SUMMARY

[0004] Applicant discloses herein that administration of miricorilant, a glucocorticoid receptor (GR) modulator (GRM) can reduce antipsychotic-induced weight gain, can ameliorate the effects of antipsychotic-induced weight gain, and can reverse antipsychotic-induced weight gain. The patient may continue to receive antipsychotic medication while receiving miricorilant and still receive the benefits of miricorilant treatment. Antipsychotic medications which may induce weight gain, and the effects of which may be ameliorated, reduced or reversed by miricorilant treatment, include olanzapine, risperidone, clozapine, quetiapine, sertindole, amisulpride, aripiprazole, asenapine, blonanserin, bifeprunox, cariprazine, clotiapine, iloperidone, lurasidone, mosapramine, melperone, paliperidone, perospirone, pimavanserin, remoxipride, sulpiride, ziprasidone, zotepine, perphenazine, thioridazine, chlorpromazine, and other such weight-inducing antipsychotic medications.

[0004a] In one aspect of the present disclosure, there is provided a cyclohexyl pyrimidine glucocorticoid receptor modulator (GRM) in the manufacture of a medicament for treating a subject suffering from antipsychotic-induced weight gain, wherein the subject is to be administered an antipsychotic medication, and wherein an effective amount of the cyclohexyl pyrimidine glucocorticoid receptor modulator (GRM) is to be administered to the subject while said subject is administered the antipsychotic medication, wherein said treatment is effective to:

reduce the body weight of a subject, as compared to baseline body weight of said subject prior to said administration of said GRM, wherein the subject has previously been administered an antipsychotic medication; or

reduce the weight gain of a subject over time while taking an antipsychotic medication and said GRM, as compared to average weight gain of subjects taking that antipsychotic medication in the absence of the GRM; or

reduce blood levels of triglycerides as compared to triglyceride levels in the blood of said subject prior to said administration of said GRM, wherein the subject has previously been administered an antipsychotic medication; or

reduce blood levels of the liver enzymes ALT, AST, or both as compared to baseline liver enzyme levels in the blood of said subject prior to said administration of said GRM, wherein the subject has previously been administered an antipsychotic medication; or

reduce plasma insulin level as compared to the baseline plasma insulin level of said subject prior to said administration of said GRM, wherein the subject has previously been administered an antipsychotic medication; or

reduce insulin resistance as compared to baseline insulin resistance of said subject prior to said administration of said GRM, wherein the subject has previously been administered an antipsychotic medication (as measured by HOMA-IR or HOMA2-IR); or

combinations thereof.

[0004b] In another aspect of the present disclosure, there is provided a use of a cyclohexyl pyrimidine glucocorticoid receptor modulator (GRM) in the manufacture of a medicament for treating a subject at risk of suffering from antipsychotic-induced weight gain, wherein the subject is to be administered an antipsychotic medication, and wherein an effective amount of the cyclohexyl pyrimidine glucocorticoid receptor modulator (GRM) is to be administered to the subject while said subject is administered the antipsychotic medication, wherein the subject has not previously been administered an antipsychotic medication, and wherein said treatment is effective to:

reduce the weight gain of a subject over time while taking said antipsychotic medication and said GRM, as compared to average weight gain of subjects administered that antipsychotic medication in the absence of the GRM; or

reduce the increase in blood levels of triglycerides as compared to the average increase in triglyceride levels in the blood of subjects administered said antipsychotic medication; or

reduce the increase in blood levels of liver enzymes ALT or AST, or both, as compared to the average increase in said liver enzyme levels in the blood of subjects administered said antipsychotic medication; or

reduce the increase in plasma insulin level as compared to the average increase in plasma insulin level in subjects administered said antipsychotic medication; or

reduce the increase in insulin resistance (as measured by HOMA-IR or HOMA2-IR) as compared to the average increase in insulin resistance of in subjects administered said antipsychotic medication; or combinations thereof.

[0005] Benefits of the methods and treatments disclosed herein include reduced weight gain, reduced rate of weight gain, reversal of weight gain, reduction in risk of developing cardiovascular disease, stroke, hypertension, and type II diabetes. Thus, the present methods

can reduce or reverse antipsychotic-induced weight gain, and can provide reduction in risk factors associated with weight gain (e.g., high blood pressure, high cholesterol, other blood lipid abnormalities, sleep disorders, insulin resistance, etc.).

[0006] The methods include administration of miricorilant (also known as CORT118335) to a patient receiving, or who has received, or who is expected to receive, an antipsychotic drug such as olanzapine, risperidone, clozapine, quetiapine, sertindole, amisulpride, aripiprazole, asenapine, blonanserin, bifeprunox, cariprazine, clotiapine, iloperidone, lurasidone, mosapramine, melperone, paliperidone, perospirone, pimavanserin, remoxipride, sulpiride, ziprasidone, zotepine, perphenazine, thioridazine, chlorpromazine, and other such weight-inducing antipsychotic medications. Miricorilant may be orally administered. The methods may reduce the amount of weight that the patient would otherwise have gained. The methods may reduce the rate of weight gain that the patient would otherwise have experienced. The methods may prevent weight gain in a patient administered antipsychotic medication. The methods may reverse weight gain that the patient experienced due to administration of antipsychotic medication.

[0007] Miricorilant is a cyclohexyl pyrimidine compound, that is, miricorilant is a GRM compound comprising a pyrimidine cyclohexyl structure, wherein the structure is as

WE CLAIM:

1. Use of a cyclohexyl pyrimidine glucocorticoid receptor modulator (GRM) in the manufacture of a medicament for ~~A method of~~ treating a subject suffering from antipsychotic-induced weight gain, wherein the subject is to be administered an antipsychotic medication, and wherein ~~the method comprising administering to the subject~~ an effective amount of the~~a~~ cyclohexyl pyrimidine glucocorticoid receptor modulator (GRM) is to be administered to the subject while said subject is administered ~~an~~the antipsychotic medication, wherein said treatment is effective to:

reduce the body weight of a subject, as compared to baseline body weight of said subject prior to said administration of said GRM, wherein the subject has previously been administered an antipsychotic medication; or

reduce the weight gain of a subject over time while taking an antipsychotic medication and said GRM, as compared to average weight gain of subjects taking that antipsychotic medication in the absence of the GRM; or

reduce blood levels of triglycerides as compared to triglyceride levels in the blood of said subject prior to said administration of said GRM, wherein the subject has previously been administered an antipsychotic medication; or

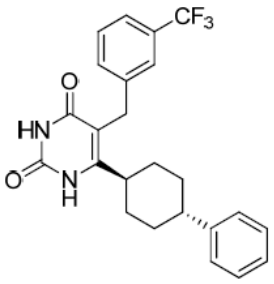
reduce blood levels of the liver enzymes ALT, AST, or both as compared to baseline liver enzyme levels in the blood of said subject prior to said administration of said GRM, wherein the subject has previously been administered an antipsychotic medication; or

reduce plasma insulin level as compared to the baseline plasma insulin level of said subject prior to said administration of said GRM, wherein the subject has previously been administered an antipsychotic medication; or

reduce insulin resistance as compared to baseline insulin resistance of said subject prior to said administration of said GRM, wherein the subject has previously been administered an antipsychotic medication (as measured by HOMA-IR or HOMA2-IR); or

combinations thereof.

2. The ~~method~~use of claim 1, wherein the cyclohexyl pyrimidine glucocorticoid receptor modulator (GRM) is miricorilant, (E)-6-(4-Phenylcyclohexyl)-5-(3-trifluoromethylbenzyl)-1H-pyrimidine-2,4-dione, which has the structure:



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3. The ~~method~~use of claim 1 or claim 2, wherein said treatment comprises ameliorating the effects of antipsychotic-induced weight gain in the ~~patient~~subject.

4. The ~~method~~use of claim 1 or claim 2, wherein said treatment comprises reducing the effects of antipsychotic-induced weight gain in the ~~patient~~subject.

5. The ~~method~~use of claim 1 or claim 2, wherein said treatment comprises reducing the amount of antipsychotic-induced weight gain in the ~~patient~~subject.

6. The ~~method~~use of claim 1 or claim 2, wherein said treatment comprises reducing the rate of antipsychotic-induced weight gain in the ~~patient~~subject.

7. The ~~method~~use of claim 1 or claim 2, wherein said treatment comprises reversing the antipsychotic-induced weight gain in the ~~patient~~subject, whereby said ~~patient~~subject loses weight.

8. Use of a cyclohexyl pyrimidine glucocorticoid receptor modulator (GRM) in the manufacture of a medicament for ~~A method of~~ treating a subject at risk of suffering from antipsychotic-induced weight gain, wherein the subject is to be administered an antipsychotic medication, and wherein ~~the method comprising administering to the subject~~ an effective amount of the~~a~~ cyclohexyl pyrimidine glucocorticoid receptor modulator (GRM) is to be administered to the subject while said subject is administered the~~an~~ antipsychotic medication, wherein the subject has not previously been administered an antipsychotic medication, and wherein said treatment is effective to:

reduce the weight gain of a subject over time while taking said antipsychotic medication and said GRM, as compared to average weight gain of subjects administered that antipsychotic medication in the absence of the GRM; or

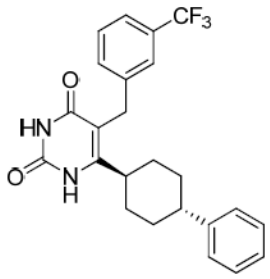
reduce the increase in blood levels of triglycerides as compared to the average increase in triglyceride levels in the blood of subjects administered said antipsychotic medication; or

reduce the increase in blood levels of liver enzymes ALT or AST, or both, as compared to the average increase in said liver enzyme levels in the blood of subjects administered said antipsychotic medication; or

reduce the increase in plasma insulin level as compared to the average increase in plasma insulin level in subjects administered said antipsychotic medication; or

reduce the increase in insulin resistance (as measured by HOMA-IR or HOMA2-IR) as compared to the average increase in insulin resistance of in subjects administered said antipsychotic medication; or combinations thereof.

9. The ~~method~~use of claim 8, wherein the cyclohexyl pyrimidine glucocorticoid receptor modulator (GRM) is miricorilant, (E)-6-(4-Phenylcyclohexyl)-5-(3-trifluoromethylbenzyl)-1H-pyrimidine-2,4-dione, which has the structure:



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10. The ~~method~~use of claim 8 or claim 9, wherein said treatment comprises ameliorating the effects of antipsychotic-induced weight gain in the ~~patient~~subject.

11. The ~~method~~use of claim 8 or claim 9, wherein said treatment comprises reducing the effects of antipsychotic-induced weight gain in the ~~patient~~subject.

12. The ~~method~~use of claim 8 or claim 9, wherein said treatment comprises reducing the amount of antipsychotic-induced weight gain in the ~~patient~~subject.

13. The ~~method~~use of claim 8 or claim 9, wherein said treatment comprises reducing the rate of antipsychotic-induced weight gain in the ~~patient~~subject.

14. ___The ~~method~~use of claim 8 or claim 9, wherein said treatment comprises reversing the antipsychotic-induced weight gain in the ~~patient~~subject, whereby said ~~patient~~subject loses weight as compared to the ~~patient~~subject's weight prior to administration of said GRM.

15. The ~~method~~use of any of claims 1 to 7, wherein said GRM administration comprises oral administration of said GRM.

16. The ~~method~~use of any of claims 8 to 14, wherein said GRM administration comprises oral administration of said GRM.

17. The ~~method~~use of any of claims 1 to 7, or claim 15, wherein said treatment comprising concomitant administration of an antipsychotic medication and said GRM is effective to reduce one or more of body weight, weight gain, liver enzyme levels in the blood, plasma insulin, and insulin resistance (HOMA-IR or HOMA2-IR) ~~-~~by about 10% or more.

18. The ~~method~~use of any of claims 8 to 14, or claim 16, wherein said treatment comprising concomitant administration of an antipsychotic medication and said GRM is effective to reduce one or more of weight gain, liver enzyme levels in the blood, plasma insulin, and insulin resistance (HOMA-IR or HOMA2-IR) ~~-~~by about 10% or more.

19. The ~~method~~use of claim 17, wherein said treatment is effective to reduce ~~reduce~~ one or more of body weight, weight gain, liver enzyme levels in the blood, plasma insulin, and insulin resistance (HOMA-IR or HOMA2-IR) ~~-~~by about 20% or more.

20. The ~~method~~use of claim 18, wherein said treatment is effective to reduce ~~reduce~~ one or more of weight gain, liver enzyme levels in the blood, plasma insulin, and insulin resistance (HOMA-IR or HOMA2-IR) by about 20% or more.