

CLAIMS

1. A method of treating or managing an autoimmune disorder, the method comprising administering to a patient in need of such treatment or management a multispecific antibody, wherein the multispecific antibody binds to B-cell maturation antigen (BCMA) and an antigen that promotes activation of one or more T cells.
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2. The method according to claim 1, wherein the autoimmune disorder is anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), rheumatoid arthritis (RA) or systemic lupus erythematosus (SLE)
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3. A method of treating or managing antineutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV), the method comprising administering to a patient in need of such treatment or management a multispecific antibody, wherein the multispecific antibody binds to BCMA and to an antigen that promotes activation of one or more T cells.
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4. The method according to any one of claims 1 to 3, wherein the antigen that promotes activation of one or more T cells is selected from the group consisting of CD3, TCR α , TCR β , TCR γ , TCR ζ , ICOS, CD28, CD27, HVEM, LIGHT, CD40, 4-1BB, OX40, DR3, GITR, CD30, TIM1, SLAM, CD2, or CD226, preferably wherein the antigen that promotes activation of one or more T cells is CD3.
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5. The method according to any one of claims 1 to 4, wherein the multispecific antibody is a bispecific antibody that binds to BCMA and CD3.
- 25 6. The method according to any one of claims 1 to 5, wherein the multispecific antibody is a bispecific antibody, optionally wherein bispecific antibody is a trivalent bispecific antibody comprising two Fab fragments of an anti-BCMA antibody, one Fab fragment of an anti-CD3 antibody, and one Fc portion, wherein the bispecific antibody is in the format BCMA Fab - Fc - CD3 Fab - BCMA Fab.
- 30 7. The method according to any one of claims 1 to 6, wherein the multispecific antibody comprises an anti-BCMA antibody, or antigen binding fragment thereof, comprising a CDR1H, CDR2H, CDR3H CDR1L, CDR2L and CDR3L region combination selected from:

- (a) CDR1H region of SEQ ID NO:21, CDR2H region of SEQ ID NO:22, CDR3H region of SEQ ID NO:17, CDR1L region of SEQ ID NO:27, CDR2L region of SEQ ID NO:28, and CDR3L region of SEQ ID NO:20;
- (b) CDR1H region of SEQ ID NO:21, CDR2H region of SEQ ID NO:22, CDR3H region of SEQ ID NO:17, CDR1L region of SEQ ID NO:25, CDR2L region of SEQ ID NO:26, and CDR3L region of SEQ ID NO:20; or
- (c) CDR1H region of SEQ ID NO:15, CDR2H region of SEQ ID NO:16, CDR3H region of SEQ ID NO:17, CDR1L region of SEQ ID NO:18, CDR2L region of SEQ ID NO:19, and CDR3L region of SEQ ID NO:20.
8. The method according to any one of claims 1 to 7, wherein the multispecific antibody comprises:
- (a) an anti-BCMA antibody, or antigen binding fragment thereof, having a variable region VH comprising an amino acid sequence that is at least 90% identical to, at least 95% identical to, at least 99% identical to, or identical to the amino acid sequence of SEQ ID NO:10 and a variable region VL comprising an amino acid sequence that is at least 90% identical to, at least 95% identical to, at least 99% identical to, or identical to the amino acid sequence of SEQ ID NO:14;
- (b) an anti-BCMA antibody, or antigen binding fragment thereof, having a variable region VH comprising an amino acid sequence that is at least 90% identical to, at least 95% identical to, at least 99% identical to, or identical to the amino acid sequence of SEQ ID NO:10 and a variable region VL comprising an amino acid sequence that is at least 90% identical to, at least 95% identical to, at least 99% identical to, or identical to the amino acid sequence of SEQ ID NO:13; or
- (c) an anti-BCMA antibody, or antigen binding fragment thereof, having a variable region VH comprising an amino acid sequence that is at least 90% identical to, at least 95% identical to, at least 99% identical to, or identical to the amino acid sequence of SEQ ID NO:9 and a variable region VL comprising an amino acid sequence that is at least 90% identical to, at least 95% identical to, at least 99% identical to, or identical to the amino acid sequence of SEQ ID NO:11.
9. The method according to any one of claims 1 to 8, wherein the multispecific antibody comprises an anti-CD3 antibody, or antigen binding fragment thereof, which comprises a heavy chain CDR1 comprising the amino acid sequence of SEQ ID NO:1, a heavy chain CDR2 comprising the amino acid sequence of SEQ ID NO:2, a heavy chain CDR3

comprising the amino acid sequence of SEQ ID NO:3, a light chain CDR1 comprising the amino acid sequence of SEQ ID NO:4, a light chain CDR2 comprising the amino acid sequence of SEQ ID NO:5, and a light chain CDR3 comprising the amino acid sequence of SEQ ID NO:6.

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10. The method according to claim 9, wherein wherein the anti-CD3 antibody or antigen binding fragment thereof comprises a variable region VH comprising an amino acid sequence that is at least 90% identical to, at least 95% identical to, at least 99% identical to, or identical to the amino acid sequence of SEQ ID NO:7 and a variable region VL comprising an amino acid sequence that is at least 90% identical to, at least 95% identical to, at least 99% identical to, or identical to the amino acid sequence of SEQ ID NO:8.
11. The method according to any one of claims 1 to 3, wherein the multispecific antibody comprises a heavy and light chain set consisting of polypeptides:
 - (a) SEQ ID NO:48, SEQ ID NO:55, SEQ ID NO:56, and two copies of SEQ ID NO:57;
 - (b) SEQ ID NO:48, SEQ ID NO:58, SEQ ID NO:59, and two copies of SEQ ID NO:60; or
 - (c) SEQ ID NO:48, SEQ ID NO:61, SEQ ID NO:62, and two copies of SEQ ID NO:63.
12. The method of any one of claims 1 to 11, wherein the autoimmune disease is selected from the group consisting of Systemic lupus erythematosus, IgA nephropathy, Membranous Nephropathy, Myasthenia gravis, Neuromyelitis optica, Pemphigus vulgaris, Anti-PAD4-activating rheumatoid arthritis, Sensitized / preformed antibodies in solid organ transplant, Guillain-Barre Syndrome (Acute inflammatory demyelinating polyneuropathy – AIDP), Chronic inflammatory demyelinating polyneuropathy (CIDP), Immune thrombocytopenic purpura, rheumatoid arthritis and ANCA-associated vasculitis (AAV).
13. The method according to any one of claims 3 to 12, wherein the AAV comprises diseases that are selected from the group consisting of granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA), microscopic polyangiitis (MPA) and renal-limited ANCA-associated vasculitis.
14. The method according to claim 13, wherein the AAV is granulomatosis with polyangiitis (GPA).

15. The method according to claim 13, wherein the AAV is eosinophilic granulomatosis with polyangiitis (EGPA).
16. The method according to claim 13, wherein the AAV is microscopic polyangiitis (MPA).
17. The method of claim 13, wherein the AAV is renal-limited ANCA-associated vasculitis.
18. The method according to any one of claims 1 to 17, wherein the autoimmune disorder (e.g. AAV) is refractory or relapsed.
19. The method according to any one of claims 1 to 18, wherein the autoimmune disorder (e.g. AAV) is newly diagnosed.
20. The method according to any one of claims 3 to 16, 18 or 19, wherein the AAV is affecting one or more body parts of the patient selected from nervous system, eyes, nose, heart, kidneys, stomach, intestine, lungs, joints, muscles and skin.
21. The method according to any one of claims 3 to 20, wherein the AAV is generalized with presence of life- or major organ-threatening manifestations.
22. The method according to claim 21, wherein the patient has diffuse alveolar hemorrhage (DAH).
23. The method according to any one of claims 3 to 20, wherein the AAV is localized without organ-threatening manifestations.
24. The method of any one of claims 1 to 23, wherein the patient is in need of plasmablast reduction.
25. The method according to any one of claims 1 to 24, wherein the patient is at risk of developing cytokine release syndrome.

26. The method of any one of claims 1 to 25, wherein the patient is at risk of developing infection.
27. The method of any one of claims 1 to 26, wherein the patient is in need of induction of remission.
28. The method of any one of claims 1 to 27, wherein the patient is in need of maintenance of remission.
29. The method of any one of claims 1 to 28, wherein the method results in a reduction of plasmablasts in the patient by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, at least 95%, or 100% relative to no treatment or a reference treatment.
30. The method of any one of claims 1 to 29, wherein the method results in a lowered incidence of cytokine release syndrome in the patient by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, at least 95%, or 100% relative to a reference treatment.
31. The method of any one of claims 1 to 30, wherein the method results in a lowered incidence of infection in the patient by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, at least 95%, or 100% relative to a reference treatment.
32. The method of any one of claims 1 to 31, wherein the method results a faster induction of remission in the patient by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, at least 95%, or 100% relative to a reference treatment.
33. The method of any one of claims 1 to 32, wherein the method results a longer maintenance of remission in the patient by at least 5%, 10%, 15%, 20%, 25%, 30%, 35%, 40%, 45%, 50%, 55%, 60%, 65%, 70%, 75%, 80%, 85%, 90%, at least 95%, or 100% relative to a reference treatment.

34. The method of any one of claims 29 to 33, wherein the reference treatment is treatment with steroids (e.g. glucocorticoids), cyclophosphamide, an anti-CD20 monoclonal antibody (e.g. rituximab), methotrexate, azathioprine, mycophenolate, mycophenolate mofetil, avacopan, anti-TNF agents (e.g. infliximab, adalimumab, golimumab, etanercept), anti-IL6R antibodies (e.g. tocilizumab, sarilumab), costimulatory blockade (e.g. abatacept), JAK inhibitors (e.g. tofacitinib, baricitinib) and/or belimumab, preferably wherein the reference treatment is treatment with steroids, cyclophosphamide or rituximab.
35. The method of any one of claims 1 to 34, wherein the method is used for the induction of remission.
36. The method of any one of claims 1 to 34, wherein the method is used for the maintenance of remission.