Heteroaryl ketone fused azadecalin compounds are disclosed in U.S. Patent 8,859,774, the entire contents of which patent is hereby incorporated by reference in its entirety.

[0008a] In one aspect, there is provided the use of an effective amount of a heteroaryl ketone fused azadecalin compound in the manufacture of a medicament for treating a patient suffering from Cushing's syndrome or Cushing's Disease (collectively "CS") without significantly prolonging said patient's QT interval, where the QT interval is the duration of the time interval between the beginning of the QRS complex of the electrocardiogram (ECG) and the end of the T wave of the ECG, wherein a patient's QT interval is significantly prolonged if the QT interval is increased by more than 10 milliseconds (ms) from the patient's baseline QT interval,

Wherein said treatment does not significantly prolong said patient's QT interval,

Whereby the patient's CS is to be treated without significantly prolonging said patient's QT interval.

[0008b] In another aspect, there is provided the use of an effective amount of a heteroaryl ketone fused azadecalin compound in the manufacture of a medicament for treating a patient suffering from Cushing's syndrome or Cushing's Disease (collectively "CS") and suffering from prolonged QT interval, where the QT interval is the duration of the time interval between the beginning of the QRS complex of the electrocardiogram (ECG) and the end of the T wave of the ECG, and wherein a prolonged QT interval is a QT interval greater than about 450 ms in men or greater than about 460 ms in women,

the use comprising:

the CS patient to be identified as suffering from prolonged QT interval,

wherein said effective amount is between about 400 milligrams (mg) and about 800 mg of said heteroaryl ketone fused azadecalin compound,

Whereby the patient's CS and prolonged QT interval are to be treated.

[0008c] In another aspect, there is provided the use of an effective amount of a heteroaryl ketone fused azadecalin compound in the manufacture of a medicament for decreasing the QT interval in a patient with a prolonged QT interval, where the QT interval is the duration of the time interval between the beginning of the QRS complex of the electrocardiogram (ECG) and the end of the T wave of the ECG, and wherein a prolonged QT interval is a QT interval greater than about 450 ms in men or greater than about 460 ms in women,

Whereby the patient's QT interval is decreased.

[0008d] In another aspect, there is provided the use of an effective amount of a heteroaryl ketone fused azadecalin compound in the manufacture of a medicament for reducing the

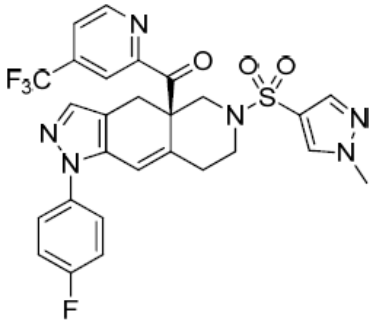
effect on QT interval in a patient receiving a drug known to prolong the QT interval of the electrocardiogram (ECG) in some patients, where the QT interval is the duration of the time interval between the beginning of the QRS complex of the ECG and the end of the T wave of the ECG, and wherein a prolonged QT interval is a QT interval greater than about 450 ms in men or greater than about 460 ms in women,

wherein the effective amount of a heteroaryl ketone fused azadecalin compound to be administered to said patient receiving said drug is known to prolong the QT interval of the electrocardiogram (ECG) in some patients,

Whereby the effect of said drug on the QT interval of the patient is decreased.

[0008e] In another aspect, there is provided the use of a heteroaryl ketone fused azadecalin compound in the manufacture of a medicament for the treatment of Cushing's syndrome or Cushing's Disease (collectively "CS") which does not lead to significant QT interval prolongation, where the QT interval is the duration of the time interval between the beginning of the QRS complex of the electrocardiogram (ECG) and the end of the T wave of the ECG, and wherein a prolonged QT interval is a QT interval greater than about 450 ms in men or greater than about 460 ms in women.

[0008f] In another aspect, the is provided the use of a pharmaceutical composition in the manufacture of a medicament for treating a patient suffering from Cushing's syndrome or Cushing's Disease (collectively "CS") which does not lead to significant QT interval prolongation, where the QT interval is the duration of the time interval between the beginning of the QRS complex of the electrocardiogram (ECG) and the end of the T wave of the ECG, and wherein a prolonged QT interval is a QT interval greater than about 450 ms in men or greater than about 460 ms in women, comprising a pharmaceutically acceptable excipient and the heteroaryl ketone fused azadecalin compound relacorilant, which is (R)-(1-(4-fluorophenyl)-6-((1-methyl-1H-pyrazol-4-yl)sulfonyl)-4,4a,5,6,7,8-hexahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridine-2-yl)methanone, which has the structure:



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[0008g] In another aspect, there is provided the use of a heteroaryl ketone fused azadecalin compound in the manufacture of a medicament for decreasing the QT interval in a patient with a prolonged QT interval, where the QT interval is the duration of the time interval between the beginning of the QRS complex of the electrocardiogram (ECG) and the end of the T wave of the ECG, and wherein a prolonged QT interval is a QT interval greater than about 450 ms in men or greater than about 460 ms in women.

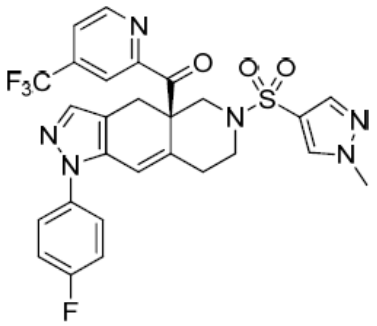
[0008h] In another aspect, there is provided the use of a heteroaryl ketone fused azadecalin compound in the manufacture of a medicament for reducing the effect on QT interval in a patient receiving a drug known to prolong the QT interval of the electrocardiogram (ECG) in some patients, where the QT interval is the duration of the time interval between the beginning of the QRS complex of the ECG and the end of the T wave of the ECG, and wherein a prolonged QT interval is a QT interval greater than about 450 ms in men or greater than about 460 ms in women.

[0009] In examples, Applicants disclose methods of treating a patient suffering from CS without significantly prolonging the QT interval or the QTc interval, comprising:

Administering an effective amount of a heteroaryl ketone fused azadecalin compound,

Wherein said treatment does not significantly prolong QT or QTc as measured by electrocardiogram (ECG), where QT is the duration of the time interval between the beginning of the QRS complex of the ECG and the end of the T wave of the ECG, and wherein QTc is the QT interval corrected for heart rate,

Whereby the Cushing's syndrome or Cushing's Disease is treated without significantly prolonging the QT interval. In examples, the heteroaryl ketone fused azadecalin compound is a GRM, and in further examples, the heteroaryl ketone fused azadecalin compound is a SGRM, such as, e.g., relacorilant. Relacorilant is ((R)-(1-(4-fluorophenyl)-6-((1-methyl-1H-pyrazol-4-yl)sulfonyl)-4,4a,5,6,7,8-hexahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridine-2-yl)methanone), which has the structure:



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[0010] In examples, the GRM (e.g., a SGRM, such as relacorilant) is orally administered. In examples, the GRM or SGRM may be administered by injection, infusion, transdermal application, or by other means or routes of administration. In examples, the GRM or SGRM (e.g., relacorilant) may be administered with food, or with water, or with both food and water. In other examples, the GRM or SGRM (e.g., relacorilant) may be administered in the absence of food.

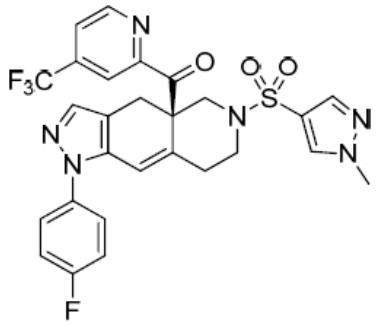
[0011] There is an unmet need for safe CS medications that ***do not cause*** QT prolongation and possibly fatal arrhythmias. Based on the present results from clinical studies in healthy volunteers and patients with CS, relacorilant is not associated with QT prolongation. Heteroaryl ketone fused azadecalin compounds such as relacorilant are believed to be able to

CLAIMS:

1. Use of an effective amount of a heteroaryl ketone fused azadecalin compound in the manufacture of a medicament for treating a patient suffering from Cushing's syndrome or Cushing's Disease (collectively "CS") without significantly prolonging said patient's QT interval, where the QT interval is the duration of the time interval between the beginning of the QRS complex of the electrocardiogram (ECG) and the end of the T wave of the ECG, wherein a patient's QT interval is significantly prolonged if the QT interval is increased by more than 10 milliseconds (ms) from the patient's baseline QT interval,
Wherein said treatment does not significantly prolong said patient's QT interval,

Whereby the patient's CS is to be treated without significantly prolonging said patient's QT interval.

2. The use of claim 1, wherein said heteroaryl ketone fused azadecalin compound is relacorilant, which is (R)-(1-(4-fluorophenyl)-6-((1-methyl-1H-pyrazol-4-yl)sulfonyl)-4,4a,5,6,7,8-hexahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridine-2-yl)methanone, which has the structure:



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3. The use of claim 1, wherein the effective amount of the heteroaryl ketone fused azadecalin compound is an amount selected from the group consisting of between about 50 milligrams per day (mg/day) and about 800 mg/day, between about 50 mg/day and about 500 mg/day, and between about 400 mg/day and about 800 mg/day.

4. The use of claim 1, wherein said administration of an effective amount of said heteroaryl ketone fused azadecalin compound does not significantly increase the patient's risk of cardiac arrhythmia.

5. The use of claim 1, wherein said administration of an effective amount of said heteroaryl ketone fused azadecalin compound does not significantly increase the patient's risk of heart attack.

6. The use of claim 1, wherein said patient has been administered a medication that prolongs QT, and wherein said administration of an effective amount of said heteroaryl ketone fused azadecalin compound does not significantly increase the patient's risk of stroke.

7. The use of claim 1, wherein said administration of an effective amount of said heteroaryl ketone fused azadecalin compound does not significantly increase the patient's risk of sudden death.

8. The use of claim 1, wherein the heteroaryl ketone fused azadecalin compound is to be orally administered.

9. The use of claim 1, wherein said heteroaryl ketone fused azadecalin compound is to be administered to a fasted patient, where a fasted patient is one that has not eaten a meal for at least 4 hours prior to administration of the heteroaryl ketone fused azadecalin compound.

10. The use of claim 1, wherein between 50 mg/day and 400 mg/day of the heteroaryl ketone fused azadecalin compound is to be administered with food to a patient, or is to be administered to a fed patient, where a fed patient is one that has eaten a meal less than one hour prior to administration of the heteroaryl ketone fused azadecalin compound.

11. The use of claim 1, wherein said patient is male.

12. Use of an effective amount of a heteroaryl ketone fused azadecalin compound in the manufacture of a medicament for treating a patient suffering from Cushing's syndrome or Cushing's Disease (collectively "CS") and suffering from prolonged QT interval, where the QT interval is the duration of the time interval between the beginning of the QRS complex of the electrocardiogram (ECG) and the end of the T wave of the ECG, and wherein a prolonged QT interval is a QT interval greater than about 450 ms in men or greater than about 460 ms in women,

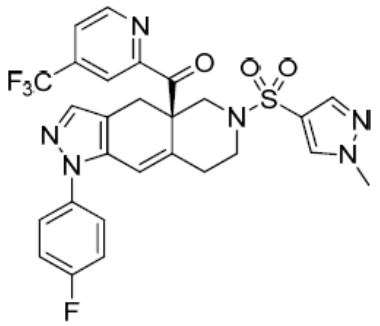
the use comprising:

the CS patient to be identified as suffering from prolonged QT interval,

wherein said effective amount is between about 400 milligrams (mg) and about 800 mg of said heteroaryl ketone fused azadecalin compound,

Whereby the patient's CS and prolonged QT interval are to be treated.

13. The use of claim 12, wherein said heteroaryl ketone fused azadecalin compound is relacorilant, which is (R)-(1-(4-fluorophenyl)-6-((1-methyl-1H-pyrazol-4-yl)sulfonyl)-4,4a,5,6,7,8-hexahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridine-2-yl)methanone, which has the structure:



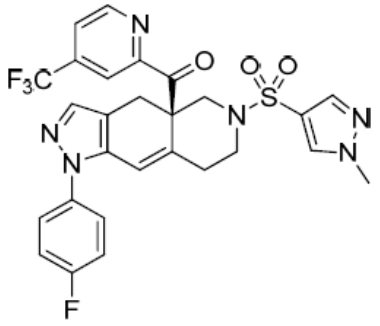
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14. The use of claim 12, wherein said effective amount of a heteroaryl ketone fused azadecalin compound is about 800 mg.

15. Use of an effective amount of a heteroaryl ketone fused azadecalin compound in the manufacture of a medicament for decreasing the QT interval in a patient with a prolonged QT interval, where the QT interval is the duration of the time interval between the beginning of the QRS complex of the electrocardiogram (ECG) and the end of the T wave of the ECG, and wherein a prolonged QT interval is a QT interval greater than about 450 ms in men or greater than about 460 ms in women,

Whereby the patient's QT interval is decreased.

16. The use of claim 15, wherein said heteroaryl ketone fused azadecalin compound is relacorilant, which is (R)-(1-(4-fluorophenyl)-6-((1-methyl-1H-pyrazol-4-yl)sulfonyl)-4,4a,5,6,7,8-hexahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridine-2-yl)methanone, which has the structure:



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17. The use of claim 15, wherein said effective amount of a heteroaryl ketone fused azadecalin compound is between about 400 milligrams (mg) and about 800 mg of said heteroaryl ketone fused azadecalin compound.

18. The use of claim 15, wherein said effective amount of a heteroaryl ketone fused azadecalin compound is about 800 mg.

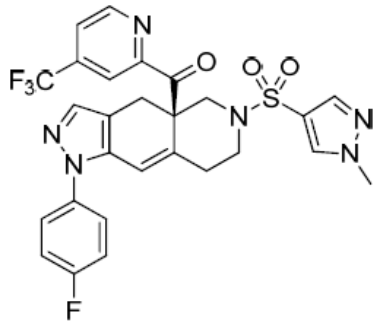
19. Use of an effective amount of a heteroaryl ketone fused azadecalin compound in the manufacture of a medicament for reducing the effect on QT interval in a patient receiving a drug known to prolong the QT interval of the electrocardiogram (ECG) in some

patients, where the QT interval is the duration of the time interval between the beginning of the QRS complex of the ECG and the end of the T wave of the ECG, and wherein a prolonged QT interval is a QT interval greater than about 450 ms in men or greater than about 460 ms in women,

wherein the effective amount of a heteroaryl ketone fused azadecalin compound to be administered to said patient receiving said drug is known to prolong the QT interval of the electrocardiogram (ECG) in some patients,

Whereby the effect of said drug on the QT interval of the patient is decreased.

20. The use of claim 19, wherein said heteroaryl ketone fused azadecalin compound is relacorilant, which is (R)-(1-(4-fluorophenyl)-6-((1-methyl-1H-pyrazol-4-yl)sulfonyl)-4,4a,5,6,7,8-hexahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridine-2-yl)methanone, which has the structure:



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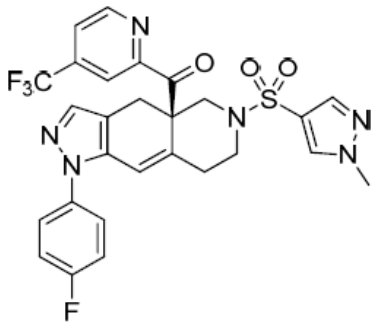
21. The use of claim 19, wherein said effective amount of a heteroaryl ketone fused azadecalin compound is between about 400 milligrams (mg) and about 800 mg of said heteroaryl ketone fused azadecalin compound.

22. The use of claim 19, wherein said effective amount of a heteroaryl ketone fused azadecalin compound is about 800 mg.

23. Use of a heteroaryl ketone fused azadecalin compound in the manufacture of a medicament for the treatment of Cushing's syndrome or Cushing's Disease (collectively "CS") which does not lead to significant QT interval prolongation, where the QT interval is the duration of the time interval between the beginning of the QRS complex of the electrocardiogram (ECG) and the end of the T wave of the ECG, and wherein a prolonged QT interval is a QT interval greater than about 450 ms in men or greater than about 460 ms in women.

24. The use of claim 23, wherein the heteroaryl ketone fused azadecalin compound is relacorilant, which is (R)-(1-(4-fluorophenyl)-6-((1-methyl-1H-pyrazol-4-

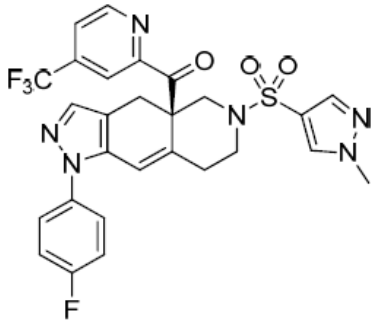
yl)sulfonyl)-4,4a,5,6,7,8-hexahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridine-2-yl)methanone, which has the structure:



, in the manufacture of a medicament for the treatment of Cushing's syndrome or Cushing's Disease (collectively "CS") which does not lead to significant QT interval prolongation, where the QT interval is the duration of the time interval between the beginning of the QRS complex of the electrocardiogram (ECG) and the end of the T wave of the ECG, and wherein a prolonged QT interval is a QT interval greater than about 450 ms in men or greater than about 460 ms in women.

25. The use of claim 24, wherein the CS patient suffers from QT interval prolongation.

26. Use of a pharmaceutical composition in the manufacture of a medicament for treating a patient suffering from Cushing's syndrome or Cushing's Disease (collectively "CS") which does not lead to significant QT interval prolongation, where the QT interval is the duration of the time interval between the beginning of the QRS complex of the electrocardiogram (ECG) and the end of the T wave of the ECG, and wherein a prolonged QT interval is a QT interval greater than about 450 ms in men or greater than about 460 ms in women, comprising a pharmaceutically acceptable excipient and the heteroaryl ketone fused azadecalin compound relacorilant, which is (R)-(1-(4-fluorophenyl)-6-((1-methyl-1H-pyrazol-4-yl)sulfonyl)-4,4a,5,6,7,8-hexahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridine-2-yl)methanone, which has the structure:

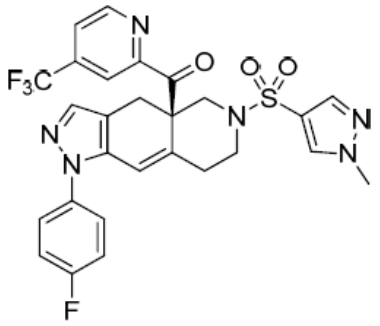


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27. The use of claim 26, wherein the CS patient suffers from QT interval prolongation.

28. Use of a heteroaryl ketone fused azadecalin compound in the manufacture of a medicament for decreasing the QT interval in a patient with a prolonged QT interval, where the QT interval is the duration of the time interval between the beginning of the QRS complex of the electrocardiogram (ECG) and the end of the T wave of the ECG, and wherein a prolonged QT interval is a QT interval greater than about 450 ms in men or greater than about 460 ms in women.

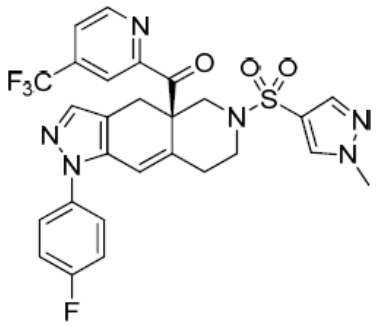
29. The use of claim 28, wherein said heteroaryl ketone fused azadecalin compound is relacorilant, which is (R)-(1-(4-fluorophenyl)-6-((1-methyl-1H-pyrazol-4-yl)sulfonyl)-4,4a,5,6,7,8-hexahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridine-2-yl)methanone, which has the structure:



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30. Use of a heteroaryl ketone fused azadecalin compound in the manufacture of a medicament for reducing the effect on QT interval in a patient receiving a drug known to prolong the QT interval of the electrocardiogram (ECG) in some patients, where the QT interval is the duration of the time interval between the beginning of the QRS complex of the ECG and the end of the T wave of the ECG, and wherein a prolonged QT interval is a QT interval greater than about 450 ms in men or greater than about 460 ms in women.

31. The use of claim 3, wherein said heteroaryl ketone fused azadecalin compound is relacorilant, which is (R)-(1-(4-fluorophenyl)-6-((1-methyl-1H-pyrazol-4-yl)sulfonyl)-4,4a,5,6,7,8-hexahydro-1H-pyrazolo[3,4-g]isoquinolin-4a-yl)(4-(trifluoromethyl)pyridine-2-yl)methanone, which has the structure:



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