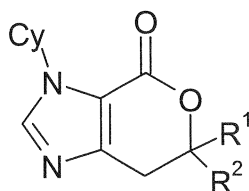


evidence that inhibitors of aldosterone synthesis will be useful for the treatment of diabetic kidney disease including diabetic nephropathy; non-diabetic kidney disease including glomerulosclerosis, glomerulonephritis, IGA nephropathy, nephritic syndrome and focal segmental glomerulosclerosis (FSGS); cardiovascular diseases including hypertension, pulmonary arterial hypertension, Conn's syndrome, systolic heart failure, diastolic heart failure, left ventricular dysfunction, left ventricular stiffness and fibrosis, left ventricular filing abnormalities, arterial stiffness, atherosclerosis and cardiovascular morbidity associated with primary or secondary hyperaldosteronism; adrenal hyperplasia and primary and secondary hyperaldosteronism.

BRIEF SUMMARY

The present disclosure provides novel compounds that inhibit aldosterone synthase (CYP11B2) and thus are useful for treating a variety of diseases and disorders that can be alleviated by lowering levels of aldosterone including renal disease, diabetic nephropathy, cardiovascular diseases and fibrotic disorders. The disclosure provides compounds that are selective for inhibition of aldosterone synthase compared to cortisol synthase (CYP11B1), CYP17A1 and CYP19A1. This disclosure also relates to pharmaceutical compositions comprising these compounds, methods of using these compounds in the treatment of various diseases and disorders, processes for preparing these compounds and intermediates useful in these processes.

In one aspect, there is provided a compound of the formula I



I

wherein:

Cy is a monocyclic or bicyclic ring system selected from C₃₋₁₀cycloalkyl, heterocyclyl, aryl and heteroaryl,

wherein each of the said C₃₋₁₀cycloalkyl, heterocyclyl, aryl and heteroaryl groups is optionally and independently substituted with one, two, or three substituent groups selected from halogen, -C₁₋₃-alkyl, -OC₁₋₃-alkyl, -CF₃, cyano, oxo, -N(C₁₋₃-alkyl)₂, -NH(C₁₋₃-alkyl), -NHCOC₁₋₃-alkyl, -C(O)C₁₋₃-alkyl, -C(O)OC₁₋₃alkyl, hydroxyC₁₋₃alkyl, or heteroaryl; and

R¹ and R² are independently selected from H, C₁₋₃alkyl, hydroxyC₁₋₃alkyl, -CH₂NHC(O)OC₁₋₄alkyl, -CH₂OC(O)C₁₋₄alkyl, -C(O)OC₁₋₄-alkyl, -C(O)H, -COOH, -C(O)NHC₁₋₄-alkyl and C(O)N(C₁₋₄-alkyl)₂; or

R¹ and R² taken together form a C₃₋₆cycloalkyl or C₃₋₆-heterocyclyl;

or a salt thereof.

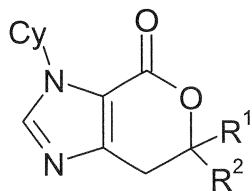
In another aspect, there is provided a pharmaceutical composition comprising a compound as defined herein and a pharmaceutically acceptable excipient or carrier.

In another aspect, there is provided a compound as defined herein for use as a medicament.

In another aspect, there is provided use of a compound as defined herein in the manufacture of a medicament for the treatment of a disease or disorder that can be alleviated by inhibition of aldosterone synthase selected from diabetic nephropathy, glomerulosclerosis, glomerulonephritis, IGA nephropathy, nephritic syndrome focal segmental glomerulosclerosis (FSGS), hypertension, pulmonary arterial hypertension, Conn's syndrome, systolic heart failure, diastolic heart failure, left ventricular dysfunction, left ventricular stiffness and fibrosis, left ventricular filing abnormalities, arterial stiffness, atherosclerosis and cardiovascular morbidity associated with primary or secondary hyperaldosteronism, adrenal hyperplasia and primary and secondary hyperaldosteronism.

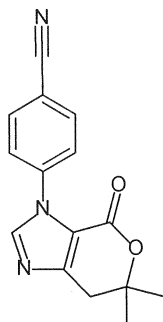
DETAILED DESCRIPTION OF THE INVENTION

In an embodiment of the invention, there are provided compounds of the formula I



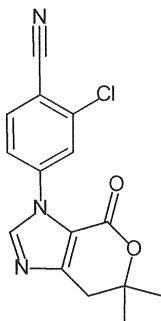
8. The compound according to claim 7 selected from the group consisting of compound numbers 1-11, 13, 15, 18, 19, 22, 23, 26, 28, 29A, 29B, 30-33, 35, 39, 41, 42, 45 and 46.

9. The compound according to claim 1, wherein said compound is



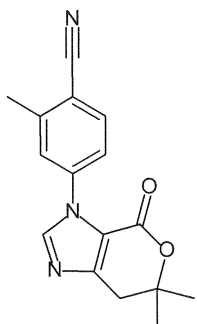
or a pharmaceutically acceptable salt thereof.

10. The compound according to claim 1, wherein said compound is



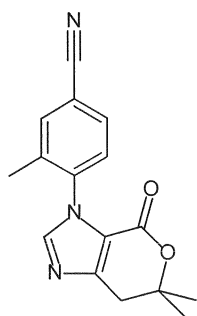
or a pharmaceutically acceptable salt thereof.

11. The compound according to claim 1, wherein said compound is



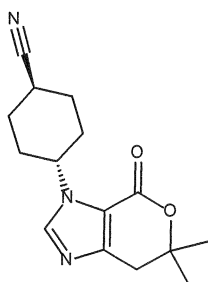
or a pharmaceutically acceptable salt thereof.

12. The compound according to claim 1, wherein said compound is



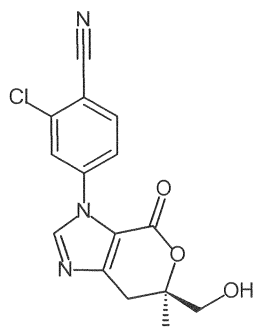
or a pharmaceutically acceptable salt thereof.

13. The compound according to claim 1, wherein said compound is



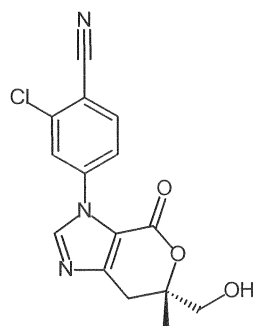
or a pharmaceutically acceptable salt thereof.

14. The compound according to claim 1, wherein said compound is



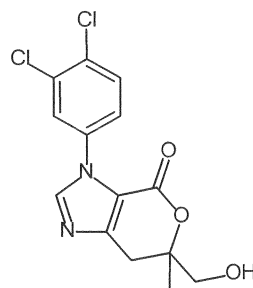
or a pharmaceutically acceptable salt thereof.

15. The compound according to claim 1, wherein said compound is



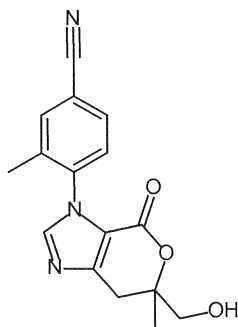
or a pharmaceutically acceptable salt thereof.

16. The compound according to claim 1, wherein said compound is



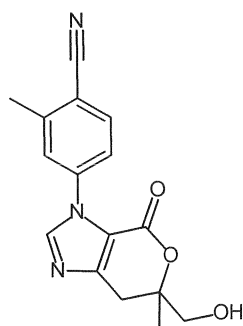
or a pharmaceutically acceptable salt thereof.

17. The compound according to claim 1, wherein said compound is



or a pharmaceutically acceptable salt thereof.

18. The compound according to claim 1, wherein said compound is



or a pharmaceutically acceptable salt thereof.

19. A pharmaceutical composition comprising a compound according to any of claims 1 to 18 and a pharmaceutically acceptable excipient or carrier.

20. A compound according to any of claims 1 to 18 for use as a medicament.

21. Use of a compound according to any of claims 1 to 18 in the manufacture of a medicament for the treatment of a disease or disorder that can be alleviated by inhibition of aldosterone synthase selected from diabetic nephropathy, glomerulosclerosis, glomerulonephritis, IGA nephropathy, nephritic syndrome focal segmental glomerulosclerosis (FSGS), hypertension, pulmonary arterial hypertension, Conn's syndrome, systolic heart failure, diastolic heart failure, left ventricular dysfunction, left ventricular stiffness and fibrosis, left ventricular filing abnormalities, arterial stiffness, atherosclerosis and cardiovascular morbidity associated with primary or secondary hyperaldosteronism, adrenal hyperplasia and primary and secondary hyperaldosteronism.

22. The use according to claim 21, wherein the disease or disorder is selected from diabetic nephropathy, glomerulosclerosis, glomerulonephritis, IGA nephropathy, nephritic syndrome and focal segmental glomerulosclerosis (FSGS).

23. The use according to claim 21, wherein the disease is diabetic nephropathy.