

CLAIMS

1. Use of an anti-CD19 antibody in the manufacture of a medicament for ~~A method of treating treatment of~~ neuromyelitis optica spectrum disorder (NMOSD), ~~the method comprising:~~

5 ~~administering wherein~~ the anti-CD19 antibody ~~VIB551 is to be administered to a subject patient~~ in need of treatment for NMOSD,

~~wherein the anti-CD19 antibody comprises Complementarity-Determining Regions (CDRs) HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3, wherein the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 comprise the amino acid sequences of SEQ~~

10 ~~ID NOs: 5, 6, 7, 8, 9, and 10, respectively, and~~

~~wherein the subject patient had been was~~ previously treated with an anti-CD20 antibody.

2. The use of claim 1, wherein the anti-CD19 antibody comprises a heavy chain variable region (VH) and a light chain variable region (VL) comprising the amino acid sequence of SEQ

15 ID NO: 1 and SEQ ID NO: 2, respectively.

3. The use of claim 1, wherein the anti-CD19 antibody is Inebilizumab.

2. ~~A method of treating NMOSD, the method comprising:~~

~~administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD,~~

~~wherein the patient had been previously treated with an anti-CD20 antibody, wherein the patient had an NMOSD attack while being treated with or within 6 months of the last~~

25 ~~dose of the anti-CD20 antibody.~~

43. ~~The use method of claim 1 or claim 2,~~ wherein the anti-CD19 antibody VIB551 is to be administered intravenously at a dose of 300 mg every 6 months.

4. ~~A method of treating NMOSD, the method comprising:~~

~~administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD,~~

~~wherein the patient is an astrocyte water channel aquaporin-4 (AQP4)-~~
~~Immunoglobulin (Ig)G⁺ patient,~~

wherein the VIB551 is administered intravenously at a dose of 300 mg every 6 months,

wherein the patient had been previously treated with an anti-CD20 antibody, and wherein the patient had an NMOSD attack while being treated with the anti-CD20 antibody.

5 5. The use of claim 1, A method of treating NMOSD, the method comprising:
administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD,
wherein the patient is an AQP4-IgG⁺ patient,
wherein the VIB551 is administered intravenously at a dose of 300 mg every 6 months,
10 wherein the patient had been previously treated with an anti-CD20 antibody; and, wherein the
subject patient had an NMOSD attack while being treated with; or within 6 months of the last
dose of the anti-CD20 antibody.

15 6. The use of claim 5, wherein the NMOSD attack comprises any one or more of an
optic neuritis, a myelitis, or a brainstem attack.

6. ~~The method of any one of claims 3-5, wherein the patient receives at least one initial dose of VIB551.~~

20 7. ~~The use method of any one of claims 13-6, wherein the anti-CD19 antibody VIB551~~
is to be administered intravenously with a first initial dose of 300 mg, a second initial dose of
300 mg two weeks after the first initial dose, and subsequent doses of 300 mg every 6 months
following the first initial dose.

25 8. ~~The use method of claim 6 or claim 7, wherein a oral corticosteroids is to be are co-~~
administered to the subject patient with the first initial ~~VIB551~~ dose.

30 9. The use of claim 1, wherein the anti-CD20 antibody is selected from the group
consisting of: rituximab, ABP-300, B-001, BAT-4306F, BAT-4406F, BCD-132, BVX-20,
CYT-202, epcoritamab, GB-261, GD-CO1620, glofitamab, HS-006, IGM-2323, IMM-0306,
MIL-62, mosunetuzumab, MRG-001, obinutuzumab, ocrelizumab, odronextamab,
ofatumumab, plamotamab, SM-09, TRS-005, Ublituximab, and YBL-031.

9. ~~The method of claim 8, wherein the oral corticosteroids are administered daily for at least 2 weeks.~~

10. The ~~use method of any one of~~ claims 1-9, wherein the anti-CD20 antibody is rituximab.

11. The use of claim 1, wherein the anti-CD19 antibody depletes peripheral blood CD20-plasmablasts and plasma cells within 8 days following the administration.

12. The use of claim 1, wherein prior to the administration,
the subject is identified as having previously been treated with the anti-CD20 antibody;
the subject is determined as:
(i) suffered at least one NMOSD attack while being treated with the anti-CD20 antibody; or
(ii) had suffered at least one NMOSD attack within 6 months of the last dose of the anti-
CD20 antibody; and
the subject is selected for the administration of the anti-CD19 antibody as a result of the
determination of (i) or (ii).

13. Use of an anti-CD19 antibody in the manufacture of a medicament for treatment of
neuromyelitis optica spectrum disorder (NMOSD), wherein the anti-CD19 antibody is to be
administered to a subject in need of treatment for NMOSD, wherein the anti-CD19 antibody
comprises Complementarity-Determining Regions (CDRs) HCDR1, HCDR2, HCDR3,
LCDR1, LCDR2, and LCDR3, wherein the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2,
and LCDR3 comprise the amino acid sequences of SEQ ID NOs: 5, 6, 7, 8, 9, and 10,
respectively, wherein the subject was previously treated with an anti-CD20 antibody, and
wherein the subject is astrocyte water channel aquaporin-4 (AQP4) Immunoglobulin (Ig)G
seropositive.

14. The use of claim 13, wherein the anti-CD19 antibody comprises a heavy chain
variable region (VH) and a light chain variable region (VL) comprising the amino acid
sequence of SEQ ID NO: 1 and SEQ ID NO: 2, respectively.

15. The use of claim 13, wherein the anti-CD19 antibody is Inebilizumab.

16. The use of claim 13, wherein the anti-CD19 antibody is to be administered intravenously at a dose of 300 mg every 6 months.

17. The use of claim 13, wherein the subject had an NMOSD attack while being treated with; or within 6 months of the last dose of the anti-CD20 antibody.

18. The use of claim 13, wherein the anti-CD19 antibody is to be administered intravenously with a first initial dose of 300 mg, a second initial dose of 300 mg two weeks after the first initial dose, and subsequent doses of 300 mg every 6 months following the first initial dose.

19. The use of claim 18, wherein a corticosteroid is to be co-administered to the subject with the first initial dose.

20. The use of claim 13, wherein the anti-CD20 antibody is selected from the group consisting of: rituximab, ABP-300, B-001, BAT-4306F, BAT-4406F, BCD-132, BVX-20, CYT-202, epcoritamab, GB-261, GD-CO1620, glofitamab, HS-006, IGM-2323, IMM-0306, MIL-62, mosunetuzumab, MRG-001, obinutuzumab, ocrelizumab, odronextamab, ofatumumab, plamotamab, SM-09, TRS-005, Ublituximab, and YBL-031.

21. The use of claim 20, wherein the anti-CD20 antibody is rituximab.

22. The use of claim 13, wherein the anti-CD19 antibody depletes peripheral blood CD20- plasmablasts and plasma cells within 8 days following the administration.

~~11. The method of any one of claims 1-10, wherein the treating is a reduction in worsening of Kurtzke Expanded Disability Severity Scale (EDSS) in the patient.~~

~~12. The method of claim 11, wherein the reduction in worsening of EDSS in the patient is:
a worsening of fewer than 2 points in EDSS score if the patient has a baseline score of 0;
a worsening of fewer than 1 point if the patient has a baseline score of 1 to 5; or
a worsening of less than 0.5 point if the patient has a baseline score of 5.5 or more.~~

13. ~~The method of any one of claims 1-10, wherein the treating is a reduction in number of active magnetic resonance imaging (MRI) lesions.~~
14. ~~The method of claim 13 wherein the active MRI lesions are enlarging T2 MRI lesions.~~
- 5 15. ~~The method of any one of claims 1-10, wherein the treating is a reduction in number of new MRI lesions.~~
16. ~~The method of any one of claims 1-10, wherein the treating is a reduction in worsening of modified Rankin Score in the patient.~~
- 10 17. ~~The method of any one of claims 1-10, wherein the treating is a reduction in frequency of in-patient hospitalizations of the patient related to NMOSD.~~
18. ~~The method of any one of claims 1-10, wherein the treating is a reduction of risk of an NMOSD-related attack of the patient.~~
19. ~~The method of claim 18, wherein the NMOSD-related attack is characterized by appearance of a new symptom or worsening of an existing symptom related to NMOSD.~~
- 15 20. ~~The method of claim 19, wherein the symptom is an eye symptom.~~
21. ~~The method of claim 20, wherein the eye symptom is eye pain, blurred vision, loss of vision, or appearance of an optic nerve lesion detected by MRI.~~
22. ~~The method of claim 19, wherein the symptom is a spinal cord symptom.~~
23. ~~The method of claim 22, wherein the spinal cord symptom is deep or radicular pain,~~
- 20 ~~extremity paraesthesia, weakness, sphincter dysfunction, Lhermitte's sign, or a spinal cord lesion detectable by MRI.~~
24. ~~The method of claim 19, wherein the symptom is a brain or brain stem symptom.~~
25. ~~The method of claim 24, wherein the brain or brainstem symptom is nausea, double vision, oculomotor palsy, vertigo, intractable vomiting, intractable hiccups, dysarthria,~~
- 25 ~~dysphagia, weakness, encephalopathy, hypothalamic dysfunction, or a brain or brain stem lesion detectable by MRI.~~
26. ~~The method of claim 18, wherein the reduction of risk of the NMOSD-related attack is between 60 and 85%.~~
27. ~~The method of any one of claims 1-10, wherein the treating is a reduction in optic~~
- 30 ~~neuritis.~~
28. ~~The method of any one of claims 1-10, wherein the treating is a reduction of severity of NMOSD-related attacks.~~
29. ~~The method of claim 28, wherein the reduction of severity of NMOSD-related attacks is~~

the reduction in NMOSD-related attacks graded as major.

30. The method of claim 28, wherein the reduction of severity of NMOSD-related attacks is the reduction in NMOSD attacks requiring in-patient hospitalization.

31. The method of any one of claims 1-10, wherein the treating is a decrease in NMOSD-related pain in the patient.

32. The method of claim 31, wherein the decrease in NMOSD-related pain is determined by measuring pain in legs of the patient.

33. The method of any one of claims 1-5, wherein two weeks prior to the first administering the 300 mg VIB551 every 6 months, an initial 300 mg VIB551 dose is administered to the subject.

34. The method of claim 33, wherein oral corticosteroids are co-administered to the patient with the initial 300 mg VIB551 dose.

35. The method of claim 1 or claim 2, wherein the patient is AQP4 IgG seropositive.

36. A method of reducing active MRI lesions in a patient diagnosed with NMOSD, the

method comprising:

administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD, wherein the patient had been previously treated with an anti-CD20 antibody, wherein the patient had an NMOSD attack while being treated with the anti-CD20 antibody.

37. — A method of reducing active MRI lesions in a patient diagnosed with NMOSD, the method comprising:

administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD, wherein the patient had been previously treated with an anti-CD20 antibody, wherein the patient had an NMOSD attack within 6 months of the last dose of the anti-CD20 antibody.

38. — The method of claim 36 or 37, wherein the VIB551 is administered intravenously at a dose of 300 mg every 6 months.

39. — A method of reducing active MRI lesions in a patient diagnosed with NMOSD, the method comprising:

administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD, wherein the patient had been previously treated with an anti-CD20 antibody, wherein the patient had an NMOSD attack while being treated with the anti-CD20 antibody; and, wherein the VIB551 is administered intravenously at a dose of 300 mg every 6 months.

40. — A method of reducing active MRI lesions in a patient diagnosed with NMOSD, the method comprising:

administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD, wherein the patient had been previously treated with an anti-CD20 antibody, wherein the patient had an NMOSD attack within 6 months of the last dose of the anti-CD20 antibody; and, wherein the VIB551 is administered intravenously at a dose of 300 mg every 6 months.

41. — A method of reducing AQP4-IgG titers in a AQP4-IgG⁺ patient in need of treatment for NMOSD, the method comprising:
administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD, wherein the patient had been previously treated with an anti-CD20 antibody, wherein the patient had an NMOSD attack while being treated with the anti-CD20 antibody.

42. — A method of reducing AQP4-IgG titers in a AQP4-IgG⁺ patient in need of treatment for NMOSD, the method comprising:
administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD, wherein the patient had been previously treated with an anti-CD20 antibody, wherein the patient had an NMOSD attack within 6 months of the last dose of the anti-CD20 antibody.

43. — The method of claim 41 or 42, wherein the VIB551 is administered intravenously at a dose of 300 mg every 6 months.

44. — A method of reducing AQP4-IgG titers in a AQP4-IgG⁺ patient in need of treatment for NMOSD, the method comprising:
administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD, wherein the patient had been previously treated with an anti-CD20 antibody, wherein the patient had an NMOSD attack while being treated with the anti-CD20 antibody; and, wherein the VIB551 is administered intravenously at a dose of 300 mg every 6 months.

45. — A method of reducing AQP4-IgG titers in a AQP4-IgG⁺ patient in need of treatment for NMOSD, the method comprising:

administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD, wherein the patient had been previously treated with an anti-CD20 antibody, wherein the patient had an NMOSD attack within 6 months of the last dose of the anti-CD20 antibody; and,

5 wherein the VIB551 is administered intravenously at a dose of 300 mg every 6 months.

46. The method of any one of claims 1-45, wherein the administration depletes at least 90% of circulating CD20+ B cells for at least six months.

10 47. — The method of any one of claims 1-46, wherein the administration does not increase risk of infections in the patient.

48. — The method of any one of claims 1-47, wherein the VIB551 depletes peripheral blood CD20⁺ plasmablasts and plasma cells within 8 days following the administering.

15 49. — A method of reducing NMOSD-related disability in a patient diagnosed with NMOSD, the method comprising:

administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD, wherein the patient had been previously treated with an anti-CD20 antibody, wherein the patient had an NMOSD attack while being treated with the anti-CD20 antibody.

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50. — A method of reducing NMOSD-related disability in a patient diagnosed with NMOSD, the method comprising:

administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD, wherein the patient had been previously treated with an anti-CD20 antibody, wherein the patient had an NMOSD attack within 6 months of the last dose of the anti-CD20 antibody.

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51. — The method of claim 49 or 50, wherein the VIB551 is administered intravenously at a dose of 300 mg every 6 months.

30 52. — A method of reducing NMOSD-related disability in a patient diagnosed with NMOSD, the method comprising:

administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD, wherein the patient had been previously treated with an anti-CD20 antibody, wherein the patient had an NMOSD attack while being treated with the anti-CD20 antibody; and,

wherein the VIB551 is administered intravenously at a dose of 300 mg every 6 months.

53. — A method of reducing NMOSD-related disability in a patient diagnosed with NMOSD, the method comprising:

5 administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD, wherein the patient had been previously treated with an anti-CD20 antibody, wherein the patient had an NMOSD attack within 6 months of the last dose of the anti-CD20 antibody; and,

wherein the VIB551 is administered intravenously at a dose of 300 mg every 6 months.

10 54. — The method of any one of claims 49-53, wherein the reducing the NMOSD-related disability in the patient is a reduction in a rate of worsening of NMOSD-related disability in the patient.

55. — The method of any one of claims 49-54, wherein the reducing the NMOSD-related disability in the patient is a lessening of NMOSD-related disability in the patient.

56. — The method of any one of claims 49-55, wherein the NMOSD-related disability is neurological disability.

57. — The method of any one of claims 49-56, wherein the reducing the NMOSD-related disability is determined using EDSS.

20 58. A method of reducing NMOSD-related attacks in a patient in need of treatment for NMOSD, the method comprising:
administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD, wherein the patient had been previously treated with an anti-CD20 antibody, wherein the patient had an NMOSD attack while being treated with the anti-CD20 antibody.

25 59. — A method of reducing NMOSD-related attacks in a patient in need of treatment for NMOSD, the method comprising:
administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD, wherein the patient had been previously treated with an anti-CD20 antibody, wherein the
30 patient had an NMOSD attack within 6 months of the last dose of the anti-CD20 antibody.

60. — The method of claim 58 or 59, wherein the VIB551 is administered intravenously at a dose of 300 mg every 6 months.

61. — A method of reducing NMOSD-related attacks in a patient in need of treatment for NMOSD, the method comprising:
administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD,
wherein the patient had been previously treated with an anti-CD20 antibody, wherein the
5 patient had an NMOSD attack while being treated with the anti-CD20 antibody; and,
wherein the VIB551 is administered intravenously at a dose of 300 mg every 6 months.

62. — A method of reducing NMOSD-related attacks in a patient in need of treatment for NMOSD, the method comprising:
10 administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD,
wherein the patient had been previously treated with an anti-CD20 antibody, wherein the
patient had an NMOSD attack within 6 months of the last dose of the anti-CD20 antibody;
and,
wherein the VIB551 is administered intravenously at a dose of 300 mg every 6 months.

15 63. The method of claim 61 or claim 62, wherein the NMOSD-related attacks suffered by the
patient comprise any one or more of an optic neuritis, a myelitis, or a brainstem attack.

20 64. The method of claim 63, wherein the NMOSD-related attacks suffered by the patient are
clinically asymptomatic.

65. — The method of any one of claims 36-64, wherein the patient receives at least one
initial dose of VIB551.

25 66. — The method of claim 65, wherein the VIB551 is administered intravenously with a
first initial dose of 300 mg, a second initial dose of 300 mg two weeks after the first initial
dose, and subsequent doses of 300 mg every 6 months following the first initial dose.

30 67. — The method of claim 66, wherein oral corticosteroids are co-administered to the
patient with the initial 300 mg VIB551 dose.

68. — The method of claim 67, wherein the oral corticosteroids are administered daily for at
least 2 weeks.

69. — The method of any one of claims 36-68, wherein the anti-CD20 antibody is rituximab.

70.—The method of any one of claims 1-69, wherein the VIB551 comprises a heavy chain variable region (VH) comprising the amino acid of SEQ ID NO:1 and a light chain variable region (VL) comprising the amino acid of SEQ ID NO: 2.

71.—A method of treating NMOSD, the method comprising:
administering an anti-CD19 antibody to a patient in need of treatment for NMOSD,
wherein the patient had been previously treated with an anti-CD20 antibody, wherein the
patient had an NMOSD attack while being treated with the anti-CD20 antibody.

72.—A method of treating NMOSD, the method comprising:
administering an anti-CD19 antibody to a patient in need of treatment for NMOSD,
wherein the patient had been previously treated with an anti-CD20 antibody, wherein the
patient had an NMOSD attack within 6 months of the last dose of the anti-CD20 antibody.

73.—A method of treating NMOSD, the method comprising:
administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD,
wherein the patient is an AQP4-IgG⁺ patient,
wherein the VIB551 is administered intravenously with a first initial dose of 300 mg, a
second initial dose of 300 mg two weeks after the first initial dose, and subsequent doses of
300 mg every 6 months following the first initial dose,
wherein patient had been previously treated with an anti-CD20 antibody, and wherein the
patient had an NMOSD attack while being treated with the anti-CD20 antibody.

74.—A method of treating NMOSD, the method comprising:
administering the anti-CD19 antibody VIB551 to a patient in need of treatment for NMOSD,
wherein the patient is an AQP4-IgG⁺ patient,
wherein the VIB551 is administered intravenously with a first initial dose of 300 mg, a
second initial dose of 300 mg two weeks after the first initial dose, and subsequent doses of
300 mg every 6 months following the first initial dose,
wherein the patient had been previously treated with an anti-CD20 antibody; and, wherein the
patient had an NMOSD attack within 6 months of the last dose of the anti-CD20 antibody.

75.—The use method of any one of claims 1-74, further comprising, wherein prior to the
administration administering:

~~identifying the subject patient is identified~~ as having previously been treated with the anti-CD20 antibody;

~~determining that the subject patient is determined as:~~

(i) suffered at least one NMOSD attack while being treated with the anti-CD20 antibody; or

5 (ii) had suffered at least one NMOSD attack within 6 months of the last dose of the anti-CD20 antibody; and

~~selecting the subject patient is selected for the administration of administering the anti-CD19 antibody as a result of the determination of determining (i) or (ii).~~