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] In one aspect, there is provided 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.

[0011] In some ~~aspect~~embodiments, the methods provided herein are methods of reducing decline due to AD in patients suffering from early, mild, or mild to moderate AD. In some embodiments, the decline is one or more of: clinical decline, cognitive decline, and functional decline. In some embodiments, the decline is clinical decline. In some embodiments, the decline is a decline in cognitive capacity or cognitive decline. In some embodiments, the decline comprises a decline in functional capacity or functional decline. Various tests and scales have been developed to measure cognitive capacity (including memory) and/or function. In various embodiments, one or more test is used to measure clinical, functional, or cognitive decline. A standard measurement of cognitive capacity is the Alzheimer's Disease Assessment Scale Cognitive (ADAS-Cog) test, for example, the 12-item ADAS-Cog or ADAS-Cog12. Thus, in some embodiments, the reduction or slowing in decline in cognitive capacity (or cognitive decline) in patients being treated with the antibodies of the ~~invention~~disclosure is determined using the ADAS-Cog12 test. An increase in ADAS-Cog12 score is indicative of worsening in a patient's condition. In some embodiments, the reduction or slowing in cognitive decline (or decline in cognitive capacity) in patients being treated with the antibodies of the ~~invention~~disclosure is determined by a Clinical Dementia Rating Scale / Sum of Boxes (CDR-SOB) score. In some embodiments, reduction or slowing in functional decline (or decline in functional ability) in patients being treated with the antibodies of the ~~invention~~disclosure is determined using the Instrumental Activities of Daily Living (or iADL) scale. In some embodiments, decline of one or more types is assessed and one or more of the foregoing tests or scales is used to measure reduction or slowing in decline.

[0012] An antibody, or antigen-binding fragment thereof, of the ~~invention~~disclosure is administered at a dose that is effective to treat the AD or other amyloidosis, as described herein. Suitable dosages are described herein and can range from about 0.3 mg/kg to 100 mg/kg. In an exemplary embodiment, the dosage is 15 mg/kg. In a further exemplary embodiment, the dosage is 30 mg/kg. In a further exemplary embodiment, the dosage is 45 mg/kg. In some embodiments, the dosage is between 500 mg and 1000mg, for example 500 mg, 700 mg, 720 mg, 750 mg, 800 mg, 820 mg, 900 mg, or between 1000 mg and 2500 mg, for example 1050 mg, 1500 mg, or 2100 mg. In the methods provided herein, a variety of dosage regimens are contemplated including dosage regimens in which the antibody is administered repeatedly, *e.g.*, on a weekly or monthly schedule, over an extended period of time, *e.g.*, months to years.

[0013] The humanized monoclonal anti- Abeta antibody of the present disclosure provides a further benefit in that it does not increase the incidence of adverse events such as

ARIA-E and ARIA-H. As shown herein, there was no increase in these adverse events in the treatment arm relative to the placebo arm. Thus, the present disclosure further provides methods of treating patients suffering from mild to moderate AD or mild AD without increasing the incidence of adverse events such as ARIA-E and/or ARIA-H.

[0014] Exploratory analyses of genetic variants revealed the association between a single nucleotide polymorphism (SNP) in the Clusterin (CLU or CLUSTERIN) gene and a treatment effect. As shown herein, crenezumab had a greater treatment effect relative to placebo in patients carrying at least one CLU allele with a T at the single nucleotide polymorphism (SNP) rs1532278 relative to patients with no CLU alleles having a T at the single nucleotide polymorphism (SNP) rs1532278. The effect was seen in patients with mild AD as well as ApoE4 positive patients.

[0015] Accordingly, in an ~~aspect~~embodiment, the present application provides methods of treating patients having early, mild to moderate, or mild AD, comprising administering to a patient suffering from early AD, mild AD, or mild to moderate AD, a humanized monoclonal anti-amyloid beta (Aβ) antibody in an amount effective to treat the AD, wherein the patient has at least one CLUSTERIN allele that comprises a T at the single nucleotide polymorphism (SNP) rs1532278 or an equivalent allele thereof. In some embodiments, the CLUSTERIN allele is an equivalent allele.

[0016] 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.

[0017] As provided herein, the methods of treating patients suffering from AD and other amyloidoses, comprise 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.

[0018] An antibody, or antigen-binding fragment thereof, of the ~~invention~~disclosure is administered at a dose that is effective to treat the AD or other amyloidosis, as described herein. Suitable dosages are described herein and can range from about 0.3 mg/kg to 100 mg/kg. In an exemplary embodiment, the dosage is 15 mg/kg. In a further exemplary embodiment, the dosage is 30 mg/kg. In a further exemplary embodiment, the dosage is 45 mg/kg. In some embodiments, the dosage is between 500 mg and 1000mg, for example 500 mg, 700 mg, 720 mg, 750 mg, 800 mg, 820 mg, 900 mg, or between 1000 mg and 2500 mg, for example 1050 mg, 1500 mg, or 2100 mg. In the methods provided herein, a variety of dosage regimens are contemplated including dosage regimens in which the antibody is administered repeatedly, *e.g.*, on a weekly or monthly schedule, over an extended period of time, *e.g.*, months to years.

[0019] 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.

[0020] Also provided herein are methods of identifying patients who are likely to benefit from treatment with a humanized monoclonal anti-amyloid beta (Aβ) antibody as well as methods of selecting patients for treatment with a humanized monoclonal anti-amyloid beta (Aβ) antibody, or antigen-binding fragment thereof. In some embodiments, the methods comprise detecting in a sample from the patient presence or absence of a CLUSTERIN allele having a T at a single nucleotide polymorphism (SNP) rs1532278, or equivalent allele

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. 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 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 ~~aspect~~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 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, or antigen-binding fragment thereof, when the sample contains at least one allele with a T nucleotide at SNP rsl532278.

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 rsl532278 is more likely to respond to treatment with an anti-Abeta antibody, or antigen-binding fragment thereof. In an ~~aspect~~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 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 ~~invention~~disclosure may be formulated for intravenous administration. In some embodiments, an antibody of the ~~invention~~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. In another aspect, there is provided ~~present disclosure provides~~ 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.

[0032] In another ~~aspect~~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, or antigen binding fragment thereof, wherein the presence of said polymorphism identifies that the patient is more likely to respond to the therapy.

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 treating Alzheimer's Disease (AD) in a patient suffering from early or mild to moderate AD, comprising comprising administering to a patient suffering from early or mild to moderate AD a humanized monoclonal anti-amyloid beta (Aβ) antibody in an amount effective to treat the AD, wherein the patient has at least one CLUSTERIN allele that comprises a T at the single nucleotide polymorphism (SNP) rs1532278.

2. The method of **claim 1**, wherein the CLUSTERIN allele is an equivalent allele thereof.

3. The method of **claim 1**, comprising detecting a polymorphism in a sample from the patient, wherein the polymorphism that is detected is in linkage disequilibrium with SNP rs1532278.

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

5. The method of **any one of claims 1 to 4**, wherein a polymorphism is detected by polymerase chain reaction.

6. The method of **any one of claims 1 to 4**, wherein a polymorphism is detected by sequencing.

7. The method of **claim 5** or **6,** wherein a 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 (single base primer extension coupled with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry), trityl mass tags, genotyping platforms (such as the Invader Assay®), single base primer extension (SBE) assays, PCR amplification (e.g. PCR amplification on magnetic nanoparticles (MNPs), restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.

8. The method of **any one of claims 1 to 4**, wherein a 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.

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

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

11. The method of **claim 9 or 10**, wherein the patient has an MMSE score of at least 20, between 20 and 30, between 20 and 26, between 24 and 30, between 24 and 26, between 22 and 26, between 22 and 28, between 23 and 26, between 24 and 26, or between 25 and 26.

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

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

14. The method of **claim 1**, wherein the anti-amyloid beta antibody binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO:1).

15. The method of **claim 14**, wherein the antibody is capable of binding oligomeric and monomeric forms of amyloid β.

16. The method of **claim 15**, wherein the antibody is an IgG4 antibody.

17. The method of **claim 15 or 16**, 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.

18. The method of **claim 17**, 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.

19. The method of **claim 17**, wherein the antibody is crenezumab.

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

21. 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 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 when a T at the single nucleotide polymorphism (SNP) rs1532278 is present in the sample.

22. The method of **claim 21**, wherein the CLUSTERIN allele is an equivalent allele thereof.

23. The method of **claim 22**, wherein the equivalent allele is in linkage disequilibrium with SNP rs1532278.

24. The method of **claim 21** or **22,** wherein the sample is a blood sample, saliva, cheek swab, tissue sample, or a sample of a bodily fluid.

25. The method of **any one of claims 21 to 24**, wherein a polymorphism is detected by polymerase chain reaction.

26. The method of **any one of claims 21 to 24**, wherein a polymorphism is detected by sequencing.

27. The method of **claim 25** or **26,** wherein a 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 (single base primer extension coupled with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry), trityl mass tags, genotyping platforms (such as the Invader Assay®), single base primer extension (SBE) assays, PCR amplification (e.g. PCR amplification on magnetic nanoparticles (MNPs), restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.

28. The method of **any one of claims 21 to 24**, wherein a 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.

29. The method of **claim 21**, wherein the patient is suffering from mild AD.

30. The method of **claim 21**, wherein the patient is suffering from early AD.

31. The method of **claim 22**, 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.

32. The method of **claim 31**, wherein the patient has an MMSE score between 22 and 26.

33. The method of any one of **claim 21** to **31**, wherein the patient is ApoE4 positive.

34. The method of **claim 21**, wherein the anti-amyloid beta antibody binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO:1).

35. The method of **claim 34**, wherein the antibody is capable of binding oligomeric and monomeric forms of amyloid β.

36. The method of **claim 35**, wherein the antibody is an IgG4 antibody.

37. The method of **claim 34** or **35**, 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.

38. The method of **claim 37**, 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.

39. The method of **claim 37**, wherein the antibody is crenezumab.

40. The method of **claim 21**, wherein the anti-amyloid beta antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab and gantenerumab.

41. 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 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.

42. The method of **claim 41**, wherein the polymorphism is a T at the single nucleotide polymorphism (SNP) rs1532278.

43. The method of **claim 41**, wherein the CLUSTERIN allele is an equivalent allele of an allele comprising SNP rs1532278.

44. The method of **claim 43**, wherein the equivalent allele is in linkage disequilibrium with SNP rs1532278.

45. The method of **claim 41** or **42,** wherein the sample is a blood sample, saliva, cheek swab, tissue sample, or a sample of a bodily fluid.

46. The method of **any one of claims 41 to 45**, wherein the polymorphism is detected by polymerase chain reaction.

47. The method of **any one of claims 41 to 45**, wherein the polymorphism is detected by sequencing.

48. The method of **claim 46** or **47,** wherein a 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 (single base primer extension coupled with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry), trityl mass tags, genotyping platforms (such as the Invader Assay®), single base primer extension (SBE) assays, PCR amplification (e.g. PCR amplification on magnetic nanoparticles (MNPs), restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.

49. The method of **any one of claims 41 to 45**, wherein a 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.

50. The method of **claim 41**, wherein the patient is suffering from mild AD.

51. The method of **claim 41**, wherein the patient is suffering from early AD.

52. The method of **claim 50**, 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..

53. The method of **claim 52**, wherein the patient has an MMSE score between 22 and 26.

54. The method of **any one of claims 41 to 52**, wherein the patient is ApoE4 positive.

55. The method of **claim 41**, wherein the anti-amyloid beta antibody binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO:1).

56. The method of **claim 55**, wherein the antibody is capable of binding oligomeric and monomeric forms of amyloid β.

57. The method of **claim 56**, wherein the antibody is an IgG4 antibody.

58. The method of **claim 56** or **57**, 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.

59. The method of **claim 58**, 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.

60. The method of **claim 59**, wherein the antibody is crenezumab.

61. The method of **claim 41**, wherein the anti-amyloid beta antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab and gantenerumab.

62. 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 from the individual and

(b) 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.

63. The method of **claim 62**, wherein the patient is suffering from mild AD.

64. The method of **claim 62**, wherein the patient is suffering from early AD.

65. The method of **claim 62**, 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.

66. The method of any one of **claim 62** to **65**, wherein the patient is ApoE4 positive.

67. The method of **claim 62**, wherein the anti-amyloid beta antibody binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO:1).

68. The method of **claim 67**, wherein the antibody is capable of binding oligomeric and monomeric forms of amyloid β.

69. The method of **claim 68**, wherein the antibody is an IgG4 antibody.

70. The method of **claim 68** or **69**, 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.

71. The method of **claim 70**, 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.

72. The method of **claim 71**, wherein the antibody is crenezumab.

73. The method of **claim 62**, wherein the anti-amyloid beta antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab, and gantenerumab.

74. 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, or antigen-binding fragment thereof.

75. The method of **claim 74**, wherein the patient is suffering from early or mild AD.

76. The method of **claim 74**, 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.

77. The method of **claim 76**, wherein the patient has an MMSE score between 22 and 26.

78. The method of any one of **claim 74** to **76**, wherein the patient is ApoE4 positive.

79. The method of **claim 74**, wherein the anti-amyloid beta antibody binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO:1).

80. The method of **claim 79**, wherein the antibody is capable of binding oligomeric and monomeric forms of amyloid β.

81. The method of **claim 80**, wherein the antibody is an IgG4 antibody.

82. The method of **claim 80** or **81**, 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.

83. The method of **claim 82**, 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.

84. The method of **claim 83**, wherein the antibody is crenezumab.

85. The method of **claim 74**, wherein the anti-amyloid beta antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab and gantenerumab.

86. 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 rs1532278 is more likely to respond to treatment with an anti-Abeta antibody than a patient who has no alleles with a T nucleotide at SNP rs1532278.

87. The method of **claim 86**, wherein the patient is suffering from early or mild AD.

88. The method of **claim 86**, 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.

89. The method of any one of **claim 86** to **88**, wherein the patient is ApoE4 positive.

90. The method of **claim 86**, wherein the anti-amyloid beta antibody binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO:1).

91. The method of **claim 90**, wherein the antibody is capable of binding oligomeric and monomeric forms of amyloid β.

92. The method of **claim 91**, wherein the antibody is an IgG4 antibody.

93. The method of **claim 91** or **92**, 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.

94. The method of **claim 93**, 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.

95. The method of **claim 94**, wherein the antibody is crenezumab.

96. The method of **claim 86**, wherein the anti-amyloid beta antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab and gantenerumab.

97. The method of **any one of claims 74 to 96**, wherein the CLUSTERIN allele is an equivalent allele of an allele comprising SNP rs1532278.

98. The method of **claim 97**, wherein the equivalent allele is in linkage disequilibrium with SNP rs1532278.

99. The method of **claim 97** or **98,** wherein the sample is a blood sample, saliva, cheek swab, tissue sample, or a sample of a bodily fluid.

100. The method of **any one of claims 97 to 99**, wherein a polymorphism is detected by polymerase chain reaction.

101. The method of **any one of claims 97 to 99**, wherein a polymorphism is detected by sequencing.

102. The method of **claim 100** or **101**, wherein a 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 (single base primer extension coupled with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry), trityl mass tags, genotyping platforms (such as the Invader Assay®), single base primer extension (SBE) assays, PCR amplification (e.g. PCR amplification on magnetic nanoparticles (MNPs), restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.

103. The method of **any one of claims 97 to 99**, wherein a 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.

104. 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.

105. The kit of **claim 104**, wherein the kit is used to detect the presence of a T at SNP rs1532278.

106. The kit of **claim 104**, wherein the reagents comprise a set of oligonucleotides specific for detecting a polymorphism in CLUSTERIN.

107. 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.

108. The use of **claim 107**, wherein 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 (single base primer extension coupled with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry), trityl mass tags, genotyping platforms (such as the Invader Assay®), single base primer extension (SBE) assays, PCR amplification (e.g. PCR amplification on magnetic nanoparticles (MNPs), restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.

109. The use of **claim 107**, wherein 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.

110. The use of **claim 107**, 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 an anti-Abeta antibody.

111. 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, or antigen binding fragment thereof, wherein the presence of said polymorphism identifies that the patient is more likely to respond to the therapy.

112. The use of **claim 111**, wherein the CLUSTERIN allele is an allele comprising SNP rs1532278 or an equivalent allele thereof.

113. The use of **claim 112**, wherein the patient has mild AD.

114. The use of **claim 112**, wherein the patient has early AD.

115. The use of **claim 112**, 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.

116. The use of **claim 112**, wherein 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 (single base primer extension coupled with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry), trityl mass tags, genotyping platforms (such as the Invader Assay®), single base primer extension (SBE) assays, PCR amplification (e.g. PCR amplification on magnetic nanoparticles (MNPs), restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.

117. The use of **claim 112**, wherein 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.

CLAIMS:

1. 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) rsl532278.

2. The use of claim 1, wherein the CLUSTERIN allele is an equivalent allele thereof.

3. The use of claim 1, comprising detecting a polymorphism in a sample from the patient, wherein the polymorphism that is detected is in linkage disequilibrium with SNP rsl532278.

4. The use of claim 3, wherein the sample is a blood sample, saliva, cheek swab, tissue sample, or a sample of a bodily fluid.

5. The use of any one of claims 1 to 4, wherein a polymorphism is detected by polymerase chain reaction.

6. The use of any one of claims 1 to 4, wherein a polymorphism is detected by sequencing.

7. The use of claim 5 or 6, wherein a 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 (single base primer extension coupled with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry), trityl mass tags, genotyping platforms (such as the Invader Assay®), single base primer extension (SBE) assays, PCR amplification (e.g. PCR amplification on magnetic nanoparticles (MNPs), restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.

8. The use of any one of claims 1 to 4, wherein a 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.

9. The use of claim 1, wherein the patient is suffering from mild AD.

10. The use of claim 1, wherein the patient is suffering from early AD.

11. The use of claim 9 or 10, 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.

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

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

14. The use of claim 1, wherein the anti-amyloid beta antibody binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: 1).

15. The use of claim 14, wherein the antibody is capable of binding oligomeric and monomeric forms of amyloid β.

16. The use of claim 15, wherein the antibody is an IgG4 antibody.

17. The use of claim 15 or 16, 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.

18. The use of claim 17, 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.

19. The use of claim 17, wherein the antibody is crenezumab.

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

21. 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 when a T at the single nucleotide polymorphism (SNP) rs1532278 is present in the sample.

22. The method of claim 21, wherein the CLUSTERIN allele is an equivalent allele thereof.

23. The method of claim 22, wherein the equivalent allele is in linkage disequilibrium with SNP rsl532278.

24. The method of claim 21 or 22, wherein the sample is a blood sample, saliva, cheek swab, tissue sample, or a sample of a bodily fluid.

25. The method of any one of claims 21 to 24, wherein a polymorphism is detected by polymerase chain reaction.

26. The method of any one of claims 21 to 24, wherein a polymorphism is detected by sequencing.

27. The method of claim 25 or 26, wherein a 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 (single base primer extension coupled with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry), trityl mass tags, genotyping platforms (such as the Invader Assay®), single base primer extension (SBE) assays, PCR amplification (e.g. PCR amplification on magnetic nanoparticles (MNPs), restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.

28. The method of any one of claims 21 to 24, wherein a 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.

29. The method of claim 21, wherein the patient is suffering from mild AD.

30. The method of claim 21, wherein the patient is suffering from early AD.

31. The method of claim 22, 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.

32. The method of claim 31, wherein the patient has an MMSE score between 22 and 26.

33. The method of any one of claim 21 to 31, wherein the patient is ApoE4 positive.

34. The method of claim 21, wherein the anti-amyloid beta antibody binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: 1).

35. The method of claim 34, wherein the antibody is capable of binding oligomeric and monomeric forms of amyloid β.

36. The method of claim 35, wherein the antibody is an IgG4 antibody.

37. The method of claim 34 or 35, 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.

38. The method of claim 37, 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.

39. The method of claim 37, wherein the antibody is crenezumab.

40. The method of claim 21, wherein the anti-amyloid beta antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab and gantenerumab.

41. 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.

42. The method of claim 41, wherein the polymorphism is a T at the single nucleotide polymorphism (SNP) rsl532278.

43. The method of claim 41, wherein the CLUSTERIN allele is an equivalent allele of an allele comprising SNP rsl532278.

44. The method of claim 43, wherein the equivalent allele is in linkage disequilibrium with SNP rsl532278.

45. The method of claim 41 or 42, wherein the sample is a blood sample, saliva, cheek swab, tissue sample, or a sample of a bodily fluid.

46. The method of any one of claims 41 to 45, wherein the polymorphism is detected by polymerase chain reaction.

47. The method of any one of claims 41 to 45, wherein the polymorphism is detected by sequencing.

48. The method of claim 46 or 47, wherein a 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 (single base primer extension coupled with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry), trityl mass tags, genotyping platforms (such as the Invader Assay®), single base primer extension (SBE) assays, PCR amplification (e.g. PCR amplification on magnetic nanoparticles (MNPs), restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.

49. The method of any one of claims 41 to 45, wherein a 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.

50. The method of claim 41, wherein the patient is suffering from mild AD.

51. The method of claim 41, wherein the patient is suffering from early AD.

52. The method of claim 50, 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..

53. The method of claim 52, wherein the patient has an MMSE score between 22 and 26.

54. The method of any one of claims 41 to 52, wherein the patient is ApoE4 positive.

55. The method of claim 41, wherein the anti-amyloid beta antibody binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: 1).

56. The method of claim 55, wherein the antibody is capable of binding oligomeric and monomeric forms of amyloid β.

57. The method of claim 56, wherein the antibody is an IgG4 antibody.

58. The method of claim 56 or 57, 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.

59. The method of claim 58, 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.

60. The method of claim 59, wherein the antibody is crenezumab.

61. The method of claim 41, wherein the anti-amyloid beta antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab and gantenerumab.

62. 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, or antigen-binding fragment thereof, when the sample contains at least one allele with a T nucleotide at SNP rs1532278.

63. The method of claim 62, wherein the patient is suffering from mild AD.

64. The method of claim 62, wherein the patient is suffering from early AD.

65. The method of claim 62, 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.

66. The method of any one of claim 62 to 65, wherein the patient is ApoE4 positive.

67. The method of claim 62, wherein the anti-amyloid beta antibody binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: 1).

68. The method of claim 67, wherein the antibody is capable of binding oligomeric and monomeric forms of amyloid β.

69. The method of claim 68, wherein the antibody is an IgG4 antibody.

70. The method of claim 68 or 69, 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.

71. The method of claim 70, 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.

72. The method of claim 71, wherein the antibody is crenezumab.

73. The method of claim 62, wherein the anti-amyloid beta antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab, and gantenerumab.

74. 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, or antigen-binding fragment thereof.

75. The method of claim 74, wherein the patient is suffering from early or mild AD.

76. The method of claim 74, 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.

77. The method of claim 76, wherein the patient has an MMSE score between 22 and 26.

78. The method of any one of claim 74 to 76, wherein the patient is ApoE4 positive.

79. The method of claim 74, wherein the anti-amyloid beta antibody binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: 1).

80. The method of claim 79, wherein the antibody is capable of binding oligomeric and monomeric forms of amyloid β.

81. The method of claim 80, wherein the antibody is an IgG4 antibody.

82. The method of claim 80 or 81, 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.

83. The method of claim 82, 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.

84. The method of claim 83, wherein the antibody is crenezumab.

85. The method of claim 74, wherein the anti-amyloid beta antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab and gantenerumab.

86. 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 than a patient who has no alleles with a T nucleotide at SNP rsl532278.

87. The method of claim 86, wherein the patient is suffering from early or mild AD.

88. The method of claim 86, 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.

89. The method of any one of claim 86 to 88, wherein the patient is ApoE4 positive.

90. The method of claim 86, wherein the anti-amyloid beta antibody binds within residues 13 and 24 of amyloid β (1-42)(SEQ ID NO: 1).

91. The method of claim 90, wherein the antibody is capable of binding oligomeric and monomeric forms of amyloid β.

92. The method of claim 91, wherein the antibody is an IgG4 antibody.

93. The method of claim 91 or 92, 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.

94. The method of claim 93, 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.

95. The method of claim 94, wherein the antibody is crenezumab.

96. The method of claim 86, wherein the anti-amyloid beta antibody is selected from the group consisting of solanezumab, bapineuzumab, aducanumab and gantenerumab.

97. The method of any one of claims 74 to 96, wherein the CLUSTERIN allele is an equivalent allele of an allele comprising SNP rs1532278.

98. The method of claim 97, wherein the equivalent allele is in linkage disequilibrium with SNP rs1532278.

99. The method of claim 97 or 98, wherein the sample is a blood sample, saliva, cheek swab, tissue sample, or a sample of a bodily fluid.

100. The method of any one of claims 97 to 99, wherein a polymorphism is detected by polymerase chain reaction.

101. The method of any one of claims 97 to 99, wherein a polymorphism is detected by sequencing.

102. The method of claim 100 or 101, wherein a 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 (single base primer extension coupled with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry), trityl mass tags, genotyping platforms (such as the Invader Assay®), single base primer extension (SBE) assays, PCR amplification (e.g. PCR amplification on magnetic nanoparticles (MNPs), restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.

103. The method of any one of claims 97 to 99, wherein a 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.

104. 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.

105. The kit of claim 104, wherein the kit is used to detect the presence of a T at SNP rs1532278.

106. The kit of claim 104, wherein the reagents comprise a set of oligonucleotides specific for detecting a polymorphism in CLUSTERIN.

107. 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.

108. The use of claim 107, wherein 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 (single base primer extension coupled with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry), trityl mass tags, genotyping platforms (such as the Invader Assay®), single base primer extension (SBE) assays, PCR amplification (e.g. PCR amplification on magnetic nanoparticles (MNPs), restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.

109. The use of claim 107, wherein 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.

110. The use of claim 107, 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 an anti-Abeta antibody.

111. 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, or

antigen binding fragment thereof, wherein the presence of said polymorphism identifies that the patient is more likely to respond to the therapy.

112. The use of claim 111, wherein the CLUSTERIN allele is an allele comprising SNP rs1532278 or an equivalent allele thereof.

113. The use of claim 112, wherein the patient has mild AD.

114. The use of claim 112, wherein the patient has early AD.

115. The use of claim 112, 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.

116. The use of claim 112, wherein 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 (single base primer extension coupled with matrix-assisted laser desorption/ionization time-of-flight mass spectrometry), trityl mass tags, genotyping platforms (such as the Invader Assay®), single base primer extension (SBE) assays, PCR amplification (e.g. PCR amplification on magnetic nanoparticles (MNPs), restriction enzyme analysis of PCR products (RFLP methods), allele-specific PCR, multiple primer extension (MPEX), and isothermal smart amplification.

117. The use of claim 112, wherein 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.