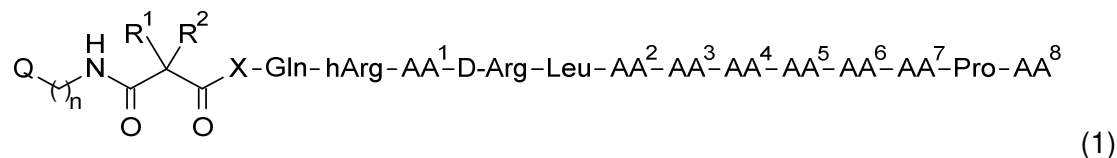


Claims

1. A compound comprising the sequence of formula (1):



wherein;

Q is selected from phenyl or a monocyclic heteroaryl ring each of which may be optionally substituted with one or more R^q groups; or Q is a polyether chain of formula -
 $(\text{OCH}_2\text{CH}_2)_m\text{OCH}_3$, wherein m is 1 to 5;

R^q is selected from halogen, hydroxyl, amino or C_{1-6} alkyl having an alkyl chain optionally containing one or more heteroatoms selected from O, N, or S;

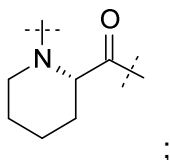
n is 1 to 3;

R^1 and R^2 are independently selected from hydrogen or a C_{1-6} alkyl group, or together with the carbon to which they are attached join to form a C_{3-8} cycloalkyl or a heterocyclyl group;

X is -DArg- or a bond;

-hArg- is a homoarginine residue;

AA^1 is the residue:

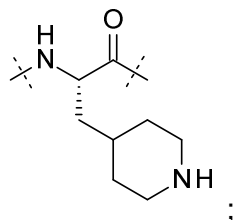


or is an aspartic acid derived residue joined to AA^3 via a lactam bridge;

AA^2 is -Gly- or is a glutamic acid derived residue joined to AA^5 via a lactam bridge;

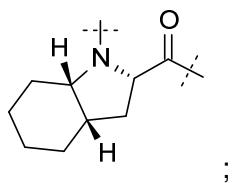
AA³ is -His-, a 4-bromophenylalanine residue or is a lysine derived residue joined to AA¹ via a lactam bridge;

5 AA⁴ is the residue:



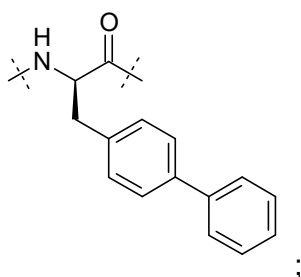
AA⁵ is -Gly- or is a lysine derived residue joined to AA² via a lactam bridge;

10 AA⁶ is the residue:



AA⁷ is a norleucine residue or a 4-bromophenylalanine residue;

15 AA⁸ is the residue:

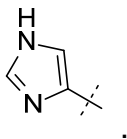


wherein the AA⁸ C-terminus is a carboxyl group or a carboxamide group and wherein the compound contains a lactam bridge;

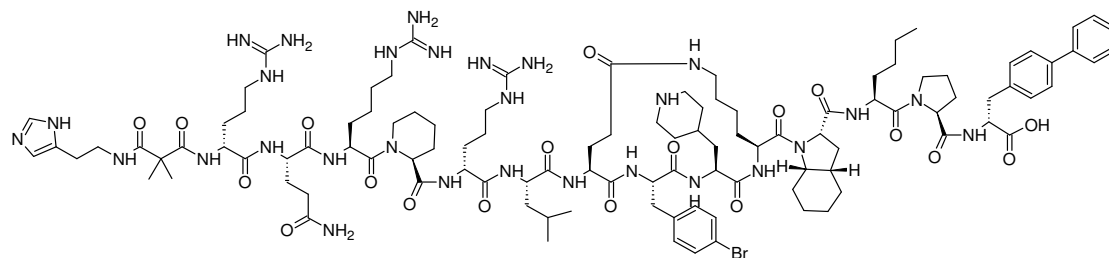
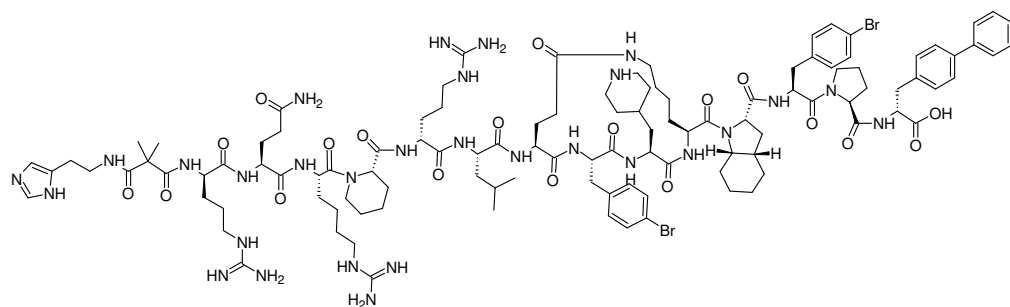
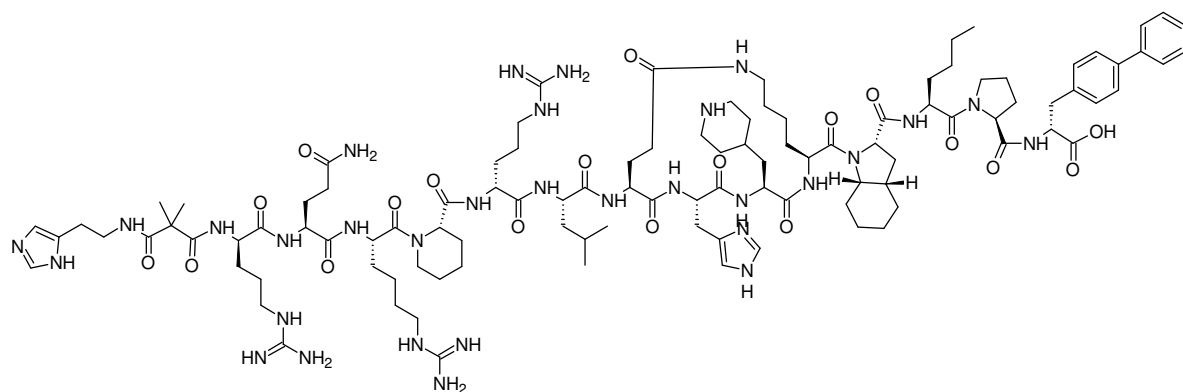
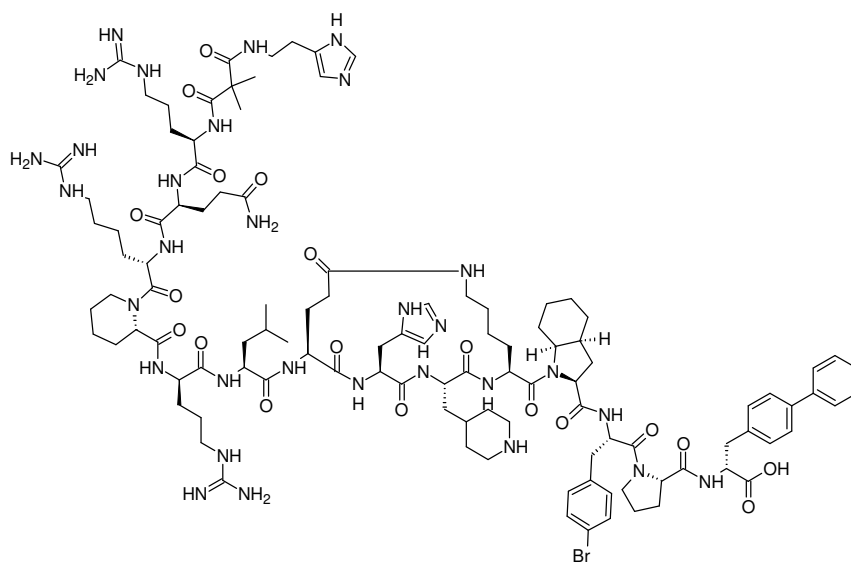
20

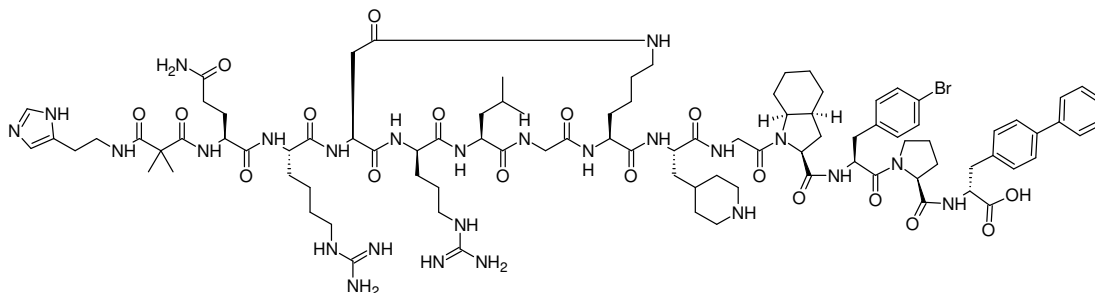
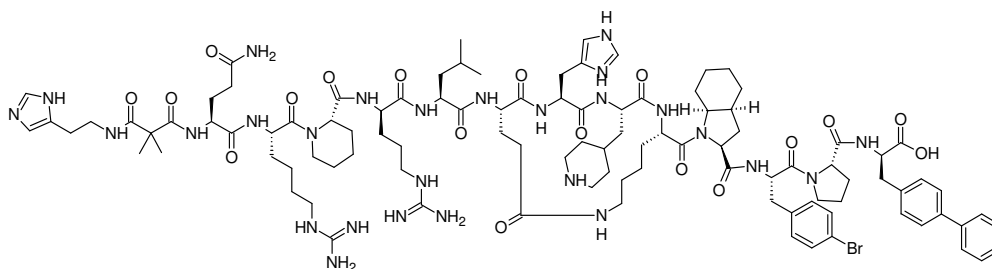
or a tautomeric or stereochemically isomeric form thereof or a prodrug, salt or zwitterion thereof.

2. The compound according to claim 1, wherein Q is:



- 5 3. The compound according to claim 1 or claim 2, wherein n is 2.
4. The compound according to any one of claims 1 to 3, wherein R¹ and R² are independently selected from hydrogen or a C₁₋₆ alkyl group.
- 10 5. The compound according to claim 4, wherein R¹ and R² are both methyl.
6. The compound according to any one of claims 1 to 5, wherein X is -DArg-.
7. The compound according to any one of claims 1 to 5, wherein X is a bond.
- 15 8. The compound according to any one of claims 1 to 7, wherein AA¹ is an aspartic acid derived residue joined via a lactam bridge to AA³ which is a lysine derived residue.
- 20 9. The compound according to any one of claims 1 to 7, wherein AA² a glutamic acid derived residue joined via a lactam bridge to AA⁵ which is a lysine derived residue.
10. The compound according to any one of claims 1 to 9, wherein the AA⁸ C-terminus is a carboxyl group.
- 25 11. The compound according to claim 1 which is selected from the group consisting of:





12. The compound according to any one of claims 1 to 11 having apelin receptor agonist activity.

13. A pharmaceutical composition comprising a compound as defined in any one of claims 1 to 12 and a pharmaceutically acceptable excipient.

14. The compound or composition according to any one of claims 1 to 13 for use in medicine.

15. Use of the compound or composition according to any one of claims 1 to 13 for use in the manufacture of a medicament for the treatment of cardiovascular disease, acute decompensated heart failure, congestive heart failure, myocardial infarction, cardiomyopathy, ischemia, ischemia/reperfusion injury, pulmonary hypertension, diabetes, obesity, cancer, metastatic disease, fluid homeostasis, pathological angiogenesis, retinopathy, HIV infection, treatment of pulmonary arterial hypertension (PAH) increasing cardiac output, reducing pulmonary vessel hypertension, reducing inflammation, improve pulmonary tissue remodelling, preserving right heart ventricular function, heart failure, congestive heart failure, cardiomyopathy, ischemia, ischemia/reperfusion injury, fluid homeostasis, kidney

5

failure, hypertension, pulmonary hypertension, polycystic kidney disease, hyponatremia, SIADH, platelet function are associated with a range of thrombotic diseases such as peripheral arterial disease (PAD), acute coronary syndrome (ACS), myocardial infarction (MI), heart attacks (HA), stroke, atherosclerosis, treatment and management of diabetes and associated related metabolic conditions, diabetic complications (for example diabetic nephropathy, retinopathy, neuropathy, non-alcoholic fatty liver disease, non-alcoholic steatosis, portal hypertension) and conditions where stimulation and/or growth and/or endurance of muscle mass may be considered beneficial.