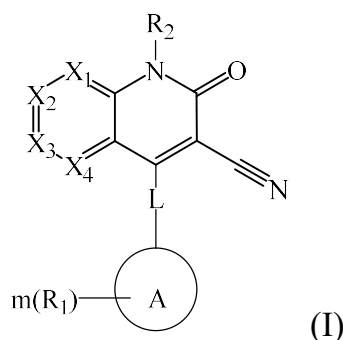


Claims

1. Use of a phosphodiesterase 9 (PDE9) inhibitor compound represented by general formula (I), ~~and~~ pharmaceutically acceptable salts, tautomers, isomers, and deuterated compounds thereof in the manufacture of a medicament for treating heart failure diseases in mammals,



wherein X₁ and X₄ are each CH; X₂ is N, and X₃ is CR₃~~X₁, X₂, X₃ and X₄ are each independently selected from CR₃ or N, and N heteroatom may be optionally~~

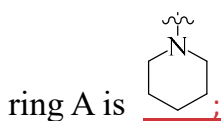
~~oxidized to~~ ;

R₃ at each occurrence is independently selected from hydrogen, deuterium, hydroxyl, amino, carboxyl, cyano, nitro, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, ~~C₁₋₆ alkylamino, (C₁₋₆-alkyl)₂-amino, halo-C₁₋₆-alkyl, halo-C₁₋₆-alkoxy, C₂₋₈-alkenyl, C₂₋₈-alkynyl, C₁₋₆-alkylsulfonyl, C₁₋₆-alkylthio, C₃₋₆-cycloalkyl, 4-6 membered heterocycyl, C₁₋₆ alkylcarbonyl, aminocarbonyl, C₁₋₆-alkylaminocarbonyl, (C₁₋₆-alkyl)₂-aminocarbonyl, 4-6 membered heterocyclylcarbonyl and 5-6 membered heteroaryl-oxy,~~ wherein the C₁₋₆ alkyl, ~~C₁₋₆-alkoxy, C₁₋₆-alkylamino, (C₁₋₆-alkyl)₂-amino, halo-C₁₋₆-alkoxy, C₂₋₈-alkenyl, C₂₋₈-alkynyl, C₁₋₆-alkylsulfonyl, C₁₋₆-alkylthio, C₃₋₆-cycloalkyl, 4-6 membered heterocycyl, C₁₋₆-alkylcarbonyl, aminocarbonyl, C₁₋₆-alkylaminocarbonyl, (C₁₋₆-alkyl)₂-aminocarbonyl, 4-6 membered heterocyclylcarbonyl and 5-6 membered heteroaryl-oxy~~ are is not substituted or optionally substituted with one or more ~~groups independently selected from~~ hydroxyl, ~~amino, carboxyl, cyano, nitro, halogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, C₁₋₆-alkoxy-C₁₋₆-alkoxy, C₁₋₆-alkylamino, (C₁₋₆-alkyl)₂-amino, C₁₋₆-alkylcarbonylamino,~~

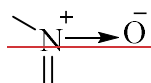
~~C₁₋₆-alkylsulfonylamino, C₁₋₆-alkylcarbonyloxy, C₃₋₆-cycloalkyl, C₂₋₈-alkynyl, halo C₁₋₆-alkyl, C₂₋₈-alkenyl, halo C₁₋₆-alkoxy, 4-6 membered heterocyclyl unsubstituted or optionally substituted with a substituent and heteroaryl unsubstituted or optionally substituted with a substituent;~~

~~the substituents of the above mentioned 4-6 membered heterocyclyl optionally substituted with a substituent and heteroaryl optionally substituted with a substituent are selected from hydroxyl, amino, carboxyl, cyano, nitro, halogen, C₁₋₆ alkyl and C₁₋₆-alkoxy;~~

L is a bond ~~and NH-(CH₂)_t~~, and t is 0, 1, 2 or 3;



~~3-12 membered heterocyclyl, aryl, 5-10 membered heteroaryl, 3-12 membered cycloalkyl, and 3-12 membered cycloalkenyl, wherein the heteroatom of the 3-12 membered heterocyclyl is selected from one of O, S, and N or any combination thereof, the S atom may be optionally oxidized to S(O) or S(O)₂, the C atom may be optionally oxidized to C(O), and the N heteroatom may be optionally oxidized to~~



~~, and the heteroatom of the 5-10 membered heteroaryl is selected from one of O, S and N or any combination thereof;~~

each R₁ is independently selected from hydrogen, deuterium, ~~hydroxyl, amino, carboxyl, cyano, nitro, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆-alkylamino, (C₁₋₆ alkyl)₂-amino, halo C₁₋₆-alkyl, halo C₁₋₆-alkoxy, C₂₋₈-alkenyl, C₂₋₈-alkynyl, C₁₋₆ alkylsulfonyl, C₁₋₆-alkylthio, 3-12 membered cycloalkyl, 3-12 membered cycloalkenyl, 3-12 membered heterocyclyl, aryl and 5-10 membered heteroaryl, wherein the C₁₋₆-alkyl, C₁₋₆-alkoxy, C₁₋₆-alkylamino, (C₁₋₆-alkyl)₂-amino, halo C₁₋₆ alkyl, halo C₁₋₆-alkoxy, C₂₋₈-alkenyl, C₂₋₈-alkynyl, C₁₋₆-alkylsulfonyl, C₁₋₆-alkylthio, 3-12 membered cycloalkyl, 3-12 membered cycloalkenyl, 3-12 membered heterocyclyl, aryl and 5-10 membered heteroaryl are not substituted or optionally substituted with groups selected from hydroxyl, amino, carboxyl, cyano, nitro, halogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, C₁₋₆-alkoxy C₁₋₆-alkoxy, C₁₋₆-alkylamino, (C₁₋₆ alkyl)₂-amino, C₁₋₆-alkylcarbonylamino and C₁₋₆-alkylsulfonylamino;~~

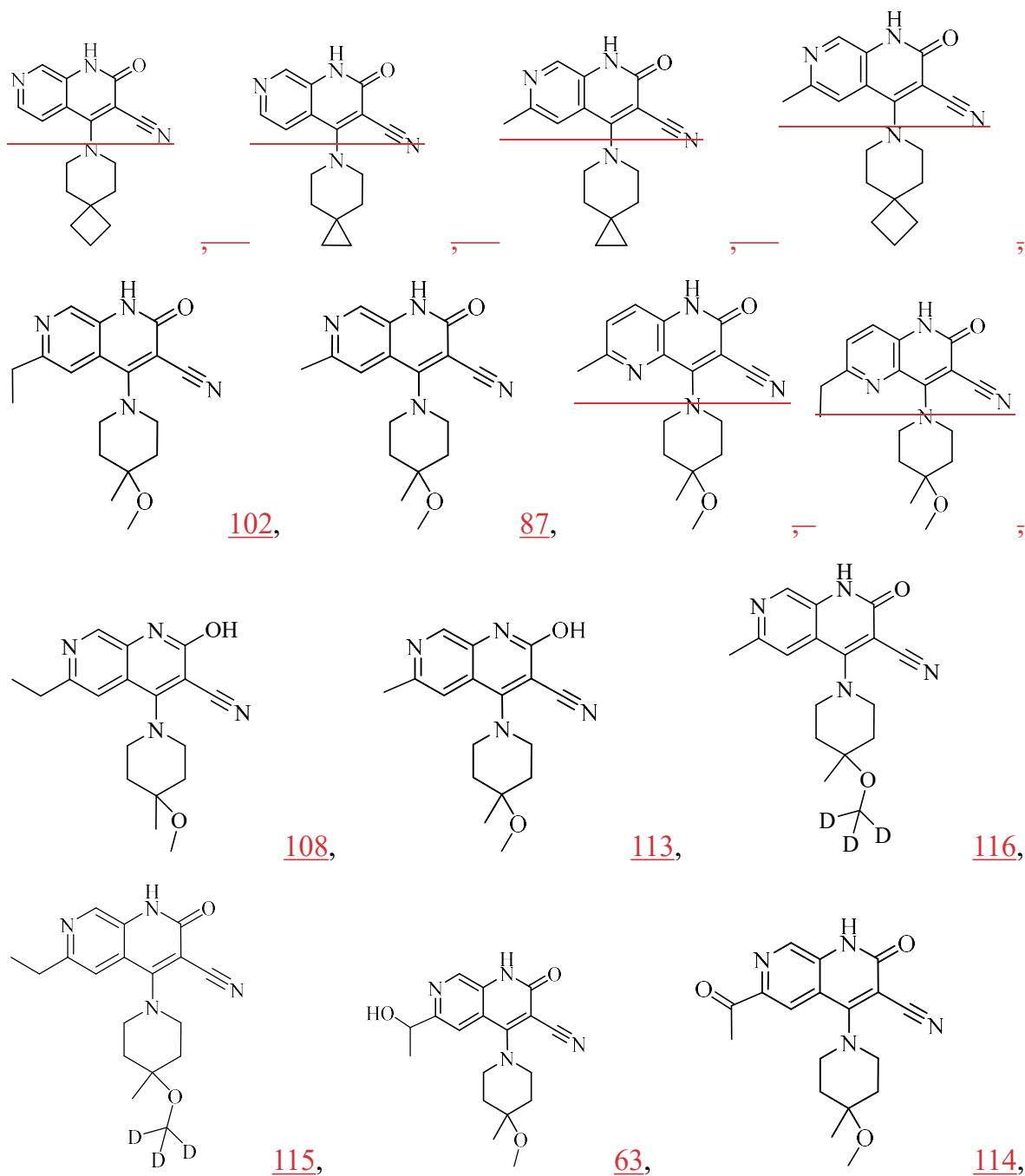
m is ~~0~~, 1, 2 or 3; _

and

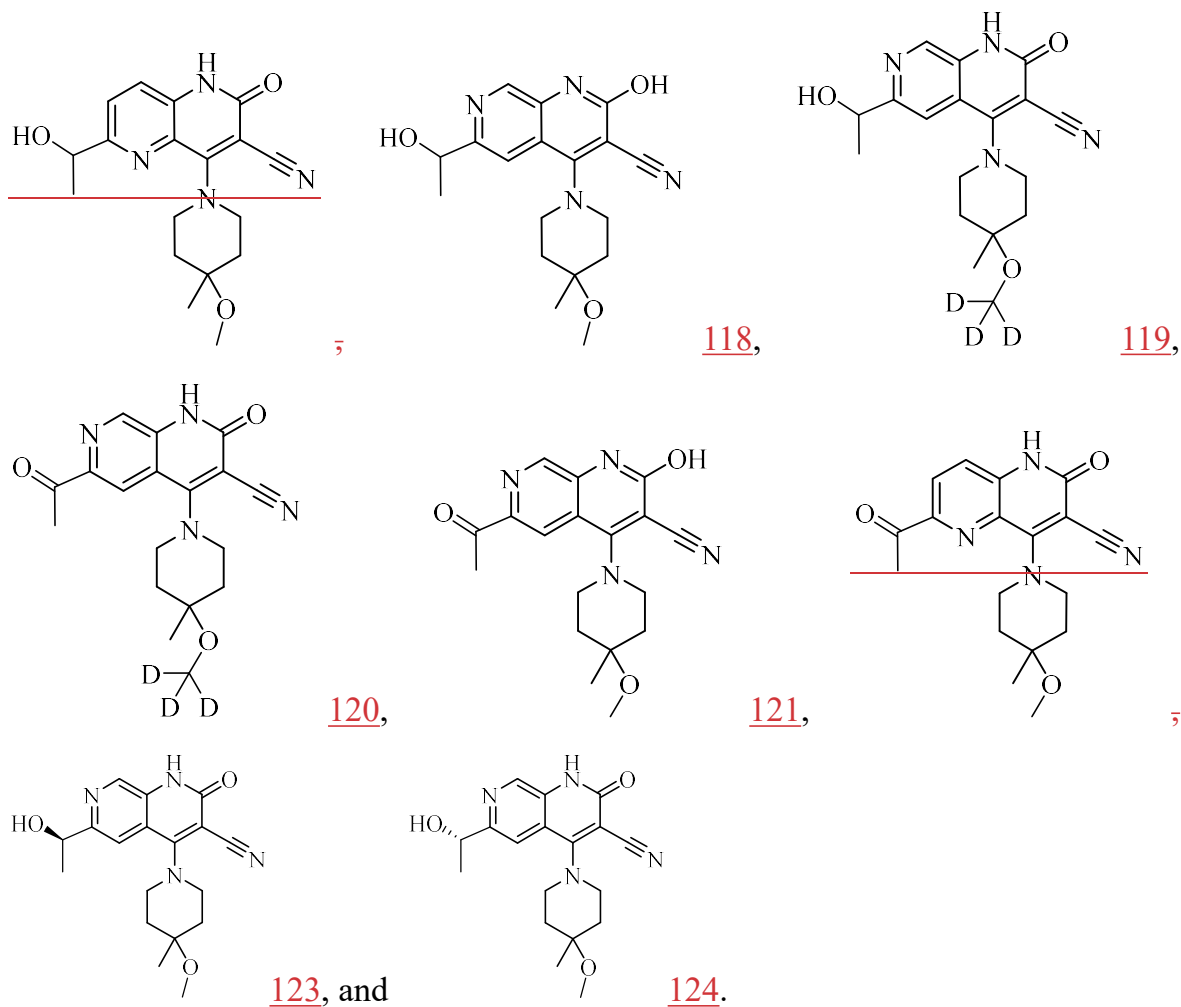
R₂ is ~~selected from~~ hydrogen, C₁₋₆-alkyl, C₂₋₈-alkenyl, C₂₋₈-alkynyl, and halo C₁₋₆-alkyl.

5

2. Use of claim 1, wherein the compound represented by the general formula (I) and pharmaceutically acceptable salts, ~~tautomers~~isomers and deuterated compounds thereof are selected from the following structures:



10



5 3. Use of claim 1 or 2, wherein the medicament for treating heart failure diseases further include a second or more therapeutic agents.

10 4. Use of claim 1 or 2, wherein the medicament for treating heart failure diseases can be prepared into any pharmaceutically acceptable pharmaceutical preparation with a pharmaceutical carrier.

15 5. Use of claim 1 or 2, wherein the medicament is formulated into the format to be administered ~~to patients or subjects in need of treatment~~ through oral, parenteral, transdermal, rectal, nasal, pulmonary, implantation, and topical administration.

6. Use of claim 1 or 2, wherein the heart failure diseases are ~~various heart failures under different classification basis, including selected from~~ left heart failure, right heart failure, and whole heart failure; acute heart failure, chronic heart failure, and decompensated heart failure; systolic and diastolic heart failure; pre-heart failure, pre-clinical heart failure, clinical heart failure and refractory end-stage heart failure; grade I, grade II, grade III, and grade IV heart failure by the New York Heart Association (NYHA) according to heart function; and heart failure with reduced left ventricular ejection fraction, heart failure with median left ventricular ejection fraction, and heart failure with preserved left ventricular ejection fraction.

7. Use of claim 1 or 2, wherein the heart failure diseases are selected from heart failure caused by ischemic heart disease, heart failure caused by toxic damage, immune-mediated heart failure and heart failure caused by inflammatory damage, heart failure caused by infiltrative lesion, heart failure caused by metabolic disorder, heart failure caused by genetic abnormality, heart failure caused by abnormal load, and heart failure caused by arrhythmia.

8. Use of claim 1 or 2, wherein the heart failure diseases are selected from systolic heart failure and diastolic heart failure.

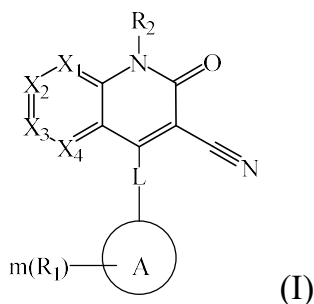
9. Use of claim 1, wherein the mammals are humans and animals.

10. Use of claim 1 or 2, wherein the ~~medicament is for compound represented by the general formula (I) and pharmaceutically acceptable salts, isomers and deuterated compounds thereof exert effects in~~ treating heart failure by means of inhibiting the activity of PDE9, and increasing the level of cyclic guanosine monophosphate.

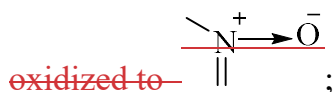
11. Use of claim 1 or 2, wherein the ~~medicament is for compound represented by the general formula (I) and pharmaceutically acceptable salts, isomers and deuterated compounds thereof exert effects in~~ treating heart failure by means of

improving the heart function of patients or subjects with heart failure and reversing the myocardial remodeling of patients or subjects with heart failure.

12. A kit, comprising (a) a phosphodiesterase 9 (PDE9) inhibitor compound represented by the general formula (I) and pharmaceutically acceptable salts, isomerstautomers, and deuterated compounds thereof and (b) an instruction for use of the compound or the pharmaceutically acceptable salts or isomerstautomers or deuterated compounds thereof in the treatment of heart failure diseases in mammals:



wherein X₁ and X₄ are each CH; X₂ is N, and X₃ is CR₃X₁; X₂, X₃ and X₄ are each independently selected from CR₃ or N, and N heteroatom may be optionally

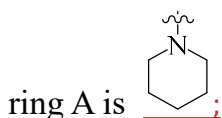


R₃ at each occurrence is independently selected from hydrogen, deuterium, hydroxyl, amino, carboxyl, cyano, nitro, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ alkylamino, (C₁₋₆-alkyl)₂ amino, halo C₁₋₆ alkyl, halo C₁₋₆ alkoxy, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₁₋₆ alkylsulfonyl, C₁₋₆ alkylthio, C₃₋₆ cycloalkyl, 4-6 membered heterocyclyl, C₁₋₆ alkylcarbonyl, aminocarbonyl, C₁₋₆ alkylaminocarbonyl, (C₁₋₆ alkyl)₂ aminocarbonyl, 4-6 membered heterocyclylcarbonyl and 5-6 membered heteroaryl-oxy, wherein the C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ alkylamino, (C₁₋₆ alkyl)₂ amino, halo C₁₋₆ alkoxy, C₂₋₈ alkenyl, C₂₋₈ alkynyl, C₁₋₆ alkylsulfonyl, C₁₋₆ alkylthio, C₃₋₆ cycloalkyl, 4-6 membered heterocyclyl, C₁₋₆ alkylcarbonyl, aminocarbonyl, C₁₋₆ alkylaminocarbonyl, (C₁₋₆ alkyl)₂ aminocarbonyl, 4-6 membered heterocyclylcarbonyl and 5-6 membered heteroaryl-oxy are is not substituted or optionally substituted with one or more groups independently selected from hydroxyl, amino, carboxyl, cyano, nitro, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆ alkoxy

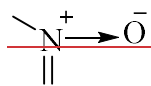
~~C₁₋₆-alkoxy, C₁₋₆-alkylamino, (C₁₋₆-alkyl)₂-amino, C₁₋₆-alkylcarbonylamino, C₁₋₆-alkylsulfonylamino, C₁₋₆-alkylcarbonyloxy, C₃₋₆-cycloalkyl, C₂₋₈-alkynyl, halo-C₁₋₆-alkyl, C₂₋₈-alkenyl, halo-C₁₋₆-alkoxy, 4-6 membered heterocyclyl unsubstituted or optionally substituted with a substituent and heteroaryl unsubstituted or optionally substituted with a substituent;~~

~~the substituents of the above mentioned 4-6 membered heterocyclyl optionally substituted with a substituent and heteroaryl optionally substituted with a substituent are selected from hydroxyl, amino, carboxyl, cyano, nitro, halogen, C₁₋₆-alkyl and C₁₋₆-alkoxy;~~

L is a bond and ~~NH-(CH₂)_t~~, and t is 0, 1, 2 or 3;



~~3-12 membered heterocyclyl, aryl, 5-10 membered heteroaryl, 3-12 membered cycloalkyl, and 3-12 membered cycloalkenyl, wherein the heteroatom of the 3-12 membered heterocyclyl is selected from one of O, S, and N or any combination thereof, the S atom may be optionally oxidized to S(O) or S(O)₂, the C atom may be optionally oxidized to C(O), and the N heteroatom may be optionally oxidized to~~



~~, and the heteroatom of the 5-10 membered heteroaryl is selected from one of O, S and N or any combination thereof;~~

each R₁ is independently selected from hydrogen, deuterium, ~~hydroxyl, amino, carboxyl, cyano, nitro, halogen, C₁₋₆ alkyl, C₁₋₆ alkoxy, C₁₋₆-alkylamino, (C₁₋₆-alkyl)₂-amino, halo-C₁₋₆-alkyl, halo-C₁₋₆-alkoxy, C₂₋₈-alkenyl, C₂₋₈-alkynyl, C₁₋₆-alkylsulfonyl, C₁₋₆-alkylthio, 3-12 membered cycloalkyl, 3-12 membered cycloalkenyl, 3-12 membered heterocyclyl, aryl and 5-10 membered heteroaryl, wherein the C₁₋₆-alkyl, C₁₋₆-alkoxy, C₁₋₆-alkylamino, (C₁₋₆-alkyl)₂-amino, halo-C₁₋₆-alkyl, halo-C₁₋₆-alkoxy, C₂₋₈-alkenyl, C₂₋₈-alkynyl, C₁₋₆-alkylsulfonyl, C₁₋₆-alkylthio, 3-12 membered cycloalkyl, 3-12 membered cycloalkenyl, 3-12 membered heterocyclyl, aryl and 5-10 membered heteroaryl are not substituted or optionally substituted with groups selected from hydroxyl, amino, carboxyl, cyano, nitro,~~

halogen, C₁₋₆-alkyl, C₁₋₆-alkoxy, C₁₋₆-alkoxy-C₁₋₆-alkoxy, C₁₋₆-alkylamino, (C₁₋₆-alkyl)₂-amino, C₁₋₆-alkylcarbonylamino and C₁₋₆-alkylsulfonylamino;

m is 0, 1, 2 or 3;

and R₂ is selected from hydrogen, C₁₋₆-alkyl, C₂₋₈-alkenyl, C₂₋₈-alkynyl, and halo-C₁₋₆-alkyl.

5