~~New~~ Claims

1. A CD33 binding agent selected from

an antibody comprising a CDR1 of SeqID No: 1, a CDR2 of SeqID No: 15, a CDR3 of SeqID No: 29, a CDR4 of SeqID No: 43, a CDR5 of SeqID No: 57 and a CDR6 of SeqID No: 71,

an antibody comprising a CDR1 of SeqID No: 2, a CDR2 of SeqID No: 16, a CDR3 of SeqID No: 30, a CDR4 of SeqID No: 44, a CDR5 of SeqID No: 58 and a CDR6 of SeqID No: 72,

an antibody comprising a CDR1 of SeqID No: 3, a CDR2 of SeqID No: 17, a CDR3 of SeqID No: 31, a CDR4 of SeqID No: 45, a CDR5 of SeqID No: 59 and a CDR6 of SeqID No: 73,

an antibody comprising a CDR1 of SeqID No: 4, a CDR2 of SeqID No: 18, a CDR3 of SeqID No: 32, a CDR4 of SeqID No: 46, a CDR5 of SeqID No: 60 and a CDR6 of SeqID No: 74,

an antibody comprising a CDR1 of SeqID No: 5, a CDR2 of SeqID No: 19, a CDR3 of SeqID No: 33, a CDR4 of SeqID No: 47, a CDR5 of SeqID No: 61 and a CDR6 of SeqID No: 75,

an antibody comprising a CDR1 of SeqID No: 6, a CDR2 of SeqID No: 20, a CDR3 of SeqID No: 34, a CDR4 of SeqID No: 48, a CDR5 of SeqID No: 62 and a CDR6 of SeqID No: 76,

an antibody comprising a CDR1 of SeqID No: 7, a CDR2 of SeqID No: 21, a CDR3 of SeqID No: 35, a CDR4 of SeqID No: 49, a CDR5 of SeqID No: 63 and a CDR6 of SeqID No: 77,

an antibody comprising a CDR1 of SeqID No: 8, a CDR2 of SeqID No: 22, a CDR3 of SeqID No: 36, a CDR4 of SeqID No: 50, a CDR5 of SeqID No: 64 and a CDR6 of SeqID No: 78,

an antibody comprising a CDR1 of SeqID No: 9, a CDR2 of SeqID No: 23, a CDR3 of SeqID No: 37, a CDR4 of SeqID No: 51, a CDR5 of SeqID No: 65 and a CDR6 of SeqID No: 79,

an antibody comprising a CDR1 of SeqID No: 10, a CDR2 of SeqID No: 24, a CDR3 of SeqID No: 38, a CDR4 of SeqID No: 52, a CDR5 of SeqID No: 66 and a CDR6 of SeqID No: 80,

an antibody comprising a CDR1 of SeqID No: 11, a CDR2 of SeqID No: 25, a CDR3 of SeqID No: 39, a CDR4 of SeqID No: 53, a CDR5 of SeqID No: 67 and a CDR6 of SeqID No: 81,

an antibody comprising a CDR1 of SeqID No: 12, a CDR2 of SeqID No: 26, a CDR3 of SeqID No: 40, a CDR4 of SeqID No: 54, a CDR5 of SeqID No: 68 and a CDR6 of SeqID No: 82,

an antibody comprising a CDR1 of SeqID No: 13, a CDR2 of SeqID No: 27, a CDR3 of SeqID No: 41, a CDR4 of SeqID No: 55, a CDR5 of SeqID No: 69 and a CDR6 of SeqID No: 83,

an antibody comprising a CDR1 of SeqID No: 14, a CDR2 of SeqID No: 28, a CDR3 of SeqID No: 42, a CDR4 of SeqID No: 56, a CDR5 of SeqID No: 70 and a CDR6 of SeqID No: 84.

2. A CD33 binding agent selected from

an antibody comprising a heavy chain variable region of SeqID No: 85 and a light chain variable region of SeqID No: 99,

an antibody comprising a heavy chain variable region of SeqID No: 86 and a light chain variable region of SeqID No: 100,

an antibody comprising a heavy chain variable region of SeqID No: 87 and a light chain variable region of SeqID No: 101,

an antibody comprising a heavy chain variable region of SeqID No: 88 and a light chain variable region of SeqID No: 102,

an antibody comprising a heavy chain variable region of SeqID No: 89 and a light chain variable region of SeqID No: 103,

an antibody comprising a heavy chain variable region of SeqID No: 90 and a light chain variable region of SeqID No: 104,

an antibody comprising a heavy chain variable region of SeqID No: 91 and a light chain variable region of SeqID No: 105,

an antibody comprising a heavy chain variable region of SeqID No: 92 and a light chain variable region of SeqID No: 106,

an antibody comprising a heavy chain variable region of SeqID No: 93 and a light chain variable region of SeqID No: 107,

an antibody comprising a heavy chain variable region of SeqID No: 94 and a light chain variable region of SeqID No: 108,

an antibody comprising a heavy chain variable region of SeqID No: 95 and a light chain variable region of SeqID No: 109,

an antibody comprising a heavy chain variable region of SeqID No: 96 and a light chain variable region of SeqID No: 110,

an antibody comprising a heavy chain variable region of SeqID No: 97 and a light chain variable region of SeqID No: 111,

an antibody comprising a heavy chain variable region of SeqID No: 98 and a light chain variable region of SeqID No: 112.

3. A CD33 binding agent selected from

an antibody comprising a heavy chain of SeqID No: 113 and a light chain of SeqID No: 127,

an antibody comprising a heavy chain of SeqID No: 114 and a light chain of SeqID No: 128,

an antibody comprising a heavy chain of SeqID No: 115 and a light chain of SeqID No: 129,

an antibody comprising a heavy chain of SeqID No: 116 and a light chain of SeqID No: 130,

an antibody comprising a heavy chain of SeqID No: 117 and a light chain of SeqID No: 131,

an antibody comprising a heavy chain of SeqID No: 118 and a light chain of SeqID No: 132,

an antibody comprising a heavy chain of SeqID No: 119 and a light chain of SeqID No: 133,

an antibody comprising a heavy chain of SeqID No: 120 and a light chain of SeqID No: 134,

an antibody comprising a heavy chain of SeqID No: 121 and a light chain of SeqID No: 135, an antibody comprising a heavy chain of SeqID No: 122 and a light chain of SeqID No: 136, an antibody comprising a heavy chain of SeqID No: 123 and a light chain of SeqID No: 137, an antibody comprising a heavy chain of SeqID No: 124 and a light chain of SeqID No: 138, an antibody comprising a heavy chain of SeqID No: 125 and a light chain of SeqID No: 139, an antibody comprising a heavy chain of SeqID No: 126 and a light chain of SeqID No: 140. ~~A CD33 binding agent binding to human CD33, the CD33 binding agent being defined by binding to an epitope within the amino acid sequence FFHPIPYYDKNSPVHGYW (SeqID No: 141) of human CD33.~~

~~2. A CD 33 binding agent according to claim 1, characterized in that having a heavy chain variable region comprising CDR1, CDR2 and CDR3, and a light chain variable region comprising CDR4, CDR5 and CDR6, wherein CDR1 has an amino acid sequence selected from SeqID No:1-14, CDR2 has an amino acid sequence selected from SeqID No:15-28, CDR3 has an amino acid sequence selected from SeqID No:29-42, CDR4 has an amino acid sequence selected from SeqID No:43-56, CDR5 has an amino acid sequence selected from SeqID No:57-70, CDR6 has an amino acid sequence selected from SeqID No:71-84~~

~~3. A CD33 binding agent according to claim 1 or 2, wherein the epitope is determined by Hydrogen Exchange Mass Spectroscopy.~~

~~4. A CD33 binding agent according to to any of the preceding claims, wherein the internalization kinetics of the CD33 binding agents are such that at least 40% of the initial amount of the CD33 binding agents remain on the cell surface at a time of 4 hours after incubation.~~

~~5. A CD33 binding agent according to any of the preceding claims, wherein the heavy chain variable region comprises an amino acid sequence selected from SeqID No:85-98 and the light chain variable region comprises an amino acid sequence selected from SeqID No:99-112.~~

~~6. A CD33 binding agent according to any of the preceding claims, wherein the CD33 binding agent has a heavy chain having an amino acid sequence selected from SeqID No:113-126 and a light chain having an amino acid sequence selected from SeqID No:127-140.~~

~~7~~4. A CD33 binding agent according to any of the preceding claims, wherein the CD33 binding agent has an affinity to both human CD33 and cynomolgus CD33 with a K_D of equal to or less than 10 nM.

~~8~~5. A CD33 binding agent according to any of the preceding claims, wherein the CD33 binding agent is humanized.

~~9~~6. A CD33 binding agent according to any of the preceding claims, wherein the CD33 binding agent is fully human.

~~10~~7. A CD33 binding agent according to any of the preceding claims, wherein the CD33 binding agent further comprises an effector function.

~~11~~8. A CD33 binding agent according to claim ~~10~~7, wherein the effector function is mediated by an F_c domain.

~~12~~9. A CD33 binding agent according to claim ~~10~~7 or claim 8, wherein the CD33 binding agent comprises one or more mutations in the F_c domain that modulate the function of the F_c domain.

~~13~~10. A CD33 binding agent according to claim ~~12~~9, wherein the modulation of the function of the Fc domain is an increase of ADCC by at least 10%~~, preferably 50% and more preferably 100%~~.

~~14~~11. A CD33 binding agent according to any of claim ~~12~~9-~~13~~ and 10, wherein the mutations in the F_c domain are located at one or more positions selected from amino acids at positions 332 and/or 239 and/or 236 according to the Kabat EU numbering index.

~~15~~12. A CD33 binding agent according to any of claim ~~12~~9-~~14~~11, wherein the mutations in the F_c domain are a combination of substitutions at positions 239 and 332~~, preferably S239D/I332E~~.

~~16. A CD33 binding agent selected from an antibody comprising a CDR1 of SeqID No: 1, a CDR2 of SeqID No: 15, a CDR3~~

~~of SeqID No: 29, a CDR4 of SeqID No: 43, a CDR5 of SeqID No: 57 and a CDR6 of SeqID No: 71,~~

~~an antibody comprising a CDR1 of SeqID No: 2, a CDR2 of SeqID No: 16, a CDR3 of SeqID No: 30, a CDR4 of SeqID No: 44, a CDR5 of SeqID No: 58 and a CDR6 of SeqID No: 72,~~

~~an antibody comprising a CDR1 of SeqID No: 3, a CDR2 of SeqID No: 17, a CDR3 of SeqID No: 31, a CDR4 of SeqID No: 45, a CDR5 of SeqID No: 59 and a CDR6 of SeqID No: 73,~~

~~an antibody comprising a CDR1 of SeqID No: 4, a CDR2 of SeqID No: 18, a CDR3 of SeqID No: 32, a CDR4 of SeqID No: 46, a CDR5 of SeqID No: 60 and a CDR6 of SeqID No: 74,~~

~~an antibody comprising a CDR1 of SeqID No: 5, a CDR2 of SeqID No: 19, a CDR3 of SeqID No: 33, a CDR4 of SeqID No: 47, a CDR5 of SeqID No: 61 and a CDR6 of SeqID No: 75,~~

~~an antibody comprising a CDR1 of SeqID No: 6, a CDR2 of SeqID No: 20, a CDR3 of SeqID No: 34, a CDR4 of SeqID No: 48, a CDR5 of SeqID No: 62 and a CDR6 of SeqID No: 76,~~

~~an antibody comprising a CDR1 of SeqID No: 7, a CDR2 of SeqID No: 21, a CDR3 of SeqID No: 35, a CDR4 of SeqID No: 49, a CDR5 of SeqID No: 63 and a CDR6 of SeqID No: 77,~~

~~an antibody comprising a CDR1 of SeqID No: 8, a CDR2 of SeqID No: 22, a CDR3 of SeqID No: 36, a CDR4 of SeqID No: 50, a CDR5 of SeqID No: 64 and a CDR6 of SeqID No: 78,~~

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~~an antibody comprising a CDR1 of SeqID No: 10, a CDR2 of SeqID No: 24, a CDR3 of SeqID No: 38, a CDR4 of SeqID No: 52, a CDR5 of SeqID No: 66 and a CDR6 of SeqID No: 80,~~

~~an antibody comprising a CDR1 of SeqID No: 11, a CDR2 of SeqID No: 25, a CDR3 of SeqID No: 39, a CDR4 of SeqID No: 53, a CDR5 of SeqID No: 67 and a CDR6 of SeqID No: 81,~~

~~an antibody comprising a CDR1 of SeqID No: 12, a CDR2 of SeqID No: 26, a CDR3 of SeqID No: 40, a CDR4 of SeqID No: 54, a CDR5 of SeqID No: 68 and a CDR6 of~~

SeqID No: 82,

an antibody comprising a CDR1 of SeqID No: 13, a CDR2 of SeqID No: 27, a CDR3 of SeqID No: 41, a CDR4 of SeqID No: 55, a CDR5 of SeqID No: 69 and a CDR6 of SeqID No: 83,

an antibody comprising a CDR1 of SeqID No: 14, a CDR2 of SeqID No: 28, a CDR3 of SeqID No: 42, a CDR4 of SeqID No: 56, a CDR5 of SeqID No: 70 and a CDR6 of SeqID No: 84.

17. A CD33 binding agent selected from

an antibody comprising a heavy chain variable region of SeqID No: 85 and a light chain variable region of SeqID No: 99,

an antibody comprising a heavy chain variable region of SeqID No: 86 and a light chain variable region of SeqID No: 100,

an antibody comprising a heavy chain variable region of SeqID No: 87 and a light chain variable region of SeqID No: 101,

an antibody comprising a heavy chain variable region of SeqID No: 88 and a light chain variable region of SeqID No: 102,

an antibody comprising a heavy chain variable region of SeqID No: 89 and a light chain variable region of SeqID No: 103,

an antibody comprising a heavy chain variable region of SeqID No: 90 and a light chain variable region of SeqID No: 104,

an antibody comprising a heavy chain variable region of SeqID No: 91 and a light chain variable region of SeqID No: 105,

an antibody comprising a heavy chain variable region of SeqID No: 92 and a light chain variable region of SeqID No: 106,

an antibody comprising a heavy chain variable region of SeqID No: 93 and a light chain variable region of SeqID No: 107,

an antibody comprising a heavy chain variable region of SeqID No: 94 and a light chain variable region of SeqID No: 108,

an antibody comprising a heavy chain variable region of SeqID No: 95 and a light chain variable region of SeqID No: 109,

an antibody comprising a heavy chain variable region of SeqID No: 96 and a light chain variable region of SeqID No: 110,

an antibody comprising a heavy chain variable region of SeqID No: 97 and a light

chain variable region of SeqID No: 111,

an antibody comprising a heavy chain variable region of SeqID No: 98 and a light chain variable region of SeqID No: 112.

18. A CD33 binding agent selected from

an antibody comprising a heavy chain of SeqID No: 113 and a light chain of SeqID No: 127,

an antibody comprising a heavy chain of SeqID No: 114 and a light chain of SeqID No: 128,

an antibody comprising a heavy chain of SeqID No: 115 and a light chain of SeqID No: 129,

an antibody comprising a heavy chain of SeqID No: 116 and a light chain of SeqID No: 130,

an antibody comprising a heavy chain of SeqID No: 117 and a light chain of SeqID No: 131,

an antibody comprising a heavy chain of SeqID No: 118 and a light chain of SeqID No: 132,

an antibody comprising a heavy chain of SeqID No: 119 and a light chain of SeqID No: 133,

an antibody comprising a heavy chain of SeqID No: 120 and a light chain of SeqID No: 134,

an antibody comprising a heavy chain of SeqID No: 121 and a light chain of SeqID No: 135,

an antibody comprising a heavy chain of SeqID No: 122 and a light chain of SeqID No: 136,

an antibody comprising a heavy chain of SeqID No: 123 and a light chain of SeqID No: 137,

an antibody comprising a heavy chain of SeqID No: 124 and a light chain of SeqID No: 138,

an antibody comprising a heavy chain of SeqID No: 125 and a light chain of SeqID No: 139,

an antibody comprising a heavy chain of SeqID No: 126 and a light chain of SeqID No: 140.

13. A CD33 binding agent according to claim 12, wherein said mutation in the Fc domain is a combination of mutations of S239D and I332E.

~~19~~14. A DNA molecule comprising a region encoding the heavy chain variable region of a CD33 binding agent according to any of the preceding claims.

~~20~~15. A DNA molecule comprising a region encoding the light chain variable region of a CD33 binding agent according to any of claims 1~~-18~~ to 13.

~~21~~16. An expression vector containing a DNA molecule of claim ~~19-~~14 or ~~20~~15.

~~22~~17. A host cell carrying ~~one or more vectors of~~a DNA molecule according to claim ~~21~~14 and a DNA molecule according to claim 15.

~~23~~18. A method for producing a CD33 binding agent of any one of claims 1~~-18~~ to 13, comprising transfecting a host cell with one or more vectors of claim ~~21~~16, culturing the host cell and recovering and purifying the antibody molecule.

~~24~~19. A pharmaceutical composition comprising, as the active ingredient, one or more CD33 binding agents according to any one of claims 1 to ~~18~~13, and at least a physiologically acceptable carrier.

~~25~~20. The pharmaceutical composition of claim ~~24~~19, further comprising one or more additional therapeutic agents.

~~26~~21. The pharmaceutical composition of any one of claims ~~24-25~~19 and 20 for depleting cells that express CD33 on their surface.

~~27~~22. The pharmaceutical composition of any one of claims ~~24-25~~19 and 20 for the treatment of myeloid cell malignancies and myelodysplastic syndrome (MDS).

~~28~~23. The pharmaceutical composition of claim ~~27~~22, wherein said myeloid malignancy is selected from acute myeloid leukemia and chronic myeloid leukemia.

~~29~~24. The pharmaceutical composition of any one of claims ~~24-25~~19 and 20 for the treatment of autoimmune and inflammatory diseases that involve myeloid cells in their pathology.

~~30~~25. Use of one or more CD33 binding agents according to any one of claims 1 to ~~18~~ 13 or a pharmaceutical composition according to any one of claims ~~24~~ 19 to ~~25~~ 20 in the manufacture of a medicament for the depletion of CD33 expressing myeloid cells in a patient.