CLAIMS

What is claimed is:

1. A composition comprising a Growth and Differentiation Factor-8 (GDF-8) inhibitor and a Glucagon-like peptide-1 (GLP-1) agonist,

wherein the GDF-8 inhibitor is an antibody or antigen-binding fragment thereof that specifically binds GDF-8, and

wherein the anti-GDF-8 antibody or antigen-binding fragment thereof comprises the heavy chain complementarity determining regions (HCDRs) of a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO:4, and the light chain complementarity determining regions (LCDRs) of a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO:5.

2. A composition comprising a Growth and Differentiation Factor-8 (GDF-8) inhibitor, an Activin A inhibitor, and a Glucagon-like peptide-1 (GLP-1) agonist,

wherein the GDF-8 inhibitor is an antibody or antigen-binding fragment thereof that specifically binds GDF-8, and

wherein the anti-GDF-8 antibody or antigen-binding fragment thereof comprises the heavy chain complementarity determining regions (HCDRs) of a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO:4, and the light chain complementarity determining regions (LCDRs) of a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO:5.

3. The composition of claim 1 or 2, wherein the anti-GDF-8 antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) comprising the amino acid sequences of SEQ ID NO:6, SEQ ID NO:7, and SEQ ID NO:8, respectively, and three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3) comprising the amino acid sequences of SEQ ID NO:9, TTS, and SEQ ID NO:11, respectively.

4. The composition of any one of claims 1-3, wherein the anti-GDF-8 antibody or antigen-binding fragment thereof comprises a heavy chain variable region (HCVR) comprising

the amino acid sequence of SEQ ID NO:4, and a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO:5.

5. The composition of any one of claims 2-4, wherein the Activin A inhibitor, if present, is an Activin A-specific binding protein.

6. The composition of any one of claims 2-5, wherein the Activin A inhibitor, if present, is an antibody or antigen-binding fragment thereof that specifically binds Activin A.

7. The composition of claim 6, wherein the anti-Activin A antibody or antigen-binding fragment thereof comprises the heavy chain complementarity determining regions (HCDRs) of a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO:12, and the light chain complementarity determining regions (LCDRs) of a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO:13.

8. The composition of claim 6 or 7, wherein the anti-Activin A antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) comprising the amino acid sequences of SEQ ID NO:14, SEQ ID NO:15, and SEQ ID NO:16, respectively, and three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3) comprising the amino acid sequences of SEQ ID NO:17, GAS, and SEQ ID NO:19, respectively.

9. The composition of any one of claims 6-8, wherein the anti-Activin A antibody or antigen-binding fragment thereof comprises a heavy chain variable region (HCVR) comprising the amino acid sequence of SEQ ID NO:12, and a light chain variable region (LCVR) comprising the amino acid sequence of SEQ ID NO:13.

10. The composition of any one of claims 1-9, wherein the GLP-1 agonist is a GLP-1 receptor agonist.

11. The composition of any one of claims 1-10, wherein the GLP-1 agonist is selected from the group consisting of Exenatide (long-acting), Dulaglutide, Liraglutide, Tirzepatide, and Semaglutide.

12. The composition of claim 11, wherein the GLP-1 agonist is Semaglutide.

13. The composition of any one of claims 1-10, wherein the GLP-1 agonist is a GLP-1-specific binding protein.

14. The composition of claim 13, wherein the GLP-1 agonist is an antibody or antigen-binding fragment thereof that specifically binds GLP-1.

15. The composition of any one of claims 1-14 for use in improving glucose control, increasing lean body mass, reducing fat mass, treating obesity, treating diabetes, and/or treating liver issues associated with increased fat mass, obesity, and/or diabetes in a subject.

16. Use of a GDF-8 inhibitor in the manufacture of a medicament for improving glucose control, increasing lean body mass, reducing fat mass, treating obesity, treating diabetes, and/or treating liver issues associated with increased fat mass, obesity, and/or diabetes in a subject,

wherein the medicament is to be used with a GLP-1 agonist,

wherein the GDF-8 inhibitor is an antibody or antigen-binding fragment thereof that specifically binds GDF-8, and

wherein the anti-GDF-8 antibody or antigen-binding fragment thereof comprises the heavy chain complementarity determining regions (HCDRs) of a heavy chain variable region (HCVR) comprising SEQ ID NO:4, and the light chain complementarity determining regions (LCDRs) of a light chain variable region (LCVR) comprising SEQ ID NO:5.

17. Use of a GDF-8 inhibitor in the manufacture of a medicament for improving glucose control, increasing lean body mass, reducing fat mass, treating obesity, treating diabetes, and/or treating liver issues associated with increased fat mass, obesity, and/or diabetes in a subject,

wherein the medicament is to be used with an Activin A inhibitor, and a GLP-1 agonist,

wherein the GDF-8 inhibitor is an antibody or antigen-binding fragment thereof that specifically binds GDF-8, and

wherein the anti-GDF-8 antibody or antigen-binding fragment thereof comprises the heavy chain complementarity determining regions (HCDRs) of a heavy chain variable region

(HCVR) comprising SEQ ID NO:4, and the light chain complementarity determining regions (LCDRs) of a light chain variable region (LCVR) comprising SEQ ID NO:5.

18. Use of an Activin A inhibitor in the manufacture of a medicament for improving glucose control, increasing lean body mass, reducing fat mass, treating obesity, treating diabetes, and/or treating liver issues associated with increased fat mass, obesity, and/or diabetes in a subject,

wherein the medicament is to be used with a GDF-8 inhibitor, and a GLP-1 agonist,

wherein the GDF-8 inhibitor is an antibody or antigen-binding fragment thereof that specifically binds GDF-8, and

wherein the anti-GDF-8 antibody or antigen-binding fragment thereof comprises the heavy chain complementarity determining regions (HCDRs) of a heavy chain variable region (HCVR) comprising SEQ ID NO:4, and the light chain complementarity determining regions (LCDRs) of a light chain variable region (LCVR) comprising SEQ ID NO:5.

19. The use of any one of claims 16 to 18, wherein the GDF-8 inhibitor and the GLP-1 agonist, and the Activin A inhibitor, if present, are in a single composition.

20. The use of any one of claims 16 to 18, wherein the GDF-8 inhibitor and the GLP-1 agonist, and the Activin A inhibitor, if present, are in at least two separate compositions.

21. The use of any one of claims 16-20, wherein the GDF-8 inhibitor is a GDF-8-specific binding protein.

22. The use of any one of claims 16-21, wherein the anti-GDF-8 antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) comprising the amino acid sequences of SEQ ID NO:6, SEQ ID NO:7, and SEQ ID NO:8, respectively, and three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3) comprising the amino acid sequences of SEQ ID NO:9, TTS, and SEQ ID NO:11, respectively.

23. The use of any one of claims 17-22, wherein the Activin A inhibitor, if present, is an Activin A-specific binding protein.

24. The use of any one of claims 17-23, wherein the Activin A inhibitor, if present, is an antibody or antigen-binding fragment thereof that specifically binds Activin A.

25. The use of claim 24, wherein the anti-Activin A antibody or antigen-binding fragment thereof comprises the heavy chain complementarity determining regions (HCDRs) of a heavy chain variable region (HCVR) comprising SEQ ID NO:12, and the light chain complementarity determining regions (LCDRs) of a light chain variable region (LCVR) comprising SEQ ID NO:13.

26. The use of claim 24 or 25, wherein the anti-Activin A antibody or antigen-binding fragment thereof comprises three heavy chain complementarity determining regions (HCDR1, HCDR2, and HCDR3) comprising the amino acid sequences of SEQ ID NO:14, SEQ ID NO:15, and SEQ ID NO:16, respectively, and three light chain complementarity determining regions (LCDR1, LCDR2, and LCDR3) comprising the amino acid sequences of SEQ ID NO:17, GAS, and SEQ ID NO:19, respectively.

27. The use of any one of claims 16-26, wherein the GLP-1 agonist is a GLP-1 receptor agonist.

28. The use of any one of claims 16-26, wherein the GLP-1 agonist is selected from the group consisting of Exenatide (long-acting), Dulaglutide, Liraglutide, Tirzepatide, and Semaglutide.

29. The use of claim 28, wherein the GLP-1 agonist is Semaglutide.

30. The use of any one of claims 16-26, wherein the GLP-1 agonist is a GLP-1-specific binding protein.

31. The use of claim 30, wherein the GLP-1 agonist is an antibody or antigen-binding fragment thereof that specifically binds GLP-1.

32. The use of any one of claims 16-31, wherein the subject, at 12 weeks from the inhibitor(s) and the agonist to be administered, exhibits at least one parameter change selected from the group consisting of:

i) at least about 35% decrease in fat mass;

ii) at least about 6% increase in lean mass;

iii) at least about 15% decrease in fasting glucose;

iv) at least about 6% decrease in HbA1c;

v) at least about 14% decrease in LDL;

vi) at least about 14% increase in HDL;

vii) at least about 35% decrease in NEFA; and

viii) at least about 55% decrease in TG.

33. The use of claim 32, wherein the subject, at 12 weeks from the inhibitor(s) and the agonist to be administered, exhibits at least one parameter change selected from the group consisting of:

i) at least about 25% decrease in fasting glucose;

iv) at least about 25% decrease in HbA1c;

v) at least about 50% decrease in LDL;

vi) at least about 60% increase in HDL;

vii) at least about 50% decrease in NEFA; and

viii) at least about 65% decrease in TG.