CLAIMS

1. A specific binding molecule that binds to an epitope within SEQ ID NO: 1 with a binding affinity greater than the binding affinity with which antibody mAb423 binds to an epitope within SEQ ID NO: 1.

2. The specific binding molecule according to claim 1 wherein the epitope of the specific binding molecule is within SEQ ID NO: 3, SEQ ID NO: 4, SEQ ID NO: 5, SEQ ID NO: 6 or SEQ ID NO: 7.

3. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises:

i. an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 8 (VEVKSEKLDFKDR);
ii. the amino acid sequence of SEQ ID NO: 9 (XXXXXXXKXXFXXR, wherein X is any amino acid); or
iii. the amino acid sequence of SEQ ID NO: 8, optionally wherein any one or more residue other than residue number 343 (K), 346 (F) and/or 349 (R) is replaced by a conservative amino acid substitution (numbering according to SEQ ID NO: 1).

4. The specific binding molecule according to any one of claims 1 to 3 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 337 to 355 of SEQ ID NO: 1 and the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 10 (N/S N A V G);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 11 (G C S S D G T/K C Y Y/H N S A L K S);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 12 (G H/F/Y Y S/P I/V Y G Y D Y L/S G T I D Y);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 13 (S G S S S N V G/- G G/R N S/D V G/A);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 14 (D/N/G T N/T S R P S);

VLCDR3 comprises the sequence set forth in SEQ ID NO: 15 (V/A T/S G D S T/S T/A H/I D/N D L/I);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto.

5. The specific binding molecule according to any one of claims 1 to 4 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 16 (NNAVG) or SEQ ID NO: 17 (SNAVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 18 (GCSSDGTCYYNSALKS), SEQ ID NO: 19 (GCSSDGKCYHNSALKS) or SEQ ID NO: 20 (GCSSDGKCYYNSALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 21 (GHYSIYGYDYLGTIDY), SEQ ID NO: 22 (GFYSIYGYDYSGTIDY), or SEQ ID NO: 23 (GYYPVYGYDYLGTIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 24 (SGSSSNVGGGNSVG) or SEQ ID NO: 25 (SGSSSNVGRNDVA);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 26 (DTNSRPS), SEQ ID NO: 27 (NTNSRPS), or SEQ ID NO: 28 (GTTSRPS);

VLCDR3 comprises the sequence set forth in SEQ ID NO: 29 (VTGDSTTHDDL), SEQ ID NO: 30 (VTGDSSTHDDL), or SEQ ID NO: 31 (ASGDSSAINDI);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 337 to 355 of SEQ ID NO: 1.

6. The specific binding molecule according to any one of claims 1 to 5 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 16 (NNAVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 18 (GCSSDGTCYYNSALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 21 (GHYSIYGYDYLGTIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 24 (SGSSSNVGGGNSVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 26 (DTNSRPS);

VLCDR3 comprises the sequence set forth in SEQ ID NO: 29 (VTGDSTTHDDL).

7. The specific binding molecule according to any one of claims 1 to 6 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 337 to 355 of SEQ ID NO: 1 with a K_D of less than around 500 pM, optionally wherein

i. The K_D for binding to SEQ ID NO: 1 is around 50 pM to around 150 pM, and/or

ii. The K_D for binding to SEQ ID NO: 5 is around 300 pM to around 400 pM.

8. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises:

i. an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 33 (GNKKIETHKLTFR);

ii. the amino acid sequence of SEQ ID NO: 34 (XXXKXXXHXXXXX, wherein X is any amino acid); or

iii. the amino acid sequence of SEQ ID NO: 33, optionally wherein any one or more residue other than residue number 370 (K) and/or 374 (H) is replaced by a conservative amino acid substitution (numbering according to SEQ ID NO: 1).

9. The specific binding molecule according to any one of claims 1, 2 or 8 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 367 to 379 of SEQ ID NO: 1. Said specific binding molecule may comprise the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 35 (S/T N/Y S/A/Y V G);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 36 (G/S/N I/V D/Y T/S D/T G E/Y/D/R E/T/A G/Y/F Y/F N P A/V L N/K S);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 37 (S/T Y/V/A R/N A/T/G/S D/- G/- L/Y/F/- A/- Y/H G/P Y/D V Q/Y A/Y I D/E Y/R/K) or SEQ ID NO: 265 (GSYYHGGGNGMVDFFDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 38 (S G S/R F/Y/D I/L/V G/S I/S/R S S/R/A/G V G) or in SEQ ID NO: 39 (SGSSSNVGYGNYVG)

VLCDR2 comprises the sequence set forth in SEQ ID NO: 40 (A/D S/A D/S/T G/S R P/A S);

VLCDR3 comprises the sequence set forth in SEQ ID NO: 41 (G/S S/I/V S/F/Y/T D/G/A/Q R/P/- T/- P/Q/D/G Y/R/H/N T/N G/Y V/I/L);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto.

10. The specific binding molecule according to any one of claims 1, 2, 8 or 9 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 42 (SNSVG), SEQ ID NO: 17 (SNAVG), SEQ ID NO: 44 (SYYVG), or SEQ ID NO: 45 (TNSVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 46 (GIDTDGEEGYNPALNS), SEQ ID NO: 47 (SVDSDGYTYYNPALKS), SEQ ID NO: 48 (GIDSDGEEGYNPALNS), SEQ ID NO: 49 (GIDSDGEEGYNPALKS), SEQ ID NO: 50 (SVDSDGDTYYNPALKS), SEQ ID NO: 51 (GIDTDGEEGYNPALKS), SEQ ID NO: 52 (NIYSTGRAFYNPALKS), or SEQ ID NO: 53 (GIDTDGEEGFNPVLKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 54 (SYRADGLAYGYVQAIDY), SEQ ID NO: 55 (SYRTDGLAYGYVQAIDY), SEQ ID NO: 56 (SVNGHPDVYYIDR), SEQ ID NO: 57 (TYRTDGYAYGYVQAIDY), SEQ ID NO: 58 (SYRSDGLAYGYVQAIDY), SEQ ID NO: 59

(SANGHPDVYYIDK), SEQ ID NO: 60 (TYRTDGFAYGYVQAIDY), SEQ ID NO: 61 (SYRTDGLAYGYVQAIEY), or SEQ ID NO: 265 (GSYYHGGGNGMVDFFDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 63 (SGSFIGISSVG); SEQ ID NO: 64 (SGSYISSSRVG); SEQ ID NO: 65 (SGSDLGSSRVG); SEQ ID NO: 66 (SGSYIGSSAVG); SEQ ID NO: 67 (SGRFIGISSVG); SEQ ID NO: 68 (SGSYIGSSGVG); or SEQ ID NO: 69 (SGSYVSRSRVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 70 (ASDGRPS); SEQ ID NO: 71 (DSSSRPS); or SEQ ID NO: 72 (AATSRAS);

VLCDR3 comprises the sequence set forth in SEQ ID NO: 73 (GSSDRTPYTGV); SEQ ID NO: 74 (GSSDRTQYTGV); SEQ ID NO: 75 (GVFGDRNYI); SEQ ID NO: 76 (GIFGDRNYI); SEQ ID NO: 77 (GSTAPTPHTGV); SEQ ID NO: 78 (SSYQRGNTGV); SEQ ID NO: 79 (GSSDRTQYTGL); or SEQ ID NO: 80 (GIYGDRNYI);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 367 to 379 of SEQ ID NO: 1.

11. The specific binding molecule according to any one of claims 1, 2, or 8 to 10 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 42 (SNSVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 46 (GIDTDGEEGYNPALNS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 54 (SYRADGLAYGYVQAIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 63 (SGSFIGISSVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 70 (ASDGRPS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 73 (GSSDRTPYTGV).

12. The specific binding molecule according to any one of claims 1, 2, or 8 to 10 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 42 (SNSVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 46 (GIDTDGEEGYNPALNS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 55 (SYRTDGLAYGYVQAIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 63 (SGSFIGISSVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 70 (ASDGRPS);

VLCDR3 comprises the sequence set forth in SEQ ID NO: 74 (GSSDRTQYTGV).

13. The specific binding molecule according to any one of claims 1, 2, or 8 to 10 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 42 (SNSVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 48 (GIDSDGEEGYNPALNS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 57 (TYRTDGYAYGYVQAIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 63 (SGSFIGISSVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 70 (ASDGRPS);

VLCDR3 comprises the sequence set forth in SEQ ID NO: 74 (GSSDRTQYTGV).

14. The specific binding molecule according to any one of claims 1, 2, or 8 to 10 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 42 (SNSVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 46 (GIDTDGEEGYNPALNS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 54 (SYRADGLAYGYVQAIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 63 (SGSFIGISSVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 70 (ASDGRPS);

VLCDR3 comprises the sequence set forth in SEQ ID NO: 74 (GSSDRTQYTGV).

15. The specific binding molecule according to any one of claims 1, 2, or 8 to 10 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 42 (SNSVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 51 (GIDTDGEEGYNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 60 (TYRTDGFAYGYVQAIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 63 (SGSFIGISSVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 70 (ASDGRPS);

VLCDR3 comprises the sequence set forth in SEQ ID NO: 74 (GSSDRTQYTGV).

16. The specific binding molecule according to any one of claims 1, 2, or 8 to 10 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 44 (SYYVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 52 (NIYSTGRAFYNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 265 (GSYYHGGGNGMVDFFDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 39 (SGSSSNVGYGNYVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 72 (AATSRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 78 (SSYQRGNTGV).

17. The specific binding molecule according to any one of claims 1, 2, or 8 to 10 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 42 (SNSVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 46 (GIDTDGEEGYNPALNS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 58 (SYRSDGLAYGYVQAIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 63 (SGSFIGISSVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 70 (ASDGRPS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 74 (GSSDRTQYTGV).

18. The specific binding molecule according to any one of claims 1, 2, or 8 to 17 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 367 to 379 of SEQ ID NO: 1 with a K_D of less than around 500 pM, optionally wherein

i. The K_D for binding to SEQ ID NO: 1 is around 100 pM to around 200 pM, and/or

ii. The K_D for binding to SEQ ID NO: 5 is around 400 pM to around 500 pM.

19. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 82 (VEVKSEKLDFKDRVQSKIGSLDNITHVPGGGN).

20. The specific binding molecule according to any one of claims 1, 2 or 19 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 337 to 368 of SEQ ID NO: 1 and the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 83 (S Y S V Y)

VHCDR2 comprises the sequence set forth in SEQ ID NO: 84 (I M Y A S G R V D Y N P A L K S)

VHCDR3 comprises the sequence set forth in SEQ ID NO: 85 (G I E N/D)

VLCDR1 comprises the sequence set forth in SEQ ID NO: 86 (R T S/N Q/E S/N V/I N/G/D N/S Y/G L S/A)

VLCDR2 comprises the sequence set forth in SEQ ID NO: 87 (Y A T Y L Y/H T)

VLCDR3 comprises the sequence set forth in SEQ ID NO: 88 (L Q Y D/G/E S/T T P L A/T);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto.

21. The specific binding molecule according to any one of claims 1, 2, 19 or 20 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 83 (SYSVY);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 84 (IMYASGRVDYNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 89 (GIEN) or SEQ ID NO: 90 (GIED);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 91 (RTSQSVNNYLS), SEQ ID NO: 92 (RTNESVGNYLS), SEQ ID NO: 93 (RTSQNIDNGLA), or SEQ ID NO 94 (RTSQSVGSYLS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 95 (YATRLYT) or SEQ ID NO: 96 (YATRLHT);

VLCDR3 comprises the sequence set forth in SEQ ID NO: 97 (LQYDSTPLA), SEQ ID NO: 98 (LQYDSTPLT), SEQ ID NO: 99 (LQYESTPLA), or SEQ ID NO: 100 (LQYGTTPLA);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 337 to 368 of SEQ ID NO: 1.

22. The specific binding molecule according to any one of claims 1, 2, or 19 to 21 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 337 to 368 of SEQ ID NO: 1 with a K_D of less than around 25 nM, optionally wherein

i. The K_D for binding to SEQ ID NO: 1 is less than around 25 nM, and/or

ii. The K_D for binding to SEQ ID NO: 5 is less than around 25 nM.

23. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 120 (SSTGSIDMVDSPQLATLADEVSASLAKQGL).

24. The specific binding molecule according to any one of claims 1, 2 or 23 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 412 to 441 of SEQ ID NO: 1 and the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 121 (S/N D/Y S/G/A V/L A/G);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 122 (A/N S/I G/Y/W S/R S/G G N/S/R K/T/I Y/E Y N P A L K S);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 123 (G I/G I/V A/G G/S V D V), or SEQ ID NO: 124 (SGGD);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 125 (S G S/G S/N N V/I G Y/R G N/D/T Y/F V G/D);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 126 (G T/A A/D/T I/S/R R A/P S/P); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 127 (A S/T Y Q/D S/Y/R N/S Y/D/N/E A/G/D/S -/G/M/V -/I F/V/I);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto.

25. The specific binding molecule according to any one of claims 1, 2, 23 or 24 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 128 (SDSVA), SEQ ID NO: 129 (NYGVG), or SEQ ID NO: 130 (SYALG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 131 (ASGSSGNKYYNPALKS), SEQ ID NO: 132 (NIWRGGRIEYNPALKS), or SEQ ID NO: 133 (NIYSGGSTYYNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 134 (GIIAGVDV), SEQ ID NO: 135 (GGVGSVDV), or SEQ ID NO: 124 (SGGD);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 39 (SGSSSNVGYGNYVG), SEQ ID NO: 137 (SGGRNNIGRGTFVD), and SEQ ID NO: 138 (SGSSSNVGYGDYVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 139 (GTAIRAS), SEQ ID NO: 140 (GAASRAS), SEQ ID NO: 141 (GATSRAS), or SEQ ID NO: 142 (GTDRRPP); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 143 (ASYQSNYAF), SEQ ID NO: 144 (ASYDRSESVV), SEQ ID NO: 145 (ASYDSSDGGV), or SEQ ID NO 146 (ATYDYSNDMII);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 412 to 441 of SEQ ID NO: 1.

26. The specific binding molecule according to any one of claims 1, 2, or 23 to 25 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 128 (SDSVA);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 131 (ASGSSGNKYYNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 134 (GIIAGVDV);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 39 (SGSSSNVGYGNYVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 139 (GTAIRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 143 (ASYQSNYAF).

27. The specific binding molecule according to any one of claims 1, 2, or 23 to 25 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 128 (SDSVA);
VHCDR2 comprises the sequence set forth in SEQ ID NO: 131 (ASGSSGNKYYNPALKS);
VHCDR3 comprises the sequence set forth in SEQ ID NO: 134 (GIIAGVDV);
VLCDR1 comprises the sequence set forth in SEQ ID NO: 138 (SGSSSNVGYGDYVG);
VLCDR2 comprises the sequence set forth in SEQ ID NO: 140 (GAASRAS); and
VLCDR3 comprises the sequence set forth in SEQ ID NO: 145 (ASYDSSDGGV).

28. The specific binding molecule according to any one of claims 1, 2, or 23 to 25 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 129 (NYGVG);
VHCDR2 comprises the sequence set forth in SEQ ID NO: 133 (NIYSGGSTYYNPALKS);
VHCDR3 comprises the sequence set forth in SEQ ID NO: 135 (GGVGSVDV);
VLCDR1 comprises the sequence set forth in SEQ ID NO: 137 (SGGRNNIGRGTFVD);
VLCDR2 comprises the sequence set forth in SEQ ID NO: 142 (GTDRRPP); and
VLCDR3 comprises the sequence set forth in SEQ ID NO: 146 (ATYDYSNDMII).

29. The specific binding molecule according to any one of claims 1, 2, or 23 to 25 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 130 (SYALG);
VHCDR2 comprises the sequence set forth in SEQ ID NO: 132 (NIWRGGRIEYNPALKS);
VHCDR3 comprises the sequence set forth in SEQ ID NO: 124 (SGGD);
VLCDR1 comprises the sequence set forth in SEQ ID NO: 39 (SGSSSNVGYGNYVG);
VLCDR2 comprises the sequence set forth in SEQ ID NO: 141 (GATSRAS); and
VLCDR3 comprises the sequence set forth in SEQ ID NO: 144 (ASYDRSESVV).

30. The specific binding molecule according to any one of claims 1, 2, or 23 to 29 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 412 to 441 of SEQ ID NO: 1 with a K_D of less than around 25 nM, optionally wherein the K_D for binding to SEQ ID NO: 1 is around 1 nM to around 10 nM.

31. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 148 (MAEPRQEFEVMEDHAGTYGLGDRKDQGGYTMHQDQEGDTDAGLKESPLQ).

32. The specific binding molecule according to any one of claims 1, 2 or 31 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 1 to 49 of SEQ ID NO: 1 and the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 149 (S N G V G);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 150 (D I S/A S S/V/G G K A/K/V Y A/S/G N/H P A L K S);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 151 (C R D G G V S/T Y G Y D I/S D Y);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 152 (S G S S/T S/G N I/V G G/S/Y G N/D Y/D L/V S/G);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 153 (G A/V T S/N/E R/L A S); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 154 (A/G S F/Y D T/S/D S/N S G G I/V);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto.

33. The specific binding molecule according to any one of claims 1, 2, 31 or 32 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 149 (SNGVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 155 (DISSSGKAYANPALKS), SEQ ID NO: 156 (DISSGGKVYGHPALKS), SEQ ID NO: 157 (DISSVGKKYANPALKS), or SEQ ID NO: 158 (DIASSGKAYSNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 159 (CRDGGVSYGYDIDY), SEQ ID NO: 160 (CRDGGVSYGYDSDY), or SEQ ID NO: 161 (CRDGGVTYGYDIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 163 (SGSSSNIGGGNYLS), SEQ ID NO: 138 (SGSSSNVGYGDYVG), SEQ ID NO: 165 (SGSSGNVGYGDYVS), or SEQ ID NO: 166 (SGSTSNVGSGNDVS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 141 (GATSRAS), SEQ ID NO: 168 (GVTERAS), SEQ ID NO: 169 (GATNLAS), or SEQ ID NO: 170 (GATNRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 171 (ASFDTSSGGI), SEQ ID NO: 172 (ASYDDSSGGI), SEQ ID NO: 173 (ASYDSSSGGV), or SEQ ID NO: 174 (GSYDSNSGGI); or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 1 to 49 of SEQ ID NO: 1.

34. The specific binding molecule according to any one of claims 1, 2, or 31 to 33 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 149 (SNGVG);
VHCDR2 comprises the sequence set forth in SEQ ID NO: 155 (DISSSGKAYANPALKS);
VHCDR3 comprises the sequence set forth in SEQ ID NO: 159 (CRDGGVSYGYDIDY);
VLCDR1 comprises the sequence set forth in SEQ ID NO: 163 (SGSSSNIGGGNYLS);
VLCDR2 comprises the sequence set forth in SEQ ID NO: 141 (GATSRAS); and
VLCDR3 comprises the sequence set forth in SEQ ID NO: 171 (ASFDTSSGGI).

35. The specific binding molecule according to any one of claims 1, 2, or 31 to 33 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 149 (SNGVG);
VHCDR2 comprises the sequence set forth in SEQ ID NO: 156 (DISSGGKVYGHPALKS);
VHCDR3 comprises the sequence set forth in SEQ ID NO: 160 (CRDGGVSYGYDSDY);
VLCDR1 comprises the sequence set forth in SEQ ID NO: 138 (SGSSSNVGYGDYVG);
VLCDR2 comprises the sequence set forth in SEQ ID NO: 168 (GVTERAS); and
VLCDR3 comprises the sequence set forth in SEQ ID NO: 172 (ASYDDSSGGI).

36. The specific binding molecule according to any one of claims 1, 2, or 31 to 33 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 149 (SNGVG);
VHCDR2 comprises the sequence set forth in SEQ ID NO: 157 (DISSVGKKYANPALKS);
VHCDR3 comprises the sequence set forth in SEQ ID NO: 161 (CRDGGVTYGYDIDY);
VLCDR1 comprises the sequence set forth in SEQ ID NO: 165 (SGSSGNVGYGDYVS);
VLCDR2 comprises the sequence set forth in SEQ ID NO: 169 (GATNLAS); and
VLCDR3 comprises the sequence set forth in SEQ ID NO: 173 (ASYDSSSGGV).

37. The specific binding molecule according to any one of claims 1, 2, or 31 to 33 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 149 (SNGVG);
VHCDR2 comprises the sequence set forth in SEQ ID NO: 158 (DIASSGKAYSNPALKS);
VHCDR3 comprises the sequence set forth in SEQ ID NO: 161 (CRDGGVTYGYDIDY);
VLCDR1 comprises the sequence set forth in SEQ ID NO: 166 (SGSTSNVGSGNDVS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 170 (GATNRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 174 (GSYDSNSGGI).

38. The specific binding molecule according to any one of claims 1, 2, or 31 to 37 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 1 to 49 of SEQ ID NO: 1 with a K_D of less than around 25 nM, optionally wherein the K_D for binding to SEQ ID NO: 1 is around 1 nM to around 20 nM.

39. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 175 (QTPTEDGSEEPGSETSDAKSTPTAEDVTAPLVDEGAPGKQAAAQPHTEIPEGTTAEEAGIGDT).

40. The specific binding molecule according to any one of claims 1, 2 or 39 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 49 to 111 of SEQ ID NO: 1 and the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 149 (S N G V G);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 176 (D I/K S S V/A G K K/T Y A/G N P A L K S);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 177 (C R D G G V T Y G Y D I/V D Y);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 178 (S G S S S N V G L/Y R/G N/D Y/V V T/S);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 179 (G A/T T S/T R A S); and VLCDR3 comprises the sequence set forth in SEQ ID NO: 180 (A S A/F D T/S N/D D/S G G V/I);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto.

41. The specific binding molecule according to any one of claims 1, 2, 39 or 40 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 149 (SNGVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 157 (DISSVGKKYANPALKS), or SEQ ID NO: 182 (DKSSAGKTYGNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 161 (CRDGGVTYGYDIDY), or SEQ ID NO: 184 (CRDGGVTYGYDVDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 185 (SGSSSNVGLRNYVT), or SEQ ID NO: 186 (SGSSSNVGYGDVVS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 141 (GATSRAS), or SEQ ID NO: 188 (GTTTRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 189 (ASADTNDGGV), or SEQ ID NO: 190 (ASFDSDSGGI);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 49 to 111 of SEQ ID NO: 1.

42. The specific binding molecule according to any one of claims 1, 2, or 39 to 41 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 149 (SNGVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 157 (DISSVGKKYANPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 161 (CRDGGVTYGYDIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 185 (SGSSSNVGLRNYVT);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 141 (GATSRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 189 (ASADTNDGGV).

43. The specific binding molecule according to any one of claims 1, 2, or 39 to 41 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 149 (SNGVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 182 (DKSSAGKTYGNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 184 (CRDGGVTYGYDVDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 186 (SGSSSNVGYGDVVS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 188 (GTTTRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 190 (ASFDSDSGGI).

44. The specific binding molecule according to any one of claims 1, 2, or 39 to 43 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 49 to 111 of SEQ ID NO: 1 with a K_D of less than around 250 nM , optionally wherein the K_D for binding to SEQ ID NO: 1 is around 50 nM to around 150 nM.

45. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 191 (GKTKIATPRGA).

46. The specific binding molecule according to any one of claims 1, 2 or 45 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 146 to 157 of SEQ ID NO: 1 and the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 192 (S N A V I/G);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 193 (L I D V/I D G D A/T A Y D/N P A L K/E S);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 194 (D/H Y G/D S/K W G Y V/A S/D D/S I D Y);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 195 (S G S D/S -/S -/N -/V I/G G/Y G A/D D/Y V G);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 196 (D N/A D/T N/T R P/A S); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 197 (G/A T/S Y S/Q G/N A/E N/R Y/S G I/V));

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto.

47. The specific binding molecule according to any one of claims 1, 2, 45 or 46 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 198 (SNAVI), or SEQ ID NO: 17 (SNAVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 200 (LIDVDGDAAYDPALKS), or SEQ ID NO: 201 (LIDIDGDTAYNPALES);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 202 (DYGSWGYVSDIDY), or SEQ ID NO: 203 (HYDKWGYADSIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 204 (SGSDIGGADVG), or SEQ ID NO: 138 (SGSSSNVGYGDYVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 206 (DNDNRPS), or SEQ ID NO: 207 (DATTRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 208 (GTYSGANYGI), or SEQ ID NO: 209 (ASYQNERSGV);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 147 to 157 of SEQ ID NO: 1.

48. The specific binding molecule according to any one of claims 1, 2, or 45 to 47 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 198 (SNAVI);
VHCDR2 comprises the sequence set forth in SEQ ID NO: 200 (LIDVDGDAAYDPALKS);
VHCDR3 comprises the sequence set forth in SEQ ID NO: 202 (DYGSWGYVSDIDY);
VLCDR1 comprises the sequence set forth in SEQ ID NO: 204 (SGSDIGGADVG);
VLCDR2 comprises the sequence set forth in SEQ ID NO: 206 (DNDNRPS); and
VLCDR3 comprises the sequence set forth in SEQ ID NO: 208 (GTYSGANYGI).

49. The specific binding molecule according to any one of claims 1, 2, or 45 to 47 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 17 (SNAVG);
VHCDR2 comprises the sequence set forth in SEQ ID NO: 201 (LIDIDGDTAYNPALES);
VHCDR3 comprises the sequence set forth in SEQ ID NO: 203 (HYDKWGYADSIDY);
VLCDR1 comprises the sequence set forth in SEQ ID NO: 138 (SGSSSNVGYGDYVG);
VLCDR2 comprises the sequence set forth in SEQ ID NO: 207 (DATTRAS); and
VLCDR3 comprises the sequence set forth in SEQ ID NO: 209 (ASYQNERSGV).

50. The specific binding molecule according to any one of claims 1, 2, or 45 to 49 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 147 to 157 of SEQ ID NO: 1 with a K_D of less than around 50 nM , optionally wherein the K_D for binding to SEQ ID NO: 1 is around 10 nM to around 20 nM .

51. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises:

i. an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 221 (RENAKAKTDHGAE);
ii. the amino acid sequence of SEQ ID NO: 222 (XXXXXXXXXXXXE, wherein X is any amino acid); or
iii. the amino acid sequence of SEQ ID NO: 221, optionally wherein any one or more residue other than residue number 391 (E) is replaced by a conservative amino acid substitution (numbering according to SEQ ID NO: 1).

52. The specific binding molecule according to any one of claims 1, 2 or 51 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence

comprising residues 379 to 391 of SEQ ID NO: 1 and the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 223 (D/S R/W G V A);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 224 (T M R S G G T/G I/T D/E Y/D N P A L K S);

VHCDR3 comprises the sequence set forth SEQ ID NO: 225 (G Y L S G D/I/V R/H Y A);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 226 (S G S R/S S D/N I/V G Y/D/A G N/D/R Y V S/G);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 227 (D/S/G T/A N/R/T T/N/S R A S); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 228 (A N/S I D S/T S/G R/N S/N H/L L/I));

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto.

53. The specific binding molecule according to any one of claims 1, 2, 51 or 52 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 229 (DRGVA), SEQ ID NO: 230 (DWGVA), or SEQ ID NO: 231 (SWGVA);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 232 (TMRSGGTIDYNPALKS), SEQ ID NO: 233 (TMRSGGGTEYNPALKS), or SEQ ID NO: 234 (TMRSGGTTDDNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 235 (GYLSGDRYA), SEQ ID NO: 236 (GYLSGIHYA), or SEQ ID NO: 237 (GYLSGVHYA);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 238 (SGSRSDIGYGNYVS), SEQ ID NO: 239 (SGSSSNVGAGNYVG), SEQ ID NO: 240 (SGSSSNVGDGDYVG), or SEQ ID NO: 241 (SGSSSNVGDGRYVS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 242 (DTNTRAS), SEQ ID NO: 243 (DTTSRAS), SEQ ID NO: 170 (GATNRAS), or SEQ ID NO: 244 (SARNRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 245 (ANIDSSRSHL), SEQ ID NO: 246 (ASIDSGNNLL), or SEQ ID NO: 247 (ASIDTSRSHI);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 379 to 391 of SEQ ID NO: 1.

54. The specific binding molecule according to any one of claims 1, 2, or 51 to 53 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 229 (DRGVA);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 232 (TMRSGGTIDYNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 235 (GYLSGDRYA);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 238 (SGSRSDIGYGNYVS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 242 (DTNTRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 245 (ANIDSSRSHL).

55. The specific binding molecule according to any one of claims 1, 2, or 51 to 53 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 230 (DWGVA);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 234 (TMRSGGTTDDNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 237 (GYLSGVHYA);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 241 (SGSSSNVGDGRYVS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 243 (DTTSRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 246 (ASIDSGNNLL).

56. The specific binding molecule according to any one of claims 1, 2, or 51 to 53 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 230 (DWGVA);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 234 (TMRSGGTTDDNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 237 (GYLSGVHYA);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 239 (SGSSSNVGAGNYVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 70 (GATNRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 247 (ASIDTSRSHI).

57. The specific binding molecule according to any one of claims 1, 2, or 51 to 53 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 231 (SWGVA);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 233 (TMRSGGGTEYNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 236 (GYLSGIHYA);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 240 (SGSSSNVGDGDYVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 244 (SARNRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 247 (ASIDTSRSHI).

58. The specific binding molecule according to any one of claims 1, 2, or 51 to 57 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 379 to 391 of SEQ ID NO: 1 with a K_D of less than around 25 nM, optionally wherein

i. The specific binding molecule has no detectable binding to SEQ ID NO: 1, and/or

ii. The K_D for binding to SEQ ID NO: 4 is around 300 pM to around 10 nM.

59. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 293 (MAEPRQEFEVMEDHAGTYGLGDRKDQGGYTMHQDQEGDTDAGLKESPLQTPTEDGSEEPGSETSDAKSTPTAEDVTAPLVDEGAPGKQAAAQPHTEIPEGTTAEEAGIGDTPSLEDEAAGHVTQARMVSKSKDGTGSDDKKAKGADGKTKIATPR).

60. The specific binding molecule according to any one of claims 1, 2, or 59 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 259 (SNGVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 157 (DISSVGKKYANPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 161 (CRDGGVTYGYDIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 165 (SGSSGNVGYGDYVS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 169 (GATNLAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 173 (ASYDSSSGGV);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 1 to 155 of SEQ ID NO: 1.

61. The specific binding molecule according to any one of claims 1, 2, or 59 to 60 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 259 (SNGVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 157 (DISSVGKKYANPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 161 (CRDGGVTYGYDIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 165 (SGSSGNVGYGDYVS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 169 (GATNLAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 173 (ASYDSSSGGV).

62. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 278 (DHAGTYGLGDRKD).

63. The specific binding molecule according to any one of claims 1, 2, or 62 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 279 (NYRVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 280 (NIRSGGTTWYNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 281 (DSSGDLYAYDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 282 (SGSSSNVGYGNYMA);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 141 (GATSRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 263 (ASYDSTSGGV);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 13 to 25 of SEQ ID NO: 25.

64. The specific binding molecule according to any one of claims 1, 2, or 62 to 63 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 279 (NYRVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 280 (NIRSGGTTWYNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 281 (DSSGDLYAYDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 282 (SGSSSNVGYGNYMA);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 141 (GATSRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 263 (ASYDSTSGGV).

65. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 283 (ADGKTKIATPRGA).

66. The specific binding molecule according to any one of claims 1, 2, or 62 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 198 (SNAVI);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 200 (LIDVDGDAAYDPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 202 (DYGSWGYVSDIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 292 (SGSYITGSSVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 284 (DNNDRPS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 285 (ASYDTSNIGL);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 145 to 157 of SEQ ID NO: 1.

67. The specific binding molecule according to any one of claims 1, 2, or 65 to 66 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 198 (SNAVI);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 200 (LIDVDGDAAYDPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 202 (DYGSWGYVSDIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 292 (SGSYITGSSVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 284 (DNNDRPS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 285 (ASYDTSNIGL).

68. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises:

i. an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 319 (TSKCGSLGNIHHK);

ii. the amino acid sequence of SEQ ID NO: 320 (XXXXGSLGNIXXX, wherein X is any amino acid); or

iii. the amino acid sequence of SEQ ID NO: 319, optionally wherein any one or more residue other than residue number 323 (G), 324 (S), 325 (L), 326 (G), 327 (N) and/or 328 (I) is replaced by a conservative amino acid substitution (numbering according to SEQ ID NO: 1).

69. The specific binding molecule according to any one of claims 1, 2, or 68 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 310 (NYPVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 311 (NIENDGSANYASALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 312 (EFGGSDGYTYFVDIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 313 (SGSSSNVGYGNYVS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 141 (GATSRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 314 (ASYDGSSSGV);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 319 to 331 of SEQ ID NO: 1.

70. The specific binding molecule according to any one of claims 1, 2, or 68 to 69 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 310 (NYPVG);
VHCDR2 comprises the sequence set forth in SEQ ID NO: 311 (NIENDGSANYASALKS);
VHCDR3 comprises the sequence set forth in SEQ ID NO: 312 (EFGGSDGYTYFVDIDY);
VLCDR1 comprises the sequence set forth in SEQ ID NO: 313 (SGSSSNVGYGNYVS);
VLCDR2 comprises the sequence set forth in SEQ ID NO: 141 (GATSRAS); and
VLCDR3 comprises the sequence set forth in SEQ ID NO: 314 (ASYDGSSSGV).

71. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 321 (KPGGGQVEVKSEKLDFKDRVQSKIGSLDNI).

72. The specific binding molecule according to any one of claims 1, 2, or 71 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 17 (SNAVG);
VHCDR2 comprises the sequence set forth in SEQ ID NO: 20 (GCSSDGKCYYNSALKS);
VHCDR3 comprises the sequence set forth in SEQ ID NO: 23 (GYYPVYGYDYLGTIDY);
VLCDR1 comprises the sequence set forth in SEQ ID NO: 25 (SGSSSNVGRNDVA);
VLCDR2 comprises the sequence set forth in SEQ ID NO: 28 (GTTSRPS); and
VLCDR3 comprises the sequence set forth in SEQ ID NO: 31 (ASGDSSAINDI);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or
(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 331 to 360 of SEQ ID NO: 1.

73. The specific binding molecule according to any one of claims 1, 2, or 71 to 72 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 17 (SNAVG);
VHCDR2 comprises the sequence set forth in SEQ ID NO: 20 (GCSSDGKCYYNSALKS);
VHCDR3 comprises the sequence set forth in SEQ ID NO: 23 (GYYPVYGYDYLGTIDY);
VLCDR1 comprises the sequence set forth in SEQ ID NO: 25 (SGSSSNVGRNDVA);
VLCDR2 comprises the sequence set forth in SEQ ID NO: 28 (GTTSRPS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 31 (ASGDSSAINDI).

74. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises:

i. an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 330 (GSLDNITHVPGGG);

ii. the amino acid sequence of SEQ ID NO: 331 (XXXDXITHXPXXX, wherein X is any amino acid); or

iii. the amino acid sequence of SEQ ID NO: 330, optionally wherein any one or more residue other than residue number 358 (D), 360 (I), 361 (T), 362 (H) and/or 364 (P) is replaced by a conservative amino acid substitution (numbering according to SEQ ID NO: 1).

75. The specific binding molecule according to any one of claims 1, 2, or 74 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 83 (SYSVY);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 84 (IMYASGRVDYNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 89 (GIEN);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 91 (RTSQSVNNYLS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 95 (YATRLYT); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 97 (LQYDSTPLA);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 355 to 367 of SEQ ID NO: 1.

76. The specific binding molecule according to any one of claims 1, 2, or 74 to 75 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 83 (SYSVY);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 84 (IMYASGRVDYNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 89 (GIEN);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 91 (RTSQSVNNYLS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 95 (YATRLYT); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 97 (LQYDSTPLA).

77. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at

least 95% or at least 99% identity to SEQ ID NO: 332 (NITHVPGGGNKKIETHKLTFRENAKAKTDHGAE).

78. The specific binding molecule according to any one of claims 1, 2, or 77 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 45 (TNSVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 53 (GIDTDGEEGFNPVLKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 55 (SYRTDGLAYGYVQAIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 68 (SGSYIGSSGVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 70 (ASDGRPS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 79 (GSSDRTQYTGL);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 350 to 391 of SEQ ID NO: 1.

79. The specific binding molecule according to any one of claims 1, 2, or 77 to 78 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 45 (TNSVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 53 (GIDTDGEEGFNPVLKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 55 (SYRTDGLAYGYVQAIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 68 (SGSYIGSSGVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 70 (ASDGRPS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 79 (GSSDRTQYTGL).

80. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 333 (ITHVPGGGNKKIETHKLTFRENAKAKTDHGA).

81. The specific binding molecule according to any one of claims 1, 2, or 80 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 334 (SVAVN);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 335 (GIISNGGTGYNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 336 (GVEWEGSMDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 337 (SGSSSNVGAGSYVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 338 (GATKRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 339 (VSYQTDFTLV);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 360 to 390 of SEQ ID NO: 1.

82. The specific binding molecule according to any one of claims 1, 2, or 80 to 81 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 334 (SVAVN);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 335 (GIISNGGTGYNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 336 (GVEWEGSMDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 337 (SGSSSNVGAGSYVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 338 (GATKRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 339 (VSYQTDFTLV).

83. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 351 (THKLTFRENAKAK).

84. The specific binding molecule according to any one of claims 1, 2, or 83 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 102 (RESIA);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 103 (GVGIDGTSYYSPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 104 (NYIDFEY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 352 (SGSSSNVGIYDVS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 353 (GTNNRPS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 354 (AAGDSSTIAV);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 373 to 385 of SEQ ID NO: 1.

85. The specific binding molecule according to any one of claims 1, 2, or 83 to 84 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 102 (RESIA);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 103 (GVGIDGTSYYSPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 104 (NYIDFEY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 352 (SGSSSNVGIYDVS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 353 (GTNNRPS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 354 (AAGDSSTIAV).

86. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 355 (VQIINKKLDLSNVQSKCGSKDNIKHVPGGGS) and/or SEQ ID NO: 356 (VEVKSEKLDFKDRVQSKIGSLDNITHVPGGGN).

87. The specific binding molecule according to any one of claims 1, 2, or 86 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 357 (SYGVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 358 (SISSGGTTFYNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 359 (DVHIYYNDYGAAYGDRDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 360 (SGSSSNIGGGNYVS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 361 (GTTSRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 362 (ASYDTNSGSV);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 275 to 305 and/or residues 337 to 368 of SEQ ID NO: 1.

88. The specific binding molecule according to any one of claims 1, 2, or 86 to 87 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 357 (SYGVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 358 (SISSGGTTFYNPALKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 359 (DVHIYYNDYGAAYGDRDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 360 (SGSSSNIGGGNYVS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 361 (GTTSRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 362 (ASYDTNSGSV).

89. The specific binding molecule according to any one of claims 1, 2, or 59 to 88 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising SEQ ID NO: 1 with a K_D of less than around 25 nM, optionally wherein the K_D for binding to SEQ ID NO: 1 is around 1 nM to around 20 nM.

90. The specific binding molecule according to any one of claims 1 or 2 wherein the epitope comprises an amino acid sequence having at least 70%, at least 75%, at least 80%, at least 90%, at least 95% or at least 99% identity to SEQ ID NO: 5 (IKHVPGGGSVQIVYKPVDLSKVTSKCGSLGNIHHKPGGGQVEVKSEKLDFKDRVQSKIGSLDNITH VPGGGNKKIETHKLTFRENAKAKTDHGA).

91. The specific binding molecule according to any one of claims 1, 2 or 90 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 297 to 390 of SEQ ID NO: 1 and the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 426 (S/T N/H S V G);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 427 (G I D T/S D G E E G Y/F N P A/V L N/K S);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 428 (S/T Y R A/T/S D G L/Y G Y V Q A I D Y);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 429 (S G S F/Y I G I/S S S/G V G);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 70 (A S D G R P S); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 432 (G S S D R T Q Y T G V/L);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto.

92. The specific binding molecule according to any one of claims 1, 2, or 90 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 42 (SNSVG), SEQ ID NO: 187 (SHSVG), SEQ ID NO: 45 (TNSVG), SEQ ID NO: 102 (RESIA), or SEQ ID NO: 199 (DYGIG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 46 (GIDTDGEEGYNPALNS), SEQ ID NO: 205 (GINYDGRTEYNSALKS), SEQ ID NO: 103 (GVGIDGTSYYSPALKS), SEQ ID NO: 53 (GIDTDGEEGFNPVLKS), or SED ID NO: 48 (GIDSDGEEGYNPALNS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 54 (SYRADGLAYGYVQAIDY), SEQ ID NO: 55 (SYRTDGLAYGYVQAIDY), SEQ ID NO: 210 (TYRSDGYAYGYVQAIDY), SEQ ID NO: 104 (NYIDFEY), or SEQ ID NO: 211 (DSKGGWGHVYQFDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 63 (SGSFIGISSVG), SEQ ID NO: 68 (SGSYIGSSGVG), SEQ ID NO: 212 (SGSNIGSASVT), or SEQ ID NO: 213 (SGSSSNVGYGDYVS);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 70 (ASDGRPS), SEQ ID NO: 214 (RNRNRPS), or SEQ ID NO: 215 (DATNRAS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 74 (GSSDRTQYTGV), SEQ ID NO: 79 (GSSDRTQYTGL), SEQ ID NO: 216 (ASHDNRISAV), or SEQ ID NO: 217 (GSYQSWGSGV);

or for each CDR sequence, an amino acid sequence with

(i) at least 85% identity thereto, and/or

(ii) one, two, or three amino acid substitutions relative thereto,

wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 297 to 390 of SEQ ID NO: 1.

93. The specific binding molecule according to any one of claims 1, 2, or 91 to 92 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 42 (SNSVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 46 (GIDTDGEEGYNPALNS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 54 (SYRADGLAYGYVQAIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 63 (SGSFIGISSVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 70 (ASDGRPS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 74 (GSSDRTQYTGV).

94. The specific binding molecule according to any one of claims 1, 2, or 91 to 92 wherein the specific binding molecule comprises the CDRs VHCDR1, VHCDR2, VHCDR3, VLCDR1, VLCDR2 and VLCDR3, wherein each of said CDRs comprises an amino acid sequence as follows:

VHCDR1 comprises the sequence set forth in SEQ ID NO: 45 (TNSVG);

VHCDR2 comprises the sequence set forth in SEQ ID NO: 53 (GIDTDGEEGFNPVLKS);

VHCDR3 comprises the sequence set forth in SEQ ID NO: 55 (SYRTDGLAYGYVQAIDY);

VLCDR1 comprises the sequence set forth in SEQ ID NO: 68 (SGSYIGSSGVG);

VLCDR2 comprises the sequence set forth in SEQ ID NO: 70 (ASDGRPS); and

VLCDR3 comprises the sequence set forth in SEQ ID NO: 79 (GSSDRTQYTGL).

95. The specific binding molecule according to any one of claims 1, 2, or 91 to 94 wherein the specific binding molecule binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 297 to 390 of SEQ ID NO: 1 with a K_D of less than around 25 nM, optionally wherein:

i. The K_D for binding to SEQ ID NO: 1 is around 500 pM to around 1 nM; or

ii. The K_D for binding to SEQ ID NO: 1 is around 1 nM to around 15 nM.

96. The specific binding molecule according to any one of claims 1 to 22, 51 to 58 and 68 to 95 wherein the specific binding molecule competes with the binding of:

a) a first region within residues 296 to 391 of SEQ ID NO: 1 to a second region within residues 296 to 391 of SEQ ID NO: 1; and/or
b) a first region within residues 296 to 390 of SEQ ID NO: 1 to a second region within residues 296 to 390 of SEQ ID NO: 1; and/or
c) a first region within residues 308 to 378 of SEQ ID NO: 1 to a second region within residues 308 to 378 of SEQ ID NO: 1.

97. The specific binding molecule according to claim 96 wherein the first and second region are within different polypeptide molecules, and wherein the specific binding molecule competes with the binding of:

a) a first polypeptide comprising residues 333 to 353 of SEQ ID NO: 1 to a second polypeptide comprising residues 333 to 353 of SEQ ID NO: 1;
b) a first polypeptide comprising residues 322 to 333 of SEQ ID NO: 1 to a second polypeptide comprising residues 322 to 333 of SEQ ID NO: 1;
c) a first polypeptide comprising residues 356 to 364 of SEQ ID NO: 1 to a second polypeptide comprising residues 356 to 364 of SEQ ID NO: 1;
d) a first polypeptide comprising residues 306 to 314 of SEQ ID NO: 1 to a second polypeptide comprising residues 306 to 314 of SEQ ID NO: 1; or
e) a first polypeptide comprising residues 369 to 378 of SEQ ID NO: 1 to a second polypeptide comprising residues 369 to 378 of SEQ ID NO: 1.

98. The specific binding molecule according to claim 96 wherein the first and second region are within the same polypeptide molecule, and wherein the specific binding molecule competes with the binding of:

a) residues 337 to 355 of SEQ ID NO: 1 to residues 337 to 355 of SEQ ID NO: 1;
b) residues 327 to 331 of SEQ ID NO: 1 to residues 356 to 363 of SEQ ID NO: 1;
c) residues 327 to 331 of SEQ ID NO: 1 to residues 356 to 363 of SEQ ID NO: 1;
d) residues 313 to 322 of SEQ ID NO: 1 to residues 368 to 378 of SEQ ID NO: 1; or
e) residues 306 to 311 of SEQ ID NO: 1 to residues 373 to 378 of SEQ ID NO: 1.

99. The specific binding molecule of any preceding claim, wherein the specific binding molecule is an antibody or a fragment thereof.

100. The specific binding molecule of claim 99, wherein the antibody or fragment thereof is humanised.

101. The specific binding molecule of any one of claims 99 or 100, wherein said specific binding molecule is an antibody, the antibody is a monoclonal antibody, or when said specific binding

molecule is a fragment of an antibody, said fragment is a Fab or $F(ab')_2$ antibody fragment, or an scFv molecule.

102. The specific binding molecule of any preceding claim, wherein the specific binding molecule binds to SEQ ID NO: 1 or a fragment thereof with a K_D of less than 10 nM.

103. A composition comprising a specific binding molecule according to any preceding claim, wherein at least 90% of the specific binding molecules in the composition that bind an epitope within SEQ ID NO: 1 bind with a K_D of less than 25 nM.

104. A nucleic acid molecule comprising a nucleic acid sequence encoding a specific binding molecule according to any one of claims 1 to 102.

105. A nucleic acid molecule according to claim 104 wherein the nucleic acid sequence is selected from the group consisting of SEQ ID Nos: 43, 219, 249, 251, 253, 380 to 411 and 431, or a nucleic acid sequence with at least 70% identity to any one of SEQ ID Nos: 43, 219, 249, 251, 253, 380 to 411 and 431.

106. A construct comprising a nucleic acid molecule according to claim 104 or claim 105.

107. A vector comprising a nucleic acid molecule of claim 104 or claim 105 or a construct of claim 106.

108. A host cell comprising a nucleic acid molecule of claim 104 or claim 105, a construct of the claim 106 or a vector of claim 107.

109. A method of preparing a specific binding molecule according to any one of claims 1 to 102 comprising:

i) introducing into a host cell a nucleic acid molecule of claim 104 or claim 105, a construct of the claim 106 or a vector of claim 107;

ii) expressing the nucleic acid molecule such that the specific binding molecule is produced; and

iii) collecting the specific binding molecule, preferably by purification.

110. A specific binding molecule obtainable by a method according to the claim 109.

111. A pharmaceutical composition comprising a specific binding molecule according any one of claims 1 to 102 or a composition according to claim 103 and one or more pharmaceutically acceptable diluents, carriers or excipients.

112. A specific binding molecule according to any one of claims 1 to 102, a composition according to claim 103 or a pharmaceutical composition according to claim 111 for use in therapy.

113. A specific binding molecule according to any one of claims 1 to 102, a composition according to claim 103 or a pharmaceutical composition according to claim 111 for use in treatment of a tauopathy.

114. A method of treating a tauopathy, comprising administering to a subject in need thereof a specific binding molecule according to any one of claims 1 to 102, a composition according to claim 103 or a pharmaceutical composition according to claim 111.

115. The specific binding molecule, composition or pharmaceutical composition for use according to claim 113 or the method of treating a tauopathy according to claim 114, wherein the tauopathy is selected from the group consisting of Alzheimer's disease, Primary age-related tauopathy (PART), Neurofibrillary tangle-predominant senile dementia, Chronic traumatic encephalopathy (CTE), Progressive supranuclear palsy (PSP), Corticobasal degeneration (CBD), Frontotemporal dementia (FTD), Frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17), Pick disease, disinhibition-dementia-parkinsonism-amyotrophy complex (DDPAC), pallido-ponto-nigral degeneration (PPND), Guam-ALS syndrome; pallido-nigro-luysian degeneration (PNLD), Dementia with Argyrophilic grains (AgD), Down's Syndrome (DS), dementia with Lewy bodies (DLB), Postencephalitic parkinsonism (PEP), Dementia pugilistica (DP), traumatic brain injury (TBI), stroke, ischemia, Lytico-bodig disease (Parkinson-dementia complex of Guam), Ganglioglioma, Gangliocytoma, Meningioangiomatosis, Postencephalitic parkinsonism, Subacute sclerosing panencephalitis (SSPE), Lead encephalopathy, tuberous sclerosis, Pantothenate kinase-associated neurodegeneration, lipofuscinosis and mild cognitive impairment (MCI).

116. An *in vitro* method of inhibiting aggregation of a tau protein or a fragment thereof comprising contacting the tau protein or a fragment thereof with a specific binding molecule according any one of claims 1 to 102.

117. An *in vitro* method for detecting a tau protein or a fragment thereof in a sample comprising contacting the sample with a specific binding molecule of any one of claims 1 to 102.

118. A diagnostic method comprising contacting a sample with a specific binding molecule of any one of claims 1 to 102.

119. The *in vitro* method for detecting a tau protein or a fragment thereof according to claim 117 or the diagnostic method according to claim 118, comprising contacting the sample with a first specific binding molecule that binds to an epitope within residues 296 to 391 of SEQ ID NO: 1 and

contacting the sample with a second specific binding molecule that binds to an epitope within SEQ ID NO: 1.

120. The *in vitro* method for detecting a tau protein or a fragment thereof according to claim 117 or 119, or the diagnostic method according to claim 118 or 119, comprising contacting the sample with at least one pair of first and second specific binding molecules, wherein the pair of first and second specific binding molecules are selected from the group consisting of:

a) A first specific binding molecule that binds to an epitope within residues 337 to 355 of SEQ ID NO: 1 and a second specific binding molecule that binds to an epitope within residues 367 to 379 of SEQ ID NO: 1;
b) A first specific binding molecule that binds to an epitope within residues 337 to 355 of SEQ ID NO: 1 and a second specific binding molecule that binds to an epitope within residues 379 to 391 of SEQ ID NO: 1; and
c) A first specific binding molecule that binds to an epitope within residues 337 to 355 of SEQ ID NO: 1 and a second specific binding molecule that binds to an epitope within residues 13 to 25 of SEQ ID NO: 1.

121. The *in vitro* method for detecting a tau protein or a fragment thereof according to any one of claims 117 or 119 to 120, or the diagnostic method according to any one of claims 118 to 120, comprising:

a) contacting the sample with a first pair of specific binding molecules comprising a specific binding molecule according to any one of claims 3 to 7 and a specific binding molecule according to any one of claims 8 to 18;
b) contacting the sample with a second pair of specific binding molecules comprising a specific binding molecule according to any one of claims 3 to 7 and a specific binding molecule according to any one of claims 50 to 58; and
c) contacting the sample with a third pair of specific binding molecules comprising a specific binding molecule according to any one of claims 3 to 7 and a specific binding molecule according to any one of claims 62 to 64;
wherein each pair of specific binding molecules is contacted to the sample in parallel.

122. The *in vitro* method for detecting a tau protein or a fragment thereof according to any one of claims 117 or 119 to 121, or the diagnostic method according to any one of claims 118 to 121, comprising:

a) contacting the sample with a first pair of specific binding molecules comprising a specific binding molecule according to claim 6 and a specific binding molecule according to claim 11;
b) contacting the sample with a second pair of specific binding molecules comprising a specific binding molecule according claim 6 and a specific binding molecule according to claim 54; and

c) contacting the sample with a third pair of specific binding molecules comprising a specific binding molecule according to claim 6 and a specific binding molecule according to claim 64; wherein each pair of specific binding molecules is contacted to the sample in parallel.

123. The *in vitro* method for detecting a tau protein or a fragment thereof according to any one of claims 117 or 119 to 122, or the diagnostic method according to any one of claims 118 to 122 wherein the sample is a plasma sample.

124. The *in vitro* method for detecting a tau protein or a fragment thereof according to any one of claims 117 or 119 to 123, or the diagnostic method according to any one of claims 118 to 123, further comprising a step of denaturing the tau protein or fragment thereof prior to contacting the sample with the specific binding molecule.

125. The diagnostic method according to any one of claims 118 to 124, comprising contacting a plasma sample with a pair of specific binding molecules comprising a first specific binding molecule according to any one of claims 3 to 7 and a second specific binding molecule according to any one of claims 8 to 18, wherein the tauopathy is Alzheimer's disease.

126. The diagnostic method according to any one of claims 118 to 125, comprising contacting a plasma sample with a pair of specific binding molecules comprising a first specific binding molecule according to claim 6 and a second specific binding molecule according to claim 11, wherein the tauopathy is Alzheimer's disease.

127. The *in vitro* method for detecting a tau protein or a fragment thereof according to any one of claims 117 or 119, or the diagnostic method according to any one of claims 118 to 119, comprising:

(a) contacting the sample with a first pair of specific binding molecules comprising a specific binding molecule according to any one of claims 3 to 7 and a specific binding molecule according to any one of claims 62 to 64; and/or

(b) contacting the sample with a first pair of specific binding molecules comprising a specific binding molecule according to any one of claims 8 to 18 and a specific binding molecule according to any one of claims 62 to 64.

128. The *in vitro* method for detecting a tau protein or a fragment thereof according to any one of claims 117 or 119, or the diagnostic method according to any one of claims 118 to 119, comprising:

(a) contacting the sample with a first pair of specific binding molecules comprising a specific binding molecule according to any one of claims 45 to 50 and a specific binding molecule according to any one of claims 62 to 64; and/or

(b) contacting the sample with a first pair of specific binding molecules comprising a specific binding molecule that binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 159 to 163 of SEQ ID NO: 1 and a specific binding molecule

according to any one of claims 62 to 64, optionally wherein the specific binding molecule that binds to a polypeptide or protein molecule comprising an amino acid sequence comprising residues 159 to 163 of SEQ ID NO: 1 is HT7.

129. A diagnostic device for use in a method according to any one of claims 117 to 128.

130. A kit comprising a specific binding molecule according to any one of claims 1 to 102 and reagents for detecting a tau protein or a fragment thereof in a sample.

CLAIMS

1. A specific binding molecule, in which the specific binding molecule comprises a VH domain comprising the sequence set forth in SEQ ID NO: 443 and a VL domain comprising the sequence set forth in SEQ ID NO: 444.

2. A specific binding molecule according to Claim 1, in which the specific binding molecule is an antibody or a fragment thereof, further optionally in which (a) the antibody or fragment thereof is humanised; and/or (b) in which the specific binding molecule is an antibody, the antibody is a monoclonal antibody, or when the specific binding molecule is a fragment of an antibody, the fragment is a Fab or $F(ab')_2$ antibody fragment, or an scFv molecule.

3. A composition comprising a specific binding molecule according to Claim 1 or 2, in which at least 90% of the specific binding molecules in the composition that bind an epitope within SEQ ID NO: 1 bind with a K_D of less than 25 nM.

4. A nucleic acid molecule comprising a nucleic acid sequence encoding a specific binding molecule according to Claim 1 or 2, optionally in which the nucleic acid sequence comprises the sequence set forth in SEQ ID No: 380.

5. A construct comprising a nucleic acid molecule according to Claim 4.

6. A vector comprising a nucleic acid molecule according to Claim 4 or a construct according to Claim 5.

7. A host cell comprising a nucleic acid molecule according to Claim 4, a construct according to Claim 5 or a vector according to Claim 6.

8. A method of preparing a specific binding molecule according to Claim 1 or 2 comprising:

(i) introducing into a host cell a nucleic acid molecule according to Claim 4, a construct according to Claim 5 or a vector according to Claim 6;

(ii) expressing the nucleic acid molecule such that the specific binding molecule is produced; and

(iii) collecting the specific binding molecule, preferably by purification.

9. A specific binding molecule obtainable by a method according to Claim 8.

10. A pharmaceutical composition comprising a specific binding molecule according to Claim 1 or 2 or a composition according to Claim 3 and one or more pharmaceutically acceptable diluents, carriers or excipients.

11. A specific binding molecule according to Claim 1 or 2, a composition according to Claim 3 or a pharmaceutical composition according to Claim 10 for use in a method of treating a tauopathy.

12. A specific binding molecule, composition or pharmaceutical composition for use according to Claim 11, in which the tauopathy is selected from the group consisting of Alzheimer's disease, Primary age-related tauopathy (PART), Neurofibrillary tangle-predominant senile dementia, Chronic traumatic encephalopathy (CTE), Progressive supranuclear palsy (PSP), Corticobasal degeneration (CBD), Frontotemporal dementia (FTD), Frontotemporal dementia and parkinsonism linked to chromosome 17 (FTDP-17), Pick disease, disinhibition-dementia-parkinsonism-amyotrophy complex (DDPAC), pallido-ponto-nigral degeneration (PPND), Guam-ALS syndrome; pallido-nigro-luysian degeneration (PNLD), Dementia with Argyrophilic grains (AgD), Down's Syndrome (DS), dementia with Lewy bodies (DLB), Postencephalitic parkinsonism (PEP), Dementia pugilistica (DP), traumatic brain injury (TBI), stroke, ischemia, Lytico-bodig disease (Parkinson-dementia complex of Guam), Ganglioglioma, Gangliocytoma, Meningioangiomatosis, Postencephalitic parkinsonism, Subacute sclerosing panencephalitis (SSPE), Lead encephalopathy, tuberous sclerosis, Pantothenate kinase-associated neurodegeneration, lipofuscinosis and mild cognitive impairment (MCI).

13. An *in vitro* method of inhibiting aggregation of a tau protein or a fragment thereof comprising contacting the tau protein or a fragment thereof with a specific binding molecule according to Claims 1 or 2.

14. An *in vitro* method for detecting a tau protein or a fragment thereof in a sample comprising contacting the sample with a specific binding molecule according to Claim 1 or 2.

15. A diagnostic method comprising contacting a sample with a specific binding molecule according to Claim 1 or 2.

16. An *in vitro* method for detecting a tau protein or a fragment thereof according to Claim 14 or a diagnostic method according to Claim 15, comprising contacting the sample with at least one pair of first and second specific binding molecules, in which the pair of first and second specific binding molecules are selected from the group consisting of:

(a) a first specific binding molecule according to Claim 1 or 2 and a second specific binding molecule that binds to an epitope within residues 367 to 379 of SEQ ID NO: 1;

(b) a first specific binding molecule according to Claim 1 or 2 and a second specific binding molecule that binds to an epitope within residues 379 to 391 of SEQ ID NO: 1; and

(c) a first specific binding molecule according to Claim 1 or 2 and a second specific binding molecule that binds to an epitope within residues 13 to 25 of SEQ ID NO: 1.

17. An *in vitro* method for detecting a tau protein or a fragment thereof according to Claim 14 or a diagnostic method according to Claim 15 in which:

(i) the sample is a plasma sample; and/or

(ii) the method further comprises a step of denaturing the tau protein or fragment thereof prior to contacting the sample with the specific binding molecule.

18. A diagnostic device for use in a method according to Claim 15, 16 or 17.

19. A kit comprising a specific binding molecule according to Claim 1 or 2 and reagents for detecting a tau protein or a fragment thereof in a sample.