CLAIMS

[Claim 1]. Use of a conjugate of an anti-human transferrin receptor antibody and a~~n agent~~ human acid α-glucosidase in the manufacture of a medicament for use in treating ~~muscle dysfunction~~Pompe disease, wherein the human acid α-glucosidase~~agent~~ has a physiological activity to be exerted in muscle.

[Claim 2]. The use according to claim 1, wherein the anti-human transferrin receptor antibody is a Fab antibody, a $F(ab')_2$ antibody, or a F(ab') antibody.

[Claim 3]. The use according to claim 1, wherein the anti-human transferrin receptor antibody is a single-chain antibody selected from the group consisting of scFab, scF(ab'), $scF(ab')_2$, and scFv.

[Claim 4]. The use according to claim 3, wherein in the single-chain antibody a light chain and a heavy chain of the anti-human transferrin receptor antibody are linked via a linker sequence.

[Claim 5]. The ~~ues~~use according to claim 4, wherein the light chain and the heavy chain of the anti-human transferrin receptor antibody are linked on the C-terminal side of the light chain via the linker sequence.

[Claim 6]. The use according to claim 4, wherein the light chain and the heavy chain of the anti-human transferrin receptor antibody are linked on the C-terminal side of the heavy chain via the linker sequence.

[Claim 7]. The use according to any one of claims 4 to 6, wherein the linker sequence comprises 8 to 50 amino acid residues.

[Claim 8]. The use according to claim 7, wherein the linker sequence comprises an amino acid sequence 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 sequence set forth as SEQ ID NO: 3, and the amino acid sequence set forth as SEQ ID NO: 4.

[Claim 9]. The use according to claim 8, wherein the linker sequence comprises 15 amino acid residues in which the amino acid sequence set forth as SEQ ID NO: ~~4~~ 3 is consecutively repeated three times.

[Claim 10]. The use according to any one of claims 1 to 9, wherein the anti-human transferrin receptor antibody comprises the amino acid sequence set forth as SEQ ID NO: 22 in the variable region of the light chain and the amino acid sequence set forth as SEQ ID NO: 23 in the variable region of the heavy chain.

~~[Claim 11]. The use according to claim 10, wherein the amino acid sequence of the variable region of the light chain has an identity not lower than 80% to the amino acid sequence set forth as SEQ ID NO: 22, and the amino acid sequence of the variable region of the heavy chain has an identity not lower than 80% to the amino acid sequence set forth as SEQ ID NO: 23.~~

~~[Claim 12]. The use according to claim 10, wherein the amino acid sequence of the variable region of the light chain has an identity not lower than 90% to the amino acid sequence set forth as SEQ ID NO: 22, and the amino acid sequence of the variable region of the heavy chain has an identity not lower than 90% to the amino acid sequence set forth as SEQ ID NO: 23.~~

~~[Claim 13]. The use according to claim 10, wherein 1 to 10 amino acids constituting the variable region of the light chain are substituted with other amino acids relative to the amino acid sequence set forth as~~

~~SEQ ID NO: 22.~~

~~[Claim 14]. The use according to claim 10, wherein 1 to 3 amino acids constituting the variable region of the light chain are substituted with other amino acids relative to the amino acid sequence set forth as SEQ ID NO: 22.~~

~~[Claim 15]. The use according to claim 10, wherein 1 to 10 amino acids constituting the variable region of the heavy chain are substituted with other amino acids relative to the amino acid sequence set forth as SEQ ID NO: 23.~~

~~[Claim 16]. The use according to claim 10, wherein 1 to 3 amino acids constituting the variable region of the heavy chain are substituted with other amino acids relative to the amino acid sequence set forth as SEQ ID NO: 23.~~

~~[Claim 17]. The use according to claim 10, wherein 1 to 10 amino acids constituting the variable region of the light chain are substituted with other amino acids relative to the amino acid sequence set forth as SEQ ID NO: 22, and 1 to 10 amino acids constituting the variable region of the heavy chain are substituted with other amino acids relative to the amino acid sequence set forth as SEQ ID NO: 23.~~

~~[Claim 18]. The use according to claim 10, wherein 1 to 3 amino acids constituting the variable region of the light chain are substituted with other amino acids relative to the amino acid sequence set forth as SEQ ID NO: 22, and 1 to 3 amino acids constituting the variable region of the heavy chain are substituted with other amino acids relative to the amino acid sequence set forth as SEQ ID NO: 23.~~

[Claim ~~19~~11]. The use according to claim 10, wherein the anti-human

transferrin receptor antibody comprises the light chain comprising an amino acid sequence set forth as SEQ ID NO: 24 and the heavy chain comprising an amino acid sequence set forth as SEQ ID NO: 25.

~~[Claim 20]. The use according to claim 19, wherein the amino acid sequence of the light chain has an identity not lower than 80% to the amino acid sequence set forth as SEQ ID NO: 24, and the amino acid sequence of the heavy chain has an identity not lower than 80% to the amino acid sequence set forth as SEQ ID NO: 25.~~

~~[Claim 21]. The use according to claim 19, wherein the amino acid sequence of the light chain has an identity not lower than 90% to the amino acid sequence set forth as SEQ ID NO: 24, and the amino acid sequence of the heavy chain has an identity not lower than 90% to the amino acid sequence set forth as SEQ ID NO: 25.~~

~~[Claim 22]. The use according to any of claims 1 to 21, wherein the agent is a peptide or a protein.~~

[Claim ~~23~~12]. The use according to any one of claims ~~22~~1 to 11, selected from the group consisting of (1) to (4) below:

(1) a conjugate in which the protein is linked to the C-terminal side of the light chain of the anti-human transferrin receptor antibody by a peptide bond,

(2) a conjugate in which the protein is linked to the N-terminal side of the light chain of the anti-human transferrin receptor antibody by a peptide bond,

(3) a conjugate in which the protein is linked to the C-terminal side of the heavy chain of the anti-human transferrin receptor antibody by a peptide bond, and

(4) a conjugate in which the protein is linked to the N-terminal side of the heavy chain of the anti-human transferrin receptor antibody by a peptide bond.

[Claim ~~24~~13]. The use according to claim ~~23~~12, wherein the protein is linked to the anti-human transferrin receptor antibody via a linker sequence.

[Claim ~~25~~14]. The use according to claim ~~24~~13, wherein the linker sequence consists of 1 to 50 amino acid residues.

[Claim ~~26~~15]. The use according to claim ~~25~~14, 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, and the amino acid sequence consisting of 1 to 10 amino acid sequences thereof that are linked consecutively.

[Claim ~~27~~16]. The use according to any one of claims 1 to ~~28~~15, wherein the anti-human transferrin receptor antibody is a humanized anti-human transferrin receptor antibody.

~~[Claim 28]. The use according to any one of claims 22 to 27, wherein the protein is a lysosomal enzyme.~~

~~[Claim 29]. The use according to claim 28, wherein the lysosomal enzyme is human α-galactosidase A.~~

~~[Claim 30]. The use according to claim 29, wherein the light chain of the humanized anti-hTfR antibody comprises the amino acid sequence set forth as SEQ ID NO: 24, and wherein the heavy chain of the humanized anti-hTfR antibody is linked on its C-terminal side to the~~

~~human α-galactosidase A via a linker sequence (Gly Ser), and the whole linked heavy chain has the amino acid sequence set forth as SEQ ID NO: 29.~~

~~[Claim 31]. The use according to claim 28, wherein the lysosomal enzyme is human acid α-glucosidase.~~

[Claim ~~32~~17]. The use according to claim ~~3~~1, wherein the light chain of the humanized anti-hTfR antibody comprises the amino acid sequence set forth as SEQ ID NO: 24, and wherein the heavy chain of the humanized anti-hTfR antibody is linked on its C-terminal side to the human acid α-glucosidase via a linker sequence (Gly Ser), and the whole linked heavy chain has the amino acid sequence set forth as SEQ ID NO: 27.

~~[Claim 33]. The use according to claim 28, wherein the muscle dysfunction comprises lysosomal disease.~~

~~[Claim 34]. The use according to claim 29 or 30, wherein the muscle dysfunction comprises Fabry disease.~~

~~[Claim 35]. The use according to claim 31 or 32, wherein the muscle dysfunction comprises Pompe disease.~~

[Claim ~~36~~18]. The use according to any one of claims ~~33~~ 1 to ~~36~~17, wherein the muscle is skeletal muscle, cardiac muscle, or smooth muscle.