

CLAIMS

1. An isotonic parenteral pharmaceutical composition, comprising:
 - a. at least about 1 mg/mL of one or more GLP-1/GLP-2 dual agonist comprising general formula A:

H[Aib]EG-X5-F-X7-SELATILD-[Ψ]-QAARDFIAWLI-X28-X29-KITD (A),

wherein X5 is T or S; X7 is T or S; X28 is Q, E, A, H, Y, L, K, R or S; X29 is H and at least one of X5 and X7 is T, and
wherein [Ψ] indicates an L or D lysine residue in which an albumin binding moiety is conjugated to the GLP-1/GLP-2 dual agonist, and
wherein said albumin binding moiety is [K([17-carboxy-heptadecanoyl]-isoGlu)]; and
 - b. about 1 mM to about 200 mM of buffer component; and
 - c. about 1 mM to about 500 mM of one or more tonicity agent, preferably about 50 mM to about 450 mM of one or more tonicity agent,wherein said one or more tonicity agent comprises or is, preferably is, an ionic or a non-ionic tonicity agent, wherein the ionic tonicity agent is selected from the group consisting of salts, alkali metals or earth metal halides, and the non-ionic tonicity agent is mannitol, such as D-mannitol,
wherein said composition further comprises a solvent, and
wherein said composition has a pH of about pH 6.0 to about pH 8.2, preferably a pH of about pH 7.0 to about pH 8.0.
2. The isotonic parenteral pharmaceutical composition of claim 1 wherein
 - a. said non-ionic tonicity agent is D-mannitol; or
 - b. said one or more tonicity agent is an ionic tonicity agent, selected from the group consisting of CaCl₂, KBr, KCl, LiCl, NaI, NaBr, NaCl or Na₂SO₄, preferably wherein the ionic tonicity agent is NaCl or KCl.
3. The parenteral pharmaceutical composition of any one of the preceding claims, wherein said one or more GLP-1/GLP-2 dual agonist comprising general formula A is of the general formula B:

H[Aib]EG-X5-FT-SELATILD-[Ψ]-QAARDFIAWLI-X28-HKITD (B),

wherein X5 is T or S; X28 is Q, E, A, H, Y, L, K, R or S and
wherein [Ψ] indicates an L or D lysine residue in which the albumin binding moiety is conjugated to the GLP-1/GLP-2 dual agonist and
wherein said albumin binding moiety is [K([17-carboxy-heptadecanoyl]-isoGlu)],
preferably wherein said one or more GLP-1/GLP-2 dual agonist comprising general formula A or B comprises the sequence:

H[Aib]EGSFTSELATILD[Ψ]QAARDFIAWLIQHKITD (SEQ ID NO: 1), preferably wherein said one or more GLP-1/GLP-2 dual agonist comprising general formula A or B is:

- a. Hy-H[Aib]EGSFTSELATILD[K([17-carboxy-heptadecanoyl]-isoGlu)]QAARDFIAWLIQHKITD-OH (CPD1OH); or
- b. Hy-H[Aib]EGSFTSELATILD[K([17-carboxy-heptadecanoyl]-isoGlu)]QAARDFIAWLIQHKITD-NH₂ (CPD1NH₂).

4. The isotonic parenteral pharmaceutical composition according to any one of the preceding claims, wherein said buffer component is selected from the group consisting of phosphate buffer, citrate buffer, histidine buffer, tris buffer or bis tris, or a combination thereof, preferably selected from the group consisting of phosphate buffer, citrate buffer, tris buffer or bis tris, or a combination thereof, preferably wherein said buffer component is phosphate buffer, preferably wherein said buffer component is a sodium phosphate buffer, preferably wherein said sodium phosphate buffer is selected from disodium phosphate or sodium dihydrogen phosphate, or a combination thereof.

5. The isotonic parenteral pharmaceutical composition according to any preceding claim wherein said buffer component is at a final concentration of about 15 mM to about 200 mM, preferably about 15mM to about 30mM, preferably wherein said buffer component is at a final concentration of about 20mM.

6. The isotonic parenteral pharmaceutical composition according to any one of claims 1 to 5 wherein said non-ionic tonicity agent is mannitol, and wherein said mannitol is at a final concentration of about 190 mM to about 240 mM, preferably about 230 mM.

7. The isotonic parenteral pharmaceutical composition according to any one of claims 1 to 5 wherein said tonicity agent is a salt, preferably NaCl or KCl, and wherein said salt is present at a final concentration of about 50 mM to about 450 mM, preferably about 115 mM, most preferably the salt is NaCl at a final concentration of about 115 mM.

8. The isotonic parenteral pharmaceutical composition of any one of the preceding claims, wherein the osmolality of the composition is about 230 mOsmol/kg to about 370 mOsmol/kg.

9. The isotonic parenteral pharmaceutical composition of any one of claims 1 to 6 or 8, wherein

a. said buffer component is a phosphate buffer at a final concentration of about 15 mM to about 200 mM, preferably about 20 mM, said one or more tonicity agent is mannitol, preferably D-mannitol, at a final concentration of about 190 mM to about 240 mM, preferably about 230 mM, and said one or more GLP-1/GLP-2 dual agonist comprises SEQ ID NO: 1 or any pharmaceutically acceptable salt thereof, wherein the pH is between about pH 7.0 and about pH 8.0, preferably about pH 8.0; or

b. said buffer component is a phosphate buffer at a final concentration of about 15 mM to about 30 mM, said one or more tonicity agent is mannitol, preferably D-mannitol, at a final concentration of about 230 mM and said one or more GLP-1/GLP-2 dual agonist comprises SEQ ID NO: 1 or any pharmaceutically acceptable salt thereof, wherein the pH is between about pH 7.0 and about pH 8.0, preferably about pH 8.0.

10. The isotonic parenteral pharmaceutical composition of any one of claims 1 to 5, 7 or 8, wherein

a. said buffer component is a phosphate buffer at a final concentration of about 15 mM to about 200 mM, preferably about 20 mM, said one or more tonicity agent is a salt, preferably NaCl or KCl, at a final concentration of about 50 mM to about 450 mM, preferably about 115 mM, and said one or more GLP-1/GLP-2 dual agonist comprises SEQ ID NO: 1 or any pharmaceutically acceptable salt thereof, wherein the pH is between about pH 7.0 and about pH 8.0, preferably about pH 8.0; or

b. said buffer component is a phosphate buffer at a final concentration of about 15 mM to about 30 mM, wherein said one or more tonicity agent is a salt, preferably NaCl or KCl, at a final concentration of about 50 mM to about 450 mM, preferably about 115 mM, and said one or more GLP-1/GLP-2 dual agonist comprises SEQ ID NO: 1 or any pharmaceutically acceptable salt thereof.

11. The isotonic parenteral pharmaceutical composition of any one of the preceding claims, wherein said one or more GLP-1/GLP-2 dual agonist is present at a concentration of about 1 mg/mL to about 15 mg/mL.

12. The isotonic parenteral pharmaceutical composition of any one of claims 1 to 6, 8, 9 or 11, comprising

a. SEQ ID NO: 1 or a chloride salt thereof, a phosphate buffer at a concentration of about 15 mM to about 30 mM, preferably about 20 mM, mannitol preferably D-mannitol at a concentration of about 230 mM, water for injection and sodium hydroxide and/or hydrochloric acid for pH adjustment to a pH of about pH 8.0, wherein said one or more GLP-1/GLP-2 dual agonist is CPD1OH or CPD1NH₂, preferably Hy-H[Aib]EGSFTSELATILD[K([17-carboxy-

heptadecanoyl]-isoGlu)]QAARDFIAWLIQHKITD-OH (CPD1OH) and is present at about 2 mg/mL; or

b. SEQ ID NO: 1 or a chloride salt thereof, a phosphate buffer at a concentration of about 15 mM to about 30 mM, preferably about 20 mM, mannitol preferably D-mannitol at a concentration of about 230 mM, water for injection and sodium hydroxide and/or hydrochloric acid for pH adjustment to a pH of about pH 8.0, wherein said one or more GLP-1/GLP-2 dual agonist is CPD1OH or CPD1NH₂, preferably Hy-H[Aib]EGSFTSELATILD[K([17-carboxy-heptadecanoyl]-isoGlu)]QAARDFIAWLIQHKITD-OH (CPD1OH) and is present at about 10 mg/mL.

13. The isotonic parenteral pharmaceutical composition of any one of claims 1 to 5, 7, 8, 10 or 11, comprising

a. SEQ ID NO: 1 or a chloride salt thereof, a phosphate buffer at a concentration of about 15 mM to about 30 mM, preferably about 20 mM, a salt, preferably NaCl or KCl, at a concentration of about 115 mM, water for injection and sodium hydroxide and/or hydrochloric acid for pH adjustment to a pH of about pH 8.0, wherein said one or more GLP-1/GLP-2 dual agonist is CPD1OH or CPD1NH₂, preferably Hy-H[Aib]EGSFTSELATILD[K([17-carboxy-heptadecanoyl]-isoGlu)]QAARDFIAWLIQHKITD-OH (CPD1OH) and is present at about 2 mg/mL; or

b. SEQ ID NO: 1 or a chloride salt thereof, a phosphate buffer at a concentration of about 15 mM to about 30 mM, preferably about 20 mM, a salt, preferably NaCl or KCl, at a concentration of about 115 mM, water for injection and sodium hydroxide and/or hydrochloric acid for pH adjustment to a pH of about pH 8.0, wherein said one or more GLP-1/GLP-2 dual agonist is CPD1OH or CPD1NH₂, preferably Hy-H[Aib]EGSFTSELATILD[K([17-carboxy-heptadecanoyl]-isoGlu)]QAARDFIAWLIQHKITD-OH (CPD1OH) and is present at about 10 mg/mL.

14. The isotonic parenteral pharmaceutical composition of claim 12 or claim 13, wherein said one or more GLP-1/GLP-2 dual agonist is Hy-H[Aib]EGSFTSELATILD[K([17-carboxy-heptadecanoyl]-isoGlu)]QAARDFIAWLIQHKITD-OH (CPD1OH).

15. The isotonic parenteral pharmaceutical composition of any one of claims 1 to 6, 8, 9, 11, 12 or 14, wherein

a. said composition comprises the ingredients:

Component	Amount per mL (CPD1OH ₂)	Function
CPD1OH	2 mg	Drug Substance
Na ₂ HPO ₄ (anhydrous)	2.65 mg	Buffer component

Disodium phosphate, anhydrous / Dibasic sodium phosphate, anhydrous		
NaH ₂ PO ₄ (anhydrous) Sodium dihydrogen phosphate, anhydrous / Monobasic sodium phosphate, anhydrous	0.16 mg	Buffer component
Mannitol (D-mannitol)	41.90 mg	Tonicity agent
Hydrochloric acid	pH adjustment to about pH 8	
Sodium Hydroxide	pH adjustment to about pH 8	
Water for Injections	To make 1 mL	Solvent

; or

b. said composition comprises the ingredients:

Component	Amount per mL (CPD1OH ₂)	Function
CPD1OH	10 mg	Drug Substance
Na ₂ HPO ₄ (anhydrous) Disodium phosphate, anhydrous / Dibasic sodium phosphate, anhydrous	2.65 mg	Buffer component
NaH ₂ PO ₄ (anhydrous) Sodium dihydrogen phosphate, anhydrous / Monobasic sodium phosphate, anhydrous	0.16 mg	Buffer component
Mannitol (D-mannitol)	41.90 mg	Tonicity agent
Hydrochloric acid	pH adjustment to about pH 8	
Sodium Hydroxide	pH adjustment to about pH 8	
Water for Injections	To make 1 mL	Solvent

16. The isotonic parenteral pharmaceutical composition of any one of claims 1 to 5, 7, 8, 10, 11, 13 or 14, wherein

a. said composition comprises the ingredients:

Component	Amount per mL (CPD1OH ₂)	Function
CPD1OH	2 mg	Drug Substance
Na ₂ HPO ₄ (anhydrous) Disodium phosphate, anhydrous / Dibasic sodium phosphate, anhydrous	2.65 mg	Buffer component
NaH ₂ PO ₄ (anhydrous) Sodium dihydrogen phosphate, anhydrous / Monobasic sodium phosphate, anhydrous	0.16 mg	Buffer component
NaCl or KCl	6.7 mg NaCl or 8.6 mg KCl	Tonicity agent
Hydrochloric acid	pH adjustment to about pH 8	
Sodium Hydroxide	pH adjustment to about pH 8	
Water for Injections	To make 1 mL	Solvent

; or

b. said composition comprises the ingredients:

Component	Amount per mL (CPD1OH ₂)	Function
CPD1OH	10 mg	Drug Substance
Na ₂ HPO ₄ (anhydrous) Disodium phosphate, anhydrous / Dibasic sodium phosphate, anhydrous	2.65 mg	Buffer component

NaH ₂ PO ₄ (anhydrous) Sodium dihydrogen phosphate, anhydrous / Monobasic sodium phosphate, anhydrous	0.16 mg	Buffer component
NaCl or KCl	6.7 mg NaCl or 8.6 mg KCl	Tonicity agent
Hydrochloric acid	pH adjustment to about pH 8	
Sodium Hydroxide	pH adjustment to about pH 8	
Water for Injections	To make 1 mL	Solvent

17. The isotonic parenteral pharmaceutical composition of any one of the preceding claims, wherein said composition

- a. is suitable for s.c. or *i.v.* injection into human subjects; and/or
- b. has a shelf-life of at least about 1, 2, 3, 4, 6, 12, 18 or 24 months, preferably at least about 24 months; and/or
- c. has a chemical stability of at least about 90% after 12 months storage; and/or
- d. has a chemical stability of at least about 97% after 12 months storage, preferably storage at about 5°C; and/or
- e. has a chemical stability of at least about 97% after 24 months storage, preferably at about 5°C.

18. A method for improving the chemical stability of an isotonic parenteral pharmaceutical composition comprising at least about 1 mg/mL of one or more GLP-1/GLP-2 dual agonist comprising general formula A:

H[Aib]EG-X5-F-X7-SELATILD-[Ψ]-QAARDFIAWLI-X28-X29-KITD (A),
wherein X5 is T or S; X7 is T or S; X28 is Q, E, A, H, Y, L, K, R or S; X29 is H and at least one of X5 and X7 is T, and
wherein [Ψ] indicates an L or D lysine residue in which an albumin binding moiety is conjugated to the GLP-1/GLP-2 dual agonist, and
wherein said albumin binding moiety is [K([17-carboxy-heptadecanoyl]-isoGlu)]; wherein said method comprises adding mannitol, preferably D-mannitol, or a salt, preferably NaCl or KCl, to said composition.

19. Use of mannitol, preferably D-mannitol, or a salt, preferably NaCl or KCl for improving the chemical stability of an isotonic parenteral pharmaceutical composition comprising at least about 1 mg/mL of one or more GLP-1/GLP-2 dual agonist comprising general formula A:

H[Aib]EG-X5-F-X7-SELATILD-[Ψ]-QAARDFIAWLI-X28-X29-KITD (A),
wherein X5 is T or S; X7 is T or S; X28 is Q, E, A, H, Y, L, K, R or S; X29 is H and at least one of X5 and X7 is T, and

wherein [Ψ] indicates an L or D lysine residue in which an albumin binding moiety is conjugated to the GLP-1/GLP-2 dual agonist, and
wherein said albumin binding moiety is [K([17-carboxy-heptadecanoyl]-isoGlu)].

20. The isotonic parenteral pharmaceutical composition of any one of the preceding claims, for use in:

- (i) increasing intestinal mass, improving intestinal function, increasing intestinal blood flow, or repairing intestinal damage or dysfunction, in a subject in need thereof; or
- (ii) the prophylaxis or treatment of malabsorption, ulcers, short-bowel syndrome, cul-de-sac syndrome, inflammatory bowel disease, irritable bowel syndrome, pouchitis, celiac sprue, tropical sprue, hypogammaglobulinemic sprue, mucositis induced by chemotherapy or radiation therapy, diarrhoea induced by chemotherapy or radiation therapy, low grade inflammation, metabolic endotoxemia, necrotising enterocolitis, primary biliary cirrhosis, hepatitis, fatty liver disease, or gastrointestinal side-effects of inflammatory conditions, in a subject in need thereof; or
- (iii) reducing or inhibiting weight gain, reducing gastric emptying or intestinal transit, reducing food intake, reducing appetite, or promoting weight loss, in a subject in need thereof; or
- (iv) the prophylaxis or treatment of obesity, morbid obesity, obesity-linked gallbladder disease, obesity-induced sleep apnoea, inadequate glucose control, glucose tolerance, dyslipidaemia, diabetes, pre-diabetes, metabolic syndrome or hypertension, in a subject in need thereof.