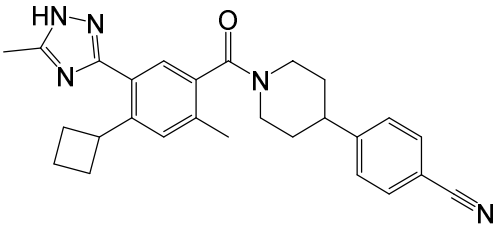
**CLAIMS**

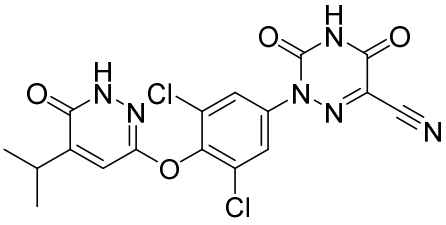
1. A pharmaceutical composition comprising a therapeutically effective amount of:

a fatty acid synthase inhibitor of formula:



(denifanstat), or a pharmaceutically acceptable salt thereof, and

a thyroid hormone receptor-beta (THR-β) agonist of formula:



(resmetirom), or a pharmaceutically acceptable salt thereof.

2. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition comprising the therapeutically effective amount is a fixed-dose combination.

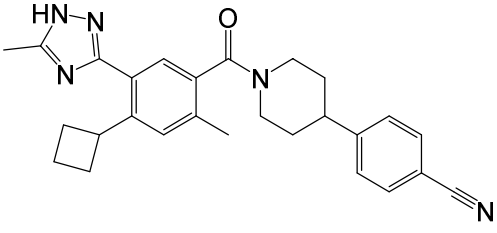
3. The pharmaceutical composition of claim 2, wherein the pharmaceutical composition comprising the therapeutically effective amount is a fixed-dose combination comprising from 25 to 50 mg of denifanstat.

4. The pharmaceutical composition of claim 3, wherein resmetirom is polymorph Form A.

5. Use of a pharmaceutical composition of any one of claims 1 to 4 in the manufacture of a medicament for treating nonalcoholic steatohepatitis/metabolic dysfunction-associated steatohepatitis (NASH/MASH) in a subject in need thereof.

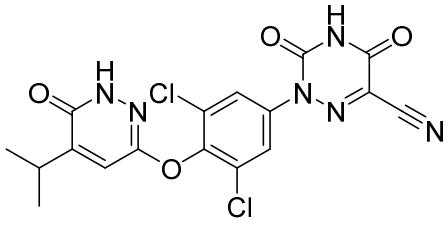
6. Use of a therapeutically effective amount of:

a fatty acid synthase inhibitor of formula:



(denifanstat), or a pharmaceutically acceptable salt thereof, and

a thyroid hormone receptor-beta (THR-β) agonist of formula:



(resmetirom), or a pharmaceutically acceptable salt thereof in the manufacture of a medicaments for a combination treatment of nonalcoholic steatohepatitis/metabolic dysfunction-associated steatohepatitis (NASH/MASH) in a subject in need thereof.

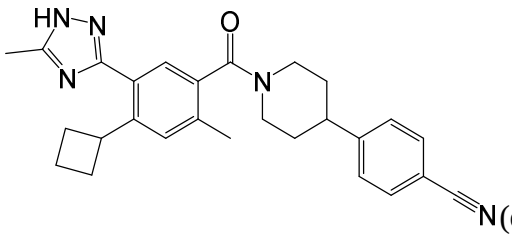
7. The use of claim 5 or 6, wherein treating the nonalcoholic steatohepatitis/metabolic dysfunction-associated steatohepatitis (NASH/MASH) comprises preventing the progression of at least one symptom of nonalcoholic steatohepatitis/metabolic dysfunction-associated steatohepatitis (NASH/MASH).

8. The use of claim 7, wherein the symptom is selected from elevated levels of AST; elevated levels of ALT; elevated levels of GGT; elevated levels of liver triglycerides; elevated levels of cholesterol; liver steatosis; liver inflammation; liver ballooning; liver fibrosis; and NAFLD activity score.

9. Use of a pharmaceutical composition of any one of claims 1 to 4 in the manufacture of a medicament for reversing established nonalcoholic steatohepatitis/metabolic dysfunction-associated steatohepatitis (NASH/MASH) in a subject in need thereof.

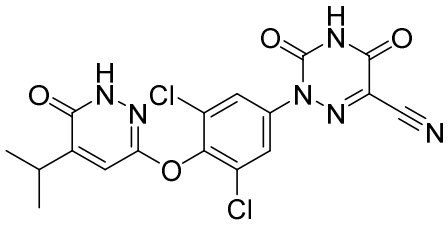
10. Use of a therapeutically effective amount of:

a fatty acid synthase inhibitor of formula:



(denifanstat), or a pharmaceutically acceptable salt thereof, and

a thyroid hormone receptor-beta (THR-β) agonist of formula:



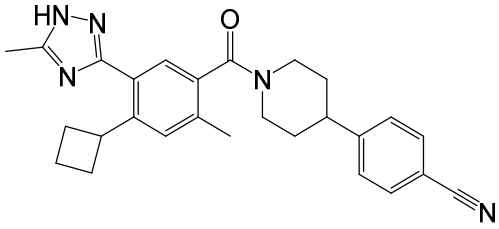
(resmetirom), or a pharmaceutically acceptable salt thereof in the manufacture of a medicaments for a combination treatment to reverse

established nonalcoholic steatohepatitis/metabolic dysfunction-associated steatohepatitis (NASH/MASH) in a subject in need thereof.

11. Use of a pharmaceutical composition of any one of claims 1 to 4 in the manufacture of a medicament for treating liver fibrosis or liver cirrhosis in a subject in need thereof.

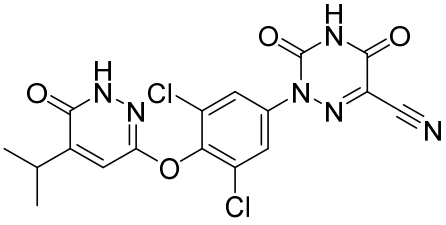
12. Use of a therapeutically effective amount of:

a fatty acid synthase inhibitor of formula:



(denifanstat), or a pharmaceutically acceptable salt thereof, and

a thyroid hormone receptor-beta (THR-β) agonist of formula:

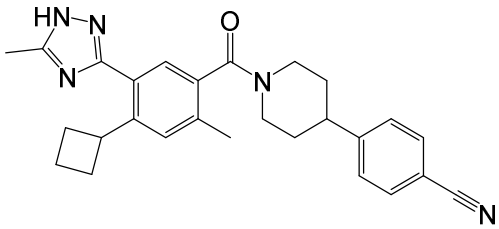


(resmetirom), or a pharmaceutically acceptable salt thereof in the manufacture of a medicaments for a combination treatment for treating liver fibrosis or liver cirrhosis in a subject in need thereof.

13. Use of a pharmaceutical composition of any one of claims 1 to 4 in the manufacture of a medicament for reducing triglycerides in a subject in need thereof.

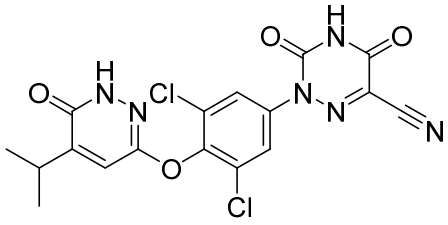
14. Use of a therapeutically effective amount of:

a fatty acid synthase inhibitor of formula:



(denifanstat), or a pharmaceutically acceptable salt thereof, and

a thyroid hormone receptor-beta (THR-β) agonist of formula:

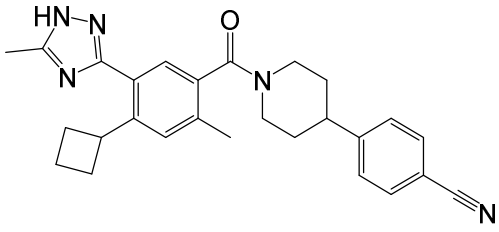


(resmetirom), or a pharmaceutically acceptable salt thereof in the manufacture of a medicaments for a combination treatment for reducing triglycerides in a subject in need thereof.

15. Use of a pharmaceutical composition of any one of claims 1 to 4 in the manufacture of a medicament for improving or restoring liver function in a subject in need thereof.

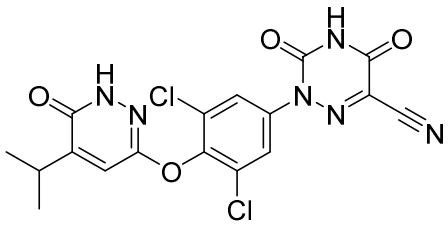
16. Use of a therapeutically effective amount of:

a fatty acid synthase inhibitor of formula:



(denifanstat), or a pharmaceutically acceptable salt thereof, and

a thyroid hormone receptor-beta (THR-β) agonist of formula:

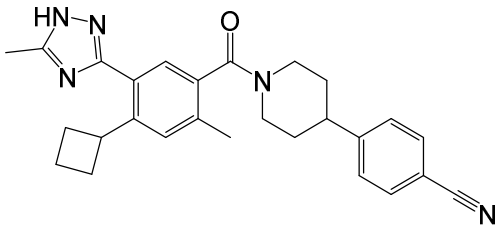


(resmetirom), or a pharmaceutically acceptable salt thereof in the manufacture of a medicaments for a combination treatment for improving or restoring liver function in a subject in need thereof

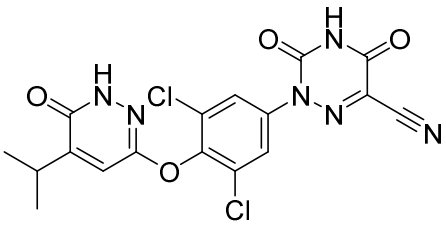
17. Use of a pharmaceutical composition of any one of claims 1 to 4 in the manufacture of a medicament for treating NASH/MASH with moderate to severe fibrosis in a subject in need thereof.

18. Use of a therapeutically effective amount of:

a fatty acid synthase inhibitor of formula:


(denifanstat), or a pharmaceutically acceptable salt thereof, and

a thyroid hormone receptor-beta (THR-β) agonist of formula:


(resmetirom), or a pharmaceutically acceptable salt thereof in the manufacture of a medicaments for a combination treatment for treating NASH/MASH with moderate to severe fibrosis in a subject in need thereof.

19. The use of claim 17 or 18, wherein the subject has an improvement in liver fibrosis ≥ 1 stage without worsening of NASH/MASH.

20. The use of claim 17 or 18, wherein the subject has resolution of NASH/MASH without worsening of fibrosis.

21. The use of any one of claims 6, 10, 12, 14, 16 and 18-20, wherein the fatty acid synthase inhibitor and the thyroid hormone receptor-beta agonist are administered sequentially.

22. The use of any one of claims 6, 10, 12, 14, 16 and 18-20, wherein the fatty acid synthase inhibitor and the thyroid hormone receptor-beta agonist are administered simultaneously.

23. The use of any one of claims 6, 10, 12, 14, 16 and 18-20, wherein the FASN inhibitor and the thyroid hormone receptor-beta agonist are administered on the same dosing schedule.

24. The use of any one of claims 6, 10, 12, 14, 16 and 18-20, wherein the FASN inhibitor and the thyroid hormone receptor-beta agonist are administered on different dosing schedules.

25. The use of any one of claims 6, 10, 12, 14, 16 and 18-24, wherein the fatty acid synthase inhibitor and the thyroid hormone receptor-beta agonist are formulated in separate dosage forms.

26. The use of any one of claims 6, 10, 12, 14, 16 and 18-20, wherein the fatty acid synthase inhibitor and the thyroid hormone receptor-beta agonist are formulated in the same dosage form.

27. The use of any one of claims 6, 10, 12, 14, 16 and 18-26, wherein the resmetirom is a polymorph of Form A.

28. The use of any one of claims 6, 10, 12, 14, 16 and 18-27, wherein the FASN inhibitor and the thyroid hormone receptor beta agonist are administered in synergistically effective amounts.

29. The use of any one of claims 6, 10, 12, 14, 16 and 18-28, wherein the FASN inhibitor is administered at a dose of 10-100 mg.

30. The use of any one of claims 6, 10, 12, 14, 16 and 18-28, wherein the FASN inhibitor is administered at a dose of 10-50 mg.

31. The use of any one of claims 6, 10, 12, 14, 16 and 18-28, wherein the FASN inhibitor is administered at a dose of 10 mg, 15 mg, 20 mg, 25 mg, 30 mg, 35 mg, 40 mg, 45 mg, or 50 mg.

32. The use of any one of claims 6, 10, 12, 14, 16 and 18-28, wherein the FASN inhibitor is administered at a dose of 50 mg.

33. The use of any one of claims 6, 10, 12, 14, 16 and 18-32, wherein the FASN inhibitor is administered once or twice daily.

34. The use of any one of claims 6, 10, 12, 14, 16 and 18-32, wherein the FASN inhibitor is administered once daily.

35. The use of any one of claims 6, 10, 12, 14, 16 and 18-34, wherein the FASN inhibitor is administered orally.

36. The use of any one of claims 6, 10, 12, 14, 16 and 18-36, wherein the thyroid hormone receptor beta agonist is administered at a dose that is equivalent to the single-agent dose indicated for treating NASH/MASH.

37. The use of any one of claims 6, 10, 12, 14, 16 and 18-36, wherein the thyroid hormone receptor beta agonist is administered at a dose that is between 10% and 90% of the single-agent dose indicated for treating NASH/MASH.

38. The use of any one of claims 6, 10, 12, 14, 16 and 18-36, wherein the thyroid hormone receptor beta agonist is administered at a dose of 80 mg once daily for a patient with a body weight of ≤100 kg and 100 mg once daily for a patient with a body weight of ≥100 kg.