

SUMMARY

[0012] Provided herein is a method of treating an HIV infection in a subject comprising administering to the subject an antibody-drug conjugate, wherein the antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding portion thereof conjugated to a monomethyl auristatin. Also provided herein is a method of treating an HIV infection in a subject consisting essentially of administering to the subject an antibody-drug conjugate, wherein the antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding portion thereof conjugated to a monomethyl auristatin. Also provided herein is a method of treating an HIV infection in a subject consisting of administering to the subject an antibody-drug conjugate, wherein the antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding portion thereof conjugated to a monomethyl auristatin. In one aspect, the present disclosure provides a use of an antibody-drug conjugate in the manufacture of a medicament for treating human immunodeficiency virus HIV infection, wherein the antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding portion thereof conjugated to a monomethyl auristatin, and treating HIV infection comprises increasing a CD4+ T-cell lymphocyte count in a subject infected with HIV. In some embodimentexamples, the HIV infection is an HIV-1 infection. In some embodimentexamples, the subject does not have a hematologic cancer at the time of administration of the antibody-drug conjugate. In some embodimentexamples, the subject has not had a hematologic cancer for at least 12 months prior to the administration of the antibody-drug conjugate. In some embodimentexamples, the subject has not had a hematologic cancer for at least 24 months prior to the administration of the antibody-drug conjugate. In some embodimentexamples, the hematologic cancer is selected from the group consisting of classical Hodgkin Lymphoma, non-Hodgkin Lymphoma, cutaneous T-cell lymphoma (CTCL), and anaplastic large cell lymphoma (ALCL). In some embodimentexamples, the hematologic cancer is classical Hodgkin Lymphoma. In some of any of the embodimentexamples herein, the classical Hodgkin Lymphoma is a stage IIA with bulky disease, stage IIB, stage III or stage IV classical Hodgkin Lymphoma. In some embodimentexamples, the anaplastic large cell lymphoma (ALCL) is a systemic anaplastic large cell lymphoma (sALCL). In some embodimentexamples, the anaplastic large cell lymphoma (ALCL) is a primary cutaneous anaplastic large cell lymphoma (pcALCL). In some embodimentexamples, the cutaneous T-cell

lymphoma (CTCL) is a mycosis fungoides (MF). In some embodiment examples, the mycosis fungoides (MF) is a CD30-positive mycosis fungoides (MF). In some embodiment examples, the anti-CD30 antibody of the antibody-drug conjugate comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises:

- (i) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 1;
- (ii) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 2; and

(iii) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 3; and
wherein the light chain variable region comprises:

- (i) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 4;
- (ii) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 5; and
- (iii) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 6. In some embodimentexamples, the anti-CD30 antibody of the antibody-drug conjugate comprises a heavy chain variable region comprising an amino acid sequence at least 85% identical to the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence at least 85% identical to the amino acid sequence of SEQ ID NO: 8. In some embodimentexamples, the anti-CD30 antibody of the antibody-drug conjugate comprises a heavy chain variable region comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 8. In some embodimentexamples, the anti-CD30 antibody of the antibody-drug conjugate comprises a heavy chain variable region comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 8. In some embodimentexamples, the anti-CD30 antibody of the antibody-drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 8. In some embodimentexamples, the anti-CD30 antibody is AC10. In some embodimentexamples, the anti-CD30 antibody is cAC10. In some embodimentexamples, the antibody-drug conjugate further comprises a linker between the anti-CD30 antibody or antigen-binding portion thereof and the monomethyl auristatin. In some embodimentexamples, the linker is a cleavable peptide linker. In some embodimentexamples, the monomethyl auristatin is monomethyl auristatin E (MMAE). In some embodimentexamples, the monomethyl auristatin is monomethyl auristatin F (MMAF). In some embodimentexamples, the antibody-drug conjugate is brentuximab vedotin. In some embodimentexamples, the antibody-drug conjugate is administered at a dose ranging from of about 0.1 mg/kg to about 1.3 mg/kg of the subject's body weight. In some embodimentexamples, the antibody-drug conjugate is administered at a dose ranging from about 0.3 mg/kg to about 0.9 mg/kg of the subject's body weight. In some embodimentexample, the antibody-drug conjugate is administered at a dose of about 0.3 mg/kg of the subject's body weight. In some embodimentexamples, the antibody-drug conjugate is administered at a

dose of about 0.6 mg/kg of the subject's body weight. In some [embodimentexamples](#), the antibody-drug conjugate is administered at a dose of about 0.9 mg/kg of the subject's body weight. In some [embodimentexamples](#), the antibody-drug conjugate is administered once about every 3 weeks. In some [embodimentexamples](#), the antibody-drug conjugate is administered once every 3 weeks. In some [embodimentexamples](#), the antibody-drug conjugate is administered for 6 3-week treatment cycles. In some [embodimentexamples](#), the antibody-drug conjugate is administered to the subject by intravenous infusion. In some [embodimentexamples](#), the intravenous infusion is about a 30 minute infusion. In some [embodimentexamples](#), the subject has a CD4 lymphocyte count of < 200 cells/mm³ prior to administration of the antibody-drug conjugate. In some [embodimentexamples](#), the subject has plasma HIV RNA ≥ 1000 copies/mL prior to administration of the antibody-drug conjugate. In some [embodimentexamples](#), the subject has had plasma HIV RNA ≥ 200 copies/mL in a 3-month period prior to administration of the antibody-drug conjugate. In some [embodimentexamples](#), the subject has a life expectancy of greater than 9 months prior to administration of the antibody-drug conjugate. In some [embodimentexamples](#), the subject has an absolute neutrophil count ≥ 750 /mm³. In some [embodimentexamples](#), the subject is male and has hemoglobin ≥ 10.5 gm/dL. In some [embodimentexamples](#), the subject is female and has hemoglobin ≥ 9.5 gm/dL. In some [embodimentexamples](#), the subject has serum alanine transaminase (SGPT/ALT) < 2.5 x upper limit of normal (ULN). In some [embodimentexamples](#), the subject has serum aspartate transaminase (SGOT/AST) < 2.5 x ULN. In some [embodimentexamples](#), the subject has bilirubin (total) < 2.5 x ULN. In some [embodimentexamples](#), the subject has creatinine < 1.5 x ULN. In some [embodimentexamples](#), the subject has received antiretroviral therapy (ART) for at least 24 weeks prior to administration of the antibody-drug conjugate. In some [embodimentexamples](#), the subject has received ART for at least 12 months prior to administration of the antibody-drug conjugate. In some [embodimentexamples](#), the subject has received ART for at least 24 months prior to administration of the antibody-drug conjugate. In some [embodimentexamples](#), the antibody-drug conjugate is administered in combination with ART. In some [embodimentexamples](#), the ART is a nucleoside reverse transcriptase inhibitor, non-nucleoside reverse transcriptase inhibitor, protease inhibitor, fusion inhibitor, CCR5 antagonist, integrase inhibitor, post-attachment inhibitor, or pharmacokinetic enhancer. In some [embodimentexamples](#), the ART comprises two or more of a nucleoside reverse transcriptase inhibitor, non-nucleoside reverse transcriptase inhibitor, protease inhibitor, fusion inhibitor, CCR5 antagonist, integrase inhibitor, post-attachment inhibitor, and pharmacokinetic enhancer. In some [embodimentexamples](#), the ART comprises three or more of a

nucleoside reverse transcriptase inhibitor, non-nucleoside reverse transcriptase inhibitor, protease inhibitor, fusion inhibitor, CCR5 antagonist, integrase inhibitor, post-attachment inhibitor, and pharmacokinetic enhancer. In some [embodimentexamples](#), the ART comprises four or more of a nucleoside reverse transcriptase inhibitor, non-nucleoside reverse transcriptase inhibitor, protease inhibitor, fusion inhibitor, CCR5 antagonist, integrase inhibitor, post-attachment inhibitor, and pharmacokinetic enhancer. In some [embodimentexamples](#), the ART comprises one or more of abacavir, emtricitabine, lamivudine, tenofovir disoproxil fumarate, zidovudine, doravirine, efavirenz, etravirine, nevirapine, rilpivirine, atazanavir, darunavir, fosamprenavir, ritonavir, saquinavir, tipranavir, enfuvirtide, maraviroc, dolutegravir, raltegravir, ibalizumab, and cobicistat. In some [embodimentexamples](#), administering the antibody-drug conjugate results in a decrease in HIV viral load in the subject relative to the viral load prior to administration of the antibody-drug conjugate. In some [embodimentexamples](#), HIV viral load is assessed by measuring CD4⁺ T-cell-associated HIV DNA. In some [embodimentexamples](#), HIV viral load is assessed by measuring CD4⁺ T-cell-associated HIV RNA. In some [embodimentexamples](#), the subject exhibits a viral load of less than or equal to 50 copies of HIV virus particles per mL of blood plasma (< 50 c/mL) after at least 24 weeks, at least 48 weeks, or at least 96 weeks after administration of the antibody-drug conjugate. In some [embodimentexamples](#), administering the antibody-drug conjugate results in elimination of the HIV infection in the subject. In some [embodimentexamples](#), administering the antibody-drug conjugate results in a decrease in the number of Treg cells relative to the number prior to the administration of the antibody-drug conjugate. In some [embodimentexamples](#), the Treg cells are CD4⁺. In some [embodimentexamples](#), the Treg cells are CD30⁺. In some [embodimentexamples](#), administering the antibody-drug conjugate results in a decrease in the number of memory T cells relative to the number prior to the administration of the antibody-drug conjugate. In some [embodimentexamples](#), the memory T cells are CD4⁺. In some [embodimentexamples](#), the memory T cells are CD30⁺. In some [embodimentexamples](#), administering the antibody-drug conjugate results in an increase in the number of CD4⁺ T cells relative to the number prior to the administration of the antibody-drug conjugate. In some [embodimentexamples](#), the subject is a human.

[0013] Also provided herein is a kit comprising (a) a dosage ranging from about 0.1 mg to about 500 mg of an of an antibody-drug conjugate that binds to CD30, wherein the antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to a monomethyl auristatin or a functional analog thereof or a functional derivative

thereof; and (b) instructions for using the antibody drug conjugate according any of the [embodimentexamples](#) herein.

[0014] Also provided herein is the use of an antibody-drug conjugate that binds to CD30 for the manufacture of a medicament for use in any of the [embodimentexamples](#) herein.

[0015] Also provided herein is an antibody-drug conjugate that binds to CD30 for use in any of the [embodimentexamples](#) herein.

[0016] Also provided herein is a method of increasing CD4⁺ T-cell lymphocyte count in a subject infected with human immunodeficiency virus (HIV) comprising administering to the subject an antibody-drug conjugate, wherein the antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding portion thereof conjugated to a monomethyl auristatin. Also provided herein is a method of increasing CD4⁺ T-cell lymphocyte count in a subject infected with human immunodeficiency virus (HIV) consisting essentially of administering to the subject an antibody-drug conjugate, wherein the antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding portion thereof conjugated to a monomethyl auristatin. Also provided herein is a method of increasing CD4⁺ T-cell lymphocyte count in a subject infected with human immunodeficiency virus (HIV) consisting of administering to the subject an antibody-drug conjugate, wherein the antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding portion thereof conjugated to a monomethyl auristatin. In some [embodimentexamples](#), the HIV infection is an HIV-1 infection. In some [embodimentexamples](#), the subject has a CD4⁺ T-cell lymphocyte count of < 200 cells/ μ L prior to administration of the antibody-drug conjugate. In some [embodimentexamples](#), the subject has a CD4⁺ T-cell lymphocyte count of >50 cells/ μ L prior to administration of the antibody-drug conjugate. In some [embodimentexamples](#), the subject has had a plasma HIV viral load $\leq$ 50 copies/mL for at least 6 months prior to administration of the antibody-drug conjugate. In some [embodimentexamples](#), the subject has had a plasma HIV viral load $\leq$ 50 copies/mL for at least 12 months prior to administration of the antibody-drug conjugate. In some [embodimentexamples](#), the subject has had a plasma HIV viral load $\leq$ 50 copies/mL for at least 24 months prior to administration of the antibody-drug conjugate. In some [embodimentexamples](#), the subject does not have a hematologic cancer at the time of administration of the antibody-drug conjugate. In some [embodimentexamples](#), the subject has not had a hematologic cancer for at least 12 months prior to the administration of the antibody-drug conjugate. In some

embodimentexamples, the subject has not had a hematologic cancer for at least 24 months prior to the administration of the antibody-drug conjugate. In some embodimentexamples, the hematologic cancer is selected from the group consisting of classical Hodgkin Lymphoma, non-Hodgkin Lymphoma, cutaneous T-cell lymphoma (CTCL), and anaplastic large cell lymphoma (ALCL). In some embodimentexamples, the hematologic cancer is classical Hodgkin Lymphoma. In some embodimentexamples, the classical Hodgkin Lymphoma is a stage IIA with bulky disease, stage IIB, stage III or stage IV classical Hodgkin Lymphoma. In some embodimentexamples, the anaplastic large cell lymphoma (ALCL) is a systemic anaplastic large cell lymphoma (sALCL). In some embodimentexamples, the anaplastic large cell lymphoma (ALCL) is a primary cutaneous anaplastic large cell lymphoma (pcALCL). In some embodimentexamples, the cutaneous T-cell lymphoma (CTCL) is a mycosis fungoides (MF). In some embodimentexamples, the mycosis fungoides (MF) is a CD30-positive mycosis fungoides (MF). In some embodimentexamples, the anti-CD30 antibody of the antibody-drug conjugate comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises:

- (i) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 1;
- (ii) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 2; and
- (iii) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 3; and

wherein the light chain variable region comprises:

- (i) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 4;
- (ii) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 5; and
- (iii) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 6. In some

embodimentexamples, the anti-CD30 antibody of the antibody-drug conjugate comprises a heavy chain variable region comprising an amino acid sequence at least 85% identical to the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence at least 85% identical to the amino acid sequence of SEQ ID NO: 8. In some embodimentexamples, the anti-CD30 antibody of the antibody-drug conjugate comprises a heavy chain variable region comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 8. In some embodimentexamples, the anti-CD30 antibody of the antibody-drug conjugate comprises a heavy chain variable region comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 7 and a light chain

variable region comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 8. In some [embodimentexamples](#), the anti-CD30 antibody of the antibody-drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 8. In some [embodimentexamples](#), the anti-CD30 antibody is AC10. In some [embodimentexamples](#), the anti-CD30 antibody is cAC10. In some [embodimentexamples](#), the antibody-drug conjugate further comprises a linker between the anti-CD30 antibody or antigen-binding portion thereof and the monomethyl auristatin. In some [embodimentexamples](#), the linker is a cleavable peptide linker. In some [embodimentexamples](#), the cleavable peptide linker has a formula: -MC-vc-PAB-. In some [embodimentexamples](#), the monomethyl auristatin is monomethyl auristatin E (MMAE). In some [embodimentexamples](#), the monomethyl auristatin is monomethyl auristatin F (MMAF). In some [embodimentexamples](#), the antibody-drug conjugate is brentuximab vedotin. In some [embodimentexamples](#), the antibody-drug conjugate is administered at a dose ranging from of about 1.2 mg/kg of the subject's body weight. In some [embodimentexamples](#), the antibody-drug conjugate is administered at a dose ranging from of 1.2 mg/kg of the subject's body weight. In some [embodimentexamples](#), the antibody-drug conjugate is administered at a dose of about 0.9 mg/kg of the subject's body weight. In some [embodimentexamples](#), the antibody-drug conjugate is administered at a dose of 0.9 mg/kg of the subject's body weight. In some [embodimentexamples](#), the antibody-drug conjugate is administered once about every 2 weeks. In some [embodimentexamples](#), the antibody-drug conjugate is administered once every 2 weeks. In some [embodimentexamples](#), the antibody-drug conjugate is administered for four 2-week treatment cycles. In some [embodimentexamples](#), the antibody-drug conjugate is administered to the subject by intravenous infusion. In some [embodimentexamples](#), the intravenous infusion is about a 30 minute infusion. In some [embodimentexamples](#), the subject has a life expectancy of greater than 9 months prior to administration of the antibody-drug conjugate. In some [embodimentexamples](#), the subject has received antiretroviral therapy (ART) for at least 24 weeks prior to administration of the antibody-drug conjugate. In some [embodimentexamples](#), the subject has received ART for at least 12 months prior to administration of the antibody-drug conjugate. In some [embodimentexamples](#), the subject has received ART for at least 24 months prior to administration of the antibody-drug conjugate. In some [embodimentexamples](#), the antibody-drug conjugate is administered in combination with ART. In some [embodimentexamples](#), the ART is a nucleoside reverse transcriptase inhibitor, non-nucleoside reverse transcriptase inhibitor, protease inhibitor, fusion inhibitor, CCR5 antagonist, integrase

inhibitor, post-attachment inhibitor, or pharmacokinetic enhancer. In some [embodimentexamples](#), the ART comprises two or more of a nucleoside reverse transcriptase inhibitor, non-nucleoside reverse transcriptase inhibitor, protease inhibitor, fusion inhibitor, CCR5 antagonist, integrase inhibitor, post-attachment inhibitor, and pharmacokinetic enhancer. In some [embodimentexamples](#), the ART comprises three or more of a nucleoside reverse transcriptase inhibitor, non-nucleoside reverse transcriptase inhibitor, protease inhibitor, fusion inhibitor, CCR5 antagonist, integrase inhibitor, post-attachment inhibitor, and pharmacokinetic enhancer. In some [embodimentexamples](#), the ART comprises four or more of a nucleoside reverse transcriptase inhibitor, non-nucleoside reverse transcriptase inhibitor, protease inhibitor, fusion inhibitor, CCR5 antagonist, integrase inhibitor, post-attachment inhibitor, and pharmacokinetic enhancer. In some [embodimentexamples](#), the ART comprises one or more of abacavir, emtricitabine, lamivudine, tenofovir disoproxil fumarate, zidovudine, doravirine, efavirenz, etravirine, nevirapine, rilpivirine, atazanavir, darunavir, fosamprenavir, ritonavir, saquinavir, tipranavir, enfuvirtide, maraviroc, dolutegravir, raltegravir, ibalizumab, and cobicistat. In some [embodimentexamples](#), the ART does not comprise a strong CYP3A4 inhibitor. In some [embodimentexamples](#), the ART does not comprise a strong P-gp inhibitor. In some [embodimentexamples](#), administering the antibody-drug conjugate results an increase in the CD4⁺ T-cell lymphocyte count in the subject to above 200 cells/ μ L. In some [embodimentexamples](#), administering the antibody-drug conjugate results in an increase in the CD4⁺ T-cell lymphocyte count by at least 50 cells/ μ L relative to the CD4⁺ T-cell lymphocyte count prior to administration. In some [embodimentexamples](#), administering the antibody-drug conjugate results an increase in the CD8⁺ T-cell lymphocyte count in the subject relative to the CD8⁺ T-cell lymphocyte count prior to administration. In some [embodimentexamples](#), administering the antibody-drug conjugate results in a decrease in the number of Treg cells relative to the number prior to the administration of the antibody-drug conjugate. In some [embodimentexamples](#), the Treg cells are CD4⁺. In some [embodimentexamples](#), the Treg cells are CD30⁺. In some [embodimentexamples](#), administering the antibody-drug conjugate results in a decrease in the number of memory T cells relative to the number prior to the administration of the antibody-drug conjugate. In some [embodimentexamples](#), the memory T cells are CD4⁺. In some [embodimentexamples](#), the memory T cells are CD30⁺. In some [embodimentexamples](#), the subject has not been administered the antibody-drug conjugate prior to the administration to increase CD4⁺ T-cell lymphocyte count in the subject. In some [embodimentexamples](#), the subject is a human.

[0017] Also provided herein is a kit comprising (a) a dosage ranging from about 0.1 mg to about 500 mg of an of an antibody-drug conjugate that binds to CD30, wherein the antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding fragment thereof conjugated to a monomethyl auristatin or a functional analog thereof or a functional derivative thereof; and (b) instructions for using the antibody drug conjugate according to any of the [embodimentexamples](#) herein.

[0018] Also provided herein is the use of an antibody-drug conjugate that binds to CD30 for the manufacture of a medicament for use in any of the [embodimentexamples](#) herein.

[0019] Also provided herein is an antibody-drug conjugate that binds to CD30 for use in any of the [embodimentexample](#)s herein.

BRIEF DESCRIPTION OF THE DRAWINGS

[0020] FIG. 1A-1B are graphs showing the effect of various concentrations of brentuximab vedotin (BV) on the total number of viable cells in various T cell populations (FIG. 1A) or the number of CD30⁺ viable cells in various T cell populations (FIG. 1B). The various T cell populations are displayed as Treg (●), naïve CD4 (◆), memory CD4 (▲), naïve CD8 (▼), and memory CD8 (■). Data are represented as viable cell counts relative to untreated control.

[0021] FIG. 2A-2B are graphs showing CD30 and CD30L expression in various T cell populations over time as monitored by flow cytometry. FIG. 2A shows a representative flow cytometry plot over a 3-day activation time-course. FIG. 2B shows the percent of each T cell population that are CD30⁺ over time. The various T cell populations are displayed as Treg (●), naïve CD4 (◆), memory CD4 (▲), naïve CD8 (▼), and memory CD8 (■).

[0022] FIG. 3A-3B are graphs showing rhodamine 123 efflux over time in various T cell populations as measured by flow cytometry. FIG. 3A shows rhodamine efflux at 37°C in Treg, naïve CD4 (CD4 TN), memory CD4 (CD4 TMEM), naïve CD8 (CD8 TM), and memory CD8 (CD8 TMEM) T cells. FIG. 3B shows rhodamine efflux over a 3-hour time course in various T cell populations. The various T cell populations are displayed as Treg (●), naïve CD4 (◆), memory CD4 (▲), naïve CD8 (▼), and memory CD8 (■).

[0023] FIG. 4 is a graph showing the effects of treating various T cell populations with a titration of free monomethyl auristatin E (MMAE) over the course of 4 days. The various T cell

CLAIMS

What is claimed is:

1. ~~Use of A method of increasing CD4⁺ T-cell lymphocyte count in a subject infected with human immunodeficiency virus (HIV) comprising administering to the subject~~ an antibody-drug conjugate ~~in the manufacture of a medicament for treating human immunodeficiency virus HIV infection,~~ wherein the antibody-drug conjugate comprises an anti-CD30 antibody or an antigen-binding portion thereof conjugated to a monomethyl auristatin, ~~and treating HIV infection comprises increasing a CD4⁺ T-cell lymphocyte count in a subject infected with HIV.~~

2. The ~~usemethod~~ of claim 1, wherein the HIV infection is an HIV-1 infection.

3. The ~~usemethod~~ of claim 1 or claim 2, wherein

~~a) the subject has a CD4⁺ T-cell lymphocyte count of < 200 cells/ μ L prior to administration of the antibody-drug conjugate; or~~

~~b) :~~

~~4. The method of any one of claims 1-3, wherein~~ the subject has a CD4⁺ T-cell lymphocyte count of >50 cells/ μ L prior to administration of the antibody-drug conjugate.

~~54. The usemethod of any one of claims 1-34, wherein~~

~~a) the subject has had a plasma HIV viral load $\leq$ 50 copies/mL for at least 6 months prior to administration of the antibody-drug conjugate; or~~

~~b) :~~

~~6. The method of any one of claims 1-4, wherein~~ the subject has had a plasma HIV viral load $\leq$ 50 copies/mL for at least 12 months prior to administration of the antibody-drug conjugate; ~~or~~

~~c) :~~

~~7. The method of any one of claims 1-4, wherein~~ the subject has had a plasma HIV viral load $\leq$ 50 copies/mL for at least 24 months prior to administration of the antibody-drug conjugate.

~~85.~~ The ~~usemethod~~ of any one of claims 1-~~74~~, wherein the subject does not have a hematologic cancer at the time of administration of the antibody-drug conjugate.

~~96.~~ The ~~usemethod~~ of ~~claim 5~~~~any one of claims 1-7~~, wherein

~~a)~~ the subject has not had a hematologic cancer for at least 12 months prior to the administration of the antibody-drug conjugate; ~~or~~

~~b) :~~

~~10.~~ ~~The method of any one of claims 1-7, wherein~~ the subject has not had a hematologic cancer for at least 24 months prior to the administration of the antibody-drug conjugate.

~~117.~~ The ~~usemethod~~ of ~~claim 5 or claim 6~~~~any one of claims 8-10~~, wherein the hematologic cancer is selected from the group consisting of classical Hodgkin Lymphoma, non-Hodgkin Lymphoma, cutaneous T-cell lymphoma (CTCL), and anaplastic large cell lymphoma (ALCL).

~~12.~~ ~~The method of claim 11, wherein the hematologic cancer is classical Hodgkin Lymphoma.~~

~~13.~~ ~~The method of claim 12, wherein the classical Hodgkin Lymphoma is a stage IIA with bulky disease, stage IIB, stage III or stage IV classical Hodgkin Lymphoma.~~

~~14.~~ ~~The method of claim 11, wherein the anaplastic large cell lymphoma (ALCL) is a systemic anaplastic large cell lymphoma (sALCL).~~

~~15.~~ ~~The method of claim 11, wherein the anaplastic large cell lymphoma (ALCL) is a primary cutaneous anaplastic large cell lymphoma (pcALCL).~~

~~16.~~ ~~The method of claim 11, wherein the cutaneous T cell lymphoma (CTCL) is a mycosis fungoides (MF).~~

~~17.~~ ~~The method of claim 16, wherein the mycosis fungoides (MF) is a CD30 positive mycosis fungoides (MF).~~

~~188.~~ The ~~use-method~~ of any one of claims 1-~~177~~, wherein the anti-CD30 antibody of the antibody-drug conjugate comprises a heavy chain variable region and a light chain variable region, wherein the heavy chain variable region comprises:

- (i) a CDR-H1 comprising the amino acid sequence of SEQ ID NO: 1;
- (ii) a CDR-H2 comprising the amino acid sequence of SEQ ID NO: 2; and
- (iii) a CDR-H3 comprising the amino acid sequence of SEQ ID NO: 3; and

wherein the light chain variable region comprises:

- (i) a CDR-L1 comprising the amino acid sequence of SEQ ID NO: 4;
- (ii) a CDR-L2 comprising the amino acid sequence of SEQ ID NO: 5; and
- (iii) a CDR-L3 comprising the amino acid sequence of SEQ ID NO: 6.

~~199.~~ The ~~usemethod~~ of any one of claims 1-~~818~~, wherein

~~a)~~ the anti-CD30 antibody of the antibody-drug conjugate comprises a heavy chain variable region comprising an amino acid sequence at least 85% identical to the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence at least 85% identical to the amino acid sequence of SEQ ID NO: 8; ~~or~~

~~b) :~~

~~20. The method of any one of claims 1-18, wherein~~ the anti-CD30 antibody of the antibody-drug conjugate comprises a heavy chain variable region comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence at least 90% identical to the amino acid sequence of SEQ ID NO: 8; ~~or c) :~~

~~21. The method of any one of claims 1-18, wherein~~ the anti-CD30 antibody of the antibody-drug conjugate comprises a heavy chain variable region comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising an amino acid sequence at least 95% identical to the amino acid sequence of SEQ ID NO: 8; ~~or d) :~~

~~22. The method of any one of claims 1-18, wherein~~ the anti-CD30 antibody of the antibody-drug conjugate comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 7 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 8.

~~23. The method of any one of claims 1-18, wherein the anti-CD30 antibody is AC10.~~

~~24~~10. The ~~use~~method of any one of claims 1-~~8~~18, wherein the anti-CD30 antibody is cAC10.

~~25. The method of any one of claims 1-24, wherein the antibody-drug conjugate further comprises a linker between the anti-CD30 antibody or antigen-binding portion thereof and the monomethyl auristatin.~~

~~26. The method of claim 25, wherein the linker is a cleavable peptide linker.~~

~~27. The method of claim 26, wherein the cleavable peptide linker has a formula: -MC-vc-PAB-.~~

~~11~~28. The ~~use~~method of any one of claims 1-~~27~~10, wherein the monomethyl auristatin is monomethyl auristatin E (MMAE).

~~29. The method of any one of claims 1-27, wherein the monomethyl auristatin is monomethyl auristatin F (MMAF).~~

~~30~~12. The ~~use~~method of any one of claims 1-~~18~~11, wherein the antibody-drug conjugate is brentuximab vedotin.

~~31. The method of any one of claims 1-30, wherein the antibody-drug conjugate is administered at a dose ranging from of about 1.2 mg/kg of the subject's body weight.~~

~~32. The method of any one of claims 1-30, wherein the antibody-drug conjugate is administered at a dose ranging from of 1.2 mg/kg of the subject's body weight.~~

~~33. The method of any one of claims 1-30, wherein the antibody-drug conjugate is administered at a dose of about 0.9 mg/kg of the subject's body weight.~~

~~34. The method of any one of claims 1-30, wherein the antibody-drug conjugate is administered at a dose of 0.9 mg/kg of the subject's body weight.~~

~~35. The method of any one of claims 1-34, wherein the antibody-drug conjugate is administered once about every 2 weeks.~~

~~36. The method of any one of claims 1-34, wherein the antibody-drug conjugate is administered once every 2 weeks.~~

~~37. The method of claim 35 or 36, wherein the antibody-drug conjugate is administered for four 2-week treatment cycles.~~

~~38. The method of any one of claims 1-37, wherein the antibody-drug conjugate is administered to the subject by intravenous infusion.~~

~~39. The method of claim 38, wherein the intravenous infusion is about a 30 minute infusion.~~

~~40. The method of any one of claims 1-39, wherein the subject has a life expectancy of greater than 9 months prior to administration of the antibody-drug conjugate.~~

~~41~~13. The ~~method-use~~ of any one of claims 1-~~12~~40, wherein
a) the subject has received antiretroviral therapy (ART) for at least 24 weeks prior to administration of the antibody-drug conjugate; or
b) :

~~42. The method of claim 41, wherein~~ the subject has received ART for at least 12 months prior to administration of the antibody-drug conjugate; or
c) :

~~43. The method of claim 41, wherein~~ the subject has received ART for at least 24 months prior to administration of the antibody-drug conjugate.

~~44~~14. The ~~use~~method of any one of claims 1-~~43~~13, wherein the antibody-drug conjugate is to be administered in combination with ART.

~~4515.~~ The ~~use~~method of ~~claim 13 or claim 14~~any one of claims 41-44, wherein the ART is a nucleoside reverse transcriptase inhibitor, non-nucleoside reverse transcriptase inhibitor, protease inhibitor, fusion inhibitor, CCR5 antagonist, integrase inhibitor, post-attachment inhibitor, or pharmacokinetic enhancer.

~~4616.~~ The ~~use~~method of claim ~~4515~~, wherein

a) the ART comprises two or more of a nucleoside reverse transcriptase inhibitor, non-nucleoside reverse transcriptase inhibitor, protease inhibitor, fusion inhibitor, CCR5 antagonist, integrase inhibitor, post-attachment inhibitor, and pharmacokinetic enhancer; or

b) :

~~47. The method of claim 45, wherein~~ the ART comprises three or more of a nucleoside reverse transcriptase inhibitor, non-nucleoside reverse transcriptase inhibitor, protease inhibitor, fusion inhibitor, CCR5 antagonist, integrase inhibitor, post-attachment inhibitor, and pharmacokinetic enhancer; or

c) :

~~48. The method of claim 45, wherein~~ the ART comprises four or more of a nucleoside reverse transcriptase inhibitor, non-nucleoside reverse transcriptase inhibitor, protease inhibitor, fusion inhibitor, CCR5 antagonist, integrase inhibitor, post-attachment inhibitor, and pharmacokinetic enhancer.

~~4917.~~ The ~~use~~method of ~~claim 13~~any one of claims 41-48, wherein the ART comprises one or more of abacavir, emtricitabine, lamivudine, tenofovir disoproxil fumarate, zidovudine, doravirine, efavirenz, etravirine, nevirapine, rilpivirine, atazanavir, darunavir, fosamprenavir, ritonavir, saquinavir, tipranavir, enfuvirtide, maraviroc, dolutegravir, raltegravir, ibalizumab, and cobicistat.

18. The use of claim 14, wherein the ART comprises one or more of abacavir, emtricitabine, lamivudine, tenofovir disoproxil fumarate, zidovudine, doravirine, efavirenz, etravirine, nevirapine, rilpivirine, atazanavir, darunavir, fosamprenavir, ritonavir, saquinavir, tipranavir, enfuvirtide, maraviroc, dolutegravir, raltegravir, ibalizumab, and cobicistat.

~~50. The method of any one of claims 41-49, wherein the ART does not comprise a strong CYP3A4 inhibitor.~~

~~51. The method of any one of claims 41-49, wherein the ART does not comprise a strong P-gp inhibitor.~~

~~52~~19. The ~~use~~method of any one of claims 1-~~51~~18, wherein ~~administering~~administration of the antibody-drug conjugate results an increase in the CD4⁺ T-cell lymphocyte count in the subject to above 200 cells/ μ L.

~~53~~20. The ~~use~~method of any one of claims 1-~~52~~19, wherein ~~administering~~administration of the antibody-drug conjugate results in an increase in the CD4⁺ T-cell lymphocyte count by at least 50 cells/ μ L relative to the CD4⁺ T-cell lymphocyte count prior to administration.

~~54. The method of any one of claims 1-53, wherein administering the antibody drug conjugate results an increase in the CD8⁺ T-cell lymphocyte count in the subject relative to the CD8⁺ T-cell lymphocyte count prior to administration.~~

~~55. The method of any one of claims 1-54, wherein administering the antibody drug conjugate results in a decrease in the number of Treg cells relative to the number prior to the administration of the antibody drug conjugate.~~

~~56. The method of claim 55, wherein the Treg cells are CD4⁺.~~

~~57. The method of claim 55 or claim 56, wherein the Treg cells are CD30⁺.~~

~~58. The method of any one of claims 1-57, wherein administering the antibody drug conjugate results in a decrease in the number of memory T cells relative to the number prior to the administration of the antibody drug conjugate.~~

~~59. The method of claim 58, wherein the memory T cells are CD4⁺.~~

~~60. The method of claim 58 or claim 59, wherein the memory T cells are CD30⁺.~~

~~61. The method of any one of claims 1-60, wherein the subject has not been administered the antibody drug conjugate prior to the administration to increase CD4⁺ T-cell lymphocyte count in the subject.~~

~~62. The method of any one of claims 1-61, wherein the subject is a human.~~

~~63. A kit comprising:~~

~~(a) a dosage ranging from about 0.1 mg to about 500 mg of an of an antibody drug conjugate that binds to CD30, wherein the antibody drug conjugate comprises an anti-CD30 antibody or an antigen binding fragment thereof conjugated to a monomethyl auristatin or a functional analog thereof or a functional derivative thereof; and~~

~~(b) —instructions for using the antibody drug conjugate according to the method of any one of claims 1-62.~~

~~64. Use of an antibody drug conjugate that binds to CD30 for the manufacture of a medicament for use in the method of any one of claims 1-62.~~

~~65. An antibody drug conjugate that binds to CD30 for use in the method of any one of claims 1-62.~~