

CLAIMS

1. Use of a composition in the preparation of a medicament for treating a metabolic disorder associated with impaired neurological signaling in a human subject,
wherein the composition comprises an antibody, or an antigen binding fragment thereof that:
(a) comprises three heavy chain complementarity determining regions (CDRs) comprising amino acid sequences of SEQ ID NO: 1 (CDRH1), SEQ ID NO: 4 (CDRH2), and SEQ ID NO: 10 (CDRH3), and three light chain CDRs comprising amino acid sequences of SEQ ID NO: 12 (CDRL1), SEQ ID NO: 18 (CDRL2), and SEQ ID NO: 22 (CDRL3), as defined by the Kabat numbering system; or three heavy chain CDRs comprising amino acid sequences of SEQ ID NO: 2 (CDRH1), SEQ ID NO: 5 (CDRH2), and SEQ ID NO: 10 (CDRH3), and three light chain CDRs comprising amino acid sequences of SEQ ID NO: 13 (CDRL1), SEQ ID NO: 19 (CDRL2), and SEQ ID NO: 22 (CDRL3), as defined by the IMGT numbering system, or an antibody or antigen-binding fragment; or
(b) competes or cross-competes with the antibody or antigen-binding fragment thereof as defined in (a);
wherein the metabolic disorder is selected from the group consisting of obesity, type II diabetes, diabetes associated with obesity, non-alcoholic steatohepatitis (NASH), and metabolic syndrome;
wherein the antibody or antigen binding fragment is in an amount effective to treat the metabolic disorder.
2. The use of claim 1, wherein the antibody or antigen binding fragment is in an amount effective to increase the level of latent myostatin in a serum sample from the subject, as compared to the level of latent myostatin in a control serum sample from the subject.
3. The use of claim 1 or claim 2, wherein the subject has spinal muscular atrophy (SMA) or spinal cord injury (SCI).
4. The use of any one of claims 1-3, wherein the impaired neurological signaling comprises partial impairment of signaling between a motor neuron and a target muscle.
5. The use of any one of claims 1-4, wherein the impaired neurological signaling is the result of nerve injury.

6. The use of claim 5, wherein the nerve injury is SCI.
7. The use according to claim 6, wherein the SCI comprises a lesion between i) C3-C8; (ii) C5-C6; (iii) C6-C7; (iv) T1-T6; or (v) T7-L5.
8. The use according to claim 6 or claim 7, wherein the subject is in an acute phase of SCI or a sub-acute phase of SCI.
9. The use according to claim 6 or claim 7, wherein the subject is in a chronic phase of SCI.
10. The use of any one of claims 1-9, wherein the metabolic disorder comprises insulin resistance, inflammation, abnormal lipid metabolism, or an increase in intramuscular fat infiltration.
11. The use of any one of claims 1-10, wherein the metabolic disorder is type II diabetes, obesity, or diabetes associated with obesity.
12. The use of any one of claims 1-11, wherein the treatment further comprises a second therapeutic agent.
13. The use of any one of claims 1-12, wherein the antibody or antigen binding fragment comprises a heavy chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 25 and a light chain variable region that is at least 90% identical to an amino acid sequence of SEQ ID NO: 31.
14. The use of any one of claims 1-13, wherein the antibody or antigen binding fragment comprises a heavy chain variable region comprising an amino acid sequence of SEQ ID NO: 25 and a light chain variable region comprising an amino acid sequence of SEQ ID NO: 31.
15. The use of any one of claims 1-14, wherein the antibody or antigen binding fragment is engineered to bind FcRn with greater affinity at pH 7.4 as compared to a non-engineered counterpart.
16. The use of any one of claims 1-15, wherein the antibody or antigen binding fragment comprises a heavy chain comprising an amino acid sequence of SEQ ID NO: 50, and a light chain comprising an amino acid sequence of SEQ ID NO: 51.

17. The use of any one of claims 1-16, wherein the composition is to be administered intravenously or subcutaneously.

18. The use of any one of claims 1-17, wherein the effective amount is an amount that causes two or more of the following in the subject:

- (i) an increase in metabolic rate;
- (ii) an increase in insulin sensitivity;
- (iii) an increase in a level of brown adipose tissue;
- (iv) an increase in a level of beige adipose tissue;
- (v) a decrease in a level of white adipose tissue;
- (vi) a decrease in a level of visceral adipose tissue;
- (vii) a decrease in ratio of adipose-to-muscle tissue in the subject;
- (viii) an increase in glucose uptake by a brown adipose tissue, a beige adipose tissue, or a muscle tissue;
- (ix) a decrease in glucose uptake by a white adipose tissue or a liver tissue;
- (x) an increase in insulin dependent glycemic control; and
- (xi) a decrease in intramuscular fat infiltration.