CLAIMS

1. A process for the manufacture of lanifibranor, said process comprising reacting N-(4-chloro-2-iodo-phenyl)-1,3-benzothiazole-6-sulfonamide with 5-hexynoic acid in the presence of Pd/C and of a copper salt.

2. The process of claim 1, wherein the copper salt is selected from copper chloride, copper acetate, copper carbonate, copper sulfate, copper bromide, trifluoroacetic acid copper, copper nitrate, copper hydroxide, copper oxide, copper iodide and mixtures thereof.

3. The process of claim 2, wherein the copper salt is copper iodide.

4. The process of any preceding claim, wherein the copper salt is used in an amount from about 0.01 to about 0.15 equivalent, based on the amount of starting N-(4-chloro-2-iodo-phenyl)-1,3-benzothiazole-6-sulfonamide.

5. The process of any preceding claim, wherein 5-hexynoic acid is used in an amount from about 1.0 to about 2.0 equivalents, based on the amount of starting N-(4-chloro-2-iodo-phenyl)-1,3-benzothiazole-6-sulfonamide.

6. The process of any preceding claim, wherein the reaction is carried out in a solvent, in particular said solvent is selected from dichloromethane, chloroform, pyridine, 4-dimethylaminopyridine, N,N-dimethylformamide, dimethyl sulfoxide, acetonitrile, tetrahydrofuran, 2-methyl tetrahydrofuran, water, ethyl acetate, toluene, acetone, methylethylketone, methylisobutylketone, cyclohexanone, methylbutylketone, and mixtures thereof.

7. The process of any preceding claim, wherein the reaction is carried out in the presence of a base, in particular the base is selected from trimethylamine, triethylamine, pyridine, imidazole, 4-dimethylaminopyridine, 2,6-lutidine, 1,4-diazabicyclo[2.2.2]octane, 1,8-diazabicyclo[5.4.0]undec-7-ene, 1,5-diazabicyclo[4.3.0]non-5-ene, N,N-dimethylphenyl-amine and mixtures thereof.

8. The process of claim 7, wherein the base is used in an amount of about 1.0 to about

20.0 equivalents, based on the amount of starting N-(4-chloro-2-iodo-phenyl)-1,3-benzothiazole-6-sulfonamide.

9. The process of any preceding claim, wherein the reaction is carried out at a temperature from about 35°C to about 200°C.

10. A process for the manufacture of crystalline form beta of lanifibranor, comprising:
a) preparing a hot slurry of lanifibranor in a suitable solvent for lanifibranor;
b) optionally, filtering the hot slurry of lanifibranor;
c) cooling the slurry of lanifibranor to a temperature from about 15°C to about 95°C; and
d) maintaining the slurry of lanifibranor to a temperature from about 15°C to about 95°C for about 15 minutes to about 72h.

11. The process of claim 10, wherein the suitable solvent for lanifibranor is selected from water, dimethyl sulfoxide, alcohol solvents, halogenated hydrocarbons solvents, ether solvents, ketone solvents, esters solvents, hydrocarbons solvents, nitrile solvents, amide solvents and mixtures thereof.

12. The process of claim 11, wherein the suitable solvent for lanifibranor is selected from toluene, tetrahydrofuran, acetic acid and mixtures thereof.

13. The process of claim 10 or claim 12, wherein the slurry of lanifibranor is heated in step a) to a temperature from about 70°C to about 120°C, such as for example from about 70°C to about 110°C, from about 80°C to about 105°C, or from about 85°C to about 100°C.

14. The process of any one of claims 10 to 13, wherein the slurry of lanifibranor is cooled in step c) to a temperature from about 15°C to 95°C, from about 20°C to 95°C, from about 25°C to 95°C, from about 30°C to 95°C, from about 35°C to 95°C, from about 40°C to 95°C, from about 45°C to 95°C, from about 50°C to about 95°C, from about 55°C to about 95°C, from about 60°C to 95°C, from about 65°C to 95°C, from about 70°C to 95°C, from about 75°C to 95°C, from about 80°C to 95°C, from about 85°C to 95°C, or from about 90°C to 95°C.

15. The process of any one of claims 10 to 14, wherein the slurry of lanifibranor is

maintained in step d) at a temperature from about 15°C to 95°C, from about 20°C to 95°C, from about 25°C to 95°C, from about 30°C to 95°C, from about 35°C to 95°C, from about 40°C to 95°C, from about 45°C to 95°C, from about 50°C to about 95°C, from about 55°C to about 95°C, from about 60°C to 95°C, from about 65°C to 95°C, from about 70°C to 95°C, from about 75°C to 95°C, from about 80°C to 95°C, from about 85°C to 95°C or from about 90°C to 95°C .

16. The process of any one of claims 10 to 15, wherein step d) is carried out for a period of time of about 15 minutes to about 72 hours, such as for example about 30 minutes to about 48 hours, about 1 hour to about 30 hours, about 1 hour to 25 hours, about 1 hour to 20 hours, about 1 hours to 15 hours.

17. The process of any one of claims 10 to 16, wherein the temperature in step d) is identical to the temperature in step c).

18. The process of any one of claims 10 to 17, wherein no seeds of crystalline form beta of lanifibranor are added during the reaction.

19. The process of any one of claims 10 to 17, wherein seeds of crystalline form beta of lanifibranor are added during step c) and/or step d).

20. The process of any one of claims 10 to 19, wherein steps c) and d) are repeated from one to ten times.

21. A crystalline form beta of lanifibranor obtained by the process of any one of claims 10 to 20, wherein said crystalline form has an angle of repose comprised between about 33° and about 37°.

22. The crystalline form beta of lanifibranor of claim 21, which has a compressibility index of about 16 to about 25, and a Hausner ratio of about 1.19 to about 1.34.

23. A pharmaceutical composition comprising the crystalline form beta of lanifibranor of any of claims 21 to 22 and a pharmaceutically acceptable carrier or excipient.

24. Use of the crystalline form beta of lanifibranor as defined in claim 21 or claim 22, or of the pharmaceutical composition as defined in claim 23, in the manufacture of a medicament for the prevention and/or treatment of a liver disease.

25. The use according to claim 24, wherein the liver disease is selected among cirrhosis, liver fibrosis, liver steatosis, fatty liver disease, acute decompensation, acute on chronic liver failure, acute liver failure, decompensated cirrhosis, non-alcoholic fatty liver disease, non-alcoholic steatohepatitis, metabolic-associated fatty liver disease, metabolic-associated steatohepatitis, liver cirrhosis, non-alcoholic steatohepatitis with moderate to advanced liver fibrosis, metabolic-associated steatohepatitis with moderate to advanced liver fibrosis, noncirrhotic non-alcoholic steatohepatitis with moderate to advanced liver fibrosis, noncirrhotic metabolic-associated steatohepatitis with moderate to advanced liver fibrosis.

26. Use of the crystalline form beta of lanifibranor as defined in claim 21 or claim 22, or of the pharmaceutical composition as defined in claim 23, in the manufacture of a medicament for the reversion of decompensated cirrhosis to compensated cirrhosis.

27. Use of the crystalline form beta of lanifibranor as defined in claim 21 or claim 22, or of the pharmaceutical composition as defined in claim 23, in the manufacture of a medicament for treating a cirrhotic subject at risk of progressing from compensated stage to decompensated stage.