

CLAIMS:

1. An isolated single domain antibody (sdAb), which binds specifically to human CD22, the sdAb comprising:

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a) a CDR1 amino acid sequence $GX_1X_2X_3DX_4YX_5$ (**SEQ ID NO: 126**), wherein:

X_1 is F or V,

X_2 is T or S,

X_3 is L, F, or S,

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X_4 is Y, D, or S, and

X_5 is V or A,

a CDR2 amino acid sequence $X_6X_7X_8X_9X_{10}GX_{11}T$ (**SEQ ID NO: 127**), wherein:

X_6 is I or M,

X_7 is T, R, G, or S,

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X_8 is S or N,

X_9 is D or S,

X_{10} is D or is absent,

X_{11} is V or A, and

a CDR3 amino acid sequence $AVDKPFYDGGX_{12}X_{13}YTCPVDFX_{14}S$ (**SEQ ID**

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NO: 128), wherein:

X_{12} is I, N, Y, or S,

X_{13} is Q, Y, R, or L, and

X_{14} is D or G;

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b) a CDR1 amino acid sequence $GSX_1FX_2X_3X_4X_5V$ (**SEQ ID NO: 129**), wherein:

X_1 is I or T,

X_2 is R or is absent,

X_3 is R, S, or I,

X_4 is I, S, or T, and

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X_5 is A, S, or T,

a CDR2 amino acid sequence $ITSX_6GX_7X_8$ (**SEQ ID NO: 130**), wherein:

X₆ is G, S, or A,

X₇ is E, D, or S,

X₈ is T or S, and

a CDR3 amino acid sequence NAX₉X₁₀GX₁₁X₁₂X₁₃X₁₄ (SEQ ID NO: 131),

5 wherein:

X₉ is K or Q,

X₁₀ is W or Y,

X₁₁ is Q, R, or G,

X₁₂ is Y, D, or R,

10 X₁₃ is E or S, and

X₁₄ is Y, D, or H;

c) a CDR1 amino acid sequence GRIX₁RSYY (SEQ ID NO: 132), wherein:

X₁ is F or S,

15 a CDR2 amino acid sequence IGX₂SDT (SEQ ID NO: 133), wherein:

X₂ is W or C, and

a CDR3 amino acid sequence AX₃X₄SPPYGPQRDEFX₅Y (SEQ ID NO: 134),

wherein:

X₃ is A or E,

20 X₄ is N or Y, and

X₅ is G or D;

d) a CDR1 amino acid sequence G X₁TX₂SVYX₃ (SEQ ID NO: 135), wherein:

X₁ is R or G,

25 X₂ is S or F, and

X₃ is G or T,

a CDR2 amino acid sequence X₄X₅X₆SX₇GX₈T (SEQ ID NO: 136), wherein:

X₄ is M or I,

X₅ is S or R,

30 X₆ is W or G,

X₇ is G or is absent, and

X₈ is P or G,

a CDR3 amino acid sequence AVRIRRTLX₉EPLTKETLYDY **SEQ ID NO: 137**), wherein:

X₉ is L or V;

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e) a CDR1 amino acid sequence as set forth in SEQ ID NO: 49,
a CDR2 amino acid sequence as set forth in SEQ ID NO: 50, and
a CDR3 amino acid sequence as set forth in SEQ ID NO: 51 (**hCD22pas-16**);

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f) a CDR1 amino acid sequence as set forth in SEQ ID NO: 4,
a CDR2 amino acid sequence as set forth in SEQ ID NO: 5, and
a CDR3 amino acid sequence as set forth in SEQ ID NO: 6 (**hCD221ug-10**);

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g) a CDR1 amino acid sequence as set forth in SEQ ID NO: 7,
a CDR2 amino acid sequence as set forth in SEQ ID NO: 8, and
a CDR3 amino acid sequence as set forth in SEQ ID NO: 9 (**hCD221ug-13**);

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h) a CDR1 amino acid sequence as set forth in SEQ ID NO: 13,
a CDR2 amino acid sequence as set forth in SEQ ID NO: 14, and
a CDR3 amino acid sequence as set forth in SEQ ID NO: 15 (**hCD221ug-36**);

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i) a CDR1 amino acid sequence as set forth in SEQ ID NO: 16,
a CDR2 amino acid sequence as set forth in SEQ ID NO: 17, and
a CDR3 amino acid sequence as set forth in SEQ ID NO: 18 (**hCD221ug-61**);

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j) a CDR1 amino acid sequence as set forth in SEQ ID NO: 40,
a CDR2 amino acid sequence as set forth in SEQ ID NO: 41, and
a CDR3 amino acid sequence as set forth in SEQ ID NO: 42 (**hCD22100ug-62**);

k) a CDR1 amino acid sequence as set forth in SEQ ID NO: 55,

a CDR2 amino acid sequence as set forth in SEQ ID NO: 56, and
a CDR3 amino acid sequence as set forth in SEQ ID NO: 57 (**hCD22pas-24**);

l) a CDR1 amino acid sequence as set forth in SEQ ID NO: 64,
a CDR2 amino acid sequence as set forth in SEQ ID NO: 65, and
a CDR3 amino acid sequence as set forth in SEQ ID NO: 66 (**hCD22pas-48**);

or

m) a CDR1 amino acid sequence as set forth in SEQ ID NO: 70,
a CDR2 amino acid sequence as set forth in SEQ ID NO: 71, and
a CDR3 amino acid sequence as set forth in SEQ ID NO: 72 (**hCD22pas-64**).

2. An isolated single domain antibody (sdAb), which binds specifically to human CD22,
the sdAb comprising:

A)

i) a CDR1 amino acid sequence as set forth in SEQ ID NO: 1, a CDR2 amino
acid sequence as set forth in SEQ ID NO: 2, and a CDR3 amino acid
sequence as set forth in SEQ ID NO: 3 (**hCD221ug-6**),

ii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 4, a CDR2 amino
acid sequence as set forth in SEQ ID NO: 5, and a CDR3 amino acid
sequence as set forth in SEQ ID NO: 6 (**hCD221ug-10**),

iii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 7, a CDR2 amino
acid sequence as set forth in SEQ ID NO: 8, and a CDR3 amino acid
sequence as set forth in SEQ ID NO: 9 (**hCD221ug-13**),

iv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 10, a CDR2 amino
acid sequence as set forth in SEQ ID NO: 11, and a CDR3 amino acid
sequence as set forth in SEQ ID NO: 12 (**hCD221ug-14**),

v) a CDR1 amino acid sequence as set forth in SEQ ID NO: 13, a CDR2 amino
acid sequence as set forth in SEQ ID NO: 14, and a CDR3 amino acid
sequence as set forth in SEQ ID NO: 15 (**hCD221ug-36**),

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- vi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 16, a CDR2 amino acid sequence as set forth in SEQ ID NO: 17, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 18 (**hCD221ug-61**),
 - vii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 19, a CDR2 amino acid sequence as set forth in SEQ ID NO: 20, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 21 (**hCD221ug-74**),
 - viii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 22, a CDR2 amino acid sequence as set forth in SEQ ID NO: 23, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 24 (**hCD221ug-75**),
 - ix) a CDR1 amino acid sequence as set forth in SEQ ID NO: 25, a CDR2 amino acid sequence as set forth in SEQ ID NO: 26, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 27 (**hCD221ug-77**),
 - x) a CDR1 amino acid sequence as set forth in SEQ ID NO: 28, a CDR2 amino acid sequence as set forth in SEQ ID NO: 29, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 30 (**hCD221ug-80**),
 - xi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 31, a CDR2 amino acid sequence as set forth in SEQ ID NO: 32, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 33 (**hCD221ug-87**),
 - xii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 34, a CDR2 amino acid sequence as set forth in SEQ ID NO: 35, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 36 (**hCD221ug-93**),
 - xiii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 37, a CDR2 amino acid sequence as set forth in SEQ ID NO: 38, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 39 (**hCD22100ug-2**),
 - xiv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 40, a CDR2 amino acid sequence as set forth in SEQ ID NO: 41, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 42 (**hCD22100ug-62**),
 - xv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 43, a CDR2 amino acid sequence as set forth in SEQ ID NO: 44, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 45 (**hCD22100ug-66**),

- xvi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 46, a CDR2 amino acid sequence as set forth in SEQ ID NO: 47, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 48 (**hCD22pas-10**),
- 5 xvii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 49, a CDR2 amino acid sequence as set forth in SEQ ID NO: 50, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 51 (**hCD22pas-16**),
- xviii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 52, a CDR2 amino acid sequence as set forth in SEQ ID NO: 53, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 54 (**hCD22pas-23**),
- 10 xix) a CDR1 amino acid sequence as set forth in SEQ ID NO: 55, a CDR2 amino acid sequence as set forth in SEQ ID NO: 56, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 57 (**hCD22pas-24**),
- xx) a CDR1 amino acid sequence as set forth in SEQ ID NO: 58, a CDR2 amino acid sequence as set forth in SEQ ID NO: 59, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 60 (**hCD22pas-32**),
- 15 xxi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 61, a CDR2 amino acid sequence as set forth in SEQ ID NO: 62, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 63 (**hCD22pas-33**),
- xxii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 64, a CDR2 amino acid sequence as set forth in SEQ ID NO: 65, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 66 (**hCD22pas-48**),
- 20 xxiii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 67, a CDR2 amino acid sequence as set forth in SEQ ID NO: 68, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 69 (**hCD22pas-55**),
- 25 xxiv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 70, a CDR2 amino acid sequence as set forth in SEQ ID NO: 71, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 72 (**hCD22pas-64**),
- xxv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 73, a CDR2 amino acid sequence as set forth in SEQ ID NO: 74, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 75 (**hCD22pas-72**),
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- xxvi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 76, a CDR2 amino acid sequence as set forth in SEQ ID NO: 77, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 78 (**hCD22pas-79**), or
- xxvii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 79, a CDR2 amino acid sequence as set forth in SEQ ID NO: 80, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 81 (**hCD22pas-82**).

3. An isolated single domain antibody (sdAb), which binds specifically to human CD22, the sdAb comprising:

A)

- i) a CDR1 amino acid sequence as set forth in SEQ ID NO: 1, a CDR2 amino acid sequence as set forth in SEQ ID NO: 2, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 3 (**hCD221ug-6**),
- ii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 4, a CDR2 amino acid sequence as set forth in SEQ ID NO: 5, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 6 (**hCD221ug-10**),
- iii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 7, a CDR2 amino acid sequence as set forth in SEQ ID NO: 8, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 9 (**hCD221ug-13**),
- iv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 10, a CDR2 amino acid sequence as set forth in SEQ ID NO: 11, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 12 (**hCD221ug-14**),
- v) a CDR1 amino acid sequence as set forth in SEQ ID NO: 13, a CDR2 amino acid sequence as set forth in SEQ ID NO: 14, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 15 (**hCD221ug-36**),
- vi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 16, a CDR2 amino acid sequence as set forth in SEQ ID NO: 17, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 18 (**hCD221ug-61**),
- vii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 19, a CDR2 amino acid sequence as set forth in SEQ ID NO: 20, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 21 (**hCD221ug-74**),

- viii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 22, a CDR2 amino acid sequence as set forth in SEQ ID NO: 23, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 24 (**hCD221ug-75**),
- ix) a CDR1 amino acid sequence as set forth in SEQ ID NO: 25, a CDR2 amino acid sequence as set forth in SEQ ID NO: 26, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 27 (**hCD221ug-77**),
- x) a CDR1 amino acid sequence as set forth in SEQ ID NO: 28, a CDR2 amino acid sequence as set forth in SEQ ID NO: 29, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 30 (**hCD221ug-80**),
- xi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 31, a CDR2 amino acid sequence as set forth in SEQ ID NO: 32, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 33 (**hCD221ug-87**),
- xii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 34, a CDR2 amino acid sequence as set forth in SEQ ID NO: 35, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 36 (**hCD221ug-93**),
- xiii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 37, a CDR2 amino acid sequence as set forth in SEQ ID NO: 38, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 39 (**hCD22100ug-2**),
- xiv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 40, a CDR2 amino acid sequence as set forth in SEQ ID NO: 41, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 42 (**hCD22100ug-62**),
- xv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 43, a CDR2 amino acid sequence as set forth in SEQ ID NO: 44, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 45 (**hCD22100ug-66**),
- xvi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 46, a CDR2 amino acid sequence as set forth in SEQ ID NO: 47, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 48 (**hCD22pas-10**),
- xvii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 49, a CDR2 amino acid sequence as set forth in SEQ ID NO: 50, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 51 (**hCD22pas-16**),

- xviii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 52, a CDR2 amino acid sequence as set forth in SEQ ID NO: 53, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 54 (**hCD22pas-23**),
- 5 xix) a CDR1 amino acid sequence as set forth in SEQ ID NO: 55, a CDR2 amino acid sequence as set forth in SEQ ID NO: 56, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 57 (**hCD22pas-24**),
- xx) a CDR1 amino acid sequence as set forth in SEQ ID NO: 58, a CDR2 amino acid sequence as set forth in SEQ ID NO: 59, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 60 (**hCD22pas-32**),
- 10 xxi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 61, a CDR2 amino acid sequence as set forth in SEQ ID NO: 62, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 63 (**hCD22pas-33**),
- xxii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 64, a CDR2 amino acid sequence as set forth in SEQ ID NO: 65, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 66 (**hCD22pas-48**),
- 15 xxiii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 67, a CDR2 amino acid sequence as set forth in SEQ ID NO: 68, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 69 (**hCD22pas-55**),
- xxiv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 70, a CDR2 amino acid sequence as set forth in SEQ ID NO: 71, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 72 (**hCD22pas-64**),
- 20 xxv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 73, a CDR2 amino acid sequence as set forth in SEQ ID NO: 74, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 75 (**hCD22pas-72**),
- 25 xxvi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 76, a CDR2 amino acid sequence as set forth in SEQ ID NO: 77, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 78 (**hCD22pas-79**), or
- xxvii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 79, a CDR2 amino acid sequence as set forth in SEQ ID NO: 80, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 81 (**hCD22pas-82**); or
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B)

CDR1, CDR2, and CDR3 amino acid sequences that are at least 80% identical to the CDR1, CDR2, and CDR3 sequences defined in any one of part A) i) to xxviii).

4. An isolated single domain antibody (sdAb), which binds specifically to human CD22,
5 the sdAb comprising:

A)

- i) a CDR3 amino acid sequence as set forth in SEQ ID NO: 3,
- ii) a CDR3 amino acid sequence as set forth in SEQ ID NO: 6,
- iii) a CDR3 amino acid sequence as set forth in SEQ ID NO: 9,
- 10 iv) a CDR3 amino acid sequence as set forth in SEQ ID NO: 12,
- v) a CDR3 amino acid sequence as set forth in SEQ ID NO: 15,
- vi) a CDR3 amino acid sequence as set forth in SEQ ID NO: 18,
- vii) a CDR3 amino acid sequence as set forth in SEQ ID NO: 21,
- viii) a CDR3 amino acid sequence as set forth in SEQ ID NO: 24,
- 15 ix) a CDR3 amino acid sequence as set forth in SEQ ID NO: 27,
- x) a CDR3 amino acid sequence as set forth in SEQ ID NO: 30,
- xi) a CDR3 amino acid sequence as set forth in SEQ ID NO: 33,
- xii) a CDR3 amino acid sequence as set forth in SEQ ID NO: 36,
- xiii) a CDR3 amino acid sequence as set forth in SEQ ID NO: 39,
- 20 xiv) a CDR3 amino acid sequence as set forth in SEQ ID NO: 42,
- xv) a CDR3 amino acid sequence as set forth in SEQ ID NO: 45,
- xvi) a CDR3 amino acid sequence as set forth in SEQ ID NO: 48,
- xvii) a CDR3 amino acid sequence as set forth in SEQ ID NO: 51,
- xviii) a CDR3 amino acid sequence as set forth in SEQ ID NO: 54,
- 25 xix) a CDR3 amino acid sequence as set forth in SEQ ID NO: 57,
- xx) a CDR3 amino acid sequence as set forth in SEQ ID NO: 60,
- xxi) a CDR3 amino acid sequence as set forth in SEQ ID NO: 63,
- xxii) a CDR3 amino acid sequence as set forth in SEQ ID NO: 66,
- xxiii) a CDR3 amino acid sequence as set forth in SEQ ID NO: 69,
- 30 xxiv) a CDR3 amino acid sequence as set forth in SEQ ID NO: 72,
- xxv) a CDR3 amino acid sequence as set forth in SEQ ID NO: 75,

- xxvi) a CDR3 amino acid sequence as set forth in SEQ ID NO: 79, or
xxvii) a CDR3 amino acid sequence as set forth in SEQ ID NO: 81.

5. The isolated single domain antibody (sdAb) of claim 4, comprising:

A)

- i) a CDR1 amino acid sequence as set forth in SEQ ID NO: 1, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 3,
ii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 4, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 6,
iii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 7, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 9,
iv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 10, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 12,
v) a CDR1 amino acid sequence as set forth in SEQ ID NO: 13, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 15,
vi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 16, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 18,
vii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 19, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 21,
viii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 22, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 24,
ix) a CDR1 amino acid sequence as set forth in SEQ ID NO: 25, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 27,
x) a CDR1 amino acid sequence as set forth in SEQ ID NO: 28, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 30,
xi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 31, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 33,
xii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 34, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 36,
xiii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 37, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 39,

- xiv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 40, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 42,
- xv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 43, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 45,
- 5 xvi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 46, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 48,
- xvii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 49, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 51,
- 10 xviii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 52, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 54,
- xix) a CDR1 amino acid sequence as set forth in SEQ ID NO: 55, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 57,
- xx) a CDR1 amino acid sequence as set forth in SEQ ID NO: 58, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 60,
- 15 xxi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 61, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 63,
- xxii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 64, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 66,
- 20 xxiii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 67, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 69,
- xxiv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 70, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 72,
- xxv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 73, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 75,
- 25 xxvi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 76, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 78, or
- xxvii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 79, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 81.

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6. The isolated isolated sdAb of claim 2 or 3, comprising A) the amino acid sequence of any one of SEQ ID NO: 85 to 112 and 120 to 125, or B) an amino acid sequence that is at least 80% identical to any one of SEQ ID NO: 82 to 108 and 120 to 125 across the full length thereof.

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7. The isolated isolated sdAb of claim 1 or 2, comprising A) the amino acid sequence of any one of SEQ ID NO: 82 to 108 and 120 to 125.

8. The isolated sdAb of any one of claims 1 to 5, which is a camelid sdAb.

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9. The isolated sdAb of claim 8, which is a lama sdAb.

10. The isolated sdAb of any one of claims 1 to 5, which is humanized.

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11. The isolated sdAb of any one of claims 1 to 10, which has an affinity for human CD22 of 2.5×10^{-7} nM or less.

12. The isolated sdAb of any one of claims 1 to 10, which has an affinity for human CD22 of 3×10^{-8} nM or less.

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13. The isolated sdAb of any one of claims 1 to 10, which has an affinity for human CD22 of 9.6×10^{-9} nM or less.

14. The isolated sdAb of any one of claims 1 to 10, which has an affinity for human CD22 of 9.3×10^{-10} nM or less.

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15. The isolated sdAb of any one of claims 1 to 10, which has an affinity for human CD22 of 7×10^{-12} nM or less.

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16. The isolated sdAb of any one of claims 1 to 15, which binds to the first Ig-like domain of human CD22.

17. The isolated sdAb of claim 16, wherein the antibody comprises SEQ ID NO: 91 (**hCD221ug-80**).

18. The isolated sdAb of any one of claims 1 to 15, which binds to the fourth Ig-like domain of human CD22.

19. The isolated sdAb of claim 18, wherein the antibody comprises SEQ ID NO: 84 (**hCD221ug-13**).

20. The isolated sdAb of any one of claims 1 to 15, which binds to the sixth Ig-like domain of human CD22.

21. The isolated sdAb of claim 20, wherein the antibody comprises SEQ ID NO: 84 (**hCD221ug-13**), SEQ ID NO: 91 (**hCD221ug-80**), SEQ ID NO: 86 (**hCD221ug-36**), or SEQ ID NO: 105 (**hCD221pas-64**).

22. The isolated sdAb of any one of claims 1 to 15, which binds to the seventh Ig-like domain of human CD22.

23. The isolated sdAb of claim 22, wherein the antibody comprises SEQ ID NO: 87 (**hCD221ug-61**), SEQ ID NO: 83 (**hCD221ug-10**), or SEQ ID NO: 100 (**hCD22pas-24**).

24. A single domain antibody (sdAb) that competes for specific binding to CD22 with the isolated sdAb as defined in claim 3 or 7.

25. The sdAb of claim 24, which is a *Camelidae* sdAb.

26. The sdAb of claim 25, which is a lama sdAb.

27. The sdAb of any one of claims 24 to 26, which is humanized.

28. A recombinant polypeptide comprising one or more sdAb as defined in any one of claims 1 to 27.

29. A multivalent antibody comprising:

- 5 a first antigen-binding portion comprising the sdAb as defined in any one of claims 1 to 27, and
 a second antigen-binding portion.

10 30. The multivalent antibody of claim 29, wherein the second antigen-binding moiety binds specifically to a cell-surface marker of an immune cell.

31. The multivalent antibody of claim 30, wherein the cell-surface marker of the immune cell comprises a T-cell marker.

15 32. The multivalent antibody of claim 31, wherein the T-cell marker comprises human CD3.

33. The multivalent antibody of any one of claims 29 to 32, comprising in N-terminal to C-terminal direction:

- 20 - the first antigen-binding portion,
 - an amino acid linker, and
 - the second antigen-binding portion.

25 34. The multivalent antibody of claim 33, which further comprises an N-terminal signal peptide.

35. The multivalent antibody of claim 34, wherein the signal peptide is a signal peptide from human CD28, preferably comprising SEQ ID NO: 110.

30 36. The multivalent antibody of any one of claims 33 to 35, wherein the amino acid linker comprises a polypeptide hinge from human CD8.

37. The multivalent antibody of claim 36, wherein the polypeptide hinge from human CD8 comprises SEQ ID NO: 112.

38. The multivalent antibody of claim 36 or 37, wherein the amino acid linker comprises, in N-terminal to C-terminal direction, SEQ ID NOs: 111, 112, and 118.

39. The multivalent antibody of any one of claims 33 to 38, which is encoded by SEQ ID NO: 119.

40. The multivalent antibody of claim 30, wherein the cell-surface marker of the immune cell marker comprises a natural killer (NK) cell marker.

41. The multivalent antibody of claim 40, wherein the NK cell marker comprises human CD16.

42. The multivalent antibody of claim 40 or 41, further comprising a cytokine for stimulating activation, expansion, and/or survival of NK cells.

43. The multivalent antibody of claim 42, wherein the cytokine for stimulating expansion of NK cells is interleukin-15 (IL15).

44. The multivalent antibody of any one of claims 40 to 43, further comprising a third antigen-binding portion that binds to a second NK cell marker.

45. The multivalent antibody of claim 44, wherein the second NK cell marker is human NKp46.

46. The multivalent antibody of any one of claims 40 to 43, further comprising at least a third antigen-binding portion that binds to a tumour-associated antigen, preferably wherein the tumour-associated antigen is distinct from human CD22.

47. The multivalent antibody of any one of claims 29 to 39, further comprising at least a third antigen-binding portion that binds to a tumour-associated antigen, preferably wherein the tumour-associated antigen is distinct from human CD22.

5 48. The multivalent antibody of any one of claims 46 or 47, wherein the third antigen-binding portion comprises a V_{HH} , V_{NAR} , or an scVF.

49. The multivalent antibody of any one of claims 29 to 47, wherein the second antigen-binding portion comprises a V_{HH} , V_{NAR} , or an scVF.

10

50. The multivalent antibody of any one of claims 29 to 49, which comprises an antigen-binding portion that binds to human serum albumin.

51. The multivalent antibody of claim 31 to 39, which is a bispecific T-cell engager.

15

52. The multivalent antibody of claim 40 or 41, which is a bispecific killer cell engager (BiKE).

53. The multivalent antibody of any one of claims 42 to 48, which is a trispecific killer cell engager (TriKE).

20

54. The multivalent antibody of any one of claims 29 to 53, wherein the sdAb comprises:

a CDR1 amino acid sequence as set forth in SEQ ID NO: 13,

a CDR2 amino acid sequence as set forth in SEQ ID NO: 14, and

25

a CDR3 amino acid sequence as set forth in SEQ ID NO: 15 (**hCD221ug36**); or

a CDR1 amino acid sequence as set forth in SEQ ID NO: 7,

a CDR2 amino acid sequence as set forth in SEQ ID NO: 8, and

a CDR3 amino acid sequence as set forth in SEQ ID NO: 9 (**hCD221ug13**).

30

55. The multivalent antibody of any one of claims 29 to 53, wherein the sdAb comprises SEQ ID NO: 86 (**hCD221ug36**) or SEQ ID NO: 84 (**hCD221ug13**).

56. A recombinant nucleic acid molecule encoding the recombinant polypeptide of claim 28,
5 or the multivalent of any one of claims 29 to 55.

57. A use of the multivalent antibody as defined in any one of claims 29 to 55 for treatment of a cancer or an autoimmune disease.

10 58. A method of treating a cancer or an autoimmune disease in subject comprising administering to the subject the multivalent antibody as defined in any one of claims 29 to 55.

59. A chimeric antibody receptor (CAR), which binds to human CD22, comprising the VHH sdAb as defined in any one of claims 1 to 27.

15 60. The CAR of claim 59 comprising in N-terminal to C-terminal direction:

- an CD22 binding domain comprising the sdAb as defined in any one of claims 1 to 27,
- a polypeptide hinge,
- 20 - a transmembrane domain, and
- a cytoplasmic domain comprising a signaling domain, preferably wherein the cytoplasmic domain further comprises a co-stimulatory domain.

61. The CAR of claim 60, wherein the polypeptide hinge is a CD8 hinge domain.

25 62. The CAR of claim 61, wherein the CD8 hinge domain comprises SEQ ID NO: 112.

63. The CAR of any one of claims 60 to 62, wherein the transmembrane domain is a CD28 transmembrane domain.

64. The CAR of claim 63, wherein the CD28 transmembrane domain comprises SEQ ID NO: 113.

65. The CAR of any one of claims 60 to 64, wherein the signaling domain is a CD3-zeta signaling domain.

66. The CAR of claim 65, wherein the CD3-zeta signaling domain comprises SEQ ID NO: 115.

67. The CAR of any one of claims 60 to 66, wherein the co-stimulatory domain is a 4-1BB co-stimulatory domain.

68. The CAR of claim 67, wherein the 4-1BB signal transduction domain comprises SEQ ID NO: 114.

69. The CAR of any of claims 60 to 68, further comprising a flexible amino acid linker between the sdAb and the polypeptide hinge.

70. The CAR of any of claim 69, wherein the flexible amino acid linker comprises SEQ ID NO: 111.

71. The CAR of any one of claims 59 to 70, further comprising a signal peptide.

72. The CAR of claim 71, wherein the signal peptide is a signal peptide from human CD28, preferably wherein the signal peptide from human CD28 comprises SEQ ID NO: 110.

73. The CAR of any one of claims 59 to 72, which is encoded by SEQ ID NO: 119.

74. The CAR of any one of claims 58 to 72, wherein the sdAb comprises SEQ ID NO: 86 (hCD221ug-36), SEQ ID NO: 83 (hCD221ug-10), SEQ ID NO: 87 (hCD221ug-61), SEQ ID

NO: 82 (**hCD221ug-6**), SEQ ID NO: 88 (**hCD221ug-74**), SEQ ID NO: 85 (**hCD221ug-14**),
SEQ ID NO: 102 (**hCD22pas-33**), or SEQ ID NO: 84 (**hCD221ug-13**).

75. The CAR of any one of claims 59 to 72, where in the VHH sdAb comprises:

- 5 a CDR1 amino acid sequence as set forth in SEQ ID NO: 4,
 a CDR2 amino acid sequence as set forth in SEQ ID NO: 5, and
 a CDR3 amino acid sequence as set forth in SEQ ID NO: 6 (**hCD221ug-10**).

76. The CAR of any one of claims 59 to 72, where in the VHH sdAb comprises:

- 10 a CDR1 amino acid sequence as set forth in SEQ ID NO: 13,
 a CDR2 amino acid sequence as set forth in SEQ ID NO: 14, and
 a CDR3 amino acid sequence as set forth in SEQ ID NO: 15 (**hCD221ug-36**).

77. The CAR of any one of claims 59 to 72, where in the VHH sdAb comprises:

- 15 a CDR1 amino acid sequence as set forth in SEQ ID NO: 19,
 a CDR2 amino acid sequence as set forth in SEQ ID NO: 20, and
 a CDR3 amino acid sequence as set forth in SEQ ID NO: 21 (**hCD221ug-74**).

78. The CAR of any one of claims 59 to 72, where in the VHH sdAb comprises:

- 20 a CDR1 amino acid sequence as set forth in SEQ ID NO: 61,
 a CDR2 amino acid sequence as set forth in SEQ ID NO: 62, and
 a CDR3 amino acid sequence as set forth in SEQ ID NO: 63 (**hCD221pas-33**).

79. The CAR of any one of claims 59 to 72, where in the VHH sdAb comprises:

- 25 a CDR1 amino acid sequence as set forth in SEQ ID NO: 1,
 a CDR2 amino acid sequence as set forth in SEQ ID NO: 2, and
 a CDR3 amino acid sequence as set forth in SEQ ID NO: 3 (**hCD221ug-6**).

80. The CAR of any one of claims 59 to 79, further comprising an additional binding domain
30 positioned N-terminally or C-terminally with respect to the CD22 binding domain, and linked
 to the CD22 binding domain by an amino acid linker.

81. The CAR of claim 80, wherein the additional binding domain binds to CD22.

82. The CAR of claim 81, wherein the additional binding domain comprises a second sdAb that is different to the sdAb of the CD22 binding domain.

5

83. The CAR of claim 82, wherein the second sdAb binds to a different epitope of CD22 compared to the sdAb of the CD22 binding domain.

84. The CAR of claim 81, wherein the additional binding domain comprises a second sdAb that comprises the same CDR1, CDR2, and CDR3 sdAb of the CD22 binding domain, preferably wherein the second sdAb is identical to the sdAb of the CD22 binding domain.

10

85. The CAR of claim 80, wherein the additional binding domain binds to a molecule different to CD22.

15

86. The CAR of claim 80, wherein the additional binding domain comprises a second sdAb.

87. The CAR of claim 85 or 86, wherein the molecule different to CD22 and CD22 are expressed by the same target cell.

20

88. A recombinant nucleic acid molecule encoding the CAR as defined in any one of claims 59 to 87.

89. A vector comprising the recombinant nucleic acid molecule as defined in claim 88.

25

90. The vector of claim 89, which is a viral vector.

91. The vector of claim 90, wherein the viral vector is a lentivirus vector.

30

92. A recombinant viral particle comprising the recombinant nucleic acid molecule of claim 88.

93. The recombinant viral particle of claim 92, which is a recombinant lentiviral particle.

94. A cell comprising the recombinant nucleic acid molecule of claim 88.

5 95. An engineered cell expressing at the cell surface membrane the CAR as defined in any one of claims 59 to 87.

96. The engineered cell of claim 95, which is an immune cell.

10 97. The engineered cell of claim 96, wherein the immune cell is derived from T-lymphocytes.

98. A use of the engineered cell of any one of claims 95 to 97 for treatment of a cancer or an autoimmune disease.

15 99. The use of claim 57 or 98, wherein the cancer is a hematological malignancy.

100. The use of claim 99, wherein the hematological malignancy is a leukemia, a lymphoma, or a myelodysplastic syndrome.

20 101. The use of claim 100, wherein the leukemia is selected from the group consisting of acute myelogenous leukemia (AML), chronic myelogenous leukemia (CML), acute lymphoid leukemia (ALL), and chronic lymphoid leukemia (CLL).

25 102. The use of claim 100, wherein the lymphoma is selected from the group consisting of multiple myeloma, non-Hodgkin's lymphoma, Burkitt's lymphoma, small cell follicular lymphoma, and large cell follicular lymphoma.

30 103. A method of treating a cancer in a subject, comprising administering to the subject the engineered cell as defined in any one of claims 92 to 97.

104. The method of claim 58 or 103, wherein the cancer is a hematological malignancy.

105. The method of claim 104, wherein the hematological malignancy is a leukemia, a lymphoma, or a myelodysplastic syndrome.

5 106. The method of claim 105, wherein the leukemia is acute lymphoid leukemia (ALL) or chronic lymphoid leukemia (CLL).

107. The method of claim 105, wherein the lymphoma is selected from the group consisting of multiple myeloma, non-Hodgkin's lymphoma, Burkitt's lymphoma, small cell follicular
10 lymphoma, and large cell follicular lymphoma.

108. A multivalent antibody comprising:

- a first antigen-binding portion,
- an amino acid linker comprising a polypeptide hinge from human CD8, and
15 - a second antigen-binding portion.

109. The multivalent antibody of claim 108, wherein the polypeptide hinge from human CD8 comprises SEQ ID NO: 112.

20 110. The multivalent antibody of claim 108 or 109, wherein the amino acid linker further comprises at least one G4S N-terminal to the polypeptide hinge from human CD8, and at least one G4S C-terminal to the polypeptide hinge from human CD8.

111. The multivalent antibody of any one of claim 108 to 110, wherein the amino acid linker is
25 at least 47 residues in length, preferably at least 52 residues in length, preferably at least 57 residues in length, more preferably at least 62 residues in length, even more preferably at least 67 residues in length.

112. The multivalent antibody of any one of claim 108 to 111, wherein the amino acid linker
30 comprises, in N-terminal to C-terminal, direction SEQ ID NOs: 111, 112, and 118.

113. The multivalent antibody of any one of claim 108 to 112, wherein the first antigen-binding portion binds specifically to human CD22.

5 114. The multivalent antibody of claim 113, wherein the first antigen-binding portion is a V_{HH} , V_{NAR} , or an scVF.

115. The multivalent antibody of any one of claim 108 to 111, wherein the first antigen-binding portion is the sdAb as defined in any one of claims 1 to 27.

10 116. The multivalent antibody of any one of claims 108 to 115, wherein the second antigen-binding moiety binds specifically to a cell-surface marker of an immune cell.

117. The multivalent antibody of claim 116, wherein the cell-surface marker of the immune cell comprises a T-cell marker.

15

118. The multivalent antibody of claim 117, wherein the T-cell marker comprises human CD3.

20 119. The multivalent antibody of any one of claims 108 to 118, wherein the second antigen binding portion is a V_{HH} , V_{NAR} , or an scVF.

CLAIMS

1. An isolated single domain antibody (sdAb) which binds specifically to human CD22, the sdAb comprising:

(A)

- 5 (i) a CDR1 amino acid sequence as set forth in SEQ ID NO: 1, a CDR2 amino acid sequence as set forth in SEQ ID NO: 2, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 3 (**hCD221ug-6**);
- (ii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 4, a CDR2 amino acid sequence as set forth in SEQ ID NO: 5, and a CDR3 amino acid sequence as
10 set forth in SEQ ID NO: 6 (**hCD221ug-10**);
- (iii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 7, a CDR2 amino acid sequence as set forth in SEQ ID NO: 8, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 9 (**hCD221ug-13**);
- (iv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 10, a CDR2 amino acid sequence as set forth in SEQ ID NO: 11, and a CDR3 amino acid sequence as
15 set forth in SEQ ID NO: 12 (**hCD221ug-14**);
- (v) a CDR1 amino acid sequence as set forth in SEQ ID NO: 13, a CDR2 amino acid sequence as set forth in SEQ ID NO: 14, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 15 (**hCD221ug-36**);
- 20 (vi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 16, a CDR2 amino acid sequence as set forth in SEQ ID NO: 17, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 18 (**hCD221ug-61**);
- (vii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 19, a CDR2 amino acid sequence as set forth in SEQ ID NO: 20, and a CDR3 amino acid sequence as
25 set forth in SEQ ID NO: 21 (**hCD221ug-74**);
- (viii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 22, a CDR2 amino acid sequence as set forth in SEQ ID NO: 23, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 24 (**hCD221ug-75**);

- (ix) a CDR1 amino acid sequence as set forth in SEQ ID NO: 25, a CDR2 amino acid sequence as set forth in SEQ ID NO: 26, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 27 (**hCD221ug-77**);
- 5 (x) a CDR1 amino acid sequence as set forth in SEQ ID NO: 28, a CDR2 amino acid sequence as set forth in SEQ ID NO: 29, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 30 (**hCD221ug-80**);
- (xi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 31, a CDR2 amino acid sequence as set forth in SEQ ID NO: 32, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 33 (**hCD221ug-87**);
- 10 (xii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 34, a CDR2 amino acid sequence as set forth in SEQ ID NO: 35, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 36 (**hCD221ug-93**);
- (xiii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 37, a CDR2 amino acid sequence as set forth in SEQ ID NO: 38, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 39 (**hCD22100ug-2**);
- 15 (xiv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 40, a CDR2 amino acid sequence as set forth in SEQ ID NO: 41, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 42 (**hCD22100ug-62**);
- (xv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 43, a CDR2 amino acid sequence as set forth in SEQ ID NO: 44, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 45 (**hCD22100ug-66**);
- 20 (xvi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 46, a CDR2 amino acid sequence as set forth in SEQ ID NO: 47, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 48 (**hCD22pas-10**);
- 25 (xvii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 49, a CDR2 amino acid sequence as set forth in SEQ ID NO: 50, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 51 (**hCD22pas-16**);
- (xviii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 52, a CDR2 amino acid sequence as set forth in SEQ ID NO: 53, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 54 (**hCD22pas-23**);
- 30

(xix) a CDR1 amino acid sequence as set forth in SEQ ID NO: 55, a CDR2 amino acid sequence as set forth in SEQ ID NO: 56, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 57 (**hCD22pas-24**);

5 (xx) a CDR1 amino acid sequence as set forth in SEQ ID NO: 58, a CDR2 amino acid sequence as set forth in SEQ ID NO: 59, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 60 (**hCD22pas-32**);

(xxi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 61, a CDR2 amino acid sequence as set forth in SEQ ID NO: 62, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 63 (**hCD22pas-33**);

10 (xxii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 64, a CDR2 amino acid sequence as set forth in SEQ ID NO: 65, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 66 (**hCD22pas-48**);

15 (xxiii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 67, a CDR2 amino acid sequence as set forth in SEQ ID NO: 68, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 69 (**hCD22pas-55**);

(xxiv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 70, a CDR2 amino acid sequence as set forth in SEQ ID NO: 71, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 72 (**hCD22pas-64**);

20 (xxv) a CDR1 amino acid sequence as set forth in SEQ ID NO: 73, a CDR2 amino acid sequence as set forth in SEQ ID NO: 74, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 75 (**hCD22pas-72**);

(xxvi) a CDR1 amino acid sequence as set forth in SEQ ID NO: 76, a CDR2 amino acid sequence as set forth in SEQ ID NO: 77, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 78 (**hCD22pas-79**); or

25 xxvii) a CDR1 amino acid sequence as set forth in SEQ ID NO: 79, a CDR2 amino acid sequence as set forth in SEQ ID NO: 80, and a CDR3 amino acid sequence as set forth in SEQ ID NO: 81 (**hCD22pas-82**).

2. An isolated sdAb according to Claim 1, comprising (A) an amino acid sequence of any of SEQ ID NOs: 85 to 112 and 120 to 125, or (B) an amino acid sequence that is at least 80% identical to any of SEQ ID NOs: 82 to 108 and 120 to 125 across the full length thereof.

30

3. An isolated sdAb according to Claim 1, comprising (A) an amino acid sequence of any of SEQ ID NOs: 82 to 108 and 120 to 125.
4. An isolated sdAb according to Claim 1, which is a camelid sdAb.
5. An isolated sdAb according to Claim 4, which is a llama sdAb.
- 5 6. An isolated sdAb according to Claim 1, which is a humanized sbAb of llama origin.
7. A recombinant polypeptide comprising one or more sdAb according to Claim 1.
8. A multivalent antibody comprising:
 - a first antigen-binding portion comprising the sdAb according to Claim 1; and
 - a second antigen-binding portion.
- 10 9. A multivalent antibody according to Claim 8, in which the second antigen-binding moiety binds specifically to a cell-surface marker of a natural killer (NK) cell.
10. A multivalent antibody according to Claim 8, in which the sdAb comprises:
 - a CDR1 amino acid sequence as set forth in SEQ ID NO: 13,
 - a CDR2 amino acid sequence as set forth in SEQ ID NO: 14, and
 - 15 a CDR3 amino acid sequence as set forth in SEQ ID NO: 15 (**hCD221ug36**); or
 - a CDR1 amino acid sequence as set forth in SEQ ID NO: 7,
 - a CDR2 amino acid sequence as set forth in SEQ ID NO: 8, and
 - a CDR3 amino acid sequence as set forth in SEQ ID NO: 9 (**hCD221ug13**).
11. A multivalent antibody according to Claim 8, in which the sdAb comprises SEQ ID NO:
 - 20 86 (**hCD221ug36**) or SEQ ID NO: 84 (**hCD221ug13**).
12. Use of a multivalent antibody according to Claim 8 in the preparation of a medicament for the treatment of a cancer or an autoimmune disease.
13. A chimeric antibody receptor (CAR), which binds to human CD22, comprising a VHH sdAb according to Claim 1.
- 25 14. A CAR according to Claim 13, in which the sdAb comprises SEQ ID NO: 86 (**hCD221ug-36**), SEQ ID NO: 83 (**hCD221ug-10**), SEQ ID NO: 87 (**hCD221ug-61**), SEQ ID

NO: 82 (**hCD221ug-6**), SEQ ID NO: 88 (**hCD221ug-74**), SEQ ID NO: 85 (**hCD221ug-14**),
SEQ ID NO: 102 (**hCD22pas-33**), or SEQ ID NO: 84 (**hCD221ug-13**).

15. A CAR according to Claim 13, in which the VHH sdAb comprises:

a CDR1 amino acid sequence as set forth in SEQ ID NO: 4,

5 a CDR2 amino acid sequence as set forth in SEQ ID NO: 5, and

a CDR3 amino acid sequence as set forth in SEQ ID NO: 6 (**hCD221ug-10**);

a CDR1 amino acid sequence as set forth in SEQ ID NO: 13,

a CDR2 amino acid sequence as set forth in SEQ ID NO: 14, and

10 a CDR3 amino acid sequence as set forth in SEQ ID NO: 15 (**hCD221ug-36**);

a CDR1 amino acid sequence as set forth in SEQ ID NO: 19,

a CDR2 amino acid sequence as set forth in SEQ ID NO: 20, and

a CDR3 amino acid sequence as set forth in SEQ ID NO: 21 (**hCD221ug-74**);

15

a CDR1 amino acid sequence as set forth in SEQ ID NO: 61,

a CDR2 amino acid sequence as set forth in SEQ ID NO: 62, and

a CDR3 amino acid sequence as set forth in SEQ ID NO: 63 (**hCD221pas-33**); or

20

a CDR1 amino acid sequence as set forth in SEQ ID NO: 1,

a CDR2 amino acid sequence as set forth in SEQ ID NO: 2, and

a CDR3 amino acid sequence as set forth in SEQ ID NO: 3 (**hCD221ug-6**).

16. A recombinant nucleic acid molecule encoding an sdAb according to Claim 1, a
multivalent antibody according to Claim 8, or a CAR according to Claim 13.

25

17. An engineered cell expressing at the cell surface membrane a CAR according to Claim
13.

18. Use of an engineered cell according to Claim 17 in the preparation of a medicament for the treatment of cancer.
19. Use according to Claim 12 or 18, in which the cancer is a hematological malignancy.