Field

[0003] The present disclosure relates in some aspects to adoptive cell therapy involving the administration of doses of cells for treating subjects with disease and conditions such as certain B cell malignancies, and related methods, compositions, uses and articles of manufacture. The cells generally express recombinant receptors such as chimeric antigen receptors (CARs). In some embodiments, the disease or condition is a non-Hodgkin lymphoma (NHL), such as relapsed or refractory NHL or specific NHL subtype; in some embodiments, the subject is of a specific group or subset of NHL subjects, such as heavily pretreated or poor-prognosis subjects.

Background

[0004] Various immunotherapy and/or cell therapy methods are available for treating diseases and conditions. For example, adoptive cell therapies (including those involving the administration of cells expressing chimeric receptors specific for a disease or disorder of interest, such as chimeric antigen receptors (CARs) and/or other recombinant antigen receptors, as well as other adoptive immune cell and adoptive T cell therapies) can be beneficial in the treatment of cancer or other diseases or disorders. Improved approaches are needed. Provided are methods and uses that meet such needs.

Summary

[0005] Provided herein are methods, uses, compositions, formulations and articles of manufacture for treating subjects having or suspected of having a disease or condition, such as a cancer or tumor, optionally a B cell malignancy such as NHL or ALL or CLL or a subtype thereof. The methods and other examples generally relate to administering to the subject T cells, generally engineered T cells, such as those expressing or containing a recombinant receptor such as a chimeric antigen receptor (CAR) or TCR.

[0005a] In one aspect, the present disclosure refers to use of a first composition comprising CD4+ T cells in the manufacture of a medicament for treating a subject having or suspected of having a disease or condition with a dose of $CD4^+$ T cells and $CD8^+$ T cells, wherein: the medicament is to be administered with a second composition comprising CD8+ T cells; each of the $CD4^+$ T cells and the $CD8^+$ T cells, individually, comprises a recombinant receptor that specifically binds to a target antigen expressed by the disease or condition or a cell or tissue thereof and/or that is associated with the disease or condition; and the dose of the CD4+ T cells

and CD8+ T cells is to be administered as a plurality of separate compositions, the plurality of separate compositions comprising the first composition comprising the $CD4^+$ T cells and the second composition comprising the $CD8^+$ T cells.

[0005b] In another aspect, the present disclosure refers to use of a first composition comprising CD8+ T cells in the manufacture of a medicament for treating a subject having or suspected of having a disease or condition with a dose of $CD4^+$ T cells and $CD8^+$ T cells, wherein: the medicament is to be administered with a second composition comprising CD4+ T cells; each of the $CD4^+$ T cells and the $CD8^+$ T cells, individually, comprises a recombinant receptor that specifically binds to a target antigen expressed by the disease or condition or a cell or tissue thereof and/or that is associated with the disease or condition; and the dose of the CD4+ T cells and CD8+ T cells is to be administered as a plurality of separate compositions, the plurality of separate compositions comprising the first composition comprising the $CD8^+$ T cells and the second composition comprising the $CD4^+$ T cells.

[0006] In some examples, the dose of cells or cells administered in connection with any examples of the provided methods, compositions, articles of manufacture and uses, contains $CD4^+$ T cells or a subtype or phenotype thereof (such as engineered or recombinant receptor-expressing $CD4^+$ T cells) and/or $CD8^+$ T cells or a subtype thereof (such as an engineered or recombinant receptor-expressing $CD4^+$ cells). In some examples, the $CD8^+$ cells or subtype or phenotype are present at a particular dose or amount or number; in some examples the $CD4^+$ cells or subtype or phenotype are present at a particular dose or amount or number. In

some examples, the $CD8^+$ cells or subtype or phenotype thereof and the $CD4^+$ cells or subtype or phenotype thereof, are present in the article or composition or combination, or are administered in the methods, at a defined ratio, such as at or about 1:1, or between at or about 1:3 and at or about 3:1. In some examples, the dose or administration contains or is of a particular amount or number of one population of the cells and the ratio is a defined ratio or is a naturally-occurring ratio, such as in the blood of the subject from which the cells are derived or ratio that occurs without selection or control for a particular ratio.

[0007] In some examples, the $CD4^+$ T cells (or subset thereof) and the $CD8^+$ T cells (or subset thereof), individually, contain a receptor that specifically binds to a target antigen expressed by the disease or condition, or a cell or tissue thereof, and/or that is associated with the disease or condition.

[0008] In some examples, the $CD4^+$ and $CD8^+$ cells are administered and/or formulated together, e.g. in a single formulation and/or from a single container.

[0009] In some examples, separate administrations are carried out of the $CD4^+$ and the $CD8^+$ cells in the dose, and/or separate formulations or containers are included, each individually enriched for the $CD4^+$ cells or the $CD4^+$ engineered cells (such as a formulation containing at least a certain percentage of, e.g., at least 80%, 85%, 90% or 95% or more of, $CD4^+$ cells and/or not comprising more than 10% or more than 5% $CD8^+$ T cells) and the $CD8^+$ Cells or the $CD8^+$ engineered cells (such as a formulation containing at least a certain percentage of, e.g., at least 80%, 85%, 90% or 95% or more of, $CD8^+$ cells and/or not comprising more than 10% or more than 5% $CD4^+$ T cells).

[0010] In some examples, the administration comprises administering a plurality of separate compositions, said plurality of separate compositions comprising a first composition comprising one of the $CD4^+$ T cells and the $CD8^+$ T cells and a second composition comprising the other of the $CD4^+$ T cells and the $CD8^+$ T cells. In certain examples of any of the provided methods, the receptor contained by the $CD4^+$ T cells and/or the receptor contained by the $CD8^+$ T cells comprises T cells a recombinant receptor, and/or wherein the $CD4^+$ T cells and/or the $CD8^+$ T cells are genetically engineered to express the receptor.

[0011] In some examples of any of the provided examples, the administration of the first composition and the administration of the second composition are carried out on the same day, are carried out between about 0 and about 12 hours apart, between about 0 and about 6 hours apart or between about 0 and 2 hours apart; and/or the initiation of administration of the

first composition and the initiation of administration of the second composition are carried out between about 1 minute and about 1 hour apart or between about 5 minutes and about 30 minutes apart. In certain examples of any of the provided methods, the first composition and second composition are administered no more than 2 hours, no more than 1 hour, no more than 30 minutes, no more than 15 minutes, no more than 10 minutes or no more than 5 minutes apart.

[0012] In certain examples of any of the provided examples, the first composition comprises the $CD4^+$ T cells. In some examples of any of the provided methods, the first composition comprises the $CD8^+$ T cells. In particular examples of any of the provided methods, the initiation of the administration of the first composition is carried out prior to the initiation of the administration of the second composition. In certain examples of any of the provided methods, the dose of cells comprises a defined ratio of $CD4^+$ cells expressing a recombinant receptor to $CD8^+$ cells expressing a recombinant receptor and/or of $CD4^+$ cells to $CD8^+$ cells, which ratio optionally is or is approximately 1:1 or is between approximately 1:3 and approximately 3:1; and/or the $CD4^+$ T cells comprising the receptor in the one of the first and second compositions and the $CD8^+$ T cells comprising the receptor in the other of the first and second compositions are present at a defined ratio, which ratio optionally is or is approximately 1:1 or is between approximately 1:3 and approximately 3:1; and/or the $CD4^+$ T cells comprising the receptor and the $CD8^+$ T cells comprising the receptor administered in the first and second compositions are present at a defined ratio, which ratio optionally is or is approximately 1:1 or is between approximately 1:3 and approximately 3:1. In some examples of any of the provided methods, the defined ratio is or is approximately 1:1. In particular examples of any of the provided methods, the dose of T cells is administered to the subject as a single dose or is administered only one time within a period of two weeks, one month, three months, six months, 1 year or more. In certain examples of any of the provided methods, the dose of T cells is administered as a double dose comprising a first dose of the T cells and a consecutive dose of the T cells, wherein one or both of the first dose and the second dose comprises administration of the plurality of compositions of T cells. In some examples of any of the provided methods, the consecutive dose is administered at a point in time that is at least or more than about 7 days or 14 days after and less than about 28 days after initiation of the administration of the first dose of cells.

[0013] In particular examples of any of the provided methods or examples, the dose of cells comprises between at or about 1 x 10^5 and at or about 5 x 10^8 total recombinant receptor-expressing T cells or total T cells, between at or about 1 x 10^5 and at or about 1 x 10^8 total recombinant receptor-expressing T cells or total T cells, between at or about 5 x 10^5 and at or about 1 x 10^7 total recombinant receptor-expressing T cells or total T cells, or from or from about 1 x 10^6 to 1 x 10^7 total recombinant receptor-expressing T cells or total T cells, each inclusive. In certain examples of any of the provided methods, the dose of T cells comprises the administration of no more than 1 x 10^8 total recombinant receptor-expressing T cells or total T cells, no more than 1 x 10^7 total recombinant receptor-expressing T cells or total T cells, no more than 0.5 x 10^7 total recombinant receptor-expressing T cells or total T cells, no more than 1 x 10^6 total recombinant receptor-expressing T cells or total T cells, no more than 0.5 x 10^6 total recombinant receptor-expressing T cells or total T cells. In some examples of any of the provided methods, the dose of T cells comprises between at or about 5 x 10^7 recombinant receptor-expressing T cells and 1 x 10^8 recombinant receptor-expressing T cells, each inclusive.

[0014] In particular examples of any of the provided methods, the recombinant receptor specifically binds to an antigen associated with the disease or condition or expressed in cells of the environment of a lesion associated with the disease or condition. In certain examples of any of the provided methods, the disease or condition is a cancer. In some examples of any of the provided methods, the disease or condition is a myeloma, leukemia or lymphoma. In particular examples of any of the provided methods, the antigen is ROR1, B cell maturation antigen (BCMA), carbonic anhydrase 9 (CAIX), tEGFR, Her2/neu (receptor tyrosine kinase erbB2), L1-CAM, CD19, CD20, CD22, mesothelin, CEA, and hepatitis B surface antigen, anti-folate receptor, CD23, CD24, CD30, CD33, CD38, CD44, EGFR, epithelial glycoprotein 2 (EPG-2), epithelial glycoprotein 40 (EPG-40), EPHa2, erb-B2, erb-B3, erb-B4, erbB dimers, EGFR vIII, folate binding protein (FBP), FCRL5, FCRH5, fetal acetylcholine receptor, GD2, GD3, HMW-MAA, IL-22R-alpha, IL-13R-alpha2, kinase insert domain receptor (kdr), kappa light chain, Lewis Y, L1-cell adhesion molecule, (L1-CAM), Melanoma-associated antigen (MAGE)-A1, MAGE-A3, MAGE-A6, Preferentially expressed antigen of melanoma (PRAME), survivin, TAG72, B7-H6, IL-13 receptor alpha 2 (IL-13Ra2), CA9, GD3, HMW-MAA, CD171, G250/CAIX, HLA-AI MAGE Al, HLA-A2 NY-ESO-1, PSCA, folate receptor-a, CD44v6, CD44v7/8, avb6 integrin, 8H9, NCAM, VEGF receptors, 5T4, Foetal AchR, NKG2D ligands, CD44v6, dual antigen, a cancer-testes antigen, mesothelin, murine CMV, mucin 1 (MUC1),

MUC16, PSCA, NKG2D, NY-ESO-1, MART-1, gp100, oncofetal antigen, ROR1, TAG72, VEGF-R2, carcinoembryonic antigen (CEA), Her2/neu, estrogen receptor, progesterone receptor, ephrinB2, CD123, c-Met, GD-2, O-acetylated GD2 (OGD2), CE7, Wilms Tumor 1 (WT-1), a cyclin, cyclin A2, CCL-1, CD138, G Protein Coupled Receptor 5D (GPCR5D), or a pathogen-specific antigen. In certain examples of any of the provided methods, the antigen is CD19.

[0015] In some examples of any of the provided methods, the disease or condition is a B cell malignancy and/or is acute lymphoblastic leukemia (ALL), adult ALL, chronic lymphoblastic leukemia (CLL), non-Hodgkin lymphoma (NHL), and Diffuse Large B-Cell Lymphoma (DLBCL). In particular examples of any of the provided methods, the disease or condition is NHL and the NHL is selected from the group consisting of aggressive NHL, diffuse large B cell lymphoma (DLBCL), NOS (not otherwise specified) (de novo and transformed from indolent), primary mediastinal large B cell lymphoma (PMBCL), T cell/histocyte-rich large B cell lymphoma (TCHRBCL), Burkitt's lymphoma, mantle cell lymphoma (MCL), and/or follicular lymphoma (FL), optionally follicular lymphoma Grade 3B (FL3B).

[0016] In some examples of any of the provided methods, the recombinant receptor includes an extracellular domain containing an antigen-binding domain. In some examples, the antigen-binding domain is or includes an antibody or an antibody fragment thereof, which optionally is a single chain fragment. In particular examples of any of the provided methods, the fragment includes antibody variable regions joined by a flexible linker. In some examples, the fragment includes an scFv. In some examples of any of the provided methods, the recombinant receptor also includes a spacer and/or a hinge region.

[0017] In certain examples of any of the provided methods, the recombinant receptor includes an intracellular signaling region. In some examples of any of the provided methods, the intracellular signaling region includes an intracellular signaling domain. In some examples of any of the provided methods, the intracellular signaling domain is or includes a primary signaling domain, a signaling domain that is capable of inducing a primary activation signal in a T cell, a signaling domain of a T cell receptor (TCR) component, and/or a signaling domain containing an immunoreceptor tyrosine-based activation motif (ITAM). In some examples, the intracellular signaling domain is or includes an intracellular signaling domain of a CD3 chain, optionally a CD3-zeta (CD3ζ) chain, or a signaling portion thereof.

[0018] In particular examples of any of the provided methods, the recombinant receptor also includes a transmembrane domain disposed between the extracellular domain and the intracellular signaling region.

[0019] In some examples of any of the provided methods, the intracellular signaling region also includes a costimulatory signaling region. In some examples, the costimulatory signaling region includes an intracellular signaling domain of a T cell costimulatory molecule or a signaling portion thereof. In certain examples of any of the provided methods, the costimulatory signaling region includes an intracellular signaling domain of a CD28, a 4-1BB or an ICOS or a signaling portion thereof. In some examples, the costimulatory signaling region is between the transmembrane domain and the intracellular signaling region.

[0020] In certain examples of any of the provided methods, the recombinant receptor is a chimeric antigen receptor (CAR), optionally wherein the recombinant receptor is a chimeric antigen receptor (CAR), optionally wherein the CAR comprises an extracellular antigen-recognition domain that specifically binds to the antigen and an intracellular signaling domain comprising an ITAM, wherein optionally, the intracellular signaling domain comprises an intracellular domain of a CD3-zeta (CD3ζ) chain; and/or wherein the CAR further comprises a costimulatory signaling region, which optionally comprises a signaling domain of CD28 or 4-1BB.

[0021] In some examples, the articles of manufacture include a container such as a vial comprising a composition comprising $CD4^+$ T cells expressing a recombinant receptor, and instructions for administering, to a subject having a disease or condition, the composition of $CD4^+$ T cells as a plurality of compositions with a composition comprising $CD8^+$ T cells expressing a recombinant receptor or a unit dose of cells comprising all or a portion of the plurality of $CD4^+$ T cells and a composition comprising $CD8^+$ T cells expressing a recombinant receptor. In some examples, the article of manufacture includes a container such as a vial comprising a composition comprising $CD8^+$ T cells expressing a recombinant receptor, and instructions for administering, to a subject having a disease or condition, the composition of $CD8^+$ T cells as a plurality of compositions with a composition comprising $CD4^+$ T cells expressing a recombinant receptor or a unit dose of cells comprising all or a portion of the plurality of $CD4^+$ T cells and a composition comprising $CD8^+$ T cells expressing a recombinant receptor.

[0021a] In another aspect, the present disclosure refers to an article of manufacture comprising (1) a vial comprising a composition comprising a plurality of $CD4^+$ T cells expressing a recombinant receptor, and (2) instructions for administering to a subject having a disease or condition: a unit dose of cells of the composition, the unit dose comprising all or a portion of the plurality of $CD4^+$ T cells, and a unit dose of a composition comprising $CD8^+$ T cells expressing a recombinant receptor, wherein the vial does not comprise the unit dose of the composition comprising CD8+ T cells expressing the recombinant receptor.

[0021b] In another aspect, the present disclosure refers to an article of manufacture comprising (1) a vial comprising a composition comprising a plurality of $CD8^+$ T cells expressing a recombinant receptor, and (2) instructions for administering to a subject having a disease or condition: a unit dose of cells of the composition, the unit dose comprising all or a portion of the plurality of $CD8^+$ T cells, and a unit dose of a composition comprising $CD4^+$ T cells expressing a recombinant receptor, wherein the vial does not comprise the unit dose of the composition comprising CD4+ T cells expressing the recombinant receptor.

[0022] In some of any of the examples, the CAR comprises, in order, the CAR includes an scFv specific for the antigen, a transmembrane domain, a cytoplasmic signaling domain derived from a costimulatory molecule, which optionally is or comprises a 4-1BB, and a cytoplasmic signaling domain derived from a primary signaling ITAM-containing molecule, which optionally is or comprises a CD3zeta signaling domain and optionally further includes a spacer between the transmembrane domain and the scFv;

[0023] In some of any of the examples, the CAR includes, in order, an scFv specific for the antigen, a transmembrane domain, a cytoplasmic signaling domain derived from a costimulatory molecule, which optionally is or comprises a 4-1BB signaling domain, and a cytoplasmic signaling domain derived from a primary signaling ITAM-containing molecule, which optionally is a CD3zeta signaling domain.

[0024] In some of any of the examples, the CAR comprises or consists of, in order, an scFv specific for the antigen, a spacer, a transmembrane domain, a cytoplasmic signaling domain derived from a costimulatory molecule, which optionally is a 4-1BB signaling domain, and a cytoplasmic signaling domain derived from a primary signaling ITAM-containing molecule, which optionally is or comprises a CD3zeta signaling domain.

[0025] In some examples, the spacer is a polypeptide spacer that (a) comprises or consists of all or a portion of an immunoglobulin hinge or a modified version thereof or

comprises about 15 amino acids or less, and does not comprise a CD28 extracellular region or a CD8 extracellular region, (b) comprises or consists of all or a portion of an immunoglobulin hinge, optionally an IgG4 hinge, or a modified version thereof and/or comprises about 15 amino acids or less, and does not comprise a CD28 extracellular region or a CD8 extracellular region, or (c) is at or about 12 amino acids in length and/or comprises or consists of all or a portion of an immunoglobulin hinge, optionally an IgG4, or a modified version thereof; or (d) has or consists of the sequence of SEQ ID NO: 1, a sequence encoded by SEQ ID NO: 2, SEQ ID NO: 30, SEQ ID NO: 31, SEQ ID NO: 32, SEQ ID NO: 33, SEQ ID O:N 34, or a variant of any of the foregoing having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto, or (e) comprises or consists of the formula X_1PPX_2P, where X_1 is glycine, cysteine or arginine and X_2 is cysteine or threonine; and/orthe costimulatory domain comprises SEQ ID NO: 12 or a variant thereof having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto; and/orthe primary signaling domain comprises SEQ ID NO: 13 or 14 or 15 or a variant thereof having at

least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto; and/orthe scFv comprises a CDRL1 sequence of RASQDISKYLN (SEQ ID NO: 35), a CDRL2 sequence of SRLHSGV (SEQ ID NO: 36), and/or a CDRL3 sequence of GNTLPYTFG (SEQ ID NO: 37) and/or a CDRH1 sequence of DYGVS (SEQ ID NO: 38), a CDRH2 sequence of VIWGSETTYYNSALKS (SEQ ID NO: 39), and/or a CDRH3 sequence of YAMDYWG (SEQ ID NO: 40) or wherein the scFv comprises a variable heavy chain region of FMC63 and a variable light chain region of FMC63 and/or a CDRL1 sequence of FMC63, a CDRL2 sequence of FMC63, a CDRL3 sequence of FMC63, a CDRH1 sequence of FMC63, a CDRH2 sequence of FMC63, and a CDRH3 sequence of FMC63 or binds to the same epitope as or competes for binding with any of the foregoing, and optionally wherein the scFv comprises, in order, a V_H, a linker, optionally comprising SEQ ID NO: 24, and a V_L, and/or the scFv comprises a flexible linker and/or comprises the amino acid sequence set forth as SEQ ID NO: 24.

[0026] In some examples, the spacer comprises or consists of SEQ ID NO: 1, the costimulatory domain comprises SEQ ID NO: 12 or variant thereof having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto, the transmembrane domain is of CD28 or comprises SEQ ID NO: 9 or a variant thereof having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto, the scFv contains the binding domain of or CDRs of or V_H and V_L of FMC63, the primary signaling domain contains SEQ ID NO: 13, 14, or 15, and/or a variant thereof having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto.

[0027] In some examples, the spacer comprises or consists of SEQ ID NO: 30, the costimulatory domain comprises SEQ ID NO: 12 or variant thereof having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto, the transmembrane domain is of CD28 or comprises SEQ ID NO: 9 or a variant thereof having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto, the scFv contains the binding domain of or CDRs of or V_H and V_L of FMC63, the primary signaling domain contains SEQ ID NO: 13, 14, or 15, and/or a variant thereof having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto.

[0028] In some examples, the spacer comprises or consists of SEQ ID NO: 31, the costimulatory domain comprises SEQ ID NO: 12 or variant thereof having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto, the transmembrane domain is of CD28 or comprises SEQ ID NO: 9 or a variant thereof having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto, the scFv contains the binding domain of or CDRs of or V_H and V_L of FMC63, the primary signaling domain contains SEQ ID NO: 13, 14, or 15, and/or a variant thereof having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto.

[0029] In some examples, the spacer comprises or consists of SEQ ID NO: 33, the costimulatory domain comprises SEQ ID NO: 12 or variant thereof having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto, the transmembrane domain is of CD28 or comprises SEQ ID NO: 9 or a variant thereof having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto, the scFv contains the binding domain of or CDRs of or V_H and V_L of FMC63, the primary signaling domain contains SEQ ID NO: 13, 14, or 15, and/or a variant thereof having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto.

[0030] In some examples, the spacer comprises or consists of SEQ ID NO: 34, the costimulatory domain comprises SEQ ID NO: 12 or variant thereof having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto, the transmembrane domain is of CD28 or comprises SEQ ID NO: 9 or a variant thereof having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto, the scFv contains the binding domain of or CDRs of or V_H and V_L of FMC63, the primary signaling domain contains SEQ ID NO: 13, 14, or 15, and/or a variant thereof having at least 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or more sequence identity thereto.

[0031] In some examples of any of the provided articles of manufacture, the recombinant receptor expressed by the $CD4^+$ cells and the recombinant receptor expressed by the $CD8^+$ T cells is the same or different. In particular examples of any of the provided articles of manufacture, vial comprises greater than or greater than about 10 x 10^6 T cells or recombinant receptor-expressing T cells, greater than or greater than about 15 x 10^6 T cells or

recombinant receptor-expressing T cells, greater than or greater than about 25 x 10^6 T cells or recombinant receptor-expressing T cell.

[0032] In certain examples of any of the provided articles of manufacture, the vial comprises between about 10 million cells per ml and about 70 million cells per ml, between about 10 million cells per ml and about 50 million cells per ml, between about 10 million cells per ml and about 25 million cells per ml, between about 10 million cells per ml and about 15 million cells per ml, 15 million cells per ml and about 70 million cells per ml, between about 15 million cells per ml and about 50 million cells per ml, between about 15 million cells per ml and about 25 million cells per ml, between about 25 million cells per ml and about 70 million cells per ml, between about 25 million cells per ml and about 50 million cells per ml, and between about 50 million cells per ml and about 70 million cells per ml. In some examples of any of the provided articles of manufacture, the composition further comprises a cryoprotectant and/or the article further includes instructions for thawing the composition prior to administration to the subject.

[0033] In some examples of any of the provided articles of manufacture, the compositions or plurality of compositions comprises a dose of cells comprising from or from about 2 x 10^7 to about 4 x 10^7 $CD8^+$ cells, such as about 2 x 10^7, 2.5 x 10^7, 3 x 10^7, 3.5 x 10^7, or 4 x 10^7 $CD8^+$ cells, and from or from about 2 x 10^7 to about 4 x 10^7 $CD4^+$ cells, such as about 2 x 10^7, 2.5 x 10^7, 3 x 10^7, 3.5 x 10^7, or 4 x 10^7 $CD4^+$ cells, each inclusive. In some examples, the compositions or plurality of compositions comprises a dose of cells comprising approximately 3 x 10^7 $CD8^+$ cells and 3.5 x 10^7 $CD4^+$ cells.

[0034] In particular examples of any of the provided articles of manufacture, the plurality of compositions of cells comprises a defined ratio of $CD4^+$ cells expressing the recombinant receptor to $CD8^+$ cells expressing the recombinant receptor and/or of $CD4^+$ cells to $CD8^+$ cells, which ratio optionally is approximately 1:1 or is between approximately 1:3 and approximately 3:1. In certain examples of any of the provided articles of manufacture, the defined ratio is or is approximately 1:1. In some examples of any of the provided articles of manufacture, the plurality of compositions, collectively, comprises a dose of cells comprising from or from about 1 x 10^5 to 5 x 10^8 total recombinant receptor-expressing T cells or total T cells, 1 x 10^5 to 1 x 10^8 total recombinant receptor-expressing T cells or total T cells, from or from about 5 x 10^5 to 1 x 10^7 total recombinant receptor-expressing T cells or total T cells, or from or from about 1 x 10^6 to 1 x 10^7 total recombinant receptor-expressing T cells or total T

cells, each inclusive.In particular examples of any of the provided articles of manufacture, the plurality of compositions, collectively, comprises a dose of cells comprising no more than 1 x 10^8 total recombinant receptor-expressing T cells or total T cells, no more than 1 x 10^7 total recombinant receptor-expressing T cells or total T cells, no more than 0.5 x 10^7 total recombinant receptor-expressing T cells or total T cells, no more than 1 x 10^6 total recombinant receptor-expressing T cells or total T cells, no more than 0.5 x 10^6 total recombinant receptor-expressing T cells or total T cells. In certain examples of any of the provided articles of manufacture, the plurality of compositions, collectively, comprises a dose of cells comprising between at or about 5 x 10^7 recombinant receptor-expressing T cells and 1 x 10^8 recombinant receptor-expressing T cells, each inclusive.

[0035] In some examples of any of the provided articles of manufacture, the instructions specify administering the composition comprising the $CD4^+$ T cells and the composition comprising the $CD8^+$ T cells 0 to 12 hours apart, 0 to 6 hours apart or 0 to 2 hours apart. In particular examples of any of the provided articles of manufacture, the instructions specify administering the composition comprising the $CD4^+$ T cells and the composition comprising the $CD8^+$ T cells no more than 2 hours, no more than 1 hour, no more than 30 minutes, no more than 15 minutes, no more than 10 minutes or no more than 5 minutes apart. In certain examples of any of the provided articles of manufacture, the instructions specify administering the composition comprising the $CD4^+$ T cells prior to administering the composition comprising the $CD8^+$ cells. In some examples of any of the provided articles of manufacture, the instructions specify administering the composition comprising the $CD8^+$ T cells prior to administering the composition comprising the $CD4^+$ cells.

[0036] In particular examples of any of the provided articles of manufacture, the recombinant receptor specifically binds to an antigen associated with the disease or condition or expressed in cells of the environment of a lesion associated with the disease or condition. In certain examples of any of the provided articles of manufacture, the disease or condition is a cancer. In some examples of any of the provided articles of manufacture, the disease or condition is a myeloma, leukemia or lymphoma.

[0037] In particular examples of any of the provided articles of manufacture, the antigen is ROR1, B cell maturation antigen (BCMA), carbonic anhydrase 9 (CAIX), tEGFR, Her2/neu (receptor tyrosine kinase erbB2), L1-CAM, CD19, CD20, CD22, mesothelin, CEA, and hepatitis B surface antigen, anti-folate receptor, CD23, CD24, CD30, CD33, CD38, CD44, EGFR,

epithelial glycoprotein 2 (EPG-2), epithelial glycoprotein 40 (EPG-40), EPHa2, erb-B2, erb-B3, erb-B4, erbB dimers, EGFR vIII, folate binding protein (FBP), FCRL5, FCRH5, fetal acetylcholine receptor, GD2, GD3, HMW-MAA, IL-22R-alpha, IL-13R-alpha2, kinase insert domain receptor (kdr), kappa light chain, Lewis Y, L1-cell adhesion molecule, (L1-CAM), Melanoma-associated antigen (MAGE)-A1, MAGE-A3, MAGE-A6, Preferentially expressed antigen of melanoma (PRAME), survivin, TAG72, B7-H6, IL-13 receptor alpha 2 (IL-13Ra2), CA9, GD3, HMW-MAA, CD171, G250/CAIX, HLA-AI MAGE Al, HLA-A2 NY-ESO-1, PSCA, folate receptor-a, CD44v6, CD44v7/8, avb6 integrin, 8H9, NCAM, VEGF receptors, 5T4, Foetal AchR, NKG2D ligands, CD44v6, dual antigen, a cancer-testes antigen, mesothelin, murine CMV, mucin 1 (MUC1), MUC16, PSCA, NKG2D, NY-ESO-1, MART-1, gp100, oncofetal antigen, ROR1, TAG72, VEGF-R2, carcinoembryonic antigen (CEA), Her2/neu, estrogen receptor, progesterone receptor, ephrinB2, CD123, c-Met, GD-2, O-acetylated GD2 (OGD2), CE7, Wilms Tumor 1 (WT-1), a cyclin, cyclin A2, CCL-1, CD138, G Protein Coupled Receptor 5D (GPCR5D), or a pathogen-specific antigen. In certain examples of any of the provided articles of manufacture, the antigen is CD19.

[0038] In some examples of any of the provided articles of manufacture, the disease or condition is a B cell malignancy and/or is acute lymphoblastic leukemia (ALL), adult ALL, chronic lymphoblastic leukemia (CLL), non-Hodgkin lymphoma (NHL), and Diffuse Large B-Cell Lymphoma (DLBCL). In particular examples of any of the provided articles of manufacture, the disease or condition is NHL and the NHL is selected from the group consisting of aggressive NHL, diffuse large B cell lymphoma (DLBCL), NOS (de novo and transformed from indolent), primary mediastinal large B cell lymphoma (PMBCL), T cell/histocyte-rich large B cell lymphoma (TCHRBCL), Burkitt's lymphoma, mantle cell lymphoma (MCL), and/or follicular lymphoma (FL), optionally follicular lymphoma Grade 3B (FL3B).

[0039] In certain examples of any of the provided articles of manufacture, the T cells are primary T cells obtained from a subject. In some examples of any of the provided articles of manufacture, the T cells are autologous to the subject. In particular examples of any of the provided articles of manufacture, the T cells are allogeneic to the subject.

[0040] In certain examples of any of the provided articles of manufacture, the recombinant receptor is or includes a functional non-TCR antigen receptor or a TCR or antigen-binding fragment thereof. In some examples, the recombinant receptor is a chimeric antigen receptor (CAR).

[0041] In particular examples any of the provided articles of manufacture, the recombinant receptor includes an extracellular domain containing an antigen-binding domain. In some examples, the antigen-binding domain is or includes an antibody or an antibody fragment thereof, which optionally is a single chain fragment. In some examples, the fragment includes antibody variable regions joined by a flexible linker. In some examples, the fragment includes an scFv.

[0042] In some examples any of the provided articles of manufacture or methods, the recombinant receptor also includes a spacer and/or a hinge region.

[0043] In certain examples any of the provided articles of manufacture or methods, the recombinant receptor includes an intracellular signaling region. In some examples, the intracellular signaling region includes an intracellular signaling domain. In some examples any of the provided articles of manufacture, the intracellular signaling domain is or includes a primary signaling domain, a signaling domain that is capable of inducing a primary activation signal in a T cell, a signaling domain of a T cell receptor (TCR) component, and/or a signaling domain containing an immunoreceptor tyrosine-based activation motif (ITAM). In some examples, the intracellular signaling domain is or includes an intracellular signaling domain of a CD3 chain, optionally a CD3-zeta (CD3ζ) chain, or a signaling portion thereof.

[0044] In particular examples any of the provided articles of manufacture or methods, the recombinant receptor also includes a transmembrane domain disposed between the extracellular domain and the intracellular signaling region.

[0045] In some examples any of the provided articles of manufacture or methods, the intracellular signaling region also includes a costimulatory signaling region. In some examples, the costimulatory signaling region includes an intracellular signaling domain of a T cell costimulatory molecule or a signaling portion thereof. In some examples any of the provided articles of manufacture, the costimulatory signaling region includes an intracellular signaling domain of a CD28, a 4-1BB or an ICOS or a signaling portion thereof. In some examples, the costimulatory signaling region is between the transmembrane domain and the intracellular signaling region.

[0046] In some examples, the methods and articles are for or capable of treating a subject having non-Hodgkin lymphoma (NHL). In some examples, the method involves, and/or the article of manufacture specifies or includes formulations capable of, administering to the subject a dose or plurality of T cells. In some examples, the T cells comprising T cells such as

$CD8^+$ T cells and/or $CD4^+$ T cells, expressing a chimeric antigen receptor (CAR) that specifically binds to a target antigen expressed by the NHL.

[0047] In some examples, the dose of T cells comprises between at or about 5 x 10^7 CAR-expressing T cells and 1 x 10^8 CAR-expressing T cells, inclusive; and the NHL comprises diffuse large B cell lymphoma (DLBCL), primary mediastinal large B cell lymphoma (PMBCL), NOS (de novo or transformed from indolent lymphoma), or follicular lymphoma Grade 3B and wherein the subject is or has been identified as having an Eastern Cooperative Oncology Group Performance Status (ECOG) status of 0 or 1.

[0047a] In another aspect, the present disclosure refers to use of a dose of T cells comprising T cells expressing a chimeric antigen receptor (CAR) in the manufacture of a medicament for treatment of a non-Hodgkin lymphoma (NHL) in a subject, wherein: the CAR specifically binds to a target antigen expressed by the NHL; the dose of T cells comprises between at or about 2.5 x 10^7 CAR-expressing T cells and 2 x 10^8 CAR-expressing T cells, inclusive; and the NHL comprises diffuse large B cell lymphoma (DLBCL), primary mediastinal large B cell lymphoma (PMBCL), NOS (de novo or transformed from indolent lymphoma) or follicular lymphoma Grade 3B, and wherein the subject is or has been identified as having an Eastern Cooperative Oncology Group Performance Status (ECOG) status of 0 or 1.

[0048] In some examples of any of the provided examples, the methods further comprise identifying, or the article of manufacture includes information specifying, treatment of a subject having diffuse large B cell lymphoma (DLBCL), primary mediastinal large B cell lymphoma (PMBCL), NOS (de novo or transformed from indolent lymphoma), or follicular lymphoma Grade 3B having an ECOG status of 0 or 1. In some examples of any of the provided examples, the dose of T cells and/or the cells administered comprises a defined ratio of $CD4^+$ cells expressing the CAR to $CD8^+$ cells expressing the CAR and/or of $CD4^+$ cells to $CD8^+$ cells, which ratio optionally is approximately 1:1 or is between approximately 1:3 and approximately 3:1.

[0049] In some examples, the examples are for treating a subject having non-Hodgkin lymphoma (NHL) and involve administering to the subject a dose of T cells comprising T cells expressing a chimeric antigen receptor (CAR) that specifically binds to a target antigen expressed by the NHL. In some examples, the dose of T cells includes a defined ratio of $CD4^+$ cells expressing the CAR to $CD8^+$ cells expressing the CAR and/or of $CD4^+$ cells to $CD8^+$ cells, which ratio in some examples is approximately or is 1:1. In some examples, the NHL comprises diffuse large B cell lymphoma (DLBCL), primary mediastinal large B cell lymphoma (PMBCL), NOS (not otherwise specificed) (de novo or transformed from indolent lymphoma), or follicular lymphoma Grade 3B.

[0049a] In another aspect, the present disclosure refers to use of a dose of T cells comprising T cells expressing a chimeric antigen receptor (CAR) in the manufacture of a medicament for treatment of a non-Hodgkin lymphoma (NHL) in a subject, wherein: the CAR specifically binds to a target antigen expressed by the NHL; the dose of T cells comprises a defined ratio of $CD4^+$ cells expressing the CAR to $CD8^+$ cells expressing the CAR and/or of $CD4^+$ cells to $CD8^+$ cells, which ratio is approximately or is 1:1; and the NHL comprises diffuse large B cell lymphoma (DLBCL), primary mediastinal large B cell lymphoma (PMBCL), NOS (de novo or transformed from indolent lymphoma) or follicular lymphoma Grade 3B.

[0050] In particular examples of any of the provided examples, the subject is or has been identified as or is specified as having an Eastern Cooperative Oncology Group Performance Status (ECOG) status of 0, 1 or 2. In certain examples of any of the provided examples, the subject is or has been identified as or is specified as having an ECOG status of 0 or 1.

[0051] In some examples of any of the provided examples, the methods and/or uses and/or administration of cells according to the articles of manufacture, achieve certain outcomes and/or are associated with certain reduced risks of toxicity, e.g., in the population of subjects treated according to the methods or according to information provided in the article of manufacture. In some examples,: at least 35%, at least 40% or at least 50% of subjects treated according to the method achieve a complete response (CR) and/or a durable CR; and/or at least 50%, at least 60% or at least 70% of the subjects treated according to the method achieve objective response (OR) and/or a durable OR. In particular examples of any of the provided methods, the response is durable for greater than 3 months or greater than 6 months. In some examples, at least 40%, at least 50%, at least 60%, at least 70% of the subjects who, at or prior to the administration of the dose of cells had or were identified to have a double/triple hit lymphoma or relapse, optionally relapse within 12 months, following administration of an autologous stem cell transplant (ASCT), achieved an OR, optionally wherein the OR is durable for at or greater than 3 months or at or greater than 6 months. In certain examples of any of the provided methods, greater than or greater than about 50% of the subjects treated according to the method do not exhibit a grade 3 or greater cytokine release syndrome (CRS) or a grade 3 or greater neurotoxicity. In some examples, such subjects do not exhibit early onset CRS and/or neurotoxicity.

[0052] Provided herein are methods of assessing likelihood of a response to a cell therapy, the methods involving: assessing the level, amount or concentration of one or more analyte in a biological sample, wherein the one or more analyte is selected from ferritin, LDH, CXCL10, G-CSF, and IL-10, wherein: the biological sample is from a subject that is a candidate for treatment with the cell therapy, said cell therapy comprising a dose of genetically engineered cells expressing a recombinant receptor; and the biological sample is obtained from the subject prior to administering the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and comparing, individually, the level, amount or concentration of the analyte in the sample to a threshold level, thereby determining a likelihood that a subject will achieve a response to the cell therapy. In some examples, the methods also involve administering the cell therapy to the subject if the subject is likely to achieve a response.

[0052a] In another aspect, the present disclosure refers to a method of assessing likelihood of a response to a cell therapy, the method comprising: (a) assessing the level, amount or concentration of one or more analyte in a biological sample, wherein the one or more analyte is selected from ferritin, LDH, CXCL10, G-CSF, and IL-10, wherein: the biological sample is from a subject that is a candidate for treatment with the cell therapy, said cell therapy comprising a dose of genetically engineered cells expressing a recombinant receptor; and the biological sample is obtained from the subject prior to administration of the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and (b) comparing, individually, the level, amount or concentration of the analyte in the sample to a threshold level, thereby determining a likelihood that a subject will achieve a response to the cell therapy.

[0053] Provided herein are methods of selecting a subject for treatment, the methods involving: assessing the level, amount or concentration of one or more analyte in a biological

sample, wherein the one or more analyte is selected from ferritin, LDH, CXCL10, G-CSF, and IL-10, wherein: the biological sample is from a subject that is a candidate for treatment with the cell therapy, said cell therapy comprising a dose of genetically engineered cells expressing a recombinant receptor; and the biological sample is obtained from the subject prior to administering the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and selecting a subject who is likely to respond to treatment based on the results of determining a likelihood that a subject will achieve a response to the cell therapy by comparing, individually, the level, amount or concentration of the analyte in the sample to a threshold level. In some examples, the methods also involve administering the cell therapy to the subject selected for treatment.

[0054] Provided herein are methods of treatment, the methods involving: selecting a subject who is likely to respond to treatment with a cell therapy based on the results of determining a likelihood that a subject will achieve a response to the cell therapy by comparing, individually, the level, amount or concentration of one or more analyte in a biological sample, wherein the one or more analyte is selected from ferritin, LDH, CXCL10, G-CSF, and IL-10, to a threshold level, wherein: the biological sample is from a subject that is a candidate for treatment with the cell therapy, said cell therapy comprising a dose of genetically engineered cells expressing a recombinant receptor; and the biological sample is obtained from the subject prior to administering the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and administering the cell therapy to a subject selected for treatment.

[0055] In some examples, the subject is likely to achieve a response if the level, amount or concentration of one or more of the analyte is below a threshold level and the subject is not likely to achieve a response if the level, amount or concentration of one or more of the analyte is above a threshold level.

[0056] In some examples, the threshold level is within 25%, within 20%, within 15%, within 10% or within 5% and/or is within a standard deviation below the median or mean level, amount or concentration, or is or is about the median or mean level, amount or concentration, of the analyte in a biological sample obtained from a group of subjects prior to receiving a cell therapy, wherein each of the subjects of the group went on to achieve a response after administration of a recombinant-receptor-expressing therapeutic cell composition for treating the same disease or condition.

[0057] In some examples, the threshold level is within 25%, within 20%, within 15%, within 10% or within 5% and/or is within a standard deviation above the median or mean level, amount or concentration of the analyte in a biological sample obtained from a group of subjects prior to receiving a cell therapy, wherein each of the subjects of the group went on to exhibit stable disease (SD) and/or progressive disease (PD) after administration of a recombinant-receptor-expressing therapeutic cell composition for treating the same disease or condition.

[0058] In some examples, the response comprises objective response. In some examples, the objective response comprises complete response (CR) or partial response (PR).

[0059] Provided herein are methods of assessing likelihood of a durable response to a cell therapy, the methods involving: assessing the level, amount or concentration of one or more analyte in a biological sample, wherein the one or more analyte is selected from LDH, ferritin, CRP, D-dimer, SAA-1, IL-6, IL-10, IL-15, IL-16, TNF-α, IFN-γ, MIP-1α, CXCL-10, IL-8, MCP-1 and MIP-1β, wherein: the biological sample is from a subject that is a candidate for treatment with the cell therapy, said cell therapy comprising a dose of genetically engineered cells expressing a recombinant receptor; and the biological sample is obtained from the subject prior to administering the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and comparing, individually, the level, amount or concentration of the analyte in the sample to a threshold level, thereby determining a likelihood that a subject will achieve a durable response to the cell therapy.

[0059a] In another aspect, the present disclosure refers to a method of assessing likelihood of a durable response to a cell therapy, the method comprising: (a) assessing the level, amount or concentration of one or more analyte in a biological sample, wherein the one or more analyte is selected from LDH, ferritin, CRP, D-dimer, SAA-1, IL-6, IL-10, IL-15, IL-16, TNF-α, IFN-γ, MIP-1α, CXCL-10, IL-8, MCP-1 and MIP-1β, wherein: the biological sample is from a subject that is a candidate for treatment with the cell therapy, said cell therapy comprising a dose of genetically engineered cells expressing a recombinant receptor; and the biological sample is obtained from the subject prior to administration of the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and (b) comparing, individually, the level, amount or concentration of the analyte in the sample to a

threshold level, thereby determining a likelihood that a subject will achieve a durable response to the cell therapy.

[0060] In some examples, the methods also involve administering the cell therapy to the subject if the subject is likely to achieve a response.

[0061] Provided herein are methods of selecting a subject for treatment, the methods involving: assessing the level, amount or concentration of one or more analyte in a biological sample, wherein the one or more analyte is selected from LDH, ferritin, CRP, D-dimer, SAA-1, IL-6, IL-10, IL-15, IL-16, TNF-α, IFN-γ, MIP-1α, CXCL-10, IL-8, MCP-1 and MIP-1β, wherein: the biological sample is from a subject that is a candidate for treatment with the cell therapy, said cell therapy comprising a dose of genetically engineered cells expressing a recombinant receptor; and the biological sample is obtained from the subject prior to administering the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and selecting a subject who is likely to respond to treatment based on the results of determining a likelihood that a subject will achieve a durable

response to the cell therapy by comparing, individually, the level, amount or concentration of the analyte in the sample to a threshold level. In some examples, the methods also involve administering the cell therapy to the subject selected for treatment.

[0061a] In another aspect, the present disclosure refers to a method of selecting a subject for treatment, the method comprising: (a) assessing the level, amount or concentration of one or more analyte in a biological sample, wherein the one or more analyte is selected from LDH, ferritin, CRP, D-dimer, SAA-1, IL-6, IL-10, IL-15, IL-16, TNF-α, IFN-γ, MIP-1α, CXCL-10, IL-8, MCP-1 and MIP-1β, wherein: the biological sample is from a subject that is a candidate for treatment with the cell therapy, said cell therapy comprising a dose of genetically engineered cells expressing a recombinant receptor; and the biological sample is obtained from the subject prior to administration of the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and (b) selecting a subject who is likely to respond to treatment based on the results of determining a likelihood that a subject will achieve a durable response to the cell therapy by comparing, individually, the level, amount or concentration of the analyte in the sample to a threshold level.

[0062] Provided herein are methods of treatment, the methods involving: selecting a subject who is likely to respond to treatment with a cell therapy based on the results of determining a likelihood that a subject will achieve a durable response to the cell therapy by comparing, individually, the level, amount or concentration of one or more analyte in a biological sample to a threshold level, wherein the one or more analyte is selected from LDH, ferritin, CRP, D-dimer, SAA-1, IL-6, IL-10, IL-15, IL-16, TNF-α, IFN-γ, MIP-1α, CXCL-10, IL-8, MCP-1 and MIP-1β, wherein: the biological sample is from a subject that is a candidate for treatment with the cell therapy, said cell therapy comprising a dose of genetically engineered cells expressing a recombinant receptor; and the biological sample is obtained from the subject prior to administering the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and administering the cell therapy to a subject selected for treatment.

[0063] In some examples, the subject is likely to achieve a durable response if the level, amount or concentration one or more of the analyte is below a threshold level and the subject is not likely to achieve a durable response if the level, amount or concentration one or more of the analyte is above a threshold level.

[0064] In some examples, the threshold level is within 25%, within 20%, within 15%, within 10% or within 5% and/or is within a standard deviation below the median or mean level, amount or concentration, or is or is about the median or mean level, amount or concentration, of the analyte in a biological sample obtained from a group of subjects prior to receiving a cell therapy, wherein each of the subjects of the group went on to achieve a durable response after administration of a recombinant-receptor-expressing therapeutic cell composition for treating the same disease or condition.

[0065] In some examples, the threshold level is within 25%, within 20%, within 15%, within 11% or within 5% and/or is within a standard deviation above the median or mean level, amount or concentration of the analyte in a biological sample obtained from a group of subjects prior to receiving a cell therapy, wherein each of the subjects of the group did not achieve a durable response after administration of a recombinant-receptor-expressing therapeutic cell composition for treating the same disease or condition.

[0066] In some examples, the durable response comprises a complete response (CR) or partial response (PR) that is durable for at or greater than 3 months, 4 months, 5 months, or 6 months.

[0067] In some examples, the durable response comprises a CR or PR that is durable for at least 3 months.

[0068] Provided herein are methods of assessing the risk of developing a toxicity after administration of a cell therapy, the methods involving assessing the level, amount or concentration of one or more analyte in a biological sample from a subject or a volumetric measure of tumor burden in a subject, wherein the one or more analyte is selected from LDH, Ferritin, C-reactive protein (CRP), D-dimer (fibrin degradation product), IL-6, IL-8, IL-10, IL-15, IL-16 TNF-α, IFN-α2, MCP-1, MIP-1α and MIP-1β, wherein: the subject is a candidate for treatment with the cell therapy, said cell therapy optionally comprising a dose or composition of genetically engineered cells expressing a recombinant receptor; and the biological sample is obtained from the subject prior to administering the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and comparing, individually, the level, amount or concentration of the analyte in the sample or the volumetric measure of tumor burden to a threshold level, thereby determining a risk of developing a toxicity after administration of the cell therapy.

[0068a] In another aspect, the present disclosure refers to amethod of assessing the risk of developing a toxicity after administration of a cell therapy, the method comprising: (a) assessing the level, amount or concentration of one or more analyte in a biological sample from a subject or a volumetric measure of tumor burden in a subject, wherein the one or more analyte is selected from LDH, Ferritin, C-reactive protein (CRP), D-dimer (fibrin degradation product), IL-6, IL-8, IL-10, IL-15, IL-16 TNF-α, IFN-α2, MCP-1, MIP-1α and MIP-1β, wherein: the subject is a candidate for treatment with the cell therapy, said cell therapy optionally comprising a dose or composition of genetically engineered cells expressing a recombinant receptor; and the biological sample is obtained from the subject prior to administration of the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and (b) comparing, individually, the level, amount or concentration of the analyte in the sample or the volumetric measure of tumor burden to a threshold level, thereby determining a risk of developing a toxicity after administration of the cell therapy.

[0069] Provided herein are methods of identifying a subject, the methods involving assessing the level, amount or concentration of one or more analyte in a biological sample from a subject or a volumetric measure of tumor burden in a subject, wherein the one or more analyte is selected from LDH, Ferritin, C-reactive protein (CRP), D-dimer (fibrin degradation product), IL-6, IL-8, IL-10, IL-15, IL-16 TNF-α, IFN-α2, MCP-1, MIP-1α and MIP-1β, wherein: the subject is a candidate for treatment with the cell therapy, said cell therapy optionally comprising a dose or composition of genetically engineered cells expressing a recombinant receptor; and the biological sample is obtained from the subject prior to administering the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and identifying a subject who has a risk of developing a toxicity after administration of a cell therapy based by comparing, individually, the level, amount or concentration of the analyte in the sample or the volumetric measure of tumor burden to a threshold level.

[0070] Provided herein are methods of treatment, comprising assessing the level, amount or concentration of one or more analyte in a biological sample from a subject or a volumetric

measure of tumor burden in the subject, wherein the one or more analyte is selected from LDH, Ferritin, C-reactive protein (CRP), D-dimer (fibrin degradation product), IL-6, IL-8, IL-10, IL-15, IL-16 TNF-α, IFN-α2, MCP-1, MIP-1α and MIP-1β, wherein: the subject is a candidate for treatment with the cell therapy, said cell therapy optionally comprising a dose or composition of genetically engineered cells expressing a recombinant receptor; and the biological sample is obtained from the subject prior to administering the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and; and comparing, individually, the level, amount or concentration of the analyte in the sample or the volumetric measure of tumor burden to a threshold level, thereby determining a risk of developing a toxicity after administration of the cell therapy; and following or based on the results of the assessment, administering to the subject the cell therapy, and, optionally, an agent or other treatment capable of treating, preventing, delaying, reducing or attenuating the development or risk of development of a toxicity.

[0071] In some examples, the biological sample is a blood or plasma sample.

[0072] In some examples, the volumetric measure of tumor burden is a sum of product dimensions (SPD) or is a volumetric measurement based on CT and/or MRI imaging or other imaging of body. In some examples, the volumetric measure of tumor burden is carried out prior to treatment, prior to apheresis, or prior to cell product manufacturing.

[0073] In some examples, the methods also involve monitoring the subject for symptoms of toxicity if the subject is administered a cell therapy and is identified as having a risk of developing a toxicity.

[0074] In some examples, the subject has a risk of developing a toxicity if the level, amount or concentration one or more of the analyte or the volumetric measure of tumor burden is above a threshold level and the subject has a low risk of developing a toxicity if the level, amount or concentration one or more of the analyte or the volumetric measure of tumor burden is below a threshold level.

[0075] In some examples, the threshold level is within 25%, within 20%, within 15%, within 10% or within 5% and/or is within a standard deviation above the median or mean level, amount or concentration, or is or is about the median or mean level, amount or concentration, of the analyte or the volumetric measure of tumor burden in a biological sample obtained from a group of subjects prior to receiving a cell therapy, wherein each of the subjects of the group

went on not to develop any toxicity after receiving a recombinant-receptor-expressing therapeutic cell composition for treating the same disease or condition.

[0076] In some examples, the threshold level is within 25%, within 20%, within 15%, within 10% or within 5% and/or is within a standard deviation below the median or mean level, amount or concentration of the analyte or the volumetric measure of tumor burden in a biological sample obtained from a group of subjects prior to receiving a cell therapy, wherein each of the subjects of the group went on to develop a toxicity after receiving a recombinant-receptor-expressing therapeutic cell composition for treating the same disease or condition.

[0077] In some examples, the toxicity is neurotoxicity or CRS.

[0078] In some examples, the toxicity is grade 1 or higher neurotoxicity or CRS.

[0079] In some examples, the toxicity is severe neurotoxicity or is grade 2 or higher neurotoxicit, a grade 3 or higher neurotoxicity, at least prolonged grade 3 neurotoxicity or is at or above grade 4 or grade 5 neurotoxixity; or the toxicity is severe CRS or comprises grade 2 or higher or grade 3 or higher CRS.

[0080] In some examples, the toxicity is neurotoxicity and the volumetric measure of tumor burden is SPD and the one or more analyte is selected from LDH, IL-10, IL-15, IL-16, TNF-α and MIP-1β .

[0081] In some examples, the toxicity is neurotoxicity and one or more analytes is assessed and the analytes are selected from LDH, Ferritin, CRP, IL-6, IL-8, IL-10, TNF-α, IFN-α2, MCP-1 and MIP-1β.

[0082] In some examples, the toxicity is neurotoxicity and one or more analytes is assessed and the analytes are selected from IL-8, IL-10 and CXCL10.

[0083] In some examples, the neurotoxicity is severe neurotoxicity or grade 3 or higher neurotoxicity.

[0084] In some examples, toxicity is CRS and the one or more analyte or volumetric measure of tumor burden is selected from LDH, SPD, CRP, d-dimer, IL-6, IL-15, TNF-α and MIP-1α.

[0085] In some examples, the CRS is severe CRS or grade 3 or higher CRS.

[0086] In some examples, if the subject is identified as having a risk of developing a toxicity, administering to the subject: (1) an agent or other treatment capable of treating, preventing, delaying, reducing or attenuating the development or risk of development of a toxicity and (2) the cell therapy, wherein administration of the agent is to be administered (i)

prior to, (ii) within one, two, or three days of, (iii) concurrently with and/or (iv) at first fever following, the initiation of administration of the cell therapy to the subject; and/or a cell therapy at a reduced dose or at a dose that is not associated with risk of developing toxicity or severe toxicity, or is not associated with a risk of developing a toxicity or severe toxicity in a majority of subjects, and/or a majority of subjects having a disease or condition that the subject has or is suspected of having, following administration of the cell therapy; and/or administering to the subject a cell therapy in an in-patient setting and/or with admission to the hospital for one or more days, optionally wherein the cell therapy is otherwise to be administered to subjects on an outpatient basis or without admission to the hospital for one or more days.

[0087] In some examples, the agent or other treatment is an anti-IL-6 antibody or an anti-IL6 receptor antibody.

[0088] In some examples, the agent or other treatment is or comprises an agent selected from among tocilizumab, siltuximab, clazakizumab, sarilumab, olokizumab (CDP6038), elsilimomab, ALD518/BMS-945429, sirukumab (CNTO 136), CPSI-2634, ARGX-109, FE301 and FM101.

[0089] In some examples, the agent or other treatment is or comprises a steroid, optionally dexamethasone.

[0090] In some examples, a volumetric measure is assessed and the volumetric measure is SPD and the threshold level is or is about 30 cm^2,is or is about 40 cm^2, is or is about 50 cm^2, is or is about 60 cm^2, or is or is about 70 cm^2. In some examples, the volumetric measure is SPD and the threshold level is or is about 50 cm^2.

[0091] In some examples, the one or more analyte is or comprises LDH and the threshold level is or is about 300 units per liter, is or is about 400 units per liter, is or is about 500 units per liter or is or is about 600 units per liter. In some examples, the analyte is LDH and the threshold level is or is about 500 units per liter.

[0092] In some examples, the recombinant receptor specifically binds to an antigen associated with the disease or condition or expressed in cells of the environment of a lesion associated with the disease or condition. In some examples, the disease or condition is a cancer. In some examples, the disease or condition is a myeloma, leukemia or lymphoma. In some examples, the disease or condition is a B cell malignancy and/or is acute lymphoblastic leukemia (ALL), adult ALL, chronic lymphoblastic leukemia (CLL), non-Hodgkin lymphoma (NHL), and Diffuse Large B-Cell Lymphoma (DLBCL).

[0093] In some examples, the recombinant receptor is a chimeric antigen receptor (CAR). In some examples, the engineered cells comprise T cells, optionally $CD4^+$ and/or $CD8^+$. In some examples, the T cells are primary T cells obtained from a subject or are autologous to the subject.

[0094] Provided herein are methods of treating a subject having non-Hodgkin lymphoma (NHL), the methods comprising administering to the subject a dose of T cells comprising T cells expressing a chimeric antigen receptor (CAR) that specifically binds to a target antigen expressed by the NHL, wherein: the dose of T cells comprises between at or about 5×10^7 recombinant receptor-expressing T cells and 1×10^8 recombinant receptor-expressing T cells, inclusive, said dose comprising a defined ratio of $CD4^+$ cells expressing the recombinant receptor to $CD8^+$ cells expressing the recombinant receptor and/or of $CD4^+$ cells to $CD8^+$ cells, which ratio is approximately or is 1:1; and the method results in (1) a complete response (CR) in at least 35%, at least 40% or at least 50% of subjects treated and/or objective response (OR) in at least 50%, at least 60% or at least 70% of subjects treated and (2) results in no more than 50% of subjects exhibiting a cytokine release syndrome (CRS) higher than grade 2 and/or a neurotoxicity higher than grade 2.

[0095] In some examples of any of the provided methods, at least 40%, at least 50%, at least 60%, at least 70% of the subjects who, at or prior to the administration of the dose of cells had or were identified to have a double/triple hit lymphoma (or high-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements with DLBCL histology (double/triple hit)) or relapse following administration of an autologous stem cell transplant (ASCT), achieved an OR, optionally wherein the OR is durable for at or greater than 3 months or at or greater than 6 months.

[0096] In some examples of any of the provided methods, the CR or the OR is durable for greater than 3 months or greater than 6 months. In particular examples of any of the provided methods, greater than or greater than about 50% of the subjects treated according to the method do not exhibit any grade of cytokine release syndrome (CRS) or neurotoxicity.

[0097] In some examples, the CR or the OR is durable for greater than 3 months or greater than 6 months; at least 20%, at least 25%, at least 35%, at least 40% or at least 50% of subjects treated according to the method achieve a CR that is durable; at least 60%, 70%, 80%, 90%, or 95% of subjects treated with the method and who achieve a CR, remain in CR or remain in response or remain surviving for at or greater than 3 months or at or greater than 6 months or

at or greater than 9 months; and/or wherein at least 60%, 70%, 80%, 90%, or 95% of subjects treated with the method who achieve a CR by one month and/or by three months remain in response, remain in CR, and/or survive or survive without progression, for greater at or greater than 3 months and/or at or greater than 6 months and/or at greater than nine months; and/or at least 50%, at least 60% or at least 70% of the subjects treated according to the method achieve objective response (OR) optionally wherein the OR is durable, or is durable in at least 60%, 70%, 80%, 90%, or 95% of subjects achieving the OR, for at or greater than 3 months or at or greater than 6 months; and/or wherein at least 60%, 70%, 80%, 90%, or 95% of subjects treated with the method and achieving an OR remain in response or surviving for greater at or greater than 3 months and/or at or greater than 6 months.

[0098] In some examples, at or prior to administration of the dose of cells, the subject is or has been identified as having a lymphoma associated with or involving central nervous system (CNS) involvement; and/or at least 70%, at least 80%, at least 90% or at least 95% of subjects treated according to the method who, at or prior to the administration of the dose of cells exhibited or were identified to exhibit a lymphoma with CNS involvement, achieved a resolution of the CNS disease.

[0099] Provided herein are methods of treating a subject, the method involving administering, to a subject that has a lymphoma a dose of T cells comprising T cells expressing a chimeric antigen receptor (CAR) that specifically binds to a target antigen expressed by the lymphoma, wherein the lymphoma in the subject is associated with or involves central nervous system (CNS) involvement. In some examples, at or prior to the time of administration of the dose of cells, the subject comprises a brain lesion, optionally a temporal lobe brain lesion. In some examples, the lymphoma is a B cell malignancy. In some examples, the lymphoma is non-Hodgkin lymphoma (NHL).

[0099a] In another aspect, the present disclosure refers to use of a dose of T cells comprising T cells expressing a chimeric antigen receptor (CAR) in the manufacture of a medicament for treatment of a lymphoma in a subject, wherein the CAR- specifically binds to a target antigen expressed by the lymphoma and the lymphoma in the subject is associated with or involves central nervous system (CNS) involvement.

[0100] In some of any such examples, at least 35%, at least 40% or at least 50% of subjects treated according to the method achieve a complete response (CR) or remission of CNS disease and/or achieve reduction in or clearance of CNS disease, optionally wherein the CR or remission or reduction or clearance of the CNS disease is durable, or is durable in at least 60%, 70%, 80%, 90%, or 95% of subjects achieving the CR, for at or greater than 3 months or at or greater than 6 months; and/or at least 60%, 70%, 80%, 90%, or 95% of subjects achieving a CR or remission or other reduction of CNS disease by one month and/or by three months remain in response, remain in remission, e.g., in CR, or remain showing signs of the reduction or

remission, and/or survive or survive without progression, for greater at or greater than 3 months and/or at or greater than 6 months and/or at greater than nine months; and/or at least 50%, at least 60% or at least 70% of the subjects treated according to the method achieve objective response (OR) or remission of CNS disease optionally wherein the OR or remission of the CNS disease is durable, or is durable in at least 60%, 70%, 80%, 90%, or 95% of subjects achieving the OR, for at or greater than 3 months or at or greater than 6 months; and/or at least 60%, 70%, 80%, 90%, or 95% of subjects achieving the OR or remission of CNS disease remain in response or surviving for greater at or greater than 3 months and/or at or greater than 6 months; and/or the brain lesion is reduced in size or volume, optionally by greater than or greater than about 25%, 50%, 75% or more. In some examples, reduction or remission or clearance of CNS disease is achieved without or without substantial signs or symptoms of a toxicity, such as a neurotoxicity such as severe neurotoxicity, e.g., neurotoxicity greater than grade 2 or greater than grade 3, and/or without toxicity caused by activation or presence of the cellular therapy cells in the brain of the subject, and/or is achieved without an increased level of the toxicity, as compared to a subject in which CNS disease remains and/or treated with the therapy but that does not exhibit CNS disease.

[0101] In some examples of any of the provided methods, greater than or greater than about 30%, 35%, 40%, or 50% of the subjects treated according to the method do not exhibit any grade of cytokine release syndrome (CRS) or neurotoxicity. In some examples of any of the provided methods, at least at or about 45%, 50%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, or 95% of subjects treated according to the method do not exhibit early onset CRS or neurotoxicity and/or do not exhibit onset of CRS earlier than 3 days following initiation of the administration and/or do not exhibit onset of neurotoxicity earlier than 5 days following initiation of the administration and/or wherein the median onset of neurotoxicity among subjects treated according to the method is at or after the median peak of, or median time to resolution of, CRS in subjects treated according to the method and/or the median onset of neurotoxicity among subjects treated according to the method is greater than at or about 8, 9, 10, or 11 days.

[0102] In certain examples of any of the provided methods, prior to initiation of administration of the dose of cells, the subject has not been administered an agent or treatment to capable of treating, preventing, delaying, reducing or attenuating the development or risk of development of a toxicity. In certain examples of any of the provided methods, the subject is not administered an agent or treatment for the treatment or prevention or reduction or

attenuation of a neurotoxicity and/or a cytokine release syndrome or risk thereof, within a period of time following administration of the dose, which period of time is optionally at or about 1, 2, 3, 4, 5 days or is optionally at or about 6, 7, 8, 9, 10, 11 days or is optionally 1, 2, 3 or 4 weeks. In certain examples of any of the provided methods, the subject is not administered an agent or treatment for the treatment or prevention or reduction or attenuation of a neurotoxicity and/or a cytokine release syndrome or risk thereof, following administration of the dose, prior to or unless the subject exhibits a sign or symptom of the toxicity and/or prior to or unless the subject exhibits a sign or symptom of the toxicity other than a fever, optionally wherein the fever is not a sustained fever or the fever is or has been reduced or reduced by more than 1ºC after treatment with an antipyretic. In certain examples of any of the provided methods, the administration and any follow-up is carried out on an outpatient basis and/or without admitting the subject to a hospital and/or without an overnight stay at a hospital and/or without requiring admission to or an overnight stay at a hospital, optionally unless or until the subject exhibits a sustained fever or a fever that is or has not been reduced or not reduced by more than 1ºC after treatment with an antipyretic.

[0103] In some examples of any of the provided methods, prior to initiation of administration of the dose of cells, the subject has not been administered an anti-IL-6 or anti-IL-6R antibody, optionally tocilizumab or situximab, and/or has not been administered a steroid, optionally dexamethasone. In certain examples of any of the provided methods, the subject is not administered an anti-IL-6 or anti-IL-6R antibody, optionally tocilizumab or siltuximab, and/or has not been administered a steroid, optionally dexamethasone, within a period of time following administration of the dose, which period of time is optionally at or about 1, 2, 3, 4, 5 days or is optionally at or about 6, 7, 8, 9, 10, 11 days or is optionally 1, 2, 3 or 4 weeks. In certain examples of any of the provided methods, the subject is not administered an anti-IL-6 or anti-IL-6R antibody, optionally tocilizumab or siltuximab, and/or has not been administered a steroid, optionally dexamethasone, following administration of the cell dose, prior to, or unless, the subject exhibits a sign or symptom of a toxicity, optionally a neurotoxicity or CRS, and/or prior to, or unless, the subject exhibits a sign or symptom of a toxicity, optionally a neurotoxicity or CRS, other than a fever, optionally wherein the fever is not a sustained fever or the fever is or has been reduced or reduced by more than 1ºC after treatment with an antipyretic. In certain examples of any of the provided methods, the administration and any follow-up is carried out on an outpatient basis and/or without admitting the subject to a hospital and/or

without an overnight stay at a hospital and/or without requiring admission to or an overnight stay at a hospital, optionally unless or until the subject exhibits a sustained fever or a fever that is or has not been reduced or not reduced by more than 1ºC after treatment with an antipyretic.

[0104] In some examples of any of the provided methods, the administration is carried out on an outpatient basis and/or without requiring admission to or an overnight stay at a hospital. In some examples of any of the provided methods, if the subject, who is or has been treated on an outpatient basis, exhibits a sustained fever or a fever that is or has not been reduced or not reduced by more than 1ºC after treatment with an antipyretic, the subject is admitted to the hospital or to an overnight stay at a hospital and/or is administered an agent or treatment for the treatment or prevention or reduction or attenuation of a neurotoxicity and/or a cytokine release syndrome or risk thereof.

[0105] In particular examples of any of the provided methods, the NHL is selected from the group consisting of aggressive NHL, diffuse large B cell lymphoma (DLBCL), NOS (de novo and transformed from indolent), primary mediastinal large B cell lymphoma (PMBCL), mantle cell lymphoma (MCL), and/or follicular lymphoma (FL), optionally follicular lymphoma Grade 3B (FL3B). In certain examples of any of the provided methods, the NHL comprises diffuse large B cell lymphoma (DLBCL), primary mediastinal large B cell lymphoma (PMBCL), NOS (de novo or transformed from indolent lymphoma), or follicular lymphoma Grade 3B. In some examples, the NHL includes DLBCL. In some examples of any of the provided methods, the DLBCL is de novo or transformed from follicular lymphoma (FL) and/or does not comprise DLBCL transformed from MZL and CLL (Richter's).

[0106] In particular examples of any of the provided methods, the subject is or has been identified as having an Eastern Cooperative Oncology Group Performance Status (ECOG) status of 0, 1 or 2. In certain examples of any of the provided methods, the subject is or has been identified as having an ECOG status of 0 or 1. In some examples of any of the provided methods, at or immediately prior to the time of the administration of the dose of cells the subject has relapsed following remission after treatment with, or become refractory to, one or more prior therapies for the NHL, optionally one, two or three prior therapies other than another dose of cells expressing the CAR.

[0107] In some examples of any of the provided methods, at or prior to administration of the dose of cells, the subject is or has been identified as having a lymphoma associated with or involving central nervous system (CNS) involvement. In some examples of any of the

provided methods, at least 70%, at least 80%, at least 90% or at least 95% of subjects treated according to the method who, at or prior to the administration of the dose of cells exhibited or were identified to exhibit a lymphoma with CNS involvement, achieved a resolution of the CNS disease.

[0108] In particular examples of any of the provided methods, at or prior to the administration of the dose of cells: the subject is or has been identified as having a double/triple hit lymphoma (or high-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements with DLBCL histology (double/triple hit)); the subject is or has been identified as having a chemorefractory lymphoma, optionally a chemorefractory DLBCL; the subject has not achieved complete remission (CR) in response to a prior therapy; and/or the subject has relapsed within 1 year or less than 1 year after receiving an autologous stem cell transplant (ASCT).

[0109] In some examples of any of the provided methods, the method includes, prior to administration of the dose of cells, identifying or selecting a subject for the administration of the dose of cells that has a double/triple hit lymphoma (or high-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements with DLBCL histology (double/triple hit)), a chemorefractory lymphoma, optionally a chemorefractory DLBCL, has not achieved complete remission (CR) in response to a prior therapy for treating the malignancy, optionally the NHL; and/or has relapsed within 1 year or less than 1 year after receiving an autologous stem cell transplant (ASCT); and/or has a lymphoma associated with or involving central nervous system (CNS) involvement.

[0110] In some examples of any of the provided methods, the method further includes administration of an additional therapeutic agent or therapy, optionally other than a cell therapy, optionally other than CAR^+ T cell therapy. In some examples, the additional therapeutic agent or therapy is for treating the NHL or malignancy and/or increases the persistence, activity and/or efficacy of the dose of cells. In some embodimetns, the additional therapeutic agent or therapy is administered if the subject does not exhibit a response, optionally does not exhibit a CR or OR, to the cell therapy within 1 month, within 2 months or within 3 months after administration of the dose of cells. In some examples, the additional therapeutic agent or therapy is administered to a subject: that is or has been identified to have stable or progressive disease (SD/PD) following treatment with a prior therapy, optionally a prior therapy with a chemotherapeutic agent, that is or has been identified with an Eastern Cooperative Oncology

Group Performance Status (ECOG) status of 2, that is or has been identified as having a transformed follicular lymphoma (tFL) and/or that is or has been identified has having a DLBCL transformed from MZL and CLL. In some examples, prior to administration of the dose of cells or the additional therapeutic agent or therapy, the method includes identifying or selecting a subject for the administration of the dose of cells that has stable or progressive disease (SD/PD) following treatment with a prior therapy, optionally a prior therapy with a chemotherapeutic agent, an Eastern Cooperative Oncology Group Performance Status (ECOG) status of 2, a transformed follicular lymphoma (tFL) and/or a DLBCL transformed from MZL and CLL. In some of any of such examples, the additional therapeutic agent or therapy is administered prior to, with or at the same time and/or subsequent to initiation of administration of the dose of cells.

[0111] In certain examples of any of the provided methods, the CAR comprises an scFv specific for the antigen, a transmembrane domain, a cytoplasmic signaling domain derived from a costimulatory molecule, which optionally is a 4-1BB, and a cytoplasmic signaling domain derived from a primary signaling ITAM-containing molecule, which optionally is a CD3zeta. In some examples of any of the provided methods, the antigen is a B cell antigen, which optionally is CD19.

[0112] In particular examples of any of the provided methods, prior to the administration, the subject has been preconditioned with a lymphodepleting therapy comprising the administration of fludarabine and/or cyclophosphamide. Certain examples of any of the provided methods further comprise, immediately prior to the administration, administering a lymphodepleting therapy to the subject comprising the administration of fludarabine and/or cyclophosphamide. In some examples of any of the provided methods, the lymphodepleting therapy comprises administration of cyclophosphamide at about 200-400 mg/m^2, optionally at or about 300 mg/m^2, inclusive, and/or fludarabine at about 20-40 mg/m^2, optionally 30 mg/m^2, daily for 2-4 days, optionally for 3 days. In particular examples of any of the provided methods, the lymphodepleting therapy comprises administration of cyclophosphamide at or about 300 mg/m^2 and fludarabine at about 30 mg/m^{2}daily for 3 days.

[0113] In certain examples of any of the provided methods, the administration of the cell dose and/or the lymphodepleting therapy is carried out via outpatient delivery. In some examples of any of the provided methods, the dose of cells is administered parenterally, optionally intravenously.

[0114] In particular examples of any of the provided methods: at least 40% or at least 50% of subjects treated according to the method achieve complete remission (CR), exhibit progression-free survival (PFS) and/or overall survival (OS) of greater than at or about 3 months, 6 months or 12 months; on average, subjects treated according to the method exhibit a median PFS or OS of greater than at or about 6 months, 12 months, or 18 months; and/or the subject exhibits PFS or OS following therapy for at least at or about 6, 12, 18 or more months. In certain examples of any of the provided methods, at or about 14 or 28 days after initiation of administration of the dose of cells, the number of CAR^+ T cells, optionally CAR^+ $CD8^+$ T cells and/or CAR^+ $CD4^+$ T cells, detectable in the blood of the subject, or in a majority of subjects so treated by the method, is greater than1 cells per μL, greater than 5 cells per μL or greater than per 10 cells per μL.

[0115] In some examples of any of the provided methods, the T cells are primary T cells obtained from a subject. In particular examples of any of the provided methods, the T cells are autologous to the subject. In certain examples of any of the provided methods, the T cells are allogeneic to the subject. In some examples of any of the provided methods, the T cells comprise $CD4^+$ and $CD8^+$ T cells administered as a plurality of compositions, said plurality of compositions comprising administration of a first composition comprising the $CD4^+$ T cells or the $CD8^+$ T cells and administration of a second composition comprising the other of the $CD4^+$ T cells or the $CD8^+$ T cells.

[0116] In particular examples of any of the provided methods, the first composition and second composition are administered 0 to 12 hours apart, 0 to 6 hours apart or 0 to 2 hours apart. In certain examples of any of the provided methods, the first composition and second composition are administered no more than 2 hours, no more than 1 hour, no more than 30 minutes, no more than 15 minutes, no more than 10 minutes or no more than 5 minutes apart. In some examples of any of the provided methods, the first composition comprises the $CD4^+$ T cell. In particular examples of any of the provided methods, the first composition comprises the $CD8^+$ T cells. In certain examples of any of the provided methods, the first composition is administered prior to the second composition.

[0117] In some examples of any of the provided methods, the dose of T cells is administered to the subject as a single dose or is administered only one time within a period of two weeks, one month, three months, six months, 1 year or more. In particular examples of any of the provided methods, the dose of T cells is administered as a double dose comprising a

first dose of the T cells and a consecutive dose of the T cells, wherein one or both of the first dose and the second dose comprises administration of the plurality of compositions of T cells. In certain examples of any of the provided methods, the consecutive dose is administered at a point in time that is at least or more than about 7 days or 14 days after and less than about 28 days after initiation of the administration of the first dose of cells.

[0118] Provided herein is an article of manufacture comprising a cell therapy comprising a dose or composition of genetically engineered cells expressing a chimeric antigen receptor (CAR), and instructions for administering the cell therapy, wherein the instructions specify: the dose of cells is to be administered to a subject having or identified to have non-Hodgkin lymphoma (NHL), the NHL selected from diffuse large B cell lymphoma (DLBCL), primary mediastinal large B cell lymphoma (PMBCL), NOS (de novo or transformed from indolent lymphoma), or follicular lymphoma Grade 3B, wherein the subject is or has been identified as having an Eastern Cooperative Oncology Group Performance Status (ECOG) status of 0 or 1; and the dose of T cells to be administered comprises between at or about 5×10^7 CAR-expressing T cells and 1×10^8 CAR-expressing T cells, inclusive. In some examples of any of the provided articles of manufacture, the instructions specify administering the dose of T cells at a defined ratio of $CD4^+$ cells expressing the CAR to $CD8^+$ cells expressing the CAR and/or of $CD4^+$ cells to $CD8^+$ cells, which ratio optionally is approximately 1:1 or is between approximately 1:3 and approximately 3:1.

[0118a] In another aspect, the present disclosure refers to an article of manufacture comprising one or more dose of a cell therapy, each dose comprising a first composition comprising one of CD4+ T cells or CD8+ T cells and a second composition comprising the other of the CD4+ or CD8+ T cells, wherein the dose comprises CD4+ T cells expressing a chimeric antigen receptor (CAR) and CD8+ T cells expressing the CAR, and instructions for administering the cell therapy, wherein the instructions specify: (i) the dose of cells is to be administered to a subject having or identified to have a non-Hodgkin lymphoma (NHL), the NHL selected from diffuse large B cell lymphoma (DLBCL), primary mediastinal large B cell lymphoma (PMBCL), NOS (de novo or transformed from indolent lymphoma), or follicular lymphoma Grade 3B, wherein the subject is or has been identified as having an Eastern Cooperative Oncology Group Performance Status (ECOG) status of 0 or 1; and administration of a number of T cells or an amount or volume of one or more formulations corresponding to or containing said specified number of cells, wherein the specified number of cells comprises between at or about 5×10^7 CAR-expressing T cells and 1×10^8 CAR-expressing T cells, inclusive, between at or about 5×10^7 CAR-expressing T cells and at or about 1.5×10^8 CAR

expressing T cells, at or about 5 x 10^7 CAR-expressing T cells, at or about 1 x 10^8 CAR-expressing T cells, or at or about 1.5 x 10^8 CAR-expressing T cells, between at or about 2.5 x 10^7 $CD8^+$CAR-expressing T cells and at or about 5 x 10^7 $CD8^+$ CAR-expressing T cells, inclusive, between at or about 2.5 x 10^7 CAR-expressing T cells and at or about 0.75 x 10^8 $CD8^+$ CAR-expressing T cells, or at or about 2.5 x 10^7 $CD8^+$ CAR-expressing T cells, at or about 5 x 10^7 CAR-expressing T cells, or at or about 0.75 x 10^8 $CD8^+$ CAR-expressing T cells, or of viable populations of any of the foregoing; (ii) the dose of T cells is to be administered at a defined ratio of $CD4^+$ cells expressing the CAR to $CD8^+$ cells expressing the CAR and/or of $CD4^+$ cells to $CD8^+$ cells, which ratio is approximately or is 1:1; and the dose of cells is to be administered to a subject having or identified to have a non-Hodgkin lymphoma (NHL), the NHL selected from diffuse large B cell lymphoma (DLBCL), primary mediastinal large B cell lymphoma (PMBCL), NOS (de novo or transformed from indolent lymphoma), or follicular lymphoma Grade 3B; and/or (iii) the dose of cells is to be administered to a subject having or identified to have a non-Hodgkin lymphoma (NHL); the dose of T cells to be administered comprises between at or about 5 x 10^7 CAR-expressing T cells and 1 x 10^8 CAR-expressing T cells, inclusive; and the dose of T cells is to be administered at a defined ratio of $CD4^+$ cells expressing the CAR to $CD8^+$ cells expressing the CAR and/or of $CD4^+$ cells to $CD8^+$ cells, which ratio is approximately or is 1:1.

[0119] Provided herein is an article of manufacture comprising a cell therapy comprising a dose or composition of genetically engineered cells expressing a chimeric antigen receptor (CAR), and instructions for administering the cell therapy, wherein the instructions specify: the dose of T cells is to be administered at a defined ratio of $CD4^+$ cells expressing the CAR to $CD8^+$ cells expressing the CAR and/or of $CD4^+$ cells to $CD8^+$ cells, which ratio is approximately or is 1:1; and the dose of cells is to be administered to a subject having or identified to have non-Hodgkin lymphoma (NHL), the NHL selected from diffuse large B cell lymphoma (DLBCL), primary mediastinal large B cell lymphoma (PMBCL), NOS (de novo or transformed from indolent lymphoma), or follicular lymphoma Grade 3B.

[0120] Provided herein is an article of manufacture comprising a cell therapy comprising a dose or composition of genetically engineered cells expressing a chimeric antigen receptor (CAR), and instructions for administering the cell therapy, wherein the instructions specify: the dose of cells is to be administered to a subject having or identified to have non-Hodgkin

lymphoma (NHL), optionally an NHL selected from aggressive NHL, diffuse large B cell lymphoma (DLBCL), NOS (de novo and transformed from indolent), primary mediastinal large B cell lymphoma (PMBCL), mantle cell lymphoma (MCL), and/or follicular lymphoma (FL), optionally follicular lymphoma Grade 3B (FL3B), the dose of T cells to be administered comprises between at or about 5 x 10^7 CAR-expressing T cells and 1 x 10^8 CAR-expressing T cells, inclusive; and the dose of T cells is to be administered at a defined ratio of $CD4^+$ cells expressing the CAR to $CD8^+$ cells expressing the CAR and/or of $CD4^+$ cells to $CD8^+$ cells, which ratio is approximately or is 1:1.

[0121] In some examples of any of the provided articles of manufacture, the instructions further specify the dose of cells is to be administered to a subject that is or has been identified as having an Eastern Cooperative Oncology Group Performance Status (ECOG) status of 0, 1 or 2, optionally an ECOG status of 0 or 1. In certain examples of any of the provided articles of manufacture, the instructions specify that the administration is in a subject that has not received, immediately prior to the administration of the dose of cells or within or about 1 month of the dose of cells, an agent or treatment capable of treating, preventing, delaying, reducing or attenuating the development or risk of development of a toxicity. In some examples of any of the provided articles of manufacture, the agent is or comprises an anti-IL-6 or anti-IL-6R antibody, optionally tocilizumab or siltuximab, and/or a steroid, optionally dexamethasone. In particular examples of any of the provided articles of manufacture, the instructions specify the dose of cells is not for administration in a subject having DLBCL transformed from MZL and CLL (Richter's) and/or is for a subject having a DLBCL that is de novo or transformed from indolent disease. In some examples of any of the provided articles of manufacture, the instructions specify the subject does not have a DLBCL transformed from MZL and CLL (Richter's).

[0122] In some examples of any of the provided articles of manufacture, the instructions specify the administration of the cell therapy is for a subject that is or has been identified as having a double/triple hit lymphoma (or high-grade B-cell lymphoma, with MYC and BCL2 and/or BCL6 rearrangements with DLBCL histology (double/triple hit)), is or has been identified as having a chemorefractory lymphoma, optionally a chemorefractory DLBCL; and/or that has not achieved complete remission (CR) in response to a prior therapy. In certain examples of any of the provided articles of manufacture, the CAR comprises an scFv specific for the antigen, a transmembrane domain, a cytoplasmic signaling domain derived from

a costimulatory molecule, which optionally is a 4-1BB, and a cytoplasmic signaling domain derived from a primary signaling ITAM-containing molecule, which optionally is a CD3zeta. In certain examples of any of the provided articles of manufacture, the antigen is a B cell antigen, which optionally is CD19.

[0123] Particular examples of any of the provided articles of manufacture further comprise instructions for use with, after or in connection with a lymphodepleting therapy, the lymphodepleting therapy optionally comprising fludarabine and/or cyclophosphamide. In certain examples of any of the provided articles of manufacture, the lymphodepleting therapy comprises administration of cyclophosphamide at about 200-400 mg/m^2, optionally at or about 300 mg/m^2, inclusive, and/or fludarabine at about 20-40 mg/m^2, optionally 30 mg/m^2, daily for 2-4 days, optionally for 3 days. In particular examples of any of the provided articles of manufacture, the lymphodepleting therapy comprises administration of cyclophosphamide at or about 300 mg/m^2 and fludarabine at about 30 mg/m^{2}daily for 3 days.

[0124] In some examples of any of the provided articles of manufacture, the instructions further specify the administration of the cell therapy is to be or may be administered to the subject on an outpatient setting and/or without admission of the subject to the hospital overnight or for one or more consecutive days and/or is without admission of the subject to the hospital for one or more days. In certain examples of any of the provided articles of manufacture, the instructions further specify the cell therapy is for parenteral administration, optionally intravenous administration. In particular examples of any of the provided articles of manufacture, the cell therapy comprises primary T cells obtained from a subject. In some examples of any of the provided articles of manufacture, the T cells are autologous to the subject. In certain examples of any of the provided articles of manufacture, the T cells are allogeneic to the subject.

[0125] In particular examples of any of the provided articles of manufacture, the article of manufacture comprises a plurality of compositions of the cell therapy, the plurality of compositions comprising a first composition of genetically engineered cells comprising CD4$^+$ T cells or CD8$^+$ T cells, wherein the instructions specify the first composition is for use in with a second composition comprising the other of the CD4$^+$ T cells or the CD8$^+$ T cells, optionally wherein the cells of the first composition and cells of the same composition are from the same subject.

[0126] In some examples of any of the provided articles of manufacture, the instructions specify the first composition and second composition are to be administered at a defined ratio of $CD4^+$ cells expressing the recombinant receptor to $CD8^+$ cells expressing the recombinant receptor and/or of $CD4^+$ cells to $CD8^+$ cells, which ratio optionally is approximately 1:1 or is between approximately 1:3 and approximately 3:1. In certain examples of any of the provided articles of manufacture, the defined ratio is or is approximately 1:1. In particular examples of any of the provided articles of manufacture, the composition further comprises a cryoprotectant and/or the article further includes instructions for thawing the composition prior to administration to the subject.

[0127] In some examples of any of the provided articles of manufacture, the instructions specify administering the composition comprising the $CD4^+$ T cells and the composition comprising the $CD8^+$ T cells 0 to 12 hours apart, 0 to 6 hours apart or 0 to 2 hours apart. In certain examples of any of the provided articles of manufacture, the instructions specify administering the composition comprising the $CD4^+$ T cells and the composition comprising the $CD8^+$ T cells no more than 2 hours, no more than 1 hour, no more than 30 minutes, no more than 15 minutes, no more than 10 minutes or no more than 5 minutes apart. In particular examples of any of the provided articles of manufacture, the instructions specify administering the composition comprising the $CD4^+$ T cells prior to administering the composition comprising the $CD8^+$ cells. In some examples of any of the provided articles of manufacture, the instructions specify administering the composition comprising the $CD8^+$ T cells prior to administering the composition comprising the $CD4^+$ cells.

[0128] Provided herein are articles of manufacture comprising one or more reagent capable of detecting one or more analytes, and instructions for using the reagent to assay a biological sample from a subject that is a candidate for treatment, optionally with a cell therapy, said cell therapy optionally comprising a dose or composition of genetically engineered cells expressing a recombinant receptor, wherein the one or more analytes is selected from LDH, ferritin, CRP, IL-6, IL-7, IL-8, IL-10, IL-15, IL-16, TNF-alpha, IFN-gamma, MCP-1, MIP-1beta, eotaxin, G-CSF, IL-1Ralpha, IL-1Rbeta, IP-10, perforin, and D-dimer (fibrin degradation product).

[0128a] In another aspect, the present disclosure refers to an article of manufacture comprising one or more reagent capable of detecting one or more analytes, and instructions for using the reagent to assay a biological sample from a subject that is a candidate for treatment with a cell therapy, said cell therapy comprising a dose or composition of genetically engineered

cells expressing a recombinant receptor, wherein the one or more analytes is selected from: (i) ferritin, LDH, CXCL10, G-CSF and IL-10; (ii) LDH, ferritin, CRP, D-dimer, SAA-1, IL-6, IL-10, IL-15, IL-16, TNF-α, IFN-γ, MIP-1α, CXCL-10, IL-8, MCP-1 and MIP-1β; or (iii) LDH, Ferritin, C-reactive protein (CRP), D-dimer (fibrin degradation product), IL-6, IL-8, IL-10, IL-15, IL-16 TNF-α, IFN-α2, MCP-1, MIP-1α and MIP-1β.

[0128b] In another aspect, the present disclosure refers to an article of manufacture comprising: a cell therapy comprising a dose of genetically engineered cells expressing a recombinant receptor, and instructions for administering the cell therapy following or based on the results of an assessment, in a biological sample of the level, or amount or concentration of one or more analyte in the biological sample, the biological sample obtained from the subject prior to administration of the cell therapy and/or the biological sample not comprising the recombinant receptor and/or the engineered cells, wherein the one or more analytes is selected from: (i) ferritin, LDH, CXCL10, G-CSF and IL-10; (ii) LDH, ferritin, CRP, D-dimer, SAA-1, IL-6, IL-10, IL-15, IL-16, TNF-α, IFN-γ, MIP-1α, CXCL-10, IL-8, MCP-1 and MIP-1β; or (iii) LDH, Ferritin, C-reactive protein (CRP), D-dimer (fibrin degradation product), IL-6, IL-8, IL-10, IL-15, IL-16 TNF-α, IFN-α2, MCP-1, MIP-1α and MIP-1β.

[0129] Particular examples of any of the provided articles of manufacture further comprise the cell therapy and/or further comprising instructions for use with, prior to and/or in connection with treatment with the cell therapy. Certain examples of any of the provided articles of manufacture further comprise one or more agents or treatments for treating,

preventing, delaying, reducing or attenuating the development or risk of development of a toxicity and/or instructions for the administration of one or more agents or treatments for treating, preventing, delaying, reducing or attenuating the development or risk of development of a toxicity in the subject.

[0130] In some examples of any of the provided articles of manufacture, the instructions further specify, if the level, amount or concentration of the analyte in the sample is at or above a threshold level for the analyte: administering to the subject an agent or other treatment capable of treating, preventing, delaying, reducing or attenuating the development or risk of development of a toxicity (i) prior to, (ii) within one, two, or three days of, (iii) concurrently with and/or (iv) at first fever following, the initiation of administration of the cell therapy to the subject; and/or administering to the subject the cell therapy at a reduced dose or at a dose that is not associated with risk of developing toxicity or severe toxicity, or is not associated with a risk of developing a toxicity or severe toxicity in a majority of subjects, and/or a majority of subjects having a disease or condition that the subject has or is suspected of having, following administration of the cell therapy; and/or administering to the subject the cell therapy in an in-patient setting and/or with admission to the hospital for one or more days, optionally wherein the cell therapy is otherwise to be administered to subjects on an outpatient basis or without admission to the hospital for one or more days.

[0131] In particular examples of any of the provided articles of manufacture, the instructions further specify, if the level, amount or concentration of the analyte is below a threshold level for the analyte, administering to the subject the cell therapy, optionally at a non-reduced dose, optionally on an outpatient basis or without admission to the hospital for one or more days.

[0132] In certain examples of any of the provided articles of manufacture, the instructions further specify administering the cell therapy to the subject and wherein the instructions further specify, if the level, amount or concentration of the analyte, is below a threshold level: the administration of the cell therapy does not comprise administering, prior to or concurrently with administering the cell therapy and/or prior to the development of a sign of symptom of a toxicity other than fever, an agent or treatment capable of treating, preventing, delaying, or attenuating the development of the toxicity; and/or the administration of the cell therapy is to be or may be administered to the subject on an outpatient setting and/or without

admission of the subject to the hospital overnight or for one or more consecutive days and/or is without admission of the subject to the hospital for one or more days.

[0133] In some examples of any of the provided articles of manufacture, the threshold level is within 25%, within 20%, within 15%, within 10% or within 5% of the average level, amount or concenration, and/or is within a standard deviation of the average level, amount or concentration, of the analyte in a biological sample obtained from a group of subjects prior to receiving a recombinant receptor-expressing therapeutic cell composition, wherein each of the subjects of the group went on to develop a toxicity after receiving a recombinant-receptor-expressing therapeutic cell composition for treating the same disease or condition. Provided herein is an article of manufacture comprising a cell therapy, said cell therapy optionally comprising a dose or composition of genetically engineered cells expressing a recombinant receptor, and instructions for administering the cell therapy following or based on the results of an assessment, in a biological sample of the level, or amount or concentration of one or more analyte in a biological sample, said biological sample obtained from the subject prior to administering the cell therapy and/or said biological sample not comprising the recombinant receptor and/or said engineered cells, wherein the one or more analytes is selected from LDH, ferritin, CRP, IL-6, IL-7, IL-8, IL-10, IL-15, IL-16, TNF-alpha, IFN-gamma, MCP-1, MIP-1beta, eotaxin, G-CSF, IL-1Ralpha, IL-1Rbeta, IP-10, perforin, and D-dimer (fibrin degradation product).

[0134] In particular examples of any of the provided articles of manufacture, said assessment comprises detection which optionally comprises contacting a reagent capable of directly or indirectly detecting the analyte with the biological sample and determining the level, amount or concentration of the analyte in the biological sample. Certain examples of any of the provided articles of manufacture further comprise the reagent and/or further comprising instructions for use with, prior to and/or in connection with the reagent for detecting the analyte. Some examples of any of the provided articles of manufacture further comprise one or more agents or treatments for treating, preventing, delaying, reducing or attenuating the development or a risk of development of a toxicity and/or instructions for the administration of one or more agents or treatments for treating, preventing, delaying, reducing or attenuating the development or risk of development of a toxicity in the subject.

[0135] In particular examples of any of the provided articles of manufacture, the instructions for administering the cell therapy specify, if the level, amount or concentration of

the analyte in the sample, is at or above a threshold level: administering to the subject an agent or other treatment capable of treating, preventing, delaying, reducing or attenuating the development or risk of development of a toxicity (i) prior to, (ii) within one, two, or three days of, (iii) concurrently with and/or (iv) at first fever following, the initiation of administration of administration of the therapeutic cell composition or the genetically engineered cells; and/or administering to the subject the cell therapy at a reduced dose or at a dose that is not associated with risk of developing toxicity or severe toxicity, or is not associated with a risk of developing a toxicity or severe toxicity in a majority of subjects, and/or a majority of subjects having a disease or condition that the subject has or is suspected of having, following administration of the cell therapy; and/or administering to the subject the cell therapy in an in-patient setting and/or with admission to the hospital for one or more days, optionally wherein the cell therapy is otherwise to be administered to subjects on an outpatient basis or without admission to the hospital for one or more days.

[0136] In certain examples of any of the provided articles of manufacture, the instructions for administering the cell therapy specify, if the level, amount or concentration of the analyte in the sample, is below a threshold level, administering to the subject the cell therapy, optionally at a non-reduced dose, optionally on an outpatient basis or without admission to the hospital for one or more days. In some examples of any of the provided articles of manufacture, the instructions further specify administering the cell therapy to the subject and wherein the instructions further specify, if the level, amount or concentration of the analyte is below a threshold level: not administering, prior to or concurrently with administering the cell therapy and/or prior to the development of a sign or symptom of a toxicity other than fever, an agent or treatment capable of treating, preventing, delaying, or attenuating the development of the toxicity; and/or the administration of the cell therapy is to be or may be administered to the subject on an outpatient setting and/or without admission of the subject to the hospital overnight or for one or more consecutive days and/or is without admission of the subject to the hospital for one or more days.

[0137] In particular examples of any of the provided articles of manufacture, the threshold level is within 25%, within 20%, within 15%, within 10% or within 5% of the average level, amount or concentration, and/or is within a standard deviation of the average level, amount or concentration, of the analyte in a biological sample obtained from a group of subjects prior to receiving a recombinant receptor-expressing therapeutic cell composition, wherein each

of the subjects of the group went on to develop a toxicity after receiving a recombinant-receptor-expressing therapeutic cell composition for treating the same disease or condition.

[0138] Provided herein are articles of manufacture comprising an agent capable of treating, preventing, delaying, reducing or attenuating the development or risk of development of a toxicity, and instructions for administering the agent following or based on the results of an assessment in a biological sample of the level, amount or concentration of one or more analytes in a biological sample, wherein the one or more analytes is selected from LDH, ferritin, CRP, IL-6, IL-7, IL-8, IL-10, IL-15, IL-16, TNF-alpha, IFN-gamma, MCP-1, MIP-1beta, eotaxin, G-CSF, IL-1Ralpha, IL-1Rbeta, IP-10, perforin, and D-dimer (fibrin degradation product). In certain examples of any of the provided articles of manufacture, said assessment comprises detection which optionally comprises contacting a reagent capable of directly or indirectly detecting the analyte with the biological sample and determining the level, amount or concentration of the analyte in the biological sample.

[0139] In some examples of any of the provided articles of manufacture, the instructions specify that the agent is to be administered i) prior to, (ii) within one, two, or three days of, (iii) concurrently with and/or (iv) at first fever following, the initiation of administration of the cell therapy to the subject and/or further comprises instructions for use with, prior to and/or in connection with treatment with the cell therapy. In particular examples of any of the provided articles of manufacture, said biological sample is obtained from the subject prior to administering the agent or cell therapy. In certain examples of any of the provided articles of manufacture, the reagent is a binding molecule that specifically binds to the marker or cells of the myeloid cell population. In some examples of any of the provided articles of manufacture, the reagent is an antibody or an antigen-binding fragment thereof. In particular examples of any of the provided articles of manufacture, the biological sample is or is obtained from a blood, plasma or serum sample. In certain examples of any of the provided articles of manufacture, comprising the reagent for detecting the analyte and/or further comprising instructions for use with, prior to and/or in connection with the reagent for detecting the analyte. Some examples of any of the provided articles of manufacture further comprise the cell therapy and/or further comprising instructions for use with, prior to and/or in connection with treatment with the cell therapy.

[0140] In particular examples of any of the provided articles of manufacture, the instructions for administering the agent specify, if the level, amount or concentration of the

analyte in the sample, is at or above a threshold level administering to the subject the agent. In certain examples of any of the provided articles of manufacture, the instruction further specify administering a cell therapy to the subject, wherein administration of the agent is to be carried out (i) prior to, (ii) within one, two, or three days of, (iii) concurrently with and/or (iv) at first fever following, the initiation of administration of the cell therapy to the subject. In some examples of any of the provided articles of manufacture, the instructions for administering the agent specify, if the level, amount or concentration is below the threshold level administering to the subject the cell therapy, optionally.wherein the instructions specify the cell therapy is to be or may be administered to the subject on an outpatient setting and/or without admission of the subject to the hospital overnight or for one or more consecutive days and/or is without admission of the subject to the hospital for one or more days.

[0141] In particular examples of any of the provided articles of manufacture, the threshold level is within 25%, within 20%, within 15%, within 10% or within 5% of the average level, amount or concentration, and/or is within a standard deviation of the average level, amount or concentration, of the analyte in a biological sample obtained from a group of subjects prior to receiving a recombinant receptor-expressing therapeutic cell composition, wherein each of the subjects of the group went on to develop a toxicity after receiving a recombinant-receptor-expressing therapeutic cell composition for treating the same disease or condition. In certain examples of any of the provided articles of manufacture, assaying or assessing cells for the analyte is by an immunoassay.

[0142] In some examples of any of the provided articles of manufacture, the toxicity comprises neurotoxicity or cytokine release syndrome (CRS), optionally grade 1 or higher neurotoxicity or CRS. In particular examples of any of the provided articles of manufacture: the toxicity comprises severe neurotoxicity and/or comprises a grade 2 or higher neurotoxicity, a grade 3 or higher neurotoxicity, at least prolonged grade 3 neurotoxicity or is at or above grade 4 or grade 5 neurotoxicity; and/or the toxicity comprises severe CRS and/or comprises grade 2 or higher or grade 3 or higher CRS. In certain examples of any of the provided articles of manufacture, the toxicity is associated with cerebral edema.

[0143] In some examples of any of the provided articles of manufacture, the agent or other treatment is or comprises one or more of a steroid; an antagonist or inhibitor of a cytokine receptor or cytokine selected from among IL-10, IL-10R, IL-6, IL-6 receptor, IFNγ, IFNGR, IL-2, IL-2R/CD25, MCP-1, CCR2, CCR4, MIP1β, CCR5, TNFalpha, TNFR1, IL-1, and IL-

1Ralpha/IL-1beta; or an agent capable of preventing, blocking or reducing microglial cell activity or function. In particular examples of any of the provided articles of manufacture, the antagonist or inhibitor is or comprises an agent selected from among an antibody or antigen-binding fragment, a small molecule, a protein or peptide and a nucleic acid. In certain examples of any of the provided articles of manufacture, the agent or other treatment is an anti-IL-6 antibody or an anti-IL6 receptor antibody.

[0144] In some examples of any of the provided articles of manufacture, the agent or other treatment is or comprises an agent selected from among tocilizumab, siltuximab, clazakizumab, sarilumab, olokizumab (CDP6038), elsilimomab, ALD518/BMS-945429, sirukumab (CNTO 136), CPSI-2634, ARGX-109, FE301 and FM101. In particular examples of any of the provided articles of manufacture, the agent or other treatment is or comprises tocilizumab. In certain examples of any of the provided articles of manufacture, the agent or other treatment is or comprises siltuximab. In some examples of any of the provided articles of manufacture, the steroid is or comprises dexamethasone.

[0145] In particular examples of any of the provided articles of manufacture, the agent capable of preventing, blocking or reducing microglial cell activity or function is selected from an anti-inflammatory agent, an inhibitor of NADPH oxidase (NOX2), a calcium channel blocker, a sodium channel blocker, inhibits GM-CSF, inhibits CSF1R, specifically binds CSF-1, specifically binds IL-34, inhibits the activation of nuclear factor kappa B (NF-κB), activates a CB_2 receptor and/or is a CB_2 agonist, a phosphodiesterase inhibitor, inhibits microRNA-155 (miR-155) or upregulates microRNA-124 (miR-124). In certain examples of any of the provided articles of manufacture, the agent capable of preventing, blocking or reducing microglial cell activation or function is a small molecule, peptide, protein, antibody or antigen-binding fragment thereof, an antibody mimetic, an aptamer, or a nucleic acid molecule.

[0146] In some examples of any of the provided articles of manufacture, the agent is selected from minocycline, naloxone, nimodipine, Riluzole, MOR103, lenalidomide, a cannabinoid (optionally WIN55 or 212-2), intravenous immunoglobulin (IVIg), ibudilast, anti-miR-155 locked nucleic acid (LNA), MCS110, PLX-3397, PLX647, PLX108-D1, PLX7486, JNJ-40346527, JNJ28312141, ARRY-382, AC-708, DCC-3014, 5-(3-methoxy-4-((4-methoxybenzyl)oxy)benzyl)pyrimidine-2,4-diamine (GW2580), AZD6495, Ki20227, BLZ945, emactuzumab, IMC-CS4, FPA008, LY-3022855, AMG-820 and TG-3003. In particular examples of any of the provided articles of manufacture, the agent is an inhibitor of colony

stimulating factor 1 receptor (CSF1R). In certain examples of any of the provided articles of manufacture, the inhibitor is selected from: PLX-3397, PLX647, PLX108-D1, PLX7486, JNJ-40346527, JNJ28312141, ARRY-382, AC-708, DCC-3014, 5-(3-methoxy-4-((4-methoxybenzyl)oxy)benzyl)pyrimidine-2,4-diamine (GW2580), AZD6495, Ki20227, BLZ945 or a pharmaceutical salt or prodrug thereof; emactuzumab, IMC-CS4, FPA008, LY-3022855, AMG-820 and TG-3003 or is an antigen-binding fragment thereof; or a combination of any of the foregoing. In some examples of any of the provided articles of manufacture, the inhibitor is PLX-3397.

[0147] In certain examples of any of the provided articles of manufacture, the disease or condition is a cancer. In particular examples of any of the provided articles of manufacture, the disease or condition is a myeloma, leukemia or lymphoma. In some examples of any of the provided articles of manufacture, the disease or condition is a B cell malignancy and/or is acute lymphoblastic leukemia (ALL), adult ALL, chronic lymphoblastic leukemia (CLL), non-Hodgkin lymphoma (NHL), and Diffuse Large B-Cell Lymphoma (DLBCL).

[0148] In certain examples of any of the provided articles of manufacture, the antigen is ROR1, B cell maturation antigen (BCMA), carbonic anhydrase 9 (CAIX), tEGFR, Her2/neu (receptor tyrosine kinase erbB2), L1-CAM, CD19, CD20, CD22, mesothelin, CEA, and hepatitis B surface antigen, anti-folate receptor, CD23, CD24, CD30, CD33, CD38, CD44, EGFR, epithelial glycoprotein 2 (EPG-2), epithelial glycoprotein 40 (EPG-40), EPHa2, erb-B2, erb-B3, erb-B4, erbB dimers, EGFR vIII, folate binding protein (FBP), FCRL5, FCRH5, fetal acetylcholine receptor, GD2, GD3, HMW-MAA, IL-22R-alpha, IL-13R-alpha2, kinase insert domain receptor (kdr), kappa light chain, Lewis Y, L1-cell adhesion molecule, (L1-CAM), Melanoma-associated antigen (MAGE)-A1, MAGE-A3, MAGE-A6, Preferentially expressed antigen of melanoma (PRAME), survivin, TAG72, B7-H6, IL-13 receptor alpha 2 (IL-13Ra2), CA9, GD3, HMW-MAA, CD171, G250/CAIX, HLA-AI MAGE Al, HLA-A2 NY-ESO-1, PSCA, folate receptor-a, CD44v6, CD44v7/8, avb6 integrin, 8H9, NCAM, VEGF receptors, 5T4, Foetal AchR, NKG2D ligands, CD44v6, dual antigen, a cancer-testes antigen, mesothelin, murine CMV, mucin 1 (MUC1), MUC16, PSCA, NKG2D, NY-ESO-1, MART-1, gp100, oncofetal antigen, ROR1, TAG72, VEGF-R2, carcinoembryonic antigen (CEA), Her2/neu, estrogen receptor, progesterone receptor, ephrinB2, CD123, c-Met, GD-2, O-acetylated GD2 (OGD2), CE7, Wilms Tumor 1 (WT-1), a cyclin, cyclin A2, CCL-1, CD138, G Protein Coupled Receptor 5D (GPCR5D), or a pathogen-specific antigen.

[0149] In particular examples of any of the provided articles of manufacture, the recombinant receptor is a T cell receptor or a functional non-T cell receptor. In some examples of any of the provided articles of manufacture, the recombinant receptor is a chimeric antigen receptor (CAR). In certain examples of any of the provided articles of manufacture, the CAR comprises an extracellular antigen-recognition domain that specifically binds to the antigen and an intracellular signaling domain comprising an ITAM, wherein optionally, the intracellular signaling domain comprises an intracellular domain of a CD3-zeta (CD3ζ) chain; and/or wherein the CAR further comprises a costimulatory signaling region, which optionally comprises a signaling domain of CD28 or 4-1BB.

[0150] In particular examples of any of the provided articles of manufacture, the engineered cells comprise T cells, optionally $CD4^+$ and/or $CD8^+$. In some examples of any of the provided articles of manufacture, the T cells are primary T cells obtained from a subject. In certain examples of any of the provided articles of manufacture, the dose that is not associated with risk of developing toxicity or severe toxicity is or comprises less than or less than about 5×10^7 total recombinant receptor-expressing cells, optionally CAR^+ cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), such as less than or less than about 2.5×10^7, less than or less than about 1.0×10^7, less than or less than about 5.0×10^6, less than or less than about 1.0×10^6, less than or less than about 5.0×10^5, or less than or less than about 1×10^5 total recombinant receptor-expressing cells, optionally CAR^+ cells, total T cells, or total peripheral blood mononuclear cells (PBMCs). In particular examples of any of the provided articles of manufacture, the dose that is not associated with risk of developing toxicity or severe toxicity is or comprises from or from about 1×10^5 to 5×10^7 total recombinant receptor-expressing cells, optionally CAR^+ cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), such as 1×10^5 to 2.5×10^7, 1×10^5 to 1.0×10^7, 1×10^5 to 5.0×10^6, 1×10^5 to 1.0×10^6, 1.0×10^5 to 5.0×10^5, 5.0×10^5 to 5×10^7, 5×10^5 to 2.5×10^7, 5×10^5 to 1.0×10^7, 5×10^5 to 5.0×10^6, 5×10^5 to 1.0×10^6, 1.0×10^6 to 5×10^7, 1×10^6 to 2.5×10^7, 1×10^6 to 1.0×10^7, 1×10^6 to 5.0×10^6, 5.0×10^6 to 5×10^7, 5×10^6 to 2.5×10^7, 5×10^6 to 1.0×10^7, 1.0×10^7 to 5×10^7, 1×10^7 to 2.5×10^7 or 2.5×10^7 to 5×10^7 total recombinant receptor-expressing cells, optionally CAR^+ cells, total T cells, or total peripheral blood mononuclear cells (PBMCs).

[0151] In certain examples of any of the provided articles of manufacture, the reagent is detectably labeled, optionally fluorescently labeled. In some examples of any of the provided articles of manufacture, the one or more analyte is LDH, ferritin, CRP, IL-6, IL-8, IL-

10, TNF-alpha, IFN-alpha2, MCP-1 and MCP-1beta. In particular examples of any of the provided articles of manufacture, the one or more analyte is or comprises LDH.

[0152] Provided herein are methods of selecting a subject for treatment, the method comprising:(a) contacting a biological sample with one or more reagent capable of detecting or that is specific for one or more analyte, wherein the one or more analyte is selected from LDH, ferritin, CRP, IL-6, IL-7, IL-8, IL-10, IL-15, IL-16, TNF-alpha, IFN-gamma, MCP-1, MIP-1beta, eotaxin, G-CSF, IL-1Ralpha, IL-1Rbeta, IP-10, perforin, and D-dimer (fibrin degradation product), wherein: the biological sample is from a subject that is a candidate for treatment with a cell therapy, said cell therapy optionally comprising a dose or composition of genetically engineered cells expressing a recombinant receptor ; and the biological sample is obtained from the subject prior to administering the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and (b) selecting a subject in which either: (i) the level, amount or concentration of the analyte in the samples at or above a threshold level, thereby identifying a subject that is at risk for developing a toxicity to the cell therapy; or (ii) the level, amount or concentration of the analyte is below a threshold level.

[0153] In certain examples of any of the provided methods: (a) a subject in (i) is selected for administering to the subject (1) an agent or other treatment capable of treating, preventing, delaying, reducing or attenuating the development or risk of development of a toxicity and (2) the cell therapy, wherein administration of the agent is to be administered (i) prior to, (ii) within one, two, or three days of, (iii) concurrently with and/or (iv) at first fever following, the initiation of administration of the cell therapy to the subject; and/or (c) a subject in (i) is selected for administering to the subject a cell therapy at a reduced dose or at a dose that is not associated with risk of developing toxicity or severe toxicity, or is not associated with a risk of developing a toxicity or severe toxicity in a majority of subjects, and/or a majority of subjects having a disease or condition that the subject has or is suspected of having, following administration of the cell therapy; and/or (b) a subject in (i) is selected for administering to the subject a cell therapy in an in-patient setting and/or with admission to the hospital for one or more days, optionally wherein the cell therapy is otherwise to be administered to subjects on an outpatient basis or without admission to the hospital for one or more days.

[0154] In some examples of any of the provided methods, a subject in (i) is selected, and the method further comprises: (a) administering to the subject (1) an agent or other treatment capable of treating, preventing, delaying, reducing or attenuating the development or risk of

development of a toxicity and (2) the cell therapy, wherein administration of the agent is carried out (i) prior to, (ii) within one, two, or three days of, (iii) concurrently with and/or (iv) at first fever following, the initiation of administration of the cell therapy to the subject; and/or (b) administering to the subject a cell therapy at a reduced dose or at a dose that is not associated with risk of developing toxicity or severe toxicity, or is not associated with a risk of developing a toxicity or severe toxicity in a majority of subjects, and/or a majority of subjects having a disease or condition that the subject has or is suspected of having, following administration of the cell therapy; and/or (c) administering to the subject a cell therapy or a dose of genetically engineered cells of a cell therapy that is not associated with risk of developing toxicity or severe toxicity, or is not associated with a risk of developing a toxicity or severe toxicity in a majority of subjects, and/or a majority of subjects having a disease or condition that the subject has or is suspected of having, following administration of the cell therapy; and/or (d) administering to the subject a cell therapy in an in-patient setting and/or with admission to the hospital for one or more days, optionally wherein the cell therapy is otherwise to be administered to subjects on an outpatient basis or without admission to the hospital for one or more days.

[0155] In particular examples of any of the provided methods: (a) a subject in (ii) is selected for administering to the subject a cell therapy, optionally at a non-reduced dose, optionally on an outpatient basis or without admission to the hospital for one or more days; (b) a subject in (ii) is selected for administering to the subject a cell therapy, wherein the cell therapy does not comprise administering, prior to or concurrently with administering the cell therapy and/or prior to the development of a sign or symptom of a toxicity other than fever, an agent or treatment capable of treating, preventing, delaying, or attenuating the development of the toxicity; and/or a subject in (ii) is selected for administering a cell therapy on an outpatient setting and/or without admission of the subject to the hospital overnight or for one or more consecutive days and/or is without admission of the subject to the hospital for one or more days.

[0156] In certain examples of any of the provided methods, a subject in (ii) is selected, and the method further comprises administering to the subject the cell therapy, optionally at a non-reduced dose, optionally on an outpatient basis or without admission to the hospital for one or more days. In some examples of any of the provided methods, a subject in (ii) is selected, and the method further comprises administering to the subject the cell therapy, wherein: the administration of the cell therapy does not comprise administering, prior to or concurrently with administering the cell therapy and/or prior to the development of a sign or symptom of a toxicity

other than fever, an agent or treatment capable of treating, preventing, delaying, or attenuating the development of the toxicity; and/or the administration of the cell therapy is to be or may be administered to the subject on an outpatient setting and/or without admission of the subject to the hospital overnight or for one or more consecutive days and/or is without admission of the subject to the hospital for one or more days.

[0157] Provided herein is a method of treatment, comprising: (a) assaying a biological sample for the level, amount or concentration of one or more analyte, wherein the biological sample is from a subject that is a candidate for treatment, optionally with a cell therapy, said cell therapy optionally comprising a dose or composition of genetically engineered cells expressing a recombinant receptor for treating a disease or condition, wherein the one or more analyte is selected from LDH, ferritin, CRP, IL-6, IL-7, IL-8, IL-10, IL-15, IL-16, TNF-alpha, IFN-gamma, MCP-1, MIP-1beta, eotaxin, G-CSF, IL-1Ralpha, IL-1Rbeta, IP-10, perforin, and D-dimer (fibrin degradation product); and (b) following or based on the results of the assay, administering to the subject the cell therapy, and, optionally, an agent or other treatment capable of treating, preventing, delaying, reducing or attenuating the development or risk of development of a toxicity.

[0158] Provided herein is a method of treatment, comprising, following or based on the results of an assay, of a biological sample from a subject, for the level, amount or concentration of one or more analyte, administering to the subject (i) a cell therapy, optionally comprising a dose or composition of genetically engineered expressing a recombinant receptor for treating a disease or condition, and, optionally, (ii) an agent or other treatment capable of treating, preventing, delaying, reducing or attenuating the development or risk of development of a toxicity, wherein: the biological sample is obtained from the subject prior to administering the cell therapy; and the one or more analyte is selected from LDH, ferritin, CRP, IL-6, IL-7, IL-8, IL-10, IL-15, IL-16, TNF-alpha, IFN-gamma, MCP-1, MIP-1beta, eotaxin, G-CSF, IL-1Ralpha, IL-1Rbeta, IP-10, perforin, and D-dimer (fibrin degradation product).

[0159] In particular examples of any of the provided methods, said assaying comprises detection which optionally comprises contacting a reagent capable of directly or indirectly detecting the analyte with the biological sample and determining the level, amount or concentration of the analyte in the biological sample. In certain examples of any of the provided methods, if the level, amount or concentration of the analyte in the sample, is at or above a threshold level: administering to the subject the agent or other treatment capable of

treating, preventing, delaying, reducing or attenuating the development or risk of development of a toxicity (i) prior to, (ii) within one, two, or three days of, (iii) concurrently with and/or (iv) at first fever following, the initiation of administration of the cell therapy to the subject; and/or administering to the subject the cell therapy at a reduced dose or at a dose that is not associated with risk of developing toxicity or severe toxicity, or is not associated with a risk of developing a toxicity or severe toxicity in a majority of subjects, and/or a majority of subjects having a disease or condition that the subject has or is suspected of having, following administration of the cell therapy; and/or administering to the subject the cell therapy in an in-patient setting and/or with admission to the hospital for one or more days, optionally wherein the cell therapy is otherwise to be administered to subjects on an outpatient basis or without admission to the hospital for one or more days.

[0160] In some examples of any of the provided methods, if the level, amount or concentration of the analyte, is at or above a threshold level: the administration of the cell therapy does not comprise administering, prior to or concurrently with administering the cell therapy and/or prior to the development of a sign or symptom of a toxicity other than fever, an agent or treatment capable of treating, preventing, delaying, or attenuating the development of the toxicity; and/or the administration of the cell therapy is to be or may be administered to the subject on an outpatient setting and/or without admission of the subject to the hospital overnight or for one or more consecutive days and/or is without admission of the subject to the hospital for one or more days.

[0161] In particular examples of any of the provided methods, administering, to a subject, an agent or other treatment capable of treating, preventing, delaying, reducing or attenuating the development or risk of development of a toxicity, wherein: the subject is a candidate for treatment optionally with a cell therapy, said cell therapy optionally comprising a dose or composition of genetically engineered cells expressing a recombinant receptor for treating a disease or condition; and the subject has been identified as at risk for developing a toxicity following or based on the results of an assay, of a biological sample from a subject, for the level, amount or concentration of one or more analyte, said biological sample obtained from the subject prior to administering the cell therapy and/or said biological sample not comprising the recombinant receptor and/or said engineered cells, wherein the one or more analyte is selected from LDH, ferritin, CRP, IL-6, IL-7, IL-8, IL-10, IL-15, IL-16, TNF-alpha, IFN-

gamma, MCP-1, MIP-1beta, eotaxin, G-CSF, IL-1Ralpha, IL-1Rbeta, IP-10, perforin, and D-dimer (fibrin degradation product).

[0162] In certain examples of any of the provided methods, said assay comprises detection which optionally comprises contacting a reagent capable of directly or indirectly detecting the analye with the biological sample and determining the level, amount or concentration of the analyte in the biological sample. In some examples of any of the provided methods, the agent is administered to the subject if the level, amount or concentration of the analyte in the sample is at or above a threshold level.

[0163] In particular examples of any of the provided methods, the agent is administered (i) prior to, (ii) within one, two, or three days of, (iii) concurrently with and/or (iv) at first fever following, the initiation of administration of the cell therapy to the subject. In certain examples of any of the provided methods, the threshold level is within 25%, within 20%, within 15%, within 10% or within 5% of the average percent or number, and/or is within a standard deviation of the average percent or number, of cells surface positive for the myeloid marker in a biological sample obtained from a group of subjects prior to receiving a recombinant receptor-expressing therapeutic cell composition, wherein each of the subjects of the group went on to develop a toxicity after receiving a recombinant-receptor-expressing therapeutic cell composition for treating the same disease or condition.

[0164] In particular examples of any of the provided methods, the threshold level is within 25%, within 20%, within 15%, within 10% or within 5% of the average level, amount or concentration, and/or is within a standard deviation of the average level, amount or concentration, of the analyte in a biological sample obtained from a group of subjects prior to receiving a recombinant receptor-expressing therapeutic cell composition, wherein each of the subjects of the group went on to develop a toxicity after receiving a recombinant-receptor-expressing therapeutic cell composition for treating the same disease or condition. In certain examples of any of the provided methods, the reagent is a binding molecule that specifically binds to the marker or cells of the myeloid cell population. In some examples of any of the provided methods, the reagent is an antibody or an antigen-binding fragment thereof. In particular examples of any of the provided methods, the biological sample is or is obtained from a blood, plasma or serum sample. In certain examples of any of the provided methods, assaying or assessing cells the analyte comprises an immunoassay.

[0165] In some examples of any of the provided methods, the toxicity comprises neurotoxicity or cytokine release syndrome (CRS), optionally grade 1 or higher neurotoxicity or CRS. In particular examples of any of the provided methods: the toxicity comprises severe neurotoxicity and/or comprises a grade 2 or higher neurotoxicity, a grade 3 or higher neurotoxicity, at least prolonged grade 3 neurotoxicity or is at or above grade 4 or grade 5 neurotoxicity; and/or the toxicity comprises severe CRS and/or comprises grade 2 or higher or grade 3 or higher CRS. In certain examples of any of the provided methods, the toxicity is associated with cerebral edema.

[0166] In some examples of any of the provided methods, the agent or other treatment is or comprises one or more of a steroid; an antagonist or inhibitor of a cytokine receptor or cytokine selected from among IL-10, IL-10R, IL-6, IL-6 receptor, IFNγ, IFNGR, IL-2, IL-2R/CD25, MCP-1, CCR2, CCR4, MIP1β, CCR5, TNFalpha, TNFR1, IL-1, and IL-1Ralpha/IL-1beta; or an agent capable of preventing, blocking or reducing microglial cell activity or function. In particular examples of any of the provided methods, the antagonist or inhibitor is or comprises an agent selected from among an antibody or antigen-binding fragment, a small molecule, a protein or peptide and a nucleic acid.

[0167] In certain examples of any of the provided methods, the agent or other treatment is an anti-IL-6 antibody or an anti-IL6 receptor antibody. In some examples of any of the provided methods, the agent or other treatment is or comprises an agent selected from among tocilizumab, siltuximab, clazakizumab, sarilumab, olokizumab (CDP6038), elsilimomab, ALD518/BMS-945429, sirukumab (CNTO 136), CPSI-2634, ARGX-109, FE301 and FM101. In particular examples of any of the provided methods, the agent or other treatment is or comprises tocilizumab. In certain examples of any of the provided methods, the agent or other treatment is or comprises siltuximab.

[0168] In some examples of any of the provided methods, the steroid is or comprises dexamethasone. In particular examples of any of the provided methods, the agent capable of preventing, blocking or reducing microglial cell activity or function is selected from an anti-inflammatory agent, an inhibitor of NADPH oxidase (NOX2), a calcium channel blocker, a sodium channel blocker, inhibits GM-CSF, inhibits CSF1R, specifically binds CSF-1, specifically binds IL-34, inhibits the activation of nuclear factor kappa B (NF-κB), activates a CB_2 receptor and/or is a CB_2 agonist, a phosphodiesterase inhibitor, inhibits microRNA-155 (miR-155) or upregulates microRNA-124 (miR-124).

[0169] In certain examples of any of the provided methods, the agent capable of preventing, blocking or reducing microglial cell activation or function is a small molecule, peptide, protein, antibody or antigen-binding fragment thereof, an antibody mimetic, an aptamer, or a nucleic acid molecule. In some examples of any of the provided methods, the agent is selected from minocycline, naloxone, nimodipine, Riluzole, MOR103, lenalidomide, a cannabinoid (optionally WIN55 or 212-2), intravenous immunoglobulin (IVIg), ibudilast, anti-miR-155 locked nucleic acid (LNA), MCS110, PLX-3397, PLX647, PLX108-D1, PLX7486, JNJ-40346527, JNJ28312141, ARRY-382, AC-708, DCC-3014, 5-(3-methoxy-4-((4-methoxybenzyl)oxy)benzyl)pyrimidine-2,4-diamine (GW2580), AZD6495, Ki20227, BLZ945, emactuzumab, IMC-CS4, FPA008, LY-3022855, AMG-820 and TG-3003.

[0170] In particular examples of any of the provided methods, the agent is an inhibitor of colony stimulating factor 1 receptor (CSF1R). In certain examples of any of the provided methods, the inhibitor is selected from: PLX-3397, PLX647, PLX108-D1, PLX7486, JNJ-40346527, JNJ28312141, ARRY-382, AC-708, DCC-3014, 5-(3-methoxy-4-((4-methoxybenzyl)oxy)benzyl)pyrimidine-2,4-diamine (GW2580), AZD6495, Ki20227, BLZ945 or a pharmaceutical salt or prodrug thereof; emactuzumab, IMC-CS4, FPA008, LY-3022855, AMG-820 and TG-3003 or is an antigen-binding fragment thereof; or a combination of any of the foregoing.

[0171] In some examples of any of the provided methods, the inhibitor is PLX-3397. In particular examples of any of the provided methods, the recombinant receptor specifically binds to an antigen associated with the disease or condition or expressed in cells of the environment of a lesion associated with the disease or condition. In certain examples of any of the provided methods, the disease or condition is a cancer. In some examples of any of the provided methods, the disease or condition is a myeloma, leukemia or lymphoma. In particular examples of any of the provided methods, the disease or condition is a B cell malignancy and/or is acute lymphoblastic leukemia (ALL), adult ALL, chronic lymphoblastic leukemia (CLL), non-Hodgkin lymphoma (NHL), and Diffuse Large B-Cell Lymphoma (DLBCL).

[0172] In certain examples of any of the provided methods,the antigen is ROR1, B cell maturation antigen (BCMA), carbonic anhydrase 9 (CAIX), tEGFR, Her2/neu (receptor tyrosine kinase erbB2), L1-CAM, CD19, CD20, CD22, mesothelin, CEA, and hepatitis B surface antigen, anti-folate receptor, CD23, CD24, CD30, CD33, CD38, CD44, EGFR, epithelial

glycoprotein 2 (EPG-2), epithelial glycoprotein 40 (EPG-40), EPHa2, erb-B2, erb-B3, erb-B4, erbB dimers, EGFR vIII, folate binding protein (FBP), FCRL5, FCRH5, fetal acetylcholine receptor, GD2, GD3, HMW-MAA, IL-22R-alpha, IL-13R-alpha2, kinase insert domain receptor (kdr), kappa light chain, Lewis Y, L1-cell adhesion molecule, (L1-CAM), Melanoma-associated antigen (MAGE)-A1, MAGE-A3, MAGE-A6, Preferentially expressed antigen of melanoma (PRAME), survivin, TAG72, B7-H6, IL-13 receptor alpha 2 (IL-13Ra2), CA9, GD3, HMW-MAA, CD171, G250/CAIX, HLA-AI MAGE Al, HLA-A2 NY-ESO-1, PSCA, folate receptor-a, CD44v6, CD44v7/8, avb6 integrin, 8H9, NCAM, VEGF receptors, 5T4, Foetal AchR, NKG2D ligands, CD44v6, dual antigen, a cancer-testes antigen, mesothelin, murine CMV, mucin 1 (MUC1), MUC16, PSCA, NKG2D, NY-ESO-1, MART-1, gp100, oncofetal antigen, ROR1, TAG72, VEGF-R2, carcinoembryonic antigen (CEA), Her2/neu, estrogen receptor, progesterone receptor, ephrinB2, CD123, c-Met, GD-2, O-acetylated GD2 (OGD2), CE7, Wilms Tumor 1 (WT-1), a cyclin, cyclin A2, CCL-1, CD138, G Protein Coupled Receptor 5D (GPCR5D), or a pathogen-specific antigen.

[0173] In some examples of any of the provided methods, the recombinant receptor is a T cell receptor or a functional non-T cell receptor. In particular examples of any of the provided methods, the recombinant receptor is a chimeric antigen receptor (CAR). In certain examples of any of the provided methods, the CAR comprises an extracellular antigen-recognition domain that specifically binds to the antigen and an intracellular signaling domain comprising an ITAM, wherein optionally, the intracellular signaling domain comprises an intracellular domain of a CD3-zeta (CD3ζ) chain; and/or wherein the CAR further comprises a costimulatory signaling region, which optionally comprises a signaling domain of CD28 or 4-1BB.

[0174] In some examples of any of the provided methods, the engineered cells comprise T cells, optionally $CD4^+$ and/or $CD8^+$. In particular examples of any of the provided methods, the T cells are primary T cells obtained from a subject. In certain examples of any of the provided methods, the cell therapy comprises the administration of from or from about 1×10^5 to 1×10^8 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), from or from about 5×10^5 to 1×10^7 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs) or from or from about 1×10^6 to 1×10^7 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), each inclusive.

[0175] In some examples of any of the provided methods, the cell therapy comprises the administration of no more than 1 x 10^8 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), no more than 1 x 10^7 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), no more than 0.5 x 10^7 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), no more than 1 x 10^6 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), no more than 0.5 x 10^6 total recombinant receptor-expressing cells, total T cells, or total peripheral blood mononuclear cells (PBMCs).

[0176] In particular examples of any of the provided methods, the dose that is not associated with risk of developing toxicity or severe toxicity is or comprises less than or less than about 5 x 10^7 total recombinant receptor-expressing cells, optionally CAR^+ cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), such as less than or less than about 2.5 x 10^7, less than or less than about 1.0 x 10^7, less than or less than about 5.0 x 10^6, less than or less than about 1.0 x 10^6, less than or less than about 5.0 x 10^5, or less than or less than about 1 x 10^5 total recombinant receptor-expressing cells, optionally CAR^+ cells, total T cells, or total peripheral blood mononuclear cells (PBMCs).

[0177] In certain examples of any of the provided methods, the dose that is not associated with risk of developing toxicity or severe toxicity is or comprises from or from about 1 x 10^5 to 5 x 10^7 total recombinant receptor-expressing cells, optionally CAR^+ cells, total T cells, or total peripheral blood mononuclear cells (PBMCs), such as 1 x 10^5 to 2.5 x 10^7, 1 x 10^5 to 1.0 x 10^7, 1 x 10^5 to 5.0 x 10^6, 1 x 10^5 to 1.0 x 10^6, 1.0 x 10^5 to 5.0 x 10^5, 5.0 x 10^5 to 5 x 10^7, 5 x 10^5 to 2.5 x 10^7, 5 x 10^5 to 1.0 x 10^7, 5 x 10^5 to 5.0 x 10^6, 5 x 10^5 to 1.0 x 10^6, 1.0 x 10^6 to 5 x 10^7, 1 x 10^6 to 2.5 x 10^7, 1 x 10^6 to 1.0 x 10^7, 1 x 10^6 to 5.0 x 10^6, 5.0 x 10^6 to 5 x 10^7, 5 x 10^6 to 2.5 x 10^7, 5 x 10^6 to 1.0 x 10^7, 1.0 x 10^7 to 5 x 10^7, 1 x 10^7 to 2.5 x 10^7 or 2.5 x 10^7 to 5 x 10^7 total recombinant receptor-expressing cells, optionally CAR^+ cells, total T cells, or total peripheral blood mononuclear cells (PBMCs). In some examples of any of the provided methods, the engineered cells are autologous to the subject. In particular examples of any of the provided methods, the engineered cells are allogeneic to the subject. In certain examples of any of the provided methods, the reagent is detectably labeled, optionally fluorescently labeled.

[0178] In some examples, the instructions provide information about a threshold level, individually for each of the one or more analytes, that is indicative of whether a subject is likely to exhibit a response to treatment with the cell therapy. In some examples, the instructions provide information about a threshold level, individually for each of the one or more analytes, that is indicative of whether a subject is likely to exhibit a durable response following administration of the cell therapy. In some examples, the instructions provide information about a threshold level, individually for each of the one or more analytes, that is indicative of whether a subject is likely to exhibit a toxicity following administration of the cell therapy.

Brief Description of the Drawings

[0179] **FIG. 1** shows the percentage of subjects who experienced laboratory abnormalities and treatment-emergent adverse events (TEAEs) that occurred in ≥20% of subjects. *: One Grade 5 AE of multi-organ failure unrelated to study treatment and due to progression of lymphoma; †: One Grade 5 AE of diffuse alveolar damage, investigator assessed as related to fludarabine, cyclophosphamide, and CAR T cell therapy, occurred on day 23 in a subject who refused mechanical ventilation for progressive respiratory failure while neutropenic on growth factors and broad spectrum antibiotics and antifungals

[0180] **FIG. 2** is a Kaplan meier curve depicting observed time to onset of CRS and neurotoxicity.

[0181] **FIG. 3A** and **FIG. 3B** depict 3 month objective response rates (ORR) among subgroups of treated subjects.

[0182] **FIG. 4A** and **FIG. 4B** show the duration of response (CR/PR, CR or PR) and overall survival in the full and core cohort of subjects.

[0183] **FIG. 5A** shows the pharmacokinetics of the CAR^+ T cells in peripheral blood at various time points post-treatment at different dose levels. **FIG. 5B** shows the pharmacokinetics of the CAR^+ T cells in peripheral blood at various time points post-treatment between responders and nonresponders. **FIG. 5C** shows the pharmacokinetics of the CAR^+ T cells in peripheral blood at various time points post-treatment in subjects that did or did not develop any neurotoxicity.

[0184] **FIG. 6A** shows the number of $CD3^+/CAR^+$, $CD4^+/CAR^+$, $CD8^+/CAR^+$ T cells in peripheral blood of a subject with chemorefractory transformed DLBCL measured at certain time points. **FIG. 6B** depicts a pretreatment axial PET-CT image showing an intracranial

CLAIMS

1. Use of a first composition comprising CD4+ T cells in the manufacture of a medicament for treating a subject having or suspected of having a disease or condition with a dose of $CD4^+$ T cells and $CD8^+$ T cells, wherein:

the medicament is to be administered with a second composition comprising CD8+ T cells;

each of the $CD4^+$ T cells and the $CD8^+$ T cells, individually, comprises a recombinant receptor that specifically binds to a target antigen expressed by the disease or condition or a cell or tissue thereof and/or that is associated with the disease or condition; and the dose of the CD4+ T cells and CD8+ T cells is to be administered as a plurality of separate compositions, the plurality of separate compositions comprising the first composition comprising the $CD4^+$ T cells and the second composition comprising the $CD8^+$ T cells.

2. Use of a first composition comprising CD8+ T cells in the manufacture of a medicament for treating a subject having or suspected of having a disease or condition with a dose of $CD4^+$ T cells and $CD8^+$ T cells, wherein:

the medicament is to be administered with a second composition comprising CD4+ T cells;

each of the $CD4^+$ T cells and the $CD8^+$ T cells, individually, comprises a recombinant receptor that specifically binds to a target antigen expressed by the disease or condition or a cell or tissue thereof and/or that is associated with the disease or condition; and

the dose of the CD4+ T cells and CD8+ T cells is to be administered as a plurality of separate compositions, the plurality of separate compositions comprising the first composition comprising the $CD8^+$ T cells and the second composition comprising the $CD4^+$ T cells.

3. The use of claim 1 or claim 2, wherein the recombinant receptor comprised by the $CD4^+$ T cells and the recombinant receptor comprised by the $CD8^+$ T cells comprises a recombinant receptor that is the same and/or wherein the $CD4^+$ T cells and the $CD8^+$ T cells are genetically engineered to express a recombinant receptor that is the same.

4. The use of any of claims 1-3, wherein:

the first composition and the second composition are to be administered on the same day, between about 0 and about 12 hours apart, between about 0 and about 6 hours apart or between about 0 and about 2 hours apart; or

the first composition and the second composition are to be administered between about 1 minute and about 1 hour apart or between about 5 minutes and about 30 minutes apart.

5. The use of any of claims 1-4, wherein the first composition and the second composition are to be administered no more than 2 hours, no more than 1 hour, no more than 30 minutes, no more than 15 minutes, no more than 10 minutes or no more than 5 minutes apart.

6. The use of any of claims 1-5, wherein the composition comprising the CD8+ T cells is to be administered prior to the composition comprising the CD4+ T cells.

7. The use of any of claims 1-6, wherein

the dose of $CD4^+$ and $CD8^+$ T cells comprises a defined ratio of $CD4^+$ cells expressing a recombinant receptor to $CD8^+$ cells expressing a recombinant receptor and/or of $CD4^+$ cells to $CD8^+$ cells, that is or is approximately 1:1 or is between approximately 1:3 and approximately 3:1.

8. The use of claim 7, wherein the defined ratio is or is approximately 1:1.

9. The use of any of claims 1-8, wherein the dose of $CD4^+$ and $CD8^+$ T cells comprises

between at or about 1 x 10^7 and at or about 2 x 10^8 total recombinant receptor-expressing T cells, inclusive.

10. The use of any of claims 1-9, wherein the disease or condition is a cancer.

11. The use of any of claims 1-10, wherein the recombinant receptor is a chimeric antigen receptor (CAR).

12. The use of any of claims 1-11, wherein the T cells are autologous to the subject.

13. An article of manufacture comprising (1) a vial comprising a composition comprising a plurality of $CD4^+$ T cells expressing a recombinant receptor, and (2) instructions for administering to a subject having a disease or condition:

a unit dose of cells of the composition, the unit dose comprising all or a portion of the plurality of $CD4^+$ T cells, and a unit dose of a composition comprising $CD8^+$ T cells expressing a recombinant receptor, wherein the vial does not comprise the unit dose of the composition comprising CD8+ T cells expressing the recombinant receptor.

14. An article of manufacture comprising (1) a vial comprising a composition comprising a plurality of $CD8^+$ T cells expressing a recombinant receptor, and (2) instructions for administering to a subject having a disease or condition:

a unit dose of cells of the composition, the unit dose comprising all or a portion of the plurality of $CD8^+$ T cells, and a unit dose of a composition comprising $CD4^+$ T cells expressing a recombinant receptor, wherein the vial does not comprise the unit dose of the composition comprising CD4+ T cells expressing the recombinant receptor.

15. The article of manufacture of claim 13 or claim 14, wherein:

the recombinant receptor expressed by the $CD4^+$ cells and the recombinant receptor expressed by the $CD8^+$ T cells is the same;

the recombinant receptor expressed by the $CD4^+$ cells and the recombinant receptor expressed by the $CD8^+$ T cells is different; or

the recombinant receptor expressed by the $CD4^+$ cells and the recombinant receptor expressed by the $CD8^+$ T cells binds to the same antigen, which is expressed by or associated with the disease or condition or cell or tissue thereof.

16. The article of manufacture of any of claims 13-15, wherein the vial comprises greater than or greater than about 10×10^6 T cells or recombinant receptor-expressing T cells, greater than or greater than about 15×10^6 T cells or recombinant receptor-expressing T cells, or greater than or greater than about 25×10^6 T cells or recombinant receptor-expressing T cell.

17. The article of manufacture of any of claims 13-16, wherein the vial comprises between about 10 million cells per mL and about 70 million cells per mL, between about 10

million cells per mL and about 50 million cells per mL, between about 10 million cells per mL and about 25 million cells per mL, between about 10 million cells per mL and about 15 million cells per mL, 15 million cells per mL and about 70 million cells per mL, between about 15 million cells per mL and about 50 million cells per mL, between about 15 million cells per mL and about 25 million cells per mL, between about 25 million cells per mL and about 70 million cells per mL, between about 25 million cells per mL and about 50 million cells per mL, or between about 50 million cells per mL and about 70 million cells per mL.

18. The article of manufacture of any of claims 13-17, wherein the composition further comprise(s) a cryoprotectant and/or the article further includes instructions for thawing the composition prior to administration to the subject.

19. The article of manufacture of any of claims 13-18, wherein the recombinant receptor is a chimeric antigen receptor (CAR).

20. Use of a dose of T cells comprising T cells expressing a chimeric antigen receptor (CAR) in the manufacture of a medicament for treatment of a non-Hodgkin lymphoma (NHL) in a subject, wherein:

the CAR specifically binds to a target antigen expressed by the NHL;

the dose of T cells comprises between at or about 2.5×10^7 CAR-expressing T cells and 2×10^8 CAR-expressing T cells, inclusive; and

the NHL comprises diffuse large B cell lymphoma (DLBCL), primary mediastinal large B cell lymphoma (PMBCL), NOS (de novo or transformed from indolent lymphoma) or follicular lymphoma Grade 3B, and wherein the subject is or has been identified as having an Eastern Cooperative Oncology Group Performance Status (ECOG) status of 0 or 1.

21. The use of claim 20, wherein the dose of T cells comprises a defined ratio of $CD4^+$ cells expressing the CAR to $CD8^+$ cells expressing the CAR and/or of $CD4^+$ cells to $CD8^+$ cells, which ratio is approximately 1:1 or is between approximately 1:3 and approximately 3:1.

22. Use of a dose of T cells comprising T cells expressing a chimeric antigen receptor (CAR) in the manufacture of a medicament for treatment of a non-Hodgkin lymphoma (NHL) in a subject, wherein:

the CAR specifically binds to a target antigen expressed by the NHL;

the dose of T cells comprises a defined ratio of $CD4^+$ cells expressing the CAR to $CD8^+$ cells expressing the CAR and/or of $CD4^+$ cells to $CD8^+$ cells, which ratio is approximately or is 1:1; and

the NHL comprises diffuse large B cell lymphoma (DLBCL), primary mediastinal large B cell lymphoma (PMBCL), NOS (de novo or transformed from indolent lymphoma) or follicular lymphoma Grade 3B.

23. The use of claim 22, wherein the subject is or has been identified as having an ECOG status of 0 or 1.

24. The use of claim 22 or claim 23 wherein

the dose of T cells comprises between at or about 5×10^7 recombinant receptor-expressing T cells and 1.5×10^8 recombinant receptor-expressing T cells, inclusive.

25. The use of any of claims 20-24, wherein:

at or prior to administration of the dose of T cells, the subject is or has been identified as having a lymphoma associated with or involving central nervous system (CNS) involvement; and/or

at least 70%, at least 80%, at least 90% or at least 95% of subjects treated according to the use who, at or prior to the administration of the dose of T cells, exhibited or were identified to exhibit a lymphoma with CNS involvement, achieve a resolution of the CNS disease.

26. Use of a dose of T cells comprising T cells expressing a chimeric antigen receptor (CAR) in the manufacture of a medicament for treatment of a lymphoma in a subject, wherein the CAR- specifically binds to a target antigen expressed by the lymphoma and the lymphoma in the subject is associated with or involves central nervous system (CNS) involvement.

27. The use of claim 26, wherein the lymphoma is a B cell malignancy.

28. The use of claim 26 or claim 27, wherein the lymphoma is a non-Hodgkin lymphoma (NHL).

29. The use of any of claims 20-28, wherein prior to initiation of administration of the dose of T cells, the subject has not been administered an agent or treatment capable of treating, preventing, delaying, reducing or attenuating the development or risk of development of a toxicity following administration of the dose of T cells.

30. The use of any of claims 20-29, wherein:

administration of the dose of T cells and any follow up is carried out on an outpatient basis and/or without requiring admission to or an overnight stay at a hospital; and

if the subject exhibits a sustained fever or a fever that is or has not been reduced by more than 1ºC after treatment with an antipyretic, the subject is to be admitted to a hospital or to an overnight stay at a hospital and/or is to be administered an agent or treatment for the treatment, prevention, reduction or attenuation of a neurotoxicity and/or a cytokine release syndrome or risk thereof.

31. The use of any of claims 20-25 and 28-30, wherein the NHL is selected from the group consisting of aggressive NHL, diffuse large B cell lymphoma (DLBCL), NOS (de novo and transformed from indolent), primary mediastinal large B cell lymphoma (PMBCL), mantle cell lymphoma (MCL), and/or follicular lymphoma Grade 3B (FL3B).

32. The use of any of claims 20-31, wherein the subject is or has been identified as having an ECOG status of 0 or 1.

33. The use of any of claims 20-25 and 28-32, wherein, at or immediately prior to administration of the dose of cells, the subject has relapsed following remission after treatment with, or become refractory to, one or more prior therapies for the NHL.

34. The use of any of claims 20-33, wherein, at or prior to administration of the dose of T cells:

the subject is or has been identified as having a double/triple hit lymphoma; and/or

the subject is or has been identified as having a chemorefractory lymphoma, or a chemorefractory DLBCL; and/or

the subject has not achieved complete remission (CR) in response to a prior therapy; and/or

the subject has relapsed within 1 year or less than 1 year after receiving an autologous stem cell transplant (ASCT).

35. The use of any of claims 20-34, wherein:

the CAR comprises an scFv specific for CD19, a transmembrane domain, a cytoplasmic signaling domain derived from a costimulatory molecule, a cytoplasmic signaling domain that comprises a CD3zeta signaling domain and a spacer between the transmembrane domain and the scFv.

36. The use of claim 35, wherein the costimulatory molecule is or comprises a 4-1BB.

37. The use of claim 35 or claim 36, wherein the spacer consists of all or a portion of an immunoglobulin hinge and is 15 amino acids or fewer in length.

38. The use of any of claims 35-37, wherein the spacer consists of at or about 12 amino acids in length.

39. The use of any of claims 35-38, wherein the spacer consists of the sequence set forth in SEQ ID NO:1.

40. The use of any of claims 35-39, wherein the scFv comprises a CDRL1 sequence of RASQDISKYLN (SEQ ID NO:35), a CDRL2 sequence of SRLHSGV (SEQ ID NO:36), and/or a CDRL3 sequence of GNTLPYTFG (SEQ ID NO:37); and/or a CDRH1 sequence of

DYGVS (SEQ ID NO:38), a CDRH2 sequence of VIWGSETTYYNSALKS (SEQ ID NO:39), and/or a CDRH3 sequence of YAMDYWG (SEQ ID NO:40).

41. The use of any of claims 35-40, wherein the scFv comprises the V_H sequence set forth in SEQ ID NO:41 and the V_L sequence set forth in SEQ ID NO:42.

42. The use of any of claims 35-41, wherein the scFv comprises the sequence set forth in SEQ ID NO:43.

43. The use of any of claims 1-12 and 20-42, wherein, prior to administration of the dose of T cells, the subject has been preconditioned with a lymphodepleting therapy comprising the administration of fludarabine and/or cyclophosphamide.

44. The use of any of claims 20-43, wherein the medicament comprises a first composition comprising one of CD4+ T cells or CD8+ T cells and is to be administered with a second composition comprising the other of the CD4+ T cells or the CD8+ T cells, for use in administering the dose of T cells, wherein the dose of T cells comprises $CD4^+$ T cells expressing the CAR and $CD8^+$ T cells expressing the CAR, and is to be administered as a plurality of separation compositions, the plurality of separate compositions comprising the first composition comprising one of the $CD4^+$ T cells and the $CD8^+$ T cells and the second composition comprising the other of the $CD4^+$ T cells or the $CD8^+$ T cells.

45. The use of claim 44, wherein:

the first composition and the second composition are to be administered 0 to 12 hours apart, 0 to 6 hours apart or 0 to 2 hours apart, or the first composition and the second composition are to be administered on the same day, between about 0 and about 12 hours apart, between about 0 and about 6 hours apart or between about 0 and 2 hours apart; and/or

the first composition and the second composition are to be administered between about 1 minute and about 1 hour apart or between about 5 minutes and about 30 minutes apart.

46. The use of claim 44 or claim 45, wherein the first composition and second composition are to be administered no more than 2 hours, no more than 1 hour, no more than 30 minutes, no more than 15 minutes, no more than 10 minutes or no more than 5 minutes apart.

47. The use of any of claims 44-46, wherein:

the first composition comprises the $CD4^+$ T cells; or

the first composition comprises the CD8+ T cells.

48. The use of any of claims 44-47, wherein the first composition is to be administered prior to the second composition.

49. The use of any of claims 1-12 and 20-48, wherein the dose of T cells comprises about 1×10^8 recombinant receptor-expressing cells.

50. A method of assessing likelihood of a response to a cell therapy, the method comprising:

(a) assessing the level, amount or concentration of one or more analyte in a biological sample, wherein the one or more analyte is selected from ferritin, LDH, CXCL10, G-CSF, and IL-10, wherein:

the biological sample is from a subject that is a candidate for treatment with the cell therapy, said cell therapy comprising a dose of genetically engineered cells expressing a recombinant receptor; and

the biological sample is obtained from the subject prior to administration of the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and

(b) comparing, individually, the level, amount or concentration of the analyte in the sample to a threshold level, thereby determining a likelihood that a subject will achieve a response to the cell therapy.

51. The method of claim 50, wherein the threshold level is within 25%, within 20%, within 15%, within 10% or within 5% and/or is within a standard deviation below the median or mean level, amount or concentration, or is or is about the median or mean level, amount or

concentration, of the analyte in a biological sample obtained from a group of subjects prior to receiving a cell therapy, wherein each of the subjects of the group went on to achieve a response after administration of a recombinant-receptor-expressing therapeutic cell composition for treating the same disease or condition.

52. The method of claim 50 or claim 51, wherein the threshold level is within 25%, within 20%, within 15%, within 10% or within 5% and/or is within a standard deviation above the median or mean level, amount or concentration of the analyte in a biological sample obtained from a group of subjects prior to receiving a cell therapy, wherein each of the subjects of the group went on to exhibit stable disease (SD) and/or progressive disease (PD) after administration of a recombinant-receptor-expressing therapeutic cell composition for treating the same disease or condition.

53. A method of assessing likelihood of a durable response to a cell therapy, the method comprising:

(a) assessing the level, amount or concentration of one or more analyte in a biological sample, wherein the one or more analyte is selected from LDH, ferritin, CRP, D-dimer, SAA-1, IL-6, IL-10, IL-15, IL-16, TNF-α, IFN-γ, MIP-1α, CXCL-10, IL-8, MCP-1 and MIP-1β, wherein:

the biological sample is from a subject that is a candidate for treatment with the cell therapy, said cell therapy comprising a dose of genetically engineered cells expressing a recombinant receptor; and

the biological sample is obtained from the subject prior to administration of the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and

(b) comparing, individually, the level, amount or concentration of the analyte in the sample to a threshold level, thereby determining a likelihood that a subject will achieve a durable response to the cell therapy.

54. A method of selecting a subject for treatment, the method comprising:

(a) assessing the level, amount or concentration of one or more analyte in a biological sample, wherein the one or more analyte is selected from LDH, ferritin, CRP, D-dimer, SAA-1,

IL-6, IL-10, IL-15, IL-16, TNF-α, IFN-γ, MIP-1α, CXCL-10, IL-8, MCP-1 and MIP-1β, wherein:

the biological sample is from a subject that is a candidate for treatment with the cell therapy, said cell therapy comprising a dose of genetically engineered cells expressing a recombinant receptor; and

the biological sample is obtained from the subject prior to administration of the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and

(b) selecting a subject who is likely to respond to treatment based on the results of determining a likelihood that a subject will achieve a durable response to the cell therapy by comparing, individually, the level, amount or concentration of the analyte in the sample to a threshold level.

55. The method of claim 53 or claim 54, wherein the threshold level is within 25%, within 20%, within 15%, within 10% or within 5% and/or is within a standard deviation below the median or mean level, amount or concentration, or is or is about the median or mean level, amount or concentration, of the analyte in a biological sample obtained from a group of subjects prior to receiving a cell therapy, wherein each of the subjects of the group went on to achieve a durable response after administration of a recombinant receptor-expressing therapeutic cell composition for treating the same disease or condition.

56. The method of any of claims 53-55, wherein the threshold level is within 25%, within 20%, within 15%, within 11% or within 5% and/or is within a standard deviation above the median or mean level, amount or concentration of the analyte in a biological sample obtained from a group of subjects prior to receiving a cell therapy, wherein each of the subjects of the group did not achieve a durable response after administration of a recombinant receptor-expressing therapeutic cell composition for treating the same disease or condition.

57. A method of assessing the risk of developing a toxicity after administration of a cell therapy, the method comprising:

(a) assessing the level, amount or concentration of one or more analyte in a biological sample from a subject or a volumetric measure of tumor burden in a subject, wherein the one or

more analyte is selected from LDH, Ferritin, C-reactive protein (CRP), D-dimer (fibrin degradation product), IL-6, IL-8, IL-10, IL-15, IL-16 TNF-α, IFN-α2, MCP-1, MIP-1α and MIP-1β, wherein:

the subject is a candidate for treatment with the cell therapy, said cell therapy optionally comprising a dose or composition of genetically engineered cells expressing a recombinant receptor; and

the biological sample is obtained from the subject prior to administration of the cell therapy and/or said biological sample does not comprise the recombinant receptor and/or said engineered cells; and

(b) comparing, individually, the level, amount or concentration of the analyte in the sample or the volumetric measure of tumor burden to a threshold level, thereby determining a risk of developing a toxicity after administration of the cell therapy.

58. The method of claim 57, wherein the volumetric measure of tumor burden is a sum of product dimensions (SPD) or is a volumetric measurement based on CT and/or MRI imaging or other imaging of the subject's body.

59. An article of manufacture comprising one or more dose of a cell therapy, each dose comprising a first composition comprising one of CD4+ T cells or CD8+ T cells and a second composition comprising the other of the CD4+ or CD8+ T cells, wherein the dose comprises CD4+ T cells expressing a chimeric antigen receptor (CAR) and CD8+ T cells expressing the CAR, and instructions for administering the cell therapy, wherein the instructions specify:

(i) the dose of cells is to be administered to a subject having or identified to have a non-Hodgkin lymphoma (NHL), the NHL selected from diffuse large B cell lymphoma (DLBCL), primary mediastinal large B cell lymphoma (PMBCL), NOS (de novo or transformed from indolent lymphoma), or follicular lymphoma Grade 3B, wherein the subject is or has been identified as having an Eastern Cooperative Oncology Group Performance Status (ECOG) status of 0 or 1; and

administration of a number of T cells or an amount or volume of one or more formulations corresponding to or containing said specified number of cells, wherein the specified number of cells comprises between at or about 5×10^7 CAR-expressing T cells and 1 x

10^8 CAR-expressing T cells, inclusive, between at or about 5 x 10^7 CAR-expressing T cells and at or about 1.5 x 10^8 CAR-expressing T cells, at or about 5 x 10^7 CAR-expressing T cells, at or about 1 x 10^8 CAR-expressing T cells, or at or about 1.5 x 10^8 CAR-expressing T cells, between at or about 2.5 x 10^7 $CD8^+$CAR-expressing T cells and at or about 5 x 10^7 $CD8^+$ CAR-expressing T cells, inclusive, between at or about 2.5 x 10^7 CAR-expressing T cells and at or about 0.75 x 10^8 $CD8^+$ CAR-expressing T cells, or at or about 2.5 x 10^7 $CD8^+$ CAR-expressing T cells, at or about 5 x 10^7 CAR-expressing T cells, or at or about 0.75 x 10^8 $CD8^+$ CAR-expressing T cells, or of viable populations of any of the foregoing;

(ii) the dose of T cells is to be administered at a defined ratio of $CD4^+$ cells expressing the CAR to $CD8^+$ cells expressing the CAR and/or of $CD4^+$ cells to $CD8^+$ cells, which ratio is approximately or is 1:1; and the dose of cells is to be administered to a subject having or identified to have a non-Hodgkin lymphoma (NHL), the NHL selected from diffuse large B cell lymphoma (DLBCL), primary mediastinal large B cell lymphoma (PMBCL), NOS (de novo or transformed from indolent lymphoma), or follicular lymphoma Grade 3B; and/or

(iii) the dose of cells is to be administered to a subject having or identified to have a non-Hodgkin lymphoma (NHL); the dose of T cells to be administered comprises between at or about 5 x 10^7 CAR-expressing T cells and 1 x 10^8 CAR-expressing T cells, inclusive; and the dose of T cells is to be administered at a defined ratio of $CD4^+$ cells expressing the CAR to $CD8^+$ cells expressing the CAR and/or of $CD4^+$ cells to $CD8^+$ cells, which ratio is approximately or is 1:1.

60. An article of manufacture comprising one or more reagent capable of detecting one or more analytes, and instructions for using the reagent to assay a biological sample from a subject that is a candidate for treatment with a cell therapy, said cell therapy comprising a dose or composition of genetically engineered cells expressing a recombinant receptor, wherein the one or more analytes is selected from:

(i) ferritin, LDH, CXCL10, G-CSF and IL-10;

(ii) LDH, ferritin, CRP, D-dimer, SAA-1, IL-6, IL-10, IL-15, IL-16, TNF-α, IFN-γ, MIP-1α, CXCL-10, IL-8, MCP-1 and MIP-1β; or

(iii) LDH, Ferritin, C-reactive protein (CRP), D-dimer (fibrin degradation product), IL-6, IL-8, IL-10, IL-15, IL-16 TNF-α, IFN-α2, MCP-1, MIP-1α and MIP-1β.

61. An article of manufacture comprising:

a cell therapy comprising a dose of genetically engineered cells expressing a recombinant receptor, and

instructions for administering the cell therapy following or based on the results of an assessment, in a biological sample of the level, or amount or concentration of one or more analyte in the biological sample, the biological sample obtained from the subject prior to administration of the cell therapy and/or the biological sample not comprising the recombinant receptor and/or the engineered cells, wherein the one or more analytes is selected from:

(i) ferritin, LDH, CXCL10, G-CSF and IL-10;

(ii) LDH, ferritin, CRP, D-dimer, SAA-1, IL-6, IL-10, IL-15, IL-16, TNF-α, IFN-γ, MIP-1α, CXCL-10, IL-8, MCP-1 and MIP-1β; or

(iii) LDH, Ferritin, C-reactive protein (CRP), D-dimer (fibrin degradation product), IL-6, IL-8, IL-10, IL-15, IL-16 TNF-α, IFN-α2, MCP-1, MIP-1α and MIP-1β.