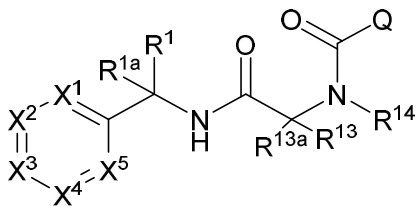
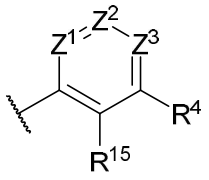
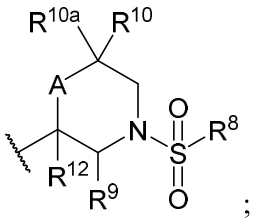
[0014a] In one aspect, the present disclosure refers to a compound or pharmaceutically acceptable salt thereof, according to Formula (I):



(I)

wherein

Q is  or  ;

A is absent, oxygen, N(H), N($C_1$-$C_6$alkyl) or $CR^{11}R^{11a}$;

$X^1$ is N or $CR^2$;

$X^2$, $X^3$, $X^4$ and $X^5$ are each independently selected from N and $CR^3$ provided that 0, 1, or 2 of $X^1$, $X^2$, $X^3$, $X^4$ and $X^5$ are N and the remainder are $CR^2$ or $CR^3$;

$R^{1a}$ is selected from the group consisting of hydrogen, $C_1$-$C_6$alkyl and halogen;

$R^1$ is selected from the group consisting of $C_1$-$C_6$alkyl, halo $C_1$-$C_6$alkyl, hydroxy $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl optionally substituted with 1 or 2 groups selected from hydroxy, halogen, and $C_1$-$C_4$alkyl, hydroxy $C_3$-$C_7$cycloalkyl, $C_3$-$C_7$cycloalkyl$C_1$-$C_4$alkyl, hydroxy $C_3$-$C_7$cycloalkyl$C_1$-$C_4$alkyl,and 4 to 7 member heterocycloalkyl having 1 or 2 ring heteroatoms independently selected from N, O and S, which heterocycloalkyl is optionally substituted with 1 or 2 groups selected from oxo, hydroxy, halogen and $C_1$-$C_4$alkyl;

$R^2$ is selected from the group consisting of hydrogen, halogen, $C_1$-$C_6$alkyl, halo$C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_3$-$C_7$cycloalkyl$C_1$-$C_4$alkyl, $C_1$-$C_6$alkoxy, halo$C_1$-$C_6$alkoxy and $SF_5$;

or

$R^1$ and $R^2$, taken in combination, form a divalent group selected from -$CH_2$-, -$CH_2CH_2$-, -$CH_2CH_2CH_2$-, -$OCH_2$-, -$CH_2OCH_2$-, -$OCH_2CH_2$, -$CH_2N(H)CH_2$- and -$CH_2N(C_1$-$C_4$alkyl)$CH_2$-, each of which is optionally substituted with $C_1$-$C_4$alkyl or hydroxy$C_1$-$C_4$alkyl and wherein the oxygen of –$OCH_2CH_2$- or –$OCH_2$- is attached to the $CR^2$ carbon;

$R^3$ is independently selected from the group consisting of hydrogen, halogen, $C_1$-$C_6$alkyl, halo$C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_3$-$C_7$cycloalkyl$C_1$-$C_4$alkyl, $C_1$-$C_6$alkoxy, halo$C_1$-$C_6$alkoxy and $SF_5$;

$Z^1$ is N or $CR^5$;

$Z^2$ is N or $CR^6$;

$Z^3$ is N or $CR^7$, wherein 0, 1, or 2 of $Z^1$, $Z^2$ and $Z^3$ can be N;

$R^4$ is halogen, $C_1$-$C_6$alkyl, $C_1$-$C_6$alkoxy, halo$C_1$-$C_6$alkyl, $C_3$-$C_7$cycloalkyl, cyano, benzoyl, $SO_2$-$R^8$ or 4 to 7 member heterocycloalkyl having a ring heteroatom selected from N, O and S which heterocycloalkyl is substituted with 0, 1 or 2 groups independently selected from the group consisting of halogen, oxo, $C_1$-$C_6$alkyl, C(O)$C_1$-$C_6$alkyl, and $SO_2$-$R^8$, and wherein when $R^4$ is $C_1$-$C_6$alkyl, halo$C_1$-$C_6$alkyl, or $C_3$-$C_7$cycloalkyl, it is optionally substituted with one or two groups independently selected from hydroxy, cyano, $CO_2H$, $CO_2C_1$-$C_6$alkyl and $C(O)NH_2$;

$R^5$ is hydrogen, $C_1$-$C_6$alkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_6$alkoxy, amino, mono- or di-$C_1$-$C_6$alkylamino, $C_3$-$C_7$cycloalkylamino or -N(H)C(O)$C_1$-$C_4$alkyl, where each alkyl or cycloalkyl is optionally substituted with hydroxy;

$R^6$ is hydrogen, $C_1$-$C_6$alkyl, halo$C_1$-$C_6$alkyl or halogen; or

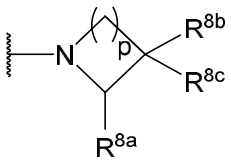
$R^5$ and $R^6$, taken in combination with the interposed atoms, form a 5- or 6- membered heteroaryl having 1 or 2 ring heteroatoms selected from N, O, and S;

$R^7$ and $R^8$ taken in combination form a divalent group selected from $–CH_2CH_2$- and $–CH_2CH_2CH_2$-; or

$R^7$ is hydrogen, $C_1$-$C_6$alkyl, or $SO_2C_1$-$C_6$alkyl;

$R^8$ is $C_1$-$C_6$alkyl, $NR^{8d}R^{8e}$, $C_3$-$C_7$cycloalkyl, halo$C_1$-$C_6$alkyl or benzyl, wherein each alkyl, cycloalkyl or haloalkyl is optionally substituted with hydroxy, $CO_2H$, $CO_2C_1$-$C_6$alkyl or $C(O)NH_2$; or

$R^8$ is a group of the formula:




wherein

p is 1 or 2;

$R^{8a}$ is hydrogen, $C_1$-$C_6$alkyl, benzyl, or phenyl optionally substituted with $C_1$-$C_6$alkyl or halogen;

$R^{8b}$ is hydrogen, halogen, $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, halo$C_1$-$C_6$alkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_6$alkoxy$C_1$-$C_4$alkyl, $C_3$-$C_7$cycloalkyl, cyano, amino, N(H)C(O)$C_1$-$C_6$alkyl, N(H)C(O)$C_3$-$C_7$cycloalkyl, N(H)C(O)halo$C_1$-$C_6$alkyl, $CO_2H$, $C(O)NH_2$, C(O)NH($C_1$-$C_6$alkyl), C(O)N($C_1$-$C_6$alkyl)$_2$, C(O)$C_1$-$C_6$alkyl, C(O)halo$C_1$-$C_6$alkyl, $SO_2C_1$-$C_6$alkyl, phenyl optionally substituted with halogen, $C_1$-$C_4$alkyl or halo$C_1$-$C_4$alkyl, benzyl optionally substituted withhalogen, phenoxy optionally substituted with halogen, 4 to 7 member heterocycloalkyl having 1 or 2 ring heteroatoms selected from N, O and S, or 5 or 6 member heteroaryl having 1 ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, which heteroaryl is optionally substituted with 1 or 2 $C_1$-$C_6$alkyl, and wherein the alkoxy is optionally substituted with halogen, phenyl or halogen-substituted phenyl;

$R^{8c}$ is hydrogen, halogen, hydroxy or $C_1$-$C_6$alkyl; or

$CR^{8b}R^{8c}$, taken in combination, forms a spirocyclic 3 to 6 member carboxycle or a 4 to 6

member heterocycle having a ring heteratom selected from N, O and S, which spirocycle is optionally substituted with hydroxy, $C_1$-$C_4$alkyl, halo$C_1$-$C_4$alkyl or $C_1$-$C_4$alkoxy;

$R^{8d}$ is hydrogen, $C_1$-$C_6$alkyl, halo$C_1$-$C_6$alkyl, $C_3$-$C_7$cycloalkyl, or 4 to 7 member heterocycloalkyl having 1 ring heteroatoms selected from N, O and S and 0 or 1 additional ring nitrogen atoms, which heterocycloalkyl is optionally substituted with 1 or 2 substituents independently selected from hydroxy, halogen, oxo, $C_1$-$C_6$alkyl, and $C_1$-$C_6$alkoxy;

$R^{8e}$ is hydrogen or $C_1$-$C_6$alkyl; or

$NR^{8d}R^{8e}$, taken in combination, forms a 4 to 7 member heterocycloalkyl optionally comprising an additional ring heteroatom selected from N, O and S, which heterocycloalkyl is optionally substituted with 1 or 2 substituents independently selected from hydroxy, halogen, oxo, $C_1$-$C_6$alkyl, $C_1$-$C_6$alkoxy and heteroaryl, which heteroaryl has 5 or 6 ring atoms and has one ring heteroatom selected from N, O and S and 0 or 1 additional ring nitrogen atom, or

$NR^{8d}R^{8e}$, taken in combination, forms a 5 or 6 member heteroaryl optionally comprising 1 additional ring heteroatom selected from N, O and S;

$R^9$ is hydrogen or $C_1$-$C_6$alkyl;

$R^{10}$ and $R^{10a}$ are each independently selected from the group consisting of hydrogen, halogen and $C_1$-$C_6$alkyl; or

$R^9$ and $R^{10}$ taken in combination form a divalent bridge selected from O, $CH_2$, and $CH_2CH_2$ and $R^{10a}$ is hydrogen;

$R^{11a}$ is hydrogen or halogen;

$R^{12}$ is hydrogen or halogen;

$R^{11}$ is selected from the group consisting of hydrogen, halogen, $C_1$-$C_6$alkyl, N(H)$C_1$-$C_6$alkyl and N(H)$C_3$-$C_7$cycloalkyl; or

$R^{11}$ and $R^{12}$, taken in combination, form a double bond;

$R^{13a}$ is hydrogen or $C_1$-$C_6$alkyl;

$R^{13}$ is $C_1$-$C_6$alkyl, $C_3$-$C_7$cycloalkyl or $C_3$-$C_7$cycloalkyl$C_1$-$C_6$alkyl;

$R^{14}$ is $C_1$-$C_6$alkyl, $C_3$-$C_7$cycloalkyl or $C_3$-$C_7$cycloalkyl$C_1$-$C_6$alkyl; and

$R^{15}$ is hydrogen or halogen;

with the proviso that

(1) when $R^4$ is $SO_2CH_3$, then at least one occurrence of $R^1$, $R^2$ or $R^3$ is not hydrogen,

(2) when $R^4$ is halogen, trifluoromethyl or cyano and $R^6$ is hydrogen or halogen, then at least one occurrence of $R^1$ or $R^2$ is not hydrogen or $R^1$ is not methyl,

(3) when $R^5$ is $C_1$-$C_6$alkoxy, then $R^4$ is not hydrogen or halogen, and

(4) when $R^4$ is $C_1$-$C_6$alkoxy or $C_1$-$C_6$alkyl, then $R^2$ is not hydrogen.

[0014b] In another aspect, the present disclosure refers to a pharmaceutical composition comprising a pharmaceutically acceptable excipient, carrier or adjuvant and a compound as described herein. In yet another aspect, the present disclosure refers to a packaged pharmaceutical composition, comprising a pharmaceutical composition as described herein and instructions for using the composition to treat a patient suffering from a heart disease.

[0014c] In another aspect, the present disclosure refers to the use of a compound as described herein, or a pharmaceutical salt thereof or a pharmaceutical composition thereof in the manufacture of a medicament for treating heart disease in a mammal.

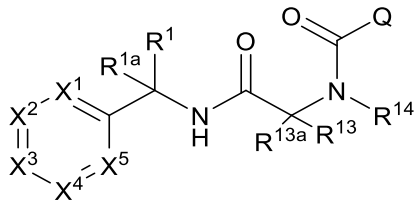
[0014d] In a further aspect, the present disclosure refers to a compound as described herein for use as a medicament. In another aspect, the present disclosure refers to the use of the compound as described herein in the manufacture of a medicament for treating heart failure.

[0015] The disclosure provides, in one example, bis-amide compounds which modulate the activity of cardiac sarcomere. Preferably, the bis-amide compounds of the disclosure are troponin activators interface to increase activity of the cardiac sarcomere. In some examples, the bis-amide compounds of the disclosure are troponin activators that activate the cardiac sarcomere. In some examples, the bis-amide compounds of the disclosure are troponin activators that increase the activity of the cardiac sarcomere. In certain preferred applications, the bis-amide compounds of the disclosure are compounds that activate the cardiac sarcomere by binding to the Troponin C and Troponin I interface.

[0016] The bis-amide compounds of the disclosure are compounds and salts according Formula (I):

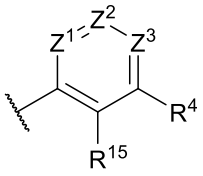
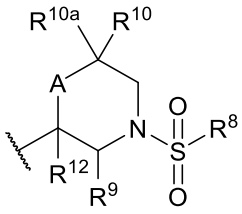
**What is Claimed:**

1. A compound or pharmaceutically acceptable salt thereof, according to Formula (I):



(I)

wherein

Q is  or  ;

A is absent, oxygen, N(H), N($C_1$-$C_6$alkyl) or $CR^{11}R^{11a}$;

$X^1$ is N or $CR^2$;

$X^2$, $X^3$, $X^4$ and $X^5$ are each independently selected from N and $CR^3$ provided that 0, 1, or 2 of $X^1$, $X^2$, $X^3$, $X^4$ and $X^5$ are N and the remainder are $CR^2$ or $CR^3$;

$R^{1a}$ is selected from the group consisting of hydrogen, $C_1$-$C_6$alkyl and halogen;

$R^1$ is selected from the group consisting of $C_1$-$C_6$alkyl, halo $C_1$-$C_6$alkyl, hydroxy $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl optionally substituted with 1 or 2 groups selected from hydroxy, halogen, and $C_1$-$C_4$alkyl, hydroxy $C_3$-$C_7$cycloalkyl, $C_3$-$C_7$cycloalkyl$C_1$-$C_4$alkyl, hydroxy $C_3$-$C_7$cycloalkyl$C_1$-$C_4$alkyl,and 4 to 7 member heterocycloalkyl having 1 or 2 ring heteroatoms independently selected from N, O and S, which heterocycloalkyl is optionally substituted with 1 or 2 groups selected from oxo, hydroxy, halogen and $C_1$-$C_4$alkyl;

$R^2$ is selected from the group consisting of hydrogen, halogen, $C_1$-$C_6$alkyl, halo$C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_3$-$C_7$cycloalkyl$C_1$-$C_4$alkyl, $C_1$-$C_6$alkoxy, halo$C_1$-$C_6$alkoxy and $SF_5$;

or

$R^1$ and $R^2$, taken in combination, form a divalent group selected from -$CH_2$-, -$CH_2CH_2$-, -$CH_2CH_2CH_2$-, -$OCH_2$-, -$CH_2OCH_2$-, -$OCH_2CH_2$, -$CH_2N(H)CH_2$- and -$CH_2N(C_1$-$C_4$alkyl$)CH_2$-, each of which is optionally substituted with $C_1$-$C_4$alkyl or hydroxy$C_1$-$C_4$alkyl and wherein the oxygen of –$OCH_2CH_2$- or –$OCH_2$- is attached to the $CR^2$ carbon;

$R^3$ is independently selected from the group consisting of hydrogen, halogen, $C_1$-$C_6$alkyl, halo$C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_3$-$C_7$cycloalkyl$C_1$-$C_4$alkyl, $C_1$-$C_6$alkoxy, halo$C_1$-$C_6$alkoxy and $SF_5$;

$Z^1$ is N or $CR^5$;

$Z^2$ is N or $CR^6$;

$Z^3$ is N or $CR^7$, wherein 0, 1, or 2 of $Z^1$, $Z^2$ and $Z^3$ can be N;

$R^4$ is halogen, $C_1$-$C_6$alkyl, $C_1$-$C_6$alkoxy, halo$C_1$-$C_6$alkyl, $C_3$-$C_7$cycloalkyl, cyano, benzoyl, $SO_2$-

$R^8$ or 4 to 7 member heterocycloalkyl having a ring heteroatom selected from N, O and S which heterocycloalkyl is substituted with 0, 1 or 2 groups independently selected from the group consisting of halogen, oxo, $C_1$-$C_6$alkyl, C(O)$C_1$-$C_6$alkyl, and $SO_2$-$R^8$, and wherein when $R^4$ is $C_1$-$C_6$alkyl, halo$C_1$-$C_6$alkyl, or $C_3$-$C_7$cycloalkyl, it is optionally substituted with one or two groups independently selected from hydroxy, cyano, $CO_2H$, $CO_2C_1$-$C_6$alkyl and $C(O)NH_2$;

$R^5$ is hydrogen, $C_1$-$C_6$alkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_6$alkoxy, amino, mono- or di-$C_1$-$C_6$alkylamino, $C_3$-$C_7$cycloalkylamino or -N(H)C(O)$C_1$-$C_4$alkyl, where each alkyl or cycloalkyl is optionally substituted with hydroxy;

$R^6$ is hydrogen, $C_1$-$C_6$alkyl, halo$C_1$-$C_6$alkyl or halogen; or

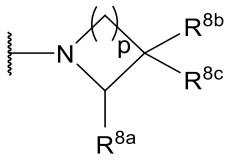
$R^5$ and $R^6$, taken in combination with the interposed atoms, form a 5- or 6- membered heteroaryl having 1 or 2 ring heteroatoms selected from N, O, and S;

$R^7$ and $R^8$ taken in combination form a divalent group selected from $–CH_2CH_2$- and $–CH_2CH_2CH_2$-; or

$R^7$ is hydrogen, $C_1$-$C_6$alkyl, or $SO_2C_1$-$C_6$alkyl;

$R^8$ is $C_1$-$C_6$alkyl, $NR^{8d}R^{8e}$, $C_3$-$C_7$cycloalkyl, halo$C_1$-$C_6$alkyl or benzyl, wherein each alkyl, cycloalkyl or haloalkyl is optionally substituted with hydroxy, $CO_2H$, $CO_2C_1$-$C_6$alkyl or $C(O)NH_2$; or

$R^8$ is a group of the formula:




wherein

p is 1 or 2;

$R^{8a}$ is hydrogen, $C_1$-$C_6$alkyl, benzyl, or phenyl optionally substituted with $C_1$-$C_6$alkyl or halogen;

$R^{8b}$ is hydrogen, halogen, $C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, halo$C_1$-$C_6$alkyl, $C_1$-$C_6$alkoxy, $C_1$-$C_6$alkoxy$C_1$-$C_4$alkyl, $C_3$-$C_7$cycloalkyl, cyano, amino, N(H)C(O)$C_1$-$C_6$alkyl, N(H)C(O)$C_3$-$C_7$cycloalkyl, N(H)C(O)halo$C_1$-$C_6$alkyl, $CO_2H$, $C(O)NH_2$, C(O)NH($C_1$-$C_6$alkyl), C(O)N($C_1$-$C_6$alkyl)$_2$, C(O)$C_1$-$C_6$alkyl, C(O)halo$C_1$-$C_6$alkyl, $SO_2C_1$-$C_6$alkyl, phenyl optionally substituted with halogen, $C_1$-$C_4$alkyl or halo$C_1$-$C_4$alkyl, benzyl optionally substituted withhalogen, phenoxy optionally substituted with halogen, 4 to 7 member heterocycloalkyl having 1 or 2 ring heteroatoms selected from N, O and S, or 5 or 6 member heteroaryl having 1 ring heteroatom selected from N, O or S and 0, 1 or 2 additional ring nitrogen atoms, which heteroaryl is optionally substituted with 1 or 2 $C_1$-$C_6$alkyl, and wherein the alkoxy is optionally substituted with halogen, phenyl or halogen-substituted phenyl;

$R^{8c}$ is hydrogen, halogen, hydroxy or $C_1$-$C_6$alkyl; or

$CR^{8b}R^{8c}$, taken in combination, forms a spirocyclic 3 to 6 member carboxycle or a 4 to 6 member heterocycle having a ring heteratom selected from N, O and S, which spirocycle is optionally substituted with hydroxy, $C_1$-$C_4$alkyl, halo$C_1$-$C_4$alkyl or $C_1$-$C_4$alkoxy;

$R^{8d}$ is hydrogen, $C_1$-$C_6$alkyl, halo$C_1$-$C_6$alkyl, $C_3$-$C_7$cycloalkyl, or 4 to 7 member

heterocycloalkyl having 1 ring heteroatoms selected from N, O and S and 0 or 1 additional ring nitrogen atoms, which heterocycloalkyl is optionally substituted with 1 or 2 substituents independently selected from hydroxy, halogen, oxo, $C_1$-$C_6$alkyl, and $C_1$-$C_6$alkoxy;

$R^{8e}$ is hydrogen or $C_1$-$C_6$alkyl; or

$NR^{8d}R^{8e}$, taken in combination, forms a 4 to 7 member heterocycloalkyl optionally comprising an additional ring heteroatom selected from N, O and S, which heterocycloalkyl is optionally substituted with 1 or 2 substituents independently selected from hydroxy, halogen, oxo, $C_1$-$C_6$alkyl, $C_1$-$C_6$alkoxy and heteroaryl, which heteroaryl has 5 or 6 ring atoms and has one ring heteroatom selected from N, O and S and 0 or 1 additional ring nitrogen atom, or

$NR^{8d}R^{8e}$, taken in combination, forms a 5 or 6 member heteroaryl optionally comprising 1 additional ring heteroatom selected from N, O and S;

$R^9$ is hydrogen or $C_1$-$C_6$alkyl;

$R^{10}$ and $R^{10a}$ are each independently selected from the group consisting of hydrogen, halogen and $C_1$-$C_6$alkyl; or

$R^9$ and $R^{10}$ taken in combination form a divalent bridge selected from O, $CH_2$, and $CH_2CH_2$ and $R^{10a}$ is hydrogen;

$R^{11a}$ is hydrogen or halogen;

$R^{12}$ is hydrogen or halogen;

$R^{11}$ is selected from the group consisting of hydrogen, halogen, $C_1$-$C_6$alkyl, N(H)$C_1$-$C_6$alkyl and N(H)$C_3$-$C_7$cycloalkyl; or

$R^{11}$ and $R^{12}$, taken in combination, form a double bond;

$R^{13a}$ is hydrogen or $C_1$-$C_6$alkyl;

$R^{13}$ is $C_1$-$C_6$alkyl, $C_3$-$C_7$cycloalkyl or $C_3$-$C_7$cycloalkyl$C_1$-$C_6$alkyl;

$R^{14}$ is $C_1$-$C_6$alkyl, $C_3$-$C_7$cycloalkyl or $C_3$-$C_7$cycloalkyl$C_1$-$C_6$alkyl; and

$R^{15}$ is hydrogen or halogen;

with the proviso that

(1) when $R^4$ is $SO_2CH_3$, then at least one occurrence of $R^1$, $R^2$ or $R^3$ is not hydrogen,

(2) when $R^4$ is halogen, trifluoromethyl or cyano and $R^6$ is hydrogen or halogen, then at least one occurrence of $R^1$ or $R^2$ is not hydrogen or $R^1$ is not methyl,

(3) when $R^5$ is $C_1$-$C_6$alkoxy, then $R^4$ is not hydrogen or halogen, and

(4) when $R^4$ is $C_1$-$C_6$alkoxy or $C_1$-$C_6$alkyl, then $R^2$ is not hydrogen.

2. The compound of claim 1, wherein

$X^1$ is $CR^2$, $X^2$ is N or $CR^3$, $X^3$ is $CR^{3a}$, $X^4$ is N or $CR^3$ and $X^5$ is $CR^3$;

$R^2$ is hydrogen, halogen, $C_1$-$C_4$alkyl, cyclopropyl, halo$C_1$-$C_4$alkyl, $C_1$-$C_4$alkoxy or halo$C_1$-$C_4$alkoxy;

$R^3$ is independently selected at each occurrence from the group consisting of hydrogen, halogen, $C_1$-$C_4$alkyl, cyclopropyl, halo$C_1$-$C_4$alkyl, $C_1$-$C_4$alkoxy and halo$C_1$-$C_4$alkoxy; and

$R^{3a}$ is halogen, $C_1$-$C_6$alkyl, halo$C_1$-$C_6$alkyl, $C_2$-$C_6$alkenyl, $C_2$-$C_6$alkynyl, $C_3$-$C_7$cycloalkyl, $C_3$-$C_7$cycloalkyl$C_1$-$C_4$alkyl, $C_1$-$C_6$alkoxy, halo$C_1$-$C_6$alkoxy or $SF_5$.

3. The compound of claim 1 or 2, wherein

$X^1$ is $CR^2$;

$R^2$ is hydrogen, halogen, $C_1$-$C_4$alkyl or $C_1$-$C_4$alkoxy;

$X^2$ is CH or N;

$X^3$ is $CR^{3a}$;

$R^{3a}$ is halogen, $C_1$-$C_4$alkyl, halo$C_1$-$C_4$alkyl, halo$C_1$-$C_6$alkoxy or $SF_5$;

$X^4$ is $CR^3$ or N;

$R^3$ is hydrogen or halogen; and

$X^5$ is CH.

4. The compound of any one of claims 1 to 3, wherein

$X^1$ is $CR^2$;

$R^2$ is hydrogen, halogen, methyl, ethyl, methoxy or ethoxy;

$X^2$ and $X^5$ are each CH;

$X^3$ is $CR^{3a}$;

$R^{3a}$ is halogen, methyl, ethyl, fluoromethyl, difluoromethyl, trifluoromethyl, trifluoromethoxy, or $SF_5$;

$X^4$ is $CR^3$; and

$R^3$ is hydrogen or halogen.

5. The compound of any one of claims 1 to 4, wherein $R^1$ is selected from the group consisting of $C_1$-$C_6$alkyl, halo $C_1$-$C_6$alkyl, $C_3$-$C_7$cycloalkyl, $C_3$-$C_7$cycloalkylmethyl, and 4 to 6 member heterocycloalkyl having a ring heteroatom selected from N and O, which heterocycloalkyl is optionally substituted with 1 or 2 groups selected from oxo, halogen, and hydroxy, and wherein the alkyl or cycloalkyl is optionally substituted with hydroxy.

6. The compound of any one of claims 1 to 5, wherein $R^1$ is $C_1$-$C_4$alkyl, trifluoromethyl, $C_3$-$C_5$cycloalkyl, $C_3$-$C_5$cycloalkylmethyl, oxetanyl, tetrahydrofuryl, or azetidinyl, wherein each alkyl, cycloalkyl, oxetanyl or azetidinyl is optionally substituted with hydroxy or halogen.

7. The compound of any one of claims 1 to 6, wherein $R^1$ is methyl, isopropyl, cyclopropyl, cyclopropylmethyl, cyclobutyl, oxetanyl, difluoromethyl, 1-hydroxycyclopropyl, 3-hydroxycyclobutyl, 3-hydroxy-3-methylcyclobutyl, 3-fluorooxetanyl or oxopyrrolidinyl.

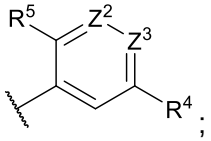
8. The compound of any one of claims 1 to 7, wherein

$R^{13}$ and $R^{14}$ are each independently selected from the group consisting of $C_1$-$C_4$alkyl, $C_3$-$C_5$cycloalkyl and $C_3$-$C_5$cycloalkylmethyl; and

$R^{13a}$ is hydrogen.

9. The compound of any one of claims 1 to 8, wherein $R^{13}$ and $R^{14}$ are each methyl and $R^{13a}$ is hydrogen.

10. The compound of any one of claims 1 to 9, wherein

Q is ;

$Z^2$ is N or $CR^6$; $Z^3$ is N or $CR^7$, wherein 0 or 1 of $Z^2$ and $Z^3$ can be N;

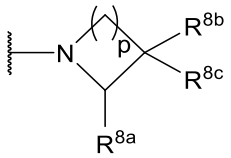
$R^4$ is $C_1$-$C_4$alkyl, $C_1$-$C_4$alkoxy, cyano, $SO_2$-$R^8$, or 4 to 7 member heterocycloalkyl having a ring heteroatom selected from N, O and S which heterocycloalkyl is substituted with 0, 1 or 2 groups independently selected from the group consisting of halogen, oxo, $C_1$-$C_6$alkyl, $C(O)C_1$-$C_6$alkyl, and $SO_2R^8$ and wherein each alkyl or cycloalkyl is optionally substituted with hydroxy, cyano, $CO_2H$ or $C(O)NH_2$;

$R^5$ is hydrogen, $C_1$-$C_4$alkyl, amino, mono- or di-$C_1$-$C_4$alkylamino, $C_3$-$C_6$cycloalkylamino or -$N(H)C(O)C_1$-$C_4$alkyl, where each alkyl or cycloalkyl is optionally substituted with hydroxy;

$R^6$ is hydrogen, $C_1$-$C_4$alkyl, halo$C_1$-$C_6$alkyl or halogen;

$R^7$ is hydrogen or $C_1$-$C_4$alkyl; and

$R^8$ is $C_1$-$C_6$alkyl, $NR^{8d}R^{8e}$, $C_3$-$C_7$cycloalkyl or halo$C_1$-$C_6$alkyl, wherein each alkyl, cycloalkyl or haloalkyl is optionally substituted with hydroxy, $CO_2H$, $CO_2C_1$-$C_6$alkyl or $C(O)NH_2$; or

$R^8$ is a group of the formula: 

p is 1 or 2;

$R^{8a}$ is hydrogen, $C_1$-$C_6$alkyl or phenyl substituted with halogen;

$R^{8b}$ is hydrogen, halogen, $C_1$-$C_4$alkyl, halo$C_1$-$C_4$alkyl, $C_1$-$C_4$alkoxy, $C_3$-$C_5$cycloalkyl, cyano, amino or $SO_2C_1$-$C_6$alkyl;

$R^{8c}$ is hydrogen, halogen, hydroxy or $C_1$-$C_6$alkyl; or

$CR^{8b}R^{8c}$, taken in combination, forms a spirocyclic 3 to 6 member carboxycle or a 4 to 6 member heterocycle having a ring heteratom selected from N, O and S, which spirocycle is optionally substituted with hydroxy, $C_1$-$C_4$alkyl, halo$C_1$-$C_4$alkyl or $C_1$-$C_4$alkoxy;

$R^{8d}$ is hydrogen, $C_1$-$C_6$alkyl, halo$C_1$-$C_6$alkyl, $C_3$-$C_7$cycloalkyl, or 4 to 7 member heterocycloalkyl having a ring heteroatoms selected from N, O and S and 0 or 1 additional ring nitrogen atoms, which heterocycloalkyl is optionally substituted with 1 or 2 substituents independently selected from hydroxy, halogen, oxo, $C_1$-$C_6$alkyl, and $C_1$-$C_6$alkoxy;

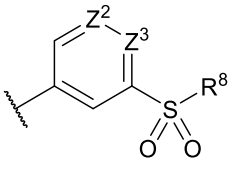
$R^{8e}$ is hydrogen or $C_1$-$C_6$alkyl; or

$NR^{8d}R^{8e}$, taken in combination, forms a 4 to 7 member heterocycloalkyl optionally comprising 1 additional ring heteroatom selected from N, O and S, which heterocycloalkyl is optionally substituted with 1 or 2 substituents independently selected from hydroxy, halogen, oxo, $C_1$-$C_6$alkyl,

$C_1$-$C_6$alkoxy and heteroaryl, which heteroaryl has 5 or 6 ring atoms and has one ring heteroatom selected from N, O and S and 0 or 1 additional ring nitrogen atom, or

$NR^{8d}R^{8e}$, taken in combination, forms a 5 or 6 member heteroaryl, which heteroaryl optionally comprises 1 additional ring heteroatom selected from N, O and S.

11. The compound of any one of claims 1 to 10, wherein

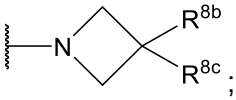
Q is 

;

$Z^2$ is CH or N;

$Z^3$ is CH or N; and

$R^8$ is $C_1$-$C_6$alkyl, $C_3$-$C_7$cycloalkyl or halo$C_1$-$C_6$alkyl; or

$R^8$ is a group of the formula: 

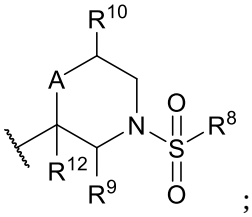
;

$R^{8b}$ is halogen, $C_1$-$C_4$alkyl, halo$C_1$-$C_4$alkyl, $C_1$-$C_4$alkoxy, $C_3$-$C_5$cycloalkyl, cyano, or amino;

$R^{8c}$ is hydrogen, halogen, hydroxy or $C_1$-$C_6$alkyl; or

$CR^{8b}R^{8c}$, taken in combination, forms a spirocyclic 3 to 4 member carboxycle or a 4 or 5 member heterocycle having a ring heteratom selected from N, O and S, which spirocycle is optionally substituted with hydroxy, $C_1$-$C_4$alkyl, halo$C_1$-$C_4$alkyl or $C_1$-$C_4$alkoxy.

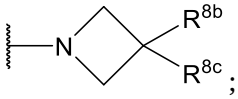
12. The compound of any one of claims 1 to 9, wherein

Q is 

;

A is oxygen, N(H), or $CHR^{11}$;

$R^8$ is $C_1$-$C_6$alkyl, $NR^{8d}R^{8e}$, $C_3$-$C_7$cycloalkyl, halo$C_1$-$C_6$alkyl or benzyl, and wherein each alkyl, cycloalkyl or haloalkyl is optionally substituted with hydroxy, $CO_2H$, $CO_2C_1$-$C_6$alkyl or $C(O)NH_2$; or

$R^8$ is a group of the formula: 

;

$R^{8b}$ is hydrogen, $C_1$-$C_4$alkyl, halo $C_1$-$C_4$alkyl, $C_1$-$C_4$alkoxy, $C_3$-$C_6$cycloalkyl, cyano, or amino;

$R^{8c}$ is hydrogen, hydroxy or $C_1$-$C_6$alkyl;

$R^{8d}$ is hydrogen, $C_1$-$C_6$alkyl, halo$C_1$-$C_6$alkyl, or $C_3$-$C_7$cycloalkyl;

$R^{8e}$ is hydrogen or $C_1$-$C_6$alkyl;

$R^9$ is hydrogen;

$R^{10}$ is hydrogen; or

$R^9$ and $R^{10}$, taken in combination, form a divalent methylene bridge; and

$R^{11}$ is hydrogen or $C_1$-$C_6$alkyl.

13. A compound of claim 1, wherein the compound is selected from the group consisting of:

3-((3-cyano-1-azetidinyl)sulfonyl)-N-methyl-N-((1R)-1-methyl-2-oxo-2-(((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)amino)ethyl)benzamide;

3-((3-cyano-1-azetidinyl)sulfonyl)-N-methyl-N-((1R)-1-methyl-2-oxo-2-(((1S)-1-(4-(trifluoromethyl)phenyl)ethyl)amino)ethyl)benzamide;

N-((1R)-2-(((1R)-1-(4-chlorophenyl)ethyl)amino)-1-methyl-2-oxoethyl)-3-((3-cyano-1-azetidinyl)sulfonyl)-N-methylbenzamide;

N-((1R)-2-(((1S)-1-(4-chlorophenyl)ethyl)amino)-1-methyl-2-oxoethyl)-3-((3-cyano-1-azetidinyl)sulfonyl)-N-methylbenzamide;

(2S)-4-((3-cyano-1-azetidinyl)sulfonyl)-N-((2R)-1-(((1R)-1-(2-fluoro-4-(trifluoromethyl)phenyl)ethyl)amino)-1-oxo-2-propanyl)-N-methyl-2-morpholinecarboxamide;

(3S)-N-((2R)-1-(((1R)-1-(4-chloro-2-fluorophenyl)ethyl)amino)-1-oxo-2-propanyl)-1-((3-cyano-1- azetidinyl)sulfonyl)-N-methyl-3-piperidinecarboxamide;

N-((1R)-2-(((1S)-1-(4-chlorophenyl)ethyl)amino)-1-methyl-2-oxoethyl)-3-((3-cyano-1-azetidinyl)sulfonyl)-N-methylbenzamide;

(3S)-1-((3-cyano-1-azetidinyl)sulfonyl)-N-methyl-N-((1R)-1-methyl-2-oxo-2-(((1R)-1-(4-(trifluoromethyl)phenyl)ethyl)amino)ethyl)-3-piperidinecarboxamide; and

(2S)-N-((2R)-1-(((1R)-1-(4-chloro-2-fluorophenyl)ethyl)amino)-1-oxo-2-propanyl)-4-((3-cyano-1- azetidinyl)sulfonyl)-N-methyl-2-morpholinecarboxamide,

or a pharmaceutically acceptable salt thereof.

14. The compound of any one of claims 1 to 13 in the form of a pharmaceutically acceptable salt.

15. A pharmaceutical composition comprising a pharmaceutically acceptable excipient, carrier or adjuvant and a compound of any one of claims 1 to 14.

16. The pharmaceutical composition of claim 15, wherein the composition is formulated in a form selected from the group consisting of an injectable fluid, an aerosol, a tablet, a pill, a capsule, a syrup, a cream, a gel and a transdermal patch.

17. A packaged pharmaceutical composition, comprising a pharmaceutical composition of claim 15 or 16 and instructions for using the composition to treat a patient suffering from a heart disease.

18. The packaged pharmaceutical composition of claim 17, wherein the heart disease is heart failure.

19. Use of a compound of any one of claims 1 to 14, or a pharmaceutical salt thereof or a pharmaceutical composition thereof in the manufacture of a medicament for treating heart disease in a mammal.

20. The use of claim 19, wherein the heart disease is heart failure.

21. The use of claim 20, wherein the heart failure is congestive heart failure.

22. The use of claim 20, wherein the heart failure is systolic heart failure.

23. A compound of any one of claims 1 to 14 for use as a medicament.

24. Use of the compound of any one of claims 1 to 14 in the manufacture of a medicament for treating heart failure.