

## CLAIMS

What is claimed is:

1. Use of an anti-TREM2 antibody in the manufacture of a medicament for~~A method of~~ treating and/or delaying the progression of a disease or injury in an individual, wherein the medicament is to be administered intravenously~~comprising administering to the individual an anti-TREM2 antibody~~ at a dose of at least about 15 mg/kg ~~intravenously~~, and wherein the anti-TREM2 antibody is an agonist.
2. Use of an anti-TREM2 antibody in the manufacture of a medicament for~~A method of~~ treating and/or delaying the progression of a disease or injury in an individual, wherein the medicament is to be administered intravenously~~comprising administering to the individual an anti-TREM2 antibody~~ at a dose of at least about 15 mg/kg ~~intravenously~~, wherein the antibody comprises a heavy chain variable region comprising an HVR-H1, HVR-H2, and HVR-H3 and a light chain variable region comprising an HVR-L1, HVR-L2, and HVR-L3, and wherein:
  - (i) the HVR-H1 comprises the amino acid sequence YAFSSQWMN (SEQ ID NO: 34), the HVR-H2 comprises the amino acid sequence RIYPGGGDTNYAGKFQG (SEQ ID NO: 35), the HVR-H3 comprises the amino acid sequence ARLLRNQPGESYAMDY (SEQ ID NO: 31), the HVR-L1 comprises the amino acid sequence RSSQSLVHSNRYTYLH (SEQ ID NO: 41), the HVR-L2 comprises the amino acid sequence KVSNRFS (SEQ ID NO: 33), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 32); or
  - (ii) the HVR-H1 comprises the amino acid sequence YAFSSDWMN (SEQ ID NO: 36), the HVR-H2 comprises the amino acid sequence RIYPGEGDTNYARKFHG (SEQ ID NO: 37), the HVR-H3 comprises the amino acid sequence ARLLRNKPGESYAMDY (SEQ ID NO: 38), the HVR-L1 comprises the amino acid sequence RTSQSLVHSNAYTYLH (SEQ ID NO: 39), the HVR-L2 comprises the amino acid sequence KVSNRVS (SEQ ID NO: 40), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 32).
3. The ~~method-use~~ of claim 1 or claim 2, wherein:
  - (a) the dose is:
    - (i) between about 15 mg/kg to about 60 mg/kg;
    - (ii) about 15 mg/kg, about 20 mg/kg, about 25 mg/kg, about 30 mg/kg, about 35 mg/kg, about 40 mg/kg, about 45 mg/kg, about 50 mg/kg, about 55 mg/kg, or about 60 mg/kg;
    - (iii) about 15 mg/kg, wherein the terminal half-life of the antibody in the plasma of the

individual is about 8.63 days;

(iv) about 30 mg/kg, wherein the terminal half-life of the antibody in the plasma of the individual is about 7.44 days;

(v) about 45 mg/kg, wherein the terminal half-life of the antibody in the plasma of the individual is about 8.40 days; or

(vi) about 60 mg/kg, wherein the terminal half-life of the antibody in the plasma of the individual is about 9.93 days; or

(b) the medicament is to be administered:

(i) about once every four weeks at a dose of at least about 15 mg/kg;

(ii) about once every week at a dose of at least about 15 mg/kg;

(iii) about once every four weeks at a dose of about 15 mg/kg;

(iv) about once every four weeks at a dose of about 20 mg/kg;

(v) about once every four weeks at a dose of about 25 mg/kg;

(vi) about once every four weeks at a dose of about 30 mg/kg;

(vii) about once every four weeks at a dose of about 35 mg/kg;

(viii) about once every four weeks at a dose of about 40 mg/kg;

(ix) about once every four weeks at a dose of about 45 mg/kg;

(x) about once every four weeks at a dose of about 50 mg/kg;

(xi) about once every four weeks at a dose of about 55 mg/kg; or

(xii) about once every four weeks at a dose of about 60 mg/kg.

~~4. The method of any one of claims 1-3, wherein the dose is about 15 mg/kg, about 20 mg/kg, about 25 mg/kg, about 30 mg/kg, about 35 mg/kg, about 40 mg/kg, about 45 mg/kg, about 50 mg/kg, about 55 mg/kg, or about 60 mg/kg.~~

~~5. The method of any one of claims 1-4, wherein the anti-TREM2 antibody is administered about once every four weeks at a dose of at least about 15 mg/kg.~~

~~6. The method of any one of claims 1-4, wherein the anti-TREM2 antibody is administered about once every week at a dose of at least about 15 mg/kg.~~

~~7. The method of any one of claims 1-5, wherein the anti-TREM2 antibody is administered about once every four weeks at a dose of about 15 mg/kg.~~

- ~~8. The method of any one of claims 1-5, wherein the anti-TREM2 antibody is administered about once every four weeks at a dose of about 20 mg/kg.~~
- ~~9. The method of any one of claims 1-5, wherein the anti-TREM2 antibody is administered about once every four weeks at a dose of about 25 mg/kg.~~
- ~~10. The method of any one of claims 1-5, wherein the anti-TREM2 antibody is administered about once every four weeks at a dose of about 30 mg/kg.~~
- ~~11. The method of any one of claims 1-5, wherein the anti-TREM2 antibody is administered about once every four weeks at a dose of about 35 mg/kg.~~
- ~~12. The method of any one of claims 1-5, wherein the anti-TREM2 antibody is administered about once every four weeks at a dose of about 40 mg/kg.~~
- ~~13. The method of any one of claims 1-5, wherein the anti-TREM2 antibody is administered about once every four weeks at a dose of about 45 mg/kg.~~
- ~~14. The method of any one of claims 1-5, wherein the anti-TREM2 antibody is administered about once every four weeks at a dose of about 50 mg/kg.~~
- ~~15. The method of any one of claims 1-5, wherein the anti-TREM2 antibody is administered about once every four weeks at a dose of about 55 mg/kg.~~
- ~~16. The method of any one of claims 1-5, wherein the anti-TREM2 antibody is administered about once every four weeks at a dose of about 60 mg/kg.~~
- ~~17.4. The method-use of any one of claims 1-316, wherein the antibody comprises:~~
- ~~(a) a heavy chain variable region comprising an HVR-H1, HVR-H2, and HVR-H3 and a light chain variable region comprising an HVR-L1, HVR-L2, and HVR-L3, wherein the HVR-H1 comprises the amino acid sequence YAFSSQWMN (SEQ ID NO: 34), the HVR-H2 comprises the amino acid sequence RIYPGGGDTNYAGKFQG (SEQ ID NO: 35), the HVR-H3 comprises the amino acid sequence ARLLRNQPGESYAMDY (SEQ ID NO: 31), the HVR-L1 comprises the amino acid sequence RSSQSLVHSNRYTYLH (SEQ ID NO: 41), the HVR-L2 comprises the amino acid sequence KVSNRFS (SEQ ID NO: 33), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 32);~~
- ~~(b) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 27 and a light~~

chain variable region comprising the amino acid sequence of SEQ ID NO: 30;

(c) a heavy chain variable region comprising an HVR-H1, HVR-H2, and HVR-H3 and a light chain variable region comprising an HVR-L1, HVR-L2, and HVR-L3, wherein the HVR-H1 comprises the amino acid sequence YAFSSDWMN (SEQ ID NO: 36), the HVR-H2 comprises the amino acid sequence RIYPGEGDTNYARKFHG (SEQ ID NO: 37), the HVR-H3 comprises the amino acid sequence ARLLRNKPGESYAMDY (SEQ ID NO: 38), the HVR-L1 comprises the amino acid sequence RTSQSLVHSNAYTYLH (SEQ ID NO: 39), the HVR-L2 comprises the amino acid sequence KVSNRVS (SEQ ID NO: 40), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 32); or

(d) a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 28 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 29.

~~18. The method of any one of claims 1-17, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 27 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 30.~~

~~19. The method of any one of claims 1-16, wherein the antibody comprises a heavy chain variable region comprising an HVR-H1, HVR-H2, and HVR-H3 and a light chain variable region comprising an HVR-L1, HVR-L2, and HVR-L3, wherein the HVR-H1 comprises the amino acid sequence YAFSSDWMN (SEQ ID NO: 36), the HVR-H2 comprises the amino acid sequence RIYPGEGDTNYARKFHG (SEQ ID NO: 37), the HVR-H3 comprises the amino acid sequence ARLLRNKPGESYAMDY (SEQ ID NO: 38), the HVR-L1 comprises the amino acid sequence RTSQSLVHSNAYTYLH (SEQ ID NO: 39), the HVR-L2 comprises the amino acid sequence KVSNRVS (SEQ ID NO: 40), and the HVR-L3 comprises the amino acid sequence SQSTRVPYT (SEQ ID NO: 32).~~

~~20. The method of any one of claims 1-16 or 19, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 28 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 29.~~

~~21.5. \_\_\_\_\_~~ The method-use of any one of claims 1-~~420~~, wherein the antibody:

(a) has a human IgG1 isotype;

(b) has a human IgG1 isotype and comprises amino acid substitutions in the Fc region at the residue positions P331S and E430G, wherein the numbering of the residues is according to EU numbering;

(c) comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 43, and a light

chain comprising the amino acid sequence of SEQ ID NO: 47;

(d) comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 44, and a light chain comprising the amino acid sequence of SEQ ID NO: 47;

(e) comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 45, and a light chain comprising the amino acid sequence of SEQ ID NO: 48; or

(f) comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 46, and a light chain comprising the amino acid sequence of SEQ ID NO: 48.

~~22. The method of any one of claims 1-21, wherein the antibody has a human IgG1 isotype and comprises amino acid substitutions in the Fe region at the residue positions P331S and E430G, wherein the numbering of the residues is according to EU numbering.~~

~~23. The method of any one of claims 1-18 or 21-22, wherein the antibody comprises:~~

~~a. a heavy chain comprising the amino acid sequence of SEQ ID NO: 43, and a light chain comprising the amino acid sequence of SEQ ID NO: 47; or~~

~~b. a heavy chain comprising the amino acid sequence of SEQ ID NO: 44, and a light chain comprising the amino acid sequence of SEQ ID NO: 47.~~

~~24. The method of any one of claims 1-16 or 19-21, wherein the antibody comprises:~~

~~a. a heavy chain comprising the amino acid sequence of SEQ ID NO: 45, and a light chain comprising the amino acid sequence of SEQ ID NO: 48; or~~

~~b. a heavy chain comprising the amino acid sequence of SEQ ID NO: 46, and a light chain comprising the amino acid sequence of SEQ ID NO: 48.~~

~~25.6. \_\_\_\_\_~~ The ~~method-use~~ of any one of claims 1-~~524~~, wherein the disease or injury is selected from the group consisting of dementia, frontotemporal dementia, Alzheimer's disease, ~~Nasu-Hakola disease~~, cognitive deficit, memory loss, a demyelination disorder, multiple sclerosis, Parkinson's disease, amyotrophic lateral sclerosis (ALS), Huntington's disease, adult-onset leukoencephalopathy with axonal spheroids and pigmented glia (ALSP), and a tauopathy disease.

~~26. The method of any one of claims 1-25, wherein the disease or injury is Alzheimer's disease.~~

~~27.7.~~ The ~~method-use~~ of claim ~~26~~, wherein ~~the disease or injury is Alzheimer's disease, and~~  
~~wherein:~~

- ~~(a) the individual has a Mini-Mental State Examination (MMSE) score of between about 16 points to about 28 points prior to administration of the anti-TREM2 antibody;~~
- ~~(b) the individual has a Clinical Dementia Rating-Global Score (CDR-GS) of 0.5, 1.0, or 2.0 prior to administration of the anti-TREM2 antibody;~~
- ~~(c) the individual has a positive amyloid-PET scan prior to administration of the anti-TREM2 antibody;~~
- ~~(d) the individual is being administered a cholinesterase inhibitor and/or memantine therapy; and/or~~
- ~~(e) the individual has symptoms of Alzheimer's disease prior to administration of the anti-TREM2 antibody, or the individual does not have symptoms of Alzheimer's disease prior to administration of the anti-TREM2 antibody.~~

~~28. The method of claim 26 or claim 27, wherein the individual has a Clinical Dementia Rating-Global Score (CDR-GS) of 0.5, 1.0, or 2.0 prior to administration of the anti-TREM2 antibody.~~

~~29. The method of any one of claims 26-28, wherein the individual has a positive amyloid-PET scan prior to administration of the anti-TREM2 antibody.~~

~~30. The method of any one of claims 26-29, wherein the individual is being administered a cholinesterase inhibitor and/or memantine therapy.~~

~~31. The method of any one of claims 26-30, wherein the individual has symptoms of Alzheimer's disease prior to administration of the anti-TREM2 antibody.~~

~~32.8.~~ The ~~method-use~~ of claim ~~734~~, wherein the symptoms ~~of Alzheimer's disease~~ are mild cognitive impairment and/or mild dementia.

~~33. The method of any one of claims 26-30, wherein the individual does not have symptoms of Alzheimer's disease prior to administration of the anti-TREM2 antibody.~~

~~34.9.~~ The ~~method-use~~ of any one of claims 1-~~833~~, wherein:

- ~~(a) the individual is heterozygous or homozygous for a mutation in TREM2;~~
- ~~(b) the individual comprises an amino acid substitution in a human TREM2 protein at residue position R47H, R62H, or both; and/or~~

(c) the individual has a positive amyloid or tau blood test prior to administration of the anti-TREM2 antibody.

~~35. The method of any one of claims 1-34, wherein the individual comprises an amino acid substitution in a human TREM2 protein at residue position R47H, R62H, or both.~~

~~36. The method of any one of claims 1-35, wherein the individual has a positive amyloid or tau blood test prior to administration of the anti-TREM2 antibody.~~

~~37.10. \_\_\_\_\_~~ The ~~method-use~~ of any one of claims 1-~~936~~, wherein:

~~(a) administration of the anti-TREM2 antibody results in at least about a 30% or at least about a 40% decrease in the levels of soluble TREM2 in the cerebrospinal fluid of the individual, compared to the levels of soluble TREM2 in the cerebrospinal fluid of the individual prior to administration of the anti-TREM2 antibody; and/or~~

~~(b) administration of the anti-TREM2 antibody results in at least about a 5% increase in the levels of soluble CSF1R in the cerebrospinal fluid of the individual, compared to the levels of soluble CSF1R in the cerebrospinal fluid of the individual prior to administration of the anti-TREM2 antibody.~~

~~38. The method of any one of claims 1-37, wherein administration of the anti-TREM2 antibody results in at least about a 40% decrease in the levels of soluble TREM2 in the cerebrospinal fluid of the individual, compared to the levels of soluble TREM2 in the cerebrospinal fluid of the individual prior to administration of the anti-TREM2 antibody.~~

~~39.11. \_\_\_\_\_~~ The ~~method-use~~ of claim ~~37 or claim 38~~~~10~~, wherein:

~~(a) the decrease in the levels of soluble TREM2 in the cerebrospinal fluid of the individual is present at about 2 days after administration of the anti-TREM2 antibody;~~

~~(b) the levels of soluble TREM2 in the cerebrospinal fluid of the individual are measured in a sample of cerebrospinal fluid obtained from the individual using an electrochemiluminescent assay;~~

~~(c) the increase in the levels of soluble CSF1R in the cerebrospinal fluid of the individual is present at about 2 days after administration of the anti-TREM2 antibody; and/or~~

~~(d) the levels of soluble CSF1R in the cerebrospinal fluid of the individual are measured in a sample of cerebrospinal fluid obtained from the individual using an ELISA assay.~~

~~40. The method of any one of claims 37-39, wherein the levels of soluble TREM2 in the cerebrospinal fluid of the individual are measured in a sample of cerebrospinal fluid obtained from the individual using an electrochemiluminescent assay.~~

- ~~41. The method of any one of claims 1-40, wherein administration of the anti-TREM2 antibody results in at least about a 5% increase in the levels of soluble CSF1R in the cerebrospinal fluid of the individual, compared to the levels of soluble CSF1R in the cerebrospinal fluid of the individual prior to administration of the anti-TREM2 antibody.~~
- ~~42. The method of claim 41, wherein the increase in the levels of soluble CSF1R in the cerebrospinal fluid of the individual is present at about 2 days after administration of the anti-TREM2 antibody.~~
- ~~43. The method of claim 41 or claim 42, wherein the levels of soluble CSF1R in the cerebrospinal fluid of the individual are measured in a sample of cerebrospinal fluid obtained from the individual using an ELISA assay.~~
- 44.12. The method use of any one of claims 1-1143, wherein the use further comprising comprises:
- (a) measuring the levels of soluble TREM2 in a sample of blood, plasma, and/or cerebrospinal fluid from the individual before and after the individual has received one or more doses of the anti-TREM2 antibody;
  - (b) measuring the levels of soluble CSF1R in a sample of blood, plasma, and/or cerebrospinal fluid from the individual before and after the individual has received one or more doses of the anti-TREM2 antibody;
  - (c) measuring the levels of brain amyloid burden in the brain of the individual before and after the individual has received one or more doses of the anti-TREM2 antibody;
  - (d) measuring one or more brain abnormalities in the brain of the individual before and after the individual has received one or more doses of the anti-TREM2 antibody;
  - (e) detecting the presence of an alteration in one or more genes in the individual selected from the group consisting of APOE, TREM2, CD33, TMEM106b, and CLUSTERIN;
  - (f) measuring the levels of one or more biomarkers of neurodegeneration in a sample of blood, plasma, and/or cerebrospinal fluid from the individual before and after the individual has received one or more doses of the anti-TREM2 antibody;
  - (g) measuring the expression levels of TREM2, CSF1R, YKL40, IL-1RA, or osteopontin in a sample of blood, plasma, and/or cerebrospinal fluid from the individual before and after the individual has received one or more doses of the anti-TREM2 antibody;
  - (h) measuring the levels of one or more biomarkers of Alzheimer's disease in a sample of blood, plasma, and/or cerebrospinal fluid from the individual before and after the individual has received one or more doses of the anti-TREM2 antibody;
  - (i) determining a score of one or more clinical assessments of the individual before and after the

individual has received one or more doses of the anti-TREM2 antibody, wherein the one or more clinical assessments are selected from the group consisting of the Mini-Mental State Examination (MMSE) score, the Clinical Dementia Rating-Global Score (CDR-GS), the Clinical Dementia Rating Sum of Boxes (CDR-SB), and the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS); and/or

(j) performing tau or amyloid positron emission tomography (PET) imaging assessments in the individual before and after the individual has received one or more doses of the anti-TREM2 antibody.

~~45. The method of any one of claims 1-44, further comprising measuring the levels of soluble CSF1R in a sample of blood, plasma, and/or cerebrospinal fluid from the individual before and after the individual has received one or more doses of the anti-TREM2 antibody.~~

~~46. The method of any one of claims 1-45, further comprising measuring the levels of brain amyloid burden in the brain of the individual before and after the individual has received one or more doses of the anti-TREM2 antibody.~~

~~47.13. The method-use of claim 1246, wherein:~~

~~(a) the levels of brain amyloid burden in the brain of the individual are measured using amyloid-positron emission tomography;~~

~~(b) the one or more brain abnormalities are measured using magnetic resonance imaging;~~

~~(c) the one or more brain abnormalities comprise brain volume;~~

~~(d) the one or more biomarkers of neurodegeneration comprise neurofilament light; and/or~~

~~(e) the one or more biomarkers of Alzheimer's disease are A $\beta$ 40, A $\beta$ 42, pTau, and/or total tau.~~

~~48. The method of any one of claims 1-47, further comprising measuring one or more brain abnormalities in the brain of the individual before and after the individual has received one or more doses of the anti-TREM2 antibody.~~

~~49. The method of claim 48, wherein the one or more brain abnormalities are measured using magnetic resonance imaging.~~

~~50. The method of claim 48 or claim 49, wherein the one or more brain abnormalities is brain volume.~~

- ~~51. The method of any one of claims 1-50, further comprising detecting the presence of an alteration in one or more genes in the individual selected from the group consisting of APOE, TREM2, CD33, TMEM106b, and CLUSTERIN.~~
- ~~52. The method of any one of claims 1-51, further comprising measuring the levels of one or more biomarkers of neurodegeneration in a sample of blood, plasma, and/or cerebrospinal fluid from the individual before and after the individual has received one or more doses of the anti-TREM2 antibody.~~
- ~~53. The method of claim 52, wherein the one or more biomarkers of neurodegeneration is neurofilament light.~~
- ~~54. The method of any one of claims 1-53, further comprising measuring the expression levels of TREM2, CSF1R, YKL40, IL-1RA, or osteopontin in a sample of blood, plasma, and/or cerebrospinal fluid from the individual before and after the individual has received one or more doses of the anti-TREM2 antibody.~~
- ~~55. The method of any one of claims 1-54, further comprising measuring the levels of one or more biomarkers of Alzheimer's disease in a sample of blood, plasma, and/or cerebrospinal fluid from the individual before and after the individual has received one or more doses of the anti-TREM2 antibody.~~
- ~~56. The method of claim 55, wherein the one or more biomarkers of Alzheimer's disease are A $\beta$ 40, A $\beta$ 42, pTau, and/or total tau.~~
- ~~57. The method of any one of claims 1-56, further comprising determining a score of one or more clinical assessments of the individual before and after the individual has received one or more doses of the anti-TREM2 antibody, wherein the one or more clinical assessments are selected from the group consisting of the Mini-Mental State Examination (MMSE) score, the Clinical Dementia Rating-Global Score (CDR-GS), the Clinical Dementia Rating Sum of Boxes (CDR-SB), and the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS).~~
- ~~58. The method of any one of claims 1-57, further comprising performing tau or amyloid positron emission tomography (PET) imaging assessments in the individual before and after the individual has received one or more doses of the anti-TREM2 antibody.~~

~~59.14.~~ The ~~method-use~~ of any one of claims 1-~~1358~~, wherein the disease or injury is Alzheimer's disease, and wherein the Alzheimer's disease is early Alzheimer's disease.

~~60.15.~~ The ~~method-use~~ of claim ~~1459~~, wherein the individual:

(a) has brain amyloidosis prior to administration of the anti-TREM2 antibody, wherein brain amyloidosis is assessed in a sample of cerebrospinal fluid obtained from the individual, or by positron emission tomography (PET);

(b) has a Mini-Mental State Examination (MMSE) score of at least about 22 points prior to administration of the anti-TREM2 antibody;

(c) has a Clinical Dementia Rating-Global Score (CDR-GS) of between about 0.5 and about 1.0 prior to administration of the anti-TREM2 antibody;

(d) has a Repeatable Battery for the Assessment of Neuropsychological Status on the Delayed Memory Index (RBANS DMI) score of 85 or less prior to administration of the anti-TREM2 antibody; and/or

(e) has a positive amyloid or tau blood test prior to administration of the anti-TREM2 antibody.

~~61. The method of claim 59 or claim 60, wherein the individual has a Mini-Mental State Examination (MMSE) score of at least about 22 points prior to administration of the anti-TREM2 antibody.~~

~~62. The method of any one of claims 59-61, wherein the individual has a Clinical Dementia Rating-Global Score (CDR-GS) of between about 0.5 and about 1.0 prior to administration of the anti-TREM2 antibody.~~

~~63. The method of any one of claims 59-62, wherein the individual has a Repeatable Battery for the Assessment of Neuropsychological Status on the Delayed Memory Index (RBANS DMI) score of 85 or less prior to administration of the anti-TREM2 antibody.~~

~~64. The method of any one of claims 59-63, wherein the individual has a positive amyloid or tau blood test prior to administration of the anti-TREM2 antibody.~~

~~65.16.~~ The ~~method-use~~ of any one of claims ~~1459-1564~~, wherein the use further comprises:

(a) ~~further comprising~~ determining a score of one or more clinical assessments of the individual before and after the individual has received one or more doses of the anti-TREM2 antibody, wherein the one or more clinical assessments are selected from the group consisting of the Clinical Dementia Rating Sum of Boxes (CDR-SB), the Mini-Mental State Examination (MMSE), the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), the Alzheimer's Disease

Assessment Scale-Cognitive Subscale-13 (ADAS-Cog13), the Alzheimer's Disease Cooperative Study-Activities of Daily Living adapted to Mild Cognitive Impairment (ADCS-ADL-MCI), and the Alzheimer's Disease Composite Score (ADCOMS);

(b) measuring the levels of one or more biomarkers of Alzheimer's disease before and after the individual has received one or more doses of the anti-TREM2 antibody, wherein the one or more biomarkers of Alzheimer's disease are measured by magnetic resonance imaging (MRI) or in a sample of blood, plasma or cerebrospinal fluid obtained from the individual;

(c) performing tau or amyloid positron emission tomography (PET) imaging assessments in the individual before and after the individual has received one or more doses of the anti-TREM2 antibody; and/or

(d) performing one or more speech assessments in the individual before and after the individual has received one or more doses of the anti-TREM2 antibody.

~~66. The method of any one of claims 59-65, further comprising measuring the levels of one or more biomarkers of Alzheimer's disease before and after the individual has received one or more doses of the anti-TREM2 antibody, wherein the one or more biomarkers of Alzheimer's disease are measured by magnetic resonance imaging (MRI), or in a sample of blood, plasma or cerebrospinal fluid obtained from the individual.~~

~~67. The method of any one of claims 59-66, further comprising performing tau or amyloid positron emission tomography (PET) imaging assessments in the individual before and after the individual has received one or more doses of the anti-TREM2 antibody.~~

~~68. The method of any one of claims 59-67, further comprising performing one or more speech assessments in the individual before and after the individual has received one or more doses of the anti-TREM2 antibody.~~

69. The method of any one of claims 1-6 and 17-68, wherein (a) the dose is about 15 mg/kg and the terminal half life of the antibody in the plasma of the individual is about 8.63 days; (b) the dose is about 30 mg/kg and the terminal half life of the antibody in the plasma of the individual is about 7.44 days; (c) the dose is about 45 mg/kg and the terminal half life of the antibody in the plasma of the individual is about 8.40 days; or (d) the dose is about 60 mg/kg and the terminal half life of the antibody in the plasma of the individual is about 9.93 days.

~~70~~.17. \_\_\_\_\_ A method of monitoring the treatment of an individual being administered an anti-TREM2 antibody, comprising:

(a) measuring the levels of soluble TREM2 in a sample of cerebrospinal fluid, blood, or plasma from the individual before and after the individual has received one or more doses of an anti-TREM2 antibody;

(b) measuring the levels of soluble CSF1R in a sample of cerebrospinal fluid, blood, or plasma from the individual before and after the individual has received one or more doses of an anti-TREM2 antibody;

(c) measuring the levels of YKL40 in a sample of cerebrospinal fluid, blood, or plasma from the individual before and after the individual has received one or more doses of an anti-TREM2 antibody;

(d) measuring the levels of IL-1RA in a sample of cerebrospinal fluid, blood, or plasma from the individual before and after the individual has received one or more doses of an anti-TREM2 antibody; or

(e) measuring the levels of osteopontin in a sample of cerebrospinal fluid, blood, or plasma from the individual before and after the individual has received one or more doses of an anti-TREM2 antibody.

~~71~~.18. \_\_\_\_\_ The method of claim ~~1770~~, further comprising a step of assessing the activity of the anti-TREM2 antibody in the individual based on the levels of soluble TREM2, soluble CSF1R, YKL40, IL-1RA, or osteopontin in the sample of cerebrospinal fluid, blood, or plasma.

~~72~~.19. \_\_\_\_\_ The method of claim ~~1874~~, wherein the anti-TREM2 antibody is determined to be active in the individual if:

(a) the levels of soluble TREM2 in the sample of cerebrospinal fluid, blood, or plasma are decreased after the individual has received one or more doses of the anti-TREM2 antibody, compared to the levels of soluble TREM2 in the sample of cerebrospinal fluid, blood, or plasma before the individual received a dose of the anti-TREM2 antibody;

(b) the levels of soluble CSF1R in the sample of cerebrospinal fluid, blood, or plasma are increased after the individual has received one or more doses of the anti-TREM2 antibody, compared to the levels of soluble CSF1R in the sample of cerebrospinal fluid, blood, or plasma before the individual received a dose of the anti-TREM2 antibody;

(c) the levels of YKL40 in the sample of cerebrospinal fluid, blood, or plasma are increased after the individual has received one or more doses of the anti-TREM2 antibody, compared to the levels of YKL40 in the sample of cerebrospinal fluid, blood, or plasma before the individual received a dose of

the anti-TREM2 antibody;

(d) the levels of IL-1RA are increased in the sample of cerebrospinal fluid, blood, or plasma after the individual has received one or more doses of the anti-TREM2 antibody, compared to the levels of IL-1RA in the sample of cerebrospinal fluid, blood, or plasma before the individual received a dose of the anti-TREM2 antibody; or

(e) the levels of osteopontin in the sample of cerebrospinal fluid, blood, or plasma are increased after the individual has received one or more doses of the anti-TREM2 antibody, compared to the levels of osteopontin in the sample of cerebrospinal fluid, blood, or plasma before the individual received a dose of the anti-TREM2 antibody.

~~73. A method of monitoring the treatment of an individual being administered an anti-TREM2 antibody, comprising measuring the levels of soluble CSF1R in a sample of cerebrospinal fluid, blood, or plasma from the individual before and after the individual has received one or more doses of an anti-TREM2 antibody.~~

~~74. The method of claim 73, further comprising a step of assessing the activity of the anti-TREM2 antibody in the individual based on the levels of soluble CSF1R in the sample of cerebrospinal fluid, blood, or plasma.~~

~~75. The method of claim 74, wherein the anti-TREM2 antibody is determined to be active in the individual if the levels of soluble CSF1R in the sample of cerebrospinal fluid, blood, or plasma are increased after the individual has received one or more doses of the anti-TREM2 antibody, compared to the levels of soluble CSF1R in the sample of cerebrospinal fluid, blood, or plasma before the individual received a dose of the anti-TREM2 antibody.~~

~~76. A method of monitoring the treatment of an individual being administered an anti-TREM2 antibody, comprising measuring the levels of YKL40 in a sample of cerebrospinal fluid, blood, or plasma from the individual before and after the individual has received one or more doses of an anti-TREM2 antibody.~~

~~77. The method of claim 76, further comprising a step of assessing the activity of the anti-TREM2 antibody in the individual based on the levels of YKL40 in the sample of cerebrospinal fluid, blood, or plasma.~~

~~78. The method of claim 77, wherein the anti-TREM2 antibody is determined to be active in the individual if the levels of YKL40 in the sample of cerebrospinal fluid, blood, or plasma are increased~~

after the individual has received one or more doses of the anti-TREM2 antibody, compared to the levels of YKL40 in the sample of cerebrospinal fluid, blood, or plasma before the individual received a dose of the anti-TREM2 antibody.

79. A method of monitoring the treatment of an individual being administered an anti-TREM2 antibody, comprising measuring the levels of IL-1RA in a sample of cerebrospinal fluid, blood, or plasma from the individual before and after the individual has received one or more doses of an anti-TREM2 antibody.

80. The method of claim 79, further comprising a step of assessing the activity of the anti-TREM2 antibody in the individual based on the levels of IL-1RA in the sample of cerebrospinal fluid, blood, or plasma.

81. The method of claim 80, wherein the anti-TREM2 antibody is determined to be active in the individual if the levels of IL-1RA in the sample of cerebrospinal fluid, blood, or plasma are increased after the individual has received one or more doses of the anti-TREM2 antibody, compared to the levels of IL-1RA in the sample of cerebrospinal fluid, blood, or plasma before the individual received a dose of the anti-TREM2 antibody.

82. A method of monitoring the treatment of an individual being administered an anti-TREM2 antibody, comprising measuring the levels of osteopontin in a sample of cerebrospinal fluid, blood, or plasma from the individual before and after the individual has received one or more doses of an anti-TREM2 antibody.

83. The method of claim 82, further comprising a step of assessing the activity of the anti-TREM2 antibody in the individual based on the levels of osteopontin in the sample of cerebrospinal fluid, blood, or plasma.

84. The method of claim 83, wherein the anti-TREM2 antibody is determined to be active in the individual if the levels of osteopontin in the sample of cerebrospinal fluid, blood, or plasma are increased after the individual has received one or more doses of the anti-TREM2 antibody, compared to the levels of osteopontin in the sample of cerebrospinal fluid, blood, or plasma before the individual received a dose of the anti-TREM2 antibody.

85.20. The method of any one of claims 1770-1984, wherein the anti-TREM2 antibody is an agonist.