CLAIMS

1. Use of a B cell depleting therapy in the manufacture of a medicament for treating neuromyelitis optica spectrum disorder (NMOSD) ~~A method of reducing neuromyelitis optica spectrum disorder (NMOSD) related damage~~ in a subject in need thereof, wherein a therapeutically effective amount of the B cell depleting therapy is to be administered to the subject in need thereof, wherein a sample of the subject has an elevated glial fibrillary acidic protein (GFAP) concentration~~the method comprising administering a composition that comprises Inebilizumab or a derivative thereof to the subject in need thereof, thereby reducing the NMODS-related damage, wherein the subject in need thereof comprises a serum glial fibrillary astrocytic protein (sGFAP) concentration of at least about 160 pg/mL~~.

2. The use of claim 1, wherein the elevated GFAP concentration is ≥ 2 standard deviations above a healthy donor mean concentration.

3. The use of claim 1, wherein the elevated GFAP concentration is at least about 170 pg/mL.

4. The use of claim 1, wherein the administration is capable of reducing: (a) a number of NMOSD-related attacks in the subject in need thereof after the administering as compared to a baseline number of NMOSD-related attacks in the subject in need thereof before the administering; or (b) a number of NMOSD-related attacks in the subject in need thereof after the administering as compared to an otherwise comparable control subject lacking the administering.

5. The use of claim 1, wherein the administration is effective at reducing: (a) a number of magnetic resonance imaging (MRI) lesions; (b) a rate of increase in new MRI lesions; or (c) both (a) and (b).

6. The use of claim 1, wherein the administration is effective at: (a) reducing a rate of worsening of expanded disability status scale (EDSS) score; or b) improving the EDSS score.

7. The use of claim 1, wherein the administration is effective at preventing NMOSD relapse in the subject as determined by: (a) a reduction in a number of MRI lesions; (b) a reduction in size of MRI lesions; or (c) both (a) and (b).

8. The use of claim 1, wherein the administration is effective at suppressing an NMOSD-related attack in the subject.

9. The use of claim 8, wherein the subject is to be administered a second therapeutic selected from the group consisting of: a steroid, plasmapheresis, immunoadsorption, and a complement inhibitor.

10. The use of claim 8, wherein the subject is to be administered a second therapeutic selected from the group consisting of: Eculizumab, Satralizumab, Ublituximab, Ravulizumab, Rituximab, Azathioprine, Mycophenolate Mofetil, a low dose corticosteroid, and any combination thereof.

11. The use of claim 1, wherein the B cell depleting therapy is selected from the group consisting of an: anti-CD19 antibody, anti-CD20 antibody, and an anti-CD22 antibody.

12. The use of claim 11, wherein the B cell depleting therapy is the anti-CD19 antibody.

13. The use of claim 12, wherein the anti-CD19 antibody comprises Inebilizumab.

14. The use of claim 13, wherein the Inebilizumab is to be administered at a dose of 300 mg.

15. The use of claim 1, wherein the administration is to be repeated every six months.

16. Use of Inebilizumab in the manufacture of a medicament for treating neuromyelitis optica spectrum disorder (NMOSD) in a subject in need thereof, wherein a therapeutically effective amount of Inebilizumab is to be administered to the subject in need thereof, wherein a serum sample of the subject has an elevated concentration of a biomarker selected from the group consisting of: glial fibrillary acidic protein (GFAP), neurofilament light chain (NfL), ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1), and TAU.

17. The use of claim 16, wherein the biomarker is GFAP.

18. The use of claim 16, wherein the biomarker is TAU.

19. The use of claim 16, wherein the biomarker is UCHL1.

20. The use of claim 16, wherein the biomarker is NfL.

21. The use of claim 16, wherein the administering comprises 300 mg of Inebilizumab administered every six months.

22. The use of claim 16, wherein prior to the administration, the subject is selected as comprising the elevated concentration of the biomarker.

23. The use of claim 16, wherein the administration is effective at reducing: (a) a number of NMOSD-related attacks in the subject in need thereof after the administering as compared to a baseline number of NMOSD-related attacks in the subject in need thereof before the administering; or (b) a number of NMOSD-related attacks in the subject in need thereof after the administering as compared to an otherwise comparable control subject lacking the administering.

24. The use of claim 16, wherein the administration is effective at reducing: (a) a number of magnetic resonance imaging (MRI) lesions; (b) a rate of increase in new MRI lesions; or (c) both (a) and (b).

25. The use of claim 16, wherein the administration is effective at: (a) reducing a rate of worsening of expanded disability status scale (EDSS) score; or b) improving the EDSS score.

26. The use of claim 16, wherein the administration is effective at preventing NMOSD relapse in the subject as determined by: (a) a reduction in a number of MRI lesions; (b) a reduction in size of MRI lesions; or (c) both (a) and (b).

27. The use of claim 16, wherein the administration is effective at suppressing an NMOSD-related attack in the subject.

28. The use of claim 17, wherein the elevated GFAP concentration is $\geq$ 2 standard deviations above a healthy donor mean concentration.

29. The use of claim 16, wherein the serum sample is positive for all of GFAP, NfL, UCH-L1, and TAU.

30. Use of Inebilizumab in the manufacture of a medicament for treating neuromyelitis optica spectrum disorder (NMOSD) in a subject in need thereof, wherein Inebilizumab is to be administered to a subject in need, wherein a sample of the subject has been determined to have an elevated concentration of a biomarker of neuronal injury.

31. The use of claim 30, wherein the biomarker of neuronal injury is selected from the group consisting of: glial fibrillary acidic protein (GFAP), neurofilament light chain (NfL), ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1), and TAU.

~~2. The method of claim 1, wherein the sGFAP concentration is at least about 165 pg/mL, about 166 pg/mL, about 167 pg/mL, about 168 pg/mL, about 169 pg/mL, about 170 pg/mL, about 171 pg/mL, about 172 pg/mL, or about 173 pg/mL or greater.~~

~~3. The method of claim 2, wherein the sGFAP concentration is at least about 170 pg/mL.~~

~~4. The method of any one of claims 1-3, wherein the composition that comprises Inebilizumab or the derivative thereof is administered intravenously.~~

~~5. The method of claim 4, wherein the intravenous administration is at a dose of about 300 mg.~~

~~6. The method of any one of claims 1-5, wherein the administering is repeated at least twice.~~

~~7. The method of claim 6, wherein the administering is repeated every 6 months.~~

~~8. The method of any of claims 1-7, wherein the reducing NMOSD-related damage is determined by at least one of:~~

~~(a) a reduction in a number of NMOSD-related attacks in the subject in need thereof after the administering as compared to a baseline number of NMOSD-related attacks in the subject in need thereof before the administering; or~~

~~(b) a reduction in a number of NMOSD-related attacks in the subject in need thereof after the administering as compared to an otherwise comparable control subject lacking the administering.~~

~~9. The method of claim 8, wherein the baseline number of NMODS-related attacks are determined over a first time period preceding the administering, wherein the number of NMODS-related attacks reduced by the administering are determined over a second time period following the administering, and wherein the first time period and the second time period are of equal length.~~

10. The method of claim 9, wherein the first time period and the second time period are at least one year.

11. The method of any of claims 1-10, wherein the reducing the NMOSD-related damage comprises reducing NMOSD-related attacks that are graded major in severity in the subject in need thereof.

12. The method of any of claims 1-10, wherein the reducing the NMOSD-related damage comprises eliminating NMOSD-related attacks that are graded major in severity in the subject in need thereof.

13. The method of any of claims 1-10, wherein the reducing the NMOSD-related damage in the subject in need thereof comprises:

(a) reducing a number of magnetic resonance imaging (MRI) lesions;

(b) reducing rate of increase in new MRI lesions; or

(c) both (a) and (b).

14. The method of any of claims 1-10, wherein the reducing the NMOSD-related damage in the subject in need thereof comprises:

(a) reducing a rate of worsening of expanded disability status scale (EDSS) score; or

(b) improving the EDSS score.

15. The method of any one of claims 1-14, further comprising identifying the subject in need thereof by determining the sGFAP concentration of at least about 160 pg/mL.

16. A method of preventing neuromyelitis optica spectrum disorder (NMOSD) relapse in a subject in need thereof, the method comprising administering a composition that comprises Inebilizumab or a derivative thereof to the subject in need thereof thereby preventing NMODS relapse, wherein the subject in need thereof comprises a serum glial fibrillary acidic protein (sGFAP) concentration of about 165 pg/mL.

17. The method of claim 16, wherein the sGFAP concentration is about: 166 pg/mL, 167 pg/mL, 168 pg/mL, 169 pg/mL, 170 pg/mL, 171 pg/mL, 172 pg/mL, 173 pg/mL, or greater.

18. The method of claim 17, wherein the sGFAP concentration is about 170 pg/mL.

19. The method of any one of claims 15-17, wherein the composition that comprises Inebilizumab or the derivative thereof is administered intravenously.

20. The method of claim 19, wherein the intravenous administration is at a dose of about 300 mg.

21. The method of any one of claims 15-20, wherein the administering is repeated at least twice.

22. The method of claim 21, wherein the administering is repeated every 6 months.

23. The method of any of claims 15-22, wherein the preventing lasts for at least 1 year after the administering.

24. The method of any of claims 15-22, wherein the preventing lasts for at least 2 years after the administering.

25. The method of any of claims 15-24, wherein the administering decreases sGFAP concentration: (a) in the subject in need thereof as compared to sGFAP concentration prior to the administering; (b) in the subject in need thereof as compared to the subject in need thereof's baseline sGFAP concentration; or (c) in an otherwise comparable subject in need thereof lacking the administering.

26. The method of any of claims 15-25, wherein the preventing results in a reduction in MRI lesions in the subject in need thereof as determined by: (a) a reduction in a number of the MRI lesions; (b) a reduction in size of the MRI lesions; or (c) both (a) and (b).

27. The method of any of claims 15-26, wherein the preventing results in an improvement in EDSS score in the subject in need thereof.

28. A method of suppressing a neuromyelitis optica spectrum disorder (NMOSD)-related attack in a subject diagnosed with NMOSD, the method comprising:

(a) identifying the subject as at-risk for an NMOSD-related attack, wherein the subject is identified as an at-risk subject if the subject comprises an increase in sGFAP concentration relative to a baseline sGFAP concentration; and

(b) administering a therapeutic to the at-risk subject in an amount effective to suppress the NMODS-related attack, wherein the administering is performed at most one week following the identifying.

29. The method of claim 28, wherein the increase in the sGFAP concentration comprises an at least 10-fold increase relative to the baseline sGFAP concentration.

30. The method of claim 28, wherein the increase in the sGFAP concentration comprises an at least 20-fold increase relative to the baseline sGFAP concentration.

31. The method of any one of claims 28-30, wherein the subject at risk for the NMOSD-related attack is not undergoing a treatment for NMOSD that comprises Inebilizumab or a derivative thereof.

32. The method of claim 28, wherein the increase in sGFAP concentration comprises an increase of 50% to 150% relative to the baseline sGFAP concentration; wherein the subject at risk for the NMOSD-related attack is undergoing treatment for NMOSD, and wherein the treatment comprises Inebilizumab or a derivative thereof.

33. The method of any of claims 28-32, wherein the therapeutic comprises one or more of a steroid, plasmapheresis, immunoadsorption, or a complement inhibitor.

34. The method of any one of claims 28-32, wherein the therapeutic comprises one or more of Eculizumab, Satralizumab, Ublituximab, Ravulizumab, Rituximab, Azathioprine, Mycophenolate Mofetil, or a low-dose corticosteroid.

35. The method of any one of claims 20-34, wherein the administering is performed at most 24 hours following the identifying.

36. The method of any of claims 20-35, wherein the suppressing the NMOSD-related attack comprises: (a) reducing a number of NMODS-related attacks; or (b) preventing a NMOSD-related attack.

37. The method of claim 36, comprising (a), wherein the reducing comprises reducing a number of NMODS-related attacks graded as major in severity.

38. The method of any of claims 28-35, wherein the suppressing the NMOSD-related attack comprises a recovery from the NMOSD-related attack that is graded as a major recovery.

~~39. The method of any of claims 28-35, wherein the suppressing the NMOSD-related attack results in a prevention of new MRI lesions in the subject at-risk for an NMOSD-related attack.~~

~~40. The method of any of claims 28-35, wherein the suppressing the NMOSD-related attack results in a reduction in NMOSD-related disability in the subject at-risk for an NMOSD-related attack.~~

~~41. The method of claim 40, wherein the reduction in NMOSD-related disability is a reduction in worsening of the subject at-risk for an NMOSD-related attack's EDSS score.~~

~~42. The method of any of claims 28-32, wherein the therapeutic comprises Inebilizumab or a derivative thereof.~~

~~43. A method of treating neuromyelitis optica spectrum disorder (NMOSD) in a subject in need thereof, the method comprising administering a therapeutically effective amount of a B cell depleting therapy to the subject in need thereof, wherein the subject has a serum glial fibrillary acidic protein (sGFAP) concentration of about 160 pg/mL.~~

~~44. The method of claim 43, wherein the sGFAP concentration is about: 165 pg/mL, 166 pg/mL, 167 pg/mL, 168 pg/mL, 169 pg/mL, 170 pg/mL, 171 pg/mL, 172 pg/mL, 173 pg/mL, or greater.~~

~~45. The method of claim 44, wherein the subject in need thereof has a sGFAP concentration of about 170 pg/mL to 171 pg/mL.~~

~~46. The method of any one of claims 43-45, wherein the B cell depleting therapy comprises Inebilizumab or a derivative thereof.~~

~~47. The method of any one of claims 43-46, wherein the therapeutically effective amount of the B cell depleting therapy is about 300 mg.~~

~~48. A method of reducing neuromyelitis optica spectrum disorder (NMOSD)-related disability in a subject in need thereof, the method comprising administering a composition that comprises Inebilizumab or a derivative thereof to the subject in need thereof, thereby reducing the NMOSD-related disability, wherein the subject in need thereof comprises: (a) an increase in serum Neurofilament light chain (sNfL) levels over a baseline level of the subject in need thereof; or (b) an increase in sNfL levels over an otherwise comparable control subject.~~

~~49. The method of claim 48, further comprising identifying the subject in need thereof.~~

~~50. A method of reducing neuromyelitis optica spectrum disorder (NMOSD)-related disability in a subject diagnosed with NMOSD, the method comprising administering a composition that comprises Inebilizumab or a derivative thereof to the subject diagnosed with NMODS, wherein the subject diagnosed with NMODS comprises: (a) an increase in serum Neurofilament light chain (sNfL) level over a baseline level of the subject diagnosed with NMODS; or (b) an increase in sNfL level over an otherwise comparable control subject.~~

~~51. A method of treating neuromyelitis optica spectrum disorder (NMOSD) in a subject in need thereof, the method comprising:~~

~~(a) identifying a subject in need thereof at increased risk for NMOSD-related disability as determined by: (i) an increased serum Neurofilament light chain (sNfL) level over a baseline level of the subject in need thereof; or (ii) an increased sNfL level over an otherwise comparable control subject; and~~

~~(b) administering a composition that comprises Inebilizumab or a derivative thereof to the subject identified in (a), thereby treating the NMODS.~~

~~52. A method of treating neuromyelitis optica spectrum disorder (NMOSD) in a subject in need thereof, the method comprising administering a composition that comprises Inebilizumab or a derivative thereof to the subject in need thereof, thereby treating the NMODS, wherein the subject in need thereof comprises: an increased serum Neurofilament light chain (sNfL) level over a baseline level of the subject in need thereof; or (b) an increased sNfL level over an otherwise comparable control subject.~~

~~53. The method of any one of claims 48-52, wherein the subject in need thereof comprises about 1.0, about 1.1, about 1.2, about 1.3, about 1.4, about 1.5, about 1.6, about 1.7, about 1.8, about 1.9, about 2.0 or greater fold change in serum Nfl over a baseline level.~~

~~54. The method of any one of claims 48-53, wherein the subject in need thereof has a sGFAP concentration of about 160 pg/mL, about 165 pg/mL, about 166 pg/mL, about 167 pg/mL, about 168 pg/mL, about 169 pg/mL, about 170 pg/mL, about 171 pg/mL, about 172 pg/mL, or about 173 pg/mL or greater.~~

55. A method of treating a subject suspected of having neuromyelitis optica spectrum disorder (NMOSD), the method comprising administering a composition that comprises Inebilizumab or a derivative thereof to the subject, wherein the subject comprises one or more NMODS-related symptoms and at least one of:

(a) an increase in serum Neurofilament light chain (sNfL) level over a baseline level of the subject; or

(b) an increase in sNfL level over an otherwise comparable control subject.

56. A method of treating a subject suspected of having neuromyelitis optica spectrum disorder (NMOSD), the method comprising:

(a) identifying a subject as having one or more NMOSD-related symptoms;

(b) determining if the subject identified in (a) is at increased risk for NMOSD-related disability as determined by (i) an increase in serum Neurofilament light chain (sNfL) level over a baseline level of the subject identified in (a); or (ii) an increase in sNfL levels over an otherwise comparable control subject; and

(c) administering a composition that comprises Inebilizumab or a derivative thereof to the subject determined to be at increased risk for NMOSD-related disability from (b).

57. A method of treating neuromyelitis optica spectrum disorder (NMOSD) in a subject in need thereof, the method comprising administering a therapeutic in an amount effective to treat the NMODS in the subject in need thereof, wherein the subject in need thereof comprises: (a) an increase in serum Neurofilament light chain (sNfL) level over a baseline level of the subject in need thereof; or (b) an increase in sNfL level over an otherwise comparable control subject.

58. A method of treating a subject suspected of having neuromyelitis optica spectrum disorder (NMOSD), the method comprising administering a therapeutic to the subject suspected of having NMOSD, wherein the subject suspected of having NMOSD comprises one or more NMODS-related symptoms and at least one of:

(a) an increase in serum Neurofilament light chain (sNfL) level over a baseline level of the subject suspected of having NMOSD; or

(b) an increase in sNfL level over an otherwise comparable control subject.

~~59. The method of claim 57 or claim 58, wherein the therapeutic comprises one or more of Eculizumab, Satralizumab, Ublituximab, Ravulizumab, Rituximab, Azathioprine, Mycophenolate Mofetil, or a low dose corticosteroid.~~