[19] Examples of metabolites or metabolic precursors are hydroxylated, carboxylated, sulphonated, glycosylated, methylated or demethylated, acetylated, covalently linked to glucuronic acid, glycine and other amino acids, glutathione, oxidized or reduced derivatives of the compounds of formula (**I**).

[20] Some compounds of formula (**I**), especially esters, can also be prodrugs of the active forms.

[21] Where the compounds of formula (**I**) can exhibit tautomerism, the formula is intended to cover all tautomers; the invention includes within its scope all the possible stereoisomers, Z and E isomers, optical isomers, enantiomers and their mixtures.

[22] Also the pharmaceutical acceptable salts are included in the scope of the invention. Pharmaceutical acceptable salts are salts which retain the biological activity of the base compound and are derived from such known pharmacologically acceptable acids such as, e. g., hydrochloric, hydrobromic, sulfuric, phosphoric, nitric, fumaric, succinic, oxalic, malic, tartaric, maleic, citric, methanesulfonic or benzoic acid and others commonly used in the art, see for example Pharmaceutical Salts and Co-crystals, Editors: Johan Wouters, Luc Quéré, RSC Publishing, 2011.

[23] Further object of the present invention are the said compounds of general formula (**I**) for use as medicaments, in particular for the treatment of HF.

[24] In some embodiments, the compound of claim 1 is selected from the group consisting of: (E)-4-(6alpha-hydroxy-17-oxoandrostane-3-yliden)butyric acid; (Z)-4-(6alpha-hydroxy-17-oxoandrostane-3-yliden) butyric acid; (E)-4-(6beta-hydroxy-17-oxoandrostane-3-yliden) butyric acid; (Z)-4-(6beta-hydroxy-17-oxoandrostane-3-yliden) butyric acid; (E)-3-[2-(azetidin-3-yl)ethyliden]-6alpha-hydroxyandrostane-17-one; (Z)-3-[2-(azetidin-3-yl)ethyliden]-6alpha-hydroxyandrostane-17-one; (E)-3-(4-aminobutyl)-6alpha-hydroxyandrost-2-ene-17-one hydroiodide; 3-[2-(piperidin-4-yl)ethyl]-6alpha-hydroxyandrost-2-ene-17-one hydroiodide; (EZ)-3-(4-aminobutyliden]-6alpha-hydroxyandrostane-17-one; (E)-3-[2-(piperidin-4-yl)ethyliden]-6alpha-hydroxyandrostane-17-one; (Z)-3-[2-(piperidin-4-yl)ethyliden]-6alpha-hydroxyandrostane-17-one; 3beta-[2-(piperidin-4-yl)ethyl]-6alpha-hydroxyandrostane-17-one; Ethyl (6alpha-hydroxy-17-ketoandrostane-3beta-yl) acetate; 4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyric acid; 4-(6beta-hydroxy-17-oxoandrostane-3-yl) butyric acid; 2-(6beta-hydroxy-17-oxoandrostane-3-yl) acetic acid; Ethyl 4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyrate~~ethylbutiroate~~; Ethyl 6~~4~~-(6alpha-hydroxy-17-oxoandrostane-3-yl) caproate~~ethylcaproate~~; ~~4~~6-(6beta-hydroxy-17-oxoandrostane-3-yl) caproic acid; (EZ)-3-(5-N-methylaminopentyliden]-6alpha-hydroxymethylandrostane-

7,17-dione; (EZ)-3-[2-(pyrrolidine-3yl~~pirrolidin-3yl~~)ethyliden]-6alpha-hydroxymethylandrostane-7,17-dione; (EZ)-3-[2-(azetidine-3-yl~~azetidin-2-yl~~)ethyliden]-6alpha-hydroxymethylandrostane-7,17-dione; (EZ)-3-[2-(piperidin-4-yl)ethyliden]-6alpha-hydroxymethylandrostane-7,17-dione; (EZ)-3-(5-N-methylaminopentyliden)-6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one; 3beta-[2-(azetidine-3-yl~~azetidin-2-yl~~)ethyl]-6alpha-hydroxymethylandrostane-7,17-dione; 3beta-[2-(azetidine-3-yl~~azetidin-2-yl~~)ethyl]-6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one; 3beta-[2-(pyrrolidine-3yl~~pirrolidin-3yl~~)ethyl]-6alpha-hydroxymethylandrostane-7,17-dione; 3beta-[2-(pyrrolidine-3yl~~pirrolidin-3yl~~)ethyl]6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one; 3beta-[2-(piperidin-4-yl)ethyl]-6alpha-hydroxymethylandrostane-7,17-dione; and 3beta-[2-(piperidin-4-yl)ethyl]-6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one.

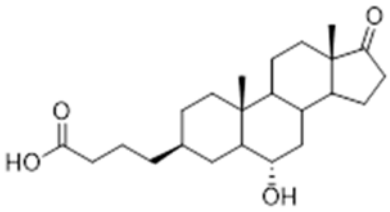
[25] A further object of the present invention are pharmaceutical compositions comprising one or more of the compounds of formula (**I**), optionally in combination with other therapeutically active ingredients. In turn, these pharmaceutical compositions may be formulated for oral administration, intravenous or intramuscular injection, inhalation, intravitreal injection, and the like. In particular embodiments, the pharmaceutical compositions disclosed herein are used in treating HF.

[26] The above and other objects of the present invention will be now disclosed in detail also by means of examples and Figures.

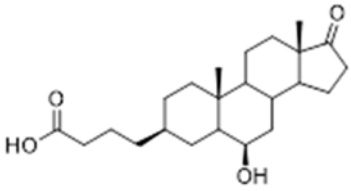
**Brief description of the drawings**

[27] **Figure 1** shows the effects of 1 µM CVie216 on sarcoplasmic reticulum (SR) $Ca^{2+}$ uptake parameters in rat ventricular myocytes isolated from STZ rats (loading protocol). The SR $Ca^{2+}$ uptake parameters included $Ca^{2+}$ transient (CaT) amplitude (Panel A); $Ca^{2+}$-induced $Ca^{2+}$ release (CICR) gain (Panel B) and the time constant ($\tau$) of $Ca^{2+}$ decay (Panel C). Differences between curves in control (N=16-18) and CVie216 (N=20-23) were statistically significant ($p<0.05$, two-way ANOVA) in panels A-C.

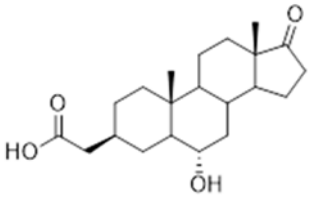
[28] **Figure 2** shows the effects of 1 µM CVie214 on sarcoplasmic reticulum (SR) $Ca^{2+}$ uptake parameters in rat ventricular myocytes isolated from STZ rats (loading protocol). The SR $Ca^{2+}$ uptake parameters included $Ca^{2+}$ transient (CaT) amplitude (Panel A); $Ca^{2+}$-induced $Ca^{2+}$ release (CICR) gain (Panel B) and the time constant ($\tau$) of $Ca^{2+}$ decay (Panel C). Differences between curves in control (N=14) and CVie214 (N=11) were statistically significant in panel B ($p<0.05$) and close to significance in panel C ($p=0.05$).



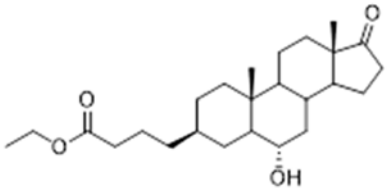

[74] 4-(6beta-hydroxy-17-oxoandrostane-3-yl) butyric acid (**CVie215**)



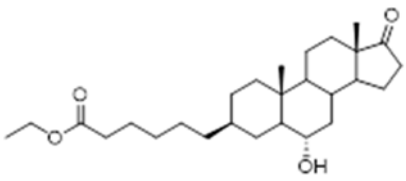

[75] 2-(6beta-hydroxy-17-oxoandrostane-3-yl) acetic acid (**CVie216**)



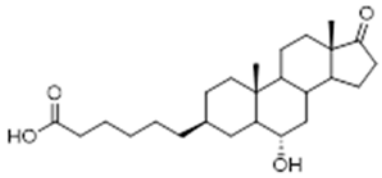

[76] Ethyl 4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyrate~~ethylbutiroate~~ (**CVie217**)



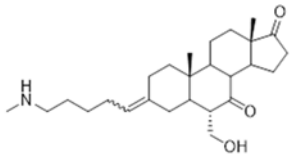

[77] Ethyl 6~~4~~-(6alpha-hydroxy-17-oxoandrostane-3-yl) caproate~~ethylcaproate~~ (**CVie218**)



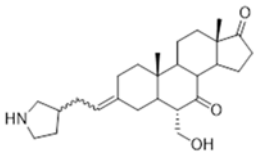

[78] 6~~4~~-(6beta-hydroxy-17-oxoandrostane-3-yl) caproic acid (**CVie219**)



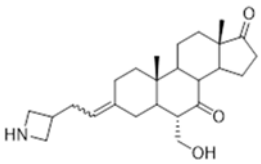
[79] (E,Z)-3-(5-N-methylaminopentyliden]-6alpha-hydroxymethylandrostane-7,17-dione (**CVie401**)



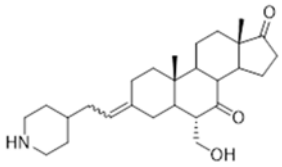
[80] (E,Z)-3-[2-(pyrrolidine-3yl~~pirrolidin-3yl~~)ethyliden]-6alpha-hydroxymethylandrostane-7,17-dione (**CVie402**)



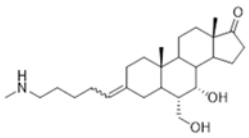
[81] (E,Z)-3-[2-(azetidine-3-yl~~azetidin-2-yl~~)ethyliden]-6alpha-hydroxymethylandrostane-7,17-dione (**CVie403**)



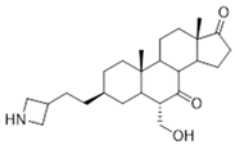
[82] (E,Z)-3-[2-(piperidin-4-yl)ethyliden]-6alpha-hydroxymethylandrostane-7,17-dione (**CVie405**)



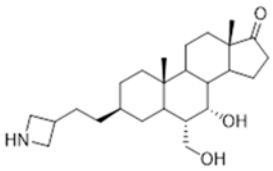
[83] (E,Z)-3-(5-N-methylaminopentyliden)-6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one (**CVie406**)



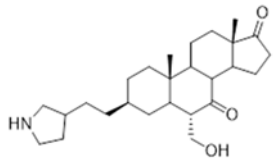
[84] 3beta-[2-(azetidine-3-yl~~azetidin-2-yl~~)ethyl]-6alpha-hydroxymethylandrostane-7,17-dione (**CVie407**)



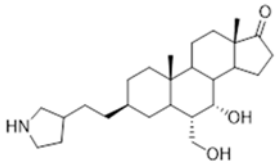
[85] 3beta-[2-(azetidine-3-yl~~azetidin-2-yl~~)ethyl]-6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one (**CVie408**)



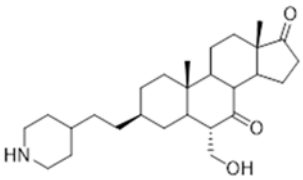
[86] 3beta-[2-(pyrrolidine-3yl~~pirrolidin-3yl~~)ethyl]-6alpha-hydroxymethylandrostane-7,17-dione (**CVie409**)



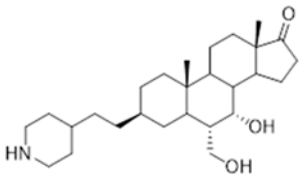

[87] 3beta-[2-(pyrrolidine-3yl~~pirrolidin-3yl~~)ethyl]6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one (**CVie410**)




[88] 3beta-[2-(piperidin-4-yl)ethyl]-6alpha-hydroxymethylandrostane-7,17-dione (**CVie411**)




[89] 3beta-[2-(piperidin-4-yl)ethyl]-6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one (**CVie412**)




[90] It is also an object of the present invention to utilize the SERCA2a-activation properties of the compound of formula (**I**) for treating, ameliorating, reversing, or abating or diminishing the symptoms of, or preventing diseases associated with diminished SERCA2a activation, such as heart failure (AHF and/or CHF). Because defective intracellular $Ca^{2+}$ distribution has a role in the myocardial remodeling process, its correction by

Y at C6 is a hydroxyl (OH) in the α- or β-configuration or a hydroxymethyl ($CH_2OH$) in the α-configuration;

Z at C7 could be either -H or -OH in an α-configuration or a ketone. The dashed line represents an optional carbonyl group (C=O) in such position.

or a pharmaceutically acceptable salt, solvate, or hydrate thereof.

[215] Aspect 2: The compound of aspect 1, wherein X is selected from the group consisting of a carboxylic acid, carboxylic ester, primary amine, secondary amine, and cyclic amine.

[216] Aspect 3: The compound of aspect 1, wherein X is a carboxylic acid or a carboxylic ester.

[217] Aspect 4: The compound of aspect 1, wherein X is not a primary amine, secondary amine, or cyclic amine.

[218] Aspect 5: The compound of aspect 1, selected from the group consisting of: (E)-4-(6alpha-hydroxy-17-oxoandrostane-3-yliden) butyric acid; (Z)-4-(6alpha-hydroxy-17-oxoandrostane-3-yliden) butyric acid; (E)-4-(6beta-hydroxy-17-oxoandrostane-3-yliden)butyric acid; (Z)-4-(6beta-hydroxy-17-oxoandrostane-3-yliden) butyric acid; (E)-3-[2-(azetidin-3-yl)ethyliden]-6alpha-hydroxyandrostane-17-one; (Z)-3-[2-(azetidin-3-yl)ethyliden]-6alpha-hydroxyandrostane-17-one; (E)-3-(4-aminobutyl)-6alpha-hydroxyandrost-2-ene-17-one hydroiodide; 3-[2-(piperidin-4-yl)ethyl]-6alpha-hydroxyandrost-2-ene-17-one hydroiodide; (EZ)-3-(4-aminobutyliden]-6alpha-hydroxyandrostane-17-one; (E)-3-[2-(piperidin-4-yl)ethyliden]-6alpha-hydroxyandrostane-17-one; (Z)-3-[2-(piperidin-4-yl)ethyliden]-6alpha-hydroxyandrostane-17-one; 3beta-[2-(piperidin-4-yl)ethyl]-6alpha-hydroxyandrostane-17-one; Ethyl (6alpha-hydroxy-17-ketoandrostane-3beta-yl) acetate; 4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyric acid; 4-(6beta-hydroxy-17-oxoandrostane-3-yl) butyric acid; 2-(6beta-hydroxy-17-oxoandrostane-3-yl) acetic acid; Ethyl 4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyrate~~ethylbutiroate~~; Ethyl 6~~4~~-(6alpha-hydroxy-17-oxoandrostane-3-yl) caproate~~ethylcaproate~~; ~~4~~6-(6beta-hydroxy-17-oxoandrostane-3-yl) caproic acid; (E,Z)-3-(5-N-methylaminopentyliden]-6alpha-hydroxymethylandrostane-7,17-dione; (E,Z)-3-[2-(pyrrolidine-3yl~~pirrolidin-3yl~~)ethyliden]-6alpha-hydroxymethylandrostane-7,17-dione; (E,Z)-3-[2-(azetidine-3-yl~~azetidin-2-yl~~)ethyliden]-6alpha-hydroxymethylandrostane-7,17-dione; (E,Z)-3-[2-(piperidin-4-yl)ethyliden]-6alpha-hydroxymethylandrostane-7,17-dione; (E,Z)-3-(5-N-methylaminopentyliden)-6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one; 3beta-[2-(azetidine-3-

yl~~azetidin-2-yl~~)ethyl]-6alpha-hydroxymethylandrostane-7,17-dione; 3beta-[2-(azetidine-3-yl~~azetidin-2-yl~~) ethyl]-6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one; 3beta-[2-(pyrrolidine-3yl~~pirrolidin-3yl~~) ethyl]-6alpha-hydroxymethylandrostane-7,17-dione; 3beta-[2-(pyrrolidine-3yl~~pirrolidin-3yl~~)ethyl] 6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one; 3beta-[2-(piperidin-4-yl) ethyl]-6alpha-hydroxymethylandrostane-7,17-dione; and 3beta-[2-(piperidin-4-yl) ethyl]-6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one.

[219] Aspect 6: The compound of aspect 1, selected from the group consisting of: (E)-4-(6alpha-hydroxy-17-oxoandrostane-3-yliden) butyric acid; (Z)-4-(6alpha-hydroxy-17-oxoandrostane-3-yliden) butyric acid; (E)-4-(6beta-hydroxy-17-oxoandrostane-3-yliden) butyric acid; (Z)-4-(6beta-hydroxy-17-oxoandrostane-3-yliden) butyric acid; Ethyl (6alpha-hydroxy-17-ketoandrostane-3beta-yl) acetate; 4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyric acid; 4-(6beta-hydroxy-17-oxoandrostane-3-yl) butyric acid; 2-(6beta-hydroxy-17-oxoandrostane-3-yl) acetic acid; Ethyl 4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyrate~~ethylbutiroate~~; Ethyl 6~~4~~-(6alpha-hydroxy-17-oxoandrostane-3-yl) caproate~~ethylcaproate~~; and ~~4~~6-(6beta-hydroxy-17-oxoandrostane-3-yl) caproic acid.

[220] Aspect 7: The compound of aspect 1, selected from the group consisting of 4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyric acid and 2-(6beta-hydroxy-17-oxoandrostane-3-yl) acetic acid.

[221] Aspect 8: The compound of any one of aspects 1-7, wherein the pharmaceutically acceptable salt is selected from chloride, bromide, sulfate, phosphate, nitrate, fumarate, succinate, oxalate, malate, tartrate, maleate, citrate, methanesulfate, and benzoate.

[222] Aspect 9: A pharmaceutical composition for use in a method for the treatment of heart failure comprising a therapeutically effective amount of one or more of the compounds of any one of aspects 1-8, in combination with at least one pharmaceutically acceptable vehicle and/or excipient.

[223] Aspect 10: The pharmaceutical composition of aspect 9, formulated for enteral administration, parenteral administration, or inhalation.

[224] Aspect 11: The pharmaceutical composition of aspect 10, formulated for oral administration.

[225] Aspect 12: The pharmaceutical composition of aspect 11, administered at a dose of between about 1 mg/kg and about 20 mg/kg, optionally, the dose is between about 1 mg/kg and about 10 mg/kg.

[242] Aspect 29: The method of aspect 28, wherein X is selected from the group consisting of a carboxylic acid, carboxylic ester, primary amine, secondary amine, and cyclic amine.

[243] Aspect 30: The method of aspect 28, wherein X is a carboxylic acid or a carboxylic ester.

[244] Aspect 31: The method of aspect 28, wherein X is not a primary amine, secondary amine, or cyclic amine.

[245] Aspect 32: The method of aspect 28, wherein the predominantly pure SERCA2a stimulator is selected from the group consisting of: (E)-4-(6alpha-hydroxy-17-oxoandrostane-3-yliden)butyric acid; (Z)-4-(6alpha-hydroxy-17-oxoandrostane-3-yliden) butyric acid; (E)-4-(6beta-hydroxy-17-oxoandrostane-3-yliden) butyric acid; (Z)-4-(6beta-hydroxy-17-oxoandrostane-3-yliden) butyric acid; (E)-3-[2-(azetidin-3-yl)ethyliden]-6alpha-hydroxyandrostane-17-one; (Z)-3-[2-(azetidin-3-yl)ethyliden]-6alpha-hydroxyandrostane-17-one; (E)-3-(4-aminobutyl)-6alpha-hydroxyandrost-2-ene-17-one hydroiodide; 3-[2-(piperidin-4-yl)ethyl]-6alpha-hydroxyandrost-2-ene-17-one hydroiodide; (E,Z)-3-(4-aminobutyliden]-6alpha-hydroxyandrostane-17-one; (E)-3-[2-(piperidin-4-yl)ethyliden]-6alpha-hydroxyandrostane-17-one; (Z)-3-[2-(piperidin-4-yl)ethyliden]-6alpha-hydroxyandrostane-17-one; 3beta-[2-(piperidin-4-yl)ethyl]-6alpha-hydroxyandrostane-17-one; Ethyl (6alpha-hydroxy-17-ketoandrostane-3beta-yl) acetate; 4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyric acid; 4-(6beta-hydroxy-17-oxoandrostane-3-yl) butyric acid; 2-(6beta-hydroxy-17-oxoandrostane-3-yl) acetic acid; Ethyl 4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyrate~~ethylbutiroate~~; Ethyl 6~~4~~-(6alpha-hydroxy-17-oxoandrostane-3-yl) caproate~~ethylcaproate~~; ~~4~~6-(6beta-hydroxy-17-oxoandrostane-3-yl) caproic acid; (E,Z)-3-(5-N-methylaminopentyliden]-6alpha-hydroxymethylandrostane-7,17-dione; (E,Z)-3-[2-(pyrrolidine-3yl~~pirrolidin-3yl~~)ethyliden]-6alpha-hydroxymethylandrostane-7,17-dione; (E,Z)-3-[2-(azetidine-3-yl~~azetidin-2-yl~~)ethyliden]-6alpha-hydroxymethylandrostane-7,17-dione; (E,Z)-3-[2-(piperidin-4-yl)ethyliden]-6alpha-hydroxymethylandrostane-7,17-dione; (E,Z)-3-(5-N-methylaminopentyliden)-6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one; 3beta-[2-(azetidine-3-yl~~azetidin-2-yl~~)ethyl]-6alpha-hydroxymethylandrostane-7,17-dione; 3beta-[2-(azetidine-3-yl~~azetidin-2-yl~~)ethyl]-6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one; 3beta-[2-(pyrrolidine-3yl~~pirrolidin-3yl~~)ethyl]-6alpha-hydroxymethylandrostane-7,17-dione; 3beta-[2-(pyrrolidine-3yl~~pirrolidin-3yl~~)ethyl]6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one; 3beta-[2-(piperidin-4-yl)ethyl]-6alpha-hydroxymethylandrostane-7,17-dione; and 3beta-[2-(piperidin-4-yl)ethyl]-6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one.

[246] Aspect 33: The method of aspect 28, wherein the predominantly pure SERCA2a stimulator is selected from the group consisting of: (E)-4-(6alpha-hydroxy-17-oxoandrostane-3-yliden) butyric acid; (Z)-4-(6alpha-hydroxy-17-oxoandrostane-3-yliden) butyric acid; (E)-4-(6beta-hydroxy-17-oxoandrostane-3-yliden) butyric acid; (Z)-4-(6beta-hydroxy-17-oxoandrostane-3-yliden) butyric acid; Ethyl (6alpha-hydroxy-17-ketoandrostane-3beta-yl)acetate; 4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyric acid; 4-(6beta-hydroxy-17-oxoandrostane-3-yl) butyric acid; 2-(6beta-hydroxy-17-oxoandrostane-3-yl) acetic acid; Ethyl 4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyrate~~ethylbutiroate~~; Ethyl 6~~4~~-(6alpha-hydroxy-17-oxoandrostane-3-yl) caproate~~ethylcaproate~~; and ~~4~~6-(6beta-hydroxy-17-oxoandrostane-3-yl) caproic acid.

[247] Aspect 34: The method of aspect 28, wherein the predominantly pure SERCA2a stimulator is selected from the group consisting of 4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyric acid and 2-(6beta-hydroxy-17-oxoandrostane-3-yl) acetic acid.

[248] Aspect 35: The method of any one of aspects 28-34, wherein the pharmaceutically acceptable salt is selected from chloride, bromide, sulfate, phosphate, nitrate, fumarate, succinate, oxalate, malate, tartrate, maleate, citrate, methanesulfate, and benzoate.

[249] Aspect 36: The method of any one of aspects 28-35, wherein the pharmaceutical composition is administered orally.

[250] Aspect 37: The method of aspect 36, wherein the pharmaceutical composition is administered at a dose of between about 1 mg/kg and about 20 mg/kg, optionally, the dose is between about 1 mg/kg and about 10 mg/kg.

[251] Aspect 38: The method of any one of aspects 28-35, wherein the pharmaceutical composition is administered intravenously.

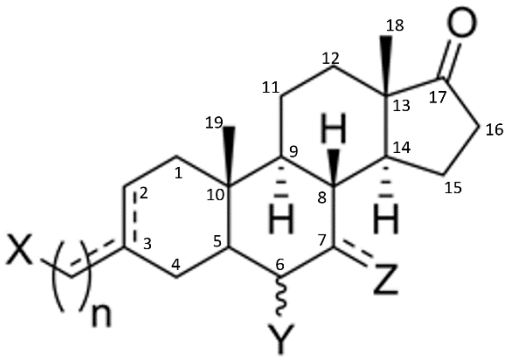
[252] Aspect 39: The method of aspect 38, wherein the pharmaceutical composition is administered at a dose of between about 0.125 mg/kg and about 10 mg/kg, optionally, the dose is between about 0.25 mg/kg and about 5 mg/kg.

[253] Aspect 40: The method of any one of aspects 28-35, wherein the pharmaceutical composition is administered intramuscularly.

[254] Aspect 41: The method of aspect 40, wherein the pharmaceutical composition is administered at a dose of between about 0.25 mg/kg and about 50 mg/kg, optionally, the dose is between about 0.25 mg/kg and about 35 mg/kg.

**CLAIMS**

1. A compound having a formula (**I**)




wherein:

X is selected from the group consisting of a carboxylic acid, carboxylic ester or a bioisoster thereof, primary alcohol, ether, and an amine group, wherein the bioisoster consists of a sulfate, sulfonic acid, phosphate, phosphonate, or a nitrogen-containing etherocyclic ring, and wherein the amine group optionally comprises a primary amine, secondary amine, or a cyclic amine;

n is 1, 2, 3, 4, or 5;

a C3-C1' dashed line represents an optional exocyclic double bond C=C at position C3-C1';

a C2-C3 dashed line represents an optional endocyclic double bond C=C;

Y at C6 is a hydroxyl (OH) in the alpha- or beta-configuration or a hydroxymethyl ($CH_2OH$) in the alpha-configuration;

Z at C7 is a -H or -OH in an alpha-configuration or a ketone, wherein a dashed line represents an optional carbonyl group (C=O) at Z; or

a pharmaceutically acceptable salt, solvate, or hydrate thereof.

2. The compound of claim 1, wherein X is selected from the group consisting of a carboxylic acid, carboxylic ester, primary amine, secondary amine, and cyclic amine.

3. The compound of claim 1, wherein X is a carboxylic acid or a carboxylic ester.

4. The compound of anyone of claims 1-3, which is selected from the group consisting of:

(E)-4-(6alpha-hydroxy-17-oxoandrostane-3-yliden) butyric acid;

(Z)-4-(6alpha-hydroxy-17-oxoandrostane-3-yliden) butyric acid;

(E)-4-(6beta-hydroxy-17-oxoandrostane-3-yliden) butyric acid;

(Z)-4-(6beta-hydroxy-17-oxoandrostane-3-yliden) butyric acid;

(E)-3-[2-(azetidin-3-yl)ethyliden]-6alpha-hydroxyandrostane-17-one;

(Z)-3-[2-(azetidin-3-yl)ethyliden]-6alpha-hydroxyandrostane-17-one;

(E)-3-(4-aminobutyl)-6alpha-hydroxyandrost-2-ene-17-one hydroiodide;

3-[2-(piperidin-4-yl)ethyl]-6alpha-hydroxyandrost-2-ene-17-one hydroiodide;

(EZ)-3-(4-aminobutyliden]-6alpha-hydroxyandrostane-17-one;

(E)-3-[2-(piperidin-4-yl)ethyliden]-6alpha-hydroxyandrostane-17-one;

(Z)-3-[2-(piperidin-4-yl)ethyliden]-6alpha-hydroxyandrostane-17-one;

3beta-[2-(piperidin-4-yl)ethyl]-6alpha-hydroxyandrostane-17-one;

Ethyl (6alpha-hydroxy-17-ketoandrostane-3beta-yl) acetate;

4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyric acid;

4-(6beta-hydroxy-17-oxoandrostane-3-yl) butyric acid;

2-(6beta-hydroxy-17-oxoandrostane-3-yl) acetic acid;

Ethyl 4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyrate ~~ethylbutiroate~~;

Ethyl 6~~4~~-(6alpha-hydroxy-17-oxoandrostane-3-yl) caproate ~~ethylcaproate~~;

6~~4~~-(6beta-hydroxy-17-oxoandrostane-3-yl) caproic acid;

(E,Z)-3-(5-N-methylaminopentyliden]-6alpha-hydroxymethylandrostane-7,17-dione;

(E,Z)-3-[2-(pyrrolidine-3yl~~pirrolidin-3yl~~)ethyliden]-6alpha-hydroxymethylandrostane-7,17-dione;

(E,Z)-3-[2-(azetidine-3-yl~~azetidin-2-yl~~)ethyliden]-6alpha-hydroxymethylandrostane-7,17-dione;

(E,Z)-3-[2-(piperidin-4-yl)ethyliden]-6alpha-hydroxymethylandrostane-7,17-dione;

(E,Z)-3-(5-N-methylaminopentyliden)-6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one;

3beta-[2-(azetidine-3-yl~~azetidin-2-yl~~)ethyl]-6alpha-hydroxymethylandrostane-7,17-dione;

3beta-[2-(azetidine-3-yl~~azetidin-2-yl~~)ethyl]-6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one;

3beta-[2-(pyrrolidine-3yl~~pirrolidin-3yl~~)ethyl]-6alpha-hydroxymethylandrostane-7,17-dione;

3beta-[2-(pyrrolidine-3yl~~pirrolidin-3yl~~)ethyl]6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one;

3beta-[2-(piperidin-4-yl)ethyl]-6alpha-hydroxymethylandrostane-7,17-dione; and

3beta-[2-(piperidin-4-yl)ethyl]-6alpha-hydroxymethyl-7alpha-hydroxyandrostane-17-one.

5. The compound of anyone of claims 1-3, which is selected from the group consisting of:

(E)-4-(6alpha-hydroxy-17-oxoandrostane-3-yliden) butyric acid;

(Z)-4-(6alpha-hydroxy-17-oxoandrostane-3-yliden) butyric acid;

(E)-4-(6beta-hydroxy-17-oxoandrostane-3-yliden) butyric acid;

(Z)-4-(6beta-hydroxy-17-oxoandrostane-3-yliden) butyric acid;

Ethyl (6alpha-hydroxy-17-ketoandrostane-3beta-yl) acetate;

4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyric acid;

4-(6beta-hydroxy-17-oxoandrostane-3-yl) butyric acid;

2-(6beta-hydroxy-17-oxoandrostane-3-yl) acetic acid;

Ethyl 4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyrate~~ethylbutiroate~~;

Ethyl 6~~4~~-(6alpha-hydroxy-17-oxoandrostane-3-yl) caproate~~ethylcaproate~~; and

6~~4~~-(6beta-hydroxy-17-oxoandrostane-3-yl) caproic acid.

6. The compound of claim 1, selected from the group consisting of 4-(6alpha-hydroxy-17-oxoandrostane-3-yl) butyric acid and 2-(6beta-hydroxy-17-oxoandrostane-3-yl) acetic acid.

7. The compound of any one of claims 1-6, wherein the pharmaceutically acceptable salt is selected from chloride, bromide, sulfate, phosphate, nitrate, fumarate, succinate, oxalate, malate, tartrate, maleate, citrate, methanesulfate, and benzoate.

8. A pharmaceutical composition comprising one or more of the compounds of any one of claims 1-7, in combination with at least one pharmaceutically acceptable vehicle and/or excipient.

9. Use of ~~A~~a pharmaceutical composition ~~for use in a method~~ for the treatment of heart failure in a subject, wherein the pharmaceutical composition comprises ~~comprising~~ one or more of the compounds of any one of claims 1-7, in combination with at least one pharmaceutically acceptable vehicle and/or excipient.

10. The pharmaceutical composition of claim 8 or the use of claim 9, wherein the pharmaceutical composition is formulated for intravenous injection, intramuscular injection, enteral administration, parenteral administration, or inhalation.

11. The pharmaceutical composition of claim 8 or the use of claim 9, wherein the pharmaceutical composition is formulated for oral administration.

12. The pharmaceutical composition of any one of claims 8-11 or the use of any one of claims 9-11, wherein~~administered at~~ a dose of between about 1 mg/kg and about 20 mg/kg is to be administered~~, optionally, the dose is between about 1 mg/kg and about 10 mg/kg~~.

13. The pharmaceutical composition or the use of claim 12, wherein the dose is between about 1 mg/kg and about 10 mg/kg.

14~~13~~. The pharmaceutical composition of any one of claims ~~8-12~~8-13 or the use of any one of claims 9-13, further comprising one or more additional therapeutically active ingredients selected from the group consisting of CE inhibitors, AIRBs, diuretics, $Ca^{2+}$ channel blockers, β-blockers, digitalis, NO donors, vasodilators, SERCA2a stimulators, neprilysin (NEP) inhibitors, myosin filament activators, recombinant relaxin-2 mediators, recombinant NP protein, activators of the soluble guanylate cyclase (sGC), and beta-arrestin ligand of angiotensin II receptor.

15~~14~~. A compound of any one of claims 1-7 for use as a medicament.

16~~15~~. A compound of any one of claims 1-7 for use for the treatment of heart failure.

17. A pharmaceutical composition comprising one or more of the compounds of any one of claims 1-7, in combination with at least one pharmaceutically acceptable vehicle and/or excipient for use in therapy.