application thus provides methods for treating and monitoring patients diagnosed with mild to moderate AD, especially mild AD, and ApoE4 positive patients, as well as patients having brain amyloid accumulation that is typically seen in patients diagnosed with AD. As exemplified herein, it has now been discovered that a humanized monoclonal anti-amyloid beta antibody with a conformational epitope specific for the middle region of amyloid beta (Aβ) peptide (*i.e.*, within amino acids 13-24, such as crenezumab) is effective to treat mild to moderate AD, especially ApoE4 positive patients and patients with milder forms of AD, such as, but not limited to, mild AD, without an increased incidence of ARIA-E or ARIA-H. Accordingly, this application provides therapeutic agents for modulating the severity of AD and improved methods of using the same.

[0009] Consequently, the present application provides methods of treating patients suffering from AD and other amyloidoses, comprising administering a humanized monoclonal anti-amyloid beta (Aβ or Abeta) antibody, or antigen-binding fragment thereof, that binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO:1). In some embodiments, the antibody, or antigen-binding fragment thereof, is capable of binding fibrillar, oligomeric, and monomeric forms of Abeta. In some embodiments, the antibody is an IgG4 antibody. In particular embodiments, the antibody, or antigen-binding fragment thereof, comprises six hypervariable regions (HVRs) wherein HVR-H1 is SEQ ID NO:2, HVR-H2 is SEQ ID NO:3, HVR-H3 is SEQ ID NO:4, HVR-L1 is SEQ ID NO:6, HVR-L2 is SEQ ID NO:7, and HVR-L3 is SEQ ID NO:8. In some embodiments, the antibody, or antigen-binding fragment thereof, comprises a heavy chain having the amino acid sequence of SEQ ID NO:5, comprising a heavy chain variable region, and a light chain having the amino acid sequence of SEQ ID NO:9, comprising a light chain variable region. In a specific example, the antibody is crenezumab.

[0010] Disclosed is use of a humanized monoclonal anti-amyloid beta (Aβ) antibody in the manufacture of a medicament for treating Alzheimer's Disease (AD) in a patient suffering from early or mild to moderate AD, wherein the patient has at least one CLUSTERIN allele that comprises a T at the single nucleotide polymorphism (SNP) rs1532278. The methods of treatment provided herein can be applied to patients suffering from AD or other amyloidosis, as described further herein. Suitable patients include patients suffering from mild to moderate AD, patients with an MMSE score of 18 to 26, patients suffering from mild AD, patients with an MMSE score of 20 or above (*e.g.*, 20-30, 20-26, 24-30, 21-26, 22-26, 22-28, 23-26, 24-26, or 25-26), patients suffering from early AD (including patients having mild cognitive impairement due to AD and patients having preclinical AD), amyloid positive patients (or patients having brain amyloid load consistent with that seen in patients diagnosed with AD), and ApoE4 positive patients suffering from mild to moderate or mild AD.

thereof. In some embodiments, the methods of identifying a patient comprise detecting in a sample from the patient presence of a CLUSTERIN allele comprising a polymorphism predictive of a response to treatment with a humanized monoclonal anti-amyloid beta (Aβ) antibody. In another aspect, there is provided a method of identifying a patient suffering from early or mild to moderate AD as more likely to respond to treatment with a humanized monoclonal anti-amyloid beta (Aβ) antibody comprising detecting in a sample that has been obtained from the patient presence of a CLUSTERIN allele comprising a polymorphism predictive of a response to treatment with a humanized monoclonal anti-amyloid beta (Aβ) antibody that binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: l) and is capable of binding oligomeric and monomeric forms of amyloid β, wherein the polymorphism is a T at the single nucleotide polymorphism (SNP) rsl532278. In some embodiments, the methods comprise selecting a patient as more likely to respond to said treatment when a T at the single nucleotide polymorphism (SNP) rs1532278 is present in a sample from the patient. In another aspect, there is provided method of selecting a patient suffering from early or mild to moderate AD for treatment with a humanized monoclonal anti-amyloid beta (Aβ) antibody comprising: (a) detecting in a sample that has been obtained from the patient presence or absence of a CLUSTERIN allele having a T at a single nucleotide polymorphism (SNP) rs1532278, and (b) selecting the patient as more likely to respond to treatment with a humanized monoclonal anti-Aβ antibody that binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: l) and is capable of binding oligomeric and monomeric forms of amyloid β when a T at the single nucleotide polymorphism (SNP) rs1532278 is present in the sample.

[0021] In some embodiments, the CLUSTERIN allele is an equivalent allele. In some embodiments, the CLUSTERIN allele is in linkage disequilibrium to rs1532278. In some embodiments, the equivalent allele comprises a SNP in linkage disequilibrium to rs1532278. In some embodiments, the linkage disequilibrium is a D' measure or an r^2 measure. In some embodiments, the D' measure between the selected SNP and the alternate SNP is ≥ 0.60. In some embodiments, the D' measure between the selected SNP and the alternate SNP is ≥ 0.70, 0.80 or 0.90. In some embodiments, the D' measure between the selected SNP and the alternate SNP is 1.0. In some embodiments, the r^2 measure between the selected SNP and the alternate SNP is ≥ 0.60. In some embodiments the r^2 measure between the selected SNP and the alternate SNP is ≥ 0.70, 0.80 or 0.90. In some embodiments, the r^2 measure between the selected SNP and the alternate SNP is 1.0.

[0022] In some embodiments, a humanized monoclonal anti-amyloid beta (Aβ or Abeta) antibody, or antigen-binding fragment thereof, binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO:1). In some embodiments, the antibody, or antigen-binding fragment thereof, is capable of binding fibrillar, oligomeric, and monomeric forms of Abeta. In some embodiments, the antibody is an IgG4 antibody. In particular embodiments, the antibody, or antigen-binding fragment thereof, comprises six hypervariable regions (HVRs) wherein HVR-H1 is SEQ ID NO:2, HVR-H2 is SEQ ID NO:3, HVR-H3 is SEQ ID NO:4, HVR-L1 is SEQ ID NO:6, HVR-L2 is SEQ ID NO:7, and HVR-L3 is SEQ ID NO:8. In some embodiments, the antibody, or antigen-binding fragment thereof, comprises a heavy chain having the amino acid sequence of SEQ ID NO:5, comprising a heavy chain variable region, and a light chain having the amino acid sequence of SEQ ID NO:9, comprising a light chain variable region. In a specific example, the antibody is crenezumab. In some embodiments, the antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab and gantenerumab.

[0023] In an embodiment, the disclosure provides methods of predicting whether an individual suffering from AD is likely to respond to treatment comprising an anti-Abeta antibody, or

antigen-binding fragment thereof. In another aspect, there is provided a method of predicting whether an individual suffering from AD is likely to respond to treatment comprising an anti-Abeta antibody, or antigen-binding fragment thereof, comprising: (a) determining the identity of a nucleotide at SNP rs1532278 in a sample that has been obtained from the individual and (b) predicting an increased likelihood of responding to treatment comprising an anti-Abeta antibody that binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: 1) and is capable of binding oligomeric and monomeric forms of amyloid β, or antigen-binding fragment thereof, when the sample contains at least one allele with a T nucleotide at SNP rs1532278.

In some embodiments, the methods comprise determining the identity of a nucleotide at SNP rs1532278 in a sample from the individual and predicting an increased likelihood of responding to treatment comprising an anti-Abeta antibody, or antigen-binding fragment thereof, when the sample contains at least one allele with a T nucleotide at SNP rs1532278, or an equivalent allele thereof. In some embodiments, the equivalent allele comprises a SNP in linkage disequilibrium to rs1532278. In some embodiments, the linkage disequilibrium is a D' measure or an r^2 measure. In some embodiments, the D' measure between the selected SNP and the alternate SNP is ≥ 0.60. In some embodiments, the D' measure between the selected SNP and the alternate SNP is ≥ 0.70, 0.80 or 0.90. In some embodiments, the D' measure between the selected SNP and the alternate SNP is 1.0. In some embodiments, the r^2 measure between the selected SNP and the alternate SNP is ≥ 0.60. In some embodiments the r^2 measure between the selected SNP and the alternate SNP is ≥ 0.70, 0.80 or 0.90. In some embodiments, the r^2 measure between the selected SNP and the alternate SNP is 1.0.

[0024] In some embodiments, the anti-Abeta antibody is a humanized monoclonal anti-amyloid beta (Aβ or Abeta) antibody, or antigen-binding fragment thereof. In some embodiments, the humanized monoclonal anti-amyloid beta (Aβ or Abeta) antibody, or antigen-binding fragment thereof, binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO:1). In some embodiments, the antibody, or antigen-binding fragment thereof, is capable of binding fibrillar, oligomeric, and monomeric forms of Abeta. In some embodiments, the antibody is an IgG4 antibody. In particular embodiments, the antibody, or antigen-binding fragment thereof, comprises six hypervariable regions (HVRs) wherein HVR-H1 is SEQ ID NO:2, HVR-H2 is SEQ ID NO:3, HVR-H3 is SEQ ID NO:4, HVR-L1 is SEQ ID NO:6, HVR-L2 is SEQ ID NO:7, and HVR-L3 is SEQ ID NO:8. In some embodiments, the antibody, or antigen-binding fragment thereof, comprises a heavy chain having the amino acid sequence of SEQ ID NO:5, comprising a heavy chain variable region, and a light chain having the amino acid sequence of SEQ ID NO:9, comprising a light chain variable region. In a specific example, the antibody is crenezumab. In some embodiments, the antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab and gantenerumab.

[0025] In another aspect, there is provided a method of optimizing therapeutic efficacy for treatment of AD comprising: determining the genotype of a patient, wherein a patient who is determined to carry at least one CLUSTERIN allele with a T nucleotide at SNP rs1532278 is more likely to respond to treatment with an anti-Abeta antibody that binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: 1) and is capable of binding oligomeric and monomeric forms of amyloid β, or antigen-binding fragment thereof. In an embodiment, the present disclosure provides methods of optimizing therapeutic efficacy for treatment of AD comprising: determining the genotype of a patient, wherein a patient who is determined to carry at least one CLUSTERIN allele with a T nucleotide at SNP

rs1532278, or an equivalent allele thereof, is more likely to respond to treatment with an anti-Abeta antibody, or antigen-binding fragment thereof. In some embodiments, the CLUSTERIN allele is an equivalent allele. In some embodiments, the CLUSTERIN allele is in linkage disequilibrium to rs1532278. In some embodiments, the equivalent allele comprises a SNP in linkage disequilibrium to rs1532278. In some embodiments, the linkage disequilibrium is a D' measure or an r^2 measure. In some embodiments, the D' measure between the selected SNP and the alternate SNP is ≥ 0.60. In some embodiments, the D' measure between the selected SNP and the alternate SNP is ≥ 0.70, 0.80 or 0.90. In some embodiments, the D' measure between the selected SNP and the alternate SNP is 1.0. In some embodiments, the r^2 measure between the selected SNP and the alternate SNP is ≥ 0.60. In some embodiments the r^2 measure between the selected SNP and the alternate SNP is ≥ 0.70, 0.80 or 0.90. In some embodiments, the r^2 measure between the selected SNP and the alternate SNP is 1.0. In another aspect, there is provided a method for determining the likelihood that a patient suffering from AD will benefit from treatment comprising an anti-Abeta antibody, or antigen-binding fragment thereof, the method comprising: determining the genotype of the patient, wherein the patient who has at least one CLUSTERIN allele with a T nucleotide at SNP rsl532278 is more likely to respond to treatment with an anti-Abeta antibody that binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: l) and is capable of binding oligomeric and monomeric forms of amyloid β than a patient who has no alleles with a T nucleotide at SNP rsl532278.

[0026] In some embodiments, the anti-Abeta antibody is a humanized monoclonal anti-amyloid beta (Aβ or Abeta) antibody, or antigen-binding fragment thereof. In some embodiments, the humanized monoclonal anti-amyloid beta (Aβ or Abeta) antibody, or antigen-binding fragment thereof, binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO:1). In some embodiments, the antibody, or antigen-binding fragment thereof, is capable of binding fibrillar, oligomeric, and monomeric forms of Abeta. In some embodiments, the antibody is an IgG4 antibody. In particular embodiments, the antibody, or antigen-binding fragment thereof, comprises six hypervariable regions (HVRs) wherein HVR-H1 is SEQ ID NO:2, HVR-H2 is SEQ ID NO:3, HVR-H3 is SEQ ID NO:4, HVR-L1 is SEQ ID NO:6, HVR-L2 is SEQ ID NO:7, and HVR-L3 is SEQ ID NO:8. In some embodiments, the antibody, or antigen-binding fragment thereof, comprises a heavy chain having the amino acid sequence of SEQ ID NO:5, comprising a heavy chain variable region, and a light chain having the amino acid sequence of SEQ ID NO:9, comprising a light chain variable region. In a specific example, the antibody is crenezumab. In some embodiments, the antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab and gantenerumab.

[0027] The methods provided herein comprise detecting the presence, and/or determining the identity, of a CLUSTERIN allele, or equivalent allele thereof. In some embodiments, presence of a CLUSTERIN allele in an individual comprises determining the identity of the nucleotide at the polymorphism from nucleic acid provided from a sample from an individual.

administration. In some embodiments, an antibody of the disclosure may be formulated for intravenous administration. In some embodiments, an antibody of the disclosure may be formulated in an arginine buffer, *e.g.*, an arginine succinate buffer. The buffer can contain one or more surfactants, *e.g.*, a polysorbate. In certain embodiments, the buffer concentration is 50 mM or greater. In some embodiments, the pH is between 4.5 and 7.0, e.g., pH 5.5. Further embodiments are described herein. The pharmaceutical formulations can be package in unit dosage forms for ease of use.

[0030] Treatment with anti-Abeta antibodies for treatment of AD or other amyloidosis, as described herein, can be combined with other therapy, including one or more anti-Abeta antibodies other than crenezumab. Non-limiting examples of other therapy include neurological drugs, corticosteroids, antibiotics, and antiviral agents. Non-limiting examples of anti-Abeta antibodies other than crenezumab include solanezumab, bapineuzumab, aducanumab, and gantenerumab.

[0031] Also provided herein are kits for determining the presence of a CLUSTERIN allele. Provided herein is a kit for determining the presence of at least one polymorphism in a biological sample, comprising reagents and instructions for detecting the presence of at least one polymorphism in CLUSTERIN, wherein the polymorphism is an allele comprising SNP rs1532278 or an equivalent allele. Reagents and methods of using the kit are further described herein. In another aspect, there is provided use of an agent that specifically binds to a polymorphism in CLUSTERIN, wherein the polymorphism is an allele comprising a T at SNP rs1532278, for the manufacture of a diagnostic for selecting patients likely to benefit from therapy with an anti-Abeta antibody that binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: 1) and is capable of binding oligomeric and monomeric forms of amyloid β, or an antigen binding fragment thereof, wherein the presence of a T at SNP rs1532278 is indicative of increased likelihood of benefit to a patient suffering with early or mild AD from therapy with the anti-Abeta antibody.

[0032] In another embodiment, the present disclosure provides agents and in vitro uses of such agents for identifying a patient having early or mild to moderate AD that is likely to respond to a therapy comprising an anti-Abeta antibody, or antigen binding fragment thereof, wherein the presence of said polymorphism, e.g., in CLUSTERIN identifies that the patient is more likely to respond to the therapy. Accordingly, agents for use in such methods include agents that are capable of detecting a CLUSTERIN allele with a T nucleotide at SNP rs1532278, or an equivalent allele thereof. In another aspect, there is provided an in vitro use of an agent that binds to at least one polymorphism wherein the polymorphism is a CLUSTERIN allele for identifying a patient having early or mild to moderate AD that is likely to respond to a therapy comprising an anti-Abeta antibody that binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: 1) and is capable of binding oligomeric and monomeric forms of amyloid β, or antigen binding fragment thereof, wherein the presence of said polymorphism identifies that the patient is more likely to respond to the therapy, and wherein the CLUSTERIN allele is an allele comprising SNP rs1532278 or an equivalent allele thereof, wherein the equivalent allele comprises a SNP in linkage disequilibrium to rs1532278.

BRIEF DESCRIPTION OF THE DRAWINGS

[0033] **FIG 1** provides the amino acid sequence of Abeta(1-42) (SEQ ID NO:1) with amino acids 13 to 24 underlined.

[0034] **FIG 2** provides the amino acid sequence of three heavy chain hypervariable regions (HVR-H1, HVR-H2, and HVR-H3, respectively) and the amino acid sequence of three light chain regions (HVR-L1, HVR-L2, HVR-L3, respectively).

CLAIMS:

1. A method of selecting a patient suffering from early or mild to moderate AD for treatment with a humanized monoclonal anti-amyloid beta (Aβ) antibody comprising:

(a) detecting in a sample that has been obtained from the patient presence or absence of a CLUSTERIN allele having a T at a single nucleotide polymorphism (SNP) rs1532278, and

(b) selecting the patient as more likely to respond to treatment with a humanized monoclonal anti-Aβ antibody that binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: 1) and is capable of binding oligomeric and monomeric forms of amyloid β when a T at the single nucleotide polymorphism (SNP) rs1532278 is present in the sample.

2. The method of claim 1, wherein the CLUSTERIN allele is an equivalent allele thereof, wherein the equivalent allele comprises a SNP in linkage disequilibrium to rs1532278.

3. The method of claim 1 or 2, wherein the sample is a blood sample, saliva, cheek swab, tissue sample, or a sample of a bodily fluid.

4. The method of any one of claims 1 to 3, wherein the polymorphism is detected by polymerase chain reaction.

5. The method of any one of claims 1 to 3, wherein the polymorphism is detected by sequencing.

6. The method of claim 4 or 5, wherein the polymorphism is detected by a technique selected from the group consisting of scanning probe and nanopore DNA sequencing, pyrosequencing, Denaturing Gradient Gel Electrophoresis (DGGE), Temporal Temperature Gradient Electrophoresis (TTGE), Zn(II)-cyclen polyacrylamide gel electrophoresis, homogeneous fluorescent PCR-based single nucleotide polymorphism analysis, phosphate-affinity polyacrylamide gel electrophoresis, high-throughput SNP genotyping platforms, molecular beacons, 5 'nuclease reaction, Taqman assay, MassArray, trityl mass tags, genotyping platforms, single base primer extension (SBE) assays, PCR amplification,

restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.

7. The method of any one of claims 1 to 3, wherein the polymorphism is detected by amplification of a target region containing the at least one polymorphism, and hybridization with at least one sequence-specific oligonucleotide that hybridizes under stringent conditions to the at least one polymorphism and detecting the hybridization.

8. The method of claim 1, wherein the patient is suffering from mild AD.

9. The method of claim 1, wherein the patient is suffering from early AD.

10. The method of claim 2, wherein the patient has an Mini-Mental State Examination (MMSE) score of at least 20, between 20 and 30, between 20 and 26, between 24 and 30, between 21 and 26, between 22 and 26, between 22 and 28, between 23 and 26, between 24 and 26, or between 25 and 26.

11. The method of claim 10, wherein the patient has an MMSE score between 22 and 26.

12. The method of any one of claim 1 to 10, wherein the patient is ApoE4 positive.

13. The method of any one of claims 1 to 12, wherein the antibody is an IgG4 antibody.

14. The method of any one of claims 1 to 13, wherein the antibody comprises six hypervariable regions (HVRs), wherein:
(i) HVR-H1 is SEQ ID NO:2;
(ii) HVR-H2 is SEQ ID NO:3;
(iii) HVR-H3 is SEQ ID NO:4;
(iv) HVR-L1 is SEQ ID NO:6;
(v) HVR-L2 is SEQ ID N0:7; and
(vi) HVR-L3 is SEQ ID NO : 8.

15. The method of claim 14, wherein the antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO: 5 and a light chain having the amino acid sequence of SEQ ID NO:9.

16. The method of claim 14, wherein the antibody is crenezumab.

17. The method of claim 1, wherein the anti-amyloid beta antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab and gantenerumab.

18. A method of identifying a patient suffering from early or mild to moderate AD as more likely to respond to treatment with a humanized monoclonal anti-amyloid beta (Aβ) antibody comprising detecting in a sample that has been obtained from the patient presence of a CLUSTERIN allele comprising a polymorphism predictive of a response to treatment with a humanized monoclonal anti-amyloid beta (Aβ) antibody that binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: 1) and is capable of binding oligomeric and monomeric forms of amyloid β, wherein the polymorphism is a T at the single nucleotide polymorphism (SNP) rsl532278.

19. The method of claim 18, wherein the CLUSTERIN allele is an equivalent allele of an allele comprising SNP rsl532278, wherein the equivalent allele comprises a SNP in linkage disequilibrium to rs1532278.

20. The method of claim 18 or 19, wherein the sample is a blood sample, saliva, cheek swab, tissue sample, or a sample of a bodily fluid.

21. The method of any one of claims 18 to 20, wherein the polymorphism is detected by polymerase chain reaction.

22. The method of any one of claims 18 to 20, wherein the polymorphism is detected by sequencing.

23. The method of claim 21 or 22, wherein the polymorphism is detected by a technique selected from the group consisting of scanning probe and nanopore DNA sequencing, pyrosequencing, Denaturing Gradient Gel Electrophoresis (DGGE), Temporal Temperature

Gradient Electrophoresis (TTGE), Zn(II)-cyclen polyacrylamide gel electrophoresis, homogeneous fluorescent PCR-based single nucleotide polymorphism analysis, phosphate-affinity polyacrylamide gel electrophoresis, high-throughput SNP genotyping platforms, molecular beacons, 5 'nuclease reaction, Taqman assay, MassArray, trityl mass tags, genotyping platforms, single base primer extension (SBE) assays, PCR amplification, restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.

24. The method of any one of claims 18 to 20, wherein the polymorphism is detected by amplification of a target region containing the at least one polymorphism, and hybridization with at least one sequence-specific oligonucleotide that hybridizes under stringent conditions to the at least one polymorphism and detecting the hybridization.

25. The method of claim 18, wherein the patient is suffering from mild AD.

26. The method of claim 18, wherein the patient is suffering from early AD.

27. The method of claim 25, wherein the patient has an MMSE score of at least 20, between 20 and 30, between 20 and 26, between 24 and 30, between 21 and 26, between 22 and 26, between 22 and 28, between 23 and 26, between 24 and 26, or between 25 and 26..

28. The method of claim 27, wherein the patient has an MMSE score between 22 and 26.

29. The method of any one of claims 18 to 27, wherein the patient is ApoE4 positive.

30. The method of any one of claims 18 to 29, wherein the antibody is an IgG4 antibody.

31. The method of any one of claims 18 to 30, wherein the antibody comprises six hypervariable regions (HVRs), wherein:
(i) HVR-H1 is SEQ ID NO:2;
(ii) HVR-H2 is SEQ ID NO:3;
(iii) HVR-H3 is SEQ ID NO:4;
(iv) HVR-L1 is SEQ ID NO:6;
(v) HVR-L2 is SEQ ID NO:7; and

(vi) HVR-L3 is SEQ ID NO:8.

32. The method of claim 31, wherein the antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO: 5 and a light chain having the amino acid sequence of SEQ ID NO:9.

33. The method of claim 32, wherein the antibody is crenezumab.

34. The method of claim 18, wherein the anti-amyloid beta antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab and gantenerumab.

35. A method of predicting whether an individual suffering from AD is likely to respond to treatment comprising an anti-Abeta antibody, or antigen-binding fragment thereof, comprising:
(a) determining the identity of a nucleotide at SNP rsl532278 in a sample that has been obtained from the individual and
(b) predicting an increased likelihood of responding to treatment comprising an anti-Abeta antibody that binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: 1) and is capable of binding oligomeric and monomeric forms of amyloid β, or antigen-binding fragment thereof, when the sample contains at least one allele with a T nucleotide at SNP rsl532278.

36. The method of claim 35, wherein the patient is suffering from mild AD.

37. The method of claim 35, wherein the patient is suffering from early AD.

38. The method of claim 35, wherein the patient has an MMSE ranging from 20 to 26, from 21 to 26, from 22 to 26, from 23 to 26, from 24 to 26, or from 25 to 26.

39. The method of any one of claim 35 to 38, wherein the patient is ApoE4 positive.

40. The method of any one of claims 35 to 39, wherein the antibody is an IgG4 antibody.

41. The method of any one of claims 35 to 40, wherein the antibody comprises six hypervariable regions (HVRs), wherein:
(i) HVR-H1 is SEQ ID NO:2;
(ii) HVR-H2 is SEQ ID NO:3;
(iii) HVR-H3 is SEQ ID NO:4;
(iv) HVR-L1 is SEQ ID NO:6;
(v) HVR-L2 is SEQ ID NO:7; and
(vi) HVR-L3 is SEQ ID NO:8.

42. The method of claim 41, wherein the antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO: 5 and a light chain having the amino acid sequence of SEQ ID NO:9.

43. The method of claim 42, wherein the antibody is crenezumab.

44. The method of claim 35, wherein the anti-amyloid beta antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab, and gantenerumab.

45. A method of optimizing therapeutic efficacy for treatment of AD comprising:
determining the genotype of a patient, wherein a patient who is determined to carry at least one CLUSTERIN allele with a T nucleotide at SNP rsl532278 is more likely to respond to treatment with an anti-Abeta antibody that binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: l) and is capable of binding oligomeric and monomeric forms of amyloid β, or antigen-binding fragment thereof.

46. The method of claim 45, wherein the patient is suffering from early or mild AD.

47. The method of claim 45, wherein the patient has an MMSE score of at least 20, between 20 and 30, between 20 and 26, between 24 and 30, between 21 and 26, between 22 and 26, between 22 and 28, between 23 and 26, between 24 and 26, or between 25 and 26.

48. The method of claim 47, wherein the patient has an MMSE score between 22 and 26.

49. The method of any one of claims 45 to 47, wherein the patient is ApoE4 positive.

50. The method of any one of claims 45 to 49, wherein the antibody is an IgG4 antibody.

51. The method of any one of claims 45 to 50, wherein the antibody comprises six hypervariable regions (HVRs), wherein:
(i) HVR-H1 is SEQ ID NO:2;
(ii) HVR-H2 is SEQ ID NO:3;
(iii) HVR-H3 is SEQ ID NO:4;
(iv) HVR-L1 is SEQ ID NO:6;
(v) HVR-L2 is SEQ ID NO:7; and
(vi) HVR-L3 is SEQ ID NO:8.

52. The method of claim 51, wherein the antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO: 5 and a light chain having the amino acid sequence of SEQ ID NO:9.

53. The method of claim 52, wherein the antibody is crenezumab.

54. The method of claim 45, wherein the anti-amyloid beta antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab and gantenerumab.

55. A method for determining the likelihood that a patient suffering from AD will benefit from treatment comprising an anti-Abeta antibody, or antigen-binding fragment thereof, the method comprising: determining the genotype of the patient, wherein the patient who has at least one CLUSTERIN allele with a T nucleotide at SNP rsl532278 is more likely to respond to treatment with an anti-Abeta antibody that binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: 1) and is capable of binding oligomeric and monomeric forms of amyloid β than a patient who has no alleles with a T nucleotide at SNP rsl532278.

56. The method of claim 55, wherein the patient is suffering from early or mild AD.

57. The method of claim 55, wherein the patient has an MMSE score of at least 20, between 20 and 30, between 20 and 26, between 24 and 30, between 21 and 26, between 22 and 26, between 22 and 28, between 23 and 26, between 24 and 26, or between 25 and 26.

58. The method of any one of claim 55 to 57, wherein the patient is ApoE4 positive.

59. The method of any one of claims 55 to 58, wherein the antibody is an IgG4 antibody.

60. The method of any one of claims 55 to 59, wherein the antibody comprises six hypervariable regions (HVRs), wherein:
(i) HVR-H1 is SEQ ID NO:2;
(ii) HVR-H2 is SEQ ID NO:3;
(iii) HVR-H3 is SEQ ID NO:4;
(iv) HVR-L1 is SEQ ID NO:6;
(v) HVR-L2 is SEQ ID NO:7; and
(vi) HVR-L3 is SEQ ID NO:8.

61. The method of claim 60, wherein the antibody comprises a heavy chain having the amino acid sequence of SEQ ID NO: 5 and a light chain having the amino acid sequence of SEQ ID NO:9.

62. The method of claim 61, wherein the antibody is crenezumab.

63. The method of claim 55, wherein the anti-amyloid beta antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab and gantenerumab.

64. The method of any one of claims 45 to 63, wherein the CLUSTERIN allele is an equivalent allele of an allele comprising SNP rsl532278, wherein the equivalent allele comprises a SNP in linkage disequilibrium to rs1532278.

65. The method of claim 64, wherein the sample is a blood sample, saliva, cheek swab, tissue sample, or a sample of a bodily fluid.

66. The method of claim 64 or 65, wherein the polymorphism is detected by polymerase chain reaction.

67. The method of claim 64 or 65, wherein the polymorphism is detected by sequencing.

68. The method of claim 66 or 67, wherein the polymorphism is detected by a technique selected from the group consisting of scanning probe and nanopore DNA sequencing, pyrosequencing, Denaturing Gradient Gel Electrophoresis (DGGE), Temporal Temperature Gradient Electrophoresis (TTGE), Zn(II)-cyclen polyacrylamide gel electrophoresis, homogeneous fluorescent PCR-based single nucleotide polymorphism analysis, phosphate-affinity polyacrylamide gel electrophoresis, high-throughput SNP genotyping platforms, molecular beacons, 5 'nuclease reaction, Taqman assay, MassArray, trityl mass tags, genotyping platforms, single base primer extension (SBE) assays, PCR amplification, restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.

69. The method of claim 64 or 65, wherein the polymorphism is detected by amplification of a target region containing the at least one polymorphism, and hybridization with at least one sequence-specific oligonucleotide that hybridizes under stringent conditions to the at least one polymorphism and detecting the hybridization.

70. Use of an agent that specifically binds to a polymorphism in CLUSTERIN, wherein the polymorphism is an allele comprising a T at SNP rsl532278, for the manufacture of a diagnostic for selecting patients likely to benefit from therapy with an anti-Abeta antibody that binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: l) and is capable of binding oligomeric and monomeric forms of amyloid β, or an antigen binding fragment thereof, wherein the presence of a T at SNP rs1532278 is indicative of increased likelihood of benefit to a patient suffering with early or mild AD from therapy with the anti-Abeta antibody.

71. In vitro use of an agent that binds to at least one polymorphism wherein the polymorphism is a CLUSTERIN allele for identifying a patient having early or mild to moderate AD that is likely to respond to a therapy comprising an anti-Abeta antibody that binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: l) and is capable of binding oligomeric and monomeric forms of amyloid β, or antigen binding fragment thereof, wherein the presence of said polymorphism identifies that the patient is more likely to respond to the therapy, and wherein the CLUSTERIN allele is an allele comprising SNP

rs1532278 or an equivalent allele thereof, wherein the equivalent allele comprises a SNP in linkage disequilibrium to rs1532278.

72. The use of claim 71, wherein the patient has mild AD.

73. The use of claim 71, wherein the patient has early AD.

74. The use of claim 71, wherein the patient has an MMSE score of at least 20, between 20 and 30, between 20 and 26, between 24 and 30, between 21 and 26, between 22 and 26, between 22 and 28, between 23 and 26, between 24 and 26, or between 25 and 26.

75. The use of claim 70 or 71, wherein the at least one polymorphism is detected by a technique selected from the group consisting of scanning probe and nanopore DNA sequencing, pyrosequencing, Denaturing Gradient Gel Electrophoresis (DGGE), Temporal Temperature Gradient Electrophoresis (TTGE), Zn(II)-cyclen polyacrylamide gel electrophoresis, homogeneous fluorescent PCR-based single nucleotide polymorphism analysis, phosphate-affinity polyacrylamide gel electrophoresis, high-throughput SNP genotyping platforms, molecular beacons, 5 'nuclease reaction, Taqman assay, MassArray, trityl mass tags, genotyping platforms , single base primer extension (SBE) assays, PCR amplification, restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.

76. The use of claim 70 or 71, wherein the at least one polymorphism is detected by amplification of a target region containing at least one polymorphism, and hybridization with at least one sequence-specific oligonucleotide that hybridizes under stringent conditions to at least one polymorphism and detecting the hybridization.