CLAIMS

1. ~~A~~ Use of a combination product~~,~~, comprising:

(i) cenicriviroc (CVC) or a pharmaceutically acceptable salt or solvate thereof; and

(ii) Elafibranor or a pharmaceutically acceptable salt thereof;

in the preparation of a medicament for the treatment of a diseases selected from liver fibrosis and cholestatic diseases.

2. ~~The combination product~~Use according to claim 1, wherein the combination product is a composition comprising components (i) and (ii) and a pharmaceutically acceptable carrier.

3. ~~The combination product~~ Useaccording to claim 1 , wherein the combination product is a kit of parts comprising components (i) and (ii), for sequential, separate or simultaneous use.

4. ~~The combination product~~Use according to any one of claims 1 to 3, wherein components (i) and (ii) are formulated in an injectable suspension, a gel, an oil, a pill, a tablet, a suppository, a powder, a capsule, an aerosol, an ointment, a cream, a patch, or means of galenic forms for a prolonged and/or slow release.

5. ~~The combination product~~Use according to any one of claims 1 to 4, further comprising at least one therapeutically active agent with known antifibrotic activity selected from :

. pirfenidone ~~or~~;

. receptor tyrosine kinase inhibitors (RTKIs) such as Nintedanib or Sorafenib; ~~,~~

. angiotensin II (AT1) receptor blockers;

. CTGF inhibitor;

. activators of the latent TGFβ complex such as MMP2, MMP9, THBS1 or cell-surface integrins;

. TGFβ receptors type I (TGFBRI) or type II (TGFBRII) and their ligands such as TGFβ, Activin, inhibin, Nodal, anti-Müllerian hormone, GDFs or BMPs, auxiliary co-receptors (also known as type III receptors); and

. components of the SMAD-dependent canonical pathway including regulatory or inhibitory SMAD proteins, or members of the SMAD-independent or non-canonical pathways including various branches of MAPK signaling, TAK1, Rho-like GTPase signaling pathways, phosphatidylinositol-3 kinase/AKT pathways, TGFβ-induced EMT process, or canonical and

non-canonical Hedgehog signaling pathways including Hh ligands or target genes, or any members of the WNT, or Notch pathways which are susceptible to influence TGFβ.

6. ~~The combination product~~Use according to any one of claims 1 to 5, further comprising at least one therapeutically active agent selected from JAK/STAT inhibitors, anti-inflammatory and/or immunosuppressant agents.

7. ~~The combination product~~Use according to claim 6, wherein the therapeutically active agent is selected from glucocorticoids, NSAIDS, cyclophosphamide, nitrosoureas, folic acid analogs, purine analogs, pyrimidine analogs, methotrexate, azathioprine, mercaptopurine, ciclosporin,myriocin, tacrolimus, sirolimus, mycophenolic acid derivatives, fingolimod, sphingosine-1-phosphate receptor modulators, monoclonal and/or polyclonal antibodies against such targets as proinflammatory cytokines and proinflammatory cytokine receptors, T-cell receptor and integrins.

~~8. The combination product according to any one of claims 1 to 7, for use as a medicament.~~

~~9. The combination product according to any one of claims 1 to 8, for use in a method for treating an inflammatory, metabolic, fibrotic and cholestatic disease.~~

~~10. The combination product for use according to claim 9, wherein the fibrotic disorder is selected in the group consisting of liver, kidney, skin, epidermis, endodermis, muscle, tendon, cartilage, heart, pancreas, lung, uterus, nervous system, testis, ovary, adrenal gland, artery, vein, colon, intestine (e.g. small intestine), biliary tract, soft tissue (e.g. mediastinum or retroperitoneum), bone marrow, joint and stomach fibrosis.~~

~~11. The combination product for use according to claim 9 or 10, wherein the fibrotic disorder is selected in the group consisting of liver, gut, lung, heart, kidney, muscle, skin, soft tissue, bone marrow, intestinal, and joint fibrosis.~~

~~12~~8. ~~The combination product for u~~Use according to any one of claims ~~9~~ 1 to ~~11~~7, wherein the disease is selected in the group consisting of ~~metabolic liver diseases, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), drug-induced liver diseases, alcohol-induced liver diseases, infectious agent induced liver diseases, inflammatory liver diseases,~~

immune system dysfunction-mediated liver diseases, dyslipidemia, cardiovascular diseases, restenosis, syndrome X, metabolic syndrome, diabetes, obesity, hypertension, chronic cholangiopathies such as Primary Sclerosing Cholangitis (PSC), Primary Biliary Cholangitis (PBC), biliary atresia, familial intrahepatic cholestasis type 3 (PFIC3), inflammatory bowel diseases, Crohn's disease, ulcerative colitis, keloid, old myocardial infarction, scleroderma/systemic sclerosis, inflammatory diseases, neurodegenerative diseases, cancers, liver cancer, hepatocallular carcinoma, gastrointestinal cancer, gastric cancer, meningioma associated with neurofibromatosis, pancreatic neuroendocrine tumors, pancreatic exocrine tumors, leukemia, myeloproliferative/myelodisplastic diseases, mastocytosis, dermatofibrosarcoma, solid tumors including breast, lung, thyroid or colorectal cancer, a prostate cancer, liver fibrosis or cirrhosis of any origin, metabolic disease-induced liver fibrosis or cirrhosis, NAFLD-induced fibrosis or cirrhosis, NASH-induced fibrosis or cirrhosis, alcohol-induced liver fibrosis or cirrhosis, drug-induced liver fibrosis or cirrhosis, infectious agent-induced liver fibrosis or cirrhosis, parasite infection-induced liver fibrosis or cirrhosis, bacterial infection-induced liver fibrosis or cirrhosis, viral infection-induced fibrosis or cirrhosis, HBV-infection induced liver fibrosis or cirrhosis, HCV-infection induced liver fibrosis or cirrhosis, HIV-infection induced liver fibrosis or cirrhosis, dual HCV and HIV-infection induced liver fibrosis or cirrhosis, radiation- or chemotherapy-induced fibrosis or cirrhosis, biliary tract fibrosis, and liver fibrosis or cirrhosis due to any chronic cholestatic disease, gut fibrosis of any etiology, Crohn's disease-induced fibrosis, ulcerative colitis-induced fibrosis, intestine (e.g. small intestine) fibrosis, colon fibrosis, stomach fibrosis, skin fibrosis, epidermis fibrosis, endodermis fibrosis, skin fibrosis due to scleroderma/systemic sclerosis, lung fibrosis, lung fibrosis consecutive to chronic inflammatory airway diseases, such as COPD, asthma, emphysema, smoker's lung,tuberculosis, pulmonary fibrosis, idiopathic pulmonary fibrosis (IPF), heart fibrosis, kidney fibrosis, nephrogenic systemic fibrosis, muscle fibrosis, soft tissue (e.g. mediastinum or retroperitoneum) fibrosis, bone marrow fibrosis, joint fibrosis, tendon fibrosis, cartilage fibrosis, pancreas fibrosis, uterus fibrosis, nervous system fibrosis, testis fibrosis, ovary fibrosis, adrenal gland fibrosis, artery fibrosis, vein fibrosis, eye fibrosis, endomyocardial fibrosis, mediastinal fibrosis, myelofibrosis, retroperitoneal fibrosis, progressive massive fibrosis (a complication of coal workers' pneumoconiosis), proliferative fibrosis, neoplastic fibrosis, peri-implantational fibrosis and asbestosis, arthrofibrosis, adhesive capsulitis.

139. The combination product for use according to any one of claims 9 1 to 118, wherein the disease is selected in the group consisting of, the disease is selected in the group consisting

of metabolic liver diseases, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), drug-induced liver diseases, alcohol-induced liver diseases, infectious agent induced liver diseases, inflammatory liver diseases, immune system dysfunction-mediated liver diseases, dyslipidemia, cardiovascular diseases, restenosis, syndrome X, metabolic syndrome, diabetes, obesity, hypertension, chronic cholangiopathies such as Primary Sclerosing Cholangitis (PSC), Primary Biliary Cholangitis (PBC), biliary atresia, familial intrahepatic cholestasis type 3 (PFIC3), inflammatory bowel diseases, Crohn's disease, ulcerative colitis, liver cancer, hepatocallular carcinoma, gastrointestinal cancer, gastric cancer, colorectal cancer, metabolic disease-induced liver fibrosis or cirrhosis, NAFLD-induced fibrosis or cirrhosis, NASH-induced fibrosis or cirrhosis, alcohol-induced liver fibrosis or cirrhosis, drug-induced liver fibrosis or cirrhosis, infectious agent-induced liver fibrosis or cirrhosis, parasite infection-induced liver fibrosis or cirrhosis, bacterial infection-induced liver fibrosis or cirrhosis, viral infection-induced fibrosis or cirrhosis, HBV-infection induced liver fibrosis or cirrhosis, HCV-infection induced liver fibrosis or cirrhosis, HIV-infection induced liver fibrosis or cirrhosis, dual HCV and HIV-infection induced liver fibrosis or cirrhosis, radiation- or chemotherapy-induced fibrosis or cirrhosis, biliary tract fibrosis, liver fibrosis or cirrhosis due to any chronic cholestatic disease, gut fibrosis of any etiology, Crohn's disease-induced fibrosis, ulcerative colitis-induced fibrosis, intestine (e.g. small intestine) fibrosis, colon fibrosis, stomach fibrosis, lung fibrosis, lung fibrosis consecutive to chronic inflammatory airway diseases, such as COPD, asthma, emphysema, smoker's lung, tuberculosis, pulmonary fibrosis, idiopathic pulmonary fibrosis (IPF).

14. Use of:

(i) cenicriviroc (CVC) or apharmaceutically acceptable salt or solvate thereof, and

(ii) Elafibranor or a pharmaceutically acceptable salt thereof

in the preparation of a medicament for the treatment of an inflammatory, metabolic, fibrotic and cholestatic disease.

15. The use according to claim 14, further comprising at least one therapeutically active agent with known antifibrotic activity selected from pirfenidone;
receptor tyrosine kinase inhibitors (RTKIs) such as Nintedanib or Sorafenib;
angiotensin II (AT1) receptor blockers;
CTGF inhibitor;
activators of the latent TGFβ complex such as MMP2, MMP9, THBS1 or cell-surface integrins;

~~TGFβ receptors type I (TGFBRI) or type II (TGFBRII) and their ligands such as TGFβ, Activin, inhibin, Nodal, anti-Müllerian hormone, GDFs or BMPs, auxiliary co-receptors (also known as type III receptors);~~

~~components of the SMAD-dependent canonical pathway including regulatory or inhibitory SMAD proteins, or members of the SMAD-independent or non-canonical pathways including various branches of MAPK signaling, TAK1, Rho-like GTPase signaling pathways, phosphatidylinositol-3-kinase/AKT pathways, TGFβ-induced EMT process, or canonical and non-canonical Hedgehog signaling pathways including Hh ligands or target genes, or any members of the WNT, or Notch pathways which are susceptible to influence TGFβ.~~

~~16. The use according to any one of claims 14 to 15, further comprising at least one therapeutically active agent selected from JAK/STAT inhibitors, anti-inflammatory and/or immunosuppressant agents.~~

~~17. Use of the combination product according to any one of claims 1 to 7, in the preparation of a combination medicament for the treatment of an inflammatory, metabolic, fibrotic and cholestatic disease.~~

~~18. The use according to any one of claims 14 to 17, wherein the fibrotic disorder is selected in the group consisting of liver, kidney, skin, epidermis, endodermis, muscle, tendon, cartilage, heart, pancreas, lung, uterus, nervous system, testis, ovary, adrenal gland, artery, vein, colon, intestine (e.g. small intestine), biliary tract, soft tissue (e.g. mediastinum or retroperitoneum), bone marrow, joint and stomach fibrosis.~~

~~19. The use according to any one of claims 14 to 18, wherein the fibrotic disorder is selected in the group consisting of liver, gut, lung, heart, kidney, muscle, skin, soft tissue, bone marrow, intestinal, and joint fibrosis.~~

~~20. The use according to any one of claims 14 to 19, wherein the disease is selected from the group consisting of metabolic liver diseases, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), drug-induced liver diseases, alcohol-induced liver diseases, infectious agent induced liver diseases, inflammatory liver diseases, immune system dysfunction-mediated liver diseases, dyslipidemia, cardiovascular diseases, restenosis, syndrome X, metabolic syndrome, diabetes, obesity, hypertension, chronic cholangiopathies~~

such as Primary Sclerosing Cholangitis (PSC), Primary Biliary Cholangitis (PBC), biliary atresia, familial intrahepatic cholestasis type 3 (PFIC3), inflammatory bowel diseases, Crohn's disease, ulcerative colitis, keloid, old myocardial infarction, scleroderma/systemic sclerosis, inflammatory diseases, neurodegenerative diseases, cancers, liver cancer, hepatocallular carcinoma, gastrointestinal cancer, gastric cancer, meningioma associated with neurofibromatosis, pancreatic neuroendocrine tumors, pancreatic exocrine tumors, leukemia, myeloproliferative/myelodisplastic diseases, mastocytosis, dermatofibrosarcoma, solid tumors including breast, lung, thyroid or colorectal cancer, a prostate cancer, liver fibrosis or cirrhosis of any origin, metabolic disease-induced liver fibrosis or cirrhosis, NAFLD-induced fibrosis or cirrhosis, NASH-induced fibrosis or cirrhosis, alcohol-induced liver fibrosis or cirrhosis, drug-induced liver fibrosis or cirrhosis, infectious agent-induced liver fibrosis or cirrhosis, parasite infection-induced liver fibrosis or cirrhosis, bacterial infection-induced liver fibrosis or cirrhosis, viral infection-induced fibrosis or cirrhosis, HBV-infection induced liver fibrosis or cirrhosis, HCV-infection induced liver fibrosis or cirrhosis, HIV-infection induced liver fibrosis or cirrhosis, dual HCV and HIV-infection induced liver fibrosis or cirrhosis, radiation- or chemotherapy-induced fibrosis or cirrhosis, biliary tract fibrosis, liver fibrosis or cirrhosis due to any chronic cholestatic disease, gut fibrosis of any etiology, Crohn's disease-induced fibrosis, ulcerative colitis-induced fibrosis, intestine (e.g. small intestine) fibrosis, colon fibrosis, stomach fibrosis, skin fibrosis, epidermis fibrosis, endodermis fibrosis, skin fibrosis due to scleroderma/systemic sclerosis, lung fibrosis, lung fibrosis consecutive to chronic inflammatory airway diseases, such as COPD, asthma, emphysema, smoker’s lung,tuberculosis, pulmonary fibrosis, idiopathic pulmonary fibrosis (IPF), heart fibrosis, kidney fibrosis, nephrogenic systemic fibrosis, muscle fibrosis, soft tissue (e.g. mediastinum or retroperitoneum) fibrosis, bone marrow fibrosis, joint fibrosis, tendon fibrosis, cartilage fibrosis, pancreas fibrosis, uterus fibrosis, nervous system fibrosis, testis fibrosis, ovary fibrosis, adrenal gland fibrosis, artery fibrosis, vein fibrosis, eye fibrosis, endomyocardial fibrosis, mediastinal fibrosis, myelofibrosis, retroperitoneal fibrosis, progressive massive fibrosis (a complication of coal workers' pneumoconiosis), proliferative fibrosis, neoplastic fibrosis, peri-implantational fibrosis and asbestosis, arthrofibrosis, adhesive capsulitis.

21. The use according to any one of claims 14 to 19, wherein the disease is selected from the group consisting of metabolic liver diseases, non-alcoholic fatty liver disease (NAFLD), non-alcoholic steatohepatitis (NASH), drug-induced liver diseases, alcohol-induced liver diseases, infectious agent induced liver diseases, inflammatory liver diseases, immune system

dysfunction-mediated liver diseases, dyslipidemia, cardiovascular diseases, restenosis, syndrome X, metabolic syndrome, diabetes, obesity, hypertension, chronic cholangiopathies such as Primary Sclerosing Cholangitis (PSC), Primary Biliary Cholangitis (PBC), biliary atresia, familial intrahepatic cholestasis type 3 (PFIC3), inflammatory bowel diseases, Crohn's disease, ulcerative colitis, liver cancer, hepatocallular carcinoma, gastrointestinal cancer, gastric cancer, colorectal cancer, metabolic disease-induced liver fibrosis or cirrhosis, NAFLD-induced fibrosis or cirrhosis, NASH-induced fibrosis or cirrhosis, alcohol-induced liver fibrosis or cirrhosis, drug-induced liver fibrosis or cirrhosis, infectious agent-induced liver fibrosis or cirrhosis, parasite infection-induced liver fibrosis or cirrhosis, bacterial infection-induced liver fibrosis or cirrhosis, viral infection-induced fibrosis or cirrhosis, HBV-infection induced liver fibrosis or cirrhosis, HCV-infection induced liver fibrosis or cirrhosis, HIV-infection induced liver fibrosis or cirrhosis, dual HCV and HIV-infection induced liver fibrosis or cirrhosis, radiation- or chemotherapy-induced fibrosis or cirrhosis, biliary tract fibrosis, liver fibrosis or cirrhosis due to any chronic cholestatic disease, gut fibrosis of any etiology, Crohn's disease-induced fibrosis, ulcerative colitis-induced fibrosis, intestine (e.g. small intestine) fibrosis, colon fibrosis, stomach fibrosis, lung fibrosis, lung fibrosis consecutive to chronic inflammatory airway diseases, such as COPD, asthma, emphysema, smoker’s lung, tuberculosis, pulmonary fibrosis, idiopathic pulmonary fibrosis (IPF).