What is Claimed is:

1. Use of an agonist of the leptin-melanocortin signaling pathway in the manufacture of a medicament for treating a subject having obesity in a subject.

2. Use of an agonist of the leptin-melanocortin signaling pathway in the manufacture of a medicament for treating a subject having elevated BMI.

3. The use according to claim 1 or claim 2, wherein the agonist of the leptin-melanocortin signaling pathway is a melanocortin-4 receptor (MC4R) agonist or a proprotein convertase subtilisin/kexin type 1 (PCSK1) agonist.

4. The use according to claim 3, wherein the MC4R agonist comprises a protein, a peptide, a nucleic acid molecule, or a small molecule.

5. The use according to claim 4, wherein the protein is a peptide analog of MC4R.

6. The use according to claim 4, wherein the peptide is setmelanotide.

7. The use according to claim 4, wherein the MC4R agonist is peptide comprising the amino acid sequence His-Phe-Arg-Trp (SEQ ID NO:32).

8. The use according to claim 4, wherein the MC4R agonist is 1,2,3R,4-tetrahydroisoquinoline-3-carboxylic acid.

9. The use according to claim 4, wherein the MC4R agonist is ALB-127158(a).

10. The use according to any one of claims 1 to 9, further comprising detecting the presence or absence of a PCSK1 variant nucleic acid molecule or PCSK1 variant polypeptide associated with an increased risk of developing obesity and/or elevated BMI in a biological sample from the subject.

11. The use according to claim 10, wherein the PCSK1 variant nucleic acid molecule associated with an increased risk of developing obesity and/or elevated BMI is a PCSK1 predicted loss-of-function variant or PCSK1 missense variant, or an mRNA molecule produced therefrom, or a cDNA molecule produced from the mRNA molecule.

12. The use according to claim 10 or claim 11, wherein detecting the presence or absence of the PCSK1 variant nucleic acid molecule or variant polypeptide associated with an increased risk of developing obesity and/or elevated BMI comprises:

determining whether the subject is heterozygous for a PCSK1 variant genomic nucleic acid molecule associated with an increased risk of developing obesity and/or elevated BMI, a PCSK1 variant mRNA molecule associated with an increased risk of developing obesity and/or elevated BMI, a PCSK1 variant cDNA molecule produced from the mRNA molecule, and/or a

PCSK1 variant polypeptide associated with an increased risk of developing obesity and/or elevated BMI, by:

obtaining or having obtained a biological sample from the subject; and

performing or having performed an assay on the biological sample to determine whether the subject is heterozygous for a PCSK1 variant nucleic acid molecule or variant polypeptide associated with an increased risk of developing obesity and/or elevated BMI.

13. The use according to claim 12, further comprising determining the subject's aggregate burden of having: a PCSK1 variant genomic nucleic acid molecule associated with an increased risk of developing obesity and/or elevated BMI, a PCSK1 variant mRNA molecule associated with an increased risk of developing obesity and/or elevated BMI, a PCSK1 variant cDNA molecule produced from the mRNA molecule, and/or a PCSK1 variant polypeptide associated with an increased risk of developing obesity and/or elevated BMI.

14. The use according to claim 13, wherein the subject is heterozygous for at least one PCSK1 loss-of-function variant.

15. The use according to claim 14, wherein the PSCK1 loss-of-function variant is a protein truncating variant.

16. A method of identifying susceptibility of an obese subject to treatment with an agonist of the leptin-melanocortin signaling pathway, the method comprising: detecting the presence or absence of one copy of a PCSK1 genetic variant associated with an increased risk of developing obesity and/or elevated BMI in a biological sample from the subject, wherein when one copy of a PCSK1 genetic variant is detected, the obese subject is susceptible to treatment with the agonist of the leptin-melanocortin signaling pathway.

17. A method of identifying susceptibility of a subject having elevated BMI to treatment with an agonist of the leptin-melanocortin signaling pathway, the method comprising: detecting the presence or absence of one copy of a PCSK1 genetic variant associated with an increased risk of developing obesity and/or elevated BMI in a biological sample from the subject, wherein when one copy of a PCSK1 genetic variant is detected, the subject is susceptible to treatment with the agonist of the leptin-melanocortin signaling pathway.

18. The method according to claim 16 or claim 17, wherein the PCSK1 genetic variant associated with an increased risk of developing obesity and/or elevated BMI is a PCSK1 loss-of-function variant or PCSK1 missense variant.

19. The method according to any one of claims 16 to 18, wherein detecting the PCSK1 genetic variant associated with an increased risk of developing obesity and/or elevated BMI comprises detecting a PCSK1 variant genomic nucleic acid molecule associated with an increased risk of developing obesity and/or elevated BMI, a PCSK1 variant mRNA molecule associated with an increased risk of developing obesity and/or elevated BMI, a PCSK1 variant cDNA molecule produced from the mRNA molecule, and/or a PCSK1 variant polypeptide associated with an increased risk of developing obesity and/or elevated BMI, by:

obtaining or having obtained a biological sample from the subject; and

performing or having performed an assay on the biological sample to determine whether the subject is heterozygous for a PCSK1 variant nucleic acid molecule or PCSK1 variant polypeptide associated with an increased risk of developing obesity and/or elevated BMI.

20. The method according to any one of claims 16 to 19, wherein the agonist of the leptin-melanocortin signaling pathway is to be further administered to the subject identified as susceptible to the leptin-melanocortin signaling pathway agonist treatment.

21. The method according to any one of claims 16 to 20, wherein the agonist of the leptin-melanocortin signaling pathway is an MC4R agonist or a PCSK1 agonist.

22. The method according to claim 21, wherein the MC4R agonist comprises a protein, a peptide, a nucleic acid molecule, or a small molecule.

23. The method according to claim 22, wherein the protein is a peptide analog of MC4R.

24. The method according to claim 22, wherein the peptide is setmelanotide.

25. The method according to claim 22, wherein the MC4R agonist is peptide comprising the amino acid sequence His-Phe-Arg-Trp.

26. The method according to claim 22, wherein the MC4R agonist is 1,2,3R,4-tetrahydroisoquinoline-3-carboxylic acid.

27. The method according to claim 22, wherein the MC4R agonist is ALB-127158(a).