

CLAIMS

What is claimed is:

1. A method of treating and/or delaying the progression of a disease or injury in an individual, comprising administering to the individual an anti-CD33 antibody intravenously at a dose of at least about 1.6 mg/kg, wherein the antibody is administered about once every twelve weeks or more frequently; and wherein the antibody comprises: a heavy chain variable region that comprises an HVR-H1 comprising the amino acid sequence GYTFTDYNLH (SEQ ID NO: 105), an HVR-H2 comprising the amino acid sequence FIYPSNRITG (SEQ ID NO: 119), and an HVR-H3 comprising the amino acid sequence SDVDYFDY (SEQ ID NO: 122); and a light chain variable region that comprises an HVR-L1 comprising the amino acid sequence RASQSVSTSTYSYMH (SEQ ID NO: 127), an HVR-L2 comprising the amino acid sequence YASNLES (SEQ ID NO: 135), and an HVR-L3 comprising the amino acid sequence QHSWEIPLT (SEQ ID NO: 146).
2. The method of claim 1, wherein the anti-CD33 antibody is administered at a dose of between about 1.6 mg/kg and about 15 mg/kg.
3. The method of claim 1 or claim 2, wherein the anti-CD33 antibody is administered at a dose of about 1.6 mg/kg, about 5 mg/kg, about 7.5 mg/kg, about 10 mg/kg, or about 15 mg/kg.
4. The method of any one of claims 1-3, wherein the anti-CD33 antibody is administered once every two weeks, once every four weeks, once every five weeks, once every six weeks, once every seven weeks, once every eight weeks, once every nine weeks, once every ten weeks, once every eleven weeks, or once every twelve weeks.
5. The method of any one of claims 1-4, wherein the anti-CD33 antibody is administered once every two weeks at a dose of about 1.6 mg/kg.
6. The method of any one of claims 1-4, wherein the anti-CD33 antibody is administered once every four weeks at a dose of about 1.6 mg/kg.
7. The method of any one of claims 1-4, wherein the anti-CD33 antibody is administered once every four weeks at a dose of about 15 mg/kg.

8. The method of any one of claims 1-4, wherein the anti- CD33 antibody is administered once every five weeks at a dose of about 15 mg/kg.
9. The method of any one of claims 1-4, wherein the anti- CD33 antibody is administered once every six weeks at a dose of about 15 mg/kg.
10. The method of any one of claims 1-4, wherein the anti-CD33 antibody is administered once every seven weeks at a dose of about 15 mg/kg.
11. The method of any one of claims 1-4, wherein the anti-CD33 antibody is administered once every eight weeks at a dose of about 15 mg/kg.
12. The method of any one of claims 1-11, wherein the cell surface level of CD33 is reduced by at least about 70% compared to the cell surface level of CD33 prior to administration of the anti-CD33 antibody.
13. The method of any one of claims 1-12, wherein the cell surface level of CD33 is reduced by at least about 80% compared to the cell surface level of CD33 prior to administration of the anti-CD33 antibody.
14. The method of any one of claims 1-13, wherein the cell surface level of CD33 is reduced by at least about 85% compared to the cell surface level of CD33 prior to administration of the anti-CD33 antibody.
15. The method of any one of claims 1-14, wherein the cell surface level of CD33 is reduced by at least about 90% compared to the cell surface level of CD33 prior to administration of the anti-CD33 antibody.
16. The method of any one of claims 12-15, wherein the reduction in the cell surface level of CD33 is present for at least about 12 days after administration of the anti-CD33 antibody.
17. The method of any one of claims 12-16, wherein the reduction in the cell surface level of CD33 is present for at least about 17 days after administration of the anti-CD33 antibody.
18. The method of any one of claims 12-17, wherein the reduction in the cell surface level of CD33 is present for at least about 29 days after administration of the anti-CD33 antibody.

19. The method of any one of claims 12-18, wherein the reduction in the cell surface level of CD33 is present for at least about 42 days after administration of the anti-CD33 antibody.
20. The method of any one of claims 12-19, wherein the reduction in the cell surface level of CD33 is present for at least about 56 days after administration of the anti-CD33 antibody.
21. The method of any one of claims 12-20, wherein the reduction in cell surface level of CD33 comprises a reduction in the cell surface level of CD33 on peripheral blood monocytes of the individual.
22. The method of any one of claims 1-21, wherein the antibody comprises a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 59 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 86.
23. The method of any one of claims 1-22, wherein the antibody has an IgG2 isotype.
24. The method of any one of claims 1-23, wherein the antibody comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 180 or SEQ ID NO: 201, and a light chain comprising the amino acid sequence of SEQ ID NO: 185.
25. The method of any one of claims 1-24, wherein the terminal half-life of the anti-CD33 antibody in plasma is about 4 days, about 5 days, about 6 days, about 7 days, about 8 days, about 9 days, about 10 days, about 11 days, or about 12 days.
26. The method of any one of claims 1-25, wherein the terminal half-life of the anti-CD33 antibody in plasma is about 10 days.
27. The method of any one of claims 1-26, wherein the disease or injury is selected from the group consisting of dementia, frontotemporal dementia, Alzheimer's disease, vascular dementia, mixed dementia, tauopathy disease, infections, and cancer.
28. The method of any one of claims 1-26, wherein the disease or injury is Alzheimer's disease.
29. The method of any one of claims 1-28, wherein the individual is diagnosed with Alzheimer's disease, or has a clinical diagnosis of probable Alzheimer's disease dementia.

30. The method of any one of claims 1-29, wherein the individual has a Mini-Mental State Examination (MMSE) score of between about 16 points to about 28 points.
31. The method of any one of claims 1-30, wherein the individual has a Clinical Dementia Rating-Global Score (CDR-GS) of about 0.5, about 1.0, or about 2.0.
32. The method of any one of claims 1-31, wherein the individual has a positive amyloid-PET scan.
33. The method of any one of claims 1-32, wherein the individual is taking a stable dose of a cholinesterase inhibitor and/or a memantine therapy for Alzheimer's disease.
34. The method of any one of claims 1-33, wherein the individual does not carry two copies of the *rs12459419^T* allele.
35. The method of any one of claims 1-34, wherein the disease or injury is Alzheimer's disease, and wherein treatment and/or delay of the progression of Alzheimer's disease is assessed using one or more clinical assessments selected from the group consisting of the Mini-Mental State Examination (MMSE), the Repeatable Battery for the Assessment of Neuropsychological Status (RBANS), the Clinical Dementia Rating (CDR) assessment, amyloid brain positron emission tomography (PET), translocator protein (TSPO)-PET imaging, and any combination thereof.