQ ID NO: 62). In some embodiments, the T_M comprises a polypeptide that is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of FWVLVVGGVLACYSLLVTVAFIIFWV (SEQ ID NO: 62).

[00170] In some embodiments, the T_M domain is from the same protein as the ECD. In some embodiments, the T_M domain is from a different protein as the ECD. In some embodiments, the T_M domain is a CD8, or CD28 T_M domain or a fragment thereof and the ECD domain is a CD8, or CD28 ECD domain or fragment thereof. In some embodiments, the T_M domain is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of IYIWAPLAGTCGVLLLSLVITLYCNHRN (SEQ ID NO: 61) and the ECD domain is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of FVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 59). In some embodiments, the T_M domain is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of IYIWAPLAGTCGVLLLSLVITLYCNHRN (SEQ ID NO: 61) and the ECD domain is at least,

or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of KIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPFPGPSKP (SEQ ID NO: 60). In some embodiments, the T_M domain is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of FWVLVVVGGLACYSLLVTVAFIIFWV (SEQ ID NO: 62) and the ECD domain is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of FVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 59). In some embodiments, the T_M domain is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of FWVLVVVGGLACYSLLVTVAFIIFWV (SEQ ID NO: 62) and the ECD domain is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of KIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPFPGPSKP (SEQ ID NO: 60).

[00171] In some embodiments, the transmembrane domain is linked to an intracellular domain (ICD) of a cellular transmembrane protein, or a fragment thereof. In some embodiments, the ICD is absent. In some embodiments, the ICD is from the same or different protein as the T_M domain. In some embodiments, the ICD comprises an Env incorporation motif. An Env incorporation motif is a molecule, e.g., polypeptide, that can help to facilitate the incorporation of a protein into the envelope of the virus. A non-limiting example of an Env incorporation motif is a polypeptide comprising the amino acid sequence of NRVRQGYS (SEQ ID NO: 63). This is a non-limiting example and other peptide sequences can be used, such as, but not limited to, GGTETSQVAPA (SEQ ID NO: 64). In some embodiments, the Env incorporation motif comprises an amino acid sequence of SEQ ID NO: 63, SEQ ID NO: 64, or a combination thereof. In some embodiments, the Env incorporation motif comprises an amino acid sequence of SEQ ID NO: 63. In some embodiments, the Env incorporation motif comprises an amino acid sequence of SEQ ID NO: 64.

[00172] In some embodiments, the target binding domain “T” is any polypeptide or polynucleotide that may be used to bind to a desired target. In some embodiments, T is any polypeptide, polynucleotide, or fragment thereof that binds to CD7, CD8, cKit (CD117), CD4, CD3, CD5, CD6, CD2, TCR alpha, TCR beta, TCR gamma, TCR delta, CD10, CD34, CD110, CD33, CD14, CD68, CCR7, CD62L, CD25, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, or CXCR3, A glycosylated CD43 epitope expressed on acute leukemia or lymphoma but not on hematopoietic progenitors; A glycosylated CD43 epitope expressed on non-hematopoietic cancers; A kinase anchor protein 4 (AKAP-4); Adrenoceptor beta 3 (ADRB3); AFP; Anaplastic lymphoma kinase (ALK); Androgen receptor; Angiopoietin-binding cell surface

receptor 2 (Tie 2); Auto antibody to desmoglein 1 (Dsg1); Auto antibody to desmoglein 3 (Dsg3); B7H3 (CD276); Biotin; Bone marrow stromal cell antigen 2 (BST2); BST1/CD157; Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-Ia); Carbonic anhydrase IX (CA1X); Carcinoembryonic antigen (CEA); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites); CCR4; CD5; CD19; CD20; CD22; CD24; CD30; CD32 (FCGR2A); CD33; CD34; CD38; CD44v6; CD72; CD79a; CD79b; CD97; CD99; CD123; CD171; CD179a; CD179b-IGLII; CD200R; CD276/B7H3; CD300 molecule-like family member f (CD300LF); CDH1-CD324; CDH6; CDH17; CDH19; Chromosome X open reading frame 61 (CXORF61); Claudin 6 (CLDN6); Claudin18.2 (CLD18A2 or CLDN18A.2); CMV pp65; C-MYC epitope Tag; Cripto; CS1 (also referred to as CD2 subset 1 or CRACC or SLAMF7 or CD319 or 19A24); CSF2RA (GM-CSFR-alpha); C-type lectin domain family 12 member A (CLEC12A); C-type lectin-like molecule-1 (CLL-1 or CLECL1); Cyclin B1; Cytochrome P450 IB 1 (CYP1B 1); DLL3; EBV-EBNA3c; EGF-bke module- containing mucin-like hormone receptor-like 2 (EMR2); Elongation factor 2 mutated (ELF2M); Ephrin B2; Ephrin type-A receptor 2 (EphA2); Epidermal growth factor receptor (EGFR); Epidermal growth factor receptor variant III (EGFRviii); Epithelial cell adhesion molecule (EPCAM); ERG; ETS translocation-variant gene 6 located on chromosome 12p (ETV6-AML); Fc fragment of IgA receptor (FCAR or CD89); Fc receptor-like 5 (FCRL5); Fibroblast activation protein alpha (FAP); FITC; Fms Like Tyrosine Kinase 3 (FLT3); Folate receptor alpha (FRA or FR1); Folate receptor beta (FRb); Follicle stimulating hormone receptor (FSHR); Fos-related antigen 1; Fucosyl-GM1; G protein coupled receptor class C group 5 member D (GPRC5D); G protein-coupled receptor 20 (GPR20); GAD; Ganglioside G2 (GD2); Ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(1-4)bDGlc(1-1)Cer); Ganglioside GM3 (aNeu5Ac(2-3)bDCIalp(1- 4)bDGlc(1-1)Cer); GD3; GFRalpha4; Glycoprotein 100 (gp100); Glypican-3 (GPC3); Gonadotropin Hormone receptor (CGHR or GR); GpA33; GpNMB; GPRC5D; Guanylyl cyclase C (GCC); Heat shock protein 70-2 mutated (mut hsp70-2); Hepatitis A virus cellular receptor 1 (HAVCR1); Hexasaccharide portion of globoH glycosphingolipid (GloboH); High molecular weight-melanoma associated antigen (HMWMAA); HIV1 envelope glycoprotein; HLA; HLA-DOA; HLA-A; HLA-A2; HLA-B; HLA-C; HLA-DM; HLA-DOB; HLA-DP; HLA-DQ; HLA-DR; HLA-G; HTLV1-Tax; Human papilloma virus E6 (HPV E6); Human papilloma virus E7 (HPV E7); Human Telomerase reverse transcriptase (hTERT); IgE; IL13Ra2; IL1 IRa; Immunoglobulin lambda-like polypeptide 1 (IGLL1); Influenza A hemagglutinin (HA); Insulin-like growth factor 1 receptor (IGF-I receptor); Interleukin 11 receptor alpha (IL-11Ra); Interleukin- 13 receptor subunit alpha-2 (IL-

13Ra2 or CD213A2); Intestinal carboxyl esterase; KIT (CD117); KSHV K8.1; KSHV-gH; LAMP1 ; Legumain; Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Leutenizing hormone receptor (LHR); Lewis(Y) antigen; Lews Ag; Livl; Locus K 9 (LY6K); Low conductance chloride channel; Lymphocyte antigen 6 complex; Lymphocyte antigen 75 (LY75); Lymphocyte-specific protein tyrosine kinase (LCK); Mammary gland differentiation antigen (NY-BR-1); Melanoma antigen recognized by T cells 1 (MelanA or MARTI); Melanoma- associated antigen 1 (MAGE-A1); Melanoma cancer testis antigen-1 (MAD-CT-1); Melanoma cancer testis antigen-2 (MAD-CT-2); Melanoma inhibitor of apoptosis (ML-IAP); Mesothelin; MPL; Mucin 1 cell surface associated (MUC1); N-Acetyl glucosaminyl-transferase V (NA17); Nectin-4; Neural cell adhesion molecule (NCAM); NKG2D; NYBR1; O-acetyl-GD2 ganglioside (OAcGD2); Olfactory receptor 51E2 (OR51E2); Oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); P53 mutant; Paired box protein Pax-3 (PAX3); Paired box protein Pax-5 (PAX5); Pannexin 3 (PANX3); PDL1; P-glycoprotein; Placenta-specific 1 (PLAC1); Platelet-derived growth factor receptor beta (PDGFR-beta); Polysialic acid; Proacrosin binding protein sp32 (OY-TES1); Prostase; Prostate carcinoma tumor antigen-1 (PCT A-1 or Galectin 8); Prostate stem cell antigen (PSCA); Prostate-specific membrane antigen (PSMA); Prostatic acid phosphatase (PAP); Prostein; Protease Serine 21 (Testisin or PRSS21); Proteasome (Prosome Macropain) Subunit Beta Type 9 (LMP2); PTK7; Ras G12V; Ras Homolog Family Member C (RhoC); Rat sarcoma (Ras) mutant; Receptor for Advanced Gly cation Endproducts (RAGE-1); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Receptor tyrosine-protein kinase ERBB2 or Her-22/neu; Renal ubiquitous 1 (RU1); Renal ubiquitous 2 (RU2); Sarcoma translocation breakpoints; Serine 2 (TMPRSS2) ETS fusion gene; Sialyl Lewis adhesion molecule (sLe); SLAMF4; SLAMF6; Slea (CA19.9 or Sialyl Lewis Antigen); Sperm protein 17 (SPA17); Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Stage-specific embryonic antigen-4 (SSEA-4); STEAP1; Survivin; Synovial sarcoma X breakpoint 2 (SSX2); TCR Gamma Alternate Reading Frame Protein (TARP); TCR-beta1 chain; TCR-beta2 chain; TCR-delta chain; TCR-gamma chain; TCRgamma-delta; Telomerase; TGFbetaR2; The antigen recognized by TNT antibody; Thyroid stimulating hormone receptor (TSHR); Timl-/HVCR1; Tissue Factor 1 (TF1); Tn ag; Tn antigen ((Tn Ag) or (GalNAca-Ser/Thr)); TNF receptor family member B cell maturation (BCMA); Transglutaminase 5 (TGS5); Transmembrane protease; TROP2; Tumor endothelial marker 1 (TEM1/CD248); Tumor endothelial marker 7-related (TEM7R); Tumor protein p53

(p53); Tumor-associated glycoprotein 72 (TAG72); Tyrosinase; Tyrosinase-related protein 2 (TRP-2); Uroplakin 2 (UPK2); Vascular endothelial growth factor receptor 2 (VEGFR2); V-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Wilms tumor protein (WT1); or X Antigen Family Member 1A (XAGE1). In some embodiments, the targeting moiety “T” binds to CD7. In some embodiments, the target binding domain “T” binds to CD8. In some embodiments, the target binding domain “T” is an antibody. It is to be understood that in the context of the present disclosure “antibody” not only refers to a “complete” antibody comprising two identical heavy chains, two identical light chains, and two antigen binding fragments, but also refers to antibodies of any isotype, fragments of antibodies including, but not limited to, Fab, Fv, scFv, and Fd fragments, chimeric antibodies, humanized antibodies, single chain antibodies (scAb), single domain antibodies (dAb), single domain heavy chain antibodies, single domain light chain antibodies, bi-specific antibodies, multi-specific antibodies, and fusion proteins comprising an antigen-binding portion of an antibody and a non-antibody protein. In some embodiments, the antibody is selected from the group comprising a scFv, Fab, VHH, single domain antibody, and the like. In some embodiments, the antibody is a scFv. In some embodiments the antibody is a Fab. In some embodiments, the antibody is a VHH. In some embodiments, the antibody is a single domain antibody.

[00173] In some embodiments, the viral particles provided for herein are pseudotyped viral particles. In some embodiments, the viral particles are pseudotyped using viral glycoproteins of viruses of the Paramyxoviridae family. In some embodiments, the pseudotyped viral-like particles are pseudotyped using viral glycoproteins of morbillivirus, such as Measles virus. In some embodiments, the pseudotyped viral-like particles are pseudotyped using viral glycoproteins of the Measles virus. In some embodiments, the pseudotyped viral-like particles are pseudotyped using viral glycoproteins of henipavirus, such as Nipah virus, Cedar virus, or Hendra virus. In some embodiments, the pseudotyped viral-like particles are pseudotyped using viral glycoproteins of the Nipah virus. In some embodiments, a polypeptide or an antibody as provided herein is linked via a linker to an envelope glycoprotein G or H of a virus of the Paramyxoviridae family. In some embodiments, the virus of the Paramyxoviridae family is a morbillivirus, such as Measles virus. In some embodiments, the virus of the Paramyxoviridae family is a henipavirus, such as Nipah virus, Cedar virus, or Hendra virus.

[00174] As provided for herein, the viruses can be pseudotyped with a VSV-G protein, either wild-type or mutant of the same. Without being bound to any particular theory, the mutant VSV-G protein that can be used to pseudotype a virus (*e.g.* lentivirus) comprising a mutation

at position 182 can be used to pseudotype a virus and transduce a cell when the virus comprises a targeting moiety. This mutation inhibits or reduces the VSV-G affinity to its natural co-receptor, the LDL-R. The mutant VSV-G proteins as provided can be used, in some embodiments, to transduce a target cell and deliver a heterologous molecule to the targeted cells.

[00175] In some embodiments, a VSV-G protein is provided that comprises a mutation at position 198 as compared to SEQ ID NO: 1 or at position 182 as compared to SEQ ID NO: 2. SEQ ID NO: 1 is the full length protein and SEQ ID NO: 2 is the ectodomain of the VSV-G protein. The 16-mer signal peptide of MKCLLYLAFLFIGVNC (SEQ ID NO: 65) as shown at the N-terminus of SEQ ID NO: 1 is cleaved leaving a protein of SEQ ID NO: 2. Thus, although a mutation may be referred to in the context of SEQ ID NO: 2, it should be understood to also be made in the context of SEQ ID NO: 1, which contains the leader sequence, and thus would be a position number that is 16 more than the position recited for SEQ ID NO: 2. In some embodiments, the mutation inhibits or decreases the binding of the VSV-G protein to the LDL receptor (LDL-R). In some embodiments, the mutation is a I182D mutation as compared to SEQ ID NO: 2. In some embodiments, the mutation is a I182E mutation as compared to SEQ ID NO: 2.

[00176] In some embodiments, a VSV-G protein is provided that comprises a mutation at position 198 as compared to SEQ ID NO: 10 or at position 182 as compared to SEQ ID NO: 11. SEQ ID NO: 10 is the full length protein and SEQ ID NO: 11 is the ectodomain of the VSV-G protein. The 16-mer signal peptide of MLSYLIFALVVSPILG (SEQ ID NO: 66) as shown at the N-terminus of SEQ ID NO: 10 is cleaved leaving a protein of SEQ ID NO: 11. Thus, although a mutation may be referred to in the context of SEQ ID NO: 11, it should be understood to also be made in the context of SEQ ID NO: 10, which contains the leader sequence, and thus would be a position number that is 16 more than the position recited for SEQ ID NO: 11. In some embodiments, the mutation inhibits or decreases the binding of the VSV-G protein to the LDL receptor (LDL-R). In some embodiments, the mutation is a T182D mutation as compared to SEQ ID NO: 11. In some embodiments, the mutation is a T182E mutation as compared to SEQ ID NO: 11.

[00177] In some embodiments, a VSV-G protein is provided that comprises a mutation at position 198 as compared to SEQ ID NO: 12 or at position 182 as compared to SEQ ID NO: 13. SEQ ID NO: 12 is the full length protein and SEQ ID NO: 13 is the ectodomain of the VSV-G protein. The 16-mer signal peptide of MLRLFLFCFLALGAHS (SEQ ID NO: 67) as shown at the N-terminus of SEQ ID NO: 12 is cleaved leaving a protein of SEQ ID NO: 13.

Thus, although a mutation may be referred to in the context of SEQ ID NO: 13, it should be understood to also be made in the context of SEQ ID NO: 12, which contains the leader sequence, and thus would be a position number that is 16 more than the position recited for SEQ ID NO: 13. In some embodiments, the mutation inhibits or decreases the binding of the VSV-G protein to the LDL receptor (LDL-R). In some embodiments, the mutation is a A182D mutation as compared to SEQ ID NO: 13. In some embodiments, the mutation is a A182E mutation as compared to SEQ ID NO: 13.

[00178] In some embodiments, a VSV-G protein is provided that comprises a mutation at position 203 as compared to SEQ ID NO: 14 or at position 182 as compared to SEQ ID NO: 15. SEQ ID NO: 14 is the full length protein and SEQ ID NO: 15 is the ectodomain of the VSV-G protein. The 21-mer signal peptide of MKMKMVIAGLILCIGILPAIG (SEQ ID NO: 68) as shown at the N-terminus of SEQ ID NO: 14 is cleaved leaving a protein of SEQ ID NO: 15. Thus, although a mutation may be referred to in the context of SEQ ID NO: 15, it should be understood to also be made in the context of SEQ ID NO: 14, which contains the leader sequence, and thus would be a position number that is 21 more than the position recited for SEQ ID NO: 15. In some embodiments, the mutation inhibits or decreases the binding of the VSV-G protein to the LDL receptor (LDL-R). In some embodiments, the mutation is a V182D mutation as compared to SEQ ID NO: 15. In some embodiments, the mutation is a V182E mutation as compared to SEQ ID NO: 15.

[00179] In some embodiments, a VSV-G protein is provided that comprises a mutation at position 199 as compared to SEQ ID NO: 16 or at position 182 as compared to SEQ ID NO: 17. SEQ ID NO: 16 is the full length protein and SEQ ID NO: 17 is the ectodomain of the VSV-G protein. The 17-mer signal peptide of MTPAFILCMLLAGSSWA (SEQ ID NO: 69) as shown at the N-terminus of SEQ ID NO: 16 is cleaved leaving a protein of SEQ ID NO: 17. Thus, although a mutation may be referred to in the context of SEQ ID NO: 17, it should be understood to also be made in the context of SEQ ID NO: 16, which contains the leader sequence, and thus would be a position number that is 17 more than the position recited for SEQ ID NO: 17. In some embodiments, the mutation inhibits or decreases the binding of the VSV-G protein to the LDL receptor (LDL-R). In some embodiments, the mutation is a V182D mutation as compared to SEQ ID NO: 17. In some embodiments, the mutation is a V182E mutation as compared to SEQ ID NO: 17.

[00180] In some embodiments, a VSV-G protein is provided that comprises a mutation at position 199 as compared to SEQ ID NO: 18 or at position 182 as compared to SEQ ID NO: 19. SEQ ID NO: 18 is the full length protein and SEQ ID NO: 19 is the ectodomain of the

VSV-G protein. The 17-mer signal peptide of MNFLLLTFFIVLPLCSHA (SEQ ID NO: 70) as shown at the N-terminus of SEQ ID NO: 18 is cleaved leaving a protein of SEQ ID NO: 19. Thus, although a mutation may be referred to in the context of SEQ ID NO: 19, it should be understood to also be made in the context of SEQ ID NO: 18, which contains the leader sequence, and thus would be a position number that is 17 more than the position recited for SEQ ID NO: 19. In some embodiments, the mutation inhibits or decreases the binding of the VSV-G protein to the LDL receptor (LDL-R). In some embodiments, the mutation is a V182D mutation as compared to SEQ ID NO: 19. In some embodiments, the mutation is a V182E mutation as compared to SEQ ID NO: 19.

[00181] In some embodiments, a VSV-G protein is provided that comprises a mutation at position 199 as compared to SEQ ID NO: 20 or at position 182 as compared to SEQ ID NO: 21. SEQ ID NO: 20 is the full length protein and SEQ ID NO: 21 is the ectodomain of the VSV-G protein. The 17-mer signal peptide of MLVLYLLLSLLALGAQC (SEQ ID NO: 71) as shown at the N-terminus of SEQ ID NO: 20 is cleaved leaving a protein of SEQ ID NO: 21. Thus, although a mutation may be referred to in the context of SEQ ID NO: 21, it should be understood to also be made in the context of SEQ ID NO: 20, which contains the leader sequence, and thus would be a position number that is 17 more than the position recited for SEQ ID NO: 21. In some embodiments, the mutation inhibits or decreases the binding of the VSV-G protein to the LDL receptor (LDL-R). In some embodiments, the mutation is a I182D mutation as compared to SEQ ID NO: 21. In some embodiments, the mutation is a I182E mutation as compared to SEQ ID NO: 21.

[00182] As used herein, when a polypeptide is said to have a mutation as compared to a reference sequence, such comparison is based on an alignment such as using BlastP or ClustalW or ClustalOmega alignment software using default parameters. For example, position 182 can be found in SEQ ID NO: 2 and also as compared to the other strains as illustrated in FIG. 3. FIG. 3 illustrates a clustal alignment of the wild-type sequences of the ectodomains of the various strains of the VSV-G protein. The residue that is bolded and underlined are the residues that align to position 182 of SEQ ID NO: 2 of the various strains. SEQ ID NO: 2 refers to ectodomain of the VSV-G protein of the Indiana strain. SEQ ID NO: 11 refers to ectodomain of the VSV-G protein of the New Jersey strain. SEQ ID NO: 13 refers to ectodomain of the VSV-G protein of the Marraba strain. SEQ ID NO: 15 refers to ectodomain of the VSV-G protein of the Carajas strain. SEQ ID NO: 17 refers to ectodomain of the VSV-G protein of the Alagoa strain. SEQ ID NO: 19 refers to ectodomain of the VSV-G protein of the Cocal strain. SEQ ID NO: 21 refers to ectodomain of the VSV-G protein of the Morreton

strain. Accordingly, the residue that aligns to residues 182 as compared to SEQ ID NO: 2 can also be mutated as provided for herein.

[00183] In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 2 is not an alanine. In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 2 is not a valine.

[00184] In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 2 is I182S, I182H, I182T, I182Q, or I182N. In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 11 is T182S, T182H, T182Q, or T182N. In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 13 is A182S, A182H, A182T, A182Q, or A182N. In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 15 is V182S, V182H, V182T, V182Q, or V182N. In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 17 is V182S, V182H, V182T, V182Q, or V182N. In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 19 is V182S, V182H, V182T, V182Q, or V182N. In some embodiments, the mutation at position 182 as compared to SEQ ID NO: 21 is I182S, I182H, I182T, I182Q, or I182N. In some embodiments, the mutation at position 182 is not a hydrophobic residue. In some embodiments, the mutation at position 182 is a charged residue. In some embodiments, the mutation at position 182 is a negatively charged residue.

[00185] Although, the mutations may be described in reference to SEQ ID NO: 1 or SEQ ID NO: 2, which is the VSV-G protein from the Indiana strain, the mutation can also be used in other strains of the VSV-G protein. For example, the mutation can be made in the New Jersey Strain of VSV-G, the Marraba strain of VSV-G, the Carajas strain of VSV-G, the Alagoa strain of VSV-G, the Cocal strain of VSV-G, or the Morreton strain of VSV-G. In some embodiments, the sequences of each are as provided herein. Examples of these can be found, for example in U.S. Patent Application Publication No. 20200216502, which is hereby incorporated by reference. For example, the wild-type full length or ectodomain of the New Jersey Strain of VSV-G are SEQ ID NO: 10 and SEQ ID NO: 11, respectively, the wild-type full length or ectodomain of Marraba strain of VSV-G are SEQ ID NO: 12 and SEQ ID NO: 13, respectively, the wild-type full length or ectodomain of Carajas strain of VSV-G are SEQ ID NO: 14 and SEQ ID NO: 15, respectively, the wild-type full length or ectodomain of Alagoa strain of VSV-G are SEQ ID NO: 16 and SEQ ID NO: 17, respectively, the wild-type full length or ectodomain of Cocal strain of VSV-G are SEQ ID NO: 18 and SEQ ID NO: 19, respectively, or the wild-type full length or ectodomain of Morreton strain of VSV-G are SEQ ID NO: 20 and SEQ ID NO: 21, respectively.

[00186] A VSV-G protein comprising a mutation at position 182 as compared to SEQ ID NO: 2 can also comprise other mutations, such as those described in U.S. Patent Application Publication No. 20200216502, which is hereby incorporated by reference in its entirety. For example, the VSV-G protein can comprise a mutation at a position that corresponds to positions of 8, 47, 209 and/or 354 of SEQ ID NO: 2.

[00187] In some embodiments, the substitution at position 8 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except Y. In some embodiments, the substitution at position 209 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except H. In some embodiments, the substitution at position 47 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except K or R. In some embodiments, the substitution at position 354 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except K or R.

[00188] In some embodiments, the substitution is at position 47 or at position 354, or at both positions 47 and 354 are substituted by A, G, F or Q. In some embodiments, the substitution is A or Q.

[00189] In some embodiments, the substitution at position 8 is an alanine, i.e., H8A.

[00190] In some embodiments, the substitution at position 47 is Q or N, i.e., K47Q or K47N.

[00191] In some embodiments, the protein comprises a mutation (substitution) at position 10. In some embodiments, the substitution/mutation is Q10A, Q10R, or Q10K.

[00192] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 2 comprises a mutation at position 182 and at least, or about, 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% identical as compared to SEQ ID NO: 2 (or SEQ ID NO: 1 if using the full length protein). In some embodiments, the polypeptide comprises a I182D or I182E mutation. In some embodiments, the VSV-G protein comprises a I182S, I182H, I182T, I182Q, or I182N mutation.

[00193] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 11 comprises a mutation at position 182 and at least, or about, 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% identical as compared to SEQ ID NO: 11 (or SEQ ID NO: 10 if using the full length protein). In some embodiments, the polypeptide comprises a T182D or T182E mutation. In some embodiments, the VSV-G protein comprises a T182S, T182H, T182Q, or T182N mutation.

[00194] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 13 comprises a mutation at position 182 and at least, or about, 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% identical as compared to SEQ ID NO: 13 (or SEQ ID NO: 12 if using the full length protein). In some embodiments, the polypeptide comprises a A182D or A182E mutation. In some embodiments, the VSV-G protein comprises a A182S, A182H, A182T, A182Q, or A182N mutation.

[00195] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 15 comprises a mutation at position 182 and at least, or about, 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% identical as compared to SEQ ID NO: 15 (or SEQ ID NO: 14 if using the full length protein). In some embodiments, the polypeptide comprises a V182D or V182E mutation. In some embodiments, the VSV-G protein comprises a V182S, V182H, V182T, V182Q, or V182N mutation.

[00196] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 17 comprises a mutation at position 182 and at least, or about, 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% identical as compared to SEQ ID NO: 17 (or SEQ ID NO: 16 if using the full length protein). In some embodiments, the polypeptide comprises a V182D or V182E mutation. In some embodiments, the VSV-G protein comprises a V182S, V182H, V182T, V182Q, or V182N mutation.

[00197] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 19 comprises a mutation at position 182 and at least, or about, 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% identical as compared to SEQ ID NO: 19 (or SEQ ID NO: 18 if using the full length protein). In some embodiments, the polypeptide comprises a V182D or V182E mutation. In some embodiments, the VSV-G protein comprises a V182S, V182H, V182T, V182Q, or V182N mutation.

[00198] In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 21 comprises a mutation at position 182 and at least, or about, 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% identical as compared to SEQ ID NO: 21 (or SEQ ID NO: 20 if using the full length protein). In some embodiments,

the polypeptide comprises a I182D or I182E mutation. In some embodiments, the VSV-G protein comprises a I182S, I182H, I182T, I182Q, or I182N mutation.

Viral Glycoproteins

[00199] The mutant VSV-G proteins can be used, for example, to pseudotype a virus, such as, but not limited to a lentivirus. Accordingly, in some embodiments, a viral particle comprising a mutant VSV-G protein as provided herein are provided. In some embodiments, the viral particle comprises a VSV-G protein comprising a mutation at position 198 as compared to SEQ ID NO: 1. In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 2 comprises a mutation at position 182 and at least, or about, 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% identical as compared to SEQ ID NO: 2 (or SEQ ID NO: 1 if using the full length protein). In some embodiments, the polypeptide comprises a I182D or I182E mutation as compared to SEQ ID NO: 2. In some embodiments, the VSV-G protein comprises a I182S, I182H, I182T, I182Q, or I182N mutation.

[00200] In some embodiments, the viral particle comprises a VSV-G protein comprising a mutation at position 198 as compared to SEQ ID NO: 10. In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 11 comprises a mutation at position 182 and at least, or about, 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% identical as compared to SEQ ID NO: 11 (or SEQ ID NO: 10 if using the full length protein). In some embodiments, the polypeptide comprises a T182D or T182E mutation as compared to SEQ ID NO: 11. In some embodiments, the VSV-G protein comprises a T182S, T182H, T182Q, or T182N mutation.

[00201] In some embodiments, the viral particle comprises a VSV-G protein comprising a mutation at position 198 as compared to SEQ ID NO: 12. In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 13 comprises a mutation at position 182 and at least, or about, 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% identical as compared to SEQ ID NO: 13 (or SEQ ID NO: 12 if using the full length protein). In some embodiments, the polypeptide comprises a A182D or A182E mutation as compared to SEQ ID NO: 13. In some embodiments, the VSV-G protein comprises a A182S, A182H, A182T, A182Q, or A182N mutation.

[00202] In some embodiments, the viral particle comprises a VSV-G protein comprising a mutation at position 203 as compared to SEQ ID NO: 14. In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 15 comprises a mutation at position 182 and at least, or about, 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% identical as compared to SEQ ID NO: 15 (or SEQ ID NO: 14 if using the full length protein). In some embodiments, the polypeptide comprises a V182D or V182E mutation as compared to SEQ ID NO: 15. In some embodiments, the VSV-G protein comprises a V182S, V182H, V182T, V182Q, or V182N mutation.

[00203] In some embodiments, the viral particle comprises a VSV-G protein comprising a mutation at position 199 as compared to SEQ ID NO: 16. In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 17 comprises a mutation at position 182 and at least, or about, 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% identical as compared to SEQ ID NO: 17 (or SEQ ID NO: 16 if using the full length protein). In some embodiments, the polypeptide comprises a V182D or V182E mutation as compared to SEQ ID NO: 17. In some embodiments, the VSV-G protein comprises a V182S, V182H, V182T, V182Q, or V182N mutation.

[00204] In some embodiments, the viral particle comprises a VSV-G protein comprising a mutation at position 199 as compared to SEQ ID NO: 18. In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 19 comprises a mutation at position 182 and at least, or about, 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% identical as compared to SEQ ID NO: 19 (or SEQ ID NO: 18 if using the full length protein). In some embodiments, the polypeptide comprises a V182D or V182E mutation as compared to SEQ ID NO: 19. In some embodiments, the VSV-G protein comprises a V182S, V182H, V182T, V182Q, or V182N mutation.

[00205] In some embodiments, the viral particle comprises a VSV-G protein comprising a mutation at position 199 as compared to SEQ ID NO: 20. In some embodiments, a protein comprising a mutation at position 182 as compared to SEQ ID NO: 21 comprises a mutation at position 182 and at least, or about, 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% identical as compared to SEQ ID NO: 21 (or SEQ ID NO: 20 if using the full length protein). In some embodiments, the polypeptide comprises a I182D or

I182E mutation as compared to SEQ ID NO: 21. In some embodiments, the VSV-G protein comprises a I182S, I182H, I182T, I182Q, or I182N mutation.

[00206] In some embodiments, the VSV-G protein further comprises a mutation at position that corresponds to positions 214 and/or 352 of SEQ ID NO: 2. In some embodiments, the residue that corresponds to position 214 of SEQ ID NO: 2 is T214. In some embodiments, the residue that corresponds to position 352 of SEQ ID NO: 2 is T352. In some embodiments, the VSV-G protein comprises mutation that corresponds to T214N mutation as compared to SEQ ID NO: 2. In some embodiments, the VSV-G protein comprises mutation that corresponds to T352A mutation as compared to SEQ ID NO: 2. In some embodiments, the VSV-G protein comprises a T214N and T352A mutations as compared to SEQ ID NO: 2. These mutations can be combined with any other mutations as provided for herein. In some embodiments, the T214N and/or T352A mutations are combined with the I182E or I182D mutations. In some embodiments, a VSV-G protein comprises an amino acid sequence of SEQ ID NO: 22 and SEQ ID NO: 23, which combines the I182D or I182E, respectively, with the T214N and T352A mutations. The sequences are also illustrated below with the leader sequences, which are removed during protein processing.

VSV-G Protein_ I196D, T230N and T368A mutations (with leader sequence and adjusted numbering)

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MKCLLYLAFLFIGVNCKFTIVFPHNQKGNWKNVPSNYHYCPSSSDLN
WHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPK
YITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVI
VQVTPHHVLVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHSDYKV
KGLCDSNLDSMDITFFSEDGELSSLGKEGTGFRSNYFAYENG GKACK
MQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSV
DVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLA PKNPGTGPAFT
IINGTLKYFETRYIRVDIAAPILSRMVGMISGTTAERELWDDWAPYEDV
EIGPNGVLR TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAA
SQLPDDESLFFGDTGLSKNPIELVEGWFSWKSSIASFFFIIGLIIGLFLVL
RVGIHL CIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 24)

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VSV-G Protein_I182D, T214N and T352A mutations (without leader sequence)

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KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPK
SHKAIQADGWMCHASKWVTTCDFRWYGPKYITHSIRSFTPSVEQCKE
SIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGE

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WVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLDSDMITFFS
EDGELSSLGKEGTGFRSNYFAYENGGKACKMQYCKHWGVRLPSGVW
FEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQ
ETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDI
AAPILSRMVGMISGTTAERELWDDWAPYEDVEIGPNGVLRRTSSGYKFP
LYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLS
KNPIELVEGWFWSSWKSSIASFFFIIGLIIGLFLVLRVGIHLCIKLKHTKKR
QIYTDIEMNRLGK (SEQ ID NO: 22)

VSV-G Protein with I196E, T230N and T368A mutations (with leader sequence and adjusted numbering)

MKCLLYLAFLFIGVNCKFTIVFPHNQKGNWKNVPSNYHYCPSSSDLN
WHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPK
YITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVI
VQVTPHHVLVDEYTGEWVDSQFINGKCSNYICPTVHNSTTWHSDYKV
KGLCDSNLESMDITFFSEDGELSSLGKEGTGFRSNYFAYENGGKACKM
QYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVD
VSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTI
NGTLKYFETRYIRVDIAAPILSRMVGMISGTTAERELWDDWAPYEDVE
IGPNGVLRRTSSGYKFP
LYMIGHGMLDSDLHLSSKAQVFEHPHIQDAAS
QLPDDESLFFGDTGLSKNPIELVEGWFWSSWKSSIASFFFIIGLIIGLFLV
RVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 25)

VSV-G Protein with I182E, T214N and T352A mutations (without leader sequences)

KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPK
SHKAIQADGWMCHASKWVTTCDFRWYGPKYITHSIRSFTPSVEQCKE
SIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGE
WVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLESMDITFFS
EDGELSSLGKEGTGFRSNYFAYENGGKACKMQYCKHWGVRLPSGVW
FEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQ
ETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDI
AAPILSRMVGMISGTTAERELWDDWAPYEDVEIGPNGVLRRTSSGYKFP
LYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLS
KNPIELVEGWFWSSWKSSIASFFFIIGLIIGLFLVLRVGIHLCIKLKHTKKR
QIYTDIEMNRLGK (SEQ ID NO: 23)

[00207] The other strains of the VSV-G protein as described herein can also comprises the mutations that correspond to T214N and/or T352A in SEQ ID NO: 2 and as illustrated in SEQ ID NO: 22 and SEQ ID NO: 23.

[00208] In some embodiments, the composition comprises a mutation as described in Hwang et al., Gene Ther 2013 Aug;20(8):807-15. (Epub 2013 Jan 31), which is hereby incorporated by reference in its entirety. For example, the mutations can be. at positions 230, 368, 66, and/or 162 that corresponds to SEQ ID NO: 1. The positions will be 16 positions less as compared to SEQ ID NO: 2, when the leader sequence is removed. In some embodiments, the mutations at those positions are, for example, T230N, T368A, K66T, S162T, or any combination thereof. In some embodiments, the VSV-G protein comprises a T230N and a T368A mutation. In some embodiments, the VSV-G polypeptide comprises a K66T, S162T, T230N, and a T368A. These positions are those that correspond to the positions in the full length protein (SEQ ID NO: 1). In some embodiments, the VSV-G protein comprises T230N mutation, a T368A mutation, a K66T mutation, a S162T mutation, or any combination thereof. In some embodiments, the VSV-G protein further comprises one or more mutations in addition to the mutation that corresponds to position 182 of SEQ ID NO: 2, such as those described in U.S. Patent Application Publication No. 20200216502, which is hereby incorporated by reference in its entirety. For example, the VSV-G protein can further comprise a mutation at a position that corresponds to positions of 8, 47, 209 and/or 354 of SEQ ID NO: 2.

[00209] In some embodiments, the substitution at position 8 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except Y. In some embodiments, the substitution at position 209 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except H. In some embodiments, the substitution at position 47 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except K or R. In some embodiments, the substitution at position 354 is by any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except K or R. In some embodiments, the substitution is at position 47 or at position 354, or at both positions 47 and 354 are substituted by A, G, F or Q. In some embodiments, the substitution is A or Q. In some embodiments, the substitution at position 8 is an alanine, i.e., H8A. In some embodiments, the substitution at position 47 is Q or N, i.e., K47Q or K47N. In some embodiments, the protein comprises a mutation (substitution) at position 10. In some embodiments, the substitution/mutation is Q10A, Q10R, or Q10K.

[00210] Additionally, in some embodiments, instead of the VSV-G protein or mutant thereof, the viruses can be pseudotyped with other viral structural proteins.

[00211] For example, the viral particle can be pseudotyped with a Spring viremia of carp virus G (SVCV-G) protein and transduce a cell when the virus comprises a targeting moiety. The Spring viremia of carp virus G protein as provided can be used, in some embodiments, to transduce a target cell and deliver a heterologous molecule to the targeted cells. In some embodiments, a Spring viremia of carp virus G protein is provided that comprises SEQ ID NO: 52. SEQ ID NO: 52 is the full length protein and SEQ ID NO: 53 is the ectodomain of the Spring viremia of carp virus G protein that has the N-terminal signal peptide removed. Accordingly, in some embodiments, the protein comprises an amino acid sequence of SEQ ID NO: 53. The Spring viremia of carp virus G protein can be used, for example, to pseudotype a virus, such as, but not limited to a lentivirus. Accordingly, in some embodiments, a viral particle comprising a Spring viremia of carp virus G protein as provided herein are provided. In some embodiments, the viral particle comprises a Spring viremia of carp virus G protein comprising SEQ ID NO: 52 or SEQ ID NO: 53 or sequence that is at least 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%, or 99% identical to a sequence of SEQ ID NO: 52 or SEQ ID NO: 53.

[00212] The sequence of Spring Viremia of Carp Virus – G (SEQ ID NO: 52-with leader sequence)

MSIISYIAFLLLLIDSNLGIPIFVPSGRNISWQPVIQPFQDYQCPIHGNNPNTMGLSATKLTIK
SPSVFSTDKVSGWICHAAEWKTTCDYRWYGPQYITHSIHPISPTIDECRRIIQRIASGTDED
LGFPFQSCGWASVTTVSNNTYRVVPHSVHLEPYGGHWIDHEFNGGECREKVCCEMKGNSIWI
TEETVQHECAKHIEEVEGIMYGNVPRGDVYANNFIIDRHHRVYRFGGSCQMKFCNKDGIKF
ARGDWVEKTAGTTLTTIHDNVPKCVDGTLVSGHRPGLDLIDTVFNLENNVEYTLCEGTRKIN
KQEKLTSDLSYLAPRIGGFGSVFVRNGLTERGSTTYIRIEVEGPIVDLSLNGTDPRTNASR
VFWDWELDGNIYQGFNGVYKGDGKIHIPLNMIESGIIDDELQHAFAQADIIPHPHYDDDEI
REDDIFFDNTGENGNPVDVAVVEWVSGWGTSLKFFGMTLVALILIFLLIRCCVACTYLMKRSK
RPATESHEMRSLV

[00213] The sequence of Spring Viremia of Carp Virus – G (SEQ ID NO: 53-without leader sequence):

IPFVPSGRNISWQPVIQPFQDYQCPIHGNNPNTMGLSATKLTIKSPSVFSTDKVSGWICHAA
EWKTTCDYRWYGPQYITHSIHPISPTIDECRRIIQRIASGTDEDLGFPFQSCGWASVTTVSN
NTYRVVPHSVHLEPYGGHWIDHEFNGGECREKVCCEMKGNSIWI TEETVQHECAKHIEEVEG
IMYGNVPRGDVYANNFIIDRHHRVYRFGGSCQMKFCNKDGIKFARGDWVEKTAGTTLTTIHD
NVPKCVDGTLVSGHRPGLDLIDTVFNLENNVEYTLCEGTRKINKQEKLTSDLSYLAPRIG
GFGSVFVRNGLTERGSTTYIRIEVEGPIVDLSLNGTDPRTNASRVFWDWELDGNIYQGFNG
VYKGDGKIHIPLNMIESGIIDDELQHAFAQADIIPHPHYDDDEIREDDIFFDNTGENGNPVD

AVVEWVSGWGTSLKFFGMTLVALILIFLLIRCCVACTYLMKRSKRPATESHEMRSLV

Targeting Moieties

[00214] In some embodiments, the viral particle comprises a targeting moiety having the formula T-S₁, wherein T is a target binding domain and S₁ is a stalk portion. The targeting moiety can be used to target the viral particle comprising the mutant VSV-G protein or the SVCV-G protein to a cell that expresses the target to which the targeting moiety binds to. In some embodiments, the target binding domain is an antibody, a scFv antibody, an antigen binding domain, an ankyrin repeat (e.g., DARPIN), a VHH domain antibody, a nanobody, single domain antibody, a FN3 domain, or any combination thereof. The target binding domain can be attached to the viral surface through a variant Fc protein (e.g. L₁-Fc-L₂-X₁) as provided for herein or through a flexible polypeptide (e.g., L₃-X₁) as provided for herein. In some embodiments, the targeting moiety is attached (fused or linked) an envelope glycoprotein G or H of a virus of the Paramyxoviridae family, such as a morbillivirus, such as Measles virus, or a henipavirus, such as Nipah virus, Cedar virus, or Hendra virus. In some embodiments, the targeting moiety can be attached (fused or linked) to a glycoprotein of a virus of the Rhabdoviridae family, such as a vesicular stomatitis New Jersey virus, a vesicular stomatitis Indiana virus, a vesicular stomatitis Alagoas virus, a vesicular stomatitis Maraba virus, a vesicular stomatitis Carajas virus, Parainfluenza virus, Spodoptera frugiperda rhabdovirus isolate Sf G, Drosophila obscura sigmavirus 10A, Wuhan insect virus 7, Perch virus, or Spring viremia of carp virus. In some embodiments, the VSV protein is the mutated proteins, such as those provided for herein. In some embodiments, the targeting moiety is attached to a glycoprotein of a virus of the Filoviridae family, such as Ebola virus or a glycoprotein of a virus of the Arenaviridae family, such as Machupo virus.

[00215] In some embodiments, the target binding domain is a scFv. In some embodiments, the target binding domain is a single domain antibody. In some embodiments, the target binding domain is a VHH.

[00216] In some embodiments, the targeting moiety binds to CD7, CD8, cKit (CD117), CD4, CD3, CD5, CD6, CD2, TCR alpha, TCR beta, TCR gamma, TCR delta, CD10, CD34, CD110, CD33, CD14, CD68, CCR7, CD62L, CD25, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, or CXCR3, A glycosylated CD43 epitope expressed on acute leukemia or lymphoma but not on hematopoietic progenitors; A glycosylated CD43 epitope expressed on non-hematopoietic cancers; A kinase anchor protein 4 (AKAP-4); Adrenoceptor beta 3 (ADRB3); AFP; Anaplastic lymphoma kinase (ALK); Androgen receptor; Angiopoietin-binding cell surface

receptor 2 (Tie 2); Auto antibody to desmoglein 1 (Dsg1); Auto antibody to desmoglein 3 (Dsg3); B7H3 (CD276); Biotin; Bone marrow stromal cell antigen 2 (BST2); BST1/CD157; Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-Ia); Carbonic anhydrase IX (CA1X); Carcinoembryonic antigen (CEA); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites); CCR4; CD5; CD19; CD20; CD22; CD24; CD30; CD32 (FCGR2A); CD33; CD34; CD38; CD44v6; CD72; CD79a; CD79b; CD97; CD99; CD123; CD171; CD179a; CD179b-IGLII; CD200R; CD276/B7H3; CD300 molecule-like family member f (CD300LF); CDH1-CD324; CDH6; CDH17; CDH19; Chromosome X open reading frame 61 (CXORF61); Claudin 6 (CLDN6); Claudin18.2 (CLD18A2 or CLDN18A.2); CMV pp65; C-MYC epitope Tag; Cripto; CS1 (also referred to as CD2 subset 1 or CRACC or SLAMF7 or CD319 or 19A24); CSF2RA (GM-CSFR-alpha); C-type lectin domain family 12 member A (CLEC12A); C-type lectin-like molecule-1 (CLL-1 or CLECL1); Cyclin B1; Cytochrome P450 IB 1 (CYP1B 1); DLL3; EBV-EBNA3c; EGF-bke module- containing mucin-like hormone receptor-like 2 (EMR2); Elongation factor 2 mutated (ELF2M); Ephrin B2; Ephrin type-A receptor 2 (EphA2); Epidermal growth factor receptor (EGFR); Epidermal growth factor receptor variant III (EGFRviii); Epithelial cell adhesion molecule (EPCAM); ERG; ETS translocation-variant gene 6 located on chromosome 12p (ETV6-AML); Fc fragment of IgA receptor (FCAR or CD89); Fc receptor-like 5 (FCRL5); Fibroblast activation protein alpha (FAP); FITC; Fms Like Tyrosine Kinase 3 (FLT3); Folate receptor alpha (FRa or FR1); Folate receptor beta (FRb); Follicle stimulating hormone receptor (FSHR); Fos-related antigen 1; Fucosyl-GM1; G protein coupled receptor class C group 5 member D (GPRC5D); G protein-coupled receptor 20 (GPR20); GAD; Ganglioside G2 (GD2); Ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(1-4)bDGlc(1-1)Cer); Ganglioside GM3 (aNeu5Ac(2-3)bDCIalp(1- 4)bDGlc(1-1)Cer); GD3; GFRalpha4; Glycoprotein 100 (gp100); Glypican-3 (GPC3); Gonadotropin Hormone receptor (CGHR or GR); GpA33; GpNMB; GPRC5D; Guanylyl cyclase C (GCC); Heat shock protein 70-2 mutated (mut hsp70-2); Hepatitis A virus cellular receptor 1 (HAVCR1); Hexasaccharide portion of globoH glycosphingolipid (GloboH); High molecular weight-melanoma associated antigen (HMWMAA); HIV1 envelope glycoprotein; HLA; HLA-DOA; HLA-A; HLA-A2; HLA-B; HLA-C; HLA-DM; HLA-DOB; HLA-DP; HLA-DQ; HLA-DR; HLA-G; HTLV1-Tax; Human papilloma virus E6 (HPV E6); Human papilloma virus E7 (HPV E7); Human Telomerase reverse transcriptase (hTERT); IgE; IL13Ra2; IL1 IRa; Immunoglobulin lambda-like polypeptide 1 (IGLL1); Influenza A hemagglutinin (HA); Insulin-like growth factor 1 receptor (IGF-I receptor); Interleukin 11 receptor alpha (IL-11Ra); Interleukin- 13 receptor subunit alpha-2 (IL-

13Ra2 or CD213A2); Intestinal carboxyl esterase; KIT (CD117); KSHV K8.1; KSHV-gH; LAMP1 ; Legumain; Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Leutenizing hormone receptor (LHR); Lewis(Y) antigen; Lews Ag; Livl; Locus K 9 (LY6K); Low conductance chloride channel; Lymphocyte antigen 6 complex; Lymphocyte antigen 75 (LY75); Lymphocyte-specific protein tyrosine kinase (LCK); Mammary gland differentiation antigen (NY-BR-1); Melanoma antigen recognized by T cells 1 (MelanA or MARTI); Melanoma- associated antigen 1 (MAGE-A1); Melanoma cancer testis antigen-1 (MAD-CT-1); Melanoma cancer testis antigen-2 (MAD-CT-2); Melanoma inhibitor of apoptosis (ML-IAP); Mesothelin; MPL; Mucin 1 cell surface associated (MUC1); N-Acetyl glucosaminyl-transferase V (NA17); Nectin-4; Neural cell adhesion molecule (NCAM); NKG2D; NYBR1; O-acetyl-GD2 ganglioside (OAcGD2); Olfactory receptor 51E2 (OR51E2); Oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); P53 mutant; Paired box protein Pax-3 (PAX3); Paired box protein Pax-5 (PAX5); Pannexin 3 (PANX3); PDL1; P-glycoprotein; Placenta-specific 1 (PLAC1); Platelet-derived growth factor receptor beta (PDGFR-beta); Polysialic acid; Proacrosin binding protein sp32 (OY-TES1); Prostate; Prostate carcinoma tumor antigen-1 (PCT A-1 or Galectin 8); Prostate stem cell antigen (PSCA); Prostate-specific membrane antigen (PSMA); Prostatic acid phosphatase (PAP); Prostein; Protease Serine 21 (Testisin or PRSS21); Proteasome (Prosome Macropain) Subunit Beta Type 9 (LMP2); PTK7; Ras G12V; Ras Homolog Family Member C (RhoC); Rat sarcoma (Ras) mutant; Receptor for Advanced Gly cation Endproducts (RAGE-1); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Receptor tyrosine-protein kinase ERBB2 or Her-22/neu; Renal ubiquitous 1 (RU1); Renal ubiquitous 2 (RU2); Sarcoma translocation breakpoints; Serine 2 (TMPRSS2) ETS fusion gene; Sialyl Lewis adhesion molecule (sLe); SLAMF4; SLAMF6; Slea (CA19.9 or Sialyl Lewis Antigen); Sperm protein 17 (SPA17); Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Stage-specific embryonic antigen-4 (SSEA-4); STEAP1; Survivin; Synovial sarcoma X breakpoint 2 (SSX2); TCR Gamma Alternate Reading Frame Protein (TARP); TCR-beta1 chain; TCR-beta2 chain; TCR-delta chain; TCR-gamma chain; TCRgamma-delta; Telomerase; TGFbetaR2; The antigen recognized by TNT antibody; Thyroid stimulating hormone receptor (TSHR); Timl-/HVCR1; Tissue Factor 1 (TF1); Tn ag; Tn antigen ((Tn Ag) or (GalNAca-Ser/Thr)); TNF receptor family member B cell maturation (BCMA); Transglutaminase 5 (TGS5); Transmembrane protease; TROP2; Tumor endothelial marker 1 (TEM1/CD248); Tumor endothelial marker 7-related (TEM7R); Tumor protein p53

(p53); Tumor-associated glycoprotein 72 (TAG72); Tyrosinase; Tyrosinase-related protein 2 (TRP-2); Uroplakin 2 (UPK2); Vascular endothelial growth factor receptor 2 (VEGFR2); V-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Wilms tumor protein (WT1); or X Antigen Family Member 1A (XAGE1). In some embodiments, the targeting moiety binds to CD7. In some embodiments, the targeting moiety binds to CD8.

[00217] In some embodiments, the targeting moiety binds to a target that is present on a cell, such as an immune cell. In some embodiments, the cell is an immune cell, such as, but not limited to, T cell, B cell; NK cell, dendritic cell, neutrophils, macrophages, a cancer cell; or, for example, CD3+ T cell; CD4+ T cell; CD7+ T cell, CD8+ T cell; CD19+ B cell; CD19+ cancer cell; CD20+ B cell; CD20+ cancer cell; CD30+ lung epithelial cell; CD34+ haematopoietic stem cell; CD105+ endothelial cell; CD105+ haematopoietic stem cell; CD117+ haematopoietic stem cell; CD133+ cancer cell; EpCAM+ cancer cell; GluA2+ neuron; GluA4+ neuron; Haematopoietic stem cell; Hepatocyte; Her2/Neu+ cancer cell; NKG2D+ natural killer cell; SLC1A3+ astrocyte; SLC7A10+ adipocyte. In some embodiments, the cell is a T cell. In some embodiments, the cell is a B cell. In some embodiments, the cell is a CD7+ T cell and/or CD8+ T cell.

CD7 binding polypeptides

[00218] In some embodiments, the targeting moiety (e.g. polypeptide) binds to CD7.

[00219] In some embodiments, the polypeptide that binds to CD7 is an antibody which binds to non-human primate CD7. In some embodiments, the polypeptide that binds to CD7 is an antibody which binds to human CD7. The sequence of human CD7 (UniProtKB P09564) is as follows (SEQ ID NO: 29):

MAGPPRLLLLPLLLALARGLPALAAQEVQQSPHCTTVPVGASVNITCSTSGG
LRGIYLRQLGPQPQDIYYEDGVVPTTDRRFRGRIDFSGSQDNLITMHLRLQLS
DTGTYTCQAITEVNVYSGTLLVLVTEEQSQGWHRCSDAPPRASALPAPTGS
ALPDPQTASALPDPPAASALPAALAVISFLLGLGLGVACVLARTQIKKLCSWR
DKNSAACVVYEDMSHSRCNTLSSPNQYQ (SEQ ID NO: 29).

[00220] In some embodiments, the CD7 that the polypeptide binds to is expressed on the surface of a cell. In some embodiments, the cell is an immune cell. In some embodiments, the immune cell is a CD7+ T cell, CD4+ T cell, CD8+ T cell, NK cell, alpha-beta T cell, gamma-delta T cell, lymphoid progenitor cell, hematopoietic stem cell, myeloid cell, monocyte, macrophage, central memory T cell, effector memory T cell, stem-cell like memory T cells,

naïve T cell, activated T cell, regulatory T cell (TReg), terminally differentiated effector memory T cell (TEMRA), resident memory T cell (TRM) or a T-cellCD8+CCR7+.

[00221] In some embodiments, the antibody comprises a Fc region. The Fc region can be linked to the heavy or light chain of the antibody. In some embodiments, the Fc region is an IgG Fc. In some embodiments, the IgG is selected from IgG1, IgG2, IgG3, or IgG4. In some embodiments, the IgG fc is IgG1 Fc. In some embodiments, the antibody comprises an Fc constant region as set forth herein, such as SEQ ID NO: 26, 27, or 28 or a mutant thereof as provided for herein.

[00222] In some embodiments, polypeptides (e.g. CD7-binding polypeptide) are provided herein. In some embodiments, antibodies (e.g. an anti-CD7 antibody) are provided herein. In some embodiments, the antibody is a recombinant antibody that binds to CD7. In some embodiments, the CD7 protein is a human CD7 protein. In some embodiments, the CD7 protein is a non-human CD7 protein (e.g., mouse, rat, pig, dog, non-human primate). As used herein, the term “recombinant antibody” refers to an antibody that is not naturally occurring. In some embodiments, the term “recombinant antibody” refers to an antibody that is not isolated from a human subject.

[00223] In some embodiments, an antibody, or antigen binding fragment thereof is provided, wherein the antibody or antibody fragment comprises a peptide selected from the following table, which illustrate the CDRs based on Kabat numbering.

Kabat CDRs						
Ab ID No	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	LCDR3
CD7AB1	GYPFTSY (SEQ ID NO: 30)	DPNSGD (SEQ ID NO: 31)	SPYYSNDNSMDY (SEQ ID NO: 32)	RASQSIGT SIH (SEQ ID NO: 33)	YASESIS (SEQ ID NO: 34)	QQSNSWPTT (SEQ ID NO: 35)

[00224] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy or light chain CDR as provided in the tables above. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy or light chain CDR as provided in the tables above and binds to non-human primate CD7. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy or light chain CDR as provided in the tables above and binds to human CD7. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence selected from SEQ ID NO: 33-35. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SEQ ID NO: 33. In some embodiments, a polypeptide,

an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SEQ ID NO: 34. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SEQ ID NO: 35. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence selected from SEQ ID NO: 30-32. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 30. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 31. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 32. The CDRs referenced in the embodiments throughout the present specification can be interchanged with the CDRs that are characterized by different formats, such as Chothia and IMGT.

[00225] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain variable region having a LCDR1, a LCDR2, and a LCDR3, wherein the LCDR1 has a sequence of SEQ ID NO: 33, the LCDR2 has a sequence of SEQ ID NO: 34, and the LCDR3 has a sequence of SEQ ID NO: 35.

[00226] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain variable region having a HCDR1, a HCDR2, and a HCDR3, wherein the HCDR1 has a sequence of SEQ ID NO: 30, the HCDR2 has a sequence of SEQ ID NO: 31, and the HCDR3 has a sequence of SEQ ID NO: 32.

[00227] In some embodiments, a polypeptide, an antibody or antibody binding fragment thereof, comprises: (i) a light chain having any one of the foregoing recited combinations of LCDR1, LCDR2, and LCDR3 sequences; and (ii) a heavy chain having any one of the foregoing recited combinations of HCDR1, HCDR2, and HCDR3 sequences.

[00228] The different CDR motifs can be combined in any combination including those not depicted in the table above. For example, the following embodiments are provided as non-limiting examples of such combinations.

[00229] In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises: (i) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 33; the light chain CDR2 has the amino acid sequence of SEQ ID NO: 34; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 35; and (ii) a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the

heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 30; the heavy chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 31; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 32; or variants of any of the foregoing. **[00230]** Although the preceding paragraphs may make reference to CDRs under the Kabat system the equivalent CDR sequences can be used from the IMGT and CHOTHIA designations.

[00231] In some embodiments, the light chain variable region CDR1 is replaced with any of the other light chain CDR1 sequences. In some embodiments, the light chain variable region CDR2 is replaced with any of the other light chain CDR2 sequences. In some embodiments, the light chain variable region CDR3 is replaced with any of the other light chain CDR3 sequences. In some embodiments, the heavy chain variable region CDR1 is replaced with any of the other heavy chain CDR1 sequences. In some embodiments, the heavy chain variable region CDR2 is replaced with any of the other heavy chain CDR2 sequences. In some embodiments, the heavy chain variable region CDR3 is replaced with any of the other heavy chain CDR3 sequences.

[00232] In some embodiments, the polypeptide comprises a heavy chain variable region peptide having one of the following sequences, or a variant thereof:

SEQ ID NO:	AB ID NO.	Sequence
36	CD7AB1	QVQLQQPGAELVKPGASVKLSCKASGYPTSYWIHWVKQRPGRGLEWLGRIDPNSGDTKYNEKFKNKATLTVDKSSTTAYMQLSSLTSEDSAVYYCARSPYYSDNSMDYWGQGTSTVTVSS

[00233] In some embodiments, the polypeptide comprises a light chain variable region peptide having one of the following sequences, or a variant thereof:

SEQ ID NO:	AB ID NO.	Sequence
37	CD7AB1	DILLTQSPAILSVSPGERVSFSCRASQSIGTSIHWYQQRTNDSPRLLIKYASESISGIPSRFSGSGSGTDFTLSINSVESEDIADYYCQQSNSWPTTFGGGTKLEIKR

[00234] In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_H peptide of SEQ ID NO: 36. In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_L peptide of SEQ ID NO: 37. In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_H peptide and a V_L peptide, wherein the wherein the V_H peptide comprises a sequence of SEQ ID NO: 36, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 37, or a variant thereof. In some embodiments, a polypeptide, an antibody, or antigen binding

fragment thereof, comprises a V_H peptide and a V_L peptide, wherein the wherein the V_H peptide comprises a sequence of SEQ ID NO: 36, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 37, or a variant thereof, and the polypeptide, the antibody, or antigen binding fragment thereof, binds to non-human primate CD7. In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_H peptide and a V_L peptide, wherein the wherein the V_H peptide comprises a sequence of SEQ ID NO: 36, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 37, or a variant thereof, and the polypeptide, the antibody, or antigen binding fragment thereof, binds to human CD7. In some embodiments, the V_H peptide comprises a sequence of SEQ ID NO: 36; and the V_L peptide comprises a sequence of SEQ ID NO: 37.

[00235] The V_H and the V_L sequences can be in any format, including, but not limited to an scFv format where the V_H and V_L regions are linked with a peptide linker. Examples of peptide linkers that can be used to link various peptides provided for herein include, but are not limited to: (GGGGS)_n (SEQ ID NO: 55), wherein each n is independently 1-5. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, n is 5. In some embodiments, the variable regions are not linked with a peptide linker. In some embodiments, the polypeptide comprises SEQ ID NO: 36 and SEQ ID NO: 37.

[00236] As provided for herein, the polypeptide, antibodies, or antigen binding fragments thereof can be variants of the sequences.

[00237] The sequences of the polypeptides or antibodies can be modified to yield human IgG antibodies. The conversion of the sequences provided herein can be modified to yield other types of antibodies. The CDRs can also be linked to other antibodies, proteins, or molecules to create antibody fragments that bind CD7.

[00238] In some embodiments, a polypeptide or an antibody as provided herein is a targeting moiety on the surface of an engineered viral particle. In some embodiments, the targeting moiety allows for binding to a target cell. In some embodiments, the targeting moiety is a CD7 binding moiety, such as a polypeptide or an antibody as provided herein. In some embodiments, the target binding domain ("T") comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38:

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DILLTQSPAILSVSPGERVSFSCRASQSIGTSIHWYQQRTNDSPRLLIKYAS
ESISGIPSRFSGSGSGTDFTLINSVESEDIADYYCQQSNSWPTTFGGGTKL
EIKRGGGGSGGGSGGGSGGGGSQVQLQQPGAELVKPGASVKLSCKASGYP
FTSYWIHWVKQRPGRGLEWLGRIDPNSGDTKYNEKFKNKATLTVDKSSTTAY
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MQLSSLTSEDSAVYYCARSPYYSDNSMDYWGQGTSTVTVSS (SEQ ID NO: 38)

or is substantially similar to SEQ ID NO: 38, or is an active fragment of SEQ ID NO: 38. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 38. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 38. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 38. In some embodiments, the target binding domain (“T”) comprises a sequence as set forth in SEQ ID NO: 38. In some embodiments, the target binding domain (“T”) as set forth in SEQ ID NO: 38 is an antibody, or an antigen binding fragment thereof. In some embodiments, the target binding domain (“T”) is an anti-CD7 antibody.

[00239] In some embodiments, a polypeptide or an antibody as provided for herein is a targeting moiety on the surface of an engineered viral particle. In some embodiments, the engineered viral particle is a pseudotyped viral-like particle. In some embodiments, the targeting moiety allows for binding to a target cell. In some embodiments, the targeting moiety is a CD7 binding moiety, such as a polypeptide or an antibody as provided herein. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 39.

QVQLQQPGAELVKPGASVKLSCKASGYPTSYWIHWVKQRPGRGLEWLGRID
PNSGDTKYNEKFKNKATLTVDKSSTTAYMQLSSLTSEDSAVYYCARSPYYSDN
SDNSMDYWGQGTSTVTVSSGGGGSGGGSGGGSGGGSGGGSDILLTQSPAILSVSP
GERVFSFSCRASQSIGTSIHVYQQRNDSPRLLIKYASESISGIPSRFSGSGS
GTDFTLSINSVESEDIADYYCQQSNSWPTTFGGGTKLEIKR (SEQ ID NO: 39)

or is substantially similar to SEQ ID NO: 39, or is an active fragment of SEQ ID NO: 39. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 39. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 39. In some embodiments, the target binding domain (“T”) comprises a sequence as set forth in SEQ ID NO: 39. In some embodiments, the target binding domain (“T”) as set forth in SEQ ID NO: 39 is an antibody, or an antigen binding fragment thereof. In some embodiments, the target binding domain (“T”) is an anti-CD7 antibody. In some embodiments, the anti-CD7 antibody

binds to non-human primate CD7. In some embodiments, the anti-CD7 antibody binds to human CD7.

CD8 binding polypeptides

[00240] In some embodiments, the targeting moiety (*e.g.* a polypeptide) can bind to CD8.

[00241] In some embodiments, the polypeptide binds to CD8. In some embodiments, the polypeptide binds to CD8-alpha. In some embodiments, the polypeptide binds to CD8-beta. In some embodiments, the polypeptide binds to CD8 heterodimer. In some embodiments, the CD8 heterodimer comprises CD8-alpha and CD8-beta subunits. In some embodiments, the polypeptide binds to CD8-alpha homodimer. In some embodiments, the polypeptide that binds to CD8 is an antibody which binds to non-human primate CD8. In some embodiments, the antibody that binds to non-human primate CD8 is an antibody which binds to non-human primate CD8-alpha. In some embodiments, the antibody that binds to non-human primate CD8 is an antibody which binds to non-human primate CD8-beta. In some embodiments, the antibody that binds to non-human primate CD8 is an antibody which binds to non-human primate CD8-alpha homodimer. In some embodiments, the antibody that binds to non-human primate CD8 is an antibody which binds to non-human primate CD8 heterodimer. In some embodiments, the polypeptide that binds to CD8 is an antibody which binds to human CD8. In some embodiments, the antibody that binds to human CD8 is an antibody which binds to human CD8-alpha. In some embodiments, the antibody that binds to human CD8 is an antibody which binds to human CD8-beta. In some embodiments, the antibody that binds to human CD8 is an antibody which binds to human CD8-alpha homodimer. In some embodiments, the antibody that binds to human CD8 is an antibody which binds to human CD8 heterodimer. The sequence of human CD8-alpha (UniProtKB Q8TAW8) is as follows (SEQ ID NO: 40):

MALPVTALLPLALLHAARPSQFRVSPLDRTWNLGETVELKQCQVLLSNPTS
GCSWLFQPRGAAASPTFLLYLSQNKPKAAEGLDTRFSGKRLGDTFVLTLSL
FRRENEGCYFCSALNSIMYFSHFVPVFLPAKPTTTPAPRPPTPAPTASQPLSL
RPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCNHRNR
RRVCKCPRPVVKS GDKPSLSARYV (SEQ ID NO: 40).

[00242] The sequence of human CD8-beta (UniProtKB Q8TD28) is as follows (SEQ ID NO: 41):

MRPRLWLLAAQLTVLHGNSVLQQTPAYIKVQTNKMVMLSCEAKISLSNMR
IYWLRQRQAPSSDSHHEFLALWDSAKGTIHGEEVEQEKIIVFRDASRFILNLT

SVKPEDSGIYFCMIVGSPELTFGKGTQLSVVDFLPTTAQPTKKSTLKKRVCRLP
RPETQKGPLCSPITLGLLVAGVLVLLVSLGVAIHLCCRRRRARLRFMKQLYK
(SEQ ID NO: 41).

[00243] In some embodiments, the CD8 that the polypeptide binds to is expressed on the surface of a cell. In some embodiments, the cell is an immune cell. In some embodiments, the immune cell is a CD7+ T cell, CD4+ T cell, CD8+ T cell, NK cell, alpha-beta T cell, gamma-delta T cell, lymphoid progenitor cell, hematopoietic stem cell, myeloid cell, monocyte, macrophage, central memory T cell, effector memory T cell, stem-cell like memory T cells, naïve T cell, activated T cell, regulatory T cell (TReg), terminally differentiated effector memory T cell (TEMRA), resident memory T cell (TRM) or a T-cell CD8+CCR7+. In some embodiments, the cell is a CD8+ T cell. In some embodiments, the cell is a CD8+ cell.

[00244] In some embodiments, the antibody comprises a Fc region. The Fc region can be linked to the heavy or light chain of the antibody. In some embodiments, the Fc region is an IgG Fc. In some embodiments, the IgG is selected from IgG1, IgG2, IgG3, or IgG4. In some embodiments, the IgG Fc is IgG1 Fc. In some embodiments, the antibody comprises an Fc constant region as set forth herein, such as SEQ ID NO: 26, 27, or 28 or a variant thereof.

[00245] In some embodiments, polypeptides (e.g. CD8-binding polypeptide) are provided herein. In some embodiments, antibodies (e.g. an anti-CD8 antibody) are provided herein. In some embodiments, the antibody is a recombinant antibody that binds to CD8. In some embodiments, the CD8 protein is a human CD8 protein. In some embodiments, the CD8 protein is a non-human CD8 protein (e.g., mouse, rat, pig, dog, non-human primate). As used herein, the term “recombinant antibody” refers to an antibody that is not naturally occurring. In some embodiments, the term “recombinant antibody” refers to an antibody that is not isolated from a human subject.

[00246] In some embodiments, an antibody, or antigen binding fragment thereof is provided, wherein the antibody or antibody fragment comprises a peptide selected from the following table, which illustrate the CDRs based on Kabat numbering.

Kabat CDRs						
Ab ID No	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	LCDR3
CD8AB1	RYTFTD Y (SEQ ID NO: 42)	YPYNGG (SEQ ID NO: 43)	DHRYNEGVSF DY (SEQ ID NO: 44)	RASESVDG FGNSFMN	LASNLES (SEQ ID NO: 46)	QQNNDPYT (SEQ ID NO: 47)

				(SEQ ID NO: 45)		
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[00247] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy or light chain CDR as provided in the tables above. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy or light chain CDR as provided in the tables above and binds to non-human primate CD8. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy or light chain CDR as provided in the tables above and binds to human CD8. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence selected from SEQ ID NO: 45-47. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SEQ ID NO: 45. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SEQ ID NO: 46. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SEQ ID NO: 47. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence selected from SEQ ID NO: 42-44. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 42. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 43. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 44. The CDRs referenced in the embodiments throughout the present specification can be interchanged with the CDRs that are characterized by different formats, such as Chothia and IMGT.

[00248] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain variable region having a LCDR1, a LCDR2, and a LCDR3, wherein the LCDR1 has a sequence of SEQ ID NO: 45, the LCDR2 has a sequence of SEQ ID NO: 46, and the LCDR3 has a sequence of SEQ ID NO: 47.

[00249] In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain variable region having a HCDR1, a HCDR2, and a HCDR3,

wherein the HCDR1 has a sequence of SEQ ID NO: 42, the HCDR2 has a sequence of SEQ ID NO: 43, and the HCDR3 has a sequence of SEQ ID NO: 44.

[00250] In some embodiments, a polypeptide, an antibody or antibody binding fragment thereof, comprises: (i) a light chain having any one of the foregoing recited combinations of LCDR1, LCDR2, and LCDR3 sequences; and (ii) a heavy chain having any one of the foregoing recited combinations of HCDR1, HCDR2, and HCDR3 sequences.

[00251] The different CDR motifs can be combined in any combination including those not depicted in the table above. For example, the following embodiments are provided as non-limiting examples of such combinations.

[00252] In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises: (i) a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 45; the light chain CDR2 has the amino acid sequence of SEQ ID NO: 46; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 47; and (ii) a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 42; the heavy chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 43; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 44; or variants of any of the foregoing.

[00253] Although the preceding paragraphs may make reference to CDRs under the Kabat system the equivalent CDR sequences can be used from the IMGT and CHOTHIA designations.

[00254] In some embodiments, the light chain variable region CDR1 is replaced with any of the other light chain CDR1 sequences. In some embodiments, the light chain variable region CDR2 is replaced with any of the other light chain CDR2 sequences. In some embodiments, the light chain variable region CDR3 is replaced with any of the other light chain CDR3 sequences. In some embodiments, the heavy chain variable region CDR1 is replaced with any of the other heavy chain CDR1 sequences. In some embodiments, the heavy chain variable region CDR2 is replaced with any of the other heavy chain CDR2 sequences. In some embodiments, the heavy chain variable region CDR3 is replaced with any of the other heavy chain CDR3 sequences.

[00255] In some embodiments, the polypeptide comprises a heavy chain variable region peptide having one of the following sequences, or a variant thereof:

SEQ ID NO:	AB ID NO.	Sequence
48	CD8AB1	EVQLQQSGPELVKPGASVKISCKASRYTFIDYNLHWVKSHEKSL EWIGFIYPYNGGTGYNQKFKNAKLTVDYSSSTAYMELRSLTSVD AAVYYCARDHRYNEGVSFDYWGQGTTLTVSS

[00256] In some embodiments, the polypeptide comprises a light chain variable region peptide having one of the following sequences, or a variant thereof:

SEQ ID NO:	AB ID NO.	Sequence
49	CD8AB1	NIVLTQSPASLAVSLGQRATISCRASESVDGFGNSFMNWWYQQKPG QSPKLLIYLASNLESGVPAFSGSGSRTDFTLTIDPVEADDAATY YCQQNNEDPYTFGGGTKLEIKR

[00257] In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_H peptide of SEQ ID NO: 48. In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_L peptide of SEQ ID NO: 49. In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_H peptide and a V_L peptide, wherein the wherein the V_H peptide comprises a sequence of SEQ ID NO: 48, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 49, or a variant thereof. In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_H peptide and a V_L peptide, wherein the wherein the V_H peptide comprises a sequence of SEQ ID NO: 48, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 49, or a variant thereof, and the polypeptide, the antibody, or antigen binding fragment thereof, binds to non-human primate CD8. In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_H peptide and a V_L peptide, wherein the wherein the V_H peptide comprises a sequence of SEQ ID NO: 48, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 49, or a variant thereof, and the polypeptide, the antibody, or antigen binding fragment thereof, binds to human CD8. In some embodiments, the V_H peptide comprises a sequence of SEQ ID NO: 48; and the V_L peptide comprises a sequence of SEQ ID NO: 49.

[00258] The V_H and the V_L sequences can be in any format, including, but not limited to an scFv format where the V_H and V_L regions are linked with a peptide linker. Examples of peptide linkers that can be used to link various peptides provided for herein include, but are not limited to: (GGGGS)_n (SEQ ID NO: 55), wherein each n is independently 1-5. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, n is 5. In some embodiments, the variable regions are not linked

with a peptide linker. In some embodiments, the polypeptide comprises SEQ ID NO: 48 and SEQ ID NO: 49.

[00259] As provided for herein, the polypeptide, antibodies, or antigen binding fragments thereof can be variants of the sequences.

[00260] The sequences of the polypeptides or antibodies can be modified to yield human IgG antibodies. The conversion of the sequences provided herein can be modified to yield other types of antibodies. The CDRs can also be linked to other antibodies, proteins, or molecules to create antibody fragments that bind CD8.

[00261] In some embodiments, a polypeptide or an antibody as provided herein is a targeting moiety on the surface of an engineered viral particle. In some embodiments, the targeting moiety allows for binding to a target cell. In some embodiments, the target binding domain (“T”) is a CD8 binding moiety, such as a polypeptide or an antibody as provided herein. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50:

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NIVLTQSPASLAVSLGQRATISCRASESVDGFGNSFMNWFYQQKPGQSPKLLI
YLASNLESGVPARFSGSGSRDFTLTIDPVEADDAATYYCQQNNEDPYTFGG
GTKLEIKRGGGSGGGSGGGSGGGSGGGSEVQLQQSGPELVKPGASVKISCKA
SRYTFTDYNLHWVKLSHEKSLEWIGFIYPYNGGTGYNQKFKNAKALTVDYSS
STAYMELRSLTSVDAAVYYCARDHRYNEGVSFQYWGQGTTLTVSS (SEQ ID
NO: 50)
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or is substantially similar to SEQ ID NO: 50, or is an active fragment of SEQ ID NO: 50. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 50. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 50. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 50. In some embodiments, the target binding domain (“T”) comprises a sequence as set forth in SEQ ID NO: 50. In some embodiments, the target binding domain (“T”) as set forth in SEQ ID NO: 50 is an antibody, or an antigen binding fragment thereof. In some embodiments, the targeting moiety is an anti-CD8 antibody.

[00262] In some embodiments, a polypeptide or an antibody as provided for herein is a targeting moiety on the surface of an engineered viral particle. In some embodiments, the engineered viral particle is a pseudotyped viral-like particle. In some embodiments, the targeting moiety allows for binding to a target cell. In some embodiments, the target binding domain (“T”) is a CD8 binding moiety, such as a polypeptide or an antibody as provided herein.

In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51:

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EVQLQQSGPELVKPGASVKISCKASRYTFTDYNLHWKLSHEKSLEWIGFIY
PYNGGTGYNQKFKNKAKLTVDYSSSTAYMELRSLTSVDAAVYYCARDHRYNE
GVSFYWGQGTTTLTVSSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGG
GQRATISCRASESVDGFGNSFMNWWYQQKPGQSPKLLIYLASNLESGVPARFS
GSGSRTDFTLTIDPVEADDAATYYCQQNNEDPYTFGGGTKLEIKR (SEQ ID
NO: 51)
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or is substantially similar to SEQ ID NO: 51, or is an active fragment of SEQ ID NO: 51. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 51. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 51. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 51. In some embodiments, the target binding domain (“T”) comprises a sequence as set forth in SEQ ID NO: 51. In some embodiments, the target binding domain (“T”) as set forth in SEQ ID NO: 51 is an antibody, or an antigen binding fragment thereof. In some embodiments, the targeting moiety is an anti-CD8 antibody. In some embodiments, the anti-CD8 antibody binds to non-human primate CD8. In some embodiments, the anti-CD8 antibody binds to human CD8.

Targeting moieties comprising an Fc domain

[00263] In some embodiments, the V_H and V_L polypeptides are linked to a stalk portion S₁ comprising an Fc region. In some embodiments, the Fc region is as provided for herein. In some embodiments, the Fc region is a variant Fc region as provided for herein. Non-limiting mutations in the Fc region are provided for herein. In some embodiments, the variant Fc region comprises a sequence that is a variant of SEQ ID NO: 26, SEQ ID NO: 27, or SEQ ID NO: 28 as provided for herein. In some embodiments, the variant of SEQ ID NO: 26 comprises one or more mutations selected from the group consisting of L234A, L235A, N297A, P329G, I253A, H310A, and H435A as provided for herein. In some embodiments, the variant of SEQ ID NO: 27 comprises one or more mutations selected from the group consisting of N297A, P329G, I253A, H310A, and H435A as provided for herein. In some embodiments, the variant of SEQ ID NO: 28 comprises one or more mutations selected from the group consisting of S228P, L235E, N297A, P329G, I253A, H310A, and H435A as provided for herein. As provided for herein, the heavy chain can be linked to a Fc region. In

some embodiments, the Fc region further comprises (*e.g.* linked to) a transmembrane domain. In some embodiments, the Fc region further comprising a transmembrane domain has a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker as provided for herein or is absent, Fc is a variant Fc region as provided for herein, L₂ is a linker as provided for herein or is absent, and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprises a polypeptide having the formula ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or is absent, T_M is a transmembrane domain as provided for herein, and ICD is an intracellular domain as provided for herein or is absent. Examples of ECD include, but are not limited to, a CD8 and/or CD28 extracellular domain as provided for herein. Examples of T_M include, but are not limited to, a CD8 and/or CD28 transmembrane domain as provided for herein. In some embodiments, X₁ comprises a T_M and the ECD and ICD are absent. In some embodiments, X₁ comprises an ECD, a T_M, and the ICD is absent. In some embodiments, X₁ comprises a T_M and an ICD and the ECD is absent. In some embodiments, X₁ comprises an ECD, a T_M, and an ICD. In any of the following embodiments, it is to be understood that the ECD, the ICD, or both may be optionally absent. Accordingly, an embodiment wherein X₁ comprises a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD comprising an Env incorporation motif is understood to encompass the following X₁ members: i) a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD comprising an Env incorporation motif; ii) a CD8 and/or CD28 T_M, and an ICD comprising an Env incorporation motif wherein the ECD is absent; iii) a CD8 and/or CD28 ECD, and a CD8 and/or CD28 T_M, wherein the ICD is absent; and iv) a CD8 and/or CD28 T_M wherein both the ECD and the ICD are absent. Similarly, an embodiment wherein X₁ comprises a CD8 and/or CD28 T_M and an ICD comprising an Env incorporation motif is understood to encompass the following X₁ members: i) a CD8 and/or CD28 T_M and an ICD comprising an Env incorporation motif; and ii) a CD8 and/or CD28 T_M wherein the ICD is absent. Similarly, an embodiment wherein X₁ comprises a CD8 and/or CD28 ECD and a CD8 and/or CD28 T_M is understood to encompass the following X₁ members: i) a CD8 and/or CD28 ECD and a CD8 and/or CD28 T_M; and ii) a CD8 and/or CD28 T_M wherein the ECD is absent. It is to be further understood that the preceding explanation is also true in embodiments where a specific ECD, T_M, or ICD are not recited. For example, an embodiment wherein X₁ comprises an ECD, a CD8 and/or CD28 T_M, and an ICD would be understood to encompass the following X₁ members: i) an ECD, a CD8 and/or CD28 T_M, and an ICD; ii) an ECD, and a CD8 and/or CD28 T_M wherein the ICD is absent; iii) a CD8 and/or CD28 T_M, and an ICD wherein the ECD is absent; and iv) a CD8

and/or CD28 T_M wherein the ECD and the ICD are absent. Similarly, an embodiment wherein X₁ comprises a CD8 and/or CD28 T_M and an ICD is understood to encompass the following X₁ members: i) a CD8 and/or CD28 T_M and an ICD; and ii) a CD8 and/or CD28 T_M wherein the ICD is absent. Similarly, an embodiment wherein X₁ comprises an ECD and a CD8 and/or CD28 T_M is understood to encompass the following X₁ members: i) an ECD and a CD8 and/or CD28 T_M; and ii) a CD8 and/or CD28 T_M wherein the ECD is absent. Unless explicitly stated, the preceding examples and explanations are applicable to any embodiments that follow.

[00264] In some embodiments, X₁ comprises a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, X₁ comprises an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, X₁ comprises a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, X₁ comprises an ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, X₁ comprises a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, X₁ comprises an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, X₁ comprises a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein.

[00265] In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising an Fc region as provided for herein. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising an Fc region comprising a transmembrane domain as provided for herein. In some embodiments, the Fc region further comprising a transmembrane domain has a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker as provided for herein or is absent, Fc is a variant Fc region as provided for herein, L₂ is a linker as provided for herein or absent, and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprises a polypeptide having the formula ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or absent, T_M is a transmembrane domain as provided for herein, and ICD is an intracellular domain as provided for herein or absent. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the V_H and V_L polypeptides provided herein are linked

to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD are anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₁, Fc, L₂, ECD, T_M, and ICD are as provided for herein. In some embodiments, the V_H and V_L polypeptides bind to an immune cell, such as those provided herein.

[00266] In some embodiments, a V_H peptide having a sequence as set forth in SEQ ID NO: 36 and a V_L peptide having a sequence as set forth in SEQ ID NO: 37 are linked to an stalk portion (S₁) comprising Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 36 and V_L peptide having a sequence as set forth in SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 36 and V_L peptide having a sequence as set forth in SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 36 and V_L peptide having a sequence as set forth in SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 36 and V_L peptide having a sequence as set forth in SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M,

and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 36 and V_L peptide having a sequence as set forth in SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 36 and V_L peptide having a sequence as set forth in SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 36 and V_L peptide having a sequence as set forth in SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 36 and V_L peptide having a sequence as set forth in SEQ ID NO: 37 linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD are anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₁, Fc, L₂, ECD, T_M, and ICD are as provided for herein. In some embodiments, the V_H and V_L polypeptides bind to an immune cell, such as those provided herein.

[00267] In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising an Fc region as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising an Fc region comprising a transmembrane domain as provided for herein. In some embodiments, the Fc region further comprising a transmembrane domain has a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker as provided for herein or is Fc is a variant Fc region as provided for herein, L₂ is a linker as provided for herein or absent, and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprises a polypeptide having

the formula ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or absent, T_M is a transmembrane domain as provided for herein, and ICD is an intracellular domain as provided for herein or absent. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising

a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD are anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₁, Fc, L₂, ECD, T_M, and ICD are as provided for herein. In some embodiments, the V_H and V_L polypeptides bind to an immune cell, such as those provided herein.

[00268] In some embodiments, a polypeptide is provided comprising a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37.

[00269] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%,

91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37; provided that the V_H peptide and a V_L peptide comprises a light chain CDR having a sequence of SEQ ID NO: 33-35; and/or a heavy chain CDR having a sequence of SEQ ID NO: 30-32. In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37; provided that the V_H peptide and a V_L peptide comprise a light chain CDR1 having a sequence of SEQ ID NO: 33; a light chain CDR2 having a sequence of SEQ ID NO: 34; a light chain CDR3 having a sequence of SEQ ID NO: 35; and/or a heavy chain CDR1 having a sequence of SEQ ID NO: 30; a heavy chain CDR2 having a sequence of SEQ ID NO: 31; and a heavy chain CDR3 having a sequence of SEQ ID NO: 32. In some embodiments, the CDRs in the V_H or V_L chain are as set forth in the combinations provided for herein.

[00270] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 33; a LCDR2 having a sequence of SEQ ID NO: 34; and a LCDR3 having a sequence of SEQ ID NO: 35; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 30; a HCDR2 having a sequence of SEQ ID NO: 31; and a HCDR3 having a sequence of SEQ ID NO: 32.

[00271] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 33, wherein the LCDR1 comprises at most 1 conservative amino acid substitution, a LCDR2 having a sequence of SEQ ID NO: 34, wherein the LCDR2 comprises at most 1 conservative

amino acid substitution, and a LCDR3 having a sequence of SEQ ID NO: 35, wherein the LCDR3 comprises at most 1 conservative amino acid substitution; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 30, wherein the HCDR1 comprises at most 1 conservative amino acid substitution, a HCDR2 having a sequence of SEQ ID NO: 31, wherein the HCDR2 comprises at most 1 conservative amino acid substitution, and a HCDR3 having a sequence of SEQ ID NO: 32, wherein the HCDR3 comprises at most 1 conservative amino acid substitution.

[00272] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence of SEQ ID NO: 36 and the V_L peptide comprises a sequence of SEQ ID NO: 37.

[00273] In some embodiments, the polypeptide as provided herein binds to non-human primate CD7. In some embodiments, the polypeptide as provided herein binds to human CD7.

[00274] As provided for herein, the different polypeptides (V_H or V_L) described herein can be linked with a peptide linker or not linked with a peptide linker and instead for a continuous sequence. In some embodiments, the peptide linker comprises a sequence of (GGGGS)_n (SEQ ID NO: 55), wherein each n is independently 1-5. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, n is 5. The linked peptide format can be represented by a formula of V_H-Z-V_L or V_L-Z-V_H, wherein Z is the peptide linker. In some embodiments, Z is (GGGGS)_n (SEQ ID NO: 55), wherein each n is independently 1-5. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, n is 5.

[00275] In some embodiments, the polypeptide comprising the linked peptide represented by a formula of V_L-Z-V_H comprises a heavy chain variable region as set forth in SEQ ID NO: 36 linked via a linker sequence GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 72) to a light chain variable region as set forth in SEQ ID NO: 37. In some embodiments, the polypeptide comprising a V_L linked via a peptide linker to a V_H has the sequence as set forth below,

DILLTQSPAILSVSPGERVSFSCRASQSIGTSHWYQQRNTDSPRLLIKAYASESIS
GIPSRFSGSGSGTDFTLSINSVESEDIADYYCQQSNSWPTTFGGGKLEIKRGG
GGSGGGGSGGGGSGGGGSQVQLQQPGAELVKPGASVKLSCKASGYPTSYW
IHWVKQRPGRGLEWLGRIDPNSGDTKYNEKFKNKATLTVDKSSTTAYMQLS
SLTSEDSAVYYCARSPYYSDNSMDYWGQGTSTVTVSS (SEQ ID NO: 38).

[00276] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to

a sequence of SEQ ID NO: 38. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 38. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 38. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 38. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 38. In some embodiments, the polypeptide as set forth in SEQ ID NO: 38 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-CD7 antibody. In some embodiments, the anti-CD7 antibody binds to non-human primate CD7. In some embodiments, the anti-CD7 antibody binds to human CD7.

[00277] In some embodiments, the polypeptide comprising the linked peptide represented by a formula of V_H -Z- V_L comprises a light chain variable region as set forth in SEQ ID NO: 37 linked via a linker sequence GGGSGGGSGGGSGGGGS (SEQ ID NO: 72) to a heavy chain variable region as set forth in SEQ ID NO: 36. In some embodiments, the polypeptide comprising a V_H linked via a peptide linker to a V_L has the sequence as set forth below,

QVQLQQPGAELVKPGASVKLSCKASGYPTSYWIHWKQRPGRGLEWLGRI
DPNSGDTKYNEKFNKATLTVDKSSTTAYMQLSSLTSEDSAVYYCARSPYY
NDNSMDYWGGQTSVTVSSGGGGSGGGSGGGSGGGGSDILLTQSPAILSVS
PGERVSFSCRASQSIGTSIHWYQQRNTDSPRLLIKYASESISGIPSRFSGSGSGT
DFTLSINSVESEDIADYYCQNSNSWPTTFGGGTKLEIKR (SEQ ID NO: 39).

[00278] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 39. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 39. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 39. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 39. In some embodiments, the polypeptide as set forth in SEQ ID NO: 39 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-CD7 antibody. In some embodiments, the anti-CD7 antibody binds to non-human primate CD7. In some embodiments, the anti-CD7 antibody binds to human CD7.

[00279] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S_1) comprising an Fc region, such as those provided herein. In some embodiments, the polypeptide comprises a sequence that is

at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region, said Fc region further comprising a transmembrane domain such as those provided herein. In some embodiments, the Fc region further comprising a transmembrane domain has a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker as provided for herein or is absent, Fc is a variant Fc region as provided for herein, L₂ is a linker as provided for herein or is absent, and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprises a polypeptide having the formula ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or is absent, T_M is a transmembrane domain as provided for herein, and ICD is an intracellular domain as provided for herein or is absent. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide

comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprising a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, is anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₁, Fc, L₂, ECD, T_M, and ICD are as provided for herein. In some embodiments, the polypeptide bind to an immune cell, such as those provided herein.

[00280] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region, such as those provided herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region, said Fc region further comprising a transmembrane domain such as those provided herein. In some embodiments, the Fc region further comprising a transmembrane domain has a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker as provided for herein or is absent, Fc is a variant Fc region as provided for herein, L₂ is a linker as provided for herein or is absent, and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprises a polypeptide having the formula ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or absent, T_M is a transmembrane domain as provided for herein, and ICD is an intracellular domain as provided for herein or absent. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD. In some embodiments, the

polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprising a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, is anchored to the surface of a viral particle, such as those provided for herein. In some

embodiments, the identities of L₁, Fc, L₂, ECD, T_M, and ICD are as provided for herein. In some embodiments, the polypeptide bind to an immune cell, such as those provided herein.

[00281] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region, such as those provided herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region, said Fc region further comprising a transmembrane domain, such as those provided herein. In some embodiments, the Fc region further comprising a transmembrane domain has a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker as provided for herein or is absent, Fc is a variant Fc region as provided for herein, L₂ is a linker as provided for herein or is absent, and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprises a polypeptide having the formula ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or is absent, T_M is a transmembrane domain as provided for herein, and ICD is an intracellular domain as provided for herein or is absent. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an

ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence having a sequence as set forth in SEQ ID NO: 38 and comprising a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, is anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₁, Fc, L₂, ECD, T_M, and ICD are as provided for herein. In some embodiments, the polypeptide bind to an immune cell, such as those provided herein.

[00282] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region, such as those provided herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region, said Fc region further comprising a transmembrane domain, such as those provided herein. In some embodiments, the Fc region further comprising a transmembrane domain has a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker as provided for herein or is absent, Fc is a variant Fc region as provided for herein, L₂ is a linker as provided for herein or is absent, and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprises a polypeptide having the formula ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or absent, T_M is a transmembrane domain as provided for herein, and ICD is an intracellular domain as provided for herein or absent. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and

comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence having a sequence as set forth in SEQ ID NO: 39 and comprising a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, is anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₁, Fc, L₂, ECD, T_M, and ICD are as provided for herein. In some embodiments, the polypeptide bind to an immune cell, such as those provided herein.

[00283] In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁, wherein T is a target binding domain and S₁ is a stalk portion, comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 98:

METDTLLLVVLLLVVPGSTGDSAQVQLQPPGAELVKPGASVKLSCKASGYPFTSYWIHWVKRPPGRGLEWLGRI
DPNSGDTKYNEKFKNKATLTVDKSSTAYMQLSSLTSEDSAVYYCARSPYYSDNSMDYWGQGTSTVTVSSGGGGG
GGGGSGGGGSGGGGSDILLTQSPAILSVPSPGERVSFSCRASQSIGTSIHWHYQQRNDSPRLIKYASESISGIPSRFSG
SGSGTDFTLINSVESEDIADYYCQSQNSWPTTFGGGKLEIKRASGGGGSGGGGSGGGGSEPKSCDKHTCPPCP
APEAAGGPSVFLFPPKPKDTLMASRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSV
LTVLAQDWLNGKEYCKVSNKALGAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE
SNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNAYTQKSLSPGKKIEVMYPPPYL
DNEKSNGTIIHVKGKHLCPSPFLPGPSKPFWVLLVVGGLVACYSLLVTVAFIIFWVRSKRSLHSDYMNVRVQGYG
(SEQ ID NO: 98)

or is substantially similar to SEQ ID NO: 98, or is an active fragment of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID

NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence of SEQ ID NO: 98.

[00284] In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁, wherein T is a target binding domain and S₁ is a stalk portion, comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 126:

SAQVQLQQPGAELVKPGASVKLSCKASGYPFTSYWIHWVKQRPGRGLEWLGRIDPNSGDTKYNEKFNKATLTV
DKSSTTAYMQLSSLTSEDSAVYYCARSPYYSDNSMDYWGQGTSTVTVSSGGGGSGGGSGGGSGGGSDILLT
QSPAILSVSPGERVFSFSCRASQSIGTSIHWYQQRNTDSPRLIKYASESISGIPSRFSGSGSGTDFTLINSVESEDIADY
YCQQNSWPTTFGGGTKEIKRASGGGGSGGGSGGGSGGGSEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTL
MASRTPVETCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLAQDWLNGKEYKCKVSN
KALGAPIEKTSKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDG
SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNAYTQKSLSLSPGKKIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSP
LFPGPSKPFWVLVVVGGVLACYSLLVTVAFIIFWVRSKRSRLHSDYMNVRVQGY (SEQ ID NO: 126)

[00285] In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 126. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 126. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 126. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence of SEQ ID NO: 126.

[00286] In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁, wherein T is a target binding domain and S₁ is a stalk portion, comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 127:

QVQLQQPGAELVKPGASVKLSCKASGYPFTSYWIHWVKQRPGRGLEWLGRIDPNSGDTKYNEKFNKATLTVDKS
STTAYMQLSSLTSEDSAVYYCARSPYYSDNSMDYWGQGTSTVTVSSGGGGSGGGSGGGSGGGSDILLTQSP
AII SVSPGERVFSFSCRASQSIGTSIHWYQQRNTDSPRLIKYASESISGIPSRFSGSGSGTDFTLINSVESEDIADYCY
QNSWPTTFGGGTKEIKRASGGGGSGGGSGGGSGGGSEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMAS
RTPVETCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLAQDWLNGKEYKCKVSNKAL
GAPIEKTSKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFL
YSKLTVDKSRWQQGNVFSCSVMHEALHNAYTQKSLSLSPGKKIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSP
LFPGPSKPFWVLVVVGGVLACYSLLVTVAFIIFWVRSKRSRLHSDYMNVRVQGY (SEQ ID NO: 127)

In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 127. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 127. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 127. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence of SEQ ID NO: 127.

[00287] In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁, wherein T is a target binding domain and S₁ is a stalk portion, comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 98, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 25-283 of SEQ ID NO: 98, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 284-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 98, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 25-283 of SEQ ID NO: 98, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 284-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 98, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 25-283 of SEQ ID NO: 98, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 284-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 98, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 25-283 of SEQ ID NO: 98, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 284-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence of SEQ ID NO: 98, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 25-283 of SEQ ID NO: 98, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 284-634 of SEQ ID NO: 98.

[00288] In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁, wherein T is a target binding domain comprising a V_H and a V_L, and S₁ is a stalk portion,

comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain corresponds to amino acids 172-283 of SEQ ID NO: 98, and wherein the stalk portion "S₁" of the polypeptide corresponds to amino acids 284-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain corresponds to amino acids 172-283 of SEQ ID NO: 98, and wherein the stalk portion "S₁" of the polypeptide corresponds to amino acids 284-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain corresponds to amino acids 172-283 of SEQ ID NO: 98, and wherein the stalk portion "S₁" of the polypeptide corresponds to amino acids 284-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain corresponds to amino acids 172-283 of SEQ ID NO: 98, and wherein the stalk portion "S₁" of the polypeptide corresponds to amino acids 284-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain corresponds to amino acids 172-283 of SEQ ID NO: 98, and wherein the stalk portion "S₁" of the polypeptide corresponds to amino acids 284-634 of SEQ ID NO: 98.

[00289] In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-X₁, wherein T is a target binding domain, L₁ is a polypeptide linker or is absent, Fc is a variant Fc domain as provided for herein, L₂ is a polypeptide linker or is absent, and X₁ is a polypeptide comprising a transmembrane domain, comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 98, wherein the target binding domain "T" of the polypeptide corresponds to amino acids 25-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO:

98, L₂ is absent, and X₁ corresponds to amino acids 543-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-X₁ comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 98, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 25-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, and X₁ corresponds to amino acids 543-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-X₁ comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 98, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 25-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, and X₁ corresponds to amino acids 543-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-X₁ comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 98, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 25-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, and X₁ corresponds to amino acids 543-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-X₁ comprises an amino acid sequence of SEQ ID NO: 98, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 25-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, and X₁ corresponds to amino acids 543-634 of SEQ ID NO: 98.

[00290] In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-X₁, wherein T is a target binding domain comprising a V_H and a V_L, L₁ is a polypeptide linker or is absent, Fc is a variant Fc domain as provided for herein, L₂ is a polypeptide linker or is absent, and X₁ is a polypeptide comprising a transmembrane domain, comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain corresponds to amino acids 172-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, and X₁ corresponds to amino acids 543-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-X₁ comprises an amino acid sequence that is at least 90% identical to a sequence

of SEQ ID NO: 98, wherein the V_H of the target binding domain corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain corresponds to amino acids 172-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, and X₁ corresponds to amino acids 543-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-X₁ comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain corresponds to amino acids 172-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, and X₁ corresponds to amino acids 543-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-X₁ comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain corresponds to amino acids 172-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, and X₁ corresponds to amino acids 543-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-X₁ comprises an amino acid sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain corresponds to amino acids 172-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, and X₁ corresponds to amino acids 543-634 of SEQ ID NO: 98.

[00291] In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD, wherein T is a target binding domain, L₁ is a polypeptide linker or is absent, Fc is a variant Fc domain as provided for herein, L₂ is a polypeptide linker or is absent, ECD is an extracellular domain, T_M is a transmembrane domain, and ICD is an intracellular domain comprising a env incorporation motif, comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 98, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 25-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, ECD comprises amino acids 543-584 of SEQ ID NO: 98, T_M comprises amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO:

98, wherein the env incorporation motif comprises amino acids 627-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 98, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 25-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, ECD comprises amino acids 543-584 of SEQ ID NO: 98, T_M comprises amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises amino acids 627-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 98, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 25-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, ECD comprises amino acids 543-584 of SEQ ID NO: 98, T_M comprises amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises amino acids 627-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 98, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 25-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, ECD comprises amino acids 543-584 of SEQ ID NO: 98, T_M comprises amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises amino acids 627-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD comprises an amino acid sequence of SEQ ID NO: 98, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 25-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, ECD comprises amino acids 543-584 of SEQ ID NO: 98, T_M comprises amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises amino acids 627-634 of SEQ ID NO: 98.

[00292] In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD, wherein T is a target binding domain comprising a V_H and a V_L, L₁

is a polypeptide linker or is absent, Fc is a variant Fc domain as provided for herein, L₂ is a polypeptide linker or is absent, ECD is an extracellular domain, T_M is a transmembrane domain, and ICD is an intracellular domain comprising a env incorporation motif, comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain corresponds to amino acids 172-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent ECD comprises amino acids 543-584 of SEQ ID NO: 98, T_M comprises amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises amino acids 627-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain corresponds to amino acids 172-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent ECD comprises amino acids 543-584 of SEQ ID NO: 98, T_M comprises amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises amino acids 627-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain corresponds to amino acids 172-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent ECD comprises amino acids 543-584 of SEQ ID NO: 98, T_M comprises amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises amino acids 627-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain corresponds to amino acids 172-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent ECD comprises amino acids

543-584 of SEQ ID NO: 98, T_M comprises amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises amino acids 627-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD comprises an amino acid of SEQ ID NO: 98, wherein the V_H of the target binding domain corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain corresponds to amino acids 172-283 of SEQ ID NO: 98, L₁ comprises amino acids 284-301 of SEQ ID NO: 98, Fc comprises amino acids 302-542 of SEQ ID NO: 98, L₂ is absent ECD comprises amino acids 543-584 of SEQ ID NO: 98, T_M comprises amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises amino acids 627-634 of SEQ ID NO: 98.

[00293] In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD, wherein T is a target binding domain, L₁ is a polypeptide linker or is absent, Fc is a variant Fc domain as provided for herein, L₂ is a polypeptide linker or is absent, ECD is an extracellular domain, T_M is a transmembrane domain, and ICD is an intracellular domain comprising a env incorporation motif, comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 98, wherein the target binding domain “T” of the polypeptide comprises an amino acid sequence SEQ ID NO: 39 and corresponds to amino acids 25-283 of SEQ ID NO: 98, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 284-301 of SEQ ID NO: 98, Fc comprises an amino acid sequence of SEQ ID NO: 104 and corresponds to amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 543-584 of SEQ ID NO: 98, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 627-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 98, wherein the target binding domain “T” of the polypeptide comprises an amino acid sequence SEQ ID NO: 39 and corresponds to amino acids 25-283 of SEQ ID NO: 98, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 284-301 of SEQ ID NO: 98, Fc comprises an amino acid sequence of SEQ ID NO: 104 and corresponds to amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, ECD comprises an amino

acid sequence of SEQ ID NO: 60 and corresponds to amino acids 543-584 of SEQ ID NO: 98, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 627-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 98, wherein the target binding domain "T" of the polypeptide comprises an amino acid sequence SEQ ID NO: 39 and corresponds to amino acids 25-283 of SEQ ID NO: 98, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 284-301 of SEQ ID NO: 98, Fc comprises an amino acid sequence of SEQ ID NO: 104 and corresponds to amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 543-584 of SEQ ID NO: 98, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 627-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 98, wherein the target binding domain "T" of the polypeptide comprises an amino acid sequence SEQ ID NO: 39 and corresponds to amino acids 25-283 of SEQ ID NO: 98, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 284-301 of SEQ ID NO: 98, Fc comprises an amino acid sequence of SEQ ID NO: 104 and corresponds to amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 543-584 of SEQ ID NO: 98, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 627-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD comprises an amino acid sequence of SEQ ID NO: 98, wherein the target binding domain "T" of the polypeptide comprises an amino acid sequence SEQ ID NO: 39 and corresponds to amino acids 25-283 of SEQ ID NO: 98, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 284-301 of SEQ ID NO: 98, Fc comprises an amino acid sequence of SEQ ID NO: 104 and corresponds to amino acids 302-542 of SEQ

ID NO: 98, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 543-584 of SEQ ID NO: 98, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 627-634 of SEQ ID NO: 98.

[00294] In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD, wherein T is a target binding domain comprising a V_H and a V_L, L₁ is a polypeptide linker or is absent, Fc is a variant Fc domain as provided for herein, L₂ is a polypeptide linker or is absent, ECD is an extracellular domain, T_M is a transmembrane domain, and ICD is an intracellular domain comprising a env incorporation motif, comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain comprises an amino acid sequence of SEQ ID NO: 36 and corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain comprises an amino acid sequence of SEQ ID NO: 37 and corresponds to amino acids 172-283 of SEQ ID NO: 98, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 284-301 of SEQ ID NO: 98, Fc comprises an amino acid sequence of SEQ ID NO: 104 and corresponds to amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 543-584 of SEQ ID NO: 98, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 627-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain comprises an amino acid sequence of SEQ ID NO: 36 and corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain comprises an amino acid sequence of SEQ ID NO: 37 and corresponds to amino acids 172-283 of SEQ ID NO: 98, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 284-301 of SEQ ID NO: 98, Fc comprises an amino acid sequence of SEQ ID NO: 104 and corresponds to amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 543-584 of SEQ ID NO: 98, T_M comprises an amino acid sequence of SEQ ID NO: 62 and

corresponds to amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 627-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain comprises an amino acid sequence of SEQ ID NO: 36 and corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain comprises an amino acid sequence of SEQ ID NO: 37 and corresponds to amino acids 172-283 of SEQ ID NO: 98, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 284-301 of SEQ ID NO: 98, Fc comprises an amino acid sequence of SEQ ID NO: 104 and corresponds to amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 543-584 of SEQ ID NO: 98, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 627-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain comprises an amino acid sequence of SEQ ID NO: 36 and corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain comprises an amino acid sequence of SEQ ID NO: 37 and corresponds to amino acids 172-283 of SEQ ID NO: 98, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 284-301 of SEQ ID NO: 98, Fc comprises an amino acid sequence of SEQ ID NO: 104 and corresponds to amino acids 302-542 of SEQ ID NO: 98, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 543-584 of SEQ ID NO: 98, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 585-612 of SEQ ID NO: 98, and ICD comprises amino acids 613-634 of SEQ ID NO: 98, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 627-634 of SEQ ID NO: 98. In some embodiments, the polypeptide provided for herein comprising the formula of T-L₁-Fc-L₂-ECD-T_M-ICD comprises an amino acid sequence of SEQ ID NO: 98, wherein the V_H of the target binding domain comprises an amino acid sequence of SEQ ID NO: 36 and corresponds to amino acids 25-150 of SEQ ID NO: 98, the V_L of the target binding domain comprises an amino acid sequence of SEQ ID NO: 37 and

sequence as set forth in SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 48 and V_L peptide having a sequence as set forth in SEQ ID NO: 49 linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD are anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₁, Fc, L₂, ECD, T_M, and ICD are as provided for herein. In some embodiments, the V_H and V_L peptides bind to an immune cell, such as those provided herein.

[00296] In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising an Fc region as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising an Fc region further comprising a transmembrane domain. In some embodiments, the Fc region further comprising a transmembrane domain has a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker as provided for herein or is absent, Fc is a variant Fc region as provided for herein, L₂ is a linker as provided for herein or is absent, and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprises a polypeptide having the formula ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or is absent, T_M is a transmembrane domain as provided for herein, and ICD is an intracellular domain as provided for herein or is absent. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to

a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein.

incorporation motif as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD are anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₁, Fc, L₂, ECD, T_M, and ICD are as provided for herein. In some embodiments, V_H and V_L peptides bind to an immune cell, such as those provided herein.

[00297] In some embodiments, a polypeptide is provided comprising a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49.

[00298] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49; provided that the V_H peptide and a V_L peptide comprises a light chain CDR having a sequence of SEQ ID NO: 45-47; and/or a heavy chain CDR having a sequence of SEQ ID NO: 42-44. In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO:

49; provided that the V_H peptide and a V_L peptide comprise a light chain CDR1 having a sequence of SEQ ID NO: 45; a light chain CDR2 having a sequence of SEQ ID NO: 46; a light chain CDR3 having a sequence of SEQ ID NO: 47; and/or a heavy chain CDR1 having a sequence of SEQ ID NO: 42; a heavy chain CDR2 having a sequence of SEQ ID NO: 43; and a heavy chain CDR3 having a sequence of SEQ ID NO: 44. In some embodiments, the CDRs in the V_H or V_L chain are as set forth in the combinations provided for herein.

[00299] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 45; a LCDR2 having a sequence of SEQ ID NO: 46; and a LCDR3 having a sequence of SEQ ID NO: 47; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 42; a HCDR2 having a sequence of SEQ ID NO: 43; and a HCDR3 having a sequence of SEQ ID NO: 44.

[00300] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 45, wherein the LCDR1 comprises at most 1 conservative amino acid substitution, a LCDR2 having a sequence of SEQ ID NO: 46, wherein the LCDR2 comprises at most 1 conservative amino acid substitution, and a LCDR3 having a sequence of SEQ ID NO: 47, wherein the LCDR3 comprises at most 1 conservative amino acid substitution; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 42, wherein the HCDR1 comprises at most 1 conservative amino acid substitution, a HCDR2 having a sequence of SEQ ID NO: 43, wherein the HCDR2 comprises at most 1 conservative amino acid substitution, and a HCDR3 having a sequence of SEQ ID NO: 44, wherein the HCDR3 comprises at most 1 conservative amino acid substitution.

[00301] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence of SEQ ID NO: 48 and the V_L peptide comprises a sequence of SEQ ID NO: 49.

[00302] In some embodiments, the polypeptide as provided herein binds to non-human primate CD8. In some embodiments, the polypeptide as provided herein binds to human CD8.

[00303] As provided for herein, the different polypeptides (V_H or V_L) described herein can be linked with a peptide linker or not linked with a peptide linker and instead for a continuous sequence. In some embodiments, the peptide linker comprises a sequence of $(GGGS)_n$ (SEQ ID NO: 55), wherein each n is independently 1-5. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, n is 5. The linked peptide format can be represented by a formula of V_H -Z- V_L or V_L -Z- V_H , wherein Z is the peptide linker. In some embodiments, Z is $(GGGS)_n$ (SEQ ID NO: 55), wherein each n is independently 1-5. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, n is 5.

[00304] In some embodiments, the polypeptide comprising the linked peptide represented by a formula of V_L -Z- V_H comprises a heavy chain variable region as set forth in SEQ ID NO: 48 linked via a linker sequence GGGSGGGSGGGSGGGGS (SEQ ID NO: 72) to a light chain variable region as set forth in SEQ ID NO: 49. In some embodiments, the polypeptide comprising a V_L linked via a peptide linker to a V_H has the sequence as set forth below,

NIVLTQSPASLAVSLGQRATISCRASESVDFGNSFMNWWYQQKPGQSPKLLIY
LASNLESGVPARFSGSGSRDFTLTIDPVEADDAATYYCQQNNEDPYTFGGGT
KLEIKRGGGSGGGSGGGSGGGSGGGSGGGSEVQLQQSGPELVKPGASVKISCKASR
YTFTDYNLHWVKLSHEKSLEWIGFIYPYNGGTGYNQKFKNKAKLTVDYSSST
AYMELRSLTSVDAAVYYCARDHRYNEGVSFDYWGGTTTLTVSS (SEQ ID
NO: 50).

[00305] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 50. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 50. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 50. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 50. In some embodiments, the polypeptide as set forth in SEQ ID NO: 50 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-CD8 antibody. In some embodiments, the anti-CD8 antibody binds to non-human primate CD8. In some embodiments, the anti-CD8 antibody binds to human CD8.

[00306] In some embodiments, the polypeptide comprising the linked peptide represented by a formula of V_H -Z- V_L comprises a light chain variable region as set forth in SEQ ID NO: 49 linked via a linker sequence GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 72) to a heavy chain variable region as set forth in SEQ ID NO: 48. In some embodiments, the polypeptide comprising a V_H linked via a peptide linker to a V_L has the sequence as set forth below,

EVQLQQSGPELVKPGASVKISCKASRYTFTDYNLHWVKLSHEKSLEWIGFIYP
YNGGTGYNQKFKNKAKLTVDYSSSTAYMELRSLTSVDAAVYYCARDHRYN
EGVSFDYWGGQTTLTVSSGGGGSGGGGSGGGGSGGGGSNIVLTQSPASLAVS
LGQRATISCRASESVDGFGNSFMNWWYQQKPGQSPKLLIYLASNLESGVPARFS
GSGSRDFTLTIDPVEADDAATYYCQQNNEDPYTFGGGTGLEIKR (SEQ ID
NO: 51).

[00307] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 51. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 51. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 51. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 51. In some embodiments, the polypeptide as set forth in SEQ ID NO: 51 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-CD8 antibody. In some embodiments, the anti-CD8 antibody binds to non-human primate CD8. In some embodiments, the anti-CD8 antibody binds to human CD8.

[00308] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising an Fc region, such as those provided herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising an Fc region, said Fc region further comprising a transmembrane domain, such as those provided herein. In some embodiments, the Fc region further comprising a transmembrane domain has a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker as provided for herein or is absent, Fc is a variant Fc region as provided for herein, L₂ is a linker as provided for herein or is absent, and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprises a polypeptide having the formula ECD-T_M-ICD,

wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or is absent, T_M is a transmembrane domain as provided for herein, and ICD is an intracellular domain as provided for herein or is absent. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD

comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprising a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, is anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₁, Fc, L₂, ECD, T_M, and ICD are as provided for herein. In some embodiments, the polypeptide bind to an immune cell, such as those provided herein.

[00309] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region, such as those provided herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region, said Fc region further comprising a transmembrane domain, such as those provided herein. In some embodiments, the Fc region further comprising a transmembrane domain has a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker as provided for herein or is absent, Fc is a variant Fc region as provided for herein, L₂ is a linker as provided for herein or is absent, and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprises a polypeptide having the formula ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or is absent, T_M is a transmembrane domain as provided for herein, and ICD is an intracellular domain as provided for herein or is absent. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%,

87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprising a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, is anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₁, Fc, L₂, ECD, T_M, and ICD are as provided for herein. In some embodiments, the polypeptide bind to an immune cell, such as those provided herein.

[00310] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising an Fc region, such as those provided herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising an Fc region, said Fc region further comprising a transmembrane domain, such as those provided herein. In some embodiments, the Fc region further comprising a transmembrane domain has

a formula of L_1 -Fc- L_2 - X_1 , wherein L_1 is a linker as provided for herein or is absent, Fc is a variant Fc region as provided for herein, L_2 is a linker as provided for herein or is absent, and X_1 is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X_1 may comprises a polypeptide having the formula ECD- T_M -ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or is absent, T_M is a transmembrane domain as provided for herein, and ICD is an intracellular domain as provided for herein or is absent. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 50 and comprises a stalk portion (S_1) comprising an Fc region (L_1 -Fc- L_2 - X_1) comprising an ECD, a T_M , and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 50 and comprises a stalk portion (S_1) comprising an Fc region (L_1 -Fc- L_2 - X_1) comprising a CD8 and/or CD28 ECD, a T_M , and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 50 and comprises a stalk portion (S_1) comprising an Fc region (L_1 -Fc- L_2 - X_1) comprising an ECD, a CD8 and/or CD28 T_M , and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 50 and comprises a stalk portion (S_1) comprising an Fc region (L_1 -Fc- L_2 - X_1) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M , and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 50 and comprises a stalk portion (S_1) comprising an Fc region (L_1 -Fc- L_2 - X_1) comprising an ECD, a T_M , and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 50 and comprises a stalk portion (S_1) comprising an Fc region (L_1 -Fc- L_2 - X_1) comprising a CD8 and/or CD28 ECD, a T_M , and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 50 and comprises a stalk portion (S_1) comprising an Fc region (L_1 -Fc- L_2 - X_1) comprising an ECD, a CD8 and/or CD28 T_M , and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 50 and comprises a stalk portion (S_1) comprising an Fc region (L_1 -Fc- L_2 - X_1) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M , and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence having a sequence as set forth in SEQ ID NO: 50 and comprising a stalk portion (S_1) comprising an Fc region (L_1 -Fc- L_2 - X_1) comprising an ECD, a T_M , and an ICD, is anchored to the surface of a viral particle, such as those provided for herein. In some

embodiments, the identities of L₁, Fc, L₂, ECD, T_M, and ICD are as provided for herein. In some embodiments, the polypeptide bind to an immune cell, such as those provided herein.

[00311] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region, such as those provided herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region, said Fc region further comprising a transmembrane domain, such as those provided herein. In some embodiments, the Fc region further comprising a transmembrane domain has a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker as provided for herein or is absent, Fc is a variant Fc region as provided for herein, L₂ is a linker as provided for herein or is absent, and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprises a polypeptide having the formula ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or is absent, T_M is a transmembrane domain as provided for herein, and ICD is an intracellular domain as provided for herein or is absent. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an

ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence having a sequence as set forth in SEQ ID NO: 51 and comprising a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, is anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₁, Fc, L₂, ECD, T_M, and ICD are as provided for herein. In some embodiments, the polypeptide bind to an immune cell, such as those provided herein.

Targeting moieties comprising flexible polypeptides

[00312] In some embodiments, the V_H and V_L polypeptides are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃) as provided for herein. In some embodiments, the V_H and V_L polypeptides are linked to a stalk portion (S₁) comprising a flexible polypeptide further comprising a polypeptide comprising a transmembrane domain as provided for herein. In some embodiments, the flexible polypeptide further comprising a polypeptide comprising a transmembrane domain is represented by the formula L₃-X₁, wherein L₃ is a flexible polypeptide as provided for herein and X₁ is as provided for herein. As provided for herein, X₁ may comprise a polypeptide having the formula of ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or is absent, T_M is a transmembrane domain as provided for herein, and ICD is an intracellular domain as provided for herein or is absent. Examples of ECD include, but are not limited to, a CD8 and/or CD28 ECD as provided for herein. Examples of T_M include, but are not limited to, a CD8 and/or CD28 transmembrane domain as provided for herein. In any of the following embodiments, it is to be understood that the ECD, the ICD, or both may be optionally absent. Accordingly, an embodiment wherein X₁ comprises a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD comprising an Env incorporation motif is understood to encompass the following X₁ members: i) a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD comprising an Env incorporation motif; ii) a CD8 and/or CD28 T_M, and an ICD comprising an Env incorporation motif wherein the ECD is absent; iii) a CD8 and/or CD28 ECD, and a CD8 and/or CD28 T_M, wherein the ICD is absent; and iv) a CD8 and/or CD28 T_M wherein both the ECD and the ICD are absent. Similarly, an embodiment wherein X₁ comprises a CD8 and/or CD28 T_M and an

ICD comprising an Env incorporation motif is understood to encompass the following X_1 members: i) a CD8 and/or CD28 T_M and an ICD comprising an Env incorporation motif; and ii) a CD8 and/or CD28 T_M wherein the ICD is absent. Similarly, an embodiment wherein X_1 comprises a CD8 and/or CD28 ECD and a CD8 and/or CD28 T_M is understood to encompass the following X_1 members: i) a CD8 and/or CD28 ECD and a CD8 and/or CD28 T_M ; and ii) a CD8 and/or CD28 T_M wherein the ECD is absent. It is to be further understood that the preceding explanation is also true in embodiments where a specific ECD, T_M , or ICD are not recited. For example, an embodiment wherein X_1 comprises an ECD, a CD8 and/or CD28 T_M , and an ICD would be understood to encompass the following X_1 members: i) an ECD, a CD8 and/or CD28 T_M , and an ICD; ii) an ECD, and a CD8 and/or CD28 T_M wherein the ICD is absent; iii) a CD8 and/or CD28 T_M , and an ICD wherein the ECD is absent; and iv) a CD8 and/or CD28 T_M wherein the ECD and the ICD are absent. Similarly, an embodiment wherein X_1 comprises a CD8 and/or CD28 T_M and an ICD is understood to encompass the following X_1 members: i) a CD8 and/or CD28 T_M and an ICD; and ii) a CD8 and/or CD28 T_M wherein the ICD is absent. Similarly, an embodiment wherein X_1 comprises an ECD and a CD8 and/or CD28 T_M is understood to encompass the following X_1 members: i) an ECD and a CD8 and/or CD28 T_M ; and ii) a CD8 and/or CD28 T_M wherein the ECD is absent. Unless explicitly stated, the preceding examples and explanations are applicable to any embodiments that follow.

[00313] In some embodiments, X_1 comprises a CD8 and/or CD28 ECD, a T_M , and an ICD. In some embodiments, X_1 comprises an ECD, a CD8 and/or CD28 T_M , and an ICD. In some embodiments, X_1 comprises a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M , and an ICD. In some embodiments, X_1 comprises an ECD, a T_M , and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, X_1 comprises a CD8 and/or CD28 ECD, a T_M , and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, X_1 comprises an ECD, a CD8 and/or CD28 T_M , and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, X_1 comprises a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M , and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein.

[00314] In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S_1) comprising a flexible polypeptide (L_3) as provided for herein. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S_1) comprising a flexible polypeptide (L_3) further comprising a polypeptide comprising a transmembrane domain as provided for herein. In some embodiments the flexible polypeptide (L_3) further comprising a polypeptide comprising a transmembrane domain is represented by

the formula L₃-X₁, wherein L₃ is a flexible polypeptide as provided for herein and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprise a polypeptide having the formula of ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein, or is absent; T_M is a transmembrane domain as provided for herein; and ICD is an intracellular domain as provided for herein. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the identities of L₃, X₁, ECD, T_M, and ICD are as provided for herein. In some embodiments, the V_H and V_L polypeptides bind to an immune cell, such as those provided herein.

[00315] In some embodiments, a V_H peptide having a sequence as set forth in SEQ ID NO: 36 and a V_L peptide having a sequence as set forth in SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 36 and V_L peptide having a sequence as set forth in SEQ ID NO: 37 are linked to a stalk portion (S₁)

comprising a flexible polypeptide (L_3 - X_1) comprising a CD8 and/or CD28 ECD, a T_M , and an ICD. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 36 and V_L peptide having a sequence as set forth in SEQ ID NO: 37 are linked to a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising an ECD, a CD8 and/or CD28 T_M , and an ICD. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 36 and V_L peptide having a sequence as set forth in SEQ ID NO: 37 are linked to a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M , and an ICD. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 36 and V_L peptide having a sequence as set forth in SEQ ID NO: 37 are linked to a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising an ECD, a T_M , and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 36 and V_L peptide having a sequence as set forth in SEQ ID NO: 37 are linked to a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising a CD8 and/or CD28 ECD, a T_M , and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 36 and V_L peptide having a sequence as set forth in SEQ ID NO: 37 are linked to a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising an ECD, a CD8 and/or CD28 T_M , and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 36 and V_L peptide having a sequence as set forth in SEQ ID NO: 37 are linked to a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M , and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 36 and V_L peptide having a sequence as set forth in SEQ ID NO: 37 are linked to a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising an ECD, a T_M , and an ICD are anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L_3 , X_1 , ECD, T_M , and ICD are as provided for herein. In some embodiments, the V_H and V_L peptides bind to an immune cell, such as those provided herein.

[00316] In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 are linked to a stalk portion (S_1) comprising a flexible

polypeptide (L₃) as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃) further comprising a polypeptide comprising a transmembrane domain as provided for herein. In some embodiments, the flexible polypeptide further comprising a polypeptide comprising a transmembrane domain is represented by the formula L₃-X₁, wherein L₃ is a flexible polypeptide as provided for herein and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprise a polypeptide having the formula of ECD-T_M-ICD, wherein ECD is an extracellular domain, or fragment thereof as provided for herein, or is absent; T_M is a transmembrane domain as provided for herein; and ICD is an intracellular domain as provided for herein, or is absent. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%,

95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37 linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD are anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₃, X₁, ECD, T_M, and ICD are as provided for herein. In some embodiments, the V_H and V_L peptides bind to an immune cell, such as those provided herein.

[00317] In some embodiments, a polypeptide is provided comprising a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%,

89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37.

[00318] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37; provided that the V_H peptide and a V_L peptide comprises a light chain CDR having a sequence of SEQ ID NO: 33-35; and/or a heavy chain CDR having a sequence of SEQ ID NO: 30-32. In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37; provided that the V_H peptide and a V_L peptide comprise a light chain CDR1 having a sequence of SEQ ID NO: 33; a light chain CDR2 having a sequence of SEQ ID NO: 34; a light chain CDR3 having a sequence of SEQ ID NO: 35; and/or a heavy chain CDR1 having a sequence of SEQ ID NO: 30; a heavy chain CDR2 having a sequence of SEQ ID NO: 31; and a heavy chain CDR3 having a sequence of SEQ ID NO: 32. In some embodiments, the CDRs in the V_H or V_L chain are as set forth in the combinations provided for herein.

[00319] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 33; a LCDR2 having a sequence of SEQ ID NO: 34; and a LCDR3 having a sequence of SEQ ID NO: 35; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 30; a HCDR2 having a sequence of SEQ ID NO: 31; and a HCDR3 having a sequence of SEQ ID NO: 32.

[00320] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%,

91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 37; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 33, wherein the LCDR1 comprises at most 1 conservative amino acid substitution, a LCDR2 having a sequence of SEQ ID NO: 34, wherein the LCDR2 comprises at most 1 conservative amino acid substitution, and a LCDR3 having a sequence of SEQ ID NO: 35, wherein the LCDR3 comprises at most 1 conservative amino acid substitution; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 30, wherein the HCDR1 comprises at most 1 conservative amino acid substitution, a HCDR2 having a sequence of SEQ ID NO: 31, wherein the HCDR2 comprises at most 1 conservative amino acid substitution, and a HCDR3 having a sequence of SEQ ID NO: 32, wherein the HCDR3 comprises at most 1 conservative amino acid substitution.

[00321] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence of SEQ ID NO: 36 and the V_L peptide comprises a sequence of SEQ ID NO: 37.

[00322] In some embodiments, the polypeptide as provided herein binds to non-human primate CD7. In some embodiments, the polypeptide as provided herein binds to human CD7.

[00323] As provided for herein, the different polypeptides (V_H or V_L) described herein can be linked with a peptide linker or not linked with a peptide linker and instead for a continuous sequence. In some embodiments, the peptide linker comprises a sequence of (GGGGS)_n (SEQ ID NO: 55), wherein each n is independently 1-5. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, n is 5. The linked peptide format can be represented by a formula of V_H-Z-V_L or V_L-Z-V_H, wherein Z is the peptide linker. In some embodiments, Z is (GGGGS)_n (SEQ ID NO: 55), wherein each n is independently 1-5. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, n is 5.

[00324] In some embodiments, the polypeptide comprising the linked peptide represented by a formula of V_L-Z-V_H comprises a heavy chain variable region as set forth in SEQ ID NO: 36 linked via a linker sequence GGGSGGGSGGGSGGGGS (SEQ ID NO: 72) to a light chain variable region as set forth in SEQ ID NO: 37. In some embodiments, the polypeptide comprising a V_L linked via a peptide linker to a V_H has the sequence as set forth below,

DILLTQSPAILSVSPGERVSFSCRASQSIGTSIHWYQQRNDSPRLLIKYASESIS
GIPSRFSGSGSGTDFTLSINSVESEDIADYYCQQSNSWPTTFGGGKLEIKRGG
GGSGGGGSGGGGSGGGGSQVQLQQPGAELVKPGASVKLSCKASGYPFTSYW
IHWVKQRPGRGLEWLGRIDPNSGDTKYNEKFKNKATLTVDKSSTTAYMQLS
SLTSEDSAVYYCARSPYYSDNNSMDYWGQGTSTVTVSS (SEQ ID NO: 38).

[00325] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 38. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 38. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 38. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 38. In some embodiments, the polypeptide as set forth in SEQ ID NO: 38 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-CD7 antibody. In some embodiments, the anti-CD7 antibody binds to non-human primate CD7. In some embodiments, the anti-CD7 antibody binds to human CD7.

[00326] In some embodiments, the polypeptide comprising the linked peptide represented by a formula of V_H -Z- V_L comprises a light chain variable region as set forth in SEQ ID NO: 37 linked via a linker sequence GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 72) to a heavy chain variable region as set forth in SEQ ID NO: 36. In some embodiments, a polypeptide comprising a V_H linked via a peptide linker to a V_L has the sequence as set forth below,

QVQLQQPGAELVKPGASVKLSCKASGYPFTSYWIHWVKQRPGRGLEWLGRID
PNNSGDTKYNEKFKNKATLTVDKSSTTAYMQLSSLTSEDSAVYYCARSPYYSD
NNSMDYWGQGTSTVTVSSGGGGSGGGGSGGGGSGGGGSDILLTQSPAILSVS
PGERVSFSCRASQSIGTSIHWYQQRNDSPRLLIKYASESISGIPSRFSGSGSGT
DFTLSINSVESEDIADYYCQQSNSWPTTFGGGKLEIKR (SEQ ID NO: 39).

[00327] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 39. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 39. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 39. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 39. In some embodiments, the polypeptide as set forth in SEQ ID

NO: 39 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-CD7 antibody. In some embodiments, the anti-CD7 antibody binds to non-human primate CD7. In some embodiments, the anti-CD7 antibody binds to human CD7.

[00328] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃) as provided for herein. In some embodiments, a polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising a flexible polypeptide further comprising a polypeptide comprising a transmembrane domain as provided for herein. In some embodiments, the flexible polypeptide further comprising a polypeptide comprising a transmembrane domain is represented by the formula L₃-X₁, wherein L₃ is a flexible polypeptide as provided for herein and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprise a polypeptide having the formula of ECD-T_M-ICD, wherein ECD is an extracellular domain, or fragment thereof as provided for herein, or is absent; T_M is a transmembrane domain as provided for herein; and ICD is an intracellular domain as provided for herein or is absent. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%,

87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprising a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD, is anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₃, ECD, T_M, and ICD are as provided for herein. In some embodiments, the polypeptide bind to an immune cell, such as those provided herein.

[00329] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃) as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising a flexible polypeptide further comprising a polypeptide comprising a transmembrane domain as provided for herein. In some embodiments, the flexible polypeptide further comprising a polypeptide comprising a transmembrane domain is represented by the formula L₃-X₁, wherein L₃ is a flexible polypeptide as provided for herein and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprise a polypeptide having the formula of ECD-T_M-ICD, wherein ECD is an extracellular domain, or fragment thereof as provided for herein, or is absent; T_M is a transmembrane domain as provided for herein; and ICD is an intracellular domain as provided

for herein, or is absent. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 39 and comprising a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD, is anchored to the surface of a viral particle, such

as those provided for herein. In some embodiments, the identities of L₃, ECD, T_M, and ICD are as provided for herein. In some embodiments, the polypeptide bind to an immune cell, such as those provided herein.

[00330] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃) as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising a flexible polypeptide further comprising a polypeptide comprising a transmembrane domain as provided for herein. In some embodiments, the flexible polypeptide further comprising a polypeptide comprising a transmembrane domain is represented by the formula L₃-X₁, wherein L₃ is a flexible polypeptide as provided for herein and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprise a polypeptide having the formula of ECD-T_M-ICD, wherein ECD is an extracellular domain, or fragment thereof as provided for herein, or is absent; T_M is a transmembrane domain as provided for herein; and ICD is an intracellular domain as provided for herein or is absent. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises

a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M , and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence having a sequence as set forth in SEQ ID NO: 38 and comprising a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising an ECD, a T_M , and an ICD, is anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L_3 , ECD, T_M , and ICD are as provided for herein. In some embodiments, the polypeptide bind to an immune cell, such as those provided herein.

[00331] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S_1) comprising a flexible polypeptide (L_3) as provided for herein. In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S_1) comprising a flexible polypeptide further comprising a polypeptide comprising a transmembrane domain as provided for herein. In some embodiments, the flexible polypeptide further comprising a polypeptide comprising a transmembrane domain is represented by the formula L_3 - X_1 , wherein L_3 is a flexible polypeptide as provided for herein and X_1 is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X_1 may comprise a polypeptide having the formula of ECD- T_M -ICD, wherein ECD is an extracellular domain or fragment thereof as provided for herein, or is absent; T_M is a transmembrane domain as provided for herein; and ICD is an intracellular domain as provided for herein, or is absent. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising a CD8 and/or CD28 ECD, a T_M , and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising an ECD, a CD8 and/or CD28 T_M , and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M , and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising an ECD, a T_M , and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S_1)

comprising a flexible polypeptide (L_3 - X_1) comprising a CD8 and/or CD28 ECD, a T_M , and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising an ECD, a CD8 and/or CD28 T_M , and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 39 and comprises a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M , and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence having a sequence as set forth in SEQ ID NO: 39 and comprising a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising an ECD, a T_M , and an ICD, is anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L_3 , ECD, T_M , and ICD are as provided for herein. In some embodiments, the polypeptide bind to an immune cell, such as those provided herein.

[00332] In some embodiments, a V_H peptide having a sequence as set forth in SEQ ID NO: 48 and a V_L peptide having a sequence as set forth in SEQ ID NO: 49 are linked to a stalk portion (S_1) comprising a flexible polypeptide (L_3) as provided for herein. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 48 and the V_L peptide having a sequence as set forth in SEQ ID NO: 49 are linked to a stalk portion (S_1) comprising a flexible polypeptide further comprising a polypeptide comprising a transmembrane domain as provided for herein. In some embodiments, the flexible polypeptide further comprising a polypeptide comprising a transmembrane domain is represented by the formula L_3 - X_1 , wherein L_3 is a flexible polypeptide as provided for herein and X_1 is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X_1 may comprise a polypeptide having the formula of ECD- T_M -ICD, wherein ECD is an extracellular domain or fragment thereof as provided for herein, or is absent; T_M is a transmembrane domain as provided for herein; and ICD is an intracellular domain as provided for herein, or is absent. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 48 and the V_L peptide having a sequence as set forth in SEQ ID NO: 49 are linked to a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising a CD8 and/or CD28 ECD, a T_M , and an ICD. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 48 and V_L peptide having a sequence as set forth in SEQ ID NO: 49 are linked to a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising an

ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 48 and V_L peptide having a sequence as set forth in SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 48 and V_L peptide having a sequence as set forth in SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 48 and V_L peptide having a sequence as set forth in SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 48 and V_L peptide having a sequence as set forth in SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 48 and V_L peptide having a sequence as set forth in SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 48 and V_L peptide having a sequence as set forth in SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 48 and V_L peptide having a sequence as set forth in SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD are anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₃, X₁, ECD, T_M, and ICD are as provided for herein. In some embodiments, the V_H and V_L peptides bind to an immune cell, such as those provided herein.

[00333] In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃) as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising

a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising a flexible polypeptide further comprising a polypeptide comprising a transmembrane domain as provided for herein. In some embodiments, the flexible polypeptide further comprising a polypeptide comprising a transmembrane domain is represented by the formula L₃-X₁, wherein L₃ is a flexible polypeptide as provided for herein and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprise a polypeptide having the formula of ECD-T_M-ICD, wherein ECD is an extracellular domain, or fragment thereof as provided for herein, or is absent; T_M is a transmembrane domain as provided for herein; and ICD is an intracellular domain as provided for herein or is absent. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some

embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 are linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49 linked to a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD are anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₃, X₁, ECD, T_M, and ICD are as provided for herein. In some embodiments, the V_H and V_L peptides bind to an immune cell, such as those provided herein.

[00334] In some embodiments, a polypeptide is provided comprising a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%,

89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49.

[00335] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49; provided that the V_H peptide and a V_L peptide comprise a light chain CDR having a sequence of SEQ ID NO: 45-47; and/or a heavy chain CDR having a sequence of SEQ ID NO: 42-44. In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49; provided that the V_H peptide and a V_L peptide comprise a light chain CDR1 having a sequence of SEQ ID NO: 45; a light chain CDR2 having a sequence of SEQ ID NO: 46; a light chain CDR3 having a sequence of SEQ ID NO: 47; and/or a heavy chain CDR1 having a sequence of SEQ ID NO: 42; a heavy chain CDR2 having a sequence of SEQ ID NO: 43; and a heavy chain CDR3 having a sequence of SEQ ID NO: 44. In some embodiments, the CDRs in the V_H or V_L chain are as set forth in the combinations provided for herein.

[00336] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 45; a LCDR2 having a sequence of SEQ ID NO: 46; and a LCDR3 having a sequence of SEQ ID NO: 47; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 42; a HCDR2 having a sequence of SEQ ID NO: 43; and a HCDR3 having a sequence of SEQ ID NO: 44.

[00337] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 48; and the V_L peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%,

91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 49; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 45, wherein the LCDR1 comprises at most 1 conservative amino acid substitution, a LCDR2 having a sequence of SEQ ID NO: 46, wherein the LCDR2 comprises at most 1 conservative amino acid substitution, and a LCDR3 having a sequence of SEQ ID NO: 47, wherein the LCDR3 comprises at most 1 conservative amino acid substitution; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 42, wherein the HCDR1 comprises at most 1 conservative amino acid substitution, a HCDR2 having a sequence of SEQ ID NO: 43, wherein the HCDR2 comprises at most 1 conservative amino acid substitution, and a HCDR3 having a sequence of SEQ ID NO: 44, wherein the HCDR3 comprises at most 1 conservative amino acid substitution.

[00338] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence of SEQ ID NO: 48 and the V_L peptide comprises a sequence of SEQ ID NO: 49.

[00339] In some embodiments, the polypeptide as provided herein binds to non-human primate CD8. In some embodiments, a polypeptide as provided herein binds to human CD8.

[00340] As provided for herein, the different polypeptides (V_H or V_L) described herein can be linked with a peptide linker or not linked with a peptide linker and instead for a continuous sequence. In some embodiments, the peptide linker comprises a sequence of (GGGGS)_n (SEQ ID NO: 55), wherein each n is independently 1-5. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, n is 5. The linked peptide format can be represented by a formula of V_H-Z-V_L or V_L-Z-V_H, wherein Z is the peptide linker. In some embodiments, Z is (GGGGS)_n (SEQ ID NO: 55), wherein each n is independently 1-5. In some embodiments, n is 1. In some embodiments, n is 2. In some embodiments, n is 3. In some embodiments, n is 4. In some embodiments, n is 5.

[00341] In some embodiments, the polypeptide comprising the linked peptide represented by a formula of V_L-Z-V_H comprises a heavy chain variable region as set forth in SEQ ID NO: 48 linked via a linker sequence GGGSGGGSGGGSGGGGS (SEQ ID NO: 72) to a light chain variable region as set forth in SEQ ID NO: 49. In some embodiments, the polypeptide comprising a V_L linked via a peptide linker to a V_H has the sequence as set forth below,

NIVLTQSPASLAVSLGQRATISCRASESVDFGNSFMNWWYQQKPGQSPKLLIY
LASNLESGVPARFSGSGSRTDFTLTIDPVEADDAATYYCQQNNEDPYTFGGGT
KLEIKRGGGSGGGSGGGSGGGSGGGGSEVQLQQSGPELVKPGASVKISKASR

YTFTDYNLHWVKLSHEKSLEWIGFIYPYNGGTGYNQKFKNKAKLTVDYSSST
AYMELRSLTSVDAAVYYCARDHRYNEGVSFDYWGQGTTLTVSS (SEQ ID
NO: 50).

[00342] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 50. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 50. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 50. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 50. In some embodiments, the polypeptide as set forth in SEQ ID NO: 50 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-CD8 antibody. In some embodiments, the anti-CD8 antibody binds to non-human primate CD8. In some embodiments, the anti-CD8 antibody binds to human CD8.

[00343] In some embodiments, the polypeptide comprising the linked peptide represented by a formula of V_H -Z- V_L comprises a light chain variable region as set forth in SEQ ID NO: 49 linked via a linker sequence GGGSGGGSGGGSGGGGS (SEQ ID NO: 72) to a heavy chain variable region as set forth in SEQ ID NO: 48. In some embodiments, the polypeptide comprising a V_H linked via a peptide linker to a V_L has the sequence as set forth below,

EVQLQQSGPELVKPGASVKISCKASRYTFTDYNLHWVKLSHEKSLEWIGFIYP
YNGGTGYNQKFKNKAKLTVDYSSSTAYMELRSLTSVDAAVYYCARDHRYN
EGVSFDYWGQGTTLTVSSGGGSGGGSGGGSGGGGSNIVLTQSPASLAVS
LGQRATISCRASESVDGFGNSFMNWWYQQKPGQSPKLLIYLASNLESGVPARFS
GSGSRDFTLTIDPVEADDAATYYCQQNNEDPYTFGGGTKLEIKR (SEQ ID
NO: 51).

[00344] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 51. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 51. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 51. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 51. In some embodiments, the polypeptide as set forth in SEQ ID NO: 51 is an antibody, or an antigen binding fragment thereof. In some embodiments, the

antibody is an anti-CD8 antibody. In some embodiments, the anti-CD8 antibody binds to non-human primate CD8. In some embodiments, the anti-CD8 antibody binds to human CD8.

[00345] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃) as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising a flexible polypeptide further comprising a polypeptide comprising a transmembrane domain as provided for herein. In some embodiments, the flexible polypeptide further comprising a polypeptide comprising a transmembrane domain is represented by the formula L₃-X₁, wherein L₃ is a flexible polypeptide as provided for herein and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprise a polypeptide having the formula of ECD-T_M-ICD, wherein ECD is an extracellular domain, or fragment thereof as provided for herein, or is absent; T_M is a transmembrane domain as provided for herein; and ICD is an intracellular domain as provided for herein or is absent. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a

sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 50 and comprising a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD, is anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₃, ECD, T_M, and ICD are as provided for herein. In some embodiments, the polypeptide bind to an immune cell, such as those provided herein.

[00346] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃) as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising a flexible polypeptide further comprising a polypeptide comprising a transmembrane domain as provided for herein. In some embodiments, the flexible polypeptide further comprising a polypeptide comprising a transmembrane domain is represented by the formula L₃-X₁, wherein L₃ is a flexible polypeptide as provided for herein and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprise a polypeptide having the formula of ECD-T_M-ICD, wherein ECD is an extracellular domain, or fragment thereof as provided for herein, or is absent; T_M is a transmembrane domain as provided for herein; and ICD is an intracellular domain as provided for herein or is absent. In some embodiments, the polypeptide comprises a sequence that is at

least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 51 and comprising a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD, is anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₃, ECD, T_M, and ICD

comprising a flexible polypeptide (L_3 - X_1) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M , and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence having a sequence as set forth in SEQ ID NO: 50 and comprising a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising an ECD, a T_M , and an ICD, is anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L_3 , ECD, T_M , and ICD are as provided for herein. In some embodiments, the polypeptide bind to an immune cell, such as those provided herein.

[00348] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S_1) comprising a flexible polypeptide (L_3) as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S_1) comprising a flexible polypeptide further comprising a polypeptide comprising a transmembrane domain as provided for herein. In some embodiments, the flexible polypeptide further comprising a polypeptide comprising a transmembrane domain is represented by the formula L_3 - X_1 , wherein L_3 is a flexible polypeptide as provided for herein and X_1 is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X_1 may comprise a polypeptide having the formula of ECD- T_M -ICD, wherein ECD is an extracellular domain, or fragment thereof as provided for herein, or is absent; T_M is a transmembrane domain as provided for herein; and ICD is an intracellular domain as provided for herein, or is absent. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising a CD8 and/or CD28 ECD, a T_M , and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising an ECD, a CD8 and/or CD28 T_M , and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M , and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising an ECD, a T_M , and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1) comprising a CD8 and/or CD28 ECD, a T_M , and an

ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 51 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence having a sequence as set forth in SEQ ID NO: 51 and comprising a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a T_M, and an ICD, is anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₃, ECD, T_M, and ICD are as provided for herein. In some embodiments, the polypeptide bind to an immune cell, such as those provided herein.

Expressed polypeptides of interest

[00349] In some embodiments, the viral particle comprising a heterologous viral glycoprotein and a targeting moiety further comprises a nucleic acid molecule encoding for a heterologous molecule of interest or “cargo.” In some embodiments, the heterologous viral glycoprotein is as provided for herein. In some embodiments, the targeting moiety is as provided for herein. As used herein, heterologous molecule of interest is meant to refer to any product that may be encoded by a nucleic acid molecule. As non-limiting examples, “cargo” or “heterologous molecule of interest” may refer to an siRNA, an shRNA, a peptide, a polypeptide, a protein, a viral payload, a viral genome, or a combination thereof. In some embodiments, the heterologous molecule of interest is an siRNA, an shRNA, a non-coding RNA (e.g. a guide RNA for a CRISPR system), a peptide, a polypeptide, a protein, a viral payload, a viral genome, a chimeric antigen receptor (“CAR”), or a combination thereof. In some embodiments, the polypeptide is a CAR.

[00350] A “chimeric antigen receptor” or “CAR” as used herein refers to an antigen-binding domain that is fused, directly, or indirectly (e.g. via a hinge or transmembrane domain to an intracellular signaling domain capable of activating or stimulating an immune cell. Most commonly, the CAR's extracellular binding domain is composed of a single chain variable fragment (scFv) derived from fusing the variable heavy and light regions of a murine or humanized monoclonal antibody. Alternatively, scFvs may be used that are derived from Fab's

(instead of from an antibody, e.g., obtained from Fab libraries). In various embodiments, this scFv is fused to a transmembrane domain and then to an intracellular signaling domain. However, the antigen binding domain can be any molecule that can bind to the target on the cell. For example, the antigen binding domain of a CAR can be an antibody, a scFv antibody, an antigen binding domain, an ankyrin repeat (e.g. DARPIN), a VHH domain antibody, a nanobody, single domain antibody, a FN3 domain, or any combination thereof. In some embodiments, a CAR includes those that solely provide CD3 ζ signals upon antigen binding. In some embodiments, the CAR includes those that provide both costimulation (e.g. CD28 or CD137) and activation (CD3 ζ). In some embodiments, the CARs include those that provide multiple costimulation (e.g. CD28 and CD137) and activation (CD3 ζ). In various embodiments, the CAR is selected to have high affinity or avidity for the antigen. In some embodiments, the antigen binding domain of the CAR binds to any appropriate antigen. In some embodiments, the antigen binding domain of the CAR binds to a target selected from, but not limited to, CD8, CCR7, CD19, CD20, CD22, CD123, CD38, FCRL5, BCMA, CD33, CD79b, CEA, ERBB2, EGFR, GD2, mesothelin, MUC1, PSMA, PSCA, STn, EGFRvIII, IL13R α , HER2, EphA2, CD70, CD133, CSPG 4, B7-H3, PDPN, MMP2, or CD147. In some embodiments, the antigen-binding domain binds to CD19. In some embodiments, the antigen-binding domain comprises a CD19 antibody, or fragment thereof. In some embodiments, the antigen-binding domain binds to CD20. In some embodiments, the antigen-binding domain comprises a CD20 antibody, or fragment thereof. In some embodiments, antibody fragments are as provided for herein, such as but not limited to a scFv antibody, an antigen binding domain, an ankyrin repeat (e.g. DARPIN), a VHH domain antibody, a nanobody, single domain antibody, a FN3 domain, or any combination thereof.

[00351] In some embodiments, the antigen-binding domain of the CAR comprises a V_H domain, a V_L domain, or a V_H and a V_L domain. In some embodiments, the V_H domain comprises an amino acid sequence having at least 75%, 80%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 89, or any value or range in-between.

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EVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVSTIS
WNSGSIGYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYCAKDIQYGN
YYYGMDVWGQGTITVTVSS (SEQ ID NO: 89)
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[00352] In some embodiments, the V_H domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 89. In some embodiments, the V_H domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 89. In some embodiments,

the V_H domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 89. In some embodiments, the V_H domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 89. In some embodiments, the V_H domain comprises an amino acid sequence having the sequence of SEQ ID NO: 89.

[00353] In some embodiments, the V_L domain comprises an amino acid sequence having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 90, or any value or range in-between.

EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDAS
NRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPITFGQGTSL
EIK (SEQ ID NO: 90)

[00354] In some embodiments, the V_L domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 90. In some embodiments, the V_L domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 90. In some embodiments, the V_L domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 90. In some embodiments, the V_L domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 90. In some embodiments, the V_L domain comprises an amino acid sequence having the sequence of SEQ ID NO: 90.

[00355] In some embodiments, the antigen-binding domain of the CAR comprises a V_H domain and a V_L domain. In some embodiments, the V_H and V_L domain are not linked by a linker peptide. In some embodiments, the V_H and V_L domain are linked by a linker peptide, such as those as provided for herein, including but not limited to: (GGGGS)_n (SEQ ID NO: 55), wherein each n is independently 1-5. In some embodiment n is 1. In some embodiment n is 2. In some embodiment n is 3. In some embodiment n is 4. In some embodiment n is 5.

[00356] In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 89, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 89, and comprises a V_L having at least 90% identity to SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%,

95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 89, and comprises a V_L having at least 95% identity to SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 89, and comprises a V_L having at least 98% identity to SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 89, and comprises a V_L having at least 99% identity to SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 89, and comprises a V_L having the sequence of SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 90% identity to SEQ ID NO: 89, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 89, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 98% identity to SEQ ID NO: 89, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 99% identity to SEQ ID NO: 89, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having an amino acid sequence of SEQ ID NO: 89, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 90% identity to SEQ ID NO: 89, and comprises a V_L having at least 90% identity to SEQ ID NO: 90. In

some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 89, and comprises a V_L having at least 90% identity to SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 90% identity to SEQ ID NO: 89, and comprises a V_L having at least 95% identity to SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 89, and comprises a V_L having at least 95% identity to SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 98% identity to SEQ ID NO: 89, and comprises a V_L having at least 98% identity to SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 99% identity to SEQ ID NO: 89, and comprises a V_L having at least 99% identity to SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having an amino acid sequence of SEQ ID NO: 89, and comprises a V_L having an amino acid sequence of SEQ ID NO: 90.

[00357] In some embodiments, the antigen-binding domain of the CAR comprises a formula of V_H-Z-V_L, wherein V_H is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 89, Z is a linker comprising the amino acid sequence GGGGSGGGGSGGGGS (SEQ ID NO: 91), and V_L is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising a formula of V_H-Z-V_L has an amino acid sequence as set forth below:

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EVQLVESGGGLVQPGPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVSTIS
WNSGSIGYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYCAKDIQYGN
YYYGMDVWGQGTITVTVSSGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERA
TLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDF
TLTISSLEPEDFAVYYCQQRSNWPITFGQGRLEIK (SEQ ID NO: 92)
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[00358] In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to a sequence of SEQ ID NO: 92. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 90% identity to a sequence of SEQ ID NO: 92. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 95% identity to a sequence of SEQ ID NO: 92. In some embodiments, the antigen-binding domain

of the CAR comprises an amino acid sequence having at least 98% identity to a sequence of SEQ ID NO: 92. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 99% identity to a sequence of SEQ ID NO: 92. In some embodiments, the antigen-binding domain of the CAR comprises the amino acid sequence of SEQ ID NO: 92.

[00359] In some embodiments, the antigen-binding domain of the CAR comprises a formula of V_L -Z- V_H , wherein V_L is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 90, Z is a linker comprising the amino acid sequence GGGGSGGGGSGGGGS (SEQ ID NO: 91), and V_H is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 89. In some embodiments, the antigen-binding domain of the CAR comprising a formula of V_L -Z- V_H has an amino acid sequence as set forth below:

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EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDAS
NRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPITFGQGTRL
EIKGGGSGGGGSGGGGSEVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAM
HWVRQAPGKGLEWVSTISWNSGSIQYADSVKGRFTISRDNAKKSLYLQMNSL
RAEDTALYYCAKDIQYGNYYYGMDVWGQGTITVTVSS (SEQ ID NO: 93)
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[00360] In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to a sequence of SEQ ID NO: 93. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 90% identity to a sequence of SEQ ID NO: 93. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 95% identity to a sequence of SEQ ID NO: 93. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 98% identity to a sequence of SEQ ID NO: 93. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 99% identity to a sequence of SEQ ID NO: 93. In some embodiments, the antigen-binding domain of the CAR comprises the amino acid sequence of SEQ ID NO: 93.

[00361] In some embodiments, the antigen-binding domain of the CAR comprises a V_H domain, a V_L domain, or a V_H and a V_L domain. In some embodiments, the V_H domain comprises an amino acid sequence having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 94, or any value or range in-between.

DIVLTQSPAILSASPGEKVTMTCRASSSVNYMDWYQKKPGSSPKPWIYATSN
 LASGVPARFSGSGSGTSLTISRVEAEDAATYYCQQWSFNPTFGGGTKLE
 IKGSTS (SEQ ID NO: 94)

[00362] In some embodiments, the V_H domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 94. In some embodiments, the V_H domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 94. In some embodiments, the V_H domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 94. In some embodiments, the V_H domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 94. In some embodiments, the V_H domain comprises an amino acid sequence having the sequence of SEQ ID NO: 94.

[00363] In some embodiments, the V_L domain comprises an amino acid sequence having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 95, or any value or range in-between.

EVQLQQSGAELVKPGASVKMSCKASGYTFTSYNMHWVKQTPGQGLEWIGAIY
 PGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSADYYCARSNYYGS
 SYWFFDVWGAGTTTVTVSS (SEQ ID NO: 95)

[00364] In some embodiments, the V_L domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 95. In some embodiments, the V_L domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 95. In some embodiments, the V_L domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 95. In some embodiments, the V_L domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 95. In some embodiments, the V_L domain comprises an amino acid sequence having the sequence of SEQ ID NO: 95.

[00365] In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 94, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 94, and comprises a V_L having at least 90% identity to SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%,

95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 94, and comprises a V_L having at least 95% identity to SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 94, and comprises a V_L having at least 98% identity to SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 94, and comprises a V_L having at least 99% identity to SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 94, and comprises a V_L having the sequence of SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 90% identity to SEQ ID NO: 94, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 94, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 98% identity to SEQ ID NO: 94, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 99% identity to SEQ ID NO: 94, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having an amino acid sequence of SEQ ID NO: 94, and comprises a V_L having at least 75%, 80%, 85%, 85%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 90% identity to SEQ ID NO: 94, and comprises a V_L having at least 90% identity to SEQ ID NO: 95. In

some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 94, and comprises a V_L having at least 90% identity to SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 90% identity to SEQ ID NO: 94, and comprises a V_L having at least 95% identity to SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 94, and comprises a V_L having at least 95% identity to SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 98% identity to SEQ ID NO: 94, and comprises a V_L having at least 98% identity to SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having at least 99% identity to SEQ ID NO: 94, and comprises a V_L having at least 99% identity to SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising a V_H domain and a V_L domain comprises a V_H domain having an amino acid sequence of SEQ ID NO: 94, and comprises a V_L having an amino acid sequence of SEQ ID NO: 95.

[00366] In some embodiments, the antigen-binding domain of the CAR comprises a formula of V_H-Z-V_L, wherein V_H is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 94, Z is a linker comprising the amino acid sequence GGGGSGGGGSGGGGS (SEQ ID NO: 91), and V_L is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising a formula of V_H-Z-V_L has an amino acid sequence as set forth below:

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DIVLTQSPAILSASPGEKVTMTCRASSSVNYMDWYQKKPGSSPKPWIYATSN
LASGVPARFSGSGSGTSYSLTISRVEAEDAATYYCQQWSFNPPTFGGGTKLE
IKGSTSGGGGSGGGGSGGGGSSEVQLQQSGAELVKPGASVKMSCKASGYTFT
SYNMHWVKQTPGQGLEWIGAIYPGNGDTSYNQKFKGKATLTADKSSSTAYMQ
LSSLTSEDSADYYCARSNYYGSSYWFFDVWGAGTTVTVSS (SEQ ID NO:
96)
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[00367] In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to a sequence of SEQ ID NO: 96. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 90% identity to a sequence of SEQ ID NO: 96. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 95% identity to a sequence of SEQ ID NO: 96. In some embodiments, the antigen-binding domain

of the CAR comprises an amino acid sequence having at least 98% identity to a sequence of SEQ ID NO: 96. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 99% identity to a sequence of SEQ ID NO: 96. In some embodiments, the antigen-binding domain of the CAR comprises the amino acid sequence of SEQ ID NO: 96.

[00368] In some embodiments, the antigen-binding domain of the CAR comprises a formula of V_L -Z- V_H , wherein V_L is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 95, Z is a linker comprising the amino acid sequence GGGGSGGGGSGGGGS (SEQ ID NO: 91), and V_H is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 94. In some embodiments, the antigen-binding domain of the CAR comprising a formula of V_L -Z- V_H has an amino acid sequence as set forth below:

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SEVQLQQSGAELVKPGASVKMSCKASGYFTSYNMHWVKQTPGQGLEWIGAI
YFGNGDTSYNQKFKGKATLTADKSSSTAYMQLSSLTSEDSADYYCARSNYYG
SSYWFFDVGAGTTVTVSSGGGGSGGGGSGGGGSDIVLTQSPAILSASPGEK
VTMTCRASSSVNYMDWYQKKPGSSPKPWIYATSNLASGVPARFSGSGSGTSY
SLTISRVEAEDAATYYCQWFSFNPPTFGGGTKLEIKGSTS (SEQ ID NO:
97)
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[00369] In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to a sequence of SEQ ID NO: 97. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 90% identity to a sequence of SEQ ID NO: 97. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 95% identity to a sequence of SEQ ID NO: 97. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 98% identity to a sequence of SEQ ID NO: 97. In some embodiments, the antigen-binding domain of the CAR comprises an amino acid sequence having at least 99% identity to a sequence of SEQ ID NO: 97. In some embodiments, the antigen-binding domain of the CAR comprises the amino acid sequence of SEQ ID NO: 97.

[00370] In some embodiments, the antigen-binding domain of the CAR comprises rituximab, ocrelizumab, obinutuzumab, ofatumumab, ibritumomab tiuxetan, tositumomab, or ublituximab. In some embodiment, the antigen-binding domain comprises rituximab. In some embodiment, the antigen-binding domain comprises ofatumumab. In some embodiments, the CAR comprises the 4-1BB domain as well.

[00371] In some embodiments, the CAR comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 99:

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MALPVTALLPLALLLHAARPGSEVQLVESGGGLVQPGRSLRLSCAASGFTF
NDYAMHWVRQAPGKGLEWVSTISWNSGSIQYADSVKGRFTISRDNAKKSLYL
QMNSLRAEDTALYYCAKDIQYGNYYYGMDVWGQGTITVTVSSGGGSGGGSG
GGGSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLI
YDASNRATGIPARFSGSGSGTDFTLTISISLEPEDFAVYYCQQRSNWPITFGQ
GTRLEIKSGLDFVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAA
GGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCNHRNKRGRKKLLYI
FKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYQQGQNQL
YNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYS
EIGMKGERRRGKRGHDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO:
99)
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or is substantially similar to SEQ ID NO: 99, or is an active fragment of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 99.

[00372] In some embodiments, the CAR comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 128:

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GSEVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVST
ISWNSGSIQYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYCAKDIQY
GNYYYGMDVWGQGTITVTVSSGGGSGGGGSGGGGSEIVLTQSPATLSLSPGE
RATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGT
DFTLTISISLEPEDFAVYYCQQRSNWPITFGQGTRLEIKSGLDFVPVFLPAKP
TTTPAPRPPTPAPTIASQPLSLRPEACRPAAAGGAVHTRGLDFACDIYIWAPL
AGTCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRF
PEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGR
DPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKRGHDGLYQGL
STATKDTYDALHMQALPPR (SEQ ID NO: 128)
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[00373] In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 128. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 128. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical

to a sequence of SEQ ID NO: 128. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 128.

[00374] In some embodiments, the CAR comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 129:

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EVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVSTIS
WNSGSIGYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYCAKDIQYGN
YYYGMDVWGQGTITVTVSSGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERA
TLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDF
TLTISSLEPEDFAVYYCQQRSNWPITFGQGTREIKSGLDFVPVFLPAKPTT
TPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAG
TCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFP
EEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDP
EMGGKPRRKNPQEGLYNELQDKMAEAYSEIGMKGERRRRGKGDGLYQGLST
ATKDTYDALHMQALPPR (SEQ ID NO: 129)
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[00375] In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 129. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 129. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 129. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 129.

[00376] In some embodiments, the CAR comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR corresponds to amino acids 24-267 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR corresponds to amino acids 24-267 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR corresponds to amino acids 24-267 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR corresponds to amino acids 24-267 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR corresponds to amino acids 24-267 of SEQ ID NO: 99.

[00377] In some embodiments, the CAR comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises a V_H and a V_L, wherein the V_H corresponds to amino acids 24-145 of SEQ ID NO: 99 and the V_L corresponds to amino acids 161-267 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises a V_H and a V_L, wherein the V_H corresponds to amino acids 24-145 of SEQ ID NO: 99 and the V_L corresponds to amino acids 161-267 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises a V_H and a V_L, wherein the V_H corresponds to amino acids 24-145 of SEQ ID NO: 99 and the V_L corresponds to amino acids 161-267 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises a V_H and a V_L, wherein the V_H corresponds to amino acids 24-145 of SEQ ID NO: 99 and the V_L corresponds to amino acids 161-267 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises a V_H and a V_L, wherein the V_H corresponds to amino acids 24-145 of SEQ ID NO: 99 and the V_L corresponds to amino acids 161-267 of SEQ ID NO: 99.

[00378] In some embodiments, the CAR comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR corresponds to amino acids 24-267 of SEQ ID NO: 99, a hinge domain of the CAR corresponds to amino acids 272-326 of SEQ ID NO: 99, a transmembrane domain of the CAR corresponds to amino acids 327-354 of SEQ ID NO: 99, a costimulatory domain of the CAR corresponds to amino acids 355-396 of SEQ ID NO: 99, and a signaling domain of the CAR corresponds to amino acids 397-508 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR corresponds to amino acids 24-267 of SEQ ID NO: 99, the hinge domain of the CAR corresponds to amino acids 272-326 of SEQ ID NO: 99, the transmembrane domain of the CAR corresponds to amino acids 327-354 of SEQ ID NO: 99, the costimulatory domain of the CAR corresponds to amino acids 355-396 of SEQ ID NO: 99, and the signaling domain of the CAR corresponds to amino acids 397-508 of SEQ ID NO: 99.

In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR corresponds to amino acids 24-267 of SEQ ID NO: 99, the hinge domain of the CAR corresponds to amino acids 272-326 of SEQ ID NO: 99, the transmembrane domain of the CAR corresponds to amino acids 327-354 of SEQ ID NO: 99, the costimulatory domain of the CAR corresponds to amino acids 355-396 of SEQ ID NO: 99, and the signaling domain of the CAR corresponds to amino acids 397-508 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR corresponds to amino acids 24-267 of SEQ ID NO: 99, the hinge domain of the CAR corresponds to amino acids 272-326 of SEQ ID NO: 99, the transmembrane domain of the CAR corresponds to amino acids 327-354 of SEQ ID NO: 99, the costimulatory domain of the CAR corresponds to amino acids 355-396 of SEQ ID NO: 99, and the signaling domain of the CAR corresponds to amino acids 397-508 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR corresponds to amino acids 24-267 of SEQ ID NO: 99, the hinge domain of the CAR corresponds to amino acids 272-326 of SEQ ID NO: 99, the transmembrane domain of the CAR corresponds to amino acids 327-354 of SEQ ID NO: 99, the costimulatory domain of the CAR corresponds to amino acids 355-396 of SEQ ID NO: 99, and the signaling domain of the CAR corresponds to amino acids 397-508 of SEQ ID NO: 99.

[00379] In some embodiments, the CAR comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises a V_H and a V_L, wherein the V_H corresponds to amino acids 24-145 of SEQ ID NO: 99 and the V_L corresponds to amino acids 161-267 of SEQ ID NO: 99, a hinge domain of the CAR corresponds to amino acids 272-326 of SEQ ID NO: 99, a transmembrane domain of the CAR corresponds to amino acids 327-354 of SEQ ID NO: 99, a costimulatory domain of the CAR corresponds to amino acids 355-396 of SEQ ID NO: 99, and a signaling domain of the CAR corresponds to amino acids 397-508 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises a V_H and a V_L, wherein the V_H corresponds to amino acids 24-145 of SEQ ID NO: 99 and the V_L corresponds to amino acids 161-267 of SEQ ID NO: 99, the hinge domain of the CAR corresponds to amino acids 272-326 of SEQ ID NO: 99, the transmembrane domain of the CAR corresponds to amino acids 327-354 of SEQ ID NO: 99, the costimulatory domain of the CAR corresponds to amino acids

355-396 of SEQ ID NO: 99, and the signaling domain of the CAR corresponds to amino acids 397-508 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises a V_H and a V_L , wherein the V_H corresponds to amino acids 24-145 of SEQ ID NO: 99 and the V_L corresponds to amino acids 161-267 of SEQ ID NO: 99, the hinge domain of the CAR corresponds to amino acids 272-326 of SEQ ID NO: 99, the transmembrane domain of the CAR corresponds to amino acids 327-354 of SEQ ID NO: 99, the costimulatory domain of the CAR corresponds to amino acids 355-396 of SEQ ID NO: 99, and the signaling domain of the CAR corresponds to amino acids 397-508 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises a V_H and a V_L , wherein the V_H corresponds to amino acids 24-145 of SEQ ID NO: 99 and the V_L corresponds to amino acids 161-267 of SEQ ID NO: 99, the hinge domain of the CAR corresponds to amino acids 272-326 of SEQ ID NO: 99, the transmembrane domain of the CAR corresponds to amino acids 327-354 of SEQ ID NO: 99, the costimulatory domain of the CAR corresponds to amino acids 355-396 of SEQ ID NO: 99, and the signaling domain of the CAR corresponds to amino acids 397-508 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises a V_H and a V_L , wherein the V_H corresponds to amino acids 24-145 of SEQ ID NO: 99 and the V_L corresponds to amino acids 161-267 of SEQ ID NO: 99, the hinge domain of the CAR corresponds to amino acids 272-326 of SEQ ID NO: 99, the transmembrane domain of the CAR corresponds to amino acids 327-354 of SEQ ID NO: 99, the costimulatory domain of the CAR corresponds to amino acids 355-396 of SEQ ID NO: 99, and the signaling domain of the CAR corresponds to amino acids 397-508 of SEQ ID NO: 99.

[00380] In some embodiments, the CAR comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises an amino acid sequence of SEQ ID NO: 92 and corresponds to amino acids 24-267 of SEQ ID NO: 99, a hinge domain of the CAR comprises an amino acid sequence of SEQ ID NO: 59 and corresponds to amino acids 272-326 of SEQ ID NO: 99, a transmembrane domain of the CAR comprises an amino acid sequence of SEQ ID NO: 61 and corresponds to amino acids 327-354 of SEQ ID NO: 99, a costimulatory domain of the CAR comprises an amino acid sequence of SEQ ID NO: 101 and corresponds to amino acids 355-396 of SEQ ID NO:

99, and a signaling domain of the CAR comprises an amino acid sequence of SEQ ID NO: 102 and corresponds to amino acids 397-508 of SEQ ID NO: 99.

KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCEL (SEQ ID NO: 101)
 RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPGEMGGKPRRK
 NPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDAL
 HMQALPPR (SEQ ID NO: 102)

In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises an amino acid sequence of SEQ ID NO: 92 and corresponds to amino acids 24-267 of SEQ ID NO: 99, the hinge domain of the CAR comprises an amino acid sequence of SEQ ID NO: 59 and corresponds to amino acids 272-326 of SEQ ID NO: 99, the transmembrane domain of the CAR comprises an amino acid sequence of SEQ ID NO: 61 and corresponds to amino acids 327-354 of SEQ ID NO: 99, the costimulatory domain of the CAR comprises an amino acid sequence of SEQ ID NO: 101 and corresponds to amino acids 355-396 of SEQ ID NO: 99, and the signaling domain of the CAR comprises an amino acid sequence of SEQ ID NO: 102 and corresponds to amino acids 397-508 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises an amino acid sequence of SEQ ID NO: 92 and corresponds to amino acids 24-267 of SEQ ID NO: 99, the hinge domain of the CAR comprises an amino acid sequence of SEQ ID NO: 59 and corresponds to amino acids 272-326 of SEQ ID NO: 99, the transmembrane domain of the CAR comprises an amino acid sequence of SEQ ID NO: 61 and corresponds to amino acids 327-354 of SEQ ID NO: 99, the costimulatory domain of the CAR comprises an amino acid sequence of SEQ ID NO: 101 and corresponds to amino acids 355-396 of SEQ ID NO: 99, and the signaling domain of the CAR comprises an amino acid sequence of SEQ ID NO: 102 and corresponds to amino acids 397-508 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises an amino acid sequence of SEQ ID NO: 92 and corresponds to amino acids 24-267 of SEQ ID NO: 99, the hinge domain of the CAR comprises an amino acid sequence of SEQ ID NO: 59 and corresponds to amino acids 272-326 of SEQ ID NO: 99, the transmembrane domain of the CAR comprises an amino acid sequence of SEQ ID NO: 61 and corresponds to amino acids 327-354 of SEQ ID NO: 99, the costimulatory domain of the CAR comprises an amino acid sequence of SEQ ID NO: 101 and corresponds to amino acids 355-

396 of SEQ ID NO: 99, and the signaling domain of the CAR comprises an amino acid sequence of SEQ ID NO: 102 and corresponds to amino acids 397-508 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises an amino acid sequence of SEQ ID NO: 92 and corresponds to amino acids 24-267 of SEQ ID NO: 99, the hinge domain of the CAR comprises an amino acid sequence of SEQ ID NO: 59 and corresponds to amino acids 272-326 of SEQ ID NO: 99, the transmembrane domain of the CAR comprises an amino acid sequence of SEQ ID NO: 61 and corresponds to amino acids 327-354 of SEQ ID NO: 99, the costimulatory domain of the CAR comprises an amino acid sequence of SEQ ID NO: 101 and corresponds to amino acids 355-396 of SEQ ID NO: 99, and the signaling domain of the CAR comprises an amino acid sequence of SEQ ID NO: 102 and corresponds to amino acids 397-508 of SEQ ID NO: 99.

[00381] In some embodiments, the CAR comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises a V_H and a V_L, wherein the V_H comprises an amino acid sequence of SEQ ID NO: 89 and corresponds to amino acids 24-145 of SEQ ID NO: 99 and the V_L comprises an amino acid sequence of SEQ ID NO: 90 and corresponds to amino acids 161-267 of SEQ ID NO: 99, a hinge domain of the CAR comprises an amino acid sequence of SEQ ID NO: 59 and corresponds to amino acids 272-326 of SEQ ID NO: 99, a transmembrane domain of the CAR comprises an amino acid sequence of SEQ ID NO: 61 and corresponds to amino acids 327-354 of SEQ ID NO: 99, a costimulatory domain of the CAR comprises an amino acid sequence of SEQ ID NO: 101 and corresponds to amino acids 355-396 of SEQ ID NO: 99, and a signaling domain of the CAR comprises an amino acid sequence of SEQ ID NO: 102 and corresponds to amino acids 397-508 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises a V_H and a V_L, wherein the V_H comprises an amino acid sequence of SEQ ID NO: 89 and corresponds to amino acids 24-145 of SEQ ID NO: 99 and the V_L comprises an amino acid sequence of SEQ ID NO: 90 and corresponds to amino acids 161-267 of SEQ ID NO: 99, the hinge domain of the CAR comprises an amino acid sequence of SEQ ID NO: 59 and corresponds to amino acids 272-326 of SEQ ID NO: 99, the transmembrane domain of the CAR comprises an amino acid sequence of SEQ ID NO: 61 and corresponds to amino acids 327-354 of SEQ ID NO: 99, the costimulatory domain of the CAR comprises an amino acid sequence of SEQ ID NO: 101 and corresponds to amino acids

355-396 of SEQ ID NO: 99, and the signaling domain of the CAR comprises an amino acid sequence of SEQ ID NO: 102 and corresponds to amino acids 397-508 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises a V_H and a V_L, wherein the V_H comprises an amino acid sequence of SEQ ID NO: 89 and corresponds to amino acids 24-145 of SEQ ID NO: 99 and the V_L comprises an amino acid sequence of SEQ ID NO: 90 and corresponds to amino acids 161-267 of SEQ ID NO: 99, the hinge domain of the CAR comprises an amino acid sequence of SEQ ID NO: 59 and corresponds to amino acids 272-326 of SEQ ID NO: 99, the transmembrane domain of the CAR comprises an amino acid sequence of SEQ ID NO: 61 and corresponds to amino acids 327-354 of SEQ ID NO: 99, the costimulatory domain of the CAR comprises an amino acid sequence of SEQ ID NO: 101 and corresponds to amino acids 355-396 of SEQ ID NO: 99, and the signaling domain of the CAR comprises an amino acid sequence of SEQ ID NO: 102 and corresponds to amino acids 397-508 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises a V_H and a V_L, wherein the V_H comprises an amino acid sequence of SEQ ID NO: 89 and corresponds to amino acids 24-145 of SEQ ID NO: 99 and the V_L comprises an amino acid sequence of SEQ ID NO: 90 and corresponds to amino acids 161-267 of SEQ ID NO: 99, the hinge domain of the CAR comprises an amino acid sequence of SEQ ID NO: 59 and corresponds to amino acids 272-326 of SEQ ID NO: 99, the transmembrane domain of the CAR comprises an amino acid sequence of SEQ ID NO: 61 and corresponds to amino acids 327-354 of SEQ ID NO: 99, the costimulatory domain of the CAR comprises an amino acid sequence of SEQ ID NO: 101 and corresponds to amino acids 355-396 of SEQ ID NO: 99, and the signaling domain of the CAR comprises an amino acid sequence of SEQ ID NO: 102 and corresponds to amino acids 397-508 of SEQ ID NO: 99. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 99, wherein the antigen binding domain of the CAR comprises a V_H and a V_L, wherein the V_H comprises an amino acid sequence of SEQ ID NO: 89 and corresponds to amino acids 24-145 of SEQ ID NO: 99 and the V_L comprises an amino acid sequence of SEQ ID NO: 90 and corresponds to amino acids 161-267 of SEQ ID NO: 99, the hinge domain of the CAR comprises an amino acid sequence of SEQ ID NO: 59 and corresponds to amino acids 272-326 of SEQ ID NO: 99, the transmembrane domain of the CAR comprises an amino acid sequence of SEQ ID NO: 61 and corresponds to amino acids 327-354 of SEQ ID NO: 99, the costimulatory domain of the CAR comprises an amino acid sequence of SEQ ID NO: 101 and

corresponds to amino acids 355-396 of SEQ ID NO: 99, and the signaling domain of the CAR comprises an amino acid sequence of SEQ ID NO: 102 and corresponds to amino acids 397-508 of SEQ ID NO: 99.

[00382] In any of the preceding embodiments, the antigen binding domain of the CAR may be directly fused to the hinge domain of the CAR. In any of the preceding embodiments, the antigen binding domain of the CAR may be connected to the hinge domain of the CAR through a polypeptide linker, such as those provided for herein. In some embodiments, the polypeptide linker comprises an amino acid sequence of SGLD (SEQ ID NO: 100). In some embodiments, the polypeptide linker connects the C-terminus of the antigen binding domain to the N-terminus of the hinge region. In some embodiments, the antigen binding domain comprises a V_H and a V_L and the polypeptide linker connects the C-terminus of the V_H to the N-terminus of the hinge region. In some embodiments, the antigen binding domain comprises a V_H and a V_L and the polypeptide linker connects the C-terminus of the V_L to the N-terminus of the hinge region.

[00383] These are merely illustrative in nature and are not limiting to the present embodiments and any chimeric antigen receptor can be delivered in conjunction with the viral particles and vectors provided for herein. These are non-limiting examples of CARs and any CAR construct could be encoded for by the nucleic acid molecule.

[00384] In some embodiments, the pseudotyped viral particle further comprises a heterologous nucleic acid molecule encoding a cargo of interest. The nucleic acid molecule may be useful for modulating the expression of a target gene. In some embodiments, the cargo can be used to modulate the activity of a cell or express a protein that is trafficked to the surface of the target cell. Therefore, in some embodiments, the nucleic acid may comprise an siRNA or an shRNA. The nucleic acid may also encode for a cargo of interest. Therefore, in some embodiments, the cargo of interest may comprise a polypeptide or portion thereof, a protein or portion thereof, a chimeric antigen receptor or portion thereof, or a tumor antigen or a portion thereof. In some embodiments, the cargo of interest is an antibody that is produced by the virus, which can then be secreted by the cell that is infected with the virus. The term “protein” can refer to any polypeptide that carries a native function in a cellular environment. Therefore, in some embodiments, the protein encoded by the nucleic acid cargo of interest may comprise an enzyme, a nuclear receptor, a transporter, a ribosomal protein, a membrane bound protein, a cytoplasmic protein, a G-protein coupled receptor, a voltage gated ion channel, a secretory protein, a mitochondria protein, a cytokine, a chimeric antigen receptor, a tumor antigen, or a portion or chimeric species thereof.

[00385] In some embodiments, the heterologous nucleic acid molecule encoding for a cargo of interest encodes for a CAR, a polypeptide comprising: i) a ligand binding extracellular domain (ECD); ii) an immune cell activating intracellular domain (ICD); and iii) a transmembrane domain linking the ECD to the ICD, or a combination thereof. In some embodiments, the CAR is as provided for herein. In some embodiments, the polypeptide comprising: i) a ligand binding extracellular domain (ECD); ii) an immune cell activating intracellular domain (ICD); and iii) a transmembrane domain linking the ECD to the ICD, is as provided for herein. In some embodiments, the CAR and the polypeptide are encoded by unique nucleic acid molecules. In some embodiments, the CAR and the polypeptide are encoded by the same nucleic acid molecule. Methods of encoding multiple proteins of interest from a single nucleic acid molecule are known in the art, and any such method is within the scope of the present disclosure. In some embodiments, the single nucleic acid molecule encodes the CAR and the polypeptide as a bicistronic molecule, wherein the CAR and the polypeptide are separated by a cleavable peptide linker. Cleavable peptide linkers are known in the art, and any such cleavable linker is within the scope of the present disclosure. In some embodiments, the cleavable peptide linker is a 2A peptide linker. In some embodiments, the nucleic acid molecule encodes for a bicistronic construct, wherein from 5' to 3' the nucleic acid molecule encodes for the CAR, the cleavable linker (e.g. a 2A linker), and the polypeptide. In some embodiments, the nucleic acid molecule encodes for a bicistronic construct, wherein from 5' to 3' the nucleic acid molecule encodes for the polypeptide, the cleavable linker (e.g. a 2A linker), and the CAR.

[00386] Without being bound to any particular theory, the viral particle comprising a heterologous viral glycoprotein as provided for herein and comprising a targeting moiety as provided for herein can be used to express the heterologous molecule of interest in the target cell. Thus, for example, the CAR and the polypeptide can be expressed in a T cell that is targeted by a viral particle pseudotyped with a VSV-G protein or a SVCV-G protein as provided for herein. Where the T cell is the intended target, the viral particle can comprise a targeting moiety that binds to a target on the surface of a T cell, such as, but not limited to CD2, CD3, CD4, CD5, CD7 or CD8. In some embodiments, the target is CD2. In some embodiments, the target is CD3. In some embodiments, the target is CD4. In some embodiments, the target is CD5. In some embodiments, the target is CD6. In some embodiments, the target is CD7. In some embodiments, the target is CD8. In some embodiments, the targeting moiety targeting CD7 is as provided for herein. In some embodiments, the targeting moiety targeting CD8 is as provided for herein.

[00387] In some embodiments, the pseudotyped viral particle is a recombinant lentivirus. In some embodiments, the recombinant pseudotyped viral particle is replication competent. In some embodiments, the recombinant pseudotyped viral particle is replication incompetent.

Exemplary viral particles comprising a targeting moiety comprising an Fc domain

[00388] In some embodiments, a viral particle is provided, the viral particle comprising a heterologous viral glycoprotein and a targeting moiety comprising a polypeptide having a formula T-S₁, wherein T is a target binding domain and S₁ is a stalk portion, wherein the heterologous viral glycoprotein comprises a sequence selected from SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 52, or SEQ ID NO: 53; wherein the target binding domain comprises a sequence selected from SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50, or SEQ ID NO: 51; wherein the stalk portion S₁ comprises a variant Fc protein comprising a sequence that is a variant of SEQ ID NO: 26, SEQ ID NO: 27, or SEQ ID NO: 28; wherein the variant of SEQ ID NO: 26 comprises one or more mutations selected from the group consisting of L234A, L235A, N297A, P329G, I253A, H310A, and H435A; wherein the variant of SEQ ID NO: 27 comprises one or more mutations selected from the group consisting of N297A, P329G, I253A, H310A, and H435A; wherein the variant of SEQ ID NO: 28 comprises one or more mutations selected from the group consisting of S228P, L235E, N297A, P329G, I253A, H310A, and H435A; and wherein the variant Fc protein further comprises a transmembrane domain comprising a sequence selected from SEQ ID NO: 61 or SEQ ID NO: 62. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 22. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 23. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 24. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 25. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 52. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 53. In some embodiments, the targeting moiety comprises an amino acid sequence of SEQ ID NO: 38. In some embodiments, the targeting moiety comprises an amino acid sequence of SEQ ID NO: 39. In some embodiments, the targeting moiety comprises an amino acid sequence of SEQ ID NO: 50. In some embodiments, the targeting moiety comprises an amino acid sequence of SEQ ID NO: 51. In some embodiments, the variant Fc protein is a variant of SEQ ID NO: 26 and comprises one or more mutations selected from the group consisting of L234A, L235A, N297A, P329G, I253A, H310A, and H435A. In some embodiments, the variant Fc protein is a variant of SEQ

ID NO: 27 and comprises one or more mutations selected from the group consisting of N297A, P329G, I253A, H310A, and H435A. In some embodiments, the variant Fc protein is a variant of SEQ ID NO: 28 and comprises one or more mutations selected from the group consisting of S228P, L235E, N297A, P329G, I253A, H310A, and H435A. In some embodiments, the transmembrane domain has an amino acid sequence of SEQ ID NO: 61. In some embodiments, the transmembrane domain has an amino acid sequence of SEQ ID NO: 62. In some embodiments, the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments, the heterologous molecule of interest is as provided for herein. In some embodiments, the heterologous molecule of interest is a CAR as provided for herein. In some embodiments, the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

[00389] In some embodiments, a viral particle is provided, said particle comprising a heterologous viral glycoprotein and a targeting moiety comprising a polypeptide having a formula T-S₁, wherein T is a target binding domain and S₁ is a stalk portion, wherein the heterologous viral glycoprotein comprises a sequence selected from SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 52, or SEQ ID NO: 53; wherein the target binding domain comprises a sequence selected from SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50, or SEQ ID NO: 51; wherein the stalk portion S₁ comprises a formula of L₁-Fc-L₂-X₁; wherein L₁ is a linker comprising a sequence selected from SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, or SEQ ID NO: 76, or is absent; Fc is a variant Fc protein comprising a sequence that is a variant of SEQ ID NO: 26, SEQ ID NO: 27, or SEQ ID NO: 28; wherein the variant of SEQ ID NO: 26 comprises one or more mutations selected from the group consisting of L234A, L235A, N297A, P329G, I253A, H310A, and H435A; wherein the variant of SEQ ID NO: 27 comprises one or more mutations selected from the group consisting of N297A, P329G, I253A, H310A, and H435A; wherein the variant of SEQ ID NO: 28 comprises one or more mutations selected from the group consisting of S228P, L235E, N297A, P329G, I253A, H310A, and H435A; L₂ is a linker comprising a sequence selected from SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, or SEQ ID NO: 76, or is absent; and X₁ is a polypeptide comprising a transmembrane domain having a formula of ECD-T_M-ICD, wherein ECD is an extracellular domain having a sequence of SEQ ID NO: 59, SEQ ID NO: 60, or any fragment thereof, or is

absent; T_M is a transmembrane domain having a sequence of SEQ ID NO: 61 or SEQ ID NO: 62 or any fragment thereof, and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64 or the ICD is absent. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 22. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 23. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 24. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 25. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 52. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 53. In some embodiments, T comprises an amino acid sequence of SEQ ID NO: 38. In some embodiments, T comprises an amino acid sequence of SEQ ID NO: 39. In some embodiments, T comprises an amino acid sequence of SEQ ID NO: 50. In some embodiments, T comprises an amino acid sequence of SEQ ID NO: 51. In some embodiments, L₁ is absent. In some embodiments, L₁ comprises an amino acid sequence of SEQ ID NO: 54. In some embodiments, L₁ comprises an amino acid sequence of SEQ ID NO: 55. In some embodiments, L₁ comprises an amino acid sequence of SEQ ID NO: 56. In some embodiments, L₁ comprises an amino acid sequence of SEQ ID NO: 57. In some embodiments, L₁ comprises an amino acid sequence of SEQ ID NO: 58. In some embodiments, L₁ comprises an amino acid sequence of SEQ ID NO: 73. In some embodiments, L₁ comprises an amino acid sequence of SEQ ID NO: 74. In some embodiments, L₁ comprises an amino acid sequence of SEQ ID NO: 75. In some embodiments, L₁ comprises an amino acid sequence of SEQ ID NO: 76. In some embodiments, the variant Fc protein is a variant of SEQ ID NO: 26 and comprises one or more mutations selected from the group consisting of L234A, L235A, N297A, P329G, I253A, H310A, and H435A. In some embodiments, the variant Fc protein is a variant of SEQ ID NO: 27 and comprises one or more mutations selected from the group consisting of N297A, P329G, I253A, H310A, and H435A. In some embodiments, the variant Fc protein is a variant of SEQ ID NO: 28 and comprises one or more mutations selected from the group consisting of S228P, L235E, N297A, P329G, I253A, H310A, and H435A. In some embodiments, L₂ is absent. In some embodiments, L₂ comprises an amino acid sequence of SEQ ID NO: 54. In some embodiments, L₂ comprises an amino acid sequence of SEQ ID NO: 55. In some embodiments, L₂ comprises an amino acid sequence of SEQ ID NO: 56. In some embodiments, L₂ comprises an amino acid sequence of SEQ ID NO: 57. In some embodiments, L₂ comprises an amino

acid sequence of SEQ ID NO: 58. In some embodiments, L₂ comprises an amino acid sequence of SEQ ID NO: 73. In some embodiments, L₂ comprises an amino acid sequence of SEQ ID NO: 74. In some embodiments, L₂ comprises an amino acid sequence of SEQ ID NO: 75. In some embodiments, L₂ comprises an amino acid sequence of SEQ ID NO: 76. In some embodiments, ECD is absent. In some embodiments, ECD comprises an amino acid sequence of SEQ ID NO: 59. In some embodiments, ECD comprises an amino acid sequence of SEQ ID NO: 60. In some embodiments, T_M comprises an amino acid sequence of SEQ ID NO: 61. In some embodiments, T_M comprises an amino acid sequence of SEQ ID NO: 62. In some embodiments, ICD is absent. In some embodiments, ICD is present and the env incorporation motif has an amino acid sequence of SEQ ID NO: 63. In some embodiments, ICD is present and the env incorporation motif has an amino acid sequence of SEQ ID NO: 64. In some embodiments, the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments, the heterologous molecule of interest is as provided for herein. In some embodiments, the heterologous molecule of interest is a CAR as provided for herein. In some embodiments, the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

~~[00390]~~ In some embodiments, a viral particle is provided, said particle comprising a heterologous viral glycoprotein and a targeting moiety comprising a polypeptide having a formula T-S₁, wherein T is a target binding domain and S₁ is a stalk portion, wherein the heterologous viral glycoprotein comprises a sequence selected from SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 52, or SEQ ID NO: 53; wherein the target binding domain comprises a sequence selected from SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50, or SEQ ID NO: 51; wherein the stalk portion S₁ comprises a formula of L₁-Fc-L₂-X₁; wherein L₁ is a linker comprising a sequence of SEQ ID NO: 55 or is absent; Fc is a variant Fc protein comprising a sequence that is a variant of SEQ ID NO: 26, SEQ ID NO: 27, or SEQ ID NO: 28; wherein the variant of SEQ ID NO: 26 comprises one or more mutations selected from the group consisting of L234A, L235A, N297A, P329G, I253A, H310A, and H435A; wherein the variant of SEQ ID NO: 27 comprises one or more mutations selected from the group consisting of N297A, P329G, I253A, H310A, and H435A; wherein the variant of SEQ ID NO: 28 comprises one or more mutations selected from the group consisting of S228P, L235E, N297A, P329G, I253A, H310A, and H435A; L₂ is a linker comprising a sequence of SEQ ID NO: 55 or is absent; and X₁ is a polypeptide comprising a transmembrane domain

having a formula of ECD-T_M-ICD, wherein ECD is an extracellular domain having a sequence of SEQ ID NO: 60, or a fragment thereof, or is absent; T_M is a transmembrane domain having a sequence of SEQ ID NO: 62 or a fragment thereof, and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64 or the ICD is absent. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 22. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 23. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 24. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 25. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 52. In some embodiments, the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 53. In some embodiments, T comprises an amino acid sequence of SEQ ID NO: 38. In some embodiments, T comprises an amino acid sequence of SEQ ID NO: 39. In some embodiments, T comprises an amino acid sequence of SEQ ID NO: 50. In some embodiments, T comprises an amino acid sequence of SEQ ID NO: 51. In some embodiments, L₁ is absent. In some embodiments, L₁ comprises an amino acid sequence of SEQ ID NO: 55. In some embodiments, the variant Fc protein is a variant of SEQ ID NO: 26 and comprises one or more mutations selected from the group consisting of L234A, L235A, N297A, P329G, I253A, H310A, and H435A. In some embodiments, the variant Fc protein is a variant of SEQ ID NO: 27 and comprises one or more mutations selected from the group consisting of N297A, P329G, I253A, H310A, and H435A. In some embodiments, the variant Fc protein is a variant of SEQ ID NO: 28 and comprises one or more mutations selected from the group consisting of S228P, L235E, N297A, P329G, I253A, H310A, and H435A. In some embodiments, L₂ is absent. In some embodiments, L₂ comprises an amino acid sequence of SEQ ID NO: 55. In some embodiments, ECD is absent. In some embodiments, ECD comprises an amino acid sequence of SEQ ID NO: 60. In some embodiments, T_M comprises an amino acid sequence of SEQ ID NO: 62. In some embodiments, ICD is absent. In some embodiments, ICD is present and the env incorporation motif has an amino acid sequence of SEQ ID NO: 63. In some embodiments, ICD is present and the env incorporation motif has an amino acid sequence of SEQ ID NO: 64. In some embodiments, the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments, the heterologous molecule of interest is as provided for herein. In some embodiments, the heterologous molecule of interest is a CAR as provided for herein. In some

embodiments, the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

[00391] In some embodiments, a viral particle is provided, said particle comprising a heterologous viral glycoprotein and a targeting moiety comprising a polypeptide having a formula T-S₁, wherein T is a target binding domain and S₁ is a stalk portion, wherein the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 23 or SEQ ID NO: 25; wherein the target binding domain comprises a sequence of SEQ ID NO: 39; wherein the stalk portion S₁ comprises a formula of L₁-Fc-L₂-X₁; wherein L₁ is a linker comprising a sequence of SEQ ID NO: 55; Fc is a variant Fc protein comprising a sequence of SEQ ID NO: 104; L₂ is a linker and is absent; and X₁ is a polypeptide comprising a transmembrane domain having a formula of ECD-T_M-ICD, wherein ECD is an extracellular domain having a sequence of SEQ ID NO: 60; T_M is a transmembrane domain having a sequence of SEQ ID NO: 62, and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63. In some embodiments, the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments, the heterologous molecule of interest is as provided for herein. In some embodiments, the heterologous molecule of interest is a CAR as provided for herein. In some embodiments, the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

[00392] In some embodiments, a viral particle is provided, said particle comprising a heterologous viral glycoprotein and a targeting moiety, wherein the heterologous viral glycoprotein comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 23 or SEQ ID NO: 25, having at least 95% identity to SEQ ID NO: 23 or SEQ ID NO: 25, having at least 99% identity to SEQ ID NO: 23 or SEQ ID NO: 25, or having at least 100% identity to SEQ ID NO: 23 or SEQ ID NO: 25; and the targeting moiety comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 98, at least 95% identity to SEQ ID NO: 98, at least 99% identity to SEQ ID NO: 98, or at least 100% identity to SEQ ID NO: 98. In some embodiments, the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments, the heterologous molecule of interest is as provided for herein. In some embodiments, the heterologous molecule of interest is a CAR as provided for herein. In some embodiments, the CAR comprises an amino acid

sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

[00393] In some embodiments, a viral particle is provided, said particle comprising a heterologous viral glycoprotein and a targeting moiety, wherein the heterologous viral glycoprotein comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 52 or SEQ ID NO: 53, having at least 95% identity to SEQ ID NO: 52 or SEQ ID NO: 53, having at least 99% identity to SEQ ID NO: 52 or SEQ ID NO: 53, or having at least 100% identity to SEQ ID NO: 52 or SEQ ID NO: 53; and the targeting moiety comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 98, at least 95% identity to SEQ ID NO: 98, at least 99% identity to SEQ ID NO: 98, or at least 100% identity to SEQ ID NO: 98. In some embodiments, the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments, the heterologous molecule of interest is as provided for herein. In some embodiments, the heterologous molecule of interest is a CAR as provided for herein. In some embodiments, the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

Exemplary viral particles comprising a targeting moiety comprising a flexible polypeptide

[00394] In some embodiments, a viral particle is provided, the viral particle comprising a heterologous viral structural protein and a targeting moiety, wherein the targeting moiety comprises a polypeptide having a formula of T-S₁, wherein T is a target binding domain and S₁ is a stalk portion; wherein the target binding domain comprises an amino acid sequence of SEQ ID NO: 38 or SEQ ID NO: 39; wherein the stalk portion S₁ comprises a formula of L₃-X₁; wherein L₃ is a flexible peptide linker having an amino acid sequence selected from SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, or SEQ ID NO: 58; and X₁ is a polypeptide comprising a transmembrane domain having a formula ECD-T_M-ICD, wherein ECD is an extracellular domain having an amino acid sequence of SEQ ID NO: 59 or SEQ ID NO: 60, or is a fragment thereof, or is absent; T_M is a transmembrane domain having an amino acid sequence of SEQ ID NO: 61 or SEQ ID NO: 62, or a fragment thereof; and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle or is absent, wherein the ICD comprises an env incorporation motif, said env incorporation motif having an amino acid sequence of SEQ ID NO: 63 or SEQ

ID NO: 64. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 38. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 39. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 54. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 55. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 56. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 57. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 58. In some embodiments, the ECD has an amino acid sequence of SEQ ID NO: 59. In some embodiments, the ECD has an amino acid sequence of SEQ ID NO: 60. In some embodiments, the T_M has an amino acid sequence of SEQ ID NO: 61. In some embodiments, the T_M has an amino acid sequence of SEQ ID NO: 62. In some embodiments, the env incorporation motif has an amino acid sequence of SEQ ID NO: 63. In some embodiments, the env incorporation motif has an amino acid sequence of SEQ ID NO: 64. In some embodiments, the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments, the heterologous molecule of interest is as provided for herein. In some embodiments, the heterologous molecule of interest is a CAR as provided for herein. In some embodiments, the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

[00395] In some embodiments, a viral particle is provided, the viral particle comprising a heterologous viral structural protein and a targeting moiety, wherein the targeting moiety comprises a polypeptide having a formula of T-S₁, wherein T is a target binding domain and S₁ is a stalk portion; wherein the target binding domain comprises an amino acid sequence of SEQ ID NO: 50 or SEQ ID NO: 51; wherein the stalk portion S₁ comprises a formula of L₃-X₁; wherein L₃ is a flexible peptide linker having an amino acid sequence selected from SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, or SEQ ID NO: 58; and X₁ is a polypeptide comprising a transmembrane domain having a formula ECD-T_M-ICD, wherein ECD is an extracellular domain having an amino acid sequence of SEQ ID NO: 59 or SEQ ID NO: 60, or is a fragment thereof, or is absent; T_M is a transmembrane domain having an amino acid sequence of SEQ ID NO: 61 or SEQ ID NO: 62, or a fragment thereof; and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle or is absent, wherein the ICD comprises an env incorporation motif, said env incorporation motif having an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64. In some embodiments, the target binding domain has an amino acid sequence of

SEQ ID NO: 50. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 51. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 54. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 55. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 56. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 57. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 58. In some embodiments, the ECD has an amino acid sequence of SEQ ID NO: 59. In some embodiments, the ECD has an amino acid sequence of SEQ ID NO: 60. In some embodiments, the T_M has an amino acid sequence of SEQ ID NO: 61. In some embodiments, the T_M has an amino acid sequence of SEQ ID NO: 62. In some embodiments, the env incorporation motif has an amino acid sequence of SEQ ID NO: 63. In some embodiments, the env incorporation motif has an amino acid sequence of SEQ ID NO: 64. In some embodiments, the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments, the heterologous molecule of interest is as provided for herein. In some embodiments, the heterologous molecule of interest is a CAR as provided for herein. In some embodiments, the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

[00396] In some embodiments, a viral particle is provided, the viral particle comprising a heterologous viral structural protein and a targeting moiety, wherein the targeting moiety comprises a polypeptide having a formula of T-S₁, wherein the heterologous viral structural protein comprises a sequence of SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 52, or SEQ ID NO: 53; wherein T is a target binding domain and S₁ is a stalk portion, wherein the target binding domain comprises an amino acid sequence of SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50, or SEQ ID NO: 51; wherein the stalk portion S₁ comprises a formula of L₃-X₁; wherein L₃ is a flexible peptide linker having an amino acid sequence selected from SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, or SEQ ID NO: 58; and X₁ is a polypeptide comprising a transmembrane domain having a formula ECD-T_M-ICD, wherein ECD is an extracellular domain having an amino acid sequence of SEQ ID NO: 59 or SEQ ID NO: 60, or is a fragment thereof, or is absent; T_M is a transmembrane domain having an amino acid sequence of SEQ ID NO: 61 or SEQ ID NO: 62, or a fragment thereof; and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle or is absent, wherein the ICD comprises an env incorporation motif, said env incorporation motif having an amino

acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64. In some embodiments, the heterologous viral structural protein comprises a sequence of SEQ ID NO: 22. In some embodiments, the heterologous viral structural protein comprises a sequence of SEQ ID NO: 23. In some embodiments, the heterologous viral structural protein comprises a sequence of SEQ ID NO: 24. In some embodiments, the heterologous viral structural protein comprises a sequence of SEQ ID NO: 25. In some embodiments, the heterologous viral structural protein comprises a sequence of SEQ ID NO: 52. In some embodiments, the heterologous viral structural protein comprises a sequence of SEQ ID NO: 53. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 38. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 39. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 50. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 51. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 54. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 55. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 56. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 57. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 58. In some embodiments, the ECD has an amino acid sequence of SEQ ID NO: 59. In some embodiments, the ECD has an amino acid sequence of SEQ ID NO: 60. In some embodiments, the T_M has an amino acid sequence of SEQ ID NO: 61. In some embodiments, the T_M has an amino acid sequence of SEQ ID NO: 62. In some embodiments, the env incorporation motif has an amino acid sequence of SEQ ID NO: 63. In some embodiments, the env incorporation motif has an amino acid sequence of SEQ ID NO: 64. In some embodiments, the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments, the heterologous molecule of interest is as provided for herein. In some embodiments, the heterologous molecule of interest is a CAR as provided for herein. In some embodiments, the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99. At least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

[00397] In some embodiments, a viral particle is provided, the viral particle comprising a heterologous viral structural protein and a targeting moiety, wherein the targeting moiety comprises a polypeptide having a formula of T-S₁, wherein the heterologous viral structural protein comprises a sequence of SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 52, or SEQ ID NO: 53; wherein T is a target binding domain and S₁ is a stalk portion, wherein the target binding domain comprises an amino acid sequence of SEQ ID

NO: 38, SEQ ID NO: 39, SEQ ID NO: 50, or SEQ ID NO: 51; wherein the stalk portion S₁ comprises a formula of L₃-X₁; wherein L₃ is a flexible peptide linker having an amino acid sequence of SEQ ID NO: 55; and X₁ is a polypeptide comprising a transmembrane domain having a formula ECD-T_M-ICD, wherein ECD is an extracellular domain having an amino acid sequence of SEQ ID NO: 59, or is a fragment thereof, or is absent; T_M is a transmembrane domain having an amino acid sequence of SEQ ID NO: 61, or a fragment thereof; and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle or is absent, wherein the ICD comprises an env incorporation motif, said env incorporation motif having an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64. In some embodiments, the heterologous viral structural protein comprises a sequence of SEQ ID NO: 22. In some embodiments, the heterologous viral structural protein comprises a sequence of SEQ ID NO: 23. In some embodiments, the heterologous viral structural protein comprises a sequence of SEQ ID NO: 24. In some embodiments, the heterologous viral structural protein comprises a sequence of SEQ ID NO: 25. In some embodiments, the heterologous viral structural protein comprises a sequence of SEQ ID NO: 52. In some embodiments, the heterologous viral structural protein comprises a sequence of SEQ ID NO: 53. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 38. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 39. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 50. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 51. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 55. In some embodiments, the ECD has an amino acid sequence of SEQ ID NO: 59. In some embodiments, the T_M has an amino acid sequence of SEQ ID NO: 61. In some embodiments, the env incorporation motif has an amino acid sequence of SEQ ID NO: 63. In some embodiments, the env incorporation motif has an amino acid sequence of SEQ ID NO: 64. In some embodiments, the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments, the heterologous molecule of interest is as provided for herein. In some embodiments, the heterologous molecule of interest is a CAR as provided for herein. In some embodiments, the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

[00398] In some embodiments, a viral particle is provided, the viral particle comprising a heterologous viral structural protein and a targeting moiety, wherein the targeting moiety

comprises a polypeptide having a formula of T-S₁, wherein the heterologous viral structural protein comprises a sequence of SEQ ID NO: 23 or SEQ ID NO: 25; wherein T is a target binding domain and S₁ is a stalk portion, wherein the target binding domain comprises an amino acid sequence of SEQ ID NO: 39; wherein the stalk portion S₁ comprises a formula of L₃-X₁; wherein L₃ is a flexible peptide linker having an amino acid sequence of SEQ ID NO: 55; and X₁ is a polypeptide comprising a transmembrane domain having a formula ECD-T_M-ICD, wherein ECD is an extracellular domain having an amino acid sequence of SEQ ID NO: 59, or is a fragment thereof, or is absent; T_M is a transmembrane domain having an amino acid sequence of SEQ ID NO: 61, or a fragment thereof; and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle or is absent, wherein the ICD comprises an env incorporation motif, said env incorporation motif having an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64. In some embodiments, the heterologous viral structural protein comprises a sequence of SEQ ID NO: 23. In some embodiments, the heterologous viral structural protein comprises a sequence of SEQ ID NO: 25. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 39. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 55. In some embodiments, the ECD has an amino acid sequence of SEQ ID NO: 59. In some embodiments, the T_M has an amino acid sequence of SEQ ID NO: 61. In some embodiments, the env incorporation motif has an amino acid sequence of SEQ ID NO: 63. In some embodiments, the env incorporation motif has an amino acid sequence of SEQ ID NO: 64. In some embodiments, the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments, the heterologous molecule of interest is as provided for herein. In some embodiments, the heterologous molecule of interest is a CAR as provided for herein. In some embodiments, the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

[00399] In some embodiments, a viral particle is provided, the viral particle comprising a heterologous viral structural protein and a targeting moiety, wherein the targeting moiety comprises a polypeptide having a formula of T-S₁, wherein the heterologous viral structural protein comprises a sequence of SEQ ID NO: 52 or SEQ ID NO: 53; wherein T is a target binding domain and S₁ is a stalk portion, wherein the target binding domain comprises an amino acid sequence of SEQ ID NO: 39; wherein the stalk portion S₁ comprises a formula of L₃-X₁; wherein L₃ is a flexible peptide linker having an amino acid sequence of SEQ ID NO:

55; and X₁ is a polypeptide comprising a transmembrane domain having a formula ECD-T_M-ICD, wherein ECD is an extracellular domain having an amino acid sequence of SEQ ID NO: 59, or is a fragment thereof, or is absent; T_M is a transmembrane domain having an amino acid sequence of SEQ ID NO: 61, or a fragment thereof; and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle or is absent, wherein the ICD comprises an env incorporation motif, said env incorporation motif having an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64. In some embodiments, the heterologous viral structural protein comprises a sequence of SEQ ID NO: 52. In some embodiments, the heterologous viral structural protein comprises a sequence of SEQ ID NO: 53. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 39. In some embodiments, L₃ has an amino acid sequence of SEQ ID NO: 55. In some embodiments, the ECD has an amino acid sequence of SEQ ID NO: 59. In some embodiments, the T_M has an amino acid sequence of SEQ ID NO: 61. In some embodiments, the env incorporation motif has an amino acid sequence of SEQ ID NO: 63. In some embodiments, the env incorporation motif has an amino acid sequence of SEQ ID NO: 64. In some embodiments, the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest. In some embodiments, the heterologous molecule of interest is as provided for herein. In some embodiments, the heterologous molecule of interest is a CAR as provided for herein. In some embodiments, the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

[00400] In some embodiments, a pharmaceutical composition is provided comprising the envelope pseudotyped viral particles or vectors as provided for herein, i.e. a particle that comprises a VSV-G mutant protein provided for herein.

[00401] In some embodiments, methods of delivering a cargo of interest to a cell are provided. In some embodiments, the methods comprise contacting the cell with the pseudotyped viral-like particles or viral vectors as provided for herein, or a pharmaceutical composition comprising the same.

[00402] In some embodiments, methods of delivering a cargo of interest to a cell in a subject are provided. In some embodiments, the methods comprise administering to the subject the pseudotyped viral-like particles or viral vectors as provided for herein, or a pharmaceutical composition comprising the same. In some embodiments, the cargo is a chimeric antigen receptor or as otherwise provided for herein.

[00403] In some embodiments, methods for of delivering a chimeric antigen receptor to a T-cell in a subject are provided. In some embodiments, the methods comprising administering to the subject the pseudotyped viral-like particles or viral vectors as provided for herein, or a pharmaceutical composition comprising the same, wherein the pseudotyped viral-like particle or viral vector comprises a heterologous nucleic acid molecule encoding the chimeric antigen receptor.

[00404] Also provided herein are nucleic acid molecules encoding a mutant VSV-G protein as provided for herein.

[00405] Methods of making the viral like particles or vectors comprising a mutant VSV-G protein are also provided. In some embodiments, the methods comprise transfecting or transducing a packaging cell line with the nucleic acid molecules encoding a mutant VSV-G protein as provided for herein under conditions sufficient to produce the pseudotyped viral-like particles or viral vectors. In some embodiments, the methods comprise transfecting or transducing a packaging cell line with the plurality of nucleic acid molecules provided for herein under conditions sufficient to produce the pseudotyped viral-like particles or viral vectors. In some embodiments, methods further comprise isolating the pseudotyped viral-like particle or viral vector. In some embodiments, the nucleic acid molecules also comprise a nucleic acid molecule encoding a targeting moiety and/or a cargo that is to be delivered by the viral vector that is produced.

Methods of Treating Cancer

[00406] Also provided for herein are methods of treating cancer in a subject. In some embodiments, the methods comprise administering to the subject the pseudotyped viral-like particles or viral vectors as provided for herein, or a pharmaceutical composition comprising the same, wherein the pseudotyped viral-like particle or viral vector comprises a heterologous nucleic acid molecule encoding the chimeric antigen receptor.

[00407] In some embodiments, the methods comprise administering to the subject immune cells that have been transduced by the pseudotyped viral-like particle or viral vectors as provided for herein. In some embodiments, the immune cells are first isolated from the subject prior to transduction by the pseudotyped viral-like particle or viral vectors as provided for herein.

[00408] Also provided herein are methods of treating a disease in a subject in need thereof.

[00409] In some embodiments, the methods provided include, but are not limited to, methods of treating a disease in a subject in need thereof, comprising administering to the subject the viral particle(s) provided herein to treat the disease.

[00410] In certain embodiments, the disease is a cancer. In addition, the compositions provided for herein can be used in methods for the treatment of any condition related to a cancer, such as a cell-mediated immune response against a tumor cell(s), where it is desirable to treat or alleviate the disease. The types of cancers to be treated include, but are not limited to, carcinoma, blastoma, sarcoma, certain leukemia or lymphoid malignancies, benign and malignant tumors, malignancies e.g., sarcomas, carcinomas, and melanomas. Other exemplary cancers include, but are not limited to, breast cancer, prostate cancer, ovarian cancer, cervical cancer, skin cancer, pancreatic cancer, colorectal cancer, renal cancer, liver cancer, brain cancer, lymphoma, leukemia, lung cancer, thyroid cancer, and the like. The cancers may be non-solid tumors (such as hematological tumors) or solid tumors. Adult tumors/cancers and pediatric tumors/cancers are also included. In one embodiment, the cancer is a hematological tumor. In one embodiment, the cancer is a carcinoma. In one embodiment, the cancer is a sarcoma. In one embodiment, the cancer is a leukemia. In one embodiment the cancer is a solid tumor.

[00411] Solid tumors are abnormal masses of tissue that usually do not contain cysts or liquid areas. Solid tumors can be benign or malignant. Different types of solid tumors are named for the type of cells that form them (such as sarcomas, carcinomas, and lymphomas). Examples of solid tumors, such as sarcomas and carcinomas, include fibrosarcoma, myxosarcoma, liposarcoma, chondrosarcoma, osteosarcoma, synovioma, mesothelioma, Ewing's tumor, leiomyosarcoma, rhabdomyosarcoma, colon carcinoma, lymphoid malignancy, pancreatic cancer, breast cancer, lung cancers, ovarian cancer, prostate cancer, hepatocellular carcinoma, squamous cell carcinoma, basal cell carcinoma, adenocarcinoma, sweat gland carcinoma, medullary thyroid carcinoma, papillary thyroid carcinoma, pheochromocytomas sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinomas, medullary carcinoma, bronchogenic carcinoma, renal cell carcinoma, hepatoma, bile duct carcinoma, choriocarcinoma, Wilms' tumor, cervical cancer, testicular tumor, seminoma, bladder carcinoma, melanoma, CNS tumors (such as a glioma (such as brainstem glioma and mixed gliomas), glioblastoma (also known as glioblastoma multiforme) astrocytoma, CNS lymphoma, germinoma, medulloblastoma, Schwannoma craniopharyngioma, ependymoma, pinealoma, hemangioblastoma, acoustic neuroma, oligodendroglioma, meningioma, neuroblastoma, retinoblastoma and brain metastases).

[00412] Carcinomas that can be amenable to therapy by the methods disclosed herein include, but are not limited to, esophageal carcinoma, hepatocellular carcinoma, basal cell carcinoma (a form of skin cancer), squamous cell carcinoma (various tissues), bladder carcinoma, including transitional cell carcinoma (a malignant neoplasm of the bladder), bronchogenic carcinoma, colon carcinoma, colorectal carcinoma, gastric carcinoma, lung carcinoma, including small cell carcinoma and non-small cell carcinoma of the lung, adrenocortical carcinoma, thyroid carcinoma, pancreatic carcinoma, breast carcinoma, ovarian carcinoma, prostate carcinoma, adenocarcinoma, sweat gland carcinoma, sebaceous gland carcinoma, papillary carcinoma, papillary adenocarcinoma, cystadenocarcinoma, medullary carcinoma, renal cell carcinoma, ductal carcinoma in situ or bile duct carcinoma, choriocarcinoma, seminoma, embryonal carcinoma, Wilm's tumor, cervical carcinoma, uterine carcinoma, testicular carcinoma, osteogenic carcinoma, epithelial carcinoma, and nasopharyngeal carcinoma.

[00413] In certain exemplary embodiments, the compositions provided herein can be used in methods to treat a myeloma, or a condition related to myeloma. Examples of myeloma or conditions related thereto include, without limitation, light chain myeloma, non-secretory myeloma, monoclonal gamopathy of undertermined significance (MGUS), plasmacytoma (e.g., solitary, multiple solitary, extramedullary plasmacytoma), amyloidosis, and multiple myeloma. In some embodiments, methods of treating multiple myeloma are provided. In some embodiments, the multiple myeloma is refractory myeloma. In some embodiments, the multiple myeloma is relapsed myeloma.

[00414] In certain exemplary embodiments, the in vivo modified immune cells produced using the compositions provided herein are used to treat a melanoma, or a condition related to melanoma. Examples of melanoma or conditions related thereto include, without limitation, superficial spreading melanoma, nodular melanoma, lentigo maligna melanoma, acral lentiginous melanoma, amelanotic melanoma, or melanoma of the skin (e.g., cutaneous, eye, vulva, vagina, rectum melanoma). In some embodiments, the melanoma is cutaneous melanoma. In some embodiments, the melanoma is refractory melanoma. In some embodiments, the melanoma is relapsed melanoma.

[00415] In some embodiments, the compositions provided herein are used to treat a sarcoma, or a condition related to sarcoma. Examples of sarcoma or conditions related thereto include, without limitation, angiosarcoma, chondrosarcoma, chordoma, endotheliosarcoma, Ewing's sarcoma, fibrosarcoma, gastrointestinal stromal tumor, leiomyosarcoma, liposarcoma, lymphangiosarcoma, lymphangioendotheliosarcoma, mesothelioma, malignant peripheral

nerve sheath tumor, myxosarcoma, osteogenic sarcoma, osteosarcoma, pleomorphic sarcoma, rhabdomyosarcoma, synovioma, synovial sarcoma, and other soft tissue sarcomas. In some embodiments, the sarcoma is synovial sarcoma. In some embodiments, the sarcoma is liposarcoma such as myxoid/round cell liposarcoma, differentiated/dedifferentiated liposarcoma, or pleomorphic liposarcoma. In some embodiments, the sarcoma is myxoid/round cell liposarcoma. In some embodiments, the sarcoma is refractory sarcoma. In some embodiments, the sarcoma is relapsed sarcoma.

[00416] In some embodiments, the subject has been treated with a therapeutic agent targeting the disease or condition, e.g. the tumor, prior to administration of the composition. In some aspects, the subject is refractory or non-responsive to the other therapeutic agent. In some embodiments, the subject has persistent or relapsed disease, e.g., following treatment with another therapeutic intervention, including chemotherapy, radiation, and/or hematopoietic stem cell transplantation (HSCT), e.g., allogenic HSCT. In some embodiments, the administration effectively treats the subject despite the subject having become resistant to another therapy.

[00417] In some embodiments, the subject is responsive to the other therapeutic agent, and treatment with the therapeutic agent reduces disease burden. In some aspects, the subject is initially responsive to the therapeutic agent, but exhibits a relapse of the disease or condition over time. In some embodiments, the subject has not relapsed. In some such embodiments, the subject is determined to be at risk for relapse, such as at a high risk of relapse, and thus the composition is administered prophylactically, e.g., to reduce the likelihood of or prevent relapse. In some aspects, the subject has not received prior treatment with another therapeutic agent.

[00418] The administration of the compositions may be carried out in any convenient manner known to those of skill in the art. For example, the compositions may be administered to a subject by aerosol inhalation, injection, ingestion, transfusion, implantation or transplantation. The compositions described herein may be administered to a patient transarterially, subcutaneously, intradermally, intratumorally, intranodally, intramedullary, intramuscularly, by intravenous (i.v.) injection, intraperitoneally, intranasally, intracranially, or intraosseously. In other instances, the compositions is injected directly into a site of a local disease site in the subject, a lymph node, an organ, a tumor, and the like.

[00419] For the prevention or treatment of disease, the appropriate dosage may depend on the type of disease to be treated, the severity and course of the disease, whether the composition is administered for preventive or therapeutic purposes, previous therapy, the subject's clinical

history and response to the treatment, and the discretion of the attending physician. The composition is, in some embodiments, suitably administered to the subject at one time or over a series of treatments.

[00420] In some embodiments, the composition is administered as part of a combination treatment, such as simultaneously with or sequentially with, in any order, another therapeutic intervention, such as an antibody or produced cell or receptor or agent, such as a cytotoxic or therapeutic agent. The composition(s), in some embodiments, is co-administered with one or more additional therapeutic agents or in connection with another therapeutic intervention, either simultaneously or sequentially in any order. In some contexts, the composition is co-administered with another therapy sufficiently close in time such that the composition enhances the effect of one or more additional therapeutic agents, or vice versa. In some embodiments, the composition is administered prior to the one or more additional therapeutic agents. In some embodiments, the composition is administered after the one or more additional therapeutic agents. In some embodiments, the one or more additional agents includes a cytokine, such as IL-2, for example, to enhance persistence. In some embodiments, the methods comprise administration of a chemotherapeutic agent. In some embodiments, the methods do not comprise the administration of a chemotherapeutic agent.

[00421] In certain embodiments, the compositions may be administered to a subject in combination with an immune checkpoint antibody (e.g., an anti-PD1, anti-CTLA-4, or anti-PDL1 antibody). For example, viral vectors may be administered in combination with an antibody or antibody fragment targeting, for example, PD-1 (programmed death 1 protein). Examples of anti-PD-1 antibodies include, but are not limited to, pembrolizumab (KEYTRUDA®, formerly lambrolizumab, also known as MK-3475), and nivolumab (BMS-936558, MDX-1106, ONO-4538, OPDIVO®) or an antigen-binding fragment thereof. In certain embodiments, the compositions may be administered in combination with an anti-PD-L1 antibody or antigen-binding fragment thereof. Examples of anti-PD-L1 antibodies include, but are not limited to, BMS-936559, MPDL3280A (TECENTRIQ®, Atezolizumab), and MEDI4736 (Durvalumab, Imfinzi). In certain embodiments, the composition may be administered in combination with an anti-CTLA-4 antibody or antigen-binding fragment thereof. An example of an anti-CTLA-4 antibody includes, but is not limited to, Ipilimumab (trade name Yervoy). Other types of immune checkpoint modulators may also be used including, but not limited to, small molecules, siRNA, miRNA, and CRISPR systems. Immune checkpoint modulators may be administered before, after, or concurrently with the viral vector. In certain embodiments, combination treatment comprising an immune checkpoint modulator

may increase the therapeutic efficacy of a therapy comprising a composition as provided herein. The other therapeutic can be administered simultaneously, before, or after the compositions provided herein are administered to the subject.

[00422] In certain embodiments, the subject is provided a secondary treatment. Secondary treatments include but are not limited to chemotherapy, radiation, surgery, and medications. In some embodiments, the subject is not provided a secondary treatment.

[00423] In some embodiments, the methods are performed without a lymphodepletion step, such as the administration of cyclophosphamide and/or fludarabine.

[00424] In some embodiments, the subject can be administered a conditioning therapy after the administration of the compositions to kill certain immune cells that are not transduced with the CAR encoded by the compositions. This can be done by including a selection marker that is encoded by the nucleic acid cargo of interest. In some embodiments, the conditioning therapy comprises administering an effective amount of cyclophosphamide to the subject. In some embodiments, the conditioning therapy comprises administering an effective amount of fludarabine to the subject. In some embodiments, the conditioning therapy comprises administering an effective amount of a combination of cyclophosphamide and fludarabine to the subject.

[00425] In some embodiments, a specific dosage regimen of the present disclosure includes a lymphodepletion step after the administration of the composition. In an exemplary embodiment, the lymphodepletion step includes administration of cyclophosphamide and/or fludarabine.

[00426] In some embodiments, the lymphodepletion step includes administration of cyclophosphamide at a dose of between about 200 mg/m²/day and about 2000 mg/m²/day (e.g., 200 mg/m²/day, 300 mg/m²/day, or 500 mg/m²/day). In an exemplary embodiment, the dose of cyclophosphamide is about 300 mg/m²/day. In some embodiments, the lymphodepletion step includes administration of fludarabine at a dose of between about 20 mg/m²/day and about 900 mg/m²/day (e.g., 20 mg/m²/day, 25 mg/m²/day, 30 mg/m²/day, or 60 mg/m²/day). In an exemplary embodiment, the dose of fludarabine is about 30 mg/m²/day.

[00427] In some embodiment, the lymphodepletion step includes administration of cyclophosphamide at a dose of between about 200 mg/m²/day and about 2000 mg/m²/day (e.g., 200 mg/m²/day, 300 mg/m²/day, or 500 mg/m²/day), and fludarabine at a dose of between about 20 mg/m²/day and about 900 mg/m²/day (e.g., 20 mg/m²/day, 25 mg/m²/day, 30 mg/m²/day, or 60 mg/m²/day). In an exemplary embodiment, the lymphodepletion step includes

administration of cyclophosphamide at a dose of about 300 mg/m²/day, and fludarabine at a dose of about 30 mg/m²/day.

[00428] In an exemplary embodiment, the dosing of cyclophosphamide is 300 mg/m²/day over three days, and the dosing of fludarabine is 30 mg/m²/day over three days.

[00429] It is known in the art that one of the adverse effects of the use of CAR T cells can be the onset of immune activation, known as cytokine release syndrome (CRS). CRS is immune activation resulting in elevated inflammatory cytokines. CRS is a known on-target toxicity, development of which likely correlates with efficacy. Clinical and laboratory measures range from mild CRS (constitutional symptoms and/or grade-2 organ toxicity) to severe CRS (sCRS; grade ≥ 3 organ toxicity, aggressive clinical intervention, and/or potentially life threatening). Clinical features include: high fever, malaise, fatigue, myalgia, nausea, anorexia, tachycardia/hypotension, capillary leak, cardiac dysfunction, renal impairment, hepatic failure, and disseminated intravascular coagulation. Dramatic elevations of cytokines including interferon-gamma, granulocyte macrophage colony-stimulating factor, IL-10, and IL-6 have been shown following CAR T-cell infusion. One CRS signature is elevation of cytokines including IL-6 (severe elevation), IFN-gamma, TNF-alpha (moderate), and IL-2 (mild). Elevations in clinically available markers of inflammation including ferritin and C-reactive protein (CRP) have also been observed to correlate with the CRS syndrome. The presence of CRS generally correlates with expansion and progressive immune activation of adoptively transferred cells. It has been demonstrated that the degree of CRS severity is dictated by disease burden at the time of infusion as patients with high tumor burden experience a more sCRS.

[00430] Accordingly, in some embodiments, the methods comprise, following the diagnosis of CRS, appropriate CRS management strategies to mitigate the physiological symptoms of uncontrolled inflammation without dampening the antitumor efficacy of the in vivo generated cells (e.g., CAR T cells). CRS management strategies are known in the art. For example, systemic corticosteroids may be administered to rapidly reverse symptoms of sCRS (e.g., grade 3 CRS) without compromising initial antitumor response.

[00431] In some embodiments, an anti-IL-6R antibody may be administered. An example of an anti-IL-6R antibody is the Food and Drug Administration-approved monoclonal antibody tocilizumab, also known as atilizumab (marketed as Actemra, or RoActemra). Tocilizumab is a humanized monoclonal antibody against the interleukin-6 receptor (IL-6R). Administration of tocilizumab has demonstrated near-immediate reversal of CRS.

[00432] CRS is generally managed based on the severity of the observed syndrome and interventions are tailored as such. CRS management decisions may be based upon clinical signs and symptoms and response to interventions, not solely on laboratory values alone.

[00433] Mild to moderate cases generally are treated with symptom management with fluid therapy, non-steroidal anti-inflammatory drug (NSAID) and antihistamines as needed for adequate symptom relief. More severe cases include patients with any degree of hemodynamic instability; with any hemodynamic instability, the administration of tocilizumab is recommended. The first-line management of CRS may be tocilizumab, in some embodiments, at the labeled dose of 8 mg/kg IV over 60 minutes (not to exceed 800 mg/dose); tocilizumab can be repeated Q8 hours. If suboptimal response to the first dose of tocilizumab, additional doses of tocilizumab may be considered. Tocilizumab can be administered alone or in combination with corticosteroid therapy. Patients with continued or progressive CRS symptoms, inadequate clinical improvement in 12-18 hours or poor response to tocilizumab, may be treated with high-dose corticosteroid therapy, generally hydrocortisone 100 mg IV or methylprednisolone 1-2 mg/kg. In patients with more severe hemodynamic instability or more severe respiratory symptoms, patients may be administered high-dose corticosteroid therapy early in the course of the CRS. CRS management guidance may be based on published standards (Lee et al. (2019) Biol Blood Marrow Transplant, doi.org/10.1016/j.bbmt.2018.12.758; Neelapu et al. (2018) Nat Rev Clin Oncology, 15:47; Teachey et al. (2016) Cancer Discov, 6(6):664-679).

[00434] Features consistent with Macrophage Activation Syndrome (MAS) or Hemophagocytic lymphohistiocytosis (HLH) have been observed in patients treated with CAR-T therapy (Henter, 2007), coincident with clinical manifestations of the CRS. MAS appears to be a reaction to immune activation that occurs from the CRS, and should therefore be considered a manifestation of CRS. MAS is similar to HLH (also a reaction to immune stimulation). The clinical syndrome of MAS is characterized by high grade non-remitting fever, cytopenias affecting at least two of three lineages, and hepatosplenomegaly. It is associated with high serum ferritin, soluble interleukin-2 receptor, and triglycerides, and a decrease of circulating natural killer (NK) activity.

[00435] In some embodiments, methods of treating cancer in a subject in need thereof are provided, the methods comprising administering to the subject any of the compositions, such as the viral particle(s), provided herein.

[00436] In some embodiments, the cell that is produced expresses the polypeptide comprising the ICD and the ECD as provided for herein. In some embodiments, when treating a patient

having such a cell, the method comprises administering to the cell or to the subject one or more compounds that bind to the ECD of the polypeptide encoded by the nucleic acid molecule. This can, for example, lead to the expansion of such cells. In some embodiments, the cell that is produced expresses the polypeptide comprising the ICD and the ECD as provided for herein and a CAR molecule as provided for herein. The CAR molecule can be any appropriate CAR molecule. In some embodiments, the antigen binding domain of the CAR molecule CAR binds to a target selected from, but not limited to, CD8, CCR7, CD19, CD20, CD22, CD123, CD38, FCRL5, BCMA, CD33, CD79b, CEA, ERBB2, EGFR, GD2, mesothelin, MUC1, PSMA, PSCA, STn, EGFRvIII, IL13R α , HER2, EphA2, CD70, CD133, CSPG 4, B7-H3, PDPN, MMP2, or CD147. In some embodiments, the antigen-binding domain binds to CD19. In some embodiments, the antigen-binding domain binds to CD20. In some embodiments, the CAR molecule is as provided for herein. Accordingly, administering to the cell or to the subject one or more compounds that bind to the ECD of the polypeptide encoded by the nucleic acid molecule can, for example, lead to the expansion of the cells expressing the polypeptide and the CAR molecule.

[00437] In some embodiments, methods of treating a disease or disorder in a subject are provided, wherein, the method comprises administering to the subject a viral as provided for herein and administering to the subject an effective amount of one or more compounds that bind to the ECD of the polypeptide encoded by the nucleic acid molecule.

[00438] In some embodiments, the ECD is a GCSFR ECD or a GHR ECD and the one or more compounds bind to the GCSFR ECD or the GHR ECD. Examples of such ECDs are provided for herein. In some embodiments, the ECD is a human GCSFR ECD or a human GHR ECD and the one or more compounds bind to the human GCSFR ECD or the human GHR ECD. Examples of such ECDs are provided for herein. Examples of such compounds include, but are not limited to, somatropin, lenograstim (Granocyte), filgrastim (Neupogen, Zarzio, Nivestim, Accofil), long acting (pegylated) filgrastim (pegfilgrastim, Neulasta, Pelmeg, Ziextenco) or lipegfilgrastim (Lonquex).

[00439] The compositions disclosed herein can comprise a pharmaceutical composition, and for example include a pharmaceutically acceptable carrier, and/or a pharmaceutical formulation.

[00440] The term “pharmaceutical formulation” refers to a preparation which is in such form as to permit the biological activity of an active ingredient contained therein to be effective, and which contains no additional components which are unacceptably toxic to a subject to which the formulation would be administered. A “pharmaceutically acceptable carrier” refers to an

ingredient in a pharmaceutical formulation, other than an active ingredient, which is nontoxic to a subject. A pharmaceutically acceptable carrier includes, but is not limited to, a buffer, excipient, stabilizer, or preservative. In some aspects, the choice of carrier is determined in part by the particular cell and/or by the method of administration. Accordingly, there are a variety of suitable formulations. For example, the pharmaceutical composition can contain preservatives. Suitable preservatives may include, for example, methylparaben, propylparaben, sodium benzoate, and benzalkonium chloride. In some aspects, a mixture of two or more preservatives is used. The preservative or mixtures thereof are typically present in an amount of about 0.0001% to about 2% by weight of the total composition. Carriers are described, e.g., by Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980). Pharmaceutically acceptable carriers are generally nontoxic to recipients at the dosages and concentrations employed, and include, but are not limited to: buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid and methionine; preservatives (such as octadecyldimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium chloride; benzethonium chloride; phenol, butyl or benzyl alcohol; alkyl parabens such as methyl or propyl paraben; catechol; resorcinol; cyclohexanol; 3-pentanol; and m-cresol); low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-forming counter-ions such as sodium; metal complexes (e.g. Zn-protein complexes); and/or non-ionic surfactants such as polyethylene glycol (PEG).

[00441] Buffering agents in some aspects are included in the compositions. Suitable buffering agents include, for example, citric acid, sodium citrate, phosphoric acid, potassium phosphate, and various other acids and salts. In some aspects, a mixture of two or more buffering agents is used. The buffering agent or mixtures thereof are typically present in an amount of about 0.001% to about 4% by weight of the total composition. Methods for preparing administrable pharmaceutical compositions are known. Exemplary methods are described in more detail in, for example, Remington: The Science and Practice of Pharmacy, Lippincott Williams & Wilkins; 21st ed. (May 1, 2005).

[00442] The formulations can include aqueous solutions. The formulation or composition may also contain more than one active ingredient useful for the particular indication, disease, or condition being treated with the composition, preferably those with activities complementary

to the composition, where the respective activities do not adversely affect one another. Such active ingredients are suitably present in combination in amounts that are effective for the purpose intended. Thus, in some embodiments, the pharmaceutical composition further includes other pharmaceutically active agents or drugs, such as chemotherapeutic agents, e.g., asparaginase, busulfan, carboplatin, cisplatin, daunorubicin, doxorubicin, fluorouracil, gemcitabine, hydroxyurea, methotrexate, paclitaxel, rituximab, vinblastine, and/or vincristine. The pharmaceutical composition in some embodiments contains the composition in amounts effective to treat or prevent the disease or condition, such as a therapeutically effective or prophylactically effective amount. Therapeutic or prophylactic efficacy in some embodiments is monitored by periodic assessment of treated subjects. The desired dosage can be delivered by a single bolus administration of the composition, by multiple bolus administrations of the composition, or by continuous infusion administration of the composition. In some embodiments, the pharmaceutical composition does not include a chemotherapeutic.

[00443] Formulations include those for oral, intravenous, intraperitoneal, subcutaneous, pulmonary, transdermal, intramuscular, intranasal, buccal, sublingual, or suppository administration. In some embodiments, the composition is administered parenterally. The term “parenteral,” as used herein, includes intravenous, intramuscular, subcutaneous, rectal, vaginal, and intraperitoneal administration. In some embodiments, the composition is administered to the subject using peripheral systemic delivery by intravenous, intraperitoneal, or subcutaneous injection. Compositions in some embodiments are provided as sterile liquid preparations, e.g., isotonic aqueous solutions, suspensions, emulsions, dispersions, or viscous compositions, which may in some aspects be buffered to a selected pH. Liquid preparations are normally easier to prepare than gels, other viscous compositions, and solid compositions. Additionally, liquid compositions are somewhat more convenient to administer, especially by injection. Viscous compositions, on the other hand, can be formulated within the appropriate viscosity range to provide longer contact periods with specific tissues. Liquid or viscous compositions can comprise carriers, which can be a solvent or dispersing medium containing, for example, water, saline, phosphate buffered saline, polyol (for example, glycerol, propylene glycol, liquid polyethylene glycol) and suitable mixtures thereof.

[00444] Sterile injectable solutions can be prepared by incorporating the composition in a solvent, such as in admixture with a suitable carrier, diluent, or excipient such as sterile water, physiological saline, glucose, dextrose, or the like. The compositions can contain auxiliary substances such as wetting, dispersing, or emulsifying agents (e.g., methylcellulose), pH buffering agents, gelling or viscosity enhancing additives, preservatives, flavoring agents,

and/or colors, depending upon the route of administration and the preparation desired. Standard texts may in some aspects be consulted to prepare suitable preparations.

[00445] Various additives which enhance the stability and sterility of the compositions, including antimicrobial preservatives, antioxidants, chelating agents, and buffers, can be added. Prevention of the action of microorganisms can be ensured by various antibacterial and antifungal agents, for example, parabens, chlorobutanol, phenol, and sorbic acid. Prolonged absorption of the injectable pharmaceutical form can be brought about by the use of agents delaying absorption, for example, aluminum monostearate and gelatin.

[00446] The formulations to be used for in vivo administration are generally sterile. Sterility may be readily accomplished, e.g., by filtration through sterile filtration membranes.

[00447] The embodiments provided for herein can be used for many purposes, since the a pseudotyped virus capable of fusing with a target cell can be used to deliver a gene or other heterologous sequence of interest.

Enumerated Embodiments

[00448] In some embodiments, the following embodiments are provided:

1. A particle or composition comprising one or more nucleic acid molecules encoding for:
 - a) a chimeric antigen receptor (CAR); and
 - b) a polypeptide comprising:
 - i) a ligand binding extracellular domain (ECD);
 - ii) an immune cell activating intracellular domain (ICD); and
 - iii) a transmembrane domain linking the ECD to the ICD.
2. The particle of embodiment 1, wherein the immune cell activating ICD comprises the ICD of hGCSF-R, or a mutant or fragment thereof.
3. The particle of embodiment 2, wherein the ICD of hGCSF-R comprise a substitution, an insertion or deletion.
4. The particle of embodiments 2 or 3, wherein the hGCSF-R ICD comprises a sequence of SEQ ID NO: 111, or an amino acid sequence having at least 50, 60, 70, 75, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to the same.
5. The particle of embodiment 4, wherein , the hGCSF-R ICD does not comprise the sequence of SEQ ID NO: 110.
6. The particle of any one of embodiments 2-5, wherein the hGCSF-R ICD comprises a sequence of SEQ ID NO: 111 and does not comprise amino acid residues 800-813, 775-813,

750-813, 725-813, or 716-813 of SEQ ID NO: 125, or a fragment thereof, positioned to the C-terminal residue of SEQ ID NO: 111.

7. The particle of any one of embodiments 2-5, wherein the hGCSF-R ICD comprises a sequence of SEQ ID NO: 111 and amino acid residues 716-812 of SEQ ID NO: 125, or a fragment thereof positioned to the C-terminal residue of SEQ ID NO: 111, provided that the ICD does not comprise the contiguous fragment of amino acid residues 716-813 of SEQ ID NO: 125.

8. The particle of any one of embodiments 1-7, wherein the ECD is a GCSF-R ECD.

9. The particle of embodiment 8, wherein the GCSF-R ECD is a human GCSF-R ECD.

10. The particle of embodiment 9, wherein the human GCSF-R ECD comprises the amino acid sequence of SEQ ID NO: 107 or SEQ ID NO: 108.

11. The particle of any one of embodiments 1-7, wherein the ECD comprises the ECD of human growth hormone receptor (hGH-R), or a mutant or fragment thereof.

12. The particle of embodiment 11, wherein the ECD of human growth hormone receptor (hGH-R) comprises the amino acid sequence encoded by exons 1-7 of hGH-R, or a mutant or fragment thereof.

13. The particle of embodiments 11 or 12, wherein the ECD of the hGH-R comprises the mutation of C259R.

14. The particle of any one of embodiments 11-13, wherein the ECD of the hGH-R comprises an amino acid sequence of SEQ ID NO: 114 or SEQ ID NO: 115, or an amino acid sequence having at least 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to the same.

15. The particle of embodiment 1, wherein the ECD comprises the ECD of human growth hormone receptor (hGH-R), or a mutant or fragment thereof.

16. The particle of embodiment 15, wherein the ECD of human growth hormone receptor (hGH-R) comprises exons 1-7 of hGH-R, or a mutant or fragment thereof.

17. The particle of embodiments 15 or 16, wherein the ECD of the hGH-R comprises the mutation of C259R.

18. The particle of any one of embodiments 15-17, wherein the ECD of the hGH-R comprises an amino acid sequence of SEQ ID NO: 114 or SEQ ID NO: 115, or an amino acid sequence having at least 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to the same.

19. The particle of any one of embodiments 1 or 15-18, wherein the ICD comprises an ICD of glycoprotein 130 ("gp130 ICD"), or a variant or fragment thereof.

20. The particle of embodiment 19, wherein the gp130 ICD comprises a fragment of the gp130 ICD.

21. The particle of embodiment 20, wherein the gp130 ICD fragment comprises a Jak1 binding site and/or a SHP-2/STAT3 binding site.
22. The particle of any one of embodiments 1 or 15-18, wherein the ICD comprises a fragment of the GCSF-R ICD.
23. The particle of embodiment 22, wherein the GCSF-R ICD fragment does not comprise the STAT3, SH3 and/or the SHC domains.
24. The particle of embodiments 22 or 23, wherein the GCSF-R ICD fragment comprises the Jak1 and/or the STAT3 binding site.
25. The particle of any one of embodiments 1 or 15-24, wherein the ICD comprises a IL-2R β ICD, or a fragment or variant thereof.
26. The particle of embodiment 25, wherein the IL-2R β ICD is a fragment of the IL-2R β ICD.
27. The particle of embodiments 25 or 26, wherein the IL-2R β ICD, or fragment thereof, comprises the SHC or STAT5 binding domains.
28. The particle of any one of embodiments 1 or 15-24, wherein the ICD comprises a IL-7R α ICD, or a fragment or variant thereof.
29. The particle of embodiment 28, wherein the IL-7R α ICD is a fragment of the IL-7R α ICD.
30. The particle of embodiments 28 or 29, wherein the ICD comprises a IL-7R α ICD, or a fragment thereof, comprises a STAT5 and/or PI3K binding domain.
31. The particle of any one of embodiments 1 or 19-30, wherein the ICD comprises a gp130 ICD, or a variant or fragment thereof, linked to an IL-2R β ICD, or fragment thereof.
32. The particle of any one of embodiments 1 or 19-30, wherein the ICD comprises a hGCSF-R ICD, or a variant or fragment thereof, linked to an IL-7R α ICD, or fragment thereof.
33. The particle of any one of embodiments 1-32, wherein the transmembrane domain, comprises a GCSF-R, gp130, or hGH-R transmembrane domain.
34. The particle of embodiment 33, wherein the transmembrane domain comprises the hGCSF-R transmembrane domain, or a variant thereof.
35. The particle of embodiment 33, wherein the transmembrane domain comprises the gp130 transmembrane domain, or a variant thereof.
36. The particle of embodiment 33, wherein the transmembrane domain comprises the hGH-R transmembrane domain, or a variant thereof.
37. The particle of any one of embodiments 1-36, wherein the polypeptide comprises:

a) an ECD that is a GCSFR-ECD, or variant thereof (e.g. as set forth herein and above); a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof (e.g. as set forth herein and above), and an immune activating ICD that is a GCSF-R ICD, or variant thereof (e.g. as set forth herein and above);

b) an ECD that is a hGH-R-ECD, or variant thereof (e.g. as set forth herein and above); a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof (e.g. as set forth herein and above), and immune activating ICD that is a GCSF-R ICD, or variant thereof (e.g. as set forth herein and above);

c) an ECD that is a hGH-R-ECD, or variant thereof (e.g. as set forth herein and above); a transmembrane domain that is a gp130 transmembrane domain, or variant thereof (e.g. as set forth herein and above), and immune activating ICD that comprises a gp130 ICD, or variant thereof (e.g. as set forth herein and above) and a IL-2R β ICD, or variant thereof (e.g. as set forth herein and above); or

d) an ECD that is a hGH-R-ECD, or variant thereof (e.g. as set forth herein and above); a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof (e.g. as set forth herein and above), and immune activating ICD that comprises a GCSF-R ICD, or variant thereof (e.g. as set forth herein and above) and a IL-7R α ICD, or variant thereof (e.g. as set forth herein and above).

38. The particle of any one of embodiments 1-37, wherein the polypeptide comprises an amino acid sequence of SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 120, or SEQ ID NO: 124, or a variant of any of the foregoing.

39. The particle of embodiment 38 wherein the variant comprises a polypeptide having at least 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%, or 99% identity to SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 120, or SEQ ID NO: 124.

40. The particle of any one of embodiments 1-39, wherein the particle is a vector (e.g., virus, a liposome, plasmid, and the like) or a cell.

41. The particle of any one of embodiments 1-40, wherein the particle is a virus or viral vector.

42. The particle of embodiment 41, wherein the viral vector is a lentiviral vector, AV vector, an AAV vector, and the like.

43. The particle of embodiments 41 or 42, wherein the viral vector is a pseudotyped viral

vector.

44. The particle of any one of embodiments 1-43, wherein the chimeric antigen receptor comprises an antigen binding domain that binds to a tumor antigen.

45. A nucleic acid molecule, including an isolated nucleic acid molecule, encoding a polypeptide comprising:

- i) a ligand binding extracellular domain (ECD);
- ii) an immune cell activating intracellular domain (ICD); and
- iii) a transmembrane domain linking the ECD to the ICD.

46. The nucleic acid molecule of embodiment 45, wherein the immune cell activating ICD comprises the ICD of hGCSF-R, or a mutant or fragment thereof.

47. The nucleic acid molecule of embodiment 46, wherein the ICD of hGCSF-R comprise a substitution, an insertion or deletion.

48. The nucleic acid molecule of embodiments 46 or 47, wherein the hGCSF-R ICD comprises a sequence of SEQ ID NO: 111, or an amino acid sequence having at least 50, 60, 70, 75, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to the same.

49. The nucleic acid molecule of embodiment 48, wherein , the hGCSF-R ICD does not comprise the sequence of SEQ ID NO: 110.

50. The nucleic acid molecule of any one of embodiments 46-49, wherein the hGCSF-R ICD comprises a sequence of SEQ ID NO: 111 and does not comprise amino acid residues 800-813, 775-813, 750-813, 725-813, or 716-813 of SEQ ID NO: 125, or a fragment thereof, positioned to the C-terminal residue of SEQ ID NO: 111.

51. The nucleic acid molecule of any one of embodiments 46-49, wherein the hGCSF-R ICD comprises a sequence of SEQ ID NO: 111 and amino acid residues 716-812 of SEQ ID NO: 125, or a fragment thereof positioned to the C-terminal residue of SEQ ID NO: 111, provided that the ICD does not comprise the contiguous fragment of amino acid residues 716-813 of SEQ ID NO: 125.

52. The nucleic acid molecule of any one of embodiments 45-51, wherein the ECD is a GCSF-R ECD.

53. The nucleic acid molecule of embodiment 52, wherein the GCSF-R ECD is a human GCSF-R ECD.

54. The nucleic acid molecule of embodiment 53, wherein the human GCSF-R ECD comprises the amino acid sequence of SEQ ID NO: 107 or SEQ ID NO: 108.

55. The nucleic acid molecule of any one of embodiments 45-51, wherein the ECD comprises the ECD of human growth hormone receptor (hGH-R), or a mutant or fragment

thereof.

56. The nucleic acid molecule of embodiment 55, wherein the ECD of human growth hormone receptor (hGH-R) comprises the amino acid sequence encoded by exons 1-7 of hGH-R, or a mutant or fragment thereof.

57. The nucleic acid molecule of embodiments 55 or 56, wherein the ECD of the hGH-R comprises the mutation of C259R.

58. The nucleic acid molecule of any one of embodiments 55-57, wherein the ECD of the hGH-R comprises an amino acid sequence of SEQ ID NO: 114 or SEQ ID NO: 115, or an amino acid sequence having at least 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to the same.

59. The nucleic acid molecule of embodiment 45, wherein the ECD comprises the ECD of human growth hormone receptor (hGH-R), or a mutant or fragment thereof.

60. The nucleic acid molecule of embodiment 59, wherein the ECD of human growth hormone receptor (hGH-R) comprises exons 1-7 of hGH-R, or a mutant or fragment thereof.

61. The nucleic acid molecule of embodiments 59 or 60, wherein the ECD of the hGH-R comprises the mutation of C259R.

62. The nucleic acid molecule of any one of embodiments 59-61, wherein the ECD of the hGH-R comprises an amino acid sequence of SEQ ID NO: 114 or SEQ ID NO: 115, or an amino acid sequence having at least 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to the same.

63. The nucleic acid molecule of any one of embodiments 45 or 59-62, wherein the ICD comprises an ICD of glycoprotein 130 ("gp130 ICD"), or a variant or fragment thereof.

64. The nucleic acid molecule of embodiment 63, wherein the gp130 ICD comprises a fragment of the gp130 ICD.

65. The nucleic acid molecule of embodiment 64, wherein the gp130 ICD fragment comprises a Jak1 binding site and/or a SHP-2/STAT3 binding site.

66. The nucleic acid molecule of any one of embodiments 45 or 59-62, wherein the ICD comprises a fragment of the GCSF-R ICD.

67. The nucleic acid molecule of embodiment 66, wherein the GCSF-R ICD fragment does not comprise the STAT3, SH3 and/or the SHC domains.

68. The nucleic acid molecule of embodiments 66 or 67, wherein the GCSF-R ICD fragment comprises the Jak1 and/or the STAT3 binding site.

69. The nucleic acid molecule of any one of embodiments 45 or 59-68, wherein the ICD comprises a IL-2R β ICD, or a fragment or variant thereof.

70. The nucleic acid molecule of embodiment 69, wherein the IL-2R β ICD is a fragment of the IL-2R β ICD.
71. The nucleic acid molecule of embodiments 69 or 70, wherein the IL-2R β ICD, or fragment thereof, comprises the SHC or STAT5 binding domains.
72. The nucleic acid molecule of any one of embodiments 45 or 59-68, wherein the ICD comprises a IL-7R α ICD, or a fragment or variant thereof.
73. The nucleic acid molecule of embodiment 72, wherein the IL-7R α ICD is a fragment of the IL-7R α ICD.
74. The nucleic acid molecule of embodiments 72 or 73, wherein the ICD comprises a IL-7R α ICD, or a fragment thereof, comprises a STAT5 and/or PI3K binding domain.
75. The nucleic acid molecule of any one of embodiments 45 or 63-74, wherein the ICD comprises a gp130 ICD, or a variant or fragment thereof, linked to an IL-2R β ICD, or fragment thereof.
76. The nucleic acid molecule of any one of embodiments 45 or 63-74, wherein the ICD comprises a hGCSF-R ICD, or a variant or fragment thereof, linked to an IL-7R α ICD, or fragment thereof.
77. The nucleic acid molecule of any one of embodiments 45-76, wherein the transmembrane domain, comprises a GCSF-R, gp130, or hGH-R transmembrane domain..
78. The nucleic acid molecule of embodiment 77, wherein the transmembrane domain comprises the hGCSF-R transmembrane domain, or a variant thereof.
79. The nucleic acid molecule of embodiment 77, wherein the transmembrane domain comprises the gp130 transmembrane domain, or a variant thereof.
80. The nucleic acid molecule of embodiment 77, wherein the transmembrane domain comprises the hGH-R transmembrane domain, or a variant thereof.
81. The nucleic acid molecule of any one of embodiments 45-80, wherein the polypeptide comprises:
- a) an ECD that is a GCSFR-ECD, or variant thereof (e.g. as set forth herein and above); a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof (e.g. as set forth herein and above), and an immune activating ICD that is a GCSF-R ICD, or variant thereof (e.g. as set forth herein and above);
 - b) an ECD that is a hGH-R-ECD, or variant thereof (e.g. as set forth herein and above); a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof (e.g. as set forth herein and above), and immune activating ICD that is a GCSF-R ICD, or

variant thereof (e.g. as set forth herein and above);

c) an ECD that is a hGH-R-ECD, or variant thereof (e.g. as set forth herein and above); a transmembrane domain that is a gp130 transmembrane domain, or variant thereof (e.g. as set forth herein and above), and immune activating ICD that comprises a gp130 ICD, or variant thereof (e.g. as set forth herein and above) and a IL-2R β ICD, or variant thereof (e.g. as set forth herein and above); or

d) an ECD that is a hGH-R-ECD, or variant thereof (e.g. as set forth herein and above); a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof (e.g. as set forth herein and above), and immune activating ICD that comprises a GCSF-R ICD, or variant thereof (e.g. as set forth herein and above) and a IL-7R α ICD, or variant thereof (e.g. as set forth herein and above).

82. The nucleic acid molecule of any one of embodiments 45-81, wherein the polypeptide comprises an amino acid sequence of SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 120, or SEQ ID NO: 124, or a variant of any of the foregoing.

83. The nucleic acid molecule of embodiment 82 wherein the variant comprises a polypeptide having at least 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%, or 99% identity to SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 16, or SEQ ID NO: 20.

84. The nucleic acid molecule of any one of embodiments 45-83, wherein the nucleic acid molecule further encodes for a chimeric antigen receptor (CAR).

85. The nucleic acid molecule of embodiment 84, wherein the CAR comprises an antigen binding domain comprising an antibody, or a fragment thereof.

86. The nucleic acid molecule of embodiment 85, wherein the antibody, or fragment thereof is an antibody, a scFv antibody, an antigen binding domain, an ankyrin repeat, a VHH domain antibody, a nanobody, a single domain antibody, or an FN3 antibody.

87. The nucleic acid molecule of embodiment 85 or 86, wherein the antigen binding domain of the CAR binds to CD20.

88. The nucleic acid molecule of embodiment 87, wherein the antigen binding domain that binds to CD20 comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 90% identity to an amino acid sequence of SEQ ID NO: 89; and a light chain variable region of the light chain having at least 90% identity to an amino acid sequence of SEQ ID NO: 90.

89. The nucleic acid molecule of embodiment 87, wherein the antigen binding domain that binds to CD20 comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 95% identity to an amino acid sequence of SEQ ID NO: 89; and a light chain variable region of the light chain having at least 95% identity to an amino acid sequence of SEQ ID NO: 90.
90. The nucleic acid molecule of embodiment 87, wherein the antigen binding domain that binds to CD20 comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 99% identity to an amino acid sequence of SEQ ID NO: 89; and a light chain variable region of the light chain having at least 99% identity to an amino acid sequence of SEQ ID NO: 90.
91. The nucleic acid molecule of embodiment 87, wherein the antigen binding domain that binds to CD20 comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain comprising an amino acid sequence of SEQ ID NO: 89; and a light chain variable region of the light chain comprising an amino acid sequence of SEQ ID NO: 90.
92. The nucleic acid molecule of any one of embodiments 88-91, wherein the heavy chain variable region and the light chain variable region are directly linked to one another and are not linked by a linker.
93. The nucleic acid molecule of any one of embodiments 88-91, wherein the antigen binding domain that binds to CD20 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 92, at least 95% sequence identity to SEQ ID NO: 92, at least 99% sequence identity to SEQ ID NO: 92, or a sequence as set forth in SEQ ID NO: 92.
94. The nucleic acid molecule of any one of embodiments 88-91, wherein the antigen binding domain that binds to CD20 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 93, at least 95% sequence identity to SEQ ID NO: 93, at least 99% sequence identity to SEQ ID NO: 93, or a sequence as set forth in SEQ ID NO: 93.
95. The nucleic acid molecule of embodiment 87, wherein the antigen binding domain that binds to CD20 comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 90% identity to an amino acid sequence of SEQ ID NO: 94; and a light chain variable region of the light chain having at least 90% identity to an amino acid sequence of SEQ ID NO: 95.

96. The nucleic acid molecule of embodiment 87, wherein the antigen binding domain that binds to CD20 comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 95% identity to an amino acid sequence of SEQ ID NO: 94; and a light chain variable region of the light chain having at least 95% identity to an amino acid sequence of SEQ ID NO: 95.
97. The nucleic acid molecule of embodiment 87, wherein the antigen binding domain that binds to CD20 comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 99% identity to an amino acid sequence of SEQ ID NO: 94; and a light chain variable region of the light chain having at least 99% identity to an amino acid sequence of SEQ ID NO: 95.
98. The nucleic acid molecule of embodiment 87, wherein the antigen binding domain that binds to CD20 comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain comprising an amino acid sequence of SEQ ID NO: 94; and a light chain variable region of the light chain comprising an amino acid sequence of SEQ ID NO: 95.
99. The nucleic acid molecule of any one of embodiments 95-98, wherein the heavy chain variable region and the light chain variable region are directly linked to one another and are not linked by a linker.
100. The nucleic acid molecule of any one of embodiments 95-98, wherein the antigen binding domain that binds to CD20 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 96, at least 95% sequence identity to SEQ ID NO: 96, at least 99% sequence identity to SEQ ID NO: 96, or a sequence as set forth in SEQ ID NO: 96.
101. The nucleic acid molecule of any one of embodiments 95-98, wherein the antigen binding domain that binds to CD20 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 97, at least 95% sequence identity to SEQ ID NO: 97, at least 99% sequence identity to SEQ ID NO: 97, or a sequence as set forth in SEQ ID NO: 97.
102. The nucleic acid molecule of any one of embodiments 84-101, wherein the CAR further comprises a hinge domain, a transmembrane domain, a costimulatory domain, and a signaling domain.
103. The nucleic acid molecule of embodiment 102, wherein the hinge domain comprises an amino acid sequence having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%,

94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to an amino acid sequence of SEQ ID NO: 59.

104. The nucleic acid molecule of embodiment 102 or 103, wherein the transmembrane domain comprises an amino acid sequence having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to an amino acid sequence of SEQ ID NO: 61.

105. The nucleic acid molecule of any one of embodiments 102-104, wherein the costimulatory domain comprises an amino acid sequence having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to an amino acid sequence of SEQ ID NO: 101.

106. The nucleic acid molecule of any one of embodiments 102-105, wherein the signaling domain comprises an amino acid sequence having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identity to an amino acid sequence of SEQ ID NO: 102.

107. The nucleic acid molecule of embodiment 87, wherein the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

108. A polypeptide comprising:

- i) a ligand binding extracellular domain (ECD);
- ii) an immune cell activating intracellular domain (ICD); and
- iii) a transmembrane domain linking the ECD to the ICD.

109. The polypeptide of embodiment 108, wherein the immune cell activating ICD comprises the ICD of hGCSF-R, or a mutant or fragment thereof.

110. The polypeptide of embodiment 109, wherein the ICD of hGCSF-R comprise a substitution, an insertion or deletion.

111. The polypeptide of embodiments 109 or 110, wherein the hGCSF-R ICD comprises a sequence of SEQ ID NO: 111, or an amino acid sequence having at least 50, 60, 70, 75, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to the same.

112. The polypeptide of embodiment 111, wherein , the hGCSF-R ICD does not comprise the sequence of SEQ ID NO: 110.

113. The polypeptide of any one of embodiments 109-112, wherein the hGCSF-R ICD comprises a sequence of SEQ ID NO: 111 and does not comprise amino acid residues 800-813, 775-813, 750-813, 725-813, or 716-813 of SEQ ID NO: 125, or a fragment thereof, positioned

to the C-terminal residue of SEQ ID NO: 111.

114. The polypeptide of any one of embodiments 109-112, wherein the hGCSF-R ICD comprises a sequence of SEQ ID NO: 111 and amino acid residues 716-812 of SEQ ID NO: 125, or a fragment thereof positioned to the C-terminal residue of SEQ ID NO: 111, provided that the ICD does not comprise the contiguous fragment of amino acid residues 716-813 of SEQ ID NO: 125.

115. The polypeptide of any one of embodiments 108-114, wherein the ECD is a GCSF-R ECD.

116. The polypeptide of embodiment 115, wherein the GCSF-R ECD is a human GCSF-R ECD.

117. The polypeptide of embodiment 116, wherein the human GCSF-R ECD comprises the amino acid sequence of SEQ ID NO: 107 or SEQ ID NO: 108.

118. The polypeptide of any one of embodiments 108-114, wherein the ECD comprises the ECD of human growth hormone receptor (hGH-R), or a mutant or fragment thereof.

119. The polypeptide of embodiment 118, wherein the ECD of human growth hormone receptor (hGH-comprises the amino acid sequence encoded by exons 1-7 of hGH-R, or a mutant or fragment thereof.

120. The polypeptide of embodiments 118 or 119, wherein the ECD of the hGH-R comprises the mutation of C259R.

121. The polypeptide of any one of embodiments 118-120, wherein the ECD of the hGH-R comprises an amino acid sequence of SEQ ID NO: 114 or SEQ ID NO: 115, or an amino acid sequence having at least 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to the same.

122. The polypeptide of embodiment 108, wherein the ECD comprises the ECD of human growth hormone receptor (hGH-R), or a mutant or fragment thereof.

123. The polypeptide of embodiment 122, wherein the ECD of human growth hormone receptor (hGH-comprises exons 1-7 of hGH-R, or a mutant or fragment thereof.

124. The polypeptide of embodiments 122 or 123, wherein the ECD of the hGH-R comprises the mutation of C259R.

125. The polypeptide of any one of embodiments 122-124, wherein the ECD of the hGH-R comprises an amino acid sequence of SEQ ID NO: 114 or SEQ ID NO: 115, or an amino acid sequence having at least 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to the same.

126. The polypeptide of any one of embodiments 108 or 122-125, wherein the ICD comprises an ICD of glycoprotein 130 ("gp130 ICD"), or a variant or fragment thereof.

127. The polypeptide of embodiment 126, wherein the gp130 ICD comprises a fragment of

the gp130 ICD.

128. The polypeptide of embodiment 127, wherein the gp130 ICD fragment comprises a Jak1 binding site and/or a SHP-2/STAT3 binding site.

129. The polypeptide of any one of embodiments 108 or 122-125, wherein the ICD comprises a fragment of the GCSF-R ICD.

130. The polypeptide of embodiment 129, wherein the GCSF-R ICD fragment does not comprise the STAT3, SH3 and/or the SHC domains.

131. The polypeptide of embodiments 129 or 130, wherein the GCSF-R ICD fragment comprises the Jak1 and/or the STAT3 binding site.

132. The polypeptide of any one of embodiments 108 or 122-131, wherein the ICD comprises a IL-2R β ICD, or a fragment or variant thereof.

133. The polypeptide of embodiment 132, wherein the IL-2R β ICD is a fragment of the IL-2R β ICD.

134. The polypeptide of embodiments 132 or 133, wherein the IL-2R β ICD, or fragment thereof, comprises the SHC or STAT5 binding domains.

135. The polypeptide of any one of embodiments 108 or 122-131, wherein the ICD comprises a IL-7R α ICD, or a fragment or variant thereof.

136. The polypeptide of embodiment 135, wherein the IL-7R α ICD is a fragment of the IL-7R α ICD.

137. The polypeptide of embodiments 135 or 136, wherein the ICD comprises a IL-7R α ICD, or a fragment thereof, comprises a STAT5 and/or PI3K binding domain.

138. The polypeptide of any one of embodiments 108 or 126-137, wherein the ICD comprises a gp130 ICD, or a variant or fragment thereof, linked to an IL-2R β ICD, or fragment thereof.

139. The polypeptide of any one of embodiments 108 or 126-137, wherein the ICD comprises a hGCSF-R ICD, or a variant or fragment thereof, linked to an IL-7R α ICD, or fragment thereof.

140. The polypeptide of any one of embodiments 108-139, wherein the transmembrane domain, comprises a GCSF-R, gp130, or hGH-R transmembrane domain.

141. The polypeptide of embodiment 140, wherein the transmembrane domain comprises the hGCSF-R transmembrane domain, or a variant thereof.

142. The polypeptide of embodiment 140, wherein the transmembrane domain comprises the gp130 transmembrane domain, or a variant thereof.

143. The polypeptide of embodiment 140, wherein the transmembrane domain comprises the hGH-R transmembrane domain, or a variant thereof.

144. The polypeptide of any one of embodiments 108-143, wherein the polypeptide comprises:

a) an ECD that is a GCSFR-ECD, or variant thereof (e.g. as set forth herein and above); a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof (e.g. as set forth herein and above), and an immune activating ICD that is a GCSF-R ICD, or variant thereof (e.g. as set forth herein and above);

b) an ECD that is a hGH-R-ECD, or variant thereof (e.g. as set forth herein and above); a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof (e.g. as set forth herein and above), and immune activating ICD that is a GCSF-R ICD, or variant thereof (e.g. as set forth herein and above);

c) an ECD that is a hGH-R-ECD, or variant thereof (e.g. as set forth herein and above); a transmembrane domain that is a gp130 transmembrane domain, or variant thereof (e.g. as set forth herein and above), and immune activating ICD that comprises a gp130 ICD, or variant thereof (e.g. as set forth herein and above) and a IL-2R β ICD, or variant thereof (e.g. as set forth herein and above); or

d) an ECD that is a hGH-R-ECD, or variant thereof (e.g. as set forth herein and above); a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof (e.g. as set forth herein and above), and immune activating ICD that comprises a GCSF-R ICD, or variant thereof (e.g. as set forth herein and above) and a IL-7R α ICD, or variant thereof (e.g. as set forth herein and above).

145. The polypeptide of any one of embodiments 108-144, wherein the polypeptide comprises an amino acid sequence of SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 120, or SEQ ID NO: 124, or a variant of any of the foregoing.

146. The polypeptide of embodiment 145 wherein the variant comprises a polypeptide having at least 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%, or 99% identity to SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 120, or SEQ ID NO: 124.

147. A particle comprising the polypeptide of any one of embodiments 108-146, wherein the particle is a vector (e.g., virus, a liposome, plasmid, and the like) or a cell.

148. The particle of embodiment 147, wherein the particle is a virus or viral vector.

149. The particle of embodiment 148, wherein the viral vector is a lentiviral vector, AV vector, an AAV vector, and the like.
150. The particle of embodiments 148 or 149, wherein the viral vector is a pseudotyped viral vector.
151. The particle of any one of embodiments 147-150, wherein the particle further comprises a chimeric antigen receptor, such as a chimeric antigen receptor comprising a an antigen binding domain that binds to a tumor antigen.
152. A viral particle comprising a heterologous viral glycoprotein, a targeting moiety, and one or more nucleic acid molecule encoding for one or more heterologous molecules of interest, wherein the targeting moiety comprises a polypeptide having the formula T-S₁, wherein T is a target binding domain and S₁ is a stalk portion, and wherein the nucleic acid molecule encoding for a heterologous molecules of interest is the nucleic acid molecule of any one of embodiments 45-107.
153. The viral particle of embodiment 152, wherein the stalk portion S₁ comprises a variant Fc protein, wherein the variant Fc protein comprises a transmembrane domain and an effector mutation, wherein the effector mutation inhibits the interaction between the Fc protein and a Fc interacting protein, such as FcγR, C1q, FcRβ, or FcRn.
154. The viral particle of embodiment 153, wherein the S₁ stalk portion is attached to the surface of the viral particle through the transmembrane domain.
155. The viral particle of embodiments 153 or 154, wherein the Fc protein is a IgG1 Fc, IgG2 Fc or IgG4 Fc protein.
156. The viral particle of any one of embodiments 153-155, wherein the variant Fc protein comprises a variant of a sequence of SEQ ID NO: 26, SEQ ID NO: 27, or SEQ ID NO: 28.
157. The viral particle of any one of embodiments 153-156, wherein the variant Fc protein is a variant IgG1 Fc protein.
158. The viral particle of embodiment 157, wherein the variant IgG1 Fc protein comprises one or more of the mutations selected from the group consisting of: L234A, L235A, N297A, P329G, I253A, H310A, and H435A.
159. The viral particle of embodiments 157 or 158, wherein the variant IgG1 Fc protein comprises a mutation that corresponds to L234A and L235A of SEQ ID NO: 26.
160. The viral particle of any one of embodiments 157-159, wherein the variant IgG1 Fc protein comprises a mutation that corresponds to N297A of SEQ ID NO: 26.

161. The viral particle of any one of embodiments 157-160, wherein the variant IgG1 Fc protein comprises a mutation that corresponds to P329G of SEQ ID NO: 26.
162. The viral particle of any one of embodiments 157-161, wherein the variant IgG1 Fc protein comprises a mutation that corresponds to L234A, L235A, N297A, and P329G of SEQ ID NO: 26.
163. The viral particle of any one of embodiments 157-162, wherein the variant IgG1 Fc protein comprises a mutation that corresponds to I253A of SEQ ID NO: 26.
164. The viral particle of any one of embodiments 157-163, wherein the variant IgG1 Fc protein comprises a mutation that corresponds to H310A of SEQ ID NO: 26.
165. The viral particle of any one of embodiments 157-164, wherein the variant IgG1 Fc protein comprises a mutation that corresponds to H435A of SEQ ID NO: 26.
166. The viral particle of any one of embodiments 157-165, wherein the variant IgG1 Fc protein comprises a mutation that corresponds to I253A, H310A, and H435A of SEQ ID NO: 26.
167. The viral particle of any one of embodiments 157-166, wherein the variant IgG1 Fc protein comprises an amino acid sequence having at least 70% identity to SEQ ID NO: 103 and further comprises one or more mutations that correspond to L19A, L20A, N82A, P114G, I38A, H95A, and/or H220A of SEQ ID NO: 103.
168. The viral particle of any one of embodiments 157-167, wherein the variant IgG1 Fc protein comprises an amino acid sequence having at least 80% identity to SEQ ID NO: 104, at least 85% identity to SEQ ID NO: 104, at least 90% identity to SEQ ID NO: 104, at least 95% identity to SEQ ID NO: 104, at least 98% identity to SEQ ID NO: 104, or at least 100% identity to SEQ ID NO: 104.
169. The viral particle of any one of embodiments 153-156, wherein the variant Fc protein is a variant IgG2 Fc protein.
170. The viral particle of embodiment 169, wherein the variant IgG2 Fc protein comprises one or more mutations selected from the group consisting of: N297A, P329G, I253A, H310A, and H435A.
171. The viral particle of embodiments 169 or 170, wherein the IgG2 Fc protein comprises a mutation that corresponds to N297A of SEQ ID NO: 27.
172. The viral particle of embodiments 169 or 170, wherein the IgG2 Fc protein comprises a mutation that corresponds to P329G of SEQ ID NO: 27.
173. The viral particle of any one of embodiments 169-172, wherein the IgG2 Fc protein comprises a mutation that corresponds to N297A and P329G of SEQ ID NO: 27.

174. The viral particle of any one of embodiments 169-173, wherein the variant IgG2 Fc protein comprises a mutation that corresponds to I253A of SEQ ID NO: 27.
175. The viral particle of any one of embodiments 169-174, wherein the variant IgG2 Fc protein comprises a mutation that corresponds to H310A of SEQ ID NO: 27.
176. The viral particle of any one of embodiments 169-175, wherein the IgG2 Fc protein comprises a mutation that corresponds to H435A of SEQ ID NO: 27.
177. The viral particle of any one of embodiments 169-176, wherein the variant IgG2 Fc protein comprises a mutation that corresponds to I253A, H310A, and H435A of SEQ ID NO: 27.
178. The viral particle of any one of embodiments 153-156, wherein the variant Fc protein is a variant IgG4 Fc protein.
179. The viral particle of embodiment 178, wherein the variant IgG4 Fc protein comprises one or more mutations selected from the group consisting of: S228P, L235E, N297A, P329G, I253A, H310A, and H435A.
180. The viral particle of embodiments 178 or 179, wherein the IgG4 Fc protein comprises a mutation that corresponds to S228P of SEQ ID NO: 28.
181. The viral particle of any one of embodiments 178-180, wherein the IgG4 Fc protein comprises a mutation that corresponds to L235E of SEQ ID NO: 28.
182. The viral particle of any one of embodiments 178-181, wherein the IgG4 Fc protein comprises a mutation that corresponds to N297A of SEQ ID NO: 28.
183. The viral particle of any one of embodiments 178-182, wherein the IgG4 Fc protein comprises a mutation that corresponds to P329G of SEQ ID NO: 28.
184. The viral particle of any one of embodiments 178-183, wherein the IgG4 Fc protein comprises a mutation that corresponds to S228P, L235E, N297A, and P329G of SEQ ID NO: 28.
185. The viral particle of any one of embodiments 178-184, wherein the variant IgG4 Fc protein comprises a mutation that corresponds to I253A of SEQ ID NO: 28.
186. The viral particle of any one of embodiments 178-185, wherein the variant IgG4 Fc protein comprises a mutation that corresponds to H310A of SEQ ID NO: 28.
187. The viral particle of any one of embodiments 178-186, wherein the IgG4 Fc protein comprises a mutation that corresponds to H435A of SEQ ID NO: 28.
188. The viral particle of any one of embodiments 178-187, wherein the variant IgG4 Fc protein comprises a mutation that corresponds to I253A, H310A, and H435A of SEQ ID NO: 28.

189. The viral particle of any one of embodiments 153-188, wherein the targeting moiety having the formula T-S₁ comprises a stalk portion S₁ having a formula of L₁-Fc-L₂-X₁.

wherein:

L₁ is a linker or absent;

Fc is a variant Fc protein;

L₂ is a linker or absent; and

X₁ is a polypeptide comprising the transmembrane domain,

wherein the targeting moiety having the formula T-S₁ has a formula of T-L₁-Fc-L₂-X₁.

190. The viral particle of embodiment 189, wherein L₁ and L₂ are each, independently, a polypeptide linker.

191. The viral particle of embodiment 190, wherein the polypeptide linker comprises (GGGGA)_n (SEQ ID NO: 54), (GGGGS)_n (SEQ ID NO: 55), (EAAAK)_n (SEQ ID NO: 73), A(EAAAK)_nA (SEQ ID NO: 74), (XP)_n (SEQ ID NO: 75), wherein X is Ala, Lys, or Glu, GSAGSAAGSGEF (SEQ ID NO: 56), KESGSVSSEQLAQFRSLD (SEQ ID NO: 57), EGKSSGSGSESKST (SEQ ID NO: 58), AEAAAKEAAKA (SEQ ID NO: 76), or a combination thereof, wherein each n is, independently, 1-5.

192. The viral particle of any one of embodiments 189-191, wherein L₁ is absent.

193. The viral particle of any one of embodiments 189-191, wherein L₁ is (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), and

wherein each n is, independently, 1-5.

194. The viral particle of any one of embodiments 189-193, wherein L₂ is absent.

195. The viral particle of any one of embodiments 189-193, wherein L₂ is (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), and

wherein each n is, independently, 1-5.

196. The viral particle of any one of embodiments 189-195, wherein X₁ comprises a polypeptide having a formula of ECD-T_M-ICD, wherein:

ECD is an extracellular domain, or a fragment thereof, of a cell surface protein, or absent;

T_M is a transmembrane domain of a transmembrane protein; and

ICD is an intracellular domain or a protein that facilitates incorporation of the targeting moiety into the envelope of the viral particle, or absent,

wherein the targeting moiety having the formula of T-L₁-Fc-L₂-X₁ has a formula of T-L₁-Fc-L₂-ECD-T_M-ICD.

197. The viral particle of embodiment 196, wherein the ECD is absent.

198. The viral particle of embodiment 196, wherein the ECD is an extracellular domain, or fragment thereof, of CD8 or CD28.

199. The viral particle of embodiment 198, wherein the ECD comprises an amino acid sequence of SEQ ID NO: 59 or SEQ ID NO: 60.

200. The viral particle of embodiment 198, wherein the ECD comprises an amino acid sequence of SEQ ID NO: 60.

201. The viral particle of any one of embodiments 196-200, wherein T_M is a transmembrane domain, or a fragment thereof, of CD8 or CD28.

202. The viral particle of embodiment 201, wherein the T_M comprises an amino acid sequence of SEQ ID NO: 61 or SEQ ID NO: 62.

203. The viral particle of embodiment 201, wherein the T_M comprises an amino acid sequence of SEQ ID NO: 62.

204. The viral particle of any one of embodiments 196-203, wherein the ICD is absent.

205. The viral particle of any one of embodiments 196-203, wherein the ICD comprises an Env incorporation motif

206. The viral particle of embodiment 205, wherein the Env incorporation motif comprises an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64.

207. The viral particle of embodiment 152, wherein the stalk portion S_1 comprises a formula of L_3 - X_1 , wherein:

L_3 is a flexible peptide linker, and

X_1 is a polypeptide comprising a transmembrane domain,

wherein the targeting moiety having the formula T - S_1 has a formula of T - L_3 - X_1 .

208. The viral particle of embodiment 207, wherein L_3 comprises a polypeptide having a sequence of $(GGGGA)_n$ (SEQ ID NO: 54), $(GGGGS)_n$ (SEQ ID NO: 55), GSAGSAAGSGEF (SEQ ID NO: 56), KESGSVSSEQLAQFRSLD (SEQ ID NO: 57), EGKSSGSGSESKST (SEQ ID NO: 58), or any combination thereof, wherein each n is, independently, 1-4.

209. The viral particle of embodiment 208, wherein n is 1, 2, or 4.

210. The viral particle of any one of embodiments 207-209, wherein X_1 comprises a polypeptide having a formula of ECD- T_M -ICD, wherein:

ECD is an extracellular domain, or a fragment thereof, of a cell surface protein, or absent;

T_M is a transmembrane domain of a transmembrane protein; and

ICD is an intracellular domain or a protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, or absent,

wherein the targeting moiety having the formula of T-L₃-X₁ has a formula of T-L₃-ECD-T_M-ICD.

211. The viral particle of embodiment 210, wherein the ECD is absent.
212. The viral particle of embodiment 210, wherein the ECD is an extracellular domain, or fragment thereof, or CD8 or CD28.
213. The viral particle of embodiment 212, wherein the ECD comprises an amino acid sequence of SEQ ID NO: 59 or SEQ ID NO: 60.
214. The viral particle of embodiment 212, wherein the ECD comprises an amino acid sequence of SEQ ID NO: 59.
215. The viral particle of any one of embodiments 210-214, wherein T_M is a transmembrane domain, or a fragment thereof, of CD8 or CD28.
216. The viral particle of embodiment 215, wherein the T_M comprises an amino acid sequence of SEQ ID NO: 61 or SEQ ID NO: 62.
217. The viral particle of embodiment 215, wherein the T_M comprises an amino acid sequence of SEQ ID NO: 61.
218. The viral particle of any one of embodiments 210-217, wherein the ICD is absent.
219. The viral particle of any one of embodiments 210-217, wherein the ICD comprises an Env incorporation motif.
220. The viral particle of embodiment 219, wherein the Env incorporation motif comprises an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64.
221. The viral particle of any one of embodiments 152-220, wherein the target binding domain (T) binds to an immune cell, wherein the immune cell is any of a T cell, B cell; NK cell, dendritic cell, neutrophils, macrophages, a cancer cell; or, for example, CD3+ T cell; CD4+ T cell; CD7+ T cell, CD8+ T cell; CD19+ B cell; CD19+ cancer cell; CD20+ B cell; CD20+ cancer cell, CD30+ lung epithelial cell; CD34+ haematopoietic stem cell; CD105+ endothelial cell; CD105+ haematopoietic stem cell; CD117+ haematopoietic stem cell; CD133+ cancer cell; EpCAM+ cancer cell; GluA2+ neuron; GluA4+ neuron; Haematopoietic stem cell; Hepatocyte; Her2/Neu+ cancer cell; NKG2D+ natural killer cell; SLC1A3+ astrocyte; SLC7A10+ adipocyte.
222. The viral particle of any one of embodiments 152-221, wherein the target binding domain (T) binds to CD7, CD8, cKit (CD117), CD4, CD3, CD5, CD6, CD2, TCR alpha, TCR beta, TCR gamma, TCR delta, CD10, CD34, CD110, CD33, CD14, CD68, CCR7, CD62L, CD25, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, or CXCR3, A glycosylated CD43 epitope

expressed on acute leukemia or lymphoma but not on hematopoietic progenitors; A glycosylated CD43 epitope expressed on non-hematopoietic cancers; A kinase anchor protein 4 (AKAP-4); Adrenoceptor beta 3 (ADRB3); AFP; Anaplastic lymphoma kinase (ALK); Androgen receptor; Angiopoietin-binding cell surface receptor 2 (Tie 2); Auto antibody to desmoglein 1 (Dsg1); Auto antibody to desmoglein 3 (Dsg3); B7H3 (CD276); Biotin; Bone marrow stromal cell antigen 2 (BST2); BST1/CD157; Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-1a); Carbonic anhydrase IX (CAIX); Carcinoembryonic antigen (CEA); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites); CCR4; CD5; CD19; CD20; CD22; CD24; CD30; CD32 (FCGR2A); CD33; CD34; CD38; CD44v6; CD72; CD79a; CD79b; CD97; CD99; CD123; CD171; CD179a; CD179b-IGLII; CD200R; CD276/B7H3; CD300 molecule-like family member f (CD300LF); CDH1-CD324; CDH6; CDH17; CDH19; Chromosome X open reading frame 61 (CXORF61); Claudin 6 (CLDN6); Claudin18.2 (CLD18A2 or CLDN18A.2); CMV pp65; C-MYC epitope Tag; Cripto; CS1 (also referred to as CD2 subset 1 or CRACC or SLAMF7 or CD319 or 19A24); CSF2RA (GM-CSFR-alpha); C-type lectin domain family 12 member A (CLEC12A); C-type lectin-like molecule-1 (CLL-1 or CLECL1); Cyclin B1; Cytochrome P450 1B1 (CYP1B1); DLL3; EBV-EBNA3c; EGF-bke module-containing mucin-like hormone receptor-like 2 (EMR2); Elongation factor 2 mutated (ELF2M); Ephrin B2; Ephrin type-A receptor 2 (EphA2); Epidermal growth factor receptor (EGFR); Epidermal growth factor receptor variant III (EGFRviii); Epithelial cell adhesion molecule (EPCAM); ERG; ETS translocation-variant gene 6 located on chromosome 12p (ETV6-AML); Fc fragment of IgA receptor (FCAR or CD89); Fc receptor-like 5 (FCRL5); Fibroblast activation protein alpha (FAP); FITC; Fms Like Tyrosine Kinase 3 (FLT3); Folate receptor alpha (Fra or FR1); Folate receptor beta (FRb); Follicle stimulating hormone receptor (FSHR); Fos-related antigen 1; Fucosyl-GM1; G protein coupled receptor class C group 5 member D (GPRC5D); G protein-coupled receptor 20 (GPR20); GAD; Ganglioside G2 (GD2); Ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(1-4)bDGlc(1-1)Cer); Ganglioside GM3 (aNeu5Ac(2-3)bDCIalp(1-4)bDGlc(1-1)Cer); GD3; GFRalpha4; Glycoprotein 100 (gp100); Glypican-3 (GPC3); Gonadotropin Hormone receptor (CGHR or GR); GpA33; GpNMB; GPRC5D; Guanylyl cyclase C (GCC); Heat shock protein 70-2 mutated (mut hsp70-2); Hepatitis A virus cellular receptor 1 (HAVCR1); Hexasaccharide portion of globoH glycosphingolipid (GloboH); High molecular weight-melanoma associated antigen (HMWMAA); HIV1 envelope glycoprotein; HLA; HLA-DOA; HLA-A; HLA-A2; HLA-B; HLA-C; HLA-DM; HLA-DOB; HLA-DP; HLA-DQ; HLA-DR; HLA-G; HTLV1-Tax; Human papilloma virus E6 (HPV E6);

Human papilloma virus E7 (HPV E7); Human Telomerase reverse transcriptase (hTERT); IgE; IL13Ra2; IL13Ra; Immunoglobulin lambda-like polypeptide 1 (IGLL1); Influenza A hemagglutinin (HA); Insulin-like growth factor 1 receptor (IGF-I receptor); Interleukin 11 receptor alpha (IL-11Ra); Interleukin-13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Intestinal carboxyl esterase; KIT (CD117); KSHV K8.1; KSHV-gH; LAMP1; Legumain; Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Leutenizing hormone receptor (LHR); Lewis(Y) antigen; Lewis Ag; Liv1; Locus K 9 (LY6K); Low conductance chloride channel; Lymphocyte antigen 6 complex; Lymphocyte antigen 75 (LY75); Lymphocyte-specific protein tyrosine kinase (LCK); Mammary gland differentiation antigen (NY-BR-1); Melanoma antigen recognized by T cells 1 (MelanA or MART1); Melanoma-associated antigen 1 (MAGE-A1); Melanoma cancer testis antigen-1 (MAD-CT-1); Melanoma cancer testis antigen-2 (MAD-CT-2); Melanoma inhibitor of apoptosis (ML-IAP); Mesothelin; MPL; Mucin 1 cell surface associated (MUC1); N-Acetyl glucosaminyl-transferase V (NA17); Nectin-4; Neural cell adhesion molecule (NCAM); NKG2D; NYBR1; O-acetyl-GD2 ganglioside (OacGD2); Olfactory receptor 51E2 (OR51E2); Oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); P53 mutant; Paired box protein Pax-3 (PAX3); Paired box protein Pax-5 (PAX5); Pannexin 3 (PANX3); PDL1; P-glycoprotein; Placenta-specific 1 (PLAC1); Platelet-derived growth factor receptor beta (PDGFR-beta); Polysialic acid; Proacrosin binding protein sp32 (OY-TES1); Prostase; Prostate carcinoma tumor antigen-1 (PCT A-1 or Galectin 8); Prostate stem cell antigen (PSCA); Prostate-specific membrane antigen (PSMA); Prostatic acid phosphatase (PAP); Prostein; Protease Serine 21 (Testisin or PRSS21); Proteasome (Prosome Macropain) Subunit Beta Type 9 (LMP2); PTK7; Ras G12V; Ras Homolog Family Member C (RhoC); Rat sarcoma (Ras) mutant; Receptor for Advanced Glycation Endproducts (RAGE-1); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Receptor tyrosine-protein kinase ERBB2 or Her-22/neu; Renal ubiquitous 1 (RU1); Renal ubiquitous 2 (RU2); Sarcoma translocation breakpoints; Serine 2 (TMPRSS2) ETS fusion gene; Sialyl Lewis adhesion molecule (sLe); SLAMF4; SLAMF6; Slea (CA19.9 or Sialyl Lewis Antigen); Sperm protein 17 (SPA17); Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Stage-specific embryonic antigen-4 (SSEA-4); STEAP1; Survivin; Synovial sarcoma X breakpoint 2 (SSX2); TCR Gamma Alternate Reading Frame Protein (TARP); TCR-beta1 chain; TCR-beta2 chain; TCR-delta chain; TCR-gamma chain; TCRgamma-delta; Telomerase; TGFbetaR2; The antigen recognized by TNT antibody; Thyroid stimulating hormone receptor (TSHR); Timl-

/HVCRI; Tissue Factor 1 (TF1); Tn ag; Tn antigen ((Tn Ag) or (GalNAca-Ser/Thr)); TNF receptor family member B cell maturation (BCMA); Transglutaminase 5 (TGS5); Transmembrane protease; TROP2; Tumor endothelial marker 1 (TEM1/CD248); Tumor endothelial marker 7-related (TEM7R); Tumor protein p53 (p53); Tumor-associated glycoprotein 72 (TAG72); Tyrosinase; Tyrosinase-related protein 2 (TRP-2); Uroplakin 2 (UPK2); Vascular endothelial growth factor receptor 2 (VEGFR2); V-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Wilms tumor protein (WT1); or X Antigen Family Member 1A (XAGE1).

223. The viral particle of embodiment 222, wherein the target binding domain (T) binds to CD7.

224. The viral particle of embodiment 223, wherein the target binding domain (T) comprises a polypeptide comprising: (i) a heavy chain comprising a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 30; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 31; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 32, or variants of any of the foregoing; and (ii) a light chain comprising a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 33; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 34; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 35; or variants of any of the foregoing.

225. The viral particle of embodiment 224, wherein the heavy chain comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 36, wherein the polypeptide comprises the sequences of HCDR1 as set forth in SEQ ID NO: 30; HCDR2 as set forth in SEQ ID NO: 31; and HCDR3 as set forth in SEQ ID NO: 32.

226. The viral particle of embodiments 224 or 225, wherein the light chain comprises: a light chain variable region having at least 90% sequence identity to SEQ ID NO: 37, wherein the polypeptide comprises the sequences of LCDR1 as set forth in SEQ ID NO: 33; LCDR2 as set forth in SEQ ID NO: 34; and LCDR3 as set forth in SEQ ID NO: 35.

227. The viral particle of any one of embodiments 224-226, wherein the polypeptide comprises a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 36, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 37, wherein polypeptide comprises the sequences of HCDR1 as set forth in SEQ ID NO: 30; HCDR2 as set

forth in SEQ ID NO: 31; HCDR3 as set forth in SEQ ID NO: 32; LCDR1 as set forth in SEQ ID NO: 33; LCDR2 as set forth in SEQ ID NO: 34; and LCDR3 as set forth in SEQ ID NO: 35.

228. The viral particle of any one of embodiments 224-227, wherein the light chain and the heavy chain comprise: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 36; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 37.

229. The viral particle of any one of embodiments 224-228, wherein the light chain and the heavy chain comprise: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 36; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 37.

230. The viral particle of any one of embodiments 224-229, wherein the light chain and the heavy chain comprise: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 36; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 37.

231. The viral particle of any one of embodiments 224-230, wherein the light chain and the heavy chain comprise: a heavy chain variable region comprising SEQ ID NO: 36, and a light chain variable region comprising SEQ ID NO: 37.

232. The viral particle of any one of embodiments 224-231, wherein the heavy chain variable region and the light chain variable region are linked by a linker, such as a peptide linker, which can be for example, a glycine/serine linker.

233. The viral particle of embodiment 232, wherein the peptide linker comprises a sequence of (GGGS)_n, wherein n is independently 1-5.

234. The viral particle of any one of embodiments 224-231, wherein the heavy chain variable region and the light chain variable region are directly linked to one another and are not linked by a linker.

235. The viral particle of any one of embodiments 223-233, wherein the target binding domain (T) that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 38, at least 95% sequence identity to SEQ ID NO: 38, at least 99% sequence identity to SEQ ID NO: 38, or a sequence as set forth in SEQ ID NO: 38.

236. The viral particle of any one of embodiments 223-233, wherein the target binding domain (T) that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 39, having at least 95% sequence identity to SEQ ID

NO: 39, having at least 99% sequence identity to SEQ ID NO: 39, or a sequence as set forth in SEQ ID NO: 39.

237. The viral particle of embodiment 222, wherein the target binding domain (T) binds to CD8.

238. The viral particle of embodiment 237, wherein the target binding domain (T) comprises a polypeptide that comprises: a heavy chain comprising a heavy chain variable region comprising heavy chain CDR1, CDR2, and CDR3 sequences, wherein the heavy chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 42; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 43; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 44, or variants of any of the foregoing; and (ii) a light chain comprising a light chain variable region comprising light chain CDR1, CDR2, and CDR3 sequences, wherein the light chain CDR1 sequence has the amino acid sequence of SEQ ID NO: 45; the light chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 46; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 47; or variants of any of the foregoing.

239. The viral particle of embodiment 238, wherein the target binding domain (T) comprises a heavy chain comprising a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 48, wherein the polypeptide comprises the sequences of HCDR1 as set forth in SEQ ID NO: 42; HCDR2 as set forth in SEQ ID NO: 43; and HCDR3 as set forth in SEQ ID NO: 44.

240. The viral particle of embodiment 238 or 239, wherein the target binding domain (T) comprises a light chain comprising a light chain variable region having at least 90% sequence identity to SEQ ID NO: 49, wherein the polypeptide comprises the sequences of LCDR1 as set forth in SEQ ID NO: 45; LCDR2 as set forth in SEQ ID NO: 46; and LCDR3 as set forth in SEQ ID NO: 47.

241. The viral particle of any one of embodiments 238-240, wherein the target binding domain (T) comprises a polypeptide comprising a heavy chain and a light chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 48, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 49, wherein polypeptide comprises the sequences of HCDR1 as set forth in SEQ ID NO: 42; HCDR2 as set forth in SEQ ID NO: 43; HCDR3 as set forth in SEQ ID NO: 44; LCDR1 as set forth in SEQ ID NO: 45; LCDR2 as set forth in SEQ ID NO: 46; and LCDR3 as set forth in SEQ ID NO: 47.

242. The viral particle of any one of embodiments 238-241, wherein the target binding domain (T) comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 90% sequence identity to SEQ ID NO: 48; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 49.

243. The viral particle of any one of embodiments 238-241, wherein the target binding domain (T) comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 95% sequence identity to SEQ ID NO: 48; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 49.

244. The viral particle of any one of embodiments 238-241, wherein the target binding domain (T) comprises a polypeptide comprising a light chain and a heavy chain comprising: a heavy chain variable region of the heavy chain having at least 99% sequence identity to SEQ ID NO: 48; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 49.

245. The viral particle of embodiment 237, wherein the target binding domain (T) comprises a polypeptide comprising a light chain and a heavy chain comprising: wherein the heavy chain comprises a heavy chain variable region comprising SEQ ID NO: 48, and the light chain comprises a light chain variable region comprising SEQ ID NO: 49.

246. The viral particle of any one of embodiments 238-245, wherein the heavy chain variable region and the light chain variable region are linked by a linker, such as a peptide linker.

247. The viral particle of embodiment 246, wherein the peptide linker is a glycine/serine linker.

248. The viral particle of embodiments 246 or 247, wherein the peptide linker comprises a sequence of (GGGGS)_n (SEQ ID NO: 55), wherein each n is independently 1-5.

249. The viral particle of any one of embodiments 238-245, wherein the heavy chain variable region and the light chain variable region are directly linked to one another and are not linked by a linker.

250. The viral particle of any one of embodiments 237-248, wherein the target binding domain (T) that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 50, at least 95% sequence identity to SEQ ID NO: 50, at least 99% sequence identity to SEQ ID NO: 50, or a sequence as set forth in SEQ ID NO: 50.

251. The viral particle of any one of embodiments 237-248, wherein the target binding domain (T) that binds to CD8 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 51, having at least 95% sequence identity to SEQ ID NO: 51, having at least 99% sequence identity to SEQ ID NO: 51, or a sequence as set forth in SEQ ID NO: 51.

252. The viral particle of any one of embodiments 152-251, wherein the target binding domain (T) is an antibody, or an antigen-binding fragment thereof, such as scFv antibody.

253. The viral particle of any one of embodiments 152-252, wherein the heterologous viral glycoprotein is a SVCV-G polypeptide.

254. The viral particle of embodiment 253, wherein the SVCV-G polypeptide comprises a polypeptide having at least 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% identity to SEQ ID NO: 52 or SEQ ID NO: 53.

255. The viral particle of embodiment 253 or 254, wherein the SVCV-G polypeptide comprises a polypeptide having at least 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% identity to SEQ ID NO: 52.

256. The viral particle of embodiment 253 or 254, wherein the SVCV-G polypeptide comprises a polypeptide having at least 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% identity to SEQ ID NO: 53.

257. The viral particle of embodiment 253 or 254, wherein the SVCV-G polypeptide comprises SEQ ID NO: 52 or SEQ ID NO: 53.

258. The viral particle of any one of embodiments 253, 254, or 257, wherein the SVCV-G polypeptide comprises SEQ ID NO: 52.

259. The viral particle of any one of embodiments 253, 254, or 257, wherein the SVCV-G polypeptide comprises SEQ ID NO: 53.

260. The viral particle of any one of embodiments 152-252, wherein the heterologous viral glycoprotein is a VSV-G polypeptide.

261. The viral particle 260, wherein the VSV-G polypeptide comprises a polypeptide of SEQ ID NO: 2 comprising a mutation that corresponds to a mutation at position 182 of SEQ ID NO: 2.

262. The viral particle 260, wherein the VSV-G polypeptide comprises an amino acid sequence having at least 70% identity to SEQ ID NO: 2 and comprising a mutation at position 182 as compared to SEQ ID NO: 2.
263. The viral particle of embodiment 261 or 262, wherein the VSV-G polypeptide comprises a I182E or I182D mutation as compared to SEQ ID NO: 2.
264. The viral particle of any one of embodiments 260-263, wherein the VSV-G polypeptide comprises the sequence having at least 70% identity to SEQ ID NO: 1 and comprising a mutation at position 198 as compared to SEQ ID NO: 1.
265. The viral particle of any one of embodiments 260-264, wherein the VSV-G polypeptide comprises a mutation that corresponds to I182D or I182E as compared to a sequence of SEQ ID NO: 2.
266. The viral particle of any one of embodiments 260-265, wherein the VSV-G polypeptide comprises a sequence at least 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% to a sequence of SEQ ID NO: 4.
267. The viral particle of any one of embodiments 260-265, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 4.
268. The viral particle of any one of embodiments 260-265, wherein the VSV-G polypeptide comprises a sequence at least 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% to a sequence of SEQ ID NO: 5.
269. The viral particle of any one of embodiments 260-265, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 5.
270. The viral particle of any one of embodiments 260-262 or 264, wherein the VSV-G polypeptide comprises a sequence at least 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% to a sequence of SEQ ID NO: 3.
271. The viral particle of any one of embodiments 260-262 or 264, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 3.
272. The viral particle of any one of embodiments 260-271, wherein the VSV-G polypeptide further comprises a mutation in the VSV-G protein that corresponds to a mutation as described in US 2020/0216502.

273. The viral particle of any one of embodiments 260-272, wherein the VSV-G polypeptide further comprises a mutation in the VSV-G protein that corresponds to a position of 8, 10, 47, 209 and/or 354 as compared to SEQ ID NO: 2.
274. The viral particle of any one of embodiments 260-273, wherein the VSV-G polypeptide further comprises a mutation that corresponds to a position 8 in SEQ ID NO: 2, wherein the mutation any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except Y.
275. The viral particle of any one of embodiments 260-274, wherein the VSV-G polypeptide further comprises a mutation that corresponds to a position 209 in SEQ ID NO: 2, wherein the mutation any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except H.
276. The viral particle of any one of embodiments 260-275, wherein the VSV-G polypeptide further comprises a mutation that corresponds to a position 47 in SEQ ID NO: 2, wherein the mutation any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except K or R.
277. The viral particle of any one of embodiments 260-276, wherein the VSV-G polypeptide further comprises a mutation that corresponds to a position 354 in SEQ ID NO: 2, wherein the mutation any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except K or R.
278. The viral particle of any one of embodiments 260-277, wherein the VSV-G polypeptide further comprises a mutation that corresponds to a position 10 in SEQ ID NO: 2, wherein the mutation any amino acid different from the amino acid indicated at that position in the sequence SEQ ID NO: 2, except Q or N.
279. The viral particle of any one of embodiments 260-278, wherein the VSV-G protein comprises a substitution at position 47 or at position 354, or at both positions 47 and 354, wherein each position is, independently, substituted by A, G, F, Q, or N.
280. The viral particle of any one of embodiments 260-279, wherein the VSV-G protein comprises a substitution at position 8, wherein the substitution is H8A, H8I, H8V, H8L, H8C, H8D, H8E, H8F, H8G, H8K, H8M, H8N, H8P, H8Q, H8R, H8S, H8T, H8W, or H8Y.
281. The viral particle of any one of embodiments 260-280, wherein the VSV-G protein comprises a substitution at position 47, wherein the substitution is K47Q or K47N.
282. The viral particle of any one of embodiments 260-281, wherein the VSV-G protein comprises a substitution H8A and/or K47Q mutation.

283. The viral particle of any one of embodiments 260-282, wherein the VSV-G protein comprises a substitution at position 10, such as Q10A, Q10R, or Q10K substitution.
284. The viral particle of any one of embodiments 260-283, wherein the VSV-G protein further comprises a mutation that corresponds to a mutation at positions 214 and/or 352 of SEQ ID NO: 2.
285. The viral particle of embodiment 284, wherein the VSV-G polypeptide comprises a T214N and/or T352A mutation.
286. The viral particle of embodiment 260, wherein the VSV-G polypeptide comprises a substitution at positions I182 and at least one of T214, and T352 of SEQ ID NO: 2.
287. The viral particle of embodiment 286, wherein the VSV-G polypeptide comprises substitutions at positions I182, T214, and T352 of SEQ ID NO: 2.
288. The viral particle of embodiments 286 or 287, wherein the substitution at position 182 is I182D or I182E, the substitution at position 214 is T214N, and the substitution at position 352 is T352A.
289. The viral particle of any one of embodiments 286-288, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24 or SEQ ID NO: 25.
290. The viral particle of any one of embodiments 286-288, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 22.
291. The viral particle of any one of embodiments 286-288, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 23.
292. The viral particle of any one of embodiments 286-288, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 24.
293. The viral particle of any one of embodiments 286-288, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 25.
294. A viral particle comprising a heterologous viral glycoprotein, a targeting moiety comprising a polypeptide having the formula T-S₁, and a nucleic acid molecule encoding for a heterologous molecule of interest,
wherein T is a target binding domain and S₁ is a stalk portion,
wherein the heterologous viral glycoprotein comprises a sequence selected from SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 52 or SEQ ID NO: 53;
wherein the target binding domain comprises a sequence selected from SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50 or SEQ ID NO: 51;

wherein the stalk portion S_1 comprises a variant Fc protein comprising a sequence that is a variant of SEQ ID NO: 26, SEQ ID NO: 27, or SEQ ID NO: 28;

wherein the variant of SEQ ID NO: 26 comprises one or more mutations selected from the group consisting of L234A, L235A, N297A, P329G, I253A, H310A, and H435A;

wherein the variant of SEQ ID NO: 27 comprises one or more mutations selected from the group consisting of N297A, P329G, I253A, H310A, and H435A;

wherein the variant of SEQ ID NO: 28 comprises one or more mutations selected from the group consisting of S228P, L235E, N297A, P329G, I253A, H310A, and H435A;

wherein the variant Fc protein further comprises a transmembrane domain comprising a sequence selected from SEQ ID NO: 61 or SEQ ID NO: 62; and

wherein the nucleic acid molecule encoding for a heterologous molecule of interest is the nucleic acid molecule of any one of embodiments 45-107.

295. A viral particle comprising a heterologous viral glycoprotein, a targeting moiety comprising a polypeptide having the formula T- S_1 , and a nucleic acid molecule encoding for a heterologous molecule of interest,

wherein T is a target binding domain and S_1 is a stalk portion,

wherein the heterologous viral glycoprotein comprises a sequence selected from SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 52 or SEQ ID NO: 53;

wherein the target binding domain comprises a sequence selected from SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50 or SEQ ID NO: 51;

wherein the stalk portion S_1 comprises a formula of L_1 -Fc- L_2 - X_1 , wherein:

L_1 is a linker comprising a sequence selected from SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, or SEQ ID NO: 76 or is absent;

Fc is a variant Fc protein comprising a sequence that is a variant of SEQ ID NO: 26, SEQ ID NO: 27, or SEQ ID NO: 28;

wherein the variant of SEQ ID NO: 26 comprises one or more mutations selected from the group consisting of L234A, L235A, N297A, P329G, I253A, H310A, and H435A;

wherein the variant of SEQ ID NO: 27 comprises one or more

mutations selected from the group consisting of N297A, P329G, I253A, H310A, and H435A;

wherein the variant of SEQ ID NO: 28 comprises one or more mutations selected from the group consisting of S228P, L235E, N297A, P329G, I253A, H310A, and H435A;

L₂ is a linker comprising a sequence selected from SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, or SEQ ID NO: 76 or is absent; and
X₁ is a polypeptide comprising a transmembrane domain having a formula of ECD-T_M-ICD, wherein:

ECD is an extracellular domain having a sequence selected from SEQ ID NO: 59 or SEQ ID NO: 60 or a fragment thereof or is absent;
T_M is a transmembrane domain having a sequence of SEQ ID NO: 61 or SEQ ID NO: 62, or a fragment thereof; and
ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64 or the ICD is absent; and

wherein the nucleic acid molecule encoding for a heterologous molecule of interest is the nucleic acid molecule of any one of embodiments 45-107.

296. A viral particle comprising a heterologous viral glycoprotein, a targeting moiety comprising a polypeptide having the formula T-S₁, and a nucleic acid molecule encoding for a heterologous molecule of interest,

wherein T is a target binding domain and S₁ is a stalk portion,

wherein the heterologous viral glycoprotein comprises a sequence selected from SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 52 or SEQ ID NO: 53;

wherein the target binding domain comprises a sequence selected from SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50 or SEQ ID NO: 51;

wherein the stalk portion S₁ comprises a formula of L₁-Fc-L₂-X₁, wherein:

L₁ is a linker comprising a sequence of SEQ ID NO: 55 or is absent;

Fc is a variant Fc protein comprising a sequence that is a variant of SEQ ID NO: 26, SEQ ID NO: 27, or SEQ ID NO: 28;

wherein the variant of SEQ ID NO: 26 comprises one or more mutations selected from the group consisting of L234A, L235A, N297A, P329G, I253A, H310A, and H435A;

wherein the variant of SEQ ID NO: 27 comprises one or more mutations selected from the group consisting of N297A, P329G, I253A, H310A, and H435A;

wherein the variant of SEQ ID NO: 28 comprises one or more mutations selected from the group consisting of S228P, L235E, N297A, P329G, I253A, H310A, and H435A;

L₂ is a linker comprising a sequence of SEQ ID NO: 55 or is absent; and

X₁ is a polypeptide comprising a transmembrane domain having a formula of ECD-T_M-ICD, wherein:

ECD is an extracellular domain having a sequence of SEQ ID NO: 60 or a fragment thereof or is absent;

T_M is a transmembrane domain having a sequence of SEQ ID NO: 62, or a fragment thereof; and

ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64 or the ICD is absent; and

wherein the nucleic acid molecule encoding for a heterologous molecule of interest is the nucleic acid molecule of any one of embodiments 45-107.

297. The viral particle of any one of embodiments 294-296, wherein the variant Fc protein comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 104, at least 90% identity to SEQ ID NO: 104, at least 95% identity to SEQ ID NO: 104, at least 98% identity to SEQ ID NO: 104, or comprises the amino acid sequence of SEQ ID NO: 104.

298. A viral particle comprising a heterologous viral glycoprotein, a targeting moiety comprising a polypeptide having the formula T-S₁, and a nucleic acid molecule encoding for a heterologous molecule of interest,

wherein T is a target binding domain and S₁ is a stalk portion,

wherein the heterologous viral glycoprotein comprises a sequence of SEQ ID NO: 23 or SEQ ID NO: 25;

wherein the target binding domain comprises a sequence of SEQ ID NO: 39;

wherein the stalk portion S₁ comprises a formula of L₁-Fc-L₂-X₁, wherein:

L₁ is a linker comprising a sequence of SEQ ID NO: 55;

Fc is a variant Fc protein comprising a sequence of SEQ ID NO: 104;

L₂ is a linker and is absent;

X₁ is a polypeptide comprising a transmembrane domain having a formula of ECD-T_M-ICD, wherein:

ECD is an extracellular domain having a sequence of SEQ ID NO: 60;

T_M is a transmembrane domain having a sequence of SEQ ID NO: 62;

and

ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63; and

wherein the nucleic acid molecule encoding for a heterologous molecule of interest encodes for a chimeric antigen receptor and a polypeptide comprising:

i) a ligand binding extracellular domain (ECD);

ii) an immune cell activating intracellular domain (ICD); and

iii) a transmembrane domain linking the ECD to the ICD.

299. A viral particle comprising a heterologous viral glycoprotein, a targeting moiety, and a nucleic acid molecule encoding for a heterologous molecule of interest, wherein;

the heterologous viral glycoprotein comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 23 or SEQ ID NO: 25, having at least 95% identity of SEQ ID NO: 23 or SEQ ID NO: 25, having at least 99% identity to SEQ ID NO: 23 or SEQ ID NO: 25, or having at least 100% identity to SEQ ID NO: 23 or SEQ ID NO: 25;

the targeting moiety comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 98, at least 95% identity to SEQ ID NO: 98, at least 99% identity to SEQ ID NO: 98, or at least 100% identity to SEQ ID NO: 98; and

wherein the nucleic acid molecule encoding for a heterologous molecule of interest encodes for a chimeric antigen receptor and a polypeptide comprising:

i) a ligand binding extracellular domain (ECD);

ii) an immune cell activating intracellular domain (ICD); and

iii) a transmembrane domain linking the ECD to the ICD.

300. A viral particle comprising a heterologous viral glycoprotein, a targeting moiety, and a nucleic acid molecule encoding for a heterologous molecule of interest, wherein;
- the heterologous viral glycoprotein comprises an amino acid sequence having at least 90% identity to of SEQ ID NO: 52 or SEQ ID NO: 53, having at least 95% identity to SEQ ID NO: 52 or SEQ ID NO: 53, having at least 99% identity to SEQ ID NO: 52 or SEQ ID NO: 53, or having at least 100% identity to SEQ ID NO: 52 or SEQ ID NO: 53;
- the targeting moiety comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 98, at least 95% identity to SEQ ID NO: 98, at least 99% identity to SEQ ID NO: 98, or at least 100% identity to SEQ ID NO: 98; and
- wherein the nucleic acid molecule encoding for a heterologous molecule of interest encodes for a chimeric antigen receptor and a polypeptide comprising:
- i) a ligand binding extracellular domain (ECD);
 - ii) an immune cell activating intracellular domain (ICD); and
 - iii) a transmembrane domain linking the ECD to the ICD.
301. A viral particle comprising a heterologous viral structural protein, a targeting moiety comprising a polypeptide having the formula T-S₁, and a nucleic acid molecule encoding for a heterologous molecule of interest,
- wherein T is a target binding domain and S₁ is a stalk portion;
- wherein the target binding domain comprises an amino acid sequence of SEQ ID NO: 38 or SEQ ID NO: 39;
- wherein the stalk portion S₁ comprises a formula of L₃-X₁; wherein
- L₃ is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, or SEQ ID NO: 58; and
- X₁ is polypeptide comprising a transmembrane domain having a formula ECD-T_M-ICD, wherein:
- ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59 or SEQ ID NO: 60, or a fragment thereof, or is absent;
- T_M is a transmembrane domain comprising an amino acid sequence of SEQ ID NO: 61 or SEQ ID NO: 62, or a fragment thereof; and
- ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle or is absent, wherein the ICD comprises an env incorporation

motif comprising an amino acid comprising a sequence of SEQ ID NO: 63 or SEQ ID NO: 64; and

wherein the nucleic acid molecule encoding for a heterologous molecule of interest is the nucleic acid molecule of any one of embodiments 45-107.

302. The viral particle of embodiment 301, wherein:

T comprises an amino acid sequence of SEQ ID NO: 38;

L₃ comprises an amino acid sequence of SEQ ID NO: 55;

ECD comprises an amino acid sequence of SEQ ID NO: 59;

T_M comprises an amino acid sequence of SEQ ID NO: 61; and

the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64.

303. The viral particle of embodiment 301, wherein:

T comprises an amino acid sequence of SEQ ID NO: 39;

L₃ comprises an amino acid sequence of SEQ ID NO: 55;

ECD comprises an amino acid sequence of SEQ ID NO: 59;

T_M comprises an amino acid sequence of SEQ ID NO: 61; and

the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64.

304. A viral particle comprising a heterologous viral structural protein, a targeting moiety comprising a polypeptide having the formula T-S₁, and a nucleic acid molecule encoding for a heterologous molecule of interest,

wherein T is a target binding domain and S₁ is a stalk portion;

wherein the target binding domain comprises an amino acid sequence of SEQ ID NO: 50 or SEQ ID NO: 51;

wherein the stalk portion S₁ comprises a formula of L₃-X₁; wherein

L₃ is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, or SEQ ID NO: 58; and

X₁ is polypeptide comprising a transmembrane domain having a formula ECD-T_M-ICD, wherein:

ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59 or SEQ ID NO: 60, or a fragment thereof, or is absent;

T_M is a transmembrane domain comprising an amino acid sequence of SEQ ID NO: 61 or SEQ ID NO: 62, or a fragment thereof; and

ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle or is absent, wherein the ICD comprises an env incorporation motif comprising an amino acid comprising a sequence of SEQ ID NO: 63 or SEQ ID NO: 64; and

wherein the nucleic acid molecule encoding for a heterologous molecule of interest is the nucleic acid molecule of any one of embodiments 45-107.

305. The viral particle of embodiment 304, wherein:
 - T comprises an amino acid sequence of SEQ ID NO: 50;
 - L₃ comprises an amino acid sequence of SEQ ID NO: 55;
 - ECD comprises an amino acid sequence of SEQ ID NO: 59;
 - T_M comprises an amino acid sequence of SEQ ID NO: 61; and
 - the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64.
306. The viral particle of embodiment 304, wherein:
 - T comprises an amino acid sequence of SEQ ID NO: 51;
 - L₃ comprises an amino acid sequence of SEQ ID NO: 55;
 - ECD comprises an amino acid sequence of SEQ ID NO: 59;
 - T_M comprises an amino acid sequence of SEQ ID NO: 61; and
 - the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64.
307. A viral particle comprising a heterologous viral structural protein, a targeting moiety comprising a polypeptide having the formula T-S₁, and a nucleic acid molecule encoding for a heterologous molecule of interest;
 - wherein the heterologous viral structural protein comprises a sequence of SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 52 or SEQ ID NO: 53;
 - wherein T is a target binding domain and S₁ is a stalk portion;
 - wherein the target binding domain comprises an amino acid sequence of SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50 or SEQ ID NO: 51;
 - wherein the stalk portion S₁ comprises a formula of L₃-X₁; wherein
 - L₃ is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, or SEQ ID NO: 58; and

X₁ is polypeptide comprising a transmembrane domain having a formula ECD-T_M-ICD, wherein:

ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59 or SEQ ID NO: 60, or a fragment thereof, or is absent;

T_M is a transmembrane domain comprising an amino acid sequence of SEQ ID NO: 61 or SEQ ID NO: 62, or a fragment thereof; and

ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid comprising a sequence of SEQ ID NO: 63 or SEQ ID NO: 64; and

wherein the nucleic acid molecule encoding for a heterologous molecule of interest is the nucleic acid molecule of any one of embodiments 45-107.

308. A viral particle comprising a heterologous viral structural protein, a targeting moiety comprising a polypeptide having the formula T-S₁, and a nucleic acid molecule encoding for a heterologous molecule of interest;

wherein the heterologous viral structural protein comprises a sequence of SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 52 or SEQ ID NO: 53;

wherein T is a target binding domain and S₁ is a stalk portion;

wherein the target binding domain comprises an amino acid sequence of SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50 or SEQ ID NO: 51;

wherein the stalk portion S₁ comprises a formula of L₃-X₁; wherein

L₃ is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 55; and

X₁ is polypeptide comprising a transmembrane domain having a formula ECD-T_M-ICD, wherein:

ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59 or a fragment thereof, or is absent;

T_M is a transmembrane domain comprising an amino acid sequence of SEQ ID NO: 61 or a fragment thereof; and

ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle or is absent, wherein the ICD comprises an env incorporation

motif comprising an amino acid comprising a sequence of SEQ ID NO: 63 or SEQ ID NO: 64; and

wherein the nucleic acid molecule encoding for a heterologous molecule of interest is the nucleic acid molecule of any one of embodiments 45-107.

309. A viral particle comprising a heterologous viral structural protein, a targeting moiety comprising a polypeptide having the formula T-S₁, and a nucleic acid molecule encoding for a heterologous molecule of interest;

wherein the heterologous viral structural protein comprises a sequence of SEQ ID NO: 23 or SEQ ID NO: 25;

wherein T is a target binding domain and S₁ is a stalk portion;

wherein the target binding domain comprises an amino acid sequence of SEQ ID NO: 39;

wherein the stalk portion S₁ comprises a formula of L₃-X₁; wherein

L₃ is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 55; and

X₁ is polypeptide comprising a transmembrane domain having a formula ECD-T_M-ICD, wherein:

ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59;

T_M is a transmembrane domain comprising an amino acid sequence of SEQ ID NO: 61; and

ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid comprising a sequence of SEQ ID NO: 63 or SEQ ID NO: 64;

wherein the nucleic acid molecule encoding for a heterologous molecule of interest is the nucleic acid molecule of any one of embodiments 45-107.

310. A viral particle comprising a heterologous viral structural protein, a targeting moiety comprising a polypeptide having the formula T-S₁, and a nucleic acid molecule encoding for a heterologous molecule of interest;

wherein the heterologous viral structural protein comprises a sequence of SEQ ID NO: 52 or SEQ ID NO: 53;

wherein T is a target binding domain and S₁ is a stalk portion;

wherein the target binding domain comprises an amino acid sequence of SEQ ID NO: 39;

wherein the stalk portion S_1 comprises a formula of L_3-X_1 ; wherein

L_3 is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 55; and

X_1 is polypeptide comprising a transmembrane domain having a formula ECD- T_M -ICD, wherein:

ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59;

T_M is a transmembrane domain comprising an amino acid sequence of SEQ ID NO: 61; and

ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid comprising a sequence of SEQ ID NO: 63 or SEQ ID NO: 64; and

wherein the nucleic acid molecule encoding for a heterologous molecule of interest is the nucleic acid molecule of any one of embodiments 45-107.

311. A viral particle comprising a heterologous viral structural protein, a targeting moiety comprising a polypeptide having the formula $T-S_1$, and a nucleic acid molecule encoding for a heterologous molecule of interest,

wherein T is a target binding domain and S_1 is a stalk portion;

wherein the target binding domain comprises an amino acid sequence of SEQ ID NO: 50 or SEQ ID NO: 51;

wherein the stalk portion S_1 comprises a formula of L_3-X_1 ; wherein

L_3 is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, or SEQ ID NO: 58; and

X_1 is polypeptide comprising a transmembrane domain having a formula ECD- T_M -ICD, wherein:

ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59 or SEQ ID NO: 60, or a fragment thereof, or is absent;

T_M is a transmembrane domain comprising an amino acid sequence of SEQ ID NO: 61 or SEQ ID NO: 62, or a fragment thereof; and

ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle or is absent, wherein the ICD comprises an env incorporation motif comprising an amino acid comprising a sequence of SEQ ID NO: 63 or SEQ ID NO: 64; and

wherein the nucleic acid molecule encoding for a heterologous molecule of interest encodes for a chimeric antigen receptor and a polypeptide comprising:

- i) a ligand binding extracellular domain (ECD);
- ii) an immune cell activating intracellular domain (ICD); and
- iii) a transmembrane domain linking the ECD to the ICD.

312. A viral particle comprising a heterologous viral structural protein, a targeting moiety comprising a polypeptide having the formula T-S₁, and a nucleic acid molecule encoding for a heterologous molecule of interest;

wherein the heterologous viral structural protein comprises a sequence of SEQ ID NO: 52 or SEQ ID NO: 53;

wherein T is a target binding domain and S₁ is a stalk portion;

wherein the target binding domain comprises an amino acid sequence of SEQ ID NO: 39;

wherein the stalk portion S₁ comprises a formula of L₃-X₁; wherein

L₃ is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 55; and

X₁ is polypeptide comprising a transmembrane domain having a formula ECD-T_M-ICD, wherein:

ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59;

T_M is a transmembrane domain comprising an amino acid sequence of SEQ ID NO: 61; and

ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid comprising a sequence of SEQ ID NO: 63 or SEQ ID NO: 64; and

wherein the nucleic acid molecule encoding for a heterologous molecule of interest encodes for a chimeric antigen receptor and a polypeptide comprising:

- i) a ligand binding extracellular domain (ECD);
- ii) an immune cell activating intracellular domain (ICD); and
- iii) a transmembrane domain linking the ECD to the ICD.

313. The viral particle of any one of embodiments 298-300 or 311-312, wherein the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

314. The viral particle of any one of embodiments 298-300 or 311-313, wherein the polypeptide encoded by the nucleic acid molecule comprises an amino acid sequence of SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 120, or SEQ ID NO: 124, or a variant of any of the foregoing.

315. The viral particle of any one of embodiments 298-300 or 311-313, wherein the polypeptide encoded by the nucleic acid molecule comprises an amino acid sequence of SEQ ID NO: 120.

316. The viral particle of any one of embodiments 298-300 or 311-315, wherein the chimeric antigen receptor and the polypeptide are encoded by separate nucleic acid molecules.

317. The viral particle of any one of embodiments 298-300 or 311-315, wherein the chimeric antigen receptor and the polypeptide are encoded by the same nucleic acid molecule.

318. The viral particle of embodiment 317, wherein the chimeric antigen receptor and the polypeptide are separated by a sequence encoding for a cleavable peptide, such as a 2A peptide.

319. A method of infecting, transfecting or transducing a cell, the method comprising contacting the cell with a particle of any one of embodiments 1-44 or a viral particle of any one of embodiments 152-318.

320. A method of infecting, transfecting or transducing a cell in a subject, the method comprising administering to the subject a pharmaceutical composition comprising a particle of any one of embodiments 1-44 or a viral particle of any one of embodiments 152-318.

321. A method of delivering one or more heterologous molecules of interest to a cell, the method comprising contacting the cell with a particle of any one of embodiments 1-44 viral particle of any one of embodiments 152-318, wherein the viral particle comprises a nucleic acid molecule encoding the heterologous molecule of interest.

322. A method of delivering one or more heterologous molecules of interest to a cell in a subject, the method comprising administering to the subject a particle of any one of embodiments 1-44 a viral particle of any one of embodiments 152-318, wherein the viral particle comprises a nucleic acid molecule encoding the heterologous molecule of interest.

323. The method of any one of embodiments 321-322, wherein the method further comprises administering to the cell or to the subject one or more compounds that bind to the ECD of the polypeptide encoded by the one or more nucleic acid molecules, such as but not limited to, somatropin, G-CSF, lenograstim (Granocyte), filgrastim (Neupogen, Zarzio, Nivestim, Accofil), long acting (pegylated) filgrastim (pegfilgrastim, Neulasta, Pelmeg, Ziextenco) or lipegfilgrastim (Lonquex).
324. The method of embodiment 323, wherein the ECD is a GCSFR ECD or a GHR ECD and the one or more compounds bind to the GCSFR ECD or the GHR ECD, such as, but not limited to, those provided for herein.
325. The method of embodiment 323 or 324, wherein the ECD is a human GCSFR ECD or a human GHR ECD and the one or more compounds bind to the human GCSFR ECD or the human GHR ECD, such as but not limited to those provided for herein.
326. The method of any one of embodiments 319-325, wherein the cell is an immune cell.
327. The method of any one of embodiments 319-326, wherein the cell is a T cell, B cell; NK cell, dendritic cell, neutrophils, macrophages, a cancer cell; or, for example, CD3+ T cell; CD4+ T cell; CD7+ T cell, CD8+ T cell; CD19+ B cell; CD19+ cancer cell; CD20+ B cell; CD20+ cancer cell, CD30+ lung epithelial cell; CD34+ haematopoietic stem cell; CD105+ endothelial cell; CD105+ haematopoietic stem cell; CD117+ haematopoietic stem cell; CD133+ cancer cell; EpCAM+ cancer cell; GluA2+ neuron; GluA4+ neuron; Haematopoietic stem cell; Hepatocyte; Her2/Neu+ cancer cell; NKG2D+ natural killer cell; SLC1A3+ astrocyte; SLC7A10+ adipocyte.
328. A method of treating a disease or disorder in a subject, the method comprising administering to the subject a particle of any one of embodiments 1-44 or a viral particle of any one of embodiments 152-318, wherein the viral particle comprises a nucleic acid molecule encoding a heterologous molecule of interest to treat the disease or disorder, wherein the nucleic acid molecule encoding a heterologous molecule of interest is the nucleic acid molecule of any one of embodiments 45-107.
329. The method of embodiment 328, wherein the method further comprises administering to the subject an effective amount of one or more compounds that bind to the ECD of the polypeptide encoded by the nucleic acid molecule.
330. The method of embodiment 329, wherein the ECD is a GCSFR ECD or a GHR ECD and the one or more compounds bind to the GCSFR ECD or the GHR ECD.
331. The method of embodiment 329 or 330, wherein the ECD is a human GCSFR ECD or a human GHR ECD and the one or more compounds bind to the human GCSFR ECD or the

human GHR ECD.

332. The method of any one of embodiments 328-331, wherein the disease or disorder is cancer (e.g. such as a T cell or B cell disorder or other type of cancer as described herein), an immune disorder, an auto-immune disorder, metabolic disorder, and the like.

333. A method of treating a disease or disorder in a subject, the method comprising:

i) administering to the subject a particle of any one of embodiments 1-44 or a viral particle of any one of embodiments 152-318, and

ii) administering to the subject an effective amount of one or more compounds capable of binding to the ECD of human GCSFR, thereby treating the disease or disorder,

wherein the viral particle comprises one or more nucleic acid molecules encoding one or more heterologous molecules of interest to treat the disease or disorder,

wherein the one or more nucleic acid molecules encoding one or more heterologous molecules of interest is the one or more nucleic acid molecules of any one of embodiments 45-107.

334. A method of treating a disease or disorder in a subject, the method comprising:

i) administering to the subject a particle of any one of embodiments 1-44 or a viral particle of any one of embodiments 152-318, and

ii) administering to the subject an effective amount of one or more compounds capable of binding to the ECD of human GHR, thereby treating the disease or disorder,

wherein the viral particle comprises one or more nucleic acid molecules encoding one or more heterologous molecules of interest to treat the disease or disorder,

wherein the one or more nucleic acid molecules encoding one or more heterologous molecules of interest is the one or more nucleic acid molecules of any one of embodiments 45-107.

335. A method of treating a disease or disorder in a subject, the method comprising:

i) administering to the subject a viral particle of any one of embodiments 152-318, and

ii) administering to the subject an effective amount of one or more compounds capable of binding to the ECD of human GHR, thereby treating the disease or disorder,

wherein the viral particle comprises a nucleic acid molecule encoding a heterologous molecule of interest to treat the disease or disorder,

wherein the nucleic acid molecule or a plurality of nucleic acid molecules encoding a heterologous molecule of interest encodes for a chimeric antigen receptor and a polypeptide comprising:

- i) a ligand binding extracellular domain (ECD);
- ii) an immune cell activating intracellular domain (ICD); and
- iii) a transmembrane domain linking the ECD to the ICD.

336. The method of embodiment 335, wherein the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

337. The method of embodiment 335 or 336, wherein the polypeptide encoded by the nucleic acid molecule comprises an amino acid sequence of SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 120, or SEQ ID NO: 124, or a variant of any of the foregoing.

338. The method of embodiment 335 or 336, wherein the polypeptide encoded by the nucleic acid molecule comprises an amino acid sequence of SEQ ID NO: 120.

339. The method of any one of embodiments 335-338, wherein the chimeric antigen receptor and the polypeptide are encoded by separate nucleic acid molecules.

340. The method of any one of embodiments 335-338, wherein the chimeric antigen receptor and the polypeptide are encoded by the same nucleic acid molecule.

341. The method of embodiment 340, wherein the chimeric antigen receptor and the polypeptide are separated by a sequence encoding for a cleavable peptide, such as a 2A peptide.

342. A method of delivering one or more heterologous molecules to a target cell, the method comprising contacting the cell with a particle of any one of embodiments 1-44 or a viral vector or particle of any one of embodiments 152-318, wherein the particle comprises one or more nucleic acid molecules encoding the one or more heterologous molecules.

[00449] The following examples are illustrative, but not limiting, of the compounds, compositions and methods described herein. Other suitable modifications and adaptations known to those skilled in the art are within the scope of the following embodiments.

Examples

[00450] Example 1: Construction of chimeric cytokine receptors.

[00451] Chimeric cytokine receptors were designed comprising a ligand binding extracellular domain (ECD); and immune cell activating intracellular domain (ICD), and a transmembrane domain linking the ECD to the ICD as provided for herein (FIG. 1). FIG. 1A illustrates select receptor designs comprising a GCSFR ECD in combination with various transmembrane and ICD domains. FIG. 1B illustrates select receptor designs comprising a growth hormone receptor (GHR) ECD in combination with various transmembrane and ICD domains. For the purposes of the following examples, the chimeric cytokine receptors were delivered to cells as part of a dual expression construct expressing a CAR as provided for herein and a chimeric cytokine receptor as provided for herein separated by a self cleavable 2A sequence. The following examples comprise experiments that deliver the CAR alone or the CAR in combination with the chimeric cytokine receptor. Examples detailing results of experiments with the chimeric cytokine receptor will explicitly mention the cytokine receptor. Otherwise, the example is referencing data generated in the absence of the cytokine receptor.

[00452] Example 2: Mutation at position 182 of VSV-G abrogates LDL-R interaction, but retains fusing properties. Plasmids/Sequences. All VSV-G plasmids were derived from pCMV-VSV-G Envelope Vector (Cell Bio Labs, catalog RV-110). Point mutations and combinations thereof were introduced using site directed mutagenesis (New England Biolabs). Individual mutations H8A and K47Q were previously shown to partially “blind” VSV-G, reducing its binding to LDL-R, the native cellular receptor for VSV (PMID: 29531262, DOI: 10.1038/s41467-018-03432-4). In this experiment, a single binder molecule consisting of a CD7-targeting scFv (clone MT701) fused to an IgG “stalk” bearing a CD28 transmembrane domain was used.

[00453] Cells. HEK293T cells were grown in DMEM with 10% FBS. SupT1 cells were maintained in RPMI media with 10% FBS. Human PBMCs were purchased from AllCells and cultured in X-Vivo 10 (Lonza) supplemented with 20ng/mL IL-2 (Peprotech). PBMCs were activated 48 hours prior to transduction using anti-CD3/CD28 Dynabeads (Cell Therapy Systems).

[00454] Generation of lentiviral particles. The recombinant lentiviral particles co-expressing VSV-G glycoprotein and binder molecules were generated by plasmid transection into HEK293T cells using Lipofectamine 3000 (ThermoFisher Scientific). A total of 5 plasmids were transfected: (1) plasmid expressing the VSV-G glycoprotein, (2) plasmid expressing the binder protein (3) plasmid expressing the lentiviral transfer genome encoding for eGFP, (4) plasmid expressing gag-pol, and (5) plasmid expressing rev. Transfected cell supernatant was harvested 48 hours later. Virus in the cell supernatant was concentrated by centrifugation

through a sucrose cushion and resuspended in PBS. Lentiviral particle titer was determined using the Lenti-X p24 Rapid Titer Kit (Takara Bio, San Jose, CA).

[00455] Lentivirus transduction assay. A series of 10-fold dilutions (in cell culture media) of the concentrated lentivirus was performed and used to infect SupT1 and activated human PBMCs. Media was replaced 6 hours later, and the transduced cells were analyzed by flow cytometry on days 4 and 7 after transduction. Cells were stained with a viability stain and an anti-CD7 antibody to detect CD7 positive cells (PeCy7 mouse-anti-human CD7, clone CD7-6B7, BD Biosciences). Expression of eGFP was measured to calculate transduction efficiency.

[00456] Structure-guided design of novel blinding mutations. Using a published crystal structures of VSV-G bound to CR2 and CR3 of the LDL-R (pdb 50YL and 50Y9, respectively), two putative positions in VSV-G with side chains oriented toward the binding interface on LDL-R were identified (FIG. 1). Residue Q10 (SEQ ID NO: 2) appeared to form several interactions with residues in both CR2 and CR3. In CR3, this included interactions with a positively charged arginine residue. Thus, three substitutions were tested: Q10A to reduce side-chain interactions that potentially stabilize LDL-R binding and Q10R and Q10K to create electrostatic repulsion.

[00457] Residue I182 (SEQ ID NO: 2) appeared to contact several residues in both CR2 and CR3 as well. Three substitutions were tested: I182A to reduce side-chain interactions that potentially stabilize LDL-R binding and I182D and I182E to create electrostatic repulsion against the primary binding interfaces on LDL-R.

[00458] Addition of negative charges in the binding interface ablate native tropism without altering fusogenicity. Titration of viral supernatants on the CD7+ T cell line SupT1 validated the structural predictions for residue I182. In the absence of any compensatory binder molecule, WT VSV-G reached titers of 3.0×10^8 while both I182D and I182E were ~3 orders of magnitude lower (Fig 2). Substitutions at residue I182 preserved fusogenicity, as titers were restored to 1×10^8 in the presence of a binder redirecting the virions to CD7.

[00459] The data is illustrated in FIG. 2, which shows that the addition of negative charges in the binding interface ablate native tropism without altering fusogenicity. FIG. 2A shows the titration of VSV-G constructs on SupT1 cells. Plotted is the percentage of SupT1 cells expressing GFP at each amount of viral input in terms of p24 antigen. Dashed lines/open circles indicate VSV-G constructs alone, solid lines/filled circles indicate the same construct with a CD7 targeting molecule expressed in trans. FIG. 2B illustrates Functional titer of each construct calculated from the titration in A, expressed as transducing units per mL of concentrated virus supernatant (TU/mL).

[00460] Thus these examples demonstrate that a mutation position 182 is sufficient to abrogate the LDL-R interaction, but retain fusogenic properties when combining with a targeting moiety that binds to a target on the target cell.

[00461] Example 3: Serum Stable VSV-G Protein

[00462] WT VSV-G is reported to be sensitive to inactivation by naïve human serum, with inactivation ranging from minimal change to about 100-fold decrease depending on study parameters. Accordingly, it was assessed i) whether substitution at position I182 produced a variant VSV-G with similar sensitivity to serum and ii) whether incorporation of known serum stabilizing VSV-G mutations into the I182 substituted constructs had an effect on the serum stability of the constructs.

[00463] WT VSV-G, Serum Stable VSV-G (T214N, T352A), LDL-R de-targeted VSV-G (I182E), and LDL-R de-targeted serum stable VSV-G (I182E, T214N, T352A) were tested for their ability to infect SupT1 cells in the presence or absence of naïve serum or heat inactivated serum (HI) (FIG. 5). As expected WT VSV-G had a dramatic decrease in percent infectivity when administered in the presence of serum with a mild rescue of infectivity if serum was heat inactivated (FIG. 5, columns 1-3). The inclusion of the CD7 targeting moiety on an IgG1 Fc stalk (WT) did not rescue the serum inactivation (FIG. 5, columns 4-6). The VSV-G constructs harboring the T214N and T352A mutations showed a similar reduction in infectivity in the presence of serum with no distinction between naïve or HI serum (FIG. 5, columns 7-9). However, the inclusion of the targeting moiety was able to partially rescue the inactivation in either serum condition (FIG. 5, columns 10-12). Surprisingly, the LDL-R de-targeted VSV-G (I182E) showed no reduction in infectivity percentage in the presence of either serum condition (FIG. 5, columns 13-15), but rather showed increased infectivity in the presence of naïve serum as compared to serum free or HI serum conditions. Further inclusion of the known serum stable mutations into VSV-G (I182E, T214N, T352A) also demonstrated increased infectivity in the presence of serum as compared to serum free conditions (FIG. 5, columns 16-18). Further, the I182E, T214N, T352A construct also demonstrates increased infectivity in the presence of HI serum (FIG. 5, column 18), which indicates that the triple mutant construct has a higher degree of serum stability than the other constructs examined.

[00464] To further characterize the effect of including serum stabilizing mutations in the viral constructs of the present application, WT VSV-G, VSV-G (I182E), and VSV-G (I182E, T230N, T352A) were assessed at a lower dose of vector (FIG. 6). In agreement with the previous assessment, WT VSV-G showed decreased infectivity in serum as compared to no-serum conditions (FIG. 6, columns 1 and 2). However, heat inactivation (HI) of serum did

appear to have a rescuing effect on WT VSV-G infectivity (FIG. 6, column 3). In further agreement with the previous assessment, VSV-G (I182E) demonstrated enhanced infectivity in the presence of serum as compared to no serum conditions (FIG. 6, columns 4 and 5). The presence of HI serum also resulted in an increased infectivity compared to no serum, with a smaller effect than naïve serum (FIG. 6, column 6). VSV-G (I182E, T214N, T352A) also demonstrated increased infectivity in serum and HI serum conditions as compared to no serum conditions (FIG. 6, columns 7-9), in agreement with the previous assessment. Further, when compared to the respective no serum condition, VSV-G (I182E, T230N, T352A) results in a greater percent increased infectivity compared to VSV-G (I182E), suggesting that inclusion of all three mutations results in greater serum stability than just I182E alone.

[00465] Thus, these examples demonstrate that i) the LDL-R detargeting mutation I182E affords an unexpected level of protection against the serum inactivation observed for WT VSV-G, ii) the LDL-R detargeting mutation I182E does not abrogate the serum stabilizing effect of the T230N + T352A mutations, and iii) the combined mutation construct VSV-G (I182E, T230N, T352A) appears to have a greater serum stabilizing effect than either I182E alone or T230N + T352A alone. Thus, VSV-G (I182E, T230N, T352A) is able to ablate native tropoism without alternating fusogenicity and additionally demonstrates a more stable profile and is not neutralized in serum.

[00466] **Example 4: Spring viremia of carp virus G protein can facilitate cell specific fusion.**

[00467] **Methods**

[00468] **Plasmids/Sequences.** All rhabdovirus GP sequences were codon optimized and synthesized by Genscript. Sequences are shown below, with accession numbers found in the following table, which are hereby incorporated by reference in its entirety, Table 1:

Table 1. Rhabdovirus glycoprotein sequences used.

Rhabdovirus	Genbank Accession
Spodoptera frugiperda rhabdovirus isolate Sf - G	KF947078.1
Drosophila obscura sigma virus 10A - G	GQ410979.1
Wuhan insect virus 7 - G	YP_009301742.1
Perch rhabdovirus - G	YP_007641366.1
Spring viremia of carp virus - G	CAA85735.1

[00469] The targeting moiety comprises an anti-CD7 antibody (clone MT701, in single chain format) anchored to the membrane via an IgG based Fc stalk, which comprises a CD28 transmembrane domain.

[00470] Cells. HEK293T cells were grown in DMEM with 10% FBS. SupT1 cells were maintained in RPMI media with 10% FBS. Human PBMCs were purchased from AllCells and cultured in X-Vivo 10 (Lonza) supplemented with 20ng/mL IL-2 (Peprotech). PBMCs were activated 48 hours prior to transduction using anti-CD3/CD28 Dynabeads (Cell Therapy Systems).

[00471] Generation of lentiviral particles. The recombinant lentiviral particles co-expressing rhabdovirus-G glycoproteins and binder molecules were generated by plasmid transection into HEK293T cells using Lipofectamine 3000 (ThermoFisher Scientific). A total 5 plasmids were transfected: (1) plasmid expressing the rhabdovirus G glycoprotein, (2) plasmid expressing the binder protein (where indicated), (3) plasmid expressing the lentiviral transfer genome encoding for CAR20, (4) plasmid expressing gag-pol, and (5) plasmid expressing rev. Transfected cell supernatant was harvested 48 hours later. Virus in the cell supernatant was concentrated by centrifugation through a sucrose cushion and resuspended in x-vivo medium. Lentiviral particle titer was determined using the Lenti-X p24 Rapid Titer Kit (Takara Bio, San Jose, CA).

[00472] Lentivirus transduction assay. A series of 5-fold dilutions (in cell culture media) of the concentrated lentivirus was performed and used to infect SupT1 and activated human PBMCs. Media was replaced 6 hours later, and the transduced cells were analyzed by flow cytometry on days 4 and 7 after transduction. Cells were stained with a viability stain, an anti-CD7 antibody to detect CD7 positive cells, and an anti-CAR antibody to detect CAR20 expression as a measure of transduction efficiency.

[00473] Results:

[00474] SVCV-G mediates fusion into human cells. Most non-mammalian rhabdovirus G proteins failed to mediate transduction in human cells, with the exception of Spring viremia of carp virus G (SVCV-G). This glycoprotein did not target SupT1 or human PBMC cells on its own as transduction was very inefficient (~1 log lower than blinded VSV-G I182E) in the absence of the CD7 binder. Targeted transduction mediated by the CD7 binder reached comparable titers to retargeted VSV-G I182E.

[00475] This surprising and unexpected result demonstrates that a viral structural protein that cannot infect an immune cell on its own can be used to infect a cell when the virus also expresses a targeting moiety, such as one that comprises an anti-CD7 scFv. This result could not have been predicted and is shown not to be an effect of the anti-CD7 scFv on its own as the presence of the anti-CD7 scFv targeting moiety was not sufficient to induce infections utilizing other non-human rhabdovirus GP proteins. The data is illustrated in FIG. 7.

[00476] Example 5: CD7 Targeting Moiety can be linked to a Fc stalk to transduce PBMCs.

[00477] Generation of Plasmids and Sequences.

[00478] The amino acid sequence including CDRs of the CD7 binder was determined via mass spectrometry (Rapid Novor). CD7 binder sequences were synthesized by IDT or GenScript (Piscataway, NJ) using codon optimization for human expression and inserted onto viral glycoprotein or IgG-based stalks and flanked by a G4S linker. An example viral glycoprotein is a Nipah-G protein with the CD7 binder attached to the extracellular region. An example IgG-based stalk was a human IgG1 Fc dimer with a CD8 or CD28 transmembrane region and an envelope incorporating motif with the CD7 binder attached to the extracellular region. The resulting binders were expressed under the direction of a CMV promoter.

[00479] Generation of Engineered Lentiviral Particles.

[00480] The recombinant lentiviral particles expressing the CD7 binder incorporated on the surface were generated by plasmid transection into HEK293T cells using Lipofectamine 3000 (ThermoFisher Scientific). In some embodiments, a total of 5 plasmids were transfected: (1) plasmid expressing the CD7 binder with the IgG stalk or a plasmid expressing the CD7 binder on a Nipah-G protein, (2) plasmid expressing a detargeted-VSV-G protein, (3) lentiviral genome expressing eGFP, (4) plasmid expressing gag-pol, (5) plasmid expressing rev. In some embodiments, a total of 5 plasmids were transfected: (1) plasmid expressing the CD7 binder with the Nipah-G protein, (2) plasmid expressing Nipah-F protein, (3) lentiviral genome expressing eGFP, (4) plasmid expressing gag-pol, (5) plasmid expressing rev. Media was changed 6 hours after transfection and cells were harvested 48 hours later. Virus in the media was concentrated by centrifugation through a sucrose cushion and resuspended in media. Lentiviral particle titer was determined using the Lenti-X p24 Rapid Titer Kit (Takara Bio, San Jose, CA)

[00481] CD7 binders attach to both human and non-human primate PBMCs, leading to CD7+ cell transduction.

[00482] Human PBMC cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect human and non-human primate cells. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on days 4 and 7 after transduction. Cells were stained with an anti-CD7 antibody to detect CD7 positive cells (PE-Cy7 mouse-anti-human CD7, clone MT-701, Biolegend) as well as GFP expression. Cell

viability was also determined. CD7 binders adhered to Paramyxoviridae glycoproteins, such as Nipah-G with Nipah-(FIG. 8A-D and FIG. 9A-D) or with Rhabdoviridae glycoproteins, such as VSV-G (FIG. 8I-L and FIG. 9I-L) successfully transduced human PBMCs (FIG. 8A-L) or NHP PBMCs (FIG. 9A-L) compared to the binder alone (FIG. 8E-H and FIG. 9E-H) which shows no transduction. When CD7 with an IgG stalk was tested, the binder alone (top row) again did not transduce human (FIG. 8M) or NHP PBMCs (FIG. 9M) but when administered with blinded VSV-G, transduction was seen in both human (FIG. 8M, bottom panel) and NHP PBMCs (FIG. 9M, bottom panel).

[00483] These examples and embodiments demonstrate that the polypeptides can be used to bind to CD7 and target viral particles to cells expressing CD7 to transduce the cells expressing CD7.

[00484] **Example 6: CD8 Targeting Moiety can be linked to a Fc stalk to transduce PBMCs.**

[00485] Generation of Plasmids and Sequences.

[00486] The amino acid sequence including CDRs of the CD8 binder was determined via mass spectrometry (Rapid Novor). CD8 binder sequences were synthesized by IDT or GenScript (Piscataway, NJ) using codon optimization for human expression and inserted onto viral glycoprotein or IgG-based stalks and flanked by a G4S linker. An example viral glycoprotein is a Nipah-G protein with the CD8 binder attached to the extracellular region. An example IgG-based stalk was a human IgG1 Fc dimer with a CD8 or CD28 transmembrane region and an envelope incorporating motif with the CD8 binder attached to the extracellular region. The resulting binders were expressed under the direction of a CMV promoter.

[00487] Generation of Engineered Lentiviral Particles.

[00488] The recombinant lentiviral particles expressing the CD8 binder incorporated on the surface were generated by plasmid transection into HEK293T cells using Lipofectamine 3000 (ThermoFisher Scientific). In some embodiments, a total of 5 plasmids were transfected: (1) plasmid expressing the CD8 binder with the IgG stalk, (2) plasmid expressing a detargeted-VSV-G protein, (3) lentiviral genome expressing eGFP, (4) plasmid expressing gag-pol, (5) plasmid expressing rev. In some embodiments, the lentiviral genome expressing eGFP was replaced with a CAR molecule. Media was changed 6 hours after transfection and cells were harvested 48 hours later. Virus in the media was concentrated by centrifugation through a sucrose cushion and resuspended in media. Lentiviral particle titer was determined using the Lenti-X p24 Rapid Titer Kit (Takara Bio, San Jose, CA).

[00489] CD8 binders attach to both human and non-human primate PBMCs, leading to CD8+ cell transduction.

[00490] Human PBMC cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect human and non-human primate cells. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on day 6 after transduction. Cells were stained with an anti-CD8 antibody to detect CD8 positive cells (BV421 mouse-anti-human CD8, clone RPA-T8, Biolegend) as well as GFP or CAR20 expression. Cell viability was also determined. CD8 binders with detargeted VSV-G successfully transduced human PBMCs (FIG. 10A) or NHP PBMCs (FIG. 10B) with GFP (FIG. 10A-10B, top row) and CAR20 (FIG. 10A-10B, bottom row).

[00491] These examples and embodiments demonstrate that the polypeptides can be used to bind to CD8 and target viral particles to cells expressing CD8 to transduce the cells expressing CD8.

[00492] **Example 7: VSV-G* pseudotyped lentiviruses harboring Fc stalk binder transduce PBMCs.**

[00493] Human PBMC cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect human and non-human primate cells. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23, SEQ ID NO: 25), as provided for herein. The binder constructs utilized for VSV-G* pseudotyped lentiviruses in the present example are the same as the CD7 binder constructs utilized in previous examples. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on day 7 after transduction to determine CAR transduction. CAR expression was observed in all human and non-human primate PBMCs assessed (FIG. 11A) compared to the binder alone (FIG. 11B) which shows no transduction. Data are also presented as percent CAR expression vs multiplicity of infection (FIG. 11C).

[00494] These examples and embodiments demonstrate that the VSV-G* pseudotyped lentiviruses are able to successfully transduce a variety of human and non-human primate PMBCs.

[00495] Example 8: CD7 Targeting Moiety can be linked to a flexible stalk to transduce PBMCs.

[00496] Human PBMC cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect human and non-human primate cells. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23, SEQ ID NO: 25), as provided for herein. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on day 7 after transduction to determine CAR transduction. CAR expression was observed in all human and non-human primate PBMCs assessed (FIG. 12A) compared to no binder (FIG. 12B) which shows no transduction. Data are also presented as percent CAR expression vs multiplicity of infection (FIG. 12C).

[00497] These examples and embodiments demonstrate that a CD7 binder with a flexible stalk is able to successfully transduce human and non-human primate PBMCs. This represents a surprising and unexpected result in light of a recent report by Dobson and colleagues (Dobson CS, Reich AN, Gaglione S, Smith BE, Kim EJ, Dong J, Ronsard L, Okonkwo V, Lingwood D, Dougan M, Dougan SK, Birnbaum ME. Antigen identification and high-throughput interaction mapping by reprogramming viral entry. *Nat Methods*. 2022 Apr;19(4):449-460. doi: 10.1038/s41592-022-01436-z. Epub 2022 Apr 8. PMID: 35396484; PMCID: PMC9012700) which showed that a VSVG (K47Q, R354A) pseudotyped virus utilizing IL-13 as a target binding domain was unable to transduce IL-13R α 1-expressing cells when utilizing a flexible (G4S)₃ surface architecture. To determine whether the number of G4S repeats is an essential variable for transduction, various constructs were utilized harboring between 0 and 4 G4S repeats (FIGs. 13A and 13B). Viruses comprising the various G4S stalks each with an anti-CD7 binding domain were transfected along with a packaging plasmid set consisting of VSV-G*, xHIV packaging, rev, and a SIN lentivector genome encoding an anti-CD20 CAR (CAR20) in HEK293T cells. Control samples were either the packaging set alone without a binder, the packaging set with an IgG Fc stalk with an anti-CD7 binding domain, or the packaging set without a binder substituting VSV-G* with VSV-G wild-type. Viral supernatant was purified by centrifugation over a 20% sucrose cushion and resuspended in X-Vivo media. Resuspended virus was analyzed by a p24 assay to determine viral protein content in solution. 10-fold dilutions by p24 mass of virus were administered to SupT1 and human PBMCs as

indicated. Flow cytometry was utilized to assess the fraction of cells with CAR20 protein on the surface at seven days after transduction. In SupT1 cells (FIG. 13A), (G₄S)₁ resulted in greater CAR expression than (G₄S)₂ or (G₄S)₃ constructs. Surprisingly, constructs harboring a (G₄S)₄ flexible stalk did not follow the trend established for (G₄S)₁₋₃ and instead the (G₄S)₄ flexible stalk constructs resulted in greater CAR expression than any of the other (G₄S)_n constructs tested. A similar result was found in human PBMCs (FIG. 13B).

[00498] Example 9: SVCV-G pseudotyped lentiviruses harboring Fc stalk binder transduce PBMCs.

[00499] Human PBMC cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect human and non-human primate cells. The CD7 binder constructs utilized for SVCV-G pseudotyped lentiviruses of the present example are the same as those utilized in previous examples. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on day 7 after transduction to determine CAR transduction. CAR expression was observed in all human and non-human primate PBMCs assessed (FIG. 14A) compared to no binder (FIG. 14B) which shows no transduction. Data are also presented as percent CAR expression vs multiplicity of infection (FIG. 14C).

[00500] These examples and embodiments demonstrate that the i) SVCV-G pseudotyped lentiviruses are able to successfully transduce PMBCs and ii) the variant Fc stalks of the present disclosure are not limited to just VSV-G pseudotyped embodiments.

[00501] Example 10: SVCV-G pseudotyped lentiviruses harboring a CD7/flexible stalk binder transduce PBMCs.

[00502] Human PBMC cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect human and non-human primate cells. The binder constructs utilized for SVCV-G pseudotyped lentiviruses are the same as those utilized in previous example 4. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on day 7 after transduction to determine CAR transduction. CAR expression was observed in all human and non-human primate PBMCs assessed (FIG. 15A) compared to no binder (FIG. 15B) which shows no transduction. Data are also presented as percent CAR expression vs multiplicity of infection (FIG. 15C).

[00503] These examples and embodiments demonstrate that the i) SVCV-G pseudotyped lentiviruses are able to successfully transduce PMBCs and ii) the flexible stalk constructs are not limited to just VSV-G pseudotyped embodiments.

[00504] Example 11: SVCV-G pseudotyped lentiviruses are comparable to VSV-G* pseudotyped lentiviruses.

[00505] The transduction efficiency of SVCV-G and VSV-G* pseudotyped lentiviruses harboring a CD7 binder with a Fc stalk were compared. Lentivirus generation and cell transduction assays were performed as in the previous examples. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23, SEQ ID NO: 25), as provided for herein. Human PBMC cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect human and non-human primate cells. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on day 7 after transduction to determine CAR transduction. CAR expression was comparable between VSV-G* and SVCV-G pseudotyped constructs across in SupT1 cells as well as several human PBMC lines and non-human primate PBMC lines (FIGs. 16A-16D).

[00506] The transduction efficiency of SVCV-G and VSV-G* pseudotyped lentiviruses harboring a CD7 binder with a flexible stalk were also compared. Lentivirus generation and cell transduction assays were performed as in the previous examples. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23, SEQ ID NO: 25), as provided for herein. Human PBMC cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect human and non-human primate cells. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on day 7 after transduction to determine CAR transduction. CAR expression was comparable between VSV-G* and SVCV-G pseudotyped constructs across in SupT1 cells as well as several human PBMC lines and non-human primate PBMC lines (FIGs. 17A-17D).

[00507] These examples and embodiments demonstrate that both VSV-G* and SVCV-G pseudotyped viral particles are able to transduce SupT1 and PBMC cells with similar potency when using a CD7 binder with either the variant Fc stalks of the present disclosure or the flexible peptide stalks of the present disclosure, suggesting that both VSV-G* and SVCV-G constructs may be useful in transducing a wide array of cell types.

[00508] Example 12: VSV-G* and SVCV-G pseudotyped lentiviruses harboring a CD7/Fc stalk binder exhibit minimal off target transduction.

[00509] The off target transduction of B-cells via VSV-G* and SVCV-G pseudotyped lentiviral constructs utilizing Fc binder stalks was assessed in several B-cell populations. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23, SEQ ID NO: 25), as provided for herein. B-cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect the various B-cell populations. The CD7 binder constructs utilized for the VSV-G* and SVCV-G pseudotyped lentiviruses are the same as those utilized in previous examples. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on day 5 after transduction to determine GFP transduction. As a control, SupT1 cells were also infected with the same lentiviral constructs. None of the B-cell populations assessed demonstrated any significant level of GFP expression (FIGs. 18A and 18B). The percent of GFP positive cells only exceeded 1% in line DB when utilizing the SVCV-G pseudotyped construct at the highest concentration of lentivirus utilized.

[00510] Lentiviral constructs delivering a CAR20-T2A-GFP transgene were also assessed in a similar manner (FIGs. 19A and 19B). VSV-G* pseudotyped lentiviruses utilizing the Fc binder stalk still exhibited minimal off target transduction of B-cells in all cell populations tested (FIGs. 19A and 19B). The percent of CAR-T2A-GFP positive cells only exceeded 1% in line DB at the highest lentiviral concentrations utilized. SVCV-G pseudotyped lentiviruses utilizing the Fc stalk also exhibited minimal off target transduction of B-cells in five of the six cell populations assessed (FIG. 19A). The percent of CAR-T2A-GFP positive cells only exceeded 1% in line HT at the highest concentration of lentivirus utilized.

[00511] These examples and embodiments demonstrate that the i) VSV-G* and SVCV-G pseudotyped lentiviruses utilizing the Fc stalks of the present disclosure have low off target

transduction of B-cells and ii) delivery of a CAR20 transgene instead of a GFP transgene does not significantly increase off target transduction in B-cells.

[00512] Example 13: VSV-G* and SVCV-G pseudotyped lentiviruses harboring a CD7/flexible stalk binder exhibit minimal off target transduction.

[00513] The off target transduction of B-cells via VSV-G* and SVCV-G pseudotyped lentiviral constructs utilizing flexible binder stalks was assessed in several B-cell populations. The utilized VSV-G protein was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23, SEQ ID NO: 25), as provided for herein. B-cells were maintained in X-Vivo10 media with 5% human serum and 20ng/mL of human IL-2. Non-human primate cells were maintained in RPMI media with 10% FBS, 1% Pen/Strep with 1mM Sodium Pyruvate and 100units/mL hIL-2. Concentrated lentivirus was used to infect the various B-cell populations. The binder constructs utilized for the VSV-G* and SVCV-G pseudotyped lentiviruses are the same as those utilized in previous Examples 4 and 6. Media was replaced 24 hours later, and the transduced cells were analyzed by flow cytometry on day 5 after transduction to determine GFP transduction. As a control, SupT1 cells were also infected with the same lentiviral constructs. None of the B-cell populations assessed demonstrated any significant level of GFP expression (FIGs. 20A and 20B).

[00514] Lentiviral constructs delivering a CAR20-T2A-GFP transgene were also assessed in a similar manner (FIGs. 20A and 20B). VSV-G* pseudotyped lentiviruses utilizing the flexible binder stalk still exhibited minimal off target transduction of B-cells in all cell populations tested (FIG. 20A). The percent of CAR-T2A-GFP positive cells did not exceed 1% in any of the B-cell cell populations at any of the lentiviral concentrations utilized. SVCV-G pseudotyped lentiviruses utilizing the flexible binder stalk also exhibited minimal off target transduction of B-cells in five of the six cell populations assessed (FIG. 20A). The percent of CAR-T2A-GFP positive cells did not exceed 1% in the Daudi, GA10, HT, Raji, or Ramos cell lines at any of the lentiviral concentrations utilized. The B-cell cell line DB did rise above 1% positive at two of the higher lentiviral concentrations utilized, but still remained less than the control SupT1 cell line.

[00515] These examples and embodiments demonstrate that the i) VSV-G* and SVCV-G pseudotyped lentiviruses utilizing a flexible binder stalk have low off target transduction of B-cells and ii) delivery of a CAR20 transgene instead of a GFP transgene does not significantly increase off target transduction in B-cells (FIGs. 21A -21B).

[00516] Example 14: VSV-G* pseudotyped lentiviruses with CD20-CAR transgene payload kills CD20 positive lymphoma cells *in vitro*

[00517] The ability of VSV-G* pseudotyped lentiviral constructs with a CD20-CAR transgene to kill CD20 positive lymphoma cells *in vitro* was assessed. The VSV-G* pseudotyped lentiviral constructs utilized CD7 binders as provided for herein. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23), as provided for herein. Human PBMCs were transduced with a lentiviral construct carrying a CD20-CAR (CAR20) transgene. The CAR20 transgenes comprised antigen binding domains of SEQ ID NO: 92 or SEQ ID NO: 93. CD20 positive lymphoma cells were then added to the CAR20 cells at a given effector to target ratio (E:T). All lentiviral constructs tested produced a dose dependent killing of CD20 positive lymphoma cells (FIGs. 22A-22B)

[00518] These examples and embodiments demonstrate that the VSV-G* pseudotyped lentiviruses utilizing the CD7 binders of the present disclosure not only transduce the appropriate target cells as demonstrated by the previous examples, but also produce robust and dose dependent killing of CD20 positive lymphoma cells *in vivo*.

[00519] Example 15: Evaluation of chimeric cytokine receptor ligand toxicity in PBMCs

[00520] The toxicity of the ligands GCSF and human growth hormone was assessed in PBMCs.

[00521] Generation of lentiviral particles. Recombinant lentiviral particles co-expressing VSV-G glycoprotein (VSV-G*, as provided for herein) and binder molecules (CD7, as provided for herein) were generated by plasmid transfection into HEK293T cells using Lipofectamine 3000 (ThermoFisher Scientific). A total of 5 plasmids were transfected: (1) plasmid expressing the VSV-G* glycoprotein, (2) plasmid expressing the binder protein (3) plasmid expressing gag-pol, (4) plasmid expressing rev, and (5) plasmid expressing the lentiviral transfer genome(s). Transfected cell supernatant was harvested 48 hours later. Virions in the cell supernatant were concentrated by centrifugation through a sucrose cushion and resuspended in PBS. Lentiviral particle titer was determined using the Lenti-X p24 Rapid Titer Kit (Takara Bio, San Jose, CA).

[00522] Transduction and population monitoring. Activated PBMCs from each donor were transduced with respective viruses, grown in complete PBMC media for 48 hours, then seeded in 96-well plates with IL-2-free media containing either 0 ng/ml, 100ng/ml, or 250 ng/ml recombinant GCSF (FIG. 23A-F) or 0 ng/ml, 7.9 ng/ml, 15.8 ng/ml, 31.75 ng/ml, 62.5 ng/ml,

125 ng/ml, 250 ng/ml, or 500 ng/ml recombinant human growth hormone (GH). Media was replaced every 48 hours. Cell viability was assessed at set intervals for 14 days by flow cytometry. For each condition expressing a chimeric cytokine receptor, the receptor was delivered in a dual expression system wherein the nucleic acid construct encoded, from 5' to 3', CAR20-2A-chimeric cytokine receptor. As a control, some PBMCs were transduced with the CAR20 construct alone.

[00523] *Toxicity assessment of GCSF*

[00524] PBMCs were transduced with CAR20 alone (FIG. 23A) or with a chimeric cytokine receptor comprising a GCSFR ECD (FIG. 23B-F). In the absence of chimeric cytokine receptor (FIG. 23A), PBMCs exhibited a drop to 40%-50% viability by day 4 post drug treatment with a steady recovery thereafter until the day 14 endpoint. The drop in viability did not appear to be the result of drug treatment, as the 0 ng/ml control exhibited a similar dip in viability. For each GCSFR ECD containing chimeric cytokine receptor tested (FIG. 23B-F), the PBMCs exhibited a dip in cell viability in the absence of GCSF. However, treatment with 100 ng/ml or 250 ng/ml GCSF ameliorated the observed dip in viability for all chimeric constructs tested, indicating that signaling through the chimeric cytokine receptor preserved cell viability even in the presence of the CAR20 construct.

[00525] *Toxicity assessment of hGH*

[00526] PBMCs were transduced with chimeric cytokine receptors comprising a GHR ECD (FIG. 24A-E). As was observed with the GCSFR ECD containing constructs, the no treatment control resulted in a dip in cell viability for all constructs tested. However, transduction with a GHR-GCSFRd15 chimeric cytokine receptor (FIG. 24A) did not result in the same protective effect against the dip in cell viability as observed for the GCSFRd15 chimeric cytokine receptor construct (FIG. 23B). The remaining GH RECD containing constructs tested (FIG 24B-E) exhibited a preservation of cell viability when treated with the indicated concentrations of hGH. This indicates that, with the exception of the GHR-GCSFRd15 construct, signaling through the chimeric cytokine receptor preserved cell viability even in the presence of the CAR20 construct.

[00527] **Example 16: Stimulation of chimeric cytokine receptors promotes PBMC expansion**

[00528] The ability of the various cytokine receptor constructs to stimulate PBMC proliferation was assessed.

[00529] **Cells.** HEK293T cells were grown in DMEM with 10% FBS. Frozen human PBMCs were purchased from AllCells and cultured in X-Vivo 10 (Lonza) supplemented with 5%

human AB serum and 20 ng/mL IL-2 (Peprotech). Human PBMCs from two donors were activated for 48 hours prior to transduction using anti-CD3/CD28 Dynabeads (Cell Therapy Systems).

[00530] Generation of lentiviral particles. The recombinant lentiviral particles co-expressing VSV-G glycoprotein (VSV-G*, as provided for herein) and binder molecules (CD7 as provided for herein) were generated by plasmid transfection into HEK293T cells using Lipofectamine 3000 (ThermoFisher Scientific). A total of 5 plasmids were transfected: (1) plasmid expressing the VSV-G* glycoprotein, (2) plasmid expressing the binder protein (3) plasmid expressing gag-pol, (4) plasmid expressing rev, and (5) plasmid expressing the lentiviral transfer genome(s). Transfected cell supernatant was harvested 48 hours later. Virions in the cell supernatant were concentrated by centrifugation through a sucrose cushion and resuspended in PBS. Lentiviral particle titer was determined using the Lenti-X p24 Rapid Titer Kit (Takara Bio, San Jose, CA). The lentiviral transfer genome encoded an EF-1a promoter driving a CD20-targeted chimeric antigen receptor followed by a 2A self-cleaving peptide and the various cytokine receptors as provided for herein.

[00531] Transduction and population monitoring. Activated PBMCs from each donor were transduced with respective viruses, grown in complete PBMC media for 48 hours, then seeded in 96-well plates with IL-2-free media containing either recombinant human growth hormone (GH, Fisher Scientific) or recombinant human granulocyte colony stimulating factor (GCSF, Sigma) at the following concentrations: GCSF at 250.00, 125.00, or 0.00 ng/mL and GH at 500.00 250.00, 125.00, 62.50, 31.25, 15.8, 7.9 or 0.00 ng/mL. Media was replaced every 48 hours. Cytometry was performed at specific intervals.

[00532] Results.

[00533] *Cell proliferation by GCSF*

[00534] In the presence of IL-2-free media, cells without a chimeric cytokine receptor (FIG. 25A) or cells harboring a receptor which did not receive GCSF did not undergo an expansion phase (FIG. 25B-F 0.0 ng/mL). In contrast, cells which harbored GCSFR ligand receptors underwent an expansion at both 250 and 125 ng/mL GCSF (FIG. 25B-F). The most significant expansion was observed when the G2R2 chimeric cytokine receptor was present (FIG. 25E).

[00535] *Cell proliferation by hGH*

[00536] Similarly, cells harboring a receptor which did not receive hGH did not undergo an expansion phase (FIG. 26A-E, 0.0 ng/mL). Interestingly, while cells expressing the GCSFRA715 receptor did respond to GCSF (FIG. 25B), cells expressing the GHR-GCSFRA715 receptor did not respond to GH at any dose (FIG. 26A). In contrast, the other

chimeric cytokines all yielded a dose responsive expansion with the GHR ligand region (FIG. 26B-E).

[00537] These results indicate that the chimeric cytokine receptors of the present disclosure are able to induce expansion of cells transduced with a CAR20 chimeric antigen receptor construct. These results, in combination of those of Example 15, indicate that the use of the chimeric cytokine receptor constructs as provided for herein results in inducible cell expansion with minimal ligand associated toxicity.

[00538] Example 17: Stimulation of chimeric cytokine receptors promotes T-cell expansion

[00539] Select chimeric cytokine receptors were further evaluated for sustaining viability and stimulating growth of CAR-T cells following transduction. PBMCs containing CAR20 and select GCSFR ECD chimeras or CAR20 and select GHR ECD chimeras were generated as described in the previous examples. Cells were then treated with either GCSF or GH at 250, 125, 62.5, 31.75 or 0.0 ng/mL of the respective agonist in IL-2-free media and evaluated at regular intervals.

[00540] **Results.** PBMCs transduced with full-length GCSFR responded well at all doses to GCSF treatment with a doubling of the cell population by the end point (FIG. 27A). Exchanging the GCSFR ligand recognition domain with that of GHR eliminated population growth effects (FIG. 27D). Transduction with GCSFRA715 yielded weak cell expansion of less than 2-fold (FIG. 27B) as did transduction with the GHR-exchanged full length GCSFR without the FNIII domain (FIG. 27E). In accordance with prior studies, G2R2 yielded a robust population expansion of up to 8-fold (FIG. 27C). Interestingly, exchanging the GCSFR ligand recognition domain with that of GHR retained the population growth effects of the IL-6R β /IL-2R β G2R2 chimeric cytokine receptor (FIG. 27F).

[00541] These results further validate the results of the previous examples and indicate that the chimeric cytokine receptors of the present disclosure are able to induce expansion of cells transduced with a CAR20 chimeric antigen receptor construct.

[00542] The above assessment was repeated with a different CAR20 construct (corresponding to SEQ ID NOs: 99, 128, and 129) and select GCSFR ECD chimeras or GHR ECD chimeras. As above, cells were treated with either GCSF or GH at 250, 125, 62.5, 31.75 or 0.0 ng/mL of the respective agonist in IL-2-free media and evaluated at regular intervals. As a control, cells were also treated with complete media containing IL-2. Two separate PBMC donor lines were assessed. The results are shown in FIG. 32.

[00543] FIG. 32A-F illustrates the results for GCSFR assessment. As shown in FIG. 32A and 32B, treatment with the indicated concentration of GCSF had no effect on total cell count when GCSFR was not present. As shown in FIG. 32C and 32D, in the presence of both the CAR20 construct and GCSFR (SEQ ID NO: 105), the CAR-T cells exhibited a minimal yet dose responsive increase in cell count when treated with GCSF. Interestingly, and as shown in FIG. 32E and 32F, when the CAR20 construct was replaced with a GFP transgene, the PBMCs exhibited no increase in cell count when treated with GCSF, even with the GCSFR (SEQ ID NO: 105) construct being present. These results indicate that both the CAR and the GCSFR ECD chimera contribute towards stimulating cell growth in response to GCSF. In other words, the quantity of CAR-T cells increased based on presence of both the activation and co-stimulation signals provided by the CAR and the cytokine signal provided by the GCSFR ECD chimera.

[00544] FIG. 33A-F illustrates the results for GHR assessment. Similar results were obtained as with the GCSFR assessment. As shown in FIG. 33A and 33B, treatment with the indicated concentration of GH had no effect on total cell count when GHR was not present. As shown in FIG. 33C and 33D, in the presence of both the CAR20 construct and GHR-G2R2 (SEQ ID NO: 120), the CAR-T cells exhibited a robust and dose responsive increase in cell count when treated with GH. Interestingly, the GH ECD chimera produced cell counts approximately equal to the cell counts obtained using the complete media. As with the GCSFR constructs discussed above, and as shown in FIG. 33E and 33F, when the CAR20 construct is replaced with a GFP transgene no increase in cell count is observed in response to GH. At time point day 11, cells were also assessed via flow cytometry to determine the percent of CAR-T cell enrichment in the cell populations for both the GH and GCSFR treatments. Data are provided in Table 2 below:

TABLE 2: Day 11 flow cytometry percentages

250 ng/ml GCSF			
	CAR20	GFP-T2A-GCSFR	CAR20-T2A-GCSFR
Donor 1	35.5	0.4	80.4
Donor 2	60.2	30.1	73.1
250 ng/ml GH			
	CAR20	GFP-T2A-GHR G2R2	CAR20-T2A-GHR G2R2
Donor 1	23.7	65.8	66.2

Donor 2	48.6	71.9	67.9
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The data in Table 2 above represent the percentage of cell population that was CD7 positive and either CAR20 positive (columns 1 and 3) or GFP positive (column 2). In comparing the results of expressing the CAR20 construct alone (column 1) vs in combination with the GCSFR ECD chimera or GH RECD chimera (column 3), co-expression of the CAR with the chimera receptors clearly results in an increase of CD7 positive CAR20 positive cells.

[00545] The data of the present example indicate that both the GCSFR and GHR chimeric receptors as provided for herein represent viable strategies to both promote T cell growth and promote enrichment of CAR-T cells. The data also highlight the surprising and unexpected result that simultaneous expression of both the CAR construct and the GCSFR or GHR chimeric receptors promotes even greater cell growth and enrichment as compared to individual expression of each respective receptor.

[00546] **Example 18: VSV-G* pseudotyped lentiviruses deplete B-cells and eliminate established tumors in mice.**

[00547] The ability of VSV-G* pseudotyped lentiviral constructs to deplete B-cell populations *in vivo* was assessed. The VSV-G* pseudotyped lentiviral constructs utilized CD7 binders as provided for herein. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23, SEQ ID NO: 25), as provided for herein. Mice were injected with lentiviral particles expressing a GFP transgene, or a CD20-CAR transgene. The mice utilized were huCD34 NSG mice which have circulating human T and B cells. Mice receiving lentiviral constructs expressing GFP saw no loss of CD20 (FIG. 28A) or CD19 (FIG. 28B) B cells. Mice receiving the CD20-CAR transgene saw a dramatic and sustained loss of B cells over three weeks as exhibited by a dramatic loss of both CD20 positive B cells (FIG. 28A) and CD19 positive B cells (FIG. 28B).

[00548] To further characterize the *in vivo* efficacy of the viral particles, the ability of VSV-G* pseudotyped lentiviral constructs to prevent tumor formation was assessed. Mice were injected with viral particles expressing a GFP transgene or a CD20-CAR transgene on protocol Day 1. On Day 9, mice were infused with Raji tumor cells and tumor progression was monitored. The experimental protocol is illustrated in FIG. 29A. Mice receiving no treatment or lentiviral constructs expressing GFP demonstrated progressive tumor development and spread as determined by IVIS imaging. In contrast, mice receiving lentiviral constructs

expressing the CD20-CAR transgene demonstrated no tumor development after Raji cell infusion (FIG. 29B).

[00549] The ability of the viral particles to affect established tumors *in vivo* was also assessed. Mice were infused with Raji tumor cells on protocol Day 0. Mice were humanized via human PBMC engraftment on protocol Day 5, and mice were either not injected with viral particles (control) or injected with viral particles expressing a CD20-CAR transgene on protocol Day 6. Tumor progression was monitored through protocol Day 30. The experimental protocol is illustrated in FIG. 30A. Control and virus treated mice demonstrated comparable tumor load on Day 5 (prior to virus administration), Day 7, and Day 8 as determined by IVIS imaging, indicating that Raji tumors were established in both groups. At Day 12, control mice continued to exhibit increased tumor load, whereas virus treated mice exhibited a dramatic decrease in tumor load. The decreased tumor load was sustained throughout the duration of the experiment (FIG. 30B).

[00550] These examples and embodiments demonstrate that the VSV-G* pseudotyped lentiviral constructs of the present disclosure are able to properly target B-cells *in vivo*, prevent tumor formation *in vivo*, and eliminate established tumors *in vivo*.

[00551] **Example 19: VSV-G* pseudotyped lentiviruses deplete B-cells in non-human primates.**

[00552] The ability of VSV-G* pseudotyped lentiviral constructs to deplete B-cell populations *in vivo* was also assessed in non-human primates (Macaques). The VSV-G* pseudotyped lentiviral constructs utilized CD7 binders as provided for herein. The VSV-G protein utilized was a variant VSV-G protein harboring a mutation to prevent binding of VSV-G to the LDL-R. The variant VSV-G is denoted VSV-G* and corresponds to VSV-G (I182E, T214N, T352A) (e.g. SEQ ID NO: 23), as provided for herein. Macaques were injected with lentiviral particles on protocol Day 0 and their CD20+ cells were monitored. Injection of the lentiviral particles results in B-cell depletion in 6/6 Macaques tested.

[00553] **Example 20: CAR-GCSF Receptor Construct Enables Tunable Expansion of Cells**

[00554] Further evaluation was conducted to determine whether the combination of a CAR and GCSF receptor (GCSFR) could modulate proliferation of CAR-T cells. FIG. 31A shows an example CAR – GCSF Receptor construct for tunable expansion of cells. In the presence of the GCSF agonist, the GCSFR receptor is turned on, thereby providing a separate signal from the signaling of the CAR. Specifically, this example involved a CD20 CAR and an engineered GCSFR constructed with a GCSF ECD and truncated GSCF ICD.

[00555] Tunable expansion of cells were first evaluated *in vitro*. Activated human PBMCs were transduced with the indicated lentiviral vectors. Two days later, cells were pelleted and resuspended in medium without IL-2 containing GCSF agonist over a dose range. FIG. 31B shows flow cytometry data demonstrating tunable CAR cell proliferation *in vitro*. FIG. 31C shows a dose response of CAR-T cells to an exogenous GCSF agonist. Cell counts and medium change (with or without agonist) were performed every other day. Flow data at days 7 and 14 after addition of agonist were similar - day 14 data are shown in FIG. 31B. Together, this demonstrates that the CAR + GCSFR construct enables tunable expansion of cells through the addition of the GCSF agonist.

[00556] Next, the CAR + GCSFR construct was further evaluated *in vivo*. FIGs. 31D and 31E depict an example *in vivo* experimental design for evaluating the CAR-GCSFR construct. NSG-MHC I/II dKO mice (Jax Labs) were engrafted with activated human PBMCs from 2 donors as indicated on day -1. As shown in FIGs. 31D and 31E, animals received GCSF alone (e.g., on Day 1), vector alone (e.g., on Day 0), or both vector (on Day 0) and GCSF (on Day 1). Animals receiving GCSF were given 100µg GCSF intraperitoneally each day for 14 days.

[00557] FIGs. 31F and 31G show significant proliferation of CAR20+ cells in the presence of GCSF agonist. Specifically, GCSF signaling through the engineered GCSFR led to significant proliferation of CAR20+ cells over a 14-day period. As shown in FIG. 31G, after GCSF was discontinued (after Day 14), a regression to baseline of CAR20+ cells occurred. Together, this data demonstrates surprisingly that the CAR + GCSFR construct enables tunable expansion of cells *in vivo*, which enhanced the expansion of these cells over cells that did not have the GCSFR chimeric construct.

[00558] This specification contains numerous citations to patents, patent applications, and publications. Each is hereby incorporated by reference for all purposes.

[00559] The specification also makes reference to various sequences, such as those provided herein and below.

VSV-G Indiana Full length WT:

MKCLLYLAFLFIGVNCFTTIVFPHNQGNWKNVPSNYHYCPSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
HASKWVTTCDFRWYGPKYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQVTPHHV
LVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDNLISMDITFFSEDGELSSLGKEGTGFRS
FAYETGGKACKMQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLC
QETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMIISGTTTERELWDD
WAPYEDVEIGPNGVLRITSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESFFGDTGLSKNP
TELVEGWFFSSWKSSIASFFFIIGLIIGLFLVLRVGIHLCKIKLHKTKRQIYTDIEMNRLGK (SEQ ID NO:
1)

VSV-G Indiana Ectodomain WT:

KFTTIVFPHNQGNWKNVPSNYHYCPSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP

KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQVTPHHVLVDEYTGWEVDSQFIN
GKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISP
DLSYLAPKNP GTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGT TTERELWDDWAPYEDVEIGPNGVLR
TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNP IELVEGW FSSWKSSIA
SFFFIIGLIIGLFLVLRVGIHL CIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 2)

VSV-G Indiana ectodomain I182A:

KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQVTPHHVLVDEYTGWEVDSQFIN
GKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISP
DLSYLAPKNP GTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGT TTERELWDDWAPYEDVEIGPNGVLR
TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNP IELVEGW FSSWKSSIA
SFFFIIGLIIGLFLVLRVGIHL CIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 3)

VSV-G Indiana ectodomain I182D:

KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQVTPHHVLVDEYTGWEVDSQFIN
GKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISP
DLSYLAPKNP GTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGT TTERELWDDWAPYEDVEIGPNGVLR
TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNP IELVEGW FSSWKSSIA
SFFFIIGLIIGLFLVLRVGIHL CIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 4)

VSV-G Indiana ectodomain I182E:

KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQVTPHHVLVDEYTGWEVDSQFIN
GKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISP
DLSYLAPKNP GTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGT TTERELWDDWAPYEDVEIGPNGVLR
TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNP IELVEGW FSSWKSSIA
SFFFIIGLIIGLFLVLRVGIHL CIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 5)

VSV-G Indiana ectodomain H8A + K47Q:

KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQVTPHHVLVDEYTGWEVDSQFIN
GKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISP
DLSYLAPKNP GTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGT TTERELWDDWAPYEDVEIGPNGVLR
TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNP IELVEGW FSSWKSSIA
SFFFIIGLIIGLFLVLRVGIHL CIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 6)

VSV-G Indiana ectodomain Q10A:

KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQVTPHHVLVDEYTGWEVDSQFIN
GKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISP
DLSYLAPKNP GTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGT TTERELWDDWAPYEDVEIGPNGVLR
TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNP IELVEGW FSSWKSSIA
SFFFIIGLIIGLFLVLRVGIHL CIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 7)

VSV-G Indiana ectodomain Q10R:

KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQVTPHHVLVDEYTGWEVDSQFIN
GKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISP
DLSYLAPKNP GTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGT TTERELWDDWAPYEDVEIGPNGVLR
TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNP IELVEGW FSSWKSSIA
SFFFIIGLIIGLFLVLRVGIHL CIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 8)

VSV-G Indiana ectodomain Q10K:

KFTIIVFPNNKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
 KYITHSIRSFPTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQVTPHHVLVDEYTGGEWVDSQFIN
 GKCSNYICPTVHNSTTWHSDYKVKGLCDNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQUYCK
 HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISP
 DLSYLAPKNPGTGPFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGTTTERELWDDWAPYEDVEIGPNGVL
 TSSGYKFPLYMIGHGMLDSDLHSSKAQVFEHPHIQDAASQLPDDSELF FGD TGLSKNP IELVEGW FSSWKSSIA
 SFFFIIGLIIGLFLVLRVGIHL CIK LKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 9)

VSV-G New Jersey Full length WT:

MLSYLIFALVSPILGKIEIVFPQHTTGDWKRVPHEYNYCPTSADKNSHGTQTGIPVELTMPKGLTTHQVDGFMCH
 HSALWMTTCDFRWYGP KYITHSIHNEEPTDYQCLEAIKAYKDGVSFNP G FPPQSCGYGTVTDAAHIVVTPHVS
 KVDEYTGGEWIDPHFIGGRCKGQICETVHNSTKWFTSSDGESVCSQLFTLVGGTFFSDSEEITSMGLPETGIRSNY
 FPYVSTEGICKMPFCRKP GYK LKNDLWFQITDPDLDTVRDLPHIKDCDLSSSIVTPGEHATDISLISDVERILD
 YALCQNTWSKIEAGEPITPVDLSYLGPKNPGAGPVFTIINGSLHYFMSKYL RVELESPIPRMEGKVAGTRIVRQ
 LWDQWFFPGEVEIGPNGVLTKQGYKFLHIIGTGEVDNDIKMERIVKHWEHPHIEAAQTFLKKDDTEEVLYYGD
 TGVSKNPVELVEGW FSGWRSSIMGVLAVIIGFVILIFLIRLIGVLSSLF RQKRRIYKSDVEMAHFR (SEQ ID
 NO: 10)

VSV-G New Jersey ectodomain WT:

KIEIVFPQHTTGDWKRVPHEYNYCPTSADKNSHGTQTGIPVELTMPKGLTTHQVDGFMCHSALWMTTCDFRWYGP
 KYITHSIHNEEPTDYQCLEAIKAYKDGVSFNP G FPPQSCGYGTVTDAAHIVVTPHVS KVDEYTGGEWIDPHFIG
 GRCKGQICETVHNSTKWFTSSDGESVCSQLFTLVGGTFFSDSEEITSMGLPETGIRSNYFPYVSTEGICKMPFCR
 KPGYK LKNDLWFQITDPDLDTVRDLPHIKDCDLSSSIVTPGEHATDISLISDVERILDYALCQNTWSKIEAGEP
 ITPVDLSYLGPKNPGAGPVFTIINGSLHYFMSKYL RVELESPIPRMEGKVAGTRIVRQLWDQWFFPGEVEIGPN
 GVLTKQGYKFLHIIGTGEVDNDIKMERIVKHWEHPHIEAAQTFLKKDDTEEVLYYGD TGVSKNPVELVEGW F
 GWRSSIMGVLAVIIGFVILIFLIRLIGVLSSLF RQKRRIYKSDVEMAHFR (SEQ ID NO: 11)

VSV-G Marraba Full length WT:

MLRFLFCFLALGAHAKFTIIVFPHHQKGNWKNVPSTYHYCPSSSDQNWHNDLTGVS LHV KIPKSHKAIQADGWMCH
 HAAKWVTTCDFRWYGP KYITHSIHMSPTLEQCKTSIEQTKQGVWINPGFPPQSCGYATVTDAAEVVVVQATPHHV
 LVDEYTGGEWIDSQLVGGKCSKEVCQTVHNSTVWHADYKITGLCESNLASVDITFFSEDGQKTS LGKPNTGFRSNH
 FAYESGEKACRMQYCTQWGIRLP SGVWFELVDKDLFQA AKLPECPRGSSISAPSQTSVDVSLIQDVERILDYSLC
 QETWSKIRAKLPVSPVDLSYLAPKNPGSGPAFTIINGTLKYFETRYIRVDISNPIIPHMVGTM SGTTTERELWND
 WYPYEDVEIGPNGVLKTP TGF KFLY MIGHGMLDSDLHKSSQAQVFEHPHAKDAASQLPDDETLFFGD TGLSKNP
 VELVEGW FSSWKSTLASFFLIIGLGVALIFIIRIIVAIRYKYKGRKTQKIYNDVEMSRLGNK (SEQ ID NO:
 12)

VSV-G Marraba ectodomain WT:

KFTIIVFPHHQKGNWKNVPSTYHYCPSSSDQNWHNDLTGVS LHV KIPKSHKAIQADGWMCHAAKWVTTCDFRWYGP
 KYITHSIHMSPTLEQCKTSIEQTKQGVWINPGFPPQSCGYATVTDAAEVVVVQATPHHV LVDEYTGGEWIDSQLV
 GKCSKEVCQTVHNSTVWHADYKITGLCESNLASVDITFFSEDGQKTS LGKPNTGFRSNHFAYESGEKACRMQYCT
 QWGIRLP SGVWFELVDKDLFQA AKLPECPRGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAKLPVSP
 DLSYLAPKNPGSGPAFTIINGTLKYFETRYIRVDISNPIIPHMVGTM SGTTTERELWNDWYPYEDVEIGPNGVLK
 TPTGFKFLY MIGHGMLDSDLHKSSQAQVFEHPHAKDAASQLPDDETLFFGD TGLSKNPVELVEGW FSSWKSTLA
 SFFLIIGLGVALIFIIRIIVAIRYKYKGRKTQKIYNDVEMSRLGNK (SEQ ID NO: 13)

VSV-G Carajas Full length WT:

MKMKMVIAGLILCIGILPAIGKITISFPQSLKGDWRPVPKGYNYCPTSADKNLHGD LIDIGLRLRAPKSFKGISA
 DGWMCHAARWITTTCDFRWYGP KYITHSIHSFRPSNDQCKEAI RLTNEGNWINPGFPPQSCGYASVTDSESVVTV
 TKHQLVLDYESGSGWIDSQLVGGKCSKEVCQTVHNSTLWHADHTLDSICDQEFVAMDAVLFTESGKFEEFGKPN
 IRSNYFPYESLKDVCQMDFCRRKGFKLP SGVWFELVDKDLFQA AKLPECPRGSSISAPSQTSVDVSLIQDVERILDYSLC
 QETWSKIRAKLPVSPVDLSYLAPKNPGSGPAFTIINGTLHYFNTRYIRVDIAGPVTKETITGFSVGT
 STSRVLWDQWFFPYGENSIGP NGLKTASGYKPLFMVGTGVLDAD IHLG EATVIEHPHAKDAQKVVDSEVIF

GDTGVSKNPVEVVEGWFSGWRSSLSMIFGIILLIVCLVLIVRILIALKYCCVRHKKRTIYKEDLEMGRIPRA
(SEQ ID NO: 14)

VSV-G Carajas ectodomain WT:

KITISFPQSLKGDWRPVPKGYNYCPTSADKNLHGDLLIDIGLRLRAPKSFKGISADGWMCHAARWITTCDFRWYGP
KYITHSIHSFRPSNDQCKEAIRLTNEGNWINPGFPPQSCGYASVTDSESVVTVTKHQVLVDEYSGSWIDSQFP
GSCTSPICDVTNHLWHADHTLSDICDQEFVAMDAVLFTESGKFEFGKPNSGIRSNYFPYESLKDVCQMDFC
RKGFKLP SGVWFEIEDAEKSHKAQVELKIKRCPHGAVISAPNQNAADINLIMDVERILDYSLCQATWSKIQNKEA
LTPIDISYLGPKNPGPGPAFTIINGTLHYFNTRYIRVDIAGPVTKEITGFVSGTSTSRVLWDQWFFPYGENSIGPN
GLLKTAGSYKYPLFMVGTGVLADIIHKLGEATVIEHPHAKAQKVDDSEVIFFGDTGVSKNPVEVVEGWFSGWR
SSLSMIFGIILLIVCLVLIVRILIALKYCCVRHKKRTIYKEDLEMGRIPRA (SEQ ID NO: 15)

VSV-G Alagoa Full length WT:

MTPAFILCMLLAGSSWAKFTIVFPQSQKGDWDPVPNNRYCPSSADQNWHDLLGVNIRAKMPKVHKAIKADGWM
CHAAKWVITTCDFRWYGPQYIITHSIHSFIPTKAQCEESIKQTKEGVWINPGFPPKNCGYASVSDAESIIIVQATAHS
VMIDEYSGDWLDSQFPTGRCTGSTCETIHNSTLWYADYQVTGLCDLSALVSTEVTFYSEDGLMTSIGRQNTGYRSN
YFPYEGAAACRMKYCTHEGIRLPSGVWFEMVDKELLESVQMPECPAGLTISAPTQTSVDVSLILDVERMLDYS
CQETWSKVHSLPISPVDLGYIAPKNPGAGPAFTIVNGTLKYFDTRYLRIDIEGVLKMTGKVSGETPTKRELWT
EWFYDDVEIGPNGVLKTPGYKFLYMIHGHLSDSLQKTSQAEVFHHPQIAEAVQKLPDDETLFFGDTGISK
PVEVIEGWFSNWRSSVMAIVFAILLVITVLMVRLCVAFRHFCCQKRHKIYNDLEMNQLRR (SEQ ID NO:
16)

VSV-G Alagoa ectodomain WT:

KFTIVFPQSQKGDWDPVPNNRYCPSSADQNWHDLLGVNIRAKMPKVHKAIKADGWMCHAAKWVITTCDFRWYGP
QYIITHSIHSFIPTKAQCEESIKQTKEGVWINPGFPPKNCGYASVSDAESIIIVQATAHSVMIDEYSGDWLDSQFPT
GRCTGSTCETIHNSTLWYADYQVTGLCDLSALVSTEVTFYSEDGLMTSIGRQNTGYRSNYPYEGAAACRMKYCT
HEGIRLPSGVWFEMVDKELLESVQMPECPAGLTISAPTQTSVDVSLILDVERMLDYSYCQETWSKVHSLPISP
VDLGYIAPKNPGAGPAFTIVNGTLKYFDTRYLRIDIEGVLKMTGKVSGETPTKRELWTEWFYDDVEIGPNGVLK
TPGYKFLYMIHGHLSDSLQKTSQAEVFHHPQIAEAVQKLPDDETLFFGDTGISKPNPVEVIEGWFSNWRSSV
MAIVFAILLVITVLMVRLCVAFRHFCCQKRHKIYNDLEMNQLRR (SEQ ID NO: 17)

VSV-G Cocal Full length WT:

MNLLLTFTIVLPLCSHAKFSIVFPQSQKGNWKNVPSYHYCPSSSDQNWHDLLGITMKVKMPKTHKAIQADGWM
CHAAKWVITTCDFRWYGPQYIITHSIHSIQPTSEQCKESIAQTKQGTWMSPGFPPQNCGYATVTDVAVVVQATPHH
VLVDEYTGWIDSQFPNGKCEETECETVHNSTVWYSDYKVTGLCDATLVDTETIFFSEDGKKEISGKPNITGYRSN
YFAYEKGDKVCKMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVGATISAPTQTSVDVSLILDVERILDYSL
CQETWSKIRSKQPVSPVDSLAPKNPGTGPAFTIINGTLKYFETRYIRIDIDNPIISKMVGKISGSQTERELWT
EWFYEGVEIGPNGILKTPGTGYKFLYMIHGMLDSDLHKTSAEVEFHPHLAEAPKQLPEEETLFFGDTGISK
PNPVELIEGWFSWKSTVVTFFFAIGVFILLYVVARIVIAVRYRYQGSNNKRIYNDIEMSRFRK (SEQ ID NO:
18)

VSV-G Cocal ectodomain WT:

KFSIVFPQSQKGNWKNVPSYHYCPSSSDQNWHDLLGITMKVKMPKTHKAIQADGWMCHAAKWVITTCDFRWYGP
KYIITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQATPHHVLVDEYTGWIDSQFP
NGKCEETECETVHNSTVWYSDYKVTGLCDATLVDTETIFFSEDGKKEISGKPNITGYRSNYPYEGKDKVCKMNYCK
HAGVRLPSGVWFEFVDQDVYAAAKLPECPVGATISAPTQTSVDVSLILDVERILDYSLCQETWSKIRSKQPVSPV
DSLAPKNPGTGPAFTIINGTLKYFETRYIRIDIDNPIISKMVGKISGSQTERELWTEWFYEGVEIGPNGILK
TPGTGYKFLYMIHGMLDSDLHKTSAEVEFHPHLAEAPKQLPEEETLFFGDTGISKPNPVELIEGWFSWKSTV
VTFFFAIGVFILLYVVARIVIAVRYRYQGSNNKRIYNDIEMSRFRK (SEQ ID NO: 19)

VSV-G Morreton Full length WT:

MLVLYLLLSLALGAQCKFTIVFPHNQKGNWKNVANYQYCPSSSDLNWNHGLIGTSLQVKMPKSHKAIQADGWM
CHAAKWVITTCDFRWYGPQYIITHSIKSMITVDQCKESIAQTKQGTWLNPGFPPQSCGYASVTDAAEAVIVKATPHQ
VLVDEYTGWVDSQFPTGKCNKDICTVHNSTTWSYKVTGLCDANLISMDITFFSEDGKLTLGKEGTGFRSN
YFAYENGDKACRMQYCKHWGVRPLSGVWFEMADKDIYNDAKFPDCPEGSSIAAPSQTSVDVSLIQDVERILDYSL

CQETWSKIRAHLPISPVDLSYLSPKNPGTGPAFTIINGTLKYFETRYIRVDIAGPIIPQMRGVISGTTTERELWT
DWYPYEDVEIGPNGVLKTATGYKFPLYMIGHGMLDSDLHISSKAQVFEHPHIQDAASQLPDDETLFFGDTGLSKN
PIELVEGWFSGWKSTIASFFFIIGLVIGLYLVLIRIGIALCIKCRVQEKRPKIYTDVEMNRLDR (SEQ ID NO:
20)

VSV-G Morreton ectodomain WT:
KFTIIVFPHNQKGNWKNVPANYQYCPSSSDLNWHNGLIGTSLQVKMPKSHKAIQADGWMCHAAKWVTTCDFRWYGP
KYVTHSIKSMIPTVDQCKESIAQTKQGTWLNPGFPPQSCGYASVTDAAEAVIVKATPHQVLVDEYTGGEWVDSQFPT
GKCNKDICTVHNSTTWHSDYKVTGLCDANLISMDITFFSEDGKLTSLGKEGTGFRSNYFAYENGDKACRMQYCK
HWGVRLPSGVWFEMADKDIYNDAKFPDCPEGSSIAAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAHLPISP
V
DLSYLSPKNPGTGPAFTIINGTLKYFETRYIRVDIAGPIIPQMRGVISGTTTERELWTDWYPYEDVEIGPNGVLK
TATGYKFPLYMIGHGMLDSDLHISSKAQVFEHPHIQDAASQLPDDETLFFGDTGLSKNPIELVEGWFSGWKSTIA
SFFFIIGLVIGLYLVLIRIGIALCIKCRVQEKRPKIYTDVEMNRLDR (SEQ ID NO: 21)

Fc IgG1 (Accession No. P01857)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS
SS
LGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHCTPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDV
S
HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQ
PREPQVYITLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRW
QQGNVFSQSVSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 26)

Fc IgG2 (Accession No. AAN76043)

STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS
SS
LGTQTYICNVNHKPSNTKVDKTKVERKCCVECPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVDVSHEDPE
VQFNWYVDGVEVHNAKTKPREEQFNSTFRVSVLTVVHQDWLNGKEYKCKVSNKGLPAPIEKTISKTKGQPREPQ
VYITLPPSRDEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPMLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 27)

Fc IgG4 (Accession No. AAB59394)

STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS
SS
LGTQTYICNVNHKPSNTKVDKRVESKYGPPCPSCPAPPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDV
SQEDP
EVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREP
QVYITLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLLTVDKSRWQEGN
VFSCSVSMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 28)

TABLE OF ADDITIONAL CDR SEQUENCES

SEQ ID NO	Sequence	Description
77	SYWIIH	CD7AB1 HCDR1- Kabat
78	RIDPNSGDTKYNEKFKN	CD7AB1 HCDR2- Kabat
32	SPYYSDNDSMDY	CD7AB1 HCDR3- Kabat
33	RASQSIGTSIH	CD7AB1 LCDR1- Kabat
34	YASESIS	CD7AB1 LCDR2- Kabat
35	QQSNSWPTT	CD7AB1 LCDR3- Kabat
79	GYPFTSYW	CD7AB1 HCDR1- IMGT
80	IDPNSGDT	CD7AB1 HCDR2- IMGT
81	ARSPYYSDNDSMDY	CD7AB1 HCDR3- IMGT
82	QSIGTS	CD7AB1 LCDR1- IMGT
-	YA	CD7AB1 LCDR2- IMGT
35	QQSNSWPTT	CD7AB1 LCDR3- IMGT
83	DYNLH	CD8AB1 HCDR1- Kabat
84	FIYPYNGGTGYNQKFKN	CD8AB1 HCDR2- Kabat
44	DHRYNEGVSFYD	CD8AB1 HCDR3- Kabat
45	RASEVDGFGNSFMN	CD8AB1 LCDR1- Kabat

SEQ ID NO	Sequence	Description
46	LASNLES	CD8AB1 LCDR2- Kabat
47	QQNNEDPYT	CD8AB1 LCDR3- Kabat
85	RYTFTDYN	CD8AB1 HCDR1- IMGT
86	IYPYNGGT	CD8AB1 HCDR2- IMGT
87	ARDHRYNEGVSFDY	CD8AB1 HCDR3- IMGT
88	ESVDGFGNSF	CD8AB1 LCDR1- IMGT
-	LA	CD8AB1 LCDR2- IMGT
47	QQNNEDPYT	CD8AB1 LCDR3- IMGT

Additional Sequences:

SEQ ID NO:	SEQUENCE	OTHER NAME
105	MARLGNCSLTWAALIILLPGSLEECGHISVSAPIVHLGDPITASC I IKQNCSHLDPEPQILWRLGAELQPGGRQQRLSDGTQESIITLPHL NHTQAFLLSCCLNWGNSLQILDQVELRAGYPPIPHNLSCLMNLTT SLICQWEPGPEPETHLPTSTFTLKSFKSRGNCQTQGDSILDCVPKDGQS HCCIPRKHLLLYQNMGIWVQAENALGTSMSPQLCLDPMDVVKLEPP MLRTMDPSPEAAPPQAGCLQCLWEPWQPGGLHINQKCELRHKPQRGE ASWALVGPLPLEALQYELCGLLPATAYTLQIRCIWFLPGHWSWDS PSLELRTTERAPTVRDLTWWRQRLDPRTVQLFWKPVPLEEDSGRI QGYVVSWRPSGQAGAILPLCNTTELSCTFHLPSEAQEVAVAYNSA GTSRPTPVVFSSESGPALTRLHAMARDPHSLWVGWEPPNPWPQGYV IEWGLGPPSASNSNKTWRMEQNGRATGFLLENIRPFQLYEIVTP LYQDTMGPSQHVYAYSQEMAPSHAPELHLKHIGKTWAQLEWVPEPP ELGKSP LTHYTI FWTNAQNQSFSAILNASSRGFVLHGLEPASLYHI HLMAASQAGATNSTVLTMTLTPEGSELHIILGLFGLLLLLTCLCG TAWLCCSPNRKNPLWPSVPDPAHSSLSGSWVPTIMEEDAFQLPGLGT PPI TKLTVLEEDEKKPVFWESHNSSETCGLPTLVQTYVLQGDPRAV STQPQSQSGTSDQVLYGQLLGSPSPGPGHYLRCDSTQPLLAGLTP SPKSYENLWFQASPLGTLVTPAPSQEDDCVFGPLLNFPLLQGIRVH GMEALGSF	hGCSFR FL (Construct A)
106	MARLGNCSLTWAALIILLPGSLE	h GCSFR ECD leader sequence

107	ECGHISVSAPIVHLGDPITASCIKQNCNSHLDPEPQILWRLGAELQ PGGRQQRLSDGTQESIITLPHLNHTQAFLLSCCLNWGNSLQILDQVE LRAGYPPAIPHNLSCLMNLTTSSLICQWEPGPETHLPTSFTLKSF SRGNCQTQGDSILDCVPKDGQSHCCIPRKHLLLYQNMGIWVQAENA LGTSMSPQLCLDPMDEVKLEPPMLRTMDPSPEAAPQAGCLQLCWE PWQPGLHINQKCELRHKPQRGEASWALVGPLPLEALQYELCGLLPA TAYTLQIRCIRWPLPGHWSWSPSLELRRTTERAPTIVRLDTWWRQRO LDPRTVQLFWKVPVPLEEDSGRIQGYVVSWRPSGQAGAILPLCNTTE LSCTFHLPSEAQEVVALVAYNSAGTSRPTPVVFSERGPALTRLHAM ARDPHSLWVGWEPNPNWPQGYVIEWGLGPPSASNSNKTWRMEQNGR ATGFLLENIRPFQLYEIIIVTPLYQDTMGPSQHVYAYSQEMAPSHA PELHLKHIGKTWAQLEWVPEPPELGKSPPLTHYTIIFWTNAQNQSFS ILNASSRGFVLHGLEPASLYHIHLMAASQAGATNSTVLTLMTLTPE GSELH	h GCSFR ECD no leader
108	MARLGNCSLTWAALIILLPGSLEECCGHISVSAPIVHLGDPITASC IIKQNCNSHLDPEPQILWRLGAELQPGGRQQRLSDGTQESIITLPHL NHTQAFLLSCCLNWGNSLQILDQVELRAGYPPAIPHNLSCLMNLTT SLICQWEPGPETHLPTSFTLKSFGRGNCQTQGDSILDCVPKDGQS HCCIPRKHLLLYQNMGIWVQAENALGTSMSPQLCLDPMDEVKLEPP MLRTMDPSPEAAPQAGCLQLCWEPPWQPGLHINQKCELRHKPQRGE ASWALVGPLPLEALQYELCGLLPAATAYTLQIRCIRWPLPGHWSW PSLELRRTTERAPTIVRLDTWWRQRLDPRVQLFWKVPVPLEEDSGRI QGYVVSWRPSGQAGAILPLCNTTELSCTFHLPSEAQEVVALVAYNSA GTSRPTPVVFSERGPALTRLHAMARDPHSLWVGWEPNPNWPQGYV IEWGLGPPSASNSNKTWRMEQNGRATGFLLENIRPFQLYEIIIVT PLYQDTMGPSQHVYAYSQEMAPSHAPELHLKHIGKTWAQLEWVPEP ELGKSPPLTHYTIIFWTNAQNQSFSAILNASSRGFVLHGLEPASLYH HLMAASQAGATNSTVLTLMTLTPEGSELH	h GCSFR ECD with leader
109	IILGLFGLLLLTCLCGTAWLCC	hGCSFR TM
110	SPNRKNPLWPSVDPFAHSSLGSWVPTIMEEDAFQLPGLGTPPITKL TVLEEDEKKPVPWESHNSSETCGLPTLVQTYVLQGDPRAVSTQPOS QSGTSDQVLYGQLLGSPSPGPGHYLRCDSTQPLLGLTPSPKSYE NLWFQASPLGLTVTPAPSQEDDCVFGPLLNFLLQGIRVHGMEALG SF	hGCSFR ICD FL
111	SPNRKNPLWPSVDPFAHSSLGSWVPTIMEEDAFQLPGLGTPPITKL TVLEEDEKKPVPWESHNSSETCGLPTLVQTYVLQGDPRAVST	hGCSFR ICD D715

112	MARLGNCSLTWAALIILLPGSLEECGHISVSAPIVHLGDPITASC IIKQNCSHLDPEPQILWRLGAELQPGGRQQLSDGTQESIITLPHL NHTQAFLSCLNWNLSQILDQVELRAGYPPAIPHNLSCLMNLTT SLICQWEPGPETHLPSTFTLKSFKSRGNCQTQGDSILDCVPKDGQS HCCIPRKHLLLYQNMGIWVQAENALGTSMSQPQLCLDPMVVKLEPP MLRTMDPSPEAAPQAGCLQCLWEPWQPLHINQKCEL RHKPQRGE ASWALVGPLPLEALQYELCGLLPATAYTLQIRCIRWPLPGHWSWDS PSLELRTTERAPT VRLDTWWRQRQLDPRTVQLFWKPVPLEEDSGRI QGYVVSWRPSGQAGAILPLCNTTEL SCTFHLPSEAQEV ALVAYNSA GTSRPTPVVFSERGPALTRLHAMARDPHSLWVGWEPNPNWPQGYV IEWGLGPPSASNSNKTWRMEQNGRATGFLLENIRPFQLYEII VTP LYQDTMGPSQHVVAYSQEMAPSHAP ELHLKHIGK TWAQLEWVPEPP ELGKSP LTHYTI FWTNAQNQSFSAI LNASSRGFVLHGLEPASLYHI HLMAASQAGATNSVLTLMTLTPEGSELHI ILGLFGLLLLTCLCG TAWLCCSPNRKNPLWPSVDP AHSSLGSWVPTIMEEDAFQLPGLGT PPI TKLTVLEEDEKKPVWESHNSSETCGLPTLVQTYVLQGDPRAV ST	hGCSFR D715 (Construct B)
113	MDLWQLLLTLALAGSSDAFSGSEATAAILSRAPWSLQSVNPGLKTN SSKEPKFTKCRSPERETFSCHWTDEVH HGTKNLGPIQLFYTRRNTQ EWTQEWKECPDYVSAGENS CYFNSSFTSIWIPYCIKLTSNGGTVDE KCF SVDEIVQPDPPIALNWTLLNVSLTGIHADIQVRWEAPRNADIQ KGWMVLEYELQYKEVNETKWMMDPILTTSPV VYSLKVDKEYEVRV RSKQRNSGNYGEFSEVLYVTLPQMSQFTCEEAPT VRLDTWWRQRQL DPRTVQLFWKPVPLEEDSGRIQGYVVSWRPSGQAGAILPLCNTTEL SCTFHLPSEAQEV ALVAYNSAGTSRPTPVVFSERGPALTRLHAMA RDPHSLWVGWEPNPNWPQGYV IEWGLGPPSASNSNKTWRMEQNGRA TGFLLENIRPFQLYEII VTPLYQDTMGPSQHVVAYSQEMAPSHAP ELHLKHIGK TWAQLEWVPEPP ELGKSP LTHYTI FWTNAQNQSFSAI LNASSRGFVLHGLEPASLYHI HLMAASQAGATNSVLTLMTLTPEG SELHI ILGLFGLLLLTCLCGTAWLCCSPNRKNPLWPSVDP AHSS LGSWVPTIMEEDAFQLPGLGTPPI TKLTVLEEDEKKPVWESHNS ETCGLPTLVQTYVLQGDPRAVST	Construct C
114	MDLWQLLLTLALAGSSDAFSGSEATAAILSRAPWSLQSVNPGLKTN SSKEPKFTKCRSPERETFSCHWTDEVH HGTKNLGPIQLFYTRRNTQ EWTQEWKECPDYVSAGENS CYFNSSFTSIWIPYCIKLTSNGGTVDE KCF SVDEIVQPDPPIALNWTLLNVSLTGIHADIQVRWEAPRNADIQ KGWMVLEYELQYKEVNETKWMMDPILTTSPV VYSLKVDKEYEVRV RSKQRNSGNYGEFSEVLYVTLPQMSQFTCEE	hGH-R ECD (with leader sequence MDLWQLLLTLALAG SSDA)
115	MDLWQLLLTLALAGSSDAFSGSEATAAILSRAPWSLQSVNPGLKTN SSKEPKFTKCRSPERETFSCHWTDEVH HGTKNLGPIQLFYTRRNTQ EWTQEWKECPDYVSAGENS CYFNSSFTSIWIPYCIKLTSNGGTVDE KCF SVDEIVQPDPPIALNWTLLNVSLTGIHADIQVRWEAPRNADIQ KGWMVLEYELQYKEVNETKWMMDPILTTSPV VYSLKVDKEYEVRV RSKQRNSGNYGEFSEVLYVTLPQMSQFTREE	hGH-R ECD C259R (with leader sequence MDLWQLLLTLALAG SSDA)

116	APTVRLDTWWRQRQLDPRTVQLFWKFPVPLEEDSGRIQGYVVSWRPS GQAGAILPLCNTTELSTFHLPSAQEVALVAYNSAGTSRPTPVVF SESRGPALTRLHAMARDPHSLWVGWEPPNPWPQGYVIEWGLGPPSA SNSNKTWRMEQNGRATGFLLENIRPFQLYEIIIVTPLYQDTMGPSQ HVYAYSQEMAPSHAPELHLKHIGKTAQLEWVPEPPELGKSPETHY TIFWTNAQNQSFSAILNASSRGFVLHGLEPASLYHIHLMAASQAGA TNSTVLTMTLTPEGSELH	hGCSFR FNIII domain
117	MDLWQLLLTLALAGSSDAFSGSEATAAILSRAPWSLQSVNPGLKTN SSKEPKFTKCRSPERETFSCHWTDVHHGTKNLGPIQLFYTRRNTQ EWTQEWKECPDYVSAGENSCYFNSSFTSIWIPYCIKLTSGGTVD KCFVDEIVQPDPPIALNWTLLNVSLTGIHADIQVRWEAPRNADIQ KGWMVLEYELQYKEVNETKWKMDPILTTSPVYSLKVDKEYEVRV RSKQRNSGNYGEFSEVLYVTLPQMSQFTCEEIILGLFGLLLLTCL CGTAWLCCSPNRKNPLWPSVPDPAHSSLSGSWVPTIMEEDAFQLPGL GTPPITKLTVLEEDEKKPVPWESHSGKNGPHVYQDLLLLSLGTTNST LPPPFSLQSGILTLPVPAQGPILTSLSGNQEEAYVTMSSFYQNQ	Construct D (comprising IL-7R α ICD denoted in SEQ ID NO: 118)
118	SGKNGPHVYQDLLLLSLGTTNSTLPPPFSLQSGILTLPVPAQGPIL TSLGSNQEEAYVTMSSFYQNQ	IL-7R α ICD
119	MDLWQLLLTLALAGSSDAFSGSEATAAILSRAPWSLQSVNPGLKTN SSKEPKFTKCRSPERETFSCHWTDVHHGTKNLGPIQLFYTRRNTQ EWTQEWKECPDYVSAGENSCYFNSSFTSIWIPYCIKLTSGGTVD KCFVDEIVQPDPPIALNWTLLNVSLTGIHADIQVRWEAPRNADIQ KGWMVLEYELQYKEVNETKWKMDPILTTSPVYSLKVDKEYEVRV RSKQRNSGNYGEFSEVLYVTLPQMSQFTCEEIILGLFGLLLLTCL CGTAWLCCSPNRKNPLWPSVPDPAHSSLSGSWVPTIMEEDAFQLPGL GTPPITKLTVLEEDEKKPVPWESHNSSETCGLPTLVQTYVLQGDPR AVSTQPQSQSSSRSLDCRESGKNGPHVYQDLLLLSLGTTNSTLPPPF SLQSGILTLPVPAQGPILTSLSGNQEEAYVTMSSFYQNQ	Construct E (comprising IL-7R α ICD of 77 amino acids: SSSRSLDCRESGKN GPHVYQDLLLLSLGT NSTLPPPFSLQSG ILTLPVPAQGPIL TSLGSNQEEAYVTM SSFYQNQ)

120	MDLWQLLLLLALAGSSDAFSGSEATAAAILSRAPWSLQSVNPGKLTN SSKEPKFTKCRSPERETF SCHWTDVHHGTKNLGPIQLFYTRRNTQ EWTQEWKECPDYVSAGENSCYFNSSFTSIWIPYCIKLTNSGGTVDE KCFSVDEIVQPDPPIALNWTLLNVSLTGIHADIQVRWEAPRNADIQ KGWMVLEYELQYKEVNETKWKMMDPILTTSPVYSLKVDKEYEVRV RSKQRNSGNYGEFSEVLYVTLPQMSQFTCEEAIIVVPVCLAFLLTTL LGVLF CFNKRDLIKKHIWPNVDP SKSHIAQWSPHTPPRHNFNSKD QMYSDGNFTDVSVEIEANDKKFPFEDLKSLDLFKKEKINTEGHSS GIGSSCMSSSRPSISASLSSNHSLTSCFTNQGYFFFHLPDALEIE ACQVYFTYDPYSEEDPDEGVAGAPTGSSPQLQPLSGEDDAYCTFP SRDDL L LFSPSLLGGPSPPTAPGGSGAGEERMPPSLQERVPRDWD PQPLGPPTPGVPDLVDFQPPPELVLRAGEEVPDAGPREGVSFPPWS RPPGQGEFRALNARLPLNTDAYLSLQELQGQDP THLV	Construct F
121	AIVVPVCLAFLLTTLGVLF CF	gp130 TM
122	NKRDLIKKHIWPNVDP SKSHIAQWSPHTPPRHNFNSKDQMYSDGN FTDVSVEIEANDKKFPFEDLKSLDLFKKEKINTEGHSSGIGSSC MSSSRPSIS	gp130 ICD
123	ASLSSNHSLTSCFTNQGYFFFHLPDALEIEACQVYFTYDPYSEEDP DEGVAGAPTGSSPQLQPLSGEDDAYCTFP SRDDL L LFSPSLLGGP SPPTAPGGSGAGEERMPPSLQERVPRDWD PQPLGPPTPGVPDLVD FQPPPELVLRAGEEVPDAGPREGVSFPPWSRPPGQGEFRALNARL PLNTDAYLSLQELQGQDP THLV	IL-2Rb ICD
124	MDLWQLLLLLALAGSSDAFSGSEATAAAILSRAPWSLQSVNPGKLTN SSKEPKFTKCRSPERETF SCHWTDVHHGTKNLGPIQLFYTRRNTQ EWTQEWKECPDYVSAGENSCYFNSSFTSIWIPYCIKLTNSGGTVDE KCFSVDEIVQPDPPIALNWTLLNVSLTGIHADIQVRWEAPRNADIQ KGWMVLEYELQYKEVNETKWKMMDPILTTSPVYSLKVDKEYEVRV RSKQRNSGNYGEFSEVLYVTLPQMSQFTCEEAIIVVPVCLAFLLTTL LGVLF CFNKRDLIKKHIWPNVDP SKSHIAQWSPHTPPRHNFNSKD QMYSDGNFTDVSVEIEANDKKFPFEDLKSLDLFKKEKINTEGHSS GIGSSCMSSSRPSISSDENESSQNTSSTVQYSTVVHSGYRHQVP SVQVFSRASLSSNHSLTSCFTNQGYFFFHLPDALEIEACQVYFTYD PYSEEDPDEGVAGAPTGSSPQLQPLSGEDDAYCTFP SRDDL L LF PSLLGGPSPPTAPGGSGAGEERMPPSLQERVPRDWD PQPLGPPTP GVPDLVDFQPPPELVLRAGEEVPDAGPREGVSFPPWSRPPGQGEFR ALNARLPLNTDAYLSLQELQGQDP THLV	Construct G

125	ECGHISVSAPIVHLGDPITASCI IKQNC SHLDPEPQILWRLGAELQ PGGRQQRLSDGTQESIITLPHLNHTQAF LSCCLNWGNSLQILDQVE LRAGYPPAIPHNLSCLMNLTTSSLICQWEPGPETHLPTSFTLKSEK SRGNCQTQGDSILDCVPKDGQSHCCIPRKHLLLYQNMGIWVQAENA LGTSMSPQLCLDPM DVVKLEPPMLRTMDPSPEAAPQAGCLQLCWE PWQPGLHINQKCELRHKPQRGEASWALVGPLPLEALQYELCGLLPA TAYTLQIRCIRWPLPGHWS DWSPSLELR TTERAPT VRLDTWWRQRQ LDPRTVQLFWKPVPLEEDSGRIQGYVVS WRPSGQAGAILPLCNTTE LSCTFHLPSEAQEVALVAYNSAGTSRPTPVVFSERGPALTRLHAM ARDPHSLWVGWEPNPWPQGYVIEWGLGPPSASNSNKTWRMEQNGR ATGFLLENIRPFQLEYEIIIVTPLYQDTMGPSQHVVAYSQEMAPSHA PELHLKHIGKTWAQLEWVPEPPELGKSPLTHYTI FWTNAQNQS FSA ILNASSRGFVLHGLEPASLYHIHLMAASQAGATNSTVLTLMTLTPE GSELHII LGLFGLLLLLTCLCGTAWLCCSPNRKNPLWPSVPDPAHS SLGSWVPTIMEEDAFQLPGLGTPPITKLTVLEEDEKKPVWESHNS SETCGLPTLVQTYVLQGDPRAVSTQPSQSGTSDQVLYGQLLGSP T SPGPGHYLRCDSTQPLLAGLTPSPKSYENLWFQASPLGTLVTPAPS QEDDCVFGPLLNFPLLQGIRVHGMEALGSF	hGCSFR FL (Construct A) no leader sequence
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What is Claimed:

1. A particle or composition comprising one or more nucleic acid molecules encoding for:
 - a) a chimeric antigen receptor (CAR); and
 - b) a polypeptide comprising:
 - i) a ligand binding extracellular domain (ECD);
 - ii) an immune cell activating intracellular domain (ICD); and
 - iii) a transmembrane domain linking the ECD to the ICD.
2. The particle of claim 1, wherein the immune cell activating ICD comprises the ICD of hGCSF-R, or a mutant or fragment thereof.
3. The particle of claim 2, wherein the hGCSF-R ICD comprises a sequence of SEQ ID NO: 111, or an amino acid sequence having at least 50, 60, 70, 75, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to the same.
4. The particle of claim 3, wherein the hGCSF-R ICD does not comprise the sequence of SEQ ID NO: 110.
5. The particle of claim 2, wherein the hGCSF-R ICD comprises a sequence of SEQ ID NO: 111 and does not comprise amino acid residues 800-813, 775-813, 750-813, 725-813, or 716-813 of SEQ ID NO: 125, or a fragment thereof, positioned to the C-terminal residue of SEQ ID NO: 111.
6. The particle of claim 2, wherein the hGCSF-R ICD comprises a sequence of SEQ ID NO: 111 and amino acid residues 716-812 of SEQ ID NO: 125, or a fragment thereof positioned to the C-terminal residue of SEQ ID NO: 111, provided that the ICD does not comprise the contiguous fragment of amino acid residues 716-813 of SEQ ID NO: 125.
7. The particle of claim 1, wherein the ECD is a GCSF-R ECD, optionally wherein the GCSF-R ECD is a human GCSF-R ECD comprising the amino acid sequence of SEQ ID NO: 107 or SEQ ID NO: 108.

8. The particle of claim 1, wherein the ECD comprises the ECD of human growth hormone receptor (hGH-R), or a mutant or fragment thereof, wherein the ECD of human growth hormone receptor (hGH-R) comprises the amino acid sequence encoded by exons 1-7 of hGH-R, or a mutant or fragment thereof.
9. The particle of claim 8, wherein the ECD of the hGH-R comprises the mutation of C259R.
10. The particle of claim 8, wherein the ECD of the hGH-R comprises an amino acid sequence of SEQ ID NO: 114 or SEQ ID NO: 115, or an amino acid sequence having at least 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identity to the same.
11. The particle of claim 1, wherein the ICD comprises an ICD of glycoprotein 130 ("gp130 ICD"), or a variant or fragment thereof.
12. The particle of claim 1, wherein the ICD comprises a fragment of the GCSF-R ICD, wherein the GCSF-R ICD fragment does not comprise the STAT3, SH3 and/or the SHC domains.
13. The particle of claim 1, wherein the ICD comprises a IL-2R β ICD, or a fragment or variant thereof.
14. The particle of claim 1, wherein the ICD comprises a IL-7R α ICD, or a fragment or variant thereof.
15. The particle of claim 1, wherein the ICD comprises a gp130 ICD, or a variant or fragment thereof, linked to an IL-2R β ICD, or fragment thereof.

16. The particle of claim 1, wherein the transmembrane domain, comprises a GCSF-R, gp130, or hGH-R transmembrane domain.

17. The particle of claim 1, wherein the polypeptide comprises:

a) an ECD that is a GCSFR-ECD, or variant thereof ; a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof ; and an immune activating ICD that is a GCSF-R ICD, or variant thereof;

b) an ECD that is a hGH-R-ECD, or variant thereof ; a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof ; and immune activating ICD that is a GCSF-R ICD, or variant thereof;

c) an ECD that is a hGH-R-ECD, or variant thereof; a transmembrane domain that is a gp130 transmembrane domain, or variant thereof; and an immune activating ICD that comprises a gp130 ICD, or variant thereof and a IL-2R β ICD, or variant thereof; or

d) an ECD that is a hGH-R-ECD, or variant thereof; a transmembrane domain that is a GCSF-R transmembrane domain, or variant thereof; and an immune activating ICD that comprises a GCSF-R ICD, or variant thereof and a IL-7R α ICD, or variant thereof.

18. The particle of claim 1, wherein the polypeptide comprises an amino acid sequence of SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 120, or SEQ ID NO: 124, or a variant of any of the foregoing.

19. The particle of claim 18 wherein the variant comprises a polypeptide having at least 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%, or 99% identity to SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 120, or SEQ ID NO: 124.

20. The particle of claim 1, wherein the CAR comprises an antigen binding domain that binds to CD20.

21. The particle of claim 20, wherein the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, SEQ ID NO: 128, or SEQ ID NO: 129, at least 90%

identity to SEQ ID NO: 99, SEQ ID NO: 128, or SEQ ID NO: 129, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, SEQ ID NO: 128, or SEQ ID NO: 129, or at least 100% identity to SEQ ID NO: 99, SEQ ID NO: 128, or SEQ ID NO: 129.

22. The particle of any one of claims 1-21, wherein the particle is a vector, a virus, a liposome, a plasmid, or a cell.

23. The particle of any one of claims 1-22, wherein the particle is a viral vector, wherein the viral vector is a lentiviral vector, AV vector, an AAV vector, and the like.

24. A nucleic acid molecule, including an isolated nucleic acid molecule, encoding a polypeptide comprising:

- i) a ligand binding extracellular domain (ECD);
- ii) an immune cell activating intracellular domain (ICD); and
- iii) a transmembrane domain linking the ECD to the ICD.

25. The nucleic acid molecule of claim 24, wherein the nucleic acid molecule encodes for the polypeptide of any one of claims 1-19.

26. The nucleic acid molecule of claim 24, wherein the polypeptide comprises an amino acid sequence of SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 120, or SEQ ID NO: 124, or a variant of any of the foregoing.

27. The nucleic acid molecule of claim 26 wherein the variant comprises a polypeptide having at least 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%, or 99% identity to SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 13, SEQ ID NO: 15, SEQ ID NO: 16, or SEQ ID NO: 20.

28. The nucleic acid molecule of any one of claims 24-27, wherein the nucleic acid molecule further encodes for a chimeric antigen receptor (CAR).

29. A viral particle comprising a heterologous viral glycoprotein, a targeting moiety, and one or more nucleic acid molecules encoding for one or more heterologous molecules of interest,

wherein the targeting moiety comprises a polypeptide having the formula T-S₁, wherein T is a target binding domain and S₁ is a stalk portion, and

wherein the nucleic acid molecule encoding for a heterologous molecules of interest is the nucleic acid molecule of any one of claims 24-28.

30. The viral particle of claim 29, wherein the target binding domain (T) binds to CD7, CD8, cKit (CD117), CD4, CD3, CD5, CD6, CD2, TCR alpha, TCR beta, TCR gamma, TCR delta, CD10, CD34, CD110, CD33, CD14, CD68, CCR7, CD62L, CD25, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, or CXCR3, A glycosylated CD43 epitope expressed on acute leukemia or lymphoma but not on hematopoietic progenitors; A glycosylated CD43 epitope expressed on non-hematopoietic cancers; A kinase anchor protein 4 (AKAP-4); Adrenoceptor beta 3 (ADRB3); AFP; Anaplastic lymphoma kinase (ALK); Androgen receptor; Angiopoietin-binding cell surface receptor 2 (Tie 2); Auto antibody to desmoglein 1 (Dsg1); Auto antibody to desmoglein 3 (Dsg3); B7H3 (CD276); Biotin; Bone marrow stromal cell antigen 2 (BST2); BST1/CD157; Cancer/testis antigen 1 (NY-ESO-1); Cancer/testis antigen 2 (LAGE-Ia); Carbonic anhydrase IX (CA1X); Carcinoembryonic antigen (CEA); CCCTC-Binding Factor (Zinc Finger Protein)-Like (BORIS or Brother of the Regulator of Imprinted Sites); CCR4; CD5; CD19; CD20; CD22; CD24; CD30; CD32 (FCGR2A); CD33; CD34; CD38; CD44v6; CD72; CD79a; CD79b; CD97; CD99; CD123; CD171; CD179a; CD179b-IGLII; CD200R; CD276/B7H3; CD300 molecule-like family member f (CD300LF); CDH1-CD324; CDH6; CDH17; CDH19; Chromosome X open reading frame 61 (CXORF61); Claudin 6 (CLDN6); Claudin18.2 (CLDN18A2 or CLDN18A.2); CMV pp65; C-MYC epitope Tag; Cripto; CS1 (also referred to as CD2 subset 1 or CRACC or SLAMF7 or CD319 or 19A24); CSF2RA (GM-CSFR-alpha); C-type lectin domain family 12 member A (CLEC12A); C-type lectin-like molecule-1 (CLL-1 or CLECL1); Cyclin B1; Cytochrome P450 IB 1 (CYP1B1); DLL3; EBV-EBNA3c; EGF-bke module- containing mucin-like hormone receptor-like 2 (EMR2); Elongation factor 2 mutated (ELF2M); Ephrin B2; Ephrin type-A receptor 2 (EphA2); Epidermal growth factor receptor (EGFR); Epidermal growth factor receptor variant III (EGFRviii); Epithelial cell adhesion molecule (EPCAM); ERG; ETS translocation-variant

gene 6 located on chromosome 12p (ETV6-AML); Fc fragment of IgA receptor (FCAR or CD89); Fc receptor-like 5 (FCRL5); Fibroblast activation protein alpha (FAP); FITC; Fms Like Tyrosine Kinase 3 (FLT3); Folate receptor alpha (Fra or FR1); Folate receptor beta (FRb); Follicle stimulating hormone receptor (FSHR); Fos-related antigen 1; Fucosyl-GM1; G protein coupled receptor class C group 5 member D (GPRC5D); G protein-coupled receptor 20 (GPR20); GAD; Ganglioside G2 (GD2) ; Ganglioside GD3 (aNeu5Ac(2-8)aNeu5Ac(2-3)bDGalp(1-4)bDGlc(1-1)Cer); Ganglioside GM3 (aNeu5Ac(2-3)bDCIalp(1- 4)bDGlc(1-1)Cer); GD3; GFRalpha4; Glycoprotein 100 (gp100); Glypican-3 (GPC3); Gonadotropin Hormone receptor (CGHR or GR); GpA33; GpNMB; GPRC5D; Guanylyl cyclase C (GCC); Heat shock protein 70-2 mutated (mut hsp70-2); Hepatitis A virus cellular receptor 1 (HAVCR1); Hexasaccharide portion of globoH glycosphingolipid (GloboH); High molecular weight-melanoma associated antigen (HMWMAA); HIV1 envelope glycoprotein; HLA; HLA-DOA; HLA-A; HLA-A2; HLA-B; HLA-C; HLA-DM; HLA-DOB; HLA-DP; HLA-DQ; HLA-DR; HLA-G; HTLV1-Tax; Human papilloma virus E6 (HPV E6); Human papilloma virus E7 (HPV E7); Human Telomerase reverse transcriptase (hTERT); IgE; IL13Ra2; IL13Ra; Immunoglobulin lambda-like polypeptide 1 (IGLL1); Influenza A hemagglutinin (HA); Insulin-like growth factor 1 receptor (IGF-I receptor); Interleukin 11 receptor alpha (IL-11Ra); Interleukin- 13 receptor subunit alpha-2 (IL-13Ra2 or CD213A2); Intestinal carboxyl esterase; KIT (CD117); KSHV K8.1; KSHV-gH; LAMP1 ; Legumain; Leukocyte immunoglobulin-like receptor subfamily A member 2 (LILRA2); Leukocyte-associated immunoglobulin-like receptor 1 (LAIR1); Leutenizing hormone receptor (LHR); Lewis(Y) antigen; Lews Ag; Livl; Locus K 9 (LY6K); Low conductance chloride channel; Lymphocyte antigen 6 complex; Lymphocyte antigen 75 (LY75); Lymphocyte-specific protein tyrosine kinase (LCK); Mammary gland differentiation antigen (NY-BR-1); Melanoma antigen recognized by T cells 1 (MelanA or MART1); Melanoma- associated antigen 1 (MAGE-A1); Melanoma cancer testis antigen-1 (MAD-CT-1); Melanoma cancer testis antigen-2 (MAD-CT-2); Melanoma inhibitor of apoptosis (ML-IAP); Mesothelin; MPL; Mucin 1 cell surface associated (MUC1); N-Acetyl glucosaminyl-transferase V (NA17); Nectin-4; Neural cell adhesion molecule (NCAM); NKG2D; NYBR1; O-acetyl-GD2 ganglioside (OacGD2); Olfactory receptor 51E2 (OR51E2); Oncogene fusion protein consisting of breakpoint cluster region (BCR) and Abelson murine leukemia viral oncogene homolog 1 (Abl) (bcr-abl); P53 mutant; Paired box protein Pax-3 (PAX3); Paired box protein Pax-5 (PAX5); Pannexin 3 (PANX3); PDL1; P-glycoprotein; Placenta-specific 1 (PLAC1); Platelet-derived growth factor receptor beta (PDGFR-beta); Polysialic acid; Proacrosin binding protein sp32 (OY-TES1); Prostase; Prostate carcinoma

tumor antigen-1 (PCT A-1 or Galectin 8); Prostate stem cell antigen (PSCA); Prostate-specific membrane antigen (PSMA); Prostatic acid phosphatase (PAP); Prostein; Protease Serine 21 (Testisin or PRSS21); Proteasome (Prosome Macropain) Subunit Beta Type 9 (LMP2); PTK7; Ras G12V; Ras Homolog Family Member C (RhoC); Rat sarcoma (Ras) mutant; Receptor for Advanced Glycation Endproducts (RAGE-1); Receptor tyrosine kinase-like orphan receptor 1 (ROR1); Receptor tyrosine-protein kinase ERBB2 or Her-22/neu; Renal ubiquitous 1 (RU1); Renal ubiquitous 2 (RU2); Sarcoma translocation breakpoints; Serine 2 (TMPRSS2) ETS fusion gene; Sialyl Lewis adhesion molecule (sLe); SLAMF4; SLAMF6; Slea (CA19.9 or Sialyl Lewis Antigen); Sperm protein 17 (SPA17); Squamous Cell Carcinoma Antigen Recognized By T Cells 3 (SART3); Stage-specific embryonic antigen-4 (SSEA-4); STEAP1; Survivin; Synovial sarcoma X breakpoint 2 (SSX2); TCR Gamma Alternate Reading Frame Protein (TARP); TCR-beta1 chain; TCR-beta2 chain; TCR-delta chain; TCR-gamma chain; TCRgamma-delta; Telomerase; TGFbetaR2; The antigen recognized by TNT antibody; Thyroid stimulating hormone receptor (TSHR); Timl-/HVCR1; Tissue Factor 1 (TF1); Tn ag; Tn antigen ((Tn Ag) or (GalNAc-Ser/Thr)); TNF receptor family member B cell maturation (BCMA); Transglutaminase 5 (TGS5); Transmembrane protease; TROP2; Tumor endothelial marker 1 (TEM1/CD248); Tumor endothelial marker 7-related (TEM7R); Tumor protein p53 (p53); Tumor-associated glycoprotein 72 (TAG72); Tyrosinase; Tyrosinase-related protein 2 (TRP-2); Uroplakin 2 (UPK2); Vascular endothelial growth factor receptor 2 (VEGFR2); V-myc avian myelocytomatosis viral oncogene neuroblastoma derived homolog (MYCN); Wilms tumor protein (WT1); or X Antigen Family Member 1A (XAGE1).

31. The viral particle of claim 30, wherein the target binding domain (T) binds to CD7.

32. The viral particle of claim 31, wherein the target binding domain (T) that binds to CD7 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 38 or SEQ ID NO: 39, having at least 95% sequence identity to SEQ ID NO: 38 or SEQ ID NO: 39, having at least 99% sequence identity to SEQ ID NO: 38 or SEQ ID NO: 39, or a sequence as set forth in SEQ ID NO: 38 or SEQ ID NO: 39.

33. The viral particle of any one of claims 29-32, wherein the heterologous viral glycoprotein is a VSV-G polypeptide.

34. The viral particle of claim 33, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 22, SEQ ID NO: 23, SEQ ID NO: 24 or SEQ ID NO: 25.

35. A viral particle comprising a heterologous viral glycoprotein, a targeting moiety, and a nucleic acid molecule encoding for a heterologous molecule of interest, wherein;
- the heterologous viral glycoprotein comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 23 or SEQ ID NO: 25, having at least 95% identity of SEQ ID NO: 23 or SEQ ID NO: 25, having at least 99% identity to SEQ ID NO: 23 or SEQ ID NO: 25, or having at least 100% identity to SEQ ID NO: 23 or SEQ ID NO: 25;
- the targeting moiety comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 98, SEQ ID NO: 126, or SEQ ID NO: 127, at least 95% identity to SEQ ID NO: 98, SEQ ID NO: 126, or SEQ ID NO: 127, at least 99% identity to SEQ ID NO: 98, SEQ ID NO: 126, or SEQ ID NO: 127, or at least 100% identity to SEQ ID NO: 98, SEQ ID NO: 126, or SEQ ID NO: 127; and
- wherein the nucleic acid molecule encoding for a heterologous molecule of interest encodes for a chimeric antigen receptor and a polypeptide comprising:
- i) a ligand binding extracellular domain (ECD);
 - ii) an immune cell activating intracellular domain (ICD); and
 - iii) a transmembrane domain linking the ECD to the ICD.
36. The viral particle of claim 35, wherein the CAR comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 99, SEQ ID NO: 128, or SEQ ID NO: 129, at least 90% identity to SEQ ID NO: 99, SEQ ID NO: 128, or SEQ ID NO: 129, at least 95% identity to SEQ ID NO: 99, SEQ ID NO: 128, or SEQ ID NO: 129, at least 99% identity to SEQ ID NO: 99, SEQ ID NO: 128, or SEQ ID NO: 129, or at least 100% identity to SEQ ID NO: 99, SEQ ID NO: 128, or SEQ ID NO: 129.
37. The viral particle of claim 35 or 36, wherein the polypeptide encoded by the nucleic acid molecule comprises an amino acid sequence of SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 120, or SEQ ID NO: 124, or a variant of any of the foregoing.
38. The viral particle of any one of claims 35-37, wherein the chimeric antigen receptor and the polypeptide are encoded by separate nucleic acid molecules.

39. The viral particle of any one of claims 35-37, wherein the chimeric antigen receptor and the polypeptide are encoded by the same nucleic acid molecule.

40. The viral particle of claim 39, wherein the chimeric antigen receptor and the polypeptide are separated by a sequence encoding for a cleavable peptide, such as a 2A peptide.

41. A method of infecting, transfecting or transducing a cell, the method comprising contacting the cell with a particle of any one of claims 1-23 or a viral particle of any one of claims 29-40.

42. A method of delivering one or more heterologous molecules of interest to a cell, the method comprising contacting the cell with a particle of any one of claims 1-23 or a viral particle of any one of claims 29-40, wherein the viral particle comprises a nucleic acid molecule encoding the heterologous molecule of interest.

43. The method of claim 41 or 42, wherein the method further comprises administering to the cell or to the subject one or more compounds that bind to the ECD of the polypeptide encoded by the one or more nucleic acid molecules, such as but not limited to, somatropin, G-CSF, lenograstim (Granocyte), filgrastim (Neupogen, Zarzio, Nivestim, Accofil), long acting (pegylated) filgrastim (pegfilgrastim, Neulasta, Pelmeg, Ziextenco) or lipegfilgrastim (Lonquex).

44. A method of treating a disease or disorder in a subject, the method comprising administering to the subject a particle of any one of claims 1-23 or a viral particle of any one of claims 29-40, wherein the viral particle comprises a nucleic acid molecule encoding a heterologous molecule of interest to treat the disease or disorder, wherein the nucleic acid molecule encoding a heterologous molecule of interest is the nucleic acid molecule of any one of claims 24-28.

45. A method of treating a disease or disorder in a subject, the method comprising:
i) administering to the subject a particle of any one of claims 1-23 or a viral particle of any one of claims 29-40, and

ii) administering to the subject an effective amount of one or more compounds capable of binding to the ECD of human GCSFR, thereby treating the disease or disorder,

wherein the viral particle comprises one or more nucleic acid molecules encoding one or more heterologous molecules of interest to treat the disease or disorder,

wherein the one or more nucleic acid molecules encoding one or more heterologous molecules of interest is the one or more nucleic acid molecules of any one of claims 24-28.

46. A method of treating a disease or disorder in a subject, the method comprising:

i) administering to the subject a particle of any one of claims 1-23 or a viral particle of any one of claims 29-40, and

ii) administering to the subject an effective amount of one or more compounds capable of binding to the ECD of human GHR, thereby treating the disease or disorder,

wherein the viral particle comprises one or more nucleic acid molecules encoding one or more heterologous molecules of interest to treat the disease or disorder,

wherein the one or more nucleic acid molecules encoding one or more heterologous molecules of interest is the one or more nucleic acid molecules of any one of claims 24-28.

47. A method of treating a disease or disorder in a subject, the method comprising:

i) administering to the subject a viral particle of any one of claims 29-40, and

ii) administering to the subject an effective amount of one or more compounds capable of binding to the ECD of human GHR, thereby treating the disease or disorder,

wherein the viral particle comprises a nucleic acid molecule encoding a heterologous molecule of interest to treat the disease or disorder,

wherein the nucleic acid molecule or a plurality of nucleic acid molecules encoding a heterologous molecule of interest encodes for a chimeric antigen receptor and a polypeptide comprising:

i) a ligand binding extracellular domain (ECD);

ii) an immune cell activating intracellular domain (ICD); and

iii) a transmembrane domain linking the ECD to the ICD.

48. The method of claim 47, wherein the CAR comprises an amino acid sequence having

at least 85% identity to SEQ ID NO: 99, at least 90% identity to SEQ ID NO: 99, at least 95% identity to SEQ ID NO: 99, at least 99% identity to SEQ ID NO: 99, or at least 100% identity to SEQ ID NO: 99.

49. The method of claim 47 or 48, wherein the polypeptide encoded by the nucleic acid molecule comprises an amino acid sequence of SEQ ID NO: 112, SEQ ID NO: 113, SEQ ID NO: 117, SEQ ID NO: 119, SEQ ID NO: 120, or SEQ ID NO: 124, or a variant of any of the foregoing.

50. A method of delivering one or more heterologous molecules to a target cell, the method comprising contacting the cell with a particle of any one of claims 1-23 or a viral vector or particle of any one of claims 29-40, wherein the particle comprises one or more nucleic acid molecules encoding the one or more heterologous molecules.