

CLAIMS

1. An antibody which binds to human CD37 comprising: (a) a variable heavy chain (VH) region comprising the CDR1, CDR2, and CDR3 sequences set forth in SEQ ID NOs: 23, 24, and 25, respectively, and a variable light chain (VL) region comprising the CDR1, CDR2, and CDR3 sequences set forth in SEQ ID NO: 27, the sequence YAS, and SEQ ID NO: 31, respectively, or (b) a VH region comprising the CDR1, CDR2, and CDR3 sequences set forth in SEQ ID NOs: 16, 17, and 18, respectively, and a VL region comprising the CDR1, CDR2, and CDR3 sequences set forth in SEQ ID NO: 20, the sequence KAS, and SEQ ID NO: 21, respectively.
2. The antibody of claim 1, which comprises the VH region comprising the CDR1, CDR2, and CDR3 sequences set forth in SEQ ID NOs: 23, 24, and 25, respectively, and the VL region comprising the CDR1, CDR2, and CDR3 sequences set forth in SEQ ID NO: 27, the sequence YAS, and SEQ ID NO: 31, respectively.
3. The antibody of claim 1, which comprises the VH region comprising the CDR1, CDR2, and CDR3 sequences set forth in SEQ ID NOs: 16, 17, and 18, respectively, and the VL region comprising the CDR1, CDR2, and CDR3 sequences set forth in SEQ ID NO: 20, the sequence KAS, and SEQ ID NO: 21, respectively.
4. The antibody of claim 2, which comprises a VH region comprising the amino acid sequence set forth in SEQ ID NO: 22 and a VL region comprising the amino acid sequence set forth in SEQ ID NO: 29.
5. The antibody of claim 3, which comprises a VH region comprising the amino acid sequence set forth in SEQ ID NO: 15 and a VL region comprising the amino acid sequence set forth in SEQ ID NO: 19.
6. The antibody of claim 2, which comprises a human IgG1 heavy chain constant region.
7. The antibody of claim 3, which comprises a human IgG1 heavy chain constant region.
8. The antibody of claim 6, wherein the human IgG1 heavy chain constant region comprises a substitution of glutamic acid at position 430 for glycine, and wherein the amino acid residue is numbered according to the EU Index.
9. The antibody of claim 7, wherein the human IgG1 heavy chain constant region comprises a substitution of glutamic acid at position 430 for glycine, and wherein the amino acid residue is numbered according to the EU Index.
10. The antibody of claim 2, which comprises a kappa light chain constant region.

11. The antibody of claim 3, which comprises a kappa light chain constant region.

12. A bispecific antibody comprising a first and second antigen-binding region arm and a second binding to human CD37 having arm, wherein the sequence of SEQ ID NO: 62, and first binding arm comprises a first and antigen-binding region and the second Fc region of a human immunoglobulin, wherein the first and binding arm comprises a second antigen-binding regions bind different epitopes on CD37, and region, wherein both the first antigen-binding region and second Fc regions comprise one or more amino acid mutations which mutation(s) enhances the Fc-Fc interaction between the bispecific antibodies upon binding to membrane-bound target compared to the Fc-Fc interaction between bispecific antibodies not having said mutation(s). antigen-binding region bind to human CD37, and wherein (a) the first antigen-binding region comprises a variable heavy chain (VH) region comprising the CDR1, CDR2, and CDR3 sequences set forth in SEQ ID NOS: 23, 24, and 25, respectively, and a variable light chain (VL) region comprising the CDR1, CDR2, and CDR3 sequences set forth in SEQ ID NO: 27, the sequence YAS, and SEQ ID NO: 31, respectively, and (b) the second antigen-binding region comprises a VH region comprising the CDR1, CDR2, and CDR3 sequences set forth in SEQ ID NOS: 16, 17, and 18, respectively, and a VL region comprising the CDR1, CDR2, and CDR3 sequences set forth in SEQ ID NO: 20, the sequence KAS, and SEQ ID NO: 21.

13. The bispecific antibody of claim 12, wherein said: (a) the first antigen-binding region is obtained from an antibody which competes for binding to human CD37 with comprises a CD37 antibody VH region comprising the CDR sequences:

VH CDR1 amino acid sequence set forth in SEQ ID NO: 16,

VH CDR222 and a VL region comprising the amino acid sequence set forth in SEQ ID NO: 17,

VH CDR329, and (b) the second antigen-binding region comprises a VH region comprising the amino acid sequence set forth in SEQ ID NO: 18,

VL CDR115 and a VL region comprising the amino acid sequence set forth in SEQ ID NO: 20, 19.

VL CDR2 sequence: KAS, and

VL CDR3 sequence set forth in SEQ ID NO: 21. [010].

14. The bispecific antibody of any one of the preceding claims claim 13, wherein said the first antigen-binding region binds to the same epitope on human CD37 as a CD37 antibody comprising the CDR sequences: arm comprises a first human IgG1 heavy chain constant

region and the second binding arm comprises a second human IgG1 heavy chain constant region.

~~VH CDR1 sequence set forth in SEQ ID NO: 16,~~

~~VH CDR2 sequence set forth in SEQ ID NO: 17,~~

~~VH CDR3 sequence set forth in SEQ ID NO: 18,~~

~~VL CDR1 sequence set forth in SEQ ID NO: 20,~~

~~VL CDR2 sequence: KAS, and~~

~~VL CDR3 sequence set forth in SEQ ID NO: 21. [010].~~

4.15. The bispecific antibody of any one of the preceding claims claim 14, wherein said both the first antigen binding and second human IgG1 heavy chain constant regions comprise a substitution of glutamic acid at position 430 for glycine, and wherein the amino acid residue is numbered according to the EU Index.

16. The bispecific antibody of claim 14, wherein the first human IgG1 heavy chain constant region comprises the CDR sequences: a substitution of phenylalanine at position 405 for leucine, wherein the second human IgG1 heavy chain constant region comprises a substitution of lysine at position 409 for arginine, and wherein the amino acid residues are numbered according to the EU Index.

~~VH CDR1 sequence set forth in SEQ ID NO: 16,~~

~~VH CDR2 sequence set forth in SEQ ID NO: 17,~~

~~VH CDR3 sequence set forth in SEQ ID NO: 18,~~

~~VL CDR1 sequence set forth in SEQ ID NO: 20,~~

~~VL CDR2 sequence: KAS, and~~

~~VL CDR3 sequence set forth in SEQ ID NO: 21. [010].~~

5.17. The bispecific antibody of claim 14, wherein the first human IgG1 heavy chain constant region comprises a substitution of lysine at position 409 for arginine, wherein the second human IgG1 heavy chain constant region comprises a substitution of phenylalanine at position 405 for leucine, and wherein the amino acid residues are numbered according to the EU Index.

18. The bispecific antibody of any one of the preceding claims claim 13, wherein said both the first antigen-binding arm and second binding arm comprise a human kappa light chain constant region comprises the VH and VL sequences:

(i) ~~VH sequence set forth in SEQ ID NO: 15 and VL sequence set forth in SEQ ID NO: 19 or~~

(ii) ~~VH sequence having at least 90% identity, such as at least 95% identity, such as at least 98% identity, such as at least 99% identity and a VL sequence having at least 90% identity, such as at least 95% identity, such as at least 98% identity, such as at least 99% identity with the VH sequence and VL sequences of SEQ ID Nos 15 and 19.~~

~~6. The 19. A bispecific antibody of any one of the claims 1 to 6, wherein said first antigen binding region binds to a functional epitope comprising one or more of the amino acids selected from the group consisting of :Y182, D189, T191, I192, D194, K195, V196, I197 and P199 of SEQ ID No: 62 (CD37).~~

~~7. The bispecific antibody of claim 1, wherein said first antigen binding region is obtained from an antibody which competes for binding to human CD37 with a CD37 antibody comprising the CDR sequences:~~

~~VH CDR1 sequence set forth in SEQ ID NO: 9,~~

~~VH CDR2 sequence set forth in SEQ ID NO: 10,~~

~~VH CDR3 comprising a first binding arm comprising a first heavy chain and a first light chain and a second binding arm comprising a second heavy chain and a second light chain, wherein both the first binding arm and second binding arm bind to human CD37, and wherein: (a) the first heavy chain comprises a variable heavy chain (VH) region comprising the amino acid sequence set forth in SEQ ID NO: 11,~~

~~VL CDR1 sequence set forth in SEQ ID NO: 13,~~

~~VL CDR2 sequence: AAS, and~~

~~VL CDR3 22, and the first light chain comprises a variable light chain (VL) region comprising the amino acid sequence set forth in SEQ ID NO: 14. [005].~~

8. ~~The bispecific antibody of claims 1 or 7, wherein said first antigen binding region binds to the same epitope on human CD37 as a CD37 antibody comprising the CDR sequences:~~

~~VH-CDR1~~29, and (b) the second heavy chain comprises a VH region comprising the amino acid sequence set forth in SEQ ID NO: 9,

~~VH-CDR2~~15, and the second light chain comprises a VL region comprising the amino acid sequence set forth in SEQ ID NO: 10,

~~VH-CDR3~~ sequence 19, wherein the first heavy chain and second heavy chain comprise heavy chain constant regions comprising the amino acid sequences set forth in SEQ ID NO: 11,

~~VL-CDR1~~NOs: 59 and 60, respectively, and wherein both the first light chain and second light chain comprise a light chain constant region comprising the amino acid sequence set forth in SEQ ID NO: ~~13~~, 61.

~~VL-CDR2~~ sequence: AAS, and

~~VL-CDR3~~ 20. A bispecific antibody comprising a first binding arm comprising a first heavy chain and a first light chain and a second binding arm comprising a second heavy chain and a second light chain, wherein both the first binding arm and second binding arm bind to human CD37, and wherein: (a) the first heavy chain comprises a variable heavy chain (VH) region comprising the amino acid sequence set forth in SEQ ID NO: ~~14~~. **[005]**.

9. ~~The bispecific antibody of claims 1, 7 or 8, wherein said first antigen binding region comprises the CDR sequences:~~

~~VH-CDR1~~22, and the first light chain comprises a variable light chain (VL) region comprising the amino acid sequence set forth in SEQ ID NO: 9,

~~VH-CDR2~~29, and (b) the second heavy chain comprises a VH region comprising the amino acid sequence set forth in SEQ ID NO: ~~10~~,

~~VH-CDR3~~ 15, and the second light chain comprises a VL region comprising the amino acid sequence set forth in SEQ ID NO: ~~11~~,

~~VL CDR1 sequence 19, wherein the first heavy chain and second heavy chain comprise heavy chain constant regions comprising the amino acid sequences set forth in SEQ ID NO: 13,~~

~~VL CDR2 sequence: AAS, and~~

- 5 ~~VL CDR3 NOs: 60 and 59, respectively, and wherein both the first light chain and second light chain comprise a light chain constant region comprising the amino acid sequence set forth in SEQ ID NO: 14. [005] 61.~~

10 ~~10. The bispecific antibody of any of claims 1 or 7 to 9, wherein said first antigen binding region comprises the VH and VL sequences:~~

~~(iii) VH sequence set forth in SEQ ID NO: 8 and VL sequence set forth in SEQ ID NO: 12 or~~

15 ~~(iv) VH sequence having at least 90% identity, such as at least 95% identity, such as at least 98% identity, such as at least 99% identity and a VL sequence having at least 90% identity, such as at least 95% identity, such as at least 98% identity, such as at least 99% identity with the VH sequence and VL sequences of SEQ ID Nos 8 and 12.~~

20 ~~11. The bispecific antibody of any one of the preceding claims, wherein said second antigen binding region is obtained from an antibody which competes for binding to human CD37 with a CD37 antibody comprising the CDR sequences selected from the group comprising:~~

25 ~~(i) VH CDR1 sequence set forth in SEQ ID NO: 23,
VH CDR2 sequence set forth in SEQ ID NO: 24,
VH CDR3 sequence set forth in SEQ ID NO: 25,
VL CDR1 sequence set forth in SEQ ID NO: 27,
VL CDR2 sequence: YAS, and
VL CDR3 sequence set forth in SEQ ID NO: 28; [016]~~

(ii) ~~VH CDR1 sequence set forth in SEQ ID NO: 2,~~
~~VH CDR2 sequence set forth in SEQ ID NO: 3,~~
~~VH CDR3 sequence set forth in SEQ ID NO: 4,~~
~~VL CDR1 sequence set forth in SEQ ID NO: 6,~~
~~VL CDR2 sequence: EAS, and~~
~~VL CDR3 sequence set forth in SEQ ID NO: 7; [004]~~

(iii) ~~VH CDR1 sequence set forth in SEQ ID NO: 40,~~
~~VH CDR2 sequence set forth in SEQ ID NO: 41,~~
~~VH CDR3 sequence set forth in SEQ ID NO: 42,~~
~~VL CDR1 sequence set forth in SEQ ID NO: 44,~~
~~VL CDR2 sequence: FAK, and~~
~~VL CDR3 sequence set forth in SEQ ID NO: 45; [G28.1] and~~

(iv) ~~VH CDR1 sequence set forth in SEQ ID NO: 47,~~
~~VH CDR2 sequence set forth in SEQ ID NO: 48,~~
~~VH CDR3 sequence set forth in SEQ ID NO: 49,~~
~~VL CDR1 sequence set forth in SEQ ID NO: 51,~~
~~VL CDR2 sequence: VAT and~~
~~VL CDR3 sequence set forth in SEQ ID NO: 52. [37.3]~~

12. ~~The bispecific antibody of any one of the preceding claims, wherein said second antigen binding region binds to the same epitope on human CD37 as a CD37 antibody comprising the CDR sequences selected from the group comprising:~~

(i) ~~VH CDR1 sequence set forth in SEQ ID NO: 23,~~
~~VH CDR2 sequence set forth in SEQ ID NO: 24,~~
~~VH CDR3 sequence set forth in SEQ ID NO: 25,~~
~~VL CDR1 sequence set forth in SEQ ID NO: 27,~~

~~VL CDR2 sequence: YAS, and~~
~~VL CDR3 sequence set forth in SEQ ID NO: 28; [016]~~

(ii) ~~VH CDR1 sequence set forth in SEQ ID NO: 2,~~
~~VH CDR2 sequence set forth in SEQ ID NO: 3,~~
~~VH CDR3 sequence set forth in SEQ ID NO: 4,~~
~~VL CDR1 sequence set forth in SEQ ID NO: 6,~~
~~VL CDR2 sequence: EAS, and~~
~~VL CDR3 sequence set forth in SEQ ID NO: 7; [004]~~

(iii) ~~VH CDR1 sequence set forth in SEQ ID NO: 40,~~
~~VH CDR2 sequence set forth in SEQ ID NO: 41,~~
~~VH CDR3 sequence set forth in SEQ ID NO: 42,~~
~~VL CDR1 sequence set forth in SEQ ID NO: 44,~~
~~VL CDR2 sequence: FAK, and~~
~~VL CDR3 sequence set forth in SEQ ID NO: 45; [G28.1] and~~

(iv) ~~VH CDR1 sequence set forth in SEQ ID NO: 47,~~
~~VH CDR2 sequence set forth in SEQ ID NO: 48,~~
~~VH CDR3 sequence set forth in SEQ ID NO: 49,~~
~~VL CDR1 sequence set forth in SEQ ID NO: 51,~~
~~VL CDR2 sequence: VAT and~~
~~VL CDR3 sequence set forth in SEQ ID NO: 52. [37.3].~~

~~13. The bispecific antibody of any one of the preceding claims, wherein said second antigen binding region binds to a functional epitope comprising one or more of the amino acids selected from the group consisting of: E124, F162, Q163, V164, L165 and H175 of SEQ ID No: 62 (CD37).~~

~~14. The bispecific antibody of any one of the preceding claims, wherein said second antigen binding region comprises the CDR sequences selected from the group comprising:~~

~~(i) VH CDR1 sequence set forth in SEQ ID NO: 23,
VH CDR2 sequence set forth in SEQ ID NO: 24,
VH CDR3 sequence set forth in SEQ ID NO: 25,
VL CDR1 sequence set forth in SEQ ID NO: 27,
VL CDR2 sequence: YAS, and
VL CDR3 sequence set forth in SEQ ID NO: 28; [016]~~

~~(ii) VH CDR1 sequence set forth in SEQ ID NO: 2,
VH CDR2 sequence set forth in SEQ ID NO: 3,
VH CDR3 sequence set forth in SEQ ID NO: 4,
VL CDR1 sequence set forth in SEQ ID NO: 6,
VL CDR2 sequence: EAS, and
VL CDR3 sequence set forth in SEQ ID NO: 7; [004]~~

~~(iii) VH CDR1 sequence set forth in SEQ ID NO: 40,
VH CDR2 sequence set forth in SEQ ID NO: 41,
VH CDR3 sequence set forth in SEQ ID NO: 42,
VL CDR1 sequence set forth in SEQ ID NO: 44,
VL CDR2 sequence: FAK, and
VL CDR3 sequence set forth in SEQ ID NO: 45; [G28.1] and~~

~~(iv) VH CDR1 sequence set forth in SEQ ID NO: 47,
VH CDR2 sequence set forth in SEQ ID NO: 48,
VH CDR3 sequence set forth in SEQ ID NO: 49,
VL CDR1 sequence set forth in SEQ ID NO: 51,
VL CDR2 sequence: VAT and~~

~~VL CDR3 sequence set forth in SEQ ID NO: 52. [37.3].~~

~~15. The bispecific antibody of any of the above claims, wherein said second antigen binding region comprises the VH and VL sequences selected from the group comprising:~~

~~(v) VH sequence set forth in SEQ ID NO: 22 and VL sequence set forth in SEQ ID NO: 26 or~~

~~(vi) VH sequence set forth in SEQ ID NO: 1 and VL sequence set forth in SEQ ID NO: 5 or~~

~~(vii) VH sequence set forth in SEQ ID NO: 39 and VL sequence set forth in SEQ ID NO: 43 or~~

~~(viii) VH sequence set forth in SEQ ID NO: 46 and VL sequence set forth in SEQ ID NO: 50 or~~

~~(ix) a VH sequence having at least 90% identity, such as at least 95% identity, such as at least 98% identity, such as at least 99% identity and a VL sequence having at least 90% identity, such as at least 95% identity, such as at least 98% identity, such as at least 99% identity with the VH sequence and VL sequence, respectively, as set forth in any one of (i) to (iv).~~

~~16. The bispecific antibody of any of the above claims, wherein the one or more Fc-Fc interaction enhancing mutations in said first and second Fc regions are amino acid substitutions.~~

~~17. The bispecific antibody of any of the above claims, wherein the one or more Fc-Fc interaction enhancing mutations in said first and second Fc regions are amino acid substitutions at one or more positions corresponding to amino acid positions 430, 440 and 345 in human IgG1 when using the EU numbering system.~~

~~18. The bispecific antibody of any of the above claims comprising at least one substitution in said first and second Fc regions selected from the group comprising: E430G, E345K, E430S, E430F, E430T, E345Q, E345R, E345Y, S440Y and S440W.~~

~~19. The bispecific antibody of any of the above claims comprising at least one substitution in said first and second Fc regions selected from E430G or E345K, preferably E430G.~~

~~20. The bispecific antibody of any of the above claims, wherein said Fc-Fc interaction enhancing mutations in said first and second Fc regions are identical substitutions in said first and second Fc regions.~~

~~21. The bispecific antibody of any of the above claims, wherein the bispecific antibody is an IgG1, IgG2, IgG3 or IgG4 isotype or a combination thereof, preferably it is an IgG1 isotype.~~

~~22. The bispecific antibody of any of the above claims, wherein the bispecific antibody is a full length antibody.~~

~~23. The bispecific antibody of any of the above claims, wherein the bispecific antibody is human, humanized or chimeric or a combination thereof.~~

~~24. The bispecific antibody of any of the above claims, wherein the bispecific antibody binds human and cynomolgus CD37, having the sequences set forth in SEQ ID Nos 62 and 63, respectively.~~

~~25. The bispecific antibody of any of the above claims, wherein~~

~~A) the first Fc region comprises a further mutation corresponding to F405L in human IgG1 and the second Fc region comprises a further mutation corresponding to K409R in human IgG1, or~~

~~B) the second Fc region comprises a further mutation corresponding to F405L in human IgG1 and the first Fc region comprises a further mutation corresponding to K409R in human IgG1~~

~~when using EU numbering.~~

26. ~~The bispecific antibody of any of the above claims which has increased CDC or increased CDC and ADCC effector functions compared to an identical bispecific antibody but which does not have the Fc-Fc interaction enhancing mutations.~~

5 27. ~~An anti-CD37 antibody binding to the same epitope on human CD37 as an anti-CD37 antibody which antibody comprises:~~

10 (x) ~~a VH region comprising a CDR1 sequence set forth in SEQ ID NO: 16, a CDR2 sequence set forth in SEQ ID NO: 17 and a CDR3 sequence set forth in SEQ ID NO: 18, and a VL region comprising a CDR1 sequence set forth in SEQ ID NO: 20, and CDR2 sequence: KAS, and CDR3 sequence set forth in SEQ ID NO: 21[010]; or~~

15 (xi) ~~a VH region comprising a CDR1 sequence set forth in SEQ ID NO: 9, a CDR2 sequence set forth in SEQ ID NO: 10 and a CDR3 sequence set forth in SEQ ID NO: 11, and a VL region comprising a CDR1 sequence set forth in SEQ ID NO: 113, and CDR2 sequence: AAS, and CDR3 sequence set forth in SEQ ID NO: 14[005].~~

28. ~~The anti-CD37 antibody of claim 27 which comprises:~~

20 (xii) ~~a VH region comprising a CDR1 sequence set forth in SEQ ID NO: 16, a CDR2 sequence set forth in SEQ ID NO: 17 and a CDR3 sequence set forth in SEQ ID NO: 18, and a VL region comprising a CDR1 sequence set forth in SEQ ID NO: 20, and CDR2 sequence: KAS, and CDR3 sequence set forth in SEQ ID NO: 21[010]; or~~

25 (xiii) ~~a VH region comprising a CDR1 sequence set forth in SEQ ID NO: 9, a CDR2 sequence set forth in SEQ ID NO: 10 and a CDR3 sequence set forth in SEQ ID NO: 11, and a VL region comprising a CDR1 sequence set forth in SEQ ID NO: 113, and CDR2 sequence: AAS, and CDR3 sequence set forth in SEQ ID NO: 14[005].~~

29. An anti-CD37 antibody which binds to human CD37 which antibody comprises:

(xiv) — a VH region comprising a CDR1 sequence set forth in SEQ ID NO: 23, a CDR2 sequence set forth in SEQ ID NO: 24 and a CDR3 sequence set forth in SEQ ID NO: 25, and a VL region comprising a CDR1 sequence set forth in SEQ ID NO: 27, and CDR2 sequence: YAS, and CDR3 sequence set forth in SEQ ID NO: 28; **[016]** or

(xv) — a VH region comprising a CDR1 sequence set forth in SEQ ID NO: 2, a CDR2 sequence set forth in SEQ ID NO: 3 and a CDR3 sequence set forth in SEQ ID NO: 4, and a VL region comprising a CDR1 sequence set forth in SEQ ID NO: 6, and CDR2 sequence: EAS, and CDR3 sequence set forth in SEQ ID NO: 7. **[004]**

30. The antibody of any of claims 27-29, wherein said antibody comprises an Fc region which comprises one or more amino acid mutations which mutation(s) enhances the Fc-Fc interaction between the antibodies upon target binding compared to the Fc-Fc interaction between antibodies not having said mutation(s).

31. The antibody of claim 30, wherein the one or more amino acid mutations in the Fc region of the antibody is amino acid substitutions at one or more positions corresponding to amino acid positions 430, 440 and 345 in human IgG1 when using the EU numbering system.

32. The antibody of claim 31 comprising at least one amino acid substitution in the Fc region selected from the group comprising: E430G, E345K, E430S, E430F, E430T, E345Q, E345R, E345Y, S440Y and S440W.

33. The antibody of claim 32 comprising at least one substitution in said Fc region selected from E430G or E345K, preferably E430G.

~~34. The antibody of any of claims 27-33 comprising a mutation corresponding to F405L or K409R in human IgG1.~~

~~35. An anti-CD37 antibody which binds to human CD37 which antibody comprises:~~

5 ~~(xvi) — a VH region comprising a CDR1 sequence set forth in SEQ ID NO: 40, a CDR2 sequence set forth in SEQ ID NO: 41 and a CDR3 sequence set forth in SEQ ID NO: 42, and a VL region comprising a CDR1 sequence set forth in SEQ ID NO: 44, and CDR2 sequence: FAK, and CDR3 sequence set forth in SEQ ID NO: 45 [G28.1] or~~

10 ~~(xvii) — a VH region comprising a CDR1 sequence set forth in SEQ ID NO: 47, a CDR2 sequence set forth in SEQ ID NO: 48 and a CDR3 sequence set forth in SEQ ID NO: 49, and a VL region comprising a CDR1 sequence set forth in SEQ ID NO: 51, and CDR2 sequence: VAT, and CDR3 sequence set forth in SEQ ID NO: 52 [37.3];~~

15 ~~(xviii) — and wherein the antibody of (i) or (ii) comprises an Fc region comprising at least one amino acid substitution selected from the group comprising: E430G, E345K, E430S, E430F, E430T, E345Q, E345R, E345Y, S440Y and S440W; and~~

~~(xix) — wherein optionally the Fc region further comprises a mutation of either K409R ————— or ————— F405L.~~

20 ~~36. The antibody of any of claims 27-35, wherein the antibody is an IgG1, IgG2, IgG3 or IgG4 isotype.~~

~~37. The antibody of any of claims 27-36, wherein the antibody is human, humanized or chimeric.~~

25 ~~38. The antibody of any of claims 27-37, wherein the antibody binds to both human and cynomolgus CD37.~~

~~39. A pharmaceutical composition comprising the bispecific antibody of any of claims 1-26 or the antibody of any of claims 27-38 and a pharmaceutically acceptable carrier.~~

~~40. The bispecific antibody of any of claims 1-26 or the antibody of any of claims 27-38 or the composition of claim 39 for use as a medicament.~~

~~41. The bispecific antibody of any of claims 1-26 or the antibody of any of claims 27-38 or the composition of claim 39 for use in the treatment of cancer or an autoimmune disease or inflammatory disorders.~~

~~42. The bispecific antibody of any of claims 1-26 or the antibody of any of claims 27-38 or the composition of claim 39 for use in the treatment of allergy, transplantation rejection or a B-cell malignancy, such as non-Hodgkin lymphoma (NHL), chronic lymphocytic leukemia (CLL), follicular lymphoma (FL), mantle cell lymphoma (MCL), plasma cell leukemia (PCL), diffuse large B-cell lymphoma (DLBCL), or acute lymphoblastic leukemia (ALL).~~

~~43. The bispecific antibody of any of claims 1-26 or the antibody of any of claims 27-38 or the composition of claim 39 for use of any of claims 40-42 in combination with one or more further therapeutic agents.~~

~~44. The bispecific antibody of any of claims 1-26 or the antibody of any of claims 27-38 or the composition of claim 39 for use of any of claims 40-43 wherein the one or more further therapeutic agents is selected from the group comprising: doxorubicin, cisplatin, bleomycin, carmustine, cyclophosphamide, chlorambucil, bendamustine, vincristine, fludarabine, ibrutinib and an anti-CD 20 antibody such as rituximab or ofatumumab.~~

~~45. The bispecific antibody of any of claims 43-44 or the antibody of any of claims 43-44 or the composition of claim 43-44 for use of claim 43-44, wherein the further therapeutic agent is an anti-CD20 antibody capable of binding to human CD20 comprising the CDR sequences selected from the group consisting of:~~

- ~~i) VH CDR1 sequence set forth in SEQ ID NO:75,~~
- ~~VH CDR2 sequence set forth in SEQ ID NO:76,~~

~~VH CDR3 sequence set forth in SEQ ID NO:77,~~
~~VL CDR1 sequence set forth in SEQ ID NO:79~~
~~VL CDR2 sequence DAS, and~~
~~VL CDR3 sequence set forth in SEQ ID NO: 80;~~

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~~ii) VH CDR1 sequence set forth in SEQ ID NO:82,~~
~~VH CDR2 sequence set forth in SEQ ID NO:83,~~
~~VH CDR3 sequence set forth in SEQ ID NO:84,~~
~~VL CDR1 sequence set forth in SEQ ID NO:85~~
~~VL CDR2 sequence DAS, and~~
~~VL CDR3 sequence set forth in SEQ ID NO: 86;~~

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~~iii) VH CDR1 sequence set forth in SEQ ID NO:95,~~
~~VH CDR2 sequence set forth in SEQ ID NO:96,~~
~~VH CDR3 sequence set forth in SEQ ID NO:97,~~
~~VL CDR1 sequence set forth in SEQ ID NO:99,~~
~~VL CDR2 sequence ATS, and~~
~~VL CDR3 sequence set forth in SEQ ID NO: 100;~~

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~~iv) VH CDR1 sequence set forth in SEQ ID NO:88,~~
~~VH CDR2 sequence set forth in SEQ ID NO:89,~~
~~VH CDR3 sequence set forth in SEQ ID NO:90,~~
~~VL CDR1 sequence set forth in SEQ ID NO:92~~
~~VL CDR2 sequence DAS, and~~
~~VL CDR3 sequence set forth in SEQ ID NO: 93;; and~~

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~~v) VH CDR1 sequence set forth in SEQ ID NO:102,~~
~~VH CDR2 sequence set forth in SEQ ID NO:103,~~
~~VH CDR3 sequence set forth in SEQ ID NO:104,~~
~~VL CDR1 sequence set forth in SEQ ID NO:106~~

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~~VL CDR2 sequence QMS, and
—— VL CDR3 sequence set forth in SEQ ID NO: 107.~~

5 ~~46. Use of the bispecific antibody of any of claims 1-26 or the antibody of any of claims 27-38 or the composition of claim 39 for the manufacture of a medicament.~~

~~47. The use of claim 46 for the manufacture of a medicament for the treatment of cancer, autoimmune disease or an inflammatory disease.~~

10 ~~48. The use of claim 47 for the manufacture of a medicament for the treatment of allergy, transplantation rejection or a B-cell malignancy, such as non-Hodgkin lymphoma (NHL), chronic lymphocytic leukemia (CLL), follicular lymphoma (FL), mantle cell lymphoma (MCL), plasma cell leukemia (PCL), diffuse large B-cell lymphoma (DLBCL), or acute lymphoblastic leukemia (ALL).~~

~~49. The use of any of claims 46-48 in combination with one or more further therapeutic agents.~~

15 ~~50. The use of claim 49, wherein the one or more further therapeutic agents is selected from the group comprising: doxorubicin, cisplatin, bleomycin, carmustine, cyclophosphamide, chlorambucil, bendamustine, vincristine, fludarabine, ibrutinib and an anti-CD 20 antibody such as rituximab or ofatumumab.~~

20 ~~51. A method of inducing cell death, or inhibiting growth and/or proliferation of a tumor cell expressing CD37 comprising administering to an individual in need thereof an effective amount of the bispecific antibody of any of claims 1-26 or the antibody of any of claims 27-38 or the composition of claim 39.~~

25 ~~52. A method of treating an individual having allergy, an autoimmune disease, an inflammatory disease, transplantation rejection or a B-cell malignancy, such as non-Hodgkin lymphoma (NHL), chronic lymphocytic leukemia (CLL), follicular lymphoma (FL), mantle cell lymphoma (MCL), plasma cell leukemia (PCL), diffuse large B-cell lymphoma (DLBCL), or~~

~~acute lymphoblastic leukemia (ALL), comprising administering to said individual an effective amount of the bispecific antibody of any of claims 1-25 or the antibody of any of claims 27-38 or the composition of claim 39.~~

5 ~~53. The method of any of claims 51-52 comprising administering one or more further therapeutic agents in combination with said antibody or said bispecific antibody.~~

~~54. The method of claim 53, wherein the one or more further therapeutic agents is selected from the group comprising: doxorubicin, cisplatin, bleomycin, carmustine, cyclophosphamide, chlorambucil, bendamustine, vincristine, fludarabine, ibrutinib and an anti-CD 20 antibody such as rituximab or ofatumumab.~~

10 ~~55. A nucleic acid construct encoding one or more sequences selected from the group comprising SEQ ID Nos: 1, 2, 3, 4, 5, 6, 6a, 7, 8, 9, 10, 11, 12, 13, 13a, 14, 15, 16, 17, 18, 19, 20, 20a, 21, 22, 23, 24, 25, 26, 27, 27a, 28, 29, 30, 30a and 31 as set out in Table 1.~~

~~56. A nucleic acid construct encoding the bispecific antibody of any of claims 1-26 or the antibody of any of claims 27-38.~~

15 ~~57. An expression vector comprising one or more nucleic acid constructs of claims 55-56.~~

~~58. A host cell comprising an expression vector according to claim 57.~~

~~59. The host cell according to claim 58, wherein the host cell is a recombinant host cell, such as a recombinant prokaryotic cell, recombinant eukaryotic cell or recombinant microbial host cell.~~

20 ~~60. An anti-idiotypic antibody, which binds to the antibody of any of claims 27-38.~~

~~61. An *in vitro* method for detecting the presence of a human CD37 antigen or a cell expressing human CD37 in a sample, said method comprising:~~

(xx) — contacting the sample with the bispecific antibody of any of claims 1-26 or the antibody of any of claims 27-38 under conditions that allow for formation of a complex between the antibody or the bispecific antibody and CD37; and

(xxi) — detecting the formation of a complex.

5 62. An *in vivo* method for detecting the presence of a human CD37 antigen, or a cell expressing human CD37 in a subject, said method comprising:

(xxii) — administering the bispecific antibody of any of claims 1-26 or the antibody of any of claims 27-38 under conditions that allow for formation of a complex between the antibody or the bispecific antibody and CD37; and

10 (xxiii) — detecting the formed complex.