CLAIMS

[Claim 1]. An anti-human transferrin receptor antibody, wherein in the heavy chain variable region of the antibody,

(a) CDR1 comprises the amino acid sequence set forth as SEQ ID NO: 62 or SEQ ID NO: 63,

(b) CDR2 comprises the amino acid sequence set forth as SEQ ID NO: 13 or SEQ ID NO: 14, and

(c) CDR3 comprises the amino acid sequence set forth as SEQ ID NO: 15 or SEQ ID NO: 16, and

in the light chain variable region of the antibody,

(a) CDR1 comprises the amino acid sequence set forth as SEQ ID NO: 6 or SEQ ID NO: 7,

(b) CDR2 comprises the amino acid sequence set forth as SEQ ID NO: 8 or SEQ ID NO: 9, or the amino acid sequence Lys-Val-Ser, and

(c) CDR3 comprises the amino acid sequence set forth as SEQ ID NO: 10,

wherein the framework region 3 of the heavy chain comprises the amino acid sequence set forth as SEQ ID NO: 64.

[Claim 2]. The antibody according to claim 1, wherein the heavy chain variable region comprises the amino acid sequence set forth as SEQ ID NO: 65.

[Claim 3]. The antibody according to claim 2, wherein the heavy chain comprises the amino acid sequence set forth as SEQ ID NO: 66 or

SEQ ID NO: 68.

[Claim 4]. The antibody according to claim 1, wherein the light chain variable region of the antibody comprises the amino acid sequence set forth as SEQ ID NO: 17, SEQ ID NO: 18, SEQ ID NO: 19, SEQ ID NO: 20, SEQ ID NO: 21 or SEQ ID NO: 22.

[Claim 5]. The antibody according to claim 1, wherein the light chain of the antibody comprises the amino acid sequence set forth as SEQ ID NO: 23, SEQ ID NO: 25, SEQ ID NO: 27 or SEQ ID NO: 29.

[Claim 6]. The antibody according to any one of claims 1 to 5, wherein the antibody has an affinity to both the extracellular region of human transferrin receptor and the extracellular region of monkey transferrin receptor.

[Claim 7]. The antibody according to claim 6, wherein the dissociation constant of its complex with the extracellular region of human transferrin receptor is not greater than 1×10^{-10} M, and the dissociation constant of its complex with the extracellular region of monkey transferrin receptor is not greater than 1×10^{-9} M.

[Claim 8]. The antibody according to claim 1, wherein the antibody is Fab antibody, $F(ab')_2$ antibody, or F(ab') antibody.

[Claim 9]. The anti-human transferrin receptor antibody according to

claim 1, wherein the antibody is a single-chain antibody selected from the group consisting of scFab, scF(ab'), scF(ab')$_2$ and scFv.

[Claim 10].The antibody according to claim 9, wherein the light chain and the heavy chain of the antibody are linked via a linker sequence.

[Claim 11]. The antibody according to claim 10, wherein the heavy chain is linked, via a linker sequence, to the light chain on the C-terminal side of the light chain.

[Claim 12]. The antibody according to claim 9, wherein the light chain is linked, via a linker sequence, to the heavy chain on the C-terminal side of the heavy chain.

[Claim 13]. The antibody according to claim 10, wherein the linker sequence consists of 2 to 50 amino acid residues.

[Claim 14]. The antibody according to claim 13, wherein the linker sequence is selected from the group consisting of the amino acid sequence Gly-Ser, the amino acid sequence Gly-Gly-Ser, the amino acid sequence Gly-Gly-Gly, the amino acid sequences set forth as SEQ ID NO: 3, SEQ ID NO: 4, and SEQ ID NO: 5, the amino acid sequence consisting of three consecutively linked amino acid sequences each set forth as SEQ ID NO: 3, and the amino acid sequences consisting of 2 to 10 repeats of any of the aforementioned sequences that are consecutively linked.

[Claim 15]. A fusion protein comprising an anti-human transferrin receptor antibody and a different protein (A),

wherein the anti-human transferrin receptor antibody is the antibody according to any one of claims 1 to 14, and

wherein the protein (A) is linked to the light chain of the antibody on the C-terminal side or the N-terminal side of the light chain.

[Claim 16]. The fusion protein according to claim 15, wherein the protein (A) is linked, directly or via a linker, to the light chain on the C-terminal side or the N-terminal side of the light chain.

[Claim 17]. The fusion protein according to claim 15, wherein the protein (A) is linked, via a linker, to the light chain on the C-terminal side or the N-terminal side of the light chain.

[Claim 18]. The fusion protein according to claim 17, wherein the linker is a peptide consisting of 1 to 50 amino acid residues.

[Claim 19]. The fusion protein according to claim 18, wherein the linker is a peptide comprising an amino acid sequence selected from the group consisting of a single glycine, a single serine, the amino acid sequence Gly-Ser, the amino acid sequence Gly-Gly-Ser, the amino acid sequence set forth as SEQ ID NO: 3, the amino acid sequence set forth as SEQ ID NO: 4, the amino acid sequence set forth as SEQ ID NO: 5, and the amino acid sequences consisting of 2 to 10 of any of the aforementioned sequences that are consecutively linked.

[Claim 20]. A fusion protein of an anti-human transferrin receptor antibody and a different protein (A),

wherein the anti-human transferrin receptor antibody is the antibody according to any one of claims 1 to 14, and

wherein the protein (A) is linked to the heavy chain of the antibody on the C-terminal side or the N-terminal side of the heavy chain.

[Claim 21]. The fusion protein according to claim 20, wherein the protein (A) is linked, directly or via a linker, to the heavy chain on the C-terminal side or the N-terminal side of the heavy chain.

[Claim 22]. The fusion protein according to claim 20, wherein the protein (A) is linked, via a linker, to the heavy chain on the C-terminal side or the N-terminal side of the heavy chain.

[Claim 23]. The fusion protein according to claim 22, wherein the linker sequence is a peptide consisting of 1 to 50 amino acid residues.

[Claim 24]. The fusion protein according to claim 23, wherein the linker is a peptide comprising an amino acid sequence selected from the group consisting of a single glycine, a single serine, the amino acid sequence Gly-Ser, the amino acid sequence Gly-Gly-Ser, the amino acid sequence set forth as SEQ ID NO: 3, the amino acid sequence set forth as SEQ ID NO: 4, the amino acid sequence set forth as SEQ ID NO: 5, and the amino acid sequences consisting of 2 to 10 of any of the

aforementioned sequences that are consecutively linked.

[Claim 25]. The fusion protein according to any one of claims 15 to 24, wherein the protein (A) is a protein originating from human.

[Claim 26]. The fusion protein according to any one of claims 15 to 24, wherein the protein (A) is selected from the group consisting of nerve growth factor (NGF), lysosomal enzymes, ciliary neurotrophic factor (CNTF), glial cell line-derived neurotrophic factor (GDNF), neurotrophin-3, neurotrophin-4/5, neurotrophin-6, neuregulin-1, erythropoietin, darbepoetin, activin, basic fibroblast growth factor (bFGF), fibroblast growth factor 2 (FGF2), epidermal growth factor (EGF), vascular endothelial growth factor (VEGF), interferon α, interferon β, interferon γ, interleukin 6, granulocyte-macrophage colony stimulating factor (GM-CSF), granulocyte colony stimulating factor (G-CSF), macrophage colony stimulating factor (M-CSF), cytokines, tumor necrosis factor α receptor (TNF-α receptor), PD-L1, and PD-L2.

[Claim 27]. The fusion protein according to any one of claims 15 to 24, wherein the protein (A) is a lysosomal enzyme, wherein the lysosomal enzyme is selected from the group consisting of α-L-iduronidase, iduronate 2-sulfatase, human acidic α-glucosidase, glucocerebrosidase, β-galactosidase, GM2 activator protein, β-hexosaminidase A, β-hexosaminidase B, N-acetylglucosamine-1-phosphotransferase, α-mannosidase, β-mannosidase, galactosylceramidase, saposin C, arylsulfatase A, α-L-fucosidase, aspartylglucosaminidase,

α-N-acetylgalactosaminidase, acidic sphingomyelinase, α-galactosidase A, β-glucuronidase, heparan N-sulfatase, α-N-acetylglucosaminidase, acetyl CoA:α- glucosaminide N-acetyltransferase, N-acetylglucosamine-6-sulfate sulfatase, acid ceramidase, amylo-1,6-glucosidase, sialidase, palmitoyl protein thioesterase 1, tripeptidyl-peptidase 1, hyaluronidase 1, CLN1 and CLN2.

[Claim 28]. The fusion protein according to any one of claims 15 to 24, wherein the protein (A) is human iduronate 2-sulfatase, human acidic α-glucosidase, or human α-L-iduronidase.

[Claim 29]. The fusion protein according to claim 20, wherein the protein (A) is human acidic α-glucosidase, wherein

(1) the light chain of the antibody comprises the amino acid sequence set forth as SEQ ID NO: 23, and

(2) the heavy chain of the antibody is linked, on the C-terminal side of the heavy chain and via the amino acid sequence Gly-Ser, to the human acidic α-glucosidase, thereby forming the amino acid sequence set forth as SEQ ID NO: 57 or SEQ ID NO: 58.

[Claim 30]. The fusion protein according to claim 20, wherein the protein (A) is human acidic α-glucosidase, wherein

(1) the light chain of the antibody comprises the amino acid sequence set forth as SEQ ID NO: 23, and

(2) the heavy chain of the antibody comprises the amino acid sequence set forth as SEQ ID NO: 66 or SEQ ID NO: 68, and the heavy

chain is linked, on the C-terminal side of the heavy chain and via the amino acid sequence Gly-Ser, to the human acidic α-glucosidase having the amino acid sequence set forth as SEQ ID NO: 55 or 56.

[Claim 31]. The fusion protein according to claim 20, wherein the protein (A) is human acidic α-glucosidase, wherein the antibody is Fab antibody, and wherein

(1) the light chain of the antibody comprises the amino acid sequence set forth as SEQ ID NO: 23, and

(2) the heavy chain of the antibody is linked, on the C-terminal side of the heavy chain and via the amino acid sequence consisting of three consecutively linked amino acid sequences each set forth as SEQ ID NO: 3, to the human acidic α-glucosidase, thereby forming the amino acid sequence set forth as SEQ ID NO: 89.

[Claim 32]. The fusion protein according to claim 20, wherein the protein (A) is human acidic α-glucosidase, wherein the antibody is Fab antibody, and wherein

(1) the light chain of the antibody comprises the amino acid sequence set forth as SEQ ID NO: 23, and

(2) the heavy chain of the antibody comprises the amino acid sequence set forth as SEQ ID NO: 61, and the heavy chain is linked, on the C-terminal side of the heavy chain and via the amino acid sequence consisting of three consecutively linked amino acid sequences each set forth as SEQ ID NO: 3, to the human acidic α-glucosidase having the amino acid sequence set forth as SEQ ID NO: 55 or 56.

[Claim 33]. The fusion protein according to claim 20, wherein the protein (A) is human α-L-iduronidase, wherein the antibody is Fab antibody, and wherein

(1) the light chain of the antibody comprises the amino acid sequence set forth as SEQ ID NO: 23, and

(2) the heavy chain of the antibody is linked, on the C-terminal side of the heavy chain and via the amino acid sequence consisting of three consecutively linked amino acid sequences each set forth as SEQ ID NO: 3, to the human α-L-iduronidase, thereby forming the amino acid sequence set forth as SEQ ID NO: 93.

[Claim 34]. The fusion protein according to claim 20, wherein the protein (A) is human α-L-iduronidase, wherein the antibody is Fab antibody, and wherein

(1) the light chain of the antibody comprises the amino acid sequence set forth as SEQ ID NO: 23, and

(2) the heavy chain of the antibody comprises the amino acid sequence set forth as SEQ ID NO: 61, and the heavy chain is linked, on the C-terminal side of the heavy chain and via the amino acid sequence consisting of three consecutively linked amino acid sequences each set forth as SEQ ID NO: 3, to the human α-L-iduronidase having the amino acid sequence set forth as SEQ ID NO: 75 or 76.

[Claim 35]. The fusion protein according to claim 15 or 20, wherein a human IgG Fc region or part of the human IgG Fc region is introduced between the protein (A) and the antibody.

[Claim 36]. The fusion protein according to claim 35, wherein the human IgG Fc region is linked, directly or via a linker sequence, to the protein (A) on the C-terminal side of the protein (A), and the heavy chain or the light chain of the antibody is linked, directly or via a linker sequence, to the human IgG Fc region on the C-terminal side of the human IgG Fc region.

[Claim 37]. The fusion protein according to claim 35, wherein the human IgG Fc region comprises the amino acid sequence set forth as SEQ ID NO: 70.

[Claim 38]. The fusion protein according to claim 37, wherein the human IgG Fc region is linked, via a linker sequence, to a Fab heavy chain consisting of the amino acid sequence set forth as SEQ ID NO: 61, and comprises the amino acid sequence set forth as SEQ ID NO: 71 formed thereby.

[Claim 39]. A DNA fragment encoding the amino acid sequence of the anti-human transferrin receptor antibody according to any one of claims 1 to 14.

[Claim 40]. A DNA fragment encoding the amino acid sequence of the fusion protein according to any one of claims 15 to 38.

[Claim 41]. An expression vector comprising the DNA fragment

according to claim 39 or 40 that is incorporated therein.

[Claim 42]. A mammalian cell transformed with the expression vector according to claim 41.

[Claim 43]. Use of the anti-human transferrin receptor antibody according to any one of claims 1 to 14 in the production of a pharmaceutical agent by linking thereto the molecule of a physiologically active protein or a pharmacologically active low-molecular-weight compound for the treatment of a disease condition of the central nervous system, wherein the pharmaceutical agent is to be parenterally administered.

[Claim 44]. Use of the fusion protein according to any one of claims 15 to 32 and 35 to 38 for the production of a pharmaceutical agent for the treatment of a disease condition of the central nervous system accompanying Pompe's disease, wherein the protein (A) is human acidic α-glucosidase, and wherein the pharmaceutical agent is to be parenterally administered.

[Claim 45]. Use of the fusion protein according to any one of claims 15 to 28 and 33 to 38, for the production of a pharmaceutical agent for the treatment of a disease condition of the central nervous system accompanying Hurler syndrome or Hurler-Scheie syndrome, wherein the protein (A) is human α-L-iduronidase, and wherein the pharmaceutical agent is to be parenterally administered.