CLAIMS

1. Use of a myostatin pathway inhibitor in the manufacture of a medicament for the treatment of a metabolic disorder,

wherein the medicament is used in conjunction with a composition comprising a GLP-1 analog;

wherein the metabolic disorder is selected from: type 2 diabetes, metabolic syndrome, pre-diabetes, obesity, cardiovascular diseases (such as congestive heart failure), spinal cord injury (SCI) (e.g., complete or incomplete/partial SCI), hypo-metabolic states, double diabetes, Cushing's disease (also referred to as Cushing's syndrome), obesity syndrome (e.g., diet-associated or diet-induced obesity), insulin resistance, insulin insufficiency, hyperinsulinemia, impaired glucose tolerance (IGT), abnormal glycogen metabolism, hyperlipidemia, hypoalbuminemia, hypertriglyceridemia, kidney disease, syndrome X, fatty liver disease, and metabolic bone diseases; and,

wherein optionally the myostatin pathway inhibitor is an antibody or antigen-binding fragment thereof.

2. Use of a myostatin pathway inhibitor and a GLP-1 analog in the manufacture of a medicament for weight management (for the treatment of obesity or overweight), wherein optionally the myostatin pathway inhibitor and the GLP-1 analog are formulated as a single formulation or as part of a single molecular construct.

3. Use of a myostatin pathway inhibitor in the manufacture of a medicament for the prevention of muscle loss in a subject receiving a GLP-1 analog therapy.

4. The use according to claim 3, wherein the subject suffers from a muscle disorder, wherein optionally the muscle disorder is a neuromuscular disorder.

5. Use of a myostatin pathway inhibitor in the manufacture of a medicament for the treatment of a metabolic disorder,

wherein the medicament is intended for a subject with central adiposity, cardiovascular disease, kidney disease, fatty liver disease, sleep apnea, high blood pressure, high blood triglyceride levels, high blood cholesterol levels, low high-density lipoprotein (HDL) levels, and a hemoglobin A1c (HbA1c) level of 6% or greater (e.g., 6.5%-10%);

wherein, optionally, the subject has a body mass index (BMI) of greater than 25;

wherein, further optionally, the subject has a BMI of between 28 and 40, inclusive of endpoints; and,

wherein the subject is on a GLP-1 analog therapy.

6. The use according to any one of claims 1-5, wherein the GLP-1 analog is semaglutide, exenatide ER, liraglutide, lixisenatide, tirzepatide, XW003, Noiiglutide, MEDI0382, dulaglutide, or albiglutide.

7. The use according to any one of claims 1-6, wherein the medicament is used in conjunction with: danuglipron (Pfizer), GLP-1 receptor agonist/GIP receptor antagonist combination such as AMG 133 (Amgen), mas receptor activators, e.g., Sarconeos, GLP-1/GIP combination such as tirzepatide (Eli Lilly), amylin/GLP-1 combination such as cagrilintide/semaglutide combination (Novo Nordisk), GLP-1/glucagon combination such as DD01 (Neuraly), GLP-1/glucagon combination such as ALT-801 (Altimmune), GLP-1/GIP such as CT-388 (Carmot), GLP-1/glucagon dual agonist such as IBI362 (mazdutide), LY-330567 (Innovent/Eli Lilly), danuglipron (PF-06882961) (Pfizer),

setmelanotide (Rhythm), GLP-1/GIP/Glucagon triple receptor agonist such as LY3437943 (Eli Lilly) and/or a dual GIP/GLP-1 receptor agonist such as LY3298176 (Eli Lilly).

8. The use according to any one of claims 1-7, wherein the myostatin pathway inhibitor is an antibody or antigen-binding fragment thereof.

9. The use according to any one of claims 1-7, wherein the myostatin pathway inhibitor is a ligand trap that binds mature myostatin.

10. The use according to claim 8, wherein the antibody or the antigen-binding fragment binds ActRII receptor, mature myostatin, or pro/latent myostatin.

11. The use according to claim 8, wherein the myostatin pathway inhibitor is an anti-myostatin Adnectin.

12. The use according to claim 8, wherein the myostatin pathway inhibitor is a myostatin-selective inhibitor, wherein optionally the antibody binds pro/latent myostatin.

13. The use according to claim 12, wherein the antibody or the antigen-binding fragment binds an epitope on pro/latent myostatin that comprises one or more amino acid resides of KALDEN (SEQ ID NO: 118) and/or FVQILRLIKPMKDGTRYTGIRSLK (SEQ ID NO: 57), wherein optionally the antibody or antigen-binding fragment binds an epitope comprising one or more of the amino acid residues F147, Q149, L151, Y186, S168, K170, K205, and/or L207, as numbered according to SEQ ID NO: 52.

14. The use according to any one of claims 8, 10, 12 and 13, wherein the antibody is not apitegromab.

15. The use according to any one of claims 1-14, wherein the medicament is formulated for subcutaneous administration.

16. The use according to any one of claims 1-15, wherein the medicament is provided as a kit.

17. A pharmaceutical composition comprising a myostatin pathway inhibitor and a GLP-1 pathway activator formulated as a single formulation or as part of a single molecular construct.

18. The pharmaceutical composition of claim 17, wherein the GLP-1 pathway activator is selected from: danuglipron (Pfizer), GLP-1 receptor agonist/GIP receptor antagonist combination such as AMG 133 (Amgen), mas receptor activators, e.g., Sarconeos, GLP-1/GIP combination such as tirzepatide (Eli Lilly), amylin/GLP-1 combination such as cagrilintide/semaglutide combination (Novo Nordisk), GLP-1/glucagon combination such as DD01 (Neuraly), GLP-1/glucagon combination such as ALT-801 (Altimmune), GLP-1/GIP such as CT-388 (Carmot), GLP-1/glucagon dual agonist such as IBI362 (mazdutide) ,LY-330567 (Innovent/Eli Lilly), danuglipron (PF-06882961) (Pfizer), setmelanotide (Rhythm), GLP-1/GIP/Glucagon triple receptor agonist such as LY3437943 (Eli Lilly) and a dual GIP/GLP-1 receptor agonist such as LY3298176 (Eli Lilly).

19. The pharmaceutical composition of claim 17, wherein the GLP-1 pathway activator is a GLP-1 analog.

20. The pharmaceutical composition according to claim 18 or 19, wherein the myostatin pathway inhibitor is an anti-myostatin Adnectin, a ligand trap that binds mature myostatin, or an antibody or antigen-binding fragment thereof that binds ActRII receptor, mature myostatin, or pro/latent myostatin.

21. The pharmaceutical composition according to any one of claims 18-20, wherein the myostatin pathway inhibitor is a myostatin-selective inhibitor.

22. The pharmaceutical composition according to claim 21, wherein the myostatin-selective inhibitor is trevogrumab, GYM329, MST1032, apitegromab, or a variant thereof, or an antibody or antigen-binding fragment that competes or cross-competes with trevogrumab, GYM329, MST1032, apitegromab, or a variant thereof.

23. The pharmaceutical composition according to claim 22, wherein the antibody or antigen-binding fragment thereof that competes or cross-competes with apitegromab is not apitegromab and binds an epitope on pro/latent myostatin that comprises one or more amino acid resides of KALDEN (SEQ ID NO: 118) and/or FVQILRLIKPMKDGTRYTGIRSLK (SEQ ID NO: 57), wherein optionally the antibody or antigen-binding fragment binds an epitope comprising one or more of the amino acid residues F147, Q149, L151, Y186, S168, K170, K205, and/or L207, as numbered according to SEQ ID NO: 52.

24. A kit comprising the pharmaceutical composition of any one of claims 17-23.

25. Use of a myostatin-selective inhibitor in the manufacture of a medicament for the treatment of a metabolic disorder,

wherein the medicament is used in conjunction with a composition comprising a GLP-1 pathway activator;

wherein the myostatin-selective inhibitor comprises an antibody or antigen-binding fragment thereof that binds to an epitope on pro/latent myostatin that comprises one or more amino acid residues of KALDEN (SEQ ID NO: 118) and/or FVQILRLIKPMKDGTRYTGIRSLK (SEQ ID NO: 57);

wherein the myostatin-selective inhibitor is not apitegromab; and

wherein composition comprising the GLP-1 pathway activator comprises: danuglipron (Pfizer), a GLP-1 receptor agonist/GIP receptor antagonist combination such as AMG 133 (Amgen), a mas receptor activator such as Sarconeos, a GLP-1/GIP combination such as tirzepatide (Eli Lilly), an amylin/GLP-1 combination such as cagrilintide/semaglutide combination (Novo Nordisk), a GLP-1/glucagon combination such as DD01 (Neuraly), a GLP-1/glucagon combination such as ALT-801 (Altimmune), a GLP-1/GIP such as CT-388 (Carmot), a GLP-1/glucagon dual agonist such as IBI362 (mazdutide), LY-330567 (Innovent/Eli Lilly), danuglipron (PF-06882961) (Pfizer), or setmelanotide (Rhythm), a GLP-1/GIP/Glucagon triple receptor agonist such as LY3437943 (Eli Lilly), and/or a dual GIP/GLP-1 receptor agonist such as LY3298176 (Eli Lilly).