

CLAIMS

1. Use of an anti-CD43 antibody or antigen-binding fragment thereof for use in the manufacture of a medicament for a method of treating a CD43 positive cancer,
5 comprising:

~~—administering a therapeutically effective amount of the anti-CD43 antibody or antigen-binding fragment to a patient having a CD43 positive cancer,~~

~~—wherein the anti-CD43 antibody or antigen-binding fragment binds an epitope within amino acids 61-91 of wild-type CD43;~~

10 wherein the antibody or the antigen-binding fragment thereof comprises a heavy chain variable domain (VH) and a light chain variable domain (VL),

wherein the VH comprises framework regions and complementarity determining regions (CDRs) having the sequences SEQ ID NO: 1; SEQ ID NO: 43; and SEQ ID NO: 3, and the VL comprises framework regions and CDRs having the sequences SEQ
15 ID NO: 4; SEQ ID NO: 5; and SEQ ID NO: 6,

and wherein the CD43 positive cancer is selected from the group consisting of: diffuse large B cell lymphoma, MALT lymphoma, Burkitt's lymphoma, anaplastic large cell lymphoma, follicular lymphoma, mantle cell lymphoma, multiple myeloma, melanoma, testicular cancer, nephroblastoma, neuroblastoma, endodermal sinus carcinoma, retinoblastoma, hepatoblastoma, medulloblastoma, choroid plexus
20 papilloma, glioblastoma, ependymoma, primitive neuroectodermal tumor, alveolus rhabdomyosarcoma, immaturity teratoma, and leiomyosarcoma.

2. The use according to claim 1, wherein the anti-CD43 antibody or antigen-binding fragment binds an epitope within amino acids 61-91 of wild-type CD43.
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~~32. The anti-CD43 antibody or antigen-binding fragment for use according to claim 1 or 2, wherein the anti-CD43 antibody or antigen-binding fragment binds amino acids 71-78 of wild-type CD43.~~

~~43. The anti-CD43 antibody or antigen-binding fragment for use according to claim 1 or 2, wherein the anti-CD43 antibody or antigen-binding fragment binds amino acids 73-78 of wild-type CD43.~~

5 ~~4. The anti-CD43 antibody or antigen-binding fragment for use according to any of the preceding claims, wherein the anti-CD43 antibody or antigen-binding fragment comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein the VH domain comprises:~~
~~— the VH CDR1 sequence of SEQ ID NO: 1;~~
10 ~~— the VH CDR2 sequence of SEQ ID NO: 43; and~~
~~— the VH CDR3 sequence of SEQ ID NO: 3;~~
~~— and wherein the VL domain comprises:~~
~~— the VL CDR1 sequence of SEQ ID NO: 4;~~
~~— the VL CDR2 sequence of SEQ ID NO: 5; and~~
15 ~~— the VL CDR3 sequence of SEQ ID NO: 6.~~

~~5. The anti-CD43 antibody or antigen-binding fragment for use according to claim 4, wherein the VH sequence is SEQ ID NO: 7 and the VL sequence is SEQ ID NO: 12.~~

20 ~~6. The anti-CD43 antibody or antigen-binding fragment for use according to claim 4 or 5, wherein the anti-CD43 antibody is a murine antibody produced by the hybridoma cell line deposited under ICLC accession number ICLC PD number 16001 (UMG1).~~

~~7. The anti-CD43 antibody or antigen-binding fragment for use according to claim 4 or 5, wherein the anti-CD43 antibody is a chimeric antibody further comprising human constant region domains.~~

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~~8. The anti-CD43 antibody or antigen-binding fragment for use according to claim 7, wherein the human constant region domains are IgG domains.~~

9. The ~~anti-CD43 antibody or antigen-binding fragment~~ for use according to claim 8, wherein the antibody heavy chain sequence is SEQ ID NO: 34 and the antibody light chain sequence is SEQ ID NO: 35.
- 5 10. The ~~anti-CD43 antibody or antigen-binding fragment~~ for use according to claim ~~4~~1, wherein the anti-CD43 antibody or antigen-binding fragment comprises human variable domain framework regions.
- 10 11. The ~~anti-CD43 antibody or antigen-binding fragment~~ for use according to claim 10, wherein the VH domain has a sequence selected from: SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, and SEQ ID NO: 11; and the VL domain has a sequence selected from: SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, and SEQ ID NO: 16.
- 15 12. The ~~anti-CD43 antibody or antigen-binding fragment~~ for use according to any of the preceding claims, wherein the anti-CD43 antibody is a monoclonal antibody.
- 20 13. The ~~anti-CD43 antibody or antigen-binding fragment~~ for use according to any of the preceding claims, wherein the anti-CD43 antibody or antigen-binding fragment is an F(ab), an F(ab)'₂, an scFv, a diabody, a single domain antibody, a tandab, or a flexibody.
- 25 14. The ~~anti-CD43 antibody or antigen-binding fragment~~ for use according to any of the preceding claims, wherein the anti-CD43 antibody or antigen-binding fragment is capable of inducing antibody dependent cellular cytotoxicity (ADCC) in the presence of an effector cell.
- 30 15. The ~~anti-CD43 antibody or antigen-binding fragment~~ for use according to any of the preceding claims, wherein the anti-CD43 antibody or antigen-binding fragment is capable of depleting tumor-associated macrophages (TAMs).

16. The ~~anti-CD43 antibody or antigen-binding fragment~~ for use according to any of the preceding claims, wherein the anti-CD43 antibody or antigen-binding fragment is conjugated to a toxic drug.

5 17. The ~~anti-CD43 antibody or antigen-binding fragment~~ for use according to any of the preceding claims, wherein the patient has diffuse large B cell lymphoma, MALT lymphoma, Burkitt lymphoma, anaplastic large cell lymphoma, follicular lymphoma, or mantle cell lymphoma.

10 18. The ~~anti-CD43 antibody or antigen-binding fragment~~ for use according to any one of claims 1 to 16, wherein the patient has multiple myeloma.

19. The ~~anti-CD43 antibody or antigen-binding fragment~~ for use according to any one of claims 1 to 16, wherein the patient has melanoma.

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20. The ~~anti-CD43 antibody or antigen-binding fragment~~ for use according to any one of claims 1 to 16, wherein the patient has testicular cancer.

21. The ~~anti-CD43 antibody or antigen-binding fragment~~ for use according to claim 20, wherein the testicular cancer is selected from the group consisting of: seminoma, embryonal carcinoma, yolk sac tumor, and teratoma.

22. The ~~anti-CD43 antibody or antigen-binding fragment~~ for use according to any one of claims 1 to 16, wherein the patient has neuroblastoma, endodermal sinus carcinoma, retinoblastoma, hepatoblastoma, medulloblastoma, choroid plexus papilloma, glioblastoma, ependymoma, primitive neuroectodermal tumor, alveolus rhabdomyosarcoma, immaturity teratoma, or leiomyosarcoma.

23. Use of a bispecific antibody for use in the manufacture of a medicament for
30 method of treating a CD43 positive cancer, comprising:

~~—administering a therapeutically effective amount of the bispecific antibody to a patient having a CD43 positive cancer,~~

wherein the bispecific antibody has a first binding specificity for an epitope within amino acids 71-78 of wild-type CD43,

5 and wherein the CD43 positive cancer is selected from the group consisting of: diffuse large B cell lymphoma, MALT lymphoma, Burkitt's lymphoma, anaplastic large cell lymphoma, follicular lymphoma, mantle cell lymphoma, multiple myeloma, melanoma, testicular cancer, nephroblastoma, neuroblastoma, endodermal sinus carcinoma, retinoblastoma, hepatoblastoma, medulloblastoma, choroid plexus
10 papilloma, glioblastoma, ependymoma, primitive neuroectodermal tumor, alveolus rhabdomyosarcoma, immaturity teratoma, and leiomyosarcoma.

24. ~~The bispecific antibody for use according to claim 23, wherein the bispecific antibody has a second binding specificity for CD3.~~

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25. Use of a CAR-T cell for use in the manufacture of a medicament for a method of treating a CD43 positive cancer, comprising:

~~—administering a therapeutically effective amount of the CAR-T cell to a patient having a CD43 positive cancer,~~

20 wherein the CAR-T cell binds an epitope within amino acids 71-78 of wild-type CD43,

and wherein the CD43 positive cancer is selected from the group consisting of: diffuse large B cell lymphoma, MALT lymphoma, Burkitt's lymphoma, anaplastic large cell lymphoma, follicular lymphoma, mantle cell lymphoma, multiple myeloma,
25 melanoma, testicular cancer, nephroblastoma, neuroblastoma, endodermal sinus carcinoma, retinoblastoma, hepatoblastoma, medulloblastoma, choroid plexus papilloma, glioblastoma, ependymoma, primitive neuroectodermal tumor, alveolus rhabdomyosarcoma, immaturity teratoma, and leiomyosarcoma.

26. ~~An anti-CD43 antibody or antigen-binding fragment thereof for use in a method of identifying a CD43-positive cancer, comprising:~~
~~—detectably contacting a sample comprising a CD43-positive cancer cell with the anti-CD43 antibody or antigen-binding fragment,~~
5 ~~—wherein the anti-CD43 antibody or antigen-binding fragment binds an epitope within amino acids 71-78 of wild-type CD43,~~
~~—and wherein the CD43-positive cancer is selected from the group consisting of: diffuse large B-cell lymphoma, MALT lymphoma, Burkitt's lymphoma, anaplastic large cell lymphoma, follicular lymphoma, mantle cell lymphoma, multiple myeloma,~~
10 ~~melanoma, testicular cancer, nephroblastoma, neuroblastoma, endodermal sinus carcinoma, retinoblastoma, hepatoblastoma, medulloblastoma, choroid plexus papilloma, glioblastoma, ependymoma, primitive neuroectodermal tumor, alveolus rhabdomyosarcoma, immaturity teratoma, and leiomyosarcoma.~~
- 15 27. ~~An anti-CD43 antibody or antigen-binding fragment thereof for use in a method of diagnosing and treating a CD43-positive cancer, comprising:~~
~~—detectably contacting a sample from a patient with the anti-CD43 antibody or antigen-binding fragment,~~
~~—diagnosing the patient with a CD43-positive cancer if a binding to the anti-CD43~~
20 ~~antibody or antigen-binding fragment is detected,~~
~~—and administering a therapeutically effective amount of the anti-CD43 antibody or antigen-binding fragment to the patient,~~
~~—wherein the anti-CD43 antibody or antigen-binding fragment binds an epitope within amino acids 71-78 of wild-type CD43,~~
25 ~~—and wherein the CD43-positive cancer is selected from the group consisting of: diffuse large B-cell lymphoma, MALT lymphoma, Burkitt's lymphoma, anaplastic large cell lymphoma, follicular lymphoma, mantle cell lymphoma, multiple myeloma, melanoma, testicular cancer, nephroblastoma, neuroblastoma, endodermal sinus carcinoma, retinoblastoma, hepatoblastoma, medulloblastoma, choroid plexus~~

~~papilloma, glioblastoma, ependymoma, primitive neuroectodermal tumor, alveolus rhabdomyosarcoma, immaturity teratoma, and leiomyosarcoma.~~

~~28. A method of treating a CD43 positive cancer, the method comprising:~~

- 5 ~~— administering a therapeutically effective amount of an anti-CD43 antibody or antigen-binding fragment thereof to a patient having a CD43 positive cancer,~~
~~— wherein the anti-CD43 antibody or antigen-binding fragment binds an epitope within amino acids 61-91 of wild-type CD43,~~
~~— and wherein the CD43 positive cancer is selected from the group consisting of:~~
- 10 ~~diffuse large B-cell lymphoma, MALT lymphoma, Burkitt's lymphoma, anaplastic large cell lymphoma, follicular lymphoma, mantle cell lymphoma, multiple myeloma, melanoma, testicular cancer, nephroblastoma, neuroblastoma, endodermal sinus carcinoma, retinoblastoma, hepatoblastoma, medulloblastoma, choroid plexus papilloma, glioblastoma, ependymoma, primitive neuroectodermal tumor, alveolus~~
- 15 ~~rhabdomyosarcoma, immaturity teratoma, and leiomyosarcoma.~~

~~29. The method of claim 28, wherein the anti-CD43 antibody or antigen-binding fragment binds amino acids 71-78 of wild-type CD43.~~

- 20 ~~30. The method of claim 28, wherein the anti-CD43 antibody or antigen-binding fragment binds amino acids 73-78 of wild-type CD43.~~

- ~~31. The method of any one of claims 28 to 30, wherein the anti-CD43 antibody or antigen-binding fragment comprises a heavy chain variable (VH) domain and a light~~
- 25 ~~chain variable (VL) domain,~~

- ~~— wherein the VH domain comprises:~~
~~— the VH CDR1 sequence of SEQ ID NO: 1;~~
~~— the VH CDR2 sequence of SEQ ID NO: 43; and~~
~~— the VH CDR3 sequence of SEQ ID NO: 3;~~
- 30 ~~— and wherein the VL domain comprises:~~

~~—the VL CDR1 sequence of SEQ ID NO: 4;
—the VL CDR2 sequence of SEQ ID NO: 5; and
—the VL CDR3 sequence of SEQ ID NO: 6.~~

5 ~~32. The method of claim 31, wherein the VH sequence is SEQ ID NO: 7 and the VL sequence is SEQ ID NO: 12.~~

10 ~~33. The method of claim 31 or 32, wherein the anti CD43 antibody is a murine antibody produced by the hybridoma cell line deposited under ICLC accession number ICLC PD number 16001 (UMG1).~~

~~34. The method of claim 31 or 32, wherein the anti CD43 antibody is a chimeric antibody further comprising human constant region domains.~~

15 ~~35. The method of claim 34, wherein the human constant region domains are IgG domains.~~

~~36. The method of claim 35, wherein the antibody heavy chain sequence is SEQ ID NO: 34 and the antibody light chain sequence is SEQ ID NO: 35.~~

20 ~~37. The method of claim 31, wherein the anti CD43 antibody or antigen-binding fragment comprises human variable domain framework regions.~~

25 ~~38. The method of claim 37, wherein the VH domain has a sequence selected from: SEQ ID NO: 8, SEQ ID NO: 9, SEQ ID NO: 10, and SEQ ID NO: 11; and the VL domain has a sequence selected from: SEQ ID NO: 13, SEQ ID NO: 14, SEQ ID NO: 15, and SEQ ID NO: 16.~~

30 ~~39. The method of any one of claims 28 to 38, wherein the anti CD43 antibody is a monoclonal antibody.~~

~~40. The method of any one of claims 28 to 39, wherein the anti-CD43 antibody or antigen binding fragment is an F(ab), an F(ab)'2, an scFv, a diabody, a single domain antibody, a tandab, or a flexibody.~~

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~~41. The method of any one of claims 28 to 40, wherein the anti-CD43 antibody or antigen binding fragment is capable of inducing antibody dependent cellular cytotoxicity (ADCC) in the presence of an effector cell.~~

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~~42. The method of any one of claims 28 to 41, wherein the anti-CD43 antibody or antigen binding fragment is capable of depleting tumor associated macrophages (TAMs).~~

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~~43. The method of any one of claims 28 to 42, wherein the anti-CD43 antibody or antigen binding fragment is conjugated to a toxic drug.~~

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~~44. The method of any one of claims 28 to 43, wherein the patient has diffuse large B cell lymphoma, MALT lymphoma, Burkitt lymphoma, anaplastic large cell lymphoma, follicular lymphoma, or mantle cell lymphoma.~~

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~~45. The method of any one of claims 28 to 43, wherein the patient has multiple myeloma.~~

~~46. The method of any one of claims 28 to 43, wherein the patient has melanoma.~~

~~47. The method of any one of claims 28 to 43, wherein the patient has testicular cancer.~~

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~~48. The method of claim 47, wherein the testicular cancer is selected from the group consisting of seminoma, embryonal carcinoma, yolk sac tumor, and teratoma.~~

49. The method of any one of claims 28 to 43, wherein the patient has ~~nephroblastoma, neuroblastoma, endodermal sinus carcinoma, retinoblastoma, hepatoblastoma, medulloblastoma, choroid plexus papilloma, glioblastoma, ependymoma, primitive neuroectodermal tumor, alveolus rhabdomyosarcoma, immaturity teratoma, or leiomyosarcoma.~~

50. A method of treating a CD43 positive cancer, the method comprising:

—administering a therapeutically effective amount of a bispecific antibody to a patient having a CD43 positive cancer,

—wherein the bispecific antibody has a first binding specificity for an epitope within amino acids 71-78 of wild type CD43,

—and wherein the CD43 positive cancer is selected from the group consisting of: diffuse large B-cell lymphoma, MALT lymphoma, Burkitt's lymphoma, anaplastic large cell lymphoma, follicular lymphoma, mantle cell lymphoma, multiple myeloma, melanoma, testicular cancer, nephroblastoma, neuroblastoma, endodermal sinus carcinoma, retinoblastoma, hepatoblastoma, medulloblastoma, choroid plexus papilloma, glioblastoma, ependymoma, primitive neuroectodermal tumor, alveolus rhabdomyosarcoma, immaturity teratoma, and leiomyosarcoma.

51. The method of claim 50, wherein the bispecific antibody has a second binding specificity for CD3.

52. A method of treating a CD43 positive cancer, the method comprising:

—administering a therapeutically effective amount of a CAR-T cell to a patient having a CD43 positive cancer,

—wherein the CAR T cell binds an epitope within amino acids 71-78 of wild type CD43,

—and wherein the CD43 positive cancer is selected from the group consisting of: diffuse large B-cell lymphoma, MALT lymphoma, Burkitt's lymphoma, anaplastic large cell lymphoma, follicular lymphoma, mantle cell lymphoma, multiple myeloma,

~~melanoma, testicular cancer, nephroblastoma, neuroblastoma, endodermal sinus carcinoma, retinoblastoma, hepatoblastoma, medulloblastoma, choroid plexus papilloma, glioblastoma, ependymoma, primitive neuroectodermal tumor, alveolus rhabdomyosarcoma, immaturity teratoma, and leiomyosarcoma.~~

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~~2653.~~ An *in vitro* method of identifying a CD43 positive cancer, the method comprising:

detectably contacting an *in vitro* sample comprising a CD43 positive cancer cell with an anti-CD43 antibody or antigen-binding fragment thereof,

10 wherein the anti-CD43 antibody or antigen-binding fragment binds an epitope within amino acids 71-78 of wild-type CD43,

and wherein the CD43 positive cancer is selected from the group consisting of: diffuse large B cell lymphoma, MALT lymphoma, Burkitt's lymphoma, anaplastic large cell lymphoma, follicular lymphoma, mantle cell lymphoma, multiple myeloma,
15 melanoma, testicular cancer, nephroblastoma, neuroblastoma, endodermal sinus carcinoma, retinoblastoma, hepatoblastoma, medulloblastoma, choroid plexus papilloma, glioblastoma, ependymoma, primitive neuroectodermal tumor, alveolus rhabdomyosarcoma, immaturity teratoma, and leiomyosarcoma.

20 ~~2754.~~ An *in vitro* method of diagnosing ~~and treating~~ a CD43 positive cancer, the method comprising:

detectably contacting an *in vitro* sample from a patient with the anti-CD43 antibody or antigen-binding fragment, and

diagnosing the patient with a CD43 positive cancer if a binding to the anti-CD43
25 antibody or antigen-binding fragment is detected,

~~—and administering a therapeutically effective amount of an anti-CD43 antibody or antigen-binding fragment to the patient thereof,~~

wherein the anti-CD43 antibody or antigen-binding fragment binds an epitope within amino acids 71-78 of wild-type CD43,

and wherein the CD43 positive cancer is selected from the group consisting of:
diffuse large B cell lymphoma, MALT lymphoma, Burkitt's lymphoma, anaplastic large
cell lymphoma, follicular lymphoma, mantle cell lymphoma, multiple myeloma,
melanoma, testicular cancer, nephroblastoma, neuroblastoma, endodermal sinus
5 carcinoma, retinoblastoma, hepatoblastoma, medulloblastoma, choroid plexus
papilloma, glioblastoma, ependymoma, primitive neuroectodermal tumor, alveolus
rhabdomyosarcoma, immaturity teratoma, and leiomyosarcoma.