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(71) Applicant: AC IMMUNE SA [CH/CH]; EPFL Innovation Park, Building B, 1015 Lausanne (CH).

(72) Inventors: ADOLFSSON, Oskar; c/o AC Immune SA, EPFL Innovation Park, Building B, 1015 Lausanne (CH).

PIORKOWSKA, Katarzyna Ewa; c/o AC Immune SA, EPFL Innovation Park, Building B, 1015 Lausanne (CH).

(74) Agent: BOULT WADE TENNANT LLP; Salisbury Square House, 8 Salisbury Square, London EC4Y 8AP (GB).

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(54) Title: NOVEL MOLECULES FOR DIAGNOSIS

(57) Abstract: The present invention relates to novel amyloid-beta (abeta) binding molecules, in particular to abeta antibodies or antigen-binding fragments thereof and/or uses thereof. The provided molecules can also be used for determining a predisposition to amyloid-beta associated diseases, disorders or conditions, monitoring residual disorder of a disease or condition, or predicting the responsiveness of a patient who is suffering from such disease or condition to the treatment with a certain medicament. Thus, the invention relates to novel molecules that can be employed for the diagnosis of diseases, disorders or conditions associated with amyloid-beta. A sandwich immunoassay may be based on capture and detection amyloid-beta binding antibodies or antigen-binding fragments thereof in which one or other of the capture or detection antibody or antigen-binding fragment thereof displays no cross-reactivity to soluble amyloid precursor protein (APP). The other amyloid-beta binding antibody or antigen-binding fragment may display cross-reactivity to soluble amyloid precursor protein (APP) without compromising the specificity of the assay against soluble APP.



Novel molecules for diagnosis

FIELD OF THE INVENTION

The present invention relates to novel amyloid-beta (abeta, Abeta, A β) binding molecules, in particular to abeta antibodies or antigen-binding fragments thereof and/or uses thereof. The provided molecules can also be used for determining a predisposition to amyloid-beta associated diseases, disorders or conditions, monitoring the disease, disorder or condition, or predicting the responsiveness of a patient who is suffering from such disease, disorder or condition to the treatment with a certain medicament. Thus, the invention relates to novel molecules that can be employed for the diagnosis and/or treatment of diseases, disorders or conditions associated with amyloid-beta.

BACKGROUND OF THE INVENTION

Alzheimer's disease (AD) is the most common cause of dementia in the elderly affecting an estimated 15 million people worldwide and 40% of the population above 85 years. The disease is characterized by progressive loss of memory, speech, and movement with a total incapacitation of the patient and eventually death. AD takes a big and devastating toll on those with the disease as well as their families, friends and caregivers.

Today, therapy focuses on controlling the symptoms of AD and its various stages. Currently available AD treatment options may help delay AD symptoms from becoming worse for a limited period of time. However, there is no evidence that these medications have any effect on the underlying progression of the disease. No cure is currently available for AD, thus early AD treatment is warranted. With no disease modifying treatment options currently available, the need for good biomarkers for earlier diagnosis is as crucial as ever. The single most prominent and early biochemical characteristic of AD is the formation of extracellular amyloid-beta (A β) plaques in the brain (Calderon-Garciduenas & Duyckaerts, 2017), primarily containing the 42-amino acid form of A β . A β plaques are formed by the 39 to 43 amino acid long A β peptide (resulting from the cleavage of the amyloid precursor protein (APP)), which is in random coil conformation in its natural non-pathological form. During the transition to the pathological state, it transforms mainly into a β -sheet secondary structure, spontaneously aggregating into insoluble deposits. Even if the precise role of A β in the development of AD is still debated, it is widely accepted that soluble A β oligomers impair synapse structure and function, and that the smallest synaptotoxic species are dimers or small soluble multimers, whereas neither A β monomers nor plaque cores significantly alter neuronal viability or synaptic plasticity (Shankar et al., 2008).

Down syndrome (DS), also known as trisomy 21, is one of the most common causes of intellectual disability, affecting 1 in 800 newborns. This condition most commonly involves triplication of chromosome 21 (Belichenko, 2016). Subjects with DS have characteristic facial features, deficits in the immune and endocrine systems, and delayed cognitive development. A key feature of adult subjects with DS is their increased risk of developing similar clinical symptoms of Alzheimer's Disease (AD), characterized by a decline in specific cognitive domains suggestive of a diagnosis of dementia. Virtually all subjects with DS older than 40 years exhibit neuropathological changes similar to AD, in the form of senile plaque formation and neurofibrillary tangles (Head, 2012). It is well accepted that the

neuropathology for AD-like cognitive decline involves the β -amyloid ($A\beta$) peptide deposition and subsequent plaque formation, neurofibrillary tangles, vascular damage, neuro-inflammation and ultimately neuronal cell death. The gene of the amyloid protein precursor (APP), which encodes the precursor protein of $A\beta$, resides on chromosome 21. In subjects with DS, the entire or at least a part of chromosome 21 is present in triplicate. Consequently, this leads to three copies of the gene that encodes APP, which results in the generation of an excess of $A\beta$. An increased $A\beta$ protein production has been shown to correlate with AD-like symptoms in DS subjects as well as in the general population that develops AD (Head, 2012). These findings show conclusively that lifelong overexpression of wild-type APP causes cognitive decline in subjects with DS, in a similar way to the amyloid cascade hypothesis used to describe subjects with AD. Down syndrome-related Alzheimer's Disease is characterized by the presence of brain neuropathological hallmarks of Alzheimer's Disease (including notably the accumulation of brain amyloid plaques and neurofibrillary tangles) which can lead, when the brain lesions are sufficiently developed, to the appearance of clinical symptoms like cognitive decline and functional impairment.

The amyloid-beta associated disease, disorder or condition is a neurological disorder such as Alzheimer's Disease (AD). Other examples of amyloid-beta associated diseases, disorders or conditions according to the invention include mild cognitive impairment (MCI), Down syndrome (DS), Down syndrome-related Alzheimer's Disease, cardiac amyloidosis, cerebral amyloid angiopathy (CAA), multiple sclerosis, Parkinson's disease (PD), Parkinson's Disease with Dementia (PDD), Dementia with Lewy Body, ALS (amyotrophic lateral sclerosis), Adult Onset Diabetes, inclusion body myositis (IBM), ocular amyloidosis, glaucoma, macular degeneration, lattice dystrophy, optic neuritis, Myotonic dystrophy and hepatic dysfunction or failure. Many of these conditions are characterized by, or associated with, loss of cognitive memory capacity. Conditions characterized by, or associated with, loss of cognitive memory capacity according to the invention therefore include AD, mild cognitive impairment (MCI), Down syndrome (DS), Down syndrome-related Alzheimer's Disease, cardiac amyloidosis, cerebral amyloid angiopathy (CAA), multiple sclerosis, Parkinson's disease, Parkinson's disease with Dementia (PDD), Dementia with Lewy body, ALS (amyotrophic lateral sclerosis), Myotonic dystrophy, hepatic dysfunction or failure and inclusion body myositis (IBM).

Currently, there are no clinically validated biomarkers of patient samples (e.g., blood, cerebral spinal fluid, urine, etc.) that can be used to specifically diagnose, stratify, or monitor the progression or regression of an amyloid-beta associated disease, disorder or condition in a subject. The majority of AD biomarker studies are focused on the quantitative changes in Tau and $A\beta$ proteins and modifications of these protein levels in the cerebral spinal fluid from AD patients, with Abeta levels showing an earlier change (Buchhave et al., 2012). For the AD biomarker and diagnostic field, there is a great need for $A\beta$ antibodies that can be engineered and optimized for a given biomarker use and a specific diagnostic technology platform.

The early diagnosis of AD and other conditions where $A\beta$ plays a role in the pathology, and/or the $A\beta$ level is altered in accessible body tissue as a marker of disease progress, is crucial for early intervention. The progression of biochemical alterations in AD is slow, with a relatively long time that passes before the first clinical signs of disease are visible. An even longer time passes before a reliable diagnosis of AD can be made and it can be distinguished from

other forms of dementia (Knopman et al., 2001). With neurodegeneration starting 20 or more years before clinical symptoms with a reliable diagnosis is possible, symptoms of mild cognitive impairment (MCI) may be noted, suggestive of a prodromal stage of AD (Britt et al., 2011). Although MCI is a feature at the prodromal AD stage, it has highly variable natural history with fluctuation of cognitive status over time making it an unreliable predictor of progress towards AD clinical diagnosis (Gauthier et al., 2006). Alterations of biomarkers in accessible tissues serving as surrogates of disease progress are thought to occur early during the preclinical prodromal stage of AD (Robb et al., 2017). Here we describe an antibody generated for use in A β biomarker assays for early diagnosis and/or treatment of diseases, disorders or conditions associated with amyloid-beta.

DESCRIPTION OF THE INVENTION

It is an object of the present invention to provide a binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, that can be employed in uses related to amyloid-beta associated diseases, disorders or conditions, such as for example diagnosis. The binding molecule, in particular the amyloid-beta antibody or antigen-binding fragment thereof, of the invention may selectively bind to or capture any amyloid-beta peptides or species in solution, in particular in body fluid or buffer solution. It was surprisingly found that the amyloid-beta antibody or antigen-binding fragment thereof, of the invention may further selectively bind to or capture any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species and/or no cross-reactivity to soluble amyloid precursor protein (APP), in particular with no cross-reactivity to soluble APP produced from cleavage by alpha-secretase (referred to herein as “soluble APP alpha” or “sAPPalpha”). Reference to selective binding or selective capture means that the binding molecule does not significantly bind to any other species present in solution (apart from amyloid-beta, irrespective of conformational state), such as a body fluid. This may be applicable in both an *in vitro* and an *in vivo* context. Selectivity is important for effective performance in various diagnostic applications as described herein. Thus, in preferred embodiments, the binding molecules of the invention do not significantly bind to other protein species found in plasma (which include apolipoproteins, immunoglobulins, albumin, fibrinogens etc.). That is to say, the binding molecules of the invention are specific for amyloid-beta, irrespective of conformational state, when bound or captured in a plasma sample. The extent of binding of a binding molecule, in particular an amyloid-beta antibody or an antigen-binding fragment thereof, of the invention to an unrelated, non-amyloid-beta protein may be less than about 10% of the binding of the antibody to amyloid-beta as measured, e.g., by a radioimmunoassay (RIA). When reference is made to “no cross-reactivity” to sAPPalpha this is intended to mean that there is no appreciable binding of the binding molecule to sAPPalpha. This may be measured for example by comparing the binding to sAPPalpha with binding to Abeta1-42. When normalized against Abeta1-42 binding, the level of binding to sAPPalpha may be less than 10%, preferably less than 5% or more preferably less than 3% of binding to Abeta1-42. Such comparison may be performed by ELISA, for example an indirect ELISA. A suitable assay is described in Example 3 with reference to Figure 8A. These antibodies are particularly useful in the invention, in particular as capture and/or detection antibodies in a sandwich immunoassay format. The terms “capture” and “detection” are terms of art. The capture antibody binds to the antigen and captures it, typically to a solid surface (to which the capture antibody is attached). The detection antibody also binds the antigen, typically to a non-

overlapping epitope as the capture and detection antibodies bind at the same time. The detection antibody generates the signal for the assay. Detection may be direct (e.g. via a directly labelled antibody, such as an enzyme or fluorescent label) or indirect (e.g. using a secondary antibody which is in turn labelled). It has been found that, provided one of the capture or detection antibodies is an antibody with no cross-reactivity to sAPPalpha the sandwich immunoassay will overall be specific and give no signal for sAPPalpha, even if the other antibody does react with sAPPalpha. Specific antibodies showing no cross-reactivity to sAPPalpha are shown in Table 1 (last column, “-“ indicates no binding). In some aspects of the invention an antibody with no cross-reactivity to sAPPalpha is used as both capture and detection antibody. Such an assay provides sensitive detection of abeta without detecting sAPPalpha (i.e. good specificity as well).

Thus, some binding molecules of the invention may show low cross-reactivity with sAPPalpha. They are usefully employed in combination with a binding molecule of the invention showing no cross-reactivity. Again, low cross-reactivity may be measured for example by comparing the binding to sAPPalpha with binding to Abeta1-42. When normalized against Abeta1-42 binding, the level of binding to sAPPalpha may be between greater than 10 and 60% of binding to Abeta1-42, such as around 50%. Such comparison may be performed by ELISA, for example an indirect ELISA. A suitable assay is described in Example 3 with reference to Figure 8A. Results are shown in Table 1 for the tested antibodies of the invention. It was determined that binding molecules with low levels of cross-reactivity to sAPPalpha may be particularly advantageous when used in combination with binding molecules with no cross-reactivity to sAPPalpha. Thus, the combination of a binding molecule with low levels of cross-reactivity to sAPPalpha and a binding molecule with no cross-reactivity to sAPPalpha may be utilized according to the invention for performing sandwich immunoassays. In particular, the binding molecule with low levels of cross-reactivity to sAPPalpha may be used as capture or detection antibody and the binding molecule with no cross-reactivity to sAPPalpha may be used as detection or capture antibody. A suitable assay of the invention of this type is described in Example 3 with reference to Figure 8B. Thus, for example, antibody ACI-31-25B1-Ab2 may be used as capture antibody and ACI-24-41F12-Ab2 used as detection antibody.

Some binding molecules of the invention may show high cross-reactivity with sAPPalpha. Again, this may be measured for example by comparing the binding to sAPPalpha with binding to Abeta1-42. When normalized against Abeta1-42 binding, the level of binding to sAPPalpha may be greater than 60%, such as between 70 and 90%, such as around 80%, of binding to Abeta1-42. Such comparison may be performed by ELISA, for example an indirect ELISA. A suitable assay is described in Example 3 with reference to Figure 8A. Results are shown in Table 1 for the tested antibodies of the invention. Binding molecules with high levels of cross-reactivity to sAPPalpha may be used in combination with binding molecules with no cross-reactivity to sAPPalpha. Thus, the combination of a binding molecule with high levels of cross-reactivity to sAPPalpha and a binding molecule with no cross-reactivity to sAPPalpha may be utilized according to the invention for performing sandwich immunoassays, giving high sensitivity for Abeta, and no detection of soluble APPalpha (i.e. high specificity). In such an assay, the selectivity is provided by the binding molecule of the invention which does not cross-react with sAPPalpha. In particular, the binding molecule with high levels of cross-reactivity to sAPPalpha may be used as capture or detection antibody and the binding

molecule with no cross-reactivity to sAPPalpha may be used as detection or capture antibody. Antibodies of the invention with high cross-reactivity to sAPPalpha include ACI-8037-103H5-Ab2 and ACI-8037-109F4-Ab1. In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 32; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 36; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 32; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 36; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 41; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 42; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 43; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 45; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 46; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 47. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 41; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 42; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 43; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 45; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 46; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 47.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 61; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 62; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 63; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 65; VL-CDR2 comprising the amino acid sequence of SEQ ID

NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 61; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 62; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 63; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 65; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 73; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 75; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 73; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 75; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 61; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 62; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 83; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 85; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 87. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 61; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 62; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 83; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 85; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 87.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 91; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 92; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 93; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 95; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 96; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 97. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 91; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 92; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 93; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 95; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 96; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 97.

comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 131; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 132; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 133; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 135; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 137.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 141; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 142; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 133; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 137. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 141; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 142; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 133; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 137.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 151; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 152; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 153; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 155; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 156; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 157. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 151; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 152; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 153; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 155; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 156; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 157. In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 161; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 162; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 163; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 165; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 166; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 167. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 161; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 162; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 163; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 165; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 166; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 167.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 171; VH-CDR2 comprising the amino acid

sequence of SEQ ID NO: 172; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 173; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 175; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 156; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 157. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 171; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 172; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 173; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 175; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 156; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 157.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 181; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 182; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 183; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 95; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 96; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 187. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 181; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 182; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 183; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 95; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 96; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 187.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 181; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 182; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 183; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 195; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 196; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 197. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 181; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 182; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 183; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 195; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 196; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 197.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 40 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 44. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 40 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 44.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 60 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 64. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 60 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 64.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 70 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 74. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 70 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 74.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 80 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 84. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 80 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 84.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 90 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 94. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a

Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 90 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 94.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 100 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 104. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 100 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 104.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 110 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 114. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 110 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 114.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 120 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 124. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 120 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 124.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 130 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 134. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 130 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 134.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 140 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 144. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 140 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 144.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 and a Light Chain

Variable Region (VL) comprising the sequence of SEQ ID NO: 154. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 154.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 160 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 164. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 160 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 164.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 170 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 174. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 170 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 174.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 180 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 184. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 180 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 184.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 180 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 194. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 180 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 194.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 or a

Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 or a Heavy Chain Variable Region (VH) having at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 30; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34 or a Light Chain Variable Region (VL) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 34. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 or a Heavy Chain Variable Region (VH) having at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 30; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34 or a Light Chain Variable Region (VL) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 34.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 40 or a Heavy Chain Variable Region (VH) having at least 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 40; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 44 or a Light Chain Variable Region (VL) having at least 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 44. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 40 or a Heavy Chain Variable Region (VH) having at least 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 40; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 44 or a Light Chain Variable Region (VL) having at least 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 44.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 60 or a Heavy Chain Variable Region (VH) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 60; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 64 or a Light Chain Variable Region (VL) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 64. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 60 or a Heavy Chain Variable Region (VH) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 60; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 64 or a Light Chain Variable Region (VL) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 64.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 70 or a Heavy Chain Variable Region (VH) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 70; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 74 or a Light Chain Variable Region (VL) having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 74. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 70 or a Heavy Chain Variable Region (VH) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 70; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 74 or a Light Chain Variable Region (VL) having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 74.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 80 or a Heavy Chain Variable Region (VH) having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 80; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 84. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 80 or a Heavy Chain Variable Region (VH) having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 80; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 84.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 90 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 90; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 94 or a Light Chain Variable Region (VL) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 94. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 90 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 90; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 94 or a Light Chain Variable Region (VL) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 94.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 100 or a Heavy Chain Variable Region (VH) having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 100; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 104. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 100 or a Heavy Chain

Variable Region (VH) having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 100; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 104.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 110 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 110; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 114 or a Light Chain Variable Region (VL) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 114. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 110 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 110; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 114 or a Light Chain Variable Region (VL) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 114.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 120 or a Heavy Chain Variable Region (VH) having at least 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 120; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 124 or a Light Chain Variable Region (VL) having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 124. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 120 or a Heavy Chain Variable Region (VH) having at least 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 120; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 124 or a Light Chain Variable Region (VL) having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 124.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 130 or a Heavy Chain Variable Region (VH) having at least 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 130; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 134. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 130 or a Heavy Chain Variable Region (VH) having at least 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 130; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 134.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 140 or a Heavy Chain

Variable Region (VH) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 140; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 144. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 140 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 140; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 144.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 or a Heavy Chain Variable Region (VH) having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 150; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 154 or a Light Chain Variable Region (VL) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 154. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 or a Heavy Chain Variable Region (VH) having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 150; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 154 or a Light Chain Variable Region (VL) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 154.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 160 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 160; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 164 or a Light Chain Variable Region (VL) having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 164. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 160 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 160; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 164 or a Light Chain Variable Region (VL) having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 164.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 170 or a Heavy Chain Variable Region (VH) having at least 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 170; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 174. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 170 or a Heavy Chain Variable Region (VH) having at least 92%, 93%, 94%, 95%, 96%, 97%, 98%, or

99% sequence identity to the amino acid sequence of SEQ ID NO: 170; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 174.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 180 or a Heavy Chain Variable Region (VH) having at least 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 180; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 184. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 180 or a Heavy Chain Variable Region (VH) having at least 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 180; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 184.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 180 or a Heavy Chain Variable Region (VH) having at least 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 180; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 194. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 180 or a Heavy Chain Variable Region (VH) having at least 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 180; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 194.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 10. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 10.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 or a Heavy Chain Variable Region (VH) having at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 30. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 or a Heavy Chain Variable Region (VH) having at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 30.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 40 or a Heavy Chain Variable Region (VH) having at least 93%, 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 40. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 40 or a Heavy Chain Variable Region (VH) having at least 93%, 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 40.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 60 or a Heavy Chain Variable Region (VH) having at least 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 60. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 60 or a Heavy Chain Variable Region (VH) having at least 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 60.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 70 or a Heavy Chain Variable Region (VH) having at least 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 70. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 70 or a Heavy Chain Variable Region (VH) having at least 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 70.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 80 or a Heavy Chain Variable Region (VH) having at least 99%, sequence identity to the amino acid sequence of SEQ ID NO: 80. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 80 or a Heavy Chain Variable Region (VH) having at least 99%, sequence identity to the amino acid sequence of SEQ ID NO: 80.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 90 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 90. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 90 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 90.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 100 or a Heavy Chain Variable Region (VH) having at least 99%, sequence identity to the amino acid sequence of SEQ ID NO: 100. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 100 or a Heavy Chain Variable Region (VH) having at least 99%, sequence identity to the amino acid sequence of SEQ ID NO: 100.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 110 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 110. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 110 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 110.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 120 or a Heavy Chain Variable Region (VH) having at least 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 120. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 120 or a Heavy Chain Variable Region (VH) having at least 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 120.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 130 or a Heavy Chain Variable Region (VH) having at least 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 130. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 130 or a Heavy Chain Variable Region (VH) having at least 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 130.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 140 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 140. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 140 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 140.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 or a Heavy Chain Variable Region (VH) having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 150. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 or a Heavy Chain Variable Region (VH) having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 150.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 160 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 160. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 160 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 160.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 170 or a Heavy Chain Variable Region (VH) having at least 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 170. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 170 or a Heavy Chain Variable Region (VH) having at least 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 170.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 180 or a Heavy Chain Variable Region (VH) having at least 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 180. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 180 or a Heavy Chain Variable Region (VH) having at least 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 180.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34 or a Light Chain Variable

Region (VL) having at least 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 34. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34 or a Light Chain Variable Region (VL) having at least 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 34.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 44 or a Light Chain Variable Region (VL) having at least 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 44. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 44 or a Light Chain Variable Region (VL) having at least 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 44.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 64 or a Light Chain Variable Region (VL) having at least 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 64. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 64 or a Light Chain Variable Region (VL) having at least 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 64.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 74 or a Light Chain Variable Region (VL) having at least 99%, sequence identity to the amino acid sequence of SEQ ID NO: 74. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 74 or a Light Chain Variable Region (VL) having at least 99%, sequence identity to the amino acid sequence of SEQ ID NO: 74.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 84. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 84.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 94 or a Light Chain Variable Region (VL) having at least 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 94. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 94.

or a Light Chain Variable Region (VL) having at least 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 94.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 104. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 104.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 114 or a Light Chain Variable Region (VL) having at least 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 114. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 114 or a Light Chain Variable Region (VL) having at least 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 114.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 124 or a Light Chain Variable Region (VL) having at least 99%, sequence identity to the amino acid sequence of SEQ ID NO: 124. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 124 or a Light Chain Variable Region (VL) having at least 99%, sequence identity to the amino acid sequence of SEQ ID NO: 124.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 134. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 134.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 144. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 144.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 154 or a Light Chain Variable Region (VL) having at least 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 154. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID

NO: 154 or a Light Chain Variable Region (VL) having at least 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 154.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 164 or a Light Chain Variable Region (VL) having at least 99%, sequence identity to the amino acid sequence of SEQ ID NO: 164. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 164 or a Light Chain Variable Region (VL) having at least 99%, sequence identity to the amino acid sequence of SEQ ID NO: 164.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 174. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 174.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 184. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 184.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 194. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 194.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 32; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; VH-CDR2

comprising the amino acid sequence of SEQ ID NO: 32; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 41; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 42; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 43. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 41; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 42; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 43.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 61; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 62; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 63. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 61; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 62; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 63.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 73. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 73.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 61; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 62; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 83. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 61; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 62; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 83.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 91; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 92; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 93. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 91; VH-CDR2

comprising the amino acid sequence of SEQ ID NO: 92; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 93.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 101; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 102; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 103. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 101; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 102; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 103.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 111; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 112; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 113. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 111; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 112; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 113.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 121; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 122; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 123. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 121; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 122; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 123.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 131; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 132; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 133. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 131; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 132; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 133.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 141; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 142; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 133. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 141; VH-CDR2

comprising the amino acid sequence of SEQ ID NO: 142; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 133.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 151; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 152; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 153. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 151; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 152; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 153.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 161; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 162; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 163. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 161; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 162; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 163.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 171; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 172; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 173. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 171; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 172; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 173.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 181; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 182; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 183. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 181; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 182; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 183.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; VL-CDR2

comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 36; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 36; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 45; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 46; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 47. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 45; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 46; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 47.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 65; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 65; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 75; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 75; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 85; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 87. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 85; VL-CDR2

comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 87.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 95; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 96; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 97. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 95; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 96; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 97.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 105; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 106; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 107. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 105; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 106; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 107.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 115; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 116; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 117. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 115; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 116; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 117.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 125; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 126; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 127. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 125; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 126; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 127.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 135; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 136; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 137. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 135; VL-CDR2

comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 137.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 137. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 137.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 155; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 156; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 157. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 155; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 156; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 157.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 175; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 156; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 157. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 175; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 156; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 157.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 95; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 96; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 187. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 95; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 96; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 187.

In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 195; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 196; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 197. Thus, the invention also provides an amyloid-beta binding molecule, in particular an amyloid-beta antibody or antigen-binding fragment thereof, which comprises VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 195; VL-CDR2

comprising the amino sequence of SEQ ID NO: 21. In some embodiments, the binding molecule, in particular the antibody, or the antigen-binding fragment thereof, comprises a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 22 and comprises a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 23. In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 24 and comprises a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 25. In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 27 and comprises a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 28. In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 38 and comprises a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 39. In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 48 and comprises a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 49. In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 50 and comprises a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 51. In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 56 and comprises a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 57. In some embodiments, the binding molecule, in particular the antibody or the antigen-binding fragment thereof, comprises a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 58 and comprises a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 59.

The binding molecules, antibodies or antigen-binding fragments thereof, may additionally or alternatively comprise amino acid changes in the CDR sequences comprised therein and as compared to the CDR sequences provided in VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17. The binding molecules, antibodies or antigen-binding fragments thereof, may additionally or alternatively comprise amino acid changes in the CDR sequences comprised therein and as compared to the CDR sequences provided in VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 32; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 36; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37. The binding molecules, antibodies or antigen-binding fragments thereof, may additionally or alternatively comprise amino acid changes in the CDR sequences comprised therein and as compared to the CDR sequences provided in VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 41; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 42; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 43; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 45; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 46; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 47. The binding molecules, antibodies

or antigen-binding fragments thereof, may additionally or alternatively comprise amino acid changes in the CDR sequences comprised therein and as compared to the CDR sequences provided in VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 61; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 62; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 63; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 65; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17. The binding molecules, antibodies or antigen-binding fragments thereof, may additionally or alternatively comprise amino acid changes in the CDR sequences comprised therein and as compared to the CDR sequences provided in VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 73; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 75; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17. The binding molecules, antibodies or antigen-binding fragments thereof, may additionally or alternatively comprise amino acid changes in the CDR sequences comprised therein and as compared to the CDR sequences provided in VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 61; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 62; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 83; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 85; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 87. The binding molecules, antibodies or antigen-binding fragments thereof, may additionally or alternatively comprise amino acid changes in the CDR sequences comprised therein and as compared to the CDR sequences provided in VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 91; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 92; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 93; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 95; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 96; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 97. The binding molecules, antibodies or antigen-binding fragments thereof, may additionally or alternatively comprise amino acid changes in the CDR sequences comprised therein and as compared to the CDR sequences provided in VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 101; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 102; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 103; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 105; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 106; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 107. The binding molecules, antibodies or antigen-binding fragments thereof, may additionally or alternatively comprise amino acid changes in the CDR sequences comprised therein and as compared to the CDR sequences provided in VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 111; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 112; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 113; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 115; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 116; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 117. The binding molecules, antibodies or antigen-binding fragments thereof, may additionally or alternatively comprise amino acid changes in the CDR sequences comprised therein and as compared to the CDR sequences provided in VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 121; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 122; and VH-CDR3 comprising the amino acid

[illegible]

comprise amino acid changes in the CDR sequences comprised therein and as compared to the CDR sequences provided in VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 181; VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 182; and VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 183; VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 195; VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 196; and VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 197. In particular, the CDR sequences comprised in the binding molecules, antibodies or antigen-binding fragments thereof, may comprise one, two or three amino acid changes with respect to the CDR sequences provided herein. An "amino acid change" may relate to a mutation, deletion or addition of an amino acid. It may also relate to the chemical alteration of an amino acid, such as for example the formation of a non-natural amino acid.

Amino acid sequence variants of the binding molecules, in particular antibodies or antigen-binding fragments thereof provided herein are contemplated. For example, it may be desirable to improve the binding affinity and/or other biological properties of the antibody. Amino acid sequence variants of an antibody may be prepared by introducing appropriate modifications into the nucleotide sequence encoding the antibody, or by peptide synthesis. Such modifications include, for example, deletions from, and/or insertions into and/or substitutions of residues within the amino acid sequences of the antibody. Any combination of deletion, insertion, and substitution can be made to arrive at the final construct, provided that the final construct possesses the desired characteristics, *e.g.*, antigen-binding.

In certain embodiments, antibody variants having one or more amino acid substitutions are provided. Sites of interest for substitutional mutagenesis include the CDRs and framework regions (FRs). Conservative substitutions are shown in Table A under the heading of "preferred substitutions." More substantial changes are provided in Table A under the heading of "exemplary substitutions," and as further described below in reference to amino acid side chain classes. Amino acid substitutions may be introduced into an antibody of interest and the products screened for a desired activity, *e.g.*, retained/improved antigen binding or improved selectivity.

TABLE A

Original Residue	Exemplary Substitutions	Preferred Substitutions
Ala (A)	Val; Leu; Ile	Val
Arg (R)	Lys; Gln; Asn	Lys
Asn (N)	Gln; His; Asp, Lys; Arg	Gln
Asp (D)	Glu; Asn	Glu
Cys (C)	Ser; Ala	Ser
Gln (Q)	Asn; Glu	Asn

Glu (E)	Asp; Gln	Asp
Gly (G)	Ala	Ala
His (H)	Asn; Gln; Lys; Arg	Arg
Ile (I)	Leu; Val; Met; Ala; Phe; Norleucine	Leu
Leu (L)	Norleucine; Ile; Val; Met; Ala; Phe	Ile
Lys (K)	Arg; Gln; Asn	Arg
Met (M)	Leu; Phe; Ile	Leu
Phe (F)	Trp; Leu; Val; Ile; Ala; Tyr	Tyr
Pro (P)	Ala	Ala
Ser (S)	Thr	Thr
Thr (T)	Val; Ser	Ser
Trp (W)	Tyr; Phe	Tyr
Tyr (Y)	Trp; Phe; Thr; Ser	Phe
Val (V)	Ile; Leu; Met; Phe; Ala; Norleucine	Leu

Amino acids may be grouped according to common side-chain properties:

- (1) hydrophobic: Norleucine, Met, Ala, Val, Leu, Ile;
- (2) neutral hydrophilic: Cys, Ser, Thr, Asn, Gln;
- (3) acidic: Asp, Glu;
- (4) basic: His, Lys, Arg;
- (5) residues that influence chain orientation: Gly, Pro;
- (6) aromatic: Trp, Tyr, Phe.

Non-conservative substitutions will entail exchanging a member of one of these classes for another class.

One type of substitutional variant involves substituting one or more hypervariable region residues of a parent antibody (*e.g.* a humanized or human antibody). Generally, the resulting variant(s) selected for further study will have modifications (*e.g.*, improvements) in certain biological properties (*e.g.*, increased affinity, reduced immunogenicity) relative to the parent antibody and/or will have substantially retained certain biological properties of the parent antibody. An exemplary substitutional variant is an affinity matured antibody, which may be conveniently generated, *e.g.*, using phage display-based affinity maturation techniques. Briefly, one or more CDR residues are mutated and the variant antibodies displayed on phage and screened for a particular biological activity *e.g.* binding affinity).

Alterations (*e.g.*, substitutions) may be made in CDRs, *e.g.*, to improve antibody affinity. Such alterations may be made in CDR "hotspots," *i.e.*, residues encoded by codons that undergo mutation at high frequency during the somatic maturation process (*see, e.g.*, Chowdhury, *Methods Mol. Biol.* 207:179-196 (2008)), and/or SDRs (a-CDRs), with the resulting variant VH or VL being tested for binding affinity. Affinity maturation by constructing and reselecting from secondary libraries has been described, *e.g.*, in Hoogenboom et al., in *Methods in Molecular Biology* 178:1-37 (O'Brien et al., ed., Human Press, Totowa, NJ, (2001).) In some embodiments of affinity maturation, diversity is introduced into the variable genes chosen for maturation by any of a variety of methods (*e.g.*, error-prone PCR, chain shuffling, or oligonucleotide-directed mutagenesis). A secondary library is then created. The library is then screened to identify any antibody variants with the desired affinity. Another method to introduce diversity involves CDR-directed approaches, in which several CDR residues (*e.g.*, 4-6 residues at a time) are randomized. CDR residues involved in antigen binding may be specifically identified, *e.g.*, using alanine scanning mutagenesis or modeling. CDR H3 and CDR-L3 in particular are often targeted.

In certain embodiments, substitutions, insertions, or deletions may occur within one or more CDRs so long as such alterations do not substantially reduce the ability of the antibody to bind antigen. For example, conservative alterations (*e.g.*, conservative substitutions as provided herein) that do not substantially reduce binding affinity may be made in CDRs. Such alterations may be outside of CDR "hotspots" or SDRs. In certain embodiments of the variant VH and VL sequences provided above, each CDR either is unaltered, or contains no more than one, two or three amino acid substitutions.

A useful method for identification of residues or regions of an antibody that may be targeted for mutagenesis is called "alanine scanning mutagenesis" as described by Cunningham and Wells (1989) *Science*, 244: 1081-1085. In this method, a residue or group of target residues (*e.g.*, charged residues such as Arg, Asp, His, Lys, and Glu) are identified and replaced by a neutral or negatively charged amino acid (*e.g.*, alanine or polyalanine) to determine whether the interaction of the antibody with antigen is affected. Further substitutions may be introduced at the amino acid locations demonstrating functional sensitivity to the initial substitutions. Alternatively, or additionally, a crystal structure of an antigen-antibody complex is used to identify contact points between the antibody and antigen. Such contact residues and neighboring residues may be targeted or eliminated as candidates for substitution. Variants may be screened to determine whether they contain the desired properties.

Amino acid sequence insertions include amino- and/or carboxyl-terminal fusions ranging in length from one residue to polypeptides containing a hundred or more residues, as well as intrasequence insertions of single or multiple amino acid residues. Examples of terminal insertions include an antibody with an N-terminal methionyl residue. Other insertional variants of the antibody molecule include the fusion to the N- or C-terminus of the antibody to an enzyme or other label (*e.g.* HRP or AP) or a polypeptide which increases the serum half-life of the antibody.

Within the scope of the present invention, amyloid-beta may have the sequence of abeta1-43 (SEQ ID NO: 3), abeta1-42 (SEQ ID NO: 1), abeta1-41 (SEQ ID NO: 4), abeta1-40 (SEQ ID NO: 5), or abeta1-39 (SEQ ID NO: 6) or fragment thereof.

The term “amyloid-beta peptides or species” refers to amyloid-beta produced by cleavage of amyloid precursor protein (APP) by beta- and gamma-secretase activity. Thus, “amyloid-beta peptides or species” refers to amyloid-beta produced by the amyloidogenic pathway. However, the term is intended to also encompass synthetically produced peptides. Those peptides will have the same amino acid sequence but are not produced by the process that occurs *in vivo*. Methods of peptide synthesis are well known in the art and commercially available. The amyloid-beta peptides or species may mainly comprise amyloid-beta 1-42 (Abeta1-42) or 1-43 (Abeta1-43) and (shorter) fragments thereof. The amyloid-beta peptides or species may incorporate post-translational modifications (PTM), including, but not limited to, phosphorylation (such as phosphorylation of serine at amino acid residue 8 of amyloid-beta (pS8-Abeta)), glycosylation, oligomerization and/or proteolytic cleavage. A synthetic process may be used in order to add some PTMs. This may involve natural components, such as kinases, used in an *in vitro* environment for example. The amyloid-beta peptides or species may include (but are not limited to) the following amyloid-beta peptides: Abeta1-38, Abeta1-39, Abeta1-40, pS8-Abeta1-40, Abeta1-42, pS8-Abeta1-42, and Abeta1-43 and (shorter) fragments thereof. Abeta peptide fragments will include the epitope recognized by the binding molecule. The amyloid-beta peptides or species may adopt different conformational states, such as monomers, oligomers or fibrillar structures.

The amyloid precursor protein (APP), an integral membrane protein, undergoes proteolytic processing to generate multiple peptide fragments some of which are released and are present in sample of body fluids (which may be referred to herein as “biofluids”). The most prominent APP peptide fragments found in biofluids include peptides in the Abeta family (Abeta1-43, Abeta1-42, Abeta1-41, Abeta1-40, and Abeta1-39) released by beta- and gamma-secretase activities of the amyloidogenic pathway. Another cleavage product of APP that is found in biofluids is the soluble APP alpha (sAPPalpha), released by the alpha-secretases of the non-amyloidogenic pathway. The binding molecules of the invention with no cross reactivity to sAPPalpha when used in a combination, such as when paired with a second Abeta antibody in a sandwich assay, advantageously do not detect sAPPalpha.

Thus, a binding molecule, in particular an antibody or antigen-binding fragment thereof, of the invention may selectively bind or capture any amyloid-beta peptides or species in solution, independently of the conformational state of the amyloid-beta peptides or species, with no cross-reactivity to soluble APP alpha. Some binding molecules, in particular an antibody or antigen-binding fragment thereof, of the invention may selectively bind or capture any amyloid-beta peptides or species in solution, independently of the conformational state of the amyloid-beta peptides

or species, with low cross-reactivity to soluble APP alpha. Some binding molecules of the invention may show higher cross-reactivity with sAPPalpha. The binding molecules demonstrating no, low or high cross-reactivity to soluble APP alpha may be combined, for use in sandwich immunoassays, with the proviso that one of the binding molecules of the inventions is employed demonstrating no cross reactivity to sAPPalpha. In this event, the assay displays an overall pair specific signal for Abeta and no signal for sAPPalpha. Preferably, the solution is a body fluid, as described herein, or a buffer solution. More preferably, the solution is a body fluid. Body fluid sample is defined as saliva, urine, nasal secretion, blood, brain and/or CSF, brain and/or ISF, more particularly a blood, brain and/or CSF or brain and/or ISF. Blood samples may be whole blood, serum or plasma samples for example, but are preferably plasma samples.

Binding molecules, in particular antibodies or antigen-binding fragments thereof, of the invention bind to an epitope within the amino acid sequence of SEQ ID NO: 1. SEQ ID NO: 1 is the amino acid sequence of human Abeta 1-42. It will be appreciated that equivalent binding regions exist in non-human Abeta. Thus, for example, the mouse Abeta 1-42 amino acid sequence is 93% (39/42 residues) identical with the human sequence. The invention encompasses binding molecules, in particular antibodies or antigen-binding fragments thereof, that bind to equivalent regions/peptides to those specified above with reference to SEQ ID NO: 1 in non-human Abeta, especially murine Abeta. The Abeta 1-42 amino acid sequence is identical between mouse and rat. In certain embodiments, binding molecules, in particular antibodies or antigen-binding fragments thereof, of the invention bind to an epitope within amino acids residues 1-8 (SEQ ID NO: 2) of SEQ ID NO: 1. In certain embodiments, binding molecules, in particular antibodies or antigen-binding fragments, of the invention bind to an epitope within amino acids residues 1-8 (SEQ ID NO: 2), 1-5 (SEQ ID NO: 7), 17-23 (SEQ ID NO: 9), 22-35 (SEQ ID NO: 29) or 26-34 (SEQ ID NO: 8) of SEQ ID NO: 1. In some embodiments, amino acids 1 and 2 of Abeta 1-42 are essential to antibody binding, in particular for antibody ACI-24-41F12-Ab2 and related (e.g. by common CDR and/or VH/VL sequences) as described herein (see SEQ ID Nos 10-25 and associated embodiments). Without wishing to be bound by theory, this antibody is thought to bind to an epitope that is inaccessible in soluble APPalpha. Soluble APPalpha includes amino acids 1-5 and 1-8 of Abeta1-42 but this antibody does not bind to sAPPalpha with high affinity.

In certain embodiments, a binding molecule, in particular an antibody or antigen-binding fragment thereof, of the invention and as provided herein has a dissociation constant (KD) of $\leq 1\mu\text{M}$, $\leq 100\text{ nM}$, $\leq 10\text{ nM}$, $\leq 1\text{ nM}$, $\leq 0.1\text{ nM}$, $\leq 0.01\text{ nM}$, or $\leq 0.001\text{ nM}$ (e.g. 10^{-8} M or less, e.g. from 10^{-8} M to 10^{-13} M , e.g., from 10^{-9} M to 10^{-13} M), in particular with respect to binding abeta1-42. In some embodiments, a binding molecule, in particular an antibody or antigen-binding fragment thereof, that binds human amyloid-beta is provided, wherein the binding molecule, in particular the antibody or antigen-binding fragment thereof, binds abeta with a KD of less than 100 nM, less than 10 nM, less than 1 nM, less than 200 pM, or less than 100 pM. Within the present invention, it is preferred that the KD is determined using ELISA, such as described in Example 3 provided herein.

The terms "binding molecule", "amyloid-beta antibody", "anti-amyloid-beta antibody", "abeta antibody" or simply "antibody" as used herein refer to a binding molecule, more particularly an antibody that is capable of binding A β monomer and/or soluble A β oligomers with sufficient affinity such that the binding molecule, antibody or antigen-binding fragment thereof, is useful as a diagnostic and/or therapeutic agent in targeting amyloid-beta. In one

embodiment, the extent of binding of a binding molecule, in particular an amyloid-beta antibody or an antigen-binding fragment thereof, of the invention to an unrelated, non-amyloid-beta protein is less than about 10% of the binding of the antibody to amyloid-beta as measured, e.g., by a radioimmunoassay (RIA).

In general, the term "antibody" is used herein in the broadest sense and encompasses various antibody structures, including but not limited to monoclonal antibodies, polyclonal antibodies, multispecific antibodies (e.g., bispecific, biparatopic antibodies), fully-human antibodies and antibody fragments so long as they exhibit the desired antigen-binding activity. Antibodies within the present invention may also be chimeric antibodies, recombinant antibodies, antigen-binding fragments of recombinant antibodies, humanized antibodies or antibodies displayed upon the surface of a phage or displayed upon the surface of a chimeric antigen receptor (CAR) T-cell.

An "antigen-binding fragment" of an antibody refers to a molecule other than an intact antibody that comprises a portion of an intact antibody and that binds the antigen to which the intact antibody binds. Examples of antibody fragments include but are not limited to Fv, Fab, Fab', Fab' -SH, F(ab')₂; diabodies; linear antibodies; single-chain antibody molecules (e.g. scFv); and multispecific antibodies formed from antibody fragments.

The term "monoclonal antibody" as used herein, refers to an antibody obtained from a population of substantially homogeneous antibodies, i.e., the individual antibodies comprising the population are identical except for possible naturally occurring mutations that may be present in minor amounts. Monoclonal antibodies are highly specific, being directed against a single antigenic site. The modified "monoclonal" indicates the character of the antibody as being amongst a substantially homogeneous population of antibodies and is not to be construed as requiring production of the antibody by any particular method. The monoclonal antibodies to be used in accordance with the present invention may be made by the hybridoma method described by Kohler, Nature 256 (1975), 495.

Accordingly, in context of the present invention, the term "antibody" relates to full immunoglobulin molecules as well as to parts of such immunoglobulin molecules (i.e., "antigen-binding fragment thereof"). Furthermore, the term relates, as discussed above, to modified and/or altered antibody molecules. The term also relates to recombinantly or synthetically generated/synthesized antibodies. The term also relates to intact antibodies as well as to antibody fragments thereof, like, separated light and heavy chains, Fab, Fv, Fab', Fab'-SH, F(ab')₂. The term antibody also comprises but is not limited to fully human antibodies, chimeric antibodies, humanized antibodies, CDR-grafted antibodies and antibody constructs, like single chain Fvs (scFv) or antibody-fusion proteins.

The term "CDR" as employed herein relates to "complementary determining region", which is well known in the art. The CDRs are parts of immunoglobulins that determine the specificity of said molecules and make contact with a specific ligand. The CDRs are the most variable part of the molecule and contribute to the diversity of these molecules. There are three CDR regions CDR1, CDR2 and CDR3 in each V domain. VH-CDR, or CDR-H depicts a CDR region of a Variable Heavy Chain and VL-CDR or CDR-L relates to a CDR region of a Variable Light Chain. VH means the Variable Heavy Chain and VL means the Variable Light Chain. The CDR regions of an Ig-derived region may be determined as described in Kabat "Sequences of Proteins of Immunological Interest", 5th edit. NIH Publication no. 91-3242 U.S. Department of Health and Human Services (1991); Chothia J., Mol. Biol. 196 (1987), 901-917 or

Chothia, Nature 342 (1989), 877-883. CDR sequences provided herein are defined according to Kabat. However, it will be understood by the skilled person that the invention is intended to encompass binding molecules in which the CDR sequences are defined according to any useful identification/numbering scheme. For example, Chothia (Canonical structures for the hypervariable regions of immunoglobulins. Chothia C, Lesk AM. J Mol Biol. 1987 Aug 20; 196(4):901-17), IMGT (IMGT, the international ImMunoGeneTics database. Giudicelli V, Chaume D, Bodmer J, Müller W, Busin C, Marsh S, Bontrop R, Marc L, Malik A, Lefranc MP. Nucleic Acids Res. 1997 Jan 1; 25(1):206-11 and Unique database numbering system for immunogenetic analysis. Lefranc MP. Immunol Today. 1997 Nov; 18(11):509), MacCallum (MacCallum RM, Martin AC, Thornton JM, J Mol Biol. 1996 Oct 11; 262(5):732-45) and Martin (Abhinandan KR, Martin ACR. Analysis and improvements to Kabat and structurally correct numbering of antibody variable domains. Mol Immunol. (2008) 45:3832–9. 10.1016/j.molimm.2008.05.022) numbering schemes may be adopted in order to define the CDRs.

An "Fc" region contains two heavy chain fragments comprising the CH2 and CH3 domains of an antibody. The two heavy chain fragments are held together by two or more disulfide bonds and by hydrophobic interactions of the CH3 domains.

The "Fv region" comprises the variable regions from both the heavy and light chains, but lacks the constant regions.

An "antibody that binds to an epitope" within a defined region of a protein is an antibody that requires the presence of one or more of the amino acids within that region for binding to the protein.

In certain embodiments, one or more amino acid modifications may be introduced into the Fc region of an antibody provided herein, thereby generating an Fc region variant. The Fc region variant may comprise a murine Fc region sequence, an antibody isotype or class (e.g. IgG1, IgG2a, IgG2b or IgG2c) comprising an amino acid modification (e.g. substitution) at one or more amino acid positions. The Fc region variant may comprise a human Fc region sequence (an antibody isotype or class, e.g., a human IgM, IgG1, IgG2, IgG3 or IgG4 Fc region) comprising an amino acid modification (e.g. a substitution) at one or more amino acid positions. An antibody isotype or class refers to the type of constant domain, region, or sequence contained within its heavy chain. There are five major classes of antibodies: IgA, IgD, IgE, IgG, and IgM, and several of these may be further divided into subclasses or isotypes, e.g., IgA1, IgA2, IgG1, IgG2, IgG2a (for murine only), IgG2b (for murine only), IgG2c (for murine only), IgG3, and IgG4. The heavy chain constant domains that correspond to the different classes of immunoglobulins are called α , δ , ϵ , γ , and μ , respectively. The antibody light chain constant domain, region, or sequence can be one of two major classes; kappa (κ) or lambda (λ). When the light chain class is not specified it is assumed to be the more common κ light chain. In some embodiments, the antibody or the antigen-binding fragment thereof, of the invention comprises murine IgG2a or chimeric (mouse/human) IgG1 isotypes.

In some embodiments, an antibody or an antigen-binding fragment thereof, of the invention may be produced recombinantly. In some embodiments, a(n isolated) nucleic acid is provided, wherein the (isolated) nucleic acid encodes a binding molecule, in particular an antibody or an antigen-binding fragment thereof of the invention. The term "nucleic acid" as used herein refers to a nucleic acid molecule. In some embodiments, a host cell or a cell-free

expression system is provided, wherein the host cell or the cell-free expression system comprises a(n isolated) nucleic acid that encodes a binding molecule, in particular an antibody or an antigen-binding fragment thereof of the invention. In some embodiments, a host cell is transfected with a vector comprising a(n isolated) nucleic acid encoding a binding molecule, in particular an antibody or an antigen-binding fragment thereof, of the invention. In some embodiments, a host cell is transfected with a vector comprising a(n isolated) nucleic acid encoding the Heavy Chain (HC) and the Light Chain (LC) of a binding molecule, in particular an antibody or an antigen-binding fragment thereof, of the invention. In some embodiments, a host cell is transfected with a) a first vector comprising a(n isolated) nucleic acid encoding the Heavy Chain (HC) of a binding molecule, in particular an antibody or an antigen-binding fragment thereof, of the invention, and with b) a second vector comprising a(n isolated) nucleic acid encoding the Light Chain (LC) of a binding molecule, in particular an antibody or an antigen-binding fragment thereof, of the invention. In some embodiments, the host cell can be, but is not limited to, a Chinese Hamster Ovary (CHO) cell. Suitable host cells may be prokaryote, yeast, or higher eukaryote cells, specifically mammalian cells. Examples of useful mammalian host cell lines are monkey kidney CV1 line transformed by SV40 (COS-7, ATCC CRL 1651); human embryonic kidney line (293 or 293 cells subcloned for growth in suspension culture, Graham et al., J. Gen. Virol. 36:59 (1977)); baby hamster kidney cells (BHK, ATCC CCL 10); Chinese hamster ovary cells/-DHFR (CHO, Urlaub et al., Proc. Natl. Acad. Sci. USA 77:4216 (1980)); mouse sertoli cells (TM4, Mather, Biol. Reprod. 23:243-251 (1980)); mouse myeloma cells SP2/0-AG14 (ATCC CRL 1581; ATCC CRL 8287) or NS0 (HPA culture collections no. 85110503); monkey kidney cells (CV1 ATCC CCL 70); African green monkey kidney cells (VERO-76, ATCC CRL-1587); human cervical carcinoma cells (HELA, ATCC CCL 2); canine kidney cells (MDCK, ATCC CCL 34); buffalo rat liver cells (BRL 3A, ATCC CRL 1442); human lung cells (W138, ATCC CCL 75); human liver cells (Hep G2, HB 8065); mouse mammary tumor (MMT 060562, ATCC CCL51); TRI cells (Mather et al., Annals N.Y. Acad. Sci. 383:44-68 (1982)); MRC 5 cells; FS4 cells; and a human hepatoma line (Hep G2), as well as DSM's PERC-6 cell line. Expression vectors suitable for use in each of these host cells are also generally known in the art. The term "host cell" generally refers to a cultured cell line. Accordingly, whole human beings into which an expression vector encoding an antigen binding polypeptide according to the invention has been introduced are explicitly excluded from the definition of a "host cell". Cell-free expression systems may be based on use of cell lysates or extracts, such as CHO cell lysates (Stech, M., Nikolaeva, O., Thoring, L. *et al.* Cell-free synthesis of functional antibodies using a coupled *in vitro* transcription-translation system based on CHO cell lysates. *Sci Rep* 7, 12030 (2017)).

In some embodiments, a(n isolated) nucleic acid is provided, wherein the (isolated) nucleic acid encodes a binding molecule, in particular an antibody or an antigen-binding fragment thereof, of the invention as provided herein. In some embodiments, a host cell is provided, wherein the host cell comprises a(n isolated) nucleic acid that encodes a binding molecule, in particular an antibody or an antigen-binding fragment thereof, of the invention as provided herein. In some embodiments, a method of producing a binding molecule, in particular an antibody or an antigen-binding fragment thereof, of the invention as provided herein, comprising culturing the host cell or a cell-free expression system under conditions suitable for producing the binding molecule, in particular the antibody or the antigen-binding fragment thereof. In some embodiments, a method for producing a(n isolated) binding molecule, in particular an antibody or an antigen-binding fragment thereof, of the invention as provided herein, comprising the steps of: a)

culturing the host cell or the cell-free expression system under conditions suitable for producing the binding molecule, in particular antibody or antigen-binding fragment thereof, and b) recovering the binding molecule, in particular antibody or antigen-binding fragment thereof. Recovery of the binding molecule, in particular antibody or antigen-binding fragment thereof may be performed by any suitable means as would be understood by one skilled in the art. Recovery may comprise purification to a desired level of purity. Recovery may comprise isolation of the antibody from the culture. Recovery may involve use of chromatography for example. Such production methods may be performed at scale and thus may enable large-scale production of the binding molecules of the invention. A binding molecule produced according to this method is also provided, which may be considered an isolated binding molecule.

As used herein, the term "isolated" means that the molecule, e.g. the nucleic acid or antibody, has been separated and/or recovered from its natural environment. Within the present invention, the molecule is preferably chemically synthesized, or synthesized in a cellular system different from the cell from which it naturally originates, and is thus "isolated" from its naturally associated components. The molecule may be isolated from its natural environment by e.g. purification or produced by means of a technical process (including but not limited to gene synthesis, polymerase chain reaction (PCR), vector purification and protein (antibody) purification). Such molecules may be, in particular, a nucleic acid, such as DNA-, RNA-, or cDNA-sequence, or a peptide, antibody or protein.

The present invention is not limited to an isolated antibody or an isolated nucleic acid in accordance with the above definition, but also relates to an antibody or nucleic acid as such irrespective of its origin.

The same applies to peptides, nucleic acids, DNA, RNA and/or cDNA sequences provided by the present invention, which are encompassed in isolated form, as defined above, or in any other form. Different techniques known in the art, including (but not limited to) SDS-polyacrylamide gel electrophoresis (SDS-PAGE), column chromatography, filtration, isoelectrofocusing, dialysis, recrystallization, ultrafiltration, salting-out, solvent precipitation, solvent extraction, distillation and immunoprecipitation, can be used to purify, isolate or separate the binding molecules, in particular antibodies or antigen-binding fragments or derivatives thereof, of the present invention from inside the cells or from outside the cells (e.g. medium).

In some embodiments, a(n isolated) nucleic acid is provided, wherein the (isolated) nucleic acid comprises SEQ ID NO: 18 encoding an abeta antibody or antigen-binding fragment thereof. In some embodiments, a(n isolated) nucleic acid is provided, wherein the (isolated) nucleic acid comprises SEQ ID NO: 19 encoding an abeta antibody or antigen-binding fragment thereof. In some embodiments, a(n isolated) nucleic acid is provided, wherein the (isolated) nucleic acid comprises SEQ ID NO: 52 encoding an abeta antibody or antigen-binding fragment thereof. In some embodiments, a(n isolated) nucleic acid is provided, wherein the (isolated) nucleic acid comprises SEQ ID NO: 53 encoding an abeta antibody or antigen-binding fragment thereof. In some embodiments, a(n isolated) nucleic acid is provided, wherein the (isolated) nucleic acid comprises SEQ ID NO: 54 encoding an abeta antibody or antigen-binding fragment thereof. In some embodiments, a(n isolated) nucleic acid is provided, wherein the (isolated) nucleic acid comprises SEQ ID NO: 55 encoding an abeta antibody or antigen-binding fragment thereof. In some embodiments, a(n isolated) nucleic acid is provided, wherein the (isolated) nucleic acid comprises SEQ ID NO: 68 encoding an abeta

[illegible]

a(n isolated) nucleic acid is provided, wherein the (isolated) nucleic acid comprises SEQ ID NO: 179 encoding an abeta antibody or antigen-binding fragment thereof. In some embodiments, a(n isolated) nucleic acid is provided, wherein the (isolated) nucleic acid comprises SEQ ID NO: 188 encoding an abeta antibody or antigen-binding fragment thereof. In some embodiments, a(n isolated) nucleic acid is provided, wherein the (isolated) nucleic acid comprises SEQ ID NO: 189 encoding an abeta antibody or antigen-binding fragment thereof. In some embodiments, a(n isolated) nucleic acid is provided, wherein the (isolated) nucleic acid comprises SEQ ID NO: 199 encoding an abeta antibody or antigen-binding fragment thereof.

In some embodiments, a diagnostic composition is provided, comprising a binding molecule, in particular an antibody or antigen-binding fragment thereof, of the invention (and as provided herein) and an acceptable carrier and/or excipient. For example, the binding molecule, in particular the antibody or antigen-binding fragment thereof, may be combined, as appropriate, with acceptable carriers or media such as sterilized water or saline solution, vegetable oils, emulsifiers, suspensions, surfactants, stabilizers, flavoring agents, excipients, vehicles, preservatives, and binders, for example, and formulated into a diagnostic preparation. Preferred diagnostic compositions of the invention are compatible with use of body fluids as the test sample. Thus, the diagnostic compositions may permit direct use with body fluid samples without requiring further processing of the body fluid sample. For cellular and/or tissue applications, the diagnostic compositions may be identically, or differently, formulated in some embodiments to facilitate use with such samples.

In some embodiments, a diagnostic composition is provided, comprising at least two amyloid-beta binding antibodies or antigen-binding fragments thereof of the invention and an acceptable carrier and/or excipient.

In some embodiments, a diagnostic composition is provided comprising:

- a. a first amyloid-beta binding antibody or antigen-binding fragment thereof that selectively binds to any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species, and
- b. a second amyloid-beta binding antibody or antigen-binding fragment thereof that selectively binds to any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species

wherein at least one, or both, of the first and second antibodies displays no cross-reactivity to soluble amyloid precursor protein (APP), in particular with no cross-reactivity to soluble APP alpha.

One or both antibodies may be an antibody of the invention. Either antibody may be used as capture antibody. It may, therefore, be provided for attachment, or attached, to a solid support. The other antibody may be used as detection antibody. It may, therefore, be conjugated with a suitable label. Conjugated antibodies are described herein, which description applies *mutatis mutandis*.

In some embodiments, both, of the first and second antibodies display no cross-reactivity to soluble amyloid precursor protein (APP), in particular with no cross-reactivity to soluble APP alpha. In other embodiments, one of the first and second antibody or antigen-binding fragment thereof displays cross-reactivity to soluble amyloid precursor protein (APP). The cross-reactivity may be low or high. The other antibody or antigen-binding fragment thereof displays no cross-reactivity to soluble amyloid precursor protein (APP). In some embodiments, a diagnostic composition is provided, comprising at least two amyloid-beta binding antibodies or antigen-binding fragments thereof and an acceptable carrier and/or excipient, wherein the amyloid-beta binding antibodies or antigen-binding fragments are selected from:

- a) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17; and/or
- b) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 32; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 36; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37; and/or
- c) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 151; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 152; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 153; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 155; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 156; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 157.

In specific embodiments, a diagnostic composition is provided comprising a) and b) above or a) and c) above.

In a more preferred embodiment, a diagnostic composition is provided, comprising at least two amyloid-beta binding antibodies or antigen-binding fragments thereof and an acceptable carrier and/or excipient, wherein the amyloid-beta binding antibodies or antigen-binding fragments are selected from:

- a) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17; and
- b) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 32; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 36; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37.

In some embodiments, a diagnostic composition is provided, comprising at least two amyloid-beta binding antibodies or antigen-binding fragments thereof and an acceptable carrier and/or excipient, wherein the amyloid-beta binding antibodies or antigen-binding fragments are selected from:

- a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14; and/or
- b) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34; and/or
- c) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 154.

In specific embodiments, a diagnostic composition is provided comprising a) and b) above or a) and c) above.

In a more preferred embodiment, a diagnostic composition is provided, comprising at least two amyloid-beta binding antibodies or antigen-binding fragments thereof and an acceptable carrier and/or excipient, wherein the amyloid-beta binding antibodies or antigen-binding fragments are selected from:

- a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14; and
- b) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34.

In some embodiments, a diagnostic composition is provided, comprising at least two amyloid-beta binding antibodies or antigen-binding fragments thereof and an acceptable carrier and/or excipient, wherein the amyloid-beta binding antibodies or antigen-binding fragments are selected from:

- a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14; and/or
- b) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 or a Heavy Chain Variable Region (VH) having at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 30; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34 or a Light Chain Variable Region (VL) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 34; and/or
- c) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 or a Heavy Chain Variable Region (VH) having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 150; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 154 or a Light Chain Variable Region (VL) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 154.

In specific embodiments, a diagnostic composition is provided comprising a) and b) above or a) and c) above.

In some embodiments, a diagnostic composition is provided, comprising at least two amyloid-beta binding antibodies or antigen-binding fragments thereof and an acceptable carrier and/or excipient, wherein the amyloid-beta binding antibodies or antigen-binding fragments are selected from:

- a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14; and
- b) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 or a Heavy Chain Variable Region (VH) having at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 30; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34 or a Light Chain Variable Region (VL) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 34

In some embodiments, a diagnostic composition is provided, comprising at least one amyloid-beta binding antibody or antigen-binding fragment thereof of the invention, in particular an antibody or antigen-binding fragment thereof that displays no cross-reactivity to soluble amyloid precursor protein (APP), in combination with at least one amyloid-beta antibody known in the art and an acceptable carrier and/or excipient. In some embodiments, the amyloid-beta antibody known in the art is a commercially available abeta binding antibody. In some embodiments, the antibody is selected from: NAB228 (Invitrogen), 6E10 (Covance), 2C8 (Invitrogen), 4G8 (Chemicon), W0-2 (Merck) and DE2 (Chemicon). Such antibodies may be used as capture antibody and the antibody of the invention used as detection antibody (or vice versa).

In some embodiments, a conjugated binding molecule, in particular antibody or antigen-binding fragment thereof, is provided, comprising a binding molecule, in particular an antibody or antigen-binding fragment thereof, described herein and a conjugated molecule. Conjugates of the invention may be referred to as immunoconjugates. Any suitable conjugated molecule may be employed according to the invention. Suitable examples include, but are not limited to enzymes (e.g. alkaline phosphatase or horseradish peroxidase), avidin, streptavidin, biotin, Protein A/G, magnetic beads, fluorophores, radioactive isotopes (i.e., radioconjugates), nucleic acid molecules, detectable labels, therapeutic agents, toxins and blood brain barrier penetration moieties. Conjugation methods are well known in the art and several technologies are commercially available for conjugating antibodies to a label or other molecule. Conjugation is typically through amino acid residues contained within the binding molecules of the invention (such as lysine, histidine or cysteine). They may rely upon methods such as the NHS (Succinimidyl) ester method, isothiocyanate method, carbodiimide method and periodate method. Conjugation may be achieved through creation of fusion proteins for example. This is appropriate where the binding molecule is conjugated with another protein molecule. Thus, suitable genetic constructs may be formed that permit the expression of a fusion of the binding molecule of the invention with the label or other molecule. Conjugation may be via a suitable linker moiety to ensure suitable spatial separation of the antibody and conjugated molecule, such as detectable label. However, a linker may not be required in all instances.

In some embodiments, a diagnostic composition is provided, comprising an isolated binding molecule, in particular an antibody or antigen-binding fragment thereof, described herein and an acceptable carrier and/or excipient.

The binding molecules, in particular amyloid-beta binding antibody or antigen-binding fragment thereof, of the invention have many uses. They may be employed for research use, in particular as an analytical tool or reference molecule. They may be used in detecting amyloid-beta aggregates, including plaques, *in vitro* or *in vivo*. The binding molecules may be used to stain amyloid-beta aggregates. For example, the binding molecules may be used for histochemical detection in postmortem brain tissue. The binding molecules are typically labelled and may be directly or indirectly labelled as discussed herein. Such uses may be performed in relation to any suitable animal, in particular mammal. Preferred subjects are human and mice.

In some embodiments, a method of diagnosing an amyloid-beta associated disease, disorder or condition, such as Alzheimer's Disease (AD), mild cognitive impairment (MCI), Down syndrome (DS), Down syndrome-related Alzheimer's Disease, cardiac amyloidosis, cerebral amyloid angiopathy (CAA), multiple sclerosis, Parkinson's disease (PD), Parkinson's Disease with Dementia (PDD), Lewy body dementia, ALS (amyotrophic lateral sclerosis), Adult Onset Diabetes, inclusion body myositis (IBM), ocular amyloidosis, glaucoma, macular degeneration, lattice dystrophy, optic neuritis, Myotonic dystrophy and hepatic dysfunction or failure is provided. The method comprises administering a binding molecule, in particular an antibody or an antigen-binding fragment thereof, of the invention or a diagnostic composition of the invention to the subject. More particularly in some embodiments, a method of diagnosing an amyloid-beta associated disease, disorder or condition is provided, wherein the amyloid-beta associated disease, disorder or condition is selected from the group consisting of Alzheimer's Disease (AD), Down syndrome (DS), Down syndrome-related Alzheimer's Disease, cerebral amyloid angiopathy (CAA), Myotonic dystrophy and Lewy body dementia. The subject is typically a mammalian subject, preferably a human. For *in vivo* methods, the binding molecule is typically labelled with a suitable label for visualization purposes.

In certain embodiments, a binding molecule, in particular an antibody or antigen-binding fragment thereof, of the invention and as provided herein is useful for detecting the presence of abeta in a biological sample. In certain embodiments, a binding molecule, in particular an antibody or antigen-binding fragment thereof, of the invention and as provided herein is useful for detecting the presence of abeta in a body fluid sample. The term "body fluid sample" includes samples derived from a body fluid by further processing, such as concentration, centrifugation and addition of further substances such as buffers and preservatives. In particular embodiments, a binding molecule, in particular an antibody or antigen-binding fragment thereof, of the invention as provided herein is useful for detecting the presence of pathological abeta in a biological sample. The term "detecting" as used herein encompasses quantitative and/or qualitative detection. The biological sample is typically obtained from a mammal, in particular a human. The biological sample is typically a clinical sample from a subject suspected of, or being screened for, an amyloid-beta associated disease, disorder or condition according to any of the methods described herein. The obtaining of a sample does not form an essential step of the methods of the invention, which may therefore begin with an already isolated sample. Obtaining a sample may be performed according to any suitable technique, determined by the sample in question. In certain embodiments, a biological sample comprises a cell, tissue and/or a body fluid (nasal secretions,

urine, blood, etc.) from the subject. Examples of suitable biological samples include cerebrospinal fluid (CSF), interstitial fluid (ISF), a cell or tissue of the brain (e.g., brain cortex or hippocampus). Examples of suitable body fluids include cerebrospinal fluid (CSF), interstitial fluid (ISF), blood (to include whole blood and derivatives such as serum and plasma), urine and nasal secretions. In some embodiments, a biological sample is cerebrospinal fluid (CSF) or blood. In some embodiments, the biological sample is plasma.

In certain embodiments, a method for detecting abeta in a biological sample is provided, wherein the method comprises contacting the biological sample with a binding molecule, in particular an abeta antibody or antigen-binding fragment thereof, of the invention as provided herein under conditions permissive for binding of the binding molecule, in particular the abeta antibody or antigen-binding fragment thereof, to abeta, and detecting whether a complex is formed between the binding molecule, in particular the abeta antibody or antigen-binding fragment thereof, and abeta. If formation of a complex is detected, it may be determined that the sample contains abeta. In the absence of complex formation or complex formation below a pre-determined threshold, it may be determined that the sample is free of abeta. Such method may be an *in vitro* or *in vivo* method. Further, the complex formed between the binding molecule, the abeta antibody or the antigen-binding fragment thereof, and abeta in a test biological sample can be compared to the complex formed in a control biological sample (e.g., a biological sample from a healthy subject or subjects). The amount of the complex formed between the binding molecule, the abeta antibody or the antigen-binding fragment thereof, and abeta in a test biological sample can also be quantified and compared to the amount of the complex formed in a control biological sample (e.g., a biological sample from a healthy subject or subjects) or to the average amount of the complex known to be formed in healthy subjects.

In certain embodiments, a binding molecule, in particular an antibody or antigen-binding fragment thereof, of the invention and as provided herein is useful for detecting the presence of abeta in a biological sample. In particular embodiments, the binding molecule, in particular an antibody or antigen-binding fragment thereof, of the invention and as provided herein is useful as an assay reagent, positive control, biomarker detection reagent and/or calibrator for an immunoassay, (including, but not limited to an ELISA, MSD (Meso Scale Discovery Inc., USA), Luminex (Luminex Corp., USA), AlphaLISA (PerkinElmer, Inc., USA), Gyrolab (Gyros Protein Technologies AB, Sweden), Simoa (Quanterix Corp., USA), Gyros™ (Given et al., 2012), Singulex Erenna (EMD Millipore, Corp., USA), iR-SENSE/Immuno-Infrared assay (Nabers et al, 2016), MITOMI (Piraino et al, 2016), Immunoprecipitation combined with liquid chromatography mass spectrometry (IP LC-MS/MS; Shimadzu, Germany), Surface plasmon resonance (SPR; Cytiva Europe, Switzerland), Atomic force microscope (AFM) (Kiio and Park, 2020) or any other assay technology or kit that relies on antibodies for target immunocapture and/or detection). As such, the binding molecule, in particular antibody or antigen-binding fragments thereof, may be used in assays for validating/screening binding molecules, abeta or abeta fragments, abeta antibodies or antigen-binding fragments thereof. The binding molecules, in particular an antibody or antigen-binding fragment thereof, of the invention may be used as detection tools and/or positive controls as they bind to all abeta species in the sample in selective fashion. In one embodiment, at least two amyloid-beta antibodies or antigen-binding fragments thereof may be used as assay reagents, positive controls, biomarker detection reagent and/or calibrators for an immunoassay as listed above. In one embodiment, at least two

amyloid-beta antibodies or antigen-binding fragments thereof may be used in an immunoassay, preferably a sandwich assay (ELISA), resulting in a sandwich pairing of antibodies, wherein preferably the antibodies are selected from ACI-24-41F12-Ab3, ACI-31-25B1-Ab2 and ACI-8041-5A2D4-Ab1, even more preferably the antibodies are ACI-24-41F12-Ab3 and ACI-31-25B1-Ab2. In one embodiment, the at least two amyloid-beta antibodies or antigen-binding fragments thereof may be used in a sandwich assay (ELISA), resulting in a sandwich pairing of antibodies, wherein one antibody or antigen-binding fragment thereof is used for capturing the target (including but not limited to abeta), preferably ACI-31-25B1-Ab2, and wherein another antibody or antigen-binding fragment thereof is used for detecting the captured target, preferably ACI-24-41F12-Ab3, more preferably ACI-24-41F12-Ab3 that is conjugated to a detectable label.

The invention relates to a method of detecting amyloid-beta in a sample obtained from a subject, the method comprising:

- a. capturing amyloid beta with an amyloid-beta binding antibody or antigen-binding fragment thereof that selectively binds to any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species, and
- b. detecting captured amyloid beta with an amyloid-beta binding antibody or antigen-binding fragment thereof that selectively binds to any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species

wherein at least one, or both, of the capture (a) and detection (b) antibody or antigen-binding fragment thereof displays no cross-reactivity to soluble amyloid precursor protein (APP), in particular with no cross-reactivity to soluble APP alpha. One or both of the capture and detection antibodies may be an antibody of the invention. The capture antibody may be provided for attachment, or attached, to a solid support. The detection antibody may be conjugated with a suitable label. Conjugated antibodies are described herein, which description applies *mutatis mutandis*.

In some embodiments, both the capture and detection antibodies display no cross-reactivity to soluble amyloid precursor protein (APP), in particular with no cross-reactivity to soluble APP alpha. In other embodiments, one of the capture and detection antibody or antigen-binding fragment thereof displays cross-reactivity to soluble amyloid precursor protein (APP). The cross-reactivity may be low or high. The other antibody or antigen-binding fragment thereof displays no cross-reactivity to soluble amyloid precursor protein (APP).

In some embodiments, the capture antibody or antigen-binding fragment is immobilized on a solid support, such as on the surface of a well (e.g. in a multiwell plate). In some embodiments, the detection antibody or antigen-binding fragment is labelled with a detectable label.

In some embodiments, the capture or detection (preferably detection) amyloid-beta binding antibody or antigen-binding fragment comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; a VL-CDR2 comprising the amino acid

sequence of SEQ ID NO: 16; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17. In some embodiments, the capture or detection (preferably detection) amyloid-beta binding antibody or antigen-binding fragment comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14. In some embodiments, the capture or detection (preferably detection) amyloid-beta binding antibody or antigen-binding fragment comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14

In some embodiments, the capture or detection (preferably capture) amyloid-beta binding antibody or antigen-binding fragment comprises:

- a. a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 32; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 36; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37; or
- b. a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 151; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 152; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 153; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 155; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 156; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 157.

The preferred capture amyloid-beta binding antibody or antigen-binding fragment comprises a) above.

In some embodiments, the capture or detection (preferably capture) amyloid-beta binding antibody or antigen-binding fragment comprises:

- a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34; or
- b) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 154.

In some embodiments, the capture or detection (preferably capture) amyloid-beta binding antibody or antigen-binding fragment comprises:

- a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 or a Heavy Chain Variable Region (VH) having at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 30; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34 or a Light Chain Variable Region (VL) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 34; and/or

- b) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 or a Heavy Chain Variable Region (VH) having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 150; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 154 or a Light Chain Variable Region (VL) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 154.

The invention also relates to a method of detecting amyloid-beta in a sample obtained from a subject, the method comprising:

- a. capturing amyloid beta with an amyloid-beta binding antibody or antigen-binding fragment thereof that selectively binds to any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species and displays no cross-reactivity to soluble amyloid precursor protein (APP), in particular with high cross-reactivity to soluble APP alpha; and
- b. detecting captured amyloid beta with an amyloid-beta binding antibody or antigen-binding fragment thereof that selectively binds to any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species and displays cross-reactivity (low or high) to soluble amyloid precursor protein (APP), in particular with no cross-reactivity to soluble APP alpha.

In some embodiments, the capture antibody or antigen-binding fragment is immobilized on a solid support, such as on the surface of a well (e.g. in a multiwell plate). In some embodiments, the capture and/or detection antibody or antigen-binding fragment has high affinity for abeta. In some embodiments, the detection antibody or antigen-binding fragment is labelled with a detectable label. In some embodiments, the capture amyloid-beta binding antibody or antigen-binding fragment comprises:

- a. a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 32; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 36; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37; or
- b. a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 151; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 152; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 153; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 155; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 156; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 157.

The preferred capture amyloid-beta binding antibody or antigen-binding fragment comprises a) above.

In some embodiments, the capture amyloid-beta binding antibody or antigen-binding fragment comprises:

- a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34; or

- b) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 154.

In some embodiments, the capture amyloid-beta binding antibody or antigen-binding fragment comprises:

- a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 or a Heavy Chain Variable Region (VH) having at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 30; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34 or a Light Chain Variable Region (VL) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 34; and/or

a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 or a Heavy Chain Variable Region (VH) having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 150; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 154 or a Light Chain Variable Region (VL) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 154. In some embodiments, the detection amyloid-beta binding antibody or antigen-binding fragment comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17. In some embodiments, the detection amyloid-beta binding antibody or antigen-binding fragment comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14. In some embodiments, the detection amyloid-beta binding antibody or antigen-binding fragment comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14.

In some embodiments, the invention comprises a method of detecting amyloid-beta in a sample obtained from a subject, the method comprising the step of capturing amyloid beta with a first amyloid-beta binding antibody or fragment thereof and the step of detecting captured amyloid-beta in the sample with a second amyloid-beta binding antibody or fragment thereof, wherein each amyloid-beta binding antibody or antigen-binding fragment thereof is independently selected from: ACI-24-41F12-Ab3, ACI-31-25B1-Ab2 and ACI-8041-5A2D4-Ab1, preferably the antibodies are ACI-24-41F12-Ab3 and ACI-31-25B1-Ab2, more preferably ACI-24-41F12-Ab3 that is conjugated to a detectable label. In another embodiment of the invention, the step of capturing amyloid beta is performed with a first amyloid-beta binding antibody or fragment thereof selected from ACI-24-41F12-Ab3, ACI-31-25B1-Ab2 and ACI-8041-5A2D4-Ab1, preferably the antibodies are ACI-24-41F12-Ab3 and ACI-31-25B1-Ab2, more preferably ACI-31-25B1-Ab2. In another embodiment of the invention, the step of detecting the captured amyloid beta is performed with a second amyloid-beta binding antibody or fragment thereof that is conjugated to a detectable label and selected from ACI-24-41F12-Ab3, ACI-31-25B1-Ab2 and ACI-8041-5A2D4-Ab1, preferably the antibodies are ACI-24-

41F12-Ab3 and ACI-31-25B1-Ab2, more preferably ACI-24-41F12-Ab3. In some embodiments, the step of detecting captured amyloid-beta in the sample is performed with a second amyloid-beta binding antibody or fragment thereof, wherein each amyloid-beta binding antibody or antigen-binding fragment thereof is conjugated to a detectable label known in the art.

The invention therefore provides a method of detecting amyloid-beta in a sample obtained from a subject, the method comprising contacting the sample with a binding molecule, in particular an antibody or antigen-binding fragment of the invention and detecting binding of the antibody or antigen-binding fragment thereof in order to detect amyloid-beta in the sample. Similarly, the invention provides a method of quantifying amyloid-beta in a sample obtained from a subject, the method comprising contacting the sample with a binding molecule, in particular an antibody or antigen-binding fragment of the invention and performing quantification based on the binding of the binding molecule to amyloid-beta. This method may comprise comparing the amyloid-beta levels in the sample to those in a control sample or samples. The levels in control samples represent known levels against which the levels in the test sample may be determined. The control samples are not, therefore, necessarily tested at the same time as the method of quantification is performed. However, in some embodiments, reference levels are determined in parallel with the test sample. For example, a quantitative ELISA, ELISA, MSD (Meso Scale Discovery Inc., USA), Luminex (Luminex Corp., USA), AlphaLISA (PerkinElmer, Inc., USA), Gyrolab (Gyros Protein Technologies AB, Sweden), Simoa (Quanterix Corp., USA), Gyros™ (Given et al., 2012), Singulex Erenna (EMD Millipore, Corp., USA), iR-SENSE/Immuno-InfraRed assay (Nabers et al, 2016), MITOMI (Piraino et al, 2016), Immunoprecipitation combined with liquid chromatography mass spectrometry (IP LC-MS/MS; Shimadzu, Germany), Surface plasmon resonance (SPR; Cytiva Europe, Switzerland), Atomic force microscope (AFM) (Kiio and Park, 2020) may be performed. A standard curve may be generated to permit quantification based on a dilution series (serial dilution) of abeta. Diagnostic compositions of the invention may be used in such methods. The sandwich immunoassays described herein, incorporating a suitable capture and detection antibody or antigen binding fragment thereof, may be used in the methods of quantifying amyloid-beta in a sample obtained from a subject.

The invention also provides a method for diagnosing a disease, disorder and/or condition associated with amyloid-beta comprising contacting the sample with a binding molecule, in particular an antibody or antigen-binding fragment of the invention and comparing the amyloid-beta levels in the sample to those in a control sample or samples. Higher levels of amyloid-beta in the sample compared with a control level based on healthy subjects are indicative of a disease, disorder and/or condition associated with amyloid-beta. Additionally or alternatively similar or higher levels of amyloid-beta in the sample compared with a diseased control (i.e. one or more samples from a subject having the disease, disorder and/or condition associated with amyloid-beta) are indicative of a disease, disorder and/or condition associated with amyloid-beta. Diagnostic compositions of the invention may be used in such methods. The sandwich immunoassays described herein, incorporating a suitable capture and detection antibody or antigen binding fragment thereof, may be used in the methods of diagnosing a disease, disorder and/or condition associated with amyloid-beta.

The binding molecules of the invention are also useful in classification methods, for example, to indicate the relative stage of the disease, disorder and/or condition associated with amyloid-beta. The invention therefore also provides a

method for classifying a disease, disorder and/or condition associated with amyloid-beta comprising contacting a sample from a subject with a binding molecule, in particular an antibody or antigen-binding fragment of the invention and comparing the amyloid-beta levels in the sample to those in a control sample or samples in order to classify the disease. A range of controls representative of different classes of disease may be employed in order to classify the sample. The test sample may be classified based on the best match to the control samples. Higher levels of amyloid-beta in the sample compared with a control level based on healthy subjects are indicative of a disease, disorder and/or condition associated with amyloid-beta. Similar or higher levels of amyloid-beta in the sample compared with a diseased control at a certain stage of disease are indicative of that stage of disease, disorder and/or condition associated with amyloid-beta. Such methods may be performed in relation to subjects known to have the disease, disorder and/or condition associated with amyloid-beta and/or in relation to subjects not already known to have the disease, disorder and/or condition associated with amyloid-beta. Diagnostic compositions of the invention may be used in such methods. The sandwich immunoassays described herein, incorporating a suitable capture and detection antibody or antigen binding fragment thereof, may be used in the classification methods of the invention.

The invention also provides a method for monitoring a disease, disorder and/or condition associated with amyloid-beta at two or more time points using samples from a subject, the method comprising contacting the samples with a binding molecule, in particular an antibody or antigen-binding fragment of the invention and comparing the amyloid-beta levels in the samples, wherein higher levels of amyloid-beta in the later sample compared with one or more earlier samples are indicative of progression of a disease, disorder and/or condition associated with amyloid-beta. Similarly, the invention provides a method for monitoring a disease, disorder and/or condition associated with amyloid-beta at two or more time points using samples from a subject, the method comprising contacting the samples with a binding molecule, in particular an antibody or antigen-binding fragment of the invention and comparing the amyloid-beta levels in the samples, wherein lower levels of amyloid-beta in the later sample compared with one or more earlier samples are indicative of regression of a disease, disorder and/or condition associated with amyloid-beta. These methods also permit a lack of progression of the disease to be monitored, where there is no significant change in levels of amyloid-beta in the later sample compared with one or more earlier samples. Such methods are typically performed in relation to subjects known to have the disease, disorder and/or condition associated with amyloid-beta. Diagnostic compositions of the invention may be used in such methods. The sandwich immunoassays described herein, incorporating a suitable capture and detection antibody or antigen binding fragment thereof, may be used in the monitoring methods of the invention.

Monitoring methods are useful to determine whether a particular therapy is successful or otherwise. The invention therefore also provides a method for monitoring a disease, disorder and/or condition associated with amyloid-beta at two or more time points using samples from a subject, the method comprising contacting the samples with a binding molecule, in particular an antibody or antigen-binding fragment of the invention, wherein lower levels of amyloid-beta in the later sample compared with one or more earlier samples are indicative of successful treatment of a disease, disorder and/or condition associated with amyloid-beta. The therapy may be any suitable candidate therapeutic agent, such as an antibody or small molecule therapeutic. These methods also permit a lack of progression of the disease to

be monitored, where there is no significant change in levels of amyloid-beta in the later sample compared with one or more earlier samples. This may also be considered successful treatment in some circumstances. Indeed, a decline in the rate of increase of abeta levels between samples, compared with the rate of increase prior to therapy, may also be considered indicative of successful treatment. Such methods are typically performed in relation to subjects known to have the disease, disorder and/or condition associated with amyloid-beta. Unsuccessful treatment may be determined where the treatment provides no decline in the rate of increase of abeta levels between samples, compared with the rate of increase prior to therapy. Diagnostic compositions of the invention may be used in such methods. The sandwich immunoassays described herein, incorporating a suitable capture and detection antibody or antigen binding fragment thereof, may be used in the methods of monitoring therapy of the invention.

The binding molecules of the invention may also be used to assist with therapy selection. Thus, the invention provides a method for selecting a therapy for treatment of a disease, disorder and/or condition associated with amyloid-beta, the method comprising contacting samples taken before and after treatment with a binding molecule, in particular an antibody or antigen-binding fragment of the invention, wherein lower levels of amyloid-beta in the sample taken after treatment compared with the sample taken before treatment are indicative of successful treatment of a disease, disorder and/or condition associated with amyloid-beta and thus the therapy is selected for treatment. The therapy may be any suitable candidate therapeutic agent, such as an antibody or small molecule therapeutic. A therapy halting progression of the disease may also be selected, where there is no significant change in levels of amyloid-beta in the later sample compared with one or more earlier samples. This may also be considered successful treatment in some circumstances. Indeed, a decline in the rate of increase of abeta levels between samples, compared with the rate of increase prior to therapy, may also be considered indicative of successful treatment and therefore result in selection of the particular therapy. Such methods are typically performed in relation to subjects known to have the disease, disorder and/or condition associated with amyloid-beta. Unsuccessful treatment may be determined where the treatment provides no decline in the rate of increase of abeta levels between samples, compared with the rate of increase prior to therapy. Such therapy is not selected for treatment. Alternatively, higher levels of amyloid-beta in the sample taken after treatment compared with the sample taken before may be indicative of unsuccessful treatment of a disease, disorder and/or condition associated with amyloid-beta and thus the therapy is not selected for treatment. Diagnostic compositions of the invention may be used in such methods. The sandwich immunoassays described herein, incorporating a suitable capture and detection antibody or antigen binding fragment thereof, may be used in the therapy selection methods of the invention (as applied to individual subjects).

Methods of the invention are also useful to determine whether a particular therapy is successful or otherwise in the context of a larger, controlled study, such as a clinical trial. Thus, these methods are typically applied to a treatment group of subjects that is compared with a group of subjects not treated with the therapy. In such a context, control samples not treated with the therapy are also available for comparative purposed (placebo group). The invention therefore also provides a method for assessing a candidate therapy for a disease, disorder and/or condition associated with amyloid-beta, the method comprising, following treatment of one or more subjects, contacting samples from the one or more treated subjects with a binding molecule, in particular an antibody or antigen-binding fragment of the

invention, wherein lower levels of amyloid-beta in the samples compared with levels in corresponding samples from subjects not treated with the therapy are indicative of successful treatment of a disease, disorder and/or condition associated with amyloid-beta. The methods are typically performed in relation to a plurality (i.e. at least two) treated subjects and a plurality of control subjects. The treated and control groups may or may not be of the same size. They may each comprise 3 or more, 4 or more, 5 or more, 10 or more, 20 or more, 50 or more subjects in some embodiments. The therapy may be any suitable candidate therapeutic agent, such as a biologic, in particular an antibody, a vaccine or small molecule therapeutic. The methods may be performed at multiple time points in matched samples between the treatment and placebo groups in order to monitor the effectiveness of the candidate therapy over a defined time period. An initial pre-therapy sample is typically also taken. Thus, the methods may comprise contacting samples from the one or more treated subjects and the subjects not treated with the therapy with a binding molecule, in particular an antibody or antigen-binding fragment of the invention prior to treatment to determine base levels of amyloid-beta. "Prior to treatment" means prior to administration of the therapy or the placebo depending upon the subject group. The binding molecules of the invention may therefore also be used to assist with assessment of candidate therapies in the context of clinical trials. Candidate therapies providing successful treatment may be selected and, ultimately, approved for marketing. Diagnostic compositions of the invention may be used in such methods. The sandwich immunoassays described herein, incorporating a suitable capture and detection antibody or antigen binding fragment thereof, may be used in the therapy selection methods of the invention (as applied to clinical trials).

According to all of the relevant methods, the disease, disorder and/or condition associated with amyloid-beta may be selected from the group consisting of Alzheimer's Disease (AD), mild cognitive impairment (MCI), Down syndrome (DS), Down syndrome-related Alzheimer's Disease, cardiac amyloidosis, cerebral amyloid angiopathy (CAA), multiple sclerosis, Parkinson's disease, Parkinson's Disease with Dementia (PDD), Lewy body dementia, ALS (amyotrophic lateral sclerosis), Adult Onset Diabetes, inclusion body myositis (IBM), ocular amyloidosis, glaucoma, macular degeneration, lattice dystrophy, optic neuritis, Myotonic dystrophy and hepatic dysfunction or failure. In specific embodiments, the amyloid-beta associated disease, disorder or condition is Alzheimer's Disease (AD), Down syndrome (DS), Down syndrome-related Alzheimer's Disease, cerebral amyloid angiopathy (CAA), Myotonic dystrophy, or Lewy body dementia.

Suitable samples employed with the various methods are typically biological samples, particularly body fluids as discussed herein. Suitable immunoassay formats are known to the skilled person including, but not limited to an ELISA, MSD (Meso Scale Discovery Inc., USA), Luminex (Luminex Corp., USA), AlphaLISA (PerkinElmer, Inc., USA), Gyrolab (Gyros Protein Technologies AB, Sweden), Simoa (Quanterix Corp., USA), Gyros™ (Given et al., 2012), Singulex Erenna (EMD Millipore, Corp., USA), iR-SENSE/Immuno-InfraRed assay (Nabers et al, 2016), MITOMI (Piraino et al, 2016), Immunoprecipitation combined with liquid chromatography mass spectrometry (IP LC-MS/MS; Shimadzu, Germany), Surface plasmon resonance (SPR; Cytiva Europe, Switzerland), Atomic force microscope (AFM) (Kiio and Park, 2020).

In some embodiments, a binding molecule, an abeta antibody or antigen-binding fragment thereof, of the invention is part of a diagnostic kit comprising such a binding molecule, abeta antibody or antigen-binding fragment thereof. Such

kits may comprise all necessary components for performing the herein provided methods and/or assays, such as, for example, buffers, detectable dyes, laboratory equipment, reaction containers, instructions and the like. The binding molecules, in particular antibodies or antigen-binding fragment thereof, may be conjugated with a label or other molecule as discussed herein. They may be labelled or expressed with dyes or tags, such as fluorophores or fluorescent dyes, or be coupled to an enzyme or to a solid support (such as an assay chip), as required for each corresponding assay technology. In a further embodiment, a binding molecule, in particular an antibody or antigen-binding fragment thereof, of the invention may be conjugated to radioactive isotopes (i.e., radioconjugates), nucleic acid molecules, detectable labels, therapeutic agents, toxins or to blood brain barrier penetration moieties, forming immunoconjugates. The kits may be used to perform any of the methods of the invention and thus may incorporate any suitable components, including reagents, necessary to perform those methods. The invention is further directed to a kit comprising an antibody or antigen-binding fragment thereof of the invention. The kits typically contain the antibody or antigen-binding fragment thereof of the invention in a suitable container. The antibody or antigen-binding fragment thereof may be provided in the form of a diagnostic composition ready for application or it may be provided in the kit with suitable agents for reconstitution of the product, such as saline solution. The kit may be provided with instructions for use. The discussion of the methods of the invention therefore applies *mutatis mutandis*. Kits for performing the sandwich immunoassays of the invention are also provided. They incorporate a suitable capture and detection antibody or antigen binding fragment thereof. Thus, the invention relates to a kit for detecting amyloid-beta in a sample obtained from a subject, the kit comprising:

- a. a capture amyloid-beta binding antibody or antigen-binding fragment thereof that selectively binds to any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species ; and
- b. a detection amyloid-beta binding antibody or antigen-binding fragment thereof that selectively binds to any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species

wherein at least one of the capture and detection antibody or antigen-binding fragment thereof displays no cross-reactivity to soluble amyloid precursor protein (APP), in particular with no cross-reactivity to soluble APP alpha.

One or both antibodies may be an antibody of the invention.

In some embodiments, the capture antibody or antigen-binding fragment is immobilized on a solid support, such as on the surface of a well (e.g. in a multiwell plate) or is provided with a solid support and/or means for immobilizing the capture antibody or antigen-binding fragment on a solid support. In some embodiments, the detection antibody or antigen-binding fragment is labelled with a detectable label or is provided with a label and means for conjugating the antibody to the label, either directly or indirectly.

In some embodiments, both of the capture and detection antibodies display no cross-reactivity to soluble amyloid precursor protein (APP), in particular with no cross-reactivity to soluble APP alpha. In other embodiments, one of the

capture and detection antibody or antigen-binding fragment thereof displays cross-reactivity to soluble amyloid precursor protein (APP). The cross-reactivity may be low or high. The other antibody or antigen-binding fragment thereof (either capture or detection antibody) displays no cross-reactivity to soluble amyloid precursor protein (APP).

In some embodiments, the capture or detection (preferably detection) amyloid-beta binding antibody or antigen-binding fragment comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17. In some embodiments, the capture or detection (preferably detection) amyloid-beta binding antibody or antigen-binding fragment comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14. In some embodiments, the capture or detection (preferably detection) amyloid-beta binding antibody or antigen-binding fragment comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14.

In some embodiments, the capture or detection (preferably capture) amyloid-beta binding antibody or antigen-binding fragment comprises:

- a. a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 32; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 36; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37; or
- b. a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 151; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 152; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 153; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 155; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 156; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 157.

The preferred capture amyloid-beta binding antibody or antigen-binding fragment comprises a) above.

In some embodiments, the capture or detection (preferably capture) amyloid-beta binding antibody or antigen-binding fragment comprises:

- a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34; or
- b) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 154.

In some embodiments, the capture or detection (preferably capture) amyloid-beta binding antibody or antigen-binding fragment comprises:

- a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 or a Heavy Chain Variable Region (VH) having at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 30; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34 or a Light Chain Variable Region (VL) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 34; and/or
- b) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 or a Heavy Chain Variable Region (VH) having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 150; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 154 or a Light Chain Variable Region (VL) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 154.

The invention also relates to a kit for detecting amyloid-beta in a sample obtained from a subject, the kit comprising:

- a. a capture amyloid-beta binding antibody or antigen-binding fragment thereof that selectively binds to any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species and displays no cross-reactivity to soluble amyloid precursor protein (APP), in particular with high cross-reactivity to soluble APP alpha; and
- b. A detection amyloid-beta binding antibody or antigen-binding fragment thereof that selectively binds to any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species and displays cross-reactivity (low or high) to soluble amyloid precursor protein (APP), in particular with no cross-reactivity to soluble APP alpha.

In some embodiments, the capture antibody or antigen-binding fragment is immobilized on a solid support, such as on the surface of a well (e.g. in a multiwell plate) or is provided with a solid support and/or means for immobilizing the capture antibody or antigen-binding fragment on a solid support. In some embodiments, the detection antibody or antigen-binding fragment has high affinity for abeta. In some embodiments, the detection antibody or antigen-binding fragment is labelled with a detectable label or is provided with a label and means for conjugating the antibody to the label, either directly or indirectly. In some embodiments, the capture amyloid-beta binding antibody or antigen-binding fragment comprises:

- a. a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 32; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 36; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37; or
- b. a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 151; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 152; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 153; a

VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 155; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 156; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 157.

The preferred capture amyloid-beta binding antibody or antigen-binding fragment comprises a) above.

In some embodiments, the capture amyloid-beta binding antibody or antigen-binding fragment comprises:

- a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34; or
- b) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 154.

In some embodiments, the capture amyloid-beta binding antibody or antigen-binding fragment comprises:

- a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 or a Heavy Chain Variable Region (VH) having at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 30; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34 or a Light Chain Variable Region (VL) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 34; and/or
- b) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 or a Heavy Chain Variable Region (VH) having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 150; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 154 or a Light Chain Variable Region (VL) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 154.

In some embodiments, the detection amyloid-beta binding antibody or antigen-binding fragment comprises a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17. In some embodiments, the detection amyloid-beta binding antibody or antigen-binding fragment comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14. In some embodiments, the detection amyloid-beta binding antibody or antigen-binding fragment comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14.

The invention may be further defined in the following numbered clauses:

1. An antibody or antigen-binding fragment thereof comprising a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; a VH-

CDR3 comprising the amino acid sequence of SEQ ID NO: 13; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17, wherein the antibody or antigen-binding fragment thereof binds to amyloid-beta.

2. An antibody or antigen-binding fragment thereof of clause 1, wherein the antibody or antigen-binding fragment binds to amino acids residues 1-8 (SEQ ID NO: 2) of human amyloid beta SEQ ID NO: 1.
3. The antibody or antigen-binding fragment thereof of clauses 1-2, wherein the antibody comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 or a heavy chain variable region (VH) having at least 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 10.
4. The antibody or antigen-binding fragment thereof of any of the preceding clauses, wherein the antibody comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 or a heavy chain variable region (VH) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14.
5. The antibody or antigen-binding fragment thereof of any of the preceding clauses, wherein the antibody comprises a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14.
6. The antibody or antigen-binding fragment thereof of any of the preceding clauses, wherein the antibody comprises a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 20, a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 21.
7. The antibody or antigen-binding fragment thereof of any of the preceding clauses, wherein the antibody comprises a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 22 and a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 23.
8. The antibody or antigen-binding fragment thereof of any of the preceding clauses, wherein the antibody comprises a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 24 a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 25.
9. The antibody or antigen-binding fragment thereof of any of the preceding clauses, for use in the diagnosis of an amyloid-beta associated disease or condition in a subject.
10. The antibody or antigen-binding fragment thereof of any of the preceding clauses, for use in the detection of amyloid-beta in a sample.
11. The antibody or antigen-binding fragment thereof of any of the preceding clauses, for use in the detection of amyloid-beta in a sample, wherein the sample is a saliva, urine, blood, brain and/or CSF sample, more particularly a blood and/or CSF sample.
12. The antibody or antigen-binding fragment thereof of any of the preceding clauses, for use in the diagnosis of an amyloid-beta associated disease or condition wherein the amyloid-beta associated disease or condition is selected from the group consisting of Alzheimer's Disease (AD), mild cognitive impairment (MCI), Down

syndrome, Down syndrome-related Alzheimer's Disease, cardiac amyloidosis, cerebral amyloid angiopathy (CAA), multiple sclerosis, Parkinson's disease, Lewy body dementia, ALS (amyotrophic lateral sclerosis), Adult Onset Diabetes, inclusion body myositis (IBM), ocular amyloidosis, glaucoma, macular degeneration, lattice dystrophy and optic neuritis.

13. The antibody or antigen-binding fragment thereof of any of the preceding clauses, for use in the diagnosis of an amyloid-beta associated disease or condition wherein the amyloid-beta associated disease or condition is Alzheimer's Disease (AD), Down syndrome, Down syndrome-related Alzheimer's Disease, cerebral amyloid angiopathy (CAA), Myotonic dystrophy, Lewy body dementia.
14. The antibody or antigen-binding fragment thereof of any of the preceding clauses, for use in the diagnosis of an amyloid-beta associated disease or condition wherein the amyloid-beta associated disease or condition is Alzheimer's Disease (AD).
15. The antibody or antigen-binding fragment thereof of any of the clauses 1 to 13, for use in the diagnosis of an amyloid-beta associated disease or condition wherein the amyloid-beta associated disease or condition is Down Syndrome.
16. A diagnostic composition comprising an isolated antibody or antigen-binding fragment thereof of any of the preceding clauses and an acceptable carrier and/or excipient.
17. An isolated nucleic acid encoding an antibody of any of the clauses 1-15.
18. A nucleic acid comprising a nucleotide sequence as provided in SEQ ID NO: 18 or SEQ ID NO: 19.
19. A recombinant vector comprising the nucleic acid of clauses 17 or 18.
20. A host cell comprising the nucleic acid of clauses 17 or 18 and/or the vector of clause 19.
21. An isolated host cell that expresses the antibody or antigen-binding fragment of any of the clauses 1-15.
22. A method for producing an isolated binding molecule, in particular an antibody comprising the steps of: a) culturing the host cell of clauses 20 or 21 under conditions suitable for producing the antibody or antigen-binding fragment thereof, and b) isolating the antibody or antigen-binding fragment thereof.

The invention may be further defined in the following numbered clauses:

1. An amyloid-beta binding antibody or antigen-binding fragment thereof comprising:
 - a) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17; or
 - b) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 32; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 36; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37; or

- c) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 41; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 42; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 43; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 45; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 46; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 47.
- 2. The amyloid-beta binding antibody or antigen-binding fragment thereof of clause 1, wherein the antibody or the antigen-binding fragment thereof comprises:
 - a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 10; or
 - b) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 or a Heavy Chain Variable Region (VH) having at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 30; or
 - c) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 40 or a Heavy Chain Variable Region (VH) having at least 93%, 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 40.
- 3. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding clauses, wherein the antibody or the antigen-binding fragment thereof comprises:
 - a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14; or
 - b) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 or a Heavy Chain Variable Region (VH) having at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 30; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34 or a Light Chain Variable Region (VL) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 34; or
 - c) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 40 or a Heavy Chain Variable Region (VH) having at least 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 40; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 44 or a Light Chain Variable Region (VL) having at least 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 44.
- 4. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding clauses, wherein the antibody or the antigen-binding fragment thereof comprises:

- a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14; or
 - b) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34; or
 - c) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 40 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 44.
5. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding clauses, wherein the antibody comprises:
- a) a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 20 and a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 21; or
 - b) a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 22 and a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 23; or
 - c) a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 24 and a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 25; or
 - d) a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 27 and a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 28; or
 - e) a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 38 and a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 39; or
 - f) a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 48 and a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 49; or
 - g) a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 50 and a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 51.
6. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding clauses, which binds to an epitope within amino acids residues 1-5 (SEQ ID NO: 7), 1-8 (SEQ ID NO: 2), 22-35 (SEQ ID NO: 29) or 26-34 (SEQ ID NO: 8) of SEQ ID NO: 1 or to an equivalent epitope in non-human amyloid-beta.
7. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding clauses, which is a murine, a chimeric, a humanized or a human antibody or an antigen-binding fragment thereof.
8. The amyloid-beta binding antibody or antigen-binding fragment thereof of any one of the preceding clauses, which is an IgM, IgG1, IgG2, IgG2a, IgG2b, IgG3 or IgG4 antibody or antigen-binding fragment thereof.
9. The amyloid-beta binding antibody or antigen-binding fragment thereof of any one of the preceding clauses, which is conjugated to another molecule, in particular a detectable label.
10. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding clauses, for use in the diagnosis of an amyloid-beta associated disease, disorder or condition in a subject.
11. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding clauses, for use in the detection of amyloid-beta in a biological sample.

12. The amyloid-beta binding antibody or antigen-binding fragment thereof of clause 11 wherein the biological sample is a body fluid sample or a buffer solution.
13. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of clause 1 to 12, for use in the detection of amyloid-beta in a body fluid sample, wherein the body fluid sample is saliva, urine, nasal secretion, blood (including whole blood, plasma and serum, preferably plasma), brain and/or CSF sample, brain and/or ISF sample, more particularly blood, brain, CSF and/or ISF sample.
14. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding clauses, for use in the diagnosis of an amyloid-beta associated disease, disorder or condition wherein the amyloid-beta associated disease, disorder or condition is selected from the group consisting of Alzheimer's Disease (AD), mild cognitive impairment (MCI), Down syndrome (DS), Down syndrome-related Alzheimer's Disease, cardiac amyloidosis, cerebral amyloid angiopathy (CAA), multiple sclerosis, Parkinson's disease, Parkinson's Disease with Dementia (PDD), Lewy body dementia, ALS (amyotrophic lateral sclerosis), Adult Onset Diabetes, inclusion body myositis (IBM), ocular amyloidosis, glaucoma, macular degeneration, lattice dystrophy, optic neuritis, Myotonic dystrophy and hepatic dysfunction or failure.
15. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding clauses, for use in the diagnosis of an amyloid-beta associated disease, disorder or condition wherein the amyloid-beta associated disease, disorder or condition is Alzheimer's Disease (AD), Down syndrome (DS), Down syndrome-related Alzheimer's Disease, cerebral amyloid angiopathy (CAA), Myotonic dystrophy, or Lewy body dementia.
16. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding clauses, for use in the diagnosis of an amyloid-beta associated disease, disorder or condition wherein the amyloid-beta associated disease, disorder or condition is Alzheimer's Disease (AD).
17. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the clauses 1 to 15 for use in the diagnosis of an amyloid-beta associated disease, disorder or condition wherein the amyloid-beta associated disease, disorder or condition is Down Syndrome (DS).
18. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the clauses 1 to 15 for use in the diagnosis of an amyloid-beta associated disease, disorder or condition wherein the amyloid-beta associated disease, disorder or condition is Down Syndrome-related Alzheimer's disease.
19. A method of detecting amyloid-beta in a sample obtained from a subject, the method comprising contacting the sample with the amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding clauses and detecting binding of the antibody or antigen-binding fragment thereof in order to detect amyloid-beta in the sample.
20. A method of quantifying amyloid-beta in a sample obtained from a subject, the method comprising contacting the sample with the amyloid-beta binding antibody or antigen-binding fragment thereof of any of clauses 1-18 and quantifying amyloid-beta in a sample based on the level of binding of the antibody or antigen-binding fragment thereof to amyloid-beta.
21. A method for diagnosing a disease, disorder and/or condition associated with amyloid-beta comprising performing the method of clauses 19 or 20 wherein higher levels of amyloid-beta in the sample compared with a

control level based on healthy subjects are indicative of a disease, disorder and/or condition associated with amyloid-beta.

22. A method for diagnosing a disease, disorder and/or condition associated with amyloid-beta comprising performing the method of clause 19 or 20 wherein similar or higher levels of amyloid-beta in the sample compared with a diseased control level are indicative of a disease, disorder and/or condition associated with amyloid-beta.
23. A method for classifying a disease, disorder and/or condition associated with amyloid-beta comprising:
 - a. performing the method of clause 21 and/or 22,
 - b. classifying the disease, disorder and/or condition associated with amyloid-beta.
24. A method for monitoring a disease, disorder and/or condition associated with amyloid-beta at two or more time points using samples from a subject comprising contacting the samples with an amyloid-beta binding antibody or antigen-binding fragment thereof of any of clauses 1-18, wherein:
 - a. higher levels of amyloid-beta in the later sample compared with one or more earlier samples are indicative of progression of a disease, disorder and/or condition associated with amyloid-beta;
 - b. lower levels of amyloid-beta in the later sample compared with one or more earlier samples are indicative of regression of a disease, disorder and/or condition associated with amyloid-beta; and/or
 - c. no significant change of levels of amyloid-beta in the later sample compared with one or more earlier samples are indicative of lack of progression of a disease, disorder and/or condition associated with amyloid-beta.
25. A method for selecting a therapy for treatment of a disease, disorder and/or condition associated with amyloid-beta comprising contacting samples taken before and after treatment with the therapy with an amyloid-beta binding antibody or antigen-binding fragment thereof of any of clauses 1-18, wherein:
 - a. lower levels of amyloid-beta in the sample taken after treatment compared with the sample taken before treatment are indicative of successful treatment of a disease, disorder and/or condition associated with amyloid-beta and thus the therapy is selected for treatment;
 - b. no significant change of levels of amyloid-beta in the sample taken after treatment compared with the sample taken before treatment are indicative of successful treatment of a disease, disorder and/or condition associated with amyloid-beta and thus the therapy is selected for treatment;
 - c. a decline in the rate of increase of levels of amyloid-beta between samples taken during treatment compared with samples taken before treatment are indicative of successful treatment of a disease, disorder and/or condition associated with amyloid-beta and thus the therapy is selected for treatment;
 - d. higher levels of amyloid-beta in the sample taken after treatment compared with the sample taken before treatment are indicative of unsuccessful treatment of a disease, disorder and/or condition associated with amyloid-beta and thus the therapy is not selected for treatment; or
 - e. no decline in the rate of increase of levels of amyloid-beta between samples taken during treatment compared with samples taken before treatment are indicative of unsuccessful treatment of a disease, disorder and/or condition associated with amyloid-beta and thus the therapy is not selected for treatment.

26. A method for assessing a candidate therapy for a disease, disorder and/or condition associated with amyloid-beta, the method comprising, following treatment of one or more subjects, contacting samples from the one or more treated subjects with an antibody or antigen-binding fragment of any of clauses 1-18, wherein lower levels of amyloid-beta in the samples compared with levels in corresponding samples from subjects not treated with the therapy are indicative of successful treatment of a disease, disorder and/or condition associated with amyloid-beta.
27. The method of clause 26 performed at multiple time points in matched samples between the treatment and placebo groups in order to monitor the effectiveness of the candidate therapy over a defined time period.
28. The method of clause 26 or 27 which comprises contacting samples from the one or more treated subjects and the subjects not treated with the therapy with an antibody or antigen-binding fragment of any of clauses 1-18 prior to treatment, with the therapy or placebo respectively, to determine base levels of amyloid-beta.
29. The method according to any one of clauses 19 to 28 wherein the disease, disorder and/or condition associated with amyloid-beta is selected from the group consisting of Alzheimer's Disease (AD), mild cognitive impairment (MCI), Down syndrome (DS), Down syndrome-related Alzheimer's Disease, cardiac amyloidosis, cerebral amyloid angiopathy (CAA), multiple sclerosis, Parkinson's disease, Parkinson's Disease with Dementia (PDD), Lewy body dementia, ALS (amyotrophic lateral sclerosis), Adult Onset Diabetes, inclusion body myositis (IBM), ocular amyloidosis, glaucoma, macular degeneration, lattice dystrophy, optic neuritis, Myotonic dystrophy and hepatic dysfunction or failure.
30. The method according to clause 29 wherein the amyloid-beta associated disease, disorder or condition is Alzheimer's Disease (AD), Down syndrome (DS), Down syndrome-related Alzheimer's Disease, cerebral amyloid angiopathy (CAA), Myotonic dystrophy, or Lewy body dementia.
31. The method according to clause 29 or 30 wherein the amyloid-beta associated disease, disorder or condition is Alzheimer's Disease (AD).
32. The method according to clause 29 or 30 wherein the amyloid-beta associated disease, disorder or condition is Down Syndrome (DS).
33. A diagnostic composition comprising the amyloid-beta binding antibody or antigen-binding fragment thereof of any one of clauses 1 to 18 and an acceptable carrier and/or excipient.
34. A nucleic acid encoding the amyloid-beta binding antibody or antigen-binding fragment thereof of any one of clauses 1 to 18.
35. A nucleic acid comprising a nucleotide sequence as provided in SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 54 or SEQ ID NO: 55.
36. A recombinant vector comprising the nucleic acid of clause 34 or 35.
37. A host cell comprising the nucleic acid of clause 34 or 35 and/or the vector of clause 36.
38. An isolated host cell that expresses the amyloid-beta binding antibody or antigen-binding fragment of any one of clauses 1 to 18.
39. A method for producing an amyloid-beta binding antibody or antigen-binding fragment thereof, comprising the steps of:

- a. culturing the host cell of clause 37 or 38 under conditions suitable for producing the amyloid-beta binding antibody or antigen-binding fragment thereof, and
 - b. recovering the amyloid-beta binding antibody or antigen-binding fragment thereof.
40. A kit for diagnosis of a disease, disorder or condition associated with amyloid-beta, or a kit for use in a method of any one of clauses 19 to 32, comprising the amyloid-beta binding antibody or antigen-binding fragment thereof according to any one of clauses 1 to 18.
41. The amyloid-beta binding antibody or antigen-binding fragment thereof of any one of clauses 1-18 for research use, in particular as an analytical tool or reference molecule.
42. The amyloid-beta binding antibody or antigen-binding fragment thereof of any one of clauses 1-18 for use in detecting amyloid-beta aggregates, including plaques, *in vitro* or *in vivo*.
43. The amyloid-beta binding antibody or antigen-binding fragment thereof for use of clause 42 which is used for histochemical detection in brain tissue.

BRIEF DESCRIPTION OF FIGURES AND TABLES

Figure 1. ACI-24-41F12-Ab3 (murine IgG2a isotype) binds Abeta1-42 with a Kd of 66 pM. No binding was observed to BSA protein. Data are expressed as O.D., and shown as mean $\pm$ SD of a single assay duplicate.

Figure 2. Antibody ACI-31-25B1-Ab2 (murine IgG2a isotype) binds to Abeta1-42 with a Kd of 41 pM. No binding was observed to BSA protein. Data are expressed as O.D.

Figure 3. Antibody ACI-31-30C11-Ab1 (murine IgG2a isotype) binds to Abeta1-42 with a Kd of 196 pM. No binding was observed to BSA protein. Data are expressed as O.D.

Figure 4. Antibody ACI-31-25B1-Ab2 (murine IgG2a isotype) captures soluble Abeta1-42 with a Kd of 312 pM. Data are expressed as O.D.

Figure 5. Antibody ACI-8041-1F11B5-Ab1 (a murine IgG2a isotype) captures soluble Abeta1-42 with a Kd of 343 pM. Data are expressed as O.D.

Figure 6. Antibody ACI-8041-9D7E1-Ab1 (a murine IgG2a isotype) captures soluble Abeta1-42 with a Kd of 1.1 nM. Data are expressed as O.D.

Figure 7. Antibody ACI-8041-10H3B11-Ab1 (a murine IgG2a isotype) captures soluble Abeta1-42 with a Kd of 2.6 nM. Data are expressed as O.D.

Figure 8. A) An indirect ELISA comparing the binding of individual antibodies ACI-24-41F12-Ab3 (a murine IgG2a isotype) and ACI-31-25B1-Ab2 (a murine IgG2a/lambda isotype) to sAPPalpha, normalized to Abeta1-42 binding. Scrambled Abeta1-42 was used as a control, showing no binding. Antibody ACI-24-41F12-Ab3 shows binding to sAPPalpha whereas no binding is observed for antibody ACI-31-25B1-Ab2. B) A sandwich pairing of antibodies ACI-24-41F12-Ab3 (detecting) and ACI-31-25B1-Ab2 (capturing) detects soluble Abeta1-42 with a Kd of 9.7 nM with

selectivity for Abeta1-42 over scrambled Abeta1-42 or sAPPalpha. Data are expressed as O.D. or as % of Abeta1-42 binding.

Table 1. Abeta1-42 binding regions and epitopes, and interaction with sAPPalpha.

Table 2. Nucleotide sequences of the Heavy Chain and Light Chain Variable domains (VH and VL).

Table 3. Amino acid sequences of the Heavy Chain and Light Chain Variable domains (VH and VL).

Table 4. Amino acid sequences of Heavy Chain (HC) and Light Chain (LC) variable and constant regions.

Table 5. Amino acid sequences of Heavy Chain (HC) and Light Chain (LC) constant regions.

The invention is further described with reference to the following non-limiting examples:

METHODS

Example 1. Antibody generation

1.1. Preparation of an abeta liposomal vaccine composition

The liposome-based antigenic constructs were prepared according to the protocols published in WO2012/055933. The liposomal vaccine with tetrapalmitoylated human Abeta1-15 peptide as antigen was used for generating antibodies ACI-24-41F12-Ab2 (murine IgG2b) and ACI-24-41F12-Ab3 (murine IgG2a isotype and a chimeric mouse/human IgG1 isotype), or with tetrapalmitoylated human Abeta22-35 peptide as antigen for generating ACI-31-25B1-Ab2 (murine IgG2b/lambda, murine IgG2a/lambda and a chimeric mouse/human IgG1 isotype),) and ACI-31-30C11-Ab1 (murine IgG2b), or with tetrapalmitoylated human Abeta1-23 peptide as antigen for generating ACI-8037-103H5-Ab2 (murine IgG2a) and ACI-8037-109F4-Ab1 (murine IgG2a), or with tetrapalmitoylated human Abeta5-23 peptide as antigen for generating ACI-8039-306H5-Ab1 (murine IgG2a), ACI-8039-307F7-Ab2 (murine IgG2a), and ACI-8039-309D9-Ab2 (murine IgG2a), or with tetrapalmitoylated human Abeta10-29 peptide as antigen for generating ACI-8041-1F11B5-Ab1 (murine IgG2a), ACI-8041-2B9H5-Ab1 (murine IgG2a), ACI-8041-3G11B3-Ab1 (murine IgG2a), ACI-8041-4G6D2-Ab1 (murine IgG2a), ACI-8041-5A2D4-Ab1 (murine IgG2a), ACI-8041-5A6H9-Ab1 (murine IgG2a), ACI-8041-6C3C4-Ab1 (murine IgG2a), ACI-8041-9D7E1-Ab1 (murine IgG2a), and ACI-8041-10H3B11-Ab1 (murine IgG2a). Mice (C57BL/6, 9 weeks old, female) were injected with the vaccine by subcutaneous (s.c.) injections on three occasions with a two-week interval between each immunization (at days 0, 14, and 28). Blood samples were collected and plasma were prepared 7 days before the first immunization and seven days after each immunization (at days 7, 21, and 35). After the last bleeding, mice were selected based on vaccine response and splenocytes used for fusions with mouse myeloma cells, 65 days after study initiation. Hybridomas binding to the target were selected, sub-cloned to obtain monoclonal antibodies, and then ranked for target-binding properties to select hybridoma clones for sequencing and recombinant antibody production. The data below describe the properties of ACI-24-41F12-Ab2, a hybridoma-derived murine IgG2b/kappa antibody, and a recombinant murine IgG2a/kappa

antibody (hereafter referred as ACI-24-41F12-Ab3 (IgG2a isotype)) and a recombinant chimeric mouse/human IgG1 isotype (hereafter referred as ACI-24-41F12-Ab3 (hIgG1 isotype)) having the same variable heavy (VH) and light (VL) chain sequences, and binding properties (data not shown), as the ACI-24-41F12-Ab2 antibody. The data below further describe some properties of ACI-31-25B1-Ab2 in the form of a murine IgG2a/lambda, and ACI-31-30C11-Ab1, ACI-8037-103H5-Ab2, ACI-8037-109F4-Ab1, ACI-8039-306H5-Ab1, ACI-8039-307F7-Ab2, ACI-8039-309D9-Ab2, ACI-8041-1F11B5-Ab1, ACI-8041-2B9H5-Ab1, ACI-8041-3G11B3-Ab1, ACI-8041-4G6D2-Ab1, ACI-8041-5A2D4-Ab1, ACI-8041-5A6H9-Ab1, ACI-8041-6C3C4-Ab1, ACI-8041-9D7E1-Ab1, and ACI-8041-10H3B11-Ab1, with a murine IgG2a isotype constant region heavy chain and kappa constant region light chain (Table 5).

Example 2. Preparation of Abeta1-42 for assays

Abeta1-42 lyophilized powder (Bachem) was reconstituted in hexafluoroisopropanol (HFIP, Sigma) to 1 mM. The peptide solution was sonicated for 15 min at room temperature, agitated overnight, and aliquots made into non-siliconized microcentrifuge tubes. The HFIP was then evaporated under a stream of argon. The resulting peptide film was vacuum dried for 10 min and stored at -80°C until use. Alternatively, to assay for target capture in solution, a biotinylated version of the Abeta1-42 peptide was used. This was prepared in a similar manner to that described above.

Example 3. Target binding

Antibody target binding was evaluated by an enzyme-linked immunosorbent assay (ELISA). Briefly, Nunc MaxiSorp 96-well plates (Nunc) were coated for 18 h at 4°C with 50 µL of 10 µg/mL Abeta1-42 or bovine serum albumin (BSA, Sigma) diluted in PBS. In selected assays, the full-length sAPPalpha fragment (Sigma) was additionally included by coating wells as described above, but at 4 µg/mL (0.04 µM). Plates were then washed 4-times with 300 µL of PBS containing 0.05% Tween20 (Millipore). To block non-specific binding to the plate, freshly prepared solution of PBS containing 0.05% Tween20 and 1% BSA, was added to each well (100 µL/well) and the plates were incubated for 1 h at 37°C. Primary antibodies were diluted to 100 nM in PBS containing 1% BSA and 0.05% Tween20, followed by 3-fold serial dilutions in duplicates. Solutions were added to plates at 50 µL/well and incubated for 1 h at 37°C. Subsequently, the plates were washed 4-times with 300 µL of PBS containing 0.05% Tween20. Plates were then incubated with horseradish peroxidase (HRP) conjugated goat anti-mouse secondary IgG (Abcam) for 1 h at 37°C. After final wash step (4-times with 300 µL of PBS containing 0.05% Tween20), plates were incubated with 3,3',5,5'-tetramethylbenzidine (TMB) substrate (BD Biosciences) and reaction stopped with a Stop Solution (Sigma). Finally, optical densities (O.D.) were read at 450 nm absorption wavelength using a Tecan Infinite plate reader. Measured values are expressed as mean O.D. from a duplicate run $\pm$ 1 standard deviation of the mean (S.D.).

An ELISA assay was used to evaluate binding of antibody ACI-24-41F12-Ab3 (a recombinant murine IgG2a isotype, also known as ACI-24-41F12-Ab3-rec1), antibody ACI-31-25B1-Ab2 (a murine IgG2a/lambda isotype), and antibody ACI-31-30C11-Ab1 (a murine IgG2a isotype) to Abeta1-42. Antibody ACI-24-41F12-Ab3 bound to Abeta1-42 with a K_d of 66 pM, and no cross-reactivity to BSA at identical protein concentration was observed (Figure 1). The assay

was repeated at least four independent times with comparable results. Antibody ACI-31-25B1-Ab2 bound to Abeta1-42 with a K_d of 41 pM (Figure 2), and antibody ACI-31-30C11-Ab1 with a K_d of 196 pM (Figure 3), with no cross-reactivity to BSA.

A target capture assay by ELISA was used to further evaluate binding of antibodies ACI-31-25B1-Ab2, ACI-8041-1F11B5-Ab1, ACI-8041-9D7E1-Ab1 and ACI-8041-10H3B11-Ab1 to Abeta1-42 in solution as an indication of soluble target capture in biological fluids. Briefly, a Nunc MaxiSorp 96-well plate (Nunc) was coated for 18 h at 4°C with 50 μ L of 5 μ g/mL goat anti-mouse IgG, Fc-gamma fragment specific antibody (Jackson Immune Research) diluted in carbonate-bicarbonate buffer. The plate was then washed 4-times with 300 μ L of PBS containing 0.05% Tween20 (Millipore). To block non-specific binding to the plate, freshly prepared solution of PBS containing 0.05% Tween20 and 1% BSA, was added to each well (100 μ L/well) and the plate was incubated for 1 h at 37°C. Primary antibody was diluted at 5 μ g/mL (33.3 nM) in PBS containing 1% BSA and 0.05% Tween20, 50 μ L/well was added to each well and the plate was incubated for 1 h at 37°C. Subsequently, the plate was washed 4-times with 300 μ L of PBS containing 0.05% Tween20. Human Abeta1-42 biotinylated at the peptide C-terminus was diluted to 10 μ g/mL (2.2 μ M) in PBS containing 1% BSA and 0.05% Tween20, followed by 3-fold serial dilutions, 50 μ L was added to each well and the plate was incubated for 1 h at 37°C. After washing 4-times with 300 μ L of PBS containing 0.05% Tween20, the plate was incubated for 45 min at ambient temperature with 50 μ L/well of streptavidin-HRP (R&D systems) diluted 1:200 in PBS containing 1% BSA and 0.05% Tween20. The plate was again washed 4-times with 300 μ L of PBS containing 0.05% Tween20 before incubating at ambient temperature for 20 or 30 min with 50 or 100 μ L/well of 3,3',5,5'-tetramethylbenzidine (TMB) enzyme substrate (BD Bioscience). Reaction was stopped with a 1.2 M HCl (Sigma) solution. Finally, optical densities (O.D.) were read at 450 nm absorption wavelength using a Tecan Infinite plate reader. Measured values are expressed as O.D. Antibody ACI-31-25B1-Ab2 captured Abeta1-42 in solution with a K_d of 312 pM (Figure 4), antibody ACI-8041-1F11B5-Ab1 captured Abeta1-42 in solution with a K_d of 343 pM (Figure 5), antibody ACI-8041-9D7E1-Ab1 captured Abeta1-42 in solution with a K_d of 1.1 nM (Figure 6), and antibody ACI-8041-10H3B11-Ab1 captured Abeta1-42 in solution with a K_d of 2.6 nM (Figure 7). Antibodies ACI-24-41F12-Ab3, ACI-31-30C11-Ab1, ACI-8037-103H5-Ab2, ACI-8037-109F4-Ab1, ACI-8039-306H5-Ab1, ACI-8039-307F7-Ab2, ACI-8039-309D9-Ab2, ACI-8041-2B9H5-Ab1, ACI-8041-3G11B3-Ab1, ACI-8041-4G6D2-Ab1, ACI-8041-5A2D4-Ab1, ACI-8041-5A6H9-Ab1, and ACI-8041-6C3C4-Ab1 also captured Abeta1-42 in solution (data not shown).

Furthermore, selected antibodies were assayed to verify binding and selectivity for Abeta1-42 by using a pairing or sandwich ELISA. Briefly, a Nunc MaxiSorp 96-well plate (Nunc) was coated for 18 h at 4°C with 50 μ L of capture antibody at 5 μ g/mL, diluted in carbonate-bicarbonate buffer. The plate was then washed and blocked as described in the preceding paragraph. Subsequently, analyte proteins were diluted to 666 nM for Abeta1-42 (Bachem) and scrambled Abeta1-42 (Anaspec), or 165 nM for sAPPalpha (Sigma) in PBS containing 1% BSA and 0.05% Tween20, followed by 3-fold serial dilutions and 50 μ L added to each well. The plate was incubated for 2 h at 37°C and then washed as previously described and then incubated for 1 h at 37°C with 50 μ L/well of biotinylated detection antibody, diluted to 2 μ g/mL in PBS containing 1% BSA and 0.05% Tween20. The subsequent steps are the same as described

in the preceding paragraph for Abeta1-42 target capture, except that incubation with TMB was only done with 100 μ L/well for 30 min.

Sandwich ELISAs run with selected antibody pairs detected Abeta1-42 in solution with Kds ranging from 100 pM. Results for an example of a sandwich ELISA using antibody ACI-24-41F12-Ab3, an N-terminus Abeta1-42 binder that cross-reacts with sAPPalpha, and one mid-domain binder that does not bind sAPPalpha are shown in Figure 8A. This demonstrates assay selectivity for soluble Abeta1-42 over sAPPalpha and a Kd of 9.7 nM for soluble Abeta1-42 (Figure 8B). The sandwich pairing of antibodies ACI-24-41F12-Ab3 (detecting) and ACI-31-25B1-Ab2 (capturing) detects soluble Abeta1-42. Additionally, selectivity for soluble Abeta1-42 was further substantiated with total lack of signal when using scrambled Abeta1-42 as the assay analyte, consisting of all the same 42 amino acids present in the human Abeta1-42 peptide.

Example 4. Epitope mapping

Epitope mapping of ACI-24-41F12-Ab2, ACI-31-25B1-Ab2, and ACI-31-30C11-Ab1 was performed by ELISA using a peptide library spanning the amino acid sequence of Abeta1-42 consisting of 33 overlapping biotinylated peptides of 8, 9, or 10 residues each (Mimotopes Ltd., Melbourne, Australia). Biotinylated Abeta1-42 (Bachem) was used as a control peptide. Epitope mapping ELISA was done according to the manufacturer's instructions. Briefly, streptavidin-coated plates (Nunc) were blocked with 0.1% BSA in PBS for 18 hours at 4°C on a horizontal shaker at 50 rpm. After washing with PBS containing 0.05% Tween20, plates were coated with each peptide from the library, diluted to the final concentration of 10 μ M in 0.1% BSA containing 0.1% sodium azide in PBS for 1 hour at ambient temperature. After washing, plates were incubated for 1 hour at ambient temperature with ACI-24-41F12-Ab2, ACI-31-25B1-Ab2, or ACI-31-30C11-Ab1 at 1 μ g/mL diluted in 2% BSA containing 0.1% sodium azide in PBS. Plates were washed again and incubated with alkaline phosphatase (AP) conjugated goat anti-mouse IgG (Jackson Immune Research) for 1 hour at ambient temperature. After final wash, plates were incubated for 2 hours with phosphatase substrate (pNPP, Sigma) and absorbance was read at 405 nm using a plate reader (Tecan).

To determine the epitope of ACI-24-41F12-Ab2 and ACI-31-25B1-Ab2, on Abeta1-42, binding of the antibodies to 33 overlapping 8, 9, or 10-mer peptides covering the entire sequence of Abeta1-42 was analysed by ELISA using streptavidin plates and peptides labelled with a terminal biotin (Table 1). In the cases where epitope was not mapped, the binding region was determined using the same assay as described above, but with target peptides corresponding to the different vaccine antigen sequences used to generate the antibodies. Binding to the full length Abeta1-42 was used as positive control. The epitope of ACI-24-41F12-Ab2 mapped to the N-terminus region and was identified to be within residues number 1 to 8 (more precisely within amino acids residues 1-5, wherein amino acids 1 and 2 of Abeta 1-42 are essential to antibody binding) of the Abeta1-42 peptide sequence. The epitope of ACI-31-25B1-Ab2 was mapped to the mid-domain region and identified to be within residues 22-35, more precisely within amino acids residues 26-34 of the Abeta1-42 peptide sequence (Table 1). The Abeta1-42 binding regions were Abeta1-5 for ACI-8037-103H5-Ab2 and ACI-8037-109F4-Ab1, Abeta17-23 for ACI-8039-306H5-Ab1, ACI-8039-307F7-Ab2, ACI-8039-309D9-Ab2, ACI-8041-1F11B5-Ab1, ACI-8041-2B9H5-Ab1, ACI-8041-3G11B3-Ab1, ACI-8041-4G6D2-

Ab1, ACI-8041-5A2D4-Ab1, ACI-8041-5A6H9-Ab1, ACI-8041-6C3C4-Ab1, ACI-8041-9D7E1-Ab1, ACI-8041-10H3B11-Ab1, and Abeta22-35 for ACI-31-30C11-Ab1. Cross-reactivity to sAPPalpha, that shares the same amino acid sequence with human Abeta1-42 between residues 1 and 16 is additionally shown in Table 1. Cross-reactivity was determined for antibodies ACI-24-41F12-Ab2, ACI-8037-103H5-Ab2, and ACI-8037-109F4-Ab1. No cross-reactivity was determined for antibodies ACI-31-25B1-Ab2, ACI-31-30C11-Ab1, ACI-8039-306H5-Ab1, ACI-8039-307F7-Ab2, ACI-8039-309D9-Ab2, ACI-8041-1F11B5-Ab1, ACI-8041-2B9H5-Ab1, ACI-8041-3G11B3-Ab1, ACI-8041-4G6D2-Ab1, ACI-8041-5A2D4-Ab1, ACI-8041-5A6H9-Ab1, ACI-8041-6C3C4-Ab1, ACI-8041-9D7E1-Ab1 and ACI-8041-10H3B11-Ab1.

Table 1. Abeta1-42 binding regions and epitopes, and interaction with sAPPalpha:

	Binding regions, aa	Epitopes, aa	sAPPalpha binding
ACI-24-41F12-Ab2 and ACI-24-41F12-Ab3	1-8 (SEQ ID NO: 2)	1-5 (SEQ ID NO: 7)	+
ACI-31-25B1-Ab2	22-35 (SEQ ID NO: 29)	26-34 (SEQ ID NO: 8)	-
ACI-31-30C11-Ab1	22-35 (SEQ ID NO: 29)	ND	-
ACI-8037-103H5-Ab2	1-5 (SEQ ID NO: 7)	ND	+++
ACI-8037-109F4-Ab1	1-5 (SEQ ID NO: 7)	ND	+++
ACI-8039-306H5-Ab1	17-23 (SEQ ID NO: 9)	ND	-
ACI-8039-307F7-Ab2	17-23 (SEQ ID NO: 9)	ND	-
ACI-8039-309D9-Ab2	17-23 (SEQ ID NO: 9)	ND	-
ACI-8041-1F11B5-Ab1	17-23 (SEQ ID NO: 9)	ND	-
ACI-8041-2B9H5-Ab1	17-23 (SEQ ID NO: 9)	ND	-
ACI-8041-3G11B3-Ab1	17-23 (SEQ ID NO: 9)	ND	-
ACI-8041-4G6D2-Ab1	17-23 (SEQ ID NO: 9)	ND	-
ACI-8041-5A2D4-Ab1	17-23 (SEQ ID NO: 9)	ND	-
ACI-8041-5A6H9-Ab1	17-23 (SEQ ID NO: 9)	ND	-
ACI-8041-6C3C4-Ab1	17-23 (SEQ ID NO: 9)	ND	-
ACI-8041-9D7E1-Ab1	17-23 (SEQ ID NO: 9)	ND	-
ACI-8041-10H3B11-Ab1	17-23 (SEQ ID NO: 9)	ND	-

ND: not determined, -: no binding, +: low binding, +++: high binding

Example 5. Antibody variable region gene sequencing

Mouse hybridoma cells were harvested and lysed using a lysis buffer containing guanidinium salts that deactivate RNases. The genomic DNA was then eliminated by adding RNase-free DNase to the sample. After cell disruption and elimination of genomic DNA, the RNA was purified to a silica-based affinity column using multiple washes and eluted from the column using RNase-free water. Once RNA was extracted, its purity and concentration was measured

spectrophotometrically. The integrity of the RNA was assessed on a denaturing agarose gel and RNA was reverse transcribed into cDNA using reverse transcriptase (RT). Before adding the reaction mixture, the RNA was heated to 70°C for 10 min to disrupt RNA secondary structures. The RT products were directly used for PCR amplification. For high-fidelity PCR amplification of the cDNA, each of the variable region primers corresponding to the different gene families encoding for antibodies were individually mixed with the constant primer, for variable heavy chain domain (VH) and variable light chain domain (VL) separately. Initially, a degenerate primer pool was used (12 for VH and 12 for VL) and, depending on results, a second pool was used to obtain PCR products. After the PCR reaction, the products were analysed by gel electrophoresis on 2% agarose gels stained with ethidium bromide. The PCR products for VL and VH were individually purified on an agarose gel using tris-acetate-EDTA (TAE). The purified fragments excised from the gel were then sequenced using the dye-terminator sequencing method. The same primers as those used for the PCR were used for the sequencing reaction. Sequencing was carried out in both directions to provide overlap at both ends. Sequencing data were analysed on the Ig Blast / Kabat database. Nucleotide sequences for VH and VL are shown in Table 2. Protein sequences for VH and VL, and their complementarity-determining regions (CDRs) are shown in Table 3. Protein sequences for HC and LC of mouse IgG2b, mouse IgG2a, and mouse/human chimeric IgG1 are shown in Table 4.

Table 2. Nucleotide sequences of the Heavy Chain and Light Chain Variable domains (VH and VL)

Antibody	VH	VL
ACI-24-41F12-Ab2 and ACI-24-41F12-Ab3 (IgG2a isotype) and ACI-24-41F12-Ab3 (hIgG1 isotype)	CAGGTTACTCTGAAAGAGTCTGGCCCTGG GATATTGCAGTCCTCCCAGACCCTCAGTC TGACTTGTTCTTTCTCTGGGTTTTCACTGA GCACTTCTGGTATGGGTGTGAGCTGGATT CGTCAGCCTTCAGGAAAGGGTCTGGAGT GGCTGGCACACATTTACTGGGATGATGA CAAGCGCTATAACCCATCCCTGAAGAGC CGGCTCACAATCTCCAAGGATACCTCCAG AAACCAGGTATTCTCAAGATCACCAGT GTGGACACTGCAGATACTGCCACATACT ACTGTGCTCGAAGGAGGAATGGTTACGA CGGGGGGTTTGCTTACTGGGGCCAAGGG ACTCTGGTCACTGTCTCTGCA (SEQ ID NO: 18)	GATGTTTTGATGACCCAACTCCACTCTC CCTGCCTGTCAGTCTTGGAGATCAAGCCT CCATCTCTTGCAGATCTAGTCAGAGCATT GTACATAGTAATGGAAACACCTATTTAG AATGGTACCTGCAGAAACCAGGCCAGTC TCCAAAGCTCCTGATCTACAAAGTTTCCA ACCGATTTTCTGGGGTCCCAGACAGGTTC AGTGGCAGTGGATCAGGGACAGATTTCA CACTCAAGATCAGCAGAGTGGAGGCTGA GGATCTGGGAGTTTATTACTGCTTTCAAG GTTCACATGTTCCGCTCACGTTCCGGTGCT GGGACCAAGCTGGAGCTGAAA (SEQ ID NO: 19)
ACI-31-25B1-Ab2 (IgG2b isotype)	GAGGTGCAGCTGGTGGAGTCTGGGGGAG ACTTAGTGAAGCCTGGAGGGTCCCTGAA ACTCTCCTGTGCAGCCTCTAGATTCACTT TCAGTACCTATGGCATGTCTTGGGTTTCGC	CAACTTGTGCTCACTCAGTCATCTTCAGC CTCTTTCTCCCTGGGAGCCTCAGCAAAAC TCACGTGCACCTTGAGTAGTCAGCACATT ACGTACACCATTGAGTGGTATCAGCAAC

with a lambda light chain and IgG2a isotype with a lambda light chain)	CAGACTCCAGACAAGAGGCTGGAATGGG TCGCAACCATTAGTAGTGGTAGAAGTTAC ACCTACTATGCAGACAGTGTGAAGGGGC GATTCACCATCTCCAGAGACAATGCCAA GAACACCCTGTACCTGCAAATGAGCAGT CTGAAGTCTGAGGACACAGCCATGTATT ACTGTGCAAGAAATAGTAACAACCAGAG GGATTACTATGCTATGGACTACTGGGGTC AAGGAACCTCAGTCACCGTCTCCTCA (SEQ ID NO: 52)	AGCCACTCAAGCCTCCTAAGTATGTGATG GTACTTGAGAAAGATGGAAGCCACAGCA CAGGTGATGGGATTCCCTGATCGCTTCTCT GGATCCAGCTCTGGTGCTGATCGTTACCT TAGCATTTCCAACATCCAGCCTGAAGATG AAGCAGTATACATCTGTGGTGTGGGTGAT GCAATTAAGGAACAATTTGTGTATGTTTT CGGCGGTGGAACCAAGGTCAGTGTCTCA (SEQ ID NO: 53)
ACI-31- 30C11- Ab1 (two isotypes: IgG2b with a kappa light chain and IgG2a with a kappa light chain)	CAGGTTTCAGCTGCAGCAGTCTGGACCTG AGCTGGTGAAGCCTGGGGCCTCAGTGAA GATTTCTGCAAGGCTTCTGGCTACGCAT TCAGTAGCTCCTGGCTGAACTGGGTGAA GCAGAGGCCTGGAGAGGGTCTTGAGTGG ATTGGACGGATTTATCCTGGAGATGGAG ATATTAACCTACAATGGGAAGTTCAAGGG CAAGGCCACACTGACTGCAGACAAATCC TCCAGCACAGCCTACATGCAACTCAGCA GCCTGACATCTGACGACTCTGCGGTCTAC TTCTGTACAAAGCGGGGACGCTATGCTTT GGACTACTGGGGTCAAGGAACCTCAGTC ACCGTCTCCTCA (SEQ ID NO: 54)	GACATTGTGCTGACCCAATCTCCAGCTTC TTTGGCTGTGTCTCTAGGGCAGAGGGCCA CCATATCCTGCAGAGCCAGTAAAAGTGTT GATAATTATGGCAAAAGTTTTATGCACTG GTTCCAGCAGAAACCAGGACAGCCACCC AAACTCCTCATCTATCGTGCATCCAACCT AGAATCTGGGATCCCTGCCAGGTTTCAGTG GCAGTGGGTCTAGGACAGACTTCACCTC ACCATTAATCCTGTGGAGGCTGATGATGT TGCAACCTATTACTGTCAGCAAAGTAATG AGGATCCGTACACGTTCCGGAGGGGGGAC CAAGCTGGAAATGAAA (SEQ ID NO: 55)
ACI-8037- 103H5- Ab2 (a murine IgG2a isotype with a kappa light chain)	CAAGTTACTCTAAAAGAGTCTGGCCCTGG GATATTGAAGCCCTCACAGACCCTCAGTC TGACTTGTTCTTTCTCTGGGTTTTCACTGA GCACTTCTGGTATGGGTGTTGGCTGGATT CGTCAGCCTTCCGGGAAGGGTCTGGAGT GGCTGGCACACATTTGGTGGGATGATGA TAAGTACTATAACCCATCCCTGAAGAGCC GGCTCACAATCTCCAAGGATTCTCCAGA AACCAGGTATTCTCAAGATCACCAGTGT GGACACTGCAGATACTGCCACTTACTACT GTGTTCTGAAGGGGGACTAGGTTAGAGGA CTACTTTGACTTCTGGGGCCAAGGCACCA CTCTCACAGTCTCCTCA	GATGTTTTGATGACCCAACTCCACTCTC CCTGCCTGTCAGTCTTGGGGATCAAGCCT CCATCTCTTGCAGATCTAGTCGGAGCATT GTTTCATAGTAATGGAAACACCTATTTAGA ATGGTACCTGCAGAAACCAGGCCAGTCT CCAAAGCTCCTGATCTTCAAAGTTTCCAA CCGATTTTCTGGGGTCCCAGACAGGTTCA GTGGCAGTGGATCAGGGACAGATTTTAC ACTCAAGATCAGCAGAGTGGAGGCTGAG GATCAGGGAGTTTATTACTGCTTTCAAGG TTCACATGTTCCGCTCACGTTCCGTGCTG GGACCAAGCTGGAGCTGAAA (SEQ ID NO: 69)

	(SEQ ID NO: 68)	
ACI-8037-109F4-Ab1 (a murine IgG2a isotype with a kappa light chain)	CAGGTTACTCTGAAAGAGTCTGGCCCTGG GATATTGCAGCCCTCCCAGACCCTCAGTC TGA CT TGT TCT TCT CT GGG TTT TCA CT GA GCA CT TCT GGT AT GGG TGT GAG CT GG ATT CGTCAGCCTTCAGGAAAGGGTCTGGAGT GGCTGGCACACATTTACTGGGATGATGA CAAGCGCTATAACCCATCCCTGAAGAGC CGGCTCACAATCTCCAAGGATACCTCCAG AAACCAGGTTTTCTCAAGATCACCAGTG TGGACACTGCAGATGCTGGCACATACTA CTGTGCTCGAAGACCTATTAGAACGGTA GTAGATGCTATGGACTACTGGGGTCAAG GAACCTCAGTCACCGTCTCCTTA (SEQ ID NO: 78)	GATGTTTTGATGACCCAACTCCACTCTC CCTGCCTGTCAGTCTTGGAGATCAGGCCT CCATCTCTTGCAGATCTAGTCAGACCATT GTACATAGTAATGGAAACACCTATTTGG AATGGTACCTGCAGAAACCAGGCCAGTC TCCAAACCTCCTGATCTACAAAGTTTCCA ACCGATTTTCTGGGGTCCCAGACAGGTTC AGTGGCAGTGGATCAGGGACAGATTTCA CACTCAAGATCAGCAGAGTGGAGGCTGA GGATCTGGGAGTTTATTACTGCTTTCAAG GTTCACATGTTCCGCTCACGTTCCGGTGCT GGGACCAAGCTGGAGCTGAAA (SEQ ID NO: 79)
ACI-8039-306H5-Ab1 (a murine IgG2a isotype with a kappa light chain)	CAAGTTACTCTAAAAGAGTCTGGCCCTGG GATATTGAAGCCCTCACAGACCCTCAGTC TGA CT TGT TCT TCT CT GGG TTT TCA CT GA GCA CT TCT GGT AT GGG TGT AGG CT GG ATT CGTCAGCCTTCAGGGAAGGGTCTGGAGT GGCTGGCACACATTTGGTGGGATGATGA TAAGTACTATAACCCATCCCTGAAGAGTC AGCTCACAATCTCCAAGGATACCTCCAG AAACCAGATATTCCTCAAGATCACCAGT GTGGACACTGCAGATACTGCCACTTACTA CTGTGTTCTGAAGCCTGTACTTTGACTACT GGGGCCAAGGCACCACTCTCACAGTCTC CTCA (SEQ ID NO: 88)	GATGTTGTGATGACCCAACTCCACTCTC CCTGCCTGTCAGTCTTGGAGATCAAGCCT CCATCTCTTGCAGATCTAGTCAGAGCCTT GTACACAGTAATGGAAACACCTATTTAC ATTGGTACCTGCAGAAGCCAGGCCAGTC TCCAAAGCTCCTGATCTACAAAGTTTCCA ACCGATTTTCTGGGGTCCCAGACAGGTTC AGTGGCAGTGGATCAGGGACAGATTTCA CACTCAAGATCAGCAGAGTGGAGGCTGA GGATCTGGGAGTTTATTTCTGCTCTCAAA GTACACATGTTCCGCTCACGTTCCGGTGCT GGGACCAAGCTGGAGCTGAAA (SEQ ID NO: 89)
ACI-8039-307F7-Ab2 (a murine IgG2a isotype with a kappa light chain)	CAGGTCCAAGTGCAGCAGCCTGGGGCTG AGCTGGTGAGGCCTGGAGGTTCAAGTAA GCTGTCCTGCAAGGCTTCTGGCTACTCCT TCACCAACTACTGGATGAACTGGGTGAA GCAGAGGCCTGGACAAGGCCTTGAGTGG ATTGGCATGATTATCCTTCCGATAGTGA AACTAGGTTAAATCAGAAATTCAAGGAC AAGGCCACATTGACTGTAGACAAATCAT	GACATTGTGATGACACAGTCTCCATCCTC CCTGGCTATGTCAGTAGGACAGAAGGTC ACTATGAGCTGCAAGTCCAGTCAGAGCC TTTTAAATAGTAGCAATCAAAAGAACTAT TTGGCCTGGTACCAGCAGAAACCAGGAC AGTCTCCTAAAATTCTGGTATACTTTGCA TCCACTAGGGAATCTGGGGTCCCTGATCG CTTCAAGAGGCAGTGGATCTGGGACAGAT

kappa light chain)	CCAGCACAGCCTACTTGCAACTCAGCAG CCCGACATCTGAGGACTCTGCGGTCTATT ACTGTGCAAAATTACTACTATACTACTTT GACTACTGGGGCCAAGGCACCACTCTCA CAGTCTCCTCA (SEQ ID NO: 98)	TTCACCTCTAACCATCAGCAGTGTGCAGGC TGAAGACCTGGCAGATTACTTCTGTCTCAGC AACATTATAGCCCTCCTCCGACGTTCCGGT GGAGGCACCAAGCTGGAAATCAAA (SEQ ID NO: 99)
ACI-8039-309D9-Ab2 (a murine IgG2a isotype with a kappa light chain)	CAGGTGCAACTGCAGCAGTCTGGGCCTC AGCTGGTTAGACCTGGGGCTTCAGTGAA GATATCCTGCAAGGCTTCTGGTAACTCAT TCACCAGCTACTGGATGCACTGGGTGAA GCAGAGGCCTGGACAAGGTCTTGAGTGG ATTGGCATGATTGATCCTTCCGATAGTGA GACTAGGTTAAATCAGAAGTTCAAGGAC AAGGCCACATTGACTGTAGACAAATCCT CCAGCACAGCCTACATGCAACTCAGCAG CCCGACATCTGAGGACTCTGCGGTCTATT ACTGTGCGGGGCTGTACTTTACTTTGGAC TACTGGGGTCAAGGAACCTCAGTCACCG TCTCCTCA (SEQ ID NO: 108)	GACATTTTGATGACCCAGTCTCCATCCTC CCTGACTGTGTCTCAGCAGGAGAGAAGGTC ACTATGAGCTGCAAGTCCAGTCAGAGTCT TTTAGCTAGTGGCAACCAAAATAACTACT TGGCCTGGCACCAGCAGAAACCAGGACG ATCTCCTAAAATACTGATAATTTGGGCAT CCACTAGGGTATCTGGAGTCCCTGATCGC TTCATAGGCAGTGGGTCTGGGACGGATTT CACTCTGACCATCAACAGTGTGCAGGCTG AAGATCTGGCTGTTTATTACTGTCAGCAG TCCTACAGCGCTCCGCTCACGTTCCGGTGC TGGGACCAAGCTGGAGCTGAAA (SEQ ID NO: 109)
ACI-8041-1F11B5-Ab1 (a murine IgG2a isotype with a kappa light chain)	CAGGTGCAGCTGAAGGAGTCAGGACCTG GCCTGGTGGCGCCCTCACAGAGCCTGTCC ATCACATGCACTGTCTCAGGGTTCTCATT AACCAACTATGGTGTAAAGCTGGATTTCGCC AGCCTCCAGGAAAGGGTCTGGAGTGGCT GGGAGTAATATGGGGTGACGGGAGCACA AATTATCATTGAGCTCTCATATCCAGACT GAGCATCAGCAAGGATAACTCCAAGAGC CAAGTTTTCTTAAACTGAACAGTCTGCA AACTGATGACACAGCCACGTACTACTGT ACCAAAGGAGCTGGCTCTTGGGGCCAAG GGATTCCGGTCACTGTCTCTGCA (SEQ ID NO: 118)	GATGTTGTGCTGACCCAGACTCCACTCAC TTTGTCCGTTACCATTGGACAACCAGCCT CCATCTCTTGCAAGTCAAGTCAGAGCCTC TTAGATAGTGATGGAAGGACATATTTAAT TTGGTTGTTACAGAGGCCAGGCCAGTCTC CAAAGCGCCTAATCTATCTGGTGTCAACA CTGGACTCTGGAGTCCCTGACAGGTTTAC TGGCAGTGGATCAGGGACAGATTTTACA CTGAAAATCAGCAGAGTGGAGGCTGAGG ATTTGGGAGTTTATTATTGCTGGCAAGGT ACACATTTTCCGTGGACGTTCCGGTGGAGG CACCAAGCTGGAAATCAAA (SEQ ID NO: 119)
ACI-8041-2B9H5-Ab1 (a murine)	CAGGTTTCAGCTGCAACAGTCTGACGCTG AGTTGGTGAAACCTGGAGCTTCAGTGAA GATATCCTGCAAGGTTTCTGGCTACACCT TCACTGACCATCCTATTCACTGGATGAAG	GACATCAAGATGACCCAGTCTCCATCTTC CATGTATGCATCTCTAGGAGAGAGAGTC ACTATCACTTGCAAGGCGAGTCAGGACA TTAATAGCTATTTAAGCTGGTTCCAGCAG

IgG2a isotype with a kappa light chain)	CAGAGGCCTGACCAGGGCCTGGAATGGA TTGGATATTTTATCCTAGAGATAGTAGT ACTCACTACAATGAGAAGTTCAAGGGCA AGGCCACATTGACTGCAGACAAATCCTC CAGCACAGCCTACATGCAGCTCAACAGC CTGACATCTGAGGACTCTGCAGTCTACTT CTGTGCAAGATCGATGGGCTACTGGGGT CAAGGAACCTCAGTCACCGTCTCCTCA (SEQ ID NO: 128)	AAACCAGGGAAATCTCCTAAGACCCTGA TCTATCGTGCAAACAGATTGGTAGATGG GGTCCCATCAAGGTTCACTGGCAGTGGA TCTGGGCAAGATTATTCTCTCACCATCAG CAGTCTGGACTATGAAGATATGGGAATTT ATTATTGTCTACAGTATGATGAGTTTCCT CCCACGTTCCGGTGCTGGGACCAAGCTGG AGCTGAAA (SEQ ID NO: 129)
ACI-8041-3G11B3-Ab1 (a murine IgG2a isotype with a kappa light chain)	CAGGTCCAAGTGCAGCAGTCTGGGGCTG AACTGGTGAAGCCTGGGGCTTCAGTGAA GTTGTCCTGCAAGGCTTCTGGCTACACCT TCATCAACTACTATATATACTGGGTGAAA CAGAGGCCTGGACAAGGCCTTGAGTGGA TTGGAGAGATTATTCCTAGCAATGATGGT ACTAACTTCAATGAGAAGTTCAAGACCA AGGCCACACTGACTGTAGACAAATCCTC CAGCACAGCATACATGCAACTCAGCAGC CTGACATCTGAGGACTCTGCGGTCTATTA CTGTACCGCGACAGGGACGGTCTGGGGC CAAGGGACTCTGGTCACTGTCTCTGCA (SEQ ID NO: 138)	GATGTTTTGATGACCCAAACTCCACTCTC CCTGCCTGTCTAGTCTTGAGATCAAGCCT CCATCTCTTGCAAGATCTAGTCAGAGCATT GTACATAGTAATGGAATCACCTATTTAGA ATGGTACCTGCAGAAACCAGGCCAGTCT CCAAAGCTCCTAATCTACAAAGTTTCCAA CCGATTTTCTGGGGTCCCAGACAGGTTCA GTGGCAGTGGATCAGGGACAGATTTTCA ACTCAAGATCAGCAGAGTGGAGGCTGAG GATCTGGGAGTTTATTACTGCTTTCAAGG TTCACATGTTCCGTGGACGTTCCGGTGGAG GCACCAAGCTGGAAATCAAA (SEQ ID NO: 139)
ACI-8041-4G6D2-Ab1 (a murine IgG2a isotype with a kappa light chain)	CAGGTCCAAGTGCAGCAGTCTGGGGCTG AACTGGTGAAGCCTGGGGCTTCAGTGAA GTTGTCCTGCAAGGCTTCTGGCTACACCT TCACCAGCTATTATATGTACTGGGTGAAG CAGAGGCCTGGACAAGGCCTTGAGTGGA TTGGAGAGATTATTCCTAGTAATGGTGAT ACTAACTTCAATGAGAAGTTCAAGGAGCA AGGCCACACTGACTGTAGACAAATCCTC CAGCACAGCATATATGCAACTCAGCAGC CTGACATCTGAGGACTCTGCGGTCTATTA CTGTACCGCGACAGGGACGGTCTGGGGC CAAGGGACTCTGGTCACTGTCTCTGCA (SEQ ID NO: 148)	GATGTTTTGATGACCCAAACTCCACTCTC CCTGCCTGTCTAGTCTTGAGATCAAGCCT CCATCTCTTGCAAGATCTAGTCAGAGCATT GTACATAGTAATGGAACACCTATTTAG AATGGTACCTGCAGAAACCAGGCCAGTC TCCAAAGCTCCTGATCTACAAAGTTTCCA ACCGATTTTCTGGGGTCCCAGACAGGTTT AGTGGCAGTGGATCAGGGACAGATTTCA CACTCAAGATCAGCAGAGTGGAGGCTGA GGATCTGGGAGTTTATTACTGCTTTCAAG GTTACATGTTCCGTGGACGTTCCGGTGGGA GGCACCAAGCTGGAAATCAAA (SEQ ID NO: 149)
ACI-8041-5A2D4-	GAGGTCCAGCTGCAACAGTCTGGACCTG AGCTGGTGAAGCCTGGGGCTTCAGTGAA	GAAATTGTGCTCACCCAGTCTCCAACCAC CATGGCTGCATCTCCCGGGGAGAAGATC

Ab1 (a murine IgG2a isotype with a kappa light chain)	GATATCCTGCAAGACTTCTGGATACACAT TCACTGAAAACACCATGCACTGGGTGAA GCAGATCCATGGAAAGAGCCTTGAGTGG ATTGGAGGTATTAATCCTAACAATGGTGT TACTAACAACAACCAGAAGTTCGAGGGC AAGGCCACTTTGACTGTAGACAAGTCCTC CAGCACAGCCTACATGGAGCTCCGCAGC CTGACATCTGAGGATTCTGCAGTCTATTA CTGTGCAAGATCTGATTACGACGCCCTTT ACTATTCTATGGACTGCTGGGGTCAAGGA ACCTCAGTCACCGTCTCCTCA (SEQ ID NO: 158)	ACTATCACCTGCAGTGGTAGCTCAAGTAT AATTTCCAATTACTTGCATTGGTATCAGC AGAAGCCAGGATTCTCCCCTAACTCTTG ATTTATAGGACATCCAATCTGGCTTCTGG AGTCCCAACTCGCTTCAGTGGCAGTGGGT CTGGGACCTCTTACTCTCTCACAATTGGC ACCATGGAGGCTGAAGATGTTGCCACTT ACTACTGCCAGCAGGGTAGTAGTATACC ATTCACGTTCCGGCTCGGGGACAAAGTTG GAAATAAAA (SEQ ID NO: 159)
ACI-8041-5A6H9-Ab1 (a murine IgG2a isotype with a kappa light chain)	GATGTGCAGCTTCAGGAGTCGGGACCTG GCCTGGTGAAACCTTCTCAGTCTCTGTCC CTCACCTGCACTGTCACTGGCTACTCAAT CACCAGTGATTATGCCTGGAAGTGGATCC GGCAGTTTCCAGGAAACAACTGGAGTG GATGGGCTACATAGACTACAGTGGTATC ACTAGCTACAACCCATCTCTCAAAAGTCG AATCTCTATCACTCGAGACACATCCAAGA ACCAGTTCTTCTGCAGTTGAATTCTGTG ACTACTGAGGACTCAGCCACATATTACTG TGCAAGAATCTCTGGACTGGATTACGAC GTGAGGGCTGGCTGGTTTGCTTCTGGGG CCAAGGGACTCTGGTCACTGTCTCTGCA (SEQ ID NO: 168)	GATATTGTGATGACGCAGGCTGCATTCTC CAATCCAGTCACTCTTGAACATCAGTTT CCATCTCCTGCAGGTCTAGTAAGAGTCTC CTACATAGTAATGGCATCACTTATTTGTA TTGGTATCTGCAGAAGCCAGGCCAGTCTC CTCAGCTCCTGATTTATCAGATGTCCAAC CTTGCTCAGGAGTCCCAGACAGGTTTCAG TAGCAGTGGGTCAGGAAGTGAATTCACA CTGAGAATCAGCAGAGTGGAGGCTGAGG ATGTGGGTGTTTATTACTGTGCTCAAAAT CTAGAACGTCCGCTCACGTTCCGGTGCTGG GACCAAGCTGGAGCTGAAA (SEQ ID NO: 169)
ACI-8041-6C3C4-Ab1 (a murine IgG2a isotype with a kappa light chain)	GAGGTCCAGCTGCAACAGTCTGGACCTG AGCTGGTGAAAGCCTGGGGCTTCAGTGAA CATATCCTGCAAGACTTCTGGATACACAT TCACTGAATACACCATGCACTGGATGAA GCAGAGCCATGGAAAGAGCCTTGAGTGG ATTGGAGGTATTAATCCTAACAATGGTGT TACTGGCTACAACCAGAAGTTCAAGGGC AGGGCCACATTGACTGTAGACAAGTCCT CCAGCACAGCCTACATGGAGCTCCGCAG CCTGACATCTGAGGATTCTGCAGTCTATT ACTGTGCAAGATCTGATTACGACGACCTT	GAAATTGTGCTCACCCAGTCTCCAACCAC CATGGCTGCATCTCCCGGGGAGAAGATC ACTATCACCTGCAGTGCCAGCTCAAGTAT AAGTTCCAATTACTTGCATTGGTATCAGC AGAAGCCAGGATTCTCCCCTAACTCTTG ATTTATAGGACATCCAATCTGGCTTCTGG AGTCCCAGCTCGCTTCAGTGGCAGTGGGT CTGGGACCTCTTACTCTCTCACAATTGGC ACCATGGAGGCTGAAGATGTTGCCACTT ACTACTGCCAGCAGGGTAGTAGTATACC

	TACTATGCTATGGACTACTGGGGTCAAGG AACCTCAGTCACCGTCTCCTCA (SEQ ID NO: 178)	ATTCACGTTCGGCTCGGGGACAAAGTTG GAAATAAAA (SEQ ID NO: 179)
ACI-8041- 9D7E1- Ab1 (a murine IgG2a isotype with a kappa light chain)	GAAGTGATGCTGGTGGAGTCTGGGGGAG GCTTAGTGAAGCCTGGAGGGTCCCTGAA ACTCTCCTGTGCAGCCTCTGGATTCACTT TCAGTAGCTATGCCATGTCTTGGGTTCGC CAGACTCCGGAGAAGAGGCTGGAGTGGG TCGCAACCATTAGTAGTGGTGGTAATTAC ACCTACTGTCCCGACAGTGTGAAGGGGC GATTCACCATCTCCAGAGACAATGCCAA GAACACCCTGTACCTGCAAATGAGCAGT CTGAGGTCTGAGGACACGGCCATGTATT ACTGTGCAGCCTATGCTTACGACGACGG GTACTACTTTGACTACTGGGGCCAAGGCA CCACTCTCACAGTCTCCTCA (SEQ ID NO: 188)	GACATTGTGATGACACAGTCTCCATCCTC CCTGGCTATGTCAGTAGGACAGAAGGTC ACTATGAGCTGCAAGTCCAGTCAGAGCC TTTTAAATAGTAGCAATCAAAAGAACTAT TTGGCCTGGTACCAGCAGAAACCAGGAC AGTCTCCTAAACTTCTGGTATACTTTGCA TCCACTAGGGAATCTGGGGTCCCTGATCG CTTCATAGGCAGTGGATCTGGGACAGATT TCACTCTTACCATCAGCAGTGTGCAGGCT GAAGACCTGGCAGATTACTTCTGTCAGCA ACATTATAGCACTCCTCTCACGTTCCGGTG CTGGGACCAAGCTGGAGCTGAAA (SEQ ID NO: 189)
ACI-8041- 10H3B11- Ab1 (a murine IgG2a isotype with a kappa light chain)	GAAGTGATGCTGGTGGAGTCTGGGGGAG GCTTAGTGAAGCCTGGAGGGTCCCTGAA ACTCTCCTGTGCAGCCTCTGGATTCACTT TCAGTAGCTATGCCATGTCTTGGGTTCGC CAGACTCCGGAGAAGAGGCTGGAGTGGG TCGCAACCATTAGTAGTGGTGGTAATTAC ACCTACTGTCCCGACAGTGTGAAGGGGC GATTCACCATCTCCAGAGACAATGCCAA GAACACCCTGTACCTGCAAATGAGCAGT CTGAGGTCTGAGGACACGGCCATGTATT ACTGTGCAGCCTATGCTTACGACGACGG GTACTACTTTGACTACTGGGGCCAAGGCA CCACTCTCACAGTCTCCTCA (SEQ ID NO: 188)	GACATCCAGATGACACAGTCTCCATCCTC ACTGTCTGCATCTCTGGGAGGCAAAGTCA CCATCACTTGCAAGGCAAGCCAAGACAT TAACAAGTATATAGCTTGGTACCAACAC AAGCCTGGAAAAGGTCCTAGGCTGCTCA TTCATTACACATCTACCTTACAGCCAGGC ATCCCATCAAGGTTTCAAGTGAAGTGGGT CTGGGAGAGATTATTCCTTACGATCAGC AACCTGGGGCCTGAAGATATTGCAACTT ATTATTGTCTACAGTATGATAATCTTCTG ACGTTCCGGTGGAGGCACCAAGCTGGAAA TCAAA (SEQ ID NO: 199)

Table 3. Amino acid sequences of the Heavy Chain and Light Chain Variable domains (VH and VL)

Antibody	VH	VH CDR1	VH CDR2	VH CDR3
	QVTLKESGPGILQSSQTLS LTCSFSGFSLSTSGMGVS	TSGMGVS (SEQ ID NO: 11)	HIYWDDDKRYNP SLKS	RRNGYDGGFAY (SEQ ID NO: 13)

ACI-24-41F12-Ab2 and ACI-24-41F12-Ab3 (a murine IgG2a isotype) and ACI-24-41F12-Ab3 (a human IgG1 isotype)	WIRQPSGKGLEWLAHIYW DDDKRYNP SLK S RL TISK DTSRNQVFLKITSVDTAD TATYYCARRRNGYDGGF AYWGQGT LVT VSA (SEQ ID NO: 10)		(SEQ ID NO: 12)	
	VL	VL CDR1	VL CDR2	VL CDR3
	DVLTMTQTPLSLPVS LGDQ ASISCRSSQSIVHSNGNTY LEWYLQKPGQSPKLLIYK VSNRFSGVPDRFSGSGSGT DFTLKISRVEAEDLGVYY CFQGSHVPLTFGAGTKLE LK (SEQ ID NO: 14)	RSSQSIVHSNGNT YLE (SEQ ID NO: 15)	KVSNRFS (SEQ ID NO: 16)	FQGSHVPLT (SEQ ID NO: 17)
Antibody	VH	VH CDR1	VH CDR2	VH CDR3
ACI-31-25B1-Ab2 (two isotypes: a murine IgG2b with a lambda light chain and a murine IgG2a with a lambda light chain)	EVQLVESGGDLVKPGGSL KLSCAASRFTFSTYGM SW VRQTPDKRLEWVATISSG RSYTTYADSVKGRFTISR DNAKNTLYLQMSSLKSED TAMYYCARN SNNQRDYY AMDYWGQGT SVTVSS (SEQ ID NO: 30)	TYGMS (SEQ ID NO: 31)	TISSGRSYTTYAD SVKG (SEQ ID NO: 32)	NSNNQRDYYAM DY (SEQ ID NO: 33)
	VL	VL CDR1	VL CDR2	VL CDR3
	QLVLTQSSSASFSLGASAK LTCTLSSQHITYTIEWYQQ QPLKPPKYVMVLEKDGSH STGDGIPDRFSGSSSGADR YLSISNIQPEDEAVYICGV GDAIKEQFVYVFGGGTKV TVL (SEQ ID NO: 34)	TLSSQHITYTIE (SEQ ID NO: 35)	GSHSTGD (SEQ ID NO: 36)	GVGDAIKEQFVY V (SEQ ID NO: 37)
Antibody	VH	VH CDR1	VH CDR2	VH CDR3

ACI-31-30C11-Ab1 (two isotypes: a murine IgG2b with a kappa light chain and a murine IgG2a with a kappa light chain)	QVQLQQSGPELVKPGASV KISCKASGYAFSSSWLNW VKQRPGEGLWIGRIYPG DGDINYNGKFKGKATLTA DKSSSTAYMQLSSLTSDD SAVYFCTKRGRYALDYW GQGTSTVTVSS (SEQ ID NO: 40)	SSWLN (SEQ ID NO: 41)	RIYPGDGDINYNG KFKG (SEQ ID NO: 42)	RGRYALDY (SEQ ID NO: 43)
	VL	VL CDR1	VL CDR2	VL CDR3
	DIVLTQSPASLAVSLGQRA TISCRASKSVDNYGKSFM HWFQQKPGQPPKLLIYRA SNLESGIPARFSGSGSRTD FTLTINPVEADDVATYYC QQSNEDPYTFGGGTKLEM K (SEQ ID NO: 44)	RASKSVDNYGKS FMH (SEQ ID NO: 45)	RASNLES (SEQ ID NO: 46)	QQSNEDPYT (SEQ ID NO: 47)
Antibody	VH	VH CDR1	VH CDR2	VH CDR3
ACI-8037-103H5-Ab2 (a murine IgG2a isotype with a kappa light chain)	QVTLKESGPGILKPSQTL LTCSFSGFSLSTSGMGVG WIRQPSGKGLEWLAHIW WDDDKYYNPSLKSRLTIS KDSSRNQVFLKITSVDTA DTATYYCVRRGTRLEDYF DFWGQGTTLTVSS (SEQ ID NO: 60)	TSGMGVG (SEQ ID NO: 61)	HIWWDDDKYYN PSLKS (SEQ ID NO: 62)	RGTRLEDYFDF (SEQ ID NO: 63)
	VL	VL CDR1	VL CDR2	VL CDR3
	DVLMTQTPLSLPVSLGDQ ASISCRSSRSIVHSNGNTY LEWYLQKPGQSPKLLIFK VSNRFSGVPDRFSGSGSGT DFTLKISRVEAEDQGVYY CFQGSHVPLTFGAGTKLE LK (SEQ ID NO: 64)	RSSRSIVHSNGNT YLE (SEQ ID NO: 65)	KVSNRFS (SEQ ID NO: 16)	FQGSHVPLT (SEQ ID NO: 17)
Antibody	VH	VH CDR1	VH CDR2	VH CDR3

ACI-8037-109F4-Ab1 (a murine IgG2a isotype with a kappa light chain)	QVTLKESGPGILQPSQTL LTCSFSGFSLSTSGMGVS WIRQPSGKGLEWLAHIYW DDDKRYNPSLKSRLTISK DTSRNQVFLKITSVDTAD AGTYYCARRPIRTVVDAM DYWGQGTSTVTVSL (SEQ ID NO: 70)	TSGMGVS (SEQ ID NO: 11)	HIYWDDDKRYNP SLKS (SEQ ID NO: 12)	RPIRTVVDAMDY (SEQ ID NO: 73)
	VL	VL CDR1	VL CDR2	VL CDR3
	DVLMQTPLSLPVS LGDQ ASISCRSSQTIVHSNGNTY LEWYLQKPGQSPNLLIYK VSNRFSGVPDRFSGSGSGT DFTLKISRVEAEDLGVYY CFQGSHVPLTFGAGTKLE LK (SEQ ID NO: 74)	RSSQTIVHSNGNT YLE (SEQ ID NO: 75)	KVSNRFS (SEQ ID NO: 16)	FQGSHVPLT (SEQ ID NO: 17)
Antibody	VH	VH CDR1	VH CDR2	VH CDR3
ACI-8039-306H5-Ab1 (a murine IgG2a isotype with a kappa light chain)	QVTLKESGPGILKPSQTL LTCSFSGFSLSTSGMGVG WIRQPSGKGLEWLAHIW WDDDKYYNPSLKSQLTIS KDTSRNQIFLKITSVDTAD TATYYCVRSLYFDYWGQ GTTLTVSS (SEQ ID NO: 80)	TSGMGVG (SEQ ID NO: 61)	HIWWDDDKYYN PSLKS (SEQ ID NO: 62)	SLYFDY (SEQ ID NO: 83)
	VL	VL CDR1	VL CDR2	VL CDR3
	DVVMQTPLSLPVS LGDQ ASISCRSSQSLVHSNGNTY LHWYLQKPGQSPKLLIYK VSNRFSGVPDRFSGSGSGT DFTLKISRVEAEDLGVYFC SQSTHVPLTFGAGTKLEL K (SEQ ID NO: 84)	RSSQSLVHSNGN TYLH (SEQ ID NO: 85)	KVSNRFS (SEQ ID NO: 16)	SQSTHVPLT (SEQ ID NO: 87)
Antibody	VH	VH CDR1	VH CDR2	VH CDR3

ACI-8039-307F7-Ab2 (a murine IgG2a isotype with a kappa light chain)	QVQLQQPGAELVRPGGSV KLCKASGYSFTNYWMN WVKQRPQGQLEWIGMIH PSDSETRLNQKFKDKATL TVDKSSSTAYLQLSSPTSE DSAVYYCAKLLLYYFDY WGQGTTTLTVSS (SEQ ID NO: 90)	NYWMN (SEQ ID NO: 91)	MIHPDSETRLNQ KFKD (SEQ ID NO: 92)	LLLYYFDY (SEQ ID NO: 93)
	VL	VL CDR1	VL CDR2	VL CDR3
	DIVMTQSPSSLAMSVGQK VTMSCKSSQSLLNSSNQK NYLAWYQQKPGQSPKILV YFASTRESGVPDRFRGSGS GTDFTLTISVQAEDLADY FCQQHYSPPTFGGGTKL EIK (SEQ ID NO: 94)	KSSQSLLNSSNQK NYLA (SEQ ID NO: 95)	FASTRES (SEQ ID NO: 96)	QQHYSPPT (SEQ ID NO: 97)
Antibody	VH	VH CDR1	VH CDR2	VH CDR3
ACI-8039-309D9-Ab2 (a murine IgG2a isotype with a kappa light chain)	QVQLQQSGPQLVRPGASV KISCKASGNSFTSYWMH WVKQRPQGQLEWIGMID PSDSETRLNQKFKDKATL TVDKSSSTAYMQLSSPTSE DSAVYYCAGLYFTLDYW GQGTSVTVSS (SEQ ID NO: 100)	SYWMH (SEQ ID NO: 101)	MIDPSDSETRLNQ KFKD (SEQ ID NO: 102)	LYFTLDY (SEQ ID NO: 103)
	VL	VL CDR1	VL CDR2	VL CDR3
	DILMTQSPSSLTVSAGEKV TMSCKSSQSLLASGNQNN YLAWHQQKPGRSPKILII WASTRVSGVPDRFIGSGS GTDFTLTINSVQAEDLAV YYCQQSYSAPLTFGAGTK LELK (SEQ ID NO: 104)	KSSQSLLASGNQ NNYLA (SEQ ID NO: 105)	WASTRV (SEQ ID NO: 106)	QQSYSAPLT (SEQ ID NO: 107)
Antibody	VH	VH CDR1	VH CDR2	VH CDR3

ACI-8041-1F11B5-Ab1 (a murine IgG2a isotype with a kappa light chain)	QVQLKESGPGLVAPSQL SITCTVSGFSLTNYGVSWI RQPPGKGLEWLGVWGD GSTNYHSALISRLSISKDN SKSQVFLKLSLQTDDTA TYYCTKGAGSWGQGIPVT VSA (SEQ ID NO: 110)	NYGVS (SEQ ID NO: 111)	VIWGDGSTNYHS ALIS (SEQ ID NO: 112)	GAGS (SEQ ID NO: 113)
	VL	VL CDR1	VL CDR2	VL CDR3
	DVVLVTQTPLTSLVTIGQPA SISCKSSQSLLDSDGRTYLI WLLQRPQGQSPKRLIYLV SLDGSVPDRFTGSGSGTD FTLKISRVEAEDLGVYYC WQGTTHFPWTFGGGTKLEI K (SEQ ID NO: 114)	KSSQSLLDSDGRT YLI (SEQ ID NO: 115)	LVSTLDS (SEQ ID NO: 116)	WQGTTHFPWT (SEQ ID NO: 117)
Antibody	VH	VH CDR1	VH CDR2	VH CDR3
ACI-8041-2B9H5-Ab1 (a murine IgG2a isotype with a kappa light chain)	QVQLQQSDAELVKPGASV KISCKVSGYTFTDHPH MKQRPDQGLEWIGYFYPR DSSTHYNEKFKGKATLTA DKSSSTAYMQLNSLTSED SAVYFCARSMGYWGQGT SVTVSS (SEQ ID NO: 120)	DHPIH (SEQ ID NO: 121)	YFYPRDSSTHYN EKFKG (SEQ ID NO: 122)	SMGY (SEQ ID NO: 123)
	VL	VL CDR1	VL CDR2	VL CDR3
	DIKMTQSPSSMYASLGER VTITCKASQDINSYLSWFQ QKPGKSPKTLIYRANRLV DGVPSRFSGSGSGQDYS LTISSLDYEDMGIYYCLQY DEFPTFGAGTKLELK (SEQ ID NO: 124)	KASQDINSYLS (SEQ ID NO: 125)	RANRLVD (SEQ ID NO: 126)	LQYDEFPT (SEQ ID NO: 127)
Antibody	VH	VH CDR1	VH CDR2	VH CDR3
ACI-8041-3G11B3-	QVQLQQSGAELVKPGASV KLSCASGYTFINYYIYW	NYYIY (SEQ ID NO: 131)	EIIPSDGNTFNE KFKT	TGTV (SEQ ID NO: 133)

Ab1 (a murine IgG2a isotype with a kappa light chain)	VKQRPQGQLEWIGEIPSN DGTNFNEKFKTKATLTVD KSSSTAYMQLSSLTSEDSA VYYCTATGTVWGQGT TVSA (SEQ ID NO: 130)		(SEQ ID NO: 132)	
	VL	VL CDR1	VL CDR2	VL CDR3
	DVLTMTQTPLSLPVS LGDQ ASISCRSSQSIVHSNGITYL EWYLQKPGQSPKLLIYKV SNRFSGVPDRFSGSGSGTD FTLKISRVEAEDLGVYYCF QGSHVPWTFGGGTKLEIK (SEQ ID NO: 134)	RSSQSIVHSNGIT YLE (SEQ ID NO: 135)	KVSNRFS (SEQ ID NO: 16)	FQGSHVPWT (SEQ ID NO: 137)
Antibody	VH	VH CDR1	VH CDR2	VH CDR3
ACI-8041-4G6D2-Ab1 (a murine IgG2a isotype with a kappa light chain)	QVQLQQSGAELVRPGASV KLSCASGYTFTSYMY WVKQRPQGQLEWIGEIPSN NGDTNFNEKFRSKATLTV DKSSSTAYMQLSSLTSEDS AVYYCTATGTVWGQGT VTVSA (SEQ ID NO: 140)	SYMY (SEQ ID NO: 141)	EIIPSNNGDTNFNE KFRS (SEQ ID NO: 142)	TGTV (SEQ ID NO: 133)
	VL	VL CDR1	VL CDR2	VL CDR3
	DVLTMTQTPLSLPVS LGDQ ASISCRSSQSIVHSNGNTY LEWYLQKPGQSPKLLIYK VSNRFSGVPDRFSGSGSGT DFTLKISRVEAEDLGVYY CFQGSHVPWTFGGGTKLE IK (SEQ ID NO: 144)	RSSQSIVHSNGNT YLE (SEQ ID NO: 15)	KVSNRFS (SEQ ID NO: 16)	FQGSHVPWT (SEQ ID NO: 137)
Antibody	VH	VH CDR1	VH CDR2	VH CDR3
ACI-8041-5A2D4-Ab1 (a murine	EVQLQQSGPELVKPGASV KISCKTSGYTFTENTMHW VKQIHGKSLEWIGGINPN NGVTNNNQKFEGKATLT	ENTMH (SEQ ID NO: 151)	GINPNNGVTNNN QKFEG (SEQ ID NO: 152)	SDYDALYYSMDC (SEQ ID NO: 153)

IgG2a isotype with a kappa light chain)	VDKSSSTAYMELRSLTSE DSAVYYCARSDYDALYY SMDCWGQGTSVTVSS (SEQ ID NO: 150)			
	VL	VL CDR1	VL CDR2	VL CDR3
	EIVLTQSPTTMAASPGEKI TITCSGSSSIISNYLHWYQ QKPGFSPKLLIYRTSNLAS GVPTRFSGSGSGTSYSLTI GTMEAEDVATYYCQQGS SIPFTFGSGTKLEIK (SEQ ID NO: 154)	SGSSSIISNYLH (SEQ ID NO: 155)	RTSNLAS (SEQ ID NO: 156)	QQGSSIPFT (SEQ ID NO: 157)
Antibody	VH	VH CDR1	VH CDR2	VH CDR3
ACI-8041- 5A6H9- Ab1 (a murine IgG2a isotype with a kappa light chain)	DVQLQESGPGLVKPSQSL SLTCTVTGYSITSDYAWN WIRQFPGNKLEWMGYID YSGITSYNPSLKSRIITRD TSKNQFFLQLNSVTTEDS ATYYCARISGLDYDVRAG WFASWGQGTLLTVSA (SEQ ID NO: 160)	SDYAWN (SEQ ID NO: 161)	YIDYSGITSYNPS LKS (SEQ ID NO: 162)	ISGLDYDVRAGW FAS (SEQ ID NO: 163)
	VL	VL CDR1	VL CDR2	VL CDR3
	DIVMTQAAFSNPVTLGTS VSISCRSSKSLLSNGITYL YWYLQKPGQSPQLLIYQM SNLASGVPDRFSSSGSGTD FTLRISRVEAEDVGVYYC AQNLERPLTFGAGTKLEL K (SEQ ID NO: 164)	RSSKSLLSNGIT YLY (SEQ ID NO: 165)	QMSNLAS (SEQ ID NO: 166)	AQNLERPLT (SEQ ID NO: 167)
Antibody	VH	VH CDR1	VH CDR2	VH CDR3
ACI-8041- 6C3C4- Ab1 (a murine IgG2a	EVQLQQSGPELVKPGASV NISCKTSGYTFTEYTMHW MKQSHGKSLEWIGGINPN NGVTGYNQKFKGRATLT VDKSSSTAYMELRSLTSE	EYTMH (SEQ ID NO: 171)	GINPNNGVTGYN QKFKG (SEQ ID NO: 172)	SDYDDLYYAMD Y (SEQ ID NO: 173)

isotype with a kappa light chain)	DSAVYYCARSDYDDLYY AMDYWGQGTSVTVSS (SEQ ID NO: 170)			
	VL	VL CDR1	VL CDR2	VL CDR3
	EIVLTQSPTTMAASPGKI TITCSASSISSNYLHWYQ QKPGFSPKLLIYRTSNLAS GVPARFSGSGSGTSYSLTI GTMEAEDVATYYCQQGS SIPFTFGSGTKLEIK (SEQ ID NO: 174)	SASSISSNYLH (SEQ ID NO: 175)	RTSNLAS (SEQ ID NO: 156)	QQGSSIPFT (SEQ ID NO: 157)
Antibody	VH	VH CDR1	VH CDR2	VH CDR3
ACI-8041- 9D7E1- Ab1 (a murine IgG2a isotype with a kappa light chain)	EVMLVESGGGLVKPGGSL KLSCAASGFTFSSYAMSW VRQTPEKRLEWVATISSG GNYTYCPDSVKGRFTISR DNAKNTLYLQMSSLRSED TAMYYCAAYAYDDGYF DYWGQGTTLTVSS (SEQ ID NO: 180)	SYAMS (SEQ ID NO: 181)	TISSGGNYTYCPD SVKG (SEQ ID NO: 182)	YAYDDGYFDFY (SEQ ID NO: 183)
	VL	VL CDR1	VL CDR2	VL CDR3
	DIVMTQSPSSLAMSVGQK VTMSCKSSQSLLNSSNQK NYLAWYQKPGQSPKLL VYFASTRESGVPDRFIGSG SGTDFTLTISVQAEDLAD YFCQQHYSTPLTFGAGTK LELK (SEQ ID NO: 184)	KSSQSLLNSSNQK NYLA (SEQ ID NO: 95)	FASTRES (SEQ ID NO: 96)	QQHYSTPLT (SEQ ID NO: 187)
Antibody	VH	VH CDR1	VH CDR2	VH CDR3
ACI-8041- 10H3B11- Ab1 (a murine IgG2a isotype with a	EVMLVESGGGLVKPGGSL KLSCAASGFTFSSYAMSW VRQTPEKRLEWVATISSG GNYTYCPDSVKGRFTISR DNAKNTLYLQMSSLRSED TAMYYCAAYAYDDGYF DYWGQGTTLTVSS	SYAMS (SEQ ID NO: 181)	TISSGGNYTYCPD SVKG (SEQ ID NO: 182)	YAYDDGYFDFY (SEQ ID NO: 183)

kappa light chain)	(SEQ ID NO: 180)			
	VL	VL CDR1	VL CDR2	VL CDR3
	DIQMTQSPSSLSASLGKV TITCKASQDINKYIAWYQ HKPGKGPRLLIHYTSTLQP GIPSRFSGSGSGRDYSFIS NLGPEDIATYYCLQYDNL LTFGGGTKLEIK (SEQ ID NO: 194)	KASQDINKYIA (SEQ ID NO: 195)	YTSTLQP (SEQ ID NO: 196)	LQYDNLLT (SEQ ID NO: 197)

Table 4. Amino acid sequences of the Heavy Chain (HC) and Light Chain (LC) variable and constant regions

Antibody	HC	LC
ACI-24-41F12-Ab2	QVTLKESGPGILQSSQTLSTCSFSGFSLSTS GMGVSWIRQPSGKGLEWLAHIYWDDDKR YNPSLKSRLTISKDTSRNQVFLKITSVDTAD TATYYCARRRNGYDGGFAYWGQGLVTV SAAKTTTPSVYPLAPGCGDTTGSSVTLGCL VKGYPFESVTVTWNSGSLSSSVHTFPALLQ SGLYTMSSSVTPSSTWPSQTVTCSVAHPA SSTTVDKKLEPSGPISTINPCPPCKECHKCPA PNLEGGPSVFIFPPNIKDVLMI SLTPKVTCV VVDVSEDDPDVQISWVFNNEVHTAQTQT HREDYNSTIRVVSTLPIQH QDWMSGKEFKC KVNNKDLPSPIERTISKIKGLVRAPQVYILPP PAEQLSRKDVSLTCLVVGFNPGDISVEWTS NGHTEENYKDTAPVLDSG SYFIYSKLN M KTSKWEKTD SFSCNVRHEGLKNYYL KKTIS RSPGK (SEQ ID NO: 20)	DVLMTQTPLSLPVSLGDQASISCRSSQSIVH SNGNTYLEWYLQKPGQSPKLLIYKVS NRFS GVPDRFSGSGSGTDFTLKISRVEAEDLGVY YCFQGSHVPLTFGAGTKLELKRADAAPT VS IFPPSSEQLTSGGASVVCFLNNFY PKDINVK WKIDGSERQNGVLNSWTDQDSKDSTYSMS STLT LTKDEYERHNSYTCEATHKTSTSPIVK SFNRNEC (SEQ ID NO: 21)
ACI-24-41F12-Ab3 (IgG2a isotype)	QVTLKESGPGILQSSQTLSTCSFSGFSLSTS GMGVSWIRQPSGKGLEWLAHIYWDDDKR YNPSLKSRLTISKDTSRNQVFLKITSVDTAD TATYYCARRRNGYDGGFAYWGQGLVTV SAAKTTAPSVYPLAPVCGDTTGSSVTLGCL VKGYPPEPVTLTWNSGSLSSGVHTFP AVLQ	DVLMTQTPLSLPVSLGDQASISCRSSQSIVH SNGNTYLEWYLQKPGQSPKLLIYKVS NRFS GVPDRFSGSGSGTDFTLKISRVEAEDLGVY YCFQGSHVPLTFGAGTKLELKRADAAPT VS IFPPSSEQLTSGGASVVCFLNNFY PKDINVK WKIDGSERQNGVLNSWTDQDSKDSTYSMS

	SDLYTLSSSVTVTSSTWPSQSITCNVAHPAS STKVDKKIEPRGPTIKPCPPCKCPAPNLLGG PSVFIFPPKIKDVLMSLSPIVTCVVVDVSED DPDVQISWVFNVEVHTAQTQTHREDYNS TLRVVSALPIQHQDWMSGKEFKCKVNNKD LPAPIERTISKPKGSVRAPQVYVLPPEEEM TKKQVTLTCMVTDMPEDIYVEWTNNGKT ELNYKNTEPVLDSDGSYFMYSKLRVEKKN WVERNYSYSCSVVHEGLHNHHTTKSFSRTP GK (SEQ ID NO: 22)	STLTLTKDEYERHNSYTCEATHKTSTSPIVK SFNRNEC (SEQ ID NO: 23)
ACI-24- 41F12- Ab3 (hIgG1 isotype)	QVTLKESGPGILQSSQTLSTCSFSGFSLSTS GMGVSWIRQPSGKGLEWLAHIYWDDDKR YNPSLKSRLTISKDTSRNQVFLKITSVDTAD TATYYCARRRNGYDGGFAYWGQGLVTV SAASTKGPSVFPLAPSSKSTSGGTAALGCL VKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVTVPSSSLGTQTYICNVNHK PSNTKVDKRVEPKSCDKTHTCPPCPAPELL GGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSHEDPEVKFNWYVDGVEVHNAKTKPREE QYNSTYRVVSVLTVLHQDWLNGKEYKCK VSNKALPAPIEKTISKAKGQPREPQVYTLPP SREEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTPPVLDSDGSFFLYSKLTVD KSRWQQGNVFSCSVMHEALHNHYTQKSLS LSPGK (SEQ ID NO: 24)	DVLMTQTPLSLPVSLGDQASISCRSSQSIVH SNGNTYLEWYLQKPGQSPKLLIYKVSNRFS GVPDRFSGSGSGTDFTLKISRVEAEDLGVY YCFQGSHTVPLTFGAGTKLELKRTVAAPSVF IFPPSDEQLKSGTASVVCLLNNFYPREAKV QWKVDNALQSGNSQESVTEQDSKDSTYSL SSTLTLSKADYEKHKVYACEVTHQGLSSPV TKSFNRGEC (SEQ ID NO: 25)
ACI-31- 25B1-Ab2 (murine IgG2b with a lambda light chain)	EVQLVESGGDLVKPGGSLKLSCAASRFTFS TYGMSWVRQTPDKRLEWVATISSGRSYTY YADSVKGRFTISRDNANKNTLYLQMSSLKSE DTAMYYCARNNSNNQRDYYAMDYWGQGT SVTVSSAKTTPPSVYPLAPGCGDTTGSSVTL GCLVKGYFPEPVTVTWNSGSLSSSVHTFPA LLQSGLYTMSSSVTVPSSTWPSQTVTCSVA HPASSTTVDKKLEPSGPISTINPCPPCKECH KCPAPNLEGGPSVFIFPPNIKDVLMISLTPK	QLVLTQSSASFSLGASAKLTCTLSSQHITY TIEWYQQQLKPPKYVMVLEKDGSHSTGD GIPDRFSGSSSGADRYLSISNIQPEDEAVYIC GVGDALKEQFVYVFGGGTKVTVLGQPKSS PSVTLPSPSSEETNKAATLVCTITDFYPGV VTVDWKVDGTPVTQGMETTQPSKQSNK YMASSYLTLTARAWERHSSYSCQVTHEGH TVEKSLSRADCS (SEQ ID NO: 28)

	VTCVVVDVSEDDPDVQISWVFNNEVHTA QTQTHREDYNSTIRVVSTLPIQHQDWMMSG KEFKCKVNNKDLPSPIERTISKIKGLVRAPQ VYILPPPAEQLSRKDVSLTCLVVGFNPGDIS VEWTSNGHTEENYKDTAPVLSDSGSYFIYS KLNMKTSKWEKTDSEFSCNVRHEGLKNYYL KKTISRSPGK (SEQ ID NO: 27)	Note that glycine at position 116 is optional and included for improving expression levels.
ACI-31- 25B1-Ab2 (murine IgG2a with a lambda light chain)	EVQLVESGGDLVKPGGSLKLSAASRFTFS TYGMSWVRQTPDKRLEWVATISSGRSYTY YADSVKGRFTISRDNANKNTLYLQMSSLKSE DTAMYYCARNSSNNQRDYYAMDYWGQGT SVTVSSAKTTAPSVYPLAPVCGDTTGSSVT LGCLVKGYFPEPVTLTWNSGSLSSGVHTFP AVLQSDLYTLSSSVTVTSSTWPSQSITCNVA HPASSTKVDKKIEPRGPTIKPCPPCKCPAPN LLGGPSVFIFPPKIKDVLMISSLPIVTCVVVD VSEDDPDVQISWVFNNEVHTAQTQTHRE DYNSTLRVVSALPIQHQDWMMSGKEFKCKV NNKDLPAPIERTISKPKGSVRAPQVYVLPPP EEEMTKKQVTLTCMVTDFMPEDIYVEWTN NGKTELNYKNTEPVLDSDGSYFMYSKLRV EKKNWVERNSYSCSVVHEGLHNHHTTKSF SRTPGK (SEQ ID NO: 38)	QLVLTQSSASFSLGASAKLTCTLSSQHITY TIEWYQQQLKPPKYVMVLEKDGSHTGD GIPDRFSGSSSGADRYLSISNIQPEDEAVYIC GVGDAIKEQFVYVFGGGTKVTVLGQPKSS PSVTLFPPSSEETNKATLVCTITDFYPGV VTVDWKVDGTPVTQGMETTQPSKQSNK YMASSYLTLTARAWERHSSYSCQVTHEGH TVEKSLSRADCS (SEQ ID NO: 39)
ACI-31- 25B1-Ab2 (human IgG1/ Lambda isotype)	EVQLVESGGDLVKPGGSLKLSAASRFTFS TYGMSWVRQTPDKRLEWVATISSGRSYTY YADSVKGRFTISRDNANKNTLYLQMSSLKSE DTAMYYCARNSSNNQRDYYAMDYWGQGT SVTVSSASTKGPSVFPLAPSSKSTSGGTAAL GCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVTVPSSSLGTQTYICNV NHKPSNTKVDKRVEPKSCDKTHTCPPCPAP ELLGGPSVFLFPPKPKDTLMISRTPEVTCVV VDVSHEDPEVKFNWYVDGVEVHNAKTKP REEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVY	QLVLTQSSASFSLGASAKLTCTLSSQHITY TIEWYQQQLKPPKYVMVLEKDGSHTGD GIPDRFSGSSSGADRYLSISNIQPEDEAVYIC GVGDAIKEQFVYVFGGGTKVTVLGQPKAN PTVTLFPPSSEELQANKATLVCLISDFYPGA VTVAWKADGSPVKAGVETTKPSKQSNK YAASSYLSLTPEQWKSHRSYSCQVTHEGST VEKTVAPTECS (SEQ ID NO: 59)

	TLPPSREEMTKNQVSLTCLVKGFYPSDIAV EWESNGQPENNYKTTPPVLDSDGSFFLYSK LTVDKSRWQQGNVFCFSVMHEALHNHYT QKSLSLSPGK (SEQ ID NO: 58)	
ACI-31- 30C11- Ab1 (murine IgG2b with a kappa light chain)	QVQLQQSGPELVKPGASVKISCKASGYAFS SSWLNWVKQRPGEGLWIGRIYPGDGDIN YNGKFKGKATLTADKSSSTAYMQLSSLTS DDSAVYFCTKRGYALDYWGQGTSTVTVSS AKTTPPSVYPLAPGCGDTTGSSVTLGCLVK GYFPESVTVTWNSGSLSSSVHTFPALLQSG LYTMSSSVTVPSSTWPSQTVTCSVAHPASS TTVDKKLEPSGPSTINPCPPCKECKCPAP NLEGGPSVFIFPPNIKDVLMLSLTPKVTCTVV VDVSEDDPDVQISWVFNNEVHTAQTQTH REDYNSTIRVVSTLPIQHQQDWMSGKEFKCK VNNKDLPSPIERTISKIKGLVRAPQVYILPPP AEQLSRKDVSLTCLVVGFPNGDISVEWTSN GHTEENYKDTAPVLDSDGSYFIYSKLNMK TSKWEKTDSFSCNVRHEGLKNYYLKKTISR SPGK (SEQ ID NO: 48)	DIVLTQSPASLA VSLGQRATISCRASKSVDN YGKSFMHWFQQKPGQPPKLLIYRASNL GIPARFSGSGSRTDFTLTINPVEADDVATYY CQQSNEDPYTFGGGT KLEMKRADAAPT VS IFPPSSEQLTSGGASVVCFLNFPKDI NVK WKIDGSERQNGVLNSWTDQDSKD STYSMS STLTLTKDEYERHNSYTCEATH KTSTSPIVK SFNRNEC (SEQ ID NO: 49)
ACI-31- 30C11- Ab1 (murine IgG2a with a kappa light chain)	QVQLQQSGPELVKPGASVKISCKASGYAFS SSWLNWVKQRPGEGLWIGRIYPGDGDIN YNGKFKGKATLTADKSSSTAYMQLSSLTS DDSAVYFCTKRGYALDYWGQGTSTVTVSS AKTTAPSVYPLAPVCGDTTGSSVTLGCLVK GYFPEPVTLTWNSGSLSSGVHTFPAVLQSD LYTLSSSVTVTSSTWPSQSITCNVAHPASST KVDKKIEPRGPTIKPCPPCKCPAPNLLGGPS VFIFPPKIKDVLMLSLSPIVTCVVVDVSEDDP DVQISWVFNNEVHTAQTQTHREDYNSTL RVVSALPIQHQQDWMSGKEFKCKVNNKDL PAPIERTISKPKGSVRAPQVYVLPPEEEMTK KQVTLTCMVTDFMPEDIYVEWTNNGKTEL NYKNTEPVLDSDGSYFMYSKLRVEKKNW VERNSYSCSVVHEGLHNHHTTKSFSRTPGK	DIVLTQSPASLA VSLGQRATISCRASKSVDN YGKSFMHWFQQKPGQPPKLLIYRASNL GIPARFSGSGSRTDFTLTINPVEADDVATYY CQQSNEDPYTFGGGT KLEMKRADAAPT VS IFPPSSEQLTSGGASVVCFLNFPKDI NVK WKIDGSERQNGVLNSWTDQDSKD STYSMS STLTLTKDEYERHNSYTCEATH KTSTSPIVK SFNRNEC (SEQ ID NO: 51)

	(SEQ ID NO: 50)	
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Table 5. Amino acid sequences of Heavy Chain (HC) and Light Chain (LC) murine IgG2a/kappa isotype constant regions.

Immunoglobulin region	Amino acid sequence
Murine IgG2a HC constant domains	AKTTAPSVYPLAPVCGDTTGSSVTLGCLVKG YFPEPVTLTWNSGSLSSGVHTFPAVL QSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKV DKKIEPRGPTIKPCPPCKCPAPNL LGGPSVFIFPPKIKDVLMISLSPIVTCVVVDVSEDDPDVQISWFVNNVEVHTAQTQTH REDYNSTLRVVSALPIQH QDWM S GKEFKCKVNNKDLPAPIERTISKPKGSVRAPQVY VLPPPEEEMTKKQVTLTCMVTD FMPEDIYVEWTNNGKTELNYKNTEPVLDS DGSYF MYSKLRVEKKNWVERN SYSCSVVHEGLHNHHTTKSFSRTPGK (SEQ ID NO: 56)
Murine LC kappa domain	RADAAPTVSIFPPSSEQLTSGGASVVCFLNNFY PKDINVKWKIDG SERQNGVLNSWT DQDSK DSTYSMSSTLT LTKDEYERHNSYTCEATHKTSTSPIVKSFNRNEC (SEQ ID NO: 57)

Unless defined otherwise, all technical and scientific terms used herein have the same meanings as commonly understood by one of ordinary skill in the art to which this invention belongs. All publications and patents specifically mentioned herein are incorporated by reference in their entirety for all purposes in connection with the invention.

The present invention is not to be limited in scope by the specific embodiments described herein. Indeed, various modifications of the invention in addition to those described herein will become apparent to those skilled in the art from the foregoing description and accompanying figures. Such modifications are intended to fall within the scope of the appended claims. Moreover, all aspects and embodiments of the invention described herein are considered to be broadly applicable and combinable with any and all other consistent embodiments, including those taken from other aspects of the invention (including in isolation) as appropriate.

REFERENCES

- Belichenko PV, Madani R, Rey-Bellet L, et al. An Anti- β -Amyloid Vaccine for Treating Cognitive Deficits in a Mouse Model of Down Syndrome. *PLOS ONE*. 2016;11(3):e0152471.
- Britt, W. G., 3rd, Hansen, A. M., Bhaskerrao, S., Larsen, J. P., Petersen, F., Dickson, A., . . . Kirsch, W. M. (2011). Mild cognitive impairment: prodromal Alzheimer's disease or something else? *J Alzheimers Dis*, 27(3), 543-551. doi:10.3233/JAD-2011-110740
- Buchhave, P., Minthon, L., Zetterberg, H., Wallin, A. K., Blennow, K., & Hansson, O. (2012). Cerebrospinal fluid levels of beta-amyloid 1-42, but not of tau, are fully changed already 5 to 10 years before the onset of Alzheimer dementia. *Arch Gen Psychiatry*, 69(1), 98-106. doi:10.1001/archgenpsychiatry.2011.155
- Calderon-Garciduenas, A. L., & Duyckaerts, C. (2017). Alzheimer disease. *Handb Clin Neurol*, 145, 325-337. doi:10.1016/B978-0-12-802395-2.00023-7
- Gauthier, S., Reisberg, B., Zaudig, M., Petersen, R. C., Ritchie, K., Broich, K., . . . International Psychogeriatric Association Expert Conference on mild cognitive, i. (2006). Mild cognitive impairment. *Lancet*, 367(9518), 1262-1270. doi:10.1016/S0140-6736(06)68542-5
- Given, AM, Whalen, PM, O'Brien, PJ and Ray, CA (2012). Development and validation of an alpha fetoprotein immunoassay using Gyros technology. *J Pham Biomed Anal.*, 64-65: 8-15. doi: 10.1016/j.jpba.2012.02.001
- Graham et al., *J. Gen. Virol.* 36:59 (1977)
- Head E, Powell D, Gold BT, Schmitt FA. Alzheimer's Disease in Down Syndrome. *European journal of neurodegenerative disease*. 2012;1(3):353-364.
- Knopman, D. S., DeKosky, S. T., Cummings, J. L., Chui, H., Corey-Bloom, J., Relkin, N., . . . Stevens, J. C. (2001). Practice parameter: diagnosis of dementia (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology*, 56(9), 1143-1153. doi:10.1212/wnl.56.9.1143
- Kiio and Soyeun Park. Nano-scientific Application of Atomic Force Microscopy in Pathology: from Molecules to Tissues. *International Journal of Medical Sciences* (2020); 17(7): 844-858. doi: 10.7150/ijms.41805
- Mather, *Biol. Reprod.* 23:243-251 (1980)
- Mather et al., *Annals N.Y. Acad. Sci.* 383:44-68 (1982)
- Nabers A, Ollesch J, Schartner J, Kötting C, Genius J, Haußmann U, Klafki H, Wiltfang J, Gerwert K. J. An infrared sensor analysing label-free the secondary structure of the Abeta peptide in presence of complex fluids. *Biophotonics*. 2016 Mar;9(3):224-34. doi: 10.1002/jbio.201400145. Epub 2015 Mar 23. PMID: 25808829

Piraino F, Volpetti F, Watson C, Maerkl SJ. A Digital-Analog Microfluidic Platform for Patient-Centric Multiplexed Biomarker Diagnostics of Ultralow Volume Samples. *ACS Nano*. 2016 Jan 26;10(1):1699-710. doi: 10.1021/acsnano.5b07939. Epub 2016 Jan 12. PMID: 26741022

Robb, C., Udeh-Momoh, C., Wagenpfeil, S., Schope, J., Alexopoulos, P., Perneczky, R., & Alzheimer's Disease Neuroimaging, I. (2017). Biomarkers and Functional Decline in Prodromal Alzheimer's Disease. *J Alzheimers Dis*, 58(1), 69-78. doi:10.3233/JAD-161162

Shankar, G. M., Li, S., Mehta, T. H., Garcia-Munoz, A., Shepardson, N. E., Smith, I., . . . Selkoe, D. J. (2008). Amyloid-beta protein dimers isolated directly from Alzheimer's brains impair synaptic plasticity and memory. *Nat Med*, 14(8), 837-842. doi:10.1038/nm1782

Stech, M., Nikolaeva, O., Thoring, L. *et al.* Cell-free synthesis of functional antibodies using a coupled *in vitro* transcription-translation system based on CHO cell lysates. *Sci Rep* 7, 12030 (2017)

Urlaub et al., *Proc. Natl. Acad. Sci. USA* 77:4216 (1980)

CLAIMS

1. An amyloid-beta binding antibody or antigen-binding fragment thereof comprising:
 - a) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17; or
 - b) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 32; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 36; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37; or
 - c) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 41; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 42; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 43; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 45; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 46; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 47; or
 - d) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 61; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 62; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 63; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 65; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17; or
 - e) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 73; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 75; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17; or
 - f) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 61; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 62; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 83; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 85; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 87; or
 - g) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 91; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 92; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 93; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 95; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 96; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 97; or

- [illegible]

- NO: 173; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 175; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 156; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 157; or
- p) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 181; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 182; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 183; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 95; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 96; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 187; or
- q) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 181; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 182; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 183; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 195; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 196; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 197.
2. The amyloid-beta binding antibody or antigen-binding fragment thereof of claim 1, wherein the antibody or the antigen-binding fragment thereof comprises:
- a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 10; or
 - b) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 or a Heavy Chain Variable Region (VH) having at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 30; or
 - c) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 40 or a Heavy Chain Variable Region (VH) having at least 93%, 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 40; or
 - d) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 60 or a Heavy Chain Variable Region (VH) having at least 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 60; or
 - e) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 70 or a Heavy Chain Variable Region (VH) having at least 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 70; or
 - f) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 80 or a Heavy Chain Variable Region (VH) having at least 99%, sequence identity to the amino acid sequence of SEQ ID NO: 80; or
 - g) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 90 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 90; or

- h) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 100 or a Heavy Chain Variable Region (VH) having at least 99%, sequence identity to the amino acid sequence of SEQ ID NO: 100; or
 - i) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 110 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 110; or
 - j) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 120 or a Heavy Chain Variable Region (VH) having at least 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 120; or
 - k) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 130 or a Heavy Chain Variable Region (VH) having at least 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 130; or
 - l) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 140 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 140; or
 - m) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 or a Heavy Chain Variable Region (VH) having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 150; or
 - n) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 160 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 160; or
 - o) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 170 or a Heavy Chain Variable Region (VH) having at least 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 170; or
 - p) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 180 or a Heavy Chain Variable Region (VH) having at least 94%, 95%, 96%, 97%, 98%, or 99%, sequence identity to the amino acid sequence of SEQ ID NO: 180.
3. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding claims, wherein the antibody or the antigen-binding fragment thereof comprises:
- a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 10; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14; or
 - b) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 or a Heavy Chain Variable Region (VH) having at least 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 30; and a Light Chain Variable Region (VL)

- comprising the sequence of SEQ ID NO: 34 or a Light Chain Variable Region (VL) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 34; or
- c) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 40 or a Heavy Chain Variable Region (VH) having at least 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 40; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 44 or a Light Chain Variable Region (VL) having at least 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 44; or
 - d) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 60 or a Heavy Chain Variable Region (VH) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 60; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 64 or a Light Chain Variable Region (VL) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 64; or
 - e) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 70 or a Heavy Chain Variable Region (VH) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 70; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 74 or a Light Chain Variable Region (VL) having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 74; or a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 80 or a Heavy Chain Variable Region (VH) having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 80; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 84; or
 - f) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 90 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 90; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 94 or a Light Chain Variable Region (VL) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 94; or
 - g) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 100 or a Heavy Chain Variable Region (VH) having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 100; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 104; or
 - h) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 110 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 110; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 114 or a Light Chain Variable Region (VL) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 114; or
 - i) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 120 or a Heavy Chain Variable Region (VH) having at least 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 120; and a Light Chain Variable Region (VL) comprising the sequence

- of SEQ ID NO: 124 or a Light Chain Variable Region (VL) having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 124; or
- j) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 130 or a Heavy Chain Variable Region (VH) having at least 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 130; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 134; or
 - k) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 140 or a Heavy Chain Variable Region (VH) having at least 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 140; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 144; or
 - l) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 or a Heavy Chain Variable Region (VH) having at least 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 150; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 154 or a Light Chain Variable Region (VL) having at least 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 154; or
 - m) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 160 or a Heavy Chain Variable Region (VH) having at least 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 160; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 164 or a Light Chain Variable Region (VL) having at least 99% sequence identity to the amino acid sequence of SEQ ID NO: 164; or
 - n) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 170 or a Heavy Chain Variable Region (VH) having at least 92%, 93%, 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 170; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 174; or
 - o) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 180 or a Heavy Chain Variable Region (VH) having at least 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 180; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 184; or
 - p) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 180 or a Heavy Chain Variable Region (VH) having at least 94%, 95%, 96%, 97%, 98%, or 99% sequence identity to the amino acid sequence of SEQ ID NO: 180; and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 194.
4. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding claims, wherein the antibody or the antigen-binding fragment thereof comprises:
- a) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 10 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14; or

- b) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34; or
 - c) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 40 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 44; or
 - d) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 60 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 64; or
 - e) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 70 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 74; or
 - f) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 80 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 84; or
 - g) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 90 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 94; or
 - h) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 100 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 104; or
 - i) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 110 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 114; or
 - j) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 120 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 124; or
 - k) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 130 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 134; or
 - l) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 140 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 144; or
 - m) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 154; or
 - n) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 160 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 164; or
 - o) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 170 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 174; or
 - p) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 180 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 184; or
 - q) a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 180 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 194; or.
5. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding claims, wherein the antibody comprises:
- a) a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 20 and a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 21; or

- b) a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 22 and a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 23; or
 - c) a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 24 and a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 25; or
 - d) a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 27 and a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 28; or
 - e) a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 38 and a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 39; or
 - f) a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 48 and a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 49; or
 - g) a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 50 and a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 51; or
 - h) a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 56 and a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 57; or
 - i) a Heavy Chain (HC) comprising the amino sequence of SEQ ID NO: 58 and a Light Chain (LC) comprising the amino sequence of SEQ ID NO: 59.
6. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding claims, which selectively binds to or captures any amyloid-beta peptides or species in solution independent of the conformational state of the amyloid-beta peptides or species.
 7. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding claims, which binds to an epitope within amino acids residues 1-5 (SEQ ID NO: 7), 1-8 (SEQ ID NO: 2), 17-23 (SEQ ID NO: 9), 22-35 (SEQ ID NO: 29) or 26-34 (SEQ ID NO: 8) of SEQ ID NO: 1 or to an equivalent epitope in non-human amyloid-beta.
 8. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding claims, which is a murine, a chimeric, a humanized or a human antibody or an antigen-binding fragment thereof.
 9. The amyloid-beta binding antibody or antigen-binding fragment thereof of any one of the preceding claims, which is an IgM, IgG1, IgG2, IgG2a, IgG2b, IgG3 or IgG4 antibody or antigen-binding fragment thereof.
 10. The amyloid-beta binding antibody or antigen-binding fragment thereof of any one of the preceding claims, which is conjugated to another molecule, in particular a detectable label.
 11. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding claims, for use in the diagnosis of an amyloid-beta associated disease, disorder or condition in a subject.
 12. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding claims, for use in the detection of amyloid-beta in a biological sample.
 13. The amyloid-beta binding antibody or antigen-binding fragment thereof of claim 12 wherein the biological sample is a body fluid sample or a buffer solution.
 14. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of claims 1 to 13, for use in the detection of amyloid-beta in a body fluid sample, wherein the body fluid sample is saliva, urine, nasal secretion,

blood (including whole blood, plasma and serum, preferably plasma), brain and/or CSF sample, brain and/or ISF sample, more particularly blood, brain, CSF and/or ISF sample.

15. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding claims, for use in the diagnosis of an amyloid-beta associated disease, disorder or condition wherein the amyloid-beta associated disease, disorder or condition is selected from the group consisting of Alzheimer's Disease (AD), mild cognitive impairment (MCI), Down syndrome (DS), Down syndrome-related Alzheimer's Disease, cardiac amyloidosis, cerebral amyloid angiopathy (CAA), multiple sclerosis, Parkinson's disease, Parkinson's Disease with Dementia (PDD), Lewy body dementia, ALS (amyotrophic lateral sclerosis), Adult Onset Diabetes, inclusion body myositis (IBM), ocular amyloidosis, glaucoma, macular degeneration, lattice dystrophy, optic neuritis, Myotonic dystrophy and hepatic dysfunction or failure.
16. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding claims, for use in the diagnosis of an amyloid-beta associated disease, disorder or condition wherein the amyloid-beta associated disease, disorder or condition is Alzheimer's Disease (AD), Down syndrome (DS), Down syndrome-related Alzheimer's Disease, cerebral amyloid angiopathy (CAA), Myotonic dystrophy, or Lewy body dementia.
17. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding claims, for use in the diagnosis of an amyloid-beta associated disease, disorder or condition wherein the amyloid-beta associated disease, disorder or condition is Alzheimer's Disease (AD).
18. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the claims 1 to 16 for use in the diagnosis of an amyloid-beta associated disease, disorder or condition wherein the amyloid-beta associated disease, disorder or condition is Down Syndrome (DS).
19. The amyloid-beta binding antibody or antigen-binding fragment thereof of any of the claims 1 to 16 for use in the diagnosis of an amyloid-beta associated disease, disorder or condition wherein the amyloid-beta associated disease, disorder or condition is Down Syndrome-related Alzheimer's disease.
20. A method of detecting amyloid-beta in a sample obtained from a subject, the method comprising contacting the sample with the amyloid-beta binding antibody or antigen-binding fragment thereof of any of the preceding claims and detecting binding of the antibody or antigen-binding fragment thereof in order to detect amyloid-beta in the sample.
21. A method of quantifying amyloid-beta in a sample obtained from a subject, the method comprising contacting the sample with the amyloid-beta binding antibody or antigen-binding fragment thereof of any of claims 1-19 and quantifying amyloid-beta in a sample based on the level of binding of the antibody or antigen-binding fragment thereof to amyloid-beta.
22. A method for diagnosing a disease, disorder and/or condition associated with amyloid-beta comprising performing the method of claim 20 or 21 wherein higher levels of amyloid-beta in the sample compared with a control level based on healthy subjects are indicative of a disease, disorder and/or condition associated with amyloid-beta.

23. A method for diagnosing a disease, disorder and/or condition associated with amyloid-beta comprising performing the method of claim 20 or 21 wherein similar or higher levels of amyloid-beta in the sample compared with a diseased control level are indicative of a disease, disorder and/or condition associated with amyloid-beta.
24. A method for classifying a disease, disorder and/or condition associated with amyloid-beta comprising:
 - a. performing the method of claim 22 and/or 23,
 - b. classifying the disease, disorder and/or condition associated with amyloid-beta.
25. A method for monitoring a disease, disorder and/or condition associated with amyloid-beta at two or more time points using samples from a subject comprising contacting the samples with an amyloid-beta binding antibody or antigen-binding fragment thereof of any of claims 1-19, wherein;
 - a. higher levels of amyloid-beta in the later sample compared with one or more earlier samples are indicative of progression of a disease, disorder and/or condition associated with amyloid-beta;
 - b. lower levels of amyloid-beta in the later sample compared with one or more earlier samples are indicative of regression of a disease, disorder and/or condition associated with amyloid-beta; and/or
 - c. no significant change of levels of amyloid-beta in the later sample compared with one or more earlier samples are indicative of lack of progression of a disease, disorder and/or condition associated with amyloid-beta.
26. A method for selecting a therapy for treatment of a disease, disorder and/or condition associated with amyloid-beta comprising contacting samples taken before and after treatment with the therapy with an amyloid-beta binding antibody or antigen-binding fragment thereof of any of claims 1-19, wherein;
 - a. lower levels of amyloid-beta in the sample taken after treatment compared with the sample taken before treatment are indicative of successful treatment of a disease, disorder and/or condition associated with amyloid-beta and thus the therapy is selected for treatment;
 - b. no significant change of levels of amyloid-beta in the sample taken after treatment compared with the sample taken before treatment are indicative of successful treatment of a disease, disorder and/or condition associated with amyloid-beta and thus the therapy is selected for treatment;
 - c. a decline in the rate of increase of levels of amyloid-beta between samples taken during treatment compared with samples taken before treatment are indicative of successful treatment of a disease, disorder and/or condition associated with amyloid-beta and thus the therapy is selected for treatment;
 - d. higher levels of amyloid-beta in the sample taken after treatment compared with the sample taken before treatment are indicative of unsuccessful treatment of a disease, disorder and/or condition associated with amyloid-beta and thus the therapy is not selected for treatment; or
 - e. no decline in the rate of increase of levels of amyloid-beta between samples taken during treatment compared with samples taken before treatment are indicative of unsuccessful treatment of a disease, disorder and/or condition associated with amyloid-beta and thus the therapy is not selected for treatment.
27. A method for assessing a candidate therapy for a disease, disorder and/or condition associated with amyloid-beta, the method comprising, following treatment of one or more subjects, contacting samples from the one or more

treated subjects with an antibody or antigen-binding fragment of any of claims 1-19, wherein lower levels of amyloid-beta in the samples compared with levels in corresponding samples from subjects not treated with the therapy are indicative of successful treatment of a disease, disorder and/or condition associated with amyloid-beta.

28. The method of claim 27 performed at multiple time points in matched samples between the treatment and placebo groups in order to monitor the effectiveness of the candidate therapy over a defined time period.
29. The method of claim 27 or 28 which comprises contacting samples from the one or more treated subjects and the subjects not treated with the therapy with an antibody or antigen-binding fragment of any of claims 1-19 prior to treatment, with the therapy or placebo respectively, to determine base levels of amyloid-beta.
30. The method according to any one of claims 20 to 29 wherein the disease, disorder and/or condition associated with amyloid-beta is selected from the group consisting of Alzheimer's Disease (AD), mild cognitive impairment (MCI), Down syndrome (DS), Down syndrome-related Alzheimer's Disease, cardiac amyloidosis, cerebral amyloid angiopathy (CAA), multiple sclerosis, Parkinson's disease, Parkinson's Disease with Dementia (PDD), Lewy body dementia, ALS (amyotrophic lateral sclerosis), Adult Onset Diabetes, inclusion body myositis (IBM), ocular amyloidosis, glaucoma, macular degeneration, lattice dystrophy, optic neuritis, Myotonic dystrophy and hepatic dysfunction or failure.
31. The method according to claim 30 wherein the amyloid-beta associated disease, disorder or condition is Alzheimer's Disease (AD), Down syndrome (DS), Down syndrome-related Alzheimer's Disease, cerebral amyloid angiopathy (CAA), Myotonic dystrophy, or Lewy body dementia.
32. The method according to claim 30 or 31 wherein the amyloid-beta associated disease, disorder or condition is Alzheimer's Disease (AD).
33. The method according to claim 30 or 31 wherein the amyloid-beta associated disease, disorder or condition is Down Syndrome (DS).
34. A diagnostic composition comprising the amyloid-beta binding antibody or antigen-binding fragment thereof of any one of claims 1 to 19 and an acceptable carrier and/or excipient.
35. A nucleic acid encoding the amyloid-beta binding antibody or antigen-binding fragment thereof of any one of claims 1 to 19.
36. A nucleic acid comprising a nucleotide sequence as provided in SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 52, SEQ ID NO: 53, SEQ ID NO: 54, SEQ ID NO: 55, SEQ ID NO: 68, SEQ ID NO: 69, SEQ ID NO: 78, SEQ ID NO: 79, SEQ ID NO: 88, SEQ ID NO: 89, SEQ ID NO: 98, SEQ ID NO: 99, SEQ ID NO: 108, SEQ ID NO: 109, SEQ ID NO: 118, SEQ ID NO: 119, SEQ ID NO: 128, SEQ ID NO: 129, SEQ ID NO: 138, SEQ ID NO: 139, SEQ ID NO: 148, SEQ ID NO: 149, SEQ ID NO: 158, SEQ ID NO: 159, SEQ ID NO: 168, SEQ ID NO: 169, SEQ ID NO: 178, SEQ ID NO: 179, SEQ ID NO: 188, SEQ ID NO: 189 or SEQ ID NO: 199.
37. A recombinant vector comprising the nucleic acid of claim 35 or 36.
38. A host cell comprising the nucleic acid of claim 35 or 36 and/or the recombinant vector of claim 37.
39. An isolated host cell that expresses the amyloid-beta binding antibody or antigen-binding fragment of any one of claims 1 to 19.

40. A method for producing an amyloid-beta binding antibody or antigen-binding fragment thereof, comprising the steps of:
- a. culturing the host cell of claim 38 or 39 under conditions suitable for producing the amyloid-beta binding antibody or antigen-binding fragment thereof, and
 - b. recovering the amyloid-beta binding antibody or antigen-binding fragment thereof.
41. A kit for diagnosis of a disease, disorder or condition associated with amyloid-beta, or a kit for use in a method of any one of claims 20 to 33, comprising the amyloid-beta binding antibody or antigen-binding fragment thereof according to any one of claims 1 to 19 and a container.
42. The amyloid-beta binding antibody or antigen-binding fragment thereof of any one of claims 1-19 for research use, in particular as an analytical tool or reference molecule.
43. The amyloid-beta binding antibody or antigen-binding fragment thereof of any one of claims 1-19 for use in detecting amyloid-beta aggregates, including plaques, *in vitro* or *in vivo*.
44. The amyloid-beta binding antibody or antigen-binding fragment thereof for use of claim 43 which is used for histochemical detection in brain tissue.
45. A diagnostic composition comprising at least two amyloid-beta binding antibodies or antigen-binding fragments thereof according to any one of claims 1 to 19 and an acceptable carrier and/or excipient.
46. The diagnostic composition of claim 45, wherein two amyloid-beta binding antibodies or antigen-binding fragments selectively bind to or capture any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species, and wherein at least one of the two amyloid-beta binding antibodies or antigen-binding fragments does not display any cross-reactivity to soluble APPalpha.
47. A diagnostic composition comprising two amyloid-beta binding antibodies or antigen-binding fragments comprising a first amyloid-beta binding antibody or antigen-binding fragment thereof according to claims 1 to 19 and a second amyloid-beta binding antibody or antigen-binding fragment thereof that is not an antibody according to claims 1 to 19, and an acceptable carrier and/or excipient.
48. The diagnostic composition comprising at least two amyloid-beta binding antibodies or antigen-binding fragments thereof and an acceptable carrier and/or excipient according to claim 46 or 47, wherein at least one, or two, of the amyloid-beta binding antibody or antigen-binding fragments are selected from:
- a) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17; and/or
 - b) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 32; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; a VL-CDR2 comprising the amino acid

sequence of SEQ ID NO: 36; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37; and/or

- c) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 151; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 152; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 153; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 155; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 156; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 157.

49. The diagnostic composition comprising at least two amyloid-beta binding antibodies or antigen-binding fragments thereof and an acceptable carrier and/or excipient according to claim 46 or 47, wherein at least one, or two, of the amyloid-beta binding antibody or antigen-binding fragment are selected from:

- a) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17; and
- b) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 32; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 36; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37.

50. An amyloid-beta binding antibody or antigen-binding fragment selected from:

- a) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17; and/or
- b) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 32; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 36; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37; and/or
- c) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 151; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 152; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 153; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 155; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 156; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 157;

for use in an immunoassay involving at least two amyloid-beta binding antibodies or antigen-binding fragments thereof.

51. A method of detecting amyloid-beta in a sample obtained from a subject, the method comprising the step of capturing amyloid beta with a first amyloid-beta binding antibody or fragment thereof and the step of detecting captured amyloid-beta in the sample with a second amyloid-beta binding antibody or fragment thereof, wherein:
 - a) each amyloid-beta binding antibody or antigen-binding fragment thereof is selected from the antibodies or antigen-binding fragments according to claims 1 to 19, or
 - b) one amyloid-beta binding antibody or antigen-binding fragment thereof according to claims 1 to 19 and the other antibody an amyloid-beta binding antibody or antigen-binding fragment thereof different to the antibody according to claims 1 to 19.
52. A method of detecting amyloid-beta in a sample obtained from a subject, the method comprising the step of capturing amyloid beta with a first amyloid-beta binding antibody or fragment thereof and the step of detecting captured amyloid-beta in the sample with a second amyloid-beta binding antibody or fragment thereof, wherein the first and second amyloid-beta binding antibodies or antigen-binding fragments thereof are selected from claims 1 to 19, and wherein at least one of the first and second antibody or antigen-binding fragment thereof does not display any cross-reactivity to soluble APPalpha.
53. A method of detecting amyloid-beta in a sample obtained from a subject, the method comprising the step of capturing amyloid beta with a first amyloid-beta binding antibody or fragment thereof and the step of detecting captured amyloid-beta in the sample with a second amyloid-beta binding antibody or fragment thereof, wherein each amyloid-beta binding antibody or antigen-binding fragment thereof is independently selected from:
 - a) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17; and/or
 - b) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 32; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 36; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37; and/or
 - c) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 151; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 152; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 153; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 155; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 156; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 157.
54. A method of detecting amyloid-beta in a sample obtained from a subject, the method comprising the step of capturing amyloid beta with a first amyloid-beta binding antibody or fragment thereof and the step of detecting captured amyloid-beta in the sample with a second amyloid-beta binding antibody or fragment thereof, wherein each amyloid-beta binding antibody or antigen-binding fragment thereof is independently selected from:

- a) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 11; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 12; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 13; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 15; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 16; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 17; and
 - b) a VH-CDR1 comprising the amino acid sequence of SEQ ID NO: 31; a VH-CDR2 comprising the amino acid sequence of SEQ ID NO: 32; a VH-CDR3 comprising the amino acid sequence of SEQ ID NO: 33; a VL-CDR1 comprising the amino acid sequence of SEQ ID NO: 35; a VL-CDR2 comprising the amino acid sequence of SEQ ID NO: 36; and a VL-CDR3 comprising the amino acid sequence of SEQ ID NO: 37.
55. A diagnostic composition comprising:
- a. a first amyloid-beta binding antibody or antigen-binding fragment thereof that selectively binds to any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species, and
 - b. a second amyloid-beta binding antibody or antigen-binding fragment thereof that selectively binds to any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species,
- wherein at least one, or both, of the first and second antibodies displays no cross-reactivity to soluble amyloid precursor protein (APP), in particular with no cross-reactivity to soluble APP alpha.
56. The diagnostic composition of claim 55 wherein at least one of the first and second antibody or antigen-binding fragment thereof that displays no cross-reactivity to soluble amyloid precursor protein (APP), in particular with no cross-reactivity to soluble APP alpha is an antibody or antigen-binding fragment thereof according to any one of claims 1 to 19.
57. The diagnostic composition of claim 56 wherein the antibody or antigen-binding fragment thereof that displays no cross-reactivity to soluble amyloid precursor protein (APP), in particular with no cross-reactivity to soluble APP alpha comprises:
- i. a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 30 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 34; or
 - ii. a Heavy Chain Variable Region (VH) comprising the sequence of SEQ ID NO: 150 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 154.
58. The diagnostic composition of any of claims 55 to 57 wherein one of the first and second antibody or antigen-binding fragment thereof displays cross-reactivity (which may be low or high) to soluble amyloid precursor protein (APP).
59. The diagnostic composition of claim 58 wherein the antibody or antigen-binding fragment thereof displaying cross-reactivity (which may be low or high) to soluble amyloid precursor protein (APP) is an antibody or antigen-binding fragment thereof according to any one of claims 1 to 19.
60. The diagnostic composition of claim 59 wherein the antibody or antigen-binding fragment thereof displaying cross-reactivity (which may be low or high) to soluble amyloid precursor protein (APP) comprises a Heavy Chain

Variable Region (VH) comprising the sequence of SEQ ID NO: 10 and a Light Chain Variable Region (VL) comprising the sequence of SEQ ID NO: 14.

61. A method of detecting amyloid-beta in a sample obtained from a subject, the method comprising:
- a. capturing amyloid beta with an amyloid-beta binding antibody or antigen-binding fragment thereof that selectively binds to any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species, and
 - b. detecting captured amyloid beta with an amyloid-beta binding antibody or antigen-binding fragment thereof that selectively binds to any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species and displays no, low or high cross-reactivity to soluble amyloid precursor protein (APP), in particular with no, low or high cross-reactivity to soluble APP alpha,

wherein at least one, or both, of the capture and detection antibody or antigen-binding fragment thereof displays no cross-reactivity to soluble amyloid precursor protein (APP), in particular with no cross-reactivity to soluble APP alpha.

62. The method of claim 61 wherein at least one of the capture and detection antibody or antigen-binding fragment thereof that displays no cross-reactivity to soluble amyloid precursor protein (APP), in particular with no cross-reactivity to soluble APP alpha is an antibody or antigen-binding fragment thereof according to any one of claims 1 to 19.
63. The method of claim 61 or 62 wherein one of the capture and detection antibody or antigen-binding fragment thereof displays cross-reactivity (which may be low or high) to soluble amyloid precursor protein (APP).
64. The method of claim 63 wherein the antibody or antigen-binding fragment thereof displaying cross-reactivity (which may be low or high) to soluble amyloid precursor protein (APP) is an antibody or antigen-binding fragment thereof according to any one of claims 1 to 19.
65. A kit for detecting amyloid-beta in a sample obtained from a subject, the kit comprising:
- a. a capture amyloid-beta binding antibody or antigen-binding fragment thereof that selectively binds to any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species ; and
 - b. a detection amyloid-beta binding antibody or antigen-binding fragment thereof that selectively binds to any amyloid-beta peptides or species in solution independently of the conformational state of the amyloid-beta peptides or species

wherein at least one of the capture and detection antibody or antigen-binding fragment thereof displays no cross-reactivity to soluble amyloid precursor protein (APP), in particular with no cross-reactivity to soluble APP alpha.

66. The kit of claim 65 wherein at least one of the capture and detection antibody or antigen-binding fragment thereof that displays no cross-reactivity to soluble amyloid precursor protein (APP), in particular with no cross-reactivity to soluble APP alpha is an antibody or antigen-binding fragment thereof according to any one of claims 1 to 19.
67. The kit of claim 65 or 66 wherein one of the capture and detection antibody or antigen-binding fragment thereof displays cross-reactivity (which may be low or high) to soluble amyloid precursor protein (APP).
68. The kit of claim 67 wherein the antibody or antigen-binding fragment thereof displaying cross-reactivity (which may be low or high) to soluble amyloid precursor protein (APP) is an antibody or antigen-binding fragment thereof according to any one of claims 1 to 19.
69. The method of any one of claims 20-33, 51-54 or 61-64, or the kit of any one of claims 65-68 wherein the sample is a body fluid sample, preferably wherein the body fluid sample is saliva, urine, nasal secretion, blood (including whole blood, plasma and serum, preferably plasma), brain and/or CSF sample, brain and/or ISF sample, more particularly blood, brain, CSF and/or ISF sample.
70. The diagnostic composition of any one of claims 45-49 or 55-60 further comprising a sample, in particular a body fluid sample, preferably wherein the body fluid sample is saliva, urine, nasal secretion, blood (including whole blood, plasma and serum, preferably plasma), brain and/or CSF sample, brain and/or ISF sample, more particularly blood, brain, CSF and/or ISF sample.

Figure 1

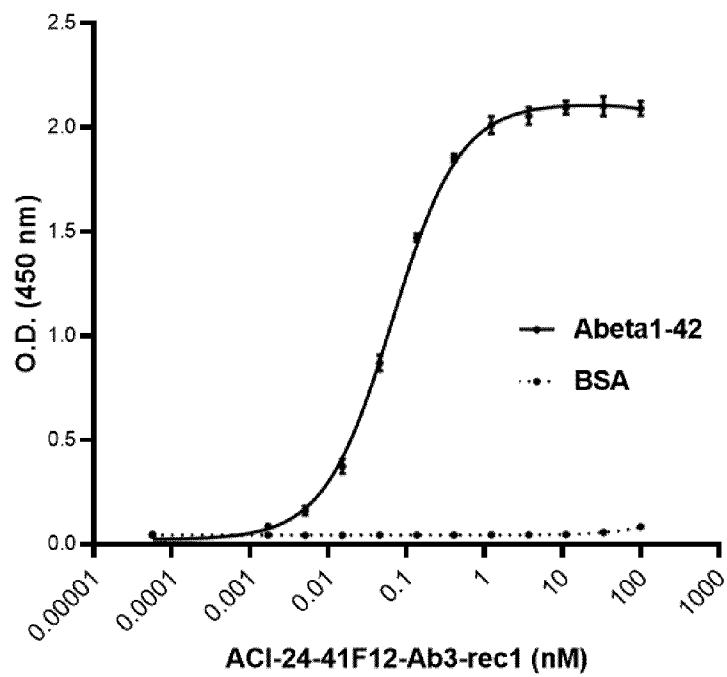


Figure 2

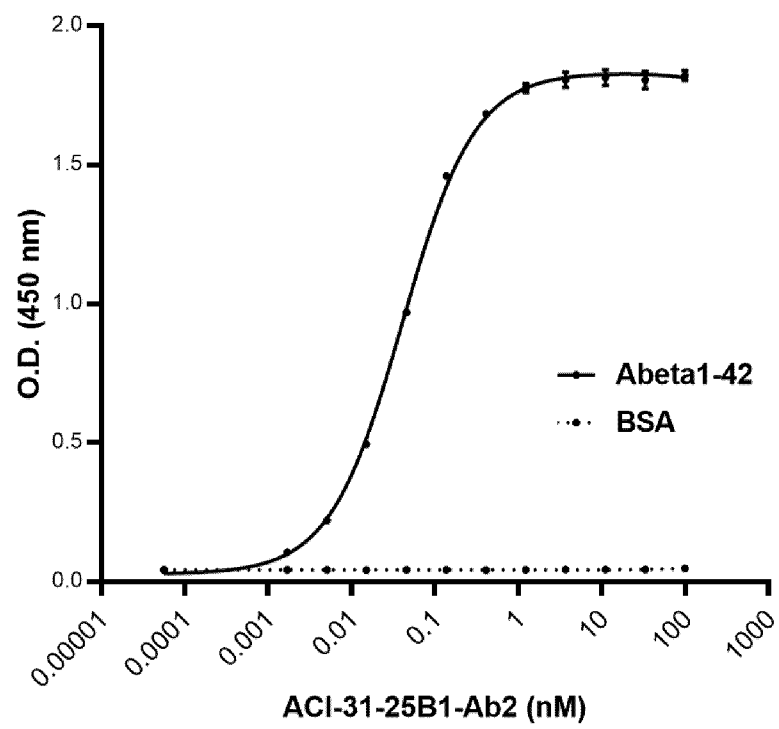


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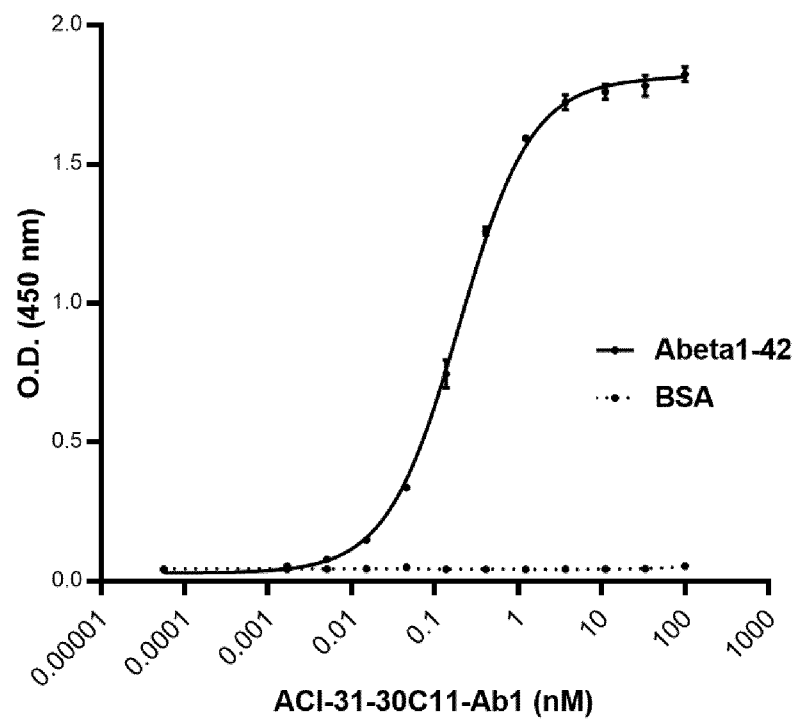


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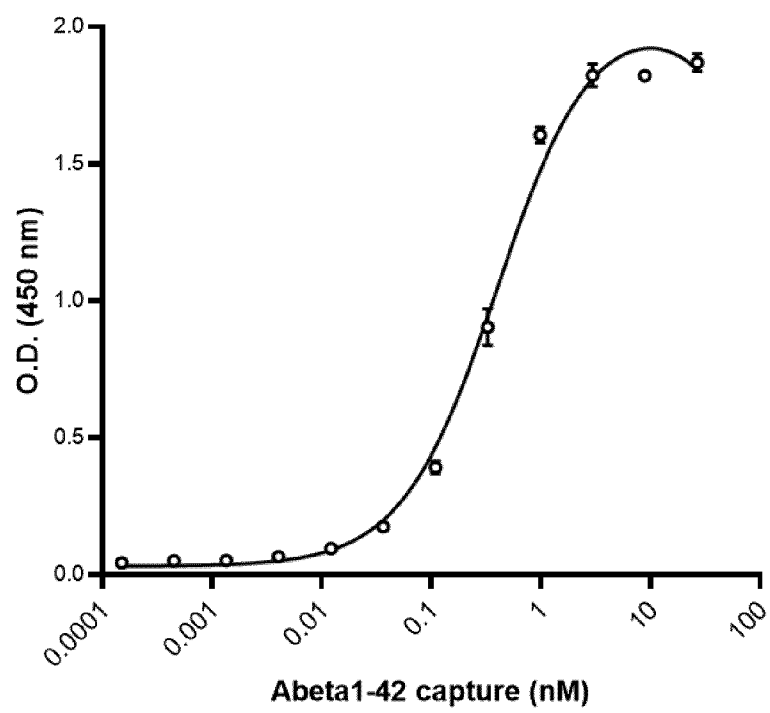


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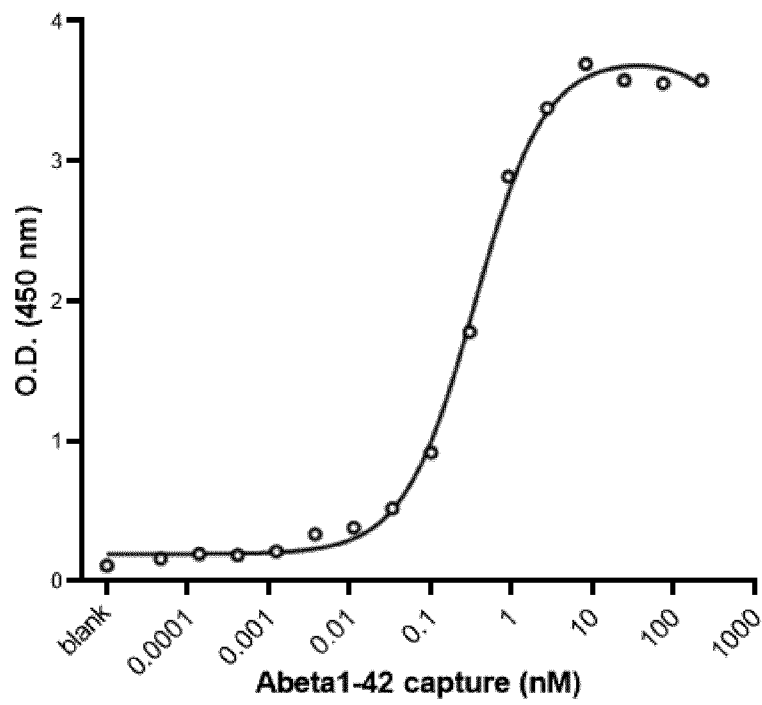


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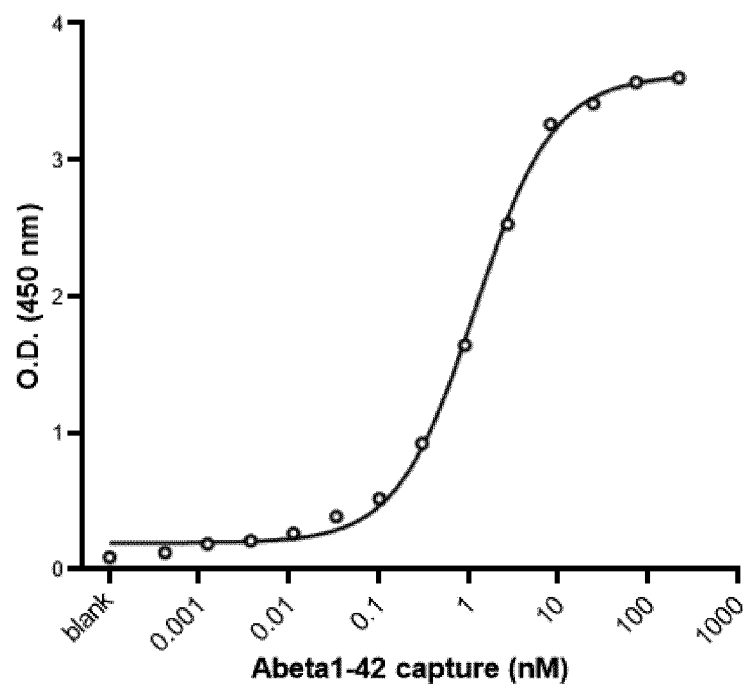


Figure 7

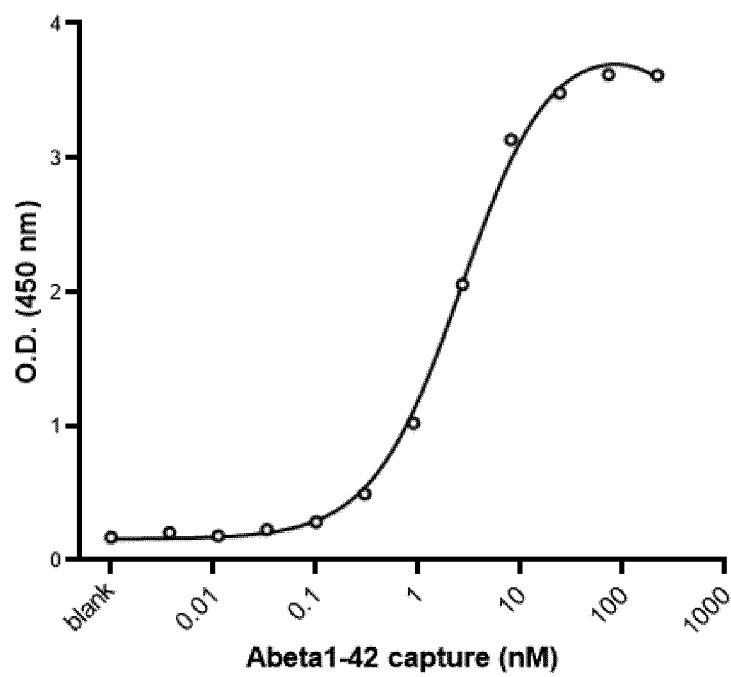
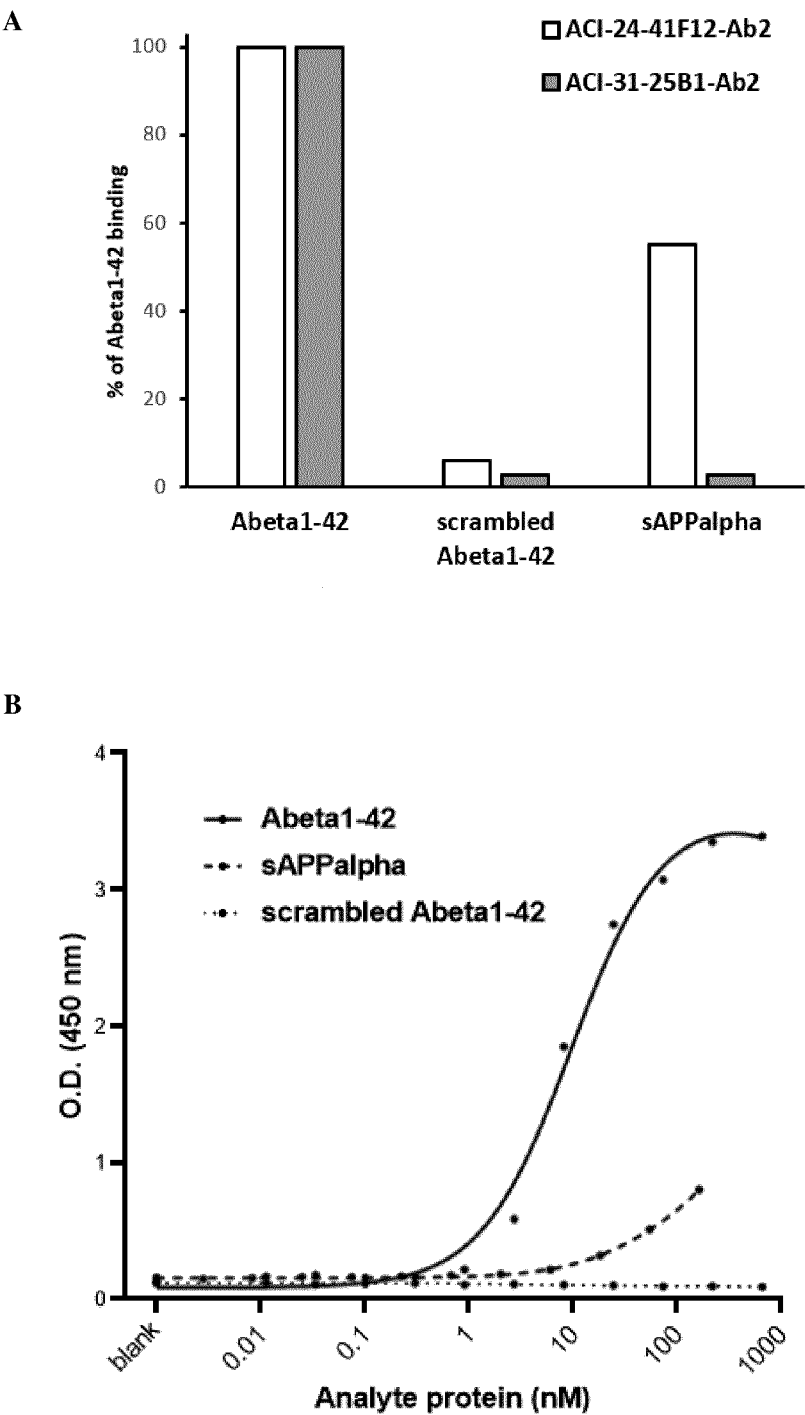


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          50          55          60
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65          70          75          80
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Ser His Val Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
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Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser
          165         170         175
Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu
          180         185         190
Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser
          195         200         205
Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys
          210         215
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<210> 26

<400> 26

000

<210> 27

<211> 458

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-31-25B1-Ab2 (murine IgG2b with a lambda LC) HC

<400> 27

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Glu Val Gln Leu Val Glu Ser Gly Gly Asp Leu Val Lys Pro Gly Gly
1          5          10          15
Ser Leu Lys Leu Ser Cys Ala Ala Ser Arg Phe Thr Phe Ser Thr Tyr
          20          25          30
Gly Met Ser Trp Val Arg Gln Thr Pro Asp Lys Arg Leu Glu Trp Val
          35          40          45
Ala Thr Ile Ser Ser Gly Arg Ser Tyr Thr Tyr Tyr Ala Asp Ser Val
          50          55          60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65          70          75          80
Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys
          85          90          95
Ala Arg Asn Ser Asn Asn Gln Arg Asp Tyr Tyr Ala Met Asp Tyr Trp
          100         105         110
Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Lys Thr Thr Pro Pro
          115         120         125
Ser Val Tyr Pro Leu Ala Pro Gly Cys Gly Asp Thr Thr Gly Ser Ser
          130         135         140
```

Val	Thr	Leu	Gly	Cys	Leu	Val	Lys	Gly	Tyr	Phe	Pro	Glu	Ser	Val	Thr	
145					150					155						160
Val	Thr	Trp	Asn	Ser	Gly	Ser	Leu	Ser	Ser	Ser	Val	His	Thr	Phe	Pro	
				165					170							175
Ala	Leu	Leu	Gln	Ser	Gly	Leu	Tyr	Thr	Met	Ser	Ser	Ser	Val	Thr	Val	
			180					185								190
Pro	Ser	Ser	Thr	Trp	Pro	Ser	Gln	Thr	Val	Thr	Cys	Ser	Val	Ala	His	
		195					200					205				
Pro	Ala	Ser	Ser	Thr	Thr	Val	Asp	Lys	Lys	Leu	Glu	Pro	Ser	Gly	Pro	
	210					215					220					
Ile	Ser	Thr	Ile	Asn	Pro	Cys	Pro	Pro	Cys	Lys	Glu	Cys	His	Lys	Cys	
225				230						235						240
Pro	Ala	Pro	Asn	Leu	Glu	Gly	Gly	Pro	Ser	Val	Phe	Ile	Phe	Pro	Pro	
			245						250							255
Asn	Ile	Lys	Asp	Val	Leu	Met	Ile	Ser	Leu	Thr	Pro	Lys	Val	Thr	Cys	
		260						265								270
Val	Val	Val	Asp	Val	Ser	Glu	Asp	Pro	Asp	Val	Gln	Ile	Ser	Trp		
		275					280					285				
Phe	Val	Asn	Asn	Val	Glu	Val	His	Thr	Ala	Gln	Thr	Gln	Thr	His	Arg	
	290					295					300					
Glu	Asp	Tyr	Asn	Ser	Thr	Ile	Arg	Val	Val	Ser	Thr	Leu	Pro	Ile	Gln	
305					310					315						320
His	Gln	Asp	Trp	Met	Ser	Gly	Lys	Glu	Phe	Lys	Cys	Lys	Val	Asn	Asn	
			325						330							335
Lys	Asp	Leu	Pro	Ser	Pro	Ile	Glu	Arg	Thr	Ile	Ser	Lys	Ile	Lys	Gly	
		340						345					350			
Leu	Val	Arg	Ala	Pro	Gln	Val	Tyr	Ile	Leu	Pro	Pro	Pro	Ala	Glu	Gln	
		355					360					365				
Leu	Ser	Arg	Lys	Asp	Val	Ser	Leu	Thr	Cys	Leu	Val	Val	Gly	Phe	Asn	
	370					375					380					
Pro	Gly	Asp	Ile	Ser	Val	Glu	Trp	Thr	Ser	Asn	Gly	His	Thr	Glu	Glu	
385					390					395						400
Asn	Tyr	Lys	Asp	Thr	Ala	Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Tyr	Phe	
			405						410							415
Ile	Tyr	Ser	Lys	Leu	Asn	Met	Lys	Thr	Ser	Lys	Trp	Glu	Lys	Thr	Asp	
		420						425					430			
Ser	Phe	Ser	Cys	Asn	Val	Arg	His	Glu	Gly	Leu	Lys	Asn	Tyr	Tyr	Leu	
		435					440					445				
Lys	Lys	Thr	Ile	Ser	Arg	Ser	Pro	Gly	Lys							
	450					455										

<210> 28
 <211> 221
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ACI-31-25B1-Ab2 (murine IgG2b with a lambda LC) LC

<400> 28																
Gln	Leu	Val	Leu	Thr	Gln	Ser	Ser	Ser	Ala	Ser	Phe	Ser	Leu	Gly	Ala	
1				5					10					15		
Ser	Ala	Lys	Leu	Thr	Cys	Thr	Leu	Ser	Ser	Gln	His	Ile	Thr	Tyr	Thr	
		20						25					30			
Ile	Glu	Trp	Tyr	Gln	Gln	Gln	Pro	Leu	Lys	Pro	Pro	Lys	Tyr	Val	Met	
		35					40					45				
Val	Leu	Glu	Lys	Asp	Gly	Ser	His	Ser	Thr	Gly	Asp	Gly	Ile	Pro	Asp	
	50					55				60						
Arg	Phe	Ser	Gly	Ser	Ser	Ser	Gly	Ala	Asp	Arg	Tyr	Leu	Ser	Ile	Ser	
65					70				75						80	
Asn	Ile	Gln	Pro	Glu	Asp	Glu	Ala	Val	Tyr	Ile	Cys	Gly	Val	Gly	Asp	
			85					90						95		
Ala	Ile	Lys	Glu	Gln	Phe	Val	Tyr	Val	Phe	Gly	Gly	Gly	Thr	Lys	Val	
		100						105					110			
Thr	Val	Leu	Gly	Gln	Pro	Lys	Ser	Ser	Pro	Ser	Val	Thr	Leu	Phe	Pro	
		115					120					125				
Pro	Ser	Ser	Glu	Glu	Leu	Glu	Thr	Asn	Lys	Ala	Thr	Leu	Val	Cys	Thr	
	130					135					140					

Ile	Thr	Asp	Phe	Tyr	Pro	Gly	Val	Val	Thr	Val	Asp	Trp	Lys	Val	Asp
145					150					155					160
Gly	Thr	Pro	Val	Thr	Gln	Gly	Met	Glu	Thr	Thr	Gln	Pro	Ser	Lys	Gln
			165						170					175	
Ser	Asn	Asn	Lys	Tyr	Met	Ala	Ser	Ser	Tyr	Leu	Thr	Leu	Thr	Ala	Arg
			180					185					190		
Ala	Trp	Glu	Arg	His	Ser	Ser	Tyr	Ser	Cys	Gln	Val	Thr	His	Glu	Gly
		195					200					205			
His	Thr	Val	Glu	Lys	Ser	Leu	Ser	Arg	Ala	Asp	Cys	Ser			
	210					215					220				

<210> 29
 <211> 14
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> Binding epitope

<400> 29
 Glu Asp Val Gly Ser Asn Lys Gly Ala Ile Ile Gly Leu Met
 1 5 10

<210> 30
 <211> 122
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ACI-31-25B1-Ab2 HCVR

<400> 30
 Glu Val Gln Leu Val Glu Ser Gly Gly Asp Leu Val Lys Pro Gly Gly
 1 5 10 15
 Ser Leu Lys Leu Ser Cys Ala Ala Ser Arg Phe Thr Phe Ser Thr Tyr
 20 25 30
 Gly Met Ser Trp Val Arg Gln Thr Pro Asp Lys Arg Leu Glu Trp Val
 35 40 45
 Ala Thr Ile Ser Ser Gly Arg Ser Tyr Thr Tyr Tyr Ala Asp Ser Val
 50 55 60
 Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
 65 70 75 80
 Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys
 85 90 95
 Ala Arg Asn Ser Asn Asn Gln Arg Asp Tyr Tyr Ala Met Asp Tyr Trp
 100 105 110
 Gly Gln Gly Thr Ser Val Thr Val Ser Ser
 115 120

<210> 31
 <211> 5
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ACI-31-25B1-Ab2 VH-CDR1

<400> 31
 Thr Tyr Gly Met Ser
 1 5

<210> 32
 <211> 17
 <212> PRT
 <213> Artificial Sequence

<220>

<223> ACI-31-25B1-Ab2 VH-CDR2

<400> 32

Thr Ile Ser Ser Gly Arg Ser Tyr Thr Tyr Tyr Ala Asp Ser Val Lys
1 5 10 15
Gly

<210> 33

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-31-25B1-Ab2 VH-CDR3

<400> 33

Asn Ser Asn Asn Gln Arg Asp Tyr Tyr Ala Met Asp Tyr
1 5 10

<210> 34

<211> 115

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-31-25B1-Ab2 LCVR

<400> 34

Gln Leu Val Leu Thr Gln Ser Ser Ser Ala Ser Phe Ser Leu Gly Ala
1 5 10 15
Ser Ala Lys Leu Thr Cys Thr Leu Ser Ser Gln His Ile Thr Tyr Thr
20 25 30
Ile Glu Trp Tyr Gln Gln Gln Pro Leu Lys Pro Pro Lys Tyr Val Met
35 40 45
Val Leu Glu Lys Asp Gly Ser His Ser Thr Gly Asp Gly Ile Pro Asp
50 55 60
Arg Phe Ser Gly Ser Ser Ser Gly Ala Asp Arg Tyr Leu Ser Ile Ser
65 70 75 80
Asn Ile Gln Pro Glu Asp Glu Ala Val Tyr Ile Cys Gly Val Gly Asp
85 90 95
Ala Ile Lys Glu Gln Phe Val Tyr Val Phe Gly Gly Gly Thr Lys Val
100 105 110
Thr Val Leu
115

<210> 35

<211> 12

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-31-25B1-Ab2 VL-CDR1

<400> 35

Thr Leu Ser Ser Gln His Ile Thr Tyr Thr Ile Glu
1 5 10

<210> 36

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-31-25B1-Ab2 VL-CDR2

<400> 36

Gly Ser His Ser Thr Gly Asp

1 5

<210> 37

<211> 13

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-31-25B1-Ab2 VL-CDR3

<400> 37

Gly Val Gly Asp Ala Ile Lys Glu Gln Phe Val Tyr Val

1 5 10

<210> 38

<211> 452

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-31-25B1-Ab2 (murine IgG2a with a lambda LC) HC

<400> 38

Glu Val Gln Leu Val Glu Ser Gly Gly Asp Leu Val Lys Pro Gly Gly

1 5 10 15

Ser Leu Lys Leu Ser Cys Ala Ala Ser Arg Phe Thr Phe Ser Thr Tyr

20 25 30

Gly Met Ser Trp Val Arg Gln Thr Pro Asp Lys Arg Leu Glu Trp Val

35 40 45

Ala Thr Ile Ser Ser Gly Arg Ser Tyr Thr Tyr Tyr Ala Asp Ser Val

50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr

65 70 75 80

Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys

85 90 95

Ala Arg Asn Ser Asn Asn Gln Arg Asp Tyr Tyr Ala Met Asp Tyr Trp

100 105 110

Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Lys Thr Thr Ala Pro

115 120 125

Ser Val Tyr Pro Leu Ala Pro Val Cys Gly Asp Thr Thr Gly Ser Ser

130 135 140

Val Thr Leu Gly Cys Leu Val Lys Gly Tyr Phe Pro Glu Pro Val Thr

145 150 155 160

Leu Thr Trp Asn Ser Gly Ser Leu Ser Ser Gly Val His Thr Phe Pro

165 170 175

Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr Val

180 185 190

Thr Ser Ser Thr Trp Pro Ser Gln Ser Ile Thr Cys Asn Val Ala His

195 200 205

Pro Ala Ser Ser Thr Lys Val Asp Lys Lys Ile Glu Pro Arg Gly Pro

210 215 220

Thr Ile Lys Pro Cys Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu Leu

225 230 235 240

Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu

245 250 255

Met Ile Ser Leu Ser Pro Ile Val Thr Cys Val Val Val Asp Val Ser

260 265 270

Glu Asp Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu

275 280 285

Val His Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser Thr

290 295 300

Leu Arg Val Val Ser Ala Leu Pro Ile Gln His Gln Asp Trp Met Ser

305					310					315				320
Gly	Lys	Glu	Phe	Lys	Cys	Lys	Val	Asn	Asn	Lys	Asp	Leu	Pro	Ala
				325					330				335	
Ile	Glu	Arg	Thr	Ile	Ser	Lys	Pro	Lys	Gly	Ser	Val	Arg	Ala	Pro
			340					345					350	
Val	Tyr	Val	Leu	Pro	Pro	Pro	Glu	Glu	Glu	Met	Thr	Lys	Lys	Gln
		355					360					365		
Thr	Leu	Thr	Cys	Met	Val	Thr	Asp	Phe	Met	Pro	Glu	Asp	Ile	Tyr
	370					375					380			
Glu	Trp	Thr	Asn	Asn	Gly	Lys	Thr	Glu	Leu	Asn	Tyr	Lys	Asn	Thr
385					390					395				400
Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Tyr	Phe	Met	Tyr	Ser	Lys	Leu
			405						410					415
Val	Glu	Lys	Lys	Asn	Trp	Val	Glu	Arg	Asn	Ser	Tyr	Ser	Cys	Ser
		420						425					430	
Val	His	Glu	Gly	Leu	His	Asn	His	His	Thr	Thr	Lys	Ser	Phe	Ser
	435					440						445		
Thr	Pro	Gly	Lys											
	450													

<210> 39
 <211> 221
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ACI-31-25B1-Ab2 (murine IgG2a with a lambda LC) LC

<400> 39														
Gln	Leu	Val	Leu	Thr	Gln	Ser	Ser	Ser	Ala	Ser	Phe	Ser	Leu	Gly
1			5					10					15	
Ser	Ala	Lys	Leu	Thr	Cys	Thr	Leu	Ser	Ser	Gln	His	Ile	Thr	Tyr
		20					25					30		
Ile	Glu	Trp	Tyr	Gln	Gln	Gln	Pro	Leu	Lys	Pro	Pro	Lys	Tyr	Val
	35					40					45			
Val	Leu	Glu	Lys	Asp	Gly	Ser	His	Ser	Thr	Gly	Asp	Gly	Ile	Pro
50					55					60				
Arg	Phe	Ser	Gly	Ser	Ser	Ser	Gly	Ala	Asp	Arg	Tyr	Leu	Ser	Ile
65				70					75				80	
Asn	Ile	Gln	Pro	Glu	Asp	Glu	Ala	Val	Tyr	Ile	Cys	Gly	Val	Gly
		85					90						95	
Ala	Ile	Lys	Glu	Gln	Phe	Val	Tyr	Val	Phe	Gly	Gly	Gly	Thr	Lys
	100						105						110	
Thr	Val	Leu	Gly	Gln	Pro	Lys	Ser	Ser	Pro	Ser	Val	Thr	Leu	Phe
	115					120					125			
Pro	Ser	Ser	Glu	Glu	Leu	Glu	Thr	Asn	Lys	Ala	Thr	Leu	Val	Cys
	130				135					140				
Ile	Thr	Asp	Phe	Tyr	Pro	Gly	Val	Val	Thr	Val	Asp	Trp	Lys	Val
145				150				155						160
Gly	Thr	Pro	Val	Thr	Gln	Gly	Met	Glu	Thr	Thr	Gln	Pro	Ser	Lys
			165					170					175	
Ser	Asn	Asn	Lys	Tyr	Met	Ala	Ser	Ser	Tyr	Leu	Thr	Leu	Thr	Ala
	180						185					190		
Ala	Trp	Glu	Arg	His	Ser	Ser	Tyr	Ser	Cys	Gln	Val	Thr	His	Glu
	195					200					205			
His	Thr	Val	Glu	Lys	Ser	Leu	Ser	Arg	Ala	Asp	Cys	Ser		
	210					215					220			

<210> 40
 <211> 117
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ACI-31-30C11-Ab1 HCVR

<400> 40

Gln	Val	Gln	Leu	Gln	Gln	Ser	Gly	Pro	Glu	Leu	Val	Lys	Pro	Gly	Ala	
1				5					10					15		
Ser	Val	Lys	Ile	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Ala	Phe	Ser	Ser	Ser	
			20					25					30			
Trp	Leu	Asn	Trp	Val	Lys	Gln	Arg	Pro	Gly	Glu	Gly	Leu	Glu	Trp	Ile	
		35					40					45				
Gly	Arg	Ile	Tyr	Pro	Gly	Asp	Gly	Asp	Ile	Asn	Tyr	Asn	Gly	Lys	Phe	
	50					55				60						
Lys	Gly	Lys	Ala	Thr	Leu	Thr	Ala	Asp	Lys	Ser	Ser	Ser	Thr	Ala	Tyr	
65					70					75					80	
Met	Gln	Leu	Ser	Ser	Leu	Thr	Ser	Asp	Asp	Ser	Ala	Val	Tyr	Phe	Cys	
			85					90					95			
Thr	Lys	Arg	Gly	Arg	Tyr	Ala	Leu	Asp	Tyr	Trp	Gly	Gln	Gly	Thr	Ser	
			100					105					110			
Val	Thr	Val	Ser	Ser												
			115													

<210> 41
 <211> 5
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ACI-31-30C11-Ab1 VH-CDR1

<400> 41
 Ser Ser Trp Leu Asn
 1 5

<210> 42
 <211> 17
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ACI-31-30C11-Ab1 VH-CDR2

<400> 42
 Arg Ile Tyr Pro Gly Asp Gly Asp Ile Asn Tyr Asn Gly Lys Phe Lys
 1 5 10 15
 Gly

<210> 43
 <211> 8
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ACI-31-30C11-Ab1 VH-CDR3

<400> 43
 Arg Gly Arg Tyr Ala Leu Asp Tyr
 1 5

<210> 44
 <211> 111
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ACI-31-30C11-Ab1 LCVR

<400> 44
 Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly

1				5					10					15					
Gln	Arg	Ala	Thr	Ile	Ser	Cys	Arg	Ala	Ser	Lys	Ser	Val	Asp	Asn	Tyr				
			20					25					30						
Gly	Lys	Ser	Phe	Met	His	Trp	Phe	Gln	Gln	Lys	Pro	Gly	Gln	Pro	Pro				
		35					40					45							
Lys	Leu	Leu	Ile	Tyr	Arg	Ala	Ser	Asn	Leu	Glu	Ser	Gly	Ile	Pro	Ala				
	50					55					60								
Arg	Phe	Ser	Gly	Ser	Gly	Ser	Arg	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Asn				
65					70					75					80				
Pro	Val	Glu	Ala	Asp	Asp	Val	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Ser	Asn				
				85				90						95					
Glu	Asp	Pro	Tyr	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Met	Lys					
			100					105						110					

<210> 45
 <211> 15
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ACI-31-30C11-Ab1 VL-CDR1

<400> 45																			
Arg	Ala	Ser	Lys	Ser	Val	Asp	Asn	Tyr	Gly	Lys	Ser	Phe	Met	His					
1				5					10					15					

<210> 46
 <211> 7
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ACI-31-30C11-Ab1 VL-CDR2

<400> 46																			
Arg	Ala	Ser	Asn	Leu	Glu	Ser													
1				5															

<210> 47
 <211> 9
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ACI-31-30C11-Ab1 VL-CDR3

<400> 47																			
Gln	Gln	Ser	Asn	Glu	Asp	Pro	Tyr	Thr											
1				5															

<210> 48
 <211> 453
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ACI-31-30C11-Ab1 (murine IgG2b with a kappa LC) HC

<400> 48																			
Gln	Val	Gln	Leu	Gln	Gln	Ser	Gly	Pro	Glu	Leu	Val	Lys	Pro	Gly	Ala				
1				5				10					15						
Ser	Val	Lys	Ile	Ser	Cys	Lys	Ala	Ser	Gly	Tyr	Ala	Phe	Ser	Ser	Ser				
		20					25					30							
Trp	Leu	Asn	Trp	Val	Lys	Gln	Arg	Pro	Gly	Glu	Gly	Leu	Glu	Trp	Ile				
		35				40						45							

Gly Arg Ile Tyr Pro Gly Asp Gly Asp Ile Asn Tyr Asn Gly Lys Phe
 50 55 60
 Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
 65 70 75 80
 Met Gln Leu Ser Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys
 85 90 95
 Thr Lys Arg Gly Arg Tyr Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser
 100 105 110
 Val Thr Val Ser Ser Ala Lys Thr Thr Pro Pro Ser Val Tyr Pro Leu
 115 120 125
 Ala Pro Gly Cys Gly Asp Thr Thr Gly Ser Ser Val Thr Leu Gly Cys
 130 135 140
 Leu Val Lys Gly Tyr Phe Pro Glu Ser Val Thr Val Thr Trp Asn Ser
 145 150 155 160
 Gly Ser Leu Ser Ser Val His Thr Phe Pro Ala Leu Leu Gln Ser
 165 170 175
 Gly Leu Tyr Thr Met Ser Ser Ser Val Thr Val Pro Ser Ser Thr Trp
 180 185 190
 Pro Ser Gln Thr Val Thr Cys Ser Val Ala His Pro Ala Ser Ser Thr
 195 200 205
 Thr Val Asp Lys Lys Leu Glu Pro Ser Gly Pro Ile Ser Thr Ile Asn
 210 215 220
 Pro Cys Pro Pro Cys Lys Glu Cys His Lys Cys Pro Ala Pro Asn Leu
 225 230 235 240
 Glu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro Asn Ile Lys Asp Val
 245 250 255
 Leu Met Ile Ser Leu Thr Pro Lys Val Thr Cys Val Val Val Asp Val
 260 265 270
 Ser Glu Asp Asp Pro Asp Val Gln Ile Ser Trp Phe Val Asn Asn Val
 275 280 285
 Glu Val His Thr Ala Gln Thr Gln Thr His Arg Glu Asp Tyr Asn Ser
 290 295 300
 Thr Ile Arg Val Val Ser Thr Leu Pro Ile Gln His Gln Asp Trp Met
 305 310 315 320
 Ser Gly Lys Glu Phe Lys Cys Lys Val Asn Asn Lys Asp Leu Pro Ser
 325 330 335
 Pro Ile Glu Arg Thr Ile Ser Lys Ile Lys Gly Leu Val Arg Ala Pro
 340 345 350
 Gln Val Tyr Ile Leu Pro Pro Pro Ala Glu Gln Leu Ser Arg Lys Asp
 355 360 365
 Val Ser Leu Thr Cys Leu Val Val Gly Phe Asn Pro Gly Asp Ile Ser
 370 375 380
 Val Glu Trp Thr Ser Asn Gly His Thr Glu Glu Asn Tyr Lys Asp Thr
 385 390 395 400
 Ala Pro Val Leu Asp Ser Asp Gly Ser Tyr Phe Ile Tyr Ser Lys Leu
 405 410 415
 Asn Met Lys Thr Ser Lys Trp Glu Lys Thr Asp Ser Phe Ser Cys Asn
 420 425 430
 Val Arg His Glu Gly Leu Lys Asn Tyr Tyr Leu Lys Lys Thr Ile Ser
 435 440 445
 Arg Ser Pro Gly Lys
 450

<210> 49

<211> 218

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-31-30C11-Ab1 (murine IgG2b with a kappa LC) LC

<400> 49

Asp Ile Val Leu Thr Gln Ser Pro Ala Ser Leu Ala Val Ser Leu Gly
 1 5 10 15
 Gln Arg Ala Thr Ile Ser Cys Arg Ala Ser Lys Ser Val Asp Asn Tyr
 20 25 30
 Gly Lys Ser Phe Met His Trp Phe Gln Gln Lys Pro Gly Gln Pro Pro
 35 40 45

Lys Leu Leu Ile Tyr Arg Ala Ser Asn Leu Glu Ser Gly Ile Pro Ala
 50 55 60
 Arg Phe Ser Gly Ser Gly Ser Arg Thr Asp Phe Thr Leu Thr Ile Asn
 65 70 75 80
 Pro Val Glu Ala Asp Asp Val Ala Thr Tyr Tyr Cys Gln Gln Ser Asn
 85 90 95
 Glu Asp Pro Tyr Thr Phe Gly Gly Gly Thr Lys Leu Glu Met Lys Arg
 100 105 110
 Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu Gln
 115 120 125
 Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe Tyr
 130 135 140
 Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg Gln
 145 150 155 160
 Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser Thr
 165 170 175
 Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu Arg
 180 185 190
 His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser Pro
 195 200 205
 Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
 210 215

<210> 50

<211> 447

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-31-30C11-Ab1 (murine IgG2a with a kappa LC) HC

<400> 50

Gln Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
 1 5 10 15
 Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Tyr Ala Phe Ser Ser Ser
 20 25 30
 Trp Leu Asn Trp Val Lys Gln Arg Pro Gly Glu Gly Leu Glu Trp Ile
 35 40 45
 Gly Arg Ile Tyr Pro Gly Asp Gly Asp Ile Asn Tyr Asn Gly Lys Phe
 50 55 60
 Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
 65 70 75 80
 Met Gln Leu Ser Ser Leu Thr Ser Asp Asp Ser Ala Val Tyr Phe Cys
 85 90 95
 Thr Lys Arg Gly Arg Tyr Ala Leu Asp Tyr Trp Gly Gln Gly Thr Ser
 100 105 110
 Val Thr Val Ser Ser Ala Lys Thr Thr Ala Pro Ser Val Tyr Pro Leu
 115 120 125
 Ala Pro Val Cys Gly Asp Thr Thr Gly Ser Ser Val Thr Leu Gly Cys
 130 135 140
 Leu Val Lys Gly Tyr Phe Pro Glu Pro Val Thr Leu Thr Trp Asn Ser
 145 150 155 160
 Gly Ser Leu Ser Ser Gly Val His Thr Phe Pro Ala Val Leu Gln Ser
 165 170 175
 Asp Leu Tyr Thr Leu Ser Ser Ser Val Thr Val Thr Ser Ser Thr Trp
 180 185 190
 Pro Ser Gln Ser Ile Thr Cys Asn Val Ala His Pro Ala Ser Ser Thr
 195 200 205
 Lys Val Asp Lys Lys Ile Glu Pro Arg Gly Pro Thr Ile Lys Pro Cys
 210 215 220
 Pro Pro Cys Lys Cys Pro Ala Pro Asn Leu Leu Gly Gly Pro Ser Val
 225 230 235 240
 Phe Ile Phe Pro Pro Lys Ile Lys Asp Val Leu Met Ile Ser Leu Ser
 245 250 255
 Pro Ile Val Thr Cys Val Val Val Asp Val Ser Glu Asp Asp Pro Asp
 260 265 270
 Val Gln Ile Ser Trp Phe Val Asn Asn Val Glu Val His Thr Ala Gln
 275 280 285

Thr	Gln	Thr	His	Arg	Glu	Asp	Tyr	Asn	Ser	Thr	Leu	Arg	Val	Val	Ser
290						295					300				
Ala	Leu	Pro	Ile	Gln	His	Gln	Asp	Trp	Met	Ser	Gly	Lys	Glu	Phe	Lys
305				310						315					320
Cys	Lys	Val	Asn	Asn	Lys	Asp	Leu	Pro	Ala	Pro	Ile	Glu	Arg	Thr	Ile
			325						330					335	
Ser	Lys	Pro	Lys	Gly	Ser	Val	Arg	Ala	Pro	Gln	Val	Tyr	Val	Leu	Pro
			340					345					350		
Pro	Pro	Glu	Glu	Glu	Met	Thr	Lys	Lys	Gln	Val	Thr	Leu	Thr	Cys	Met
		355				360						365			
Val	Thr	Asp	Phe	Met	Pro	Glu	Asp	Ile	Tyr	Val	Glu	Trp	Thr	Asn	Asn
370						375					380				
Gly	Lys	Thr	Glu	Leu	Asn	Tyr	Lys	Asn	Thr	Glu	Pro	Val	Leu	Asp	Ser
385					390					395					400
Asp	Gly	Ser	Tyr	Phe	Met	Tyr	Ser	Lys	Leu	Arg	Val	Glu	Lys	Lys	Asn
				405					410					415	
Trp	Val	Glu	Arg	Asn	Ser	Tyr	Ser	Cys	Ser	Val	Val	His	Glu	Gly	Leu
			420					425					430		
His	Asn	His	His	Thr	Thr	Lys	Ser	Phe	Ser	Arg	Thr	Pro	Gly	Lys	
	435						440					445			

<210> 51
 <211> 218
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ACI-31-30C11-Ab1 (murine IgG2a with a kappa LC) LC

Asp	Ile	Val	Leu	Thr	Gln	Ser	Pro	Ala	Ser	Leu	Ala	Val	Ser	Leu	Gly
1				5					10					15	
Gln	Arg	Ala	Thr	Ile	Ser	Cys	Arg	Ala	Ser	Lys	Ser	Val	Asp	Asn	Tyr
			20					25					30		
Gly	Lys	Ser	Phe	Met	His	Trp	Phe	Gln	Gln	Lys	Pro	Gly	Gln	Pro	Pro
		35				40					45				
Lys	Leu	Leu	Ile	Tyr	Arg	Ala	Ser	Asn	Leu	Glu	Ser	Gly	Ile	Pro	Ala
	50					55				60					
Arg	Phe	Ser	Gly	Ser	Gly	Ser	Arg	Thr	Asp	Phe	Thr	Leu	Thr	Ile	Asn
65					70				75					80	
Pro	Val	Glu	Ala	Asp	Asp	Val	Ala	Thr	Tyr	Tyr	Cys	Gln	Gln	Ser	Asn
			85					90					95		
Glu	Asp	Pro	Tyr	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Met	Lys	Arg
		100					105						110		
Ala	Asp	Ala	Ala	Pro	Thr	Val	Ser	Ile	Phe	Pro	Pro	Ser	Ser	Glu	Gln
		115					120					125			
Leu	Thr	Ser	Gly	Gly	Ala	Ser	Val	Val	Cys	Phe	Leu	Asn	Asn	Phe	Tyr
	130					135				140					
Pro	Lys	Asp	Ile	Asn	Val	Lys	Trp	Lys	Ile	Asp	Gly	Ser	Glu	Arg	Gln
145				150					155						160
Asn	Gly	Val	Leu	Asn	Ser	Trp	Thr	Asp	Gln	Asp	Ser	Lys	Asp	Ser	Thr
				165				170					175		
Tyr	Ser	Met	Ser	Ser	Thr	Leu	Thr	Leu	Thr	Lys	Asp	Glu	Tyr	Glu	Arg
		180					185					190			
His	Asn	Ser	Tyr	Thr	Cys	Glu	Ala	Thr	His	Lys	Thr	Ser	Thr	Ser	Pro
		195					200					205			
Ile	Val	Lys	Ser	Phe	Asn	Arg	Asn	Glu	Cys						
	210					215									

<210> 52
 <211> 366
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> ACI-31-25B1-Ab2 (IgG2b and IgG2a) HCVR

<400> 52
gaggtgcagc tgggtggagtc tgggggagac ttagtgaagc ctggagggtc cctgaaactc 60
tcctgtgcag cctctagatt cactttcagt acctatggca tgtcttgggt tcgccagact 120
ccagacaaga ggctggaatg ggtcgcaacc attagtagtg gtagaagtta cacctactat 180
gcagacagtg tgaaggggcg attcaccatc tccagagaca atgccaagaa caccctgtac 240
ctgcaaatga gcagtctgaa gtctgaggac acagccatgt attactgtgc aagaaatagt 300
aacaaccaga gggattacta tgctatggac tactggggtc aaggaacctc agtcaccgtc 360
tcctca 366

<210> 53
<211> 345
<212> DNA
<213> Artificial Sequence

<220>
<223> ACI-31-25B1-Ab2 (IgG2b and IgG2a) LCVR

<400> 53
caacttgtgc tcactcagtc atcttcagcc tctttctccc tgggagcctc agcaaaactc 60
acgtgcacct tgagtagtca gcacattacg tacaccattg agtggtatca gcaacagcca 120
ctcaagcctc ctaagtatgt gatggtactt gagaaagatg gaagccacag cacaggtgat 180
gggattcctg atcgcttctc tggatccagc tctggtgctg atcgttacct tagcatttcc 240
aacatccagc ctgaagatga agcagtatac atctgtggtg tgggtgatgc aattaaggaa 300
caatttgtgt atgttttcgg cggtggaacc aaggctactg tccta 345

<210> 54
<211> 351
<212> DNA
<213> Artificial Sequence

<220>
<223> ACI-31-30C11-Ab1 (IgG2b and IgG2a) HCVR

<400> 54
caggttcagc tgcagcagtc tggacctgag ctggtgaagc ctggggcctc agtgaagatt 60
tcctgcaagg cttctggcta cgcattcagt agctcctggc tgaactgggt gaagcagagg 120
cctggagagg gtcttgagtg gattggacgg atttatcctg gagatggaga tattaactac 180
aatgggaagt tcaagggcaa ggccacactg actgcagaca aatcctccag cacagcctac 240
atgcaactca gcagcctgac atctgacgac tctgcggtct acttctgtac aaagcgggga 300
cgctatgctt tggactactg gggtaagga acctcagtca cctctcctc a 351

<210> 55
<211> 333
<212> DNA
<213> Artificial Sequence

<220>

<223> ACI-31-30C11-Ab1 (IgG2b and IgG2a) LCVR

<400> 55

```
gacattgtgc tgaccaatc tccagcttct ttggctgtgt ctctagggca gagggccacc      60
atatcctgca gagccagtaa aagtgttgat aattatggca aaagttttat gcactggttc      120
cagcagaaac caggacagcc acccaaactc ctcatctatc gtgcatccaa cctagaatct      180
gggatccctg ccaggttcag tggcagtggg tctaggacag acttcaccct caccattaat      240
cctgtggagg ctgatgatgt tgcaacctat tactgtcagc aaagtaatga ggatccgtac      300
acgttcggag gggggaccaa gctggaaatg aaa                                  333
```

<210> 56

<211> 330

<212> PRT

<213> Artificial Sequence

<220>

<223> Murine IgG2a HC constant domain

<400> 56

```
Ala Lys Thr Thr Ala Pro Ser Val Tyr Pro Leu Ala Pro Val Cys Gly
1      5      10      15
Asp Thr Thr Gly Ser Ser Val Thr Leu Gly Cys Leu Val Lys Gly Tyr
      20      25      30
Phe Pro Glu Pro Val Thr Leu Thr Trp Asn Ser Gly Ser Leu Ser Ser
      35      40      45
Gly Val His Thr Phe Pro Ala Val Leu Gln Ser Asp Leu Tyr Thr Leu
      50      55      60
Ser Ser Ser Val Thr Val Thr Ser Ser Thr Trp Pro Ser Gln Ser Ile
      65      70      75      80
Thr Cys Asn Val Ala His Pro Ala Ser Ser Thr Lys Val Asp Lys Lys
      85      90      95
Ile Glu Pro Arg Gly Pro Thr Ile Lys Pro Cys Pro Pro Cys Lys Cys
      100      105      110
Pro Ala Pro Asn Leu Leu Gly Gly Pro Ser Val Phe Ile Phe Pro Pro
      115      120      125
Lys Ile Lys Asp Val Leu Met Ile Ser Leu Ser Pro Ile Val Thr Cys
      130      135      140
Val Val Val Asp Val Ser Glu Asp Asp Pro Asp Val Gln Ile Ser Trp
      145      150      155      160
Phe Val Asn Asn Val Glu Val His Thr Ala Gln Thr Gln Thr His Arg
      165      170      175
Glu Asp Tyr Asn Ser Thr Leu Arg Val Val Ser Ala Leu Pro Ile Gln
      180      185      190
His Gln Asp Trp Met Ser Gly Lys Glu Phe Lys Cys Lys Val Asn Asn
      195      200      205
Lys Asp Leu Pro Ala Pro Ile Glu Arg Thr Ile Ser Lys Pro Lys Gly
      210      215      220
Ser Val Arg Ala Pro Gln Val Tyr Val Leu Pro Pro Pro Glu Glu Glu
      225      230      235      240
Met Thr Lys Lys Gln Val Thr Leu Thr Cys Met Val Thr Asp Phe Met
      245      250      255
Pro Glu Asp Ile Tyr Val Glu Trp Thr Asn Asn Gly Lys Thr Glu Leu
      260      265      270
Asn Tyr Lys Asn Thr Glu Pro Val Leu Asp Ser Asp Gly Ser Tyr Phe
      275      280      285
Met Tyr Ser Lys Leu Arg Val Glu Lys Lys Asn Trp Val Glu Arg Asn
      290      295      300
Ser Tyr Ser Cys Ser Val Val His Glu Gly Leu His Asn His His Thr
      305      310      315      320
Thr Lys Ser Phe Ser Arg Thr Pro Gly Lys
      325      330
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<210> 57
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> Murine LC kappa domain

<400> 57
Arg Ala Asp Ala Ala Pro Thr Val Ser Ile Phe Pro Pro Ser Ser Glu
1 5 10 15
Gln Leu Thr Ser Gly Gly Ala Ser Val Val Cys Phe Leu Asn Asn Phe
20 25 30
Tyr Pro Lys Asp Ile Asn Val Lys Trp Lys Ile Asp Gly Ser Glu Arg
35 40 45
Gln Asn Gly Val Leu Asn Ser Trp Thr Asp Gln Asp Ser Lys Asp Ser
50 55 60
Thr Tyr Ser Met Ser Ser Thr Leu Thr Leu Thr Lys Asp Glu Tyr Glu
65 70 75 80
Arg His Asn Ser Tyr Thr Cys Glu Ala Thr His Lys Thr Ser Thr Ser
85 90 95
Pro Ile Val Lys Ser Phe Asn Arg Asn Glu Cys
100 105

<210> 58
<211> 452
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-31-25B1-Ab2 human IgG1 HC

<400> 58
Glu Val Gln Leu Val Glu Ser Gly Gly Asp Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Lys Leu Ser Cys Ala Ala Ser Arg Phe Thr Phe Ser Thr Tyr
20 25 30
Gly Met Ser Trp Val Arg Gln Thr Pro Asp Lys Arg Leu Glu Trp Val
35 40 45
Ala Thr Ile Ser Ser Gly Arg Ser Tyr Thr Tyr Tyr Ala Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Ser Ser Leu Lys Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Arg Asn Ser Asn Asn Gln Arg Asp Tyr Tyr Ala Met Asp Tyr Trp
100 105 110
Gly Gln Gly Thr Ser Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro
115 120 125
Ser Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr
130 135 140
Ala Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr
145 150 155 160
Val Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro
165 170 175
Ala Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr
180 185 190
Val Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn
195 200 205
His Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser
210 215 220
Cys Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu
225 230 235 240
Gly Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu
245 250 255
Met Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser
260 265 270

His	Glu	Asp	Pro	Glu	Val	Lys	Phe	Asn	Trp	Tyr	Val	Asp	Gly	Val	Glu
	275						280					285			
Val	His	Asn	Ala	Lys	Thr	Lys	Pro	Arg	Glu	Glu	Gln	Tyr	Asn	Ser	Thr
	290						295				300				
Tyr	Arg	Val	Val	Ser	Val	Leu	Thr	Val	Leu	His	Gln	Asp	Trp	Leu	Asn
	305				310					315					320
Gly	Lys	Glu	Tyr	Lys	Cys	Lys	Val	Ser	Asn	Lys	Ala	Leu	Pro	Ala	Pro
				325					330					335	
Ile	Glu	Lys	Thr	Ile	Ser	Lys	Ala	Lys	Gly	Gln	Pro	Arg	Glu	Pro	Gln
			340					345					350		
Val	Tyr	Thr	Leu	Pro	Pro	Ser	Arg	Glu	Glu	Met	Thr	Lys	Asn	Gln	Val
		355					360					365			
Ser	Leu	Thr	Cys	Leu	Val	Lys	Gly	Phe	Tyr	Pro	Ser	Asp	Ile	Ala	Val
	370					375					380				
Glu	Trp	Glu	Ser	Asn	Gly	Gln	Pro	Glu	Asn	Asn	Tyr	Lys	Thr	Thr	Pro
	385				390					395					400
Pro	Val	Leu	Asp	Ser	Asp	Gly	Ser	Phe	Phe	Leu	Tyr	Ser	Lys	Leu	Thr
				405					410					415	
Val	Asp	Lys	Ser	Arg	Trp	Gln	Gln	Gly	Asn	Val	Phe	Ser	Cys	Ser	Val
			420					425					430		
Met	His	Glu	Ala	Leu	His	Asn	His	Tyr	Thr	Gln	Lys	Ser	Leu	Ser	Leu
	435						440					445			
Ser	Pro	Gly	Lys												
	450														

<210> 59

<211> 221

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-31-25B1-Ab2 human IgG1/ Lambda LC

<400> 59

Gln	Leu	Val	Leu	Thr	Gln	Ser	Ser	Ser	Ala	Ser	Phe	Ser	Leu	Gly	Ala
1				5					10					15	
Ser	Ala	Lys	Leu	Thr	Cys	Thr	Leu	Ser	Ser	Gln	His	Ile	Thr	Tyr	Thr
			20					25					30		
Ile	Glu	Trp	Tyr	Gln	Gln	Gln	Pro	Leu	Lys	Pro	Pro	Lys	Tyr	Val	Met
		35					40					45			
Val	Leu	Glu	Lys	Asp	Gly	Ser	His	Ser	Thr	Gly	Asp	Gly	Ile	Pro	Asp
	50					55					60				
Arg	Phe	Ser	Gly	Ser	Ser	Ser	Gly	Ala	Asp	Arg	Tyr	Leu	Ser	Ile	Ser
	65				70				75					80	
Asn	Ile	Gln	Pro	Glu	Asp	Glu	Ala	Val	Tyr	Ile	Cys	Gly	Val	Gly	Asp
			85					90					95		
Ala	Ile	Lys	Glu	Gln	Phe	Val	Tyr	Val	Phe	Gly	Gly	Gly	Thr	Lys	Val
			100					105					110		
Thr	Val	Leu	Gly	Gln	Pro	Lys	Ala	Asn	Pro	Thr	Val	Thr	Leu	Phe	Pro
		115					120					125			
Pro	Ser	Ser	Glu	Glu	Leu	Gln	Ala	Asn	Lys	Ala	Thr	Leu	Val	Cys	Leu
	130					135					140				
Ile	Ser	Asp	Phe	Tyr	Pro	Gly	Ala	Val	Thr	Val	Ala	Trp	Lys	Ala	Asp
	145				150					155					160
Gly	Ser	Pro	Val	Lys	Ala	Gly	Val	Glu	Thr	Thr	Lys	Pro	Ser	Lys	Gln
				165					170					175	
Ser	Asn	Asn	Lys	Tyr	Ala	Ala	Ser	Ser	Tyr	Leu	Ser	Leu	Thr	Pro	Glu
			180					185					190		
Gln	Trp	Lys	Ser	His	Arg	Ser	Tyr	Ser	Cys	Gln	Val	Thr	His	Glu	Gly
	195					200						205			
Ser	Thr	Val	Glu	Lys	Thr	Val	Ala	Pro	Thr	Glu	Cys	Ser			
	210					215						220			

<210> 60

<211> 121

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8037-103H5-Ab2 HCVR

<400> 60

Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Lys Pro Ser Gln
1 5 10 15
Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30
Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu
35 40 45
Trp Leu Ala His Ile Trp Trp Asp Asp Asp Lys Tyr Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Ser Ser Arg Asn Gln Val
65 70 75 80
Phe Leu Lys Ile Thr Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr
85 90 95
Cys Val Arg Arg Gly Thr Arg Leu Glu Asp Tyr Phe Asp Phe Trp Gly
100 105 110
Gln Gly Thr Thr Leu Thr Val Ser Ser
115 120

<210> 61

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8037-103H5-Ab2 HC CDR1

<400> 61

Thr Ser Gly Met Gly Val Gly
1 5

<210> 62

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8037-103H5-Ab2 HC CDR2

<400> 62

His Ile Trp Trp Asp Asp Asp Lys Tyr Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 63

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8037-103H5-Ab2 HC CDR3

<400> 63

Arg Gly Thr Arg Leu Glu Asp Tyr Phe Asp Phe
1 5 10

<210> 64

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8037-103H5-Ab2 LCVR

<400> 64

```
Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1          5          10          15
Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Arg Ser Ile Val His Ser
          20          25          30
Asn Gly Asn Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
          35          40          45
Pro Lys Leu Leu Ile Phe Lys Val Ser Asn Arg Phe Ser Gly Val Pro
          50          55          60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65          70          75          80
Ser Arg Val Glu Ala Glu Asp Gln Gly Val Tyr Tyr Cys Phe Gln Gly
          85          90          95
Ser His Val Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
          100          105          110
```

<210> 65

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8037-103H5-Ab2 LC CDR1

<400> 65

```
Arg Ser Ser Arg Ser Ile Val His Ser Asn Gly Asn Thr Tyr Leu Glu
1          5          10          15
```

<210> 66

<400> 66

000

<210> 67

<400> 67

000

<210> 68

<211> 363

<212> DNA

<213> Artificial Sequence

<220>

<223> ACI-8037-103H5-Ab2 HCVR

<400> 68

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caagttactc taaaagagtc tggccctggg atattgaagc cctcacagac ctcagtcctg      60
acttgttcct tctctggggtt ttcactgagc acttctggta tgggtggttg ctggattcgt      120
cagccttcgc ggaagggtct ggagtggtct gcacacattt ggtgggatga tgataagtac      180
tataacccat ccctgaagag ccggctcaca atctccaagg attcctccag aaaccaggta      240
ttcctcaaga tcaccagtgt ggacactgca gatactgcc a ttactactg tgttcgaagg      300
gggactaggt tagaggacta ctttgacttc tggggccaag gcaccactct cacagtctcc      360
tca                                             363
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<210> 69
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<223> ACI-8037-103H5-Ab2 LCVR

<400> 69
gatgttttga tgacccaaac tccactctcc ctgcctgtca gtcttgggga tcaagcctcc 60
atctcttgca gatctagtcg gagcattgtt catagtaatg gaaacaccta tttagaatgg 120
tacctgcaga aaccaggcca gtctccaaag ctctgatct tcaaagtttc caaccgattt 180
tctgggggtcc cagacagggtt cagtggcagt ggatcaggga cagatttcac actcaagatc 240
agcagagtgg aggctgagga tcaggaggtt tattactgct ttcaagggtc acatgttccg 300
ctcacgttcg gtgctgggac caagctggag ctgaaa 336

<210> 70
<211> 122
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8037-109F4-Ab1 HCVR

<400> 70
Gln Val Thr Leu Lys Glu Ser Gly Pro Gly Ile Leu Gln Pro Ser Gln
1 5 10 15
Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser
20 25 30
Gly Met Gly Val Ser Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu
35 40 45
Trp Leu Ala His Ile Tyr Trp Asp Asp Asp Lys Arg Tyr Asn Pro Ser
50 55 60
Leu Lys Ser Arg Leu Thr Ile Ser Lys Asp Thr Ser Arg Asn Gln Val
65 70 75 80
Phe Leu Lys Ile Thr Ser Val Asp Thr Ala Asp Ala Gly Thr Tyr Tyr
85 90 95
Cys Ala Arg Arg Pro Ile Arg Thr Val Val Asp Ala Met Asp Tyr Trp
100 105 110
Gly Gln Gly Thr Ser Val Thr Val Ser Leu
115 120

<210> 71
<400> 71
000

<210> 72
<400> 72
000

<210> 73
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8037-109F4-Ab1 HC CDR3

<400> 73
Arg Pro Ile Arg Thr Val Val Asp Ala Met Asp Tyr

1 5 10

<210> 74
<211> 112
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8037-109F4-Ab1 LCVR

<400> 74
Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15
Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Thr Ile Val His Ser
20 25 30
Asn Gly Asn Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Asn Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Gly
85 90 95
Ser His Val Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105 110

<210> 75
<211> 16
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8037-109F4-Ab1 VL CDR1

<400> 75
Arg Ser Ser Gln Thr Ile Val His Ser Asn Gly Asn Thr Tyr Leu Glu
1 5 10 15

<210> 76
<400> 76
000

<210> 77
<400> 77
000

<210> 78
<211> 366
<212> DNA
<213> Artificial Sequence

<220>
<223> ACI-8037-109F4-Ab1 HCVR

<400> 78
caggttactc tgaaagagtc tggccctggg atattgcagc cctcccagac cctcagtcgt 60
acttgttctt tctctggggtt ttcactgagc acttctggta tgggtgtgag ctggattcgt 120
cagccttcag gaaaggtct ggagtggtc gcacacattt actgggatga tgacaagcgc 180
tataacccat ccctgaagag cgggtcaca atctccaagg atacctccag aaaccaggtt 240

ttcctcaaga tcaccagtgt ggacactgca gatgctggca catactactg tgctcgaaga	300
cctattagaa cggtagtaga tgctatggac tactgggggtc aaggaacctc agtcaccgtc	360
tcctta	366

<210> 79
 <211> 336
 <212> DNA
 <213> Artificial Sequence

<220>
 <223> ACI-8037-109F4-Ab1 LCVR

<400> 79	
gatgttttga tgacccaaac tccactctcc ctgcctgtca gtcttggaga tcaggcctcc	60
atctcttgca gatctagtca gaccattgta catagtaatg gaaacaccta tttggaatgg	120
tacctgcaga aaccaggcca gtctccaaac ctctgatct acaaagtttc caaccgattt	180
tctgggggtcc cagacagggtt cagtggcagt ggatcaggga cagatttcac actcaagatc	240
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ctcacgttcg gtgctgggac caagctggag ctgaaa	336

<210> 80
 <211> 116
 <212> PRT
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<220>
 <223> ACI-8039-306H5-Ab1 HCVR

<400> 80	
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Thr Leu Ser Leu Thr Cys Ser Phe Ser Gly Phe Ser Leu Ser Thr Ser	
20 25 30	
Gly Met Gly Val Gly Trp Ile Arg Gln Pro Ser Gly Lys Gly Leu Glu	
35 40 45	
Trp Leu Ala His Ile Trp Trp Asp Asp Lys Tyr Tyr Asn Pro Ser	
50 55 60	
Leu Lys Ser Gln Leu Thr Ile Ser Lys Asp Thr Ser Arg Asn Gln Ile	
65 70 75 80	
Phe Leu Lys Ile Thr Ser Val Asp Thr Ala Asp Thr Ala Thr Tyr Tyr	
85 90 95	
Cys Val Arg Ser Leu Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Thr Leu	
100 105 110	
Thr Val Ser Ser	
115	

<210> 81
 <400> 81
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<210> 82
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<210> 83
 <211> 6
 <212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8039-306H5-Ab1 HC CDR3

<400> 83

Ser Leu Tyr Phe Asp Tyr
1 5

<210> 84

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8039-306H5-Ab1 HCVR

<400> 84

Asp Val Val Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly
1 5 10 15
Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Val His Ser
20 25 30
Asn Gly Asn Thr Tyr Leu His Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile
65 70 75 80
Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Phe Cys Ser Gln Ser
85 90 95
Thr His Val Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105 110

<210> 85

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8039-306H5-Ab1 LC CDR1

<400> 85

Arg Ser Ser Gln Ser Leu Val His Ser Asn Gly Asn Thr Tyr Leu His
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<210> 86

<400> 86

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<210> 87

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8039-306H5-Ab1 LC CDR3

<400> 87

Ser Gln Ser Thr His Val Pro Leu Thr
1 5

<210> 88
<211> 348
<212> DNA
<213> Artificial Sequence

<220>
<223> ACI-8039-306H5-Ab1 HCVR

<400> 88
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cagccttcag ggaagggctc ggagtggctg gcacacattt ggtgggatga tgataagtac 180
tataacccat ccctgaagag tcagctcaca atctccaagg atacctccag aaaccagata 240
ttcctcaaga tcaccagtgt ggacactgca gatactgcc a ttactactg tgttcgaagc 300
ctgtactttg actactgggg ccaaggcacc actctcacag tctcctca 348

<210> 89
<211> 336
<212> DNA
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<220>
<223> ACI-8039-306H5-Ab1 LCVR

<400> 89
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tacctgcaga agccaggcca gtctccaaag ctctgatct acaaagtttc caaccgattt 180
tctgggggtcc cagacagggtt cagtggcagt ggatcaggga cagatttcac actcaagatc 240
agcagagtgg aggctgagga tctgggagtt tatttctgct ctcaaagtac acatgttccg 300
ctcacgttcg gtgctgggac caagctggag ctgaaa 336

<210> 90
<211> 117
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8039-307F7-Ab2 HCVR

<400> 90
Gln Val Gln Leu Gln Gln Pro Gly Ala Glu Leu Val Arg Pro Gly Gly
1 5 10 15
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Ser Phe Thr Asn Tyr
20 25 30
Trp Met Asn Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45
Gly Met Ile His Pro Ser Asp Ser Glu Thr Arg Leu Asn Gln Lys Phe
50 55 60
Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80
Leu Gln Leu Ser Ser Pro Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95
Ala Lys Leu Leu Leu Tyr Tyr Phe Asp Tyr Trp Gly Gln Gly Thr Thr

100
Leu Thr Val Ser Ser
115

105

110

<210> 91
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8039-307F7-Ab2 HC CDR1

<400> 91
Asn Tyr Trp Met Asn
1 5

<210> 92
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8039-307F7-Ab2 HC CDR2

<400> 92
Met Ile His Pro Ser Asp Ser Glu Thr Arg Leu Asn Gln Lys Phe Lys
1 5 10 15
Asp

<210> 93
<211> 8
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8039-307F7-Ab2 HC CDR3

<400> 93
Leu Leu Leu Tyr Tyr Phe Asp Tyr
1 5

<210> 94
<211> 113
<212> PRT
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<220>
<223> ACI-8039-307F7-Ab2 LCVR

<400> 94
Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ala Met Ser Val Gly
1 5 10 15
Gln Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30
Ser Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45
Ser Pro Lys Ile Leu Val Tyr Phe Ala Ser Thr Arg Glu Ser Gly Val
50 55 60
Pro Asp Arg Phe Arg Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80
Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Asp Tyr Phe Cys Gln Gln
85 90 95
His Tyr Ser Pro Pro Pro Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile
100 105 110

Lys

<210> 95
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8039-307F7-Ab2 LC CDR1

<400> 95
Lys Ser Ser Gln Ser Leu Leu Asn Ser Ser Asn Gln Lys Asn Tyr Leu
1 5 10 15
Ala

<210> 96
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8039-307F7-Ab2 LC CDR2

<400> 96
Phe Ala Ser Thr Arg Glu Ser
1 5

<210> 97
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8039-307F7-Ab2 LC CDR3

<400> 97
Gln Gln His Tyr Ser Pro Pro Pro Thr
1 5

<210> 98
<211> 351
<212> DNA
<213> Artificial Sequence

<220>
<223> ACI-8039-307F7-Ab2 HCVR

<400> 98
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cctggacaag gccttgagtg gattggcatg attcatcctt ccgatagtga aactagggtta 180
aatcagaaat tcaaggacaa ggccacattg actgtagaca aatcatccag cacagcctac 240
ttgcaactca gcagcccgac atctgaggac tctgcggtct attactgtgc aaaattacta 300
ctatactact ttgactactg gggccaaggc accactctca cagtctcctc a 351

<210> 99
<211> 339

<212> DNA
<213> Artificial Sequence

<220>
<223> ACI-8039-307F7-Ab2 LCVR

<400> 99
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atgagctgca agtccagtca gagcctttta aatagtagca atcaaaagaa ctatttggcc 120
tgggtaccagc agaaaccagg acagtctcct aaaattctgg tatactttgc atccactagg 180
gaatctgggg tccctgatcg cttcagaggc agtggatctg ggacagattt cactctaacc 240
atcagcagtg tgcaggctga agacctggca gattacttct gtcagcaaca ttatagccct 300
cctccgacgt tcggtggagg caccaagctg gaaatcaaa 339

<210> 100
<211> 116
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8039-309D9-Ab2 HCVR

<400> 100
Gln Val Gln Leu Gln Gln Ser Gly Pro Gln Leu Val Arg Pro Gly Ala
1 5 10 15
Ser Val Lys Ile Ser Cys Lys Ala Ser Gly Asn Ser Phe Thr Ser Tyr
20 25 30
Trp Met His Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45
Gly Met Ile Asp Pro Ser Asp Ser Glu Thr Arg Leu Asn Gln Lys Phe
50 55 60
Lys Asp Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80
Met Gln Leu Ser Ser Pro Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95
Ala Gly Leu Tyr Phe Thr Leu Asp Tyr Trp Gly Gln Gly Thr Ser Val
100 105 110
Thr Val Ser Ser
115

<210> 101
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8039-309D9-Ab2 HC CDR1

<400> 101
Ser Tyr Trp Met His
1 5

<210> 102
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8039-309D9-Ab2 HC CDR2

<400> 102

Met Ile Asp Pro Ser Asp Ser Glu Thr Arg Leu Asn Gln Lys Phe Lys
1 5 10 15
Asp

<210> 103

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8039-309D9-Ab2 HC CDR3

<400> 103

Leu Tyr Phe Thr Leu Asp Tyr
1 5

<210> 104

<211> 113

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8039-309D9-Ab2 LCVR

<400> 104

Asp Ile Leu Met Thr Gln Ser Pro Ser Ser Leu Thr Val Ser Ala Gly
1 5 10 15
Glu Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Ala Ser
20 25 30
Gly Asn Gln Asn Asn Tyr Leu Ala Trp His Gln Gln Lys Pro Gly Arg
35 40 45
Ser Pro Lys Ile Leu Ile Ile Trp Ala Ser Thr Arg Val Ser Gly Val
50 55 60
Pro Asp Arg Phe Ile Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80
Ile Asn Ser Val Gln Ala Glu Asp Leu Ala Val Tyr Tyr Cys Gln Gln
85 90 95
Ser Tyr Ser Ala Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu
100 105 110
Lys

<210> 105

<211> 17

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8039-309D9-Ab2 LC CDR1

<400> 105

Lys Ser Ser Gln Ser Leu Leu Ala Ser Gly Asn Gln Asn Asn Tyr Leu
1 5 10 15
Ala

<210> 106

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8039-309D9-Ab2 LC CDR2

<400> 106

Trp Ala Ser Thr Arg Val Ser

1 5

<210> 107

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8039-309D9-Ab2 LC CDR3

<400> 107

Gln Gln Ser Tyr Ser Ala Pro Leu Thr

1 5

<210> 108

<211> 348

<212> DNA

<213> Artificial Sequence

<220>

<223> ACI-8039-309D9-Ab2 HCVR

<400> 108

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cctggacaag gtcttgagtg gattggcatg attgatcctt ccgatagtga gactaggtta 180

aatcagaagt tcaaggacaa ggccacattg actgtagaca aatcctccag cacagcctac 240

atgcaactca gcagcccgac atctgaggac tctgcggtct attactgtgc ggggctgtac 300

tttactttgg actactgggg tcaaggaacc tcagtcaccg tctcctca 348

<210> 109

<211> 339

<212> DNA

<213> Artificial Sequence

<220>

<223> ACI-8039-309D9-Ab2 LCVR

<400> 109

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atgagctgca agtccagtc gagtctttta gctagtggca accaaaataa ctacttggcc 120

tggcaccagc agaaaccagg acgatctcct aaaatactga taatttgggc atccactagg 180

gtatctggag tccctgatcg cttcataggc agtgggtctg ggacggattt cactctgacc 240

atcaacagtg tgcaggctga agatctggct gtttattact gtcagcagtc ctacagcgct 300

ccgctcacgt tcggtgctgg gaccaagctg gagctgaaa 339

<210> 110

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-1F11B5-Ab1 HCVR

<400> 110

Gln Val Gln Leu Lys Glu Ser Gly Pro Gly Leu Val Ala Pro Ser Gln
1 5 10 15
Ser Leu Ser Ile Thr Cys Thr Val Ser Gly Phe Ser Leu Thr Asn Tyr
20 25 30
Gly Val Ser Trp Ile Arg Gln Pro Pro Gly Lys Gly Leu Glu Trp Leu
35 40 45
Gly Val Ile Trp Gly Asp Gly Ser Thr Asn Tyr His Ser Ala Leu Ile
50 55 60
Ser Arg Leu Ser Ile Ser Lys Asp Asn Ser Lys Ser Gln Val Phe Leu
65 70 75 80
Lys Leu Asn Ser Leu Gln Thr Asp Asp Thr Ala Thr Tyr Tyr Cys Thr
85 90 95
Lys Gly Ala Gly Ser Trp Gly Gln Gly Ile Pro Val Thr Val Ser Ala
100 105 110

<210> 111

<211> 5

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-1F11B5-Ab1 HC CDR1

<400> 111

Asn Tyr Gly Val Ser
1 5

<210> 112

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-1F11B5-Ab1 HC CDR2

<400> 112

Val Ile Trp Gly Asp Gly Ser Thr Asn Tyr His Ser Ala Leu Ile Ser
1 5 10 15

<210> 113

<211> 4

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-1F11B5-Ab1 HC CDR3

<400> 113

Gly Ala Gly Ser
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<210> 114

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-1F11B5-Ab1 LCVR

<400> 114

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Gln	Pro	Ala	Ser	Ile	Ser	Cys	Lys	Ser	Ser	Gln	Ser	Leu	Leu	Asp	Ser
			20					25					30		
Asp	Gly	Arg	Thr	Tyr	Leu	Ile	Trp	Leu	Leu	Gln	Arg	Pro	Gly	Gln	Ser
			35				40					45			
Pro	Lys	Arg	Leu	Ile	Tyr	Leu	Val	Ser	Thr	Leu	Asp	Ser	Gly	Val	Pro
	50					55					60				
Asp	Arg	Phe	Thr	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Lys	Ile
65					70					75					80
Ser	Arg	Val	Glu	Ala	Glu	Asp	Leu	Gly	Val	Tyr	Tyr	Cys	Trp	Gln	Gly
				85					90					95	
Thr	His	Phe	Pro	Trp	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys
			100					105						110	

<210> 115

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-1F11B5-Ab1 LC CDR1

<400> 115

Lys	Ser	Ser	Gln	Ser	Leu	Leu	Asp	Ser	Asp	Gly	Arg	Thr	Tyr	Leu	Ile
1				5					10					15	

<210> 116

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-1F11B5-Ab1 LC CDR2

<400> 116

Leu	Val	Ser	Thr	Leu	Asp	Ser
1				5		

<210> 117

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-1F11B5-Ab1 LC CDR3

<400> 117

Trp	Gln	Gly	Thr	His	Phe	Pro	Trp	Thr
1				5				

<210> 118

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> ACI-8041-1F11B5-Ab1 HCVR

<400> 118

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ccaggaaagg gtctggagtg gctgggagta atatgggggtg acgggagcac aaattatcat      180
tcagctctca tatccagact gagcatcagc aaggataact ccaagagcca agttttctta      240
aaactgaaca gtctgcaaac tgatgacaca gccacgtact actgtaccaa aggagctggc      300
tcttggggcc aagggtattcc ggtcactgtc tctgca                                336
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<210> 119

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> ACI-8041-1F11B5-Ab1 LCVR

<400> 119

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atctcttgca agtcaagtca ggcctctta gatagtgatg gaaggacata ttttaatttg      120
ttgttacaga ggccaggcca gtctccaaag cgcctaactc atctgggtgc aacactggac      180
tctggagtcc ctgacagggt cactggcagt ggatcaggga cagatttcac actgaaaatc      240
agcagagtgg aggctgagga tttgggagtt tattattgct ggcaaggtag acattttccg      300
tggacgttcg gtggaggcac caagctggaa atcaaa                                336
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<210> 120

<211> 113

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-2B9H5-Ab1 HCVR

<400> 120

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Ser Val Lys Ile Ser Cys Lys Val Ser Gly Tyr Thr Phe Thr Asp His
          20         25         30
Pro Ile His Trp Met Lys Gln Arg Pro Asp Gln Gly Leu Glu Trp Ile
          35         40         45
Gly Tyr Phe Tyr Pro Arg Asp Ser Ser Thr His Tyr Asn Glu Lys Phe
          50         55         60
Lys Gly Lys Ala Thr Leu Thr Ala Asp Lys Ser Ser Ser Thr Ala Tyr
65         70         75         80
Met Gln Leu Asn Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Phe Cys
          85         90         95
Ala Arg Ser Met Gly Tyr Trp Gly Gln Gly Thr Ser Val Thr Val Ser
          100        105        110
Ser
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<210> 121

<211> 5

<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-2B9H5-Ab1 HC CDR1

<400> 121
Asp His Pro Ile His
1 5

<210> 122
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-2B9H5-Ab1 HC CDR2

<400> 122
Tyr Phe Tyr Pro Arg Asp Ser Ser Thr His Tyr Asn Glu Lys Phe Lys
1 5 10 15
Gly

<210> 123
<211> 4
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-2B9H5-Ab1 HC CDR3

<400> 123
Ser Met Gly Tyr
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<210> 124
<211> 107
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-2B9H5-Ab1 LCVR

<400> 124
Asp Ile Lys Met Thr Gln Ser Pro Ser Ser Met Tyr Ala Ser Leu Gly
1 5 10 15
Glu Arg Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Ser Tyr
20 25 30
Leu Ser Trp Phe Gln Gln Lys Pro Gly Lys Ser Pro Lys Thr Leu Ile
35 40 45
Tyr Arg Ala Asn Arg Leu Val Asp Gly Val Pro Ser Arg Phe Ser Gly
50 55 60
Ser Gly Ser Gly Gln Asp Tyr Ser Leu Thr Ile Ser Ser Leu Asp Tyr
65 70 75 80
Glu Asp Met Gly Ile Tyr Tyr Cys Leu Gln Tyr Asp Glu Phe Pro Pro
85 90 95
Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105

<210> 125
<211> 11
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-2B9H5-Ab1 LC CDR1

<400> 125
Lys Ala Ser Gln Asp Ile Asn Ser Tyr Leu Ser
1 5 10

<210> 126
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-2B9H5-Ab1 LC CDR2

<400> 126
Arg Ala Asn Arg Leu Val Asp
1 5

<210> 127
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-2B9H5-Ab1 LC CDR3

<400> 127
Leu Gln Tyr Asp Glu Phe Pro Pro Thr
1 5

<210> 128
<211> 339
<212> DNA
<213> Artificial Sequence

<220>
<223> ACI-8041-2B9H5-Ab1 HCVR

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cctgaccagg gcctggaatg gattggatat ttttatccta gagatagtag tactcactac 180
aatgagaagt tcaagggcaa ggccacattg actgcagaca aatcctccag cacagcctac 240
atgcagctca acagcctgac atctgaggac tctgcagtct acttctgtgc aagatcgatg 300
ggctactggg gtcaaggaac ctcagtcacc gtctcctca 339

<210> 129
<211> 321
<212> DNA
<213> Artificial Sequence

<220>
<223> ACI-8041-2B9H5-Ab1 LCVR

<400> 129
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 gggaaatctc ctaagaccct gatctatcgt gcaaacagat tggtagatgg ggtcccatca 180
 aggttcagtg gcagtggatc tgggcaagat tattctctca ccatcagcag tctggactat 240
 gaagatatgg gaatttatta ttgtctacag tatgatgagt ttctctccac gttcgggtgct 300
 gggaccaagc tggagctgaa a 321

<210> 130
 <211> 113
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ACI-8041-3G11B3-Ab1 HCVR

<400> 130
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 1 5 10 15
 Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Ile Asn Tyr
 20 25 30
 Tyr Ile Tyr Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
 35 40 45
 Gly Glu Ile Ile Pro Ser Asn Asp Gly Thr Asn Phe Asn Glu Lys Phe
 50 55 60
 Lys Thr Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Thr Ala Tyr
 65 70 75 80
 Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
 85 90 95
 Thr Ala Thr Gly Thr Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser
 100 105 110
 Ala

<210> 131
 <211> 5
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ACI-8041-3G11B3-Ab1 HC CDR1

<400> 131
 Asn Tyr Tyr Ile Tyr
 1 5

<210> 132
 <211> 17
 <212> PRT
 <213> Artificial Sequence

<220>
 <223> ACI-8041-3G11B3-Ab1 HC CDR2

<400> 132
 Glu Ile Ile Pro Ser Asn Asp Gly Thr Asn Phe Asn Glu Lys Phe Lys
 1 5 10 15
 Thr

<210> 133
 <211> 4
 <212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-3G11B3-Ab1 HC CDR3

<400> 133

Thr Gly Thr Val

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<210> 134

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-3G11B3-Ab1 LCVR

<400> 134

Asp	Val	Leu	Met	Thr	Gln	Thr	Pro	Leu	Ser	Leu	Pro	Val	Ser	Leu	Gly
1				5				10					15		
Asp	Gln	Ala	Ser	Ile	Ser	Cys	Arg	Ser	Ser	Gln	Ser	Ile	Val	His	Ser
			20					25					30		
Asn	Gly	Ile	Thr	Tyr	Leu	Glu	Trp	Tyr	Leu	Gln	Lys	Pro	Gly	Gln	Ser
			35				40					45			
Pro	Lys	Leu	Leu	Ile	Tyr	Lys	Val	Ser	Asn	Arg	Phe	Ser	Gly	Val	Pro
	50					55					60				
Asp	Arg	Phe	Ser	Gly	Ser	Gly	Ser	Gly	Thr	Asp	Phe	Thr	Leu	Lys	Ile
65					70					75				80	
Ser	Arg	Val	Glu	Ala	Glu	Asp	Leu	Gly	Val	Tyr	Tyr	Cys	Phe	Gln	Gly
			85					90						95	
Ser	His	Val	Pro	Trp	Thr	Phe	Gly	Gly	Gly	Thr	Lys	Leu	Glu	Ile	Lys
			100					105						110	

<210> 135

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-3G11B3-Ab1 LC CDR1

<400> 135

Arg	Ser	Ser	Gln	Ser	Ile	Val	His	Ser	Asn	Gly	Ile	Thr	Tyr	Leu	Glu
1				5					10					15	

<210> 136

<400> 136

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<210> 137

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-3G11B3-Ab1 LC CDR3

<400> 137

Phe	Gln	Gly	Ser	His	Val	Pro	Trp	Thr
1				5				

<210> 138
<211> 339
<212> DNA
<213> Artificial Sequence

<220>
<223> ACI-8041-3G11B3-Ab1 HCVR

<400> 138
caggtccaac tgcagcagtc tggggctgaa ctggtgaagc ctggggcttc agtgaagttg 60
tcctgcaagg cttctggcta caccttcatt aactactata tatactgggt gaaacagagg 120
cctggacaag gccttgagtg gattggagag attattccta gcaatgatgg tactaacttc 180
aatgagaagt tcaagaccaa ggccacactg actgtagaca aatcctccag cacagcatac 240
atgcaactca gcagcctgac atctgaggac tctgcggtct attactgtac cgcgacaggg 300
acggctctggg gccaaggagc tctggtcact gtctctgca 339

<210> 139
<211> 336
<212> DNA
<213> Artificial Sequence

<220>
<223> ACI-8041-3G11B3-Ab1 LCVR

<400> 139
gatgttttga tgacccaaac tccactctcc ctgcctgtca gtcttggaga tcaagcctcc 60
atctcttgca gatctagtca gagcattgta catagtaatg gaatcaccta tttagaatgg 120
tacctgcaga aaccaggcca gtctccaaag ctctaatct acaaagtttc caaccgattt 180
tctgggggtcc cagacagggt cagtggcagt ggatcagga cagatttcac actcaagatc 240
agcagagtgg aggctgagga tctgggagtt tattactgct ttcaaggttc acatgttccg 300
tggacgttcg gtggaggcac caagctggaa atcaaa 336

<210> 140
<211> 113
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-4G6D2-Ab1 HCVR

<400> 140
Gln Val Gln Leu Gln Gln Ser Gly Ala Glu Leu Val Arg Pro Gly Ala
1 5 10 15
Ser Val Lys Leu Ser Cys Lys Ala Ser Gly Tyr Thr Phe Thr Ser Tyr
20 25 30
Tyr Met Tyr Trp Val Lys Gln Arg Pro Gly Gln Gly Leu Glu Trp Ile
35 40 45
Gly Glu Ile Ile Pro Ser Asn Gly Asp Thr Asn Phe Asn Glu Lys Phe
50 55 60
Arg Ser Lys Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80
Met Gln Leu Ser Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95
Thr Ala Thr Gly Thr Val Trp Gly Gln Gly Thr Leu Val Thr Val Ser

	100	105	110
Ala			
<210> 141			
<211> 5			
<212> PRT			
<213> Artificial Sequence			
<220>			
<223> ACI-8041-4G6D2-Ab1 HC CDR1			
<400> 141			
Ser Tyr Tyr Met Tyr			
1 5			
<210> 142			
<211> 17			
<212> PRT			
<213> Artificial Sequence			
<220>			
<223> ACI-8041-4G6D2-Ab1 HC CDR2			
<400> 142			
Glu Ile Ile Pro Ser Asn Gly Asp Thr Asn Phe Asn Glu Lys Phe Arg			
1 5 10 15			
Ser			
<210> 143			
<400> 143			
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<210> 144			
<211> 112			
<212> PRT			
<213> Artificial Sequence			
<220>			
<223> ACI-8041-4G6D2-Ab1 LCVR			
<400> 144			
Asp Val Leu Met Thr Gln Thr Pro Leu Ser Leu Pro Val Ser Leu Gly			
1 5 10 15			
Asp Gln Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Ile Val His Ser			
20 25 30			
Asn Gly Asn Thr Tyr Leu Glu Trp Tyr Leu Gln Lys Pro Gly Gln Ser			
35 40 45			
Pro Lys Leu Leu Ile Tyr Lys Val Ser Asn Arg Phe Ser Gly Val Pro			
50 55 60			
Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile			
65 70 75 80			
Ser Arg Val Glu Ala Glu Asp Leu Gly Val Tyr Tyr Cys Phe Gln Gly			
85 90 95			
Ser His Val Pro Trp Thr Phe Gly Gly Gly Thr Lys Leu Glu Ile Lys			
100 105 110			
<210> 145			
<400> 145			
000			
<210> 146			
<400> 146			

000

<210> 147

<400> 147

000

<210> 148

<211> 339

<212> DNA

<213> Artificial Sequence

<220>

<223> ACI-8041-4G6D2-Ab1 HCVR

<400> 148

caggtccaac tgcagcagtc tggggctgaa ctggtgaggc ctggggcttc agtgaagttg 60

tcctgcaagg cttctggcta caccttcacc agctattata tgtactgggt gaagcagagg 120

cctggacaag gccttgagtg gattggagag attattccta gtaatggtga tactaacttc 180

aatgagaagt tcaggagcaa ggccacactg actgtagaca aatcctccag cacagcatat 240

atgcaactca gcagcctgac atctgaggac tctgcggtct attactgtac cgcgacaggg 300

acggtctggg gccaagggac tctggtcact gtctctgca 339

<210> 149

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> ACI-8041-4G6D2-Ab1 LCVR

<400> 149

gatgttttga tgacccaaac tccactctcc ctgcctgtca gtcttgaga tcaagcctcc 60

atctcttgca gatctagtca gagcattgta catagtaatg gaaacaccta tttagaatgg 120

tacctgcaga aaccaggcca gtctccaaag ctctgatct acaaagtttc caaccgattt 180

tctgggggcc cagacagggt cagtggcagt ggatcaggga cagatttcac actcaagatc 240

agcagagtgg aggctgagga tctgggagtt tattactgct ttcaagggtc acatgttccg 300

tggacgttcg gtggaggcac caagctggaa atcaaa 336

<210> 150

<211> 121

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-5A2D4-Ab1 HCVR

<400> 150

Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala

1 5 10 15

Ser Val Lys Ile Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Glu Asn

20 25 30

Thr Met His Trp Val Lys Gln Ile His Gly Lys Ser Leu Glu Trp Ile

35 40 45

Gly Gly Ile Asn Pro Asn Asn Gly Val Thr Asn Asn Asn Gln Lys Phe

Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Gly Thr Met Glu
65 70 75 80
Ala Glu Asp Val Ala Thr Tyr Tyr Cys Gln Gln Gly Ser Ser Ile Pro
85 90 95
Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 155
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-5A2D4-Ab1 LC CDR1

<400> 155
Ser Gly Ser Ser Ser Ile Ile Ser Asn Tyr Leu His
1 5 10

<210> 156
<211> 7
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-5A2D4-Ab1 LC CDR2

<400> 156
Arg Thr Ser Asn Leu Ala Ser
1 5

<210> 157
<211> 9
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-5A2D4-Ab1 LC CDR3

<400> 157
Gln Gln Gly Ser Ser Ile Pro Phe Thr
1 5

<210> 158
<211> 363
<212> DNA
<213> Artificial Sequence

<220>
<223> ACI-8041-5A2D4-Ab1 HCVR

<400> 158
gaggctccagc tgcaacagtc tggacctgag ctggtgaagc ctggggcctc agtgaagata 60
tcctgcaaga cttctggata cacattcact gaaaacacca tgcactgggt gaagcagatc 120
catggaaaga gccttgagt gattggaggt attaatccta acaatggtgt tactaacaac 180
aaccagaagt tcgagggcaa ggccactttg actgtagaca agtcctccag cacagcctac 240
atggagctcc gcagcctgac atctgaggat tctgcagtct attactgtgc aagatctgat 300
tacgacgcc tttactattc tatggactgc tggggtcaag gaacctcagt caccgtctcc 360
tca 363

<210> 159
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> ACI-8041-5A2D4-Ab1 LCVR

<400> 159
gaaattgtgc tcacccagtc tccaaccacc atggctgcat ctcccgggga gaagatcact 60
atcacctgca gtggtagctc aagtataatt tccaattact tgcattggta tcagcagaag 120
ccaggattct cccctaaact cttgatttat aggacatcca atctggcttc tggagtcca 180
actcgcttca gtggcagtgg gtctgggacc tcttactctc tcacaattgg caccatggag 240
gctgaagatg ttgccactta ctactgccag cagggtagta gtataccatt cacgttcggc 300
tcggggacaa agttggaaat aaaa 324

<210> 160
<211> 124
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-5A6H9-Ab1 HCVR

<400> 160
Asp Val Gln Leu Gln Glu Ser Gly Pro Gly Leu Val Lys Pro Ser Gln
1 5 10 15
Ser Leu Ser Leu Thr Cys Thr Val Thr Gly Tyr Ser Ile Thr Ser Asp
20 25 30
Tyr Ala Trp Asn Trp Ile Arg Gln Phe Pro Gly Asn Lys Leu Glu Trp
35 40 45
Met Gly Tyr Ile Asp Tyr Ser Gly Ile Thr Ser Tyr Asn Pro Ser Leu
50 55 60
Lys Ser Arg Ile Ser Ile Thr Arg Asp Thr Ser Lys Asn Gln Phe Phe
65 70 75 80
Leu Gln Leu Asn Ser Val Thr Thr Glu Asp Ser Ala Thr Tyr Tyr Cys
85 90 95
Ala Arg Ile Ser Gly Leu Asp Tyr Asp Val Arg Ala Gly Trp Phe Ala
100 105 110
Ser Trp Gly Gln Gly Thr Leu Val Thr Val Ser Ala
115 120

<210> 161
<211> 6
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-5A6H9-Ab1 HC CDR1

<400> 161
Ser Asp Tyr Ala Trp Asn
1 5

<210> 162
<211> 16
<212> PRT
<213> Artificial Sequence

<220>

<223> ACI-8041-5A6H9-Ab1 HC CDR2

<400> 162

Tyr Ile Asp Tyr Ser Gly Ile Thr Ser Tyr Asn Pro Ser Leu Lys Ser
1 5 10 15

<210> 163

<211> 15

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-5A6H9-Ab1 HC CDR3

<400> 163

Ile Ser Gly Leu Asp Tyr Asp Val Arg Ala Gly Trp Phe Ala Ser
1 5 10 15

<210> 164

<211> 112

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-5A6H9-Ab1 LCVR

<400> 164

Asp Ile Val Met Thr Gln Ala Ala Phe Ser Asn Pro Val Thr Leu Gly
1 5 10 15
Thr Ser Val Ser Ile Ser Cys Arg Ser Ser Lys Ser Leu Leu His Ser
20 25 30
Asn Gly Ile Thr Tyr Leu Tyr Trp Tyr Leu Gln Lys Pro Gly Gln Ser
35 40 45
Pro Gln Leu Leu Ile Tyr Gln Met Ser Asn Leu Ala Ser Gly Val Pro
50 55 60
Asp Arg Phe Ser Ser Ser Gly Ser Gly Thr Asp Phe Thr Leu Arg Ile
65 70 75 80
Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Ala Gln Asn
85 90 95
Leu Glu Arg Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu Lys
100 105 110

<210> 165

<211> 16

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-5A6H9-Ab1 LC CDR1

<400> 165

Arg Ser Ser Lys Ser Leu Leu His Ser Asn Gly Ile Thr Tyr Leu Tyr
1 5 10 15

<210> 166

<211> 7

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-5A6H9-Ab1 LC CDR2

<400> 166

Gln Met Ser Asn Leu Ala Ser
1 5

<210> 167

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-5A6H9-Ab1 LC CDR3

<400> 167

Ala Gln Asn Leu Glu Arg Pro Leu Thr
1 5

<210> 168

<211> 372

<212> DNA

<213> Artificial Sequence

<220>

<223> ACI-8041-5A6H9-Ab1 HCVR

<400> 168

gatgtgcagc ttcaggagtc gggacctggc ctggtgaaac cttctcagtc tctgtccctc	60
acctgcactg tctactggcta ctcaatcacc agtgattatg cctggaactg gatccggcag	120
tttccaggaa acaaactgga gtggatgggc tacatagact acagtggat cactagctac	180
aaccatctc tcaaaagtcg aatctctatc actcgagaca catccaagaa ccagttcttc	240
ctgcagttga attctgtgac tactgaggac tcagccacat attactgtgc aagaatctct	300
ggactggatt acgacgtgag ggctggctgg tttgcttcct ggggccaagg gactctggtc	360
actgtctctg ca	372

<210> 169

<211> 336

<212> DNA

<213> Artificial Sequence

<220>

<223> ACI-8041-5A6H9-Ab1 LCVR

<400> 169

gatattgtga tgacgcaggc tgcattctcc aatccagtca ctcttggaac atcagtttcc	60
atctcctgca ggtctagtaa gagtctccta catagtaatg gcatcactta tttgtattgg	120
tatctgcaga agccaggcca gtctcctcag ctcttgattt atcagatgtc caaccttgcc	180
tcaggagtcc cagacagggt cagtagcagt gggtcaggaa ctgatttcac actgagaatc	240
agcagagtgg aggctgagga tgtgggtgtt tattactgtg ctcaaatct agaacgtccg	300
ctcacgttcg gtgctgggac caagctggag ctgaaa	336

<210> 170
<211> 121
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-6C3C4-Ab1 HCVR

<400> 170
Glu Val Gln Leu Gln Gln Ser Gly Pro Glu Leu Val Lys Pro Gly Ala
1 5 10 15
Ser Val Asn Ile Ser Cys Lys Thr Ser Gly Tyr Thr Phe Thr Glu Tyr
20 25 30
Thr Met His Trp Met Lys Gln Ser His Gly Lys Ser Leu Glu Trp Ile
35 40 45
Gly Gly Ile Asn Pro Asn Asn Gly Val Thr Gly Tyr Asn Gln Lys Phe
50 55 60
Lys Gly Arg Ala Thr Leu Thr Val Asp Lys Ser Ser Ser Thr Ala Tyr
65 70 75 80
Met Glu Leu Arg Ser Leu Thr Ser Glu Asp Ser Ala Val Tyr Tyr Cys
85 90 95
Ala Arg Ser Asp Tyr Asp Asp Leu Tyr Tyr Ala Met Asp Tyr Trp Gly
100 105 110
Gln Gly Thr Ser Val Thr Val Ser Ser
115 120

<210> 171
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-6C3C4-Ab1 HC CDR1

<400> 171
Glu Tyr Thr Met His
1 5

<210> 172
<211> 17
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-6C3C4-Ab1 HC CDR2

<400> 172
Gly Ile Asn Pro Asn Asn Gly Val Thr Gly Tyr Asn Gln Lys Phe Lys
1 5 10 15
Gly

<210> 173
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-6C3C4-Ab1 HC CDR3

<400> 173
Ser Asp Tyr Asp Asp Leu Tyr Tyr Ala Met Asp Tyr
1 5 10

<210> 174
<211> 108
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-6C3C4-Ab1 LCVR

<400> 174
Glu Ile Val Leu Thr Gln Ser Pro Thr Thr Met Ala Ala Ser Pro Gly
1 5 10 15
Glu Lys Ile Thr Ile Thr Cys Ser Ala Ser Ser Ser Ile Ser Ser Asn
20 25 30
Tyr Leu His Trp Tyr Gln Gln Lys Pro Gly Phe Ser Pro Lys Leu Leu
35 40 45
Ile Tyr Arg Thr Ser Asn Leu Ala Ser Gly Val Pro Ala Arg Phe Ser
50 55 60
Gly Ser Gly Ser Gly Thr Ser Tyr Ser Leu Thr Ile Gly Thr Met Glu
65 70 75 80
Ala Glu Asp Val Ala Thr Tyr Tyr Cys Gln Gln Gly Ser Ser Ile Pro
85 90 95
Phe Thr Phe Gly Ser Gly Thr Lys Leu Glu Ile Lys
100 105

<210> 175
<211> 12
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-6C3C4-Ab1 LC CDR1

<400> 175
Ser Ala Ser Ser Ser Ile Ser Ser Asn Tyr Leu His
1 5 10

<210> 176
<400> 176
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<210> 177
<400> 177
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<210> 178
<211> 363
<212> DNA
<213> Artificial Sequence

<220>
<223> ACI-8041-6C3C4-Ab1 HCVR

<400> 178
gaggtccagc tgcaacagtc tggacctgag ctggtgaagc ctggggcttc agtgaacata 60
tcctgcaaga cttctggata cacattcact gaatacacca tgcactggat gaagcagagc 120
catggaaaga gccttgagtg gattggaggt attaatccta acaatggtgt tactggctac 180
aaccagaagt tcaagggcag ggccacattg actgtagaca agtcctccag cacagcctac 240
atggagctcc gcagcctgac atctgaggat tctgcagtct attactgtgc aagatctgat 300
tacgacgacc ttctactatgc tatggactac tggggctcaag gaacctcagt caccgtctcc 360

<210> 179
<211> 324
<212> DNA
<213> Artificial Sequence

<220>
<223> ACI-8041-6C3C4-Ab1 LCVR

<400> 179
gaaattgtgc tcacccagtc tccaaccacc atggctgcat ctcccgggga gaagatcact 60
atcacctgca gtgccagctc aagtataagt tccaattact tgcattggta tcagcagaag 120
ccaggattct cccctaaact cttgatttat aggacatcca atctggcttc tggagtcca 180
gctcgcttca gtggcagtgg gtctgggacc tcttactctc tcacaattgg caccatggag 240
gctgaagatg ttgccactta ctactgccag cagggtagta gtataccatt cacgttcggc 300
tcgggggacaa agttggaaat aaaa 324

<210> 180
<211> 120
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-9D7E1-Ab1 HCVR

<400> 180
Glu Val Met Leu Val Glu Ser Gly Gly Gly Leu Val Lys Pro Gly Gly
1 5 10 15
Ser Leu Lys Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr
20 25 30
Ala Met Ser Trp Val Arg Gln Thr Pro Glu Lys Arg Leu Glu Trp Val
35 40 45
Ala Thr Ile Ser Ser Gly Gly Asn Tyr Thr Tyr Cys Pro Asp Ser Val
50 55 60
Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Thr Leu Tyr
65 70 75 80
Leu Gln Met Ser Ser Leu Arg Ser Glu Asp Thr Ala Met Tyr Tyr Cys
85 90 95
Ala Ala Tyr Ala Tyr Asp Asp Gly Tyr Tyr Phe Asp Tyr Trp Gly Gln
100 105 110
Gly Thr Thr Leu Thr Val Ser Ser
115 120

<210> 181
<211> 5
<212> PRT
<213> Artificial Sequence

<220>
<223> ACI-8041-9D7E1-Ab1 HC CDR1

<400> 181
Ser Tyr Ala Met Ser
1 5

<210> 182
<211> 17
<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-9D7E1-Ab1 HC CDR2

<400> 182

Thr Ile Ser Ser Gly Gly Asn Tyr Thr Tyr Cys Pro Asp Ser Val Lys
1 5 10 15
Gly

<210> 183

<211> 11

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-9D7E1-Ab1 HC CDR3

<400> 183

Tyr Ala Tyr Asp Asp Gly Tyr Tyr Phe Asp Tyr
1 5 10

<210> 184

<211> 113

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-9D7E1-Ab1 LCVR

<400> 184

Asp Ile Val Met Thr Gln Ser Pro Ser Ser Leu Ala Met Ser Val Gly
1 5 10 15
Gln Lys Val Thr Met Ser Cys Lys Ser Ser Gln Ser Leu Leu Asn Ser
20 25 30
Ser Asn Gln Lys Asn Tyr Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln
35 40 45
Ser Pro Lys Leu Leu Val Tyr Phe Ala Ser Thr Arg Glu Ser Gly Val
50 55 60
Pro Asp Arg Phe Ile Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr
65 70 75 80
Ile Ser Ser Val Gln Ala Glu Asp Leu Ala Asp Tyr Phe Cys Gln Gln
85 90 95
His Tyr Ser Thr Pro Leu Thr Phe Gly Ala Gly Thr Lys Leu Glu Leu
100 105 110
Lys

<210> 185

<400> 185

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<210> 186

<400> 186

000

<210> 187

<211> 9

<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-9D7E1-Ab1 LC CDR3

<400> 187
Gln Gln His Tyr Ser Thr Pro Leu Thr
1 5

<210> 188
<211> 360
<212> DNA
<213> Artificial Sequence

<220>
<223> ACI-8041-9D7E1-Ab1 HCVR

<400> 188
gaagtgatgc tggaggagtc tgggggaggc ttagtgaagc ctggagggtc cctgaaactc 60
tcctgtgcag cctctggatt cactttcagt agctatgcc tgtcttgggt tcgccagact 120
ccggagaaga ggctggagtg ggtcgcaacc attagtagtg gtgtaatta cacctactgt 180
cccagacgtg tgaaggggcg attcaccatc tccagagaca atgccaagaa caccctgtac 240
ctgcaaatga gcagtctgag gtctgaggac acggccatgt attactgtgc agcctatgct 300
tacgacgacg ggtactactt tgactactgg ggccaaggca ccactctcac agtctcctca 360

<210> 189
<211> 339
<212> DNA
<213> Artificial Sequence

<220>
<223> ACI-8041-9D7E1-Ab1 LCVR

<400> 189
gacattgtga tgacacagtc tccatcctcc ctggctatgt cagtaggaca gaaggtcact 60
atgagctgca agtccagtca gagcctttta aatagtagca atcaaaagaa ctatttggcc 120
tggtaccagc agaaaccagg acagtctcct aaacttctgg tatactttgc atccactagg 180
gaatctgggg tccctgatcg cttcataggc agtggatctg ggacagattt cactcttacc 240
atcagcagtg tgcaggctga agacctggca gattacttct gtcagcaaca ttatagcact 300
cctctcacgt tcggtgctgg gaccaagctg gagctgaaa 339

<210> 190
<400> 190
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<210> 191
<400> 191
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<210> 192
<400> 192
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<210> 193
<400> 193
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<210> 194
<211> 106
<212> PRT

<213> Artificial Sequence

<220>

<223> ACI-8041-10H3B11-Ab1 LCVR

<400> 194

Asp Ile Gln Met Thr Gln Ser Pro Ser Ser Leu Ser Ala Ser Leu Gly
1 5 10 15
Gly Lys Val Thr Ile Thr Cys Lys Ala Ser Gln Asp Ile Asn Lys Tyr
20 25 30
Ile Ala Trp Tyr Gln His Lys Pro Gly Lys Gly Pro Arg Leu Leu Ile
35 40 45
His Tyr Thr Ser Thr Leu Gln Pro Gly Ile Pro Ser Arg Phe Ser Gly
50 55 60
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accaagctgg aaatcaaa	318