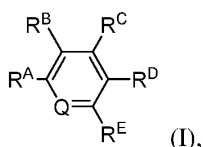


We claim:

1. A compound according to formula I, or a stereoisomer, tautomer, pharmaceutically acceptable salt, hydrate, or solvate thereof



wherein:

R^A is $-N(R^1)R^2$ and R^B is H, aliphatic, $-O$ -aliphatic, $-S$ -aliphatic, $-O-C(O)$ -aliphatic, or halogen, or R^A is $N(R^1)$ or $-CH_2N(R^1)-$ and R^A together with R^B forms a 5- or 6-membered heteroaliphatic or heteroaryl ring;

10 R^C is H, aliphatic, $-S$ -aliphatic, or $-O-C(O)$ -aliphatic, and R^D is substituted aliphatic or $-Y-X-(CR^7)_m-N(R^4)R^5$, or R^C and R^D together form a 5- or 6-membered heteroaliphatic or heteroaryl ring, wherein the 5- or 6-membered heteroaliphatic or heteroaryl ring is substituted with $-X-(CR^7)_m-N(R^4)R^5$;

R^E is H, $-O$ -aliphatic, aliphatic, $-S$ -aliphatic, $-O-C(O)$ -aliphatic, or halogen;

15 Q is $C-R^3$ or N;

X is $N(R^6)$, O, $C(O)$, $-S(O_2)O-$, $-OS(O_2)-$, $-P(O)(OH)O-$, $-OP(O)OH-$, $-N(H)-C(H)(CF_3)-$, or $-C(H)(CF_3)-N(H)-$, or X is absent;

Y is $-(CR^7)_n-$ or a divalent azole ring;

R^1 and R^2 independently are H or aliphatic;

20 R^3 is H, aliphatic, $-O$ -aliphatic, or $-S$ -aliphatic;

R^4 and R^5 independently are H, aliphatic, aryl or heteroaryl, or R^4 and R^5 together with N form a heterocycloaliphatic or heteroaryl ring;

R^6 is H or aliphatic;

each R^7 independently is H, halogen, or aliphatic; and

25 m and n independently are integers from 1 to 10,

wherein at least one of the following conditions applies

(i) if Q is $C-R^3$, then at least one of R^B , R^C , R^E , and R^3 is other than H, or

(ii) if R^D is $-Y-X-(CH_2)_m-N(R^4)R^5$ where X is absent, then Y is not $-(CH_2)_n-$, or

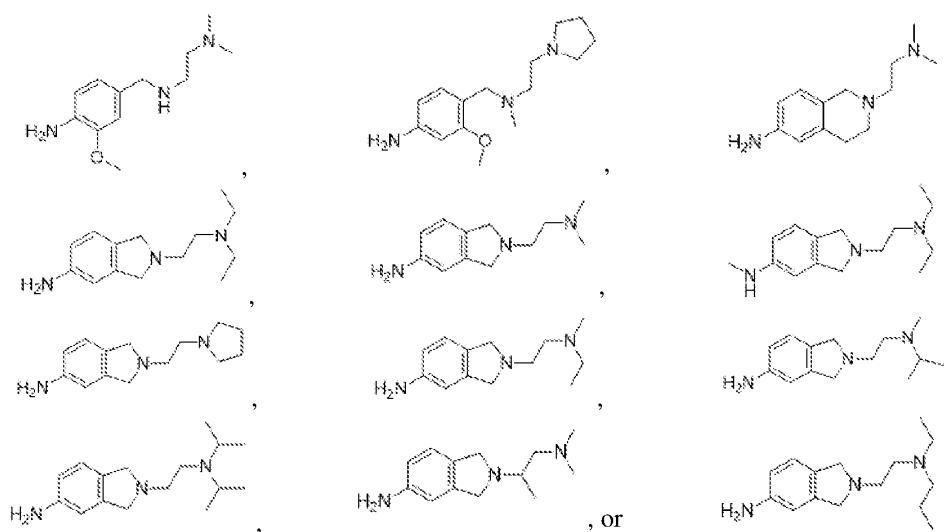
(iii) the compound includes $-Y-X-(CR^7)_m-N(R^4)R^5$ or $-X-(CR^7)_m-N(R^4)R^5$, where

30 X is present, or

(iv) if Y is a divalent azole ring, then X is absent, or

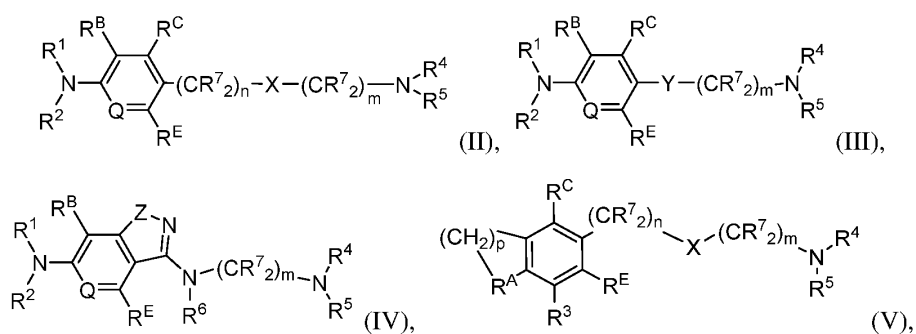
(v) if R⁴ and R⁵ together with N form a heterocycloaliphatic or heteroaryl ring and Q is C-R³, then at least of one of R^B, R^C, R^E, and R³ is other than H, or at least one of R¹ and R² is other than H or -CH₃; and

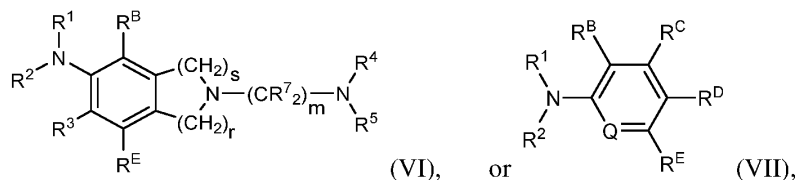
5 wherein the compound is not



2. The compound according to claim 1, wherein R^D is -Y-X-(CR⁷₂)_m-N(R⁴)R⁵.

3. The compound according to claim 1, wherein the compound has a structure according to
10 one of formulas II, III, IV, V, VI, or VII





wherein:

R^A is $N(R^1)$ or $-CH_2N(R^1)-$;

R^B is H, aliphatic, $-O$ -aliphatic, $-S$ -aliphatic, or halogen;

5 R^C is H or aliphatic;

R^D is $-(CH_2)_qSO_3M$, $-(CH_2)_qNH_2$, or $-(CH_2)_qOH$, where q is an integer from 1 to 10 and M is a monatomic cation;

X is $N(R^6)$, O , $C(O)$, $-S(O_2)O-$, $-OS(O_2)-$, $-P(O)(OH)O-$, $-OP(O)(OH)-$, $-N(H)-C(H)(CF_3)-$ or $-C(H)(CF_3)-N(H)-$;

10 Y is an azole;

Z is O , $N(H)$, or CH_2 ;

p is 1, 2, or 3 when R^A is $N(R^1)$, or p is 1 or 2 when R^A is $-CH_2N(R^1)-$;

q is an integer from 1 to 10; and

r is 1 or 2, s is 1 or 2, and $r+s = 2$ or 3,

15 wherein if the compound has a structure according to formula II, then at least one of the following conditions applies

(i) at least one of R^1 and R^2 is other than H, or

(ii) at least one of R^C and R^E is other than H, or

(iii) X is other than $N(H)$, or

20 (iv) m is not 2, or

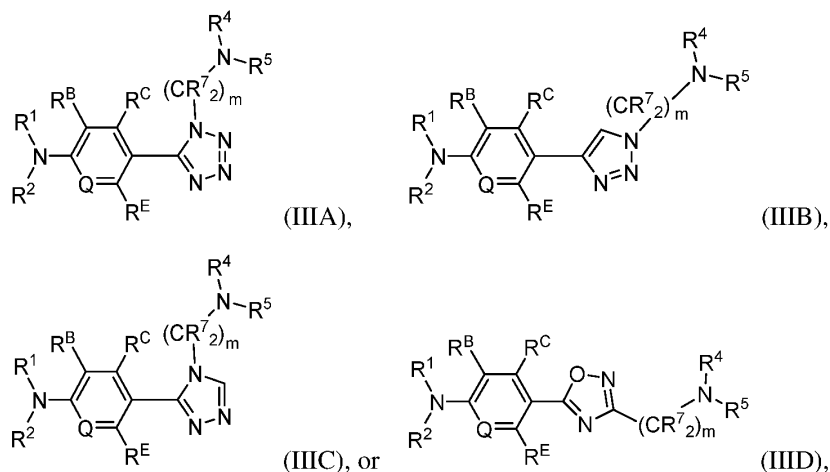
(v) n is not 1, or

(vi) if Q is CH then R^B is not $-O$ -aliphatic, or

(vii) if R^B is H then Q is not $C-R^3$ where R^3 is $-O$ -aliphatic.

25 4. The compound according to claim 3, wherein the compound has a structure according to formula III, and Y is an imidazolyl, pyrazolyl, triazolyl, tetrazolyl, oxazolyl, isoxazolyl, oxadiazolyl, furazanyl, thiazolyl, isothiazolyl, or thiadiazolyl group.

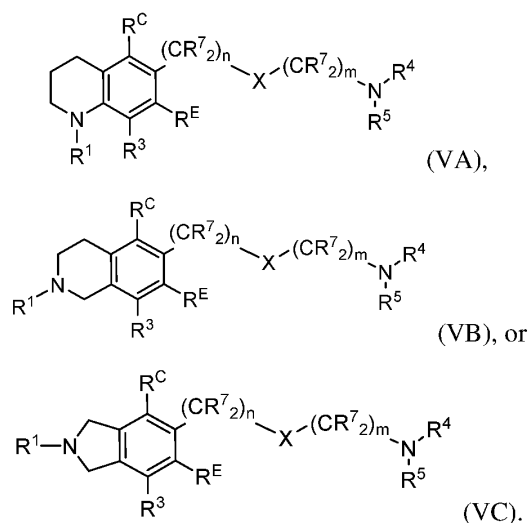
5. The compound according to claim 3, wherein the compound has a structure according to one of formulas IIIA, IIIB, IIIC, or IIID



- 5 wherein if the compound has a structure according to formula IIIA, then at least one of R^1 and R^2 is other than H, or at least one of R^B , R^C , and R^E is other than H, or Q is other than CH.

6. The compound of any one of claims 1-5, wherein Q is $C-R^3$.

- 10 7. The compound of claim 3, wherein the compound has a structure according to one of formulas VA, VB, or VC



8. The compound according to claim 7, wherein:

R^1 is H or alkyl;

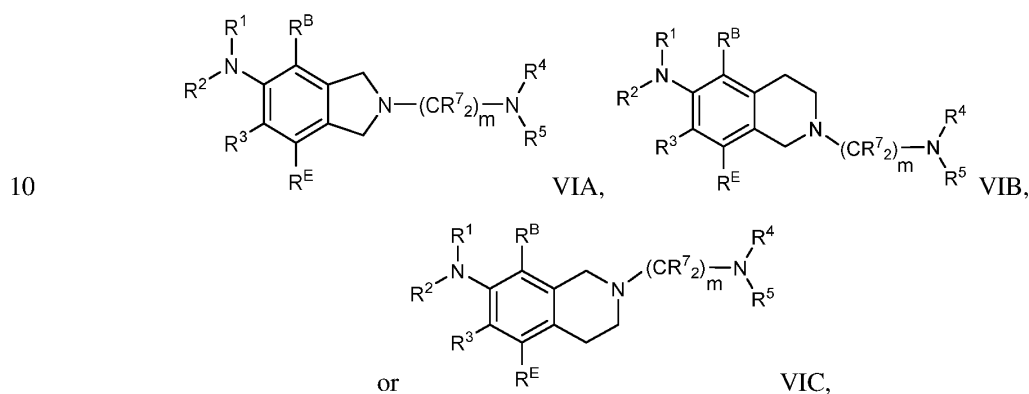
each R^7 independently is H or halogen; and

(i) R^4 and R^5 are H, or

5 (ii) R^4 is H and R^5 is alkyl, or

(iii) R^4 and R^5 are alkyl.

9. The compound according to claim 3, wherein the compound has a structure according to one of formulas VIA, VIB, or VIC



wherein:

if the compound has a structure according formula VIA, then at least one of R^B , R^E , or R^3 is other than H, or m is not 2, or if one of R^1 and R^2 is H, then the other of R^1 and R^2 is other than H or CH_3 , or

if the compound has a structure according to formula VIB, then at least one of R^B , R^E , or R^3 is other than H, or m is not 2, or at least one of R^1 and R^2 is other than H, or at least one of R^4 and R^5 is other than $-CH_3$.

10. The compound according to any one of claims 1-7 or 9, wherein R^4 and R^5 are alkyl.

11. The compound of any one of claims 3-10, wherein R^C is H.

12. The compound according to any one of claims 1-11, wherein m is 2, or n is 1, or m is 2 and n is 1.

13. The compound according to any one of claims 1-12, wherein R^6 is H, or each R^7 is H, or R^6 is H and each R^7 is H.
14. The compound according to any one of claims 2-13, wherein X is N(H), O, C(O),
5 -S(O₂)O-, -OS(O₂)-, -P(O)(OH)O-, -OP(O)(OH)-, -N(H)-C(H)(CF₃)-, or -C(H)(CF₃)-N(H)-.
15. The compound according to any one of claims 2-13, wherein X is N(H), O, C(O), -S(O₂)O-, or -P(O)(OH)O-.
- 10 16. The compound according to any one of claims 2-13, wherein X is N(H), O, or -S(O₂)O-.
17. The compound according to claim 1, wherein:
 R^A is -N(R¹)R² where R¹ is H or aliphatic and R² is H or aliphatic;
 R^B is H, aliphatic, -O-aliphatic, -S-aliphatic, -O-C(O)-aliphatic, or halogen;
15 R^C is H, aliphatic, -S-aliphatic, or -O-C(O)-aliphatic; and
 R^D is substituted aliphatic.
18. The compound according to claim 17, wherein R^D is -(CH₂)_qNH₂, -(CH₂)_qOH,
or -(CH₂)_qSO₃M where q is an integer from 1 to 10 and M is a monatomic cation.
- 20 19. The compound according to claim 17, wherein R^D is -CH₂SO₃M, -CH₂NH₂, or -CH₂OH.
20. The compound according to any one of claims 1-19, wherein at least one H atom is replaced
by a deuterium atom.
- 25 21. The compound according to claim 1, wherein the compound is:
*N*¹-(4-amino-2-methoxybenzyl)-*N*²,*N*²-diethylethane-1,2-diamine;
3-methoxy-4-(((2-(pyrrolidin-1-yl)ethyl)amino)methyl)aniline;
sodium (4-amino-2-methoxyphenyl)methanesulfonate;
30 *N*-butyl-2-(2-(diethylamino)ethyl)isoindolin-5-amine;
N-butyl-2-(2-(pyrrolidin-1-yl)ethyl)isoindolin-5-amine;
sodium (4-(dibutylamino)-3-methoxyphenyl)methanesulfonate;
sodium (4-amino-3-methoxyphenyl)methanesulfonate;

- 4-((2-(diethylamino)ethoxy)methyl)-2,3-dimethoxyaniline;
N-butyl-4-(3-((diethylamino)methyl)-1,2,4-oxadiazol-5-yl)-3-methoxyaniline;
N-butyl-4-(3-((dimethylamino)methyl)-1,2,4-oxadiazol-5-yl)-3-methoxyaniline;
N-butyl-4-(3-((dibutylamino)methyl)-1,2,4-oxadiazol-5-yl)-3-methoxyaniline;
5 *N*-butyl-4-(3-((dibutylamino)methyl)-1,2,4-oxadiazol-5-yl)-2-methylaniline;
N-butyl-5-((2-(diethylamino)ethoxy)methyl)pyridin-2-amine;
*N*¹-((1-butyl-1,2,3,4-tetrahydroquinolin-6-yl)methyl)-*N*²,*N*²-dimethylethane-1,2-diamine;
N-butyl-4-(1-(2-(dibutylamino)ethyl)-1*H*-tetrazol-5-yl)-2-methylaniline;
2-(2-(diethylamino)ethyl)-1,2,3,4-tetrahydroisoquinolin-6-amine;
10 *N*³-(2-(diethylamino)ethyl)-1*H*-indazole-3,6-diamine;
*N*⁶,*N*⁶-dibutyl-*N*³-(2-(diethylamino)ethyl)-1*H*-indazole-3,6-diamine;
*N*¹-((1-butyl-1,2,3,4-tetrahydroquinolin-6-yl)methyl)-*N*²,*N*²-diethylethane-1,2-diamine;
*N*¹-(4-amino-3-methylbenzyl)-*N*²,*N*²-diethylethane-1,2-diamine;
*N*¹-((6-aminopyridin-3-yl)methyl)-*N*²,*N*²-dibutylethane-1,2-diamine;
15 *N*¹-((6-(butylamino)pyridin-3-yl)methyl)-*N*²,*N*²-diethylethane-1,2-diamine;
N-butyl-5-(((2-(pyrrolidin-1-yl)ethyl)amino)methyl)pyridin-2-amine;
N-butyl-2-(2-(diethylamino)ethyl)-1,2,3,4-tetrahydroisoquinolin-6-amine; or
N-butyl-2-(2-(pyrrolidin-1-yl)ethyl)-1,2,3,4-tetrahydroisoquinolin-6-amine.
- 20 22. A pharmaceutical composition, comprising:
a therapeutically effective amount of at least one compound according to any one of claims 1-21, or a stereoisomer, tautomer, pharmaceutically acceptable salt, hydrate, or solvate thereof; and
at least one pharmaceutically acceptable additive.
- 25 23. A method, comprising:
for modulating activity of a calcium ion channel by contacting the calcium ion channel with
an effective amount of a compound according to any one of claims 1-21, or a stereoisomer,
tautomer, pharmaceutically acceptable salt, hydrate, or solvate thereof.
- 30 24. The method of claim 23, wherein contacting the calcium ion channel with the compound
inhibits activity of the calcium ion channel.

25. The method of claim 23 or claim 24, wherein the calcium ion channel is a ryanodine receptor.
26. The method of claim 25, wherein the ryanodine receptor is RyR2.
- 5 27. The method of any one of claims 23-26, wherein contacting the calcium ion channel comprises administering the effective amount of the compound, or stereoisomer, tautomer, pharmaceutically acceptable salt, hydrate, or solvate thereof, to a subject.
- 10 28. The method of claim 27, wherein the subject is a subject identified as having, or being at risk of having, a cardiac arrhythmia or heart failure.
29. The method of claim 28, wherein administering the effective amount of the compound, or stereoisomer, tautomer, pharmaceutically acceptable salt, hydrate, or solvate thereof, comprises
- 15 administering an amount of a pharmaceutical composition comprising the effective amount of the compound to the subject.
30. The method of any one of claims 23-29, wherein the compound is:
*N*¹-(4-amino-2-methoxybenzyl)-*N*²,*N*²-diethylethane-1,2-diamine;
20 3-methoxy-4-(((2-(pyrrolidin-1-yl)ethyl)amino)methyl)aniline;
sodium (4-amino-2-methoxyphenyl)methanesulfonate;
N-butyl-2-(2-(diethylamino)ethyl)isoindolin-5-amine;
N-butyl-2-(2-(pyrrolidin-1-yl)ethyl)isoindolin-5-amine; or
any combination thereof.
- 25 31. A method for ameliorating at least one sign or symptom of a cardiac arrhythmia or heart failure, the method comprising:
administering one or more therapeutically effective doses of a compound according to any one of claims 1-21, or a stereoisomer, tautomer, pharmaceutically acceptable salt, hydrate, or
- 30 solvate thereof, over an effective period of time to a subject identified as having, or being at risk of having, a cardiac arrhythmia or heart failure, thereby ameliorating at least one sign or symptom of the cardiac arrhythmia or heart failure.

32. The method of claim 31, wherein administering the therapeutically effective dose of the compound, or stereoisomer, tautomer, pharmaceutically acceptable salt, hydrate, or solvate thereof, comprises administering an amount of a pharmaceutical composition comprising the therapeutically effective dose of the compound, or stereoisomer, tautomer, pharmaceutically acceptable salt,
5 hydrate, or solvate thereof, to the subject.
33. The method of claim 31 or claim 32, wherein administering is performed by an oral, parenteral, transmucosal, or transdermal route.
- 10 34. The method of any one of claims 31-33, wherein administering is performed by an oral, intramuscular, subcutaneous, intravenous, or intra-arterial route.
35. The method of any one of claims 31-34, wherein the compound is:
*N*¹-(4-amino-2-methoxybenzyl)-*N*²,*N*²-diethylethane-1,2-diamine;
15 3-methoxy-4-(((2-(pyrrolidin-1-yl)ethyl)amino)methyl)aniline;
sodium (4-amino-2-methoxyphenyl)methanesulfonate;
N-butyl-2-(2-(diethylamino)ethyl)isoindolin-5-amine;
N-butyl-2-(2-(pyrrolidin-1-yl)ethyl)isoindolin-5-amine; or
any combination thereof.