CLAIMS

1. A combination comprising an FGF21 (fibroblast growth factor 21) compound and a GLP-1R (glucagon-like peptide-1 receptor) agonist,

wherein the FGF21 compound has an FGF21 activity which is the same as or is in the range of 50% to 150% of the FGF21 activity of native FGF21, and

wherein the GLP-1R agonist has a GLP-1R agonistic activity which is 9- to 531-fold reduced as compared to the GLP-1R agonistic activity of native GLP-1(7-36), wherein the GLP-1R agonist comprises or consists of the amino acid sequence

H-G-E-G-T-F-T-S-D-X_{10}-S-X_{12}-Q-X_{14}-X_{15}-E-E-X_{18}-V-X_{20}-X_{21}-F-I-E-W-L-X_{27}-X_{28}-X_{29}-X_{30}
(SEQ ID NO: 37),

wherein

X_{10} is L or K;

X_{12} is K or I;

X_{14} is L;

X_{15} is E or D;

X_{18} is A or R;

X_{20} is R or Q;

X_{21} is L or E;

X_{27} is L, E, K or V;

X_{28} is A;

X_{29} is T or G;

X_{30} is G or R;

wherein, optionally, the amino acid sequence comprises at least one additional amino acid residue at its N-terminus; and

wherein, optionally, the amino acid sequence comprises a peptide extension consisting of up to 12, 11 or 10 amino acid residues at its C-terminus.

2. The combination according to claim 1, wherein the GLP-1R agonist has a GLP-1R agonistic activity which is 9- to 482-fold or 9- to 319-fold or 9- to 121-fold reduced as compared to the GLP-1R agonistic activity of native GLP-1(7-36); or wherein the GLP-1R agonist has a GLP-1R agonistic activity which is 18- to 501-fold or 18- to 469-fold or 18- to 313-fold or 18- to 123-fold reduced as compared to the GLP-1R agonistic activity of native GLP-1(7-36).

3. The combination according to claim 1 or 2, wherein the FGF21 compound is native FGF21 or an FGF21 variant having at least 80% or at least 90% or at least 95% amino acid sequence identity to the amino acid sequence of native FGF21.

4. The combination according to any of claims 1 to 3, wherein the GLP-1R agonist comprises or consists of an amino acid sequence selected from the group consisting of SEQ ID NOs: 9, 10, 12, 14, 16, 17, 19 and 20.

5. A pharmaceutical composition comprising an FGF21 (fibroblast growth factor 21) compound and a GLP-1R (glucagon-like peptide-1 receptor) agonist together with a pharmaceutically acceptable carrier and/or excipient,
wherein the FGF21 compound has an FGF21 activity which is the same as or is in the range of 50% to 150% of the FGF21 activity of native FGF21, and
wherein the GLP-1R agonist has a GLP-1R agonistic activity which is 9- to 531-fold reduced as compared to the GLP-1R agonistic activity of native GLP-1(7-36), wherein the GLP-1R agonist comprises or consists of the amino acid sequence

H-G-E-G-T-F-T-S-D-X_{10}-S-X_{12}-Q-X_{14}-X_{15}-E-E-X_{18}-V-X_{20}-X_{21}-F-I-E-W-L-X_{27}-X_{28}-X_{29}-X_{30}
(SEQ ID NO: 37),

wherein
X_{10} is L or K;
X_{12} is K or I;
X_{14} is L;
X_{15} is E or D;
X_{18} is A or R;
X_{20} is R or Q;
X_{21} is L or E;
X_{27} is L, E, K or V;
X_{28} is A;
X_{29} is T or G;
X_{30} is G or R;
wherein, optionally, the amino acid sequence comprises at least one additional amino acid residue at its N-terminus; and
wherein, optionally, the amino acid sequence comprises a peptide extension consisting of up to 12, 11 or 10 amino acid residues at its C-terminus.

6. A fusion molecule comprising an FGF21 (fibroblast growth factor 21) compound and a GLP-1R (glucagon-like peptide-1 receptor) agonist,
wherein the FGF21 compound has an FGF21 activity which is the same as or is in the range of 50% to 150% of the FGF21 activity of native FGF21, and
wherein the GLP-1R agonist has a GLP-1R agonistic activity which is 9- to 531-fold reduced as compared to the GLP-1R agonistic activity of native GLP-1(7-36), wherein the GLP-1R agonist comprises or consists of the amino acid sequence

H-G-E-G-T-F-T-S-D-X_{10}-S-X_{12}-Q-X_{14}-X_{15}-E-E-X_{18}-V-X_{20}-X_{21}-F-I-E-W-L-X_{27}-X_{28}-X_{29}-X_{30}
(SEQ ID NO: 37),

wherein
X_{10} is L or K;
X_{12} is K or I;
X_{14} is L;
X_{15} is E or D;
X_{18} is A or R;
X_{20} is R or Q;
X_{21} is L or E;
X_{27} is L, E, K or V;
X_{28} is A;
X_{29} is T or G;
X_{30} is G or R;
wherein, optionally, the amino acid sequence comprises at least one additional amino acid residue at its N-terminus; and
wherein, optionally, the amino acid sequence comprises a peptide extension consisting of up to 12, 11 or 10 amino acid residues at its C-terminus.

7. The pharmaceutical composition according to claim 5 or the fusion molecule according to claim 6, wherein the GLP-1R agonist and/or the FGF21 compound are as defined in any of claims 2 to 4.

8. A nucleic acid molecule encoding a fusion molecule according to claim 6 or 7.

9. A host cell containing a nucleic acid molecule according to claim 8.

10. A kit comprising a combination according to any of claims 1 to 4, a pharmaceutical composition according to claim 5 or 7, a fusion molecule according to claim 6 or 7, a nucleic acid molecule according to claim 8 or a host cell according to claim 9.

11. A combination according to any of claims 1 to 4, a pharmaceutical composition according to claim 5 or 7, a fusion molecule according to claim 6 or 7, a nucleic acid molecule according to claim 8 or a host cell according to claim 9 for use as a medicament.

12. A combination according to any of claims 1 to 4, a pharmaceutical composition according to claim 5 or 7, a fusion molecule according to claim 6 or 7, a nucleic acid molecule according to claim 8 or a host cell according to claim 9 for use in the treatment of a disease or disorder selected from the group consisting of obesity, metabolic syndrome, diabetes mellitus, diabetic retinopathy, hyperglycemia, dyslipidemia, Non-Alcoholic SteatoHepatitis (NASH) and atherosclerosis.

13. The combination, pharmaceutical composition, fusion molecule, nucleic acid molecule or host cell for use according to claim 12, wherein the diabetes mellitus is type 1 diabetes mellitus or type 2 diabetes mellitus.

14. A GLP-1R agonist having a GLP-1R agonistic activity which is 9- to 531-fold reduced as compared to the GLP-1R agonistic activity of native GLP-1(7-36), wherein the GLP-1R agonist comprises or consists of the amino acid sequence

H-G-E-G-T-F-T-S-D-X_{10}-S-X_{12}-Q-X_{14}-X_{15}-E-E-X_{18}-V-X_{20}-X_{21}-F-I-E-W-L-X_{27}-X_{28}-X_{29}-X_{30}
(SEQ ID NO:37),

wherein
X_{10} is L or K;
X_{12} is K or I;
X_{14} is L;
X_{15} is E or D;
X_{18} is A or R;
X_{20} is R or Q;
X_{21} is L or E;
X_{27} is L, E, K or V;
X_{28} is A;
X_{29} is T or G;
X_{30} is G or R;

wherein, optionally, the amino acid sequence comprises at least one additional amino acid residue at its N-terminus; and

wherein, optionally, the amino acid sequence comprises a peptide extension consisting of up to 12, 11 or 10 amino acid residues at its C-terminus.

15. The GLP-1R agonist according to claim 14 comprising or consisting of an amino acid sequence selected from the group consisting of SEQ ID NOs: 9, 10, 12, 14, 16, 17, 19 and 20.