

CLAIMS

1. Use of a composition in the preparation of a medicament for inhibiting myostatin activation in a subject,

wherein the composition comprises an antibody, or antigen binding fragment thereof, that specifically binds pro/latent-myostatin and blocks release of mature myostatin, in an amount effective to cause two or more of the following in the subject upon administration:

- (a) an increase in mass and/or function of a muscle tissue in the subject;
- (b) an increase in the metabolic rate of the subject;
- (c) an increase in insulin sensitivity of the subject;
- (d) an increase in a level of brown adipose tissue in the subject;
- (e) an increase in a level of beige adipose tissue in the subject;
- (f) a decrease in a level of white adipose tissue in the subject;
- (g) a decrease in a level of visceral adipose tissue in the subject;
- (h) a decrease in ratio of adipose-to-muscle tissue in the subject;
- (i) an increase in glucose uptake by a brown adipose tissue, a beige adipose tissue, or a muscle tissue in the subject;
- (j) a decrease in glucose uptake by a white adipose tissue or a liver tissue;
- (k) a decrease in muscle catabolism of protein and/or muscle release of amino acids in the subject;
- (l) an increase in insulin dependent glycemic control in the subject;
- (m) a decrease in intramuscular fat infiltration in the subject;
- (n) an improvement in quality of life, as assessed by a standardized quality of life test;
- (o) prevention of muscle loss or atrophy in the subject; and/or,
- (p) prevention of developing a metabolic dysregulation associated with muscle dysfunction

in the subject,

wherein the subject is a human subject that benefits from reduced myostatin signaling.

2. A pharmaceutical composition for use in a method for treating a muscle condition or disorder in a human subject,

wherein the pharmaceutical composition comprises an antibody, or antigen binding fragment thereof, that specifically binds pro/latent-myostatin and blocks release of mature myostatin, in an amount effective to cause two or more of the following in the subject:

- (a) an increase in mass and/or function of a muscle tissue in the subject;
- (b) an increase in the metabolic rate of the subject;
- (c) an increase in insulin sensitivity of the subject;

- (d) an increase in a level of brown adipose tissue in the subject;
 - (e) an increase in a level of beige adipose tissue in the subject;
 - (f) a decrease in a level of white adipose tissue in the subject;
 - (g) a decrease in a level of visceral adipose tissue in the subject;
 - (h) a decrease in ratio of adipose-to-muscle tissue in the subject;
 - (i) an increase in glucose uptake by a brown adipose tissue, a beige adipose tissue, or a muscle tissue in the subject;
 - (j) a decrease in glucose uptake by a white adipose tissue or a liver tissue;
 - (k) a decrease in muscle catabolism of protein and/or muscle release of amino acids in the subject;
 - (l) an increase in insulin dependent glycemic control in the subject;
 - (m) a decrease in intramuscular fat infiltration in the subject;
 - (n) an improvement in quality of life, as assessed by a standardized quality of life test;
 - (o) prevention of muscle loss or atrophy in the subject; and/or,
 - (p) prevention of developing a metabolic dysregulation associated with muscle dysfunction in the subject.
3. The use of claim 1, wherein the subject has been selected as suffering from a muscle condition or disorder.
 4. The use of claim 1, wherein the subject has been selected as suffering from, or at risk of developing, a metabolic disorder.
 5. The use of any one of claims 1, 3 or 4, or the pharmaceutical composition for use according to claim 2, wherein the amount is an amount that causes an increase in a level of latent myostatin in a circulation serum sample, as compared to a control.
 6. The use of any one of claims 1 or 3-5, or the pharmaceutical composition for use according to claim 2 or claim 5, wherein the subject has a muscle condition selected from the group consisting of: myopathy, muscular atrophy, muscular dystrophy, and nerve injury.
 7. The use of claim 6, or the pharmaceutical composition for use according to claim 6, wherein the muscular atrophy is associated with a defect in motor neurons.
 8. The use of claim 7, or the pharmaceutical composition for use according to claim 7, wherein the defect comprises a genetic mutation.

9. The use of claim 8, or the pharmaceutical composition for use according to claim 8, wherein the muscular atrophy is associated with spinal muscular atrophy (SMA), amyotrophic lateral sclerosis (ALS), or myasthenia gravis.
10. The use of claim 6, or the pharmaceutical composition for use according to claim 6, wherein the nerve injury comprises partial denervation of neurons that innervate muscle, or impaired signaling between a motor neuron and a target muscle.
11. The use of claim 6, or the pharmaceutical composition for use according to claim 6, wherein the muscle atrophy comprises glucocorticoid-induced muscle atrophy.
12. The use of any one of claims 1 or 3-5, or the pharmaceutical composition for use according to claim 2, wherein the subject has a metabolic disease selected from the group consisting of type I diabetes, type II diabetes, obesity, metabolic syndrome/pre-diabetes, cardiovascular disease, non-alcoholic steatohepatitis (NASH), a hypo-metabolic state, double diabetes, Cushings disease, metabolic myopathy, androgen deficiency, and an obesity syndrome.
13. The use of claim 12, or the pharmaceutical composition of claim 12, wherein the androgen deficiency is associated with the metabolic disease.
14. The use of claim 13, wherein the subject has a cancer.
15. The use, or the pharmaceutical composition, of claim 12, wherein the metabolic myopathy is a glycogen storage disease or lipid storage disorder.
16. The use of any one of claims 1 or 3-12, or the pharmaceutical composition for use according to any one of claims 2-12, wherein the subject is treated with a second therapy.
17. The use of claim 16, or the pharmaceutical composition for use according to claim 16, wherein the second therapy comprises neuroprotective therapy.
18. The use of claim 17, or the pharmaceutical composition for use according to claim 17, wherein the neuroprotective therapy comprises a stem cell therapy.
19. Use of a composition in the preparation of a medicament for treating or preventing a disease associated with an impaired neurological signaling between a neuron and a target tissue in a human subject, wherein the human subject has been selected as suffering from a disease associated with an

impaired neurological signaling between a neuron and a target tissue expressing a myostatin precursor; and

wherein the composition comprises an antibody, or antigen binding fragment thereof, that specifically binds pro/latent-myostatin and blocks release of mature myostatin in an amount effective to treat or prevent the disease.

20. A composition comprising an antibody, or antigen binding fragment thereof, that specifically binds pro/latent-myostatin and blocks release of mature myostatin, for use in a method of treating or preventing a disease associated with an impaired neurological signaling between a neuron and a target tissue in a human subject,

the method comprising selecting the human subject suffering from the disease associated with an impaired neurological signaling between a neuron and a target tissue expressing a myostatin precursor; and administering the composition to the human subject.

21. The use of claim 19, or the composition for use according to claim 20, wherein the target tissue is selected from the group consisting of a muscle, an adipose tissue, a brain tissue, a liver tissue, and a blood vessel tissue.

22. The use of claim 21, or the composition for use according to claim 21, wherein the target tissue is a skeletal muscle.

23. A composition for treating or preventing myasthenia gravis, amyotrophic lateral sclerosis (ALS), or spinal muscular atrophy (SMA) in a human subject, the composition comprising an antibody, or antigen binding fragment thereof, that specifically binds pro/latent-myostatin and blocks release of mature myostatin.

24. Use of a composition in the preparation of a medicament for treating a lesion that causes an impaired, but not complete loss of, signaling between a neuron and a target muscle in a subject, wherein the composition comprises a myostatin inhibitor in an amount effective to treat the muscle located below the lesion in the subject.

25. The use of claim 24, wherein the amount is an amount effective to prevent muscle loss or muscle atrophy below the lesion.

26. The use of claim 24, wherein the amount is an amount effective to increase muscle mass and/or function below the lesion.

27. The use of claim 24, wherein the muscle contains fast-twitch muscle fibers.

28. The use of claim 24, wherein the muscle contains slow-twitch muscle fibers.
29. The use of any one of claims 24-28, wherein the muscle located below the lesion is selected from the group of a soleus muscle, a gastrocnemius muscle, a bicep muscle and a tricep muscle.
30. The use of any one of claims 24-29, wherein the amount is effective to increase mass and/or function of a muscle above the lesion in the subject.
31. The use of any one of claims 24-30, wherein the myostatin inhibitor is an antibody, or antigen-binding portion thereof, a small molecule, or gene therapy.
32. The use of claim 31, wherein the antibody binds i) mature myostatin; ii) myostatin receptor; and/or, iii) GDF11.
33. The use of any one of claims 19, 21-22 or 24-32, wherein the amount is effective to treat a metabolic condition in the subject.
34. The use of claim 33, wherein the amount is effective to cause in the subject:
- (a) an increase in mass and/or function of a muscle tissue in the subject;
 - (b) an increase in the metabolic rate of the subject;
 - (c) an increase in insulin sensitivity of the subject;
 - (d) an increase in a level of brown adipose tissue in the subject;
 - (e) an increase in a level of beige adipose tissue in the subject;
 - (f) a decrease in a level of white adipose tissue in the subject;
 - (g) a decrease in a level of visceral adipose tissue in the subject;
 - (h) a decrease in ratio of adipose-to-muscle tissue in the subject;
 - (i) an increase in glucose uptake by a brown adipose tissue, a beige adipose tissue, or a muscle tissue in the subject;
 - (j) a decrease in glucose uptake by a white adipose tissue or a liver tissue;
 - (k) a decrease in muscle catabolism of protein and/or muscle release of amino acids in the subject;
 - (l) an increase in insulin dependent glycemic control in the subject;
 - (m) a decrease in intramuscular fat infiltration in the subject;
 - (n) an improvement in quality of life, as assessed by a standardized quality of life test;
 - (o) prevention of muscle loss or atrophy in the subject; and/or,
 - (p) prevention of developing a metabolic dysregulation associated with muscle dysfunction in the subject.