

-CH₂-O-(CH₂)_{m16}-[#], wherein m16 is 0-6; [#]-CH₂-O-(CH₂)_{m17}-, wherein m17 is 0-6;

(CH₂)_{m18}-NH-CO-CH₂-NH-CO-(CH₂)_{n5}-[#], wherein m18 is 0-3, and n5 is 0 or 1, with the proviso that m18+n5= 0-3; [#]-(CH₂)_{m19}-NH-CO-CH₂-NH-CO-(CH₂)_{n6}-, wherein m19 is 0-3, and n6 is 0 or 1, with the proviso that m19+n6= 0-3;

(CH₂)_{m20}-NH-CO-CH(CH₃)-NH-CO-(CH₂)_{n7}-[#], wherein m20 is 0-3, and n7 is 0 or 1, with the proviso that m20+n7= 0-3; [#]-(CH₂)_{m21}-NH-CO-CH(CH₃)-NH-CO-(CH₂)_{n8}-, wherein m21 is 0-3, and n8 is 0 or 1, with the proviso that m21+n8= 0-3;

(CH₂)_{m22}-NH-CO-CH(CH₂-C(CH₃)₂)-NH-CO-(CH₂)_{n9}-[#], wherein m22 is 0-3, and n9 is 0 or 1, with the proviso that m22+n9= 0-3; [#]-(CH₂)_{m23}-NH-CO-CH(CH₂-C(CH₃)₂)-NH-CO-(CH₂)_{n10}-, wherein m23 is 0-3, and n10 is 0 or 1, with the proviso that m23+n10= 0-3;

(CH₂)_{m24}-NH-CO-CH(CH(CH₃)C₂H₅)-NH-CO-(CH₂)_{n11}-[#], wherein m24 is 0-3, and n11 is 0 or 1, with the proviso that m24+n11= 0-3; [#]-(CH₂)_{m25}-NH-CO-CH(CH(CH₃)C₂H₅)-NH-CO-(CH₂)_{n12}-, wherein m25 is 0-3, and n12 is 0 or 1, with the proviso that m25+n12= 0-3;

(CH₂)_{m26}-NH-CO-CH(CH₂(C₆H₅))-NH-CO-(CH₂)_n-[#], wherein m26 is 0-3, and n13 is 0 or 1, with the proviso that m26+n13= 0-3; [#]-(CH₂)_{m27}-NH-CO-CH(CH₂(C₆H₅))-NH-CO-(CH₂)_{n14}-, wherein m27 is 0-3, and n14 is 0 or 1, with the proviso that m27+n14= 0-3;

(CH₂)_{m28}-NH-CO-(CH₂)₃-NH-CO-(CH₂)_{n15}-[#], wherein m28 is 0 or 1, and n15 is 0 or 1, with the proviso that m28+n15=0-1; [#]-(CH₂)_{m29}-NH-CO-(CH₂)₃-NH-CO-(CH₂)_{n16}-, wherein m29 is 0 or 1, and n16 is 0 or 1, with the proviso that m29+n16=0-1;

(CH₂)_{m30}-NH-CO-NH-(CH₂)_{n17}-[#], wherein m30 is 0-5, and n17 is 0-5, with the proviso that m30+n17=0-5; [#]-(CH₂)_{m31}-NH-CO-NH-(CH₂)_{n18}-, wherein m31 is 0-5, and n18 is 0-5, with the proviso that m31+n18=0-5;

(CH₂)_{m32}-O-CO-NH-(CH₂)_{n19}-[#], wherein m32 is 0-5, and n19 is 0-5, with the proviso that m32+n19=0-5; [#]-(CH₂)_{m33}-O-CO-NH-(CH₂)_{n20}-, wherein m33 is 0-5, and n20 is 0-5, with the proviso that m33+n20=0-5;

*(CH₂)_{m34}-O-CO-O-(CH₂)_{n21}-[#], wherein m 34 is 0-5, and n21 is 0-5, with the proviso that m34+n21=0-5;

*(CH₂)_{m35}-NH-CO-(CH₂)_{n22}-NH-(CH₂)_{p1}-, wherein m35 is 0-4, n22 is 0-4, and p1 is 0-4, with the proviso that m35+n22+p1=0-4; and

$^*-(\text{CH}_2)_{m36}-\text{NH}-\text{CO}-(\text{CH}=\text{CH})-\text{CO}-\text{NH}-(\text{CH}_2)_{n23}-^{\#}$, wherein $m36$ is 0-2, and $n23$ is 0-2, with the proviso that $m36+n23=0-2$;

wherein * and $^{\#}$ reflect where X^1 is bound within the ring structure; and

X^2 is absent, is hydrogen, or is an amino acid or amino acid sequence selected from the group consisting of G^{14} , K^{14} , F^{14} , SEQ ID NO:1 [$Y^1\text{RQSMNNFQGLRSF}^{14}$], SEQ ID NO:2 [$R^2\text{QSMNNFQGLRSF}^{14}$], SEQ ID NO:3 [$Q^3\text{SMNNFQGLRSF}^{14}$], SEQ ID NO:4 [$S^4\text{MNNFQGLRSF}^{14}$], SEQ ID NO:5 [$M^5\text{NNFQGLRSF}^{14}$], SEQ ID NO:6 [$N^6\text{NFQGLRSF}^{14}$], SEQ ID NO:7 [$N^7\text{FQGLRSF}^{14}$], SEQ ID NO:8 [$F^8\text{QGLRSF}^{14}$], SEQ ID NO:9 [$Q^9\text{GLRSF}^{14}$], SEQ ID NO:10 [$G^{10}\text{LRSF}^{14}$], SEQ ID NO:11 [$L^{11}\text{RSF}^{14}$], SEQ ID NO:12 [$R^{12}\text{SF}^{14}$], and SEQ ID NO:13 [$S^{13}\text{F}^{14}$], which is covalently linked by an amide bond to the N-terminal G^{15} of the amino acid sequence of formula (I), wherein any amino acid of X^2 may optionally be replaced by a natural or unnatural amino acid;

wherein A is L-Alanine; R is L-Arginine; N is L-Asparagine; D is L-Aspartic acid; Q is L-Glutamine; G is L-Glycine; H is L-Histidine; I is L-Isoleucine; L is L-Leucine; K is L-Lysine; M is L-Methionine; F is L-Phenylalanine; P is L-Proline; S is L-Serine; T is L-Threonine; Y is L-Tyrosine; V is L-Valine;

wherein the numbering of amino acids in formula (I) and in the definition of X^2 refers to the corresponding human ADM sequence;

X^3 is absent or is a heterologous moiety which is covalently linked to the N-terminus or to a functional group of the side chain of any amino acid of X^2 , to the N-terminus of G^{15} or to Z;

Z is absent or is a cleavable linker covalently bound between the N terminus of any amino acid of X^2 or of G^{15} and X^3 or between a functional group of the side chain of any amino acid of X^2 and X^3

wherein if X^3 is absent, then

Z is also absent and X^2 is hydrogen or is an amino acid or amino acid sequence as defined above;

wherein if X^3 is a heterologous moiety, then

X^2 is absent or is an amino acid or amino acid sequence as defined above; Z is absent or is a cleavable linker covalently bound between the N terminus of any

amino acid of X^2 or of G^{15} and X^3 or between a functional group of the side chain of any amino acid of X^2 and X^3 ;

or a physiologically acceptable salt, a solvate or a solvate of a salt thereof.

2. The compound of formula (I) as claimed in claim 1, wherein X^1 is selected from the group consisting of

$^*-(CH_2)_{m1}-S-^{\#}$, wherein $m1$ is 0-6; $^{\#}-(CH_2)_{m2}-S-^*$, wherein $m2$ is 0-6;

$^*-(CH_2)_{m3}-^{\#}$, wherein $m3$ is 1-8;

$^*-(CH_2)_{m6}-CO-NH-(CH_2)_{n3}-^{\#}$, wherein $m6$ is 0-4, and $n3$ is 0-4, with the proviso that $m6+n3=0-6$;

$^{\#}-(CH_2)_{m7}-CO-NH-(CH_2)_{n4}-^*$, wherein $m7$ is 0-4, and $n4$ is 0-4, with the proviso that $m7+n4=0-6$;

X^2 is G^{14} or K^{14} , which is covalently linked by an amide bond to the N-terminal G^{15} of the compound of formula (I);

X^3 is absent or is a heterologous moiety which is covalently linked to the N-terminus of G^{14} or K^{14} or to a functional group of the side chain of K^{14} , or to Z;

Z is absent or is a cleavable linker covalently bound between the N terminus of G^{14} or K^{14} and X^3 , or between a functional group of the side chain of K^{14} and X^3 ;

wherein if X^3 is absent, then Z is also absent;

wherein if X^3 is a heterologous moiety, then Z is absent or is a cleavable linker covalently bound between the N terminus of G^{14} or K^{14} and X^3 , or between a functional group of the side chain of K^{14} and X^3 ;

or a physiologically acceptable salt, a solvate or a solvate of a salt thereof.

3. The compound of formula (I) as claimed in claim 1 or 2, wherein X^3 is a heterologous moiety selected from the group consisting of a polymer, a Fc, a FcRn binding ligand, albumin and an albumin-binding ligand; and

X^1 , X^2 , and Z are as defined in any of claims 1 to 4;

or a physiologically acceptable salt, a solvate or a solvate of a salt thereof.

4. The compound of formula (I) as claimed in claim 3, wherein X^3 is a polymer and the polymer is selected from the group consisting of linear or branched C_3 - C_{100} carboxylic acids, preferably C_4 - C_{30} carboxylic acids, optionally substituted with halo, hydroxy, alkoxy, amino, alkylamino, dialkylamino, sulfate, or phosphate, and which may be saturated, or mono- or di-unsaturated, a PEG moiety, a PPG moiety, a PAS moiety and a HES moiety; and

X^1 , X^2 , and Z are as defined in any of claims 1 to 5;

or a physiologically acceptable salt, a solvate or a solvate of a salt thereof.

5. The compound of formula (I) as claimed in claim 4, wherein the carboxylic acid is selected from the group consisting of arachidic acid, arachidonic acid, behenic acid, capric acid, caproic acid, caprylic acid, ceroplastic acid, cerotic acid, docosahexaenoic acid, eicosapentaenoic acid, elaidic acid, enanthic acid, erucic acid, geddic acid, henatriacontylic acid, heneicosylic acid, heptacosylic acid, hexatriacontylic acid, lacceroic acid, lauric acid, lignoceric acid, linoelaidic acid, linoleic acid, margaric acid, melissic acid, montanic acid, myristic acid, myristoleic acid, nonacosylic acid, nonadecylic acid, oleic acid, palmitic acid, palmitoleic acid, pantothenic acid, pelargonic acid, pentacosylic acid, pentadecylic acid, psyllic acid, sapienic acid, stearic acid, tricosylic acid, tridecylic acid, undecylic acid, vaccenic acid, valeric acid, α -linolenic acid and derivatives thereof; and

X^1 , X^2 , and Z are as defined in any of claims 1 to 6;

or a physiologically acceptable salt, a solvate or a solvate of a salt thereof.

6. The compound of formula (I) as claimed in any of claims 1 to 5, wherein Z is absent and X^1 , X^2 , and X^3 are as defined in any of claims 1 to 7;

or a physiologically acceptable salt, a solvate or a solvate of a salt thereof.

7. The compound of formula (I) as claimed in any of claims 1 to 5, wherein Z is a cleavable linker as defined in any of claims 1 to 8; and X^1 , X^2 , and X^3 are as defined in any of claims 1 to 8;

or a physiologically acceptable salt, a solvate or a solvate of a salt thereof.

8. The compound of formula (I) as claimed in any of claims 1 to 7, wherein the compound is further modified by N-methylation of at least one amide bond; and

X^1 , X^2 , X^3 , and Z are as defined in any of claims 1 to 7;

or a physiologically acceptable salt, a solvate or a solvate of a salt thereof.

9. The compound of formula (I) as claimed in any of claims 1 to 8, wherein

X^1 is selected from the group consisting of $^*-(CH_2)_{m1}-S-^{\#}$, wherein $m1$ is 0-4; $^{\#}-(CH_2)_{m2}-S-^*$, wherein $m2$ is 0-4; $^*-(CH_2)_{m6}-CO-NH-(CH_2)_{n3}-^{\#}$, wherein $m6$ is 0-4, and $n3$ is 0-4, with the proviso that $m6+n3=0-6$;

X^2 is G^{14} or K^{14} , which is covalently linked by an amide bond to the N-terminal G^{15} of the compound of formula (I);

X^3 is absent or is a heterologous moiety which is covalently linked to the N-terminus of G^{14} or K^{14} or to a functional group of the side chain of K^{14} , or to Z;

Z is absent or is a cleavable linker covalently bound between the N terminus of G^{14} or K^{14} and X^3 , or between a functional group of the side chain of K^{14} and X^3 ;

wherein if X^3 is absent, then Z is also absent;

wherein if X^3 is a heterologous moiety, then Z is absent or is a cleavable linker covalently bound between the N terminus of G^{14} or K^{14} and X^3 , or between a functional group of the side chain of K^{14} and X^3 ;

or a physiologically acceptable salt, a solvate or a solvate of a salt thereof.

10. A compound as claimed in any of claims 1 to 9 for use in therapy.
11. Use of a compound as claimed in any of claims 1 to 9 in the manufacture of a medicament for the treatment and/or prevention of cardiovascular, edematous and/or inflammatory disorders.
12. Use of a compound according to claim 11 for the treatment and/or prevention of heart failure, chronic heart failure, worsening heart failure, acute heart failure, acute decompensated heart failure, diastolic and systolic (congestive) heart failure, coronary heart disease, ischemic and/or hemorrhagic stroke, hypertension, pulmonary hypertension, peripheral arterial occlusive disease, pre-eclampsia, chronic obstructive pulmonary disease, asthma, acute and/or chronic pulmonary edema, allergic alveolitis and/or pneumonitis due to inhaled organic dust and particles of fungal, actinomycetic or other origin, and/or acute chemical bronchitis, acute and/or chronic chemical pulmonary edema, neurogenic pulmonary edema, acute and/or chronic pulmonary manifestations due to radiation, acute and/or chronic interstitial lung disorders, acute lung injury/acute respiratory distress syndrome (ALI/ARDS) in adult or child including newborn, ALI/ARDS secondary to pneumonia and sepsis, aspiration pneumonia and ALI/ARDS

secondary to aspiration, ALI/ARDS secondary to smoke gas inhalation, transfusion-related acute lung injury (TRALI), ALI/ARDS and/or acute pulmonary insufficiency following surgery, trauma and/or burns, and/or ventilator induced lung injury (VILI), lung injury following meconium aspiration, pulmonary fibrosis, mountain sickness, chronic kidney diseases, glomerulonephritis, acute kidney injury, cardiorenal syndrome, lymphedema, inflammatory bowel disease, sepsis, septic shock, systemic inflammatory response syndrome (SIRS) of non-infectious origin, anaphylactic shock, inflammatory bowel disease, urticaria and/or edematous ocular disorders or ocular disorders associated with disturbed vascular function, including, age-related macular degeneration (AMD), diabetic retinopathy, in particular diabetic macula edema (DME), subretinal edema, and intraretinal edema.

13. A medicament comprising a compound as claimed in any of claims 1 to 9 in combination with an inert nontoxic pharmaceutically suitable excipient.
14. A medicament comprising a compound as claimed in any of claims 1 to 9 in combination with a further active ingredient selected from the group consisting of ACE inhibitors, angiotensin receptor antagonists, beta-2 receptor agonists, phosphodiesterase (PDE) inhibitors, glucocorticoid receptor agonists, diuretics, recombinant angiotensin converting enzyme-2, acetylsalicylic acid, natriuretic peptides and derivatives thereof, and neprilysin inhibitors.