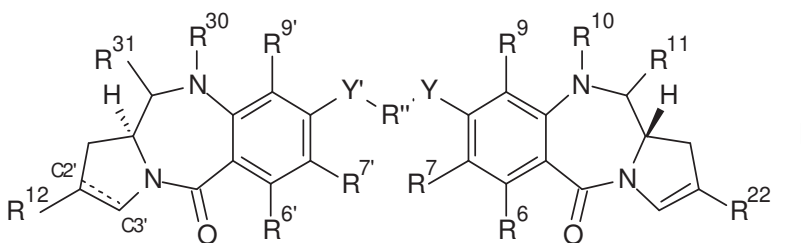
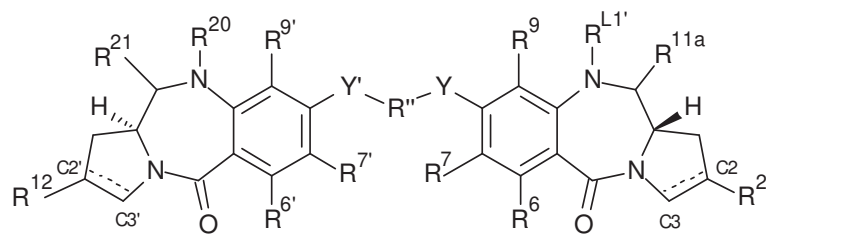


ibid.; Wang et al., Cell Res. 27 (1) (2017) 11–37); specific and effective molecular adjuvants are an essential part of these strategies.

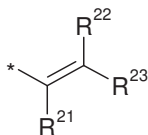
5 SUMMARY

The present authors have studied the effects of administering CD25-ADCs in a number of different disease models, including models with CD25-ve tumor target cells. Their observations indicated an efficacy beyond what was expected for either of direct target cell killing by the ADC combined with the so-called ‘bystander effect’ indirect cell killing, as described in WO/2016/083468. Building on these observations, the present authors reasoned that increased efficacy of ADCx25 arose from targeted cell-killing of AD25+ve regulatory immune cells, such as Tregs. That is, the present authors have determined that the CD25-ADCs described herein have applications as powerful and specific molecular adjuvants.

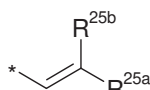
The therapies described herein include those that induce or enhance a subject’s immune response. In one aspect, the present disclosure is directed to of a CD25-ADC for the manufacture of a medicament for treating or preventing a CD25-ve solid tumour in a subject by targeting CD25+ve regulatory immune cells; wherein the CD25-ADC is a conjugate of formula L - (D^L)_p, where D^L is of formula I or II:



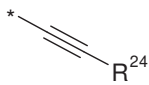
wherein: L is an antibody (Ab) which is an antibody that binds to CD25; when there is a double bond present between C2' and C3', R¹² is selected from the group consisting of: (ia) C₅₋₁₀ aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C₁₋₇ alkyl, C₃₋₇ heterocyclyl and bis-oxy-C₁₋₃ alkylene; (ib) C₁₋₅ saturated aliphatic alkyl; (ic) C₃₋₆ saturated cycloalkyl;



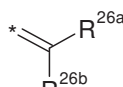
(id) _____, wherein each of R²¹, R²² and R²³ are independently selected from H, C₁₋₃ saturated alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl and cyclopropyl, where the total number of carbon atoms in the R¹² group is no more than 5;



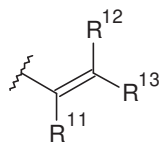
(ie) , wherein one of R^{25a} and R^{25b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and



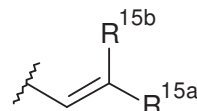
(if) , where R²⁴ is selected from: H; C₁₋₃ saturated alkyl; C₂₋₃ alkenyl; C₂₋₃ alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; when there is a single bond present between C2' and C3',



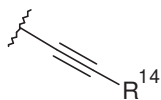
R¹² is , where R^{26a} and R^{26b} are independently selected from H, F, C₁₋₄ saturated alkyl, C₂₋₃ alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C₁₋₄ alkyl amido and C₁₋₄ alkyl ester; or, when one of R^{26a} and R^{26b} is H, the other is selected from nitrile and a C₁₋₄ alkyl ester; R⁶ and R⁹ are independently selected from H, R, OH, OR, SH, SR, NH₂, NHR, NRR', nitro, Me₃Sn and halo; where R and R' are independently selected from optionally substituted C₁₋₁₂ alkyl, C₃₋₂₀ heterocyclyl and C₅₋₂₀ aryl groups; R⁷ is selected from H, R, OH, OR, SH, SR, NH₂, NHR, NHRR', nitro, Me₃Sn and halo; R'' is a C₃₋₁₂ alkylene group, which chain may be interrupted by one or more heteroatoms, e.g. O, S, NR^{N2} (where R^{N2} is H or C₁₋₄ alkyl), and/or aromatic rings, e.g. benzene or pyridine; Y and Y' are selected from O, S, or NH; R⁶, R⁷, R⁹ are selected from the same groups as R⁶, R⁷ and R⁹ respectively; **[Formula I]** R^{L1'} is a linker for connection to the antibody (Ab); R^{11a} is selected from OH, OR^A, where R^A is C₁₋₄ alkyl, and SO₂M, where z is 2 or 3 and M is a monovalent pharmaceutically acceptable cation; R²⁰ and R²¹ either together form a double bond between the nitrogen and carbon atoms to which they are bound or; R²⁰ is selected from H and R^C, where R^C is a capping group; R²¹ is selected from OH, OR^A and SO₂M; when there is a double bond present between C2 and C3, R² is selected from the group consisting of: (ia) C₅₋₁₀ aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C₁₋₇ alkyl, C₃₋₇ heterocyclyl and bis-oxy-C₁₋₃ alkylene; (ib) C₁₋₅ saturated aliphatic alkyl; (ic) C₃₋₆ saturated cycloalkyl;



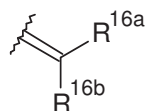
(id) , wherein each of R¹¹, R¹² and R¹³ are independently selected from H, C₁₋₃ saturated alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl and cyclopropyl, where the total number of carbon atoms in the R² group is no more than 5;



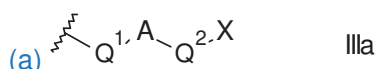
(ie) , wherein one of R^{15a} and R^{15b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and



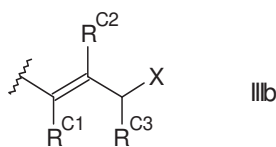
(if) _____, where R^{14} is selected from: H; C_{1-3} saturated alkyl; C_{2-3} alkenyl; C_{2-3} alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; when there is a single bond present between C2 and C3,



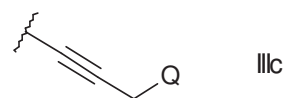
R^2 is _____, where R^{16a} and R^{16b} are independently selected from H, F, C_{1-4} saturated alkyl, C_{2-3} alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C_{1-4} alkyl amido and C_{1-4} alkyl ester; or, when one of R^{16a} and R^{16b} is H, the other is selected from nitrile and a C_{1-4} alkyl ester; **[Formula II]** R^{22} is of formula IIIa, formula IIIb or formula IIIc:



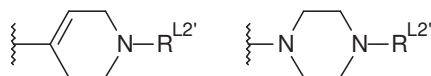
where A is a C_{5-7} aryl group, and either (i) Q^1 is a single bond, and Q^2 is selected from a single bond and $-Z-(CH_2)_n-$, where Z is selected from a single bond, O, S and NH and n is from 1 to 3; or (ii) Q^1 is $-CH=CH-$, and Q^2 is a single bond;



where; R^{C1} , R^{C2} and R^{C3} are independently selected from H and unsubstituted C_{1-2} alkyl;

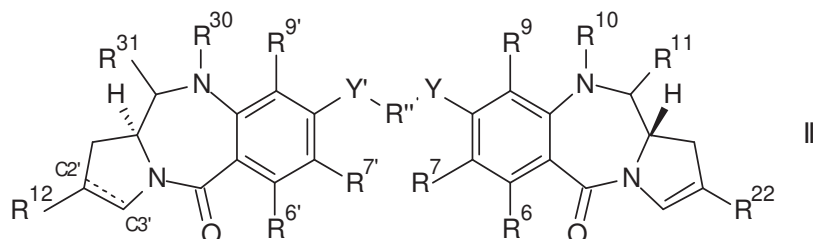
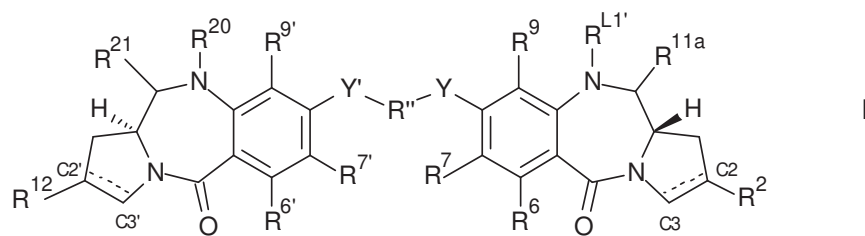


where Q is selected from $O-R^{L2'}$, $S-R^{L2'}$ and $NR^N-R^{L2'}$, and R^N is selected from H, methyl and ethyl X is selected from the group comprising: $O-R^{L2'}$, $S-R^{L2'}$, $CO_2-R^{L2'}$, $CO-R^{L2'}$, $NH-C(=O)-$



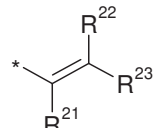
$R^{L2'}$, $NHNH-R^{L2'}$, $CONHNH-R^{L2'}$, $NR^N-R^{L2'}$, wherein R^N is selected from the group comprising H and C_{1-4} alkyl; $R^{L2'}$ is a linker for connection to the antibody (Ab); R^{10} and R^{11} either together form a double bond between the nitrogen and carbon atoms to which they are bound or; R^{10} is H and R^{11} is selected from OH, OR^A and SO_2M ; R^{30} and R^{31} either together form a double bond between the nitrogen and carbon atoms to which they are bound or; R^{30} is H and R^{31} is selected from OH, OR^A and SO_2M . In

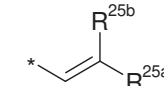
~~one~~ another aspect, the present disclosure refers to use of a CD25-ADC in the manufacture of a medicament for inducing or enhancing an immune response in a subject by targeting CD25+ve regulatory immune cells, wherein the CD25-ADC is a conjugate of formula L - $(D^L)_p$, where D^L is of formula I or II:

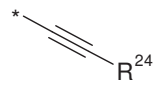


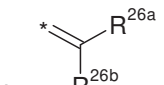
wherein:

- 5 L is an antibody (Ab) which is an antibody that binds to CD25; when there is a double bond present between C2' and C3', R¹² is selected from the group consisting of: (ia) C₅₋₁₀ aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C₁₋₇ alkyl, C₃₋₇ heterocyclyl and bis-oxy-C₁₋₃ alkylene; (ib) C₁₋₅ saturated aliphatic alkyl; (ic) C₃₋₆ saturated cycloalkyl;

- 10 (id) , wherein each of R²¹, R²² and R²³ are independently selected from H, C₁₋₃ saturated alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl and cyclopropyl, where the total number of carbon atoms in the R¹² group is no more than 5;

- (ie) , wherein one of R^{25a} and R^{25b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and

- 15 (if) , where R²⁴ is selected from: H; C₁₋₃ saturated alkyl; C₂₋₃ alkenyl; C₂₋₃ alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; when there is a single bond present between C2' and C3',

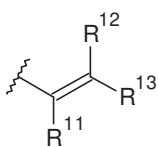
- 20 R¹² is , where R^{26a} and R^{26b} are independently selected from H, F, C₁₋₄ saturated alkyl, C₂₋₃ alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C₁₋₄ alkyl amido and C₁₋₄ alkyl ester; or, when one of R^{26a} and R^{26b} is H, the other is selected from nitrile and a C₁₋₄ alkyl ester; R⁶ and R⁹ are independently selected from H, R, OH, OR, SH, SR, NH₂, NHR, NRR', nitro, Me₃Sn and halo; where R and R' are independently selected from optionally substituted C₁₋₁₂ alkyl, C₃₋₂₀ heterocyclyl and C₅₋₂₀ aryl groups; R⁷ is selected from H, R, OH, OR, SH, SR, NH₂, NHR, NHRR', nitro, Me₃Sn and
- 25

halo; R" is a C₃₋₁₂ alkylene group, which chain may be interrupted by one or more heteroatoms, e.g. O, S, NR^{N2} (where R^{N2} is H or C₁₋₄ alkyl), and/or aromatic rings, e.g. benzene or pyridine; Y and Y' are selected from O, S, or NH; R^{6'}, R^{7'}, R^{9'} are selected from the same groups as R⁶, R⁷ and R⁹ respectively;

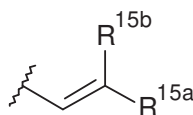
5 **[Formula I]**

R^{L1'} is a linker for connection to the antibody (Ab);

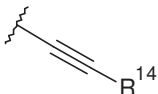
- R^{11a} is selected from OH, OR^A, where R^A is C₁₋₄ alkyl, and SO₂M, where z is 2 or 3 and M is a monovalent pharmaceutically acceptable cation; R²⁰ and R²¹ either together form a double bond between the nitrogen and carbon atoms to which they are bound or; R²⁰ is selected from H and R^C, where R^C is a capping group; R²¹ is selected from OH, OR^A and SO₂M; when there is a double bond present between C2 and C3, R² is selected from the group consisting of: (ia) C₅₋₁₀ aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C₁₋₇ alkyl, C₃₋₇ heterocyclyl and bis-oxy-C₁₋₃ alkylene; (ib) C₁₋₅ saturated aliphatic alkyl; (ic) C₃₋₆ saturated cycloalkyl;



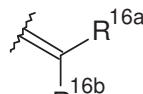
- (id) , wherein each of R¹¹, R¹² and R¹³ are independently selected from H, C₁₋₃ saturated alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl and cyclopropyl, where the total number of carbon atoms in the R² group is no more than 5;



- 20 (ie) , wherein one of R^{15a} and R^{15b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and



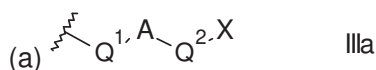
- (if) , where R¹⁴ is selected from: H; C₁₋₃ saturated alkyl; C₂₋₃ alkenyl; C₂₋₃ alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; when there is a single bond present between C2 and C3,



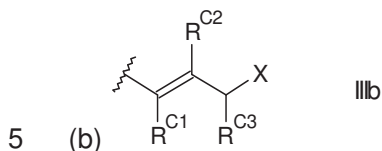
- R² is , where R^{16a} and R^{16b} are independently selected from H, F, C₁₋₄ saturated alkyl, C₂₋₃ alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C₁₋₄ alkyl amido and C₁₋₄ alkyl ester; or, when one of R^{16a} and R^{16b} is H, the other is selected from nitrile and a C₁₋₄ alkyl ester;

30 **[Formula II]**

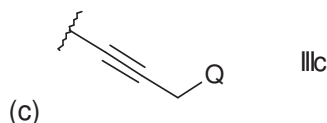
R²² is of formula IIIa, formula IIIb or formula IIIc:



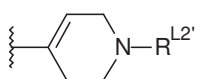
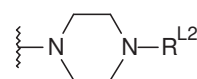
where A is a C₅₋₇ aryl group, and either (i) Q¹ is a single bond, and Q² is selected from a single bond and -Z-(CH₂)_n-, where Z is selected from a single bond, O, S and NH and n is from 1 to 3; or (ii) Q¹ is -CH=CH-, and Q² is a single bond;



where; R^{C1}, R^{C2} and R^{C3} are independently selected from H and unsubstituted C₁₋₂ alkyl;



where Q is selected from O-R^{L2'}, S-R^{L2'} and NR^N-R^{L2'}, and R^N is selected from H, methyl and ethyl, X is selected from the group comprising: O-R^{L2'}, S-R^{L2'}, CO₂-R^{L2'}, CO-R^{L2'}, NH-C(=O)-

10 R^{L2'}, NHNH-R^{L2'}, CONHNH-R^{L2'}, , , NR^NR^{L2'}, wherein R^N is selected from the group comprising H and C₁₋₄ alkyl; R^{L2'} is a linker for connection to the antibody (Ab); R¹⁰ and R¹¹ either together form a double bond between the nitrogen and carbon atoms to which they are bound or; R¹⁰ is H and R¹¹ is selected from OH, OR^A and SO₂M; R³⁰ and R³¹ either together form a double bond between the nitrogen and carbon atoms to which they are bound or; R³⁰ is H and R³¹ is selected from OH, OR^A and SO₂M.

20 ~~In another aspect, the present disclosure refers to use of a CD25-ADC as disclosed herein for the manufacture of a medicament for treating or preventing a disorder a subject, wherein the disorder is characterized by a disorder associated antigen (DAA). In another aspect, the present disclosure refers to a use of a CD25-ADC as disclosed herein in the manufacture of a medicament for treating or preventing a proliferative disorder, or a pathogen-associated disorder in a subject. In another aspect, the present disclosure refers to a use of a CD25-ADC as disclosed herein in the manufacture of a medicament for treating a disorder a subject, wherein the disorder is characterized by a disorder associated antigen (DAA), wherein the subject: (i) has received an adoptive cell transfer; or (ii) has been selected for treatment on the basis they have received an adoptive cell transfer. In another aspect, the present disclosure refers to a use of a CD25-ADC as disclosed herein in the manufacture of a medicament for use in combinatorial therapy for enhancing the efficacy of cell therapy in a subject, wherein said medicament is to be administered in combination with the cell therapy.~~

25 ~~In yet another aspect, the present disclosure refers to a use of a CD25-ADC as disclosed in the manufacture of a medicament for use in combinatorial therapy for treating a disorder a subject, wherein the disorder is characterized by a disorder associated antigen (DAA), wherein said medicament is to be administered in combination with a cell therapy. In another aspect, the present disclosure refers to a method of selecting a subject as suitable for treatment with a CD25-ADC, the method comprising the steps of: (a) identifying a subject who: (i) has, is suspected of having, has been diagnosed with, or is at risk of, a disorder characterized by a disorder associated antigen (DAA), and/or (ii) has received an adoptive~~

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~~cell transfer, and/or (iii) has been selected for treatment with cell therapy; and (b) selecting the subject for treatment with the CD25-ADC.~~

In particular, in certain examples the therapies include treating a disorder by inducing or enhancing the immune response of a subject against an antigen associated with the disorder. In some examples the therapies described herein enhance or induce an immune response by targeting immune regulatory cells with a CD25-ADC. The targeting of immune regulatory cells in this manner allows for a reduction in the negative regulation of the subject's immune responses to an existing or newly presented antigen.

In some examples the therapies described herein enhance or induce an immune response by directly killing target cells through cytotoxic ADC binding to the target cells and/or, through a 'bystander effect', indirectly killing target cells in the proximity of cells that are directly bound by the cytotoxic ADC (see, for example, WO/2016/083468). Without wishing to be bound by theory, it is believed that this killing of target cells causes the release of target antigens, 'stranger signals', 'neo-epitopes', and/or 'danger signals' into the extracellular environment where they can interact with and further stimulate a subject's immune system (see, for example, Virgil EJC Schijns & Ed C Lavelle (2011) Expert Review of Vaccines, 10:4, 539-550).

Thus, in one example, the present disclosure provides a method of inducing or enhancing an immune response in a subject, the method comprising the step of administering a CD25-ADC to the subject. The immune response may be disorder-associated antigen (DAA) specific immune response, such as a CD8+ T cell response, a CD4+ T cell response, an antibody response, or a memory cell response.

In another example, the present disclosure provides a method of treating or preventing a disorder a subject, wherein the disorder is characterized by a disorder-associated antigen (DAA), the method comprising administering a CD25-ADC to the subject.

In some examples the CD25-ADC is administered in combination with a DAA. The DAA may be administered as part of a vaccine composition, optionally wherein the CD25-ADC is also part of the same vaccine composition.

The CD25-ADC may be administered in combination with the DAA or vaccine composition, although they may be administered concomitantly. Preferably, the CD25-ADC is administered before the DAA or vaccine composition. The immune-suppressive activity or size of a population of regulatory immune cells in the subject may be reduced by at least 90% before the DAA or vaccine composition is administered. Preferably the regulatory immune cells are Treg cells.

The DAA may be tumour-associated antigen (TAA) or a pathogen-associated antigen (PAA). The PAA is derived from a pathogen selected from the group consisting of a virus, bacterium, fungus, protozoa, parasite, prion protein, or protein aggregate.

In some cases the subject has, is suspected of having, has been diagnosed with, or is at risk of, a disorder characterized by a disorder-associated antigen (DAA). In some cases the subject has been selected for treatment on the basis that the subject has, is suspected of having, has been diagnosed with, or is at risk of, a disorder characterized by a disorder-associated antigen (DAA).

The disorder may be a proliferative disorder such as cancer. In some cases, the proliferative disorder or cancer is a solid tumour, which may comprise or consist of CD25+ve neoplastic cells. The solid tumour may be associated with CD25+ve infiltrating cells, in some cases high levels of CD25+ve infiltrating cells. In some cases the solid tumour is selected from the group consisting of pancreatic cancer, breast cancer (including triple negative breast cancer), colorectal cancer, gastric and oesophageal cancer, melanoma, non-small cell lung cancer, ovarian cancer, hepatocellular carcinoma, renal cell carcinoma, bladder, and head and neck cancer.

In some cases the proliferative disorder or cancer is lymphoma or leukaemia, such as Hodgkin's Lymphoma; non-Hodgkin's, including diffuse large B-cell lymphoma (DLBCL), follicular lymphoma, (FL), Mantle Cell lymphoma (MCL), chronic lymphatic lymphoma (CLL) Marginal Zone B-cell lymphoma (MZBL); and leukemias, including Hairy cell leukemia (HCL), Hairy cell leukemia variant (HCL-v), Acute Myeloid Leukaemia (AML), and Acute Lymphoblastic Leukaemia (ALL) such as Philadelphia chromosome-positive ALL (Ph+ALL) or Philadelphia chromosome-negative ALL (Ph-ALL). The proliferative disorder or cancer may be associated with elevated levels of regulatory immune cells, such as Treg cells.

The subject may be selected for treatment on the basis that the subject has received an adoptive cell transfer, such as a bone marrow transplant. The adoptive cell transfer may be an autologous cell transfer or an allogenic cell transfer, and may be a stem cell transfer and/or an immune cell transfer. In some cases, the subject received the adoptive cell transfer at least 3 months prior to the administration of the CD25-ADC, such as at least 6 months, at least 12 months, at least 18 months, or at least 24 months prior to the administration of the CD25-ADC.

The CD25-ADC may be administered in combination with a cell therapy. Preferably, the CD25-ADC is administered before the cell therapy, such as at least 7 days before the cell therapy. The immune-suppressive activity or size of a population of regulatory immune cells in the subject may be reduced by at least 90% before the cell therapy is administered. Preferably the regulatory immune cells are Treg cells. The cell therapy may comprise the administration of autologous cells, allogenic cells, stem cells, and/or immune cells.

Preferably, the administered cells are immune cells such as T-cells, Natural Killer (NK) cells, Natural Killer T-cell (NKT), Lymphokine-activated Killer (LAK) cells, or macrophages. The immune cells express a chimeric antigen receptor (CAR). In some examples the immune cells are CAR T-cells, such as a 1st generation CAR T-cell, a 2nd generation CAR T-cell, a 3rd generation CAR T-cell, a 4th generation CAR T-cell, a TRUCK, a smart CAR, or an iCAR.

In another example, the disclosure also provides an antibody-drug conjugate compound as disclosed herein for use in a method of treatment as disclosed herein.

- 5 In another example, the disclosure also provides a composition or pharmaceutical composition comprising an antibody-drug conjugate compound as disclosed herein for use in a method of treatment as disclosed herein.

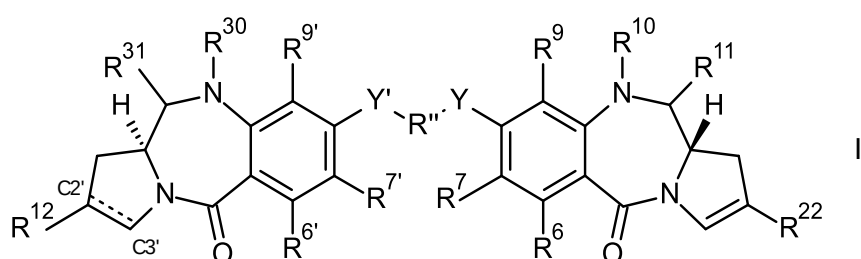
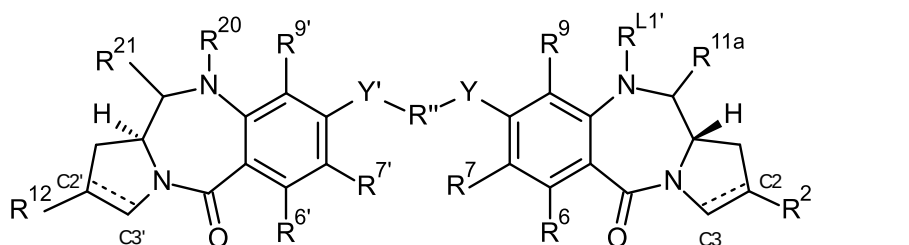
- 10 In another example, the disclosure also provides a use of an antibody-drug conjugate compound as disclosed herein in the preparation of a medicament for use in a method of treatments as disclosed herein.

CLAIMS

1. Use of a CD25-ADC for the manufacture of a medicament for treating or preventing a CD25-ve solid tumour in a subject by targeting CD25+ve regulatory immune cells;

wherein the CD25-ADC is a conjugate of formula L - $(D^L)_p$, where D^L is of formula I or

II:



wherein:

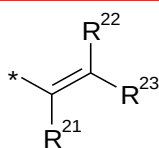
L is an antibody (Ab) which is an antibody that binds to CD25;

when there is a double bond present between C2' and C3', R¹² is selected from the group consisting of:

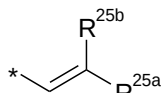
(ia) C₅₋₁₀ aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C₁₋₇ alkyl, C₃₋₇ heterocyclyl and bis-oxy-C₁₋₃ alkylene;

(ib) C₁₋₅ saturated aliphatic alkyl;

(ic) C₃₋₆ saturated cycloalkyl;



(id) _____, wherein each of R²¹, R²² and R²³ are independently selected from H, C₁₋₃ saturated alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl and cyclopropyl, where the total number of carbon atoms in the R¹² group is no more than 5;

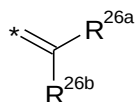


(ie) _____, wherein one of R^{25a} and R^{25b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and



(if) _____, where R²⁴ is selected from: H; C₁₋₃ saturated alkyl; C₂₋₃ alkenyl; C₂₋₃ alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl;

when there is a single bond present between C2' and C3',



R¹² is , where R^{26a} and R^{26b} are independently selected from H, F, C₁₋₄ saturated alkyl, C₂₋₃ alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C₁₋₄ alkyl amido and C₁₋₄ alkyl ester; or, when one of R^{26a} and R^{26b} is H, the other is selected from nitrile and a C₁₋₄ alkyl ester;

R⁶ and R⁹ are independently selected from H, R, OH, OR, SH, SR, NH₂, NHR, NRR', nitro, Me₃Sn and halo;

where R and R' are independently selected from optionally substituted C₁₋₁₂ alkyl, C₃₋₂₀ heterocyclyl and C₅₋₂₀ aryl groups;

R⁷ is selected from H, R, OH, OR, SH, SR, NH₂, NHR, NHRR', nitro, Me₃Sn and halo;

R'' is a C₃₋₁₂ alkylene group, which chain may be interrupted by one or more heteroatoms, e.g. O, S, NR^{N2} (where R^{N2} is H or C₁₋₄ alkyl), and/or aromatic rings, e.g. benzene or pyridine;

Y and Y' are selected from O, S, or NH;

R⁶, R⁷, R⁹ are selected from the same groups as R⁶, R⁷ and R⁹ respectively;

[Formula I]

R^{L1'} is a linker for connection to the antibody (Ab);

R^{11a} is selected from OH, OR^A, where R^A is C₁₋₄ alkyl, and SO_zM, where z is 2 or 3 and M is a monovalent pharmaceutically acceptable cation;

R²⁰ and R²¹ either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R²⁰ is selected from H and R^C, where R^C is a capping group;

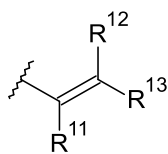
R²¹ is selected from OH, OR^A and SO_zM;

when there is a double bond present between C2 and C3, R² is selected from the group consisting of:

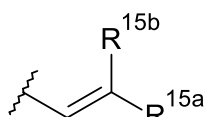
(ia) C₅₋₁₀ aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C₁₋₇ alkyl, C₃₋₇ heterocyclyl and bis-oxy-C₁₋₃ alkylene;

(ib) C₁₋₅ saturated aliphatic alkyl;

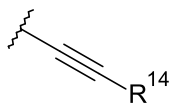
(ic) C₃₋₆ saturated cycloalkyl;



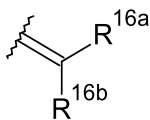
(id) , wherein each of R¹¹, R¹² and R¹³ are independently selected from H, C₁₋₃ saturated alkyl, C₂₋₃ alkenyl, C₂₋₃ alkynyl and cyclopropyl, where the total number of carbon atoms in the R² group is no more than 5;



(ie) , wherein one of R^{15a} and R^{15b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and



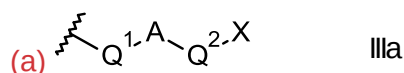
(if) ---R^{14} , where R^{14} is selected from: H; C_{1-3} saturated alkyl; C_{2-3} alkenyl; C_{2-3} alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; when there is a single bond present between C2 and C3.



R^2 is ---R^{16a} , where R^{16a} and R^{16b} are independently selected from H, F, C_{1-4} saturated alkyl, C_{2-3} alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C_{1-4} alkyl amido and C_{1-4} alkyl ester; or, when one of R^{16a} and R^{16b} is H, the other is selected from nitrile and a C_{1-4} alkyl ester;

[Formula III]

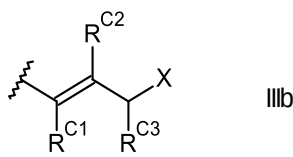
R^{22} is of formula IIIa, formula IIIb or formula IIIc:



where A is a C_{5-7} aryl group, and either

(i) Q^1 is a single bond, and Q^2 is selected from a single bond and $-\text{Z}-(\text{CH}_2)_n-$, where Z is selected from a single bond, O, S and NH and n is from 1 to 3; or

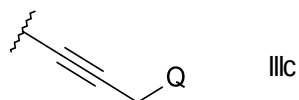
(ii) Q^1 is $-\text{CH}=\text{CH}-$, and Q^2 is a single bond;



(b)

where:

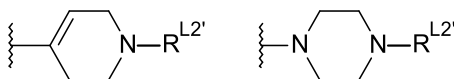
$\text{R}^{\text{C}1}$, $\text{R}^{\text{C}2}$ and $\text{R}^{\text{C}3}$ are independently selected from H and unsubstituted C_{1-2} alkyl;



(c)

where Q is selected from $\text{O-R}^{\text{L}2'}$, $\text{S-R}^{\text{L}2'}$ and $\text{NR}^{\text{N}}-\text{R}^{\text{L}2'}$, and R^{N} is selected from H, methyl and ethyl

X is selected from the group comprising: $\text{O-R}^{\text{L}2'}$, $\text{S-R}^{\text{L}2'}$, $\text{CO}_2-\text{R}^{\text{L}2'}$, $\text{CO-R}^{\text{L}2'}$, $\text{NH-C(=O)-R}^{\text{L}2'}$,



$\text{NHNH-R}^{\text{L}2'}$, $\text{CONHNH-R}^{\text{L}2'}$, $\text{NR}^{\text{N}}-\text{R}^{\text{L}2'}$, wherein R^{N} is selected from the group comprising H and C_{1-4} alkyl;

$\text{R}^{\text{L}2'}$ is a linker for connection to the antibody (Ab);

R^{10} and R^{11} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{10} is H and R^{11} is selected from OH, OR^{A} and SO_2M ;

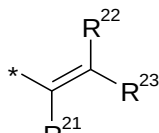
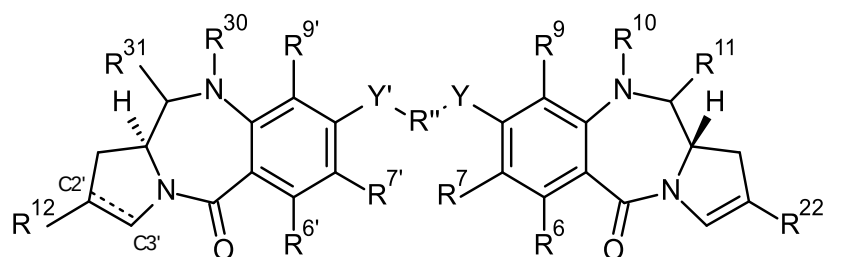
R^{30} and R^{31} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

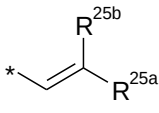
R^{30} is H and R^{31} is selected from OH, OR^{A} and SO_2M .

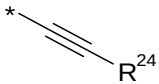
2. The use of claim 1, wherein the CD25+ve regulatory immune cells are Tregs.
3. The use of any one of claims 1 to 2, wherein the CD25+ve solid tumour is an established tumour or a metastatic tumour.
4. The use of claim 3, wherein the established tumour is a tumour diagnosed or identified in a naïve subject.
5. The use of claim 3, wherein the established tumour is a relapsed tumour.
6. The use of any one of claims 1 to 5, wherein the CD25+ve solid tumour comprises or consists of CD25+ve neoplastic cells.
7. The use of any one of claims 1 to 6, wherein the CD25+ve solid tumour is associated with CD25+ve infiltrating cells; optionally wherein the CD25+ve solid tumour is associated with high levels of CD25+ve infiltrating cells.
8. The use of any one of claims 1 to 7, wherein the solid tumour is selected from the group consisting of pancreatic cancer, breast cancer (including triple negative breast cancer), colorectal cancer, gastric and oesophageal cancer, melanoma, non-small cell lung cancer, ovarian cancer, hepatocellular carcinoma, renal cell carcinoma, bladder, and head and neck cancer.
9. The use of any one of claims 1 to 8, wherein the use comprises that the subject is to be selected for treatment on the basis that the subject has received an adoptive cell transfer; and wherein the CD25-ADC is to be administered to the subject.
10. The use of claim 9, wherein the adoptive cell transfer is a bone marrow transplant.
11. The use of claims 9 to 10, wherein the subject received the adoptive cell transfer at least 3 months prior to the administration of the CD25-ADC, such as at least 6 months, at least 12 months, at least 18 months, or at least 24 months prior to the administration of the CD25-ADC.
12. The use of any one of claims 1 to 11, wherein the CD25-ADC is to be administered in combination with a cell therapy.
13. The use of claim 12, wherein the CD25-ADC is to be administered before the cell therapy; optionally wherein the CD25-ADC is to be administered 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, or 14 days before the cell therapy.
14. The use of any one of claims 12 to 13, wherein the size of a population of Treg cells in the subject is reduced by at least 90% before the cell therapy is to be administered.

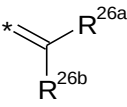
16. The use of any one of claims 12 to 15, wherein the cell therapy comprises **that** T-cells, Natural Killer (NK) cells, Natural Killer T-cell (NKT), Lymphokine-activated Killer (LAK) cells, or macrophages **are to be administered**.

118. Use of a CD25-ADC in the manufacture of a medicament for inducing or enhancing an immune response in a subject by targeting CD25+ve regulatory immune cells, wherein the CD25-ADC is a conjugate of formula L - (D^L)_p, where D^L is of formula I or



(ie) , wherein one of R^{25a} and R^{25b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and

(if) , where R²⁴ is selected from: H; C₁₋₃ saturated alkyl; C₂₋₃ alkenyl; C₂₋₃ alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; when there is a single bond present between C2' and C3',

R¹² is , where R^{26a} and R^{26b} are independently selected from H, F, C₁₋₄ saturated alkyl, C₂₋₃ alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C₁₋₄ alkyl amido and C₁₋₄ alkyl ester; or, when one of R^{26a} and R^{26b} is H, the other is selected from nitrile and a C₁₋₄ alkyl ester;

R⁶ and R⁹ are independently selected from H, R, OH, OR, SH, SR, NH₂, NHR, NRR', nitro, Me₃Sn and halo;

where R and R' are independently selected from optionally substituted C₁₋₁₂ alkyl, C₃₋₂₀ heterocyclyl and C₅₋₂₀ aryl groups;

R⁷ is selected from H, R, OH, OR, SH, SR, NH₂, NHR, NHRR', nitro, Me₃Sn and halo;

R'' is a C₃₋₁₂ alkylene group, which chain may be interrupted by one or more heteroatoms, e.g. O, S, NR^{N2} (where R^{N2} is H or C₁₋₄ alkyl), and/or aromatic rings, e.g. benzene or pyridine;

Y and Y' are selected from O, S, or NH;

R^{6'}, R^{7'}, R^{9'} are selected from the same groups as R⁶, R⁷ and R⁹ respectively;

[Formula I]

R^{L1'} is a linker for connection to the antibody (Ab);

R^{11a} is selected from OH, OR^A, where R^A is C₁₋₄ alkyl, and SO_zM, where z is 2 or 3 and M is a monovalent pharmaceutically acceptable cation;

R²⁰ and R²¹ either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R²⁰ is selected from H and R^C, where R^C is a capping group;

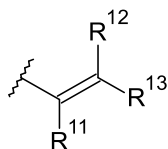
R²¹ is selected from OH, OR^A and SO_zM;

when there is a double bond present between C2 and C3, R² is selected from the group consisting of:

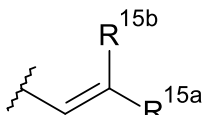
(ia) C₅₋₁₀ aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C₁₋₇ alkyl, C₃₋₇ heterocyclyl and bis-oxy-C₁₋₃ alkylene;

(ib) C₁₋₅ saturated aliphatic alkyl;

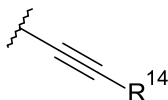
(ic) C₃₋₆ saturated cycloalkyl;



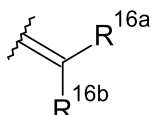
(id) , wherein each of R^{11} , R^{12} and R^{13} are independently selected from H, C_{1-3} saturated alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl and cyclopropyl, where the total number of carbon atoms in the R^2 group is no more than 5;



(ie) , wherein one of R^{15a} and R^{15b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and



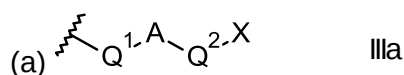
(if) , where R^{14} is selected from: H; C_{1-3} saturated alkyl; C_{2-3} alkenyl; C_{2-3} alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; when there is a single bond present between C2 and C3,



R^2 is , where R^{16a} and R^{16b} are independently selected from H, F, C_{1-4} saturated alkyl, C_{2-3} alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C_{1-4} alkyl amido and C_{1-4} alkyl ester; or, when one of R^{16a} and R^{16b} is H, the other is selected from nitrile and a C_{1-4} alkyl ester;

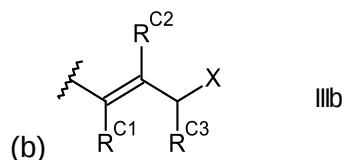
[Formula II]

R^{22} is of formula IIIa, formula IIIb or formula IIIc:



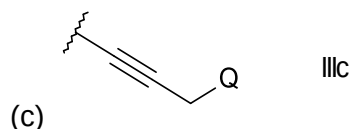
where A is a C_{5-7} aryl group, and either

- (i) Q^1 is a single bond, and Q^2 is selected from a single bond and $-Z-(CH_2)_n-$, where Z is selected from a single bond, O, S and NH and n is from 1 to 3; or
 (ii) Q^1 is $-CH=CH-$, and Q^2 is a single bond;



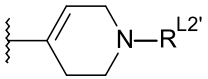
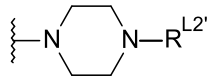
where;

R^{C1} , R^{C2} and R^{C3} are independently selected from H and unsubstituted C_{1-2} alkyl;



where Q is selected from $O-R^{L2'}$, $S-R^{L2'}$ and $NR^N-R^{L2'}$, and R^N is selected from H, methyl and ethyl

X is selected from the group comprising: O-R^{L2'}, S-R^{L2'}, CO₂-R^{L2'}, CO-R^{L2'}, NH-C(=O)-R^{L2'},

NHNH-R^{L2'}, CONHNH-R^{L2'}, , , NR^NR^{L2'}, wherein R^N is

selected from the group comprising H and C₁₋₄ alkyl;

R^{L2'} is a linker for connection to the antibody (Ab);

R¹⁰ and R¹¹ either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R¹⁰ is H and R¹¹ is selected from OH, OR^A and SO₂M;

R³⁰ and R³¹ either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

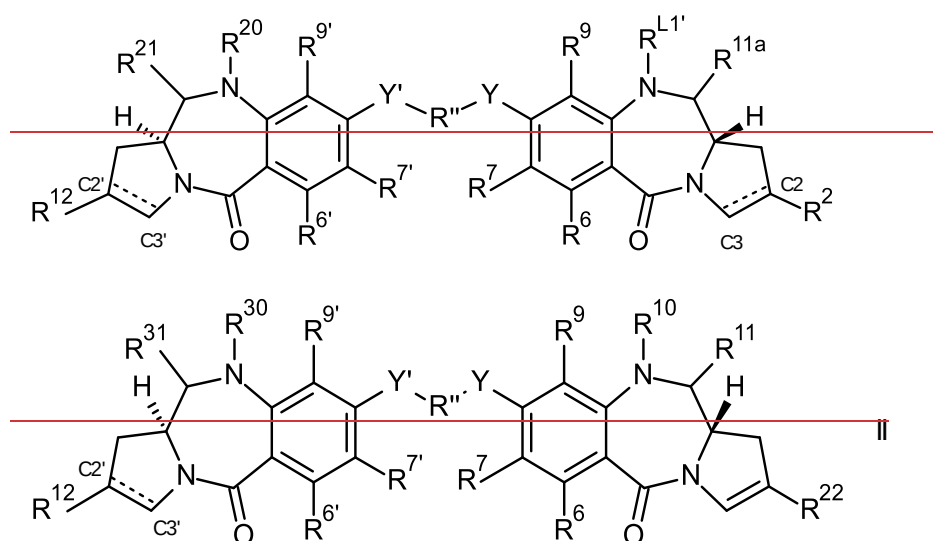
R³⁰ is H and R³¹ is selected from OH, OR^A and SO₂M.

192. The use of claim **181**, wherein the immune response is a disorder-associated antigen (DAA) specific immune response.

203. The use of either one of claims **118** and **192**, wherein the DAA-specific immune response is a CD8+ T cell response, a CD4+ T cell response, or an antibody response.

4. ~~Use of a CD25-ADC for the manufacture of a medicament for treating or preventing a disorder in a subject, wherein the disorder is characterized by a disorder-associated antigen (DAA);~~

~~wherein the CD25-ADC is a conjugate of formula L—(D^L)_p, where D^L is of formula I or II:~~



~~wherein:~~

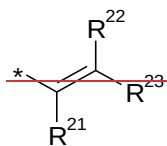
~~L is an antibody (Ab) which is an antibody that binds to CD25;~~

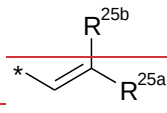
~~when there is a double bond present between C2' and C3', R¹² is selected from the group consisting of:~~

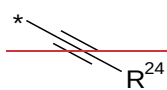
~~(ia) C₅₋₁₀-aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C₁₋₇-alkyl, C₃₋₇-heterocyclyl and bis-oxy-C₁₋₃-alkylene;~~

~~(ib) C₁₋₅-saturated aliphatic alkyl;~~

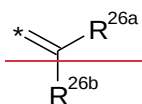
~~(ic) C₃₋₆-saturated cycloalkyl;~~

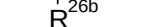
~~(id) , wherein each of R²¹, R²² and R²³ are independently selected from H, C₁₋₃ saturated alkyl, C₂₋₃-alkenyl, C₂₋₃-alkynyl and cyclopropyl, where the total number of carbon atoms in the R¹²-group is no more than 5;~~

~~(ie) , wherein one of R^{25a} and R^{25b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and~~

~~(if) , where R²⁴ is selected from: H; C₁₋₃-saturated alkyl; C₂₋₃-alkenyl; C₂₋₃ alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl;~~

~~when there is a single bond present between C2' and C3',~~



~~R¹² is~~ , where ~~R^{26a} and R^{26b} are independently selected from H, F, C₁₋₄-saturated alkyl, C₂₋₃-alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C₁₋₄-alkyl amido and C₁₋₄-alkyl ester; or, when one of R^{26a} and R^{26b} is H, the other is selected from nitrile and a C₁₋₄-alkyl ester;~~

~~R⁶ and R⁹ are independently selected from H, R, OH, OR, SH, SR, NH₂, NHR, NRR', nitro, Me₃Sn and halo;~~

~~where R and R' are independently selected from optionally substituted C₁₋₁₂-alkyl, C₃₋₂₀ heterocyclyl and C₅₋₂₀-aryl groups;~~

~~R⁷ is selected from H, R, OH, OR, SH, SR, NH₂, NHR, NHRR', nitro, Me₃Sn and halo;~~

~~R'' is a C₃₋₁₂-alkylene group, which chain may be interrupted by one or more heteroatoms, e.g. O, S, NR^{N2} (where R^{N2} is H or C₁₋₄-alkyl), and/or aromatic rings, e.g. benzene or pyridine;~~

~~Y and Y' are selected from O, S, or NH;~~

~~R^{6'}, R^{7'}, R^{9'} are selected from the same groups as R⁶, R⁷ and R⁹ respectively;~~

[Formula I]

~~R^{L4'} is a linker for connection to the antibody (Ab);~~

~~R^{11a} is selected from OH, OR^A, where R^A is C₁₋₄-alkyl, and SO_zM, where z is 2 or 3 and M is a monovalent pharmaceutically acceptable cation;~~

~~R²⁰ and R²¹ either together form a double bond between the nitrogen and carbon atoms to which they are bound or;~~

~~R²⁰ is selected from H and R^C, where R^C is a capping group;~~

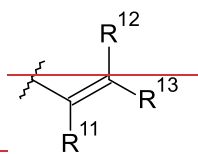
~~R²¹ is selected from OH, OR^A and SO_zM;~~

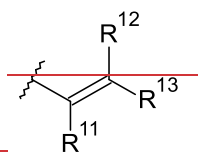
~~when there is a double bond present between C2 and C3, R² is selected from the group consisting of:~~

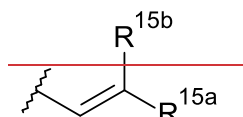
~~(ia) C₅₋₁₀-aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C₁₋₇-alkyl, C₃₋₇-heterocyclyl and bis-oxy-C₁₋₃-alkylene;~~

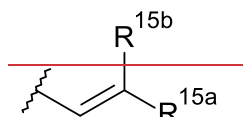
~~(ib) C₁₋₅-saturated aliphatic alkyl;~~

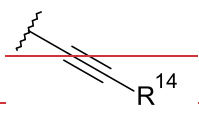
~~(ic) C₃₋₆-saturated cycloalkyl;~~

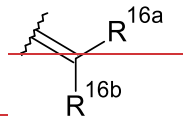


~~(id) , wherein each of R¹¹, R¹² and R¹³ are independently selected from H, C₁₋₃-saturated alkyl, C₂₋₃-alkenyl, C₂₋₃-alkynyl and cyclopropyl, where the total number of carbon atoms in the R²-group is no more than 5;~~



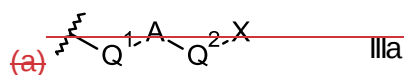
~~(ie) , wherein one of R^{15a} and R^{15b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy, pyridyl; and thiophenyl; and~~

(if) , where R^{14} is selected from: H; C_{1-3} -saturated alkyl; C_{2-3} -alkenyl; C_{2-3} -alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; when there is a single bond present between C2 and C3,

R^2 is , where R^{16a} and R^{16b} are independently selected from H, F, C_{1-4} -saturated alkyl, C_{2-3} -alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C_{1-4} -alkyl amido and C_{1-4} -alkyl ester; or, when one of R^{16a} and R^{16b} is H, the other is selected from nitrile and a C_{1-4} -alkyl ester;

[Formula II]

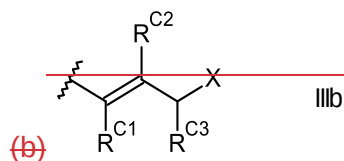
R^{22} is of formula IIIa, formula IIIb or formula IIIc:



where A is a C_{5-7} -aryl group, and either

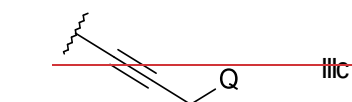
(i) Q^1 is a single bond, and Q^2 is selected from a single bond and $-Z-(CH_2)_n-$, where Z is selected from a single bond, O, S and NH and n is from 1 to 3; or

(ii) Q^1 is $-CH=CH-$, and Q^2 is a single bond;



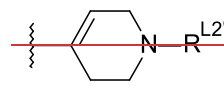
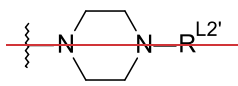
where;

R^{C1} , R^{C2} and R^{C3} are independently selected from H and unsubstituted C_{1-2} -alkyl;



where Q is selected from $O-R^{L2'}$, $S-R^{L2'}$ and $NR^N-R^{L2'}$, and R^N is selected from H, methyl and ethyl

X is selected from the group comprising: $O-R^{L2'}$, $S-R^{L2'}$, $CO_2-R^{L2'}$, $CO-R^{L2'}$, $NH-C(=O)-R^{L2'}$,

$NHNH-R^{L2'}$, $CONHNH-R^{L2'}$, , , $NR^N-R^{L2'}$, wherein R^N is selected from the group comprising H and C_{1-4} -alkyl;

$R^{L2'}$ is a linker for connection to the antibody (Ab);

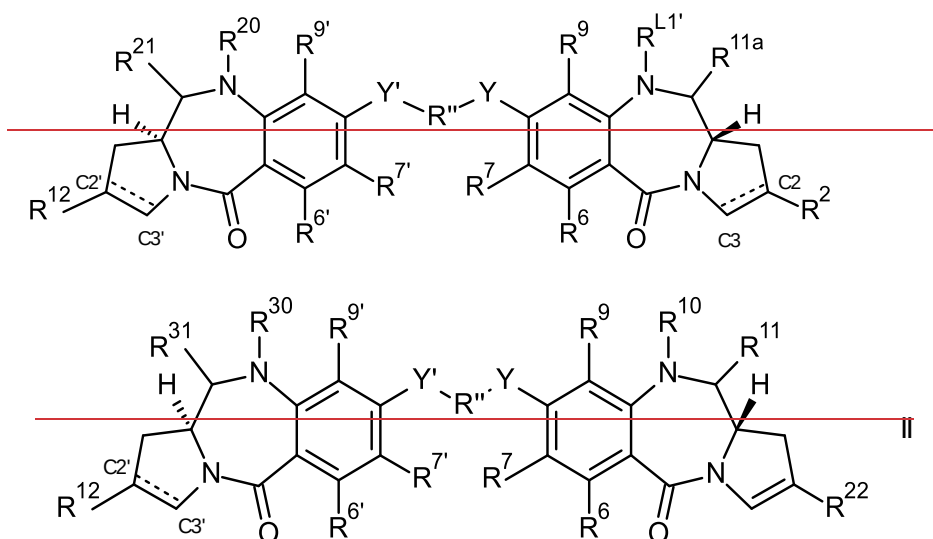
R^{10} and R^{11} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{10} is H and R^{11} is selected from OH, OR^A and SO_zM ;

R^{30} and R^{31} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{30} is H and R^{31} is selected from OH, OR^A and SO_zM .

5. ~~Use of a CD25-ADC in the manufacture of a medicament for treating or preventing a proliferative disorder, or a pathogen-associated disorder in a subject,~~
~~wherein the CD25-ADC is a conjugate of formula L—(D^L)_p, where D^L is of formula I or~~
II:

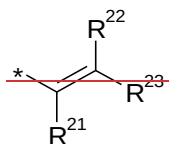


wherein:

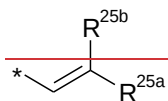
L is an antibody (Ab) which is an antibody that binds to CD25;

when there is a double bond present between C2' and C3', R¹² is selected from the group consisting of:

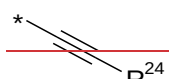
- (ia) C₅₋₁₀-aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C₁₋₇-alkyl, C₃₋₇-heterocyclyl and bis-oxy-C₁₋₃-alkylene;
- (ib) C₁₋₅-saturated aliphatic alkyl;
- (ic) C₃₋₆-saturated cycloalkyl;



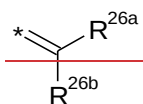
- (id) —, wherein each of R²¹, R²² and R²³ are independently selected from H, C₁₋₃ saturated alkyl, C₂₋₃-alkenyl, C₂₋₃-alkynyl and cyclopropyl, where the total number of carbon atoms in the R¹²-group is no more than 5;



- (ie) —, wherein one of R^{25a} and R^{25b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and



- (if) —, where R²⁴ is selected from: H; C₁₋₃-saturated alkyl; C₂₋₃-alkenyl; C₂₋₃ alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl;
- when there is a single bond present between C2' and C3',



~~R¹² is —, where R^{26a} and R^{26b} are independently selected from H, F, C₁₋₄-saturated alkyl, C₂₋₃-alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C₁₋₄-alkyl amido and C₁₋₄-alkyl ester; or, when one of R^{26a} and R^{26b} is H, the other is selected from nitrile and a C₁₋₄-alkyl ester;~~

~~R⁶ and R⁹ are independently selected from H, R, OH, OR, SH, SR, NH₂, NHR, NRR', nitro, Me₃Sn and halo;~~

~~where R and R' are independently selected from optionally substituted C₁₋₁₂-alkyl, C₃₋₂₀ heterocyclyl and C₅₋₂₀-aryl groups;~~

~~R⁷ is selected from H, R, OH, OR, SH, SR, NH₂, NHR, NHRR', nitro, Me₃Sn and halo;~~

~~R'' is a C₃₋₁₂-alkylene group, which chain may be interrupted by one or more heteroatoms, e.g. O, S, NR^{N2} (where R^{N2} is H or C₁₋₄-alkyl), and/or aromatic rings, e.g. benzene or pyridine;~~

~~Y and Y' are selected from O, S, or NH;~~

~~R^{6'}, R^{7'}, R^{9'} are selected from the same groups as R⁶, R⁷ and R⁹ respectively;~~

~~[Formula I]~~

~~R^{L1} is a linker for connection to the antibody (Ab);~~

~~R^{11a} is selected from OH, OR^A, where R^A is C₁₋₄-alkyl, and SO_zM, where z is 2 or 3 and M is a monovalent pharmaceutically acceptable cation;~~

~~R²⁰ and R²¹ either together form a double bond between the nitrogen and carbon atoms to which they are bound or;~~

~~R²⁰ is selected from H and R^C, where R^C is a capping group;~~

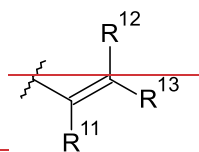
~~R²¹ is selected from OH, OR^A and SO_zM;~~

~~when there is a double bond present between C2 and C3, R² is selected from the group consisting of:~~

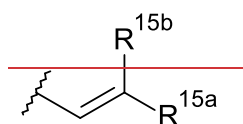
~~(ia) C₅₋₁₀-aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C₁₋₇-alkyl, C₃₋₇-heterocyclyl and bis-oxy-C₁₋₃-alkylene;~~

~~(ib) C₁₋₅-saturated aliphatic alkyl;~~

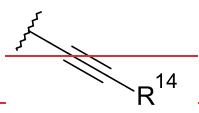
~~(ic) C₃₋₆-saturated cycloalkyl;~~

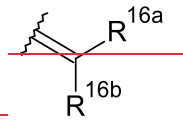


~~(id) —, wherein each of R¹¹, R¹² and R¹³ are independently selected from H, C₁₋₃-saturated alkyl, C₂₋₃-alkenyl, C₂₋₃-alkynyl and cyclopropyl, where the total number of carbon atoms in the R² group is no more than 5;~~



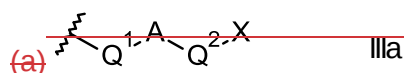
~~(ie) —, wherein one of R^{15a} and R^{15b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and~~

(if) , where R^{14} is selected from: H; C_{1-3} -saturated alkyl; C_{2-3} -alkenyl; C_{2-3} -alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; when there is a single bond present between C2 and C3,

R^2 is , where R^{16a} and R^{16b} are independently selected from H, F, C_{1-4} -saturated alkyl, C_{2-3} -alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C_{1-4} -alkyl amido and C_{1-4} -alkyl ester; or, when one of R^{16a} and R^{16b} is H, the other is selected from nitrile and a C_{1-4} -alkyl ester;

[Formula II]

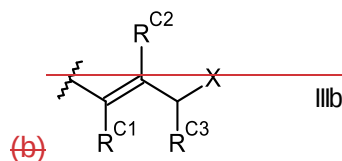
R^{22} is of formula IIIa, formula IIIb or formula IIIc:



where A is a C_{5-7} -aryl group, and either

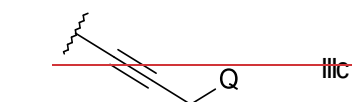
(i) Q^1 is a single bond, and Q^2 is selected from a single bond and $-Z-(CH_2)_n-$, where Z is selected from a single bond, O, S and NH and n is from 1 to 3; or

(ii) Q^1 is $-CH=CH-$, and Q^2 is a single bond;



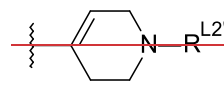
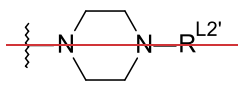
where;

R^{C1} , R^{C2} and R^{C3} are independently selected from H and unsubstituted C_{1-2} -alkyl;



where Q is selected from $O-R^{L2'}$, $S-R^{L2'}$ and $NR^N-R^{L2'}$, and R^N is selected from H, methyl and ethyl

X is selected from the group comprising: $O-R^{L2'}$, $S-R^{L2'}$, $CO_2-R^{L2'}$, $CO-R^{L2'}$, $NH-C(=O)-R^{L2'}$,

$NHNH-R^{L2'}$, $CONHNH-R^{L2'}$, , , $NR^N-R^{L2'}$, wherein R^N is selected from the group comprising H and C_{1-4} -alkyl;

$R^{L2'}$ is a linker for connection to the antibody (Ab);

R^{10} and R^{11} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{10} is H and R^{11} is selected from OH, OR^A and SO_zM ;

R^{30} and R^{31} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{30} is H and R^{31} is selected from OH, OR^A and SO_zM .

216. The use of any one of claims 181 to 204, wherein the CD25-ADC is to be administered in combination with a disorder-associated antigen (DAA).

227. The use of any one of claims 192 to 216, wherein the DAA is a:
(a) protein, polypeptide, peptide, peptide mimetic;
(b) a nucleic acid encoding a protein, polypeptide, peptide, peptide mimetic
(c) a sugar or oligosaccharide;
(d) a lipid, phospholipid, liposaccharide, or lipoprotein;
optionally wherein the DAA is a cell-surface antigen.

238. The use of either one of claims 216 or 227, wherein the DAA is to be administered as part of a vaccine composition, optionally wherein the CD25-ADC is also part of the same vaccine composition.

249. The use of any one of claims 227 to 823, wherein the CD25-ADC is to be administered before the DAA or vaccine composition.

2510. The use of any one of claims 216 to 249, wherein the size of a population of Treg cells in the subject is reduced by at least 90% before the DAA or vaccine composition is to be administered.

2611. The use of any one of claims 216 to 238, wherein the CD25-ADC is to be administered concomitantly with the DAA or vaccine composition.

2712. The use of any one of claims 192 to 1611, wherein the DAA is a tumour-associated antigen (TAA);

optionally wherein the TAA is selected from the group consisting of *BMPR1B*, *E16*, *STEAP1*, *0772P*, *MPF*, *Napi3b*, *Sema 5b*, *PSCA* hlg, *ETB*, *MSG783*, *STEAP2*, *TrpM4*, *CRIPTO*, *CD21*, *CD79b*, *FcRH2*, *HER2*, *NCA*, *MDP*, *IL20R-alpha*, *Brevican*, *EphB2R*, *ASLG659*, *PSCA*, *GEDA*, *BAFF-R*, *CD22*, *CD79a*, *CXCR5*, *HLA-DOB*, *P2X5*, *CD72*, *LY64*, *FcRH1*, *IRTA2*, *TENB2*, *PSMA*, *SST*, *ITGAV*, *ITGB6*, *CEACAM5*, *MET*, *MUC1*, *CA9*, *EGFRvIII*, *CD33*, *CD19*, *IL2RA*, *AXL*, *CD30*, *BCMA*, *CT Ags*, *CD174*, *CLEC14A*, *GRP78* – *HSPA5*, *CD70*, *Stem Cell specific antigens*, *ASG-5*, *ENPP3*, *PRR4*, *GCC* – *GUCY2C*, *Liv-1* – *SLC39A6*, *5T4*, *CD56* – *NCMA1*, *CanAg*, *FOLR1*, *GPNMB*, *TIM-1* – *HAVCR1*, *RG-1*, *B7-H4* – *VTCN1*, *PTK7*, *CD37*, *CD138*, *CD74*, *Claudins*, *EGFR*, *Her3*, *RON* – *MST1R*, *EPHA2*, *CD20* – *MS4A1*, *Tenascin C* – *TNC*, *FAP*, *DKK-1*, *CD52*, *CS1* – *SLAMF7*, *Endoglin*, *Annexin A1*, *V-CAM (CD106)*, *DLK-1*, and *KAAG1*.

2813. The use of any one of claims 192 to 2611, wherein the DAA is a pathogen-associated antigen (PAA).

2914. The use of claim 2813, wherein the PAA is derived from a pathogen selected from the group consisting of a virus, bacterium, fungus, protozoa, parasite, prion protein, or protein aggregate;
optionally wherein the pathogen is selected from:

Adeno-associated virus, Aichi virus, Australian bat lyssavirus, BK polyomavirus, Banna virus, Barmah forest virus, Bunyamwera virus, Bunyavirus La Crosse, Bunyavirus snowshoe hare, Cercopithecine herpesvirus, Chandipura virus, Chikungunya virus, Cosavirus A, Cowpox virus, Coxsackievirus, Crimean-Congo hemorrhagic fever virus, Dengue virus, Dhori virus, Dugbe virus, Duvenhage virus, Eastern equine encephalitis virus, Ebolavirus, Echovirus, Encephalomyocarditis virus, Epstein-Barr virus, European bat lyssavirus, GB virus C/Hepatitis G virus Pegivirus, Hantaan virus, Hendra virus, Hepatitis A virus, Hepatitis B virus, Hepatitis C virus, Hepatitis E virus, Hepatitis delta virus, Horsepox virus, Human adenovirus, Human astrovirus, Human coronavirus, Human cytomegalovirus, Human enterovirus 68, 70, Human herpesvirus 1, Human herpesvirus 2, Human herpesvirus 6, Human herpesvirus 7, Human herpesvirus 8, Human immunodeficiency virus, Human papillomavirus 1, Human papillomavirus 2, Human papillomavirus 16,18, Human parainfluenza, Human parvovirus B19, Human respiratory syncytial virus, Human rhinovirus, Human SARS coronavirus, Human spumaretrovirus, Human T-lymphotropic virus, Human torovirus, Influenza A virus, Influenza B virus, Isfahan virus, JC polyomavirus, Japanese encephalitis virus, Junin arenavirus, KI Polyomavirus, Kunjin virus, Lagos bat virus, Lake Victoria Marburgvirus, Langat virus, Lassa virus, Lordsdale virus, Louping ill virus, Lymphocytic choriomeningitis virus, Machupo virus, Mayaro virus, MERS coronavirus, Measles virus, Mengo encephalomyocarditis virus, Merkel cell polyomavirus, Mokola virus, Molluscum contagiosum virus, Monkeypox virus, Mumps virus, Murray valley encephalitis virus, New York virus, Nipah virus, Norwalk virus, O'nyong-nyong virus, Orf virus, Oropouche virus, Pichinde virus, Poliovirus, Punta toro phlebovirus, Puumala virus, Rabies virus, Rift valley fever virus, Rosavirus A, Ross river virus, Rotavirus A, Rotavirus B, Rotavirus C, Rubella virus, Sagiyama virus, Salivirus A, Sandfly fever sicilian virus, Sapporo virus, Semliki forest virus, Seoul virus, Simian foamy virus, Simian virus 5, Sindbis virus, Southampton virus, St. Louis encephalitis virus, Tick-borne powassan virus, Torque teno virus, Toscana virus, Uukuniemi virus, Vaccinia virus, Varicella-zoster virus, Variola virus O, Venezuelan equine encephalitis virus, Vesicular stomatitis virus, Western equine encephalitis virus, WU polyomavirus, West Nile virus, Yaba monkey tumor virus, Yaba-like disease virus, Yellow fever virus, and Zika virus;

Acetobacter aurantius, *Acinetobacter baumannii*, *Actinomyces israelii*, *Agrobacterium radiobacter*, *Agrobacterium tumefaciens*, *Anaplasma* sp. inc. *Anaplasma phagocytophilum*, *Azorhizobium caulinodans*, *Azotobacter vinelandii*, *Bacillus*, *Bacillus anthracis*, *Bacillus brevis*, *Bacillus cereus*, *Bacillus fusiformis*, *Bacillus licheniformis*, *Bacillus megaterium*, *Bacillus mycoides*, *Bacillus stearothermophilus*, *Bacillus subtilis*, *Bacillus Thuringiensis*, *Bacteroides* sp. inc. *Bacteroides fragilis*, *Bacteroides gingivalis*, *Bacteroides melaninogenicus*, *Prevotella melaninogenica*, *Bartonella* sp. inc. *Bartonella henselae*, *Bartonella Quintana*, *Bordetella* sp. inc. *Bordetella bronchiseptica*, *Bordetella pertussis*, *Borrelia burgdorferi*, *Brucella* sp. inc. *Brucella abortus*, *Brucella melitensis*, *Brucella suis*, *Burkholderia* sp. inc. *Burkholderia mallei*, *Burkholderia pseudomallei*, *Burkholderia cepacia*, *Calymmatobacterium granulomatis*, *Campylobacter* sp. inc. *Campylobacter coli*, *Campylobacter fetus*, *Campylobacter jejuni*, *Campylobacter pylori*, *Chlamydia* sp. inc. *Chlamydia trachomatis*, *Chlamydophila* sp. inc. *Chlamydophila pneumoniae*, *Chlamydophila psittaci*, *Clostridium* sp. inc. *Clostridium botulinum*, *Clostridium difficile*, *Clostridium perfringens*, *Clostridium tetani*, *Corynebacterium* sp. inc. *Corynebacterium diphtheriae*, *Corynebacterium fusiforme*, *Coxiella burnetii*, *Ehrlichia chaffeensis*, *Enterobacter cloacae*,

Enterococcus sp. inc. *Enterococcus avium*, *Enterococcus durans*, *Enterococcus faecalis*, *Enterococcus faecium*, *Enterococcus gallinarum*, *Enterococcus maloratus*, *Escherichia coli*, *Francisella tularensis*, *Fusobacterium nucleatum*, *Gardnerella vaginalis*, *Haemophilus* sp. inc. *Haemophilus ducreyi*, *Haemophilus influenzae*, *Haemophilus parainfluenzae*, *Haemophilus pertussis*, *Haemophilus vaginalis*, *Helicobacter pylori*, *Klebsiella pneumoniae*, *Lactobacillus* sp. inc. *Lactobacillus acidophilus*, *Lactobacillus bulgaricus*, *Lactobacillus casei*, *Lactococcus lactis*, *Legionella pneumophila*, *Listeria monocytogenes*, *Methanobacterium extroquens*, *Microbacterium multiforme*, *Micrococcus luteus*, *Moraxella catarrhalis*, *Mycobacterium* sp. inc. *Mycobacterium avium*, *Mycobacterium bovis*, *Mycobacterium diphtheria*, *Mycobacterium intracellulare*, *Mycobacterium leprae*, *Mycobacterium lepraemurium*, *Mycobacterium phlei*, *Mycobacterium smegmatis*, *Mycobacterium tuberculosis*, *Mycoplasma* sp. inc. *Mycoplasma fermentans*, *Mycoplasma genitalium*, *Mycoplasma hominis*, *Mycoplasma penetrans*, *Mycoplasma pneumoniae*, *Neisseria* sp. inc. *Neisseria gonorrhoeae*, *Neisseria meningitides*, *Pasteurella* sp. inc. *Pasteurella multocida*, *Pasteurella tularensis*, *Peptostreptococcus*, *Porphyromonas gingivalis*, *Prevotella melaninogenica*, *Pseudomonas aeruginosa*, *Rhizobium radiobacter*, *Rickettsia* sp. inc. *Rickettsia prowazekii*, *Rickettsia psittaci*, *Rickettsia quintana*, *Rickettsia rickettsia*, *Rickettsia trachomae*, *Rochalimaea* sp. inc. *Rochalimaea henselae*, *Rochalimaea quintana*, *Rothia dentocariosa*, *Salmonella* sp. inc. *Salmonella enteritidis*, *Salmonella typhi*, *Salmonella typhimurium*, *Serratia marcescens*, *Shigella dysenteriae*, *Spirillum volutans*, *Staphylococcus* sp. inc. *Staphylococcus aureus*, *Staphylococcus epidermidis*, *Stenotrophomonas maltophilia*, *Streptococcus* sp. inc. *Streptococcus agalactiae*, *Streptococcus avium*, *Streptococcus bovis*, *Streptococcus cricetus*, *Streptococcus faecium*, *Streptococcus faecalis*, *Streptococcus ferus*, *Streptococcus gallinarum*, *Streptococcus lactis*, *Streptococcus mitior*, *Streptococcus mitis*, *Streptococcus mutans*, *Streptococcus oralis*, *Streptococcus pneumoniae*, *Streptococcus pyogenes*, *Streptococcus rattus*, *Streptococcus salivarius*, *Streptococcus sanguis*, *Streptococcus sobrinus*, *Treponema* sp. inc. *Treponema pallidum*, *Treponema denticola*, *Vibrio* sp. inc. *Vibrio cholerae*, *Vibrio comma*, *Vibrio parahaemolyticus*, *Vibrio vulnificus*, *Wolbachia*, *Yersinia* sp. inc. *Yersinia enterocolitica*, *Yersinia pestis*, and *Yersinia pseudotuberculosis*;

Aspergillus sp., *Candida* sp. including *C.albicans* and *C.auris*, *Coccidioides* sp., *Cryptococcus gattii*, *Pneumocystis jirovecii*, *Sporothrix* sp., *Blastomyces* sp., *Cryptococcus neoformans*, *Histoplasma* sp., *Talaromyces* sp. including *T.marneffeii*, *Anncaliia algerae*, *A. connori*, *A. vesicularum*, *Encephalitozoon cuniculi*, *E. hellem*, *E. intestinalis*, *Enterocytozoon bieneusi*, *Microsporidium ceylonensis*, *M. africanum*, *Nosema ocularum*, *Pleistophora* sp., *Trachipleistophora hominis*, *T. anthropophthera*, *Vittaforma corneae*, and *Tubulinosema acridophagus*;

Acanthamoeba, *Trypanosoma* sp. including *T.brucei*, *T.cruzi*, and *T.evansi*, *Plasmodium* sp. including *P.falciparum*, *P.vivax*, *P.ovale*, *P.malariae*, *P.knowlesi*, *P.relictum*, *P.anasum*, and *P.gallinaceum*, *Hemoproteus* sp., *Babesia* sp., *Besnoitia* sp., *Blastocystis* sp., *Cryptosporidium* sp. including *C.parvum* and *C.hominis*, *Cyclospora cayetanensis*, *Dientamoeba fragilis*, *Giardia* so. including *G.lambliia* and *G.intestinalis*, *Histomonas meleagridis*, *Sappinia* sp. including *S.diploidea* and *S.pedata*, *Toxoplasma gondii*, and *Trichomonas vaginalis*;

Echinococcus sp. including *E.granulosus* and *E.multilocularis*, *Entamoeba histolytica*, *Ancylostoma* sp. including *A.brazilense*, *A.caninum*, and *A. ceylanicum*, *Uncinaria*

stenocephala, *Angiostrongylus* sp. including *Angiostrongylus cantonensis*, *Ascaris* sp. including *A.lumbricoides* and *A.suum*, *Balantidium coli*, *Balamuthia mandrillaris*, *Baylisascaris procyonis*, *Schistosoma* sp. including *S.mansoni*, *S. haematobium*, and *S. japonicum*, *Capillaria hepatica*, *Capillaria philippinensis*, *Clonorchis* sp., *Taenia* sp. including *T.solium*, *T.saginata*, and *T.asiatica*, *Diphyllbothrium* sp. including *Diphyllbothrium latum*, *Dipylidium* sp., *Dracunculus medinensis*, *Enterobius vermicularis*, *Fasciola* sp. including *Fasciola hepatica*, *Fasciolopsis buski*, *Gnathostoma* sp., *Heterophyes heterophyes*, *Naegleria fowleri*, *Onchocerca volvulus*, *Paragonimus* sp., *Sarcocystis* sp., *Strongyloides* sp., *Toxocara canis*, *Toxocara cati*, and *Trichinella* sp.; and PrP^C, PrP^{res}, and PrP^{Sc}.

~~15. The use of any one of claims 1 to 14, wherein the subject has, is suspected of having, has been diagnosed with, or is at risk of, a disorder characterized by a disorder-associated antigen (DAA).~~

~~16. The use of any one of claims 1 to 15, wherein the subject has been selected for treatment on the basis that the subject has, is suspected of having, has been diagnosed with, or is at risk of, a disorder characterized by a disorder-associated antigen (DAA).~~

~~17. The use of any one of claims 1 to 16, comprising the steps of: selecting the subject for treatment on the basis that the subject has, is suspected of having, has been diagnosed with, or is at risk of, a disorder characterized by a disorder-associated antigen (DAA), and wherein the CD25-ADC is to be administered to the subject.~~

~~18. The use of any one of claims 5 to 17, wherein the proliferative disorder is a cancer.~~

~~19. The use of either one of claims 5 or 18, wherein the cancer is a solid tumour.~~

~~20. The use of claim 19, wherein the solid tumour comprises or consists of CD25-ve neoplastic cells.~~

~~21. The use of any one of claims 18 to 20, wherein the solid tumour is associated with CD25+ve infiltrating cells;
— optionally wherein the solid tumour is associated with high levels of CD25+ve infiltrating cells.~~

~~22. The use of claim 21, wherein the solid tumour is selected from the group consisting of pancreatic cancer, breast cancer (including triple negative breast cancer), colorectal cancer, gastric and oesophageal cancer, melanoma, non-small cell lung cancer, ovarian cancer, hepatocellular carcinoma, renal cell carcinoma, bladder, and head and neck cancer.~~

~~23. The use of claim 18, wherein the pathogen-associated disorder is viral, bacterial, fungal, protozoan, parasitical, prion, or protein aggregate.~~

24. The use of either one of claims 18 or 23, wherein the pathogen-associated disorder is selected from:

~~Adenovirus infection, HIV/AIDS, Alphavirus Encephalitis, Arenavirus, Argentine hemorrhagic fever, Arthropod-borne viral encephalitis, Avian Influenza, Bolivian Hemorrhagic Fever, Borna disease, Chickenpox, Chikungunya, Coxsackievirus Infection, Crimean-Congo Hemorrhagic Fever, Cytomegalovirus infection, Dengue fever, Eastern equine encephalitis, Ebola, Echovirus Infection, Epstein-Barr Virus infection, Epstein-Barr Virus Related Tumours, Fifth Disease, Filovirus, Flavivirus, German measles, Hand, foot & mouth disease, Hemorrhagic fever with renal syndrome, Herpes Virus (Herpesviridae) infection, Herpes Simplex Virus Infection, Herpes Zoster Virus, Human Papilloma Virus Associated Epidermal Lesions, Human Papilloma Virus related Cervical Cancer, Mononucleosis, Influenza, Japanese Encephalitis, Kaposi Sarcoma, Korean Hemorrhagic Fever, Kyasanur Forest Disease, Lassa Fever, Lymphocytic choriomeningitis, Marburg Virus Disease, Measles, Molluscum Contagiosum, Mumps, Murray Valley encephalitis, Norwalk Virus related Diarrhea, Omsk hemorrhagic fever, Orthomyxoviruses, Parainfluenza Virus Infection, Paramyxovirus, Parvovirus B19 Infection, Picornavirus, Poxviruses, Rabies, Respiratory syncytial virus infection, Rift Valley Fever, Rotavirus diarrhea, Rubella, Rubeola, Smallpox, St. Louis Encephalitis, Tick-borne Encephalitis, Varicella, Variola, Venezuelan equine encephalitis, Viral hemorrhagic fevers, Western equine encephalitis, West Nile Virus disease, Yellow Fever, and Zika;~~

~~Actinomycosis, Acute prostatitis, Anaerobic infection, Bacillary peliosis, Bacteremia, Bacterial pneumonia, Bacteroides ureolyticus, Baggio-Yoshinari syndrome, Barcoo fever, Bartonellosis, Biliary fever, Botryomycosis, Bovine campylobacteriosis, Brazilian purpuric fever, Brazilian Purpuric Fever, Brodie abscess, Burkholderia cepacia complex, Buruli ulcer, Campylobacteriosis, Capnocytophaga canimorsus, Cariogram, Carrion's disease, Chlamydia suis, Cholera, bacterial prostatitis, osteomyelitis, endodontic lesions, bovine pleuropneumonia, dermatitis, Diphtheria, Diphtheritic stomatitis, Epidural abscess, Epiglottitis, Erysipelas, Legionnaires' disease, Far East scarlet-like fever, Fitz-Hugh-Curtis syndrome, Foot rot, Gardnerella vaginalis, Garre's sclerosing osteomyelitis, Granuloma inguinale, Haemophilus meningitis, monocytotropic ehrlichiosis, Lemierre's syndrome, Leprosy, Listeriosis, Lyme disease, Meningococcal disease, Mycobacterium avium-intracellulare infection, Necrotizing fasciitis, Nocardiosis, Noma, Omphalitis, Orbital cellulitis, Periodontal abscess, Periorbital cellulitis, Peritonsillar abscess, Pott disease, Proctitis, Pseudomonas infection, Psittacosis, Pyaemia, Pyomyositis, Q fever, Retropharyngeal abscess, Salmonellosis, Serratia infection, Shigellosis, Southern tick-associated rash illness, Staphylococcal scalded skin syndrome, brucellosis, Syphilis, Tetanus, Toxic shock syndrome, Trench fever, Tropical ulcer, Tubo-ovarian abscess, Ureaplasma urealyticum infection, Tuberculosis, Vertebral osteomyelitis, Waterhouse-Friderichsen syndrome, Whooping cough, Xanthogranulomatous osteomyelitis, and Yersiniosis;~~

~~Aspergillosis, Candidiasis, Coccidioidomycosis, Cryptococcus gattii infection, onychomycosis, microsporidiosis, mucormycosis, pneumocystis pneumonia, sporotrichosis, blastomycosis, Candida auris infection, Cryptococcus neoformans infection, fungal eye infection including keratitis and endophthalmitis, Histoplasmosis, mycetoma, dermatophytosis inc. tinea pedis tinea corporis, and talaromycosis;~~

~~Acanthamoeba keratitis, African trypanosomiasis, Avian malaria, Babesiosis, Besnoitiosis, Blastocystosis, Chagas disease, Cryptosporidiosis, Cyclosporiasis,~~

Dientamoebiasis, Giardiasis, Histomoniasis, Malaria, Premunity, Sappinia amoebic encephalitis, Surra, Toxoplasmosis, Trichomoniasis, and Trypanosomiasis;
 Echinococcosis, Amebiasis, Ancylostomiasis, Angiostrongyliasis, Anisakiasis, Ascariasis, Balantidiasis, Granulomatous Amebic Encephalitis, Baylisascariasis, Schistosomiasis, Capillariasis, Clonorchiasis, Cysticercosis, Diphyllbothriasis, Filariasis, Enterobiasis, Fascioliasis, Fasciolopsiasis, gnathostomiasis, Heterophyiasis, Hymenolepiasis, Leishmaniasis, Opisthorchiasis, Loiasis, Onchocerciasis, Paragonimiasis, Sarcocystosis, Taeniasis, Toxocariasis, Trichinellosis, and Trichuriasis;
 Creutzfeldt-Jakob disease (CJD) including iatrogenic, variant, familial, and sporadic sub-types, fatal familial insomnia (FFI), Gertsman-Straussler-Scheinker syndrome (GSS), kuru, and variably protease-sensitive prionopathy (VPSPr);
 Alzheimer's disease, Cerebral β -amyloid angiopathy, Retinal ganglion cell degeneration in glaucoma, Parkinson's disease and other synucleinopathies, Tauopathies, Frontotemporal lobar degeneration, FTL-D-FUS, Amyotrophic lateral sclerosis (ALS), Huntington's disease, Familial British dementia, Familial Danish dementia, Hereditary cerebral hemorrhage with amyloidosis, CADASIL, Alexander disease, Serpinopathies, Familial amyloidotic neuropathy, Senile systemic amyloidosis, Serpinopathies, AL amyloidosis, AH amyloidosis, AA amyloidosis, Type II diabetes, Aortic medial amyloidosis, ApoAI amyloidosis, ApoAII amyloidosis, ApoAIV amyloidosis, Familial amyloidosis of the Finnish type (FAF), Lysozyme amyloidosis, Fibrinogen amyloidosis, Dialysis amyloidosis, Inclusion body myositis/myopathy, Cat Retinitis pigmentosa with rhodopsin mutations, Medullary thyroid carcinoma, Cardiac atrial amyloidosis, Pituitary prolactinoma, Hereditary lattice corneal dystrophy, Cutaneous lichen amyloidosis, Mallory bodies, Multiple System Atrophy, Corneal lactoferrin amyloidosis, Pulmonary alveolar proteinosis, Odontogenic (Pindborg) tumor amyloid, Seminal vesicle amyloid, Apolipoprotein C2 amyloidosis, Apolipoprotein C3 amyloidosis, Lect2 amyloidosis, Insulin amyloidosis, Galectin-7 amyloidosis (primary localized cutaneous amyloidosis), Corneodesmosin amyloidosis, Enfuvirtide amyloidosis, Cystic fibrosis, and Sickle cell disease.

25.—The use of any one of claims 1 to 24, wherein the use comprises that the subject is to be selected for treatment on the basis that the subject has received an adoptive cell transfer; and wherein the CD25-ADC is to be administered to the subject.

26.—The use of claim 25, wherein the adoptive cell transfer is a bone marrow transplant.

27.—The use of claims 25 to 26, wherein the subject received the adoptive cell transfer at least 3 months prior to the administration of the CD25-ADC, such as at least 6 months, at least 12 months, at least 18 months, or at least 24 months prior to the administration of the CD25-ADC.

28.—The use of any one of claims 1 to 5 or 15 to 27, wherein the CD25-ADC is to be administered in combination with a cell therapy.

29.—The use of claim 28, wherein the CD25-ADC is to be administered before the cell therapy;

~~optionally wherein the CD25-ADC is to be administered 1 day, 2 days, 3 days, 4 days, 5 days, 6 days, 7 days, 8 days, 9 days, 10 days, 11 days, 12 days, 13 days, or 14 days before the cell therapy.~~

~~30. The use of any one of claims 28 to 29, wherein the size of a population of Treg cells in the subject is reduced by at least 90% before the cell therapy is to be administered.~~

~~31. The use of any one of claims 28 to 30, wherein the cell therapy comprises the administration of T-cells, Natural Killer (NK) cells, Natural Killer T-cell (NKT), Lymphokine-activated Killer (LAK) cells, or macrophages.~~

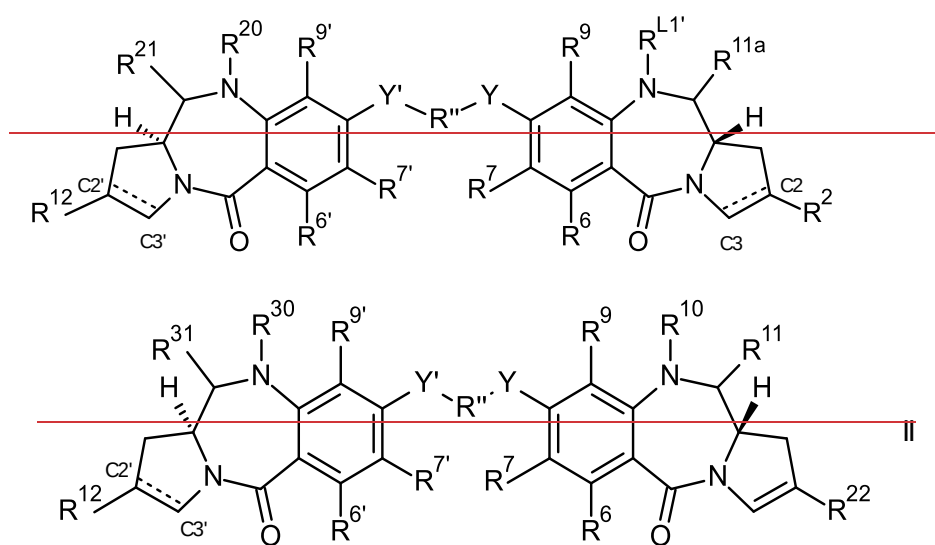
~~32. The use of any one of claims 28 to 31, wherein the cell therapy comprises the administration of CAR T-cells.~~

~~33. Use of a CD25-ADC in the manufacture of a medicament for treating a disorder a subject, wherein the disorder is characterized by a disorder-associated antigen (DAA), wherein the subject:~~

- ~~(i) has received an adoptive cell transfer; or~~
~~(ii) has been selected for treatment on the basis they have received an adoptive cell transfer;~~

~~wherein the CD25-ADC is a conjugate of formula L—(D^L)_p, where D^L is of formula I or~~

~~II:~~

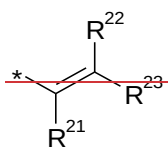


~~wherein:~~

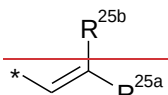
~~L is an antibody (Ab) which is an antibody that binds to CD25;~~

~~when there is a double bond present between C2' and C3', R¹² is selected from the group consisting of:~~

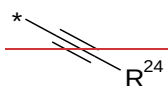
- ~~(ia) C₅₋₁₀-aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C₁₋₇-alkyl, C₃₋₇-heterocyclyl and bis-oxy-C₁₋₃-alkylene;~~
~~(ib) C₁₋₅-saturated aliphatic alkyl;~~
~~(ic) C₃₋₆-saturated cycloalkyl;~~



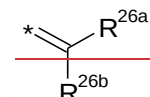
(id) ~~—, wherein each of R^{21} , R^{22} and R^{23} are independently selected from H, C_{1-3} saturated alkyl, C_{2-3} alkenyl, C_{2-3} alkynyl and cyclopropyl, where the total number of carbon atoms in the R^{12} group is no more than 5;~~



(ie) ~~—, wherein one of R^{25a} and R^{25b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and~~



(if) ~~—, where R^{24} is selected from: H; C_{1-3} saturated alkyl; C_{2-3} alkenyl; C_{2-3} alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; when there is a single bond present between $C2'$ and $C3'$;~~



R^{12} is ~~—, where R^{26a} and R^{26b} are independently selected from H, F, C_{1-4} saturated alkyl, C_{2-3} alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C_{1-4} alkyl amido and C_{1-4} alkyl ester; or, when one of R^{26a} and R^{26b} is H, the other is selected from nitrile and a C_{1-4} alkyl ester;~~

R^6 and R^9 are independently selected from H, R, OH, OR, SH, SR, NH_2 , NHR, NRR' , nitro, Me_3Sn and halo;

where R and R' are independently selected from optionally substituted C_{1-12} alkyl, C_{3-20} heterocyclyl and C_{5-20} aryl groups;

R^7 is selected from H, R, OH, OR, SH, SR, NH_2 , NHR, $NHRR'$, nitro, Me_3Sn and halo;

R'' is a C_{3-12} alkylene group, which chain may be interrupted by one or more heteroatoms, e.g. O, S, NR^{N2} (where R^{N2} is H or C_{1-4} alkyl), and/or aromatic rings, e.g. benzene or pyridine;

Y and Y' are selected from O, S, or NH;

$R^{6'}$, $R^{7'}$, $R^{9'}$ are selected from the same groups as R^6 , R^7 and R^9 respectively;

[Formula I]

$R^{L1'}$ is a linker for connection to the antibody (Ab);

R^{11a} is selected from OH, OR^A , where R^A is C_{1-4} alkyl, and SO_zM , where z is 2 or 3 and M is a monovalent pharmaceutically acceptable cation;

R^{20} and R^{21} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{20} is selected from H and R^C , where R^C is a capping group;

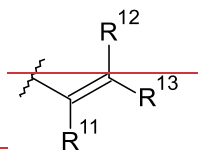
R^{21} is selected from OH, OR^A and SO_zM ;

when there is a double bond present between C2 and C3, R^2 is selected from the group consisting of:

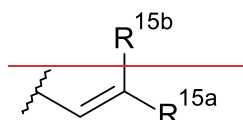
(ia) C_{5-10} aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C_{1-7} alkyl, C_{3-7} heterocyclyl and bis-oxy C_{1-3} alkylene;

~~(ib) C₁₋₅-saturated aliphatic alkyl;~~

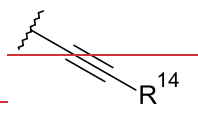
~~(ic) C₃₋₆-saturated cycloalkyl;~~



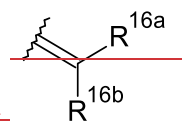
~~(id) —, wherein each of R¹¹, R¹² and R¹³ are independently selected from H, C₁₋₃-saturated alkyl, C₂₋₃-alkenyl, C₂₋₃-alkynyl and cyclopropyl, where the total number of carbon atoms in the R² group is no more than 5;~~



~~(ie) —, wherein one of R^{15a} and R^{15b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and~~



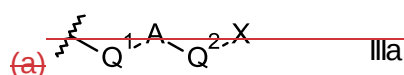
~~(if) —, where R¹⁴ is selected from: H; C₁₋₃-saturated alkyl; C₂₋₃-alkenyl; C₂₋₃-alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; when there is a single bond present between C2 and C3,~~



~~R² is —, where R^{16a} and R^{16b} are independently selected from H, F, C₁₋₄-saturated alkyl, C₂₋₃-alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C₁₋₄-alkyl amido and C₁₋₄-alkyl ester; or, when one of R^{16a} and R^{16b} is H, the other is selected from nitrile and a C₁₋₄-alkyl ester;~~

[Formula II]

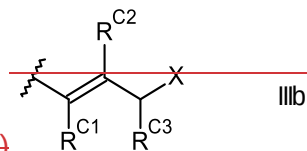
~~R²² is of formula IIIa, formula IIIb or formula IIIc:~~



~~where A is a C₅₋₇-aryl group, and either~~

~~(i) Q¹ is a single bond, and Q² is selected from a single bond and Z-(CH₂)_n, where Z is selected from a single bond, O, S and NH and n is from 1 to 3; or~~

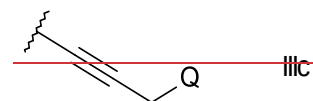
~~(ii) Q¹ is -CH=CH-, and Q² is a single bond;~~



~~(b)~~

~~where;~~

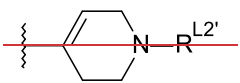
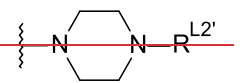
~~R^{C1}, R^{C2} and R^{C3} are independently selected from H and unsubstituted C₁₋₂-alkyl;~~



~~(c)~~

where Q is selected from $O-R^{L2'}$, $S-R^{L2'}$ and $NR^N-R^{L2'}$, and R^N is selected from H, methyl and ethyl

X is selected from the group comprising: $O-R^{L2'}$, $S-R^{L2'}$, $CO_2-R^{L2'}$, $CO-R^{L2'}$, $NH-C(=O)-R^{L2'}$,

$NHNH-R^{L2'}$, $CONHNH-R^{L2'}$, , , $NR^N-R^{L2'}$, wherein R^N is

selected from the group comprising H and C_{1-4} alkyl;

$R^{L2'}$ is a linker for connection to the antibody (Ab);

R^{10} and R^{11} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{10} is H and R^{11} is selected from OH, OR^A and SO_2M ;

R^{30} and R^{31} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{30} is H and R^{31} is selected from OH, OR^A and SO_2M .

34. The use of claim 33 further comprising the step of selecting the subject for treatment on the basis that the subject has received an adoptive cell transfer.

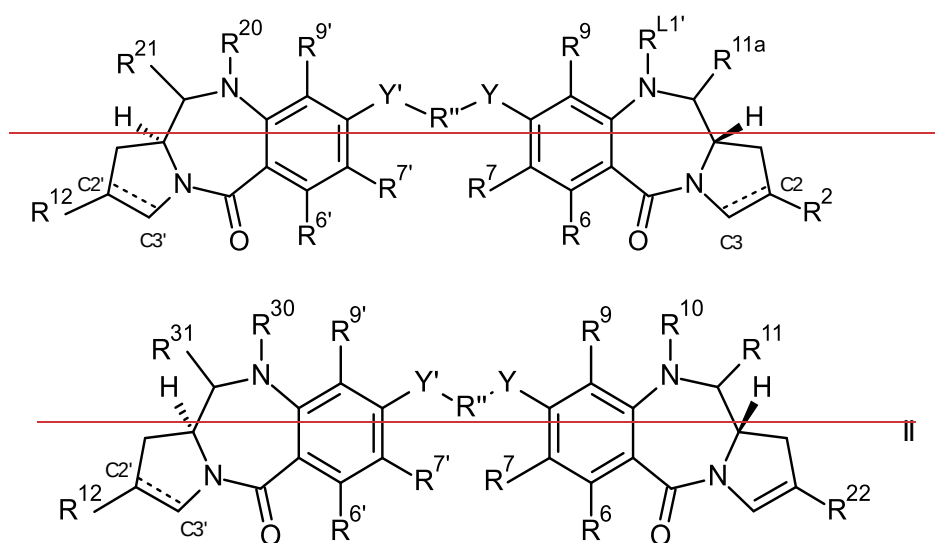
35. The use of either one of claims 33 or 34, wherein the disorder is as defined in any one of claims 17 to 22.

36. The use of any one of claims 33 to 35, wherein the adoptive cell transfer is as defined in any one of claims 23 to 24.

37. Use of a CD25-ADC in the manufacture of a medicament for use in combinatorial therapy for enhancing the efficacy of cell therapy in a subject, wherein said medicament is to be administered in combination with the cell therapy;

wherein the CD25-ADC is a conjugate of formula $L-(D^L)_p$, where D^L is of formula I or

II:



wherein:

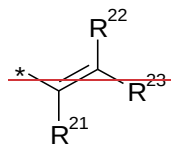
L is an antibody (Ab) which is an antibody that binds to CD25;

when there is a double bond present between C2' and C3', R¹² is selected from the group consisting of:

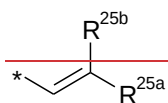
(ia) C₅₋₁₀-aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C₁₋₇-alkyl, C₃₋₇-heterocyclyl and bis-oxy-C₁₋₃-alkylene;

(ib) C₁₋₅-saturated aliphatic alkyl;

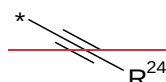
(ic) C₃₋₆-saturated cycloalkyl;



(id) —, wherein each of R²¹, R²² and R²³ are independently selected from H, C₁₋₃ saturated alkyl, C₂₋₃-alkenyl, C₂₋₃-alkynyl and cyclopropyl, where the total number of carbon atoms in the R¹²-group is no more than 5;

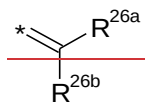


(ie) —, wherein one of R^{25a} and R^{25b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and



(if) —, where R²⁴ is selected from: H; C₁₋₃-saturated alkyl; C₂₋₃-alkenyl; C₂₋₃ alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl;

when there is a single bond present between C2' and C3',



R¹² is —, where R^{26a} and R^{26b} are independently selected from H, F, C₁₋₄-saturated alkyl, C₂₋₃-alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C₁₋₄-alkyl amido and C₁₋₄-alkyl ester; or, when one of R^{26a} and R^{26b} is H, the other is selected from nitrile and a C₁₋₄-alkyl ester;

R⁶ and R⁹ are independently selected from H, R, OH, OR, SH, SR, NH₂, NHR, NRR', nitro, Me₃Sn and halo;

where R and R' are independently selected from optionally substituted C₁₋₁₂-alkyl, C₃₋₂₀ heterocyclyl and C₅₋₂₀-aryl groups;

R⁷ is selected from H, R, OH, OR, SH, SR, NH₂, NHR, NHRR', nitro, Me₃Sn and halo;

R'' is a C₃₋₁₂-alkylene group, which chain may be interrupted by one or more heteroatoms, e.g. O, S, NR^{N2} (where R^{N2} is H or C₁₋₄-alkyl), and/or aromatic rings, e.g. benzene or pyridine;

Y and Y' are selected from O, S, or NH;

R^{6'}, R^{7'}, R^{9'} are selected from the same groups as R⁶, R⁷ and R⁹ respectively;

[Formula I]

R^{L1} is a linker for connection to the antibody (Ab);

R^{11a} is selected from OH, OR^A, where R^A is C₁₋₄-alkyl, and SO_{zM}, where z is 2 or 3 and M is a monovalent pharmaceutically acceptable cation;

R²⁰ and R²¹ either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{20} is selected from H and R^G , where R^G is a capping group;

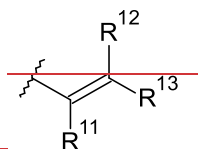
R^{21} is selected from OH, OR^A and SO_2M ;

when there is a double bond present between C2 and C3, R^2 is selected from the group consisting of:

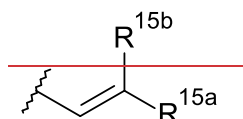
(ia) C_{5-10} -aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C_{1-7} -alkyl, C_{3-7} -heterocyclyl and bis-oxy- C_{1-3} -alkylene;

(ib) C_{1-5} -saturated aliphatic alkyl;

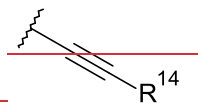
(ic) C_{3-6} -saturated cycloalkyl;



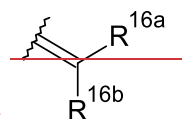
(id) —, wherein each of R^{11} , R^{12} and R^{13} are independently selected from H, C_{1-3} -saturated alkyl, C_{2-3} -alkenyl, C_{2-3} -alkynyl and cyclopropyl, where the total number of carbon atoms in the R^2 -group is no more than 5;



(ie) —, wherein one of R^{15a} and R^{15b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and



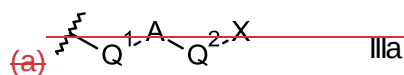
(if) —, where R^{14} is selected from: H; C_{1-3} -saturated alkyl; C_{2-3} -alkenyl; C_{2-3} -alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; when there is a single bond present between C2 and C3,



R^2 is —, where R^{16a} and R^{16b} are independently selected from H, F, C_{1-4} -saturated alkyl, C_{2-3} -alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C_{1-4} -alkyl amido and C_{1-4} -alkyl ester; or, when one of R^{16a} and R^{16b} is H, the other is selected from nitrile and a C_{1-4} -alkyl ester;

[Formula II]

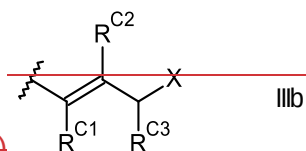
R^{22} is of formula IIIa, formula IIIb or formula IIIc:



where A is a C_{5-7} -aryl group, and either

(i) Q^1 is a single bond, and Q^2 is selected from a single bond and $-Z(CH_2)_n-$, where Z is selected from a single bond, O, S and NH and n is from 1 to 3; or

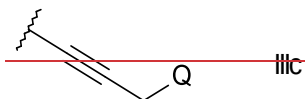
(ii) Q^1 is $-CH=CH-$, and Q^2 is a single bond;



(b)

where;

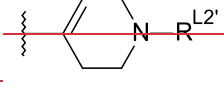
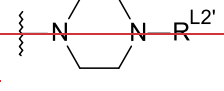
R^{C1} , R^{C2} and R^{C3} are independently selected from H and unsubstituted C_{1-2} -alkyl;



(c)

where Q is selected from $O-R^{L2'}$, $S-R^{L2'}$ and $NR^N-R^{L2'}$, and R^N is selected from H, methyl and ethyl

X is selected from the group comprising: $O-R^{L2'}$, $S-R^{L2'}$, $CO_2-R^{L2'}$, $CO-R^{L2'}$, $NH-C(=O)-R^{L2'}$,

$NHNH-R^{L2'}$, $CONHNH-R^{L2'}$, , , $NR^N-R^{L2'}$, wherein R^N is selected from the group comprising H and C_{1-4} -alkyl;

$R^{L2'}$ is a linker for connection to the antibody (Ab);

R^{10} and R^{11} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{10} is H and R^{11} is selected from OH, OR^A and SO_2M ;

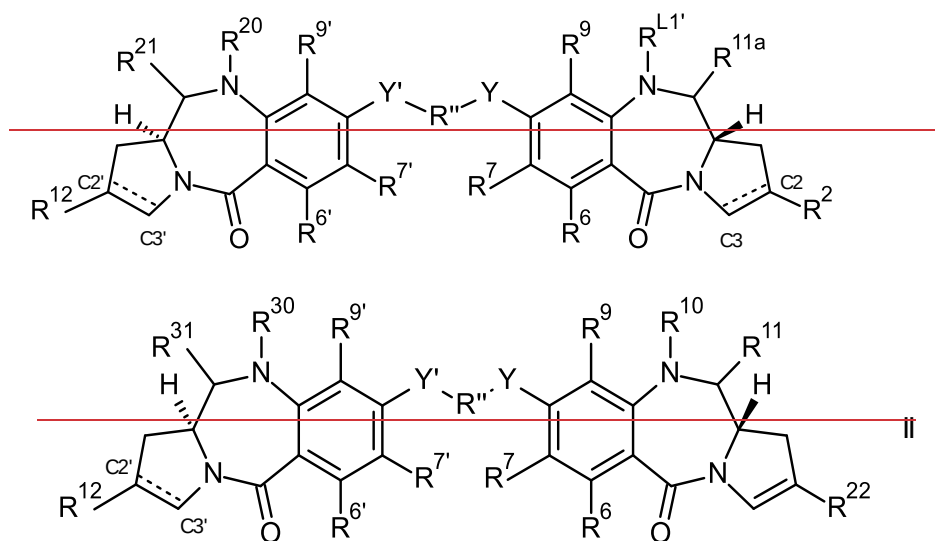
R^{30} and R^{31} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{30} is H and R^{31} is selected from OH, OR^A and SO_2M .

38. Use of a CD25-ADC in the manufacture of a medicament for use in combinatorial therapy for treating a disorder a subject, wherein the disorder is characterized by a disorder-associated antigen (DAA), wherein said medicament is to be administered in combination with a cell therapy;

wherein the CD25-ADC is a conjugate of formula L - $(D^L)_p$, where D^L is of formula I or

II:



wherein:

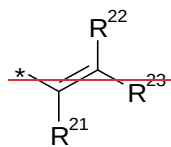
L is an antibody (Ab) which is an antibody that binds to CD25;

when there is a double bond present between C2' and C3', R¹² is selected from the group consisting of:

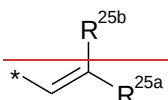
(ia) C₅₋₁₀-aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C₁₋₇-alkyl, C₃₋₇-heterocyclyl and bis-oxy-C₁₋₃-alkylene;

(ib) C₁₋₅-saturated aliphatic alkyl;

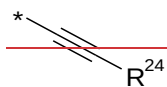
(ic) C₃₋₆-saturated cycloalkyl;



(id) —, wherein each of R²¹, R²² and R²³ are independently selected from H, C₁₋₃ saturated alkyl, C₂₋₃-alkenyl, C₂₋₃-alkynyl and cyclopropyl, where the total number of carbon atoms in the R¹² group is no more than 5;

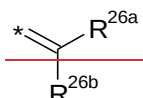


(ie) —, wherein one of R^{25a} and R^{25b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and



(if) —, where R²⁴ is selected from: H; C₁₋₃ saturated alkyl; C₂₋₃-alkenyl; C₂₋₃ alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl;

when there is a single bond present between C2' and C3',



R¹² is —, where R^{26a} and R^{26b} are independently selected from H, F, C₁₋₄ saturated alkyl, C₂₋₃-alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C₁₋₄-alkyl amido and C₁₋₄-alkyl ester; or, when one of R^{26a} and R^{26b} is H, the other is selected from nitrile and a C₁₋₄-alkyl ester;

R⁶ and R⁹ are independently selected from H, R, OH, OR, SH, SR, NH₂, NHR, NRR', nitro, Me₃Sn and halo;

where R and R' are independently selected from optionally substituted C₁₋₁₂-alkyl, C₃₋₂₀ heterocyclyl and C₅₋₂₀-aryl groups;

R⁷ is selected from H, R, OH, OR, SH, SR, NH₂, NHR, NHRR', nitro, Me₃Sn and halo;

R'' is a C₃₋₁₂-alkylene group, which chain may be interrupted by one or more heteroatoms, e.g. O, S, NR^{N2} (where R^{N2} is H or C₁₋₄-alkyl), and/or aromatic rings, e.g. benzene or pyridine;

Y and Y' are selected from O, S, or NH;

R^{6'}, R^{7'}, R^{9'} are selected from the same groups as R⁶, R⁷ and R⁹ respectively;

[Formula I]

R^{L1} is a linker for connection to the antibody (Ab);

R^{11a} is selected from OH, OR^A, where R^A is C₁₋₄-alkyl, and SO_zM, where z is 2 or 3 and M is a monovalent pharmaceutically acceptable cation;

~~R²⁰ and R²¹ either together form a double bond between the nitrogen and carbon atoms to which they are bound or;~~

~~R²⁰ is selected from H and R^G, where R^G is a capping group;~~

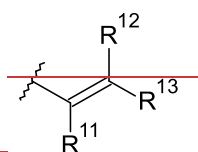
~~R²¹ is selected from OH, OR^A and SO₂M;~~

~~when there is a double bond present between C2 and C3, R² is selected from the group consisting of:~~

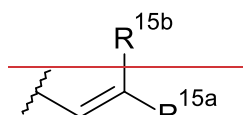
~~(ia) C₅₋₁₀-aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C₁₋₇-alkyl, C₃₋₇-heterocyclyl and bis-oxy-C₁₋₃-alkylene;~~

~~(ib) C₁₋₅-saturated aliphatic-alkyl;~~

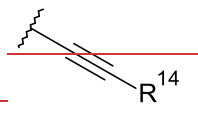
~~(ic) C₃₋₆-saturated cycloalkyl;~~



~~(id) —, wherein each of R¹¹, R¹² and R¹³ are independently selected from H, C₁₋₃-saturated alkyl, C₂₋₃-alkenyl, C₂₋₃-alkynyl and cyclopropyl, where the total number of carbon atoms in the R²-group is no more than 5;~~

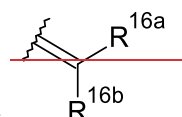


~~(ie) —, wherein one of R^{15a} and R^{15b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and~~



~~(if) —, where R¹⁴ is selected from: H; C₁₋₃-saturated alkyl; C₂₋₃-alkenyl; C₂₋₃-alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl;~~

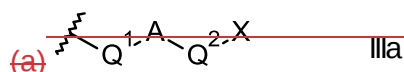
~~when there is a single bond present between C2 and C3,~~



~~R² is —, where R^{16a} and R^{16b} are independently selected from H, F, C₁₋₄-saturated alkyl, C₂₋₃-alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C₁₋₄-alkyl-amido and C₁₋₄-alkyl-ester; or, when one of R^{16a} and R^{16b} is H, the other is selected from nitrile and a C₁₋₄-alkyl-ester;~~

[Formula II]

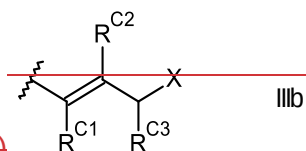
~~R²² is of formula IIIa, formula IIIb or formula IIIc:~~



~~where A is a C₅₋₇-aryl group, and either~~

~~(i) Q¹ is a single bond, and Q² is selected from a single bond and —Z(CH₂)_n—, where Z is selected from a single bond, O, S and NH and n is from 1 to 3; or~~

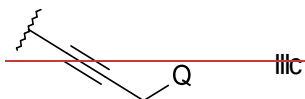
~~(ii) Q¹ is —CH=CH—, and Q² is a single bond;~~



(b)

where;

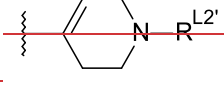
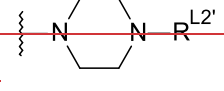
R^{C1} , R^{C2} and R^{C3} are independently selected from H and unsubstituted C_{1-2} -alkyl;



(c)

where Q is selected from $O-R^{L2'}$, $S-R^{L2'}$ and $NR^N-R^{L2'}$, and R^N is selected from H, methyl and ethyl

X is selected from the group comprising: $O-R^{L2'}$, $S-R^{L2'}$, $CO_2-R^{L2'}$, $CO-R^{L2'}$, $NH-C(=O)-R^{L2'}$,

$NHNH-R^{L2'}$, $CONHNH-R^{L2'}$, , , $NR^N-R^{L2'}$, wherein R^N is selected from the group comprising H and C_{1-4} -alkyl;

$R^{L2'}$ is a linker for connection to the antibody (Ab);

R^{10} and R^{11} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{10} is H and R^{11} is selected from OH, OR^A and SO_2M ;

R^{30} and R^{31} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{30} is H and R^{31} is selected from OH, OR^A and SO_2M .

39. The use of claim 38, wherein the disorder is as defined in any one of claims 18 to 24.

40. The use of any one of claims 37 to 39, wherein the CD25-ADC is to be administered before the cell therapy.

41. The use of any one of claims 37 to 40, wherein the size of a population of Treg cells in the subject is reduced by at least 90% before the DAA or vaccine composition is to be administered.

42. The use of any one of claims 37 to 41, wherein the cell therapy is as defined in any one of claims 31 to 32.

43. A method of selecting a subject as suitable for treatment with a CD25-ADC, the method comprising the steps of:

(a) identifying a subject who:

(i) has, is suspected of having, has been diagnosed with, or is at risk of, a disorder characterized by a disorder-associated antigen (DAA), and/or

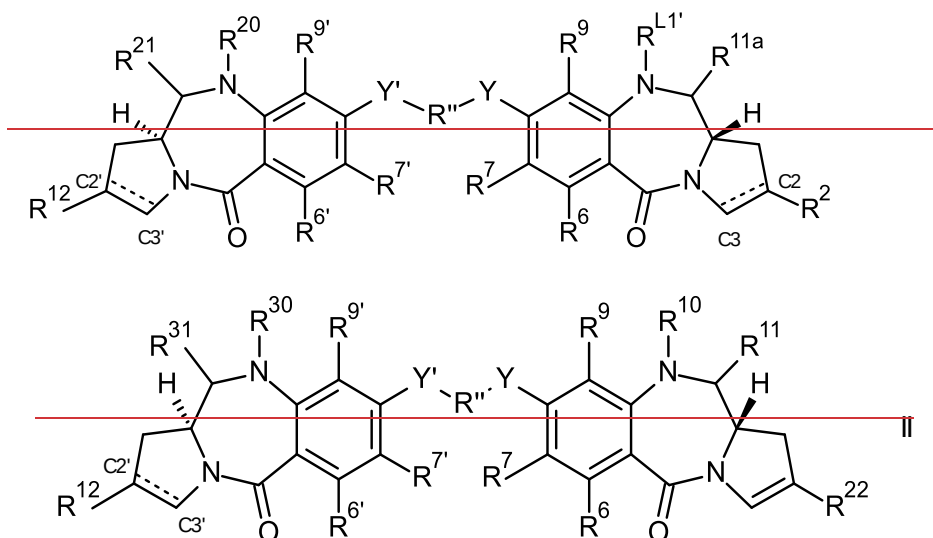
(ii) has received an adoptive cell transfer, and/or

(iii) has been selected for treatment with cell therapy; and

(b) selecting the subject for treatment with the CD25-ADC;

wherein the CD25-ADC is a conjugate of formula L—(D^L)_p, where D^L is of formula I or

II:

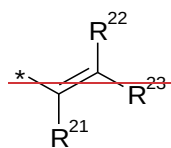


wherein:

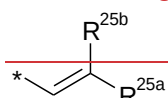
L is an antibody (Ab) which is an antibody that binds to CD25;

when there is a double bond present between C2' and C3', R¹² is selected from the group consisting of:

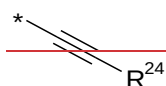
- (ia) C₅₋₁₀-aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C₁₋₇-alkyl, C₃₋₇-heterocyclyl and bis-oxy-C₁₋₃-alkylene;
- (ib) C₁₋₅-saturated aliphatic-alkyl;
- (ic) C₃₋₆-saturated cycloalkyl;



- (id) —, wherein each of R²¹, R²² and R²³ are independently selected from H, C₁₋₃ saturated alkyl, C₂₋₃-alkenyl, C₂₋₃-alkynyl and cyclopropyl, where the total number of carbon atoms in the R¹²-group is no more than 5;

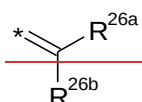


- (ie) —, wherein one of R^{25a} and R^{25b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and



- (if) —, where R²⁴ is selected from: H; C₁₋₃-saturated alkyl; C₂₋₃-alkenyl; C₂₋₃-alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl;

when there is a single bond present between C2' and C3',

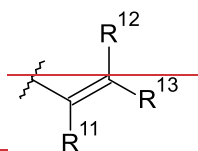


R¹² is —, where R^{26a} and R^{26b} are independently selected from H, F, C₁₋₄-saturated alkyl, C₂₋₃-alkenyl, which alkyl and alkenyl groups are optionally substituted by a group

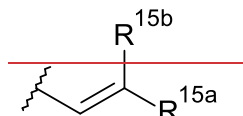
selected from C_{1-4} -alkyl amide and C_{1-4} -alkyl ester; or, when one of R^{26a} and R^{26b} is H, the other is selected from nitrile and a C_{1-4} -alkyl ester;
 R^6 and R^9 are independently selected from H, R, OH, OR, SH, SR, NH_2 , NHR, NRR' , nitro, Me_3Sn and halo;
 where R and R' are independently selected from optionally substituted C_{1-12} -alkyl, C_{3-20} heterocyclyl and C_{5-20} -aryl groups;
 R^7 is selected from H, R, OH, OR, SH, SR, NH_2 , NHR, $NHRR'$, nitro, Me_3Sn and halo;
 R'' is a C_{3-12} -alkylene group, which chain may be interrupted by one or more heteroatoms, e.g. O, S, NR^{N2} (where R^{N2} is H or C_{1-4} -alkyl), and/or aromatic rings, e.g. benzene or pyridine;
 Y and Y' are selected from O, S, or NH;
 $R^{6'}$, $R^{7'}$, $R^{9'}$ are selected from the same groups as R^6 , R^7 and R^9 respectively;

[Formula I]

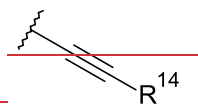
$R^{14'}$ is a linker for connection to the antibody (Ab);
 R^{11a} is selected from OH, OR^A , where R^A is C_{1-4} -alkyl, and SO_zM , where z is 2 or 3 and M is a monovalent pharmaceutically acceptable cation;
 R^{20} and R^{21} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;
 R^{20} is selected from H and R^C , where R^C is a capping group;
 R^{21} is selected from OH, OR^A and SO_zM ;
 when there is a double bond present between C2 and C3, R^2 is selected from the group consisting of:
 (ia) C_{5-10} -aryl group, optionally substituted by one or more substituents selected from the group comprising: halo, nitro, cyano, ether, carboxy, ester, C_{1-7} -alkyl, C_{3-7} -heterocyclyl and bis-oxy- C_{1-3} -alkylene;
 (ib) C_{1-5} -saturated aliphatic alkyl;
 (ic) C_{3-6} -saturated cycloalkyl;



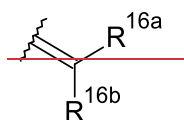
(id) —, wherein each of R^{11} , R^{12} and R^{13} are independently selected from H, C_{1-3} -saturated alkyl, C_{2-3} -alkenyl, C_{2-3} -alkynyl and cyclopropyl, where the total number of carbon atoms in the R^2 group is no more than 5;



(ie) —, wherein one of R^{15a} and R^{15b} is H and the other is selected from: phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl; and



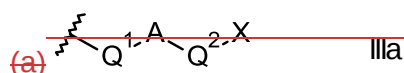
(if) —, where R^{14} is selected from: H; C_{1-3} -saturated alkyl; C_{2-3} -alkenyl; C_{2-3} alkynyl; cyclopropyl; phenyl, which phenyl is optionally substituted by a group selected from halo, methyl, methoxy; pyridyl; and thiophenyl;
 when there is a single bond present between C2 and C3,



R^{22} is ~~where R^{16a} and R^{16b} are independently selected from H, F, C_{1-4} saturated alkyl, C_{2-3} alkenyl, which alkyl and alkenyl groups are optionally substituted by a group selected from C_{1-4} alkyl amido and C_{1-4} alkyl ester; or, when one of R^{16a} and R^{16b} is H, the other is selected from nitrile and a C_{1-4} alkyl ester;~~

[Formula II]

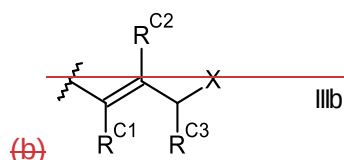
R^{22} is of formula IIIa, formula IIIb or formula IIIc:



where A is a C_{5-7} aryl group, and either

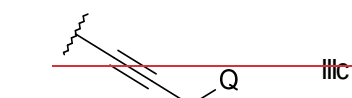
(i) Q^1 is a single bond, and Q^2 is selected from a single bond and $-Z-(CH_2)_n-$, where Z is selected from a single bond, O, S and NH and n is from 1 to 3; or

(ii) Q^1 is $-CH=CH-$, and Q^2 is a single bond;



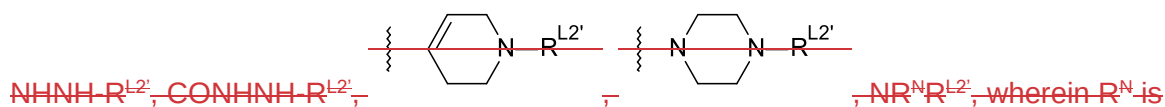
where;

R^{C1} , R^{C2} and R^{C3} are independently selected from H and unsubstituted C_{1-2} alkyl;



where Q is selected from $O-R^{L2'}$, $S-R^{L2'}$ and $NR^N-R^{L2'}$, and R^N is selected from H, methyl and ethyl

X is selected from the group comprising: $O-R^{L2'}$, $S-R^{L2'}$, $CO_2-R^{L2'}$, $CO-R^{L2'}$, $NH-C(=O)-R^{L2'}$,



selected from the group comprising H and C_{1-4} alkyl;

$R^{L2'}$ is a linker for connection to the antibody (Ab);

R^{10} and R^{11} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{10} is H and R^{11} is selected from OH, OR^A and SO_2M ;

R^{30} and R^{31} either together form a double bond between the nitrogen and carbon atoms to which they are bound or;

R^{30} is H and R^{31} is selected from OH, OR^A and SO_2M .

44. The method of claim 43, wherein the disorder is as defined in any one of claims 18 to 24.

45. The method of either one of claims 43 or 44, wherein the adoptive cell transfer is as defined in claim 26.

~~46. The method of any one of claims 43 to 44, wherein the subject received the adoptive cell transfer at least 3 months prior to the administration of the CD25-ADC, such as at least 6 months, at least 12 months, at least 18 months, or at least 24 months prior to the administration of the CD25-ADC.~~

~~47. The method of any one of claims 43 to 46, wherein the cell therapy is as defined in any one of claims 31 to 32.~~

3048. The ~~method or~~ use of any one of claims 1 to 2947, wherein the CD25-ADC is to be administered in combination with a checkpoint inhibitor or other immunostimulatory agent.

3149. The ~~method or~~ use of claim 3048, wherein the CD25-ADC ~~is may be~~ to be administered before the checkpoint inhibitor or other immunostimulatory agent, simultaneous with the checkpoint inhibitor or other immunostimulatory agent, or after the checkpoint inhibitor or other immunostimulatory agent.

3250. The ~~method or~~ use of either one of claims 3048 or 3149, wherein the checkpoint inhibitor is a PD1 antagonist.

3351. The ~~method or~~ use of claim 3250, wherein the PD1 antagonist is selected from pembrolizumab, nivolumab, MEDI0680, PDR001 (spartalizumab), Camrelizumab, AUNP12, Pidilizumab Cemiplimab (REGN-2810), AMP-224, BGB-A317 (Tisleizumab), and BGB-108.

3452. The ~~method or~~ use of either one of claims 3048 or 3149, wherein the checkpoint inhibitor is a PD-L1 antagonist.

3553. The ~~method or~~ use of claim 3452, wherein the PD-L1 antagonist is selected from atezolizumab (Tecentrig), BMS-936559/MDX-1105, durvalumab/MEDI4736, and MSB0010718C (Avelumab).

3654. The ~~method or~~ use of either one of claims 3048 or 3149, wherein the checkpoint inhibitor is a G1TR (Glucocorticoid-Induced INFR-Related protein) agonist.

3755. The ~~method or~~ use of claim 3654, wherein the G1TR (Glucocorticoid-Induced INFR-Related protein) agonist is selected from MEDI1873, TRX518, GWN323, MK-1248, MK 4166, BMS-986156 and INCAGN1876.

3856. The ~~method or~~ use of either one of claims 3048 or 3149, wherein the checkpoint inhibitor is an OX40 agonist.

3957. The ~~method or~~ use of claim 3856, wherein the OX40 agonist is selected from MEDI0562, MEDI6383, MOXR0916, RG7888, OX40mAb24, INCAGN1949, GSK3174998, and PF-04518600.

4058. The ~~method or~~ use of either one of claims 3048 or 3149, wherein the checkpoint inhibitor is a CTLA-4 antagonist.

4159. The ~~method or~~ use of claim 4058, wherein the CTLA-4 antagonist is selected from ipilimumab and Tremelimumab.

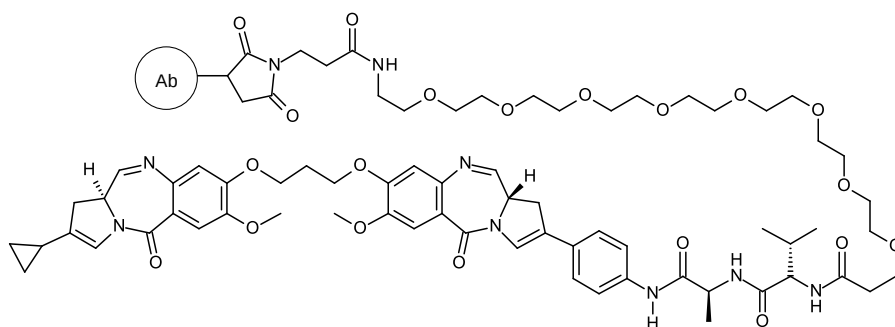
4260. The ~~method or~~ use of either one of claims 3048 or 3149, wherein the other immunostimulatory agent is a bi-specific T-cell engager (BiTE).

4361. The ~~method or~~ use of claim 4260, wherein the BiTE specifically binds CD3.

4462. The ~~method or~~ use of either one of claims 4260 or 4361, wherein the BiTE specifically binds the DAA.

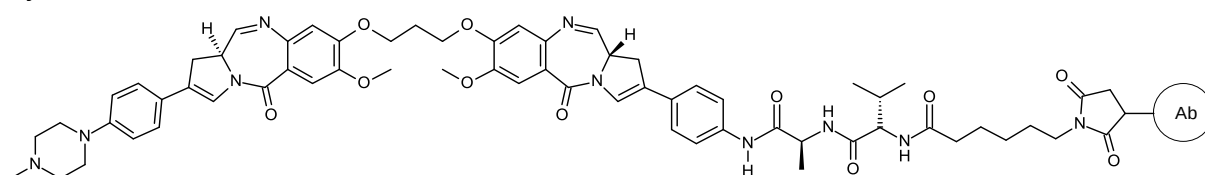
4563. The ~~method or~~ use of any one of claims 1 to 4462, wherein the CD25-ADC is to be administered in combination with radiotherapy.

4664. The ~~method or~~ use of any one of claims 1 to 4563, wherein the CD25-ADC is of formula ConjA:



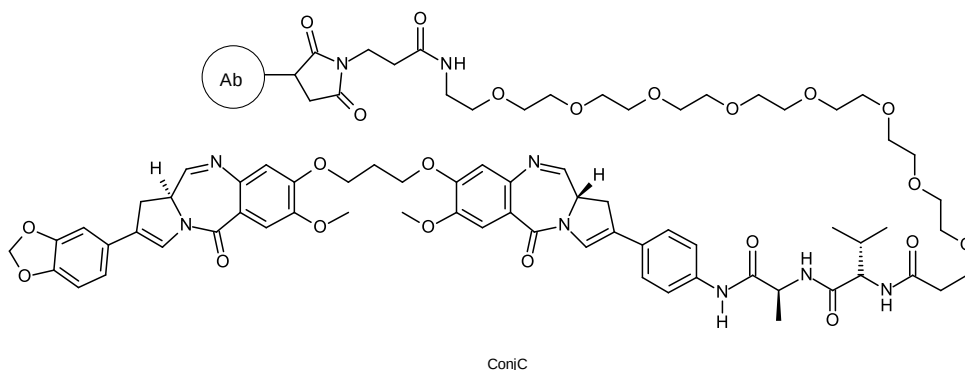
ConjA

ConjB:

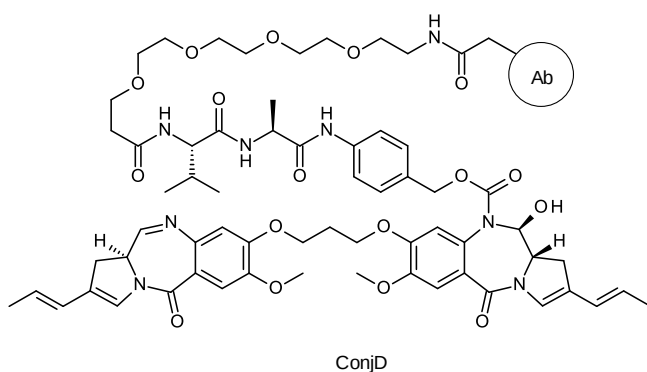


ConjB

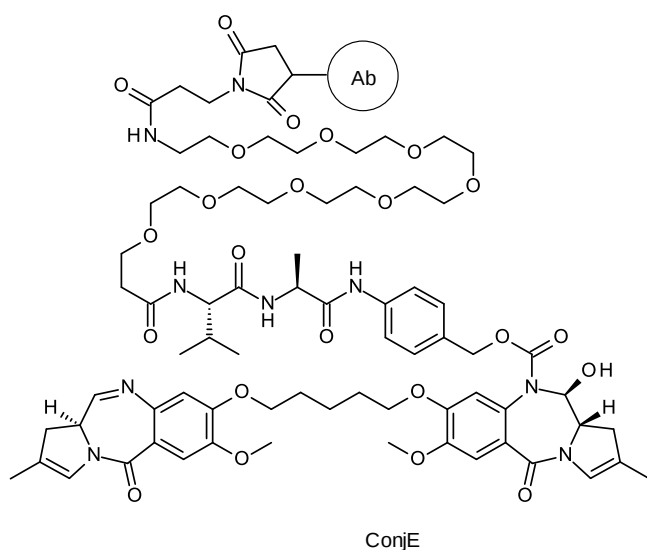
ConjC:



ConjD:



Or ConjE:



4765. The ~~method or~~ use according to any one of claims 1 to **4664** wherein the CD25-ADC comprises an antibody comprising:

a VH domain having a VH CDR1 with the amino acid sequence of SEQ ID NO.3, a VH CDR2 with the amino acid sequence of SEQ ID NO.4, and a VH CDR3 with the amino acid sequence of SEQ ID NO.5.

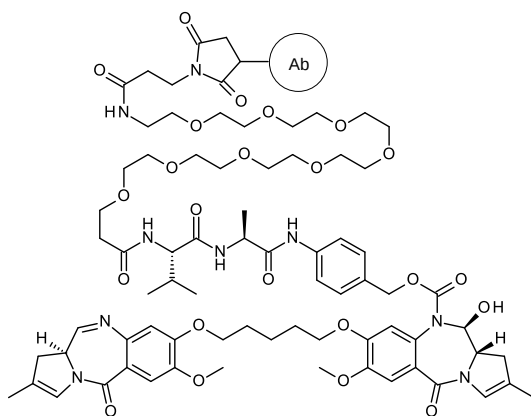
~~4866.~~ The ~~method or~~ use according to any one of claims 1 to ~~4765~~ wherein the CD25-ADC comprises an antibody comprising a VH domain having the sequence according to SEQ ID NO. 1.

~~4967.~~ The ~~method or~~ use according to any one of claims 1 to ~~4866~~ wherein the CD25-ADC comprises an antibody comprising:

a VL domain comprising a VL CDR1 with the amino acid sequence of SEQ ID NO.6, a VL CDR2 with the amino acid sequence of SEQ ID NO.7, and a VL CDR3 with the amino acid sequence of SEQ ID NO.8.

~~5068.~~ The ~~method or~~ use according to any one of claims 1 to ~~4967~~ wherein the CD25-ADC comprises an antibody comprising a VL domain having the sequence according to SEQ ID NO. 2.

51. The use according to any of claims 1 to 45, wherein the CD25-ADC has the chemical structure:



, where the Ab is an antibody that binds to CD25, the antibody having a VH domain comprising a VH CDR1 with the amino acid sequence of SEQ ID NO.3, a VH CDR2 with the amino acid sequence of SEQ ID NO.4, and a VH CDR3 with the amino acid sequence of SEQ ID NO.5; and a VL domain comprising a VL CDR1 with the amino acid sequence of SEQ ID NO.6, a VL CDR2 with the amino acid sequence of SEQ ID NO.7, and a VL CDR3 with the amino acid sequence of SEQ ID NO.8; and wherein the drug to antibody ratio (DAR) is between 1 and 8.

~~69. The method or use of any one of claims 1 to 68, wherein the CD25-ADC is ADCx25.~~

~~70. The method or use of any one of claims 1 to 68, wherein the CD25-ADC is ADCT-301.~~

~~5271.~~ The ~~method or~~ use of any one of claims 1 to ~~5168~~, wherein the CD25-ADC is Camidanlumab Tesirine.