

CLAIMS

We claim:

1. ~~_____ A method of treating generalized myasthenia gravis (MG) in a subject, the method comprising administering to the subject an effective amount of an isolated FcRn antagonist, thereby treating MG in the subject.~~
2. ~~_____ The method of claim 1, wherein the isolated FcRn antagonist comprises a variant Fc region, or FcRn-binding fragment thereof.~~
3. ~~_____ The method of claim 2, wherein the Fc domains of the variant Fc region, or FcRn-binding fragment thereof, comprise the amino acids Y, T, E, K, F, and Y at EU positions 252, 254, 256, 433, 434, and 436, respectively.~~
4. ~~_____ The method of any one of claims 1-3, wherein the FcRn antagonist is an anti-FcRn antibody comprising an antigen binding region comprising variable domains which specifically bind human FcRn.~~
5. ~~_____ The method of any one of claims 1-3, wherein the FcRn antagonist does not comprise an antibody variable region.~~
6. ~~_____ The method of any one of claims 1-3 and 5, wherein the FcRn antagonist does not comprise a CH1 domain.~~
7. ~~_____ The method of any one of claims 1-3, 5, and 6, wherein the FcRn antagonist does not comprise a free cysteine residue.~~
8. ~~_____ The method of any one of claims 2-7, wherein the variant Fc region is a variant IgG Fc region.~~
9. ~~_____ The method of any one of claims 2-8, wherein the variant Fc region is a variant IgG1 Fc region.~~

- ~~10. The method of any one of claims 2-9, wherein the amino acid sequence of the Fc domains of the variant Fc region comprises an amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 2, and 3.~~
- ~~11. The method of any one of claims 1-9, wherein the isolated FcRn antagonist consists of a variant Fc region, wherein said variant Fc region consists of two Fc domains which form a homodimer, wherein the amino acid sequence of each of the Fc domains of the variant Fc region consists of SEQ ID NO: 1.~~
- ~~12. The method of any one of claims 1-9, wherein the isolated FcRn antagonist consists of a variant Fc region, wherein said variant Fc region consists of two Fc domains which form a homodimer, wherein the amino acid sequence of the Fc domains of the variant Fc region consists of SEQ ID NO: 2.~~
- ~~13. The method of any one of claims 1-9, wherein the isolated FcRn antagonist consists of a variant Fc region, wherein said variant Fc region consists of two Fc domains which form a homodimer, wherein the amino acid sequence of the Fc domains of the variant Fc region consists of SEQ ID NO: 3.~~
- ~~14. The method of any one of claims 2-13, wherein the variant Fc region binds to FcRn with increased affinity and reduced pH dependence relative to a native Fc region, for example a wild-type IgG Fc region, preferably a wild-type IgG1 Fc region.~~
- ~~15. The method of any one of claims 2-14, wherein the variant Fc region has increased affinity for CD16a.~~
- ~~16. The method of any one of claims 2-14, wherein the variant Fc region does not have increased affinity for CD16a.~~
- ~~17. The method of any one of claims 2-16, wherein the Fc domains of the variant Fc region comprise an N-linked glycan at EU position 297.~~
- ~~18. The method of any one of claims 2-17, wherein the Fc domains of the variant Fc region comprise a fucosylated N-linked glycan at EU position 297.~~

19. — ~~The method of any one of claims 2-18, wherein the Fc domains of the variant Fc region comprise an N-linked glycan having a bisecting GlcNAc at EU position 297.~~

20. — ~~The method of any one of claims 2-17, wherein the Fc domains of the variant Fc region comprise an afucosylated N-linked glycan at EU position 297.~~

21. — ~~The method of any one of claims 1-20, wherein the FcRn antagonist comprises a plurality of FcRn antagonist molecules, wherein at least 50% of the plurality of FcRn antagonist molecules comprise a variant Fc region or FcRn-binding fragment thereof.~~

22. — ~~The method of any one of the preceding claims, wherein the FcRn antagonist is administered to the subject 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, or 22 times in 22 days.~~

23. — ~~The method of claim 22, wherein the FcRn antagonist is administered to the subject at a frequency of once every 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, or 22 days.~~

24. — ~~The method of claim 23, wherein the FcRn antagonist is administered to the subject at a frequency of once every 3 days.~~

25. — ~~The method of claim 23, wherein the FcRn antagonist is administered to the subject at a frequency of once every 7 days.~~

26. — ~~The method of any one of the preceding claims, wherein the FcRn antagonist is administered to the subject in a dose of between about 1 and about 200 mg/kg.~~

27. — ~~The method of claim 26, wherein the FcRn antagonist is administered to the subject in a dose of about 1, 2, 3, 5, 10, 20, 25, 30, 50, 70, 100, or 200 mg/kg.~~

28. — ~~The method of claim 26, wherein the FcRn antagonist is administered to the subject in a dose of about 5 mg/kg.~~

29. — ~~The method of claim 26, wherein the FcRn antagonist is administered to the subject in a dose of about 10 mg/kg.~~

30. — ~~The method of claim 26, wherein the FcRn antagonist is administered to the subject in a dose of about 20 mg/kg.~~

31. — ~~The method of claim 26, wherein the FcRn antagonist is administered to the subject in a dose of about 25 mg/kg.~~

32. — ~~The method of any one of the previous claims, wherein the FcRn antagonist is administered to the subject in a dose selected from the group consisting of about 150, 300, 450, 600, 750, 900, 1050, and 1200 mg.~~

33. — ~~The method of claim 32, wherein the FcRn antagonist is administered to the subject in a dose of about 150 mg.~~

34. — ~~The method of claim 32, wherein the FcRn antagonist is administered to the subject in a dose of about 300 mg.~~

35. — ~~The method of claim 32, wherein the FcRn antagonist is administered to the subject in a dose of about 450 mg.~~

36. — ~~The method of any one of claims 22-35, wherein at least one additional dose of the FcRn antagonist is administered to the subject.~~

37. — ~~The method of any one of claims 1-36, wherein the FcRn antagonist is administered intravenously.~~

38. — ~~The method of any one of claims 1-36, wherein the FcRn antagonist is administered subcutaneously.~~

39. — ~~The method of any one of claims 1-36, wherein a first one or more doses are administered to the subject intravenously, and wherein one or more subsequent doses are administered subcutaneously.~~

40. — ~~The method of claim 39, wherein the first 1, 2, 3, or 4 doses are administered to the subject intravenously, and wherein 1, 2, 3, or 4 subsequent doses are administered to the subject subcutaneously.~~

41. — ~~The method of claim 39, wherein the first 4 doses are administered to the subject intravenously, and wherein 1, 2, 3, or 4 subsequent doses are administered to the subject subcutaneously.~~

42. — ~~The method of claim 39, wherein 1 dose is administered to the subject intravenously and 4 subsequent doses are administered to the subject subcutaneously.~~

43. — ~~The method of claim 39, wherein 2 doses are administered to the subject intravenously and 4 subsequent doses are administered to the subject subcutaneously.~~

44. — ~~A method of treating generalized myasthenia gravis in a subject, the method comprising administering to the subject an isolated FcRn antagonist using a phased dosing schedule with an induction phase comprising about 1-5 doses of the isolated FcRn antagonist within 1 month, followed by a maintenance phase comprising a dose of FcRn antagonist every week (q1w), every two weeks (q2w), every three weeks (q3w), or every 4 weeks (q4w) thereafter, thereby treating the generalized myasthenia gravis in the subject.~~

45. — ~~The method of claim 44, wherein the isolated FcRn antagonist consists of a variant Fc region, wherein said variant Fc region consists of two Fc domains which form a homodimer, wherein the amino acid sequence of each of the Fc domains of the variant Fc region consists of SEQ ID NO: 1.~~

46. — ~~The method of claim 44, wherein the isolated FcRn antagonist consists of a variant Fc region, wherein said variant Fc region consists of two Fc domains which form a homodimer, wherein the amino acid sequence of the Fc domains of the variant Fc region consists of SEQ ID NO: 2.~~

47. — ~~The method of claim 44, wherein the isolated FcRn antagonist consists of a variant Fc region, wherein said variant Fc region consists of two Fc domains which form a homodimer,~~

~~wherein the amino acid sequence of the Fc domains of the variant Fc region consists of SEQ ID NO: 3.~~

~~48. The method of any one of claims 44-47, wherein the induction phase comprises administration of 1, 2, 3, 4, or 5 doses of about 5 mg/kg, about 10 mg/kg, about 15 mg/kg or about 20 mg/kg of FcRn antagonist.~~

~~49. The method of any one of claims 44-48, wherein the 1-5 doses of the induction phase are administered intravenously (i.v.).~~

~~50. The method of any one of claims 44-49, wherein the maintenance phase doses comprise fixed dose of about 150 mg or about 300 mg of FcRn antagonist.~~

~~51. The method of any one of claims 44-50, wherein the maintenance phase doses are administered on an as-needed basis depending on clinical symptoms of the subject.~~

~~52. The method of any one of claims 44-51, wherein the maintenance phase doses are administered subcutaneously (s.c.) to the subject.~~

~~53. The method of claim 49, wherein 1 dose is administered to the subject intravenously and 1, 2 or 3 subsequent doses are administered to the subject subcutaneously.~~

~~54. The method of claim 49, wherein 1 dose is administered to the subject intravenously and 4 subsequent doses are administered to the subject subcutaneously.~~

~~55. The method of claim 49, wherein 2 doses are administered to the subject intravenously and 1 subsequent dose is administered to the subject subcutaneously.~~

~~56. The method of claim 49, wherein 2 doses are administered to the subject intravenously and 2 subsequent doses are administered to the subject subcutaneously.~~

~~57. The method of claim 49, wherein 2 doses are administered to the subject intravenously and 3 subsequent doses are administered to the subject subcutaneously.~~

58. — ~~The method of claim 49, wherein 2 doses are administered to the subject intravenously and 4 subsequent doses are administered to the subject subcutaneously.~~

59. — ~~The method of claim 49, wherein 3 doses are administered to the subject intravenously and 1 subsequent dose is administered to the subject subcutaneously.~~

60. — ~~The method of claim 49, wherein 3 doses are administered to the subject intravenously and 2 subsequent doses are administered to the subject subcutaneously.~~

61. — ~~The method of claim 49, wherein 3 doses are administered to the subject intravenously and 3 subsequent doses are administered to the subject subcutaneously.~~

62. — ~~The method of claim 49, wherein 3 doses are administered to the subject intravenously and 4 subsequent doses are administered to the subject subcutaneously.~~

63. — ~~The method of claim 49, wherein 4 doses are administered to the subject intravenously and 1 subsequent dose is administered to the subject subcutaneously.~~

64. — ~~The method of claim 49, wherein 4 doses are administered to the subject intravenously and 2 subsequent doses are administered to the subject subcutaneously.~~

65. — ~~The method of claim 49, wherein 4 doses are administered to the subject intravenously and 3 subsequent doses are administered to the subject subcutaneously.~~

66. — ~~The method of claim 49, wherein 4 doses are administered to the subject intravenously and 4 subsequent doses are administered to the subject subcutaneously.~~

67. — ~~The method of any one of claims 44-66, wherein one or more doses of the FcRn antagonist are administered as a retreatment, a maintenance dose, or a tapering dose.~~

68. — ~~The method of any one of claims 1-67, wherein the FcRn antagonist is administered to the subject simultaneously with an additional therapeutic agent.~~

69. — The method of any one of claims 1-67, wherein the FcRn antagonist is administered to the subject sequentially with an additional therapeutic agent.

70. — The method of claim 68 or claim 69, wherein dosage of the additional therapeutic agent is tapered in conjunction with treatment with the FcRn antagonist.

71. — The method of any one of the preceding claims, wherein administration of the isolated FcRn antagonist treats one or more exacerbations of the generalized myasthenia gravis.

72. — The method of any one of the preceding claims, wherein administration of the isolated FcRn antagonist improves one or more clinical symptoms of the generalized myasthenia gravis selected from the group consisting of ocular muscle fatigue or weakness, skeletal muscle fatigue or weakness, respiratory muscle fatigue or weakness, disabling fatigue, slurred speech, choking, impaired swallowing, double or blurred vision, immobility requiring assistance, shortness of breath, and respiratory failure.

73. — The method of claim 72, wherein the FcRn antagonist is administered to the subject 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, or 22 times in 22 days.

74. — The method of any one of the preceding claims, wherein administration of the isolated FcRn antagonist improves one or more therapeutic evaluation scores in the subject selected from the group consisting of Quantitative Myasthenia Gravis (QMG) score, Myasthenia Gravis activities of daily living (MG-ADL) score, Myasthenia Gravis composite (MGC) score, 15-item Quality of life scale for Myasthenia Gravis (MGQoL15r), and EuroQoL 5-Dimension (EQ-5D) score.

75. — The method of claim 74, wherein the score on at least one scale selected from the group consisting of QMG, MG-ADL, MGC, MGQoL15r, and EQ-5D is improved by at least one point at day 8, 15, 22, 29, or 36 compared to a baseline score as measured using the same scale prior to administration of the isolated FcRn antagonist at day 1.

76. — The method of claim 75, wherein the QMG score is improved at day 8, 15, 22, 29, or 36 compared to a baseline QMG score as measured prior to administration of the isolated FcRn antagonist at day 1.

77. — ~~The method of claim 76, wherein the QMG score is decreased by at least 3 points at day 8, 15, 22, 29, or 36 compared to a baseline QMG score as measured prior to administration of the isolated FcRn antagonist at day 1.~~

78. — ~~The method of claim 76, wherein the QMG score is decreased by at least 4 points at day 8, 15, 22, 29, or 36 compared to a baseline QMG score as measured prior to administration of the isolated FcRn antagonist at day 1.~~

79. — ~~The method of claim 75, wherein the MG-ADL score is improved at day 8, 15, 22, 29, or 36 compared to a baseline MG-ADL score as measured prior to administration of the isolated FcRn antagonist at day 1.~~

80. — ~~The method of claim 79, wherein the MG-ADL score is decreased by at least 2 points at day 8, 15, 22, 29, or 36 compared to a baseline MG-ADL score as measured prior to administration of the isolated FcRn antagonist at day 1.~~

81. — ~~The method of claim 79, wherein the MG-ADL score is decreased by at least 3 points at day 8, 15, 22, 29, or 36 compared to a baseline MG-ADL score as measured prior to administration of the isolated FcRn antagonist at day 1.~~

82. — ~~The method of claim 75, wherein the MGC score is improved at day 8, 15, 22, 29, or 36 compared to a baseline MGC score as measured prior to administration of the isolated FcRn antagonist at day 1.~~

83. — ~~The method of claim 82, wherein the MGC score is decreased by at least 4 points at day 8, 15, 22, 29, or 36 compared to a baseline MGC score as measured prior to administration of the isolated FcRn antagonist at day 1.~~

84. — ~~The method of claim 82, wherein the MGC score is decreased by at least 5 points at day 8, 15, 22, 29, or 36 compared to a baseline MGC score as measured prior to administration of the isolated FcRn antagonist at day 1.~~

85. — ~~The method of claim 75, wherein the MGQoL15r score is improved at day 8, 15, 22, 29, or 36 compared to a baseline MGQoL15r score as measured prior to administration of the isolated FcRn antagonist at day 1.~~

86. — ~~The method of claim 85, wherein the MGQoL15r score is decreased by at least 3 points at day 8, 15, 22, 29, or 36 compared to a baseline MGQoL15r score as measured prior to administration of the isolated FcRn antagonist at day 1.~~

87. — ~~The method of claim 85, wherein the MGQoL15r score is decreased by at least 4 points at day 8, 15, 22, 29, or 36 compared to a baseline MGQoL15r score as measured prior to administration of the isolated FcRn antagonist at day 1.~~

88. — ~~The method of claim 75, wherein the EQ-5D score is improved at day 8, 15, 22, 29, or 36 compared to a baseline EQ-5D score as measured prior to administration of the isolated FcRn antagonist at day 1.~~

89. — ~~The method of any one of the preceding claims, wherein administration of the isolated FcRn antagonist reduces serum level of at least one IgG antibody selected from the group consisting of total serum IgG, anti-acetylcholine receptor (AChR) antibody, anti-MuSK antibody, and anti-LRP4 antibody.~~

90. — ~~The method of claim 89, wherein the FcRn antagonist is administered to the subject 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, or 22 times in 22 days, and wherein the serum level of the at least one IgG antibody is reduced at day 8, 15, 22, 29, or 36 compared to a baseline serum level of the at least one IgG antibody as measured prior to administration of the isolated FcRn antagonist at day 1.~~

91. — ~~The method of claim 90, wherein the serum level of the at least one IgG antibody is reduced by at least about 25% at day 8, 15, 22, 29, or 36.~~

92. — ~~The method of claim 90, wherein the serum level of the at least one IgG antibody is reduced by at least about 50% at day 8, 15, 22, 29, or 36.~~

~~93. The method of any one of claims to 89-92, wherein the at least one IgG antibody is total serum IgG antibody.~~

~~94. The method of any one of claims to 89-92, wherein the at least one IgG antibody is an anti-AChR antibody.~~

~~95. The method of any one of claims to 89-92, wherein the at least one IgG antibody is an anti-MuSK antibody.~~

~~96. The method of any one of claims to 89-92, wherein the at least one IgG antibody is an anti-LRP4 antibody.~~

~~97. The method of any one of the preceding claims, wherein the subject has a QMG score of at least 11 points with no more than 25% of the total points due to ocular symptoms as measured prior to first administration of the isolated FcRn antagonist.~~

~~98. The method of any one of the preceding claims, wherein the subject has a MG-ADL score of at least 5 points with no more than 25% of the total points due to ocular symptoms as measured prior to first administration of the isolated FcRn antagonist.~~

~~99. The method of any one of the preceding claims, wherein the subject, prior to first administration of the isolated FcRn antagonist, has confirmed diagnosis generalized MG, has Class II-IVa disease according to the Myasthenia Gravis Foundation of America (MGFA) classification system, and has an MG-ADL score of at least 5 with more than 50% of the score attributable to non-ocular items.~~

~~100. The method of any one of the preceding claims, wherein the subject concurrently is receiving standard myasthenia gravis therapy.~~

~~101. The method of any one of one of the preceding claims, wherein the generalized myasthenia gravis is refractory generalized myasthenia gravis.~~

~~102. The method of any one of claims 1-101, wherein the generalized myasthenia gravis is not responsive to a standard myasthenia gravis therapy selected from the group consisting of~~

~~intravenous immunoglobulin (IVIg), plasmapheresis, azathioprine, non-steroidal immunosuppressant drugs, steroids, cholinesterase inhibitors, immunoadsorption, and eculizumab.~~

~~103. The method of any one of claims 1-101, wherein the subject is intolerant to a standard myasthenia gravis therapy selected from the group consisting of intravenous immunoglobulin (IVIg), plasmapheresis, azathioprine, non-steroidal immunosuppressant drugs, steroids, cholinesterase inhibitors, immunoadsorption, and eculizumab.~~

~~104. The method of any one of claims 1-101, wherein the subject shows marked generalized weakness or bulbar signs and symptoms of myasthenia gravis while receiving therapy for myasthenia gravis including anticholinesterase inhibitor therapy and immunosuppressant therapy and requires chronic plasma exchange or chronic IVIg to maintain clinical stability.~~

~~105. The method of any one of claims 1-104, wherein the subject is positive for auto-antibodies binding to nicotinic acetylcholine receptor (anti-AChR).~~

~~106. The method of any one of claims 1-104, wherein the subject is negative for auto-antibodies binding to nicotinic acetylcholine receptor (anti-AChR).~~

~~107. The method of any one of claims 1-106, wherein the subject is anti-MuSK antibody positive.~~

~~108. The method of any one of claims 1-106, wherein the subject is anti-MuSK antibody negative.~~

~~109. The method of any one of claims 1-108, wherein the subject is anti-LRP4 antibody positive.~~

~~110. The method of any one of claims 1-108, wherein the subject is anti-LRP4 antibody negative.~~

~~111. The method of any one of the preceding claims, wherein the subject is a human.~~

~~112. The method of any one of the preceding claims, wherein the subject is an adult human.~~

~~113. A method of treating generalized myasthenia gravis (MG) in a subject, the method comprising administering to the subject an effective amount of an isolated FcRn antagonist, thereby treating MG in the subject, wherein:~~

~~the subject, prior to first administration of the isolated FcRn antagonist, has confirmed diagnosis generalized MG, has Class II-IVa disease according to the Myasthenia Gravis Foundation of America (MGFA) classification system, and has an MG-ADL score of at least 5 with more than 50% of the score attributable to non-ocular items,~~

~~the isolated FcRn antagonist consists of a variant Fc region, wherein said variant Fc region consists of two Fc domains which form a homodimer, wherein the amino acid sequence of each of the Fc domains of the variant Fc region consists of SEQ ID NO: 2, and~~

~~the isolated FcRn antagonist is administered to the subject in a dose of about 10 mg/kg.~~

~~114. A method of treating generalized myasthenia gravis in a subject, the method comprising administering to the subject an isolated FcRn antagonist using a phased dosing schedule with an induction phase comprising about 1-5 doses of the isolated FcRn antagonist within 1 month, followed by a maintenance phase comprising a dose of FcRn antagonist every week (q1w), every two weeks (q2w), every three weeks (q3w), or every 4 weeks (q4w) thereafter, thereby treating the generalized myasthenia gravis in the subject, wherein:~~

~~the subject, prior to first administration of the isolated FcRn antagonist, has confirmed diagnosis generalized MG, has Class II-IVa disease according to the Myasthenia Gravis Foundation of America (MGFA) classification system, and has an MG-ADL score of at least 5 with more than 50% of the score attributable to non-ocular items,~~

~~the isolated FcRn antagonist consists of a variant Fc region, wherein said variant Fc region consists of two Fc domains which form a homodimer, wherein the amino acid sequence of each of the Fc domains of the variant Fc region consists of SEQ ID NO: 2, and~~

~~the isolated FcRn antagonist is administered to the subject in a dose of about 10 mg/kg.~~

~~115. A method of treating generalized myasthenia gravis in a subject, the method comprising administering to the subject an isolated FcRn antagonist using a phased dosing schedule with an induction phase comprising about 1-5 doses of the isolated FcRn antagonist within 1 month, followed by a maintenance phase comprising one or more cycles as needed based on clinical need thereafter, each cycle comprising administering to the subject about 1-5 doses of the~~

~~isolated FcRn antagonist within 1 month, thereby treating the generalized myasthenia gravis in the subject, wherein:~~

~~the subject, prior to first administration of the isolated FcRn antagonist in the induction phase, has confirmed diagnosis generalized MG, has Class II-IVa disease according to the Myasthenia Gravis Foundation of America (MGFA) classification system, and has an MG-ADL score of at least 5 with more than 50% of the score attributable to non-ocular items,~~

~~the subject, prior to first administration of the isolated FcRn antagonist in any cycle of the maintenance phase, has an MG-ADL score of at least 5 with more than 50% of the score attributable to non-ocular items,~~

~~the isolated FcRn antagonist consists of a variant Fc region, wherein said variant Fc region consists of two Fc domains which form a homodimer, wherein the amino acid sequence of each of the Fc domains of the variant Fc region consists of SEQ ID NO: 2, and~~

~~the isolated FcRn antagonist is administered to the subject in a dose of about 10 mg/kg.~~

~~116. The method of any one of claims 113-115, wherein the subject is an adult human with generalized myasthenia gravis.~~

~~117. The method of any one of claims 113-116, wherein the subject is an adult human with generalized myasthenia gravis whose symptoms are inadequately controlled with acetylcholinesterase inhibitors, steroids, or immunosuppressive therapies.~~

~~118. The method of any one of claims 113-117, wherein the subject is an adult human with generalized myasthenia gravis who is positive for auto-antibodies binding to nicotinic acetylcholine receptor (anti-AChR).~~

~~119. The method of any one of claims 113-118, wherein the subject is an adult human with generalized myasthenia gravis who is positive for auto-antibodies binding to nicotinic acetylcholine receptor (anti-AChR) and whose symptoms are inadequately controlled with acetylcholinesterase inhibitors, steroids, or immunosuppressive therapies.~~

~~120. The method of any one of claims 113-117, wherein the subject is an adult human with generalized myasthenia gravis who is negative for auto-antibodies binding to nicotinic acetylcholine receptor (anti-AChR).~~

~~121. The method of any one of claims 113-118, wherein the subject is an adult human with generalized myasthenia gravis who is negative for auto-antibodies binding to nicotinic acetylcholine receptor (anti-AChR) and whose symptoms are inadequately controlled with acetylcholinesterase inhibitors, steroids, or immunosuppressive therapies.~~

~~122. The method of any one of claims 113-118, wherein the subject is an adult human with generalized myasthenia gravis who is positive for auto-antibodies binding to nicotinic acetylcholine receptor (anti-AChR) and positive for auto-antibodies binding to muscle-specific kinase (MuSK).~~

~~123. The method of any one of claims 113-118, wherein the subject is an adult human with generalized myasthenia gravis who is positive for auto-antibodies binding to nicotinic acetylcholine receptor (anti-AChR) and positive for auto-antibodies binding to muscle-specific kinase (MuSK) and whose symptoms are inadequately controlled with acetylcholinesterase inhibitors, steroids, or immunosuppressive therapies.~~

~~124. The method of any one of claims 113-118, wherein the subject is an adult human with generalized myasthenia gravis who is negative for auto-antibodies binding to nicotinic acetylcholine receptor (anti-AChR) and negative for auto-antibodies binding to muscle-specific kinase (MuSK).~~

~~125. The method of any one of claims 113-118, wherein the subject is an adult human with generalized myasthenia gravis who is negative for auto-antibodies binding to nicotinic acetylcholine receptor (anti-AChR) and negative for auto-antibodies binding to muscle-specific kinase (MuSK) and whose symptoms are inadequately controlled with acetylcholinesterase inhibitors, steroids, or immunosuppressive therapies.~~

1. An invention not claimed in any divisional application.