

HEPATOCTYTE TARGETING MOLECULES AND METHODS OF USE THEREOF

RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application Ser. No. 63/507,817 filed June 13, 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 May 10, 2024, is named "INH-026WO_SL.xml" and is 138,150 bytes in size.

FIELD

[0003] Embodiments provided herein relate to hepatocyte targeting molecules, compositions comprising 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 that can then be combined with other targeting domains to target specific cell types, such as, but not limited to, liver cells. 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 that targets the viral particle to the liver 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: 91, at least 85% identity to SEQ ID NO: 91, at least 90% identity to SEQ ID NO: 91, at least 95% identity to SEQ ID NO: 91, at least 98% identity to SEQ ID NO: 91, or at least 100% identity to SEQ ID NO: 91.

[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 ASGR1. 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 HCDR 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 comprising the amino acid sequence of GKN, and an LCDR of SEQ ID NO: 34, 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: 35. In some embodiments, the light chain comprises a light chain variable region having at least 90% sequence identity to SEQ ID NO: 36. In some embodiments, the targeting moiety that binds to ASGR1 comprises a polypeptide having a sequence having at least 90% sequence identity to SEQ ID NO: 37. In some embodiments, the targeting moiety that binds to ASGR1 comprises a polypeptide having a sequence having at least 90% sequence identity to SEQ ID NO: 38.

[0019] In some embodiments, the heterologous viral glycoprotein is a SVCV-G polypeptide as provided for herein.

[0020] 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.

[0021] 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 chimeric antigen receptor ("CAR"), ATP7B, GAA, SERPINA1, OTC, GUSB, UGT1A1, PAH, BCKDHA, BCKDHB, DBT, ATP8B1, ABCB11, ABCB4, FAH, TAT, HPD, HMBS, ASS1, SLC25A13, F8, F9, AGXT, GRHPR, HOGA1, INS, glucagon-like peptide-1 (GLP-1) hormone, glucagon-like peptide-2 (GLP-2) hormone, glicentin, PYY, CCK, glucagon, amylin, activin type II inhibitors, or miR-22 inhibitors.

[0022] In some embodiments, the viral particle further comprises at least one nucleic acid molecule encoding for a gene editing system.

[0023] In some embodiments, the viral particle is a non-integrating lentiviral vector (NILV) particle.

[0024] 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.

[0025] 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.

[0026] 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.

[0027] 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.

[0028] 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.

[0029] 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.

[0030] 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: 37 or SEQ ID NO: 38. 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.

[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 target binding domain comprises a sequence selected from SEQ ID NO: 37 or SEQ ID NO: 38. In some embodiments, the stalk portion S₁ comprises a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker comprising a sequence selected from SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, or SEQ ID NO: 76, or is absent; Fc is a variant Fc protein comprising a sequence that is a variant of SEQ ID NO: 26, SEQ ID NO: 27, or SEQ ID NO: 28, L₂ is a linker comprising a sequence selected from SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, or SEQ ID NO: 76, or is absent; and X₁ is a polypeptide comprising a transmembrane domain. In some embodiments, the variant of SEQ ID NO: 26 comprises one or more mutations selected from the group consisting of L234A, L235A, N297A, P329G, I253A, H310A, and H435A. In some embodiments, the variant of SEQ ID NO: 27 comprises one or more mutations selected from the group consisting of N297A, P329G, I253A, H310A, and H435A. In some embodiments, the variant of SEQ ID NO: 28 comprises one or more mutations selected from the group consisting of S228P, L235E, N297A, P329G, I253A, H310A and H435A. In some embodiments, the polypeptide comprising a transmembrane domain (X₁) has a formula of ECD-T_M-ICD, wherein ECD is an extracellular domain having a sequence selected from SEQ ID NO: 59 or SEQ ID NO: 60, or is a fragment thereof, or is absent; T_M is a transmembrane domain having a sequence of SEQ ID NO: 61 or SEQ ID NO: 62 or a fragment thereof; and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64, or the ICD is absent.

[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: 37 or SEQ ID NO: 38. 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.

[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, 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: 37 or SEQ ID NO: 38. 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: 91, 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.

[0034] 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: 89 or SEQ ID NO: 92, at least 95% identity to SEQ ID NO: 89 or SEQ ID NO: 92, at least 99% identity to SEQ ID NO: 89 or SEQ ID NO: 92, or at least 100% identity to SEQ ID NO: 89 or SEQ ID NO: 92.

[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: 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: 89 or SEQ ID NO: 92, at least 95% identity to SEQ ID NO: 89 or SEQ ID NO: 92, at least 99% identity to SEQ ID NO: 89 or SEQ ID NO: 92, or at least 100% identity to SEQ ID NO: 89 or SEQ ID NO: 92.

[0036] 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: 37 or SEQ ID NO: 38. 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.

[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 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: 37 or SEQ ID NO: 38. 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 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: 37 or SEQ ID NO: 38. In some embodiments, the stalk portion S₁ comprises a formula L₃-X₁, wherein L₃ is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 55, and X₁ is a polypeptide linker comprising a transmembrane domain. In some embodiments, the polypeptide comprising a transmembrane domain (X₁) has a formula of ECD-T_M-ICD, wherein ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59 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: 23 or SEQ ID NO: 25. In some embodiments, the target binding domain comprises an amino acid sequence of SEQ ID NO: 37 or SEQ ID NO: 38. In some embodiments, the stalk portion S₁ comprises a formula L₃-X₁, wherein L₃ is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 55, and X₁ is a polypeptide linker comprising a transmembrane domain. In some embodiments, the polypeptide comprising a transmembrane domain (X₁) has a formula of ECD-T_M-ICD, wherein ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59, T_M is a transmembrane domain comprising an amino acid sequence of SEQ ID NO: 61, and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64.

[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: 52 or SEQ ID NO: 53. In some embodiments, the target binding domain comprises an amino acid sequence of SEQ ID NO: 37 or SEQ ID NO: 38. In some embodiments, the stalk portion S₁ comprises a formula L₃-X₁, wherein L₃ is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 55, and X₁ is a polypeptide linker comprising a transmembrane domain. In some embodiments, the polypeptide comprising a transmembrane domain (X₁) has a formula of ECD-T_M-ICD, wherein ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59, T_M is a transmembrane domain comprising an amino acid sequence of SEQ ID NO: 61, and ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, wherein the ICD comprises an env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64.

BRIEF DESCRIPTION OF FIGURES

[0041] 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.

[0042] 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.

[0043] FIG. 3 illustrates an alignment of the ectodomains of different VSV-G proteins from different strains.

[0044] FIG. 4 illustrates the effect of various VSV-G mutations on the serum stability of viral constructs in combination with a CD7 binder.

[0045] FIG. 5 illustrates the effect of various VSV-G mutations on the serum stability of viral constructs in combination with a CD7 binder.

[0046] FIG. 6 illustrates the ability of various rhabdovirus G proteins to transduce SupT1 and PBMC cells alone or in combination with a CD7 binder.

[0047] FIG. 7A and FIG. 7B illustrate the ability of the lentiviral particles harboring ASGR1 binders to successfully transduce ASGR1+ cells. FIG. 7A illustrates results for an ASGR1 binder comprising SEQ ID NO: 38. FIG. 7B illustrates results for an ASGR1 binder comprising SEQ ID NO: 37.

DETAILED DESCRIPTION

[0048] 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.

[0049] 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.

[0050] 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.

[0051] 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.

[0052] As used herein, the terms “a” or “an” means that “at least one” or “one or more” unless the context clearly indicates otherwise.

[0053] 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.

[0054] 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.

[0055] 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.”

[0056] 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.

[0057] 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.

[0058] 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.

[0059] “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.

[0060] “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.

[0061] “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.

[0062] 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.

[0063] “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.

[0064] 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.

[0065] 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.

[0066] 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.

[0067] 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.

[0068] 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.

[0069] “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.

[0070] 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.

[0071] 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.

[0072] 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.

[0073] 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).

[0074] 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.”

[0075] “Parenteral” administration of a composition includes, e.g., subcutaneous (s.c.), intravenous (i.v.), intramuscular (i.m.), or intrasternal injection, or infusion techniques.

[0076] 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.

[0077] 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.

[0078] 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.

[0079] 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.

[0080] 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.

[0081] 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.

[0082] 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.

[0083] 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.

[0084] 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.

[0085] 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.

[0086] 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.

[0087] 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.

Viral Particles Comprising Heterologous Viral Glycoprotein and Targeting Moiety

[0088] 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 that targets the viral particle to the liver, 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.

[0089] 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).

[0090] In some embodiments, the variant Fc protein is a variant IgG1 Fc protein (SEQ ID NO: 26). In some embodiments, the variant IgG1 Fc protein comprises one or more of the mutations that corresponds to those selected from the group consisting of: L234A, L235A,

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

[0091] In some embodiments, the variant Fc protein comprising a variant IgG1 Fc protein comprises a truncation of the IgG1 Fc sequence. The truncation can comprise the deletion of any number of amino acids from the N-terminus, the C-terminus, or both of the IgG1 Fc sequence. In some embodiments, the variant Fc protein comprising a variant IgG1 Fc protein comprises a truncation of SEQ ID NO: 26. The truncation can comprises the deletion of any number of amino acids from the N-terminus, the C-terminus, or both of SEQ ID NO: 26. In some embodiments, the truncation comprises the deletion of amino acids from the N-terminus of SEQ ID NO: 26. In some embodiments, the truncation comprises the deletion of amino acids from the C-terminus of SEQ ID NO: 26. In some embodiments, the truncation comprises the deletion of amino acids from both the N-terminus and the C-terminus of SEQ ID NO: 26. In some embodiments, the truncation of SEQ ID NO: 26 comprises an amino acid sequence of SEQ ID NO: 90:

EPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVDS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY

KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKG
 FYP SDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVF
 SCSVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 90)

[0092] In some embodiments, the variant IgG1 Fc protein comprises one or more mutations relative to SEQ ID NO: 90 selected from the group consisting of: L19A, L20A, N82A, P114G, I38A, H95A, and H220A. It is to be understood that the positions L19, L20, N82, P114, I38, H95, and H220 are in reference to SEQ ID NO: 90 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: 90. Any of the mutations L19A, L20A, N82A, P114G, I38A, H95A, and H220A of SEQ ID NO: 90 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: 90. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to N82A of SEQ ID NO: 90. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to P114G of SEQ ID NO: 90. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to L19A, L20A, N82A, and P114G of SEQ ID NO: 90. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to I38A of SEQ ID NO: 90. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to H95A of SEQ ID NO: 90. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to H220A of SEQ ID NO: 90. In some embodiments, the variant IgG1 Fc protein comprises a mutation that corresponds to I38A, H95A, and H220A of SEQ ID NO: 90. 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: 90. 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: 90. 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: 91:

EPKSCDKTHTCPPCPAPEAAGGPSVFLFPPKPKDTLMASRTPEVTCVVVDVS
 HEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLAQDWLNGKEY
 KCKVSNKALGAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKG
 FYP SDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVF
 SCSVMHEALHNAYTQKSLSLSPGK (SEQ ID NO: 91)

[0093] 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.

[0094] 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.

[0095] 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.

[0096] In some embodiments, the variant Fc protein comprising a variant IgG4 Fc protein comprises a truncation of the IgG4 Fc sequence. The truncation can comprise the deletion of any number of amino acids from the N-terminus, the C-terminus, or both of the IgG4 Fc sequence. In some embodiments, the variant Fc protein comprising a variant IgG4 Fc protein comprises a truncation of SEQ ID NO: 28. The truncation can comprises the deletion of any number of amino acids from the N-terminus, the C-terminus, or both of SEQ ID NO: 28. In some embodiments, the truncation comprises the deletion of amino acids from the N-terminus of SEQ ID NO: 28. In some embodiments, the truncation comprises the deletion of amino acids from the C-terminus of SEQ ID NO: 28. In some embodiments, the truncation comprises the deletion of amino acids from both the N-terminus and the C-terminus of SEQ ID NO: 28.

[0097] In some embodiments, the stalk portion S₁ comprising a variant Fc protein is given by the formula L₁-Fc-L₂-X₁, wherein L₁ is a linker or absent; Fc is the variant Fc protein; L₂ is a linker or absent; and X₁ is a polypeptide comprising the transmembrane domain. Accordingly, the targeting moiety comprising the formula T-S₁ may also be given by the formula T-L₁-Fc-L₂-X₁, wherein: T is a target binding domain that targets the viral particle to the liver; L₁ is a linker or absent; Fc is the variant Fc protein; L₂ is a linker or absent; and X₁ is a polypeptide comprising the transmembrane domain. Therefore, it is to be understood that, in some embodiments, the stalk portion S₁ may be given by the formula L₁-Fc-L₂- X₁. 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.

[0098] In some embodiments, L₁ and L₂ 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, L₁ 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.

[0099] 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 that targets the viral particle to the liver; L₁ is a linker or absent; Fc is the

variant Fc protein; L_2 is a linker or absent; ECD is an extracellular domain, or a fragment thereof, of a cell surface protein, or is absent; T_M is a transmembrane domain of a transmembrane protein; and ICD is an intracellular domain of a protein or a protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle, or is absent. Therefore, it is to be understood that, in some embodiments, the stalk portion S_1 may be given by the formula L_1 -Fc- L_2 -ECD- T_M -ICD.

[00100] 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 that targets the viral particle to the liver, 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.

[00101] 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, L₃ is (GGGGA)_n (SEQ ID NO: 54) and n is greater than 10. 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 (GGGGS)_n (SEQ ID NO: 55) and n is 5. In some embodiments, L₃ is (GGGGS)_n (SEQ ID NO: 55) and n is 6. In some embodiments, L₃ is (GGGGS)_n (SEQ ID NO: 55) and n is 7. In some embodiments, L₃ is (GGGGS)_n (SEQ ID NO: 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 EGKSSSGSGSESKST (SEQ ID NO: 58).

[00102] 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), EGKSSSGSGSESKST (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 EGKSSSGSGSESKST (SEQ ID NO: 58).

[00103] 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), EGKSSSGSGSESKST (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).

[00104] 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 that targets the viral particle to the liver, 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.

[00105] In some embodiments, the ECD is absent. In some embodiments, the ECD can be any appropriate extracellular domain or fragment thereof. In some embodiments, the ECD is from a different protein as compared to the transmembrane domain. The ECD domain can be the entire ECD domain or a fragment thereof. In some embodiments, the ECD domain is a CD8 or CD28 ECD domain, or a fragment thereof. In some embodiments, the ECD domain is a CD8 ECD domain or fragment thereof. In some embodiments, the CD8 ECD domain comprises the polypeptide of FVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 59). In some embodiments, the CD8 ECD domain consists or consists essentially of the polypeptide of FVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 59). In some embodiments, the ECD domain comprises a polypeptide that is 25-45 amino acids in length. In some embodiments, the ECD comprises a polypeptide that is at least,

or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of FVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 59). In some embodiments, the ECD domain is a CD28 ECD domain or fragment thereof. In some embodiments, the CD28 ECD domain comprises the polypeptide of KIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPFPGPSKP (SEQ ID NO: 60). In some embodiments, the CD28 ECD domain consists or consists essentially of the polypeptide of KIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPFPGPSKP (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 KIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPFPGPSKP (SEQ ID NO: 60).

[00106] 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 FWVLVVVGVLACYSLLVTVAFIIFWV (SEQ ID NO: 62). In some embodiments, the CD28 T_M domain consists or consists essentially of the polypeptide of FWVLVVVGVLACYSLLVTVAFIIFWV (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 FWVLVVVGVLACYSLLVTVAFIIFWV (SEQ ID NO: 62).

[00107] In some embodiments, the T_M domain is from the same protein as the ECD. In some embodiments, the T_M domain is from a different protein as the ECD. In some embodiments, the T_M domain is a CD8, or CD28 T_M domain or a fragment thereof and the ECD domain is a CD8, or CD28 ECD domain or fragment thereof. In some embodiments, the T_M domain is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of IYIWAPLAGTCGVLLLSLVITLYCNHRN (SEQ ID NO: 61) and the ECD domain is at least,

or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of FVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 59). In some embodiments, the T_M domain is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of IYIWAPLAGTCGVLLLSLVITLYCNHRN (SEQ ID NO: 61) and the ECD domain is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of KIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPFPGPSKP (SEQ ID NO: 60). In some embodiments, the T_M domain is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of FWVLVVVGGLACYSLLVTVAFIIFWV (SEQ ID NO: 62) and the ECD domain is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of FVPVFLPAKPTTTPAPRPPTPAPTIASQPLSLRPEACRPAAGGAVHTRGLDFACD (SEQ ID NO: 59). In some embodiments, the T_M domain is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of FWVLVVVGGLACYSLLVTVAFIIFWV (SEQ ID NO: 62) and the ECD domain is at least, or is about, 80, 85, 90, 91, 92, 93, 94, 95, 96, 97, 98, or 99% identical to a peptide of KIEVMYPPPYLDNEKSNGTIIHVKGKHLCPSPFPGPSKP (SEQ ID NO: 60).

[00108] In some embodiments, the transmembrane domain is linked to an intracellular domain (ICD) of a cellular transmembrane protein, or a fragment thereof. In some embodiments, the ICD is absent. In some embodiments, the ICD is from the same or different protein as the T_M domain. In some embodiments, the ICD comprises an Env incorporation motif. An Env incorporation motif is a molecule, e.g., polypeptide, that can help to facilitate the incorporation of a protein into the envelope of the virus. A non-limiting example of an Env incorporation motif is a polypeptide comprising the amino acid sequence of NRVQRGYS (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.

[00109] 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, the desired target is a liver cell. In some embodiments, the liver cell is a hepatocyte. In some embodiments, T is any polypeptide, polynucleotide, or fragment thereof that binds to ASGPR,

including a subunit thereof, such as ASGR1, or ASGR2. In some embodiments, the targeting moiety “T” binds to ASGPR. In some embodiments, the target binding domain “T” binds to the ASGR1 subunit of ASGPR. In some embodiments, the target binding domain “T” binds to the ASGR2 subunit of ASGPR. In some embodiments, the target binding domain “T” binds to both the ASGR1 and the ASGR2 subunits of ASGPR, such as through a conserved epitope on both ASGR1 and ASGR2 or through an epitope that spans ASGR1 and ASGR2. 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.

[00110] 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.

[00111] 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.

[00112] 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.

[00113] 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.

[00114] 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.

[00115] 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 MKMKMVIAGLLCIGILPAIG (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.

[00116] 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.

[00117] In some embodiments, a VSV-G protein is provided that comprises a mutation at position 199 as compared to SEQ ID NO: 18 or at position 182 as compared to SEQ ID NO:

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

[00118] 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.

[00119] 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.

[00120] 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.

[00121] 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.

[00122] 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.

[00123] 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.

[00124] 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.

[00125] 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.

[00126] In some embodiments, the substitution at position 8 is an alanine, i.e., H8A.

[00127] In some embodiments, the substitution at position 47 is Q or N, i.e., K47Q or K47N.

[00128] In some embodiments, the protein comprises a mutation (substitution) at position 10. In some embodiments, the substitution/mutation is Q10A, Q10R, or Q10K.

[00129] 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.

[00130] 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.

[00131] 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.

[00132] 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.

[00133] 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.

[00134] 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.

[00135] 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

[00136] 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.

[00137] 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.

[00138] 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.

[00139] 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.

[00140] 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.

[00141] 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.

[00142] 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.

[00143] In some embodiments, the VSV-G protein further comprises a mutation at position that corresponds to positions 214 and/or 352 of SEQ ID NO: 2. In some embodiments, the residue that corresponds to position 214 of SEQ ID NO: 2 is T214. In some embodiments, the residue that corresponds to position 352 of SEQ ID NO: 2 is T352. In some embodiments, the VSV-G protein comprises mutation that corresponds to T214N mutation as compared to SEQ ID NO: 2. In some embodiments, the VSV-G protein comprises mutation that corresponds to T352A mutation as compared to SEQ ID NO: 2. In some embodiments, the VSV-G protein comprises a T214N and T352A mutations as compared to SEQ ID NO: 2. These mutations can be combined with any other mutations as provided for herein. In some embodiments, the T214N and/or T352A mutations are combined with the I182E or I182D mutations. In some embodiments, a VSV-G protein comprises an amino acid sequence of SEQ ID NO: 22 and SEQ ID NO: 23, which combines the I182D or I182E, respectively, with the T214N and T352A mutations. The sequences are also illustrated below with the leader sequences, which are removed during protein processing.

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

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MKCLLYLAFLFIGVNCKFTIVFPHNQKGNWKNVPSNYHYCPSSSDLN
WHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGPK
YITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVI
VQVTPHHVLVDEYTG EWVDSQFINGKCSNYICPTVHNSTTWHSDYKV
KGLCDSNLDSMDITFFSEDGELSSLGKEGTGFRS NYFAYENG GKACK
MQYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSV
DVSLIQDVERILDYSLCQETWSKIRAGLPISPVDLSYLAPKNPGTGPAFT
IINGTLKYFETRYIRVDIAAPILSRMVGMISGTTAERELWDDWAPYEDV
EIGPNGVLR TSSGYKFPLYMIGHGMLDSLHLSSKAQVFEHPHIQDAA
SQLPDDESLFFGDTGLSKNPIELVEGW FSSWKSSIASFFFHIGLIIGLFLVL
RVGIHLCIKLKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 24)

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VSV-G Protein_ I182D, T214N and T352A mutations (without leader sequence)

KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPK
SHKAIQADGWMCHASKWVTTCDFRWYGPKYITHSIRSFTPSVEQCKE
SIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGE
WVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLDSDMDITFFS
EDGESSLGKEGTGFRSNYFAYENGGKACKMQYCKHWGVRLPSGVW
FEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQ
ETWSKIRAGLPISPDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDI
AAPILSRMVGMI SGTTAERELWDDWAPYEDVEIGPNGVLR TSSGYKFP
LYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLFFGDTGLS
KNPIELVEGWFSWKSSIASFFFIIGLIIGLFLVLRVGIHLCKLKH TKKR
QIYTDIEMNRLGK (SEQ ID NO: 22)

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

MKCLLYLAFLFIGVNCKFTIVFPHNQKGNWKNVPSNYHYCPSSSDLN
WHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAEAVI
VQVTPHHVLVDEYTGEWVDSQFINGKCSNYICPTVHNSTTWHSYK
VKGLCDSNLESMDITFFSEEDGESSLGKEGTGFRSNYFAYENGGKACKM
QYCKHWGVRLPSGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVD
VSLIQDVERILDYSLCQETWSKIRAGLPISPDLSYLAPKNPGTGPAFTII
NGTLKYFETRYIRVDIAAPILSRMVGMI SGTTAERELWDDWAPYEDVE
IGPNGVLR TSSGYKFP LYMIGHGMLDSDLHLSSKAQVFEHPHIQDAAS
QLPDDESLFFGDTGLSKNPIELVEGWFSWKSSIASFFFIIGLIIGLFLVL
RVGIHLCKLKH TKKRQIYTDIEMNRLGK (SEQ ID NO: 25)

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

KFTIVFPHNQKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPK
SHKAIQADGWMCHASKWVTTCDFRWYGPKYITHSIRSFTPSVEQCKE
SIEQTKQGTWLNPGFPPQSCGYATVTDAEAVIVQVTPHHVLVDEYTGE
WVDSQFINGKCSNYICPTVHNSTTWHSYKVKGLCDSNLESMDITFFS
EDGESSLGKEGTGFRSNYFAYENGGKACKMQYCKHWGVRLPSGVW
FEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQ
ETWSKIRAGLPISPDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDI
AAPILSRMVGMI SGTTAERELWDDWAPYEDVEIGPNGVLR TSSGYKFP

LYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDESLLFFGDTGLS
KNPIELVEGWFWSSWKSSIASFFFIIGLIIGLFLVLRVGIHLCKLKHHTKKR
QIYTDIEMNRLGK (SEQ ID NO: 23)

[00144] 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.

[00145] 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.

[00146] 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.

[00147] Additionally, in some embodiments, instead of the VSV-G protein or mutant thereof, the viruses can be pseudotyped with other viral structural proteins.

[00148] 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.

[00149] The sequence of Spring Viremia of Carp Virus – G (SEQ ID NO: 52-with leader sequence)

MSIISYIAFLLLLIDSNLGIPIFVPSGRNISWQPVIQPFQDYQCPIHGNNLNTMGLSATKLTIK
SPSVFSTDKVSGWICHAAEWKTTCDYRWYGPQYITHSIHPISPTIDECRRIIQRIASGTDED
LGFPFQSCGWASVTTVSNTNYRVVPHSVHLEPYGGHWIDHEFNNGGECREKVCCEMKGNSIWI
TEETVQHECAKHIEEVEGIMYGNVPRGDVMYANFIIDRHHRVYRFGGSCQMFKCNKDGIKF
ARGDWVEKTAGTLTTIHDNVPKCVDTLVSGHRPGLDLIDTVFNLENNVEYTLCEGTRKIN
KQEKLTSDLSYLAPRIGGFGSVFRVNRGTLERGSTTYIRIEVEGPIVDSLNGTDPRTNASR
VFWDWELDGNIIYQGFNGVYKKGDKGIHIPLNMIESGIIDDELQHAFQADIIPHPHYDDDEI
REDDIFFDNTGNGNPVDAVVEWVSGWGTSLKFFGMTLVALILIFLLIRCCVACTYLMKRSK
RPATESHEMRSLV

[00150] The sequence of Spring Viremia of Carp Virus – G (SEQ ID NO: 53-without leader sequence):

IPFVPSGRNISWQPVIQPFQDYQCPIHGNNLNTMGLSATKLTIKSPSVFSTDKVSGWICHAA
EWKTTCDYRWYGPQYITHSIHPISPTIDECRRIIQRIASGTDEDLGFPFQSCGWASVTTVS
NTNYRVVPHSVHLEPYGGHWIDHEFNNGGECREKVCCEMKGNSIWIETVQHECAKHIEEVEG
IMYGNVPRGDVMYANFIIDRHHRVYRFGGSCQMFKCNKDGIKFARGDWVEKTAGTLTTIHD

NVPKCVDTLVSGHRPGLDLIDTVFNLENVVEYTLCEGTRKINKQEKLTSDLSYLAPRIG
 GFGSVFRVRNGTLERGSTTYIRIEVEGPVDSLNGTDPRTNASRVFWDDWELDGNIYQGFNG
 VYKKGDKIHIPLNMIESGIIDDELQHAFQADIIPHPHYDDDEIREDDIFFDNTGENGNPVD
 AVVEWVSGWGTSLKFFGMTLVALILIFLLIRCCVACTYLMKRSKRPATESHEMRSLV

Targeting Moieties

[00151] In some embodiments, the viral particle comprises a targeting moiety having the formula T-S₁, wherein T is a target binding domain that targets the viral particle to the liver 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 liver 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 the stalk portion S₁ comprising a variant Fc protein (e.g. L₁-Fc-L₂-X₁) as provided for herein or through a stalk portion S₁ comprising 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.

[00152] 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.

[00153] In some embodiments, the targeting moiety binds to asialoglycoprotein receptors (ASGPR). ASGPR comprises two subunits, asialoglycoprotein receptor 1 (ASGR1) and asialoglycoprotein receptor 2 (ASGR2). Accordingly, in some embodiments, the targeting moiety binds to ASGR1, ASGR2, or a combination thereof. In some embodiments, the

targeting moiety binds to ASGR1. In some embodiments, the targeting moiety binds to ASGR2. In some embodiments, the targeting moiety binds to both ASGR1 and ASGR2. In binding to both ASGR1 and ASGR2, the targeting moiety may recognize and bind a region of conserved epitope similarity between ASGR1 and ASGR2. Alternatively, the targeting moiety may recognize an epitope that spans both subunits. ASGPR consists of an extracellular carbohydrate recognition domain (CRD), a transmembrane domain, a stalk region connecting the CRD to the transmembrane domain, and a cytoplasmic domain. The targeting moiety may bind to any accessible region on ASGPR. In some embodiments, the targeting moiety binds to the CRD of ASGPR. In some embodiments, the targeting moiety binds to the stalk region of ASGPR. Each of the subunits (ASGR1 and ASGR2) making up ASGPR also share the same composition of a CRD, stalk region, transmembrane domain, and cytoplasmic domain. Accordingly, in some embodiments, the targeting moiety binds to the CRD of ASGR1. In some embodiments, the targeting moiety binds to the CRD of ASGR2. In some embodiments, the targeting moiety binds to the CRD of both ASGR1 and ASGR2. In some embodiments, the targeting moiety binds to the stalk region of ASGR1. In some embodiments, the targeting moiety binds to the stalk region of ASGR2. In some embodiments, the targeting moiety binds to the stalk region of both ASGR1 and ASGR2.

[00154] In some embodiments, the targeting moiety binds to a target that is present on a cell, such as a liver cell. In some embodiments, the cell is a hepatocyte. In some embodiments, the cell is a ASGR1+ hepatocyte. In some embodiments, the cell is a ASGR2+ hepatocyte.

ASGR binding polypeptides

[00155] In some embodiments, the targeting moiety (e.g. polypeptide) binds to ASGR1.

[00156] In some embodiments, the polypeptide that binds to ASGR1 is an antibody which binds to non-human primate ASGR1. In some embodiments, the polypeptide that binds to ASGR1 is an antibody which binds to human ASGR1. The sequence of human ASGR1 (UniProt P07306-1) is as follows (SEQ ID NO: 29):

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MTKEYQDLQHLDNEESDHHQLRKGPPLQRLCSGPRLLLSLGLSLLL
VVVCVIGSQNSQLQEELRGLRETFNFTASTEAVKGLSTQGGNVGRKMKSL
ESQLEKQKDLSEDHSSLLLVHKQFVSDLRSLSCQMAALQGNGSERTCCPVN
WVEHERSCYWFSRSGKAWADADNYCRLEDAHLVVVTSWEEQKFVQHHIGP
VNTWMGLHDQNGPWKWVDGTDYETGFKNWRPEQPDDWYGHGLGGGEDC
AHFTDDGRWNDDVCQRPYRWVCETELDKASQEPPLL (SEQ ID NO: 29).
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[00157] In some embodiments, the ASGR1 that the polypeptide binds to is expressed on the surface of a cell. In some embodiments, the cell is a liver cell. In some embodiments, the liver cell is a ASGR1+ hepatocyte.

[00158] 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 or variant thereof as provided for herein.

[00159] In some embodiments, polypeptides (e.g. ASGR1-binding polypeptide) are provided herein. In some embodiments, antibodies (e.g. an anti-ASGR1 antibody) are provided herein. In some embodiments, the antibody is a recombinant antibody that binds to ASGR1. In some embodiments, the ASGR1 protein is a human ASGR1 protein. In some embodiments, the ASGR1 protein is a non-human ASGR1 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.

[00160] In some embodiments, the targeting moiety (e.g. polypeptide) binds to ASGR2.

[00161] In some embodiments, the polypeptide that binds to ASGR2 is an antibody which binds to non-human primate ASGR2. In some embodiments, the polypeptide that binds to ASGR2 is an antibody which binds to human ASGR2. The sequence of human ASGR2 (UniProt P07307-1) is as follows (SEQ ID NO: 131):

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MAKDFQDIQQLSSEENDHPFHQGE GPGTRRLNPRRGNPFLKGPPPAQPLAQR  
LCSMVCFSLLALSFNILLVVICVTGSQSEGHGGAQLQAE LRS LKEAFS NFSSS  
TLTEVQAISTHGGSVGDKITSLGAKLEKQQDLKADHDALLFHLKHFPVDLR  
FVACQMELLHSNGSQR TCCPVNWVEHQGSCYWFSHSGKAWAEAEKYCQLE  
NAHLVVINSWEEQKFIVQHTNP FNTWIGLTDS DGSWKWVDGTDYRHNYKN  
WAVTQPDNWHGHELGGS EDCVEVQPDGRWNDDFCLQVYRWVCEKRRNAT  
GEVA (SEQ ID NO: 131).
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[00162] In some embodiments, the ASGR2 that the polypeptide binds to is expressed on the surface of a cell. In some embodiments, the cell is a liver cell. In some embodiments, the liver cell is a ASGR2+ hepatocyte.

[00163] 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 or variant thereof as provided for herein.

[00164] In some embodiments, polypeptides (e.g. ASGR2-binding polypeptide) are provided herein. In some embodiments, antibodies (e.g. an anti-ASGR2 antibody) are provided herein. In some embodiments, the antibody is a recombinant antibody that binds to ASGR2. In some embodiments, the ASGR2 protein is a human ASGR2 protein. In some embodiments, the ASGR2 protein is a non-human ASGR2 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.

[00165] In some embodiments, the targeting moiety (e.g. polypeptide) binds to ASGR1. In some embodiments, an antibody, or antigen binding fragment thereof is provided, wherein the antibody or antibody fragment binds to ASGR1. In some embodiments, the ASGR1 binding antibody, or antigen binding fragment thereof, is as described in U.S. Patent Serial No. 9,771,427; U.S. Patent Serial No. 10,975,151; U.S. Patent Publication No. 202110324085A1; Bon, Charlotte et al. “Capacity limits of asialoglycoprotein receptor-mediated liver targeting.” *mAbs* vol. 9,8 (2017): 1360-1369. doi:10.1080/19420862.2017.1373924; Trahtenherts, Alla, and Itai Benhar. “An internalizing antibody specific for the human asialoglycoprotein receptor.” *Hybridoma* (2005) vol. 28,4 (2009): 225-33. doi:10.1089/hyb.2009.0019; Coulstock, Edward et al. “Liver-targeting of interferon-alpha with tissue-specific domain antibodies.” *PloS one* vol. 8,2 (2013): e57263. doi:10.1371/journal.pone.0057263; and Born, Rita. “Benefit and application of antibodies against the H1 carbohydrate recognition domain of the human hepatic asialoglycoprotein receptor.” 2005. University of Basel. Doctoral Thesis. Doi: 10.5451/unibas-004136448; each of which is hereby incorporated by reference in their entirety. In some embodiments, the antibody, or antigen binding fragment thereof that binds to ASGR1 comprises a peptide selected from the following table, which illustrate the CDRs based on IMGT numbering.

IMGT CDRs						
Ab ID No	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	LCDR3

ASGR1 4F3	GFTFSSYA (SEQ ID NO: 30)	ISGSGGST (SEQ ID NO: 31)	AKDFSSRRWYLE Y (SEQ ID NO: 32)	LRSYY (SEQ ID NO: 33)	GKN	NSLERIGYLS YV (SEQ ID NO: 34)
ASGR1 8D7	GYTFTSY (SEQ ID NO: 39)	ISPSSGYT (SEQ ID NO: 40)	ARKGGYLDY (SEQ ID NO: 41)	QNVDTN (SEQ ID NO: 42)	SA	QQYNSYPFT (SEQ ID NO: 43)
ASGR1 B11	GFTFSDYY (SEQ ID NO: 46)	ITTGGGSP (SEQ ID NO: 47)	ARDRTAGYFDY (SEQ ID NO: 48)	SSGIGNAY (SEQ ID NO: 49)	KN	AAWDDSLNGW V (SEQ ID NO: 50)
ASGR1 C11	GYTFTSYW (SEQ ID NO: 80)	IFPGTGTS (SEQ ID NO: 81)	ARTNNYRSYALD Y (SEQ ID NO: 82)	KSVSTSGYSY (SEQ ID NO: 83)	LV	QQIRGGAYT (SEQ ID NO: 84)

[00166] Although the above table presents exemplary CDRs in IMGT numbering format, it is to be understood that other numbering systems may also be utilized. For example, the antibody, or antigen binding fragment thereof may comprise a peptide of the Chothia, AbM, or Kabat numbering systems, or any other applicable numbering system. Exemplary sequences for the Chothia, AbM, and Kabat numbering systems are presented in the following tables:

Chothia CDRs						
Ab ID No	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	LCDR3
ASGR1 4F3	GFTFSSY (SEQ ID NO: 93)	SGSGGS (SE Q ID NO: 94)	DFSSRRWYLEY (SEQ ID NO: 95)	QGDSLRSYYA S (SEQ ID NO: 96)	GKNNRPS (SEQ ID NO: 97)	NSLERIGYLS YV (SEQ ID NO: 34)
ASGR1 8D7	GYTFTSY (SEQ ID NO: 102)	SPSSGY (SEQ ID NO: 103)	KGGYLDY (SEQ ID NO: 104)	KASQNVDTNV A (SEQ ID NO: 105)	SASYRYS (SEQ ID NO: 106)	QQYNSYPFT (SEQ ID NO: 43)
ASGR1 B11	GFTFSDY (SEQ ID NO: 111)	TTGGGS (SEQ ID NO: 112)	DRTAGYFDY (SEQ ID NO: 113)	TGSSGIGNAY VS (SEQ ID NO: 114)	KNGQRPS (SEQ ID NO: 115)	AAWDDSLNGW V (SEQ ID NO: 50)
ASGR1 C11	GYTFTSY (SEQ ID NO: 120)	FPGTGT (SEQ ID NO: 121)	TNNYRSYALDY (SEQ ID NO: 122)	RASKSVSTSG YSYMH (SEQ ID NO: 123)	LVSNNLES (SEQ ID NO: 124)	QQIRGGAYT (SEQ ID NO: 84)

AbM CDRs						
Ab ID No	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	LCDR3
ASGR1 4F3	GFTFSSYAM S (SEQ ID NO: 98)	AISGSGGST Y (SEQ ID NO: 99)	DFSSRRWYLEY (SEQ ID NO: 95)	QGDSLRSYYA S (SEQ ID NO: 96)	GKNNRPS (SEQ ID NO: 97)	NSLERIGYLS YV (SEQ ID NO: 34)
ASGR1 8D7	GYTFTSYPM H (SEQ ID NO: 107)	YISPSSGYT K (SEQ ID NO: 108)	KGGYLDY (SEQ ID NO: 104)	KASQNVDTNV A (SEQ ID NO: 105)	SASYRYS (SEQ ID NO: 106)	QQYNSYPFT (SEQ ID NO: 43)
ASGR1 B11	GFTFSDYYM S (SEQ ID NO: 116)	AITTGGGSP N (SEQ ID NO: 117)	DRTAGYFDY (SEQ ID NO: 113)	TGSSGIGNAY VS (SEQ ID NO: 114)	KNGQRPS (SEQ ID NO: 115)	AAWDDSLNGW V (SEQ ID NO: 50)
ASGR1 C11	GYTFTSYWI Q (SEQ ID NO: 125)	EIFPGTGTS Y (SEQ ID NO: 126)	TNNYRSYALDY (SEQ ID NO: 122)	RASKSVSTSG YSYMH SEQ ID NO: 123)	LVSNNLES (SEQ ID NO: 124)	QQIRGGAYT (SEQ ID NO: 84)

Kabat CDRs						
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Ab ID No	HCDR1	HCDR2	HCDR3	LCDR1	LCDR2	LCDR3
ASGR1 4F3	STAMS (SEQ ID NO: 100)	AISGSGGST YYADSVKG (SEQ ID NO: 101)	DFSSRRWYLEY (SEQ ID NO: 95)	QGDSLRSYYA S (SEQ ID NO: 96)	GKNNRPS (SEQ ID NO: 97)	NSLERIGYLS YV (SEQ ID NO: 34)
ASGR1 8D7	SYPMH (SEQ ID NO: 109)	YISPSSGYT KYNQKFTD (SEQ ID NO: 110)	KGGYLDY (SEQ ID NO: 104)	KASQNVDTNV A (SEQ ID NO: 105)	SASYRYS (SEQ ID NO: 106)	QQYNSYPFT (SEQ ID NO: 43)
ASGR1 B11	DYYS (SEQ ID NO: 118)	AITGGGSP NYADSVKG (SEQ ID NO: 119)	DRTAGYFDY (SEQ ID NO: 113)	TGSSGIGNAY VS (SEQ ID NO: 114)	KNGQRPS (SEQ ID NO: 115)	AAWDDSLNGW V (SEQ ID NO: 50)
ASGR1 C11	SYWIQ (SEQ ID NO: 127)	EIFPGTGTS YYNENFKG (SEQ ID NO: 128)	TNNYSYALDY (SEQ ID NO: 122)	RASKSVSTSG YSYMH (SEQ ID NO: 123)	LVSNLIES (SEQ ID NO: 124)	QQIRGGAYT (SEQ ID NO: 84)

[00167] Accordingly, it is to be understood that while the following embodiments may refer only to the sequences as provided in the IMGT numbering system, said embodiments also encompass the corresponding combination or recitation of the Chothia, AbM, and Kabat numbering sequences as provided for herein.

[00168] 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 ASGR1. 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 ASGR1. 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, the amino acid sequence GKN, or SEQ ID NO: 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 GKN. 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 heavy chain CDR having a sequence selected from SEQ ID NO: 30-32. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 30. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 31. In some

embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 32. The CDRs referenced in the embodiments throughout the present specification can be interchanged with the CDRs that are characterized by different formats, such as Chothia, AbM, or Kabat.

[00169] 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 GKN, and the LCDR3 has a sequence of SEQ ID NO: 34.

[00170] 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.

[00171] 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.

[00172] 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.

[00173] 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 GKN; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 34; 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.

[00174] Although the preceding paragraphs may make reference to CDRs under the IMGT system the equivalent CDR sequences can be used from the Chothia, Kabat, or AbM designations.

[00175] 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.

[00176] 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 ASGR1. 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 ASGR1. 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: 42, the amino acid sequence SA, or SEQ ID NO: 43. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SEQ ID NO: 42. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SA. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light 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 selected from SEQ ID NO: 39-41. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 39. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 40. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 41.

[00177] 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: 42, the LCDR2 has a sequence of SA, and the LCDR3 has a sequence of SEQ ID NO: 43.

[00178] 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: 39, the HCDR2 has a sequence of SEQ ID NO: 40, and the HCDR3 has a sequence of SEQ ID NO: 41.

[00179] 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.

[00180] 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.

[00181] 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: 42; the light chain CDR2 has the amino acid sequence of SA; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 43; 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: 39; the heavy chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 40; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 41; or variants of any of the foregoing.

[00182] 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.

[00183] 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 ASGR1. 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 ASGR1. 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: 49, the amino acid sequence KN, or SEQ ID NO: 50. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SEQ ID NO: 49. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of KN. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SEQ ID NO: 50. 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: 46-48. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 46. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy 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 of SEQ ID NO: 48.

[00184] 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: 49, the LCDR2 has a sequence of KN, and the LCDR3 has a sequence of SEQ ID NO: 50.

[00185] 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: 46, the HCDR2 has a sequence of SEQ ID NO: 47, and the HCDR3 has a sequence of SEQ ID NO: 48.

[00186] 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.

[00187] 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.

[00188] 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: 49; the light chain CDR2 has the amino acid sequence of KN; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 50; 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: 46; the heavy chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 47; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 48; or variants of any of the foregoing.

[00189] 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.

[00190] 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 ASGR1. 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 ASGR1. 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: 83, the amino acid sequence LV, or SEQ ID NO: 84. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SEQ ID NO: 83. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of LV. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a light chain CDR having a sequence of SEQ ID NO: 84. 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: 80-82. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 80. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 81. In some embodiments, a polypeptide, an antibody, or antibody binding fragment thereof, comprises a heavy chain CDR having a sequence of SEQ ID NO: 82.

[00191] 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: 83, the LCDR2 has a sequence of LV, and the LCDR3 has a sequence of SEQ ID NO: 84.

[00192] 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: 80, the HCDR2 has a sequence of SEQ ID NO: 81, and the HCDR3 has a sequence of SEQ ID NO: 82.

[00193] 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.

[00194] 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.

[00195] 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: 83; the light chain CDR2 has the amino acid sequence of LV; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 84; 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: 80; the heavy chain CDR2 sequence has the amino acid sequence of SEQ ID NO: 81; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 82; or variants of any of the foregoing.

[00196] 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.

[00197] 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
35	ASGR1 4F3	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGL EWVSAISGSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAED TAVYYCAKDFSSRRWYLEYWGQGTLLTVSS
44	ASGR1 8D7	QVQLQQSAAELARPGASVKMSCKASGYTFTSYPMHWVKQRPGQGL EWIAYISPSGGYTKYNQKFTDKTTLTADKSSSTAYMQLSSLTSDD SAVYYCARKGGYLDYWGQGTLLTVSS
51	ASGR1 B11	EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMSWVRQAPGKGL EWVSAITGGGSPNYADSVKGRFTISRDN SKNTLYLQMNSLRAED TAVYYCARDRTAGYFDYWGQALVTSS
85	ASGR1 C11	QVQLQQSGAELVKPGASVKLSCKTSGYTFTSYWIQWVKQRPGQGL GWIGEIPFGTGTSYNENFKGKATLTIDTSSSTAYMQPSSLTSED SAVYFCARTNNYRSYALDYWGQGTNYRS

[00198] 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
36	ASGR1 4F3	SSELTQDPAVSVALGQTVRITCQGD SLRSYYASWYQQKPGQAPVL VIYGKNNRPSGIPDRFSGSSSGNTASLTITGAQAEDEADYYCNSL ERIGYLSYVFGGGTKLTVL
45	ASGR1 8D7	DIVMTQSQKFMSTSVGDRVSVTCKASQNVDTNVAWFQQKPGQYPK VLIYSASYRYSGVPDRFTGSGSGTDFTLTISNVQSEDLAEYFCQQ YNSYPFTFGAGTKLELKRA
77	ASGR1 B11	DIVLTQPPSASGTPGQRTVITSGTSSSGIGNAYVSWYQQLPGKAP KLLIYKNGQRPSGVSDRFSGSKSGTSASLAISGLRSEDEADYYCA AWDDSLNGWVFGGGTKVTVL
86	ASGR1 C11	DIVMTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKPG QPPRLLIYLVNLESGVPA RFSGSGSGTDFTLTNIHPVEEEDAATY YCQQIRGGAYTFGGGTKLEIKR

[00199] In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_H peptide of SEQ ID NO: 35, SEQ ID NO: 44, SEQ ID NO: 51, or SEQ ID NO: 85. In some embodiments, the V_H peptide comprises the amino acid sequence of SEQ ID NO: 35. In some embodiments, the V_H peptide comprises the amino acid sequence of SEQ ID NO: 44. In some embodiments, the V_H peptide comprises the amino acid sequence of SEQ ID NO: 51. In some embodiments, the V_H peptide comprises the amino acid sequence of SEQ ID NO: 85. In some embodiments, a polypeptide, an antibody, or antigen binding fragment thereof, comprises a V_L peptide of SEQ ID NO: 36, SEQ ID NO: 45, SEQ ID NO: 77, or SEQ ID NO: 86. In some embodiments, the V_L peptide comprises the amino acid sequence of SEQ ID NO: 36. In some embodiments, the V_L peptide comprises the amino acid sequence of SEQ

ID NO: 45. In some embodiments, the V_L peptide comprises the amino acid sequence of SEQ ID NO: 77. In some embodiments, the V_L peptide comprises the amino acid sequence of SEQ ID NO: 86. 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: 35, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 36, or a variant thereof. In some embodiments, the V_H peptide comprises a sequence of SEQ ID NO: 44, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 45, or a variant thereof. In some embodiments, the V_H peptide comprises a sequence of SEQ ID NO: 51, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 77, or a variant thereof. In some embodiments, the V_H peptide comprises a sequence of SEQ ID NO: 85, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 86, 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 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 ASGR1. In some embodiments, the V_H peptide comprises a sequence of SEQ ID NO: 44, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 51, or a variant thereof, and the polypeptide, the antibody, or antigen binding fragment thereof, binds to non-human primate ASGR1. In some embodiments, the V_H peptide comprises a sequence of SEQ ID NO: 51, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 77, or a variant thereof, and the polypeptide, the antibody, or antigen binding fragment thereof, binds to non-human primate ASGR1. In some embodiments, the V_H peptide comprises a sequence of SEQ ID NO: 85, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 86, or a variant thereof, and the polypeptide, the antibody, or antigen binding fragment thereof, binds to non-human primate ASGR1. 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 ASGR1. In some embodiments, the V_H peptide comprises a sequence of SEQ ID NO: 44, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 45, or a variant thereof, and the polypeptide, the antibody, or antigen binding fragment thereof, binds to human ASGR1. In some embodiments, the V_H peptide comprises a sequence of SEQ ID NO: 51, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 77, or a variant thereof;

thereof, and the polypeptide, the antibody, or antigen binding fragment thereof, binds to human ASGR1. In some embodiments, the V_H peptide comprises a sequence of SEQ ID NO: 85, or a variant thereof; and the V_L peptide comprises a sequence of SEQ ID NO: 86, or a variant thereof, and the polypeptide, the antibody, or antigen binding fragment thereof, binds to human ASGR1. 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. In some embodiments, the V_H peptide comprises a sequence of SEQ ID NO: 44; and the V_L peptide comprises a sequence of SEQ ID NO: 45. In some embodiments, the V_H peptide comprises a sequence of SEQ ID NO: 51; and the V_L peptide comprises a sequence of SEQ ID NO: 77. In some embodiments, the V_H peptide comprises a sequence of SEQ ID NO: 85; and the V_L peptide comprises a sequence of SEQ ID NO: 86.

[00200] 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. In some embodiments, the polypeptide comprises SEQ ID NO: 44 and SEQ ID NO: 45. In some embodiments, the polypeptide comprises SEQ ID NO: 51 and SEQ ID NO: 77. In some embodiments, the polypeptide comprises SEQ ID NO: 85 and SEQ ID NO: 86.

[00201] As provided for herein, the polypeptide, antibodies, or antigen binding fragments thereof can be variants of the sequences.

[00202] 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 ASGR1.

[00203] 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 ASGR1 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: 37:

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SSELTQDPAVSVALGQTVRITCQGDSLRSYYASWYQQKPGQAPVLVIYGKNN
RPSGIPDRFSGSSSGNTASLTITGAQAEDEADYYCNSLERIGYLSYVFGGGT
KLTIVLGGGGSGGGSGGGGSEVQLLESGLVQPGGSLRLSCAASGFTFSSY
AMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDN SKNTLYLQMN
SLRAEDTAVYYCAKDFSSRRWYLEYWGQGTILTVSS (SEQ ID NO: 37)
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or is substantially similar to SEQ ID NO: 37, or is an active fragment of SEQ ID NO: 37. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 37. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 37. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 37. In some embodiments, the target binding domain (“T”) comprises a sequence as set forth in SEQ ID NO: 37. In some embodiments, the target binding domain (“T”) as set forth in SEQ ID NO: 37 is an antibody, or an antigen binding fragment thereof. In some embodiments, the target binding domain (“T”) is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

~~[00204]~~ 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 ASGR1 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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EVQLLESGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAIS
GSGGSTYYADSVKGRFTISRDN SKNTLYLQMN SLRAEDTAVYYCAKDFSSRR
WYLEYWGQGTILTVSSGGGGSGGGSGGGGSSSELTQDPAVSVALGQTVRIT
CQGDSLRSYYASWYQQKPGQAPVLVIYGKNNRPSGIPDRFSGSSSGNTASLT
ITGAQAEDEADYYCNSLERIGYLSYVFGGGTKLTVL (SEQ ID NO: 38)
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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-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00205] 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 ASGR1 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: 129:

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DIVMTQSQKFMSTSVGDRVSVTCKASQNVDTNVAWFQQKPGQYPKVLIIYSAS
YRYSQVPDRFTGSGSGTDFTLTISNVQSEDLAEYFCQQYNSYPFTFGAGTKL
ELKRAGGGGSGGGGSGGGGSGVQLQQSAELARPGASVKMSCKASGYTFTSY
PMHWVKQRPQGQGLEWIAIYISPSGKYTKYNQKFTDKTTLTADKSSTTAYMQLS
SLTSDDSAVYYCARKGGYLDYWGGQTTLTVSS (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 target binding domain (“T”) comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 129. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 129. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 129. In some embodiments, the target binding domain (“T”) comprises a sequence as set forth in SEQ ID NO: 129. In some embodiments, the target binding domain (“T”) as set forth in SEQ ID NO: 129 is an antibody, or an antigen binding fragment thereof. In some embodiments, the target binding domain (“T”) is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[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 ASGR1 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: 130:

QVQLQQSAAELARPGASVKMSCKASGYTFTSYPMHWVKQRPGGLEWIAIYIS
PSSGYTKYNQKFTDKTTLTADKSSTTAYMQLSSLTSDDSAVYYCARKGGYLD
YWGQGTTLTVSSGGGGSGGGSGGGGSDIVMTQSQKFMSTSVGDRVSVTCKA
SQNVDTNVAWFQQKPGQYPKVLIIYSASYRYSVGPDRFTGSGSGTDFTLTISN
VQSEDLAEYFCQQYNSYPFTFGAGTKLELKRA (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 target binding domain (“T”) comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 130. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 130. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 130. In some embodiments, the target binding domain (“T”) comprises a sequence as set forth in SEQ ID NO: 130. In some embodiments, the target binding domain (“T”) as set forth in SEQ ID NO: 130 is an antibody, or an antigen binding fragment thereof. In some embodiments, the target binding domain (“T”) is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00207] 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 ASGR1 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: 78:

DIVLTQPPSASGTPGQRTISCTGSSSGIGNAYVSWYQQLPKGAPKLLIYKN
GQRPSGVSDRFSGSKSGTSASLAISGLRSEADYYCAAWDDSLNGWVFGGG
TKVTVLGGGGSGGGSGGGGSEVQLLESGGGLVQPGGSLRLSCAASGFTFSD
YYMSWVRQAPGKLEWVSAITGGGSPNYADSVKGRFTISRDN SKNTLYLQM
NSLRAEDTAVYYCARDRTAGYFDYWGQALVTVSS (SEQ ID NO: 78)

or is substantially similar to SEQ ID NO: 78, or is an active fragment of SEQ ID NO: 78. In some embodiments, the target binding domain (“T”) comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 78. In some embodiments, the target binding domain

("T") comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 78. In some embodiments, the target binding domain ("T") comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 78. In some embodiments, the target binding domain ("T") comprises a sequence as set forth in SEQ ID NO: 78. In some embodiments, the target binding domain ("T") as set forth in SEQ ID NO: 78 is an antibody, or an antigen binding fragment thereof. In some embodiments, the target binding domain ("T") is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00208] 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 ASGR1 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: 79:

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EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMSWVRQAPGKGLEWVSAIT
TGGGSPNYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCARDRTAGY
FDYWGQALVTVSSGGGGSGGGGSGGGGSDIVLTQPPSASGTPGQRVTISCT
GSSSGIGNAYVSWYQQLPGKAPKLLIYKNGQRPSGVSDRFSGSKSGTSASLA
ISGLRSEDEADYYCAAWDDSLNGWVFGGGTKVTVL (SEQ ID NO: 79)
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or is substantially similar to SEQ ID NO: 79, or is an active fragment of SEQ ID NO: 79. In some embodiments, the target binding domain ("T") comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 79. In some embodiments, the target binding domain ("T") comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 79. In some embodiments, the target binding domain ("T") comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 79. In some embodiments, the target binding domain ("T") comprises a sequence as set forth in SEQ ID NO: 79. In some embodiments, the target binding domain ("T") as set forth in SEQ ID NO: 79 is an antibody, or an antigen binding fragment thereof. In some embodiments, the target binding domain ("T") is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00209] 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 ASGR1 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: 87:

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DIVMTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKPGQPPRLLI
YLVSNLESGVPARFSGSGTDFTLNIHPVEEEDAATYYCQXXGGAYTFGG
GTKLEIKRGGGGSGGGSGGGGSQVQLQQSGAELVKPGASVKLSCKTSGYTF
TSYWIQWVKQRPQGGLGWIGEIFPGTGTSYNENFKGKATLTIDTSSSTAYM
QPSSLTSEDSAVYFCARTNNYRSYALDYWGQGTNYRS (SEQ ID NO: 87)
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or is substantially similar to SEQ ID NO: 87, or is an active fragment of SEQ ID NO: 87. In some embodiments, the target binding domain ("T") comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 87. In some embodiments, the target binding domain ("T") comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 87. In some embodiments, the target binding domain ("T") comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 87. In some embodiments, the target binding domain ("T") comprises a sequence as set forth in SEQ ID NO: 87. In some embodiments, the target binding domain ("T") as set forth in SEQ ID NO: 87 is an antibody, or an antigen binding fragment thereof. In some embodiments, the target binding domain ("T") is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00210] 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 ASGR1 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: 88:

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QVQLQQSGAELVKPGASVKLSCKTSGYTFTSYWIQWVKQRPQGGLGWIGEIF
PGTGTSYNENFKGKATLTIDTSSSTAYMQPSSLTSEDSAVYFCARTNNYRS
YALDYWGQGTNYRSGGGGSGGGGSGGGGSDIVMTQSPASLAVSLGQRATISY
RASKSVSTSGYSYMHWNQQKPGQPPRLLIYLVSNLESGVPARFSGSGTDF
TLNIHPVEEEDAATYYCQXXGGAYTFGGGTKLEIKR (SEQ ID NO: 88)
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or is substantially similar to SEQ ID NO: 88, or is an active fragment of SEQ ID NO: 88. In some embodiments, the target binding domain ("T") comprises a sequence that is at least 90%

identical to a sequence of SEQ ID NO: 88. In some embodiments, the target binding domain ("T") comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 88. In some embodiments, the target binding domain ("T") comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 88. In some embodiments, the target binding domain ("T") comprises a sequence as set forth in SEQ ID NO: 88. In some embodiments, the target binding domain ("T") as set forth in SEQ ID NO: 88 is an antibody, or an antigen binding fragment thereof. In some embodiments, the target binding domain ("T") is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

Targeting moieties comprising an Fc domain

[00211] In some embodiments, the V_H and V_L polypeptides are linked to a stalk portion S₁ comprising an Fc region. In some embodiments, the Fc region is as provided for herein. In some embodiments, the Fc region is a variant Fc region as provided for herein. Non-limiting mutations in the Fc region are provided for herein. In some embodiments, the variant Fc region comprises a sequence that is a variant of SEQ ID NO: 26, SEQ ID NO: 27, or SEQ ID NO: 28 as provided for herein. In some embodiments, the variant of SEQ ID NO: 26 comprises one or more mutations selected from the group consisting of L234A, L235A, N297A, P329G, I253A, H310A, and H435A as provided for herein. In some embodiments, the variant of SEQ ID NO: 27 comprises one or more mutations selected from the group consisting of N297A, P329G, I253A, H310A, and H435A as provided for herein. In some embodiments, the variant of SEQ ID NO: 28 comprises one or more mutations selected from the group consisting of S228P, L235E, N297A, P329G, I253A, H310A, and H435A as provided for herein. As provided for herein, the heavy chain can be linked to a Fc region. In some embodiments, the Fc region further comprises (*e.g.* linked to) a transmembrane domain. In some embodiments, the Fc region further comprising a transmembrane domain has a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker as provided for herein or is absent, Fc is a variant Fc region as provided for herein, L₂ is a linker as provided for herein or is absent, and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprises a polypeptide having the formula ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or is absent, T_M is a transmembrane domain as provided for herein, and ICD is an intracellular domain as provided for herein or is absent. Examples of ECD include, but are not limited to, a CD8 and/or CD28 extracellular domain as provided for herein. Examples of T_M include, but are

not limited to, a CD8 and/or CD28 transmembrane domain as provided for herein. In some embodiments, X₁ comprises a T_M and the ECD and ICD are absent. In some embodiments, X₁ comprises an ECD, a T_M, and the ICD is absent. In some embodiments, X₁ comprises a T_M and an ICD and the ECD is absent. In some embodiments, X₁ comprises an ECD, a T_M, and an ICD. In any of the following embodiments, it is to be understood that the ECD, the ICD, or both may be optionally absent. Accordingly, an embodiment wherein X₁ comprises a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD comprising an Env incorporation motif is understood to encompass the following X₁ members: i) a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD comprising an Env incorporation motif; ii) a CD8 and/or CD28 T_M, and an ICD comprising an Env incorporation motif wherein the ECD is absent; iii) a CD8 and/or CD28 ECD, and a CD8 and/or CD28 T_M, wherein the ICD is absent; and iv) a CD8 and/or CD28 T_M wherein both the ECD and the ICD are absent. Similarly, an embodiment wherein X₁ comprises a CD8 and/or CD28 T_M and an ICD comprising an Env incorporation motif is understood to encompass the following X₁ members: i) a CD8 and/or CD28 T_M and an ICD comprising an Env incorporation motif; and ii) a CD8 and/or CD28 T_M wherein the ICD is absent. Similarly, an embodiment wherein X₁ comprises a CD8 and/or CD28 ECD and a CD8 and/or CD28 T_M is understood to encompass the following X₁ members: i) a CD8 and/or CD28 ECD and a CD8 and/or CD28 T_M; and ii) a CD8 and/or CD28 T_M wherein the ECD is absent. It is to be further understood that the preceding explanation is also true in embodiments where a specific ECD, T_M, or ICD are not recited. For example, an embodiment wherein X₁ comprises an ECD, a CD8 and/or CD28 T_M, and an ICD would be understood to encompass the following X₁ members: i) an ECD, a CD8 and/or CD28 T_M, and an ICD; ii) an ECD, and a CD8 and/or CD28 T_M wherein the ICD is absent; iii) a CD8 and/or CD28 T_M, and an ICD wherein the ECD is absent; and iv) a CD8 and/or CD28 T_M wherein the ECD and the ICD are absent. Similarly, an embodiment wherein X₁ comprises a CD8 and/or CD28 T_M and an ICD is understood to encompass the following X₁ members: i) a CD8 and/or CD28 T_M and an ICD; and ii) a CD8 and/or CD28 T_M wherein the ICD is absent. Similarly, an embodiment wherein X₁ comprises an ECD and a CD8 and/or CD28 T_M is understood to encompass the following X₁ members: i) an ECD and a CD8 and/or CD28 T_M; and ii) a CD8 and/or CD28 T_M wherein the ECD is absent. Unless explicitly stated, the preceding examples and explanations are applicable to any embodiments that follow.

[00212] 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, X_1 comprises a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M , and an ICD. In some embodiments, X_1 comprises an ECD, a T_M , and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, X_1 comprises a CD8 and/or CD28 ECD, a T_M , and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, X_1 comprises an ECD, a CD8 and/or CD28 T_M , and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, X_1 comprises a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M , and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein.

[00213] In some embodiments, the V_H and V_L polypeptides provided herein are linked to a stalk portion (S_1) 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 (S_1) 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 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 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 V_H and V_L polypeptides provided herein are linked to 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 V_H and V_L polypeptides provided herein are linked to 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 V_H and V_L polypeptides provided herein are linked to 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 V_H and V_L polypeptides provided herein are linked to 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 V_H and V_L polypeptides provided herein are linked to 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 V_H and V_L polypeptides provided herein are linked to 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

sequence as set forth in SEQ ID NO: 36 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: 35 and V_L peptide having a sequence as set forth in SEQ ID NO: 36 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 a liver cell, such as those provided herein.

[00215] 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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 comprise 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 are linked to a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein.

incorporation motif as provided for herein. In some embodiments, the V_H peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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 a liver cell, such as those provided herein.

[00216] 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: 35; 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: 36.

[00217] 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: 35; 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: 36; provided that the V_H peptide and a V_L peptide comprises a light chain CDR having a sequence of SEQ ID NO: 33, and amino acid sequence of GKN, and a sequence of SEQ ID NO: 34; 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: 35; 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: 36; 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 GKN; a light chain CDR3 having a sequence of SEQ ID NO: 34; 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.

[00218] 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: 35; 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: 36; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 33; a LCDR2 having a sequence of GKN; and a LCDR3 having a sequence of SEQ ID NO: 34; 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.

[00219] 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: 35; 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: 36; 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 GKN, wherein the LCDR2 comprises at most 1 conservative amino acid substitution, and a LCDR3 having a sequence of SEQ ID NO: 34, 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.

[00220] In some embodiments, a V_H peptide having a sequence as set forth in SEQ ID NO: 44 and a V_L peptide having a sequence as set forth in SEQ ID NO: 45 are linked to an stalk portion (S₁) comprising Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD. In

some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 44 and V_L peptide having a sequence as set forth in SEQ ID NO: 45 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: 44 and V_L peptide having a sequence as set forth in SEQ ID NO: 45 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: 44 and V_L peptide having a sequence as set forth in SEQ ID NO: 45 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: 44 and V_L peptide having a sequence as set forth in SEQ ID NO: 45 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: 44 and V_L peptide having a sequence as set forth in SEQ ID NO: 45 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: 44 and V_L peptide having a sequence as set forth in SEQ ID NO: 45 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: 44 and V_L peptide having a sequence as set forth in SEQ ID NO: 45 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: 44 and V_L peptide having a sequence as set forth in SEQ ID NO: 45 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 a liver cell, such as those provided herein.

[00221] 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: 44; 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: 45 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: 44; 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: 45 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: 44; 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: 45 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: 44; 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: 45 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: 44; 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: 45 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: 44; 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: 45 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: 44; 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: 45 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: 44; 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: 45 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: 44; 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: 45 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: 44; 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: 45 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: 44; 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: 45 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 a liver cell, such as those provided herein.

[00222] 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: 44; 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: 45.

[00223] 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: 44; 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: 45; provided that the V_H peptide and a V_L peptide comprises a light chain CDR having a sequence of SEQ ID NO: 42, and amino acid sequence of SA, and a sequence of SEQ ID NO: 43; and/or a heavy chain CDR having a sequence of SEQ ID NO: 39-41. 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: 44; 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: 45; provided that the V_H peptide and a V_L peptide comprise a light chain CDR1 having a sequence of SEQ ID NO: 42; a light chain CDR2 having a sequence of SA; a light chain CDR3 having a sequence of SEQ ID NO: 43; and/or a heavy chain CDR1 having a sequence of SEQ ID NO: 39; a heavy chain CDR2 having a sequence of SEQ ID NO: 40; and a heavy chain CDR3 having a sequence of SEQ ID NO: 41. In some embodiments, the CDRs in the V_H or V_L chain are as set forth in the combinations provided for herein.

[00224] 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: 44; 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:

45; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 42; a LCDR2 having a sequence of SA; and a LCDR3 having a sequence of SEQ ID NO: 43; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 39; a HCDR2 having a sequence of SEQ ID NO: 40; and a HCDR3 having a sequence of SEQ ID NO: 41.

[00225] 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: 44; 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: 45; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 42, wherein the LCDR1 comprises at most 1 conservative amino acid substitution, a LCDR2 having a sequence of SA, wherein the LCDR2 comprises at most 1 conservative amino acid substitution, and a LCDR3 having a sequence of SEQ ID NO: 43, 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: 39, wherein the HCDR1 comprises at most 1 conservative amino acid substitution, a HCDR2 having a sequence of SEQ ID NO: 40, wherein the HCDR2 comprises at most 1 conservative amino acid substitution, and a HCDR3 having a sequence of SEQ ID NO: 41, wherein the HCDR3 comprises at most 1 conservative amino acid substitution.

[00226] In some embodiments, a V_H peptide having a sequence as set forth in SEQ ID NO: 51 and a V_L peptide having a sequence as set forth in SEQ ID NO: 77 are linked to an stalk portion (S₁) comprising Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 51 and V_L peptide having a sequence as set forth in SEQ ID NO: 77 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: 51 and V_L peptide having a sequence as set forth in SEQ ID NO: 77 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: 51 and V_L peptide having a sequence as set forth in SEQ ID NO: 77 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: 51 and V_L peptide having a sequence as set forth in SEQ ID NO: 77 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: 51 and V_L peptide having a sequence as set forth in SEQ ID NO: 77 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: 51 and V_L peptide having a sequence as set forth in SEQ ID NO: 77 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: 51 and V_L peptide having a sequence as set forth in SEQ ID NO: 77 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: 51 and V_L peptide having a sequence as set forth in SEQ ID NO: 77 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 a liver cell, such as those provided herein.

[00227] 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: 51; 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: 77 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: 51; 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: 77 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: 51; 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: 77 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: 51; 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: 77 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: 51; 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: 77 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: 51; 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: 77 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: 51; 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: 77 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: 51; 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: 77 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: 51; 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: 77 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: 51; 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: 77 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 a liver cell, such as those provided herein.

[00228] 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: 51; 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: 77.

[00229] 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: 51; 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: 77; provided that the V_H peptide and a V_L peptide comprises a light chain CDR having a sequence of SEQ ID NO: 49, and amino acid sequence of KN, and a sequence of SEQ ID NO: 50; and/or a heavy chain CDR having a sequence of SEQ ID NO: 46-48. 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: 51; 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: 77; provided that the V_H peptide and a V_L peptide comprise a light chain CDR1 having a sequence of SEQ ID NO: 49; a light chain CDR2 having a sequence of KN; a light chain CDR3 having a sequence of SEQ ID NO: 50; and/or a heavy chain CDR1 having a sequence of SEQ ID NO: 46; a heavy chain CDR2 having a sequence of SEQ ID NO: 47; and a heavy chain CDR3 having a sequence of SEQ ID NO: 48. In some embodiments, the CDRs in the V_H or V_L chain are as set forth in the combinations provided for herein.

[00230] 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: 51; 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: 77; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 49; a LCDR2 having a sequence of KN; and a LCDR3 having a sequence of SEQ ID NO: 50; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 46; a HCDR2 having a sequence of SEQ ID NO: 47; and a HCDR3 having a sequence of SEQ ID NO: 48.

[00231] 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: 51; 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: 77; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 49, wherein the LCDR1 comprises at most 1 conservative amino acid substitution, a LCDR2 having a sequence of KN, wherein the LCDR2 comprises at most 1 conservative amino acid

substitution, and a LCDR3 having a sequence of SEQ ID NO: 50, 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: 46, wherein the HCDR1 comprises at most 1 conservative amino acid substitution, a HCDR2 having a sequence of SEQ ID NO: 47, wherein the HCDR2 comprises at most 1 conservative amino acid substitution, and a HCDR3 having a sequence of SEQ ID NO: 48, wherein the HCDR3 comprises at most 1 conservative amino acid substitution.

[00232] In some embodiments, a V_H peptide having a sequence as set forth in SEQ ID NO: 85 and a V_L peptide having a sequence as set forth in SEQ ID NO: 86 are linked to an stalk portion (S₁) comprising Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD. In some embodiments, the V_H peptide having a sequence as set forth in SEQ ID NO: 85 and V_L peptide having a sequence as set forth in SEQ ID NO: 86 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: 85 and V_L peptide having a sequence as set forth in SEQ ID NO: 86 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: 85 and V_L peptide having a sequence as set forth in SEQ ID NO: 86 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: 85 and V_L peptide having a sequence as set forth in SEQ ID NO: 86 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: 85 and V_L peptide having a sequence as set forth in SEQ ID NO: 86 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: 85 and V_L peptide having a sequence as set forth in SEQ ID NO: 86 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: 85 and V_L peptide having a sequence as set forth in SEQ ID NO: 86 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: 85 and V_L peptide having a sequence as set forth in SEQ ID NO: 86 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 a liver cell, such as those provided herein.

[00233] 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: 85; 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: 86 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: 85; 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: 86 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: 85; 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: 86 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: 85; 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: 86 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: 85; 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: 86 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: 85; 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: 86 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: 85; 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: 86 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: 85; 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: 86 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: 85; 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: 86 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: 85; 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: 86 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.

97%, 98%, or 99% identical to a sequence of SEQ ID NO: 85; 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: 86 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: 85; 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: 86 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 a liver cell, such as those provided herein.

[00234] 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: 85; 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: 86.

[00235] 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: 85; 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: 86; provided that the V_H peptide and a V_L peptide comprises a light chain CDR having a sequence of SEQ ID NO: 83, and amino acid sequence of LV, and a sequence of SEQ ID NO: 84; and/or a heavy chain CDR having a sequence of SEQ ID NO: 80-82. 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: 85; 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: 86; provided that the V_H peptide and a V_L peptide comprise a light chain CDR1 having a sequence of SEQ ID NO: 83; a light

chain CDR2 having a sequence of LV; a light chain CDR3 having a sequence of SEQ ID NO: 84; and/or a heavy chain CDR1 having a sequence of SEQ ID NO: 80; a heavy chain CDR2 having a sequence of SEQ ID NO: 81; and a heavy chain CDR3 having a sequence of SEQ ID NO: 82. In some embodiments, the CDRs in the V_H or V_L chain are as set forth in the combinations provided for herein.

[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: 85; 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: 86; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 83; a LCDR2 having a sequence of LV; and a LCDR3 having a sequence of SEQ ID NO: 84; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 80; a HCDR2 having a sequence of SEQ ID NO: 81; and a HCDR3 having a sequence of SEQ ID NO: 82.

[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: 85; 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: 86; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 83, wherein the LCDR1 comprises at most 1 conservative amino acid substitution, a LCDR2 having a sequence of LV, wherein the LCDR2 comprises at most 1 conservative amino acid substitution, and a LCDR3 having a sequence of SEQ ID NO: 84, 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: 80, wherein the HCDR1 comprises at most 1 conservative amino acid substitution, a HCDR2 having a sequence of SEQ ID NO: 81, wherein the HCDR2 comprises at most 1 conservative amino acid substitution, and a HCDR3 having a sequence of SEQ ID NO: 82, wherein the HCDR3 comprises at most 1 conservative amino acid substitution.

[00238] 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: 35 and the V_L peptide comprises a sequence of SEQ ID NO: 36. 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: 44 and the V_L peptide comprises a sequence of SEQ ID NO: 45. 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: 51 and the V_L peptide comprises a sequence of SEQ ID NO: 77. 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: 85 and the V_L peptide comprises a sequence of SEQ ID NO: 86.

[00239] In some embodiments, the polypeptide as provided herein binds to non-human primate ASGR1. In some embodiments, the polypeptide as provided herein binds to human ASGR1.

[00240] 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.

[00241] 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: 35 linked via a linker sequence GGGSGGGSGGGSGGGGS (SEQ ID NO: 72) to a light chain variable region as set forth in SEQ ID NO: 36. 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,

SSSELTQDPAVSVALGQTVRITCQGDLSRYSYASWYQQKPGQAPVLVIYGKNN
RPSGIPDRFSGSSSGNTASLTITGAQAEDEADYYCNSLERIGYLSYVFGGGTKL
TVLGGGGSGGGSGGGGSEVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAM
SWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNKNTLYLQMNSL
RAEDTAVYYCAKDFSSRRWYLEYWGQGLTVTVSS (SEQ ID NO: 37).

[00242] 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: 37. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 37. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 37. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 37. In some embodiments, the polypeptide comprises a sequence

as set forth in SEQ ID NO: 37. In some embodiments, the polypeptide as set forth in SEQ ID NO: 37 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00243] 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: 36 linked via a linker sequence GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 72) to a heavy chain variable region as set forth in SEQ ID NO: 35. 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,

EVQLLES GGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAIS
GSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKDFSSRR
WYLEYWGQGT LVT VSSGGGGSGGGGSGGGGSSSELTQDPAVSVALGQTVRI
TCQGDSLRSYYASWYQQKPGQAPVLVIYGKNNRPSGIPDRFSGSSSGNTASLT
ITGAQAEDEADYYCNSLERIGYLSYVFGGGTKLTVL (SEQ ID NO: 38).

[00244] 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-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00245] 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: 44 linked via a linker sequence GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 72) to a light chain variable region as set forth in SEQ ID NO: 45. 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,

DIVMTQSQKFMSTSVGDRVSVTCKASQNVDTNVAWFQQKPGQYPKVLIYSA
SYRYSGVPDRFTGSGSGTDFTLTISNVQSEDLAEYFCQQYNSYPFTFGAGTKL

ELKRAGGGGSGGGGSGGGGSQVQLQQSAAELARPGASVKMSCASGYTFTS
YPMHWVKQRPGQGLEWIA YISPSSGYTKYNQKFTDKTTLTADKSSTTAYMQ
LSSLTSDDSAVYYCARKGGYLDYWGQGTTLTVSS (SEQ ID NO: 129).

[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: 129. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 129. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 129. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 129. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 129. In some embodiments, the polypeptide as set forth in SEQ ID NO: 129 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00247] 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: 45 linked via a linker sequence GGGSGGGSGGGSGGGGS (SEQ ID NO: 72) to a heavy chain variable region as set forth in SEQ ID NO: 44. 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,

QVQLQQSAAELARPGASVKMSCASGYTFTSYPMHWVKQRPGQGLEWIA YI
SPSSGYTKYNQKFTDKTTLTADKSSTTAYMQLSSLTSDDSAVYYCARKGGYL
DYWGQGTTLTVSSGGGSGGGSGGGSGGGSDIVMTQSQKFMSTSVGDRVSVTC
KASQNVDTNVAWFQKPGQYPKVLISASRYSGVPDRFTGSGSGTDFTLTI
SNVQSEDLAEYFCQQYNSYPFTFGAGTKLELKRA (SEQ ID NO: 130).

[00248] 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: 130. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 130. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 130. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 130. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 130. In some embodiments, the polypeptide as set forth in SEQ ID NO: 130 is an antibody, or an antigen binding fragment thereof. In some

embodiments, the antibody is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00249] 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: 51 linked via a linker sequence GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 72) to a light chain variable region as set forth in SEQ ID NO: 77. 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,

DIVLTQPPSASGTPGQRTISCTGSSSGIGNAYVSWYQQLPGKAPKLLIYKNG
QRPSGVSDRFGSKSGTSASLAISGLRSEDEADYYCAAWDDSLNGWVFGGGT
KVTVLGGGGSGGGGSGGGGSEVQLLESGGGLVQPGGSLRLSCAASGFTFSDY
YMSWVRQAPGKGLEWVSAITGGGSPNYADSVKGRFTISRDN SKNTLYLQM
NSLRAEDTAVYYCARDRTAGYFDYWQGALVTVSS (SEQ ID NO: 78).

[00250] 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: 78. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 78. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 78. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 78. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 78. In some embodiments, the polypeptide as set forth in SEQ ID NO: 78 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00251] 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: 77 linked via a linker sequence GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 72) to a heavy chain variable region as set forth in SEQ ID NO: 51. 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,

EVQLLESGGGLVQPGGSLRLSCAASGFTFSDYYMSWVRQAPGKGLEWVSAIT
TGGGSPNYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCARDRTAG
YFDYWQGALVTVSSGGGGSGGGGSGGGGSDIVLTQPPSASGTPGQRTISC

TGSSSGIGNAYVSWYQQLPGKAPKLLIYKNGQRPSGVSDRFSGSKSGTSASLA
ISGLRSEDEADYYCAAWDDSLNGWVFGGGTKVTVL (SEQ ID NO: 79).

[00252] 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: 79. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 79. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 79. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 79. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 79. In some embodiments, the polypeptide as set forth in SEQ ID NO: 79 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00253] 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: 85 linked via a linker sequence GGGSGGGSGGGSGGGGS (SEQ ID NO: 72) to a light chain variable region as set forth in SEQ ID NO: 86. 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,

DIVMTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKPGQPPRLLIY
LVSNLESGVPARFSGSGSDFTLNIHPVEEEDAATYYCQXXGGAYTFGGG
TKLEIKRGGGSGGGSGGGGSQVQLQSGAELVKPGASVKLSCKTSGYTFT
SYWIQWVKQRPQGGLGWIGEIFPGTGTSYYNENFKGKATLTIDTSSSTAYMQ
PSSLTSEDSAVYFCARTNNYRSYALDYWGQGTNYRS (SEQ ID NO: 87).

[00254] 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: 87. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 87. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 87. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 87. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 87. In some embodiments, the polypeptide as set forth in SEQ ID NO: 87 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds

to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00255] 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: 86 linked via a linker sequence GGGSGGGSGGGSGGGGS (SEQ ID NO: 72) to a heavy chain variable region as set forth in SEQ ID NO: 85. 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,

QVQLQQSGAELVKPGASVKLSCKTSGYTFTSYWIQWVKRPGQGLGWIGEIF
PGTGTSYYNENFKGKATLTIDTSSSTAYMQPSSLTSEDSAVYFCARTNNYRSY
ALDYWGQGTNYRSGGGSGGGSGGGSGGGSDIVMTQSPASLAVSLGQRATISY
RASKSVSTSGYSYMHWNQKPGQPPRLLIYLVSNLESGVPARFSGSGSGTDFT
LNHPVEEEDAATYYCQQXXGGAYTFGGGTKLEIKR (SEQ ID NO: 88).

[00256] 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: 88. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 88. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 88. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 88. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 88. In some embodiments, the polypeptide as set forth in SEQ ID NO: 88 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00257] 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: 37 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: 37 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 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: 37 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: 37 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: 37 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: 37 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: 37 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: 37 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: 37 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: 37 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: 37 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 a liver cell, such as those provided herein.

[00258] 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, such as those provided herein. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region, said Fc region further comprising a transmembrane domain such as those provided herein. In some embodiments, the Fc region further comprising a transmembrane domain has a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker as provided for herein or is absent, Fc is a variant Fc region as provided for herein, L₂ is a linker as provided for herein or is absent, and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprises a polypeptide having the formula ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or 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: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising

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

[00259] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 37 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: 37 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: 37 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: 37 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: 37 and comprises a stalk portion (S_1) comprising an Fc region (L_1 -Fc- L_2 - X_1) comprising 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: 37 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: 37 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: 37 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: 37 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: 37 and comprising a stalk portion (S_1) comprising an Fc region (L_1 -Fc- L_2 - X_1) comprising an ECD, a T_M , and an ICD, is

anchored to the surface of a viral particle, such as those provided for herein. In some embodiments, the identities of L₁, Fc, L₂, ECD, T_M, and ICD are as provided for herein. In some embodiments, the polypeptide bind to a liver cell, such as those provided herein.

[00260] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region, such as those provided herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region, said Fc region further comprising a transmembrane domain, such as those provided herein. In some embodiments, the Fc region further comprising a transmembrane domain has a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker as provided for herein or is absent, Fc is a variant Fc region as provided for herein, L₂ is a linker as provided for herein or is absent, and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprises a polypeptide having the formula ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or 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: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M, and an ICD. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 38 and comprises a stalk portion (S₁)

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

[00261] 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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 a liver cell, such as those provided herein.

[00262] 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: 130 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: 130 and comprises a stalk portion (S₁) comprising an Fc region, said Fc region further comprising a transmembrane domain such as those provided herein. In some embodiments, the Fc region further comprising a transmembrane domain has a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker as provided for herein or is absent, Fc is a variant Fc region as provided for herein, L₂ is a linker as provided for herein or is absent, and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprises a polypeptide having the formula ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or absent, T_M is a transmembrane domain as provided for herein, and ICD is an intracellular domain as provided for herein or absent. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 130 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: 130 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: 130 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: 130 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: 130 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: 130 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: 130 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: 130 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: 130 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 a liver cell, such as those provided herein.

[00263] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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 a liver cell, such as those provided herein.

[00264] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 130 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: 130 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: 130 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: 130 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: 130 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: 130 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: 130 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: 130 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: 130 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence having a sequence as set forth in SEQ ID NO: 130 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 a liver cell, such as those provided herein.

[00265] 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: 78 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: 78 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: 78 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: 78 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: 78 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: 78 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: 78 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: 78 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: 78 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: 78 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: 78 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 a liver cell, such as those provided herein.

[00266] 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: 79 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: 79 and comprises a stalk portion (S₁) comprising an Fc region, said Fc region further comprising a transmembrane domain such as those provided herein. In some embodiments, the Fc region further comprising a transmembrane domain has a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker as provided for herein or is absent, Fc is a variant Fc region as provided for herein, L₂ is a linker as provided for herein or is absent, and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprises a polypeptide having the formula ECD-T_M-ICD,

wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or absent, T_M is a transmembrane domain as provided for herein, and ICD is an intracellular domain as provided for herein or absent. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 79 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: 79 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: 79 and comprises a stalk portion (S₁) comprising an Fc region (L₁-Fc-L₂-X₁) comprising 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: 79 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: 79 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: 79 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: 79 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: 79 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: 79 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 a liver cell, such as those provided herein.

[00267] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 78 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: 78 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: 78 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: 78 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: 78 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: 78 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: 78 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: 78 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: 78 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: 78 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: 78 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 a liver cell, such as those provided herein.

[00268] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 79 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: 79 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: 79 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: 79 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: 79 and comprises a stalk portion (S₁) 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: 79 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: 79 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: 79 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: 79 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: 79 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: 79 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 a liver cell, such as those provided herein.

[00269] 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: 87 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: 87 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 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: 87 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: 87 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: 87 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 87 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 87 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 87 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 87 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 87 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: 87 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 a liver cell, such as those provided herein.

[00270] 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: 88 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: 88 and comprises a stalk portion (S₁) comprising an Fc region, said Fc region further comprising a transmembrane domain such as those provided herein. In some embodiments, the Fc region further comprising a transmembrane domain has a formula of L₁-Fc-L₂-X₁, wherein L₁ is a linker as provided for herein or is absent, Fc is a variant Fc region as provided for herein, L₂ is a linker as provided for herein or is absent, and X₁ is a polypeptide comprising a transmembrane domain as provided for herein. As provided for herein, X₁ may comprises a polypeptide having the formula ECD-T_M-ICD, wherein ECD is an extracellular domain, or a fragment thereof as provided for herein or absent, T_M is a transmembrane domain as provided for herein, and ICD is an intracellular domain as provided for herein or absent. In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 88 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: 88 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: 88 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: 88 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: 88 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: 88 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: 88 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: 88 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: 88 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 a liver cell, such as those provided herein.

[00271] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 87 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: 87 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: 87 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: 87 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: 87 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: 87 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: 87 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: 87 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: 87 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: 87 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: 87 and comprising a stalk portion (S_1) comprising an Fc region (L_1 -Fc- L_2 - X_1) comprising an ECD, a T_M , and an ICD, is anchored to the surface of a viral particle, such as those provided for herein. In some

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

[00272] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 88 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: 88 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: 88 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: 88 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: 88 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: 88 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: 88 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: 88 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: 88 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: 88 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: 88 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 a liver cell, such as those provided herein.

[00273] 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: 89:

METDTLLLVLLLVWVPGSTGDSASSELTQDPAVSVALGQTVRITCQGDSLRSYASWYQQKPGQAPVLIYGKNN
RPSGIPDRFSGSSSGNTASLTITGAQAEDEADYYCNSLERIGYLSYVFGGGTKLTVLGGGGSGGGGSGGGGSEVQLL
ESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDNKNTLYL
QMNSLRAEDTAVYYCAKDFSSRRWYLEYWGQGLTVTVSSASGGGGSGGGGSGGGGSEPKSCDKTHTCPPCPAP
EAAGGPSVFLFPPKPKDTLMASRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLT
VLAQDWLNGKEYKCKVSNKALGAPIEKTSKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESN
GQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSSVMHEALHNAYTQKSLSLSPGKKIEVMYPPPYLD
NEKSNGTIIHVKGKHLCPSPFLPGPSKPFVWLVVVGGLVACYSLLVTVAFIIFWVRSKRSLHSDYMNRRVRQGY
(SEQ ID NO: 89)

or is substantially similar to SEQ ID NO: 89, or is an active fragment of SEQ ID NO: 89. 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: 89. 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: 89. 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: 89. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence of SEQ ID NO: 89.

[00274] 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: 89, wherein the target binding

domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 89, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 89. 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: 89, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 89, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 89. 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: 89, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 89, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 89. 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: 89, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 89, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 89. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence of SEQ ID NO: 89, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 89, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 89.

[00275] 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: 89, wherein the V_L of the target binding domain corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain corresponds to amino acids 148-267 of SEQ ID NO: 89, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 89. 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: 89, wherein the V_L of the target binding domain corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain corresponds to amino acids 148-267 of SEQ ID NO: 89, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 89. 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: 89, wherein the V_L of the target binding domain corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain corresponds to amino acids 148-267 of SEQ ID NO: 89, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 89. 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: 89, wherein the V_L of the target binding domain corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain corresponds to amino acids 148-267 of SEQ ID NO: 89, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 89. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence of SEQ ID NO: 89, wherein the V_L of the target binding domain corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain corresponds to amino acids 148-267 of SEQ ID NO: 89, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 89.

[00276] 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: 89, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 89. 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: 89, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 89, L₁ comprises amino acids 268-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 89. 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: 89, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 89. 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: 89, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 89. 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: 89, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 89.

[00277] 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: 89, wherein the V_L of the target binding domain corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain corresponds to amino acids 148-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 89. 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: 89, wherein the V_L of the target binding domain corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain corresponds to amino acids 148-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 89. 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: 89, wherein the V_L of the target binding domain corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain corresponds to amino acids 148-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 89. 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: 89, wherein the V_L of the target binding domain corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain corresponds to amino acids 148-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 89. 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: 89, wherein the V_L of the target binding domain corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain corresponds to amino acids 148-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 89.

[00278] 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: 89, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, ECD comprises amino acids 517-556 of SEQ ID NO: 89, T_M comprises amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 89. 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: 89, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, ECD comprises amino acids 517-556 of SEQ ID NO: 89, T_M comprises amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 89. 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: 89, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 89,

L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, ECD comprises amino acids 517-556 of SEQ ID NO: 89, T_M comprises amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 89. 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: 89, wherein the target binding domain "T" of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, ECD comprises amino acids 517-556 of SEQ ID NO: 89, T_M comprises amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 89. 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: 89, wherein the target binding domain "T" of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, ECD comprises amino acids 517-556 of SEQ ID NO: 89, T_M comprises amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 89.

[00279] 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: 89, wherein the V_L of the target binding domain corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain corresponds to amino acids 148-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent ECD comprises amino acids 517-556 of SEQ ID NO: 89, T_M comprises amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 89. 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: 89, wherein the V_L of the target binding domain corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain corresponds to amino acids 148-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent ECD comprises amino acids 517-556 of SEQ ID NO: 89, T_M comprises amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 89. 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: 89, wherein the V_L of the target binding domain corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain corresponds to amino acids 148-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent ECD comprises amino acids 517-556 of SEQ ID NO: 89, T_M comprises amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 89. 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: 89, wherein the V_L of the target binding domain corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain corresponds to amino acids 148-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent ECD comprises amino acids 517-556 of SEQ ID NO: 89, T_M comprises amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 89. 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: 89, wherein the V_L of the target binding domain corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain corresponds to amino acids 148-267 of SEQ ID NO: 89, L₁ comprises amino acids 270-284 of SEQ ID NO: 89, Fc comprises amino acids 285-516 of SEQ ID NO: 89, L₂ is absent ECD comprises amino acids 517-556 of SEQ ID NO: 89, T_M comprises amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 89.

[00280] 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: 89, wherein the target binding domain “T” of the polypeptide comprises an amino acid sequence SEQ ID NO: 37 and corresponds to amino acids 24-267 of SEQ ID NO: 89, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 89, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 89, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 89. 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: 89, wherein the target binding domain “T” of the polypeptide comprises an amino acid sequence SEQ ID NO: 37 and corresponds to amino acids 24-267 of SEQ ID NO: 89, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 89, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 89, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 89. 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: 89, wherein the target binding domain “T” of the polypeptide comprises an amino acid sequence SEQ ID NO: 37 and corresponds to amino acids 24-267 of SEQ ID NO: 89, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 89, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ

ID NO: 89, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 89, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 89. 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: 89, wherein the target binding domain “T” of the polypeptide comprises an amino acid sequence SEQ ID NO: 37 and corresponds to amino acids 24-267 of SEQ ID NO: 89, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 89, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 89, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 89. 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: 89, wherein the target binding domain “T” of the polypeptide comprises an amino acid sequence SEQ ID NO: 37 and corresponds to amino acids 24-267 of SEQ ID NO: 89, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 89, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 89, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 89.

[00281] 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: 89, wherein the V_L of the target binding domain comprises an amino acid sequence of SEQ ID NO: 36 and corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain comprises an amino acid sequence of SEQ ID NO: 35 and corresponds to amino acids 148-267 of SEQ ID NO: 89, L_1 comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 89, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 89, L_2 is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 89, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 89. In some embodiments, the polypeptide provided for herein comprising the formula of T- L_1 -Fc- L_2 -ECD- T_M -ICD comprises an amino acid sequence that is at least 90% identical to a sequence of SEQ ID NO: 89, wherein the V_L of the target binding domain comprises an amino acid sequence of SEQ ID NO: 36 and corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain comprises an amino acid sequence of SEQ ID NO: 35 and corresponds to amino acids 148-267 of SEQ ID NO: 89, L_1 comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 89, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 89, L_2 is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 89, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 89. In some embodiments, the polypeptide provided for herein comprising the formula of T- L_1 -Fc- L_2 -ECD- T_M -ICD comprises an amino acid sequence that is at least 95% identical to a sequence of SEQ ID NO: 89, wherein the V_L of the target binding domain comprises an amino acid sequence of SEQ ID NO: 36 and corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain comprises an amino acid sequence of SEQ ID NO: 35 and corresponds to amino acids 148-267 of SEQ ID NO: 89, L_1 comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 89, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ

ID NO: 89, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 89, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 89. 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: 89, wherein the V_L of the target binding domain comprises an amino acid sequence of SEQ ID NO: 36 and corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain comprises an amino acid sequence of SEQ ID NO: 35 and corresponds to amino acids 148-267 of SEQ ID NO: 89, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 89, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 89, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 89. 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: 89, wherein the V_L of the target binding domain comprises an amino acid sequence of SEQ ID NO: 36 and corresponds to amino acids 24-132 of SEQ ID NO: 89, the V_H of the target binding domain comprises an amino acid sequence of SEQ ID NO: 35 and corresponds to amino acids 148-267 of SEQ ID NO: 89, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 89, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 89, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 89, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 89, and ICD comprises amino acids 584-604 of SEQ ID NO: 89, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 89.

[00282] 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: 92:

METDTLLLWVLLWVPGSTGDSAEVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAI
SGSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKDFSSRRWYLEYWGQGLTVTVSSGGGGSG
GGGSGGGGSSSELTQDPAVSVALGQTVRITCQGDSLRSYYASWYQKPGQAPVLIYGKNNRPSGIPDRFSGSSS
GNTASLTITGAQAEDEADYYCNSLERIGYLSYVFGGGTKLTVLASGGGGSGGGGSGGGGSEPKCDKTHTCPPCPA
PEAAGGPSVFLFPKPKDTLMASRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVSVL
TVLAQDWLNGKEYCKKVSNAKALGAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWES
NGQPENNYKTTTPVLDSGSEFFLYSKLTVDKSRWQQGNVFSCSVMHEALHNAYTQKSLSLSPGKKIEVMYPPPYL
DNEKSGTIIHVKGKHLCPSPFLPGPSKPFVWLVVVGGLVACYSLLVTVAFIIFWVRSKRSLHSDYMNRRVQGYG
(SEQ ID NO: 92)

or is substantially similar to SEQ ID NO: 92, or is an active fragment of SEQ ID NO: 92. 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: 92. 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: 92. 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: 92. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence of SEQ ID NO: 92.

[00283] In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁, wherein T is a target binding domain and S₁ is a stalk portion, comprises an amino acid sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99%, or 100% identical to a sequence of SEQ ID NO: 92, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 92, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 92. 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: 92, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 92, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 92. 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: 92, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 92, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 92. 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: 92, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 92, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 92. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence of SEQ ID NO: 92, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 92, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 92.

[00284] 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: 92, wherein the V_H of the target binding domain corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain corresponds to amino acids 161-267 of SEQ ID NO: 92, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 92. 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: 92, wherein the V_H of the target binding domain corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain corresponds to amino acids 161-267 of SEQ ID NO: 92, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 92. 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: 92, wherein the V_H of the target binding domain corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain corresponds to amino acids 161-267 of SEQ ID NO: 92, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 92. 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: 92, wherein the V_H of the target binding domain corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain corresponds to amino acids 161-267 of SEQ ID NO: 92, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 92. In some embodiments, the polypeptide provided for herein comprising the formula of T-S₁ comprises an amino acid sequence of SEQ ID NO: 92, wherein the V_H of the target binding domain corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target

binding domain corresponds to amino acids 161-267 of SEQ ID NO: 92, and wherein the stalk portion “S₁” of the polypeptide corresponds to amino acids 268-604 of SEQ ID NO: 92.

[00285] 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: 92, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 92. 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: 92, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 92, L₁ comprises amino acids 268-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 92. 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: 92, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 92. 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: 92, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 92. 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: 92, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 92.

[00286] 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: 92, wherein the V_H of the target binding domain corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain corresponds to amino acids 161-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 92. 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: 92, wherein the V_H of the target binding domain corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain corresponds to amino acids 161-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 92. 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: 92, wherein the V_H of the target binding domain corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain corresponds to amino acids 161-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 92. 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: 92, wherein the V_H of the target binding domain corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain corresponds to amino acids 161-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 92. 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: 92, wherein the V_H of the target binding domain corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain corresponds to amino acids 161-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, and X₁ corresponds to amino acids 517-604 of SEQ ID NO: 92.

[00287] 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: 92, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, ECD comprises amino acids 517-556 of SEQ ID NO: 92, T_M comprises amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 92. 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: 92, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, ECD comprises amino acids 517-556 of SEQ ID NO: 92, T_M comprises amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 92. 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: 92, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, ECD comprises amino acids 517-556 of SEQ ID NO: 92, T_M comprises amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 92. 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: 92, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, ECD comprises amino acids 517-556 of SEQ ID NO: 92, T_M comprises amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92,

wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 92. 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: 92, wherein the target binding domain “T” of the polypeptide corresponds to amino acids 24-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, ECD comprises amino acids 517-556 of SEQ ID NO: 92, T_M comprises amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 92.

~~{00288}~~ 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: 92, wherein the V_H of the target binding domain corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain corresponds to amino acids 161-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent ECD comprises amino acids 517-556 of SEQ ID NO: 92, T_M comprises amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 92. 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: 92, wherein the V_H of the target binding domain corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain corresponds to amino acids 161-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent ECD comprises amino acids 517-556 of SEQ ID NO: 92, T_M comprises amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 92. 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: 92, wherein the V_H of the target binding domain corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of

the target binding domain corresponds to amino acids 161-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent ECD comprises amino acids 517-556 of SEQ ID NO: 92, T_M comprises amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 92. 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: 92, wherein the V_H of the target binding domain corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain corresponds to amino acids 161-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent ECD comprises amino acids 517-556 of SEQ ID NO: 92, T_M comprises amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 92. 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: 92, wherein the V_H of the target binding domain corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain corresponds to amino acids 161-267 of SEQ ID NO: 92, L₁ comprises amino acids 270-284 of SEQ ID NO: 92, Fc comprises amino acids 285-516 of SEQ ID NO: 92, L₂ is absent ECD comprises amino acids 517-556 of SEQ ID NO: 92, T_M comprises amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises amino acids 597-604 of SEQ ID NO: 92.

[00289] 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: 92, wherein the target binding domain “T” of the polypeptide comprises an amino acid sequence SEQ ID NO: 38 and corresponds to amino acids 24-267 of SEQ ID NO: 92, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 92, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino

acids 517-556 of SEQ ID NO: 92, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 92. 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: 92, wherein the target binding domain "T" of the polypeptide comprises an amino acid sequence SEQ ID NO: 38 and corresponds to amino acids 24-267 of SEQ ID NO: 92, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 92, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 92, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 92. 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: 92, wherein the target binding domain "T" of the polypeptide comprises an amino acid sequence SEQ ID NO: 38 and corresponds to amino acids 24-267 of SEQ ID NO: 92, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 92, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 92, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 92. 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: 92, wherein the target binding domain "T" of the polypeptide comprises an amino acid sequence SEQ ID NO: 38 and corresponds to amino acids 24-267 of SEQ ID NO: 92, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 92, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 92, L₂ is absent,

ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 92, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 92. 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: 92, wherein the target binding domain "T" of the polypeptide comprises an amino acid sequence SEQ ID NO: 38 and corresponds to amino acids 24-267 of SEQ ID NO: 92, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 92, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 92, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 92.

[00290] 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: 92, wherein the V_H of the target binding domain comprises an amino acid sequence of SEQ ID NO: 35 and corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain comprises an amino acid sequence of SEQ ID NO: 36 and corresponds to amino acids 161-267 of SEQ ID NO: 92, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 92, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 92, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises an amino acids sequence of SEQ

ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 92. 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: 92, wherein the V_H of the target binding domain comprises an amino acid sequence of SEQ ID NO: 35 and corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain comprises an amino acid sequence of SEQ ID NO: 36 and corresponds to amino acids 161-267 of SEQ ID NO: 92, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 92, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 92, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 92. 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: 92, wherein the V_H of the target binding domain comprises an amino acid sequence of SEQ ID NO: 35 and corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain comprises an amino acid sequence of SEQ ID NO: 36 and corresponds to amino acids 161-267 of SEQ ID NO: 92, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 92, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 92, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 92. 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: 92, wherein the V_H of the target binding domain comprises an amino acid sequence of SEQ ID NO: 35 and corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain comprises an amino acid sequence of SEQ ID NO: 36 and corresponds to amino acids 161-267 of SEQ ID NO: 92, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID

NO: 92, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 92, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 92. 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: 92, wherein the V_H of the target binding domain comprises an amino acid sequence of SEQ ID NO: 35 and corresponds to amino acids 24-143 of SEQ ID NO: 92, the V_L of the target binding domain comprises an amino acid sequence of SEQ ID NO: 36 and corresponds to amino acids 161-267 of SEQ ID NO: 92, L₁ comprises an amino acid sequence of SEQ ID NO: 72 and corresponds to amino acids 270-284 of SEQ ID NO: 92, Fc comprises an amino acid sequence of SEQ ID NO: 91 and corresponds to amino acids 285-516 of SEQ ID NO: 92, L₂ is absent, ECD comprises an amino acid sequence of SEQ ID NO: 60 and corresponds to amino acids 517-556 of SEQ ID NO: 92, T_M comprises an amino acid sequence of SEQ ID NO: 62 and corresponds to amino acids 557-583 of SEQ ID NO: 92, and ICD comprises amino acids 584-604 of SEQ ID NO: 92, wherein the env incorporation motif comprises an amino acids sequence of SEQ ID NO: 63 and corresponds to amino acids 597-604 of SEQ ID NO: 92.

Targeting moieties comprising flexible polypeptides

[00291] 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 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.

[00292] In some embodiments, X_1 comprises a CD8 and/or CD28 ECD, a T_M , and an ICD. In some embodiments, X_1 comprises an ECD, a CD8 and/or CD28 T_M , and an ICD. In some embodiments, X_1 comprises a CD8 and/or CD28 ECD, a CD8 and/or CD28 T_M , and an ICD. In some embodiments, X_1 comprises an ECD, a T_M , and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, X_1 comprises a CD8 and/or CD28 ECD, a T_M , and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, X_1 comprises an ECD, a CD8 and/or CD28 T_M ,

[00294] In some embodiments, a V_H peptide having a sequence as set forth in SEQ ID NO: 35 and a V_L peptide having a sequence as set forth in SEQ ID NO: 36 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: 35 and V_L peptide having a sequence as set forth in SEQ ID NO: 36 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: 35 and V_L peptide having a sequence as set forth in SEQ ID NO: 36 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: 35 and V_L peptide having a sequence as set forth in SEQ ID NO: 36 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: 35 and V_L peptide having a sequence as set forth in SEQ ID NO: 36 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: 35 and V_L peptide having a sequence as set forth in SEQ ID NO: 36 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: 35 and V_L peptide having a sequence as set forth in SEQ ID NO: 36 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: 35 and V_L peptide having a sequence as set forth in SEQ ID NO: 36 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: 35 and V_L peptide having a sequence as set forth in SEQ ID NO: 36 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: 35 and V_L peptide having a sequence as set forth in SEQ ID NO: 36 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.

(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 a liver cell, such as those provided herein.

[00295] 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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: 35; and the V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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: 35; and the

V_L peptide comprising a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 36 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 a liver cell, such as those provided herein.

[00296] 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: 35; 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: 36.

[00297] 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: 35; 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: 36; provided that the V_H peptide and a V_L peptide comprises a light chain CDR having a sequence of SEQ ID NO: 33, and an amino acid sequence of GKN, and a sequence of SEQ ID NO: 34; 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: 35; 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: 36; 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 GKN; a light chain CDR3 having a sequence of SEQ ID NO: 34; 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.

[00298] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO:

35; 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: 36; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 33; a LCDR2 having a sequence of GKN; and a LCDR3 having a sequence of SEQ ID NO: 34; 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.

[00299] In some embodiments, the polypeptide comprises a V_H peptide and a V_L peptide, wherein the V_H peptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 35; 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: 36; 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 GKN, wherein the LCDR2 comprises at most 1 conservative amino acid substitution, and a LCDR3 having a sequence of SEQ ID NO: 34, 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.

[00300] In some embodiments, a V_H peptide having a sequence as set forth in SEQ ID NO: 44 and a V_L peptide having a sequence as set forth in SEQ ID NO: 45 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: 44 and V_L peptide having a sequence as set forth in SEQ ID NO: 45 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: 44 and V_L peptide having a sequence as set forth in SEQ ID NO: 45 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: 44 and V_L peptide having a sequence as set forth in SEQ ID NO: 45 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: 44 and V_L peptide having a sequence as set forth in SEQ ID NO: 45 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: 44 and V_L peptide having a sequence as set forth in SEQ ID NO: 45 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: 44 and V_L peptide having a sequence as set forth in SEQ ID NO: 45 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: 44 and V_L peptide having a sequence as set forth in SEQ ID NO: 45 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: 44 and V_L peptide having a sequence as set forth in SEQ ID NO: 45 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 a liver cell, such as those provided herein.

[00301] 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: 44; 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: 45 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: 44; 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: 45 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 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: 44; 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: 45 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: 44; 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: 45 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: 44; 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: 45 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: 44; 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: 45 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: 44; 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: 45 are linked to a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1)

comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H peptide 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: 44; 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: 45 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: 44; 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: 45 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: 44; 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: 45 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 a liver cell, such as those provided herein.

[00302] 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: 44; 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: 45.

[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: 44; 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:

45; provided that the V_H peptide and a V_L peptide comprises a light chain CDR having a sequence of SEQ ID NO: 42, and an amino acid sequence of SA, and a sequence of SEQ ID NO: 43; and/or a heavy chain CDR having a sequence of SEQ ID NO: 39-41. 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: 44; 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: 45; provided that the V_H peptide and a V_L peptide comprise a light chain CDR1 having a sequence of SEQ ID NO: 42; a light chain CDR2 having a sequence of SA; a light chain CDR3 having a sequence of SEQ ID NO: 43; and/or a heavy chain CDR1 having a sequence of SEQ ID NO: 39; a heavy chain CDR2 having a sequence of SEQ ID NO: 40; and a heavy chain CDR3 having a sequence of SEQ ID NO: 41. In some embodiments, the CDRs in the V_H or V_L chain are as set forth in the combinations provided for herein.

[00304] 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: 44; 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: 45; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 42; a LCDR2 having a sequence of SA; and a LCDR3 having a sequence of SEQ ID NO: 43; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 39; a HCDR2 having a sequence of SEQ ID NO: 40; and a HCDR3 having a sequence of SEQ ID NO: 41.

[00305] 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: 44; 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: 45; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 42, wherein the LCDR1 comprises at most 1 conservative amino acid substitution, a LCDR2 having a sequence of SA, wherein the LCDR2 comprises at most 1 conservative amino acid substitution, and a LCDR3 having a sequence of SEQ ID NO: 43, 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: 39, wherein the HCDR1 comprises at most 1

conservative amino acid substitution, a HCDR2 having a sequence of SEQ ID NO: 40, wherein the HCDR2 comprises at most 1 conservative amino acid substitution, and a HCDR3 having a sequence of SEQ ID NO: 41, wherein the HCDR3 comprises at most 1 conservative amino acid substitution.

[00306] In some embodiments, a V_H peptide having a sequence as set forth in SEQ ID NO: 51 and a V_L peptide having a sequence as set forth in SEQ ID NO: 77 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: 51 and V_L peptide having a sequence as set forth in SEQ ID NO: 77 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: 51 and V_L peptide having a sequence as set forth in SEQ ID NO: 77 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: 51 and V_L peptide having a sequence as set forth in SEQ ID NO: 77 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: 51 and V_L peptide having a sequence as set forth in SEQ ID NO: 77 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: 51 and V_L peptide having a sequence as set forth in SEQ ID NO: 77 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: 51 and V_L peptide having a sequence as set forth in SEQ ID NO: 77 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: 51 and V_L peptide having a sequence as set forth in SEQ ID NO: 77 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: 51 and V_L peptide having a sequence as set forth in SEQ ID NO: 77 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 a liver cell, such as those provided herein.

[00307] 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: 51; 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: 77 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: 51; 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: 77 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: 51; 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: 77 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: 51; 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: 77 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: 51; 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: 77 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: 51; 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: 77 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: 51; 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: 77 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: 51; 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: 77 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: 51; 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: 77 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: 51; 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: 77 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 a liver cell, such as those provided herein.

[00308] 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: 51; 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: 77.

[00309] 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: 51; 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: 77; provided that the V_H peptide and a V_L peptide comprises a light chain CDR having a sequence of SEQ ID NO: 49, and an amino acid sequence of KN, and a sequence of SEQ ID NO: 50; and/or a heavy chain CDR having a sequence of SEQ ID NO: 46-48. 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: 51; 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: 77; provided that the V_H peptide and a V_L peptide comprise a light chain CDR1 having a sequence of SEQ ID NO: 49; a light chain CDR2 having a sequence of KN; a light chain CDR3 having a sequence of SEQ ID NO: 50; and/or a heavy chain CDR1 having a sequence of SEQ ID NO: 46; a heavy chain CDR2 having a sequence of SEQ ID NO: 47; and a heavy chain CDR3 having a sequence of SEQ ID NO: 48. In some embodiments, the CDRs in the V_H or V_L chain are as set forth in the combinations provided for herein.

[00310] 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:

51; 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: 77; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 49; a LCDR2 having a sequence of KN; and a LCDR3 having a sequence of SEQ ID NO: 50; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 46; a HCDR2 having a sequence of SEQ ID NO: 47; and a HCDR3 having a sequence of SEQ ID NO: 48.

[00311] 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: 51; 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: 77; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 49, wherein the LCDR1 comprises at most 1 conservative amino acid substitution, a LCDR2 having a sequence of KN, wherein the LCDR2 comprises at most 1 conservative amino acid substitution, and a LCDR3 having a sequence of SEQ ID NO: 50, 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: 46, wherein the HCDR1 comprises at most 1 conservative amino acid substitution, a HCDR2 having a sequence of SEQ ID NO: 47, wherein the HCDR2 comprises at most 1 conservative amino acid substitution, and a HCDR3 having a sequence of SEQ ID NO: 48, wherein the HCDR3 comprises at most 1 conservative amino acid substitution.

[00312] In some embodiments, a V_H peptide having a sequence as set forth in SEQ ID NO: 85 and a V_L peptide having a sequence as set forth in SEQ ID NO: 86 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: 85 and V_L peptide having a sequence as set forth in SEQ ID NO: 86 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: 85 and V_L peptide having a sequence as set forth in SEQ ID NO: 86 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: 85 and V_L peptide having a sequence as set forth in SEQ ID NO: 86 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: 85 and V_L peptide having a sequence as set forth in SEQ ID NO: 86 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: 85 and V_L peptide having a sequence as set forth in SEQ ID NO: 86 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: 85 and V_L peptide having a sequence as set forth in SEQ ID NO: 86 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: 85 and V_L peptide having a sequence as set forth in SEQ ID NO: 86 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: 85 and V_L peptide having a sequence as set forth in SEQ ID NO: 86 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 a liver cell, such as those provided herein.

[00313] 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: 85; 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: 86 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: 85; 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: 86 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 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: 85; 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: 86 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: 85; 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: 86 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: 85; 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: 86 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: 85; 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: 86 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: 85; 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: 86 are linked to a stalk portion (S_1) comprising a flexible polypeptide (L_3 - X_1)

comprising a CD8 and/or CD28 ECD, a T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the V_H peptide 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: 85; 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: 86 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: 85; 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: 86 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: 85; 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: 86 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 a liver cell, such as those provided herein.

[00314] 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: 85; 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: 86.

[00315] 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: 85; 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:

86; provided that the V_H peptide and a V_L peptide comprises a light chain CDR having a sequence of SEQ ID NO: 83, and an amino acid sequence of LV, and a sequence of SEQ ID NO: 84; and/or a heavy chain CDR having a sequence of SEQ ID NO: 80-82. 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: 85; 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: 86; provided that the V_H peptide and a V_L peptide comprise a light chain CDR1 having a sequence of SEQ ID NO: 83; a light chain CDR2 having a sequence of LV; a light chain CDR3 having a sequence of SEQ ID NO: 84; and/or a heavy chain CDR1 having a sequence of SEQ ID NO: 80; a heavy chain CDR2 having a sequence of SEQ ID NO: 81; and a heavy chain CDR3 having a sequence of SEQ ID NO: 82. In some embodiments, the CDRs in the V_H or V_L chain are as set forth in the combinations provided for herein.

[00316] 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: 85; 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: 86; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 83; a LCDR2 having a sequence of LV; and a LCDR3 having a sequence of SEQ ID NO: 84; and the V_H peptide comprises a HCDR1 having a sequence of SEQ ID NO: 80; a HCDR2 having a sequence of SEQ ID NO: 81; and a HCDR3 having a sequence of SEQ ID NO: 82.

[00317] 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: 85; 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: 86; provided that the V_L peptide comprises a LCDR1 having a sequence of SEQ ID NO: 83, wherein the LCDR1 comprises at most 1 conservative amino acid substitution, a LCDR2 having a sequence of LV, wherein the LCDR2 comprises at most 1 conservative amino acid substitution, and a LCDR3 having a sequence of SEQ ID NO: 84, 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: 80, wherein the HCDR1 comprises at most 1

conservative amino acid substitution, a HCDR2 having a sequence of SEQ ID NO: 81, wherein the HCDR2 comprises at most 1 conservative amino acid substitution, and a HCDR3 having a sequence of SEQ ID NO: 82, wherein the HCDR3 comprises at most 1 conservative amino acid substitution.

[00318] 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: 35 and the V_L peptide comprises a sequence of SEQ ID NO: 36. 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: 44 and the V_L peptide comprises a sequence of SEQ ID NO: 45. 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: 51 and the V_L peptide comprises a sequence of SEQ ID NO: 77. 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: 85 and the V_L peptide comprises a sequence of SEQ ID NO: 86.

[00319] In some embodiments, the polypeptide as provided herein binds to non-human primate ASGR1. In some embodiments, the polypeptide as provided herein binds to human ASGR1.

[00320] 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.

[00321] 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: 35 linked via a linker sequence GGGSGGGSGGGSGGGGS (SEQ ID NO: 72) to a light chain variable region as set forth in SEQ ID NO: 36. 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,

SSELTQDPAVSVALGQTVRITCQGDSLRSYYASWYQQKPGQAPVLVIYGKNN
RPSGIPDRFSGSSSGNTASLTITGAQAEDEADYYCNSLERIGYLSYVFGGGTKL
TVLGGGGSGGGSGGGGSEVQLLESGLLVQPGGSLRLSCAASGFTFSSYAM

SWVRQAPGKGLEWVSAISGSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSL
RAEDTAVYYCAKDFSSRRWYLEYWGQGLTVTVSS (SEQ ID NO: 37).

[00322] 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: 37. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 37. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 37. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 37. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 37. In some embodiments, the polypeptide as set forth in SEQ ID NO: 37 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00323] 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: 36 linked via a linker sequence GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 72) to a heavy chain variable region as set forth in SEQ ID NO: 35. 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,

EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYAMSWVRQAPGKGLEWVSAIS
GSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKDFSSRR
WYLEYWGQGLTVTVSSGGGGSGGGGSGGGGSSSELTQDPAVSVALGQTVRI
TCQGDSLRSYYASWYQQKPGQAPVLVIYGKNNRPSGIPDRFSGSSSGNTASLT
ITGAQAEDEADYYCNSLERIGYLSYVFGGGTKLTVL (SEQ ID NO: 38).

[00324] 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-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds

to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00325] 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: 44 linked via a linker sequence GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 72) to a light chain variable region as set forth in SEQ ID NO: 45. 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,

DIVMTQSQKFMSTSVGDRVSVTCKASQNVDTNVAWFQQKPGQYPKVLIIYSA
SYRYSGVPDRFTGSGSGTDFTLTISNVQSEDLAEYFCQQYNSYPFTFGAGTKL
ELKRAGGGGSGGGGSGGGGSQVQLQQSAAELARPGASVKMSCKASGYTFTS
YPMHWVKQRPGQGLEWIAIYISPSSGYTKYNQKFTDKTTLTADKSSTTAYMQ
LSSLTSDDSAVYYCARKGGYLDYWGGQTTLTVSS (SEQ ID NO: 129).

[00326] 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: 129. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 129. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 129. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 129. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 129. In some embodiments, the polypeptide as set forth in SEQ ID NO: 129 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00327] 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: 45 linked via a linker sequence GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 72) to a heavy chain variable region as set forth in SEQ ID NO: 44. 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,

QVQLQQSAAELARPGASVKMSCKASGYTFTSYPMHWVKQRPGQGLEWIAIYI
SPSSGYTKYNQKFTDKTTLTADKSSTTAYMQLSSLTSDDSAVYYCARKGGYL
DYWGQTTLTVSSGGGGSGGGGSGGGGSDIVMTQSQKFMSTSVGDRVSVTC

KASQNVDTNVAWFQQKPGQYPKVLIYSASYRYSQVPDRFTGSGSGTDFTLTI
SNVQSEDLAEYFCQQYNSYPFTFGAGTKLELKRA (SEQ ID NO: 130).

[00328] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 130. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 130. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 130. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 130. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 130. In some embodiments, the polypeptide as set forth in SEQ ID NO: 130 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00329] 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: 51 linked via a linker sequence GGGGSGGGGSGGGGSGGGGS (SEQ ID NO: 72) to a light chain variable region as set forth in SEQ ID NO: 77. 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,

DIVLTQPPSASGTPGQRVTISCTGSSSGIGNAYVSWYQQLPGKAPKLLIYKNG
QRPSGVSDRFSGSKSGTSASLAISGLRSEDEADYYCAAWDDSLNGWVFGGGT
KVTVLGGGGSGGGGSGGGGSEVQLLESGGGLVQPGGSLRLSCAASGFTFSDY
YMSWVRQAPGKGLEWVSAITTGGGSPNYADSVKGRFTISRDN SKNTLYLQM
NSLRAEDTAVYYCARDRTAGYFDYWGGALVTVSS (SEQ ID NO: 78).

[00330] 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: 78. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 78. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 78. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 78. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 78. In some embodiments, the polypeptide as set forth in SEQ ID NO: 78 is an antibody, or an antigen binding fragment thereof. In some

embodiments, the antibody is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00331] 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: 77 linked via a linker sequence GGGSGGGSGGGSGGGGS (SEQ ID NO: 72) to a heavy chain variable region as set forth in SEQ ID NO: 51. 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,

EVQLLESQGGLVQPGGSLRLSCAASGFTFSDYYMSWVRQAPGKGLEWVSAIT
TGGGSPNYADSVKGRFTISRDNKNTLYLQMNSLRAEDTAVYYCARDRTAG
YFDYWGGQALVTVSSGGGSGGGSGGGSDIVLTQPPSASGTPGQRVTISC
TGSSSGIGNAYVSWYQQLPKGAPKLLIYKNGQRPSGVSDRFSGSKSGTSASLA
ISGLRSEDEADYYCAAWDDSLNGWVFGGGTKVTVL (SEQ ID NO: 79).

[00332] 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: 79. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 79. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 79. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 79. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 79. In some embodiments, the polypeptide as set forth in SEQ ID NO: 79 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00333] 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: 85 linked via a linker sequence GGGSGGGSGGGSGGGGS (SEQ ID NO: 72) to a light chain variable region as set forth in SEQ ID NO: 86. 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,

DIVMTQSPASLAVSLGQRATISYRASKSVSTSGYSYMHWNQQKPGQPPRLLIY
LVSNLESGVPARFSGSGGTDFTLNIHPVEEEDAATYYCQXXGGAYTFGGG

TKLEIKRGGGGSGGGSGGGGSQVQLQQSGAELVKPGASVKLSCKTSGYTFT
SYWIQWVKQRPQGGLGWIGEIPGTGTSYYNENFKGKATLTIDTSSSTAYMQ
PSSLTSEDSAVYFCARTNNYRSYALDYWGQGTNYRS (SEQ ID NO: 87).

[00334] 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: 87. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 87. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 87. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 87. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 87. In some embodiments, the polypeptide as set forth in SEQ ID NO: 87 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1.

[00335] 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: 86 linked via a linker sequence GGGSGGGSGGGSGGGGS (SEQ ID NO: 72) to a heavy chain variable region as set forth in SEQ ID NO: 85. 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,

QVQLQQSGAELVKPGASVKLSCKTSGYTFTSYWIQWVKQRPQGGLGWIGEIP
PGTGTSYYNENFKGKATLTIDTSSSTAYMQPSSLTSEDSAVYFCARTNNYRSY
ALDYWGQGTNYRSGGGSGGGSGGGSGGGSDIVMTQSPASLAVSLGQRATISY
RASKSVSTSGYSYMHWNQQKPGQPPRLIYLVSNLESGVPARFSGSGSGTDFT
LNIHPVEEEDAATYYCQQXXGGAYTFGGGTKLEIKR (SEQ ID NO: 88).

[00336] 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: 88. In some embodiments, the polypeptide comprises a sequence that is at least 90% identical to a sequence of SEQ ID NO: 88. In some embodiments, the polypeptide comprises a sequence that is at least 95% identical to a sequence of SEQ ID NO: 88. In some embodiments, the polypeptide comprises a sequence that is at least 99% identical to a sequence of SEQ ID NO: 88. In some embodiments, the polypeptide comprises a sequence as set forth in SEQ ID NO: 88. In some embodiments, the polypeptide as set forth in SEQ ID

NO: 88 is an antibody, or an antigen binding fragment thereof. In some embodiments, the antibody is an anti-ASGR1 antibody. In some embodiments, the anti-ASGR1 antibody binds to non-human primate ASGR1. In some embodiments, the anti-ASGR1 antibody binds to human ASGR1

[00337] 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: 37 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: 37 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: 37 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: 37 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: 37 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: 37 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: 37 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: 37 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: 37 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: 37 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 a liver cell, such as those provided herein.

[00338] 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, 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 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 a liver cell, such as those provided herein.

[00339] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 37 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: 37 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: 37 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: 37 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: 37 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: 37 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: 37 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: 37 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: 37 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: 37 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 a liver cell, such as those provided herein.

[00340] 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, a 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 a liver cell, such as those provided herein.

[00341] 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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 a liver cell, such as those provided herein.

[00342] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 130 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: 130 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: 130 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: 130 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: 130 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: 130 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: 130 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: 130 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: 130 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: 130 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 a liver cell, such as those provided herein.

[00343] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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: 129 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 a liver cell, such as those provided herein.

[00344] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 130 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: 130 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: 130 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: 130 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: 130 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: 130 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: 130 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: 130 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: 130 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: 130 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 a liver cell, such as those provided herein.

[00345] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 78 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: 78 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: 78 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: 78 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: 78 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: 78 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: 78 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: 78 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 78 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 78 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 a liver cell, such as those provided herein.

[00346] In some embodiments, the polypeptide comprises a sequence that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 79 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 79 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 79 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID

NO: 79 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: 79 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: 79 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: 79 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: 79 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: 79 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: 79 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 a liver cell, such as those provided herein.

[00347] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 78 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: 78 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: 78 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: 78 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: 78 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: 78 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: 78 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: 78 and comprises a stalk portion (S₁) comprising a flexible polypeptide (L₃-X₁) comprising an ECD, a CD8 and/or CD28 T_M, and an ICD, wherein the ICD comprises an Env incorporation motif as provided for herein. In some embodiments, the polypeptide comprising a sequence having a sequence as set forth in SEQ ID NO: 78 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 a liver cell, such as those provided herein.

[00348] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 79 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: 79 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: 79 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: 79 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: 79 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: 79 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: 79 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: 79 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: 79 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: 79 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 a liver cell, such as those provided herein.

~~{00349}~~ 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: 87 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: 87 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: 87 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: 87 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: 87 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: 87 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: 87 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: 87 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: 87 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: 87 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 a liver cell, such as those provided herein.

[00350] 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: 88 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: 88 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 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 88 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 88 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 88 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 88 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 88 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 88 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 88 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 that is at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% identical to a sequence of SEQ ID NO: 88 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 a liver cell, such as those provided herein.

[00351] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 87 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: 87 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: 87 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: 87 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: 87 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: 87 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: 87 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: 87 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: 87 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: 87 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 a liver cell, such as those provided herein.

[00352] In some embodiments, the polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 88 and comprises a stalk portion (S_1) comprising a flexible polypeptide (L_3) as provided for herein. In some embodiments, a polypeptide comprises a sequence having a sequence as set forth in SEQ ID NO: 88 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: 88 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: 88 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: 88 and comprises a stalk portion (S_1)

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: 88 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: 88 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: 88 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: 88 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: 88 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 a liver cell, such as those provided herein.

Expressed polypeptides of interest

[00353] In some embodiments, the viral particle comprising a heterologous viral glycoprotein and a targeting moiety further comprises a nucleic acid molecule encoding for a heterologous molecule of interest or “cargo.” In some embodiments, the heterologous viral glycoprotein is as provided for herein. In some embodiments, the targeting moiety is as provided for herein. As used herein, heterologous molecule of interest is meant to refer to any product that may be encoded by a nucleic acid molecule. As non-limiting examples, “cargo” or “heterologous molecule of interest” may refer to an siRNA, an shRNA, a peptide, a polypeptide, a protein, a viral payload, a viral genome, or a combination thereof. In some embodiments, the heterologous molecule of interest is an siRNA, an shRNA, a non-coding RNA (e.g. a guide RNA for a CRISPR system), a peptide, a polypeptide, a protein, a viral payload, a viral genome,

a chimeric antigen receptor (“CAR”), or a combination thereof. In some embodiments, the polypeptide is a CAR.

[00354] 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 an 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.

[00355] 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.

[00356] In some embodiments, the heterologous molecule of interest comprises a gene or genes that are useful for the treatment of a disease or disorder. In some embodiments, the heterologous molecule of interest comprises a gene or genes that are useful for the treatment of liver-related diseases or disorders. In some embodiments, the heterologous molecule of interest comprises a gene or genes that are useful for the treatment of inherited liver disorders, inherited systemic disorders, acquired disorders, or any combination thereof. In some embodiments, the heterologous molecule of interest comprises a gene or genes that are useful for the treatment a disease or disorder selected from the group comprising, but not limited to, Wilson disease, glycogen storage disease, alpha-1 antitrypsin (AAT) deficiency, ornithine transcarbamylase (OTC) deficiency, mucopolysaccharidosis VII, Crigler-Najjar Syndrome Type 1, phenylketonuria, maple syrup urine disease, progressive familial intrahepatic cholestasis, tyrosinemia, acute intermittent porphyria, citrullinemia type 1, type 1 diabetes, hemophilia A, hemophilia B, a hemoglobinopathy (e.g., alpha/beta thalassemia or sickle cell), obesity, oxalosis, Type II diabetes, gestational diabetes, malignant neoplasms, or extrahepatic tumors. In some embodiments, the heterologous molecule of interest comprises a gene or genes that are useful for the treatment of an inherited liver disorder, wherein the inherited liver disorder is selected from the group comprising, but not limited to, Wilson disease, glycogen storage disease, alpha-1 antitrypsin (AAT) deficiency, ornithine transcarbamylase (OTC) deficiency, mucopolysaccharidosis VII, Crigler-Najjar Syndrome Type 1, phenylketonuria, maple syrup urine disease, progressive familial intrahepatic cholestasis, tyrosinemia, acute intermittent porphyria, citrullinemia type 1, or type 1 diabetes. In some embodiments, the heterologous molecule of interest comprises a gene or genes that are useful for the treatment of an inherited systemic disorder, wherein the inherited systemic disorder is selected from the group comprising, but not limited to, hemophilia A, hemophilia B, a hemoglobinopathy (e.g., alpha/beta thalassemia or sickle cell), obesity, or oxalosis. In some embodiments, the heterologous molecule of interest comprises a gene or genes that are useful for the treatment of an acquired disorder, wherein the acquired disorder is selected from the group comprising, but not limited to, Type II diabetes, gestational diabetes, malignant neoplasms, obesity, or extrahepatic tumors.

[00357] In some embodiments, the heterologous molecule of interest is Wilson disease protein (ATP7B), acid alpha-glucosidase (GAA), plasminogen activator inhibitor-1 (SERPINA1), ornithine transcarbamylase (OTC), Beta-glucuronidase (GUSB), UDP-glucuronosyltransferase 1-1 (UGT1A1), phenylketonuria (PAH), branched chain keto acid dehydrogenase E1 subunit alpha (BCKDHA), branched chain keto acid dehydrogenase E1 subunit beta (BCKDHB), branched chain keto acid dehydrogenase E2 (DBT), ATPase phospholipid transporting 8B1 (ATP8B1), bile salt export pump (ABCB11), ATP binding cassette subfamily A member 4 (ABCB4), fumarylacetoacetate hydrolase (FAH), Tyrosine aminotransferase (TAT), 4-hydroxyphenylpyruvate dioxygenase (HPD), hydroxymethylbilane synthase (HMBS), argininosuccinate synthase 1 (ASS1), citrin (SLC25A13), Factor VIII (F8), Factor IX (F9), alanine-glyoxylate aminotransferase (AGXT), glyoxylate and hydroxypyruvate reductase (GRHPR), 4-hydroxy-2-oxoglutarate aldolase (HOGA1), insulin (INS), glucagon-like peptide-1 (GLP-1) hormone, glucagon-like peptide-2 (GLP-2) hormone, glicentin, peptide YY (PYY), cholecystokinin (CCK), glucagon, amylin, activin type II inhibitors, or miR-22 inhibitors. In some embodiments, the heterologous molecule of interest is or encodes for ATP7B. In some embodiments, the heterologous molecule of interest is or encodes for GAA. In some embodiments, the heterologous molecule of interest is or encodes for SERPINA1. In some embodiments, the heterologous molecule of interest is or encodes for OTC. In some embodiments, the heterologous molecule of interest is or encodes for GUSB. In some embodiments, the heterologous molecule of interest is or encodes for UGT1A1. In some embodiments, the heterologous molecule of interest is or encodes for PAH. In some embodiments, the heterologous molecule of interest is or encodes for BCKDHA. In some embodiments, the heterologous molecule of interest is or encodes for BCKDHB. In some embodiments, the heterologous molecule of interest is or encodes for DBT. In some embodiments, the heterologous molecule of interest is or encodes for ATP8B1. In some embodiments, the heterologous molecule of interest is or encodes for ABCB11. In some embodiments, the heterologous molecule of interest is or encodes for ABCB4. In some embodiments, the heterologous molecule of interest is or encodes for FAH. In some embodiments, the heterologous molecule of interest is or encodes for TAT. In some embodiments, the heterologous molecule of interest is or encodes for HPD. In some embodiments, the heterologous molecule of interest is or encodes for HMBS. In some embodiments, the heterologous molecule of interest is or encodes for ASS1. In some embodiments, the heterologous molecule of interest is or encodes for SLC25A13. In some embodiments, the heterologous molecule of interest is or encodes for F8. In some

embodiments, the heterologous molecule of interest is or encodes for F9. In some embodiments, the heterologous molecule of interest is or encodes for AGXT. In some embodiments, the heterologous molecule of interest is or encodes for GRHPR. In some embodiments, the heterologous molecule of interest is or encodes for HOGA1. In some embodiments, the heterologous molecule of interest is or encodes for INS. In some embodiments, the heterologous molecule of interest is or encodes for glucagon-like peptide-1 (GLP-1) hormone. In some embodiments, the heterologous molecule of interest is or encodes for glucagon-like peptide-2 (GLP-2) hormone. In some embodiments, the heterologous molecule of interest is or encodes for glicentin. In some embodiments, the heterologous molecule of interest is or encodes for PYY. In some embodiments, the heterologous molecule of interest is or encodes for CCK. In some embodiments, the heterologous molecule of interest is or encodes for glucagon. In some embodiments, the heterologous molecule of interest is or encodes for amylin. In some embodiments, the heterologous molecule of interest is or encodes for activin type II inhibitors. In some embodiments, the heterologous molecule of interest is or encodes for miR-22 inhibitors.

[00358] 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 a heterologous molecule of interest as provided for herein in the target cell. Thus, for example, any of ATP7B, GAA, SERPINA1, OTC, GUSB, UGT1A1, PAH, BCKDHA, BCKDHB, DBT, ATP8B1, ABCB11, ABCB4, FAH, TAT, HPD, HMBS, ASS1, SLC25A13, F8, F9, AGXT, GRHPR, HOGA1, INS, glucagon-like peptide-1 (GLP-1) hormone, glucagon-like peptide-2 (GLP-2) hormone, glicentin, PYY, CCK, glucagon, amylin, activin type II inhibitors, or miR-22 inhibitors can be expressed in a liver 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 liver cell is the intended target, the viral particle can comprise a targeting moiety that binds to a target on the surface of the liver cell, such as, but not limited to ASGPR, including a subunit thereof, such as ASGR1, or ASGR2. In some embodiments, the targeting moiety targeting ASGR1 is as provided for herein.

[00359] 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.

[00360] In some embodiments, the pseudotyped viral particle is a lentivirus. In some embodiments, the pseudotyped viral particle is a non-integrating lentiviral vector (NILV). NILV constructs are known in the art and any such construct is within the scope of the present

disclosure. In some embodiments, the NILV contains mutations in the viral enzyme responsible for integration of viral genome into host chromosomes rendering the integration activity of the enzyme dramatically reduced or non-operable. In some embodiments, the NILV contains mutations to or deletion of the attachment (att) sites at the end of the 5'-LTR and 3'-LTR to prevent binding of the viral integrase to the att sites. In some embodiments, the NILV contains both mutations to the viral integrase and mutations to or deletion of the att sites.

[00361] In some embodiments, the viral integrase is from HIV-1. In some embodiments, the HIV-1 viral integrase contains a mutation at D64, D116, E152, or any combination thereof which results in a catalytically dead HIV-1 integrase. In some embodiments, the HIV-1 integrase comprises a mutation selected from H12A, N120L, Q148A, Q168L, F185A, W235E, K264R, K266R, K273R, or any combination thereof, which results in a diminished HIV-1 integrase.

[00362] In some embodiments, the NILV is as described in Gallinaro, Alessandra et al. "Integrase Defective Lentiviral Vector as a Vaccine Platform for Delivering Influenza Antigens." *Frontiers in immunology* vol. 9 171. 5 Feb. 2018, doi:10.3389/fimmu.2018.00171; Hu, Junhui et al. "A Non-integrating Lentiviral Approach Overcomes Cas9-Induced Immune Rejection to Establish an Immunocompetent Metastatic Renal Cancer Model." *Molecular therapy. Methods & clinical development* vol. 9 203-210. 23 Feb. 2018, doi:10.1016/j.omtm.2018.02.009; Lu, Baisong et al. "Delivering SaCas9 mRNA by lentivirus-like bionanoparticles for transient expression and efficient genome editing." *Nucleic acids research* vol. 47,8 (2019): e44. doi:10.1093/nar/gkz093; Wang, Yan et al. "Generation of a caged lentiviral vector through an unnatural amino acid for photo-switchable transduction." *Nucleic acids research* vol. 47,19 (2019): e114. doi:10.1093/nar/gkz659; Wanisch, Klaus, and Rafael J Yáñez-Muñoz. "Integration-deficient lentiviral vectors: a slow coming of age." *Molecular therapy : the journal of the American Society of Gene Therapy* vol. 17,8 (2009): 1316-32. doi:10.1038/mt.2009.122; Luis, Apolonia. "The Old and the New: Prospects for Non-Integrating Lentiviral Vector Technology." *Viruses* vol. 12,10 1103. 29 Sep. 2020, doi:10.3390/v12101103; Chen, Yanhao et al. "A Self-restricted CRISPR System to Reduce Off-target Effects." *Molecular therapy : the journal of the American Society of Gene Therapy* vol. 24,9 (2016): 1508-10. doi:10.1038/mt.2016.172; and Chen, Feng et al. "Episomal lentiviral vectors confer erythropoietin expression in dividing cells." *Plasmid* vol. 90 (2017): 15-19. doi:10.1016/j.plasmid.2017.02.001; each of which is incorporated by reference herein in their entirety.

Gene Editing Systems and Methods of Use Thereof

[00363] In some embodiments, the viral particles provided for herein further comprise at least one nucleic acid molecule encoding a gene editing system. The term “gene editing system” refers to some or all of the components necessary for a functional gene editing complex. For example, a CRISPR/Cas9 gene editing system may include a guide RNA or single guide RNA and a Cas9 protein. In another embodiment, a CRISPR/Cas9 gene editing system could include a nucleic acid molecule, or molecules, that encode a single guide RNA and a Cas9 protein. In other embodiments, a gene editing system may include a Zinc finger nuclease system, a Transcription Activator-like Effector nuclease (TALEN) system, or a meganuclease system.

[00364] In some embodiments, the gene editing system is a CRISPR-Cas system. In some embodiments, the gene editing system is a zinc finger nuclease system. In some embodiments, the gene editing system is TALEN. In some embodiments, the gene editing system is a meganuclease. In some embodiments, the gene editing system is a gene product regulating nucleic acid molecule. Gene products that regulate a nucleic acid molecule are known in the art and any such product may be utilized. In some embodiments, the gene product regulating nucleic acid molecule is selected from the group including, but not limited to, siRNA, piRNA, miRNA, RNAi, mRNA, shRNA, and antisense RNA. In some embodiments, the gene product regulating nucleic acid molecule is siRNA. In some embodiments, the gene product regulating nucleic acid molecule is piRNA. In some embodiments, the gene product regulating nucleic acid molecule is miRNA. In some embodiments, the gene product regulating nucleic acid molecule is RNAi. In some embodiments, the gene product regulating nucleic acid molecule is mRNA. In some embodiments, the gene product regulating nucleic acid molecule is shRNA. In some embodiments, the gene product regulating nucleic acid molecule is antisense RNA.

[00365] In some embodiments, the gene editing system may be a CRISPR-Cas system. A CRISPR-Cas system may comprise a CRISPR system guide or a polynucleotide encoding the guide. The guide may direct sequence-specific binding of a CRISPR complex to a target sequence in a genomic locus of the cell to be engineered. The targeted sequence may be modified by the CRISPR-Cas system. Alternatively or additionally, CRISPR-Cas system may comprise a CRISPR-Cas protein or a polynucleotide encoding the CRISPR protein. In some cases, a CRISPR-Cas system may further comprise a template or a polynucleotide encoding the template. The template may comprise a nucleic acid sequence capable of modifying the target sequence. In some embodiments, the nucleic acid molecule encodes a CRISPR-Cas system comprising a Cas protein, and a guide RNA, a single guide RNA, or at least one nucleic acid molecule that targets the Cas protein to a target nucleic acid molecule. In some

embodiments, the CRISPR-Cas system is a Class 1 or Class 2 CRISPR-Cas system. In some embodiments, the CRISPR-Cas system is a Class 1 CRISPR-Cas system. In some embodiments, the CRISPR-Cas system is a Class 2 CRISPR-Cas system. In some embodiments, the Class 2 CRISPR-Cas system comprises a Type II Cas protein. In some embodiments, the Type II Cas protein is a Cas9 protein. In some embodiments, the Class 2 CRISPR-Cas system comprises a Type V Cas protein. In some embodiments, the type V Cas protein is selected from the group including, but not limited to, Cas12a, Cas12b, Cas12c, Cas12d, Cas12e, or Cas 14. In some embodiments, the type V Cas protein is Cas12a. In some embodiments, the type V Cas protein is Cas12b. In some embodiments, the type V Cas protein is Cas12c. In some embodiments, the type V Cas protein is Cas12d. In some embodiments, the type V Cas protein is Cas12e. In some embodiments, the type V Cas protein is Cas 14. In some embodiments, the Class 2 CRISPR-Cas system comprises a Type VI Cas protein. In some embodiments, the Type VI Cas protein is selected from the group including, but not limited to, Cas13a, Cas13b, Cas13c, or Cas13d. In some embodiments, the Type VI Cas protein is Cas13a. In some embodiments, the Type VI Cas protein is Cas13b. In some embodiments, the Type VI Cas protein is Cas13c. In some embodiments, the Type VI Cas protein is Cas13d. In some embodiments, the CRISPR-Cas system is a base editing system. In some embodiments, the CRISPR-Cas base editing system comprises a dCas linked to a cytidine deaminase or an adenosine deaminase. In some embodiments, the CRISPR-Cas base editing system comprises a dCas linked to a cytidine deaminase. In some embodiments, the CRISPR-Cas base editing system comprises a dCas linked to an adenosine deaminase. In some embodiments, the CRISPR-Cas system is a prime editing system. In some embodiments, the CRISPR-Cas prime editing system comprises CRISPRa, CRISPRi, Cas 3, or CasMINI protein. In some embodiments, the CRISPR-Cas prime editing system comprises CRISPRa. In some embodiments, the CRISPR-Cas prime editing system comprises CRISPRi. In some embodiments, the CRISPR-Cas prime editing system comprises Cas 3. In some embodiments, the CRISPR-Cas prime editing system comprises a CasMINI protein.

[00366] In some embodiments, the gene editing system is a TALEN system. For example, the TALEN system may comprise a transcription activator-like effector nuclease (TALEN), an engineered variant thereof, or nucleic acids encoding thereof.

[00367] In some embodiments, the gene editing system is a ZFN system. For example, the ZFN system may comprise a zinc-finger nuclease, an engineered variant thereof, or nucleic acid encoding thereof. The ZFN system may use artificial restriction enzymes generated by

fusing a zinc finger DNA-binding domain to a DNA-cleavage domain that can be engineered to target desired DNA sequences.

[00368] In some embodiments, the gene editing system is a meganuclease system. For example, the meganuclease system may comprise a meganuclease, an engineered variant thereof, or nucleic acids encoding thereof. The meganuclease may be endodeoxyribonucleases characterized by a large recognition site (double-stranded DNA sequences of 12 to 40 base pairs).

[00369] The term “endogenous” is used herein to indicate that a molecule is native to a particular cell, cell population, cell type, tissue, or organism. For example, an endogenous gene refers to a gene that is native to a particular cell, cell population, cell type, tissue, or organism. In some embodiments, a target nucleic acid molecule is edited, wherein the target nucleic acid molecule is an endogenous gene.

[00370] In some embodiments, a method of editing a target nucleic acid molecule in a cell is provided. In some embodiments, the method comprises contacting the cell with a viral particle as provided for herein, wherein the nucleic acid molecule encoding the gene editing system is expressed in the cell and edits the target nucleic acid molecule in the cell. In some embodiments, the viral particle is a NILV particle as provided for herein. In some embodiments, the cell is a liver cell as provided for herein. In some embodiments, the cell is a hepatocyte, as provided for herein.

Exemplary viral particles comprising a targeting moiety comprising an Fc domain

[00371] 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: 37 or SEQ ID NO: 38; 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: 37. In some embodiments, the targeting moiety comprises an amino acid sequence of SEQ ID NO: 38. 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.

[00372] 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: 37 or SEQ ID NO: 38; 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: 37. In some embodiments, T comprises an amino acid sequence of SEQ ID NO: 38. 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.

[00373] 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: 37 or SEQ ID NO: 38; 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: 37. In some embodiments, T comprises an amino acid sequence of SEQ ID NO: 38. 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.

[00374] 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: 37 or SEQ ID NO: 38; 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: 91; 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.

[00375] 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: 89 or SEQ ID NO: 92, at least 95% identity to SEQ ID NO: 89 or SEQ ID NO: 92, at least 99% identity to SEQ ID NO: 89 or SEQ ID NO: 92, or at least 100% identity to SEQ ID NO: 89 or SEQ ID NO: 92. 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.

[00376] 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: 89 or SEQ ID NO: 92, at least 95% identity to SEQ ID NO: 89 or SEQ ID NO: 92, at least 99% identity to SEQ ID NO: 89 or SEQ ID NO: 92, or at least 100% identity to SEQ ID NO: 89 or SEQ ID NO: 92. 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.

Exemplary viral particles comprising a targeting moiety comprising a flexible polypeptide

[00377] 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: 37 or SEQ ID NO: 38; 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: 37. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 38. 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.

[00378] 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: 37 or SEQ ID NO: 38; 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: 37. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 38. 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.

~~{00379}~~ 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: 37, SEQ ID NO: 38; 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: 37. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 38. 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.

[00380] 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: 37 or SEQ ID NO: 38; 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: 37. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 38. 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.

[00381] 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: 37 or SEQ ID NO: 38; 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: 37. In some embodiments, the target binding domain has an amino acid sequence of SEQ ID NO: 38. 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.

Pharmaceutical Compositions and Methods

[00382] 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.

[00383] 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.

[00384] 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 as provided for herein.

[00385] Also provided herein are nucleic acid molecules encoding a mutant VSV-G protein as provided for herein.

[00386] 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 Diseases or Disorders

[00387] Also provided for herein are methods of treating a disease or disorder in a subject in need thereof. 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 a molecule of interest to treat the disease or disorder.

[00388] In certain embodiments, the disease is a liver disease. In some embodiments, the disease or disorder is an inherited liver disorder. In some embodiments, the disease or disorder is an inherited systemic disorder. In some embodiments, the disease or disorder is an acquired disorder. In some embodiments, the disease or disorder is selected from, but not limited to, Wilson disease, a glycogen storage disease (e.g. von Gierke's disease, Pompe's disease, and the like), alpha-1 antitrypsin (AAT) deficiency, ornithine transcarbamylase (OTC) deficiency, mucopolysaccharidosis VII, Crigler-Najjar Syndrome Type 1, phenylketonuria, maple syrup urine disease, progressive familial intrahepatic cholestasis, tyrosinemia, acute intermittent porphyria, citrullinemia type 1, type 1 diabetes such as hemophilia A, hemophilia B, a

hemoglobinopathy (e.g., alpha/beta thalassemia or sickle cell), obesity, oxalosis, Type II diabetes, gestational diabetes, malignant neoplasms, or extrahepatic tumors. In some embodiments, the inherited liver disorder is selected from, but not limited to, Wilson disease, a glycogen storage disease (e.g. von Gierke's disease, Pompe's disease, and the like), alpha-1 antitrypsin (AAT) deficiency, ornithine transcarbamylase (OTC) deficiency, mucopolysaccharidosis VII, Crigler-Najjar Syndrome Type 1, phenylketonuria, maple syrup urine disease, progressive familial intrahepatic cholestasis, tyrosinemia, acute intermittent porphyria, citrullinemia type 1, or type 1 diabetes. In some embodiments, the inherited systemic disorder is selected from, but not limited to, hemophilia A, hemophilia B, a hemoglobinopathy (e.g., alpha/beta thalassemia or sickle cell), obesity, or oxalosis. In some embodiments, the acquired disorder is selected from, but not limited to, Type II diabetes, gestational diabetes, malignant neoplasms, obesity, or extrahepatic tumors.

[00389] In addition, the compositions provided for herein can be used in methods for the treatment of any condition related to a liver disease or disorder.

[00390] In certain exemplary embodiments, the in vivo modified liver cells produced using the compositions provided herein are used to treat the liver disease or disorder.

[00391] In some embodiments, the subject has been treated with a therapeutic agent targeting the disease or condition, e.g. the liver disease or disorder, 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. In some embodiments, the administration effectively treats the subject despite the subject having become resistant to another therapy.

[00392] 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.

[00393] The administration of the compositions may be carried out in any convenient manner known to those of skill in the art. For example, the compositions may be administered to a subject by aerosol inhalation, injection, ingestion, transfusion, implantation or transplantation.

The compositions described herein may be administered to a patient transarterially, subcutaneously, intradermally, intratumorally, intranodally, intramedullary, intramuscularly, by intravenous (i.v.) injection, intraperitoneally, intranasally, intracranially, or intraosseously. In other instances, the compositions is injected directly into a site of a local disease site in the subject, a lymph node, an organ, a tumor, and the like.

[00394] 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.

[00395] 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.

[00396] 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.

[00397] 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.

[00398] In some embodiments, the methods are performed without a lymphodepletion step, such as the administration of cyclophosphamide and/or fludarabine.

[00399] In embodiments wherein the heterologous molecule of interest is a CAR, 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.

[00400] 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.

[00401] 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.

[00402] 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.

[00403] 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.

[00404] 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.

[00405] 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.

[00406] 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 atlizumab (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.

[00407] 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.

[00408] 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).

[00409] 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.

[00410] 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.

[00411] The compositions disclosed herein can comprise a pharmaceutical composition, and for example include a pharmaceutically acceptable carrier, and/or a pharmaceutical formulation.

[00412] The term “pharmaceutical formulation” refers to a preparation which is in such form as to permit the biological activity of an active ingredient contained therein to be effective, and which contains no additional components which are unacceptably toxic to a subject to which the formulation would be administered. A “pharmaceutically acceptable carrier” refers to an ingredient in a pharmaceutical formulation, other than an active ingredient, which is nontoxic to a subject. A pharmaceutically acceptable carrier includes, but is not limited to, a buffer, excipient, stabilizer, or preservative. In some aspects, the choice of carrier is determined in part by the particular cell and/or by the method of administration. Accordingly, there are a variety of suitable formulations. For example, the pharmaceutical composition can contain preservatives. Suitable preservatives may include, for example, methylparaben, propylparaben, sodium benzoate, and benzalkonium chloride. In some aspects, a mixture of two or more preservatives is used. The preservative or mixtures thereof are typically present in an amount of about 0.0001% to about 2% by weight of the total composition. Carriers are described, e.g., by Remington's Pharmaceutical Sciences 16th edition, Osol, A. Ed. (1980). Pharmaceutically acceptable carriers are generally nontoxic to recipients at the dosages and concentrations employed, and include, but are not limited to: buffers such as phosphate, citrate, and other organic acids; antioxidants including ascorbic acid and methionine; preservatives (such as octadecyldimethylbenzyl ammonium chloride; hexamethonium chloride; benzalkonium chloride; benzethonium chloride; phenol, butyl or benzyl alcohol; alkyl parabens such as methyl or propyl paraben; catechol; resorcinol; cyclohexanol; 3-pentanol; and m-cresol); low molecular weight (less than about 10 residues) polypeptides; proteins, such as serum albumin, gelatin, or immunoglobulins; hydrophilic polymers such as polyvinylpyrrolidone; amino acids such as glycine, glutamine, asparagine, histidine, arginine, or lysine; monosaccharides, disaccharides, and other carbohydrates including glucose, mannose, or dextrans; chelating agents such as EDTA; sugars such as sucrose, mannitol, trehalose or sorbitol; salt-forming

counter-ions such as sodium; metal complexes (e.g. Zn-protein complexes); and/or non-ionic surfactants such as polyethylene glycol (PEG).

[00413] 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).

[00414] 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.

[00415] 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.

[00416] 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.

[00417] 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.

[00418] 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.

[00419] 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

[00420] 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 that targets the viral particle to the liver 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 FcγR, C1q, FcRβ, 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: 90 and further comprises one or more mutations that correspond to L19A, L20A, N82A, P114G, I38A, H95A, and/or H220A of SEQ ID NO: 90.
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: 91, at least 85% identity to SEQ ID NO: 91, at least 90% identity to SEQ ID NO: 91, at least 95% identity to SEQ ID NO: 91, at least 98% identity to SEQ ID NO: 91, or at least 100% identity to SEQ ID NO: 91.
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 27-33, 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 S_1 comprises a formula of L_3 - X_1 , wherein:
- L_3 is a flexible peptide linker, and
- X_1 is a polypeptide comprising a transmembrane domain,
- wherein the targeting moiety having the formula T - S_1 has a formula of T - L_3 - X_1 .
57. The viral particle of embodiment 56, wherein L_3 comprises a polypeptide having a sequence of $(GGGGA)_n$ (SEQ ID NO: 54), $(GGGGS)_n$ (SEQ ID NO: 55), GSAGSAAGSGEF (SEQ ID NO: 56), KESGSVSSEQLAQFRSLD (SEQ ID NO: 57), EGKSSGSGSESKST (SEQ ID NO: 58), or any combination thereof, wherein each n is, independently, 1-4.
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) targets hepatocytes.
71. The viral particle of any one of embodiments 1-70, wherein the target binding domain (T) binds to ASGR1, ASGR2, or a combination thereof
72. The viral particle of embodiment 71, wherein the target binding domain (T) binds to ASGR1.
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 GKN; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 34; 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: 35, 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: 36, wherein the polypeptide comprises the sequences of LCDR1 as set forth in SEQ ID NO: 33; LCDR2 of GKN; and LCDR3 as set forth in SEQ ID NO: 34.
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: 35, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 36, 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 of GKN; and LCDR3 as set forth in SEQ ID NO: 34.

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: 35; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 36.

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: 35; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 36.

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: 35; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 36.

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: 35, and a light chain variable region comprising SEQ ID NO: 36.

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 ASGR1 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 37, at least 95% sequence identity to SEQ ID NO: 37, at least 99% sequence identity to SEQ ID NO: 37, or a sequence as set forth in SEQ ID NO: 37.

85. The viral particle of any one of embodiments 72-82, wherein the target binding domain (T) that binds to ASGR1 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 38, having at least 95% sequence identity to SEQ ID NO: 38, having at least 99% sequence identity to SEQ ID NO: 38, or a sequence as set forth in SEQ ID NO: 38.

86. 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: 39; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 40; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 41, 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: 42; the light chain CDR2 sequence has the amino acid sequence of SA; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 43; or variants of any of the foregoing.

87. The viral particle of embodiment 86, wherein the heavy chain comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 44, wherein the polypeptide comprises the sequences of HCDR1 as set forth in SEQ ID NO: 39; HCDR2 as set forth in SEQ ID NO: 40; and HCDR3 as set forth in SEQ ID NO: 41.

88. The viral particle of embodiments 86 or 87, wherein the light chain comprises: a light chain variable region having at least 90% sequence identity to SEQ ID NO: 45, wherein the polypeptide comprises the sequences of LCDR1 as set forth in SEQ ID NO: 42; LCDR2 of SA; and LCDR3 as set forth in SEQ ID NO: 43.

89. The viral particle of any one of embodiments 86-88, 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: 44, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 45, wherein polypeptide comprises the sequences of HCDR1 as set forth in SEQ ID NO: 39; HCDR2 as set forth in SEQ ID NO: 40; HCDR3 as set forth in SEQ ID NO: 41; LCDR1 as set forth in SEQ ID NO: 42; LCDR2 of SA; and LCDR3 as set forth in SEQ ID NO: 43.

90. The viral particle of any one of embodiments 86-89, 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: 44; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 45.

91. The viral particle of any one of embodiments 86-90, 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: 44; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 45.

92. The viral particle of any one of embodiments 86-91, 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: 44; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 45.

93. The viral particle of any one of embodiments 86-92, wherein the light chain and the heavy chain comprise: a heavy chain variable region comprising SEQ ID NO: 44, and a light chain variable region comprising SEQ ID NO: 45.

94. The viral particle of any one of embodiments 86-93, 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.

95. The viral particle of embodiment 94, wherein the peptide linker comprises a sequence of (GGGGS)_n, wherein n is independently 1-5.

96. The viral particle of any one of embodiments 86-93, 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.

97. The viral particle of any one of embodiments 72 or 86-95, wherein the target binding domain (T) that binds to ASGR1 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 129, at least 95% sequence identity to SEQ ID NO: 129, at least 99% sequence identity to SEQ ID NO: 129, or a sequence as set forth in SEQ ID NO: 129.

98. The viral particle of any one of embodiments 72 or 86-95, wherein the target binding domain (T) that binds to ASGR1 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 130, having at least 95% sequence identity to SEQ ID NO: 130, having at least 99% sequence identity to SEQ ID NO: 130, or a sequence as set forth in SEQ ID NO: 130.

99. 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: 46; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 47; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 48, 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: 49; the light chain CDR2 sequence has the amino acid sequence of KN; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 50; or variants of any of the foregoing.

100. The viral particle of embodiment 99, wherein the heavy chain comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 51, wherein the polypeptide comprises the sequences of HCDR1 as set forth in SEQ ID NO: 46; HCDR2 as set forth in SEQ ID NO: 47; and HCDR3 as set forth in SEQ ID NO: 48.

101. The viral particle of embodiments 99 or 100, wherein the light chain comprises: a light chain variable region having at least 90% sequence identity to SEQ ID NO: 77, wherein the polypeptide comprises the sequences of LCDR1 as set forth in SEQ ID NO: 48; LCDR2 of KN; and LCDR3 as set forth in SEQ ID NO: 49.

102. The viral particle of any one of embodiments 99-101, 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: 51, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 77, wherein polypeptide comprises the sequences of HCDR1 as set forth in SEQ ID NO: 46; HCDR2 as set forth in SEQ ID NO: 47; HCDR3 as set forth in SEQ ID NO: 48; LCDR1 as set forth in SEQ ID NO: 49; LCDR2 of KN; and LCDR3 as set forth in SEQ ID NO: 50.

103. The viral particle of any one of embodiments 99-102, 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: 51; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 77.

104. The viral particle of any one of embodiments 99-103, 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: 51; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 77.

105. The viral particle of any one of embodiments 99-104, 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: 51; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 77.

106. The viral particle of any one of embodiments 99-105, wherein the light chain and the heavy chain comprise: a heavy chain variable region comprising SEQ ID NO: 51, and a light chain variable region comprising SEQ ID NO: 77.

107. The viral particle of any one of embodiments 99-106, 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.

108. The viral particle of embodiment 107, wherein the peptide linker comprises a sequence of (GGGGS)_n, wherein n is independently 1-5.

109. The viral particle of any one of embodiments 99-106, 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.

110. The viral particle of any one of embodiments 72 or 99-108, wherein the target binding domain (T) that binds to ASGR1 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 78, at least 95% sequence identity to SEQ ID NO: 78, at least 99% sequence identity to SEQ ID NO: 78, or a sequence as set forth in SEQ ID NO: 78.

111. The viral particle of any one of embodiments 72 or 99-108, wherein the target binding domain (T) that binds to ASGR1 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 79, having at least 95% sequence identity to SEQ ID NO: 79, having at least 99% sequence identity to SEQ ID NO: 79, or a sequence as set forth in SEQ ID NO: 79.

112. 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: 80; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 81; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 82, 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: 83; the light chain CDR2 sequence has the amino acid sequence of LV; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 84; or variants of any of the foregoing.

113. The viral particle of embodiment 112, wherein the heavy chain comprises a heavy chain variable region having at least 90% sequence identity to SEQ ID NO: 85, wherein the polypeptide comprises the sequences of HCDR1 as set forth in SEQ ID NO: 80; HCDR2 as set forth in SEQ ID NO: 81; and HCDR3 as set forth in SEQ ID NO: 82.

114. The viral particle of embodiments 112 or 113, wherein the light chain comprises: a light chain variable region having at least 90% sequence identity to SEQ ID NO: 86, wherein the polypeptide comprises the sequences of LCDR1 as set forth in SEQ ID NO: 83; LCDR2 of LV; and LCDR3 as set forth in SEQ ID NO: 84.

115. The viral particle of any one of embodiments 112-114, 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: 85, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 86, wherein polypeptide comprises the sequences of HCDR1 as set forth in SEQ ID NO: 80; HCDR2 as set forth in SEQ ID NO: 81; HCDR3 as set forth in SEQ ID NO: 82; LCDR1 as set forth in SEQ ID NO: 83; LCDR2 of LV; and LCDR3 as set forth in SEQ ID NO: 84.

116. The viral particle of any one of embodiments 112-115, 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: 85; and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 86.

117. The viral particle of any one of embodiments 112-116, 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: 85; and a light chain variable region of the light chain having at least 95% sequence identity to SEQ ID NO: 86.

118. The viral particle of any one of embodiments 112-117, 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: 85; and a light chain variable region of the light chain having at least 99% sequence identity to SEQ ID NO: 86.

119. The viral particle of any one of embodiments 112-118, wherein the light chain and the heavy chain comprise: a heavy chain variable region comprising SEQ ID NO: 85, and a light chain variable region comprising SEQ ID NO: 86.

120. The viral particle of any one of embodiments 112-119, 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.

121. The viral particle of embodiment 120, wherein the peptide linker comprises a sequence of (GGGS)_n, wherein n is independently 1-5.
122. The viral particle of any one of embodiments 112-119, 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.
123. The viral particle of any one of embodiments 72 or 112-121, wherein the target binding domain (T) that binds to ASGR1 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 87, at least 95% sequence identity to SEQ ID NO: 87, at least 99% sequence identity to SEQ ID NO: 87, or a sequence as set forth in SEQ ID NO: 87.
124. The viral particle of any one of embodiments 72 or 112-121, wherein the target binding domain (T) that binds to ASGR1 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 88, having at least 95% sequence identity to SEQ ID NO: 88, having at least 99% sequence identity to SEQ ID NO: 88, or a sequence as set forth in SEQ ID NO: 88.
125. The viral particle of any one of embodiments 1-124, wherein the target binding domain (T) is an antibody, or an antigen-binding fragment thereof, such as scFv antibody.
126. The viral particle of any one of embodiments 1-125, wherein the heterologous viral glycoprotein is a SVCV-G polypeptide.
127. The viral particle of embodiment 126, 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.
128. The viral particle of embodiment 126 or 127, 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.
129. The viral particle of embodiment 126 or 127, 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.
130. The viral particle of embodiment 126 or 127, wherein the SVCV-G polypeptide comprises SEQ ID NO: 52 or SEQ ID NO: 53.

131. The viral particle of any one of embodiments 126, 127, or 130, wherein the SVCV-G polypeptide comprises SEQ ID NO: 52.
132. The viral particle of any one of embodiments 126, 127, or 130, wherein the SVCV-G polypeptide comprises SEQ ID NO: 53.
133. The viral particle of any one of embodiments 1-125, wherein the heterologous viral glycoprotein is a VSV-G polypeptide.
134. The viral particle 133, 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.
135. The viral particle 133, 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.
136. The viral particle of embodiment 134 or 135, wherein the VSV-G polypeptide comprises a I182E or I182D mutation as compared to SEQ ID NO: 2.
137. The viral particle of any one of embodiments 133-136, 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.
138. The viral particle of any one of embodiments 133-137, wherein the VSV-G polypeptide comprises a mutation that corresponds to I182D or I182E as compared to a sequence of SEQ ID NO: 2.
139. The viral particle of any one of embodiments 133-138, 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.
140. The viral particle of any one of embodiments 133-138, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 4.
141. The viral particle of any one of embodiments 133-138, 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.
142. The viral particle of any one of embodiments 133-138, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 5.
143. The viral particle of any one of embodiments 133-135 or 137, 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.

144. The viral particle of any one of embodiments 133-135 or 137, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 3.

145. The viral particle of any one of embodiments 133-144, 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.

146. The viral particle of any one of embodiments 133-145, 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.

147. The viral particle of any one of embodiments 133-146, 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.

148. The viral particle of any one of embodiments 133-147, 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.

149. The viral particle of any one of embodiments 133-148, 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.

150. The viral particle of any one of embodiments 133-149, 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.

151. The viral particle of any one of embodiments 133-150, 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.

152. The viral particle of any one of embodiments 133-151, 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.

153. The viral particle of any one of embodiments 133-152, 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.
154. The viral particle of any one of embodiments 133-153, wherein the VSV-G protein comprises a substitution at position 47, wherein the substitution is K47Q or K47N.
155. The viral particle of any one of embodiments 133-154, wherein the VSV-G protein comprises a substitution H8A and/or K47Q mutation.
156. The viral particle of any one of embodiments 133-155, wherein the VSV-G protein comprises a substitution at position 10, such as Q10A, Q10R, or Q10K substitution.
157. The viral particle of any one of embodiments 133-156, 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.
158. The viral particle of embodiment 157, wherein the VSV-G polypeptide comprises a T214N and/or T352A mutation.
159. The viral particle of embodiment 133, wherein the VSV-G polypeptide comprises a substitution at positions I182 and at least one of T214, and T352 of SEQ ID NO: 2.
160. The viral particle of embodiment 159, wherein the VSV-G polypeptide comprises substitutions at positions I182, T214, and T352 of SEQ ID NO: 2.
161. The viral particle of embodiments 159 or 160, 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.
162. The viral particle of any one of embodiments 159-161, 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.
163. The viral particle of any one of embodiments 159-161, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 22.
164. The viral particle of any one of embodiments 159-161, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 23.
165. The viral particle of any one of embodiments 159-161, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 24.
166. The viral particle of any one of embodiments 159-161, wherein the VSV-G polypeptide comprises a sequence of SEQ ID NO: 25.
167. The viral particle of any one of embodiments 1-166, wherein the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest.

168. The viral particle of embodiment 167, 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.
169. The viral particle of embodiments 167 or 168, wherein the heterologous molecule of interest is a chimeric antigen receptor ("CAR"), ATP7B, GAA, SERPINA1, OTC, GUSB, UGT1A1, PAH, BCKDHA, BCKDHB, DBT, ATP8B1, ABCB11, ABCB4, FAH, TAT, HPD, HMBS, ASS1, SLC25A13, F8, F9, AGXT, GRHPR, HOGA1, INS, glucagon-like peptide-1 (GLP-1) hormone, glucagon-like peptide-2 (GLP-2) hormone, glicentin, PYY, CCK, glucagon, amylin, activin type II inhibitors, or miR-22 inhibitors.
170. The viral particle of any one of embodiments 1-169, wherein the viral particle further comprises at least one nucleic acid molecule encoding a gene editing system.
171. The viral particle of embodiment 130 wherein the gene editing system is a CRISPR-Cas system, a zinc finger nuclease system, a TALEN, a meganuclease, or a gene product regulating nucleic acid molecule.
172. The viral particle of embodiment 171, wherein the nucleic acid molecule encodes a CRISPR-Cas system comprising a Cas protein, and a guide RNA, a single guide RNA, or at least one nucleic acid molecule that targets the Cas protein to a target nucleic acid molecule.
173. The viral particle of any one of embodiments 171-172, wherein the CRISPR-Cas system is a Class 1 or Class 2 CRISPR-Cas system.
174. The viral particle of embodiment 173, wherein the Class 2 CRISPR-Cas system comprises a Type II Cas protein.
175. The viral particle of embodiment 174, wherein the Type II Cas protein is a Cas9 protein.
176. The viral particle of embodiment 173, wherein the Class 2 CRISPR-Cas system comprises a Type V Cas protein.
177. The viral particle of embodiment 176, wherein the Type V Cas protein is selected from Cas12a, Cas12b, Cas12c, Cas12d, Cas12e, or Cas 14.
178. The viral particle of embodiment 173, wherein the Class 2 CRISPR-Cas system comprises a Type VI Cas protein.
179. The viral particle of embodiment 178, wherein the Type VI Cas protein is selected from Cas13a, Cas13b, Cas13c, or Cas13d.
180. The viral particle of any one of embodiments 171-172, wherein the CRISPR-Cas system is a base editing system.
181. The viral particle of embodiment 180, wherein the CRISPR-Cas system comprises a dCas linked to a cytidine deaminase or an adenosine deaminase.

182. The viral particle of any one of embodiments 171-172, wherein the CRISPR-Cas system is a prime editing system.
183. The viral particle of any one of embodiments 171-172, wherein the CRISPR-Cas system comprises CRISPRa, CRISPRi, Cas 3, or CasMINI protein.
184. The viral particle of embodiment 171, wherein the gene product regulating nucleic acid molecule encodes at least one molecule selected from siRNA, piRNA, miRNA, RNAi RNA, mRNA, shRNA, and antisense RNA.
185. A method of infecting a cell, the method comprising contacting the cell with a viral particle of any one of embodiments 1-184.
186. 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 1-184.
187. 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 1-184, wherein the viral particle comprises a nucleic acid molecule encoding the heterologous molecule of interest.
188. 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 1-184, wherein the viral particle comprises a nucleic acid molecule encoding the heterologous molecule of interest.
189. A method of editing a target nucleic acid molecule in a cell, the method comprising contacting the cell with the viral particle of any one of embodiments 170-184, wherein the nucleic acid molecule encoding the gene editing system is expressed in the cell and edits the target nucleic acid molecule in the cell.
190. The method of any one of embodiments 185-189, wherein the cell is a liver cell.
191. The method of any one of embodiments 185-190, wherein the cell is a hepatocyte.
192. 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 1-184, wherein the viral particle comprises a nucleic acid molecule encoding the heterologous molecule of interest to treat the disease or disorder.
193. The method of embodiment 192, wherein the disease or disorder is an inherited liver disorder, such as Wilson disease, a glycogen storage disease (e.g. von Gierke's disease, Pompe's disease, and the like), alpha-1 antitrypsin (AAT) deficiency, ornithine transcarbamylase (OTC) deficiency, mucopolysaccharidosis VII, Crigler-Najjar Syndrome

Type 1, phenylketonuria, maple syrup urine disease, progressive familial intrahepatic cholestasis, tyrosinemia, acute intermittent porphyria, citrullinemia type 1, or type 1 diabetes.

194. The method of embodiment 192, wherein the disease or disorder is an inherited systemic disorder, such as hemophilia A, hemophilia B, obesity, or oxalosis.

195. The method of embodiment 192, wherein the disease or disorder is an acquired disorder, such as Type II diabetes, gestational diabetes, malignant neoplasms, obesity, or extrahepatic tumors.

196. 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 1-184, wherein the particle comprises a nucleic acid molecule encoding the heterologous molecule.

197. 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: 37, or SEQ ID NO: 38;

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.

198. 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: 37, or SEQ ID NO: 38;
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.

199. 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: 37, or SEQ ID NO: 38;

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.

200. The viral particle of any one of embodiments 197-199, wherein the variant Fc protein comprises an amino acid sequence having at least 85% identity to SEQ ID NO: 91, at least 90% identity to SEQ ID NO: 91, at least 95% identity to SEQ ID NO: 91, at least 98% identity to SEQ ID NO: 91, or comprises the amino acid sequence of SEQ ID NO: 91.

201. 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: 37 or SEQ ID NO: 38;

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: 91;

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.

202. 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: 89 or SEQ ID NO: 92, at least 95% identity to SEQ ID NO: 89 or SEQ

ID NO: 92, at least 99% identity to SEQ ID NO: 89 or SEQ ID NO: 92, or at least 100% identity to SEQ ID NO: 89 or SEQ ID NO: 92.

203. 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: 89 or SEQ ID NO: 92, at least 95% identity to SEQ ID NO: 89 or SEQ ID NO: 92, at least 99% identity to SEQ ID NO: 89 or SEQ ID NO: 92, or at least 100% identity to SEQ ID NO: 89 or SEQ ID NO: 92.

204. 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: 37 or SEQ ID NO: 38;

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.

205. The viral particle of embodiment 204, wherein:

T comprises an amino acid sequence of SEQ ID NO: 37;
 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.

206. The viral particle of embodiment 204, 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.

207. 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:
 37, or SEQ ID NO: 38;

wherein the stalk portion S₁ comprises a formula of L₃-X₁; wherein

L₃ is a flexible peptide linker comprising an amino acid sequence of SEQ ID
 NO: 54, SEQ ID NO: 55, SEQ ID NO: 56, SEQ ID NO: 57, or SEQ ID NO:
 58; and

X₁ is polypeptide comprising a transmembrane domain having a formula
 ECD-T_M-ICD, wherein:

ECD is an extracellular domain comprising an amino acid sequence of
 SEQ ID NO: 59 or SEQ ID NO: 60, or a fragment thereof, or is absent;

T_M is a transmembrane domain comprising an amino acid sequence of
 SEQ ID NO: 61 or SEQ ID NO: 62, or a fragment thereof; and

ICD is an intracellular domain or protein that facilitates the
 incorporation of the targeting moiety into the envelope of the viral
 particle, wherein the ICD comprises an env incorporation motif

comprising an amino acid comprising a sequence of SEQ ID NO: 63 or
SEQ ID NO: 64.

208. 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: 37, or SEQ ID NO: 38;

wherein the stalk portion S₁ comprises a formula of L₃-X₁; wherein

L₃ is a flexible peptide linker comprising an amino acid sequence of SEQ ID NO: 55; and

X₁ is polypeptide comprising a transmembrane domain having a formula ECD-T_M-ICD, wherein:

ECD is an extracellular domain comprising an amino acid sequence of SEQ ID NO: 59 or a fragment thereof, or is absent;

T_M is a transmembrane domain comprising an amino acid sequence of SEQ ID NO: 61 or a fragment thereof; and

ICD is an intracellular domain or protein that facilitates the incorporation of the targeting moiety into the envelope of the viral particle or is absent, wherein the ICD comprises an env incorporation motif comprising an amino acid comprising a sequence of SEQ ID NO: 63 or SEQ ID NO: 64.

209. 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: 37 or SEQ ID NO: 38;

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.

210. 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: 37 or SEQ ID NO: 38;

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.

211. The viral particle of any one of embodiments 197-210, wherein the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest.

212. The viral particle of embodiment 211, wherein the heterologous molecule of interest is a CAR, ATP7B, GAA, SERPINA1, OTC, GUSB, UGT1A1, PAH, BCKDHA, BCKDHB, DBT, ATP8B1, ABCB11, ABCB4, FAH, TAT, HPD, HMBS, ASS1, SLC25A13, F8, F9, AGXT, GRHPR, HOGA1, INS, glucagon-like peptide-1 (GLP-1) hormone, glucagon-like peptide-2 (GLP-2) hormone, glicentin, PYY, CCK, glucagon, amylin, activin type II inhibitors, or miR-22 inhibitors.
213. The viral particle of any one of embodiments 197-212, wherein the viral particle further comprises at least one nucleic acid molecule encoding a gene editing system.
214. The viral particle of embodiment 213 wherein the gene editing system is a CRISPR-Cas system, a zinc finger nuclease system, a TALEN, a meganuclease, or a gene product regulating nucleic acid molecule.
215. The viral particle of embodiment 214, wherein the nucleic acid molecule encodes a CRISPR-Cas system comprising a Cas protein, and a guide RNA, a single guide RNA, or at least one nucleic acid molecule that targets the Cas protein to a target nucleic acid molecule.
216. The viral particle of any one of embodiments 214-215, wherein the CRISPR-Cas system is a Class 1 or Class 2 CRISPR-Cas system.
217. The viral particle of embodiment 216, wherein the Class 2 CRISPR-Cas system comprises a Type II Cas protein.
218. The viral particle of embodiment 217, wherein the Type II Cas protein is a Cas9 protein.
219. The viral particle of embodiment 216, wherein the Class 2 CRISPR-Cas system comprises a Type V Cas protein.
220. The viral particle of embodiment 219, wherein the Type V Cas protein is selected from Cas12a, Cas12b, Cas12c, Cas12d, Cas12e, or Cas 14.
221. The viral particle of embodiment 216, wherein the Class 2 CRISPR-Cas system comprises a Type VI Cas protein.
222. The viral particle of embodiment 221, wherein the Type VI Cas protein is selected from Cas13a, Cas13b, Cas13c, or Cas13d.
223. The viral particle of any one of embodiments 214-215, wherein the CRISPR-Cas system is a base editing system.
224. The viral particle of embodiment 223, wherein the CRISPR-Cas system comprises a dCas linked to a cytidine deaminase or an adenosine deaminase.
225. The viral particle of any one of embodiments 214-215, wherein the CRISPR-Cas system is a prime editing system.
226. The viral particle of any one of embodiments 214-215, wherein the CRISPR-Cas

system comprises CRISPRa, CRISPRi, Cas 3, or CasMINI protein.

227. The viral particle of embodiment 214, wherein the gene product regulating nucleic acid molecule encodes at least one molecule selected from siRNA, piRNA, miRNA, RNAi RNA, mRNA, shRNA, and antisense RNA.

[00421] 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

[00422] **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.

[00423] **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).

[00424] **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).

[00425] **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.

[00426] Structure-guided design of novel binding 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.

[00427] 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.

[00428] 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.

[00429] 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).

[00430] 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.

[00431] Example 2: Serum Stable VSV-G Protein

[00432] 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.

[00433] 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.

[00434] 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.

[00435] Thus, these examples demonstrate that i) the LDL-R detargeting mutation I182E affords an unexpected level of protection against the serum inactivation observed for WT VSV-G, ii) the LDL-R detargeting mutation I182E does not abrogate the serum stabilizing effect of the T230N + T352A mutations, and iii) the combined mutation construct VSV-G (I182E, T230N, T352A) appears to have a greater serum stabilizing effect than either I182E alone or T230N + T352A alone. Thus, VSV-G (I182E, T230N, T352A) is able to ablate native tropoism without alternating fusogenicity and additionally demonstrates a more stable profile and is not neutralized in serum.

[00436] **Example 3: Spring viremia of carp virus G protein can facilitate cell specific fusion.**

[00437] **Methods**

[00438] **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

[00439] 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.

[00440] **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).

[00441] 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).

[00442] 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.

[00443] Results:

[00444] 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.

[00445] 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.

[00446] Example 4: Generation of SupT1 ASGR1 model cell lines

[00447] Model SupT1 cell lines containing human, cynomolgus monkey, and mouse ASGR1 were generated. Parental SupT1 cells were transduced with wild-type VSV-G pseudotyped lentiviral vectors encoding EF-1 α driven human ASGR1 (NP_001662.1), cyno ASGR1 (XP_005582755.1), or mouse ASGR1 (NP_001278060.1). Specifically, lentiviral vector

particles were produced in HEK239T cells following transfection of xHIV, WT VSV-G, Rev, and the noted lentiviral genomes. Supernatant was isolated, centrifuged at 1000 x g for 5 min, then centrifuged over a 20% sucrose cushion overnight at 4C. Virus pellets were isolated and resuspended in TSSM with 3% human serum albumin. SupT1 cells were transduced with a 6x dilution series for each transgene. 7 days after transduction, cells were stained with anti-ASGPR1 PE (clone 8D7, BD Biosciences 563655) and analyzed by flow cytometry. Results are depicted in the table below:

	SupT1 Construct			
	Control (parental)	h-ASGR1	c-ASGR1	m-ASGR1
Percent ASGR1 positive	0.72	57.1	61.2	1.41

[00448] Both human and cyno constructs successfully achieved ASGR1 overexpression in SupT1 cells. Little murine ASGR1 was detected, however this may be attributed to the species selectivity of the 8D7 ASGR1 antibody. Transduced cells demonstrating 40-60% ASGR1 positivity were utilized for subsequent studies.

[00449] **Example 5: ASGR1 binders target lentiviral constructs to ASGR1 positive model cells**

[00450] ASGR1 immuno-adhesion constructs as provided for herein were generated and tested for their ability to successfully transduce a mixed population of ASGR1 positive and negative cells with a GFP transgene. The ASGR1 positive cells utilized were the ASGR1+ SupT1 model cells as described in Example 4. VSV-G* pseudotyped lentiviral particles were produced as in Example 3 with the lentiviral transfer genome encoding green fluorescent protein instead of a CAR. Results of transduction of the ASGR1 cell models with GFP-encoding lentiviral vector particles are shown in the table below:

Cell line	Percent dual GFP positive ASGR1 positive cells					
	VSV-G no binder	VSV-G* no binder	VSV-G* + SEQ ID NO: 79	VSV-G* + SEQ ID NO: 87	VSV-G* + SEQ ID NO: 38	VSV-G* + SEQ ID NO: 37
SupT1 (parental)	0	0	0	0	0	0
h-ASGR1+ SupT1	54.6	0.63	0.11	1.32	34.9	36.5
c-ASGR1+ SupT1	47.9	1.54	0.15	1.60	30.9	32.5

[00451] The ASGR1 immuno-adhesion constructs tested exhibited minimal “leaky” GFP expression (i.e. GFP positive ASGR1 negative) as shown in the table below:

Cell line	Percent GFP positive ASGR1 negative cells					
	VSV-G no binder	VSV-G* no binder	VSV-G* + SEQ ID NO: 79	VSV-G* + SEQ ID NO: 87	VSV-G* + SEQ ID NO: 38	VSV-G* + SEQ ID NO: 37
SupT1 (parental)	98.9	0.29	0.015	0.12	0.11	0.21
h-ASGR1+ SupT1	42.2	0.13	0.048	0.021	2.83	3.24
c-ASGR1+ SupT1	50.2	0.14	9.10E-03	0.083	9.64	9.42

[00452] Generally, WT VSV-G was able to successfully transduce the parental and the ASGR1 containing SupT1 cells with a distribution of ASGR1 positive and ASGR1 negative transduced cells matching the distribution outlined in example 4. Specifically, WT VSV-G successfully transduced SupT1 parental cells, yielding 98.9% GFP+ with 0.0% ASGR1+. WT VSV-G further successfully transduced h-ASGR1+ SupT1 cells (42.2% GFP+ ASGR1- and 54.6% GFP+ ASGR1+) and c-ASGR1+ SupT1 cells (50.2% GFP+ ASGR1- and 47.9% GFP+ ASGR1+). As expected, the VSV-G construct blinded to its native LDL receptor (VSV-G I182E, T230N, T352A; SEQ ID NO: 23; denoted VSV-G* in the table) successfully ablated transduction of both ASGR1 positive and ASGR1 negative SupT1 cells. Specifically, VSV-G* yielded only 0.29% GFP+ SupT1 parental cells, with 0.0% ASGR1+. ASGR1 immuno-adhesion constructs containing SEQ ID NO: 79 or SEQ ID NO: 87 were not able to successfully rescue transduction of the ASGR1 positive SupT1 cells. However, VSV-G* pseudotyped particles supplemented with ASGR1 immuno-adhesion constructs containing SEQ ID NO: 37 or SEQ ID NO: 38 were able to successfully transduce the ASGR1 positive SupT1 cells. These results indicate that an immuno-adhesion construct containing an ASGR1 scFv as a target binding domain is able to successfully target a viral particle to an ASGR1 positive cell and facilitate delivery and transduction of a heterologous molecule of interest.

Therefore, the same ASGR1 immuno-adhesion constructs were also tested for their ability to transduce the model m-ASGR1+ SupT1 cell line. As detailed in Example 4, it was hypothesized that the m-ASGR1 model cell line exhibited minimal ASGR1 signal because of the species selectivity of the 8D7 ASGR1 antibody clone used to assess the cell lines. Based on this hypothesis and on the results above, an increase in GFP positive ASGR1 negative cell populations in the mASGR1 SupT1 cell line would indicate that the cells did in fact contain mASGR1 and that it was recognized by the immuno-adhesion constructs. The results are depicted in the table below:

Cell line	Percent GFP positive ASGR1 negative cells					
	VSV-G no binder	VSV-G* no binder	VSV-G* + SEQ ID NO: 79	VSV-G* + SEQ ID NO: 87	VSV-G* + SEQ ID NO: 38	VSV-G* + SEQ ID NO: 37
SupT1 (parental)	98.9	0.29	0.015	0.12	0.11	0.21
m-ASGR1+ SupT1	97.7	0.16	0.037	0.10	22.0	22.0

These results suggest that the m-ASGR1 SupT1 model cell line comprises ASGR1 positive cells. It was expected that there would not be an increase in ASGR1 positive cells because the 8D7 ASGR1 antibody clone was used for ASGR1 detection in the flow cytometry analysis. Therefore, the increase in GFP positive ASGR1 negative cell population, which was more than 2X greater than observed for the c-ASGR1+ SupT1 cell line and more than 6X greater than observed for the h-ASGR1+ SupT1 cell line, indicates that the m-ASGR1 SupT1 model cell line does in fact contain overexpressed m-ASGR1.

[00453] Example 6: ASGR1 binders containing SEQ ID NO: 37 or SEQ ID NO: 38 dose-dependently transduce ASGR1 positive model cell lines

[00454] Pseudotyped lentiviral particles comprising VSV-G* glycoprotein and ASGR1 immuno-adhesion constructs containing SEQ ID NO: 37 or SEQ ID NO: 38 were tested for their ability to dose dependently transduce the h-ASGR1+, c-ASGR1+, and m-ASGR1+ SupT1 model cell lines described above with a GFP gene. As shown in FIG 7A and FIG 7B, the lentiviral constructs did not transduce the SupT1 parental cell line which does not contain ASGR1. However, the pseudotyped lentiviral constructs comprising ASGR1 immuno-adhesion constructs containing SEQ ID NO: 38 (FIG 7A) or SEQ ID NO: 37 (FIG 7B) dependently transduced each of the h-ASGR1+, c-ASGR1+, and m-ASGR1+ SupT1 model cell lines.

[00455] These results demonstrate the selectivity of the pseudotyped lentiviral particles comprising VSV-G* glycoprotein and ASGR1 immuno-adhesion constructs containing SEQ ID NO: 37 or SEQ ID NO: 38 in that neither immuno-adhesion construct significantly transduced the parental SupT1 cell line which does not contain ASGR1. Further, these results support the conclusions of Example 5 that both immuno-adhesion constructs transduce the m-ASGR1+ SupT1 model cell line in the same dose dependent manner as the h-ASGR1+ and c-ASGR1+ SupT1 cell lines. Lastly, these results further demonstrate that immuno-adhesion constructs containing an ASGR1 scFv as a target binding domain were able to successfully target a viral particle to an ASGR1 positive cell and facilitate delivery and transduction of a heterologous molecule of interest.

[00456] Example 7: ASGR1 binders containing SEQ ID NO: 37 transduce ASGR1 positive model cell lines with liver disease associated genes

[00457] Pseudotyped lentiviral particles comprising VSV-G* glycoprotein and ASGR1 immuno-adhesion constructs containing SEQ ID NO: 37 were tested for their ability to dose dependently transduce the h-ASGR1+ and c-ASGR1+ SupT1 model cell lines described above with a mSEAP-T2A-GFP gene construct. To assess whether epitope location plays a significant role in gene delivery, an immuno-adhesion construct was generated using the anti-ASGPR antibody DOM26H-196-61 (DOM26H-196-61 as disclosed in Coulstock, Edward et al. “Liver-targeting of interferon-alpha with tissue-specific domain antibodies.” *PloS one* vol. 8,2 (2013): e57263. doi:10.1371/journal.pone.0057263; which is hereby incorporated by reference in its entirety). The DOM scFv containing construct binds to the carbohydrate recognition domain (CRD) of ASGPR whereas the immuno-adhesion constructs containing SEQ ID NO: 37 or SEQ ID NO: 38 bind to the stalk region of ASGPR. The results are depicted in the table below:

Cell line	Percent GFP positive ASGR1 positive cells			
	VSV-G* no binder	VSV-G* + DOM26null isotype control	VSV-G* + DOM26	VSV-G* + SEQ ID NO: 37
SupT1 (parental)	0.019	0	5.08E-3	9.97E-3
h-ASGR1+ SupT1	0.039	0.062	2.67	22.4
c-ASGR1+ SupT1	0.23	0.20	3.97	23.2

[00458] These results demonstrate that a pseudotyped lentiviral particle comprising VSV-G* glycoprotein and an ASGR1 immuno-adhesion construct containing SEQ ID NO: 37 is able to successfully transduce the model SupT1 cell lines with liver disease associate genes. Further, these results indicate that epitope location is essential for the function of the lentiviral particle, as an immuno-adhesion molecule targeting the CRD provided only minimal transduction, whereas the immuno-adhesion molecule targeting the stalk region of ASGPR (i.e. the immuno-adhesion molecule comprising SEQ ID NO: 37) successfully transduced the SupT1 cells at an amount about 10X that of the CRD binding targeting molecule.

[00459] The above constructs were also tested for their ability to transduce the m-ASGR1+ SupT1 cells using the same paradigm as outlined in Example 5. The results are depicted in the table below:

Cell line	Percent GFP positive ASGR1 negative cells
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	VSV-G* no binder	VSV-G* + DOM26null isotype control	VSV-G* + DOM26	VSV-G* + SEQ ID NO: 37
SupT1 (parental)	0.057	0.11	0.13	0.085
m-ASGR1+ SupT1	0.046	0.029	0.13	11.0

[00460] These results demonstrate that, similar to the h-ASGR1+ and c-ASGR1+ SupT1 cells, a pseudotyped lentiviral particle comprising VSV-G* glycoprotein and an ASGR1 immuno-adhesion construct containing SEQ ID NO: 37 is able to successfully transduce the m-ASGR1+ model SupT1 cell line with liver disease associated gene. Also similar to the h-ASGR1+ and c-ASGR1+ SupT1 cells, binding epitope is essential, as only the immuno-adhesion molecule targeting the stalk region of ASGPR (i.e. the immuno-adhesion molecule comprising SEQ ID NO: 37) successfully transduced the SupT1 cells.

[00461] Example 8: ASGR1 binders containing SEQ ID NO: 37 or SEQ ID NO: 38 transduce ASGR1 positive model cell lines with liver disease associated genes

[00462] Pseudotyped lentiviral particles comprising VSV-G* glycoprotein and ASGR1 immuno-adhesion constructs containing SEQ ID NO: 37 or SEQ ID NO: 38 were tested for their ability to dose dependently transduce the h-ASGR1+, c-ASGR1+, and m-ASGR1+ SupT1 model cell lines described above with a liver disease or disorder associated heterologous molecule of interest. The liver disease or disorder associated heterologous molecules of interest are as provided for herein. The transduction will be assessed in a similar manner as to outlined in the Examples above.

[00463] Example 9: ASGR1 binders containing SEQ ID NO: 37 or SEQ ID NO: 38 successfully transduce ASGR1 positive cells *in vivo*

[00464] Pseudotyped lentiviral particles comprising VSV-G* glycoprotein and ASGR1 immuno-adhesion constructs containing SEQ ID NO: 37 or SEQ ID NO: 38 are tested for their ability to transduce murine cells *in vivo*. Specifically, mSEAP-2A-GFP or luciferase-GFP fusion particles are delivered via tail vein to mice. Blood draws are taken at regular intervals (e.g., 5, 7, 14, 21, 28 days) to evaluate SEAP activity and IVIS imaging is utilized for live imaging of luciferase expression at similar intervals. Terminal evaluation of mice is conducted through histology of liver organs to identify GFP+ cells.

[00465] This specification contains numerous citations to patents, patent applications, and publications. Each is hereby incorporated by reference for all purposes.

[00466] The specification also makes reference to various sequences, such as those provided herein and below.

VSV-G Indiana Full length WT:

MKCLLYLAFLFIGVNCKFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
LVDEYTGGEWVDSQFINGKCSNYICPTVHNSTTWHSDYKVKGLCDSNLSMDITFFSEDGELSSLGKEGTGFRSNY
FAYETGGKACKMQYCKHWGVRPSPGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLC
QETWSKIRAGLPISPVDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGTTTERELWDDWAPYEDVEIGP
NGVLR TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNPIELVEGWFS
SWKSSIA SFFFIIIGLIIGLFLVLRVGIHLCKIKLHKKRQIYTDIEMNRLGK (SEQ ID NO: 1)

VSV-G Indiana Ectodomain WT:

KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQVTPHHVLVDEYTGGEWVDSQFIN
GKCSNYICPTVHNSTTWHSDYKVKGLCDSNLSMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
HWGVRPSPGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISP
VDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGTTTERELWDDWAPYEDVEIGP
NGVLR TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNPIELVEGWFS
SWKSSIA SFFFIIIGLIIGLFLVLRVGIHLCKIKLHKKRQIYTDIEMNRLGK (SEQ ID NO: 2)

VSV-G Indiana ectodomain I182A:

KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQVTPHHVLVDEYTGGEWVDSQFIN
GKCSNYICPTVHNSTTWHSDYKVKGLCDSNLSMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
HWGVRPSPGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISP
VDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGTTTERELWDDWAPYEDVEIGP
NGVLR TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNPIELVEGWFS
SWKSSIA SFFFIIIGLIIGLFLVLRVGIHLCKIKLHKKRQIYTDIEMNRLGK (SEQ ID NO: 3)

VSV-G Indiana ectodomain I182D:

KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQVTPHHVLVDEYTGGEWVDSQFIN
GKCSNYICPTVHNSTTWHSDYKVKGLCDSNLSMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
HWGVRPSPGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISP
VDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGTTTERELWDDWAPYEDVEIGP
NGVLR TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNPIELVEGWFS
SWKSSIA SFFFIIIGLIIGLFLVLRVGIHLCKIKLHKKRQIYTDIEMNRLGK (SEQ ID NO: 4)

VSV-G Indiana ectodomain I182E:

KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQVTPHHVLVDEYTGGEWVDSQFIN
GKCSNYICPTVHNSTTWHSDYKVKGLCDSNLSMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
HWGVRPSPGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISP
VDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGTTTERELWDDWAPYEDVEIGP
NGVLR TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNPIELVEGWFS
SWKSSIA SFFFIIIGLIIGLFLVLRVGIHLCKIKLHKKRQIYTDIEMNRLGK (SEQ ID NO: 5)

VSV-G Indiana ectodomain H8A + K47Q:

KFTIVFPHNQGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAEAVIVQVTPHHVLVDEYTGGEWVDSQFIN
GKCSNYICPTVHNSTTWHSDYKVKGLCDSNLSMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
HWGVRPSPGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISP
VDLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGTTTERELWDDWAPYEDVEIGP
NGVLR TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDDES LFFGDTGLSKNPIELVEGWFS
SWKSSIA SFFFIIIGLIIGLFLVLRVGIHLCKIKLHKKRQIYTDIEMNRLGK (SEQ ID NO: 6)

VSV-G Indiana ectodomain Q10A:

KFTIVFPHNAKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
 KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAVIVQVTPHHVLVDEYTG EWVDSQFIN
 GKCSNYICPTVHNSTTWHSDYKVKGLCDNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
 HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISP
 V DLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGT TTERELWDDWAPYEDVEIGPNGVLR
 TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDSLFFGDTGLSKNP IELVEGWFSWKS
 SIA SFFFIIGLIIGLFLVLRVGIHLCKIKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 7)

VSV-G Indiana ectodomain Q10R:

KFTIVFPHNRKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
 KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAVIVQVTPHHVLVDEYTG EWVDSQFIN
 GKCSNYICPTVHNSTTWHSDYKVKGLCDNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
 HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISP
 V DLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGT TTERELWDDWAPYEDVEIGPNGVLR
 TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDSLFFGDTGLSKNP IELVEGWFSWKS
 SIA SFFFIIGLIIGLFLVLRVGIHLCKIKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 8)

VSV-G Indiana ectodomain Q10K:

KFTIVFPHNRKGNWKNVPSNYHYCPSSSDLNWHNDLIGTALQVKMPKSHKAIQADGWMCHASKWVTTCDFRWYGP
 KYITHSIRSFTPSVEQCKESIEQTKQGTWLNPGFPPQSCGYATVTDAAVIVQVTPHHVLVDEYTG EWVDSQFIN
 GKCSNYICPTVHNSTTWHSDYKVKGLCDNLISMDITFFSEDGELSSLGKEGTGFRSNYFAYETGGKACKMQYCK
 HWGVRLP SGVWFEMADKDLFAAARFPECPEGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAGLPISP
 V DLSYLAPKNPGTGPAFTIINGTLKYFETRYIRVDIAAPILSRMVGMI SGT TTERELWDDWAPYEDVEIGPNGVLR
 TSSGYKFPLYMIGHGMLDSDLHLSSKAQVFEHPHIQDAASQLPDDSLFFGDTGLSKNP IELVEGWFSWKS
 SIA SFFFIIGLIIGLFLVLRVGIHLCKIKHTKKRQIYTDIEMNRLGK (SEQ ID NO: 9)

VSV-G New Jersey Full length WT:

MLSYLIFALVVPILGKIEIVFPQHTTGDWKRVPHEYNYCPTSADKNSHGTQTGIPVELTMPKGLTTHQVDGFMCH
 SALWMTTCDFRWYGP KYITHSIHNEEPTDYQCLEAIKAYKDGVSFNP G F P P Q S C G Y A T V T D A E A H I V T P H S V
 K D G V S F N P G F P P Q S C G Y A T V T D A E A H I V T P H S V K V D E Y T G E W I D P H F I G
 G R C K G Q I C E T V H N S T K W F T S S D G E S V C S Q L F T L V G G T F F S D S E E I T S M G L P E T G I R S N Y
 F P Y V S T E G I C K M P F C R K P G Y K L K N D L W F Q I T D P D L K T V R D L P H I K D C D L S S I V T P G E H A T D I S L I S D V E R I L D
 Y A L C Q N T W S K I E A G E P I T P V D L S Y L G P K N P G A G P V F T I I N G S L H Y F M S K Y L R V E L E S P V I P R M E G K V A G T R I V R Q
 L W D Q W F P F G E V E I G P N G V L K T Q G Y K F P L H I I G T G E V D N D I K M E R I V K H W E H P H I E A A Q T F L K K D D T E E V L Y Y G D
 T G V S K N P V E L V E G W F S G W R S S I M G V L A V I I G F V I L I F L I R L I G V L S S L F R Q K R R P I Y K S D V E M A H F R (SEQ ID
 NO: 10)

VSV-G New Jersey ectodomain WT:

KIEIVFPQHTTGDWKRVPHEYNYCPTSADKNSHGTQTGIPVELTMPKGLTTHQVDGFMCHSALWMTTCDFRWYGP
 KYITHSIHNEEPTDYQCLEAIKAYKDGVSFNP G F P P Q S C G Y A T V T D A E A H I V T P H S V K V D E Y T G E W I D P H F I G
 G R C K G Q I C E T V H N S T K W F T S S D G E S V C S Q L F T L V G G T F F S D S E E I T S M G L P E T G I R S N Y F P Y V S T E G I C K M P F C R
 K P G Y K L K N D L W F Q I T D P D L K T V R D L P H I K D C D L S S I V T P G E H A T D I S L I S D V E R I L D Y A L C Q N T W S K I E A G E P
 I T P V D L S Y L G P K N P G A G P V F T I I N G S L H Y F M S K Y L R V E L E S P V I P R M E G K V A G T R I V R Q L W D Q W F P F G E V E I G P N
 G V L K T Q G Y K F P L H I I G T G E V D N D I K M E R I V K H W E H P H I E A A Q T F L K K D D T E E V L Y Y G D T G V S K N P V E L V E G W F S
 G W R S S I M G V L A V I I G F V I L I F L I R L I G V L S S L F R Q K R R P I Y K S D V E M A H F R (SEQ ID NO: 11)

VSV-G Marraba Full length WT:

MLRFLFCFLALGAHSKFTIVFPHHQGNWKNVPSTYHYCPSSSDQNWHNDLTGVS LHV KIPKSHKAIQADGWMCH
 HA AKWVTTCDFRWYGP KYITHSIHMSPTLEQCKTSIEQTKQGVWVNP G F P P Q S C G Y A T V T D A E V V V V Q A T P H H V
 L V D E Y T G E W I D S Q L V G G K S K E V C Q T V H N S T V W H A D Y K I T G L C E S N L A S V D I T F F S E D G Q K T S L G K P N T G F R S N H
 F A Y E S G E K A C R M Q Y C T Q W G I R L P S G V W F E L V D K D L F Q A A K L P E C P R G S S I S A P S Q T S V D V S L I Q D V E R I L D Y S L C
 Q E T W S K I R A K L P V S P V D L S Y L A P K N P G S G P A F T I I N G T L K Y F E T R Y I R V D I S N P I I P H M V G T M S G T T T E R E L W N D
 W Y P Y E D V E I G P N G V L K T P T G F K F P L Y M I G H G M L D S D L H K S S Q A Q V F E H P H A K D A A S Q L P D D E T L F F G D T G L S K N P
 V E L V E G W F S W K S T L A S F F L I I G L G V A L I F I I R I I V A I R Y K Y K R K T Q K I Y N D V E M S R L G N K (SEQ ID NO:
 12)

VSV-G Marraba ectodomain WT:

KFTIVFPHHQKGNWKNVPSTYHYCPSSSDQNWHNDLTGVSLHVKIPKSHKAIQADGWMCHAAKWVTTCDFRWYGP
 KYITHSIHSMSPtleQCKTSIEQTKQGVWINPGFPPQSCGYATVTDAEVVVVQATPHHVLVDEYTG EWIDSQLVG
 GKCSKEVCQT VHNSTVWHADYKITGLCESNLASVDITFFSEDGQKTSLGKPN TGFRSNHFAYESGEKACRMQYCT
 QWGIRLPSGVWFELVDKDLFQA AKLPECPRGSSISAPSQTSVDVSLIQDVERILDYSLCQETWSKIRAKLPVSPV
 DLSYLAPKNPGSGPAFTIINGTLKYFETRYIRVDISNPIIPH MVGTMSGTTTERELWNDWYPYEDVEIGPNGVLK
 TPTGKFPLYMIGHGMLDSDLHKSSQAQVFEHPHAKDAASQLPDDETLFFGDTGLSKNPVELVEGWFSWWSKSTLA
 SFFLIIGLVALIFIIRIIVAIRYKYKGRKTQKIYNDVEMSRLGNK (SEQ ID NO: 13)

VSV-G Carajas Full length WT:

MKMKMVIAGLILCIGILPAIGKITISFPQSLKGDWRPVPKGYNYCPTSADKNLHGDLDIDIGLRLRAPKSFKGIS
 DGWMCHAARWTTTCDFRWYGPKYITHSIHSFRPSNDQCKEAI RL TNEGNWINPGFPPQSCGYASVTDSES VVVTV
 TKHQVLVDEYSGSWIDSQFP GSGCTSPICDTVHNSTLWHADHTLDSICDQEFVAMDAVLFTESGKFEEFGKPN SG
 IRSNYFPYESLKDVCQMDFCRKGKFLPSGVWFEIEDAEKSHKAQVELKIKRCPHGAVISAPNQNAADINLIMDV
 ERILDYSLCQATWSKIQNKEALTPIDISYLGPKNPGP GPAFTIINGTLHYFNTRYIRVDIAGPVTKEITG FVSGT
 STSRVLWDQWFPYGENSIGPNGLLK TASGYKYP LFMVGTGVL DADIHKLGEATVIEHPHAKAQKVVDSEVIF F
 GDTGVSKNPVEVVEGWFSGWRSSLSIFGIILLIVCLVLIVRILIALKYCCVRHKKRTIYKEDLEMGRIPRA
 (SEQ ID NO: 14)

VSV-G Carajas ectodomain WT:

KITISFPQSLKGDWRPVPKGYNYCPTSADKNLHGDLDIDIGLRLRAPKSFKGISADGWMCHAARWTTCDFRWYGP
 KYITHSIHSFRPSNDQCKEAI RL TNEGNWINPGFPPQSCGYASVTDSES VVVTVTKHQVLVDEYSGSWIDSQFP G
 GCTSPICDTVHNSTLWHADHTLDSICDQEFVAMDAVLFTESGKFEEFGKPN SGIRSNYFPYESLKDVCQMDFC K
 RKGKFLPSGVWFEIEDAEKSHKAQVELKIKRCPHGAVISAPNQNAADINLIMDVERILDYSLCQATWSKIQNKEA
 LTPIDISYLGPKNPGP GPAFTIINGTLHYFNTRYIRVDIAGPVTKEITG FVSGTSTSRVLWDQWFPYGENSIGPN
 GLLKTASGYKYP LFMVGTGVL DADIHKLGEATVIEHPHAKAQKVVDSEVIF FGD TGVSKNPVEVVEGWFSGWR
 SSLMSIFGIILLIVCLVLIVRILIALKYCCVRHKKRTIYKEDLEMGRIPRA (SEQ ID NO: 15)

VSV-G Alagoa Full length WT:

MTPAFILCMLLAGSSWAKFTIVFPQSQKGDWKDVPPNYRYCPSSADQNWHGDL LGVNIRAKMPKVHKA IKADGWM
 CHAAKWVTTCDYRWYGPQYITHSIHSFIPTKAQCEESIKQTKEGVWINPGFPPKNCGYASVSDAES IIVQATAHS
 VMIDEYSGDWLDSQFP TGRCTGSTCETIHNSTLWYADYQVTGLCD SALVSTEVTFYSEDGLMTSIGRQNTGYRSN
 YFPYEEKGAAACRMKYCTHEGIRLPSGVWFEMVDKELLESVQMPECPAGLTISAPTQTSVDVSLILDVERMLDYS L
 CQETWSKVHSGLPISPVDLGYIAPKNPGAGP AFTIIVNGTLKYFDTRYLRIDIEGPVLKMTGKVSGTPTKRELWT
 EWFYDDVEIGPNGVLKTP EGYKFLPYMIGHGLDSDLQKTSQAEVFHHPQIAEAVQKL PDDETLFFGDTGISK N
 PVEVIEGWFSNWRSSVMAIVFAILLVITVLMVRLCVAFRHFCCQKRHKIYNDLEMNQLRR (SEQ ID NO:
 16)

VSV-G Alagoa ectodomain WT:

KFTIVFPQSQKGDWKDVPPNYRYCPSSADQNWHGDL LGVNIRAKMPKVHKA IKADGWMCHAAKWVTTCDYRWYGP
 QYITHSIHSFIPTKAQCEESIKQTKEGVWINPGFPPKNCGYASVSDAES IIVQATAHSVMIDEYSGDWLDSQFP T
 GRCTGSTCETIHNSTLWYADYQVTGLCD SALVSTEVTFYSEDGLMTSIGRQNTGYRSNYFPYEEKGAAACRMKYCT
 HEGIRLPSGVWFEMVDKELLESVQMPECPAGLTISAPTQTSVDVSLILDVERMLDYS LCQETWSKVHSGLPISP V
 DLGYIAPKNPGAGP AFTIIVNGTLKYFDTRYLRIDIEGPVLKMTGKVSGTPTKRELWTEWFPYDDVEIGPNGVLK
 TPEGYKFLPYMIGHGLDSDLQKTSQAEVFHHPQIAEAVQKL PDDETLFFGDTGISK NPVEVIEGWFSNWRSSVM
 AIVFAILLVITVLMVRLCVAFRHFCCQKRHKIYNDLEMNQLRR (SEQ ID NO: 17)

VSV-G Cocal Full length WT:

MNLLLLTIVLPLCSHAKFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWHNDLLGITMKVKMPKTHKAIQADGWM
 CHAAKWTTTCDFRWYGPKYITHSIHSIQPTSEQCKESIKQTKQGTWMSFGFPPQNCGYATVTDVAVVVQATPHH
 VLVDEYTG EWIDSQLVNGKCEETECETVHNSTVWYSYKVTGLCDATLVDTETFFSEDGKKE SIGKPN TGYSN
 YFAYEKGDKVKCMNYCKHAGVRLPSGVWFEFVDQDVYAAAKLPECPV GATISAPTQTSVDVSLILDVERILDYSL
 CQETWSKIRSKQPVSPVDLSYLAPKNPGTGP AFTIINGTLKYFETRYIRIDIDNPIISKMVGKISGSGTRELWT
 EWFYEGVEIGPNGILKTP TGYKFLPYMIGHGMLDSDLHKTSQAEVFHHPHLAEAPKQLPEEETLFFGDTGISK N

PVELIEGWFSWSTVVTFFFAIGVFILLYVVARIVIAVRYRYQGSNNKRIYNDIEMSRFRK (SEQ ID NO: 18)

VSV-G Cocal ectodomain WT:

KFSIVFPQSQKGNWKNVPSSYHYCPSSSDQNWNHNDLLGITMKVKMPKTHKAIQADGWMCHAAKWITTCDFRWYGP
KYITHSIHSIQPTSEQCKESIKQTKQGTWMSPGFPPQNCGYATVTDVAVVVQATPHHVLVDEYTGEWIDSQFPN
GKCETEECETVHNSTVWYSDYKVTGLCDATLVDTEITFFSEDKKESIGKPNTRYRSNYFAYEKGDKVKCMNYCK
HAGVRLPSGVWFEFVDQDVYAAAKLPECPVGATISAPTQTSVDVSLILDVERILDYSLCOETWSKIRSKQPVSPV
DLSYLAPKNP GTGPAFTIINGTLKYFETRYIRIDIDNPIISKMVGKISGSQTERELWTEWFPYEGVEIGPNGILK
TPTGYKFPLFMIGHGMLDSDLHKTSQAEVFEHPLAEAPKQLPEEETLFFGDTGISKNPVELIEGWFSWSTV
TFFFAIGVFILLYVVARIVIAVRYRYQGSNNKRIYNDIEMSRFRK (SEQ ID NO: 19)

VSV-G Morreton Full length WT:

MLVLYLLLSLLALGAQCKFTIVFPHNQKGNWKNVPANYQYCPSSSDLNWNHNLIGTSLQVKMPKSHKAIQADGWM
CHAAKWITTCDFRWYGPKYVTHSIKSMIPTVDQCKESIAQTKQGTWLNPGFPPQSCGYASVTDAAEAVIVKATPHQ
VLVDEYTGWDVDSQFP TGKCNKDICTVHNSTTWHSDYKVTGLCDANLISMDITFFSEDKGLTSLGKEGTGFRSN
YFAYENGDKACRMQYCKHWGVRPLSGVWFEMADKDIYNDAKFPDCPEGSSIAAPSQTSVDVSLIQDVERILDYSL
CQETWSKIRAHLPISPVDLSYLSKPNPGTGPFTIINGTLKYFETRYIRVDIAGPIIPQMRGVISGTTTERELWT
DWYPYEDVEIGPNGVLKTATGYKFPLYMIGHGMLDSDLHSSKAQVFEHPIQDAASQLPDDETLFFGDTGLSKN
PIELVEGWFSGWKSTIASFFFIIGLVIGLYLVLRIALCIKCRVQEKRPKIYTDVEMNRLDR (SEQ ID NO: 20)

VSV-G Morreton ectodomain WT:

KFTIVFPHNQKGNWKNVPANYQYCPSSSDLNWNHNLIGTSLQVKMPKSHKAIQADGWMCHAAKWITTCDFRWYGP
KYVTHSIKSMIPTVDQCKESIAQTKQGTWLNPGFPPQSCGYASVTDAAEAVIVKATPHQVLVDEYTGWDVDSQFP
TGKCNKDICTVHNSTTWHSDYKVTGLCDANLISMDITFFSEDKGLTSLGKEGTGFRSNYFAYENGDKACRMQYCK
HWGVRPLSGVWFEMADKDIYNDAKFPDCPEGSSIAAPSQTSVDVSLIQDVERILDYSLCOETWSKIRAHLPISP
V DLSYLSKPNPGTGPFTIINGTLKYFETRYIRVDIAGPIIPQMRGVISGTTTERELWTDWYPYEDVEIGPNGVLK
TATGYKFPLYMIGHGMLDSDLHSSKAQVFEHPIQDAASQLPDDETLFFGDTGLSKNPIELVEGWFSGWKSTIA
SFFFIIGLVIGLYLVLRIALCIKCRVQEKRPKIYTDVEMNRLDR (SEQ ID NO: 21)

Fc IgG1 (Accession No. P01857)

ASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSS
LGTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKDTLMISRTPEVTCVVDVDS
HEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYCKCKVSNKALPAPIEKTIKAKGQ
PREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRW
QQGNVFCSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 26)

Fc IgG2 (Accession No. AAN76043)

STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSL
GTQTYICNVDHKPSNTKVDKTVKCCVECPPEPPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVDVDSHEDPE
VQFNWYVDGVEVHNAKTKPREEQFNSTFRVSVLTVVHQDWLNGKEYCKCKVSNKGLPAPIEKTIKAKGQPREPQ
VYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPMLDSDGSFFLYSKLTVDKSRWQQGNV
FSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 27)

Fc IgG4 (Accession No. AAB59394)

STKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSL
GKTKTYICNVDHKPSNTKVDKRVESKYGPPCSCPAPPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVDSQEDP
EVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYCKCKVSNKGLPSSIEKTIKAKGQPREP
QVYTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGN
VFSCVMHEALHNHYTQKSLSLSPGK (SEQ ID NO: 28)

What is Claimed:

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 that targets the viral particle to the liver, and S₁ is a stalk portion, wherein T binds to ASGR1, ASGR2, or a combination thereof.
2. The viral particle of claim 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 FcγR, C1q, FcRβ, or FcRn.
3. The viral particle of claim 2, 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.
4. The viral particle of claim 2, wherein the variant Fc protein comprises an amino acid sequence having at least 80% identity to SEQ ID NO: 91, at least 85% identity to SEQ ID NO: 91, at least 90% identity to SEQ ID NO: 91, at least 95% identity to SEQ ID NO: 91, at least 98% identity to SEQ ID NO: 91, or at least 100% identity to SEQ ID NO: 91.
5. The viral particle of claim 1, wherein the target binding domain (T) binds to ASGR2.
6. The viral particle of claim 1, wherein the target binding domain (T) binds to ASGR1.
7. The viral particle of claim 6, 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 GKN; and the light

chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 34; or variants of any of the foregoing.

8. The viral particle of claim 7, 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: 35, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 36, 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 of GKN; and LCDR3 as set forth in SEQ ID NO: 34.

9. The viral particle of claim 7, wherein the light chain and the heavy chain comprise: a heavy chain variable region comprising SEQ ID NO: 35, and a light chain variable region comprising SEQ ID NO: 36.

10. The viral particle of claim 7, wherein the target binding domain (T) that binds to ASGR1 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 37 or SEQ ID NO: 38, at least 95% sequence identity to SEQ ID NO: 37 or SEQ ID NO: 38, at least 99% sequence identity to SEQ ID NO: 37 or SEQ ID NO: 38, or a sequence as set forth in SEQ ID NO: 37 or SEQ ID NO: 38.

11. The viral particle of claim 6, 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: 39; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 40; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 41, 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: 42; the light chain CDR2 sequence has the amino acid sequence of SA; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 43; or variants of any of the foregoing.

12. The viral particle of claim 11, 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: 44, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 45, wherein polypeptide comprises the sequences of HCDR1 as set forth in SEQ ID NO: 39; HCDR2 as set forth in SEQ ID NO: 40; HCDR3 as set forth in SEQ ID NO: 41; LCDR1 as set forth in SEQ ID NO: 42; LCDR2 of SA; and LCDR3 as set forth in SEQ ID NO: 43.

13. The viral particle of claim 11, wherein the light chain and the heavy chain comprise: a heavy chain variable region comprising SEQ ID NO: 44, and a light chain variable region comprising SEQ ID NO: 45.

14. The viral particle of claim 11, wherein the target binding domain (T) that binds to ASGR1 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 129 or SEQ ID NO: 130, at least 95% sequence identity to SEQ ID NO: 129 or SEQ ID NO: 130, at least 99% sequence identity to SEQ ID NO: 129 or SEQ ID NO: 130, or a sequence as set forth in SEQ ID NO: 129 or SEQ ID NO: 130.

15. The viral particle of claim 6, 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: 46; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 47; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 48, 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: 49; the light chain CDR2 sequence has the amino acid sequence of KN; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 50; or variants of any of the foregoing.

16. The viral particle of claim 15, 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: 51, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 77, wherein polypeptide comprises the

sequences of HCDR1 as set forth in SEQ ID NO: 46; HCDR2 as set forth in SEQ ID NO: 47; HCDR3 as set forth in SEQ ID NO: 48; LCDR1 as set forth in SEQ ID NO: 49; LCDR2 of KN; and LCDR3 as set forth in SEQ ID NO: 50.

17. The viral particle of claim 15, wherein the light chain and the heavy chain comprise: a heavy chain variable region comprising SEQ ID NO: 51, and a light chain variable region comprising SEQ ID NO: 77.

18. The viral particle of claim 15, wherein the target binding domain (T) that binds to ASGR1 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 78 or SEQ ID NO: 79, at least 95% sequence identity to SEQ ID NO: 78 or SEQ ID NO: 79, at least 99% sequence identity to SEQ ID NO: 78 or SEQ ID NO: 79, or a sequence as set forth in SEQ ID NO: 78 or SEQ ID NO: 79.

19. The viral particle of claim 6, 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: 80; the heavy chain CDR2 has the amino acid sequence of SEQ ID NO: 81; and the heavy chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 82, 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: 83; the light chain CDR2 sequence has the amino acid sequence of LV; and the light chain CDR3 sequence has the amino acid sequence of SEQ ID NO: 84; or variants of any of the foregoing.

20. The viral particle of claim 19, 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: 85, and a light chain variable region of the light chain having at least 90% sequence identity to SEQ ID NO: 86, wherein polypeptide comprises the sequences of HCDR1 as set forth in SEQ ID NO: 80; HCDR2 as set forth in SEQ ID NO: 81; HCDR3 as set forth in SEQ ID NO: 82; LCDR1 as set forth in SEQ ID NO: 83; LCDR2 of LV; and LCDR3 as set forth in SEQ ID NO: 84.

21. The viral particle of claim 19, wherein the light chain and the heavy chain comprise: a heavy chain variable region comprising SEQ ID NO: 85, and a light chain variable region comprising SEQ ID NO: 86.

22. The viral particle of claim 19, wherein the target binding domain (T) that binds to ASGR1 comprises a polypeptide comprising a sequence having at least 90% sequence identity to SEQ ID NO: 87 or SEQ ID NO: 88, at least 95% sequence identity to SEQ ID NO: 87 or SEQ ID NO: 88, at least 99% sequence identity to SEQ ID NO: 87 or SEQ ID NO: 88, or a sequence as set forth in SEQ ID NO: 87 or SEQ ID NO: 88.

23. The viral particle of claim 1, wherein the target binding domain (T) is an antibody, or an antigen-binding fragment thereof, such as scFv antibody.

24. The viral particle of any one of claims 1-23, 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.

25. The viral particle of claim 24, wherein L₁ and L₂ are each, independently, absent or a polypeptide linker comprising an amino acid sequence of SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 73, SEQ ID NO: 74, SEQ ID NO: 75, SEQ ID NO: 56, SEQ ID NO: 57, SEQ ID NO: 58, or SEQ ID NO: 76.

26. The viral particle of claim 24, wherein L₁ and L₂ each, independently, comprise an amino acid sequence of (GGGGA)_n (SEQ ID NO: 54) or (GGGGS)_n (SEQ ID NO: 55), and wherein each n is, independently, 1-5.

27. The viral particle of claim 24, 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.

28. The viral particle of claim 27, wherein the ECD comprises an amino acid sequence of SEQ ID NO: 59 or SEQ ID NO: 60.

29. The viral particle of claim 27, wherein the T_M comprises an amino acid sequence of SEQ ID NO: 61 or SEQ ID NO: 62.

30. The viral particle of claim 27, wherein the ICD comprises an Env incorporation motif comprising an amino acid sequence of SEQ ID NO: 63 or SEQ ID NO: 64.

31. The viral particle of any one of claims 1-30, wherein the heterologous viral glycoprotein is a VSV-G polypeptide.

32. The viral particle of claim 31, 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.

33. The viral particle of any one of claims 1-32, wherein the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest.

34. The viral particle of claim 33, wherein the heterologous molecule of interest is a chimeric antigen receptor ("CAR"), ATP7B, GAA, SERPINA1, OTC, GUSB, UGT1A1, PAH, BCKDHA, BCKDHB, DBT, ATP8B1, ABCB11, ABCB4, FAH, TAT, HPD, HMBS, ASS1, SLC25A13, F8, F9, AGXT, GRHPR, HOGA1, INS, glucagon-like peptide-1 (GLP-1) hormone, glucagon-like peptide-2 (GLP-2) hormone, glicentin, PYY, CCK, glucagon, amylin, activin type II inhibitors, or miR-22 inhibitors.

35. The viral particle of any one of claims 1-34, wherein the viral particle further comprises at least one nucleic acid molecule encoding a gene editing system.
36. The viral particle of claim 35 wherein the gene editing system is a CRISPR-Cas system, a zinc finger nuclease system, a TALEN, a meganuclease, or a gene product regulating nucleic acid molecule.
37. A method of infecting a cell, the method comprising contacting the cell with a viral particle of any one of claims 1-36.
38. 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 claims 1-36.
39. 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 claims 1-36, wherein the viral particle comprises a nucleic acid molecule encoding the heterologous molecule of interest.
40. 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 claims 1-36, wherein the viral particle comprises a nucleic acid molecule encoding the heterologous molecule of interest.
41. A method of editing a target nucleic acid molecule in a cell, the method comprising contacting the cell with the viral particle of any one of claims 35-36, wherein the nucleic acid molecule encoding the gene editing system is expressed in the cell and edits the target nucleic acid molecule in the cell
42. The method of any one of claims 37-41, wherein the cell is a liver cell, optionally a hepatocyte.
43. 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 1-36, wherein the viral particle comprises a nucleic acid molecule encoding the heterologous molecule of interest to

treat the disease or disorder.

44. The method of claim 43, wherein the disease or disorder is Wilson disease, a glycogen storage disease (e.g. von Gierke's disease, Pompe's disease, and the like), alpha-1 antitrypsin (AAT) deficiency, ornithine transcarbamylase (OTC) deficiency, mucopolysaccharidosis VII, Crigler-Najjar Syndrome Type 1, phenylketonuria, maple syrup urine disease, progressive familial intrahepatic cholestasis, tyrosinemia, acute intermittent porphyria, citrullinemia type 1, type 1 diabetes, hemophilia A, hemophilia B, a hemoglobinopathy, obesity, oxalosis, Type II diabetes, gestational diabetes, malignant neoplasms, or extrahepatic tumors.

45. 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: 37, or SEQ ID NO: 38;

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.

46. 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: 37, or SEQ ID NO: 38;

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.

47. 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: 89 or SEQ ID NO: 92, at least 95% identity to SEQ ID NO: 89 or SEQ ID NO: 92, at least 99% identity to SEQ ID NO: 89 or SEQ ID NO: 92, or at least 100% identity to SEQ ID NO: 89 or SEQ ID NO: 92.

48. The viral particle of any one of claims 45-47, wherein the viral particle further comprises a nucleic acid molecule encoding a heterologous molecule of interest.

49. The viral particle of claim 48, wherein the heterologous molecule of interest is a CAR, ATP7B, GAA, SERPINA1, OTC, GUSB, UGT1A1, PAH, BCKDHA, BCKDHB, DBT, ATP8B1, ABCB11, ABCB4, FAH, TAT, HPD, HMBS, ASS1, SLC25A13, F8, F9, AGXT, GRHPR, HOGA1, INS, glucagon-like peptide-1 (GLP-1) hormone, glucagon-like peptide-2

(GLP-2) hormone, glicentin, PYY, CCK, glucagon, amylin, activin type II inhibitors, or miR-22 inhibitors.

50. The viral particle of any one of claims 45-49, wherein the viral particle further comprises at least one nucleic acid molecule encoding a gene editing system.