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(54) **Title**: ANTI-PRO/LATENT MYOSTATIN ANTIBODIES AND METHODS OF USE THEREOF

(57) **Abstract**: The present invention relates to antibodies that specifically bind pro-myostatin and/or latent myostatin, and methods and uses thereof.

AMENDED CLAIMS
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We claim:

1. A pharmaceutical composition for use in a method for treating a muscle condition in a subject,

wherein the pharmaceutical composition comprises an antibody or fragment thereof that specifically binds pro/latent myostatin and inhibits release of mature myostatin; and,

wherein the pharmaceutical composition causes 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.

2. The pharmaceutical composition for use according to claim 1, wherein the muscle condition is associated with impaired neurological signaling between a neuron and a target muscle.

3. The pharmaceutical composition for use according to claim 2, wherein the muscle condition comprises motor neuron dysfunction.

4. The pharmaceutical composition for use according to claim 2, wherein the muscle condition is caused by an injury.

5. The pharmaceutical composition for use according to claim 2, wherein the injury comprises incomplete SCI.

6. The pharmaceutical composition for use according to claim 2, wherein the muscle condition is associated with a genetic defect.

7. The pharmaceutical composition for use according to claim 2, wherein the muscle condition is amyotrophic lateral sclerosis (ALS), spinal muscular atrophy (SMA), or myasthelia gravis.

8. The pharmaceutical composition for use according to any one of the preceding claims, wherein the subject has or is at risk of developing a metabolic disorder.

9. The pharmaceutical composition for use according to any one of the preceding claims, wherein the antibody or fragment does not bind mature myostatin or GDF11.

10. The pharmaceutical composition for use according to any one of the preceding claims, wherein the antibody is a fully human or humanized antibody.

11. The pharmaceutical composition for use according to any one of the preceding claims, wherein the antibody is a IgG_4 subtype.

12. The pharmaceutical composition for use according to any one of the preceding claims, wherein the antibody is a pH-sensitive antibody.

AMENDED SHEET (ARTICLE 19)

13. The pharmaceutical composition for use according to any one of the preceding claims, wherein the method comprises administration of the pharmaceutical composition at dosage of 0.1-30 mg/kg of the antibody.

14. The pharmaceutical composition for use according to any one of the preceding claims, wherein the method comprises weekly, biweekly or monthly administration.

15. The pharmaceutical composition for use according to any one of the preceding claims, wherein the method comprises IV injection or subcutaneous administration.