

Claims

1. A multispecific antibody or multispecific binding fragment comprising:
 - a) a first antigen-binding arm that binds cluster of differentiation 79B protein (CD79B), comprising a first variable heavy domain (VH1) and further comprising a first variable light domain (VL1); and
 - b) a second antigen-binding arm that binds cluster of differentiation 22 (CD22), comprising a second variable heavy domain (VH2) and further comprising a second variable light domain (VL2).
2. The multispecific antibody or multispecific binding fragment of claim 1, wherein:
 - (a) the VH1 comprises the HCDR1 of SEQ ID NO:9, the HCDR2 of SEQ ID NO:10, and the HCDR3 of SEQ ID NO:11; and the VL1 comprises the LCDR1 of SEQ ID NO:12, the LCDR2 of SEQ ID NO:13, and the LCDR3 of SEQ ID NO:14;
 - (b) the VH1 comprises the HCDR1 of SEQ ID NO:17, the HCDR2 of SEQ ID NO:18, and the HCDR3 of SEQ ID NO:19; and the VL1 comprises the LCDR1 of SEQ ID NO:20, the LCDR2 of SEQ ID NO:21, and the LCDR3 of SEQ ID NO:22;
 - (c) the VH1 comprises the HCDR1 of SEQ ID NO:25, the HCDR2 of SEQ ID NO:26, and the HCDR3 of SEQ ID NO:27; and the VL1 comprises the LCDR1 of SEQ ID NO:28, the LCDR2 of SEQ ID NO:29, and the LCDR3 of SEQ ID NO:30;
 - (d) the VH1 comprises the HCDR1 of SEQ ID NO:33, the HCDR2 of SEQ ID NO:34, and the HCDR3 of SEQ ID NO:35; and the VL1 comprises the LCDR1 of SEQ ID NO:36, the LCDR2 of SEQ ID NO:37, and the LCDR3 of SEQ ID NO:38;
 - (e) the VH1 comprises the HCDR1 of SEQ ID NO:41, the HCDR2 of SEQ ID NO:42, and the HCDR3 of SEQ ID NO:43; and the VL1 comprises the LCDR1 of SEQ ID NO:44, the LCDR2 of SEQ ID NO:45, and the LCDR3 of SEQ ID NO:46;
 - (f) the VH1 comprises the HCDR1 of SEQ ID NO:49, the HCDR2 of SEQ ID NO:50, and the HCDR3 of SEQ ID NO:51; and the VL1 comprises the LCDR1 of SEQ ID NO:52, the LCDR2 of SEQ ID NO:53, and the LCDR3 of SEQ ID NO:54; or
 - (g) the VH1 comprises the HCDR1 of SEQ ID NO:57, the HCDR2 of SEQ ID NO:58, and the HCDR3 of SEQ ID NO:59; and the VL1 comprises the LCDR1 of SEQ ID NO:60, the LCDR2 of SEQ ID NO:61, and the LCDR3 of SEQ ID NO:62.

3. The multispecific antibody or multispecific binding fragment of claim 1 or claim 2, wherein the first antigen-binding arm that binds CD79b comprises a VH and VL selected from the group consisting of:

- a) the VH of SEQ ID NO: 15 and the VL of SEQ ID NO: 16;
- 5 b) the VH of SEQ ID NO: 23 and the VL of SEQ ID NO: 24;
- c) the VH of SEQ ID NO: 31 and the VL of SEQ ID NO: 32;
- d) the VH of SEQ ID NO: 39 and the VL of SEQ ID NO: 40;
- e) the VH of SEQ ID NO: 47 and the VL of SEQ ID NO: 48;
- f) the VH of SEQ ID NO: 55 and the VL of SEQ ID NO: 56;
- 10 g) the VH of SEQ ID NO: 63 and the VL of SEQ ID NO: 64; and
- h) the VH of SEQ ID NO: 80 and the VL of SEQ ID NO: 81.

4. The multispecific antibody or multispecific binding fragment of any one of claim 1-3, wherein the antigen-binding arm that binds CD79b comprises: a VH1 comprising the HCDR1 of SEQ
15 ID NO:9, the HCDR2 of SEQ ID NO:10, and the HCDR3 of SEQ ID NO:11; and a VL1 comprising the LCDR1 of SEQ ID NO:12, the LCDR2 of SEQ ID NO:13, and the LCDR3 of SEQ ID NO:14.

5. The multispecific antibody or multispecific binding fragment of any one of claim 1-4, wherein the antigen-binding arm that binds CD79b comprises the VH1 of SEQ ID NO: 80 and the
20 VL1 of SEQ ID NO: 81.

6. The multispecific antibody or multispecific binding fragment of any one of claims 1-5, wherein the second antigen-binding arm that binds CD22 comprises a VH2 comprising the HCDR1 of SEQ ID NO:1, the HCDR2 of SEQ ID NO:2, and the HCDR3 of SEQ ID NO:3, and a VL2
25 comprising the LCDR1 of SEQ ID NO:4, the LCDR2 of SEQ ID NO:5, and the LCDR3 of SEQ ID NO:6.

7. The multispecific antibody or multispecific binding fragment of any one of claims 1-6, wherein the VH2 comprises SEQ ID NO:7 and the VL2 comprises SEQ ID NO:8.

30 8. The multispecific antibody or multispecific binding fragment of any one of claims 1-7, wherein the first or second antigen-binding arm comprises at least one selected from the group consisting of a single-chain variable fragment (scFv), an (scFv)₂, an antigen-binding fragment (Fab), a F(ab')₂, a Fd, a Fv, a VHH, and a dAB.

9. The multispecific antibody or multispecific binding fragment of claim 8, wherein the first antigen-binding arm comprises an scFv, and the second antigen-binding arm comprises a Fab.

10. The multispecific antibody or multispecific binding fragment of any one of claims 1-9, wherein the first antigen-binding arm comprises an scFv having the amino acid sequence of SEQ ID NO:82.

11. The multispecific antibody or multispecific binding fragment of any one of claims 1-10, wherein the first antigen-binding arm that binds CD79b comprises or is operably linked to a first Fragment crystallizable (Fc) domain, and wherein the second antigen-binding arm that binds CD22 comprises or is operably linked to a second Fc domain.

12. The multispecific antibody or multispecific binding fragment of claim 11, wherein at least one of the first and second Fc domain comprises one or more mutations that promote heterodimerization of the Fc domains, reduce Fc binding to a Fcγ receptor, reduce Fc binding to protein A, extend the half-life of the multispecific antibody or multispecific binding fragment, or any combination thereof.

13. The multispecific antibody or multispecific binding fragment of claim 12, wherein the one or more mutations that promote heterodimerization of the Fc domains are selected from T366S, L368A, T366W, and Y407V (EU numbering).

14. The multispecific antibody or multispecific binding fragment of claim 13, wherein the first Fc domain comprise mutation T366W, and wherein the second Fc domain comprises mutations T366S, L368A, and Y407V.

15. The multispecific antibody or multispecific binding fragment of any one of claims 12-14, wherein the one or more mutations that reduce Fc binding to a Fcγ receptor are selected from L234A, L235A, and D265S (EU numbering).

16. The multispecific antibody or multispecific binding fragment of claim 15, wherein both the first Fc domain and the second Fc domain comprise mutations L234A, L235A, and D265S.

17. The multispecific antibody or multispecific binding fragment of any one of claims 12-16, wherein the one or more mutations that reduce Fc binding to protein A are selected from H435R and Y436F (EU numbering).

18. The multispecific antibody or multispecific binding fragment of claim 17, wherein the second Fc domain comprises mutations H435R and Y436F.

19. The multispecific antibody or multispecific binding fragment of any one of claims 12-18, wherein the one or more mutations that extend the half-life of the multispecific antibody or multispecific binding fragment are selected from M252Y, S254T, and T256E (EU numbering).

20. The multispecific antibody or multispecific binding fragment of claim 19, wherein both the first Fc domain and the second Fc domain comprise mutations M252Y, S254T, and T256E.

21. The multispecific antibody or multispecific binding fragment of any one of claims 11-20, wherein the first Fc domain comprises SEQ ID NO:89, and wherein the second Fc domain comprises SEQ ID NO:90.

22. The multispecific antibody or multispecific binding fragment of any one of claims 1-21, comprising the amino acid sequences of SEQ ID NO:79, SEQ ID NO: 83, and SEQ ID NO: 84.

23. An immunoconjugate comprising the multispecific antibody or multispecific binding fragment of any one of claims 1-22 conjugated to a therapeutic agent or an imaging agent.

24. A pharmaceutical composition comprising the multispecific antibody or multispecific binding fragment of any one of claims 1-22 and a pharmaceutically acceptable carrier.

25. A polynucleotide encoding the multispecific antibody or multispecific binding fragment of any one of claims 1-22.

26. A vector comprising the polynucleotide of claim 25.

27. A host cell comprising the vector of claim 27.

28. Use of the multispecific antibody or multispecific binding fragment of any one of claims 1-22 in the manufacture of a medicament for the treatment of an autoimmune disease in a subject, wherein a therapeutically effective amount of the medicament is to be administered to the subject for a time sufficient to treat the autoimmune disease.

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29. The use of claim 28, wherein the autoimmune disease is Systemic lupus erythematosus (SLE), Sjögren's syndrome (SjS), Rheumatoid arthritis, Autoimmune myopathies, Type I diabetes, Addison disease, Pernicious anemia, Autoimmune hepatitis, Primary biliary cholangitis (PBC), Autoimmune pancreatitis, Celiac disease, Focal segmental glomerulosclerosis, Primary membranous nephropathy, Ovarian insufficiency, Autoimmune orchitis, Dry eye disease, Idiopathic interstitial pneumonias, Thyroid disease (e.g, Grave's), Systemic sclerosis (Scleroderma), Myasthenic syndromes, Autoimmune encephalitis, Bullous skin diseases, TTP, ITP, AIHA, Anca vasculitis, Myocarditis/dilatory CM, NMOSD, Maternal-fetal alloimmunity, Maternal-fetal autoimmunity, Anti-cardiolipin/antiphospholipid syndrome, Hypergammaglobulinemia, Transplant-associated ID, or Multifocal motor neuropathy.

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30. Use of the multispecific antibody or multispecific binding fragment of any one of claims 1-22 in the manufacture of a medicament for use in a method of modulating B cell activation or inhibiting aberrant B cell activation in a subject, wherein a therapeutically effective amount of the medicament is to be administered to the subject for a time sufficient to modulate B cell activation or inhibit aberrant B cell activation.

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31. Use of the multispecific antibody or multispecific binding fragment of any one of claims 1-22 in the manufacture of a medicament for use in a method of decreasing B cell proliferation, decreasing cytokine production or reducing B cell activation in a subject, wherein a therapeutically effective amount of the medicament is to be administered to the subject for a time sufficient to decrease B cell proliferation, decrease cytokine production or reduce B cell activation.

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32. The multispecific antibody or multispecific binding fragment of any one of claims 1-22 for use in therapy, wherein an effective amount of the multispecific antibody or multispecific binding fragment is to be administered to the subject.