WHAT IS CLAIMED IS:

1. An isolated antibody or antigen-binding fragment thereof which specifically binds to the same Sp35 epitope as a reference monoclonal antibody selected from the group consisting of 3B5.2, 7P1D5.1G9 and Li81.

2. An isolated antibody or antigen-binding fragment thereof which specifically binds to Sp35, wherein said antibody or fragment thereof competitively inhibits a reference monoclonal antibody selected from the group consisting of 3B5.2, 7P1D5.1G9 and Li81.

3. An isolated antibody or antigen-binding fragment thereof which specifically binds to Sp35, wherein said antibody or fragment thereof is selected from the group consisting of 3B5.2, 7P1D5.1G9 and Li81.

4. The antibody or fragment thereof of any one of claims 1 to 3, which binds to a linear epitope.

5. The antibody or fragment thereof of any one of claims 1 to 3, which binds to a non-linear conformational epitope.

6. The antibody or fragment thereof of any one of claims 1 to 5, which binds to the Sp35 LRR domain.

7. The antibody or fragment thereof of any one of claims 1 to 5, which binds to the Sp35 LRRNT or LRRCT domain.

8. The antibody or fragment thereof of any one of claims 1 to 5, which binds to the region of Sp35 from amino acids 417-532 of SEQ ID NO:2 or amino acids 495-532 of SEQ ID NO:2.

9. The antibody or fragment thereof of any one of claims 1 to 5, which binds to the Sp35 basic region domain.

10. The antibody of fragment thereof of claim 9 which binds to amino acids 415 to 424 of SEQ ID NO:2 or amino acids 417 to 424 of SEQ ID NO:2.

11. The antibody or fragment thereof of any one of claims 1 to 5, which binds to the Sp35 immunoglobulin domain.

12. The antibody or fragment thereof of claim 11 which binds to amino acids 419 to 493 of SEQ ID NO:2.

13. The antibody or fragment thereof of any one of claims 1 to 5, which binds to the Sp35 LLRCT domain.

14. The antibody of fragment thereof of claim 13 which binds to amino acids 363 to 414 of SEQ ID NO:2 or amino acids 363 to 416 of SEQ ID NO:2.

15. The antibody or fragment thereof of any one of claims 1 to 14, which is a multivalent, and comprises at least two heavy chains and at least two light chains.

16. The antibody or fragment thereof of any one of claims 1 to 15, which is multispecific.

17. The antibody or fragment thereof of claim 16, which is bispecific.

18. The antibody or fragment thereof of any one of claims 1 to 17 which is humanized.

19. The antibody or fragment thereof of any one of claims 1 to 17, which is chimeric.

20. The antibody or fragment thereof of any one of claims 1 to 17, which is primatized.

21. The antibody or fragment thereof of any one of claims 1 to 17, which is fully human.

22. The antibody or fragment thereof of any one of claims 1 to 21, which is an Fab fragment.

23. The antibody or fragment thereof of any one of claims 1 to 21, which is an Fab' fragment.

24. The antibody or fragment thereof of any one of claims 1 to 21, which is an $F(ab)_2$ fragment.

25. The antibody or fragment thereof of any one of claims 1 to 21, which is an Fv fragment.

26. The antibody or fragment thereof of any one of claims 1 to 21, which is a single chain antibody.

27. The antibody or fragment thereof of any one of claims 1, 2, or 4 to 26, which specifically binds to a Sp35 polypeptide or fragment thereof, or an Sp35 variant polypeptide, with an affinity characterized by a dissociation constant (K_D) which is less than the K_D for said reference monoclonal antibody.

28. The antibody or fragment thereof of any one of claims 1 to 26, which specifically binds to a Sp35 polypeptide or fragment thereof, or a Sp35 variant polypeptide with an affinity characterized by a dissociation constant (K_D) no greater than 5×10^{-2} M, 10^{-2} M, 5×10^{-3} M, 10^{-3} M, 5×10^{-4} M, 10^{-4} M, 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, 10^{-13} M, 5×10^{-14} M, 10^{-14} M, 5×10^{-15} M, or 10^{-15} M.

29. The antibody or fragment thereof of any one of claims 1 to 28, which preferentially binds to a human Sp35 polypeptide or fragment thereof, relative to a murine Sp35 polypeptide or fragment thereof.

30. The antibody or fragment thereof of any one of claims 1 to 29, which is an antagonist of Sp35 mediated neurite outgrowth inhibition.

31. The antibody or fragment thereof of any one of claims 1 to 29, which is an antagonist of Sp35 mediated neuronal cell death.

32. The antibody or fragment thereof of any one of claims 1 to 29, which is an antagonist of Sp35-mediated myelination inhibition.

33. The antibody or fragment thereof of any one of claims 1 to 29, which is an antagonist of Sp35 mediated oligodendrocyte cell death.

34. The antibody or fragment thereof of any one of claims 1 to 29, which is an antagonist of Sp35 mediated oligodendrocyte differentiation inhibition.

35. The antibody or fragment thereof of any one of claims 1 to 29, which is an antagonist of Sp35 mediated oligodendrocyte proliferation inhibition.

36. The antibody or fragment thereof of any one of claims 1 to 35, further comprising a heterologous polypeptide fused thereto.

37. The antibody or fragment thereof of any one of claims 1 to 36, wherein said antibody is conjugated to an agent selected from the group consisting of a therapeutic agent, a prodrug, a peptide, a protein, an enzyme, a virus, a lipid, a biological response modifier, a pharmaceutical agent, or PEG.

38. A composition comprising the antibody or fragment thereof of any one of claims 1 to 37, and a carrier.

39. An isolated antibody or antigen binding fragment thereof comprising a VH region and a VL region wherein said VH and VL regions comprise, respectively, polypeptide sequences at least 90% identical to the reference polypeptides SEQ ID NO:416 and SEQ ID NO:417; SEQ ID NO:433 and SEQ ID NO:434; or SEQ ID NO:435 and SEQ ID NO:434 and wherein an antibody or antigen-binding fragment thereof comprising said VH and VL specifically binds to Sp35.

40. An isolated antibody or antigen binding fragment thereof comprising a VH region and a VL region wherein said VH and VL regions, respectively, are identical, except for less than 20 conservative amino acid substitutions, to reference polypeptides SEQ ID NO:416 and SEQ ID NO:417; SEQ ID NO:433 and SEQ ID NO:434; or SEQ ID NO:435 and SEQ ID NO:434 and wherein an antibody or antigen-binding fragment thereof comprising said VH and VL specifically binds to Sp35.

41. An isolated antibody or antigen binding fragment thereof comprising a VH region and a VL region wherein said VH and VL regions comprise, respectively, the polypeptides selected from the group consisting of

(i) SEQ ID NO:416 and SEQ ID NO:417; and

(ii) SEQ ID NO:430 and 432;

(iii) SEQ ID NO:431 and 432;

(iv) SEQ ID NO:433 and 434; and

(v) SEQ ID NO:435 and 434..

42. An isolated polynucleotide comprising a nucleic acid encoding an immunoglobulin heavy chain variable region (VH), wherein the CDR1, CDR2, and CDR3 regions of said VH are at least 90% identical, respectively, to reference heavy chain CDR1, CDR2, and CDR3 polypeptide sequences SEQ ID NO:410, SEQ ID NO:411, and SEQ ID NO:412; or SEQ ID NO:436, SEQ ID NO;437 and SEQ ID NO:438 and wherein an antibody or antigen-binding fragment thereof comprising said VH specifically binds to Sp35.

43. An isolated polynucleotide comprising a nucleic acid encoding an immunoglobulin heavy chain variable region (VH), wherein the CDR1, CDR2, and CDR3 regions of said VH are identical respectively, except for less than 20 conservative amino acid substitutions, to reference heavy chain CDR1, CDR2, and CDR3 polypeptide sequences SEQ ID NO:410, SEQ ID NO:411, and SEQ ID NO:412; or SEQ ID NO:436, SEQ ID NO;437 and SEQ ID NO:438 and wherein an antibody or antigen-binding fragment thereof comprising said VH specifically binds to Sp35.

44. The polynucleotide of any one of claims 42 or 43, wherein the CDR1, CDR2, and CDR3 regions of said VH comprise, respectively, polypeptide sequences SEQ ID NO:410, SEQ ID NO:411, and SEQ ID NO:412 or SEQ ID NO:436, SEQ ID NO;437 and SEQ ID NO:438.

45. An isolated polynucleotide comprising a nucleic acid encoding an immunoglobulin heavy chain (VH), wherein said CDR1, CDR2, and CDR3 regions of said VH

are encoded by the nucleic acid sequences of SEQ ID NO:424, SEQ ID NO:425, and SEQ ID NO:426; or SEQ ID NO:439, SEQ ID NO;440 and SEQ ID NO:441.

46. An isolated polynucleotide comprising a nucleic acid encoding a VH region at least 90% identical to the reference VH polypeptide sequence of SEQ ID NO:416, SEQ ID NO:433 or SEQ ID NO:435 wherein an antibody or antigen-binding fragment thereof comprising said VH specifically binds to Sp35.

47. An isolated polynucleotide comprising a nucleic acid encoding a VH region identical to the reference VH polypeptide sequence of SEQ ID NO:416, 432, 433 or 435, except for less than 20 conservative amino acid substitutions, and wherein an antibody or antigen-binding fragment thereof comprising said VH specifically binds to Sp35.

48. The polynucleotide of any one of claims 46 or 47, wherein said VH is identical to said reference VH.

49. The polynucleotide of any one of claims 46 or 47, wherein said VH is encoded by the nucleic acid sequence of SEQ ID NO:422, 448 or 450.

50. The polynucleotide of any one of claims 42 to 49, further comprising a nucleic acid encoding a signal peptide fused to said VH.

51. The polynucleotide of any one of claims 42 to 49, further comprising a nucleic acid encoding a CH1 domain fused to said VH.

52. The polynucleotide of any one of claims 42 to 49, further comprising a nucleic acid encoding a CH2 domain fused to said VH.

53. The polynucleotide of any one of claims 42 to 49, further comprising a nucleic acid encoding a CH3 domain fused to said VH.

54. The polynucleotide of any one of claims 42 to 49, further comprising a nucleic acid encoding the hinge region fused to said VH.

55. The polynucleotide of any one of claims 42 to 54, wherein an antibody or antigen-binding fragment thereof comprising said VH specifically binds to the same epitope as the monoclonal antibody 3B5.2 or Li81.

56. The polynucleotide of any one of claims 42 to 54, wherein an antibody or antigen-binding fragment thereof comprising said VH competitively inhibits the monoclonal antibody 3B5.2 or Li81 from binding to Sp35.

57. The polynucleotide of any one of claims 42 to 54, wherein an antibody or antigen-binding fragme nt thereof comprising said VH specifically binds to a Sp35 polypeptide or fragment thereof, or a Sp35 variant polypeptide, with an affinity characterized by a dissociation constant (K_D) no greater than 5×10^{-2} M, 10^{-2} M, 5×10^{-3} M, 10^{-3} M, 5×10^{-4} M, 10^{-4} M, 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, 10^{-13} M, 5×10^{-14} M, 10^{-14} M, 5×10^{-15} M, or 10^{-15} M.

58. An isolated polynucleotide comprising a nucleic acid encoding an immunoglobulin light chain variable region (VL), wherein the CDR1, CDR2, and CDR3 regions of said VL are at least 90% identical, respectively, to reference light chain CDR1, CDR2, and CDR3 sequences SEQ ID NO: 413, 414 and 415, or SEQ ID NO:442, 443 and 444 and wherein an antibody or antigen-binding fragment thereof comprising said VL specifically binds to Sp35.

59. An isolated polynucleotide comprising a nucleic acid encoding an immunoglobulin light chain variable region (VL), wherein the CDR1, CDR2, and CDR3 regions of said VL are identical respectively, except for less than 20 conservative amino acid substitutions, to reference light chain CDR1, CDR2, and CDR3 sequences SEQ ID NO: 413, 414 and 415 or SEQ ID NO;442, 443 and 444 and wherein an antibody or antigen-binding fragment thereof comprising said VL specifically binds to Sp35.

60. The polynucleotide of any one of claims 58 or 59, wherein the CDR1, CDR2, and CDR3 regions of said VL comprise, respectively, the polypeptides sequences SEQ ID NO: 413, 414 and 415 or SEQ ID NO:442, 443 and 444.

61. An isolated polynucleotide comprising a nucleic acid encoding an immunoglobulin light chain variable region (VL), wherein said CDR1, CDR2, and CDR3 regions of said VL are encoded by the nucleic acid sequence of SEQ ID NO:427, SEQ ID NO:428, and SEQ ID NO:429; or SEQ ID NO:445, SEQ ID NO:446, and SEQ ID NO:447.

62. An isolated polynucleotide comprising a nucleic acid encoding a VL region at least 90% identical to the reference VL polypeptide sequence of SEQ ID NO:417 or 434, wherein an antibody or antigen-binding fragment thereof comprising said VL specifically binds to Sp35.

63. An isolated polynucleotide comprising a nucleic acid encoding a VL region identical to the reference VL polypeptide sequence selected from the group consisting of SEQ ID NO:417; SEQ ID NO:430; SEQ ID NO:431; SEQ ID NO:442; SEQ ID NO:443 and SEQ ID NO:444; except for less than 20 conservative amino acid substitutions, and wherein an antibody or antigen-binding fragment thereof comprising said VL specifically binds to Sp35.

64. The polynucleotide of any one of claims 62 or 63, wherein said VL is identical to said reference VL.

65. The polynucleotide of claim 64, wherein said VL is encoded by the nucleic acid sequence of SEQ ID NO:423 or SEQ ID NO:449.

66. The polynucleotide of any one of claims 58 to 65, further comprising a nucleic acid encoding a signal peptide fused to said VL.

67. The polynucleotide of any one of claims 58 to 65, further comprising a nucleic acid encoding a CH1 domain fused to said VL.

68. The polynucleotide of any one of claims 58 to 65, further comprising a nucleic acid encoding a CH2 domain fused to said VL.

69. The polynucleotide of any one of claims 58 to 65, further comprising a nucleic acid encoding a CH3 domain fused to said VL.

70. The polynucleotide of any one of claims 58 to 65, further comprising a nucleic acid encoding the hinge region fused to said VL.

71. The polynucleotide of any one of claims 58 to 70, wherein an antibody or antigen-binding fragment thereof comprising said VL specifically binds to the same epitope as the monoclonal antibody 3B5.2 or Li81.

72. The polynucleotide of any one of claims 58 to 70, wherein an antibody or antigen-binding fragment thereof comprising said VL competitively inhibits the monoclonal antibody 3B5.2or Li81.

73. The polynucleotide of any one of claims 58 to 72, wherein an antibody or antigen-binding fragment thereof comprising said VL specifically binds to a Sp35 polypeptide or fragment thereof, or a Sp35 variant polypeptide, with an affinity characterized by a dissociation constant (K_D) no greater than 5×10^{-2} M, 10^{-2} M, 5×10^{-3} M, 10^{-3} M, 5×10^{-4} M, 10^{-4} M, 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, 10^{-13} M, 5×10^{-14} M, 10^{-14} M, 5×10^{-15} M, or 10^{-15} M.

74. The polynucleotide of any one of claims 42 to 73, further comprising a heterologous polynucleotide.

75. The polynucleotide of claim 74, wherein said heterologous polynucleotide encodes a heterologous polypeptide.

76. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL specifically binds to a linear epitope.

77. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL specifically binds to a non-linear conformational epitope.

78. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL specifically binds to the Sp35 LRR domain.

79. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL specifically binds to the Sp35 LRRNT domain.

80. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL specifically binds to the Sp35 LRRCT domain.

81. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL specifically binds to the Sp35 immunoglobulin domain.

82. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL specifically binds to the Sp35 basic region.

83. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL is a multivalent antibody molecule comprising at least two heavy chains and at least two light chains.

84. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL is multispecific.

85. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL is bispecific.

86. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL is monovalent, bivalent, polyvalent, or bifunctional.

87. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL is humanized.

88. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is chimeric.

89. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL is primatized.

90. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL is fully human.

91. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL is an Fab fragment.

92. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL is an Fab' fragment.

93. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL is an $F(ab)_2$ fragment.

94. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL is an Fv fragment.

95. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL is a single chain antibody.

96. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL specifically binds to a Sp35 polypeptide or fragment thereof, or a Sp35 variant polypeptide with an affinity characterized by a dissociation constant (K_D) no greater than 5×10^{-2} M, 10^{-2} M, 5×10^{-3} M, 10^{-3} M, 5×10^{-4} M, 10^{-4} M, 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, 10^{-13} M, 5×10^{-14} M, 10^{-14} M, 5×10^{-15} M, or 10^{-15} M.

97. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL preferentially binds to a human Sp35 polypeptide or fragment thereof, relative to a murine Sp35 polypeptide or fragment thereof.

98. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL is an antagonist of Sp35 mediated neurite outgrowth inhibition.

99. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL is an antagonist of Sp35-mediated myelination inhibition.

100. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL is an antagonist of Sp35 mediated oligodendrocyte cell death.

101. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL is an antagonist of Sp35 mediated oligodendrocyte differentiation inhibition.

102. The polynucleotide of any one of claims 42 to 75, wherein an antibody or antigen-binding fragment thereof comprising said VH or said VL is an antagonist of Sp35 mediated oligodendrocyte proliferation inhibition.

103. A composition comprising the polynucleotide of any one of claims 42 to 102.

104. A composition comprising a VH encoding polynucleotide and a VL encoding polynucleotide, wherein said VH encoding polynucleotide and said VL encoding polynucleotide, respectively, comprise polynucleotides encoding amino acid sequences at least 90% identical to the reference polypeptides SEQ ID NO:416 and SEQ ID NO:417; or SEQ ID NO:433 and SEQ ID NO:434; or SEQ ID NO:435 and SEQ ID NO:434 and wherein said VH and VL encoding polynucleotides together encode an antibody or binding fragment thereof which specifically binds Sp35.

105. A composition comprising a VH encoding polynucleotide and a VL encoding polynucleotide, wherein said VH encoding polynucleotide and said VL encoding polynucleotide, respectively, comprise polynucleotides encoding amino acid sequences identical, except for less than 20 conservative amino acid substitutions, to the reference polypeptides SEQ ID NO:416 and

SEQ ID NO:417; or SEQ ID NO:433 and SEQ ID NO:434; or SEQ ID NO:435 and SEQ ID NO:434 and wherein said VH and VL encoding polynucleotides together encode an antibody or binding fragment thereof which specifically binds Sp35.

106. A composition comprising a VH encoding polynucleotide and a VL encoding polynucleotide, wherein said VH encoding polynucleotide and said VL encoding polynucleotide, respectively, comprise polynucleotides encoding amino acid sequences identical to the reference polypeptides selected from the group consisting of:

(i) SEQ ID NO:416 and SEQ ID NO:417;

(ii) SEQ ID NO:430 and SEQ ID NO:432;

(iii) SEQ ID NO:431 and 432

(iv) SEQ ID NO:433 and 434; and

(v) SEQ ID NO:435 and 434.

107. The composition of any one of claims 104 to 106, wherein said VH encoding polynucleotide and said VL encoding polynucleotide comprise, respectively, the nucleotide sequences of SEQ ID NO:422 and SEQ ID NO:423; or SEQ ID NO:448 and SEQ ID NO:449; or SEQ ID NO:450 and SEQ ID NO:449.

108. The composition of any one of claims 104 to 107, wherein said VH encoding polynucleotide and said VL encoding polynucleotide are contained in the same open reading frame, such that the VH and VL polypeptide encoded by said polynucleotides are comprised in a single-chain antibody or fragment thereof.

109. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL specifically binds to a linear epitope.

110. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL specifically binds to a non-linear conformational epitope.

111. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL specifically binds to the Sp35 LRR domain.

112. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL specifically binds to the Sp35 LRRNT domain.

113. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL specifically binds to the Sp35 LRRCT domain.

114. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL specifically binds to the Sp35 immunoglobulin domain.

115. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL specifically binds to the Sp35 basic region.

116. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is a multivalent antibody molecule comprising at least two heavy chains and at least two light chains.

117. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is multispecific.

118. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is bispecific.

119. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is monovalent, bivalent, polyvalent, or bifunctional.

120. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is humanized.

121. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is chimeric.

122. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is primatized.

123. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is fully human.

124. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is an Fab fragment.

125. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is an Fab' fragment.

126. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is an $F(ab)_2$ fragment.

127. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is an Fv fragment.

128. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is a single chain antibody.

129. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL specifically binds to a Sp35 polypeptide or fragment thereof, or a Sp35 variant polypeptide with an affinity characterized by a dissociation constant (K_D) no greater than 5×10^{-2} M, 10^{-2} M, 5×10^{-3} M, 10^{-3} M, 5×10^{-4} M, 10^{-4} M, 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, 10^{-13} M, 5×10^{-14} M, 10^{-14} M, 5×10^{-15} M, or 10^{-15} M.

130. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL preferentially binds to a human Sp35 polypeptide or fragment thereof, relative to a murine Sp35 polypeptide or fragment thereof.

131. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is an antagonist of Sp35 mediated neurite outgrowth inhibition.

132. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is an antagonist of Sp35-mediated myelination inhibition.

133. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is an antagonist of Sp35 mediated oligodendrocyte cell death.

134. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is an antagonist of Sp35 mediated oligodendrocyte differentiation inhibition.

135. The composition of any one of claims 104 to 107, wherein an antibody or antigen-binding fragment thereof comprising said VH and VL is an antagonist of Sp35 mediated oligodendrocyte proliferation inhibition.

136. A vector comprising the polynucleotide of any one of claims 42 to 102.

137. The vector of claim 136, wherein said polynucleotide is operably associated with a promoter.

138. The vector of claim 136, wherein said polynucleotide encoding a VH and said polynucleotide encoding a VL are fused in frame, are co-transcribed from a single promoter operably associated therewith, and are cotranslated into a single chain antibody or antigen-binding fragment thereof.

139. The vector of claim 136, wherein said polynucleotide encoding a VH and said polynucleotide encoding a VL are co-transcribed from a single promoter operably associated therewith, but are separately translated.

140. The vector of claim 139, further comprising an IRES sequence disposed between said polynucleotide encoding a VH and said polynucleotide encoding a VL.

141. The vector of claim 139, wherein said polynucleotide encoding a VH and said polynucleotide encoding a VL are separately transcribed, each being operably associated with a separate promoter.

142. The vector of claim 141, wherein said separate promoters are copies of the same promoter.

143. The vector of claim 141, wherein said separate promoters non-identical.

144. A composition comprising the vector of any one of claims 136 to 143.

145. A composition comprising a first vector comprising a VH encoding polynucleotide of any one of claims 45 to 57 or 74 to 102 and a second vector comprising a VL encoding polynucleotide of any one of claims 58 to 73 or 74 to 102.

146. A host cell comprising the polynucleotide of any one of claims 42 to 102 or the vector of any one of claims 136 to 145.

147. A host cell comprising at least a first and a second vector, wherein said first and said second vectors are non-identical, wherein said first vector comprises the polynucleotide of any one of claims 42 to 57 or 74 to 112 which encodes an immunoglobulin heavy chain variable region, and wherein said second vector comprises the polynucleotide of any one of claims 58 to 73 or 74 to 102 which encodes an immunoglobulin light chain variable region.

148. A method of producing an anti-Sp35 antibody, comprising culturing the host cell of any one of claims 146 to 147, and recovering said antibody.

149. An anti-Sp35 antibody, or antigen-binding fragment thereof, produced by the method of claim 148.

150. An isolated polypeptide comprising an immunoglobulin heavy chain variable region (VH), wherein the CDR1, CDR2, and CDR3 regions of said VH are at least 90% identical, respectively, to reference heavy chain CDR1, CDR2, and CDR3 sequences SEQ ID NO:410, SEQ ID NO:411, and SEQ ID NO:412; or SEQ ID NO:436, SEQ ID NO:437 and SEQ ID NO:438 and wherein an antibody or antigen-binding fragment thereof comprising said VH specifically binds to Sp35.

151. An isolated polypeptide comprising an immunoglobulin heavy chain variable region (VH), wherein the CDR1, CDR2, and CDR3 regions of said VH are identical respectively, except for less than 20 conservative amino acid substitutions, to reference heavy chain CDR1, CDR2, and CDR3 sequences SEQ ID NO:410, SEQ ID NO:411, and SEQ ID NO:412; or SEQ ID NO:436, SEQ ID NO:437 and SEQ ID NO:438 and wherein an antibody or antigen-binding fragment thereof comprising said VH specifically binds to Sp35.

152. An isolated polypeptide, comprising an immunoglobulin heavy chain variable region (VH), wherein the CDR1, CDR2, and CDR3 regions of said VH are SEQ ID NO:410, SEQ ID NO:411, and SEQ ID NO:412 ; or SEQ ID NO:436, SEQ ID NO:437 and SEQ ID NO:438.

153. An isolated polypeptide comprising a VH at least 90% identical to the reference VH sequence SEQ ID NO:416, SEQ ID NO:433 or SEQ ID NO:435, wherein an antibody or antigen-binding fragment thereof comprising said VH specifically binds to Sp35.

154. An isolated polypeptide comprising a VH identical to the reference VH SEQ ID NO:416, SEQ ID NO:433 or SEQ ID NO:435, except for less than 20 conservative amino acid substitutions, and wherein an antibody or antigen-binding fragment thereof comprising said VH specifically binds to Sp35.

155. The polypeptide of claim 153, wherein said VH is SEQ ID NO:416 or SEQ ID NO:433 or SEQ ID NO:435.

156. The polypeptide of any one of claims 150 to 155, wherein an antibody or antigen-binding fragment thereof comprising said VH specifically binds to the same epitope as the monoclonal antibody 3B5.2 or Li81.

157. The polypeptide of any one of claims 150 to 155, wherein an antibody or antigen-binding fragment thereof comprising said VH competitively inhibits the monoclonal antibody 3B5.2 or Li81 from binding to Sp35.

158. The polypeptide of any one of claims 150 to 157, wherein an antibody or antigen-binding fragment thereof comprising said VH specifically binds to a Sp35 polypeptide or fragment thereof, or a Sp35 variant polypeptide, with an affinity characterized by a dissociation constant (K_D) no greater than 5×10^{-2} M, 10^{-2} M, 5×10^{-3} M, 10^{-3} M, 5×10^{-4} M, 10^{-4} M, 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, 10^{-13} M, 5×10^{-14} M, 10^{-14} M, 5×10^{-15} M, or 10^{-15} M.

159. An isolated polypeptide comprising an immunoglobulin light chain variable region (VL), wherein the CDR1, CDR2, and CDR3 regions of said VL are at least 90% identical, respectively, to reference light chain CDR1, CDR2, and CDR3 sequences SEQ ID NO:413, SEQ ID NO:414 and SEQ ID NO:415; or SEQ ID NO:442, SEQ ID NO:443 and SEQ ID NO:444 and wherein an antibody or antigen-binding fragment thereof comprising said VL specifically binds to Sp35.

160. An isolated polypeptide comprising an immunoglobulin light chain variable region (VL), wherein the CDR1, CDR2, and CDR3 regions of said VL are identical, respectively, except for less than 20 conservative amino acid substitutions, to reference light chain CDR1, CDR2, and CDR3 sequences SEQ ID NO:413, SEQ ID NO:414 and SEQ ID NO:415; or SEQ ID NO:442, SEQ ID NO:443 and SEQ ID NO:444 and wherein an antibody or antigen-binding fragment thereof comprising said VL specifically binds to Sp35.

161. An isolated polypeptide comprising an immunoglobulin light chain variable region (VL), wherein the CDR1, CDR2, and CDR3 regions of said VL are SEQ ID NO:413,

SEQ ID NO:414 and SEQ ID NO:415; or SEQ ID NO:442, SEQ ID NO:443 and SEQ ID NO:444.

162. An isolated polypeptide comprising a VL at least 90% identical to the reference VL sequence of SEQ ID NO:417 or SEQ ID NO:434 wherein an antibody or antigen-binding fragment thereof comprising said VL specifically binds to Sp35.

163. An isolated polypeptide comprising a VL identical to a reference VL sequence of SEQ ID NO:417 or SEQ ID NO:434, except for less than 20 conservative amino acid substitutions, and wherein an antibody or antigen-binding fragment thereof comprising said VL specifically binds to Sp35.

164. The polypeptide of any one of claims 162 or 163, wherein said VL is SEQ ID NO:417 or SEQ ID NO:434.

165. The polypeptide of any one of claims 159 to 164, wherein an antibody or antigen-binding fragment thereof comprising said VL specifically binds to the same epitope as the monoclonal antibody 3B5.2 or Li81.

166. The polypeptide of any one of claims 159 to 164, wherein an antibody or antigen-binding fragment thereof comprising said VL competitively inhibits the monoclonal antibody 3B5.2 or Li81 from binding to Sp35.

167. The polypeptide of any one of claims 159 to 166, wherein an antibody or antigen-binding fragment thereof comprising said VL specifically binds to a Sp35 polypeptide or fragment thereof, or a Sp35 variant polypeptide, with an affinity characterized by a dissociation constant (K_D) no greater than 5×10^{-2} M, 10^{-2} M, 5×10^{-3} M, 10^{-3} M, 5×10^{-4} M, 10^{-4} M, 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, 10^{-13} M, 5×10^{-14} M, 10^{-14} M, 5×10^{-15} M, or 10^{-15} M.

168. The polypeptide of any one of claims 150 to 167, further comprising a heterologous polypeptide fused thereto.

169. The polypeptide of any one of claims 150 to 168, wherein said polypeptide is conjugated to an agent selected from the group consisting of a therapeutic agent, a prodrug, a peptide, a protein, an enzyme, a virus, a lipid, a biological response modifier, a pharmaceutical agent, or PEG.

170. A composition comprising the polypeptide of any one of claims 150 to 169, wherein an antibody or antigen-binding fragment thereof comprising said VH and said VL specifically binds to Sp35.

171. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL specifically binds to a linear epitope.

172. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL specifically binds to a non-linear conformational epitope.

173. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL specifically binds to the Sp35 LRR domain.

174. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL specifically binds to the Sp35 LRRNT domain.

175. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL specifically binds to the Sp35 LRRCT domain.

176. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL specifically binds to the Sp35 Basic region.

177. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL specifically binds to the Sp35 immunoglobulin domain.

178. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is a multivalent antibody molecule comprising at least two heavy chains and at least two light chains.

179. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is multispecific.

180. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is bispecific.

181. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is monovalent, bivalent, polyvalent, or bifunctional.

182. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is humanized.

183. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is chimeric.

184. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is primatized.

185. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is fully human.

186. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is an Fab fragment.

187. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is an Fab' fragment.

188. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is an $F(ab)_2$ fragment.

189. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is an Fv fragment.

190. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is a single chain antibody.

191. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL specifically binds to a Sp35 polypeptide or fragment thereof, or a Sp35 variant polypeptide with an affinity characterized by a dissociation constant (K_D) no greater than 5×10^{-2} M, 10^{-2} M, 5×10^{-3} M, 10^{-3} M, 5×10^{-4} M, 10^{-4} M, 5×10^{-5} M, 10^{-5} M, 5×10^{-6} M, 10^{-6} M, 5×10^{-7} M, 10^{-7} M, 5×10^{-8} M, 10^{-8} M, 5×10^{-9} M, 10^{-9} M, 5×10^{-10} M, 10^{-10} M, 5×10^{-11} M, 10^{-11} M, 5×10^{-12} M, 10^{-12} M, 5×10^{-13} M, 10^{-13} M, 5×10^{-14} M, 10^{-14} M, 5×10^{-15} M, or 10^{-15} M..

192. The polypeptide of any one of claims 150 to 169 or the composition of claim 170, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both

said VH and VL preferentially binds to a human Sp35 polypeptide or fragment thereof, relative to a murine Sp35 polypeptide or fragment thereof.

193. A composition comprising the polypeptide of any one of claims 150 to 192, and a carrier.

194. The polypeptide of any one of claims 150 to 192 or the composition of any one of claims 170 or 193, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is an antagonist of Sp35 mediated neurite outgrowth inhibition.

195. The polypeptide of any one of claims 150 to 192 or the composition of any one of claims 170 or 193, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is an antagonist of Sp35-mediated myelination inhibition.

196. The polypeptide of any one of claims 150 to 192 or the composition of any one of claims 170 or 193, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is an antagonist of Sp35 mediated oligodendrocyte cell death.

197. The polypeptide of any one of claims 150 to 192 or the composition of any one of claims 170 or 193, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is an antagonist of Sp35 mediated oligodendrocyte differentiation inhibition.

198. The polypeptide of any one of claims 150 to 192 or the composition of any one of claims 170 or 193, wherein an antibody or antigen-binding fragment thereof comprising said VH, said VL, or both said VH and VL is an antagonist of Sp35 mediated oligodendrocyte proliferation inhibition.

199. An isolated antibody or antigen binding fragment thereof comprising the polypeptide of any one of claims 150 to 169.

CLAIMS

1. An isolated antibody or antigen-binding fragment thereof which can specifically bind to Sp35, wherein the antibody or antigen-binding fragment thereof comprises

an immunoglobulin heavy chain variable region (VH) comprising the VH CDR1, CDR2, and CDR3 amino acid sequences set forth in SEQ ID NO: 436, SEQ ID NO:437, and SEQ ID NO:438, respectively; and

an immunoglobulin light chain variable region (VL) comprising the VL CDR1, CDR2, and CDR3 amino acid sequences set forth in SEQ ID NO:442, SEQ ID NO:443, and SEQ ID NO:444, respectively.

2. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment comprises the VL of the amino acid sequence set forth in SEQ ID NO:434.

3. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment comprises the amino acid sequence set forth in SEQ ID NO:434.

4. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment comprises the VH of the amino acid sequence set forth in SEQ ID NO:433.

5. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment comprises the amino acid sequence set forth in SEQ ID NO:433.

6. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment comprises the amino acid sequence set forth in SEQ ID NO:435.

7. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody comprises the amino acid sequence set forth in SEQ ID NO:434 and the amino acid sequence set forth in SEQ ID NO:433.

8. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody comprises the amino acid sequence set forth in SEQ ID NO:434 and the amino acid sequence set forth in SEQ ID NO:435.

9. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment is an aglycosylated variant.

10. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment is conjugated to an agent selected from the group consisting of a therapeutic agent, a prodrug, a peptide, a protein, an enzyme, a virus, a lipid, a biological response modifier, a pharmaceutical agent, and PEG.

11. The antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or antigen-binding fragment is fused to a brain targeting protein or peptide.

12. The antibody or antigen-binding fragment thereof of claim 11, wherein the brain targeting protein or peptide is selected from the group consisting of FC5, mAB 83-14, B2 polypeptide, B6 polypeptide, B8 polypeptide, anti-Fc receptor, transferrin, OX26 monoclonal antibody, and anti-insulin receptor.

13. The antibody or antigen-binding fragment thereof of claim 12, wherein the brain targeting protein or peptide is FC5.

14. A composition for treating a human subject having a disease selected from the group consisting of multiple sclerosis (MS), progressive multifocal leukoencephalopathy (PML), encephalomyelitis (EPL), central pontine myelolysis (CPM), adrenoleukodystrophy, Alexander's disease, Pelizaeus Merzbacher disease (PMZ), Globoid cell Leucodystrophy (Krabbe's disease), Wallerian Degeneration, optic neuritis, transverse myelitis, amylotrophic lateral sclerosis (ALS), Huntington's disease, Alzheimer's disease, Parkinson's disease, spinal cord injury, traumatic brain injury, post radiation injury, neurologic complications of chemotherapy, stroke, acute ischemic optic neuropathy, vitamin E deficiency, isolated vitamin E deficiency syndrome, Bassen-Kornzweig syndrome, Marchiafava-Bignami syndrome, metachromatic leukodystrophy, trigeminal neuralgia, and Bell's palsy, comprising an isolated antibody or antigen-binding fragment thereof comprising
a immunoglobulin heavy chain variable region (VH) comprising the VH CDR1, CDR2, and CDR3 sequences of SEQ ID NO:436, SEQ ID NO:437, and SEQ ID NO:438, respectively; and
a immunoglobulin light chain variable region (VL) comprising the VL CDR1, CDR2, and CDR3 sequences of SEQ ID NO:442, SEQ ID NO:443, and SEQ ID NO:444, respectively;
wherein the antibody or antigen-binding fragment can specifically bind to an Sp35 polypeptide; and
wherein the composition is formulated for parenteral administration.

15. The composition of claim 14, wherein the antibody or antigen-binding fragment comprises the VH sequence of the amino acid sequence set forth in SEQ ID NO:435 and the VL sequence of the amino acid sequence set forth in of SEQ ID NO:434.

16. The composition of claim 14, wherein the antibody or antigen-binding fragment comprises the sequences of SEQ ID NO:434 and 435.

17. The composition of any one of claims 14-16, wherein the disease is multiple sclerosis.

18. The composition of any one of claims 14-16, wherein the disease is acute ischemic optic neuropathy.

19. The composition of any one of claims 14-16, wherein the disease is optic neuritis.

20. The composition of any one of claims 14-16, wherein the disease is Alzheimer's disease.

21. The composition of any one of claims 14-16, wherein the disease is Parkinson's disease.

22. The composition of any one of claims 14-16, wherein the disease is stroke.

23. The composition of any one of claims 14-16, wherein the disease is spinal cord injury.

24. The composition of any one of claims 14-16, wherein the disease is traumatic brain injury.

25. The composition of any one of claims 14-16, wherein the disease is transverse myelitis.

26. An isolated polynucleotide comprising a nucleic acid encoding an immunoglobulin heavy chain variable region (VH), wherein the CDR1, CDR2, and CDR3 regions of said VH comprise the amino acid sequences set forth in SEQ ID NO:436, SEQ ID NO:437 and SEQ ID NO:438, wherein an antibody or antigen-binding fragment thereof comprising said VH and an immunoglobulin light chain variable region (VL) whose CDR1, CDR2, and CDR3 regions comprise the amino acid sequences set forth in SEQ ID NO:442, SEQ ID NO:443, and SEQ ID NO:444 can specifically bind to Sp35.

27. The polynucleotide of claim 26, wherein the polynucleotide encodes the amino acid sequence set forth in SEQ ID NO:433.

28. The polynucleotide of claim 26, wherein the polynucleotide encodes the mature form of the amino acid sequence set forth in SEQ ID NO:474.

29. A vector comprising the polynucleotide of any one of claims 26-28.

30. A host cell comprising a VH encoding polynucleotide and a VL encoding polynucleotide, wherein said VH comprises the VH CDR1, CDR2, and CDR3 amino acid sequences set forth in SEQ ID NO: 436, SEQ ID NO:437, and SEQ ID NO:438 and wherein said VL comprises the VL CDR1, CDR2, and CDR3 amino acid sequences set forth in SEQ ID NO:442, SEQ ID NO:443, and SEQ ID NO:444 and wherein an antibody or antigen-binding fragment thereof comprising said VH and said VL can specifically bind to Sp35.

31. The host cell of claim 30, wherein the VH and VL encoding polynucleotides are present on one or more vectors.

32. An *in vitro* method of producing an anti-Sp35 antibody or antigen-binding fragment thereof, comprising culturing the host cell of claim 30 and recovering said antibody or antigen-binding fragment from the culture.

33. An anti-Sp35 antibody produced by the method of claim 32 or an antigen-binding fragment thereof.

34. A medicament for treating a human subject having a disease selected from the group consisting of multiple sclerosis (MS), progressive multifocal leukoencephalopathy (PML), encephalomyelitis (EPL), central pontine myelolysis (CPM), adrenoleukodystrophy, Alexander's disease, Pelizaeus Merzbacher disease (PMZ), Globoid cell Leucodystrophy (Krabbe's disease), Wallerian Degeneration, optic neuritis, transverse myelitis, amylotrophic lateral sclerosis (ALS), Huntington's disease, Alzheimer's disease, Parkinson's disease, spinal cord injury, traumatic brain injury, post radiation injury, neurologic complications of chemotherapy, stroke, acute ischemic optic neuropathy, vitamin E deficiency, isolated vitamin E deficiency syndrome, Bassen-Kornzweig syndrome, Marchiafava-Bignami syndrome, metachromatic leukodystrophy, trigeminal neuralgia, and Bell's palsy , wherein the medicament comprises the antibody or antigen-binding fragment thereof of any of claims 1-13 or 33.

35. The medicament of claim 34, wherein the disease is stroke.

36. The medicament of claim 34, wherein the disease is optic neuritis.

37. The medicament of claim 34, wherein the disease is transverse myelitis.

38. The medicament of claim 34, wherein the disease is Alzheimer's disease.

39. The medicament of claim 34, wherein the disease is Parkinson's disease.

40. The medicament of claim 34, wherein the disease is spinal cord injury.

41. The medicament of claim 34, wherein the disease is traumatic brain injury.

42. A medicament for treating multiple sclerosis, wherein the medicament comprises the antibody or antigen-binding fragment thereof of any of claims 1-13 or 33.

43. The medicament of claim 42, wherein the medicament is to be co-formulated or co-administered with an additional therapeutic agent.

44. A medicament for treating acute ischemic optic neuropathy, wherein the medicament comprises the antibody or antigen-binding fragment thereof of any of claims 1-13 or 33.

45. The medicament of claim 44, wherein the medicament is to be co-formulated or co-administered with an additional therapeutic agent.

46. An *in vitro* method of inhibiting signal transduction by NgR1, comprising contacting the NgR1 with the isolated Sp35 antibody or antigen-binding fragment thereof of any one of claims 1-13 or 33.

47. An *in vitro* method of decreasing inhibition of axonal growth of a central nervous system (CNS) neuron, comprising contacting the neuron with the isolated Sp35 antibody or antigen-binding fragment thereof of any one of claims 1-13 or 33.