## CLAIMS

[Claim 1]

A fusion protein comprising a humanized anti-human transferrin receptor antibody and the amino acid sequence of iduronate 2-sulfatase linked to the light chain of the antibody on the C-terminal side or the N-terminal side of the light chain, or linked to the heavy chain of the antibody on the C-terminal side or the N-terminal side of the heavy chain, wherein the light chain variable region and the heavy chain variable region of the antibody are selected from (1) or (2) below:

(1) the light chain variable region comprising the amino acid sequence having a homology not lower than 90% to the amino acid sequence set forth as SEQ ID NO:191, and comprising the amino acid sequence set forth as SEQ ID NO:16 as CDR1, the amino acid sequence set forth as SEQ ID NO:18 as CDR2, and the amino acid sequence set forth as SEQ ID NO:20 as CDR3; and the heavy chain variable region comprising the amino acid sequence having a homology not lower than 90% to the amino acid sequence set forth as SEQ ID NO:205, and comprising the amino acid sequence set forth as SEQ ID NO:88 as CDR1, the amino acid sequence set forth as SEQ ID NO:90 as CDR2, and the amino acid sequence set forth as SEQ ID NO:92 as CDR3;

(2) the light chain variable region comprising the amino acid sequence having a homology not lower than 90% to the amino acid sequence set forth as SEQ ID NO:191, and comprising the amino acid sequence set forth as SEQ ID NO:16 as CDR1, the amino acid sequence set forth as SEQ ID NO:18 as CDR2, and the amino acid sequence set forth as SEQ ID NO:20 as CDR3; and the heavy chain variable region comprising the amino acid sequence having a homology not lower than 90% to the amino acid sequence set forth as SEQ ID NO:205, and comprising the amino acid sequence set forth as SEQ

ID NO:89 as CDR1, the amino acid sequence set forth as SEQ ID NO:90 as CDR2, and the amino acid sequence set forth as SEQ ID NO:92 as CDR3.

[Claim 2]

A fusion protein comprising an anti-human transferrin receptor antibody and the amino acid sequence of iduronate 2-sulfatase, wherein the amino acid sequence of the antibody is selected from the group consisting of (1) to (4) below:

(1) an antibody, wherein the light chain variable region thereof comprises the amino acid sequence set forth as SEQ ID NO:191; and wherein the heavy chain variable region thereof comprises the amino acid sequence set forth as SEQ ID NO:205,

(2) an antibody, wherein the light chain variable region thereof comprises the amino acid sequence set forth as SEQ ID NO:193; and wherein the heavy chain variable region thereof comprises the amino acid sequence set forth as SEQ ID NO:205,

(3) an antibody, wherein the light chain variable region thereof comprises the amino acid sequence set forth as SEQ ID NO:194; and wherein the heavy chain variable region thereof comprises the amino acid sequence set forth as SEQ ID NO:205, and

(4) an antibody, wherein the light chain variable region thereof comprises the amino acid sequence set forth as SEQ ID NO:195; and wherein the heavy chain variable region thereof comprises the amino acid sequence set forth as SEQ ID NO:205.

[Claim 3]

A fusion protein comprising an anti-human transferrin receptor antibody and the amino acid sequence of iduronate 2-sulfatase, wherein the

amino acid sequence of the antibody is selected from the group consisting of (1) to (8) below:

(1) an antibody, wherein the light chain thereof comprises the amino acid sequence set forth as SEQ ID NO:196; and wherein the heavy chain thereof comprises the amino acid sequence set forth as SEQ ID NO:210,

(2) an antibody, wherein the light chain thereof comprises the amino acid sequence set forth as SEQ ID NO:198; and wherein the heavy chain thereof comprises the amino acid sequence set forth as SEQ ID NO:210,

(3) an antibody, wherein the light chain thereof comprises the amino acid sequence set forth as SEQ ID NO:200; and wherein the heavy chain thereof comprises the amino acid sequence set forth as SEQ ID NO:210,

(4) an antibody, wherein the light chain thereof comprises the amino acid sequence set forth as SEQ ID NO:202; and wherein the heavy chain thereof comprises the amino acid sequence set forth as SEQ ID NO:210,

(5) an antibody, wherein the light chain thereof comprises the amino acid sequence set forth as SEQ ID NO:196; and wherein the heavy chain thereof comprises the amino acid sequence set forth as SEQ ID NO:212,

(6) an antibody, wherein the light chain thereof comprises the amino acid sequence set forth as SEQ ID NO:198; and wherein the heavy chain thereof comprises the amino acid sequence set forth as SEQ ID NO:212,

(7) an antibody, wherein the light chain thereof comprises the amino acid sequence set forth as SEQ ID NO:200; and whereof the heavy chain thereof comprises the amino acid sequence set forth as SEQ ID NO:212, and

(8) an antibody, wherein the light chain thereof comprises the amino acid sequence set forth as SEQ ID NO:202; and wherein the heavy chain thereof comprises the amino acid sequence set forth as SEQ ID NO:212.

[Claim 4]

The fusion protein according to any one of claims 1 to 3, wherein the antibody has an affinity to both the extracellular region of human transferrin receptor and the extracellular region of monkey transferrin receptor.

[Claim 5]

The fusion protein according to claim 4, wherein the dissociation constant of its complex with the extracellular region of human transferrin receptor is not greater than $1\times10^{-8}$ M, and the dissociation constant of its complex with the extracellular region of monkey transferrin receptor is not greater than $5\times10^{-8}$ M, when analyzed by using bio-layer interferometry.

[Claim 6]

The fusion protein according to any one of claims 1 to 5, wherein the antibody is Fab antibody, F(ab')2 antibody, or F(ab') antibody.

[Claim 7]

The fusion protein according to any one of claims 1 to 5, wherein the antibody is a single-chain antibody selected from the group consisting of scFab, scF(ab'), scF(ab')2 and scFv.

[Claim 8]

The fusion protein according to claim 7, wherein the light chain and the heavy chain of the antibody are linked via a linker sequence.

[Claim 9]

The fusion protein according to claim 7, wherein the heavy chain is linked, via a linker sequence, to the light chain on the C-terminal side of the light chain.

[Claim 10]

The fusion protein according to claim 7, wherein the light chain is linked, via a linker sequence, to the heavy chain on the C-terminal side of the heavy chain.

[Claim 11]

The fusion protein according to any one of claims 8 to 10, wherein the linker sequence consists of 8 to 50 amino acid residues.

[Claim 12]

The fusion protein according to claim 11, 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, and the amino acid sequence consisting of three consecutively linked amino acid sequences each set forth as SEQ ID NO:3.

[Claim 13]

The fusion protein according to any one of claims 1 to 12, wherein the iduronate 2-sulfatase is linked, via a linker sequence, to the light chain on the C-terminal side or the N-terminal side of the light chain or to the heavy chain on the C-terminal side or the N-terminal side of the heavy chain.

[Claim 14]

The fusion protein according to claim 13, wherein the linker sequence consists of 1 to 50 amino acid residues.

[Claim 15]

The fusion protein according to claim 13, wherein the linker sequence comprises 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 sequence consisting of 1 to 10 of any of aforementioned amino acid sequences that are consecutively linked.

[Claim 16]

The fusion protein according to any one of claims 1 to 15, wherein the iduronate 2-sulfatase is a human iduronate 2-sulfatase.

[Claim 17]

The fusion protein according to claim 16, wherein the light chain of the humanized anti-hTfR antibody has the amino acid sequence set forth as SEQ ID NO:196. and wherein the heavy chain of the humanized anti-hTfR antibody is linked, on the C-terminal side thereof and via a linker sequence Gly-Ser, to the human iduronate 2-sulfatase, and the whole linked heavy chain has the amino acid sequence set forth as SEQ ID NO:251.

[Claim 18]

The fusion protein according to claim 16, comprising: the humanized anti-hTfR antibody light chain having the amino acid sequence set forth as SEQ ID NO:196; and the humanized anti-hTfR antibody heavy chain having the amino acid sequence set forth as SEQ ID NO:210 which is linked, on the

C-terminal side thereof and via a linker sequence Gly-Ser, to the human iduronate 2-sulfatase set forth as SEQ ID NO:246.

[Claim 19]

The fusion protein according to claim 16, comprising: the conjugate composed of human iduronate 2-sulfatase linked via a linker sequence Gly-Ser to the heavy chain on the C-terminal side of the heavy chain; and the light chain, wherein the amino acid sequence of the conjugate is set forth as SEQ ID NO:251, and the amino acid sequence of the light chain is set forth as SEQ ID NO:196.

[Claim 20]

A DNA fragment encoding the amino acid sequence of the fusion protein according to any one of claims 1 to 19.

[Claim 21]

An expression vector comprising the DNA fragment according to claim 20 that is incorporated therein.

[Claim 22]

A mammalian cell transformed with the expression vector according to claim 21.