[0004] Liver disorders can be categorized in different groups of diseases, such as alcohol-induced fatty liver disease (AFLD), nonalcoholic fatty liver disease (NAFLD), drug- or alcohol-related liver diseases, viral diseases, immune-mediated liver diseases, metabolic liver diseases, and complications associated with hepatic insufficiency and/or liver transplantation. Nonalcoholic fatty liver disease is a common hepatic disorder with histological features similar to those of alcohol-induced fatty liver disease, in individuals who consume little or no alcohol. Fatty liver disease is due to an abnormal retention of lipid (fats) within hepatocytes. Effective treatments for AFLD and NAFLD remain insufficient. To date, no therapeutic drug treatment is established for such patients. There is a need for novel therapeutic options for managing fatty liver disease. There is a need for novel therapeutic options for patients in need of treatment by both a drug which may cause liver toxicity and a drug which affects the GR.

SUMMARY

[0004a] In one aspect, there is provided the use of a nonsteroidal selective glucocorticoid receptor modulator (SGRM), in the manufacture of a medicament for treatment of a patient suffering from a disorder selected from a liver disorder, Cushing's syndrome, Cushing's Disease, cancer, a fungal infection**,** a bacterial infection, a viral infection, an inflammatory disease or condition, a cardiovascular disease, an endocrine condition, and a kidney disease, and combinations thereof, without adverse effects on the liver of said patient.

[0004b] In another aspect, there is provided the use of a nonsteroidal selective glucocorticoid receptor modulator (SGRM), in a manufacture of a medicament for reduction of liver steatosis in a patient suffering from a disorder selected from a liver disorder, Cushing's syndrome, Cushing's Disease, cancer, a fungal infection**,** a bacterial infection, a viral infection, an inflammatory disease or condition, a cardiovascular disease, an endocrine condition, and a kidney disease, and combinations thereof, without adverse effects on the liver of the patient, effective to reduce said liver steatosis in said patient.

[0004c] In another aspect, there is provided the use of a nonsteroidal selective glucocorticoid receptor modulator (SGRM), in the manufacture of a medicament for reduction or prevention of liver toxicity in a patient receiving a drug which may cause liver toxicity, wherein the nonsteroidal selective glucocorticoid receptor modulator (SGRM) is to be administered in addition to said drug which may cause liver toxicity.

[0004d] In another aspect, there is provided the use of a nonsteroidal selective glucocorticoid receptor modulator (SGRM), in the manufacture of a medicament for treatment of a patient receiving a drug which may cause liver toxicity, without adverse effects on the liver of said patient, wherein the nonsteroidal selective glucocorticoid receptor modulator (SGRM) is to

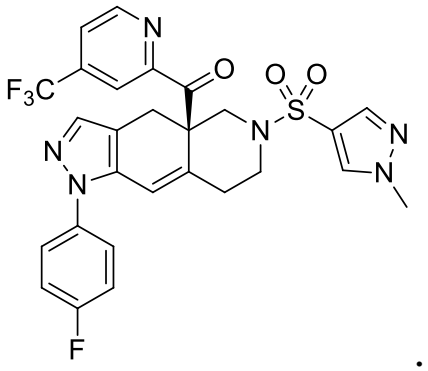
be administered to treat said patient receiving said drug which may cause liver toxicity, without adverse effects on the liver of the patient.

[0004e] In another aspect, there is provided the use of a nonsteroidal selective glucocorticoid receptor modulator in the manufacture of a medicament for treatment of a disorder selected from Cushing's syndrome, Cushing's Disease, and a fatty liver disease without adverse effects on liver enzyme levels, or on liver function, wherein said use is with a drug that may cause liver toxicity.

[0005] The present methods provide improved methods of administering selective glucocorticoid receptor modulators (SGRMs) and drugs that may cause liver toxicity to patients in need thereof. Disclosed herein are novel methods for treating Cushing's syndrome and Cushing's Disease with a favorable liver safety profile. Also disclosed herein are novel methods for treating liver disorders including fatty liver diseases, for reducing high levels of liver enzymes, and other treatments, all with a favorable liver safety profile. Applicant discloses herein the favorable liver safety profile of the SGRM relacorilant following administration to healthy and to hepatically impaired adults, and to patients with Cushing's syndrome. The methods comprise administering to the subject an effective amount of relacorilant without adverse effects on liver enzyme levels, or on liver function. In examples, the methods comprise administering to the subject an effective amount of relacorilant in combination with another drug, without adverse effects on liver enzyme levels, or on liver function. In examples, the methods include methods of reducing or preventing liver toxicity in a patient receiving a drug which may cause liver toxicity, the method comprising administering to the patient an effective amount of a nonsteroidal selective glucocorticoid receptor modulator (SGRM) in addition to said drug which may cause liver toxicity. In examples, the patient is receiving a drug which may cause liver toxicity, and is then administered a SGRM. In examples, the patient is receiving a SGRM, and is then administered a drug which may cause liver toxicity. In examples, the other drug may be a drug that may inhibit CYP3A enzymes (including CYP3A4 enzymes), such as, e.g., itraconazole or ketoconazole. In examples, the methods comprise reducing liver steatosis in a patient suffering from a liver disorder, Cushing's syndrome, Cushing's Disease, or a

combination thereof, by administering to the patient an effective amount of a nonsteroidal selective glucocorticoid receptor modulator (SGRM) effective to reduce said liver steatosis in said patient. In examples, the methods comprise co-administering an effective amount of relacorilant when the patient is being, or is to be, administered a drug with known liver toxicity (e.g., itraconazole, ketoconazole, or other CYP3A inhibitor) effective to reduce, prevent, or abolish the liver toxicity of that drug with known liver toxicity.

[0006] Relacorilant is a heteroaryl-ketone fused azadecalin compound disclosed and described in Example 18 of U.S. Patent No. 8,859,774, the entire contents of which U.S. Patent is hereby incorporated by reference in its entirety. The chemical name of 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)pyridin-2-yl)methanone; it has the following structure:



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[0007] Applicant has discovered and discloses herein that relacorilant has a favorable liver safety profile that includes a trend toward improved liver function tests (LFTs) in healthy volunteers and patients with normal and impaired liver function. Applicant has discovered and discloses herein that relacorilant may be safely administered to patients with moderate hepatic impairment as well as to patients with normal liver function. Thus, SGRMs such as relacorilant may be administered to patients with impaired liver function in the same manner, dosing, and frequency of administration as it is administered to patients with normal liver function. The findings in patients with liver impairment support the use of relacorilant in treating Cushing's syndrome and Cushing's Disease patients who have moderate hepatic impairment without need for adjustment of the relacorilant dose (as compared to the dose used for patients without moderate hepatic impairment). The findings in patients with liver impairment also support the use of relacorilant in treating patients suffering from liver disorders who have moderate hepatic impairment without need for adjustment of the relacorilant dose (as compared to the dose used for patients without liver disorders).

Relacorilant may be administered in the treatment of liver disorders including, for example, a fatty liver disorder. Fatty liver disorders include, for example, alcohol-related liver disease, and nonalcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), and other liver disorders. A SGRM such as relacorilant may be administered to a patient suffering from cancer, or from a fungal infection, or from another disorder for which a drug that may cause liver toxicity may be co-administered, without need for adjustment of the relacorilant dose (as compared to the dose used in the absence of the drug that may cause liver toxicity).

[0008] Relacorilant may be orally administered, or may be administered by other suitable means. In the studies disclosed herein, relacorilant was orally administered in doses of 100 milligrams (mg) to 400 mg per day. Relacorilant may be administered once daily, or may be administered twice, or three times, or other number of times per day.

[0009] In examples of the methods disclosed herein, the effective amounts of relacorilant may include a daily dose of between 1 and 100 mg/kg/day. In some examples, the daily relacorilant dose is 1, 2, 4, 6, 8, 10, 12, 14, 16, 18, 20, 30, 40, 50 60, 70, 80, 90 or 100 mg/kg/day. Relacorilant may be administrated for at least 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 25, 30, 35, 40, 45, 50, 55, 60, 65, 70, 75, or 80 weeks.

[0010] The present methods provide improved methods of treating patients who are administered an SGRM and a drug that may cause liver toxicity to patients. The present methods provide improved methods of treating Cushing's syndrome, Cushing's Disease, and liver disorders including fatty liver disease, excess liver enzyme levels, and other liver disorders. The present methods provide improved methods for reducing liver steatosis in a patient suffering from a liver disorder, Cushing's syndrome, Cushing's Disease, or a combination thereof. The present methods provide improved methods for reducing, preventing, or abolishing the liver toxicity of drugs with known liver toxicity by administration of a SGRM, such as relacorilant, with the drug with known liver toxicity.

BRIEF DESCRIPTION OF THE DRAWINGS

[0011] FIG. 1 shows the results of the hepatic impariment study.

[0012] FIG. 2 shows the results of the drug-drug interaction study (relacorilant – itraconazole).

[0013] FIG. 3 shows the results of the Phase 2 Cushing's syndrome study.

[0014] FIG. 4 shows the study designs of on-going clinical studies.

WE CLAIM:

1. Use of a nonsteroidal selective glucocorticoid receptor modulator (SGRM), in the manufacture of a medicament for treatment of a patient suffering from a disorder selected from a liver disorder, Cushing's syndrome, Cushing's Disease, cancer, a fungal infection**,** a bacterial infection, a viral infection, an inflammatory disease or condition, a cardiovascular disease, an endocrine condition, and a kidney disease, and combinations thereof, without adverse effects on the liver of said patient.

2. The use of claim 1, wherein the liver disorder is a fatty liver disease.

3. The use of claim 2, wherein the fatty liver disease is a fatty liver disease selected from alcohol related liver disease (ARLD) and nonalcoholic fatty liver disease (NAFLD).

4. The use of claim 3, wherein said alcohol-related liver disease (ARLD) is alcohol fatty liver disease (AFL), alcoholic steatohepatitis (ASH) or alcoholic cirrhosis.

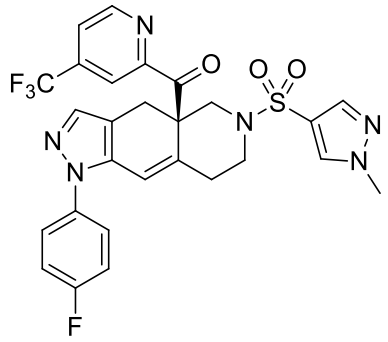
5. The use of claim 3, wherein said nonalcoholic fatty liver disease (NAFLD) is nonalcoholic steatohepatitis (NASH) or nonalcoholic cirrhosis.

6. The use of claim 1, wherein the patient suffers from Cushing's syndrome.

7. The use of claim 1, wherein the patient suffers from Cushing's Disease.

8. The use of claim 1, wherein the nonsteroidal selective glucocorticoid receptor modulator is a compound comprising a heteroaryl ketone fused azadecalin structure.

9. The use of claim 8, wherein the nonsteroidal selective glucocorticoid receptor modulator is relacorilant, (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)pyridin-2-yl)methanone, having the formula:



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10. The use of any of claims 1 to 9, further comprising a further pharmaceutical composition to be administered to the patient, without further adverse effects on the liver of said patient.

11. The use of claim 10, wherein said further pharmaceutical composition comprises itraconazole or ketoconazole.

12. The use of claim 10, wherein said further pharmaceutical composition comprises a CYP3A inhibitor selected from ketoconazole, itraconazole, nefazodone, ritonavir, nelfinavir, indinavir, boceprevir, clarithromycin, conivaptan, lopinavir, posaconazole, saquinavir, telaprevir, cobicistat, troleandomycin, tipranivir, paritaprevir and voriconazole.

13. The use of claim 10, wherein said further pharmaceutical composition comprises a drug selected from mercaptopurine, indomethacin, phenytoin, rifampin, abacavir, allopurinol, amineptine, amiodarone, bicalutamide, chlorzoxazone, dactinomycin, dantrolene, diclofenac, diflunisal, fenoprofen, flutamide, hydroxyurea, imatinib, iproniazid, ketoconazole, labetalol, leflunomide, mefenamic acid, methyldopa, nefazodone, nitrofurantoin, perhexiline, propylthiouracil, stavudine, sulindac, tamoxifen, tizanidine, tolcapone, valproic acid, zidovudine, troglitazone, fluconazole, itraconazole, clomipramine, clarithromycin, testosterone, etodolac, pemoline, nevirapine, benzbromarone, busulfan, disulfiram, isoniazid, nimesulide, minocycline, alatrofloxacin mesylate, gemtuzumab ozogamicin, acetazolamide, benoxaprofen, bromfenac, danazol, febuxostat, griseofulvin, ibufenac, sunitinib, methimazole, sulfathiazole, terbinafine, ticrynafen, trovafloxacin, etravirine, tolvaptan, pazopanib, divalproex sodium, lumiracoxib, tasosartan, oxyphenisatin, tilbroquinol, alclofenac, aplaviroc, clomacran, dermatan, isaxonine, pipamazine, pralnacasan, sulfacarbamide, triacetyldiphenolisatin, fiduxosin, pafuraidine, phenoxypropazine, oxandrolone, acarbose, alpidem, bexarotene, voriconazole, bendazac, benzarone,

benziodarone, atomoxetine, chlormezanone, erlotinib, cinchophen, tipranavir, clometacin, sorafenib, darunavir, cyclofenil, didanosine, interferon alfa-2b, interferon alfa-2a, recombinant, droxicam, ethambutol, infliximab, exifone, fialuridine, fipexide, fosphenytoin, gemcitabine, levofloxacin, mebanazine, moxisylyte, nialamide, nilutamide, niperotidine, nomifensine, nortriptyline, pirprofen, riluzole, ritonavir, sulcotidil, tolrestat, fenclozic acid, ebrotidine, nitrefazole, tetrabamate, xenazoic acid, zafirlukast, falnidamol, zimelidine, telithromycin, ximelagatran, duloxetine, glafenine, mepazine, lapatinib, alaproclate, orlistat, sitaxsentan, carbamazepine, felbamate, ciprofloxacin, oxymetholone, niacin, cyclosporine, albendazole, deferasirox, thiabendazole, raltegravir, dronedarone, bosentan, micafungin, bortezomib, milnacipran, asparaginase, efavirenz, interferon beta-1b, interferon beta-1a, interferon alfacon-1, lamotrigine, nandrolone decanoate, dacarbazine, acetaminophen, azathioprine, erythromycin, sulfasalazine, isotretinoin, atorvastatin, clozapine, 4-aminosalicylic acid, zileuton, acitretin, natalizumab, papaverine, gemfibrozil, ticlopidine, exemestane, gefitinib, eltrombopag olamine, oxaliplatin, diltiazem, estramustine, peginterferon alfa-2b, methotrexate, cytarabine, maraviroc, mexiletine, and pentostatin.

14. The use of claim 1, wherein the patient suffers from Cushing's syndrome and a liver disorder.

15. The use of claim 1, wherein the patient suffers from Cushing's Disease and a liver disorder.

16. Use of a nonsteroidal selective glucocorticoid receptor modulator (SGRM), in a manufacture of a medicament for reduction of liver steatosis in a patient suffering from a disorder selected from a liver disorder, Cushing's syndrome, Cushing's Disease, cancer, a fungal infection**,** a bacterial infection, a viral infection, an inflammatory disease or condition, a cardiovascular disease, an endocrine condition, and a kidney disease, and combinations thereof, without adverse effects on the liver of the patient, effective to reduce said liver steatosis in said patient.

17. The use of claim 16, wherein the liver disorder is a fatty liver disease.

18. The use of claim 17, wherein the fatty liver disease is a fatty liver disease selected from alcohol related liver disease (ARLD) and nonalcoholic fatty liver disease (NAFLD).

19. The use of claim 18, wherein said alcohol-related liver disease (ARLD) is alcohol fatty liver disease (AFL), alcoholic steatohepatitis (ASH) or alcoholic cirrhosis.

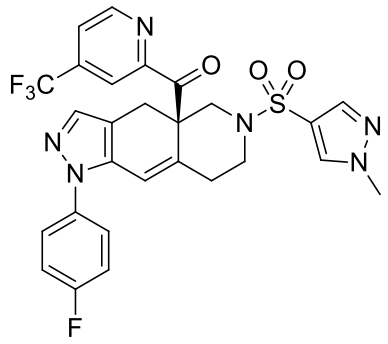
20. The use of claim 18, wherein said nonalcoholic fatty liver disease (NAFLD) is nonalcoholic steatohepatitis (NASH) or nonalcoholic cirrhosis.

21. The use of claim 16, wherein the patient suffers from Cushing's syndrome.

22. The use of claim 16, wherein the patient suffers from Cushing's Disease.

23. The use of claim 16, wherein the nonsteroidal selective glucocorticoid receptor modulator is a compound comprising a heteroaryl ketone fused azadecalin structure.

24. The use of claim 23, wherein the nonsteroidal selective glucocorticoid receptor modulator is relacorilant, (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)pyridin-2-yl)methanone, having the formula:



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25. The use of any of claims 16 to 24, further comprising a further pharmaceutical composition to be administered to the patient, without further adverse effects on the liver of said patient.

26. The use of claim 25, wherein said further pharmaceutical composition comprises itraconazole or ketoconazole.

27. The use of claim 25, wherein said further pharmaceutical composition comprises a CYP3A inhibitor selected from ketoconazole, itraconazole, nefazodone,

ritonavir, nelfinavir, indinavir, boceprevir, clarithromycin, conivaptan, lopinavir, posaconazole, saquinavir, telaprevir, cobicistat, troleandomycin, tipranivir, paritaprevir and voriconazole.

28. The use of claim 25, wherein said further pharmaceutical composition comprises a drug selected from mercaptopurine, indomethacin, phenytoin, rifampin, abacavir, allopurinol, amineptine, amiodarone, bicalutamide, chlorzoxazone, dactinomycin, dantrolene, diclofenac, diflunisal, fenoprofen, flutamide, hydroxyurea, imatinib, iproniazid, ketoconazole, labetalol, leflunomide, mefenamic acid, methyldopa, nefazodone, nitrofurantoin, perhexiline, propylthiouracil, stavudine, sulindac, tamoxifen, tizanidine, tolcapone, valproic acid, zidovudine, troglitazone, fluconazole, itraconazole, clomipramine, clarithromycin, testosterone, etodolac, pemoline, nevirapine, benzbromarone, busulfan, disulfiram, isoniazid, nimesulide, minocycline, alatrofloxacin mesylate, gemtuzumab ozogamicin, acetazolamide, benoxaprofen, bromfenac, danazol, febuxostat, griseofulvin, ibufenac, sunitinib, methimazole, sulfathiazole, terbinafine, ticrynafen, trovafloxacin, etravirine, tolvaptan, pazopanib, divalproex sodium, lumiracoxib, tasosartan, oxyphenisatin, tilbroquinol, alclofenac, aplaviroc, clomacran, dermatan, isaxonine, pipamazine, pralnacasan, sulfacarbamide, triacetyldiphenolisatin, fiduxosin, pafuraidine, phenoxypropazine, oxandrolone, acarbose, alpidem, bexarotene, voriconazole, bendazac, benzarone, benziodarone, atomoxetine, chlormezanone, erlotinib, cinchophen, tipranavir, clometacin, sorafenib, darunavir, cyclofenil, didanosine, interferon alfa-2b, interferon alfa-2a, recombinant, droxicam, ethambutol, infliximab, exifone, fialuridine, fipexide, fosphenytoin, gemcitabine, levofloxacin, mebanazine, moxisylyte, nialamide, nilutamide, niperotidine, nomifensine, nortriptyline, pirprofen, riluzole, ritonavir, sulcotidil, tolrestat, fenclozic acid, ebrotidine, nitrefazole, tetrabamate, xenazoic acid, zafirlukast, falnidamol, zimelidine, telithromycin, ximelagatran, duloxetine, glafenine, mepazine, lapatinib, alaproclate, orlistat, sitaxsentan, carbamazepine, felbamate, ciprofloxacin, oxymetholone, niacin, cyclosporine, albendazole, deferasirox, thiabendazole, raltegravir, dronedarone, bosentan, micafungin, bortezomib, milnacipran, asparaginase, efavirenz, interferon beta-1b, interferon beta-1a, interferon alfacon-1, lamotrigine, nandrolone decanoate, dacarbazine, acetaminophen, azathioprine, erythromycin, sulfasalazine, isotretinoin, atorvastatin, clozapine, 4-aminosalicylic acid, zileuton, acitretin, natalizumab, papaverine, gemfibrozil, ticlopidine, exemestane, gefitinib, eltrombopag olamine, oxaliplatin, diltiazem, estramustine, peginterferon alfa-2b, methotrexate, cytarabine, maraviroc, mexiletine, and pentostatin.

29. The use of claim 16, wherein the patient suffers from Cushing's syndrome and a liver disorder.

30. The use of claim 16, wherein the patient suffers from Cushing's Disease and a liver disorder.

31. Use of a nonsteroidal selective glucocorticoid receptor modulator (SGRM), in the manufacture of a medicament for reduction or prevention of liver toxicity in a patient receiving a drug which may cause liver toxicity, wherein the nonsteroidal selective glucocorticoid receptor modulator (SGRM) is to be administered in addition to said drug which may cause liver toxicity.

32. The use of claim 31, wherein said patient is receiving said drug which may cause liver toxicity, and is then to be administered said SGRM.

33. The use of claim 31, wherein said patient is receiving said SGRM, and is then to be administered said drug which may cause liver toxicity.

34. The use of claim 31, wherein the patient suffers from a fatty liver disease.

35. The use of claim 34, wherein the fatty liver disease is a fatty liver disease selected from alcohol related liver disease (ARLD) and nonalcoholic fatty liver disease (NAFLD).

36. The use of claim 35, wherein said alcohol-related liver disease (ARLD) is alcohol fatty liver disease (AFL), alcoholic steatohepatitis (ASH) or alcoholic cirrhosis.

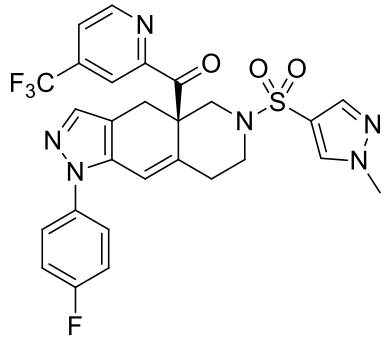
37. The use of claim 31, wherein said nonalcoholic fatty liver disease (NAFLD) is nonalcoholic steatohepatitis (NASH) or nonalcoholic cirrhosis.

38. The use of claim 31, wherein the patient suffers from Cushing's syndrome.

39. The use of claim 31, wherein the patient suffers from Cushing's Disease.

40. The use of any of claims 31 to 39, wherein the nonsteroidal selective glucocorticoid receptor modulator is a compound comprising a heteroaryl ketone fused azadecalin structure.

41. The use of claim 40, wherein the nonsteroidal selective glucocorticoid receptor modulator is relacorilant, (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)pyridin-2-yl)methanone, having the formula:



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42. The use of any of claims 31 to 41, wherein the drug which may cause liver toxicity is a CYP3A inhibitor selected from ketoconazole, itraconazole, nefazodone, ritonavir, nelfinavir, indinavir, boceprevir, clarithromycin, conivaptan, lopinavir, posaconazole, saquinavir, telaprevir, cobicistat, troleandomycin, tipranivir, paritaprevir and voriconazole.

43. The use of any of claims 31 to 41, wherein the drug which may cause liver toxicity is a drug selected from mercaptopurine, indomethacin, phenytoin, rifampin, abacavir, allopurinol, amineptine, amiodarone, bicalutamide, chlorzoxazone, dactinomycin, dantrolene, diclofenac, diflunisal, fenoprofen, flutamide, hydroxyurea, imatinib, iproniazid, ketoconazole, labetalol, leflunomide, mefenamic acid, methyldopa, nefazodone, nitrofurantoin, perhexiline, propylthiouracil, stavudine, sulindac, tamoxifen, tizanidine, tolcapone, valproic acid, zidovudine, troglitazone, fluconazole, itraconazole, clomipramine, clarithromycin, testosterone, etodolac, pemoline, nevirapine, benzbromarone, busulfan, disulfiram, isoniazid, nimesulide, minocycline, alatrofloxacin mesylate, gemtuzumab ozogamicin, acetazolamide, benoxaprofen, bromfenac, danazol, febuxostat, griseofulvin, ibufenac, sunitinib, methimazole, sulfathiazole, terbinafine, ticrynafen, trovafloxacin, etravirine, tolvaptan, pazopanib, divalproex sodium, lumiracoxib, tasosartan, oxyphenisatin, tilbroquinol, alclofenac, aplaviroc, clomacran, dermatan, isaxonine, pipamazine, pralnacasan,

sulfacarbamide, triacetyldiphenolisatin, fiduxosin, pafuraidine, phenoxypropazine, oxandrolone, acarbose, alpidem, bexarotene, voriconazole, bendazac, benzarone, benziodarone, atomoxetine, chlormezanone, erlotinib, cinchophen, tipranavir, clometacin, sorafenib, darunavir, cyclofenil, didanosine, interferon alfa-2b, interferon alfa-2a, recombinant, droxicam, ethambutol, infliximab, exifone, fialuridine, fipexide, fosphenytoin, gemcitabine, levofloxacin, mebanazine, moxisylyte, nialamide, nilutamide, niperotidine, nomifensine, nortriptyline, pirprofen, riluzole, ritonavir, sulcotidil, tolrestat, fenclozic acid, ebrotidine, nitrefazole, tetrabamate, xenazoic acid, zafirlukast, falnidamol, zimelidine, telithromycin, ximelagatran, duloxetine, glafenine, mepazine, lapatinib, alaproclate, orlistat, sitaxsentan, carbamazepine, felbamate, ciprofloxacin, oxymetholone, niacin, cyclosporine, albendazole, deferasirox, thiabendazole, raltegravir, dronedarone, bosentan, micafungin, bortezomib, milnacipran, asparaginase, efavirenz, interferon beta-1b, interferon beta-1a, interferon alfacon-1, lamotrigine, nandrolone decanoate, dacarbazine, acetaminophen, azathioprine, erythromycin, sulfasalazine, isotretinoin, atorvastatin, clozapine, 4-aminosalicylic acid, zileuton, acitretin, natalizumab, papaverine, gemfibrozil, ticlopidine, exemestane, gefitinib, eltrombopag olamine, oxaliplatin, diltiazem, estramustine, peginterferon alfa-2b, methotrexate, cytarabine, maraviroc, mexiletine, and pentostatin.

44. The use of any of claims 31 to 41, wherein the drug which may cause liver toxicity is ketoconazole.

45. The use of any of claims 31 to 41, wherein the drug which may cause liver toxicity is itraconazole.

46. The use of any of claims 31 to 45, wherein the patient suffers from Cushing’s syndrome and a liver disorder.

47. The use of any of claims 31 to 46, wherein the patient suffers from Cushing’s Disease and a liver disorder.

48. Use of a nonsteroidal selective glucocorticoid receptor modulator (SGRM), in the manufacture of a medicament for treatment of a patient receiving a drug which may cause liver toxicity, without adverse effects on the liver of said patient, wherein the nonsteroidal selective glucocorticoid receptor modulator (SGRM) is to be administered to treat said patient receiving said drug which may cause liver toxicity, without adverse effects on the liver of the patient.

49. The use of claim 48, wherein said patient is receiving said drug which may cause liver toxicity, and is then to be administered said SGRM.

50. The use of claim 48, wherein said patient is receiving said SGRM, and is then to be administered said drug which may cause liver toxicity.

51. The use of claim 48, wherein the patient suffers from a fatty liver disease.

52. The use of claim 51, wherein the fatty liver disease is a fatty liver disease selected from alcohol related liver disease (ARLD) and nonalcoholic fatty liver disease (NAFLD).

53. The use of claim 52, wherein said alcohol-related liver disease (ARLD) is alcohol fatty liver disease (AFL), alcoholic steatohepatitis (ASH) or alcoholic cirrhosis.

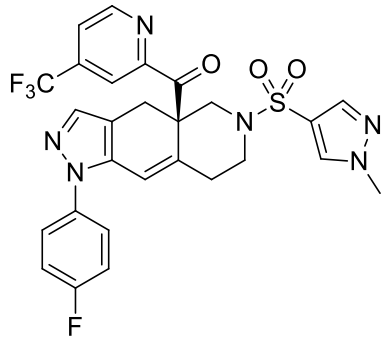
54. The use of claim 53, wherein said nonalcoholic fatty liver disease (NAFLD) is nonalcoholic steatohepatitis (NASH) or nonalcoholic cirrhosis.

55. The use of claim 48, wherein the patient suffers from Cushing's syndrome.

56. The use of claim 48, wherein the patient suffers from Cushing's Disease.

57. The use of any of claims 48 to 56, wherein the nonsteroidal selective glucocorticoid receptor modulator is a compound comprising a heteroaryl ketone fused azadecalin structure.

58. The use of claim 57, wherein the nonsteroidal selective glucocorticoid receptor modulator is relacorilant, (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)pyridin-2-yl)methanone, having the formula:



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59. The use of any of claims 48 to 58, wherein the drug which may cause liver toxicity is a CYP3A inhibitor selected from ketoconazole, itraconazole, nefazodone, ritonavir, nelfinavir, indinavir, boceprevir, clarithromycin, conivaptan, lopinavir, posaconazole, saquinavir, telaprevir, cobicistat, troleandomycin, tipranivir, paritaprevir and voriconazole.

60. The use of any of claims 48 to 58, wherein the drug which may cause liver toxicity is a drug selected from mercaptopurine, indomethacin, phenytoin, rifampin, abacavir, allopurinol, amineptine, amiodarone, bicalutamide, chlorzoxazone, dactinomycin, dantrolene, diclofenac, diflunisal, fenoprofen, flutamide, hydroxyurea, imatinib, iproniazid, ketoconazole, labetalol, leflunomide, mefenamic acid, methyldopa, nefazodone, nitrofurantoin, perhexiline, propylthiouracil, stavudine, sulindac, tamoxifen, tizanidine, tolcapone, valproic acid, zidovudine, troglitazone, fluconazole, itraconazole, clomipramine, clarithromycin, testosterone, etodolac, pemoline, nevirapine, benzbromarone, busulfan, disulfiram, isoniazid, nimesulide, minocycline, alatrofloxacin mesylate, gemtuzumab ozogamicin, acetazolamide, benoxaprofen, bromfenac, danazol, febuxostat, griseofulvin, ibufenac, sunitinib, methimazole, sulfathiazole, terbinafine, ticrynafen, trovafloxacin, etravirine, tolvaptan, pazopanib, divalproex sodium, lumiracoxib, tasosartan, oxyphenisatin, tilbroquinol, alclofenac, aplaviroc, clomacran, dermatan, isaxonine, pipamazine, pralnacasan, sulfacarbamide, triacetyldiphenolisatin, fiduxosin, pafuraidine, phenoxypropazine, oxandrolone, acarbose, alpidem, bexarotene, voriconazole, bendazac, benzarone, benziodarone, atomoxetine, chlormezanone, erlotinib, cinchophen, tipranavir, clometacin, sorafenib, darunavir, cyclofenil, didanosine, interferon alfa-2b, interferon alfa-2a, recombinant, droxicam, ethambutol, infliximab, exifone, fialuridine, fipexide, fosphenytoin, gemcitabine, levofloxacin, mebanazine, moxisylyte, nialamide, nilutamide, niperotidine, nomifensine, nortriptyline, pirprofen, riluzole, ritonavir, sulcotidil, tolrestat, fenclozic acid, ebrotidine, nitrefazole, tetrabamate, xenazoic acid, zafirlukast, falnidamol, zimelidine,

telithromycin, ximelagatran, duloxetine, glafenine, mepazine, lapatinib, alaproclate, orlistat, sitaxsentan, carbamazepine, felbamate, ciprofloxacin, oxymetholone, niacin, cyclosporine, albendazole, deferasirox, thiabendazole, raltegravir, dronedarone, bosentan, micafungin, bortezomib, milnacipran, asparaginase, efavirenz, interferon beta-1b, interferon beta-1a, interferon alfacon-1, lamotrigine, nandrolone decanoate, dacarbazine, acetaminophen, azathioprine, erythromycin, sulfasalazine, isotretinoin, atorvastatin, clozapine, 4-aminosalicylic acid, zileuton, acitretin, natalizumab, papaverine, gemfibrozil, ticlopidine, exemestane, gefitinib, eltrombopag olamine, oxaliplatin, diltiazem, estramustine, peginterferon alfa-2b, methotrexate, cytarabine, maraviroc, mexiletine, and pentostatin.

61. The use of any of claims 48 to 58, wherein the drug which may cause liver toxicity is ketoconazole.

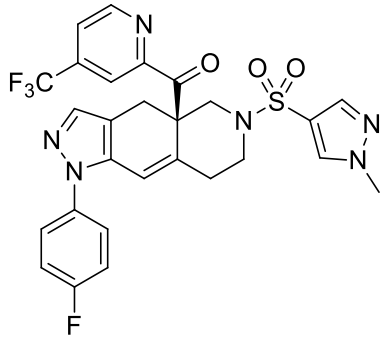
62. The use of any of claims 48 to 58, wherein the drug which may cause liver toxicity is itraconazole.

63. The use of any of claims 48 to 62, wherein the patient suffers from Cushing's syndrome and a liver disorder.

64. The use of any of claims 48 to 63, wherein the patient suffers from Cushing's Disease and a liver disorder.

65. The use of any of claims 48 to 64, wherein the nonsteroidal SGRM is a compound comprising a heteroaryl ketone fused azadecalin structure.

66. The use of claim 65, wherein the nonsteroidal SGRM is relacorilant, (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)pyridin-2-yl)methanone, having the formula:



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67. The use of any of claims 48 to 66, wherein said patient suffers from an excess liver enzyme level in the blood of the liver enzyme alanine aminotransferase, wherein said administration of said a nonsteroidal SGRM compound does not increase said liver enzyme levels in the blood.

68. The use of any of claims 48 to 67, wherein said patient suffers from an excess liver enzyme level in the blood of the liver enzyme aspartate aminotransferase, wherein said administration of said a nonsteroidal SGRM compound does not increase said liver enzyme levels in the blood.

69. The use of any of claims 48 to 68, wherein the patient has received a drug selected from ketoconazole, itraconazole, nefazodone, ritonavir, nelfinavir, indinavir, boceprevir, clarithromycin, conivaptan, lopinavir, posaconazole, saquinavir, telaprevir, cobicistat, troleandomycin, tipranivir, paritaprevir and voriconazole.

70. The use of any of claims 48 to 68, wherein the patient has received a drug selected from mercaptopurine, indomethacin, phenytoin, rifampin, abacavir, allopurinol, amineptine, amiodarone, bicalutamide, chlorzoxazone, dactinomycin, dantrolene, diclofenac, diflunisal, fenoprofen, flutamide, hydroxyurea, imatinib, iproniazid, ketoconazole, labetalol, leflunomide, mefenamic acid, methyldopa, nefazodone, nitrofurantoin, perhexiline, propylthiouracil, stavudine, sulindac, tamoxifen, tizanidine, tolcapone, valproic acid, zidovudine, troglitazone, fluconazole, itraconazole, clomipramine, clarithromycin, testosterone, etodolac, pemoline, nevirapine, benzbromarone, busulfan, disulfiram, isoniazid, nimesulide, minocycline, alatrofloxacin mesylate, gemtuzumab ozogamicin, acetazolamide, benoxaprofen, bromfenac, danazol, febuxostat, griseofulvin, ibufenac, sunitinib, methimazole, sulfathiazole, terbinafine, ticrynafen, trovafloxacin, etravirine, tolvaptan, pazopanib, divalproex sodium, lumiracoxib, tasosartan, oxyphenisatin, tilbroquinol, alclofenac, aplaviroc, clomacran, dermatan, isaxonine, pipamazine, pralnacasan, sulfacarbamide, triacetyldiphenolisatin, fiduxosin, pafuraidine, phenoxypropazine, oxandrolone, acarbose, alpidem, bexarotene, voriconazole, bendazac, benzarone, benziodarone, atomoxetine, chlormezanone, erlotinib, cinchophen, tipranavir, clometacin, sorafenib, darunavir, cyclofenil, didanosine, interferon alfa-2b, interferon alfa-2a, recombinant, droxicam, ethambutol, infliximab, exifone, fialuridine, fipexide, fosphenytoin, gemcitabine, levofloxacin, mebanazine, moxisylyte, nialamide, nilutamide, niperotidine, nomifensine, nortriptyline, pirprofen, riluzole, ritonavir, sulcotidil, tolrestat, fenclozic acid,

ebrotidine, nitrefazole, tetrabamate, xenazoic acid, zafirlukast, falnidamol, zimelidine, telithromycin, ximelagatran, duloxetine, glafenine, mepazine, lapatinib, alaproclate, orlistat, sitaxsentan, carbamazepine, felbamate, ciprofloxacin, oxymetholone, niacin, cyclosporine, albendazole, deferasirox, thiabendazole, raltegravir, dronedarone, bosentan, micafungin, bortezomib, milnacipran, asparaginase, efavirenz, interferon beta-1b, interferon beta-1a, interferon alfacon-1, lamotrigine, nandrolone decanoate, dacarbazine, acetaminophen, azathioprine, erythromycin, sulfasalazine, isotretinoin, atorvastatin, clozapine, 4-aminosalicylic acid, zileuton, acitretin, natalizumab, papaverine, gemfibrozil, ticlopidine, exemestane, gefitinib, eltrombopag olamine, oxaliplatin, diltiazem, estramustine, peginterferon alfa-2b, methotrexate, cytarabine, maraviroc, mexiletine, and pentostatin.

71. The use of any of claims 48 to 68, wherein the patient has received ketoconazole.

72. The use of any of claims 48 to 68, wherein the patient has received itraconazole.

73. Use of a nonsteroidal selective glucocorticoid receptor modulator in the manufacture of a medicament for treatment of a disorder selected from Cushing's syndrome, Cushing's Disease, and a fatty liver disease without adverse effects on liver enzyme levels, or on liver function, wherein said use is with a drug that may cause liver toxicity.

74. The use of claim 73, wherein said disorder is Cushing's syndrome.

75. The use of claim 73, wherein said disorder is Cushing's Disease.

76. The use of claim 73, wherein said disorder is a fatty liver disease.

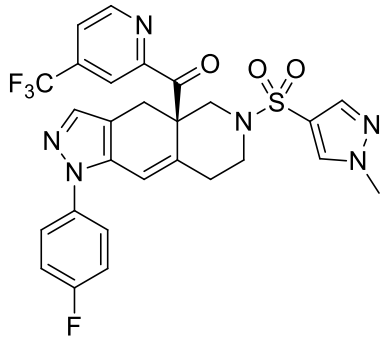
77. The use of claim 76, wherein said fatty liver disease is a fatty liver disease selected from alcohol related liver disease (ARLD) and nonalcoholic fatty liver disease (NAFLD).

78. The use of claim 77, wherein said alcohol-related liver disease (ARLD) is alcohol fatty liver disease (AFL), alcoholic steatohepatitis (ASH) or alcoholic cirrhosis.

79. The use of claim 77, wherein said nonalcoholic fatty liver disease (NAFLD) is nonalcoholic steatohepatitis (NASH) or nonalcoholic cirrhosis.

80. The use of any of claims 73 to 79, wherein said nonsteroidal selective glucocorticoid receptor modulator is a compound comprising a heteroaryl ketone fused azadecalin structure.

81. The use of claim 80, wherein said nonsteroidal selective glucocorticoid receptor modulator is relacorilant, (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)pyridin-2-yl)methanone, having the formula:



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82. The use of any of claims 73 to 81, comprising use with a CYP3A inhibitor selected from ketoconazole, itraconazole, nefazodone, ritonavir, nelfinavir, indinavir, boceprevir, clarithromycin, conivaptan, lopinavir, posaconazole, saquinavir, telaprevir, cobicistat, troleandomycin, tipranivir, paritaprevir and voriconazole.

83. The use of any of claims 73 to 81, comprising use with a drug selected from mercaptopurine, indomethacin, phenytoin, rifampin, abacavir, allopurinol, amineptine, amiodarone, bicalutamide, chlorzoxazone, dactinomycin, dantrolene, diclofenac, diflunisal, fenoprofen, flutamide, hydroxyurea, imatinib, iproniazid, ketoconazole, labetalol, leflunomide, mefenamic acid, methyldopa, nefazodone, nitrofurantoin, perhexiline, propylthiouracil, stavudine, sulindac, tamoxifen, tizanidine, tolcapone, valproic acid, zidovudine, troglitazone, fluconazole, itraconazole, clomipramine, clarithromycin, testosterone, etodolac, pemoline, nevirapine, benzbromarone, busulfan, disulfiram, isoniazid, nimesulide, minocycline, alatrofloxacin mesylate, gemtuzumab ozogamicin, acetazolamide, benoxaprofen, bromfenac, danazol, febuxostat, griseofulvin, ibufenac, sunitinib, methimazole, sulfathiazole, terbinafine, ticrynafen, trovafloxacin, etravirine, tolvaptan,

pazopanib, divalproex sodium, lumiracoxib, tasosartan, oxyphenisatin, tilbroquinol, alclofenac, aplaviroc, clomacran, dermatan, isaxonine, pipamazine, pralnacasan, sulfacarbamide, triacetyldiphenolisatin, fiduxosin, pafuraidine, phenoxypropazine, oxandrolone, acarbose, alpidem, bexarotene, voriconazole, bendazac, benzarone, benziodarone, atomoxetine, chlormezanone, erlotinib, cinchophen, tipranavir, clometacin, sorafenib, darunavir, cyclofenil, didanosine, interferon alfa-2b, interferon alfa-2a, recombinant, droxicam, ethambutol, infliximab, exifone, fialuridine, fipexide, fosphenytoin, gemcitabine, levofloxacin, mebanazine, moxisylyte, nialamide, nilutamide, niperotidine, nomifensine, nortriptyline, pirprofen, riluzole, ritonavir, sulcotidil, tolrestat, fenclozic acid, ebrotidine, nitrefazole, tetrabamate, xenazoic acid, zafirlukast, falnidamol, zimelidine, telithromycin, ximelagatran, duloxetine, glafenine, mepazine, lapatinib, alaproclate, orlistat, sitaxsentan, carbamazepine, felbamate, ciprofloxacin, oxymetholone, niacin, cyclosporine, albendazole, deferasirox, thiabendazole, raltegravir, dronedarone, bosentan, micafungin, bortezomib, milnacipran, asparaginase, efavirenz, interferon beta-1b, interferon beta-1a, interferon alfacon-1, lamotrigine, nandrolone decanoate, dacarbazine, acetaminophen, azathioprine, erythromycin, sulfasalazine, isotretinoin, atorvastatin, clozapine, 4-aminosalicylic acid, zileuton, acitretin, natalizumab, papaverine, gemfibrozil, ticlopidine, exemestane, gefitinib, eltrombopag olamine, oxaliplatin, diltiazem, estramustine, peginterferon alfa-2b, methotrexate, cytarabine, maraviroc, mexiletine, and pentostatin.

84. The use of any of claims 73 to 81, comprising use with ketoconazole.

85. The use of any of claims 73 to 81, comprising use with itraconazole.