

PSEUDOTYPED VIRAL PARTICLES COMPRISING ENGINEERED CHIMERIC RECEPTOR PROTEINS

RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application Ser. No. 63/508,169 filed June 14, 2023, which is hereby incorporated by reference in its 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 6, 2024, is named "INH-028WO_SL" and is 242,242 bytes in size.

FIELD

[0003] Embodiments provided herein relate to viral particles comprising a heterologous viral glycoprotein and a targeting moiety having the formula T-S₁, wherein T is a target binding domain and S₁ is a stalk portion. The stalk portion may comprise variant Fc domains. The stalk portion may comprise a flexible peptide domain. Embodiments provided herein further relate to compositions comprising the viral particles provided for herein and methods of using the same.

BACKGROUND

[0004] Vesicular stomatitis virus (VSV) is an enveloped, negative-strand RNA virus that belongs to the Vesiculovirus genus of the Rhabdovirus family. It is an arbovirus which can infect insects, cattle, horses and pigs. VSV genome encodes five structural proteins among which include a single transmembrane glycoprotein (G). The glycoprotein is a classic type I membrane glycoprotein with an amino-terminal signal peptide, an ectodomain of about 450 amino acids, a single alpha helical transmembrane segment and a small intraviral carboxy-terminal domain. The signal peptide is cleaved in the lumen of the endoplasmic reticulum and the native glycoprotein consists in the ectodomain, the transmembrane domain and the intraviral domain.

[0005] G plays a critical role during the initial steps of virus infection (Albertini, A. A. V., Baquero, E., Ferlin, A., and Gaudin, Y. (2012). Molecular and Cellular Aspects of Rhabdovirus Entry. *Viruses* 4, 117-139.), which is hereby incorporated by reference in its entirety. First, it is responsible for virus attachment to specific receptors. After binding, virions enter the cell by a clathrin-mediated endocytic pathway. In the acidic environment of the endocytic vesicle, G triggers the fusion between the viral and endosomal membranes, which releases the genome in

the cytosol for the subsequent steps of infection. Fusion is catalyzed by a low-pH-induced large structural transition from a pre-toward a post-fusion conformation which are both trimeric (Roche, S., Bressanelli, S., Rey, F. A., and Gaudin, Y. (2006). Crystal structure of the low-pH form of the vesicular stomatitis virus glycoprotein G. *Science* 313, 187-191. Roche, S., Rey, F. A., Gaudin, Y., and Bressanelli, S. (2007). Structure of the prefusion form of the vesicular stomatitis virus glycoprotein g. *Science* 315, 843-848), each of which is hereby incorporated by reference in its entirety).

[0006] The polypeptide chain of G ectodomain folds into three distinct domains which are the fusion domain (FD), the pleckstrin homology domain (PHD), and the trimerization domain (TrD). During the structural transition, the FD, the PHD and the TrD retain their tertiary structure. Nevertheless, they undergo large rearrangements in their relative orientation due to secondary changes in hinge segments (S1 to S5) which refold during the low-pH induced conformational change (Roche et al., 2006; Roche et al., 2007).

[0007] It has been shown that low-density lipoprotein receptor (LDL-R) and other members of this receptor family serve as VSV receptors (Finkelshtein, D., Werman, A., Novick, D., Barak, S., and Rubinstein, M. (2013). LDL receptor and its family members serve as the cellular receptors for vesicular stomatitis virus. *Proceedings of the National Academy of Sciences of the United States of America* 110, 7306-7311, which is hereby incorporated by reference in its entirety). VSV-G can be used for pseudotyping other viruses and VSV-G-pseudotyped lentiviruses (VSV-G-LVs) exhibit the same broad tropism as VSV. However, this broad tropism can inhibit the selective targeting of specific cell types. Therefore, there is a need, for modified (mutated or mutant) VSV-G proteins that can be used to pseudotype viruses that abrogate its binding to the LDL receptor. The present embodiments, fulfill these needs as well as others.

BRIEF SUMMARY

[0008] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein and a targeting moiety 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.

[0009] 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.

[0010] 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.

[0011] 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.

[0012] 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.

[0013] 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.

[0014] 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.

[0015] 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.

[0016] In some embodiments, the stalk portion S₁ comprises a formula of L₃-X₁, wherein L₃ is a flexible peptide linker, and X₁ is a polypeptide comprising a transmembrane domain; wherein the targeting moiety having the formula T-S₁ has a formula of T-L₃-X₁.

[0017] 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-L₃-X₁ has a formula of T-L₃-ECD-T_M-ICD.

[0018] 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.

[0019] 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.

[0020] In some embodiments, the heterologous viral glycoprotein is a SVCV-G polypeptide as provided for herein.

[0021] 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.

[0022] 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: 113, 89, 94, 105, or 109, 136, 137, and a light chain variable region having at least 95% identity to SEQ ID NO: 90, 95, 106, or 110. 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.

[0023] 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, 96, 107, or 111. 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, 97, 108, or 112.

[0024] In some embodiments, the CAR comprises an antigen binding domain having an amino acid sequence having at least 95% identity to SEQ ID NO: 114 or 118. In some embodiments, the CAR comprises an antigen binding domain having an amino acid sequence having at least 95% identity to SEQ ID NO: 115 or 119. In some embodiments, the CAR comprises an antigen binding domain having an amino acid sequence having at least 95% identity to SEQ ID NO: 116, 120, 122, or 124. In some embodiments, the CAR comprises an antigen binding domain having an amino acid sequence having at least 95% identity to SEQ ID NO: 117, 121, 123, or 125.

[0025] 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.

[0026] 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.

[0027] 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.

[0028] 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.

[0029] 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.

[0030] 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.

[0031] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein and a targeting moiety comprising a polypeptide having the formula T-S₁, 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.

[0032] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein and a targeting moiety comprising a polypeptide having the formula T-S₁, 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 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, L_2 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 X_1 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 (X_1) 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.

{0033} In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein and a targeting moiety comprising a polypeptide having the formula T - S_1 , wherein T is a target binding domain and S_1 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 S_1 comprises a formula of L_1 -Fc- L_2 - X_1 , wherein L_1 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, L_2 is a linker comprising a sequence of SEQ ID NO: 55 or is absent; and X_1 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 (X_1) 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.

[0034] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein and a targeting moiety comprising a polypeptide having the formula $T-S_1$, wherein T is a target binding domain and S_1 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 S_1 comprises a formula of L_1 -Fc- L_2 - X_1 , wherein L_1 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, L_2 is a linker and is absent; and X_1 is a polypeptide 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 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.

[0035] In some embodiments, a viral particle is provided, wherein the viral particle comprises a heterologous viral glycoprotein and a targeting moiety. 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.

[0036] In some embodiments, a viral particle is provided, wherein the viral particle comprises a heterologous viral glycoprotein and a targeting moiety. 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.

[0037] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein and a targeting moiety comprising a polypeptide having the formula T-S₁, 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.

[0038] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein and a targeting moiety comprising a polypeptide having the formula T-S₁, 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 (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.

[0039] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein and a targeting moiety comprising a polypeptide having the formula T-S₁, 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: 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 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.

[0040] In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein and a targeting moiety comprising a polypeptide having the formula T-S₁, 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: 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 S₁ comprises a formula L₃-X₁, wherein L₃ 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.

{0041} In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein and a targeting moiety comprising a polypeptide having the formula T-S₁, 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: 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 S₁ comprises a formula L₃-X₁, wherein L₃ 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.

{0042} In some embodiments, a viral particle is provided. In some embodiments, the viral particle comprises a heterologous viral glycoprotein and a targeting moiety comprising a polypeptide having the formula T-S₁, 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 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.

[0043] In some embodiments, the viral particle as provided for herein further comprises a nucleic acid molecule encoding for 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 amino acid sequence having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to any one of the sequences of SEQ ID NOs: 126-135.

BRIEF DESCRIPTION OF FIGURES

[0044] FIG. 1A and FIG. 1B illustrate crystal structures of VSV-G bound to LDL-R. FIG. 1A illustrates the crystal structure of VSV-G bound to CR3 of the LDL-R. FIG. 1B illustrates the crystal structure of VSV-G bound to CR2 of the LDL-R.

[0045] FIG. 2A and FIG. 2B illustrate the effect of adding negatively charged amino acids to the VSV-G:LDL-R binding interface on native tropism and fusogenicity. FIG. 2A illustrates the titration of VSV-G constructs on SupT1 cells. FIG. 2B illustrates functional titer of each construct calculated from the titration in FIG. 2A.

[0046] FIG. 3 illustrates an alignment of the ectodomains of different VSV-G proteins from different strains.

[0047] FIG. 4 illustrates the effect of various VSV-G mutations on the serum stability of viral constructs in combination with a CD7 binder.

[0048] FIG. 5 illustrates the effect of various VSV-G mutations on the serum stability of viral constructs in combination with a CD7 binder.

[0049] FIG. 6 illustrates the ability of various rhabdovirus G proteins to transduce SupT1 and PBMC cells alone or in combination with a CD7 binder.

[0050] FIG. 7A-L show flow cytometry data of human PBMCs transduced with exemplary vectors comprising CD7 binders as disclosed herein.

[0051] FIG. 7M shows flow cytometry data of human PBMCs transduced with exemplary vectors comprising CD7 binders as disclosed herein.

[0052] FIG. 8A-L shows flow cytometry data of non-human primate PBMCs transduced with exemplary vectors comprising CD7 binders as disclosed herein.

[0053] FIG. 8M shows flow cytometry data of non-human primate PBMCs transduced with exemplary vectors comprising CD7 binders as disclosed herein.

[0054] FIG. 9A shows flow cytometry data of human PBMCs transduced with exemplary vectors comprising CD8 binders as disclosed herein.

[0055] FIG. 9B shows flow cytometry data of non-human primate PBMCs transduced with exemplary vectors comprising CD8 binders as disclosed herein.

[0056] FIG. 10A 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 10B illustrates the transduction of cells in the absence of the CD7 binder. FIG. 10C 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).

[0057] FIG. 11A 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. 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).

[0058] FIG. 12A 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. 12B 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.

[0059] FIG. 13A 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 13B illustrates the transduction of cells in the absence of the CD7 binder. FIG. 13C illustrates the transduction of human and non-human primate PBMCs in terms of MOI calculated from SupT1 titration.

[0060] FIG. 14A 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. 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.

[0061] FIG. 15A-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).

[0062] 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).

[0063] FIG. 17A and FIG. 17B 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. 17A 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. 17B illustrates the data for SVCV-G pseudotyped lentiviral particles harboring a CD7 binder with a variant Fc stalk.

[0064] FIG. 18A and FIG. 18B 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. 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.

[0065] FIG. 19A and FIG. 19B is a comparison of the off target transduction of GFP in a panel of B-cell cell lines as compared to control SupT1. FIG. 19A 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. 19B illustrates the data for SVCV-G pseudotyped lentiviral particles harboring a CD7 binder with a flexible stalk.

[0066] FIG. 20A and FIG. 20B 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. 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.

[0067] FIG. 21 illustrates the ability of PBMCs transduced with a FHVH33 BCMA CAR construct as provided for herein (SEQ ID NO: 126) to kill three separate BCMA positive multiple myeloma cell lines. PBMCs were transduced with a viral particle as provided for herein.

[0068] FIG. 22A and 22B illustrate the loss of efficacy of the FHVH33 BCMA CAR (SEQ ID NO: 126) PBMCs when BCMA is knocked down in the NCI-H929 multiple myeloma cell

line. FIG. 22A illustrates the relative BCMA content in the WT and KD cell lines. FIG. 22B illustrates the CAR (SEQ ID NO: 126) efficacy against the WT and KD cell lines.

[0069] FIG. 23A and 23B illustrate the ability of PBMCs transduced with FCRL5 CAR constructs (SEQ ID Nos: 129 and 130) as provided for herein to kill FCRL5 positive Rec-1 cells. FIG. 23A illustrates the efficacy of the FCRL5 CAR construct with a V_L-V_H scFv orientation (SEQ ID NO: 129). FIG. 23B illustrates the efficacy of the FCRL5 CAR construct with a V_H-V_L scFv orientation (SEQ ID NO: 130).

[0070] FIG. 24 illustrates the ability of PBMCs transduced with a FHVH33 BCMA CAR construct (SEQ ID NO: 126), a FCRL5 CAR construct (SEQ ID NO: 130), a BCMA-FCRL5 tandem CAR construct (SEQ ID NO: 127), or a FCRL5-BCMA tandem CAR construct (SEQ ID NO: 128) to kill BCMA positive NCI-H929 WT cells.

[0071] FIG. 25 illustrates the ability of PBMCs transduced with a FHVH33 BCMA CAR construct (SEQ ID NO: 126), a FCRL5 CAR construct (SEQ ID NO: 130), a BCMA-FCRL5 (SEQ ID NO: 127) tandem CAR construct, or a FCRL5-BCMA tandem CAR construct (SEQ ID NO: 128) to kill FCRL5 positive Rec-1 WT cells.

[0072] FIG. 26A and 26B illustrate m971 HL (SEQ ID NO: 132) as being functionally preferable to m971 LH (SEQ ID NO: 133) in CD22 CARs when testing efficacy on Raji (FIG. 26A) and Daudi (FIG. 26B) cells.

[0073] FIG. 27A-C illustrate TanCAR20/22 (SEQ ID NOs: 134 and 135) overcoming the loss of CD20 or CD22 expression in Raji cells. FIG. 27A illustrates the result in Raji cells having CD20 knocked out. FIG. 27B illustrates the result in Raji cells having CD22 knocked out. FIG. 27C illustrates the result in WT Raji cells.

[0074] FIG. 28A-C, and FIG. 29 illustrate the Dual CAR 20/22 (SEQ ID NOs: 134 and 135) in the pSF backbone maintaining killing against CD20 or CD22 single knockout clones. FIG. 28A illustrates the results by luciferase assay in the provided cell lines. FIG. 28B illustrates flow cytometry results for the provided cell lines. FIG. 28C illustrates flow cytometry results for the provided cell lines at a range of E:T ratios. FIG. 29 illustrates similar results to FIGs 28A and 28C in separate PBMC clones with distinct results for TanCAR orientation.

[0075] FIG. 30A-D illustrate the effect of CD19 CAR (SEQ ID NO: 203), CD20 CAR (SEQ ID NO: 150), or CD19/CD20 TanCAR (SEQ ID NOs: 167 and 170) on inducing Raji cell death when CART cells expressing the indicated CARs were incubated at the given E:T ratios. FIG. 30A illustrates the results for Raji-GFP/luciferase cells. FIG. 30B illustrates the results for Raji-GFP/luciferase cells with both CD19 and CD20 knocked out. FIG. 30C illustrates the

results for Raji-GFP/luciferase cells with CD19 knocked out. FIG. 30D illustrates the results for Raji-GFP/luciferase cells with CD20 knocked out.

[0076] FIG. 31A and 31B illustrate the effect of TanCAR constructs on inducing Raji cell death against the given Raji cell lines when CART cells expressing the indicated CARs were incubated at the given E:T ratios. FIG. 31A illustrates the results for the CD19-CD20 TanCAR SEQ ID NO: 167. FIG. 31B illustrates the results for the CD19-CD20 TanCAR SEQ ID NO: 170.

DETAILED DESCRIPTION

[0077] Provided for herein are viral particles comprising a heterologous viral glycoprotein and a targeting moiety, 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. 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.

[0078] 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.

[0079] 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.

[0080] 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.

[0081] As used herein, the terms “a” or “an” means that “at least one” or “one or more” unless the context clearly indicates otherwise.

[0082] 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.

[0083] 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.

[0084] 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.”

[0085] 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.

[0086] 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.

[0087] 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.

[0088] “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.

[0089] “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.

[0090] “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.

[0091] 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.

[0092] “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.

[0093] 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.

[0094] 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.

[0095] 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.

[0096] 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.

[0097] 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.

[0098] “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.

[0099] 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.

[00100] 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.

[00101] 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.

[00102] 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).

[00103] 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.”

[00104] “Parenteral” administration of a composition includes, e.g., subcutaneous (s.c.), intravenous (i.v.), intramuscular (i.m.), or intrasternal injection, or infusion techniques.

[00105] 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.

[00106] 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.

[00107] 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.

[00108] 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.

[00109] 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.

[00110] 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.

[00111] 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.

[00112] 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.

[00113] 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.

[00114] 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.

[00115] 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.

[00116] 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.

[00117] Throughout the specification, reference may be made to amino acid constructs containing a leader sequence or peptide or not containing a leader sequence or peptide. While certain embodiments may refer solely to a sequence containing or not containing a leader sequence, it is to be understood that the embodiment encompasses both a sequence comprising a leader peptide and a sequence not comprising a leader peptide.

Viral Particles Comprising Heterologous Viral Glycoprotein and Targeting Moiety

[00118] 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.

[00119] 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).

[00120] 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 NO: 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.

[00121] 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 comprise 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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EPKSCDKTHTCPPCPAPPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY
KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKG
FYPDSIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVF
SCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 103)
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[00122] 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, sN82, 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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EPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMASRTPEVTCVVDVDS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLAQDNLNGKEY
KCKVSNKALGAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKG
FYPYSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVF
SCSVMHEALHNAYTQKSLSLSPGK (SEQ ID NO: 104)
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[00123] 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 position 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.

[00124] 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.

[00125] 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.

[00126] 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 comprise 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.

[00127] 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.

[00128] 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), AEAAAKEAAKA (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, L₁ is (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), wherein each n is, independently, 1-5. In some embodiments, L₁ is (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), wherein each n is, independently, 1. In some embodiments, L₁ is (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), wherein each n is, independently, 2. In some embodiments, L₁ is (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), wherein each n is, independently, 3. In some embodiments, L₁ is (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), wherein each n is, independently, 4. In some embodiments, L₁ is (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), wherein each n is, independently, 5. In some embodiments, L₁ 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, L₂ is absent. In some embodiments, L₂ is (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), wherein each n is, independently, 1-5. In some embodiments, L₂ is (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), wherein each n is, independently, 1. In some embodiments, L₂ is (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), wherein each n is, independently, 2. In some embodiments, L₂ is (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), wherein each n is, independently, 3. In some embodiments, L₂ is (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), wherein each n is, independently, 4. In some embodiments, L₂ is (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), wherein each n is, independently, 5. In some embodiments, L₂ is (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), wherein each n is, independently, greater than 5.

[00129] 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-L₁-Fc-L₂-X₁ may also be given by the formula T-L₁-Fc-L₂-ECD-T_M-ICD, wherein T is a target binding domain; L₁ is a linker or absent; Fc is the variant Fc protein; L₂ 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 S₁ may be given by the formula L₁-Fc-L₂-ECD-T_M-ICD.

[00130] 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.

[00131] 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 greater than 7.

55) and n is 8. In some embodiments, L₃ is (GGGGS)_n (SEQ ID NO: 55) and n is 9. In some embodiments, L₃ is (GGGGS)_n (SEQ ID NO: 55) and n is 10. In some embodiments, L₃ is (GGGGS)_n (SEQ ID NO: 55) and n is greater than 10. 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).

[00132] In some embodiments, the flexible peptide linker L₃ may be any flexible peptide linker. In some embodiments, L₃ 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, L₃ is (GGGGA)_n (SEQ ID NO: 54) and n is 1. In some embodiments, L₃ is (GGGGA)_n (SEQ ID NO: 54) and n is 2. In some embodiments, L₃ is (GGGGA)_n (SEQ ID NO: 54) and n is 3. In some embodiments, L₃ is (GGGGA)_n (SEQ ID NO: 54) and n is 4. In some embodiments, L₃ is (GGGGS)_n (SEQ ID NO: 55) and n is 1. In some embodiments, L₃ is (GGGGS)_n (SEQ ID NO: 55) and n is 2. In some embodiments, L₃ is (GGGGS)_n (SEQ ID NO: 55) and n is 3. In some embodiments, L₃ is (GGGGS)_n (SEQ ID NO: 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).

[00133] In some embodiments, L₃ 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, L₃ is (GGGGA)_n (SEQ ID NO: 54) and n is 1. In some embodiments, L₃ is (GGGGA)_n (SEQ ID NO: 54) and n is 2. In some embodiments, L₃ is (GGGGA)_n (SEQ ID NO: 54) and n is 4. In some embodiments, L₃ is (GGGGS)_n (SEQ ID NO: 55) and n is 1. In some embodiments, L₃ is (GGGGS)_n (SEQ ID NO: 55) and n is 2. In some embodiments, L₃ is (GGGGS)_n (SEQ ID NO: 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 EGKSSSGSGSESKST (SEQ ID NO: 58).

[00134] 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.

[00135] 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 KIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPFLPGPSKP (SEQ ID NO: 60). In some embodiments, the CD28 ECD domain consists or consists essentially of the polypeptide of

KIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPFLPGPSKP (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 KIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPFLPGPSKP (SEQ ID NO: 60).

[00136] 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 FWVLVVVGGVLACYSLVTVAFIIFWV (SEQ ID NO: 62). In some embodiments, the CD28 T_M domain consists or consists essentially of the polypeptide of FWVLVVVGGVLACYSLVTVAFIIFWV (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 FWVLVVVGGVLACYSLVTVAFIIFWV (SEQ ID NO: 62).

[00137] 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

KIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSP LFPGPSKP (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 KIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSP LFPGPSKP (SEQ ID NO: 60).

[00138] 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 TM 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.

[00139] 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; Angiotensin-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 (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- α); 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; 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 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); Tim1/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.

[00140] 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.

[00141] 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.

[00142] 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.

[00143] 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.

[00144] 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.

[00145] 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.

[00146] 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.

[00147] 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 MNFLLLTIVLPLCSHA (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.

[00148] 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.

[00149] 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.

[00150] 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.

[00151] 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.

[00152] 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.

[00153] 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.

[00154] 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.

[00155] 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.

[00156] In some embodiments, the substitution at position 8 is an alanine, i.e., H8A.

[00157] In some embodiments, the substitution at position 47 is Q or N, i.e., K47Q or K47N.

[00158] In some embodiments, the protein comprises a mutation (substitution) at position 10. In some embodiments, the substitution/mutation is Q10A, Q10R, or Q10K.

[00159] 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.

[00160] 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.

[00161] 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.

[00162] 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.

[00163] 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.

[00164] 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.

[00165] 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

[00166] 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.

[00167] 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.

[00168] 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.

[00169] 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.

[00170] 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.

[00171] 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.

[00172] 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.

[00173] 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
VQVTPHHVLVDEYTGWVDSQFINGKCSNYICPTVHNSTTWHSDYKV
KGLCDSNLDSDITFFSEDGELSSLGKEGTGFRSNYFAYENGKACK
MQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSV
DVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLA PKNPGTGPAFT
IINGTLKYFETRYIRVDIAAPILSRMVGMISGTTAERELWDDWAPYEDV
EIGPNGVLRTSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAA
SQLPDDESLFFGDTGLSKNPIELVEGWFSWKSSIASFFFIIGLIIGLFLVL
RVGIHLCIKLKHTKKRQIYTDIEMNRLGK (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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WVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLDSDMDITFFS
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
YITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVI
VQVTPHHVLVDEYTGEWVDSQFINGKCSNYICPTVHNSTTWHSDYKVK
KGLCDSNLESMDITFFSEDGELSSLGKEGTGFRSNYFAYENGGKACKM
QYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVD
VSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTII
NGTLKYFETRYIRVDIAAPILSRMVGMISGTTAERELWDDWAPYEDVE
IGPNGVLRRTSSGYKFP
LYMIGHGMLDSDLHLSSKAQVFEHPHIQDAAS
QLPDDESLFFGDTGLSKNPIELVEGWFWSSWKSSIASFFFIIGLIIGLFLV
RVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 25)

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

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

[00174] 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.

[00175] 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.

[00176] 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.

[00177] Additionally, in some embodiments, instead of the VSV-G protein or mutant thereof, the viruses can be pseudotyped with other viral structural proteins.

[00178] 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.

[00179] The sequence of Spring Viremia of Carp Virus – G (SEQ ID NO: 52-with leader sequence)

MSIISYIAFLLLIDSNLGIPIFVPSGRNISWQPVIQPFQDYQCP IHGNLPNTMGLSATKLTIK
SPSVFSTDKVSGWICHAAEWKTTCDYRWYGPQYITHSIHPISPTIDECRRIIQRIASGTDED
LGFPFQSCGWASVTTVSNTNRYVPHSVHLEPYGGHWIDHEFNNGGECREKVCCEMKGNSIWI
TEETVQHECAKHIEEVEGIMYGNVPRGDVMYANNFIIDRHHRVYRFGGSCQMKFCNKDGIKF
ARGDWVEKTAGTLTTIHDNVPKVDGTLVSGHRPGLDLIDTVFNLENVVEYTLCEGTRKIN
KQEKLTSDVLSYLAPRIGGFGSVFVRNGLTGERGSTTYIRIEVEGPVDSLNGTDPRTNASR
VFWDWELDGNIIYQGFNGVYKGDGKIHIPLNMIESGIIDDELQHAFAQADIIPHPHYDDDEI
REDDIFFDNTGENGNPVDVAVVEWVSGWGTSLKFFGMTLVALILIFLLIRCCVACTYLMKRSK
RPATESHEMRSLV

[00180] The sequence of Spring Viremia of Carp Virus – G (SEQ ID NO: 53-without leader sequence):

IPIFVPSGRNISWQPVIQPFQDYQCP IHGNLPNTMGLSATKLTIKSPSVFSTDKVSGWICHAA
EWKTTCDYRWYGPQYITHSIHPISPTIDECRRIIQRIASGTDEDLGFPFQSCGWASVTTVSNTN
RYVPHSVHLEPYGGHWIDHEFNNGGECREKVCCEMKGNSIWI TEETVQHECAKHIEEVEG
IMYGNVPRGDVMYANNFIIDRHHRVYRFGGSCQMKFCNKDGIKFARGDWVEKTAGTLTTIHD
NVPKVDGTLVSGHRPGLDLIDTVFNLENVVEYTLCEGTRKINKQEKLTSDVLSYLAPRIG
GFGSVFVRNGLTGERGSTTYIRIEVEGPVDSLNGTDPRTNASRVFWDWELDGNIIYQGFNG
VYKGDGKIHIPLNMIESGIIDDELQHAFAQADIIPHPHYDDDEIREDDIFFDNTGENGNPVD

AVVEWVSGWGTSLKFFGM TLVALILIFLLIRCCVACTYLMKRSKRPATESHEMRSLV

Targeting Moieties

[00181] 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.

[00182] 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.

[00183] 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; 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 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); Tim1/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.

[00184] 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

[00185] In some embodiments, the targeting moiety (e.g. polypeptide) binds to CD7.

[00186] 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
LRGIYLRQLGPQPQDIYYEDGVVPTTDRRFRGRIDFSGSQDNLITMHLQLS
DTGTYTCQAITEVNVYGSGLVLVTEEQSQGWHRCSDAPPRASALPAPTGS
ALPDPQTASALPDPPAASALPAALAVISFLLGLGLGVACVLARTQIKKLCSWR
DKNSAACVVYEDMSHSRCNTLSSPNQYQ (SEQ ID NO: 29).

[00187] 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+.

[00188] 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.

[00189] 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.

[00190] 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 Chothia numbering.

Chothia 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)	RASQSIGTSIH (SEQ ID NO: 33)	YASESIS (SEQ ID NO: 34)	QQSNSWPTT (SEQ ID NO: 35)

[00191] 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 Kabat and IMGT.

[00192] 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.

[00193] 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.

[00194] 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.

[00195] 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.

[00196] 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.

[00197] Although the preceding paragraphs may make reference to CDRs under the Chothia system the equivalent CDR sequences can be used from the IMGT and Kabat designations.

[00198] 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.

[00199] 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	QVQLQQPGAELVKPGASVKLSCKASGYPFTSYWIHWVKQRPGRGLEWLGRIDPNSGDTKYNEKFKNKATLTVDKSSTTAYMQLSSLTSEDSAVYYCARSPYYSDNSMDYWGQGTSTVTVSS

[00200] 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	DILLTQSPAILSVPGERVSVFSCRASQSIGTSIHWHYQQRTNDSFRLLIKYASESISGIPSRFSGSGSGTDFTLSINSVESEDIADYYCQQSNSWPTTFGGGTKLEIKR

[00201] 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 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.

[00202] 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.

[00203] As provided for herein, the polypeptide, antibodies, or antigen binding fragments thereof can be variants of the sequences.

[00204] 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.

[00205] 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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DILLTQSPAILSVSPGERVSFSCRASQSIGTSIHVYQQRTNDSPRLLIKYS
ESISGIPSRFSGSGSGTDFTLINSVESEDIADYYCQQSNSWPTTFGGGTKL
EIKRGGGGSGGGSGGGSGGGSGVQLQQPGAELVKPGASVKLSCKASGYP
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.

[00206] 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.

QVQLQQPGAELVKPGASVKLSCKASGYPFTSYWIHWVKQRPGRGLEWLGRID
PNSGDTKYNEKFKNKATLTVDKSSTTAYMQLSSLTSEDSAVYYCARSPYYSDN
NSMDYWGQGTSTVTVSSGGGGSGGGSGGGSGGGSDILLTQSPAILSVSP
GERVFSFSCRASQSIGTSIHYYQRTNDSPLLLIKYASESISGIPSRFSGSGS
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

[00207] In some embodiments, the targeting moiety (*e.g.* a polypeptide) can bind to CD8.

[00208] 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):

MALPVTALLPLALLHAARPSQFRVSPLDRTWNLGETVELKCQVLLSNPTS
GCSWLFQPRGAAASPTFLLYLSQNKPKAAEGLDTRFSGKRLGDTFVLTLS
FRRENEGCYFCSALSNSIMYFSHFVPVFLPAKPTTTPAPRPPTPAPTASQPLSL
RPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCNHRNR
RRVCKCPRPVVKSGDKPSLSARYV (SEQ ID NO: 40).

[00209] The sequence of human CD8-beta (UniProtKB Q8TD28) is as follows (SEQ ID NO: 41):

MRPRLWLLAAQLTVLHGNSVLQQTAYIKVQTNKMVMLSCEAKISLSNMR
IYWLRQRQAPSSDSHHEFLALWDSAKGTIHGEEVEQEKIIVFRDASRFILNLT

SVKPEDSGIYFCMIVGSPELTFGKGTQLSVVDFLPTTAQPTKKSTLKKRVCRLP
RPETQKGPLCSPITLGLLVAGVLVLLVSLGVAIHLCCRRRRRARLRFMKQLYK
(SEQ ID NO: 41).

[00210] 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.

[00211] 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.

[00212] 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.

[00213] 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 Chothia numbering.

Chothia 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 (SEQ ID NO: 45)	LASNLES (SEQ ID NO: 46)	QQNNEDPYT (SEQ ID NO: 47)

[00214] 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 Kabat and IMGT.

[00215] 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.

[00216] 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.

[00217] 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.

[00218] 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.

[00219] 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.

[00220] Although the preceding paragraphs may make reference to CDRs under the Chothia system the equivalent CDR sequences can be used from the IMGT and Kabat designations.

[00221] 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.

[00222] 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	EVQLQQSGPELVKPGASVKISCKASRYTFTDYNLHWVKSHEKSL EWIGFIYPYNGGTGYNQKFKNAKLTVDYSSSTAYMELRSLTSVD AAVYYCARDHRYNEGVSFDYWGQGTTLTVSS

[00223] 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	NIVLTQSPASLAVSLGQRATISCRASESVDGFGNSFMNWFQQKPG QSPKLLIYLASNLESGVFPARFSGSGSRDFTLTIDPVEADDAATY YCQQNNEDPYTFGGGTKLEIKR

[00224] 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.

[00225] 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.

[00226] As provided for herein, the polypeptide, antibodies, or antigen binding fragments thereof can be variants of the sequences.

[00227] 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.

[00228] 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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NIVLTQSPASLAVSLGQRATISCRASESVDGFGNSFMNWWYQQKPGQSPKLLI
YLASNLESGVPARFSGSGSRDFTLTIDPVEADDAATYYCQQNNEDPYTFGG
GTKLEIKRGGGSGGGGSGGGGSGGGGSEVQLQQSGPELVKPGASVKISCKA
SRYTFTDYNLHWVKSHEKSLEWIGFIYPYNGGTGYNQKFKNAKLTVDYSS
STAYMELRSLTSVDAAVYYCARDHRYNEGVSFDYWGGTTLTVSS (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.

[00229] 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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EVQLQQSGPELVKPGASVKISCKASRYTFTDYNLHWVKSHEKSLEWIGFIY
PYNGGTGYNQKFKNAKLTVDYSSSTAYMELRSLTSVDAAVYYCARDHRYNE
GVSFDYWGGTTLTVSSGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGG
GQQRATISCRASESVDGFGNSFMNWWYQQKPGQSPKLLIYLASNLESGVPARFS
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GSGSRITDFTLTIDPVEADDAATYYCQQNNEDPYTFGGGTKLEIKR (SEQ ID NO: 51)

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

[00230] 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, 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. 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, X_1 comprises a T_M and the ECD and ICD are absent. In some embodiments, X_1 comprises an ECD, a T_M , and the ICD is absent. In some embodiments, X_1 comprises a T_M and an ICD and the ECD is absent. In some embodiments, X_1 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 X_1 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 X_1 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 X_1 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.

[00231] 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.

[00232] 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 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.

[00233] 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 a 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.

[00234] 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 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 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.

[00235] 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.

[00236] 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.

[00237] 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.

[00238] 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.

[00239] 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.

[00240] 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.

[00241] 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.

[00242] 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,

DILLTQSPAILSVSPGERVSFSCRASQSIGTSIHWYQQRNDSPRLLIKAYASESIS
GIPSRFSGSGSGTDFTLSINSVESEDIADYYCQQSNSWPTTFGGGKLEIKRGG
GGSGGGSGGGSGGGGSQVQLQQPGAELVKPGASVKLSCKASGYPTSYW
IHWVKQRPGRGLEWLGRIDPNSGDTKYNEKFKNKATLTVDKSSTTAYMQLS
SLTSEDSAVYYCARSPYYSDNSMDYWGQGTSTVTVSS (SEQ ID NO: 38).

[00243] 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.

[00244] 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,

QVQLQQPGAELVKPGASVKLSCKASGYPTSYWIHWVKQRPGRGLEWLGRI
DPNSGDTKYNEKFKNKATLTVDKSSTTAYMQLSSLTSEDSAVYYCARSPYY
NDNSMDYWGGQTSVTVSSGGGGSGGGSGGGSGGGSDILLTQSPAILSVS
PGERVSFSCRASQSIGTSIHWWYQQRNTDSPRLLIKYASESISGIPSRFSGSGSGT
DFTLSINSVESEDIADYYCQNSWPTTFGGGTKLEIKR (SEQ ID NO: 39).

[00245] 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.

[00246] 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 (S_1) 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, 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 (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 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 (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 L_1 , Fc, L_2 , 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.

[00247] 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 (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: 39 and comprises a stalk portion (S_1) 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 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 (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 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 (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 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 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 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.

[00248] 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 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: 38 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: 38 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: 38 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: 38 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: 38 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: 38 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: 38 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 comprises a sequence having a sequence as set forth in SEQ ID NO: 38 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: 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.

[00249] 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.

[00250] 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:

METDTLLLWVLLWVPGSTGDSAQVQLQPGAEIVKPGASVKLSCKASGYPFTSYWIHWVKRPRGRGLEWLGRI
 DPNSGDTKYNEKFNKATLTVDKSTTAYMQLSSLTSEDSAVYYCARSPYSDNSMDYWGQGTSTVSSGGGGS
 GGGGSGGGGSGGGGSDILLTQSPAILSVSPGERVFSFSCRASQSIGTSIHWYQQRTNDSRLLIKYASESISGIPSRFSG
 SSGTDFTLSINSVESEDIADYYCQSNWPPTFGGGTKLEIKRASGGGSGGGGSGGGGSEPKSCDKTHTCPPCP
 APEAAGGPSVFLFPPKPKDTLMASRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSV
 LTVLAQDWLNGKEYCKVSNKALGAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWE
 SNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNAYTQKSLSLSPGKIEVMYPPPYL
 DNEKSGTIIHVKGKHLCPSPLPFGPSKPFVWLVVVGGLACYSLLVTVAFIIFWVRSKRSLHSDYMNVRVRQGYG
 (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.

[00251] 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: 143:

SAQVQLQQPGAELVKPGASVKLSCKASGYPFTSYWIHWVKQRPGRGLEWLGRIIDPNSGDTKYNEKFKNKATLTV
DKSSTTAYMQLSSLTSEDSAVYYCARSPYYSNDNSMDYWGQGTSTVTVSSGGGGSGGGGSGGGGSGGGGSDILLT
QSPAILSVSPGERVSFSCRASQSIGTSIHWYQRTNDSPRLIKYASESISGIPSRFSGSGSGTDFTLSINSVESEDIADY
YCQQSNSWPTTFGGGKLEIKRASGGGGSGGGGSGGGGSEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTL
MASRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLAQDWLNGKEYKCKVSN
KALGAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDG
SFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNAYTQKSLSLSPGKKIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSP
LFPGPSKPFVWLVVVGGLACYSLLVTVAFIIFWVRSKRSRLHSDYMNVRVQGY (SEQ ID NO: 143)

or is substantially similar to SEQ ID NO: 143, or is an active fragment of SEQ ID NO: 143. 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: 143. 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: 143. 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: 143. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence of SEQ ID NO: 143.

[00252] 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: 144:

QVQLQQPGAELVKPGASVKLSCKASGYPFTSYWIHWVKQRPGRGLEWLGRIIDPNSGDTKYNEKFKNKATLTVDKS
STTAYMQLSSLTSEDSAVYYCARSPYYSNDNSMDYWGQGTSTVTVSSGGGGSGGGGSGGGGSGGGGSDILLTQSP
AILSVSPGERVSFSCRASQSIGTSIHWYQRTNDSPRLIKYASESISGIPSRFSGSGSGTDFTLSINSVESEDIADYCYCQ
QNSNSWPTTFGGGKLEIKRASGGGGSGGGGSGGGGSEPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMAS
RTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLAQDWLNGKEYKCKVSNKAL
GAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFL
YSKLTVDKSRWQQGNVFSCSVMHEALHNAYTQKSLSLSPGKKIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPLPF
GPSKPFVWLVVVGGLACYSLLVTVAFIIFWVRSKRSRLHSDYMNVRVQGY (SEQ ID NO: 144)

or is substantially similar to SEQ ID NO: 144, or is an active fragment of SEQ ID NO: 144. 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: 144. 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: 144. 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: 144. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence of SEQ ID NO: 144.

[00253] 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.

[00254] 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.

[00255] 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.

[00256] 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.

[00257] 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.

[00258] 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.

[00259] 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.

[00260] 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 an 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 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.

[00261] 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 (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 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 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: 48 and V_L peptide having a 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 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 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: 48 and V_L peptide having a 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 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 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: 48 and V_L peptide having a 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 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 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 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: 48 and V_L peptide having a 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.

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.

[00262] 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 an stalk portion (S_I) 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 (S_I) 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 (S_I) 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 (S_I) 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 (S_I) 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 (S_I) 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: 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 (S_I) 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.

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.

[00263] 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.

[00264] 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.

[00265] 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.

[00266] 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.

[00267] 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.

[00268] 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.

[00269] 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.

[00270] 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,

NIVLTQSPASLA VSLGQRATISCRASESV DGF GNSFMN WYQQKPGQSPKLLIY
LASNLESGV PARFSGSGSR TDFLTIDPVEADDAATYYCQQNNEDPYTFGGGT
KLEIKRGGGSGGGSGGGSGGGSGGGGSEVQLQQSGPELVKPGASVKISCKASR
YTFTDYNLHWVKLSHEKSLEWIGFIYPYNGGTGYNQKFKNKAKLTVDYSSST
AYMELRSLTSVDAAVYYCARDHRYNEGVSFDYWGQGTTTLTVSS (SEQ ID
NO: 50).

[00271] 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.

[00272] 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
EGVSFDYWGQGTTTLTVSSGGGGSGGGGSGGGGSGGGGSGNIVLTQSPASLAVS
LGQRATISCRASESVDGFGNSFMNWWYQQKPGQSPKLLIYLASNLESGVPARFS
GSGSRITDFTLTIDPVEADDAATYYCQQNNEDPYTFGGGTKEIKR (SEQ ID
NO: 51).

[00273] 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.

[00274] 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.

[00275] 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.

[00276] 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 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, 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 L_1 , Fc, L_2 , 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.

[00277] 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 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 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

{00278} 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 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.

[00279] 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.

[00280] In some embodiments, the V_H and V_L polypeptides provided herein 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 provided herein 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 (L₃) 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 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 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 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 polypeptides bind to an immune cell, such as those provided herein.

[00281] 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 (L₃-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 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 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 (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: 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 (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: 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 (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: 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 (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: 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 (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: 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 (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.

[00282] 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) 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: 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 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 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.

[00283] 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.

[00284] 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.

[00285] 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.

[00286] 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 L_{CDR1} having a sequence of SEQ ID NO: 33, wherein the L_{CDR1} comprises at most 1 conservative amino acid substitution, a L_{CDR2} having a sequence of SEQ ID NO: 34, wherein the L_{CDR2} comprises at most 1 conservative amino acid substitution, and a L_{CDR3} having a sequence of SEQ ID NO: 35, wherein the L_{CDR3} comprises at most 1 conservative amino acid substitution; and the V_H peptide comprises a H_{CDR1} having a sequence of SEQ ID NO: 30, wherein the H_{CDR1} comprises at most 1 conservative amino acid substitution, a H_{CDR2} having a sequence of SEQ ID NO: 31, wherein the H_{CDR2} comprises at most 1 conservative amino acid substitution, and a H_{CDR3} having a sequence of SEQ ID NO: 32, wherein the H_{CDR3} comprises at most 1 conservative amino acid substitution.

[00287] 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.

[00288] 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.

[00289] 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.

[00290] 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,

DILLTQSPAILSVPGERVVSFSCRASQSIGTSIHWYQQRNDSPRLLIKYASESIS
GIPSRFSGSGSGTDFTLSINSVESEDIADYYCQQNSWPTTFGGGKLEIKRGG
GGSGGGSGGGSGGGGSQVQLQQPGAELVKPGASVKLSCKASGYPTSYW

IHWVKQRPGRGLEWLGRIDPNSGDTKYNEKFKNKATLTVDKSSTTAYMQLS
SLTSEDSAVYYCARSPYYSDNSMDYWGQGTSTVTVSS (SEQ ID NO: 38).

[00291] 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.

[00292] 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,

QVQLQQPGAELVKPGASVKLSCKASGYPTSYWIHWVKQRPGRGLEWLGRIDPNSGDTKYNEKFKNKATLTVDKSSTTAYMQLSSLTSEDSAVYYCARSPYYSDNSMDYWGQGTSTVTVSSGGGGSGGGGSGGGGSGGGGSDILLTQSPAILSVPGERVSFSCRASQSIGTSIHWYQQRNDSPRLLIKYASESISGIPSRFSGSGSGTDFTLINSINSEDIADYYCQQSNSWPTTFGGGGTKLEIKR (SEQ ID NO: 39).

[00293] 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.

[00294] 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.

[00295] 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.

[00296] 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 (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: 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.

[00297] 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 a flexible polypeptide (L₃) 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 (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: 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 having a sequence as set forth in 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 having a sequence as set forth in 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 having a sequence as set forth in 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 having a sequence as set forth in 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 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.

[00298] 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 (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: 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 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.

[00299] 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 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 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 (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 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 (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 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 (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 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 (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 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.

[00300] 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.

[00301] 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.

[00302] 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.

[00303] 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.

[00304] 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.

[00305] 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.

[00306] 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.

[00307] 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,

NIVL TQSPASLAVSLGQRATISCRASESV DGF GNSFMN WYQQKPGQSPKLLIY
LASNLESGV PARFSGSGSRTDFTLTIDPVEADDAATYYCQQNNEDPYTFGGGT
KLEIKRGGGSGGGSGGGSGGGSGGGGSEVQLQQSGPELVKPGASVKISKASR
YFTFDYNLHWVKLSHEKSLEWIGFIYPYNGGTGYNQKFKNKAKLTVDYSSST
AYMELRSLTSVDAAVYYCARDHRYNEGVSFDYWGGQTTLTVSS (SEQ ID
NO: 50).

[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. 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 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.

[00309] 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
EGVSFDYWGQGTTTLTVSSGGGSGGGGSGGGGSGGGGSNIVLTQSPASLAVS
LGQRATISCRASESVDGFGNSFMNWFYQQKPGQSPKLLIYLASNLESGVPARFS
GSGSRTDFTLTIDPVEADDAATYYCQQNNEDPYTFGGGTKLEIKR (SEQ ID
NO: 51).

[00310] 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 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.

[00311] 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.

[00312] 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 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, 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 are as provided for herein. In some embodiments, the polypeptide bind to an immune cell, such as those provided herein.

[00313] 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 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: 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 having a sequence as set forth in 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 having a sequence as set forth in 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 having a sequence as set forth in 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 having a sequence as set forth in 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 having a sequence as set forth in 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 having a sequence as set forth in 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 having a sequence as set forth in 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 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.

[00314] 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 (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: 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, 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 (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.

Expressed polypeptides of interest

[00315] 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”), a dual CAR, a tandem CAR, or a combination thereof. In some embodiments, the heterologous molecule of interest is a CAR. In some embodiments, the heterologous molecule of interest is a dual CAR. In some embodiments, the heterologous molecule of interest is a tandem CAR.

[00316] 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, 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.

[00317] As used herein, a dual CAR refers to an immune cell comprising two complete, independent CAR molecules with antigen binding domains. The antigen binding domains can be different or the same. If the antigen binding domains are the same, that is they bind the same antigen at the same epitope or have identical domains that binds to the antigen, then at least one of the other domains of the CAR would be different in a dual CAR. In some embodiments, the dual CAR polypeptides are expressed via two separate expression cassettes. In some embodiments, the dual CAR polypeptides are expressed on a single expression cassette, wherein the first and second CAR molecules are separated by a cleavable linker (i.e. a bicistronic CAR). However, in some embodiments, the nucleic acid molecules encoding the dual CARs are delivered to a cell in a viral vector, such as those provided for herein. The viral vector can have each CAR expressed from different areas of the viral genome either under the same or different promoters or other regulatory elements. In some embodiments, the antigen binding domains of the two CARs bind to the same antigen but at different epitopes. In some embodiments, the antigen binding domains bind to two different antigens. For example, in some embodiments, the antigen binding domain of the first CAR and the antigen binding domain of the second CAR may each, independently, bind one of CD19, CD20, CD22, BCMA, and FCRL5. In some embodiments, the antigen binding domain of the first CAR binds one of CD19, CD20, CD22, BCMA, and FCRL5 and the antigen binding domain of the second CAR binds one of CD19, CD20, CD22, BCMA, and FCRL5, provided that the antigen binding

domains of the first and second CAR do not bind to the same target. In some embodiments, the dual CAR binds to specific antigen pairs. In some embodiments, the antigen pairs comprise, but are not limited to, CD19/CD20, CD20/CD22, and BCMA/FCRL5. The dual CAR antigen binding domains may each, independently, comprise 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, the antigen binding domains of the first and second CAR are both antibodies. In some embodiments, the antigen binding domains of the first and second CAR are both scFv antibodies. In some embodiments, the antigen binding domain of the first CAR is an scFv antibody and the antigen binding domain of the second CAR 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. In some embodiments, the antigen binding domain of the first CAR 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, and the antigen binding domain of the second CAR is an scFv antibody.

[00318] As used herein, a tandem CAR refers to a CAR molecule that is bispecific toward a set of antigen targets, wherein the first antigen binding domain and the second antigen binding domain are part of a single polypeptide chain. In some embodiments, the first and second antigen binding domain of tandem CAR each, independently, bind one of CD19, CD20, CD22, BCMA, and FCRL5. In some embodiments, the first antigen binding domain of the tandem CAR binds one of CD19, CD20, CD22, BCMA, and FCRL5 and the second antigen binding domain of the tandem CAR binds one of CD19, CD20, CD22, BCMA, and FCRL5, provided that the first and second antigen binding domains of the tandem CAR do not bind to the same target. In some embodiments, the tandem CAR binds to specific antigen pairs. In some embodiments, the antigen pairs comprise, but are not limited to, CD19/CD20, CD20/CD22, and BCMA/FCRL5. The tandem CAR antigen binding domains may each, independently, comprise 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, the first and second antigen binding domains of the tandem CAR are both antibodies. In some embodiments, the first and second antigen binding domains of the tandem CAR are both scFv antibodies. In some embodiments, the first antigen binding domain of the tandem CAR is an scFv antibody and the second antigen binding domain of the tandem CAR 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. In some embodiments, the first antigen binding domain of the tandem CAR 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, and the second antigen binding domain of the tandem CAR is an scFv antibody.

[00319] In some embodiments, the first and second antigen binding domains of the tandem CAR are both scFv antibodies. In some embodiments, the antigen binding domain of the tandem CAR comprises a first V_H domain, a first V_L domain, a second V_H domain, and a second V_L domain, wherein the first V_H domain and the first V_L domain are derived from or associated with a first antibody, or binding fragment thereof (such as, but not limited to, an scFv) and wherein the second V_H domain and the second V_L domain are derived from or associated with a second antibody, or binding fragment thereof (such as, but not limited to, an scFv). It is to be understood that the V_H and the V_L domains may be in any orientation. For example, in some embodiments, the antigen binding domain of the tandem CAR comprises, from N-terminus to C-terminus, a first V_H polypeptide, a first V_L polypeptide, a second V_H polypeptide, and a second V_L polypeptide, wherein the first V_H domain and the first V_L domain are derived from or associated with a first antibody, or binding fragment thereof, and wherein the second V_H domain and the second V_L domain are derived from or associated with a second antibody, or binding fragment thereof. In some embodiments, the orientation of the V_H and V_L domains are as provided in the table below:

Tandem CAR Orientation number	Tandem CAR V _H /V _L Orientation
1	V _{H1} - V _{L1} - V _{H2} - V _{L2}
2	V _{H1} - V _{L1} - V _{L2} - V _{H2}
3	V _{H1} - V _{H2} - V _{L1} - V _{L2}
4	V _{H1} - V _{H2} - V _{L2} - V _{L1}
5	V _{H1} - V _{L2} - V _{H2} - V _{L1}
6	V _{H1} - V _{L2} - V _{L1} - V _{H2}
7	V _{L1} - V _{H1} - V _{H2} - V _{L2}
8	V _{L1} - V _{H1} - V _{L2} - V _{H2}
9	V _{L1} - V _{H2} - V _{H1} - V _{L2}
10	V _{L1} - V _{H2} - V _{L2} - V _{H1}

Tandem CAR Orientation number	Tandem CAR V _H /V _L Orientation
11	V _{L1} - V _{L2} - V _{H1} - V _{H2}
12	V _{L1} - V _{L2} - V _{H2} - V _{H1}
13	V _{H2} - V _{L1} - V _{H1} - V _{L2}
14	V _{H2} - V _{L1} - V _{L2} - V _{H1}
15	V _{H2} - V _{H1} - V _{L1} - V _{L2}
16	V _{H2} - V _{H1} - V _{L2} - V _{L1}
17	V _{H2} - V _{L2} - V _{H1} - V _{L1}
18	V _{H2} - V _{L2} - V _{L1} - V _{H1}
19	V _{L2} - V _{H1} - V _{H2} - V _{L1}
20	V _{L2} - V _{H1} - V _{L1} - V _{H2}
21	V _{L2} - V _{H2} - V _{H1} - V _{L1}
22	V _{L2} - V _{H2} - V _{L1} - V _{H1}
23	V _{L2} - V _{L1} - V _{H1} - V _{H2}
24	V _{L2} - V _{L1} - V _{H2} - V _{H1}

[00320] In some embodiments, the V_H and V_L domains are not linked by a linker peptide. In some embodiments, the V_H and V_L domains 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. In some embodiments, each V_H and V_L domain each, individually, are, or are not linked to the adjacent V_H or V_L domain via a linker such as a peptide linker as provided for herein.

[00321] In some embodiments, the first antigen binding domain of the tandem CAR is an scFv antibody and the second antigen binding domain of the tandem CAR is a single domain antibody (sdAb). In some embodiments, the first antigen binding domain of the tandem CAR is a sdAb and the second antigen binding domain of the tandem CAR is an scFv antibody. In some embodiments, the antigen binding domain of the tandem CAR comprises a first V_H domain, a first V_L domain, and a first sdAb, wherein the first V_H domain and the first V_L domain are derived from or associated with a first antibody, or binding fragment thereof (such as, but not limited to, an scFv) and wherein the first sdAb is derived from or associated with a second antibody, or binding fragment thereof (such as, but not limited to, an scFv). It is to be

understood that the V_H , V_L and sdAb may be in any orientation. For example, in some embodiments, the antigen binding domain of the tandem CAR comprises, from N-terminus to C-terminus, a first V_H polypeptide, a first V_L polypeptide, and a first sdAb, wherein the first V_H domain and the first V_L domain are derived from or associated with a first antibody, or binding fragment thereof, and wherein the first sdAb is derived from or associated with a second antibody, or binding fragment thereof. In some embodiments, the orientation of the V_H , V_L , and sdAb domains are as provided in the table below:

Tandem CAR Orientation number	Tandem CAR V_H/V_L /sdAb Orientation
25	$V_{H1} - V_{L1} - \text{sdAb}$
26	$V_{H1} - \text{sdAb} - V_{L1}$
27	$\text{sdAb} - V_{H1} - V_{L1}$
28	$V_{L1} - V_{H1} - \text{sdAb}$
29	$V_{L1} - \text{sdAb} - V_{H1}$
30	$\text{sdAb} - V_{L1} - V_{H1}$

[00322] In some embodiments, the V_H , V_L , and sdAb domains are not linked by a linker peptide. In some embodiments, the V_H , V_L , and sdAb domains 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. In some embodiments, each V_H , V_L , and sdAb domain each, individually, are, or are not linked to the adjacent domain via a linker such as a peptide linker as provided for herein.

[00323] In some embodiments, the tandem CAR has a first antigen binding domain targeting CD20 and a second antigen binding domain targeting CD22. In some embodiments, the antigen binding domain targeting CD20 and the antigen binding domain targeting CD22 are each, independently, 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, the antigen binding domain targeting CD20 and the antigen binding domain targeting CD22 are each an scFv antibody. In some embodiments, the antigen binding domain targeting CD20 comprises a V_H domain and a V_L domain. In some embodiments, the antigen binding domain targeting CD22 comprises a V_H domain and a V_L domain. It is to be understood that the CD20 targeting V_H and the V_L

domains and the CD22 targeting V_H and V_L domains may be in any orientation. For example, in some embodiments, the antigen binding domain of the tandem CAR comprises, from N-terminus to C-terminus, a CD20 targeting V_H polypeptide, a CD20 targeting V_L polypeptide, a CD22 targeting V_H polypeptide, and a CD22 targeting V_L polypeptide. In some embodiments, the orientation of the V_H and V_L domains are as provided in the table below:

Tandem CAR Orientation number	Tandem CAR V _H /V _L Orientation
31	V _H -CD20 – V _L -CD20 – V _H -CD22 – V _L -CD22
32	V _H -CD20 – V _L -CD20 – V _L -CD22 – V _H -CD22
33	V _H -CD20 – V _H -CD22 – V _L -CD20 – V _L -CD22
34	V _H -CD20 – V _H -CD22 – V _L -CD22 – V _L -CD20
35	V _H -CD20 – V _L -CD22 – V _H -CD22 – V _L -CD20
36	V _H -CD20 – V _L -CD22 – V _L -CD20 – V _H -CD22
37	V _L -CD20 – V _H -CD20 – V _H -CD22 – V _L -CD22
38	V _L -CD20 – V _H -CD20 – V _L -CD22 – V _H -CD22
39	V _L -CD20 – V _H -CD22 – V _H -CD20 – V _L -CD22
40	V _L -CD20 – V _H -CD22 – V _L -CD22 – V _H -CD20
41	V _L -CD20 – V _L -CD22 – V _H -CD20 – V _H -CD22
42	V _L -CD20 – V _L -CD22 – V _H -CD22 – V _H -CD20
43	V _H -CD22 – V _L -CD20 – V _H -CD20 – V _L -CD22
44	V _H -CD22 – V _L -CD20 – V _L -CD22 – V _H -CD20
45	V _H -CD22 – V _H -CD20 – V _L -CD20 – V _L -CD22
46	V _H -CD22 – V _H -CD20 – V _L -CD22 – V _L -CD20
47	V _H -CD22 – V _L -CD22 – V _H -CD20 – V _L -CD20
48	V _H -CD22 – V _L -CD22 – V _L -CD20 – V _H -CD20
49	V _L -CD22 – V _H -CD20 – V _H -CD22 – V _L -CD20
50	V _L -CD22 – V _H -CD20 – V _L -CD20 – V _H -CD22
51	V _L -CD22 – V _H -CD22 – V _H -CD20 – V _L -CD20
52	V _L -CD22 – V _H -CD22 – V _L -CD20 – V _H -CD20
53	V _L -CD22 – V _L -CD20 – V _H -CD20 – V _H -CD22
54	V _L -CD22 – V _L -CD20 – V _H -CD22 – V _H -CD20

[00324] In some embodiments, the CD20 targeting V_H and V_L domains and the CD22 targeting V_H and V_L domains are not linked by a linker peptide. In some embodiments, the CD20 targeting V_H and V_L domains and the CD22 targeting V_H and V_L domains 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. In some embodiments, each CD20 targeting V_H and V_L domain and CD22 targeting V_H and V_L domain each, individually, are, or are not linked to the adjacent V_H or V_L domain via a linker such as a peptide linker as provided for herein.

[00325] In some embodiments, the antigen binding domain targeting CD20 is an scFv antibody and the antigen binding domain targeting CD22 is a sdAb. In some embodiments, the antigen binding domain targeting CD20 is a sdAb and the antigen binding domain targeting CD22 is an scFv antibody. In some embodiments, the scFv antibody comprises a V_H and a V_L domain. It is to be understood that the V_H, V_L and sdAb may be in any orientation. For example, in some embodiments, the antigen binding domain of the tandem CAR comprises, from N-terminus to C-terminus, a CD20 targeting V_H polypeptide, a CD20 targeting V_L polypeptide, and a CD22 sdAb. In some embodiments, the orientation of the V_H, V_L, and sdAb domains are as provided in the table below:

Tandem CAR Orientation number	Tandem CAR V _H /V _L /sdAb Orientation
55	V _H -CD20 – V _L -CD20 – anti CD22 sdAb
56	V _H -CD20 – anti CD22 sdAb - V _L -CD20
57	anti CD22 sdAb - V _H -CD20 – V _L -CD20
58	V _L -CD20 – V _H -CD20 - anti CD22 sdAb
59	V _L -CD20 – anti CD22 sdAb - V _H -CD20
60	anti CD22 sdAb - V _L -CD20 – V _H -CD20
61	V _H -CD22 – V _L -CD22 – anti CD20 sdAb
62	V _H -CD22 – anti CD20 sdAb - V _L -CD22
63	anti CD20 sdAb - V _H -CD22 – V _L -CD22
64	V _L -CD22 – V _H -CD22 - anti CD20 sdAb
65	V _L -CD22 – anti CD20 sdAb - V _H -CD22
66	anti CD20 sdAb - V _L -CD22 – V _H -CD22

[00326] In some embodiments, the V_H, V_L, and sdAb domains are not linked by a linker peptide. In some embodiments, the V_H, V_L, and sdAb domains are linked by a linker peptide, such as those as provided for herein, including but not limited to: (GGGS)_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. In some embodiments, each V_H, V_L, and sdAb domain each, individually, are, or are not linked to the adjacent domain via a linker such as a peptide linker as provided for herein.

[00327] In some embodiments, the tandem CAR has a first antigen binding domain targeting BCMA and a second antigen binding domain targeting FCRL5. In some embodiments, the antigen binding domain targeting BCMA and the antigen binding domain targeting FCRL5 are each, independently, 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, the antigen binding domain targeting BCMA and the antigen binding domain targeting FCRL5 are each an scFv antibody. In some embodiments, the antigen binding domain targeting BCMA comprises a V_H domain and a V_L domain. In some embodiments, the antigen binding domain targeting FCRL5 comprises a V_H domain and a V_L domain. It is to be understood that the BCMA targeting V_H and the V_L domains and the FCRL5 targeting V_H and V_L domains may be in any orientation. For example, in some embodiments, the antigen binding domain of the tandem CAR comprises, from N-terminus to C-terminus, a BCMA targeting V_H polypeptide, a BCMA targeting V_L polypeptide, a FCRL5 targeting V_H polypeptide, and a FCRL5 targeting V_L polypeptide. In some embodiments, the orientation of the V_H and V_L domains are as provided in the table below:

Tandem CAR Orientation number	Tandem CAR V _H /V _L Orientation
67	V _H -BCMA – V _L -BCMA – V _H -FCRL5 – V _L -FCRL5
68	V _H -BCMA – V _L -BCMA – V _L -FCRL5 – V _H -FCRL5
69	V _H -BCMA – V _H -FCRL5 – V _L -BCMA – V _L -FCRL5
70	V _H -BCMA – V _H -FCRL5 – V _L -FCRL5 – V _L -BCMA
71	V _H -BCMA – V _L -FCRL5 – V _H -FCRL5 – V _L -BCMA
72	V _H -BCMA – V _L -FCRL5 – V _L -BCMA – V _H -FCRL5
73	V _L -BCMA – V _H -BCMA – V _H -FCRL5 – V _L -FCRL5
74	V _L -BCMA – V _H -BCMA – V _L -FCRL5 – V _H -FCRL5

Tandem CAR Orientation number	Tandem CAR V _H /V _L Orientation
75	V _L -BCMA – V _H -FCRL5 – V _H -BCMA – V _L -FCRL5
76	V _L -BCMA – V _H -FCRL5 – V _L -FCRL5 – V _H -BCMA
77	V _L -BCMA – V _L -FCRL5 – V _H -BCMA – V _H -FCRL5
78	V _L -BCMA – V _L -FCRL5 – V _H -FCRL5 – V _H -BCMA
79	V _H -FCRL5 – V _L -BCMA – V _H -BCMA – V _L -FCRL5
80	V _H -FCRL5 – V _L -BCMA – V _L -FCRL5 – V _H -BCMA
81	V _H -FCRL5 – V _H -BCMA – V _L -BCMA – V _L -FCRL5
82	V _H -FCRL5 – V _H -BCMA – V _L -FCRL5 – V _L -BCMA
83	V _H -FCRL5 – V _L -FCRL5 – V _H -BCMA – V _L -BCMA
84	V _H -FCRL5 – V _L -FCRL5 – V _L -BCMA – V _H -BCMA
85	V _L -FCRL5 – V _H -BCMA – V _H -FCRL5 – V _L -BCMA
86	V _L -FCRL5 – V _H -BCMA – V _L -BCMA – V _H -FCRL5
87	V _L -FCRL5 – V _H -FCRL5 – V _H -BCMA – V _L -BCMA
88	V _L -FCRL5 – V _H -FCRL5 – V _L -BCMA – V _H -BCMA
89	V _L -FCRL5 – V _L -BCMA – V _H -BCMA – V _H -FCRL5
90	V _L -FCRL5 – V _L -BCMA – V _H -FCRL5 – V _H -BCMA

[00328] In some embodiments, the BCMA targeting V_H and V_L domains and the FCRL5 targeting V_H and V_L domains are not linked by a linker peptide. In some embodiments, the BCMA targeting V_H and V_L domains and the FCRL5 targeting V_H and V_L domains are linked by a linker peptide, such as those as provided for herein, including but not limited to: (GGGS)_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. In some embodiments, each BCMA targeting V_H and V_L domain and FCRL5 targeting V_H and V_L domain each, individually, are, or are not linked to the adjacent V_H or V_L domain via a linker such as a peptide linker as provided for herein.

[00329] In some embodiments, the antigen binding domain targeting BCMA is an scFv antibody and the antigen binding domain targeting FCRL5 is a sdAb. In some embodiments, the antigen binding domain targeting BCMA is a sdAb and the antigen binding domain targeting FCRL5 is an scFv antibody. In some embodiments, the scFv antibody comprises a V_H and a V_L domain. It is to be understood that the V_H, V_L and sdAb may be in any orientation.

For example, in some embodiments, the antigen binding domain of the tandem CAR comprises, from N-terminus to C-terminus, a BCMA targeting V_H polypeptide, a BCMA targeting V_L polypeptide, and a FCRL5 sdAb. In some embodiments, the orientation of the V_H, V_L, and sdAb domains are as provided in the table below:

Tandem CAR Orientation number	Tandem CAR V _H /V _L /sdAb Orientation
91	V _H -BCMA – V _L -BCMA – anti FCRL5 sdAb
92	V _H -BCMA – anti FCRL5 sdAb - V _L -BCMA
93	anti FCRL5 sdAb - V _H -BCMA – V _L -BCMA
94	V _L -BCMA – V _H -BCMA - anti FCRL5 sdAb
95	V _L -BCMA – anti FCRL5 sdAb - V _H -BCMA
96	anti FCRL5 sdAb - V _L -BCMA – V _H -BCMA
97	V _H -FCRL5 – V _L -FCRL5 – anti BCMA sdAb
98	V _H -FCRL5 – anti BCMA sdAb - V _L -FCRL5
99	anti BCMA sdAb - V _H -FCRL5 – V _L -FCRL5
100	V _L -FCRL5 – V _H -FCRL5 - anti BCMA sdAb
101	V _L -FCRL5 – anti BCMA sdAb - V _H -FCRL5
102	anti BCMA sdAb - V _L -FCRL5 – V _H -FCRL5

[00330] In some embodiments, the V_H, V_L, and sdAb domains are not linked by a linker peptide. In some embodiments, the V_H, V_L, and sdAb domains are linked by a linker peptide, such as those as provided for herein, including but not limited to: (GGGS)_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. In some embodiments, each V_H, V_L, and sdAb domain each, individually, are, or are not linked to the adjacent domain via a linker such as a peptide linker as provided for herein.

[00331] In some embodiments, the tandem CAR has a first antigen binding domain targeting CD20 and a second antigen binding domain targeting CD19. In some embodiments, the antigen binding domain targeting CD20 and the antigen binding domain targeting CD19 are each, independently, 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, the antigen binding domain targeting CD20 and the antigen binding domain targeting CD19 are each an scFv antibody. In

some embodiments, the antigen binding domain targeting CD20 comprises a V_H domain and a V_L domain. In some embodiments, the antigen binding domain targeting CD19 comprises a V_H domain and a V_L domain. It is to be understood that the CD20 targeting V_H and the V_L domains and the CD19 targeting V_H and V_L domains may be in any orientation. For example, in some embodiments, the antigen binding domain of the tandem CAR comprises, from N-terminus to C-terminus, a CD20 targeting V_H polypeptide, a CD20 targeting V_L polypeptide, a CD19 targeting V_H polypeptide, and a CD19 targeting V_L polypeptide. In some embodiments, the orientation of the V_H and V_L domains are as provided in the table below:

Tandem CAR Orientation number	Tandem CAR V _H /V _L Orientation
31	V _H -CD20 – V _L -CD20 - V _H -CD19 - V _L -CD19
32	V _H -CD20 – V _L -CD20 - V _L -CD19 - V _H -CD19
33	V _H -CD20 – V _H -CD19 – V _L -CD20 - V _L -CD19
34	V _H -CD20 – V _H -CD19 - V _L -CD19 - V _L -CD20
35	V _H -CD20 – V _L -CD19 - V _H -CD19 - V _L -CD20
36	V _H -CD20 – V _L -CD19 - V _L -CD20 - V _H -CD19
37	V _L -CD20 – V _H -CD20 – V _H -CD19 – V _L -CD19
38	V _L -CD20 – V _H -CD20 – V _L -CD19 – V _H -CD19
39	V _L -CD20 – V _H -CD19 – V _H -CD20 – V _L -CD19
40	V _L -CD20 – V _H -CD19 – V _L -CD19 – V _H -CD20
41	V _L -CD20 – V _L -CD19 – V _H -CD20 – V _H -CD19
42	V _L -CD20 – V _L -CD19 – V _H -CD19 – V _H -CD20
43	V _H -CD19 – V _L -CD20 - V _H -CD20 - V _L -CD19
44	V _H -CD19 – V _L -CD20 - V _L -CD19 - V _H -CD20
45	V _H -CD19 – V _H -CD20 – V _L -CD20 - V _L -CD19
46	V _H -CD19 – V _H -CD20 - V _L -CD19 - V _L -CD20
47	V _H -CD19 – V _L -CD19 - V _H -CD20 - V _L -CD20
48	V _H -CD19 – V _L -CD19 - V _L -CD20 - V _H -CD20
49	V _L -CD19 – V _H -CD20 – V _H -CD19 – V _L -CD20
50	V _L -CD19 – V _H -CD20 – V _L -CD20 – V _H -CD19
51	V _L -CD19 – V _H -CD19 – V _H -CD20 – V _L -CD20
52	V _L -CD19 – V _H -CD19 – V _L -CD20 – V _H -CD20
53	V _L -CD19 – V _L -CD20 – V _H -CD20 – V _H -CD19

Tandem CAR Orientation number	Tandem CAR V _H /V _L Orientation
54	V _L -CD19 – V _L -CD20 – V _H -CD19 – V _H -CD20

[00332] In some embodiments, the CD20 targeting V_H and V_L domains and the CD19 targeting V_H and V_L domains are not linked by a linker peptide. In some embodiments, the CD20 targeting V_H and V_L domains and the CD19 targeting V_H and V_L domains 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. In some embodiments, each CD20 targeting V_H and V_L domain and CD19 targeting V_H and V_L domain each, individually, are, or are not linked to the adjacent V_H or V_L domain via a linker such as a peptide linker as provided for herein.

[00333] In some embodiments, the antigen binding domain targeting CD20 is an scFv antibody and the antigen binding domain targeting CD19 is a sdAb. In some embodiments, the antigen binding domain targeting CD20 is a sdAb and the antigen binding domain targeting CD19 is an scFv antibody. In some embodiments, the scFv antibody comprises a V_H and a V_L domain. It is to be understood that the V_H, V_L and sdAb may be in any orientation. For example, in some embodiments, the antigen binding domain of the tandem CAR comprises, from N-terminus to C-terminus, a CD20 targeting V_H polypeptide, a CD20 targeting V_L polypeptide, and a CD19 sdAb. In some embodiments, the orientation of the V_H, V_L, and sdAb domains are as provided in the table below:

Tandem CAR Orientation number	Tandem CAR V _H /V _L /sdAb Orientation
55	V _H -CD20 – V _L -CD20 – anti CD19 sdAb
56	V _H -CD20 – anti CD19 sdAb - V _L -CD20
57	anti CD19 sdAb - V _H -CD20 – V _L -CD20
58	V _L -CD20 – V _H -CD20 - anti CD19 sdAb
59	V _L -CD20 – anti CD19 sdAb - V _H -CD20
60	anti CD19 sdAb - V _L -CD20 – V _H -CD20
61	V _H -CD19 – V _L -CD19 – anti CD20 sdAb
62	V _H -CD19 – anti CD20 sdAb - V _L -CD19
63	anti CD20 sdAb - V _H -CD19 – V _L -CD19

Tandem CAR Orientation number	Tandem CAR V _H /V _L /sdAb Orientation
64	V _L -CD19 – V _H -CD19 - anti CD20 sdAb
65	V _L -CD19 – anti CD20 sdAb - V _H -CD19
66	anti CD20 sdAb - V _L -CD19 – V _H -CD19

[00334] In some embodiments, the V_H, V_L, and sdAb domains are not linked by a linker peptide. In some embodiments, the V_H, V_L, and sdAb domains are linked by a linker peptide, such as those as provided for herein, including but not limited to: (GGGS)_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. In some embodiments, each V_H, V_L, and sdAb domain each, individually, are, or are not linked to the adjacent domain via a linker such as a peptide linker as provided for herein.

[00335] In various embodiments, the antigen binding domain targeting CD19 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: 138, or any value or range in-between. In various embodiments, SEQ ID NO: 138 is a CD19 binding V_H domain.

EVQLVQSGAEVKKPGESLKISCKGSGYSFSSSWIGWVRQMPGKGLEWMGIY
PDDSDTRYSPSFQGQVTISADKSIRTAYLQWSSLKASDTAMYYCARHVTMIW
GVIIDFWGQGTLVTVSS (SEQ ID NO: 138)

[00336] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 138. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 138. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 138. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 138. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 138.

[00337] In various embodiments, the antigen binding domain targeting CD19 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: 139, or any value or range in-between. In various embodiments, SEQ ID NO: 139 is a CD19 binding V_L domain.

AIQLTQSPSSLSASVGDRTTITCRASQGISSALAWYQQKPGKAPKLLIYDAS
 SLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFNSYPYTFGQGTKL
 EIK (SEQ ID NO: 139)

[00338] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 139. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 139. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 139. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 139. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 139. In some embodiments, the antigen binding domain targeting CD19 comprises a V_H domain comprising an amino acid sequence of SEQ ID NO: 138 and a V_L domain comprising an amino acid sequence of SEQ ID NO: 139.

[00339] In various embodiments, the antigen binding domain targeting CD19 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: 140, or any value or range in-between. In various embodiments, SEQ ID NO: 140 comprises both CD19 binding V_H and V_L domains. For example, SEQ ID NO: 140 has the following architecture: V_H – linker – V_L.

EVQLVQSGAEVKKPGESLKISCKGSGYSFSSSWIGWVRQMPGKGLEWMGIY
 PDDSDTRYSPSFQGVTTISADKSIRTAYLQWSSLKASDTAMYYCARHVTMIW
 GVIIDFWGQGTILTVTVSSGGGGSGGGSGGGGSAIQLTQSPSSLSASVGDRT
 ITCRASQGISSALAWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDF
 LTISSLQPEDFATYYCQQFNSYPYTFGQGTKLEIK (SEQ ID NO: 140)

[00340] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 140. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 140. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 140. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 140. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 140.

[00341] In various embodiments, the antigen binding domain targeting CD19 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: 141, or any value or range in-between. In various embodiments, SEQ ID NO: 141 comprises both CD19 binding VH and VL domains. For example, SEQ ID NO: 141 has the following architecture: VL – linker – VH.

AIQLTQSPSSLSASVGDRVTTITCRASQGISSALAWYQQKPGKAPKLLIYDAS
SLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFNSYPYTFGQGTKL
EIKGGGGSGGGSGGGGSEVQLVQSGAEVKKPGESLKISCKGSGYSFSSSWI
GWVRQMPGKGLEWMGIIYPDDSDTRYSPSFQGQVTISADKSIRTAYLQWSSL
KASDTAMYYCARHVTMIWGVIIIDFWGQGTILVTVSS (SEQ ID NO: 141)

[00342] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 141. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 141. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 141. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 141. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 141.

[00343] In some embodiments, the antigen binding domain targeting CD19 comprises a VH and/or a VL as provided in the table below.

Exemplary CD19 VH and VL sequences		
SEQ ID NO	Domain(s)	Sequence
138	VH	EVQLVQSGAEVKKPGESLKISCKGSGYSFSSSWIGWVRQMP GKGLEWMGIIYPDDSDTRYSPSFQGQVTISADKSIRTAYLQ WSSLKASDTAMYYCARHVTMIWGVIIIDFWGQGTILVTVSS
139	VL	AIQLTQSPSSLSASVGDRVTTITCRASQGISSALAWYQQKPG KAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISSLQPED FATYYCQQFNSYPYTFGQGTKLEIK
140	VH-linker-VL	EVQLVQSGAEVKKPGESLKISCKGSGYSFSSSWIGWVRQMP GKGLEWMGIIYPDDSDTRYSPSFQGQVTISADKSIRTAYLQ WSSLKASDTAMYYCARHVTMIWGVIIIDFWGQGTILVTVSSGG GGSGGGSGGGGSAIQLTQSPSSLSASVGDRVTTITCRASQ

Exemplary CD19 VH and VL sequences		
SEQ ID NO	Domain(s)	Sequence
		ISSALAWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGT DFTLTISLQPEDFATYYCQQFNSYPYTFGQGTKLEIK
141	VL-linker-VH	AIQLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPG KAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISLQPED FATYYCQQFNSYPYTFGQGTKLEIKGGGGSGGGSGGGGSE VQLVQSGAEVKKPGESLKISCKGSGYSFSSSWIGWVRQMPG KGLEWMGI IYPDDSDTRYSPSFQGVITISADKSIRTAYLQW SSLKASDTAMYICARHVTMIWGVIIIDFWGQGTTLTVSS

[00344] In various embodiments, the antigen binding domain targeting CD19 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: 177, or any value or range in-between.

EVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQPPRKGLEWLGVIW
GSETTYNSALKSRLTIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGGS
YAMDYWGQGTSTTVSS (SEQ ID NO: 177)

[00345] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 177. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 177. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 177. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 177. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 177.

[00346] In various embodiments, the antigen binding domain targeting CD19 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: 178, or any value or range in-between.

DIQMTQTSSLSASLGDRVTISCRASQDISKYLNWYQQKPDGTVKLLIYHTS
RLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYTFGGGTKL
EIT (SEQ ID NO: 178)

[00347] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 178. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 178. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 178. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 178. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 178.

[00348] In some embodiments, the antigen-binding domain of the CAR comprises any anti-CD19 antibody, or an scFv thereof, or an active fragment thereof. In some embodiments, the antigen-binding domain of the CAR comprises axicabtagene ciloleucel (KTEX19, Yescarta), brexucabtagene autoleucel (Tecartus), lisocabtagene maraleucel (JCAR017, Breyanzi), tisagenlecleucel (CTL019, Kymriah), tafasitamab (MOR208, XmAb5574, Monjuvi), loncastuximab tesirine (ADCT-402), anti-CD19 antibody clone 21D4, 21D4a, 47G4, FMC63, SJ25C1, inebilizumab, blinatumomab (MT103, AMG103, Blincyto), coltuximab ravtansine (SAR3419), MEDI-551, Denintuzumab mafodotin (SGN-CD19A), taplitumomabpaptox, XmAb 5871, MDX-1342, IKS03, AMG562, CLN-978, TNB-486 CD19/CD3, 41BB-CD3ζ LV20.19, CD19/CD20 bispecific CAR-T cell therapy (Johnson Comprehensive Cancer Center), ALLO-501/ALLO-501A, Kyverna KYV-101, PBCAR0191, LY3541860, Merck modified B4 mAb anti-CD19 (Merck), or AFM11. In some embodiments, the antigen binding domain of the CAR is an antibody, or an scFv thereof, or an active fragment thereof, as provided in U.S. Patent Serial No. 8,097,703B2, U.S. Patent Serial No. 10,287,350B2, U.S. Patent Serial No. 11,236,161B2, U.S. Patent Publication No. 2022/0153838A1, and U.S. Patent Publication No. 2022/0204619A1; each of which are hereby incorporated by reference in their entirety. In some embodiments, the CAR comprises the 4-1BB domain as well.

[00349] In some embodiments, the antigen binding domain of the CAR comprises a VH and a VL as provided for herein. In some embodiments, the antigen binding domain of the CAR comprises a VH and/or a VL as provided in the table below.

Exemplary CD19 scFv VH and VL sequences		
Generic Name	SEQ ID NO	Sequence
Axicabtagene ciloleucel (KTEX19)	179 (VH)	EVKLQESGPGPLVAPSQSLSVTTCTVSGVSLPDYGVSWIRQPP PRKGLEWLGVWGSETTYNSSALKSRLTI IKDNSKSQVFLK KMNSLQTDDTAIYYCAKHYYYYGGSYAMDYWGQGTSTVTVSS

Exemplary CD19 scFv VH and VL sequences		
	180 (VL)	DIQMTQQTTSSLSASLGDRVTISCRASSQDISKYLNWYQQKP DGTVKLLLIYHTSRLHSGVPSRFSGSGGSGTDYSLTISNLEQ EDIATYYFCQQGNTLPYTFGGGKLEI
Brexucabtagene autoleucel	181 (VH)	EVKLQESGPGLVAPSQSLSVTTCTVSGVSLPDYGVSWIRQPP PRKGLEWLGVWGSETTYNSSALKSRLTIKDNSKSQVFLK KMNSLQTDDTAIYYCAKHYYYGGSYAMDYWGQGSTVTVSS
	182 (VL)	DIQMTQQTTSSLSASLGDRVTISCRASSQDISKYLNWYQQKP DGTVKLLLIYHTSRLHSGVPSRFSGSGGSGTDYSLTISNLEQ EDIATYYFCQQGNTLPYTFGGGKLEI
Lisocabtagene maraleucel (JCAR017)	183 (VH)	EVKLQESGPGLVAPSQSLSVTTCTVSGVSLPDYGVSWIRQPP PRKGLEWLGVWGSETTYNSSALKSRLTIKDNSKSQVFLK KMNSLQTDDTAIYYCAKHYYYGGSYAMDYWGQGSTVTVSS
	184 (VL)	DIQMTQQTTSSLSASLGDRVTISCRASSQDISKYLNWYQQKP DGTVKLLLIYHTSRLHSGVPSRFSGSGGSGTDYSLTISNLEQ EDIATYYFCQQGNTLPYTFGGGKLEI
Tisagenlecleucel (CTL019)	185 (VH)	EVKLQESGPGLVAPSQSLSVTTCTVSGVSLPDYGVSWIRQPP PRKGLEWLGVWGSETTYNSSALKSRLTIKDNSKSQVFLK KMNSLQTDDTAIYYCAKHYYYGGSYAMDYWGQGSTVTVSS
	186 (VL)	DIQMTQQTTSSLSASLGDRVTISCRASSQDISKYLNWYQQKP DGTVKLLLIYHTSRLHSGVPSRFSGSGGSGTDYSLTISNLEQ EDIATYYFCQQGNTLPYTFGGGKLEI
Tafasitamab (MOR208, XmAb5574)	187 (VH)	EVQLVESGGGLVKPGGSLKLSAASGYTFTSYVMHWVRQAPG KGLEWIGYINPYNDGTYNEKFQGRVTISSDKSISTAYMELS SLRSED TAMYYCARGTYYYGTRVFDYWGQGT LVTVSS
	188 (VL)	DIVMTQSPATLSLSPGERATLSCRSSKSLQNVNGNTYLYWFQ QKPGQSPQLLIYRMSNLNSGVPRFSGSGSGTEFTLTISLSLE PEDFAVYYCMQHLEYPITFGAGTKLEIK
Inebilizumab (MEDI- 551)	189 (VH)	EVQLVESGGGLVQPGGSLRLSAAASGFTFSSSWMNWVRQAPG KGLEWVGRIYPGDGDTNYNVFKGRFTISRDDSKNSLYLQMN SLKTEDTAVYYCARGSFITTVRDFDYWGQGT LVTVSS
	190 (VL)	EIVLTQSPDFQSVTPKEKVTITCRASEVDTFGISFMNWFQQ KPDQSPKLLIHEASNQSGVPSRFSGSGSGTDFTLTINSLEA EDAATYYCQQSKEVPFTFGGGTKVEIK
Denintuzumab mafodotin (SGN- CD19A)	191 (VH)	QVQLQESGPGLVKPSQTLSTCTVSGGSISTSGMGVGVIRQH PGKLEWIGHIWDDDKRYNPALKSRVTISVDTSKNQFSLKL SSVTAADTAVYYCARMELWSYFYFDYWGQGT LVTVSS
	192 (VL)	EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPGQA PRLLIYDTSKLASGIPARFSGSGSGTDFTLTISLSLEPEDVAV YYCFQGSVYPFTFGQGTKLEIK
Blinatumomab (MT103, AMG103)	193 (VH1)	QVQLQQSGAELVRPGSSVKISCKASGYAFSSYWMNVKQRP QGLEWIGQIWP GDGDTNNGKFKGKATLTADESSSTAYMQLS SLASEDSAVYFCARRETTTVGRYYYAMDYWGQGT TTVVSS
	194 (VL)	DIQLTQSPASLAVSLGQRATISCKASQSDYDGD SYLNWYQQ IPGQPPKLLIYDASNLVSGIPPRFSGSGSGTDFTLNHPVEK VDAATYHCQQSTEDPWTFGGGTKLEIK

Exemplary CD19 scFv VH and VL sequences		
	195 (VH2)	DIKLQSGAELARPGASVKMSCKTSGYTFTRYTMHWVKQRPQG GLEWIGYINPSRGYTNYNQKFKDKATLTDDKSSSTAYMQLSS LTSEDSAVYYCARYDDHYCLDYWGQGTTTLTVSS
	196 (VL1)	DIQLTQSPAIMASASPGEKVTMTCRASSSVSYMNWYQQKSGTS PKRWIYDTSKVASGVPYRFSGSGSGTSYSLTISSEAEADAAT YYCQQWSSNPLTFGAGTKLELK
Coltuximab ravtansine (SAR3419)	197 (VH)	QVQLVQPGAIEVVKPGASVKLSCKTSGYFTSNWMHWVKQAPG QGLEWIGEIDPDSYTNYNQNFQGKAKLTVDKSTSTAYMEVS SLRSDDTAVYYCARGSNPYYYAMDYWGQGTSTVTVSS
	198 (VL2)	EIVLTQSPAIMASAPGERVTMTCSASSGVNMYHWYQQKPGTS PRRWIYDTSKLAGVPAFSGSGSGTDYSLTISSEPEADAAT YYCHQRGSYTFGGGKLEIK
Loncastuximab tesirine (ADCT-402)	199 (VH)	QVQLVQPGAIEVVKPGASVKLSCKTSGYFTSNWMHWVKQAPG QGLEWIGEIDPDSYTNYNQNFQGKAKLTVDKSTSTAYMEVS SLRSDDTAVYYCARGSNPYYYAMDYWGQGTSTVTVSS
	200 (VL)	EIVLTQSPAIMASAPGERVTMTCSASSGVNMYHWYQQKPGTS PRRWIYDTSKLAGVPAFSGSGSGTDYSLTISSEPEADAAT YYCHQRGSYTFGGGKLEIK
FMC63, alt	201 (VH)	EVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQPPR KLEWLGVIWGSETTYNSALKSRLTIKDNSSKQVFLKMNS LQTDDTAIYYCAKHYGGSYAMDYWGQGTSTVTVSS
	202 (VL)	DIQMTQTSSLSASLGDRVTISCRASQDISKYNWYQQKPDG TVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIA TYFCQQGNTLPYTFGGGKLEIT

[00350] In various embodiments, the antigen binding domain targeting CD19 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: 179, or any value or range in-between.

EVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQPPRKLEWLGVIWGSETTYNSALKSRLTIKDNSSKQVFLKMNSLQTDDTAIYYCAKHYGGSYAMDYWGQGTSTVTVSS (SEQ ID NO: 179)

[00351] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 179. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 179. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 179. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 179. In some embodiments, the antigen

binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 179.

[00352] In various embodiments, the antigen binding domain targeting CD19 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: 180, or any value or range in-between.

DIQMTQQTTSSLSASLGDRVTISCRASSQDISKYLNWYQQKPDGTVKLLLIY
HTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYYFCQQGNTLPYTFG
GGTKLEI (SEQ ID NO: 180)

[00353] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 180. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 180. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 180. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 180. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 180.

[00354] In various embodiments, the antigen binding domain targeting CD19 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: 181, or any value or range in-between.

EVKLQESGPGLVAPSQSLSVTTCTVSGVSLPDYGVSWIRQPPPRKGLEWLGV
IWGSETTYYNSSALKSRLTIKDNSKSQVFLKKMNSLQTDDETAIYYCAKHY
YYGGSYAMDYWGQTSVTVSS (SEQ ID NO: 181)

[00355] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 181. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 181. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 181. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 181. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 181.

[00356] In various embodiments, the antigen binding domain targeting CD19 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: 182, or any value or range in-between.

DIQMTQQTTSSLSASLGDRVTISCRASSQDISKYLNWYQQKPDGTVKLLLIY
HTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYYFCQQGNTLPYTFG
GGTKLEI (SEQ ID NO: 182)

[00357] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 182. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 182. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 182. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 182. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 182.

[00358] In various embodiments, the antigen binding domain targeting CD19 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: 183, or any value or range in-between.

EVKLQESGPGLVAPSQSLSVTTCTVSGVSLPDYGVSWIRQPPPRKGLEWLGV
IWGSETTYYNSSALKSRLLTIKDNSKSQVFLKKMNSLQTDDETAIYYCAKHYY
YYGGSYAMDYWGQGTSTVTVSS (SEQ ID NO: 183)

[00359] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 183. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 183. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 183. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 183. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 183.

[00360] In various embodiments, the antigen binding domain targeting CD19 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: 184, or any value or range in-between.

DIQMTQQTSSLSASLGDRVTISCRASSQDISKYLNWYQQKPDGTVKLLLIY
HTSRLHSGVPSRFSGSGGSGTDYSLTISNLEQEDIATYYFCQQGNTLPYTFG
GGTKLEI (SEQ ID NO: 184)

[00361] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 184. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 184. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 184. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 184. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 184.

[00362] In various embodiments, the antigen binding domain targeting CD19 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: 185, or any value or range in-between.

EVKLQESGPGLVAPSQSLSVTTCTVSGVSLPDYGVSWIRQPPPRKGLEWLGV
IWGSETTYYNSSALKSRLTIKDNSKSKVFLKKMNSLQTDATAIYYCAKHYY
YYGGSYAMDYWGQGTSTVTVSS (SEQ ID NO: 185)

[00363] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 185. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 185. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 185. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 185. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 185.

[00364] In various embodiments, the antigen binding domain targeting CD19 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: 186, or any value or range in-between.

DIQMTQQTSSLSASLGDRVTISCRASSQDISKYLNWYQQKPDGTVKLLLIY
 HTSRLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYYFCQQGNTLPYTFG
 GGTKLEI (SEQ ID NO: 186)

[00365] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 186. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 186. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 186. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 186. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 186.

[00366] In various embodiments, the antigen binding domain targeting CD19 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: 187, or any value or range in-between.

EVQLVESGGGLVKPGGSLKLSAASGYTFTSYVMHWVRQAPGKGLEWIGYIN
 PYNDGTKYNEKFQGRVTISSDKSISTAYMELSSLRSEDAMYYCARGTYYYG
 TRVFDYWGQGLTVTVSS (SEQ ID NO: 187)

[00367] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 187. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 187. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 187. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 187. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 187.

[00368] In various embodiments, the antigen binding domain targeting CD19 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: 188, or any value or range in-between.

DIVMTQSPATLSLSPGERATLSCRSSKSLQNVNGNTYLYWFQQKPGQSPQLL
 IYRMSNLNSGVPDRFSGSGSGTEFTLTISLEPEDFAVYYCMQHLEYPITFG
 AGTKLEIK (SEQ ID NO: 188)

[00369] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 188. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 188. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 188. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 188. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 188.

[00370] In various embodiments, the antigen binding domain targeting CD19 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: 189, or any value or range in-between.

EVQLVESGGGLVQPGGSLRLSCAASGFTFSSSWMNWVRQAPGKGLEWVGRIY
PGDGDNTYNVVKFKGRFTISRDDSKNSLYLQMNSLKTEDTAVYYCARSGFITTT
VRDFDYWGQGTLVTVSS (SEQ ID NO: 189)

[00371] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 189. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 189. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 189. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 189. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 189.

[00372] In various embodiments, the antigen binding domain targeting CD19 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: 190, or any value or range in-between.

EIVLTQSPDFQSVTPKEKVTITCRASESVDTFGISFMNWFQQKPDQSPKLLI
HEASNQSGVPSRFSGSGSGTDFLTINSLEAEDAATYYCQQSKEVPFTFGG
GTKVEIK (SEQ ID NO: 190)

[00373] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 190. In some embodiments,

the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 190. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 190. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 190. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 190.

[00374] In various embodiments, the antigen binding domain targeting CD19 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: 191, or any value or range in-between.

QVQLQESGPGLVKPSQTLSTCTVSGGSISTSGMGVGWIRQHPGKGLEWIGH
IWWDDDKRYNPALKSRVTISVDTSKNQFSLKLSSVTAADTAVYYCARMELWS
YYFDYWGQGTLVTVSS (SEQ ID NO: 191)

[00375] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 191. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 191. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 191. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 191. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 191.

[00376] In various embodiments, the antigen binding domain targeting CD19 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: 192, or any value or range in-between.

EIVLTQSPATLSLSPGERATLSCSASSSVSYMHWYQQKPGQAPRLLIYDTSK
LASGIPARFSGSGGTDFLTITISLLEPEDVAVYYCFQGSVYPFTFGQGTKLE
IK (SEQ ID NO: 192)

[00377] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 192. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 192. In some embodiments, the antigen binding domain targeting

CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 192. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 192. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 192.

[00378] In various embodiments, the antigen binding domain targeting CD19 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: 193, or any value or range in-between.

QVQLQQSGAELVRPGSSVKISCKASGYAFSSYWMNWKQRPQGQGLEWIGQIW
PGDGDNTYNGKFKGKATLTADESSSTAYMQLSSLASEDSAVYFCARRETTTV
GRYYAMDYWGQGTTTVTVSS (SEQ ID NO: 193)

[00379] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 193. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 193. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 193. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 193. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 193.

[00380] In various embodiments, the antigen binding domain targeting CD19 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: 194, or any value or range in-between.

DIQLTQSPASLAVSLGQRATISCKASQSDYDGD SYLNWYQQIPGQPPKLLI
YDASNLVSGIPPRFSGSGSGTDFTLNIHPVEKVDAAITYHCQQSTEDPWTFGG
GTKLEIK (SEQ ID NO: 194)

[00381] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 194. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 194. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 194. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid

sequence having at least 99% identity to SEQ ID NO: 194. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 194.

[00382] In various embodiments, the antigen binding domain targeting CD19 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: 195, or any value or range in-between.

DIKLQSGAELARPGASVKMSCKTSGYTFTRYTMHWVKQRPGGLEWIGYINP
SRGYTNYNQKFKDKATLTDDKSSSTAYMQLSSLTSEDSAVYYCARYYDDHYC
LDYWGQGTTTLTVSS (SEQ ID NO: 195)

[00383] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 195. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 195. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 195. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 195. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 195.

[00384] In various embodiments, the antigen binding domain targeting CD19 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: 196, or any value or range in-between.

DIQLTQSPAIMSASPGKVTMTCRASSSVSYMNWYQQKSGTSPKRWIYDTSK
VASGVPYRFSGSGSGTSYSLTISSEAEADAATYYCQQWSSNPLTFGAGTKLE
LK (SEQ ID NO: 196)

[00385] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 196. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 196. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 196. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 196. In some embodiments, the antigen

binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 196.

[00386] In various embodiments, the antigen binding domain targeting CD19 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: 197, or any value or range in-between.

QVQLVQPGAIEVVKPGASVKLSCKTSGYTFSTSNWMHWKQAPGGGLEWIGEID
 PSDSYTNYNQNFQGKAKLTVDKSTSTAYMEVSSLRSDDTAVYYCARGSNPYY
 YAMDYWGQGTSTVTVSS (SEQ ID NO: 197)

[00387] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 197. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 197. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 197. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 197. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 197.

[00388] In various embodiments, the antigen binding domain targeting CD19 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: 198, or any value or range in-between.

EIVLTQSPAISASPGERVMTCSASSGVNYMHWYQQKPGTSPRRWIYDTSK
 LASGVPARFSGSGSDYSLTISSEPEDAATYYCHQRGSYTFGGGTKLEIK
 (SEQ ID NO: 198)

[00389] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 198. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 198. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 198. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 198. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 198.

[00390] In various embodiments, the antigen binding domain targeting CD19 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: 199, or any value or range in-between.

QVQLVQPGAIEVVKPGASVKLSCKTSGYTFTSNWMHWVKQAPGGGLEWIGEID
 PSDSYTNYNQNFQGKAKLTVDKSTSTAYMEVSSLRSDDTAVYYCARGSNPYY
 YAMDYWGQGTSVTVSS (SEQ ID NO: 199)

[00391] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 199. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 199. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 199. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 199. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 199.

[00392] In various embodiments, the antigen binding domain targeting CD19 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: 200, or any value or range in-between.

EIVLTQSPAISASPGERVMTMTCSASSGVNYMHWYQQKPGTSPRRWIYDTSK
 LASGVPARFSGSGSTSYSLTISSMEPEDAATYYCHQRGSYTFGGGTKLEIK
 (SEQ ID NO: 200)

[00393] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 200. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 200. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 200. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 200. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 200.

[00394] In various embodiments, the antigen binding domain targeting CD19 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: 201, or any value or range in-between.

EVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQPPRKGLEWLGVIW
GSETTYNSALKSRLTIIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGGS
YAMDYWGQGTSTVTVSS (SEQ ID NO: 201)

[00395] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 201. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 201. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 201. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 201. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 201.

[00396] In various embodiments, the antigen binding domain targeting CD19 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: 202, or any value or range in-between.

DIQMTQTTSSLSASLGDRVTISCRASQDISKYLNWYQQKPDGTVKLLIYHTS
RLHSGVPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYTFGGGTKL
EIT (SEQ ID NO: 202)

[00397] In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 202. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 202. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 202. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 202. In some embodiments, the antigen binding domain targeting CD19 comprises an amino acid sequence having the sequence of SEQ ID NO: 202.

[00398] 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 a FHVH33 domain disclosed in Application No US20200138865A1, which is hereby incorporated by reference in its entirety. 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: 113 or any value or range in-between.

EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSSIS
GSGDYIYYADSVKGRFTISRDISKNTLYLQMNSLRAEDTAVYYCAKEGTGAN
SSLADYRGQGTTLVTVSS (SEQ ID NO: 113)

[00399] In some embodiments, the V_H domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 113. In some embodiments, the V_H domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 113. In some embodiments, the V_H domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 113. In some embodiments, the V_H domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 113. In some embodiments, the V_H domain comprises an amino acid sequence having the sequence of SEQ ID NO: 113.

[00400] In some embodiments, the antigen-binding domain of the CAR comprises a V_H domain, a V_L domain, a V_H and a V_L domain, or two V_H domains and a single 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.

EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSSIS
GSGDYIYYADSVKGRFTISRDISKNTLYLQMNSLRAEDTAVYYCAKEGTGAN
SSLADYRGQGTTLVTVSS (SEQ ID NO: 89)

[00401] 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.

[00402] 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.

EVQLVESGPGGLVKPSETLSLTCTVSGFSLTRFGVHWVRQPPGKGLEWLGVIW
RGGSTDYNAAFVSRLTISKDNSKNQVSLKLSSVTAADTAVYYCSNHYYGSSD
YALDNWGQGTLVTVSS (SEQ ID NO: 94)

[00403] 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.

[00404] 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.

DIQMTQSPSSLSASVGDRVTITCKASQDVRNLVWFQQKPGKAPKLLIYSGS
YRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQHYSPPYTFGQGTKV
EIK (SEQ ID NO: 95)

[00405] 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.

[00406] In some embodiments, the antigen binding domain comprises a V_H and/or a V_L as provided in the table below.

Exemplary BCMA or FCRL5 VH and VL sequences			
SEQ ID NO	Target	Domain(s)	Sequence
89	BCMA	VH	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMS WVRQAPGKGLEWVSSISGSGDYIYYADSVKGRFTI SRDISKNTLYLQMNSLRAEDTAVYYCAKEGTGANS SLADYRGQGTLVTVSS
90	FCRL5	VH	EVQLVESGPGGLVKPSETLSLTCTVSGFSLTRFGVH WVRQPPGKGLEWLGVIWRRGGSTDYNAAFVSRLTIS

Exemplary BCMA or FCRL5 VH and VL sequences				
SEQ ID NO	Target	Domain(s)	Sequence	
			KDNSKNQVSLKLSSVTAADTAVYYCSNHYYGSSDY ALDNWGQGTLVTVSS	
94	FCRL5	VL	DIQMTQSPSSLSASVGDRVTITCKASQDVRNLVWV FQQKPGKAPKLLIYSGSYRYSGVPSRFSGSGSGTD FTLTISLQPEDFATYYCQQHYSPPYTFGQGTKVE IK	
107	FCRL5	VL-linker- VH	DIQMTQSPSSLSASVGDRVTITCKASQDVRNLVWV FQQKPGKAPKLLIYSGSYRYSGVPSRFSGSGSGTD FTLTISLQPEDFATYYCQQHYSPPYTFGQGTKVE IKGGGGSGGGSGGGGSEVQLVESGPGLVKPSSETL SLTCTVSGFSLTRFGVHWVRQPPGKGLEWLGVIWR GGSTDYNAAFVSRLTISKDNSKNQVSLKLSSVTAA DTAVYYCSNHYYGSSDYALDNWGQGTLVTVSS	
108	FCRL5	VH-linker- VL	EVQLVESGPGLVKPSSETLSLTCTVSGFSLTRFGVH WVRQPPGKGLEWLGVIWRGGSTDYNAAFVSRLTIS KDNSKNQVSLKLSSVTAADTAVYYCSNHYYGSSDY ALDNWGQGTLVTVSSGGGGSGGGSGGGGSDIQMT QSPSSLSASVGDRVTITCKASQDVRNLVWVWFQQKP GKAPKLLIYSGSYRYSGVPSRFSGSGSGTDFTLTI SSLQPEDFATYYCQQHYSPPYTFGQGTKVEIK	

[00407] In some embodiments, the antigen-binding domain of the CAR comprises a V_H domain, a V_L domain, a V_H and a V_L domain, or two V_H domains and a single 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: 136, or any value or range in-between.

EVQLVESGPGLVKPSSETLSLTCTVSGFSLTRFGVHWVRQPPGKGLEWLGVIW
RGGSTDYNAAFVSRLTISKDNSKNQVSLKLSSVTAADTAVYYCSNHYYGSSD
YALDNWGQGTLVTVSS (SEQ ID NO: 136)

[00408] In some embodiments, the V_H domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 136. In some embodiments, the V_H domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 136. In some embodiments, the V_H domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO:

136. In some embodiments, the V_H domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 136. In some embodiments, the V_H domain comprises an amino acid sequence having the sequence of SEQ ID NO: 136.

[00409] 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.

DIQMTQSPSSLSASVGDRVTITCKASQDVRNLVWFQQKPGKAPKLLIYSGS
YRYSQVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQHYSPPYTFGGGTKV
EIK (SEQ ID NO: 90)

[00410] 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.

[00411] 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: (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.

[00412] In some embodiments, the antigen-binding domain of the CAR comprising two V_H domains and a single 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, comprises a V_{H2} 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: 136, 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 two V_H domains and a single 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, comprises a V_{H2} 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: 136, 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 two V_H domains and a single 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, comprises a V_{H2} 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: 136, 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 two V_H domains and a single 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, comprises a V_{H2} 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: 136, 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 two V_H domains and a single 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, comprises a V_{H2} 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: 136, 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 two V_H domains and a single 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, comprises a V_{H2} 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: 136, and comprises a V_L having the sequence of SEQ ID NO: 90. In some embodiments, the antigen-binding domain of the CAR comprising two V_H domains and a single V_L domain comprises a V_H domain having at least 90% identity to SEQ ID NO: 89, comprises a V_{H2} domain having at least 90% identity to SEQ ID NO: 136, 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 two V_H domains and a single V_L domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 89, comprises a V_{H2} domain having at least 95% identity to SEQ ID NO: 136, 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 two V_H domains and a single V_L domain comprises a V_H domain having at least 98% identity to SEQ ID NO: 89, comprises a V_{H2} domain having at least 98% identity to SEQ ID NO: 136, 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 two V_H domains and a single V_L domain comprises a V_H domain having at least 99% identity to SEQ ID NO: 89, comprises a V_{H2} domain having at least 99% identity to SEQ ID NO: 136, 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 two V_H domains and a single V_L domain comprises a V_H domain having an amino acid sequence of SEQ ID NO: 89, comprises a V_{H2} domain having an amino acid sequence of SEQ ID NO: 136, 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 two V_H domains and a single V_L domain comprises a V_H domain having at least 90% identity to SEQ ID NO: 89, comprises a V_{H2} domain having at least 90% identity to SEQ ID NO: 136, 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 two V_H domains and a single V_L domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 89, comprises a V_{H2} domain having at least 95% identity to SEQ ID NO: 136, 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 two V_H domains and a single V_L domain comprises a V_H domain having at least 90% identity to SEQ ID NO: 89, comprises a V_{H2} domain having at least 90% identity to SEQ ID NO: 136, 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 two V_H domains and a single V_L domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 89, comprises a V_{H2} domain having at least 95% identity to SEQ ID NO: 136, 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 two V_H domains and a single V_L domain comprises a V_H domain having at least 98% identity to SEQ ID NO: 89, comprises a V_{H2} domain having at least 98% identity to SEQ ID NO: 136, 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 two V_H domains and a single V_L domain comprises a V_H domain having at least 99% identity to

SEQ ID NO: 89, comprises a V_{H2} domain having at least 99% identity to SEQ ID NO: 136, 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 two V_H domains and a single V_L domain comprises a V_H domain having an amino acid sequence of SEQ ID NO: 89, comprises a V_{H2} domain having an amino acid sequence of SEQ ID NO: 136, and comprises a V_L having an amino acid sequence of SEQ ID NO: 90.

[00413] In some embodiments, the antigen-binding domain of the CAR comprises a formula of V_H-Z-V_{H2}-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), V_{H2} is a heavy chain variable region comprising the amino acid sequence of 136, 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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EVQLLESQGGGLVQPGGSLRLSCAASGFTTFSSYAMSWVRQAPGKGLEWVSSIS
GSGDYIYYADSVKGRFTISRDISKNTLYLQMNSLRAEDTAVYYCAKEGTGAN
SSLADYRGQGTTLVTVSSGGGGSGGGGSGGGGSGGGGSEVQLVESGPGLVKPS
ETLSLTCTVSGFSLTRFGVHWVRQPPGKGLEWLGVIWRGGSTDYNAAFVSRL
TISKDNQVSLKLSSVTAADTAVYYCSNHYYGSSDYALDNWGQGTTLVTVS
SGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGRVTITCKASQDVRNLVWF
QQKPGKAPKLLIYSGSYRYSGVPSRFSGSGSGTDFTLTISLQPEDFATYYC
QQHYSPPYTFGQGTKVEIK (SEQ ID NO: 92)
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[00414] 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.

[00415] In some embodiments, the antigen-binding domain of the CAR comprises a formula of V_L-Z-V_H-Z-V_{H2}, 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), V_H is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 89, and V_{H2} is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 136. In some embodiments, the antigen-binding domain of the CAR comprising a formula of V_L-Z-V_H-Z-V_{H2} has an amino acid sequence as set forth below:

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DIQMTQSPSSLSASVGDRVTITCKASQDVRNLVVWFQQKPGKAPKLLIYSGS
YRYSQVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQHYSPPYTFGGQGTKV
EIKGGGGSGGGGSGGGGSEVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAM
SWVRQAPGKGLEWVSSISGSGDYIYYADSVKGRFTISRDISKNTLYLQMNSL
RAEDTAVYYCAKEGTGANSSSLADYRGQGTTLVTVSSGGGGSGGGGSGGGGSGG
GGSEVQLVESGPGGLVKPSETLSLTCTVSGFSLTRFGVHWVRQPPGKGLEWLG
VIWRGGSTDYNAAFVSRLTISKDNSKNQVSLKLSSVTAADTAVYYCSNHYYG
SSDYALDNWGQGTTLVTVSS (SEQ ID NO: 93)
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[00416] 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.

[00417] 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: 137, or any value or range in-between.

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EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSSIS
GSGDYIYYADSVKGRFTISRDISKNTLYLQMNSLRAEDTAVYYCAKEGTGAN
SSLADYRGQGTTLVTVSS (SEQ ID NO: 137)
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[00418] In some embodiments, the V_H domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 137. In some embodiments, the V_H domain comprises an

amino acid sequence having at least 95% identity to SEQ ID NO: 137. In some embodiments, the V_H domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 137. In some embodiments, the V_H domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 137. In some embodiments, the V_H domain comprises an amino acid sequence having the sequence of SEQ ID NO: 137.

[00419] 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 two V_H domains and a single 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, a V_{H2} 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: 137, 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 two V_H domains and a single 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, a V_{H2} 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: 137, 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 two V_H domains and a single 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, a V_{H2} 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: 137, 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 two V_H domains and a single 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, a V_{H2} 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: 137, 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 two V_H domains and a

single VL 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, a V_{H2} 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: 137, and comprises a V_L having the sequence of SEQ ID NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising two V_H domains and a single VL domain comprises a V_H domain having at least 90% identity to SEQ ID NO: 94, a V_{H2} 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 two V_H domains and a single VL domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 94, a V_{H2} 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 two V_H domains and a single VL domain comprises a V_H domain having at least 98% identity to SEQ ID NO: 94, a V_{H2} 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 two V_H domains and a single VL domain comprises a V_H domain having at least 99% identity to SEQ ID NO: 94, a V_{H2} 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 two V_H domains and a single VL domain comprises a V_H domain having an amino acid sequence of SEQ ID NO: 94, a V_{H2} 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 two V_H domains and a single VL domain comprises a V_H domain having at least 90% identity to SEQ ID NO: 94, a V_{H2} 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 two V_H domains and a single VL domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 94, a V_{H2} 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.

NO: 95. In some embodiments, the antigen-binding domain of the CAR comprising two V_H domains and a single V_L domain comprises a V_H domain having at least 90% identity to SEQ ID NO: 94, a V_{H2} 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 two V_H domains and a single V_L domain comprises a V_H domain having at least 95% identity to SEQ ID NO: 94, a V_{H2} 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 two V_H domains and a single V_L domain comprises a V_H domain having at least 98% identity to SEQ ID NO: 94, a V_{H2} 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 two V_H domains and a single V_L domain comprises a V_H domain having at least 99% identity to SEQ ID NO: 94, a V_{H2} 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 two V_H domains and a single V_L domain comprises a V_H domain having an amino acid sequence of SEQ ID NO: 94, a V_{H2} 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.

[00420] In some embodiments, the antigen-binding domain of the CAR comprises a formula of V_H-Z-V_{H2}-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), V_L is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 95, and V_{H2} is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 97. In some embodiments, the antigen-binding domain of the CAR comprising a formula of V_H-Z-V_{H2}-Z-V_L has an amino acid sequence as set forth below:

```
EVQLVESGPGGLVKPSETLSLTCTVSGFSLTRFGVHWVRQPPGKGLEWLGVIW
RGGSTDYNAAFVSRLTISKDNSKNQVSLKLSSVTAADTAVYYCSNHYYGSSD
YALDNWQGQGLVTVTSSGGGGSGGGGSGGGGSGGGGSEVQLLES GGGLVQPGG
SLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSSISGSGDYIYYADSVKGRF
TISRDISKNTLYLQMNSLRAEDTAVYYCAKEGTGANSSLADYRGQGLVTVS
SGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRTITCKASQDVRNLVWF
QQKPGKAPKLLIYSGSYRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC
QQHYSPPYTFGQGTKVEIK (SEQ ID NO: 96)
```

[00421] 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.

[00422] In some embodiments, the antigen-binding domain of the CAR comprises a formula of V_L -Z- V_H -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 GGGGSGGGGSGGGG (SEQ ID NO: 91), V_H is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 94, and V_H is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 137. In some embodiments, the antigen-binding domain of the CAR comprising a formula of V_L -Z- V_H -Z- V_H has an amino acid sequence as set forth below:

```
DIQMTQSPSSLSASVGDRTITCKASQDVRNLVWFQQKPGKAPKLLIYSGS
YRYSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQHYSPPYTFGQGTKV
EIKGGGSGGGGSGGGGSEVQLVESGPGLVKPSSETLSLTCTVSGFSLTRFGV
HWVRQPPGKGLEWLGVIWRGGSTDYNAAFVSRLTISKDNSKNQVSLKLSSVT
AADTAVYYCSNHYYGSSDYALDNWGQGTILTVSSGGGGSGGGGSGGGGSGGG
GSEVQLLESGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSS
ISGSGDYIYYADSVKGRFTISRDISKNTLYLQMNSLRAEDTAVYYCAKEGTG
ANSSLADYRGQGTILTVSS (SEQ ID NO: 97)
```

[00423] 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.

[00424] In some embodiments, the antigen binding domain comprises a combinations of VH and VL sequences as provided in the table below.

Exemplary combinations of BCMA-FCRL5 VH and VL sequences				
SEQ ID NO	Target	Domain(s)	Sequence	
92	BCMA and FCRL5	BCMA VH – FCRL5 VH – FCRL5 VL	EVQLLES GGG LVQP GGS LRLS CAAS GFT FSS YAM SWVR QAP GKGLEWVSSISGSGDYIYYADSVKGRFTISRDISKNTLYLQ MNSLRAEDTAVYYCAKEGTGANSS LADYRGQGT LVT VSSGG GGSGGGSGGGSGGGGSEVQLVESGPGLVKPS ETL SLTCT VSGFSLTRFGVHWVRQPPGKGLEWLGVIWRGGSTDYNAAFV SRLTISKDNSKNQVSLKLSSVTAADTAVYYCSNHYYGSSDY ALDNWGQGT LVT VSSGGGGSGGGSGGGGSDIQMTQSPSSL SASVGDRVTITCKASQDVRNLVWFQ QKPGKAPKLLIYSGS YRYSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQHYS PPYTFGQGTKVEIK	
93	BCMA and FCRL5	FCRL5 VL – BCMA VH – FCRL5 VH	DIQMTQSPSSLSASVGDRVTITCKASQDVRNLVWFQ QKPG KAPKLLIYSGSYRYSGVPSRFSGSGSGTDFTLTISLQPED FATYYCQQHYSPPYTFGQGTKVEIKGGGGSGGGSGGGGSE VQLLES GGG LVQP GGS LRLS CAAS GFT FSS YAM SWVR QAPG KGLEWVSSISGSGDYIYYADSVKGRFTISRDISKNTLYLQM NSLRAEDTAVYYCAKEGTGANSS LADYRGQGT LVT VSSGGG GSGGGSGGGSGGGGSEVQLVESGPGLVKPS ETL SLTCTV SGFSLTRFGVHWVRQPPGKGLEWLGVIWRGGSTDYNAAFVS RLTISKDNSKNQVSLKLSSVTAADTAVYYCSNHYYGSSDYA LDNWGQGT LVT VSS	
96	BCMA and FCRL5	FCRL5 VH – FCRL5 VL – BCMA VH	EVQLVESGPGLVKPS ETL SLTCTVSGFSLTRFGVHWVRQPP GKGLEWLGVIWRGGSTDYNAAFVSRLTISKDNSKNQVSLKL SSVTAADTAVYYCSNHYYGSSDYALDNWGQGT LVT VSSGGG GSGGGSGGGSGGGGSEVQLLES GGG LVQP GGS LRLS CA SGFT FSS YAM SWVR QAPGKGLEWVSSISGSGDYIYYADSVK GRFTISRDISKNTLYLQMNSLRAEDTAVYYCAKEGTGANSS LADYRGQGT LVT VSSGGGGSGGGSGGGGSDIQMTQSPSSL SASVGDRVTITCKASQDVRNLVWFQ QKPGKAPKLLIYSGS	

Exemplary combinations of BCMA-FCRL5 VH and VL sequences				
SEQ ID NO	Target	Domain(s)	Sequence	
			YRYSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQHYSPPYTFGQGTKVEIK	
97	BCMA and FCRL5	FCRL5 VL – FCRL5 VH – BCMA VH	DIQMTQSPSSLSASVGDRVTITCKASQDVRNLVVWFQQKPGKAPKLLIYSGSYRYSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQHYSPPYTFGQGTKVEIKGGGGSGGGSGGGGSEVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSSISGSGDYIYYADSVKGRFTISRDISKNTLYLQMNSLRAEDTAVYYCAKEGTGANSSLADYRGQGTILVTVSSGGGGSGGGSGGGGSEVQLVESGPGLVKVPSETLSLTCTVSGFSLTRFGVHWVRQPPGKGLEWLGVIWRGGSTDYNAAFVSRLTISKDNSKNQVSLKLSSVTAADTAVYYCSNHYYGSSDYALDNWGQGTLVTVSS	

[00425] 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 CAR comprises 1G7.v85 in L-H orientation disclosed in Application No US10323094B2, which is hereby incorporated by reference in its entirety. 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: 105, or any value or range in-between.

EVQLVESGPGLVKPSETLSLTCTVSGFSLTRFGVHWVRQPPGKGLEWLGVIWRGGSTDYNAAFVSRLTISKDNSKNQVSLKLSSVTAADTAVYYCSNHYYGSSDYALDNWGQGTLVTVSS

(SEQ ID NO: 105)

[00426] In some embodiments, the V_H domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 105. In some embodiments, the V_H domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 105. In some embodiments, the V_H domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 105. In some embodiments, the V_H domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 105. In some embodiments, the V_H domain comprises an amino acid sequence having the sequence of SEQ ID NO: 105.

[00427] 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: 106, or any value or range in-between.

DTQMTQSPSSLSASVGDRTITCKASQDVRNLVVWFQKQPGKAPKLLIYSGS
YRYSGVPSRFSGSGSGTDFTLTISSLPEDFATYYCQQHYSPPYTFGQGTKV
EIK (SEQ ID NO: 106)

[00428] In some embodiments, the V_L domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 106. In some embodiments, the V_L domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 106. In some embodiments, the V_L domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 106. In some embodiments, the V_L domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 106. In some embodiments, the V_L domain comprises an amino acid sequence having the sequence of SEQ ID NO: 106.

[00429] 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: 105, 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: 106. 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: 105, and comprises a V_L having at least 90% identity to SEQ ID NO: 106. 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: 105, and comprises a V_L having at least 95% identity to SEQ ID NO: 106. 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: 105, and comprises a V_L having at least 98% identity to SEQ ID NO: 106. 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: 105, and comprises a V_L having at least 99% identity to SEQ ID NO: 106. 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: 105, and comprises a V_L having the sequence of SEQ ID NO: 106. 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: 105, 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: 106. 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: 105, 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: 106. 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: 105, 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: 106. 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: 105, 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: 106. 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: 105, 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: 106. 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: 105, and comprises a V_L having at least 90% identity to SEQ ID NO: 106. 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: 105, and comprises a V_L having at least 90% identity to SEQ ID NO: 106. 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: 105, and comprises a V_L having at least 95% identity to SEQ ID NO: 106. 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: 105, and comprises a V_L having at least 95% identity to SEQ ID NO: 106. 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: 105, and comprises a V_L having at least 98% identity to SEQ ID NO: 106. 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: 105, and comprises a V_L having at least 99% identity to SEQ ID NO: 106. 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: 105, and comprises a V_L having an amino acid sequence of SEQ ID NO: 106.

[00430] 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: 105, 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: 106. 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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DIQMTQSPSSLSASVGDRVTITCKASQDVRNLVWFQQKPGKAPKLLIYSGS
YRYSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQHYSPPYTFGQGTKV
EIKGGGGSGGGGSGGGGSEVQLVESGPGLVKPSSETLSLTCTVSGFSLTRFGV
HWVRQPPGKGLEWLGVIWRGGSTDYNAAFVSRLTISKDNSKNQVSLKLSSVT
AADTAVYYCSNHYYGSSDYALDNWGQGTTLVTVSS (SEQ ID NO: 107)
```

[00431] 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: 107. 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: 107. 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: 107. 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: 107. 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: 107. In some embodiments, the antigen-binding domain of the CAR comprises the amino acid sequence of SEQ ID NO: 107.

[00432] 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: 106, 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: 105. 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:

```
EVQLVESGPGLVKPSETLSLTCTVSGFSLTRFGVHWVRQPPGKGLEWLGVIW
RGGSTDYNAAFVSRLTISKDNSKNQVSLKLSSVTAADTAVYYCSNHYYGSSD
YALDNWGQGTLVTVSSGGGGSGGGSGGGSDIQMTQSPSSLSASVGDRTI
TCKASQDVRNLLVWFQQKPGKAPKLLIYSGSYRYSGVPSRFSGSGSDFTL
TISSLQPEDFATYYCQQHYSPPYTFGQGTKVEIK (SEQ ID NO: 108)
```

[00433] 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: 108. 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: 108. 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: 108. 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: 108. 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: 108. In some embodiments, the antigen-binding domain of the CAR comprises the amino acid sequence of SEQ ID NO: 108.

[00434] 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 CAR comprises 1G7.v85 in H-L orientation disclosed in Application No US10323094B2 hereby incorporated by reference in its entirety. 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: 109, or any value or range in-between.

```
EVQLVESGPGLVKPSETLSLTCTVSGFSLTRFGVHWVRQPPGKGLEWLGVIW
RGGSTDYNAAFVSRLTISKDNSKNQVSLKLSSVTAADTAVYYCSNHYYGSSD
YALDNWGQGTLVTVSS (SEQ ID NO: 109)
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[00435] In some embodiments, the V_H domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 109. In some embodiments, the V_H domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 109. In some embodiments, the V_H domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 109. In some embodiments, the V_H domain comprises an amino acid sequence having at least

99% identity to SEQ ID NO: 109. In some embodiments, the VH domain comprises an amino acid sequence having the sequence of SEQ ID NO: 109.

[00436] In some embodiments, the VL 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: 110, or any value or range in-between.

DIQMTQSPSSLSASVGDRVTITCKASQDVRNLVWFQQKPKAPKLLIYSGS
YRYSQVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQHYSPPYTFGQGTKV
EIK (SEQ ID NO: 110)

[00437] In some embodiments, the VL domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 110. In some embodiments, the VL domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 110. In some embodiments, the VL domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 110. In some embodiments, the VL domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 110. In some embodiments, the VL domain comprises an amino acid sequence having the sequence of SEQ ID NO: 110.

[00438] In some embodiments, the antigen-binding domain of the CAR comprising a VH domain and a VL domain comprises a VH 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: 109, and comprises a VL 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: 110. In some embodiments, the antigen-binding domain of the CAR comprising a VH domain and a VL domain comprises a VH 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: 109, and comprises a VL having at least 90% identity to SEQ ID NO: 110. In some embodiments, the antigen-binding domain of the CAR comprising a VH domain and a VL domain comprises a VH 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: 109, and comprises a VL having at least 95% identity to SEQ ID NO: 110. In some embodiments, the antigen-binding domain of the CAR comprising a VH domain and a VL domain comprises a VH 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: 109, and comprises a VL having at least 98% identity to SEQ ID NO: 110. In some embodiments, the antigen-binding domain of the CAR comprising a VH domain and a VL domain comprises a VH 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: 109, and comprises a VL having at least 99% identity to SEQ ID NO: 110. In some embodiments, the antigen-binding domain of the CAR comprising a VH domain and a VL domain comprises a VH 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: 109, and comprises a VL having the sequence of SEQ ID NO: 110. In some embodiments, the antigen-binding domain of the CAR comprising a VH domain and a VL domain comprises a VH domain having at least 90% identity to SEQ ID NO: 109, and comprises a VL 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: 110. In some embodiments, the antigen-binding domain of the CAR comprising a VH domain and a VL domain comprises a VH domain having at least 95% identity to SEQ ID NO: 109, and comprises a VL 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: 110. In some embodiments, the antigen-binding domain of the CAR comprising a VH domain and a VL domain comprises a VH domain having at least 98% identity to SEQ ID NO: 109, and comprises a VL 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: 110. In some embodiments, the antigen-binding domain of the CAR comprising a VH domain and a VL domain comprises a VH domain having at least 99% identity to SEQ ID NO: 109, and comprises a VL 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: 110. In some embodiments, the antigen-binding domain of the CAR comprising a VH domain and a VL domain comprises a VH domain having an amino acid sequence of SEQ ID NO: 109, and comprises a VL 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: 110. In some embodiments, the antigen-binding domain of the CAR comprising a VH domain and a VL domain comprises a VH domain having at least 90% identity to SEQ ID NO: 109, and comprises a VL having at least 90% identity to SEQ ID NO: 110. In some embodiments, the antigen-binding domain of the CAR comprising a VH domain and a VL domain comprises a VH domain having at least 95% identity to SEQ ID NO: 109, and comprises a VL having at least 90% identity to SEQ ID NO: 110. In some embodiments, the antigen-binding domain of the CAR comprising a VH domain and a VL domain comprises a VH domain having at least 90% identity to SEQ ID NO: 109, and comprises a VL having at least 95% identity to SEQ ID NO: 110. In some embodiments, the antigen-binding domain of the CAR comprising a VH

domain and a VL domain comprises a VH domain having at least 95% identity to SEQ ID NO: 109, and comprises a VL having at least 95% identity to SEQ ID NO: 110. In some embodiments, the antigen-binding domain of the CAR comprising a VH domain and a VL domain comprises a VH domain having at least 98% identity to SEQ ID NO: 109, and comprises a VL having at least 98% identity to SEQ ID NO: 110. In some embodiments, the antigen-binding domain of the CAR comprising a VH domain and a VL domain comprises a VH domain having at least 99% identity to SEQ ID NO: 109, and comprises a VL having at least 99% identity to SEQ ID NO: 110. In some embodiments, the antigen-binding domain of the CAR comprising a VH domain and a VL domain comprises a VH domain having an amino acid sequence of SEQ ID NO: 109, and comprises a VL having an amino acid sequence of SEQ ID NO: 110.

[00439] In some embodiments, the antigen-binding domain of the CAR comprises a formula of VH-Z-VL, wherein VH is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 109, Z is a linker comprising the amino acid sequence GGGSGGGSGGGGS (SEQ ID NO: 91), and VL is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 110. In some embodiments, the antigen-binding domain of the CAR comprising a formula of VH-Z-VL has an amino acid sequence as set forth below:

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EVQLVESGPGGLVKPSETLSLTCTVSGFSLTRFGVHWVRQPPGKGLEWLGVIW
RGGSTDYNAAFVSRLTISKDNSKNQVSLKLSSVTAADTAVYYCSNHYYGSSD
YALDNWGQGTLVTVSSGGGGSGGGSGGGGSDIQMTQSPSSLSASVGDRTI
TCKASQDVRNLVWFQKPKGKAPKLLIYSGSYRYSGVPSRFSGSGSGTDFTL
TISSLQPEDFATYYCQQHYSPPYTFGQGTKVEIK (SEQ ID NO: 111)
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[00440] 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: 111. 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: 111. 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: 111. 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: 111. 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: 111. In

some embodiments, the antigen-binding domain of the CAR comprises the amino acid sequence of SEQ ID NO: 111.

[00441] In some embodiments, the antigen-binding domain of the CAR comprises a formula of VL-Z-VH, wherein VL is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 110, Z is a linker comprising the amino acid sequence GGGGSGGGGSGGGGS (SEQ ID NO: 91), and VH is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 109. In some embodiments, the antigen-binding domain of the CAR comprising a formula of VL-Z-VH has an amino acid sequence as set forth below:

```
DIQMTQSPSSLSASVGDRVTITCKASQDVRNLVWFQQKPGKAPKLLIYSGS
YRYSQVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQHYSPPYTFGGQTKV
EIKGGGSGGGGSGGGGSEVQLVESGPGLVKPSSETLSLTCTVSGFSLTRFGV
HWVRQPPGKGLEWLGVIWRGGSTDYNAFVSRLTISKDNSKNQVSLKLSSVT
AADTAVYYCSNHYYGSSDYALDNWGQGTLLTVSS (SEQ ID NO: 112)
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[00442] 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: 112. 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: 112. 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: 112. 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: 112. 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: 112. In some embodiments, the antigen-binding domain of the CAR comprises the amino acid sequence of SEQ ID NO: 112.

[00443] 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: 114, or any value or range in-between.

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EVQLVESGGGLVQPGPGRSLRLSCAASGFTTFNDYAMHWVRQAPGKGLEWVSTIS
WNSGSIGYADSVKGRFTISRDNAKKSLYLQMNSLR AEDTALYYCAKDIQYGN
YYYGMDVWGQGTITVTVSS (SEQ ID NO: 114)
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[00444] In some embodiments, the V_H domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 114. In some embodiments, the V_H domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 114. In some embodiments, the V_H domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 114. In some embodiments, the V_H domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 114. In some embodiments, the V_H domain comprises an amino acid sequence having the sequence of SEQ ID NO: 114.

[00445] 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: 115, or any value or range in-between.

EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDAS
NRATGIPARFSGSGSGTDFTLTISLLEPEDFAVYYCQQRSNWPITFGQGTRL
EIK (SEQ ID NO: 115)

[00446] In some embodiments, the V_L domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 115. In some embodiments, the V_L domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 115. In some embodiments, the V_L domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 115. In some embodiments, the V_L domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 115. In some embodiments, the V_L domain comprises an amino acid sequence having the sequence of SEQ ID NO: 115.

[00447] 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: 114, 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: 115. 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: 114, and comprises a V_L having at least 90% identity to SEQ ID NO: 115. 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: 114, and comprises a V_L having at least 95% identity to SEQ ID NO: 115. 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: 114, and comprises a V_L having at least 98% identity to SEQ ID NO: 115. 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: 114, and comprises a V_L having at least 99% identity to SEQ ID NO: 115. 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: 114, and comprises a V_L having the sequence of SEQ ID NO: 115. 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: 114, 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: 115. 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: 114, 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: 115. 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: 114, 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: 115. 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: 114, 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: 115. 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: 114, 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: 115. 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: 114, and comprises a V_L having at least 90% identity to SEQ ID NO: 115. 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: 114, and comprises a V_L having at least 90%

identity to SEQ ID NO: 115. 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: 114, and comprises a V_L having at least 95% identity to SEQ ID NO: 115. 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: 114, and comprises a V_L having at least 95% identity to SEQ ID NO: 115. 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: 114, and comprises a V_L having at least 98% identity to SEQ ID NO: 115. 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: 114, and comprises a V_L having at least 99% identity to SEQ ID NO: 115. 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: 114, and comprises a V_L having an amino acid sequence of SEQ ID NO: 115.

[00448] 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: 114, 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: 115. 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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EVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVSTIS
WNSGSIGYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYCAKDIQYGN
YYYGMDVWGQGTITVTVSSGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERA
TLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDF
TLTISSLEPEDFAVYYCQQRSNWPITFGQGRLEIK (SEQ ID NO: 116)
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[00449] 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: 116. 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: 116. 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: 116. 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: 116. 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: 116. In some embodiments, the antigen-binding domain of the CAR comprises the amino acid sequence of SEQ ID NO: 116.

[00450] 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: 115, 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: 114. 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:

```
EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDAS
NRATGIPARFSGSGGTDFTLTISSLEPEDFAVYYCQQRSNWPITFGQGTRL
EIKGGGSGGGGSGGGGSEVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAM
HWVRQAPGKGLEWVSTISWNSGSIGYADSVKGRFTISRDNAKKSLYLQMNSL
RAEDTALYYCAKDIQYGNYYYGMDVWGQGTITVTVSS (SEQ ID NO: 117)
```

[00451] 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: 117. 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: 117. 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: 117. 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: 117. 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: 117. In some embodiments, the antigen-binding domain of the CAR comprises the amino acid sequence of SEQ ID NO: 117.

[00452] In some embodiments, the antigen binding domain comprises a V_H and/or a V_L as provided in the table below.

Exemplary CD20 VH and VL sequences				
SEQ ID NO	Target	Domain(s)	Sequence	
114	CD20	VH	EVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVSTISWNSGSIQYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYCAKDIQYGNYYYGMDVWGQGTITVTVSS	
115	CD20	VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRTGIPARFSGSGSGTDFTLTITSSLEPEDFAVYYCQQRSNWPITFGQGTRLEIK	
116	CD20	VH-linker-VL	EVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVSTISWNSGSIQYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYCAKDIQYGNYYYGMDVWGQGTITVTVSSGGGGSGGGSGGGSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRTGIPARFSGSGSGTDFTLTITSSLEPEDFAVYYCQQRSNWPITFGQGTRLEIK	
117	CD20	VL-linker-VH	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRTGIPARFSGSGSGTDFTLTITSSLEPEDFAVYYCQQRSNWPITFGQGTRLEIKGGGGSGGGSGGGSEVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVSTISWNSGSIQYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYCAKDIQYGNYYYGMDVWGQGTITVTVSS	

[00453] 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 antigen-binding domain comprises M971 domain disclosed in Application Nos US8591889B2, US9279019B2, US9598492B2, US10494435 and PMID 20065646, which are hereby incorporated by reference in entirety. 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: 118, or any value or range in-between.

QVQLQQSGPGLVKPSQTLSTCAISGDSVSSNSAAWNWIRQSPSRGLEWLGR
TYYRSKQWYNDYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYYCAREVT
GDLEDAFDIWGQGTMTVTVSS (SEQ ID NO: 118)

[00454] In some embodiments, the V_H domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 118. In some embodiments, the V_H domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 118. In some embodiments, the V_H domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO:

118. In some embodiments, the V_H domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 118. In some embodiments, the V_H domain comprises an amino acid sequence having the sequence of SEQ ID NO: 118.

[00455] 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: 119, or any value or range in-between.

DIQMTQSPSSLSASVGDRVTITCRASQTIWSYLNWYQQRPKGAPNLLIYAAS
SLQSGVPSRFSGRGSGTDFTLTIISSLQAEDFATYYCQQSYISIPQTFGGGTKL
EIK (SEQ ID NO: 119)

[00456] In some embodiments, the V_L domain comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 119. In some embodiments, the V_L domain comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 119. In some embodiments, the V_L domain comprises an amino acid sequence having at least 98% identity to SEQ ID NO: 119. In some embodiments, the V_L domain comprises an amino acid sequence having at least 99% identity to SEQ ID NO: 119. In some embodiments, the V_L domain comprises an amino acid sequence having the sequence of SEQ ID NO: 119.

[00457] 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: 118, 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: 119. 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: 118, and comprises a V_L having at least 90% identity to SEQ ID NO: 119. 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: 118, and comprises a V_L having at least 95% identity to SEQ ID NO: 119. 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: 118, and comprises a V_L having at least 98% identity to SEQ ID NO: 119. 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: 118, 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: 118, and comprises a V_L having at least 99% identity to SEQ ID NO: 119. 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: 118, and comprises a V_L having the sequence of SEQ ID NO: 119. 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: 118, 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: 119. 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: 118, 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: 119. 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: 118, 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: 119. 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: 118, 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: 119. 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: 118, 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: 119. 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: 118, and comprises a V_L having at least 90% identity to SEQ ID NO: 119. 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: 118, and comprises a V_L having at least 90% identity to SEQ ID NO: 119. 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: 118, and comprises a V_L having at least 95% identity to SEQ ID NO: 119. 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: 118, and comprises a V_L having at least 95% identity to SEQ ID NO: 119. 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: 118, and comprises a V_L having at least 98% identity to SEQ ID NO: 119. 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: 118, and comprises a V_L having at least 99% identity to SEQ ID NO: 119. 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: 118, and comprises a V_L having an amino acid sequence of SEQ ID NO: 119.

[00458] 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: 118, 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: 119. 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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VQVLQQSGPGLVKPSQTLSTCAISGDSVSSNSAAWNWIRQSPSRGLEWLGR
TYYSKQWYNDYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYYCAREVT
GDLEDAFDIWGQGTMTVTSSGGGSGGGGSGGGGSDIQMTQSPSSLSASVGD
RVTITCRASQTIWSYLNWYQQRPGKAPNLLIYAASSLQSGVPSRFSGRGSGT
DFTLTISSLQAEDFATYYCQQSYSIPQTFGQGTKLEIK (SEQ ID NO:
120)

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[00459] 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: 120. 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: 120. 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: 120. 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: 120. 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: 120. In some embodiments, the antigen-binding domain of the CAR comprises the amino acid sequence of SEQ ID NO: 120.

[00460] 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: 119, 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: 118. 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:

DIQMTQSPSSLSASVGDRVTITCRASQTIWSYLNWYQQRPGKAPNLLIYAAS
SLQSGVPSRFSGRSGTDFTLTISSLQAEDFATYYCQQSYSIPQTFGGGTKL
EIKGGGSGGGGSGGGGSQVQLQQSGPGLVKPSQTLTLTCAISGDSVSSNSA
AWNWIRQSPSRGLEWLGRTYYRSKWYNDYAVSVKSRITINPDTSKNQFSLQL
NSVTPEDTAVYYCAREVTGDLEDAFDIWGQGMVTVS (SEQ ID NO:
121)

[00461] 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: 121. 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: 121. 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: 121. 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: 121. 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: 121. In some embodiments, the antigen-binding domain of the CAR comprises the amino acid sequence of SEQ ID NO: 121.

[00462] In some embodiments, the antigen binding domain comprises a V_H and/or a V_L as provided in the table below.

Exemplary CD22 V _H and V _L sequences			
SEQ ID NO	Target	Domain(s)	Sequence
118	CD22	V _H	QVQLQQSGPGLVKPSQTLTLTCAISGDSVSSNSAAWNWIRQ SPSRGLEWLGRTYYRSKWYNDYAVSVKSRITINPDTSKNQF SLQLNSVTPEDTAVYYCAREVTGDLEDAFDIWGQGMVTVS S

Exemplary CD22 VH and VL sequences				
SEQ ID NO	Target	Domain(s)	Sequence	
119	CD22	VL	DIQMTQSPSSLSASVGDRVTITCRASQTIWSYLNWYQQRPGKAPNLLIYAASSLQSGVPSRFSGRGSGTDFTLTISSLQAEDFATYYCQQSYSIPQTFGQGTKLEIK	
120	CD22	VH-linker-VL	QVQLQQSGPGLVKPSQTLSTCAISGDSVSSNSAAWNWIRQSPSRGLEWLGRTYYRSKWYNDYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYYCAREVTGDLEDAFDIWGQGTMTVSSGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQTIWSYLNWYQQRPGKAPNLLIYAASSLQSGVPSRFSGRGSGTDFTLTISSLQAEDFATYYCQQSYSIPQTFGQGTKLEIK	
121	CD22	VL-linker-VH	DIQMTQSPSSLSASVGDRVTITCRASQTIWSYLNWYQQRPGKAPNLLIYAASSLQSGVPSRFSGRGSGTDFTLTISSLQAEDFATYYCQQSYSIPQTFGQGTKLEIKGGGSGGGGSGGGGSQLQLQQSGPGLVKPSQTLSTCAISGDSVSSNSAAWNWIRQSPSRGLEWLGRTYYRSKWYNDYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYYCAREVTGDLEDAFDIWGQGTMTVSSGGGSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQTIWSYLNWYQQRPGKAPNLLIYAASSLQSGVPSRFSGRGSGTDFTLTISSLQAEDFATYYCQQSYSIPQTFGQGTKLEIK	

[00463] In some embodiments, the antigen-binding domain of the tandem CAR comprises a formula of V_H -Z- V_L -ZZ- V_{H2} -Z- V_{L2} , wherein V_H is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 118, Z is a linker comprising the amino acid sequence GGGGSGGGGSGGGG (SEQ ID NO: 91), V_L is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 119, ZZ is a flexible linker comprising the amino acid sequence GGGGSGGGGSGGGGSGGGG (SEQ ID NO: 72), V_{H2} is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 114, and V_{L2} is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115. In some embodiments, the antigen-binding domain of the tandem CAR comprising a formula of V_H -Z- V_L -ZZ- V_{H2} -Z- V_{L2} has an amino acid sequence as set forth below:

QVQLQQSGPGLVKPSQTLSTCAISGDSVSSNSAAWNWIRQSPSRGLEWLGRTYYRSKWYNDYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYYCAREVTGDLEDAFDIWGQGTMTVSSGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTITCRASQTIWSYLNWYQQRPGKAPNLLIYAASSLQSGVPSRFSGRGSGTDFTLTISSLQAEDFATYYCQQSYSIPQTFGQGTKLEIKGGGSGGGGSGGGGSGGGGSEVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLWVSTISWNSGSIQYADSVKGRFTISRDNAKKSLYLQMNSLRRAEDTALYYCAKDIQYGNYYYGMDVWGQGTITVTVSSGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGS

SGGTDFTLTISLLEPEDFAVYYCQQRSNWPITFGQGTRLEIK (SEQ ID NO: 122)

[00464] In some embodiments, the antigen-binding domain of the dual 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: 122. In some embodiments, the antigen-binding domain of the dual CAR comprises an amino acid sequence having at least 90% identity to a sequence of SEQ ID NO: 122. In some embodiments, the antigen-binding domain of the dual CAR comprises an amino acid sequence having at least 95% identity to a sequence of SEQ ID NO: 122. In some embodiments, the antigen-binding domain of the dual CAR comprises an amino acid sequence having at least 98% identity to a sequence of SEQ ID NO: 122. In some embodiments, the antigen-binding domain of the dual CAR comprises an amino acid sequence having at least 99% identity to a sequence of SEQ ID NO: 122. In some embodiments, the antigen-binding domain of the dual CAR comprises the amino acid sequence of SEQ ID NO: 122.

[00465] In some embodiments, the antigen-binding domain of the tandem CAR comprises a formula of V_L -Z- V_H -ZZ- V_{L2} -Z- V_{H2} , wherein V_H is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 118, Z is a linker comprising the amino acid sequence GGGGSGGGGSGGGG (SEQ ID NO: 91), V_L is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 119, ZZ is a flexible linker comprising the amino acid sequence GGGGSGGGGSGGGGSGGGG (SEQ ID NO: 72), V_{H2} is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 114, and V_{L2} is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115. In some embodiments, the antigen-binding domain of the tandem CAR comprising a formula of V_L -Z- V_H -ZZ- V_{L2} -Z- V_{H2} has an amino acid sequence as set forth below:

DIQMTQSPSSLSASVGDRVTITCRASQTIWSYLNWYQQRPGKAPNLLIYAAS
SLQSGVPSRFSGRSGTDFLTITISLQAEDEFATYYCQQSYIPQTFGGGTKL
EIKGGGGSGGGGSGGGGSGVQLQQSGPGLVKPSQTLSTCAISGDSVSSNSA
AWNIRQSPSRGLEWLGRTYYRSKYNDYAVSVKSRITINPDTSKNQFSLQL
NSVTPEDTAVYYCAREVTGDLEDAFDIWGQGMVTVSSGGGGSGGGGSGGGG
SGGGGSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRL
LIYDASNRATGIPARFSGSGTDFLTITISLLEPEDFAVYYCQQRSNWPITF
GQGTRLEIKEVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGK
GLEWVSTISWNSGSGIGYADSVKGRFTISRDAKKSLEYLQMNSLRAEDTALYY
CAKDIQYGNYYYGMDVWGQGTITVTVSS (SEQ ID NO: 123)

[00466] In some embodiments, the antigen-binding domain of the dual 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: 123. In some embodiments, the antigen-binding domain of the dual CAR comprises an amino acid sequence having at least 90% identity to a sequence of SEQ ID NO: 123. In some embodiments, the antigen-binding domain of the dual CAR comprises an amino acid sequence having at least 95% identity to a sequence of SEQ ID NO: 123. In some embodiments, the antigen-binding domain of the dual CAR comprises an amino acid sequence having at least 98% identity to a sequence of SEQ ID NO: 123. In some embodiments, the antigen-binding domain of the dual CAR comprises an amino acid sequence having at least 99% identity to a sequence of SEQ ID NO: 123. In some embodiments, the antigen-binding domain of the dual CAR comprises the amino acid sequence of SEQ ID NO: 123.

[00467] In some embodiments, the antigen-binding domain of the tandem CAR comprises a formula of $V_H\text{-}Z\text{-}V_L\text{-}ZZ\text{-}V_{H2}\text{-}Z\text{-}V_{L2}$, wherein V_H is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 114, Z is a linker comprising the amino acid sequence GGGGSGGGGSGGGG (SEQ ID NO: 91), V_L is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115, ZZ is a flexible linker comprising the amino acid sequence GGGGSGGGGSGGGGSGGGG (SEQ ID NO: 72), V_{H2} is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 118, and V_{L2} is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 119. In some embodiments, the antigen-binding domain of the tandem CAR comprising a formula of $V_H\text{-}Z\text{-}V_L\text{-}ZZ\text{-}V_{H2}\text{-}Z\text{-}V_{L2}$ has an amino acid sequence as set forth below:

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EVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVSTIS
WNSGSIGYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYCAKDIQYGN
YYYGMDVWGQGTITVTVSSGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERA
TLSCRASQSVSSYLAWYQQKPGQAPRLIYDASNRATGIPARFSGSGSGTDF
TLTISSLEPEDFAVYYCQQRSNWPITFGQGTREIKGGGSGGGGSGGGGSG
GGGSQVQLQQSGPGLVKPSQTLSTCAISGDSVSSNSAAWNWIRQSPSRGLE
WLGRTYYRSKWYNDYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYYCA
REVTGDLDAFDIWGQGTMTVTVSSGGGSGGGGSGGGGSDIQMTQSPSSLSA
SVGDRVTITCRASQTIWSYLNWYQQRPGKAPNLLIYAASSLQSGVPSRFSGR
GSGTDFTLTISSLQAEDFATYYCQQSYIPQTFGQGTKLEIK (SEQ ID
NO: 124)
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[00468] In some embodiments, the antigen-binding domain of the dual 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: 124. In some embodiments, the antigen-binding domain of the dual CAR comprises an amino acid sequence having at least 90% identity to a sequence of SEQ ID NO: 124. In some embodiments, the antigen-binding domain of the dual CAR comprises an amino acid sequence having at least

95% identity to a sequence of SEQ ID NO: 124. In some embodiments, the antigen-binding domain of the dual CAR comprises an amino acid sequence having at least 98% identity to a sequence of SEQ ID NO: 124. In some embodiments, the antigen-binding domain of the dual CAR comprises an amino acid sequence having at least 99% identity to a sequence of SEQ ID NO: 124. In some embodiments, the antigen-binding domain of the dual CAR comprises the amino acid sequence of SEQ ID NO: 124.

[00469] In some embodiments, the antigen-binding domain of the tandem CAR comprises a formula of V_L -Z- V_H -ZZ- V_{L2} -Z- V_{H2} , wherein V_H is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 114, Z is a linker comprising the amino acid sequence GGGGSGGGGSGGGG (SEQ ID NO: 91), V_L is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 115, ZZ is a flexible linker comprising the amino acid sequence GGGGSGGGGSGGGGSGGGG (SEQ ID NO: 72), V_{H2} is a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 118, and V_{L2} is a light chain variable region comprising the amino acid sequence of SEQ ID NO: 119. In some embodiments, the antigen-binding domain of the tandem CAR comprising a formula of V_L -Z- V_H -ZZ- V_{L2} -Z- V_{H2} has an amino acid sequence as set forth below:

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DIQMTQSPSSLSASVGDRTITCRASQTIWSYLNWYQQRPGKAPNLLIYAAS
SLQSGVPSRFSGRGSQTDFTLTISSLQAEDFATYYCQQSYSPQTFGGQTKL
EIKGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGGSGGGG
AWNWIQSPSRGLEWLGRTYYRSKWYNDYAVSVKSRITINPDTSKNQFSLQL
NSVTPEDTAVYYCAREVTGDLEDAFDIWGGQTMVTVSGGGGSGGGGSGGGG
GGGGSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQKPGQAPRLL
IYDASNRAITGIPARFSGSGSGTDFTLTISLEPEDFAVYYCQQRNWPITFG
QGTRLEIGGGGSGGGGSGGGGSEVQLVESGGGLVQPGRSLRLSCAASGFTFN
DYAMHWVRQAPGKGLEWVSTISWNSGSIQYADSVKGRFTISRDNAKKSLYLQ
MNSLRAEDTALYYCAKDIQYGNYYYGMDVWGQGTITVTVS (SEQ ID NO:
125)
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[00470] In some embodiments, the antigen-binding domain of the dual 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: 125. In some embodiments, the antigen-binding domain of the dual CAR comprises an amino acid sequence having at least 90% identity to a sequence of SEQ ID NO: 125. In some embodiments, the antigen-binding domain of the dual CAR comprises an amino acid sequence having at least 95% identity to a sequence of SEQ ID NO: 125. In some embodiments, the antigen-binding domain of the dual CAR comprises an amino acid sequence having at least 98% identity to a sequence of SEQ ID NO: 125. In some embodiments, the antigen-binding domain of the dual CAR comprises an amino acid sequence having at least 99% identity to a sequence of SEQ ID

NO: 125. In some embodiments, the antigen-binding domain of the dual CAR comprises the amino acid sequence of SEQ ID NO: 125.

[00471] In some embodiments, the antigen-binding domain of the CAR comprises the antigen-binding domain of any one of rituximab, ocrelizumab, obinutuzumab, ofatumumab, ibritumomab tiuxetan, tositumomab, or ublituximab. In some embodiment, the antigen-binding domain comprises the antigen binding domain of rituximab. In some embodiment, the antigen-binding domain comprises the antigen binding domain of ofatumumab. In some embodiments, the CAR comprises the 4-1BB domain as well.

[00472] 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: 126:

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EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSSIS
GSGDYIYYADSVKGRFTISRDISKNTLYLQMNSLRAEDTAVYYCAKEGTGAN
SSLADYRGQGTTLTVSSSGLDFVPVFLPAKPTTTPAPRPPTPAPTIASQPLS
LRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCNHRN
KRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADA
PAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNEL
QKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
(SEQ ID NO: 126)
```

or is substantially similar to SEQ ID NO: 126, or is an active fragment of SEQ ID NO: 126. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 126. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 126. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 126. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 126.

[00473] 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: 145:

```
MALPVTALLLPLALLLHAARPGSEVQLLESGGGLVQPGGSLRLSCAASGFTF
SSYAMSWVRQAPGKGLEWVSSISGSGDYIYYADSVKGRFTISRDISKNTLYL
QMNSLRAEDTAVYYCAKEGTGANSSLADYRGQGTTLTVSSSGLDFVPVFLPA
KPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWA
PLAGTCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCS
CRFPEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRR
GRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQ
GLSTATKDTYDALHMQALPPR (SEQ ID NO: 145)
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or is substantially similar to SEQ ID NO: 145, or is an active fragment of SEQ ID NO: 145. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 145. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 145. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 145. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 145.

[00474] 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: 155:

```
GSEVQLLES GGGVLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSS
ISGSDYIYYADSVKGRFTISRDISKNTLYLQMNSLRAEDTAVYYCAKEGTG
ANSSLADYRGQGT LVTVSSSGLDFVPVFLPAKPTTTPAPRPPTPAPTIASQP
LSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCNH
RNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFEEEEGGCELRVKFSRSA
DAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYN
ELQKDKMAEAYSEIGMKGERRRGKGDGLYQGLSTATKDTYDALHMQALPPR
(SEQ ID NO: 155)
```

or is substantially similar to SEQ ID NO: 155, or is an active fragment of SEQ ID NO: 155. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 155. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 155. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 155. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 155.

[00475] 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: 127:

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EVQLLES GGGVLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSSIS
GSGDYIYYADSVKGRFTISRDISKNTLYLQMNSLRAEDTAVYYCAKEGTGAN
SSLADYRGQGT LVTVSSGGGSGGGGSGGGGSGGGGSEVQLVESGPGLVKPS
ETLSLTCTVSGFSLTRFGVHWVRQPPGKLEWLGVWIRGGSTDYNAAFVSRL
TISKDNSKNQVSLKLSSVTAADTAVYYCSNHYYGSSDYALDNWGQGT LVTVS
SGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRTITCKASQDVRLVWVF
QQKPGKAPKLLIYSGSYRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYC
QQHYSPPYTFGQGTKVEIKSGLDFVPVFLPAKPTTTPAPRPPTPAPTIASQP
LSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCNH
RNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFEEEEGGCELRVKFSRSA
DAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYN
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ELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR
(SEQ ID NO: 127)

or is substantially similar to SEQ ID NO: 127, or is an active fragment of SEQ ID NO: 127. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 127. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 127. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 127. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 127.

[00476] 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: 146:

MALPVTALLPLALLLHAARPGSEVQLLESGGGLVQPGGSLRLSCAASGFTF
SSYAMSWVRQAPGKLEWVSSIISGSDYIYYADSVKGRFTISRDISKNTLYL
QMNSLRAEDTAVYYCAKEGTGANSSLADYRGQGLVTVSSGGGGSGGGGSGG
GGSGGGSEVQLVESGPGLVKPSSETLSLTCTVSGFSLTRFGVHWVRQPPGKG
LEWLGVWRGGSTDYNAAFVSRLTISKDNSKNQVSLKLSSVTAADTAVYYCS
NHYYGSSDYALDNWGQGLVTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSA
SVGDRVTITCKASQDVRNLVWFQQKPGKAPKLLIYSGSYRYSRVPSRFSGS
GSGTDFTLTISSLQPEDFATYYCQHHYSPPYTFGQGTKVEIKSGLDFVPVFL
PAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAGGAVHTRGLDFACDIYI
WAPLAGTCGVLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDG
CSCRFPEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDK
RRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGL
YQGLSTATKDTYDALHMQALPPR (SEQ ID NO: 146)

or is substantially similar to SEQ ID NO: 146, or is an active fragment of SEQ ID NO: 146. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 146. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 146. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 146. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 146.

[00477] 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: 156:

GSEVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKLEWVSS
ISGSDYIYYADSVKGRFTISRDISKNTLYLQMNSLRAEDTAVYYCAKEGTG

ANSSLADYRGQGTTLVTVSSGGGGSGGGGSGGGGSEVQLVESGPGLVK
 PSETLSLTCTVSGFSLTRFGVHWVRQPPGKGLEWLGVIWRGGSTDYNAAFVS
 RLTIKDNKSNQVSLKLSSVTAADTAVYYCSNHYYGSSDYALDNWGQGTTLVT
 VSSGGGGSGGGGSGGGSDIQMTQSPSSLSASVGDRVTITCKASQDVRNLV
 WFQQKPGKAPKLLIYSGSYRYSVPSRFSGSGSGTDFTLTISLQPEDFATY
 YCQQHYSPPYTFGQGTKVEIKSGLDFVPVFLPAKPTTTPAPRPPTPAPTIAS
 QPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
 NHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSR
 SADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGKPRRKNPQEGLY
 NELQKDKMAEAYSEIGMKGERRRGKGGHDGLYQGLSTATKDTYDALHMQALP
 PR (SEQ ID NO: 156)

or is substantially similar to SEQ ID NO: 156, or is an active fragment of SEQ ID NO: 156. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 156. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 156. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 156. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 156.

[00478] 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:

DIQMTQSPSSLSASVGDRVTITCKASQDVRNLVWFQQKPGKAPKLLIYSGS
 YRYSVPSRFSGSGSGTDFTLTISLQPEDFATYCYCQQHYSPPYTFGQGTKV
 EIKGGGGSGGGGSGGGGSEVQLVESGPGLVKPSSETLSLTCTVSGFSLTRFGV
 HWVRQPPGKGLEWLGVIWRGGSTDYNAAFVSRLTIKDNKSNQVSLKLSSVT
 AADTAVYYCSNHYYGSSDYALDNWGQGTTLVTVSSGGGGSGGGGSGGGG
 GSEVQLLESGGGLVQPGGSLRLSCAASGFTTFSSYAMSWVRQAPGKGLEWVSS
 ISGSGDYIYYADSVKGRFTISRDISKNTLYLQMNSLRAEDTAVYYCAKEGTG
 ANSSLADYRGQGTTLVTVSSSGLDFVPVFLPAKPTTTPAPRPPTPAPTIASQP
 LSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCNH
 RNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSR
 SADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMGKPRRKNPQEGLYN
 ELQKDKMAEAYSEIGMKGERRRGKGGHDGLYQGLSTATKDTYDALHMQALPPR
 (SEQ ID NO: 128)

or is substantially similar to SEQ ID NO: 128, or is an active fragment of SEQ ID NO: 128. 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.

[00479] 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: 147:

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MALPVTALLLPLALLLHAARPGSDIQMTQSPSSLSASVGDRVTITCKASQDV
RNLVVWFQQKPGKAPKLLIYSGSYRYSRVPSRFSGSGSGTDFTLTISSLQPE
DFATYYCQQHYSPPYTFGQGTKVEIKGGGSGGGSGGGGSEVQLVESGPG
VKPSETLSLTCTVSGFSLTRFGVHWVRQPPGKGLEWLGVIWRGGSTDYNAAF
VSRLTISKDNSKNQVSLKLSVTAADTAVYYCSNHYYGSSDYALDNWGQGT
LVTVSSGGGSGGGSGGGSGGGGSEVQLLESGLVQPGGSLRLSCAASGF
TFSSYAMSWVRQAPGKLEWVSSISGSGDYIYYADSVKGRFTISRDISKNTL
YLQMNSLR AEDTAVYYCAKEGTGANS SLADYRGQGT LVTVSSSGLDFVPVFL
PAKPTTTPAPRPPTPAPT IASQPLSLRPEACRPAAGGAVHTRGLDFACDIYI
WAPLAGTCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDG
CSCRFP EEEEEGGCEL RVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVL
DKRRGRDP EMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRRGK
GHDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO: 147)
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or is substantially similar to SEQ ID NO: 147, or is an active fragment of SEQ ID NO: 147. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 147. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 147. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 147. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 147.

[00480] 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: 157:

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GSDIQMTQSPSSLSASVGDRVTITCKASQDV RNLVVWFQQKPGKAPKLLIYS
GSYRYSRVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQHYSPPYTFGQGT
KVEIKGGGSGGGSGGGGSEVQLVESGPGLVKPSETLSLTCTVSGFSLTRF
GVHWVRQPPGKGLEWLGVIWRGGSTDYNAAFVSRLTISKDNSKNQVSLKLS
VTAADTAVYYCSNHYYGSSDYALDNWGQGT LVTVSSGGGSGGGSGGGSG
GGGSEVQLLESGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKLEWV
SSISGSGDYIYYADSVKGRFTISRDISKNTLYLQMNSLR AEDTAVYYCAKEG
TGANS SLADYRGQGT LVTVSSSGLDFVPVFLPAKPTTTPAPRPPTPAPT IAS
QPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYC
NHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFP EEEEEGGCEL RVKFSR
SADAPAYQQGQNQLYNELNLGRREEYDVL DKRRGRDP EMGGKPRRKNPQEG
LYNELQKDKMAEAYSEIGMKGERRRRGK GHDGLYQGLSTATKDTYDALHMQAL
PPR (SEQ ID NO: 157)
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or is substantially similar to SEQ ID NO: 157, or is an active fragment of SEQ ID NO: 157. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 157. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 157. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 157. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 157.

[00481] 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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DIQMTQSPSSLSASVGDRVTITCKASQDVRNLVVWFQQKPGKAPKLLIYSGS
YRYSQVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQHYSPPYTFGQGTKV
EIKGGGSGGGGSGGGGSEVQLVESGPGLVKPSSETLSLTCTVSGFSLTRFGV
HWVRQPPGKGLEWLGVIWRGGSTDYNAAFVSRLTISKDNSKNQVSLKLSSVT
AADTAVYYCSNHYYGSSDYALDNWGQGTTLTVSSSSGLDFVPVFLPAKPTTTP
APRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTC
GVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEE
EEGGCELRVKFSRSADAPAYQQGNQLYNELNLGRREEYDVLDRGRDPPEM
GGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTAT
KDTYDALHMQALPPR (SEQ ID NO: 129)
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or is substantially similar to SEQ ID NO: 129, or is an active fragment of SEQ ID NO: 129. 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.

[00482] 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: 148:

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MALPVTALLLPLALLLHAARPGSDIQMTQSPSSLSASVGDRVTITCKASQDV
RNLVVWFQQKPGKAPKLLIYSGSYRYSQVPSRFSGSGSGTDFTLTISSLQPE
DFATYYCQQHYSPPYTFGQGTKVEIKGGGSGGGGSGGGGSEVQLVESGPGLV
VKPSSETLSLTCTVSGFSLTRFGVHWVRQPPGKGLEWLGVIWRGGSTDYNAAF
VSRLTISKDNSKNQVSLKLSSVTAADTAVYYCSNHYYGSSDYALDNWGQGTTL
VTVSSSSGLDFVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGG
AVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCNHRNKRGRKKLLYIFK
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QPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYQQGQNQLYN
 ELNLGRREEYDVLDKRRGRDPGEMGGKPRRKNPQEGLYNELQKDKMAEAYSEI
 GMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO:
 148)

or is substantially similar to SEQ ID NO: 148, or is an active fragment of SEQ ID NO: 148. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 148. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 148. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 148. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 148.

[00483] 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: 158:

GSDIQMTQSPSSLSASVGDRVTITCKASQDVRNLVVWFQQKPGKAPKLLIYS
 GSYRYSGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQHYSPPYTFGQGT
 KVEIKGGGGSGGGGSGGGGSEVQLVESGPGLVKPSSETLSLTCTVSGFSLTRF
 GVHWVRQPPGKGLEWLGVIWRGGSTDYNAAFVSRLTISKDNSKNQVSLKLSS
 VTAADTAVYYCSNHYYGSSDYALDNWGQGTTLTVSSSGLDFVPVFLPAKPTT
 TPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAG
 TCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRF
 EEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDP
 EMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLST
 ATKDTYDALHMQALPPR (SEQ ID NO: 158)

or is substantially similar to SEQ ID NO: 158, or is an active fragment of SEQ ID NO: 158. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 158. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 158. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 158. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 158.

[00484] 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: 130:

EVQLVESGPGLVKPSSETLSLTCTVSGFSLTRFGVHWVRQPPGKGLEWLGVIW
 RGGSTDYNAAFVSRLTISKDNSKNQVSLKLSSVTAADTAVYYCSNHYYGSSD
 YALDNWGQGTTLTVSSGGGGSGGGGSGGGGSDIQMTQSPSSLSASVGDRVTI

TCKASQDVRLVWVFQQKPGKAPKLLIYSGSYRYSRVPSRFSGSGSGTDFTL
 TISSLPEDFATYYCQQHYSPPYTFGQGTKVEIKSGLDFVPVFLPAKPTTTP
 APRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGTC
 GVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEE
 EGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEM
 GKGPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGDGLYQGLSTAT
 KDTYDALHMQALPPR (SEQ ID NO: 130)

or is substantially similar to SEQ ID NO: 130, or is an active fragment of SEQ ID NO: 130. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 130. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 130. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 130. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 130.

[00485] 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: 149:

MALPVTALLPLALLLHAARPGSEVQLVESGPGLVKPSSETLSLTCTVSGFSL
 TRFGVHWVRQPPGKGLEWLGVIWRGGSTDYNAAFVSRLTISKDNSKNQVSLK
 LSSVTAADTAVYYCSNHYYGSSDYALDNWGQGTILTVSSGGGSGGGGSGGG
 GSDIQMTQSPSSLSASVGDRVTITCKASQDVRLVWVFQQKPGKAPKLLIYS
 GSYRYSRVPSRFSGSGSGTDFTLTISSLPEDFATYYCQQHYSPPYTFGQGT
 KVEIKSGLDFVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGG
 AVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCNHRNKRGRKKLLYIFK
 QPFMRPVQTTQEEDGCSCRFPEEEGGCELRVKFSRSADAPAYQQGQNQLYN
 ELNLGRREEYDVLDKRRGRDPEMGKPRRKNPQEGLYNELQKDKMAEAYSEI
 GMKGERRRGKGDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO:
 149)

or is substantially similar to SEQ ID NO: 149, or is an active fragment of SEQ ID NO: 149. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 149. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 149. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 149. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 149.

[00486] 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: 159:

GSEVQLVESGPGGLVKPSETLSLTCTVSGFSLTRFGVHWVRQPPGKGLEWLGV
 IWRGGSTDYNAAFVSRLTISKDNSKNQVSLKLSSVTAADTAVYYCSNHYYGS
 SDYALDNWGQGTTLVTVSSGGGGSGGGGSDIQMTQSPSSLSASVGDRV
 TITCKASQDVRNLVVWFQKPGKAPKLLIYSGSYRYSVPSRFSGSGSGTDF
 TLTISSLQPEDFATYYCQQHYSPPYTFGQGTKEIKSGLDFVPVFLPAKPTT
 TPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAG
 TCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFP
 EEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDP
 EMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRRGKGGHDGLYQGLST
 ATKDITYDALHMQALPPR (SEQ ID NO: 159)

or is substantially similar to SEQ ID NO: 159, or is an active fragment of SEQ ID NO: 159. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 159. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 159. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 159. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 159.

[00487] 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: 131:

EVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVSTIS
 WNSGSIGYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYCAKDIQYGN
 YYYGMDVWGQGTITVTVSSGGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERA
 TLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDF
 TLTISSLEPEDFAVYYCQQRSNWPITFGQGTREIKSGLDFVPVFLPAKPTT
 TPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAG
 TCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFP
 EEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDP
 EMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRRGKGGHDGLYQGLST
 ATKDITYDALHMQALPPR (SEQ ID NO: 131)

or is substantially similar to SEQ ID NO: 131, or is an active fragment of SEQ ID NO: 131. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 131. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 131. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 131. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 131.

[00488] 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: 150:

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MALPVTALLPLALLLHAARPGSEVQLVESGGGLVQPGRSLRLSCAASGFTF
NDYAMHWVRQAPGKGLEWVSTISWNSGSIGYADSVKGRFTISRDNAKKSLYL
QMNSLRAEDTALYYCAKDIQYGNYYYGMDVWGQGTITVTVSSGGGGSGGGSG
GGGSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLI
YDASNRATGIPARFSGSGGTDFLTITSSLEPEDFAVYYCQQRSNWPITFGQ
GTRLEIKSGLDFVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAA
GGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCNHRNKRGRKKLLYI
FKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYQQGQNQL
YNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYS
EIGMKGERRRRGKGDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO:
150)
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or is substantially similar to SEQ ID NO: 150, or is an active fragment of SEQ ID NO: 150. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 150. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 150. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 150. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 150.

[00489] 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: 160:

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GSEVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVST
ISWNSGSIGYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYCAKDIQY
GNYYYGMDVWGQGTITVTVSSGGGGSGGGSGGGGSEIVLTQSPATLSLSPGE
RATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGGT
DFTLTITSSLEPEDFAVYYCQQRSNWPITFGQGTRLEIKSGLDFVPVFLPAK
PTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPL
AGTCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCR
FPEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGR
DPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRRGKGDGLYQGL
STATKDTYDALHMQALPPR (SEQ ID NO: 160)
```

or is substantially similar to SEQ ID NO: 160, or is an active fragment of SEQ ID NO: 160. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 160. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 160. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a

sequence of SEQ ID NO: 160. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 160.

[00490] 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: 132:

```
QVQLQQSGPGLVKPSQTLSTCAISGDSVSSNSAAWNWIRQSPSRGLEWLGR
TYYRSKWYNDYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYYCAREVT
GDLEDAFDIWGQGTMTVTSSGGGGSGGGSGGGSDIQMTQSPSSLSASVGD
RVTITCRASQTIWSYLNWYQQRPGKAPNLLIYAASSLQSGVPSRFSGRGSGT
DFTLTITSSSLQAEDFATYYCQSYSIPQTFGQGTKLEIKSGLDFVPVFLPAKP
TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPL
AGTCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCR
FPEEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGR
DPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKRGHDGLYQGL
STATKDTYDALHMQALPPR (SEQ ID NO: 132)
```

or is substantially similar to SEQ ID NO: 132, or is an active fragment of SEQ ID NO: 132. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 132. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 132. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 132. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 132.

[00491] 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: 151:

```
MALPVTALLLPLALLLHAARPGSQVQLQQSGPGLVKPSQTLSTCAISGDSV
SSNSAAWNWIRQSPSRGLEWLGRTYYRSKWYNDYAVSVKSRITINPDTSKNQ
FSLQLNSVTPEDTAVYYCAREVTGDLEDAFDIWGQGTMTVTSSGGGGSGGGG
SGGGGSDIQMTQSPSSLSASVGDRTTITCRASQTIWSYLNWYQQRPGKAPNL
LIYAASSLQSGVPSRFSGRGSGTDFTLTITSSSLQAEDFATYYCQSYSIPQTF
GQGTKLEIKSGLDFVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRP
AAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCNHRNKRGRKKLL
YIFKQPFMRPVQTTQEEDGCSCRFPEEEEEGGCELRVKFSRSADAPAYQQGQN
QLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEA
YSEIGMKGERRRGKRGHDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID
NO: 151)
```

or is substantially similar to SEQ ID NO: 151, or is an active fragment of SEQ ID NO: 151. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 151. In some embodiments, the CAR comprises an amino acid

sequence that is at least 95% identical to a sequence of SEQ ID NO: 151. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 151. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 151.

[00492] 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: 161:

```
GSQVQLQQSGPGLVKPSQTLSTCAISGDSVSSNSAAWNWIRQSPSRGLEWL
GRTYYRSKWYNDYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYYCARE
VTGDLEDAFDIWGQGTMTVTSSGGGSGGGSGGGSDIQMTQSPSSLSASV
GDRVTTITCRASQTIWSYLNWYQQRPGKAPNLLIYAASSLQSGVPSRFSGRGS
GTDFTLTITSSSLQAEDFATYYCQSYSIPQTFGQGTKLEIKSGLDFVPVFLPA
KPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWA
PLAGTCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCS
CRFPEEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRR
GRDPFEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRRGKGGHDGLYQ
GLSTATKDTYDALHMQALPPR (SEQ ID NO: 161)
```

or is substantially similar to SEQ ID NO: 161, or is an active fragment of SEQ ID NO: 161. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 161. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 161. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 161. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 161.

[00493] 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: 133:

```
DIQMTQSPSSLSASVGDRTTITCRASQTIWSYLNWYQQRPGKAPNLLIYAAS
SLQSGVPSRFSGRSGTDFTLTITSSSLQAEDFATYYCQSYSIPQTFGQGTKL
EIKGGGSGGGGSGGGGSQVQLQQSGPGLVKPSQTLSTCAISGDSVSSNSA
AWNWIRQSPSRGLEWLGRTYYRSKWYNDYAVSVKSRITINPDTSKNQFSLQL
NSVTPEDTAVYYCAREVTGDLEDAFDIWGQGTMTVTSSGLDFVPVFLPAKP
TTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAFL
AGTCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCR
FPEEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGR
DPFEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRRGKGGHDGLYQGL
STATKDTYDALHMQALPPR (SEQ ID NO: 133)
```

or is substantially similar to SEQ ID NO: 133, or is an active fragment of SEQ ID NO: 133. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 133. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 133. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 133. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 133.

[00494] 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: 152:

```
MALPVTALLLPLALLLHAARPGSDIQMTQSPSSLSASVGDRVTITCRASQTI
WSYLNWYQQRPGKAPNLLIYAASSLQSGVPSRFSGRGSGTDFTLTISSLQAE
DFATYYCQQSYSIPQTFGQGTKLEIKGGGSGGGGSGGGGSQVQLQQSGPGL
VKPSQTLSTCAISGDSVSSNSAAWNWIWIRQSPSRGLEWLGRTYYRSKWYNDY
AVSVKSRITINPDTSKNQFSLQNSVTPEDTAVYYCAREVTGDLEDAFDIWG
QGTMTVTVSSSGLDFVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRP
AAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCNHRNKRGRKKLL
YIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYQQGQN
QLYNELNLGRREEYDVLDRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEA
YSEIGMKGERRRRGKGDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID
NO: 152)
```

or is substantially similar to SEQ ID NO: 152, or is an active fragment of SEQ ID NO: 152. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 152. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 152. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 152. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 152.

[00495] 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: 162:

```
GSDIQMTQSPSSLSASVGDRVTITCRASQTIWSYLNWYQQRPGKAPNLLIYA
ASSLQSGVPSRFSGRGSGTDFTLTISSLQAE DFATYYCQQSYSIPQTFGQGT
KLEIKGGGSGGGGSGGGGSQVQLQQSGPGLVKPSQTLSTCAISGDSVSSN
SAAWNWIWIRQSPSRGLEWLGRTYYRSKWYNDYAVSVKSRITINPDTSKNQFSL
QLNSVTPEDTAVYYCAREVTGDLEDAFDIWGQGTMTVTVSSSGLDFVPVFLPA
KPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWA
PLAGTCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCS
CRFPEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDRR
```

GRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRRGKGHDLGYQ
GLSTATKDTYDALHMQALPPR (SEQ ID NO: 162)

or is substantially similar to SEQ ID NO: 162, or is an active fragment of SEQ ID NO: 162. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 162. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 162. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 162. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 162.

[00496] In some embodiments, the CAR is a Tandem CAR which 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: 134:

QVQLQQSGPGLVKPSQTLSTCAISGDSVSSNSAAWNWIQSPSRGLEWLGR
TYYSRSKWINDYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYYCAREVT
GDLEDAFDIWGQGTMTVTVSSGGGGSGGGSGGGGSDIQMTQSPSSLSASVGD
RVTITCRASQTIWSYLNWYQQRPGKAPNLLIYAASSLQSGVPSRFSGRSGT
DFTLTISLQAEDFATYYCQSYSIPQTFGQGTKLEIKGGGGSGGGSGGGG
SGGGGSEVQLVESGGGLVQPGSLRLSCAASGFTFNDYAMHWVRQAPGKGLE
WVSTISWNSGSIYADSVKGRFTISRDNAKKSLYLQMNSLRRAEDTALYYCAK
DIQYGNYYYGMDVWGQGTITVTVSSGGGGSGGGSGGGGSEIVLTQSPATLSL
SPGERATLSCRASQSVSSYLAWYQQKPGQAPRLIYDASNRATGIPARFSGS
GSGTDFTLTISLLEPEDFAVYYCQQRSNWPIITFGQGRLEIKSGLDVFPVFL
PAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYI
WAPLAGTCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDG
CSCRFPEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDK
RRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRRGKGHDL
YQGLSTATKDTYDALHMQALPPR (SEQ ID NO: 134)

or is substantially similar to SEQ ID NO: 134, or is an active fragment of SEQ ID NO: 134. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 134. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 134. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 134. In some embodiments, the Tandem CAR comprises an amino acid sequence of SEQ ID NO: 134.

[00497] In some embodiments, the CAR is a Tandem CAR which 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: 153:

MALPVTALLLPLALLLHAARPGSQVQLQQSGPGLVKPSQTLSTLCAISGDSV
SSNSAAWNWIRQSPSRGLEWLGRTYYRSKWYNDYAVSVKSRITINPDTSKNQ
FSLQLNSVTPEDTAVYYCAREVTGDLEDAFDIWGQGTMTVTVSSGGGSGGGG
SGGGGSDIQMTQSPSSLSASVGDRVITITCRASQTIWSYLNWYQQRPGKAPNL
LIYAASSLQSGVPSRFSGRSGTDFTLTISSLQAEDFATYYCQQSYSIPQTF
GQGTKLEIKGGGSGGGGSGGGGSGGGGSEVQLVESGGGLVQPGRSLRLSCA
ASGFTFNDYAMHWVRQAPGKLEWVSTISWNSGSIYADSVKGRFTISRDN
AKKSLYLQMNSLRAEDTALYYCAKDIQYGNYYYGMDVWGQGTITVTVSSGGGGS
GGGGSGGGGSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQ
APRLLIYDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNW
PITFGQGTREIKSGLDFVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPE
ACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLSLVITLYCNHRNKRGR
KKLLYIFKQPFMRPVQTTQEEDGCSCRFEEEEGGCELRVKFSRSADAPAYQ
QQQNQLYNELNLGRREEYDVLDRRGRDPEMGGKPRRKNPQEGLYNELQKDK
MAEAYSEIGMKGERRRGKGDGLYQGLSTATKDTYDALHMQALPPR (SEQ
ID NO: 153)

or is substantially similar to SEQ ID NO: 153, or is an active fragment of SEQ ID NO: 153. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 153. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 153. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 153. In some embodiments, the Tandem CAR comprises an amino acid sequence of SEQ ID NO: 153.

[00498] In some embodiments, the CAR is a Tandem CAR which 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: 163:

GSQVQLQQSGPGLVKPSQTLSTLCAISGDSVSSNSAAWNWIRQSPSRGLEWL
GRTYYRSKWYNDYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYYCARE
VTGDLEDAFDIWGQGTMTVTVSSGGGSGGGGSGGGGSDIQMTQSPSSLSASV
GDRVITITCRASQTIWSYLNWYQQRPGKAPNLLIYAASSLQSGVPSRFSGRGS
GTDFTLTISLQAEDFATYYCQQSYSIPQTFGQGTKLEIKGGGSGGGGSGG
GGSGGGGSEVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGK
LEWVSTISWNSGSIYADSVKGRFTISRDNAAKSLYLQMNSLRAEDTALYYC
AKDIQYGNYYYGMDVWGQGTITVTVSSGGGSGGGGSGGGGSEIVLTQSPATL
SLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARF
SFGSGTDFTLTISSLEPEDFAVYYCQQRSNWPITFGQGTREIKSGLDFVPV
FLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDI
YIWAPLAGTCGVLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEE
DGCSCRFEEEEGGCELRVKFSRSADAPAYQQQNQLYNELNLGRREEYDVL
DKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGD
GLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO: 163)

or is substantially similar to SEQ ID NO: 163, or is an active fragment of SEQ ID NO: 163. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 163. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 163. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 163. In some embodiments, the Tandem CAR comprises an amino acid sequence of SEQ ID NO: 163.

[00499] In some embodiments, the CAR is a Tandem CAR which 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: 135:

```
EVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVSTIS
WNSGSIGYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYCAKDIQYGN
YYYGMDVWGQGTITVTVSSGGGGSGGGSGGGGSEIVLTQSPATLSLSPGERA
TLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDF
TLTISSELEPEDFAVYYCQQRSNWPITFGQGRLEIKGGGGSGGGSGGGGSG
GGGSQVQLQQSGPGLVKPSQTLSTCAISGDSVSSNSAAWNWIRQSPSRGLE
WLGRYYRSKWYNDYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYYCA
REVTGDLDAFDIWGQGTMTVTVSSGGGGSGGGSGGGGSDIQMTQSPSSLSA
SVGDRVTITCRASQTIWSYLNWYQQRPGKAPNLLIYAASSLQSGVPSRFSGR
GSGTDFTLTISSLQAEDFATYYCQSYSIPQTFGQGTKLEIKSGLDVFPVFL
PAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYI
WAPLAGTCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDG
CSCRFPEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDK
RRGRDPEMGKPRRKNPQEGLYNELQDKMAEAYSEIGMKGERRRRGKGDGL
YQGLSTATKDTYDALHMQALPPR (SEQ ID NO: 135)
```

or is substantially similar to SEQ ID NO: 135, or is an active fragment of SEQ ID NO: 135. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 135. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 135. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 135. In some embodiments, the Tandem CAR comprises an amino acid sequence of SEQ ID NO: 135.

[00500] In some embodiments, the CAR is a Tandem CAR which 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: 154:

```
MALPVTALLLPLALLLHAARPGSEVQLVESGGGLVQPGRSLRLSCAASGFTF
NDYAMHWVRQAPGKGLEWVSTISWNSGSIGYADSVKGRFTISRDNAKKSLYL
QMNSLRAEDTALYYCAKDIQYGNYYYGMDVWGQGTITVTVSSGGGGSGGGSG
GGGSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLI
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YDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPITFGQ
 GTRLEIKGGGSGGGGSGGGGSGGGGSGVQLQQSGPGLVKPSQTLSTCAIS
 GDSVSSNSAAWNWIRQSPSRGLEWLGRITYYRSKWYNDYAVSVKSRITINPDT
 SKNQFSLQLNSVTPEDTAVYYCAREVTGDLEDAFDIWGQGTMTVTVSSGGGGS
 GGGGSGGGGSDIOMTQSPSSLSASVGDRVTITCRASQTIWSYLNWYQQRPGK
 APNLLIYAASSLQSGVPSRFSGRGSGTDFTLTISSSLQAEDFATYYCQQSYSI
 PQTFGQGTKLEIKSGLDFVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPE
 ACRPAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCNHRNKRGR
 KKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYQ
 QGQNQLYNELNLGRREEYDVLDRRGRDPEMGGKPRRKNPQEGLYNELQKDK
 MAEAYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR (SEQ
 ID NO: 154)

or is substantially similar to SEQ ID NO: 154, or is an active fragment of SEQ ID NO: 154. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 154. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 154. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 154. In some embodiments, the Tandem CAR comprises an amino acid sequence of SEQ ID NO: 154.

[00501] In some embodiments, the CAR is a Tandem CAR which 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: 164:

GSEVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVST
 ISWNSGSGIGYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYCAKDIQY
 GNYYYGMDVWVGQGTITVTVSSGGGSGGGGSGGGGSEIVLTQSPATLSLSPGE
 RATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGT
 DFTLTISSLEPEDFAVYYCQQRSNWPITFGQGTREIKGGGSGGGGSGGGG
 SGGGSGVQLQQSGPGLVKPSQTLSTCAISGDSVSSNSAAWNWIRQSPSRG
 LEWLGRITYYRSKWYNDYAVSVKSRITINPDTSKNQFSLQLNSVTPEDTAVYY
 CAREVTGDLEDAFDIWGQGTMTVTVSSGGGSGGGGSGGGGSDIOMTQSPSS
 SASVGDRVTITCRASQTIWSYLNWYQQRPGKAPNLLIYAASSLQSGVPSRFS
 GRGSGTDFTLTISSSLQAEDFATYYCQQSYSIPQTFGQGTKLEIKSGLDFVPV
 FLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDI
 YIWAPLAGTCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEE
 DGCSCRFPEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVL
 DKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHD
 GLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO: 164)

or is substantially similar to SEQ ID NO: 164, or is an active fragment of SEQ ID NO: 164. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 164. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO:

164. In some embodiments, the Tandem CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 164. In some embodiments, the Tandem CAR comprises an amino acid sequence of SEQ ID NO: 164.

[00502] 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: 142:

```
MALPVTALLLPLALLLHAARPGSEVQLVQSGAEVKKPGESLKISCKGSGYSF
SSSWIGWVRQMPGKGLEWMGIIYPDDSDTRYSPSFQGGQVTISADKSIRTAYL
QWSSLKASDTAMYYCARHVTMIWGVIIIDFWGQGTTLTVSSGGGGSGGGGSGG
GGSAIQLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPGKAPKLLIY
DASSLESGVPSRFSGSGSGTDFTLTISSLPEDFATYYCQQFNSYPYTFGQG
TKLEIKSGLDVFPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAG
GAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCNHRNKRGRKLLYIF
KQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYQQGQNQLY
NELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSE
IGMKGERRRRGKGDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO:
142)
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or is substantially similar to SEQ ID NO: 142, or is an active fragment of SEQ ID NO: 142. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 142. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 142. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 142. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 142.

[00503] 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: 165. In various embodiments, SEQ ID NO: 165 comprises CD19 binding VH and VL domains and CD20 binding VH and VL domains. For example, SEQ ID NO: 165 has the following architecture: CD19 VL – CD19 VH – CD20 VH – CD20 VL.

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AIQLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPGKAPKLLIYDAS
SLESGVPSRFSGSGSGTDFTLTISSLPEDFATYYCQQFNSYPYTFGQGTKL
EIKGGGGSGGGSGGGSEVQLVQSGAEVKKPGESLKISCKGSGYSFSSSWI
GWVRQMPGKGLEWMGIIYPDDSDTRYSPSFQGGQVTISADKSIRTAYLQWSSL
KASDTAMYYCARHVTMIWGVIIIDFWGQGTTLTVSSGGGGSGGGGSGGGGSGG
GGSEVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVS
TISWNSGSIYADSVKGRFTISRDNAKKSLYLQMNSLRRAEDTALYYCAKDIQ
YGNYYYGMDVWGQGTITVTVSSGGGGSGGGGSGGGGSEIVLTQSPATLSLSPG
ERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRAITGIPARFSGSGSG
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TDFTLTISSLEPEDFAVYYCQQRSNWPITFGQGRLEIK (SEQ ID NO: 165)

or is substantially similar to SEQ ID NO: 165, or is an active fragment of SEQ ID NO: 165. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 165. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 165. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 165. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 165.

[00504] 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: 166. In various embodiments, SEQ ID NO: 166 comprises CD19 binding VH and VL domains and CD20 binding VH and VL domains. For example, SEQ ID NO: 166 has the following architecture: CD20 VH – CD20 VL – CD19 VL – CD19 VH.

EVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVSTIS
WNSGSIQYADSVKGRFTISRDNAKKSLYLQMNSLRRAEDTALYYCAKDIQYGN
YYYGMDVWGQGTITVTVSSGGGGSGGGSGGGGSEIVLTQSPATLSLSPGERA
TLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDF
TLTSSLEPEDFAVYYCQQRSNWPITFGQGRLEIKGGGGSGGGSGGGGSG
GGGSAIQLTQSPSSLSASVGDRTITCRASQGISSALAWYQQKPGKAPKLLI
YDASSLESQVPSRFSGSGSGTDFLTSSSLQPEDFATYYCQQFNSYPYTFGQ
GTKLEIKGGGGSGGGSGGGGSEVQLVQSGAEVKKPAGESLKISCKGSGYSFS
SSWIGWVRQMPGKGLEWGMIIYPDDSDTRYSPSFQGGVTISADKSIRTAYLQ
WSSLKASDTAMYYCARHVTMIWGVIIIDFWGQGTILTVSS (SEQ ID NO: 166)

or is substantially similar to SEQ ID NO: 166, or is an active fragment of SEQ ID NO: 166. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 166. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 166. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 166. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 166.

[00505] 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: 167.

MALPVTALLLPLALLLHAARPGSAIQLTQSPSSLSASVGDRVTITCRASQGI
 SSALAWYQQKPGKAPKLLIYDASSLESQVPSRFSGSGSGTDFTLTISSLQPE
 DFATYYCQQFNSYPYTFGQGTKLEIKGGGSGGGGSGGGGSEVQLVQSGAEV
 KKPGESESLKISCKGSGYSFSSSWIGWVRQMPGKGLEWMGIIYPDDSDTRYSPS
 FQGQVTISADKSIRTAYLQWSSLKASDTAMYICARHVTMIWGVIIIDFWGQGT
 LVTVSSGGGSGGGGSGGGGSGGGGSEVQLVESGGGLVQPGRSLRLSCAASG
 FTFNDYAMHWVRQAPGKGLEWVSTISWNSGSIYADSVKGRFTISRDNAKKS
 LYLQMNSLRAEDTALYYCAKDIQYGNYYYGMDVWGQGTITVTVSSGGGSGGGG
 GSGGGGSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPR
 LLIYDASNRTATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPIT
 FGQGTREIKSGLDFVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACR
 PAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCNHRNKRGRKKL
 LYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYQQGQ
 NQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAE
 AYSEIGMKGERRRRGKGGHDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID
 NO: 167)

or is substantially similar to SEQ ID NO: 167, or is an active fragment of SEQ ID NO: 167. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 167. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 167. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 167. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 167.

[00506] 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: 168:

GSAIQLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPGKAPKLLIYD
 ASSLESQVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFNSYPYTFGQGT
 KLEIKGGGSGGGGSGGGGSEVQLVQSGAEVKKPGESESLKISCKGSGYSFSSS
 WIGWVRQMPGKGLEWMGIIYPDDSDTRYSPSFQGQVTISADKSIRTAYLQWS
 SLKASDTAMYICARHVTMIWGVIIIDFWGQGTITVTVSSGGGSGGGGSGGGG
 GGGGSEVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEW
 VSTISWNSGSIYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYCAKD
 IQYGNYYYGMDVWGQGTITVTVSSGGGSGGGGSGGGGSEIVLTQSPATLSLS
 PGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRTATGIPARFSGS
 GSGTDFTLTISSLEPEDFAVYYCQQRSNWPITFGQGTREIKSGLDFVPVFLP
 AKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIW
 APLAGTCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGC
 SCRFPEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKR
 RGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRRGKGGHDGLY
 QGLSTATKDTYDALHMQALPPR (SEQ ID NO: 168)

or is substantially similar to SEQ ID NO: 168, or is an active fragment of SEQ ID NO: 168. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 168. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 168. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 168. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 168.

[00507] 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: 169:

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AIQLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPGKAPKLLIYDAS
SLESGVPSRFSGSGSGTDFTLTISSLPEDFATYYCQQFNSYPYTFGQGTKL
EIKGGGGSGGGSGGGGSEVQLVQSGAEVKKPGESEKISCKGSGYSFSSSWI
GWVRQMPGKGLEWVGIIYPDDSDTRYSPSFQGGVTISADKSIRTAYLQWSSL
KASDTAMYYCARHVTMIWGVIIIDFWGQGTTLTVSSGGGGSGGGSGGGSGGG
GGSEVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKLEWVS
TISWNSGSGIGYADSVKGRFTISRDNAKKSLYLQMNSLRRAEDTALYYCAKDIQ
YGNYYYGMDVWGQGTITVTVSSGGGGSGGGSGGGSGGGSEIVLTQSPATLSLSPG
ERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRAITGIPARFSGSGSG
TDFTLTISSLEPEDFAVYYCQQRSNWPITFGQGTREIKSGLDFVPVFLPAK
PTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAP
LAGTCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSC
RFPEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDRRG
RDPFEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRRGKGDGLYQG
LSTATKDTYDALHMQALPPR (SEQ ID NO: 169)
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or is substantially similar to SEQ ID NO: 169, or is an active fragment of SEQ ID NO: 169. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 169. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 169. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 169. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 169.

[00508] 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: 170:

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MALPVTALLLPLALLLHAARPGSEVQLVESGGGLVQPGRSLRLSCAASGFTF
NDYAMHWVRQAPGKLEWVSTISWNSGSGIGYADSVKGRFTISRDNAKKSLYL
QMNSLRRAEDTALYYCAKDIQYGNYYYGMDVWGQGTITVTVSSGGGGSGGGSG
GGGSEIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLI
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YDASNRATGIPARFSGSGSGTDFTLTISSLEPEDFAVYYCQQRSNWPITFGQ
 GTRLEIKGGGSGGGSGGGSGGGSSAIQLTQSPSSLSASVGDRVTITCRA
 SQGISSALAWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISS
 LQPEDFATYYCQQFNSYPYTFGQGTKLEIKGGGSGGGSGGGGSEVQLVQS
 GAEVKKPGESLKISCKGSGYSFSSSWIGWVRQMPGKGLEWMGIIYPDDSDTR
 YSPSFQGGVTTISADKSIRTAYLQWSSLKASDTAMYICARHVTMIWGVIIDFW
 GQGTLLTVSSSGLDFVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACR
 PAAGGAVHTRGLDFACDIYIWAPLAGTCGVLLLSLVITLYCNHRNKRGRKKL
 LYIFKQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYQQGQ
 NQLYNELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAE
 AYSEIGMKGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID
 NO: 170)

or is substantially similar to SEQ ID NO: 170, or is an active fragment of SEQ ID NO: 170. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 170. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 170. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 170. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 170.

{00509} 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: 171:

GSEVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVST
 ISWNSGSGIGYADSVKGRFTISRDNAKKSLYLQMNSLRAEDTALYYCAKDIQY
 GNYYYGMDVWGQGTITVTVSSGGGSGGGSGGGGSEIVLTQSPATLSLSPGE
 RATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGT
 DFTLTISSLEPEDFAVYYCQQRSNWPITFGQGTREIKGGGSGGGSGGGG
 SGGGSSAIQLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPGKAPKL
 LIYDASSLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFNSYPYTF
 GQGTKLEIKGGGSGGGSGGGGSEVQLVQSGAEVKKPGESLKISCKGSGYS
 FSSSWIGWVRQMPGKGLEWMGIIYPDDSDTRYSPSFQGGVTTISADKSIRTAY
 LQWSSLKASDTAMYICARHVTMIWGVIIDFWGQGTLLTVSSSGLDFVPVFLP
 AKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIW
 APLAGTCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGC
 SCRFPEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKR
 RGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLY
 QGLSTATKDTYDALHMQALPPR (SEQ ID NO: 171)

or is substantially similar to SEQ ID NO: 171, or is an active fragment of SEQ ID NO: 171. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 171. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 171. In some

embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 171. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 171.

[00510] 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: 172:

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EVQLVESGGGLVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVSTIS
WNSGSIQYADSVKGRFTISRDNAKKSLYLQMNSLRRAEDTALYYCAKDIQYGN
YYYGMDVWGQGTITVTVSSGGGSGGGGSGGGGSEIVLTQSPATLSLSPGERA
TLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDF
TLTISSLEPEDFAVYYCQQRSNWPITFGQGTREIKGGGSGGGGSGGGGSG
GGGSAIQLTQSPSSLSASVGDRTITCRASQGISALAWYQQKPGKAPKLLI
YDASSLESQVPSRFSGSGSGTDFTLTISSLPEDFAVYYCQQFNSYPYTFGQ
GTKLEIKGGGSGGGGSGGGGSEVQLVQSGAEVKKPGESLKISCKGSGYSFS
SSWIGWVRQMPGKGLEWMIIPDDSDTRYSPFQGGVTISADKSIRTAYLQ
WSSLKASDTAMYICARHVTMIWGVIIIDFWGQGTITVTVSSGLDFVPVFLPAK
PTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAP
LAGTCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSC
RFPEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREYDVLDRRG
RDPFEMGGKPRRKNPQEGLYNELQDKMAEAYSEIGMKGERRRRGKGDGLYQG
LSTATKDTYDALHMQALPPR (SEQ ID NO: 172)
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or is substantially similar to SEQ ID NO: 172, or is an active fragment of SEQ ID NO: 172. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 172. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 172. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 172. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 172.

[00511] 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: 173:

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METDTLLLVLLVLPVPGSTGDIVLTQSPAILSASPGEKVTMTCRASSSVNYM
DWYQKKPGSSPKPWIYATSNLASGVPARFSGSGSGTSYSLTISRVEAEDAAT
YYCQQWFSNPPTFGGGTKLEIKGSTSGGGSGGGGSGGGGSEVQLQQSGAELV
KPGASVKMCKASGYTFSTSYNMHWVKQTPGQGLEWIGAIYPNGDTSYNQKF
KGKATLTADKSSSTAYMQLSSLTSEDSADYYCARSNYYGSSYWFFDVGAGT
TVTVSSGGGSEVKLQESGPGLVAPSQSLSVCTVSGVSLPDYGVSWIRQPP
RKGLEWLGVIWGSETTYNSALKSRLLTIKDNSKSQVFLKMNSLTQDDTAIY
YCAKHYYYGGSYAMDYWGQTSVTVSSGSTSGSGKPGSGEGSTKGDIMQTQT
TSSLSASLGDRVTISCRASQDISKYLNWYQQKPDGTVKLLIYHTSRLHSGVP
SRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYTFGGGTKLEITESKY
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GPPCPPCPMFVVLVVVGGVLACYSLLVTVAFIIFWVKRGRKKLLYIFKQPFM
 RPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNL
 GRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKG
 ERRRGKGGHDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO: 173)

or is substantially similar to SEQ ID NO: 173, or is an active fragment of SEQ ID NO: 173. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 173. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 173. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 173. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 173.

[00512] 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: 174:

DIVLTQSPAILLSASPGEKVTMTCRASSSVNYMDWYQKKPGSSPKPWIYATSN
 LASGVPARFSGSGSGTSYSLTISRVEAEDAATYYCQQWSFNPPTFGGGKTLE
 IKGSTSGGGSGGGSGGGSSSEVQLQQSGAELVKPGASVKMSCKASGYTFTSY
 NMHWVKQTPGQGLEWIGAIYPGNGDTSYNQKFKGKATLTADKSSSTAYMQLS
 SLTSEDSADYYCARSNYYGSSYWFFDVWGAGTTVTVSSGGGSEVKLQESGP
 GLVAPSQSLSVTCTVSGVSLPDYGVSWIRQPPRKLEWLGVIWGSETTYNS
 ALKSRLTIKDNSKSQVFLKMNSLQTDITAIYYCAKHYYYGGSYAMDYWGQG
 TSVTVSSGSTSGSGKPGSGEGSTKGDITQMTQTSSLSASLGDRVTISCRASQ
 DISKYLNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNLE
 QEDIATYFCQQGNTLPYTFGGGKTLEITESKYGPPCPPCPMFVVLVVVGGVL
 ACYSLLVTVAFIIFWVKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEEE
 EGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEMG
 GKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGGHDGLYQGLSTATK
 DTYDALHMQALPPR (SEQ ID NO: 174)

or is substantially similar to SEQ ID NO: 174, or is an active fragment of SEQ ID NO: 174. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 174. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 174. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 174. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 174.

[00513] 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: 175:

MALPVTALLLPLALLLHAARPEIVLTQSPATLSLSPGERATLSCRASQSVSS
 YLAWYQQKPGQAPRLLIYDASNRATGIPARFSGSGSGTDFTLTISSELEPEDF
 AVYYCQQRSNWPITFGQGTRLEIKGSTSGGGSGGGSGGGSSSEVQLVESGGG
 LVQPGRSLRLSCAASGFTFNDYAMHWVRQAPGKGLEWVSTISWNSGSIGYAD
 SVKGRFTISRDNAAKSLYLQMNLSRAEDTALYYCAKDIQYGNYYYGMDVWGQ
 GTTIVTVSSGGGGSEVKLQESGPGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQ
 PPRKGLEWLGVIWGSETTYNSALKSRLTIKDNSKSQVFLKMNSLQTDDTA
 IYYCAKHYYYGGSYAMDYWGQGTSTVTVSSGSTSGSGKPGSGEGSTKGDQMT
 QTTSSLSASLGDRVTISCRASQDISKYLNWYQQKPDGTVKLLIYHTSRLHSG
 VPSRFSGSGSGTDYSLTISNLEQEDIATYFCQQGNTLPYTFGGGKLEITES
 KYGPPCPPCPMFWVLVVGVLACYSLLVTVAFIIFWVKRGRKKLLYIFKQPF
 FMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFERSADAPAYQQGQNQLYNEL
 NLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGM
 KGERRRGKGHDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO: 175)

or is substantially similar to SEQ ID NO: 175, or is an active fragment of SEQ ID NO: 175. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 175. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 175. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 175. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 175.

[00514] 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: 176:

EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDAS
 NRATGIPARFSGSGSGTDFTLTISSELEPEDFAVYYCQQRSNWPITFGQGTRL
 EIKGSTSGGGSGGGSGGGSSSEVQLVESGGGLVQPGRSLRLSCAASGFTFND
 YAMHWVRQAPGKGLEWVSTISWNSGSIGYADSVKGRFTISRDNAAKSLYLQMN
 NSLRAEDTALYYCAKDIQYGNYYYGMDVWGQGTITVTVSSGGGGSEVKLQESG
 PGLVAPSQSLSVTCTVSGVSLPDYGVSWIRQPPRKGLEWLGVIWGSETTYN
 SALKSRLTIKDNSKSQVFLKMNSLQTDDTAIYYCAKHYYYGGSYAMDYWGQ
 GTSTVTVSSGSTSGSGKPGSGEGSTKGDQMTQTTSSLSASLGDRVTISCRAS
 QDISKYLNWYQQKPDGTVKLLIYHTSRLHSGVPSRFSGSGSGTDYSLTISNL
 EQEDIATYFCQQGNTLPYTFGGGKLEITESKYGPPCPPCPMFWVLVVGVL
 LACYSLLVTVAFIIFWVKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPEE
 EEGGCELRVKFERSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPEM
 GGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTAT
 KDTYDALHMQALPPR (SEQ ID NO: 176)

or is substantially similar to SEQ ID NO: 176, or is an active fragment of SEQ ID NO: 176. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 176. In some embodiments, the CAR comprises an amino acid

sequence that is at least 95% identical to a sequence of SEQ ID NO: 176. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 176. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 176.

[00515] 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: 203:

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MALPVTALLLPLALLLHAARPGSAIQLTQSPSSLSASVGDRVTITCRASQGI
SSALAWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTLTISSLQPE
DFATYYCQQFNSYPYTFGQGTKLEIKGGGSGGGGSGGGGSEVQLVQSGAEV
KKPGESLKISCKGSGYSFSSSWIGWVRQMPGKGLEWMGIYPDDSDTRYSPS
FQQQVTISADKSIRTAYLQWSSLKASDTAMYYCARHVTMIWGVIIIDFWGQGT
LVTVSSSGLDFVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAG
GAVHTRGLDFACDIYIWAPLAGTCGVLVITLYCNHRNKRGRKKLLYIF
KQPFMRPVQTTQEEDGCSCRFPEEEEGGCELRVKFSRSADAPAYQQGQNQLY
NELNLGRREEYDVLDKRRGRDPEMGGKPRRKNPQEGLYNELQKDKMAEAYSE
IGMKGERRRRGKGGHDGLYQGLSTATKDTYDALHMQALPPR (SEQ ID NO:
203)
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or is substantially similar to SEQ ID NO: 203, or is an active fragment of SEQ ID NO: 203. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 203. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 203. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 203. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 203.

[00516] 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: 204:

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GSEVQLVQSGAEVKKPGESLKISCKGSGYSFSSSWIGWVRQMPGKGLEWMGI
IYPDDSDTRYSPSFQQQVTISADKSIRTAYLQWSSLKASDTAMYYCARHVTM
IWGVIIIDFWGQGT LVTVSSGGGSGGGGSGGGGSAIQLTQSPSSLSASVGDR
VTITCRASQGISSALAWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTD
FTLTISSLQPEDFATYYCQQFNSYPYTFGQGTKLEIKSGLDFVPVFLPAKPT
TTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLA
GTCGVLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRF
PEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRD
PEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRRGKGGHDGLYQGLS
TATKDTYDALHMQALPPR (SEQ ID NO: 204)
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or is substantially similar to SEQ ID NO: 204, or is an active fragment of SEQ ID NO: 204. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 204. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 204. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 204. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 204.

[00517] 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: 205:

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GSAIQLTQSPSSLSASVGDRVTITCRASQGISSALAWYQQKPGKAPKLLIYD
ASSLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFNSTYPTFGQGT
KLEIKGGGGSGGGSGGGGSEVQLVQSGAEVKKPGESLKISCKGSGYSFSSS
WIGWVRQMPGKGLEWMGIIYPDDSDTRYSPSFQGGVTISADKSIRTAYLQWS
SLKASDTAMYYCARHVTMIWGVIIIDFWGQGTILVTVSSSGLDFVPVFLPAKPT
TTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLA
GTCGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRF
PEEEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRD
PEMGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRRGKGGHDGLYQGLS
TATKDTYDALHMQALPPR (SEQ ID NO: 205)

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or is substantially similar to SEQ ID NO: 205, or is an active fragment of SEQ ID NO: 205. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 205. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 205. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 205. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 205.

[00518] 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: 206:

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EVQLVQSGAEVKKPGESLKISCKGSGYSFSSSWIGWVRQMPGKGLEWMGIIY
PDDSDTRYSPSFQGGVTISADKSIRTAYLQWSSLKASDTAMYYCARHVTMIW
GVIIIDFWGQGTILVTVSSGGGGSGGGSGGGGSAIQLTQSPSSLSASVGDRVT
ITCRASQGISSALAWYQQKPGKAPKLLIYDASSLESGVPSRFSGSGSGTDFTL
TISSLQPEDFATYYCQQFNSTYPTFGQGTLEIKSGGLDFVPVFLPAKPTTT
PAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGT
CGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPE
EEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPE

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MGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTA
TKDTYDALHMQALPPR (SEQ ID NO: 206)

or is substantially similar to SEQ ID NO: 206, or is an active fragment of SEQ ID NO: 206. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 206. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 206. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 206. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 206.

[00519] 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: 207:

AIQLTQSPSSLSASVGDRTTICRASQGISSALAWYQQKPGKAPKLLIYDAS
SLESGVPSRFSGSGSGTDFTLTISSLQPEDFATYYCQQFNSYPYTFGQGTKL
EIKGGGGSGGGGSGGGGSEVQLVQSGAEVKKPGESLKISCKGSGYSFSSSWI
GWVRQMPGKGLEWMGIIYPDDSDTRYSPSFQGGVTISADKSIRTAYLQWSSL
KASDTAMYCARHVTMIWGVIIIDFWGQGTLLTVSSSGLDFVPVFLPAKPTTT
PAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACDIYIWAPLAGT
CGVLLLSLVITLYCNHRNKRGRKKLLYIFKQPFMRPVQTTQEEDGCSCRFPE
EEEGGCELRVKFSRSADAPAYQQGQNQLYNELNLGRREEYDVLDKRRGRDPE
MGGKPRRKNPQEGLYNELQKDKMAEAYSEIGMKGERRRGKGHDGLYQGLSTA
TKDTYDALHMQALPPR (SEQ ID NO: 207)

or is substantially similar to SEQ ID NO: 207, or is an active fragment of SEQ ID NO: 207. In some embodiments, the CAR comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 207. In some embodiments, the CAR comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 207. In some embodiments, the CAR comprises an amino acid sequence that is at least 98% identical to a sequence of SEQ ID NO: 207. In some embodiments, the CAR comprises an amino acid sequence of SEQ ID NO: 207.

[00520] 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.

[00521] 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.

[00522] 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.

[00523] 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 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.

[00524] 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

[00525] 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, dual CAR, or tandem CAR, as provided for herein. In some embodiments, the CAR or Tandem 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 any one of the sequences of SEQ ID Nos: 126-135.

[00526] 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, a dual CAR, or a tandem CAR, as provided for herein. In some embodiments, the CAR or Tandem 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 any one of the sequences of SEQ ID Nos: 126-135.

[00527] 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, a dual CAR, or a tandem CAR, as provided for herein. In some embodiments, the CAR or Tandem 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 any one of the sequences of SEQ ID Nos: 126-135.

[00528] 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, a dual CAR, or a tandem CAR, as provided for herein. In some embodiments, the CAR or Tandem 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 any one of the sequences of SEQ ID Nos: 126-135.

[00529] 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, a dual CAR, or a tandem CAR, as provided for herein. In some embodiments, the CAR or Tandem 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 any one of the sequences of SEQ ID Nos: 126-135.

[00530] 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, a dual CAR, or a tandem CAR, as provided for herein. In some embodiments, the CAR or Tandem 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 any one of the sequences of SEQ ID Nos: 126-135.

Exemplary viral particles comprising a targeting moiety comprising a flexible polypeptide

[00531] 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, a dual CAR, or a tandem CAR, as provided for herein. In some embodiments, the CAR or Tandem 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 any one of the sequences of SEQ ID Nos: 126-135.

[00532] 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, a dual CAR, or a tandem CAR, as provided for herein. In some embodiments, the CAR or Tandem 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 any one of the sequences of SEQ ID Nos: 126-135.

[00533] 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, a dual CAR, or a tandem CAR, as provided for herein. In some embodiments, the CAR or Tandem 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 any one of the sequences of SEQ ID Nos: 126-135.

[00534] 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, a dual CAR, or a tandem CAR, as provided for herein. In some embodiments, the CAR or Tandem 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 any one of the sequences of SEQ ID Nos: 126-135.

[00535] 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, a dual CAR, or a tandem CAR, as provided for herein. In some embodiments, the CAR or Tandem 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 any one of the sequences of SEQ ID Nos: 126-135.

[00536] 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, a dual CAR, or a tandem CAR, as provided for herein. In some embodiments, the CAR or Tandem 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 any one of the sequences of SEQ ID Nos: 126-135.

[00537] 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.

[00538] 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.

[00539] 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.

[00540] 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.

[00541] Also provided herein are nucleic acid molecules encoding a mutant VSV-G protein as provided for herein.

[00542] 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

[00543] 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.

[00544] 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.

[00545] Also provided herein are methods of treating a disease in a subject in need thereof.

[00546] 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.

[00547] 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.

[00548] 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).

[00549] 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.

[00550] 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 gammopathy of undetermined 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.

[00551] 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.

[00552] 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.

[00553] 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.

[00554] 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.

[00555] 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 composition is injected directly into a site of a local disease site in the subject, a lymph node, an organ, a tumor, and the like.

[00556] 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.

[00557] 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.

[00558] 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.

[00559] 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.

[00560] In some embodiments, the methods are performed without a lymphodepletion step, such as the administration of cyclophosphamide and/or fludarabine.

[00561] 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.

[00562] 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.

[00563] 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.

[00564] 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.

[00565] 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.

[00566] 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.

[00567] 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.

[00568] 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.

[00569] 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.

[00570] 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).

[00571] 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.

[00572] 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.

[00573] The compositions disclosed herein can comprise a pharmaceutical composition, and for example include a pharmaceutically acceptable carrier, and/or a pharmaceutical formulation.

[00574] 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 dextrins; 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).

[00575] 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).

[00576] 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.

[00577] 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.

[00578] 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.

[00579] 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.

[00580] 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.

[00581] 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

[00582] In some embodiments, the following embodiments are provided:

1. A viral particle comprising a heterologous viral glycoprotein and a targeting moiety, 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.

2. The viral particle of embodiment 1, 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 Fc γ R, C1q, FcR β , or FcRn.
3. The viral particle of embodiment 2, wherein the S₁ stalk portion is attached to the surface of the viral particle through the transmembrane domain.
4. The viral particle of embodiments 2 or 3, wherein the Fc protein is a IgG1 Fc, IgG2 Fc or IgG4 Fc protein.
5. The viral particle of any one of embodiments 2-4, 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.
6. The viral particle of any one of embodiments 2-5, wherein the variant Fc protein is a variant IgG1 Fc protein.
7. The viral particle of embodiment 6, 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.
8. The viral particle of embodiments 6 or 7, wherein the variant IgG1 Fc protein comprises a mutation that corresponds to L234A and L235A of SEQ ID NO: 26.
9. The viral particle of any one of embodiments 6-8, wherein the variant IgG1 Fc protein comprises a mutation that corresponds to N297A of SEQ ID NO: 26.
10. The viral particle of any one of embodiments 6-9, wherein the variant IgG1 Fc protein comprises a mutation that corresponds to P329G of SEQ ID NO: 26.
11. The viral particle of any one of embodiments 6-10, wherein the variant IgG1 Fc protein comprises a mutation that corresponds to L234A, L235A, N297A, and P329G of SEQ ID NO: 26.

12. The viral particle of any one of embodiments 6-11, wherein the variant IgG1 Fc protein comprises a mutation that corresponds to I253A of SEQ ID NO: 26.
13. The viral particle of any one of embodiments 6-12, wherein the variant IgG1 Fc protein comprises a mutation that corresponds to H310A of SEQ ID NO: 26.
14. The viral particle of any one of embodiments 6-13, wherein the variant IgG1 Fc protein comprises a mutation that corresponds to H435A of SEQ ID NO: 26.
15. The viral particle of any one of embodiments 6-14, wherein the variant IgG1 Fc protein comprises a mutation that corresponds to I253A, H310A, and H435A of SEQ ID NO: 26.
16. The viral particle of any one of embodiments 6-15, 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.
17. The viral particle of any one of embodiments 6-16, 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.
18. The viral particle of any one of embodiments 2-5, wherein the variant Fc protein is a variant IgG2 Fc protein.
19. The viral particle of embodiment 18, wherein the variant IgG2 Fc protein comprises one or more mutations selected from the group consisting of: N297A, P329G, I253A, H310A, and H435A.
20. The viral particle of embodiments 18 or 19, wherein the IgG2 Fc protein comprises a mutation that corresponds to N297A of SEQ ID NO: 27.

21. The viral particle of embodiments 18 or 19, wherein the IgG2 Fc protein comprises a mutation that corresponds to P329G of SEQ ID NO: 27.
22. The viral particle of any one of embodiments 18-21, wherein the IgG2 Fc protein comprises a mutation that corresponds to N297A and P329G of SEQ ID NO: 27.
23. The viral particle of any one of embodiments 18-22, wherein the variant IgG2 Fc protein comprises a mutation that corresponds to I253A of SEQ ID NO: 27.
24. The viral particle of any one of embodiments 18-23, wherein the variant IgG2 Fc protein comprises a mutation that corresponds to H310A of SEQ ID NO: 27.
25. The viral particle of any one of embodiments 18-24, wherein the IgG2 Fc protein comprises a mutation that corresponds to H435A of SEQ ID NO: 27.
26. The viral particle of any one of embodiments 18-25, wherein the variant IgG2 Fc protein comprises a mutation that corresponds to I253A, H310A, and H435A of SEQ ID NO: 27.
27. The viral particle of any one of embodiments 2-5, wherein the variant Fc protein is a variant IgG4 Fc protein.
28. The viral particle of embodiment 27, 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.
29. The viral particle of embodiments 27 or 28, wherein the IgG4 Fc protein comprises a mutation that corresponds to S228P of SEQ ID NO: 28.
30. The viral particle of any one of embodiments 27-29, wherein the IgG4 Fc protein comprises a mutation that corresponds to L235E of SEQ ID NO: 28.
31. The viral particle of any one of embodiments 27-30, wherein the IgG4 Fc protein comprises a mutation that corresponds to N297A of SEQ ID NO: 28.

32. The viral particle of any one of embodiments 27-31, wherein the IgG4 Fc protein comprises a mutation that corresponds to P329G of SEQ ID NO: 28.

33. The viral particle of any one of embodiments 27-32, wherein the IgG4 Fc protein comprises a mutation that corresponds to S228P, L235E, N297A, and P329G of SEQ ID NO: 28.

34. The viral particle of any one of embodiments 37-33, wherein the variant IgG4 Fc protein comprises a mutation that corresponds to I253A of SEQ ID NO: 28.

35. The viral particle of any one of embodiments 27-34, wherein the variant IgG4 Fc protein comprises a mutation that corresponds to H310A of SEQ ID NO: 28.

36. The viral particle of any one of embodiments 27-35, wherein the IgG4 Fc protein comprises a mutation that corresponds to H435A of SEQ ID NO: 28.

37. The viral particle of any one of embodiments 27-36, wherein the variant IgG4 Fc protein comprises a mutation that corresponds to I253A, H310A, and H435A of SEQ ID NO: 28.

38. The viral particle of any one of embodiments 2-37, 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.

39. The viral particle of embodiment 38, wherein L₁ and L₂ are each, independently, a polypeptide linker.

40. The viral particle of embodiment 39, 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.

41. The viral particle of any one of embodiments 38-40, wherein L₁ is absent.

42. The viral particle of any one of embodiments 38-40, wherein L₁ is (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), and wherein each n is, independently, 1-5.

43. The viral particle of any one of embodiments 38-42, wherein L₂ is absent.

44. The viral particle of any one of embodiments 38-42, wherein L₂ is (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), and wherein each n is, independently, 1-5.

45. The viral particle of any one of embodiments 38-44, 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.

46. The viral particle of embodiment 45, wherein the ECD is absent.

47. The viral particle of embodiment 45, wherein the ECD is an extracellular domain, or fragment thereof, of CD8 or CD28.

48. The viral particle of embodiment 47, wherein the ECD comprises an amino acid sequence of SEQ ID NO: 59 or SEQ ID NO: 60.

49. The viral particle of embodiment 47, wherein the ECD comprises an amino acid sequence of SEQ ID NO: 60.

50. The viral particle of any one of embodiments 45-49, wherein T_M is a transmembrane domain, or a fragment thereof, of CD8 or CD28.

51. The viral particle of embodiment 50, wherein the T_M comprises an amino acid sequence of SEQ ID NO: 61 or SEQ ID NO: 62.

52. The viral particle of embodiment 50, wherein the T_M comprises an amino acid sequence of SEQ ID NO: 62.

53. The viral particle of any one of embodiments 45-52, wherein the ICD is absent.

54. The viral particle of any one of embodiments 45-52, wherein the ICD comprises an Env incorporation motif.

55. The viral particle of embodiment 54, wherein the Env incorporation motif comprises an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64.

56. The viral particle of embodiment 1, wherein the stalk portion S₁ comprises a formula of L₃-X₁, wherein:

L₃ is a flexible peptide linker, and

X₁ is a polypeptide comprising a transmembrane domain,

wherein the targeting moiety having the formula T-S₁ has a formula of T-L₃-X₁.

57. The viral particle of embodiment 56, wherein L₃ 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.

58. The viral particle of embodiment 57, wherein n is 1, 2, or 4.

59. The viral particle of any one of embodiments 56-58, 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 $T-L_3-X_1$ has a formula of $T-L_3$ -ECD- T_M -ICD.

60. The viral particle of embodiment 59, wherein the ECD is absent.

61. The viral particle of embodiment 59, wherein the ECD is an extracellular domain, or fragment thereof, or CD8 or CD28.

62. The viral particle of embodiment 61, wherein the ECD comprises an amino acid sequence of SEQ ID NO: 59 or SEQ ID NO: 60.

63. The viral particle of embodiment 61, wherein the ECD comprises an amino acid sequence of SEQ ID NO: 59.

64. The viral particle of any one of embodiments 59-63, wherein T_M is a transmembrane domain, or a fragment thereof, of CD8 or CD28.

65. The viral particle of embodiment 64, wherein the T_M comprises an amino acid sequence of SEQ ID NO: 61 or SEQ ID NO: 62.

66. The viral particle of embodiment 64, wherein the T_M comprises an amino acid sequence of SEQ ID NO: 61.

67. The viral particle of any one of embodiments 59-66, wherein the ICD is absent.
68. The viral particle of any one of embodiments 59-66, wherein the ICD comprises an Env incorporation motif.
69. The viral particle of embodiment 68, wherein the Env incorporation motif comprises an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64.
70. The viral particle of any one of embodiments 1-69, 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.
71. The viral particle of any one of embodiments 1-70, 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- α); 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)bDGlcp(1-l)Cer); Ganglioside GM3 (aNeu5Ac(2-3)bDClalp(1-4)bDGlcp(1-l)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 K9 (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 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).

72. The viral particle of embodiment 71, wherein the target binding domain (T) binds to CD7.

73. The viral particle of embodiment 72, 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.

74. The viral particle of embodiment 73, 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.

75. The viral particle of embodiments 73 or 74, 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.

76. The viral particle of any one of embodiments 73-75, 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.

77. The viral particle of any one of embodiments 73-76, 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.

78. The viral particle of any one of embodiments 73-77, 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.

79. The viral particle of any one of embodiments 73-78, 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.

80. The viral particle of any one of embodiments 73-79, 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.

81. The viral particle of any one of embodiments 73-80, 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.

82. The viral particle of embodiment 81, wherein the peptide linker comprises a sequence of (GGGGS)_n, wherein n is independently 1-5.

83. The viral particle of any one of embodiments 73-80, 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.

84. The viral particle of any one of embodiments 72-82, 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.

85. The viral particle of any one of embodiments 72-82, 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.

86. The viral particle of embodiment 71, wherein the target binding domain (T) binds to CD8.

87. The viral particle of embodiment 86, 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.

88. The viral particle of embodiment 87, 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.

89. The viral particle of embodiment 87 or 88, 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.

90. The viral particle of any one of embodiments 87-89, 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.

91. The viral particle of any one of embodiments 87-90, 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.

92. The viral particle of any one of embodiments 87-90, 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.

93. The viral particle of any one of embodiments 87-90, 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.

94. The viral particle of embodiment 86, 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.

95. The viral particle of any one of embodiments 87-94, wherein the heavy chain variable region and the light chain variable region are linked by a linker, such as a peptide linker.

96. The viral particle of embodiment 95, wherein the peptide linker is a glycine/serine linker.
97. The viral particle of embodiments 95 or 96, wherein the peptide linker comprises a sequence of (GGGGS)_n (SEQ ID NO: 55), wherein each n is independently 1-5.
98. The viral particle of any one of embodiments 87-94, 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.
99. The viral particle of any one of embodiments 86-97, 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.
100. The viral particle of any one of embodiments 86-97, 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.
101. The viral particle of any one of embodiments 1-100, wherein the target binding domain (T) is an antibody, or an antigen-binding fragment thereof, such as scFv antibody.
102. The viral particle of any one of embodiments 1-101, wherein the heterologous viral glycoprotein is a SVCV-G polypeptide.
103. The viral particle of embodiment 102, 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.

104. The viral particle of embodiment 102 or 103, 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.

105. The viral particle of embodiment 102 or 103, 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.

106. The viral particle of embodiment 102 or 103, wherein the SVCV-G polypeptide comprises SEQ ID NO: 52 or SEQ ID NO: 53.

107. The viral particle of any one of embodiments 102, 103, or 106, wherein the SVCV-G polypeptide comprises SEQ ID NO: 52.

108. The viral particle of any one of embodiments 102, 103, or 106, wherein the SVCV-G polypeptide comprises SEQ ID NO: 53.

109. The viral particle of any one of embodiments 1-101, wherein the heterologous viral glycoprotein is a VSV-G polypeptide.

110. The viral particle of embodiment 109, 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.

111. The viral particle of embodiment 109, 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.

112. The viral particle of embodiment 110 or 111, wherein the VSV-G polypeptide comprises a I182E or I182D mutation as compared to SEQ ID NO: 2.

113. The viral particle of any one of embodiments 109-112, 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.

114. The viral particle of any one of embodiments 109-113, wherein the VSV-G polypeptide comprises a mutation that corresponds to I182D or I182E as compared to a sequence of SEQ ID NO: 2.

115. The viral particle of any one of embodiments 109-114, 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.

116. The viral particle of any one of embodiments 109-114, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 4.

117. The viral particle of any one of embodiments 109-114, 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.

118. The viral particle of any one of embodiments 109-114, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 5.

119. The viral particle of any one of embodiments 109-111 or 113, 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.

120. The viral particle of any one of embodiments 109-111 or 113, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 3.

121. The viral particle of any one of embodiments 109-120, 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.

122. The viral particle of any one of embodiments 109-121, 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.

123. The viral particle of any one of embodiments 109-122, 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.

124. The viral particle of any one of embodiments 109-123, 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.

125. The viral particle of any one of embodiments 109-124, 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.

126. The viral particle of any one of embodiments 109-125, 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.

127. The viral particle of any one of embodiments 109-126, 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.

128. The viral particle of any one of embodiments 109-127, 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.
129. The viral particle of any one of embodiments 109-128, 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.
130. The viral particle of any one of embodiments 109-129, wherein the VSV-G protein comprises a substitution at position 47, wherein the substitution is K47Q or K47N.
131. The viral particle of any one of embodiments 109-130, wherein the VSV-G protein comprises a substitution H8A and/or K47Q mutation.
132. The viral particle of any one of embodiments 109-131, wherein the VSV-G protein comprises a substitution at position 10, such as Q10A, Q10R, or Q10K substitution.
133. The viral particle of any one of embodiments 109-132, 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.
134. The viral particle of embodiment 133, wherein the VSV-G polypeptide comprises a T214N and/or T352A mutation.
135. The viral particle of embodiment 109, wherein the VSV-G polypeptide comprises a substitution at positions I182 and at least one of T214, and T352 of SEQ ID NO: 2.
136. The viral particle of embodiment 135, wherein the VSV-G polypeptide comprises substitutions at positions I182, T214, and T352 of SEQ ID NO: 2.
137. The viral particle of embodiments 135 or 136, 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.

138. The viral particle of any one of embodiments 135-137, 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.
139. The viral particle of any one of embodiments 135-137, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 22.
140. The viral particle of any one of embodiments 135-137, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 23.
141. The viral particle of any one of embodiments 135-137, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 24.
142. The viral particle of any one of embodiments 135-137, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 25.
143. The viral particle of any one of embodiments 1-142, wherein the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest.
144. The viral particle of embodiment 141, wherein 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, or a combination thereof.
145. The viral particle of embodiment 143 or 144, wherein the heterologous molecule of interest is a chimeric antigen receptor ("CAR"), a dual CAR, or a Tandem CAR.

146. The viral particle of embodiment 145, wherein the CAR or tandem CAR comprises an antigen binding domain comprising an antibody, or a fragment thereof.

147. The viral particle of embodiment 146, 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.

148. The viral particle of embodiment 146 or 147, wherein the antigen binding domain of the CAR or tandem CAR binds to BCMA and/or FCRL5, or CD20 and/or CD22.

149. The viral particle of embodiment 148, wherein the antigen binding domain that binds to BCMA and/or FCRL5 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 any one of the amino acid sequences of SEQ ID NOs: 113, 89, 94, 105, 109, 136, or 137. 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, 95, 106, or 110.

150. The viral particle of embodiment 148, wherein the antigen binding domain that binds to BCMA and/or FCRL5 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 NOs: 113, 89, 94, 105, 109, 136, or 137; and a light chain variable region of the light chain having at least 95% identity to an amino acid sequence of SEQ ID NOs: 90, 95, 106, or 110.

151. The viral particle of embodiment 148, wherein the antigen binding domain that binds to BCMA and/or FCRL5 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 NOs: 113, 89, 94, 105, 109, 136, or 137; and a

light chain variable region of the light chain having at least 99% identity to an amino acid sequence of SEQ ID NOs: 90, 95, 106, or 110.

152. The viral particle of embodiment 148, wherein the antigen binding domain that binds to BCMA and/or FCRL5 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 NOs: 113, 89, 94, 105, 109, 136, or 137; and a light chain variable region of the light chain comprising an amino acid sequence of SEQ ID NOs: 90, 95, 106, or 110.

153. The viral particle of any one of embodiments 149-152, 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.

154. The viral particle of any one of embodiments 149-152, wherein the antigen binding domain that binds to BCMA and/or FCRL5 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NOs: 92, 96, 107, or 111, at least 95% sequence identity to SEQ ID NO: 92, 96, 107, or 111, at least 99% sequence identity to SEQ ID NO: 92, 96, 107, or 111, or a sequence as set forth in SEQ ID NO: 92, 96, 107, or 111.

155. The viral particle of any one of embodiments 149-152, wherein the antigen binding domain that binds to BCMA and/or FCRL5 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NOs: 93, 97, 108, or 112, at least 95% sequence identity to SEQ ID NOs: 93, 97, 108, or 112, at least 99% sequence identity to SEQ ID NOs: 93, 97, 108, or 112 or a sequence as set forth in SEQ ID NOs: 93, 97, 108, or 112.

156. The viral particle of embodiment 148, wherein the antigen binding domain that binds to CD20 and/or CD22 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 any one of the amino acid sequences of SEQ ID NOs: 114 or 118. and a light chain variable

region of the light chain having at least 90% identity to an amino acid sequence of SEQ ID NO: 115 or 119.

157. The viral particle of embodiment 148, wherein the antigen binding domain that binds to CD20 and/or CD22 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 NOs: 114 or 118; and a light chain variable region of the light chain having at least 95% identity to an amino acid sequence of SEQ ID NOs: 115 or 119.

158. The viral particle of embodiment 148, wherein the antigen binding domain that binds to CD20 and/or CD22 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 NOs: 114 or 118; and a light chain variable region of the light chain having at least 99% identity to an amino acid sequence of SEQ ID NOs: 115 or 119.

159. The viral particle of claim 148, wherein the antigen binding domain that binds to CD20 and/or CD22 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 NOs: 114 or 118; and a light chain variable region of the light chain comprising an amino acid sequence of SEQ ID NOs: 115 or 119.

160. The viral particle of any one of embodiments 156-159, 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.

161. The viral particle of claims any one of embodiments 156-159, wherein the antigen binding domain that binds to CD20 and/or CD22 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NOs: 116, 120, 122, or 124, at least 95% sequence identity to SEQ ID NO: 116, 120, 122, or 124, at least 99% sequence

identity to SEQ ID NO: 116, 120, 122, or 124, or a sequence as set forth in SEQ ID NO: 116, 120, 122, or 124.

162. The viral particle of claims any one of embodiments 156-159, wherein the antigen binding domain that binds to CD20 and/or CD22 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NOs: 117, 121, 123, or 125, at least 95% sequence identity to SEQ ID NOs: 117, 121, 123, or 125, at least 99% sequence identity to SEQ ID NOs: 117, 121, 123, or 125, or a sequence as set forth in SEQ ID NOs: 117, 121, 123, or 125.

163. The viral particle of any one of embodiments 145-162, wherein the CAR further comprises a hinge domain, a transmembrane domain, a costimulatory domain, and a signaling domain.

164. The viral particle of embodiment 163, 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.

165. The viral particle of embodiment 163 or 164, 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.

166. The viral particle of any one of embodiments 163-165, 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.

167. The viral particle of any one of embodiments 163-166, 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.

168. The viral particle of embodiment 148, wherein 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% identical to any one of the sequences of SEQ ID NOs: 126-135.

169. A method of infecting a cell, the method comprising contacting the cell with a viral particle of any one of embodiments 1-168.

170. A method of infecting a cell in a subject, the method comprising administering to the subject a pharmaceutical composition comprising a viral particle of any one of embodiments 1-168.

171. A method of delivering a heterologous molecule of interest to a cell, the method comprising contacting the cell with a viral particle of any one of embodiments 1-168, wherein the viral particle comprises a nucleic acid molecule encoding the heterologous molecule of interest.

172. A method of delivering a heterologous molecule of interest to a cell in a subject, the method comprising administering to the subject a viral particle of any one of embodiments 1-168, wherein the viral particle comprises a nucleic acid molecule encoding the heterologous molecule of interest.

173. The method of any one of embodiments 169-172, wherein the cell is an immune cell.

174. The method of any one of embodiments 169-173, 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.

175. A method of treating a disease or disorder in a subject, the method comprising administering to the subject a viral particle of any one of embodiments 1-168, wherein the viral particle comprises a nucleic acid molecule encoding the heterologous molecule of interest to treat the disease or disorder.

176. The method of embodiment 175, 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.

177. A method of delivering a heterologous molecule to a target cell, the method comprising contacting the cell with a viral vector or particle of any one of embodiments 1-168, wherein the particle comprises a nucleic acid molecule encoding the heterologous molecule.

178. A viral particle comprising a heterologous viral glycoprotein and a targeting moiety comprising a polypeptide having the 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.

179. A viral particle comprising a heterologous viral glycoprotein and a targeting moiety comprising a polypeptide having the 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 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.

180. A viral particle comprising a heterologous viral glycoprotein and a targeting moiety comprising a polypeptide having the 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.

181. The viral particle of any one of embodiments 178-180, 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.

182. A viral particle comprising a heterologous viral glycoprotein and a targeting moiety
 comprising a polypeptide having the 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;

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.

183. A viral 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 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; 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.

184. A viral 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 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; 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.

185. A viral particle comprising a heterologous viral structural protein and a targeting moiety comprising a polypeptide having the formula 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 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.

186. The viral particle of embodiment 185, 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.
187. The viral particle of embodiment 185, 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.
188. A viral particle comprising a heterologous viral structural protein and a targeting moiety comprising a polypeptide having the formula 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 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.

189. The viral particle of embodiment 188, 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.
190. The viral particle of embodiment 188, 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.
191. A viral particle comprising a heterologous viral structural protein and a targeting moiety comprising a polypeptide having the formula 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 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, 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.

192. A viral particle comprising a heterologous viral structural protein and a targeting moiety comprising a polypeptide having the formula $T-S_1$;

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 S_1 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 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 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.

193. A viral particle comprising a heterologous viral structural protein and a targeting moiety comprising a polypeptide having the formula 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 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.

194. A viral particle comprising a heterologous viral structural protein and a targeting moiety comprising a polypeptide having the formula 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 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.

195. The viral particle of any one of embodiments 178-194, wherein the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest.

196. The viral particle of embodiment 195, wherein the heterologous molecule of interest is a CAR.

[00583] 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

[00584] **Example 1: 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.

[00585] 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).

[00586] 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).

[00587] 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.

[00588] 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.

[00589] 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.

[00590] **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.

[00591] 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).

[00592] 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.

[00593] **Example 2: Serum Stable VSV-G Protein**

[00594] 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.

[00595] 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. 4). 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. 4, columns 1-3). The inclusion of the CD7 targeting moiety on an IgG1 Fc

stalk (WT) did not rescue the serum inactivation (FIG. 4, 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. 4, columns 7-9). However, the inclusion of the targeting moiety was able to partially rescue the inactivation in either serum condition (FIG. 4, 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. 4, 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. 4, columns 16-18). Further, the I182E, T214N, T352A construct also demonstrates increased infectivity in the presence of HI serum (FIG. 4, column 18), which indicates that the triple mutant construct has a higher degree of serum stability than the other constructs examined.

[00596] 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. 5). In agreement with the previous assessment, WT VSV-G showed decreased infectivity in serum as compared to no-serum conditions (FIG. 5, columns 1 and 2). However, heat inactivation (HI) of serum did appear to have a rescuing effect on WT VSV-G infectivity (FIG. 5, 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. 5, 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. 5, column 6). VSV-G (I182E, T214N, T352A) also demonstrated increased infectivity in serum and HI serum conditions as compared to no serum conditions (FIG. 5, 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.

[00597] 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 tropism

without alternating fusogenicity and additionally demonstrates a more stable profile and is not neutralized in serum.

[00598] **Example 3: Spring viremia of carp virus G protein can facilitate cell specific fusion.**

[00599] **Methods**

[00600] **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

[00601] 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.

[00602] **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).

[00603] **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).

[00604] **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.

[00605] Results:

[00606] **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.

[00607] 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. 6.

[00608] **Example 4: CD7 Targeting Moiety can be linked to a Fc stalk to transduce PBMCs.**

[00609] Generation of Plasmids and Sequences.

[00610] 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.

[00611] Generation of Engineered Lentiviral Particles.

[00612] 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)

[00613] CD7 binders attach to both human and non-human primate PBMCs, leading to CD7+ cell transduction.

[00614] 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. 7A-D and FIG. 8A-D) or with Rhabdoviridae glycoproteins, such as VSV-G (FIG. 7I-L and FIG. 8I-L) successfully transduced human PBMCs (FIG. 7A-L) or NHP PBMCs (FIG. 8A-L) compared to the binder alone (FIG. 7E-H and FIG. 8E-H) which shows no transduction. When CD7 with an IgG stalk was tested, the binder alone (top row) again did not transduce human (FIG. 7M) or NHP PBMCs (FIG. 8M) but when administered with blinded VSV-G, transduction was seen in both human (FIG. 7M, bottom panel) and NHP PBMCs (FIG. 8M, bottom panel).

[00615] 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.

[00616] **Example 5: CD8 Targeting Moiety can be linked to a Fc stalk to transduce PBMCs.**

[00617] Generation of Plasmids and Sequences.

[00618] 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.

[00619] Generation of Engineered Lentiviral Particles.

[00620] 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).

[00621] CD8 binders attach to both human and non-human primate PBMCs, leading to CD8+ cell transduction.

[00622] 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. 9A) or NHP PBMCs (FIG. 9B) with GFP (FIG. 9A-9B, top row) and CAR20 (FIG. 9A-9B, bottom row).

[00623] 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.

[00624] **Example 6: VSV-G* pseudotyped lentiviruses harboring Fc stalk binder transduce PBMCs.**

[00625] 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. 10A) compared to the binder alone (FIG. 10B) which shows no transduction. Data are also presented as percent CAR expression vs multiplicity of infection (FIG. 10C).

[00626] 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.

[00627] Example 7: CD7 Targeting Moiety can be linked to a flexible stalk to transduce PBMCs.

[00628] 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. 11A) compared to no binder (FIG. 11B) which shows no transduction. Data are also presented as percent CAR expression vs multiplicity of infection (FIG. 11C).

[00629] 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 (FIG. 12). 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. 12A), (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. 12B).

[00630] Example 8: SVCV-G pseudotyped lentiviruses harboring Fc stalk binder transduce PBMCs.

[00631] 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.

13A) compared to no binder (FIG. 13B) which shows no transduction. Data are also presented as percent CAR expression vs multiplicity of infection (FIG. 13C).

[00632] 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.

[00633] Example 9: SVCV-G pseudotyped lentiviruses harboring a CD7/flexible stalk binder transduce PBMCs.

[00634] 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. 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).

[00635] 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.

[00636] Example 10: SVCV-G pseudotyped lentiviruses are comparable to VSV-G* pseudotyped lentiviruses.

[00637] 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 (FIG. 15).

[00638] 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 (FIG. 16).

[00639] 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.

[00640] Example 11: VSV-G* and SVCV-G pseudotyped lentiviruses harboring a CD7/Fc stalk binder exhibit minimal off target transduction.

[00641] 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 (FIG. 17). 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.

[00642] Lentiviral constructs delivering a CAR20-T2A-GFP transgene were also assessed in a similar manner (FIG. 18). VSV-G* pseudotyped lentiviruses utilizing the Fc binder stalk still exhibited minimal off target transduction of B-cells in all cell populations tested (FIG. 18). 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. 18A). The percent of CAR-T2A-GFP positive cells only exceeded 1% in line HT at the highest concentration of lentivirus utilized.

[00643] 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.

[00644] **Example 12: VSV-G* and SVCV-G pseudotyped lentiviruses harboring a CD7/flexible stalk binder exhibit minimal off target transduction.**

[00645] 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 (FIG. 19).

[00646] Lentiviral constructs delivering a CAR20-T2A-GFP transgene were also assessed in a similar manner (FIG. 20). VSV-G* pseudotyped lentiviruses utilizing the flexible binder stalk still exhibited minimal off target transduction of B-cells in all cell populations tested (FIG. 12). 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. 12A). 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.

[00647] 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.

[00648] Example 13: anti-BCMA CAR transduced PBMCs kill multiple myeloma cells *in vitro*

[00649] PBMCs were transduced with a VSV-G* pseudotyped lentiviral construct delivering a FHVH33-BCMA CAR transgene and the ability of the PBMCs to kill BCMA positive multiple myeloma 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 FHVH33-BCMA CAR construct (SEQ ID NO: 126) as provided for herein. BCMA positive multiple myeloma cells were then added to the FHVH33-BCMA CAR cells at a given effector to target ratio (E:T). As shown in FIG. 21, the transduced PBMCs were able to kill three separate BCMA positive multiple myeloma cells.

[00650] Loss of BCMA antigen is a major determinant of resistance to BCMA-CAR therapy. Therefore, the PBMCs transduced with the FHVH33-BCMA CAR (SEQ ID NO: 126) transgene were tested for their ability to kill the multiple myeloma cell line NCI-H929 with BCMA knocked down. As expected (FIG. 22) the reduction of BCMA expression conferred resistance to the NCI-H929 cell line.

[00651] These examples and embodiments demonstrate that the VSV-G* pseudotyped lentiviruses utilizing the CD7 binders of the present disclosure are able to transduce PBMC cells with a FHVH33-BCMA CAR (SEQ ID NO: 126) transgene and generate functional FHVH33-BCMA CAR PBMC cells.

[00652] **Example 14: Generation of FCRL5 CAR PBMCs.**

[00653] The ability of VSV-G* pseudotyped lentiviral constructs to transduce PBMCs with a FCRL5 CAR transgene 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. Human PBMCs were transduced with a lentiviral construct carrying a FHVH33-BCMA CAR construct (SEQ ID NO: 126), or one of two FCRL5 CAR constructs (SEQ ID NOs: 129 or 130) as provided for herein. PBMCs were assessed for successful CAR transduction via flow cytometry analysis, staining with antibodies specific for the G4S linker present in the FCRL5 CAR constructs. As a secondary readout, transduced PBMCs were also incubated with His-tagged recombinant Human FCRL5, washed, and subsequently incubated with PE-dazzle 594-tagged anti-His tag secondary antibody. The results are shown in the table below:

	Construct			
	Non-transduced	BCMA FHVH33 CAR (SEQ ID NO: 126)	FCRL5 CAR V _L -V _H (SEQ ID NO: 129)	FCRL5 CAR V _H -V _L (SEQ ID NO: 130)
G4S positive cell percentage	0.055	0.46	19.0	19.9
Recombinant FCRL5 binding percentage	0.20	0.41	16.5	19.8

[00654] As shown in the table above, the VSV-G* pseudotyped lentiviral construct successfully transduced the PBMC cells with the FCRL5 CAR constructs (SEQ ID NO: 129 or 130), as detected via both G4S reactivity and recombinant FCRL5 protein binding. Having demonstrated the ability to generate FCRL5 CAR PBMCs, the ability of the PBMCs to kill FCRL5 positive Rec-1 cells *in vitro* was assessed. Human PBMCs were transduced with lentiviral constructs carrying either the V_L-V_H orientation FCRL5 CAR construct (SEQ ID NO: 129) or the V_H-V_L orientation FCRL5 CAR construct (SEQ ID NO: 130) as provided for herein. FCRL5 positive Rec-1 cells were then added to the FCRL5 CAR cells at multiple

effector to target (E:T) ratios. As shown in FIG 23A and FIG. 23B, the transduced PBMCs were able to kill the FCRL5 positive Rec-1 cells. Further, both orientations of the FCRL5 CAR produced similar results.

[00655] These examples and embodiments demonstrate that the VSV-G* pseudotyped lentiviruses utilizing the CD7 binders of the present disclosure are able to transduce PBMC cells with a FCRL5 CAR transgene and generate functional FCRL5 CAR PBMC cells.

[00656] **Example 15: Tandem BCMA-FCRL5 CAR constructs overcome loss of BCMA-CAR efficacy in Rec-1 cells.**

[00657] Tandem CAR constructs were generated comprising a BCMA sdAB (FHVH33) (SEQ ID NO: 126) and a FCRL5 scFv as provided for herein. The ability of VSV-G* pseudotyped lentiviral constructs to transduce PBMC cells with the tandem CAR transgenes 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 FHVH33-BCMA CAR construct (SEQ ID NO: 126), a FCRL5 CAR construct with a V_H-V_L orientation (SEQ ID NO: 130), or one of two BCMA/FCRL5 tandem CAR constructs (SEQ ID NO: 127 or 128) as provided for herein. PBMCs were assessed for successful CAR transduction via flow cytometry analysis, staining with antibodies specific for the G₄S linker present in the FCRL5 CAR and the BCMA/FCRL5 tandem CAR constructs. As an additional readout, transduced PBMCs were also incubated in parallel with either Alexafluor 647-tagged recombinant Human BCMA, or His-tagged recombinant Human FCRL5, washed, and subsequently incubated with PE-dazzle 594-tagged anti-His tag secondary antibody. The results are shown in the table below:

	Construct				
	Non-transduced	FHVH33 CAR (SEQ ID NO: 126)	FCRL5 CAR V _H -V _L (SEQ ID NO: 130)	BCMA/FCRL5 Tan CAR (SEQ ID NO: 127)	FCRL5/BCMA Tan CAR (SEQ ID NO: 128)
G ₄ S positive cell percentage	0.055	0.46	19.9	14.0	20.8
Recombinant BCMA binding percentage	0.015	39.8	0.00534	12.2	19.7

Recombinant FCRL5 binding percentage	0.20	0.41	19.8	15.2	21.5
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{00658} As shown in the table above, the VSV-G* pseudotyped lentiviral construct successfully transduced PBMCs with all of the CAR constructs. The anti-FCRL5 containing constructs demonstrated both G4S reactivity and binding to recombinant FCRL5 protein. Likewise, the FHVH33 constructs demonstrated binding to recombinant BCMA. Importantly, the tandem CAR constructs demonstrated the ability to bind to both antigens, as both tandem CAR constructs exhibited G4S reactivity as well as binding to recombinant BCMA and recombinant FCRL5. Having demonstrated the ability to generate the tandem CAR PBMCs, the ability of the PBMCs to kill BCMA positive NCI-H929 cells and FCRL5 positive Rec-1 cells *in vitro* was assessed. Human PBMCs were transduced with lentiviral constructs carrying CAR constructs outlined in the table above and as provided for herein. BCMA positive NCI-H929 cells or FCRL5 positive Rec-1 cells were then added to the CAR PBMC cells at multiple effector to target (E:T) ratios. As shown in FIG. 24, the FCRL5 CAR transduced PBMCs had reduced efficacy against the NCI-H929 cells as compared to the FHVH33 CAR transduced PBMCs. However, both tandem CAR transduced PBMCs displayed similar efficacy against the NCI-H929 cells as the FHVH33 CAR PBMCs, indicating that the potency of the bispecific antigen binding domain was similar to the BCMA CAR. As shown in FIG. 25, the FHVH33 CAR transduced PBMCs had a reduced efficacy against the Rec-1 cells as compared to the FCRL5 CAR transduced PBMCs. However, both tandem CAR transduced PBMCs displayed similar efficacy against the Rec-1 cells as the FCRL5 CAR PBMCs, indicating that the potency of bispecific antigen binding domain was similar to FCRL5 CAR.

{00659} These examples and embodiments demonstrate that the VSV-G* pseudotyped lentiviruses utilizing the CD7 binders of the present disclosure are able to transduce PBMC cells with tandem CAR transgenes and generate functional BCMA/FCRL5 tandem CAR PBMC cells. Additionally, these examples and embodiments demonstrate that the specific BCMA/FCRL5 tandem CAR combination is able to successfully overcome the loss of efficacy of an anti-BCMA CAR in a cell model having reduced BCMA content (Rec-1 cells).

{00660} **Example 16: Examination of Tandem CD20/CD22 CAR.** Fig. 26A and Fig. 26B demonstrate that M971 HL works better than LH across a range of effector cell to target cell ratios. PBMCs were transduced with VSV-G* anti-CD7 targeted vectors encoding OFA (SEQ

ID NO: 131), M971 HL (SEQ ID NO: 132), M971 LH (SEQ ID NO: 133), M971HL-OFA (SEQ ID NO: 134), or OFA-M971HL (SEQ ID NO: 135). Transduced PBMCs were then mixed with Raji or Daudi B-cell lines. M971 HL CAR22 (SEQ ID NO: 132) depletes Raji and Daudi cells with similar efficacy to Ofa HL CAR (SEQ ID NO: 131), and TanCAR 20/22 (both m971-Ofa (SEQ ID NO: 134) and Ofa-m971 (SEQ ID NO: 135) have efficacy similar to Ofa HL CAR (SEQ ID NO 131)). Fig. 27A-C illustrates that the TanCAR 20/22 is effective against B-cells expressing either CD20 or CD22. Cas9 knockout of either CD20 or CD22 was performed in the Raji B-cell line then those target cells were mixed with PBMCs from Fig. 26A-B. This experiment was performed with bulk-KO populations, so for example the OFA-CAR (SEQ ID NO: 131) was ~95% effective in the Raji-CD22-KO but reduced to 65% effective in the Raji-CD20-KO when 0% efficacy would be expected in a complete CD20 null [see Fig. 28A-C]. Importantly, the TanCAR of either orientation maintained >95% cytotoxicity. In summary, the loss of CD20 expression reduces efficacy of Ofa HL CAR (SEQ ID NO: 131) and m971 HL CAR (SEQ ID NO: 132), and TanCAR 20/22 can overcome the loss of either CD20 or CD22 expression in Raji Cells. As shown in Fig 28A-C, the same held true when the heterologous populations were purified into clonal knockouts. As expected, clonal KO of CD20 made the OFA CAR20 (SEQ ID NO: 131) <10% effective, while the M971 anti-CD22 (SEQ ID NO: 134) was less than 25% effective in the CD22KO. In all cases, the TanCAR had greater cytotoxicity. Note, the Raji from all other experiments are Raji-GFP-Luciferase cells, so reduction of luciferase activity may also be tracked as a surrogate for Raji cell health. In summary, the Dual CAR20/22 maintains killing against CD20 or CD22 single knockout clones. This is further illustrated in Fig. 29 which repeats Fig. 28A-C but with different PBMC donors.

[00661] Example 17: Examination of Tandem CD19/CD20 CAR. Similar experiments to those provided in example 16 above were performed to assess CD19/CD20 tandem CAR constructs. Briefly, PBMCs were activated with CD3/CD28 beads and incubated for 48 hours, after which activation was confirmed via flow cytometry. Activated PBMCs were transduced with lentiviral constructs as provided for herein delivering either CD19 CAR (SEQ ID NO: 203), CD20 CAR (SEQ ID NO: 150), CD19/CD20 TanCAR (SEQ ID NO: 167) or CD20/CD19 Tan CAR (SEQ ID NO: 170). CAR expression was confirmed on Day 5 post transduction, and the function of the CAR was assessed on Day 7 post transduction via incubation with Raji cell lines either i) expressing GFP/luciferase, ii) expressing GFP/luciferase and having CD19 and CD20 knocked out, iii) expressing GFP/luciferase and

having CD19 knocked out, or iv) expressing GFP/luciferase and having CD20 knocked out. B cell depletion was measured 48 hours post cell mixing.

[00662] As illustrated in FIG. 30A, each tandem CAR construct performed similarly to the single CAR constructs in Raji-GFP/LUC cells. FIG. 30B illustrates that the cell killing was due to the proper interaction of the CAR with the Raji cell, as knockout of both CD19 and CD20 ablated cell killing. FIGs. 30C and 30D illustrate that the tandem CAR constructs were able to maintain cell killing even when one of the target antigens (CD19 or CD20) was knocked out.

[00663] The CD19/CD20 TanCAR constructs were further investigated to determine if antigen binding domain orientation had an effect on cell killing. As shown in FIG. 31A, the TanCAR with a CD19-CD20 orientation (SEQ ID NO: 167) exhibited a slight reduction of cell killing in CD19 KO Raji cells, and a more modest reduction of cell killing in CD20 KO Raji cells. As expected, CD19 KO and CD20 KO dramatically reduces cell killing. As shown in FIG. 31B, the TanCAR with a CD20-CD19 orientation (SEQ ID NO: 170) maintained similar levels of cell killing across WT, CD19 KO, and CD20 KO Raji cells.

[00664] The results of these examples suggest that the CD19/CD20 TanCAR constructs as provided for herein are capable of mediating Raji cell killing and also maintain efficacy when one of the epitopes is absent from the target cell.

[00665] This specification contains numerous citations to patents, patent applications, and publications. Each is hereby incorporated by reference for all purposes.

[00666] The specification also makes reference to various sequences, such as those provided herein and below.

VSV-G Indiana Full length WT:

MKCLLYLAFLFIGVNCFTTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWNHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQVTPHHVLVDEYTGGEWVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGTTTERELWDDWAPYEDVEIGPNGVLR TSSGYKFLYMIHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGWFSWKS SIASFFFIIGLIIGLFLVLRVGIHLCKIKLHKTKRQIYTDIEMNRLGK (SEQ ID NO: 1)

VSV-G Indiana Ectodomain WT:

KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWNHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQVTPHHVLVDEYTGGEWVDSQFIN GKCSNYICPTVHNSTTWHSYKVKGLCDSNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCKHWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGTTTERELWDDWAPYEDVEIGPNGVLR TSSGYKFLYMIHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDES LFFGDTGLSKNP IELVEGWFSWKS SIASFFFIIGLIIGLFLVLRVGIHLCKIKLHKTKRQIYTDIEMNRLGK (SEQ ID NO: 2)

VSV-G Indiana ectodomain I182A:

KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHDNLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
 KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAVIVQVTPHHVLVDEYTGGEWVDSQFIN
 GKCSNYICPTVHNSTTWHSDYKVKGLCDNLASMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
 HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPV
 DLSYLAPKNP GTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGTTTERELWDDWAPYEDVEIGPNGVLR
 TSSGYKFLYMIHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGWFSWKSSIA
 SFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK (SEQ ID NO: 3)

VSV-G Indiana ectodomain I182D:

KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHDNLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
 KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAVIVQVTPHHVLVDEYTGGEWVDSQFIN
 GKCSNYICPTVHNSTTWHSDYKVKGLCDNLDSMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
 HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPV
 DLSYLAPKNP GTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGTTTERELWDDWAPYEDVEIGPNGVLR
 TSSGYKFLYMIHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGWFSWKSSIA
 SFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK (SEQ ID NO: 4)

VSV-G Indiana ectodomain I182E:

KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHDNLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
 KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAVIVQVTPHHVLVDEYTGGEWVDSQFIN
 GKCSNYICPTVHNSTTWHSDYKVKGLCDNLDSMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
 HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPV
 DLSYLAPKNP GTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGTTTERELWDDWAPYEDVEIGPNGVLR
 TSSGYKFLYMIHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGWFSWKSSIA
 SFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK (SEQ ID NO: 5)

VSV-G Indiana ectodomain H8A + K47Q:

KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHDNLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
 KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAVIVQVTPHHVLVDEYTGGEWVDSQFIN
 GKCSNYICPTVHNSTTWHSDYKVKGLCDNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
 HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPV
 DLSYLAPKNP GTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGTTTERELWDDWAPYEDVEIGPNGVLR
 TSSGYKFLYMIHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGWFSWKSSIA
 SFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK (SEQ ID NO: 6)

VSV-G Indiana ectodomain Q10A:

KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHDNLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
 KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAVIVQVTPHHVLVDEYTGGEWVDSQFIN
 GKCSNYICPTVHNSTTWHSDYKVKGLCDNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
 HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPV
 DLSYLAPKNP GTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGTTTERELWDDWAPYEDVEIGPNGVLR
 TSSGYKFLYMIHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGWFSWKSSIA
 SFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK (SEQ ID NO: 7)

VSV-G Indiana ectodomain Q10R:

KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHDNLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
 KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAVIVQVTPHHVLVDEYTGGEWVDSQFIN
 GKCSNYICPTVHNSTTWHSDYKVKGLCDNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
 HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPV
 DLSYLAPKNP GTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGTTTERELWDDWAPYEDVEIGPNGVLR
 TSSGYKFLYMIHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLSKNP IELVEGWFSWKSSIA
 SFFFIIGLIIGLFLVLRVGIHLCKIKLHTKKRQIYTDIEMNRLGK (SEQ ID NO: 8)

VSV-G Indiana ectodomain Q10K:

KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHDNLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
 KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAVIVQVTPHHVLVDEYTGGEWVDSQFIN
 GKCSNYICPTVHNSTTWHSDYKVKGLCDNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
 HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISPV

DLSYLAPKNPGTGPFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGTTTERELWDDWAPYEDVEIGPNGVLR
TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDSE LFFGDTGLSKNPIELVEGWFSWKSSIA
SFFFIIGLIIGLFLVLRVGIHLCKIKLHKTKRQIYTDIEMNRLGK (SEQ ID NO: 9)

VSV-G New Jersey Full length WT:

MLSYLIFALVSPILGKIEIVFPQHTTGDWKRVPHEYNYCPTSADKN SHGTQTGIPVELTMPKGLTTHQVDGFM C
HSALWMTTCDFRWYGP KYITHSIHNEEPTDYQCLEAIKAYKDGVSFNPGFPPQSCGYGTVTDAAEHIVTVPHSV
KVDEYTG EWIDPHFIGGRCKGQICETVHNSTKWFTSSDGESVCSQLFTLVGGTFFSDSEEITSMGLPETGIRSNY
FPYVSTEGICKMPFCRKP GYKLNLDLWFQITDPDLDKTVRDLPHIKDCDLSSSIVTPGEHATDISLISDVERILD
YALCQNTWSKIEAGEPITPVDLSYLGPKNPGAGPVFTIINGSLHYFMSKYL RVELESPVIPRMEGKVAGTRIVRQ
LWDQWFFPGEVEIGPNGVLKTKQGYKFPLHIIGTGEVDNDIKMERIVKHWEHPHIEAAQTFLKKDDTEEVLYYGD
TGVSKNPVELVEGWFSGWRSSIMGVLAVIIGFVILIFLIRLIGVLSLFRQKRRPIYKSDVEMAHFR (SEQ ID
NO: 10)

VSV-G New Jersey ectodomain WT:

KIEIVFPQHTTGDWKRVPHEYNYCPTSADKN SHGTQTGIPVELTMPKGLTTHQVDGFMCHSALWMTTCDFRWYGP
KYITHSIHNEEPTDYQCLEAIKAYKDGVSFNPGFPPQSCGYGTVTDAAEHIVTVPHSVKVDEYTG EWIDPHFIG
GRCKGQICETVHNSTKWFTSSDGESVCSQLFTLVGGTFFSDSEEITSMGLPETGIRSNYFPYVSTEGICKMPFCR
KPGYKLNLDLWFQITDPDLDKTVRDLPHIKDCDLSSSIVTPGEHATDISLISDVERILDYALCQNTWSKIEAGEP
ITPVDLSYLGPKNPGAGPVFTIINGSLHYFMSKYL RVELESPVIPRMEGKVAGTRIVRQLWDQWFFPGEVEIGPN
GVLKTKQGYKFPLHIIGTGEVDNDIKMERIVKHWEHPHIEAAQTFLKKDDTEEVLYYGD TGVSKNPVELVEGWFS
GWRSSIMGVLAVIIGFVILIFLIRLIGVLSLFRQKRRPIYKSDVEMAHFR (SEQ ID NO: 11)

VSV-G Marraba Full length WT:

MLRFLFCFLALGAHSKFTIVFPHHQKGNWKNVPSTYHYCPSSSDQNWHNDLTGVS LHVKIPKSHKAIQADGWM C
HAAKWVTTCDFRWYGP KYITHSIHMSPTLEQCKTSIEQTKQGVWINPGFPPQSCGYATVTDAAEVVVVQATPHHV
LVDEYTG EWIDSQLVGKCSKEVCQTVHNSTVWHADYKITGLCESNLASVDITFFSEDGQKTS LGKPNTGFRSNH
FAYESGEKACRMQYCTQWGIRLPSGVWFELVDKDLFQA AKLPECPRGSSISAPSQTSVDVSLIQDVERILDYSLC
QETWSKIRAKLPVSPVDLSYLAPKNPGSGPAFTIINGTLKYFETRYIRVDISNPIIPH MVGTMSGTTTERELWND
WYPYEDVEIGPNGVLKTP TGFKFPLYMIGHGMLDSDLHKSSQAQVFEHPHAKDAASQLPDDETLFFGDTGLSKNP
VELVEGWFSWKSTLASFFLIIGLVALIFIIRIIVAIRYKYKGRKTQKIYNDVEMSRLGNK (SEQ ID NO:
12)

VSV-G Marraba ectodomain WT:

KFTIVFPHHQKGNWKNVPSTYHYCPSSSDQNWHNDLTGVS LHVKIPKSHKAIQADGWMCHAAKWVTTCDFRWYGP
KYITHSIHMSPTLEQCKTSIEQTKQGVWINPGFPPQSCGYATVTDAAEVVVVQATPHHVLVDEYTG EWIDSQLVG
GKCSKEVCQTVHNSTVWHADYKITGLCESNLASVDITFFSEDGQKTS LGKPNTGFRSNHFAYESGEKACRMQYCT
QWGIRLPSGVWFELVDKDLFQA AKLPECPRGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAKLPVSPV
DLSYLAPKNPGSGPAFTIINGTLKYFETRYIRVDISNPIIPH MVGTMSGTTTERELWNDWYPYEDVEIGPNGVLK
TPTGFKFPLYMIGHGMLDSDLHKSSQAQVFEHPHAKDAASQLPDDETLFFGDTGLSKNPVELVEGWFSWKSTLA
SFFLIIGLVALIFIIRIIVAIRYKYKGRKTQKIYNDVEMSRLGNK (SEQ ID NO: 13)

VSV-G Carajas Full length WT:

MKMKMVIAGLILCIGILPAIGKITISFPQSLKGDW RVPKGYNYCPTSADKNLHGD LIDIGLRLRAPKSFKGISA
DGWMCHAARWITTCDFRWYGP KYITHSIHSFRPSNDQCKEAI RL TNEGNWINPGFPPQSCGYASVTDSESVVVTV
TKHQVLVDEYSGSWIDSQFP GGSCTSPICDTVHNSTLWHADHTLDSICDQEFVAMDAVLFTESGKFEFGKPN SG
IRSNYFPYESLKDVCMDFCKRKGKFLPSGVWFEIEDAEKSHKAQVELKIKRCPHGAVISAPNQNAADINLIMDV
ERILDYSLCQATWSKIQNKEALTP IDISYLGPKNPGPGPAFTIINGTLHYFNTRYIRVDIAGPVTK EITGFSVT
STSRVLWDQWFFPYGENSIGPNGLLKTASGYKPLFMVGTGVLDADIHKLGEATVIEHPHAKAQAQVVDSEVIF F
GDTGVSKNPVEVVEGWFSGWRSSLSMIFGIILIVCLVIVRLIALKYCCVRHKKRTIYKEDLEMGRIPRA
(SEQ ID NO: 14)

VSV-G Carajas ectodomain WT:

KITISFPQSLKGDWRVPKGYNYCPTSADKNLHGD LIDIGLRLRAPKSFKGISADGWMCHAARWITTCDFRWYGP
KYITHSIHSFRPSNDQCKEAI RL TNEGNWINPGFPPQSCGYASVTDSESVVVTVTKHQVLVDEYSGSWIDSQFP G

GSCTSPICDTVHNSTLWHADHTLDSICDQEFVAMDAVLFTESGKFEEFGKPNSGIRSNYPYFESLKDVCQMDFCR
 RKGFKLP SGVWFEIEDAEKSHKAQVELKIKRCPHGAVISAPNQNAADINLIMDVERILDYSLCQATWSKIQNKEA
 LTPIDISYLGPKNPGPGPAFTIINGTLHYFNTRYIRVDIAGPVTKEITGEVSGTSTSRVLWDQWFPYGENSIGPN
 GLLKTASGYKYPLFMVGTGVLADADIHKLGEATVIEHPHAKAQAQKVVDSEVIFFGDTGVSKNPVEVVEGWFSGWR
 SSLMSIFGIILLIVCLVILVRILIALKYCCVRHKKRTIYKEDLEMGRIPRA (SEQ ID NO: 15)

VSV-G Alagoa Full length WT:

MTPAFILCMLLAGSSWAKFTIVFPQSQKGDWKPVPNNYRYCPSSADQNWHDLLGVNIRAKMPKVHKAIKADGWM
 CHAAKWVTTCDYRWYGPQYITHSIHSFIPTKAQCEESIKQTKEGVWINPGFPPKNCGYASVSDAESIIVQATAHS
 VMIDEYSGDWLDSQFP TGRCTGSTCETIHNSTLWYADYQVTGLCDLSTEVTFYSEDGLMTSIGRQNTGYRSN
 YFYPEKGAAACRMKYCTHEGIRLPSGVWFEMVDKELLESVQMPECPAGLTISAPTQTSVDVSLILDVERMLDYSL
 CQETWSKIVHSGLPISPVDLGYIAPKNPGAGPAFTIIVNGTLKYFDTRYLRIDIEGPVLKMTGKVSPTPKRELWT
 EWFYDDVEIGPNGLKTPGYKFLYMLIGHGLDSDLQKTSQAEVFHHPQIAEAVQKLPDDETLFFGDTGISKN
 PVEVIEGWFSNWRSSVMAIVFAILLVITVLMVRLCVAFRHFCCQKRHKIYNDLEMNQLRR (SEQ ID NO:
 16)

VSV-G Alagoa ectodomain WT:

KFTIVFPQSQKGDWKPVPNNYRYCPSSADQNWHDLLGVNIRAKMPKVHKAIKADGWMCHAAKWVTTCDYRWYGP
 QYITHSIHSFIPTKAQCEESIKQTKEGVWINPGFPPKNCGYASVSDAESIIVQATAHSMIDEYSGDWLDSQFP
 TGRCTGSTCETIHNSTLWYADYQVTGLCDLSTEVTFYSEDGLMTSIGRQNTGYRSNYPYFYPEKGAAACRMKYCT
 HEGIRLPSGVWFEMVDKELLESVQMPECPAGLTISAPTQTSVDVSLILDVERMLDYSLCQETWSKIVHSGLPISP
 VDLGYIAPKNPGAGPAFTIIVNGTLKYFDTRYLRIDIEGPVLKMTGKVSPTPKRELWT EWFYDDVEIGPNGLK
 TPEGYKFLYMLIGHGLDSDLQKTSQAEVFHHPQIAEAVQKLPDDETLFFGDTGISKNPVEVIEGWFSNWRSSV
 MAIVFAILLVITVLMVRLCVAFRHFCCQKRHKIYNDLEMNQLRR (SEQ ID NO: 17)

VSV-G Cocal Full length WT:

MNLLLLTFIVLPLCSHAKFTIVFPQSQKGNWKNVPSYHYCPSSSDQNWHDLLGITMKVKMPKTHKAIQADGWM
 CHAAKWITTCDFRWYGPQYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQATPHH
 VLVDEYTGWDVDSQFPNGKCEETVEECETVHNSTVWYSDYKVTGLCDATLVDTEITFFSEDGKKESIGKPN
 TYRSNYPYFAYEKGDVKCKMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVGATISAPTQTSVDVSLILD
 VERILDYSLCQETWSKIRSKQPVSPVDSLAPKNPGTGPAFTIINGTLKYFETRYIRIDIDNPIISKMVGKISGSQ
 TERELWTEWFPYEGVEIGPNGLKTPTGYKFLYMLIGHGLDSDLHKTQAEVFHHPHAEAPKQLPEEETLFFGDT
 GISKNPVELIEGWFSWKSTVVTFFFAIGVFILLYVVARIVIAVRYRYQGSNNKRIYNDIEMSRFRK (SEQ ID
 NO: 18)

VSV-G Cocal ectodomain WT:

KFSIVFPQSQKGNWKNVPSYHYCPSSSDQNWHDLLGITMKVKMPKTHKAIQADGWMCHAAKWITTCDFRWYGP
 KYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQATPHHVLVDEYTGWDVDSQFP
 NGKCEETVEECETVHNSTVWYSDYKVTGLCDATLVDTEITFFSEDGKKESIGKPN TYRSNYPYFAYEKGDVK
 CKMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPVGATISAPTQTSVDVSLILDVERILDYSLCQETWSKIR
 SKQPVSPVDSLAPKNPGTGPAFTIINGTLKYFETRYIRIDIDNPIISKMVGKISGSQTERELWTEWFPYEGVEI
 GPNGLKTPTGYKFLYMLIGHGLDSDLHKTQAEVFHHPHAEAPKQLPEEETLFFGDTGISKNPVELIEGWFSWK
 STVVTFFFAIGVFILLYVVARIVIAVRYRYQGSNNKRIYNDIEMSRFRK (SEQ ID NO: 19)

VSV-G Morreton Full length WT:

MLVLYLLLSLLALGAQCKFTIVFPHNQKGNWKNVPANYQYCPSSSDLNWNHGLIGTSLQVKMPKSHKAIQADGWM
 CHAAKWVTTCDYRWYGPQYIVTHSIKSMIPTVDQCKESIAQTKQGTWLNPGFPPQSCGYASVTDAAEAVIVKATPHQ
 VLVDEYTGWDVDSQFP TGKCNKDICTVHNSTVWYSDYKVTGLCDANLISMDITFFSEDGKLTSLGKEGTGFRSN
 YFAYENGDKACRMQYCKHGWVRLPSGVWFEMADKDIYNDAKFPDCPEGSSIAAPSQTSVDVSLIQDVERILDYSL
 CQETWSKIRAHLPISPVDLSYSPKNPGTGPAFTIINGTLKYFETRYIRVDIAGPIIPQMRGVISGTTTERELWT
 DWYPYEDVEIGPNGLKTATGYKFLYMLIGHGLDSDLHISKAQVFEHPHIQDAASQLPDDETLFFGDTGLSKN
 PIELVEGWFSWKSTIASFFFIIGLVIGLYLVLRIALCICKRVQEKRPKIYTDVEMNRLDR (SEQ ID NO:
 20)

VSV-G Morreton ectodomain WT:

KFTIVFPHNQKGNWKNVPANYQYCPSSDLNWNHGLIGTSLQVKMPKSHKAIQADGWMCHAAKWVTTCDFRWYGP
KYVTHSIKSMIPTVDQCKESIAQTKQGTWLNPGFPPQSCGYASVTDAAEAVIVKATPHQVLVDEYTGGEWVDSQFPT
GKCNKDICTPTVHNSTTWHSDYKVTGLCDANLISMDITFFSEDGKLTSLGKEGTGFRSNYFAYENGDKACRMQYCK
HWGVRLP SGVWFEMADKDIYNDAKFDPDCPEGSSIAAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAHLPISPV
DLSYLSPKNP GTGPAFTIINGTLKYFETRYIRVDIAGPIIPQMRGVISGTTTERELWTDWYPYEDVEIGPNGVLK
TATGYKFLPYMIGHGMLDSDLHISSKAQVFEHPhiQDAASQLPDDETLFFGDTGLSKNP IELVEGWFSGWKSTIA
SFFFIIGLVIGLYLVLRI GIALCIKCRVQEKRPKIYTDVEMNRLDR (SEQ ID NO: 21)

Fc IgG1 (Accession No. P01857)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS
LGTQTYICNVNHKPSNTKVDKKVEPKCDKTHCTCPPAPELGGPSVFLFPPKPKDTLMISRTPEVTCVVDVDS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQ
PREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRW
QQGNVFSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO: 26)

Fc IgG2 (Accession No. AAN76043)

STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS
SLGTQTYICNVDHKPSNTKVDKRVESKYGPPCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVDSQEDP
EVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPAPIEKTISKAKGQPREP
QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPMLDSDGSFFLYSKLTVDKSRWQQGNV
FSCSVMEALHNHYTQKSLSLSPGK (SEQ ID NO: 27)

Fc IgG4 (Accession No. AAB59394)

STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS
SLGTKTYICNVDHKPSNTKVDKRVESKYGPPCPSCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVDSQEDP
EVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREP
QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGN
VFSCSVMEALHNHYTQKSLSLSPGK (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	SPYYSNDNSMDY	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	ARSPYYSNDNSMDY	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	DHRYNEGVSFDY	CD8AB1 HCDR3- Kabat
45	RASESVDGFGNSFMN	CD8AB1 LCDR1- Kabat
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

SEQ ID NO	Sequence	Description
47	QQNNEDPYT	CD8AB1 LCDR3- IMGT

What is Claimed:

1. A viral particle comprising one or more nucleic acid molecules, a heterologous viral glycoprotein and a targeting moiety, 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, wherein the one or more nucleic acid molecules encodes i) a tandem chimeric antigen receptor comprising a first antigen binding domain and a second antigen binding domain or ii) a first chimeric antigen receptor (first CAR) having an antigen binding domain and a second chimeric antigen receptor (second CAR) having an antigen binding domain.
2. The viral particle of claim 1, wherein:
 - the first antigen binding domain and second antigen binding domain of the tandem CAR, are each an antibody, or a fragment thereof, such as an scFv; or
 - the antigen binding domain of the first CAR and the antigen binding domain of the second CAR are each, independently, an antibody, or a fragment thereof, such as an scFv.
3. The viral particle of claim 1, wherein:
 - the first antigen binding domain and the second antigen binding domain of the tandem CAR bind to different antigens or different epitopes on the same antigen; or
 - the antigen binding domain of the first car and the antigen binding domain of the second CAR bind to different antigens or different epitopes on the same antigen.
4. The viral particle of claim 2, wherein:
 - the first and second antigen binding domains of the tandem CAR binds BCMA or FCRL5; CD19 or CD20; or CD20 and/or CD22, provided that the first and second antigen binding domains do not bind to the same antigen; or
 - the antigen binding domains of the first CAR and the second CAR binds to BCMA or FCRL5; CD19 or CD20; or CD20 and/or CD22, provided that the antigen binding domains of the first CAR and the second CAR do not bind to the same antigen.
5. The viral particle of claim 4, wherein the antigen binding domain that binds to BCMA 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 any one of the amino acid sequences of SEQ ID NOs: 89 and 94, and a light chain variable region of the light chain having at least 95% identity to the amino acid sequence of SEQ ID NO: 90.
6. The viral particle of claim 4, wherein the antigen binding domain that binds to BCMA and/or FCRL5 comprises a polypeptide comprising a light chain and a heavy chain

comprising: a heavy chain variable region of the heavy chain having any one of the amino acid sequences of SEQ ID NOs: 89 and 94, and a light chain variable region of the light chain of SEQ ID NO: 90.

7. The viral particle of claim 6 or 7, wherein the antigen binding domain that binds to BCMA and/or FCRL5 comprises a polypeptide comprising a sequence having at least 95% sequence identity to SEQ ID NOs: 92, 96, 107, or 111.
8. The viral particle of claim 6 or 7, wherein the antigen binding domain that binds to BCMA and/or FCRL5 comprises a polypeptide comprising a sequence having at least 95% sequence identity to SEQ ID NOs: 93, 97, 108, or 112.
9. The viral particle of claim 5, wherein the antigen binding domain that binds to CD19 and/or 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% sequence identity to any one of the amino acid sequences of SEQ ID NOs: 114 or 138, and a light chain variable region of the light chain having at least 95% sequence identity to an amino acid sequence of SEQ ID NO: 115 or 139.
10. The viral particle of claim 5, wherein the antigen binding domain that binds to CD19 and/or 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 NOs: 114 or 138; and a light chain variable region of the light chain comprising an amino acid sequence of SEQ ID NOs: 115 or 139.
11. The viral particle of claim 5, wherein the antigen binding domain that binds to CD20 and/or CD22 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 any one of the amino acid sequences of SEQ ID NOs: 114 or 118, and a light chain variable region of the light chain having at least 95% sequence identity to any one of the amino acid sequences of SEQ ID NO: 115 or 119.
12. The viral particle of claim 5, wherein the antigen binding domain that binds to CD20 and/or CD22 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 NOs: 114 or 118; and a light chain variable region of the light chain comprising an amino acid sequence of SEQ ID NOs: 115 or 119.
13. The viral particle of claim 5, wherein the antigen binding domain that binds to CD20 and/or CD22 comprises a polypeptide comprising a sequence having at least 95%

- sequence identity to any one of the amino acid sequences of SEQ ID NO: 116, 120, 122, or 124, or a sequence as set forth in SEQ ID NO: 116, 120, 122, or 124.
14. The viral particle of claim 5, wherein the antigen binding domain that binds to CD20 and/or CD22 comprises a polypeptide comprising a sequence having at least 95% sequence identity to any one of the amino acid sequences of SEQ ID NOs: 117, 121, 123, or 125, or a sequence as set forth in SEQ ID NOs: 117, 121, 123, or 125.
 15. The viral particle of any one of claims 3-14, wherein the CAR further comprises a hinge domain, a transmembrane domain, a costimulatory domain, and a signaling domain.
 16. The viral particle of claim 15, 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.
 17. The viral particle of claim 15 or 16, 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.
 18. The viral particle of any one of claims 15-17, 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.
 19. The viral particle of any one of claims 15-18, 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.
 20. The viral particle of claim 5, wherein the CAR or tandem 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% identical to any one of the sequences of SEQ ID NOs: 126-135, 138-142, and 145-207.
 21. The viral particle of claim 5, wherein the CAR or tandem 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% identical to any one of the sequences of SEQ ID NOs: 126-135, 142, 145-164, 203-207.
 22. The viral particle of claim 5, wherein the CAR or tandem 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% identical to any one of the sequences of SEQ ID NOs: 150, 167, 170, or 203.
23. The viral particle of claim 5, wherein the CAR or tandem CAR comprises an amino acid sequence or SEQ ID NO: 150.
 24. The viral particle of claim 5, wherein the CAR or tandem CAR comprises an amino acid sequence or SEQ ID NO: 167.
 25. The viral particle of claim 5, wherein the CAR or tandem CAR comprises an amino acid sequence or SEQ ID NO: 170.
 26. The viral particle of claim 5, wherein the CAR or tandem CAR comprises an amino acid sequence or SEQ ID NO: 203.
 27. The viral particle of any one of claims 1-26, wherein the S₁ stalk portion comprises a variant Fc protein and is attached to a surface of the viral particle through a transmembrane domain.
 28. The viral particle of claims 27, wherein the variant Fc protein is a IgG1 Fc, IgG2 Fc or IgG4 Fc protein.
 29. The viral particle of claim 28, 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.
 30. The viral particle of claim 28, wherein the variant Fc protein is a variant IgG1 Fc protein.
 31. The viral particle of claim 30, 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.
 32. The viral particle of any one of claims 1-31, 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.
 33. The viral particle of claim 32, wherein L₁ and L₂ are each, independently, a polypeptide linker.
 34. The viral particle of claim 33, 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.
35. The viral particle of any one of claims 32-34, 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.
36. The viral particle of claim 35, wherein the ECD comprises an amino acid sequence of SEQ ID NO: 59 or SEQ ID NO: 60.
37. The viral particle of claim 35, wherein the T_M comprises an amino acid sequence of SEQ ID NO: 61 or SEQ ID NO: 62.
38. The viral particle of any one of claims 35-37, wherein the ICD comprises an Env incorporation motif.
39. The viral particle of claim 38, wherein the Env incorporation motif comprises an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64.
40. The viral particle of any one of claims 1-39, wherein the target binding domain (T) binds to CD7.
41. The viral particle of any one of claims 1-39, wherein the target binding domain (T) binds to CD8.
42. The viral particle of any one of claims 1-41, wherein the heterologous viral glycoprotein is a VSV-G polypeptide.
43. The viral particle of claim 42, 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.
44. The viral particle of claim 43, wherein the VSV-G polypeptide comprises a I182E or I182D mutation as compared to SEQ ID NO: 2.
45. A method of infecting a cell, the method comprising contacting the cell with a viral particle of any one of claims 1-44.
46. A method of treating a disease or disorder in a subject, the method comprising administering to the subject a viral particle of any one of claims 1-44.

47. The method of claim 46, 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.
48. 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: 22, SEQ ID NO: 23, SEQ ID NO: 24, SEQ ID NO: 25, SEQ ID NO: 52 or SEQ ID NO: 53, having at least 95% identity to 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, having at least 99% identity to 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, or having at least 100% identity to 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;
the targeting moiety comprises an amino acid sequence having at least 90% identity to SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50 or SEQ ID NO: 51, at least 95% identity to SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50 or SEQ ID NO: 51, at least 99% identity to SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50 or SEQ ID NO: 51, or at least 100% identity to SEQ ID NO: 38, SEQ ID NO: 39, SEQ ID NO: 50 or SEQ ID NO: 51; and
the heterologous molecule of interest is a chimeric antigen receptor (CAR), a dual CAR, or a Tandem CAR that binds to BCMA and/or FCRL5, CD19 and/or CD20, or CD20 and/or CD22, wherein the CAR, dual CAR, or Tandem CAR comprises an amino acid sequence having at least 85%, 90%, 95%, 99%, or 100% identity to any one of the sequences of SEQ ID NOs: 126-135, 138-142, and 145-207.
49. The viral particle of claim 48, wherein the CAR, dual CAR, or Tandem 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% identical to any one of the sequences of SEQ ID NOs: 150, 167, 170, or 203.