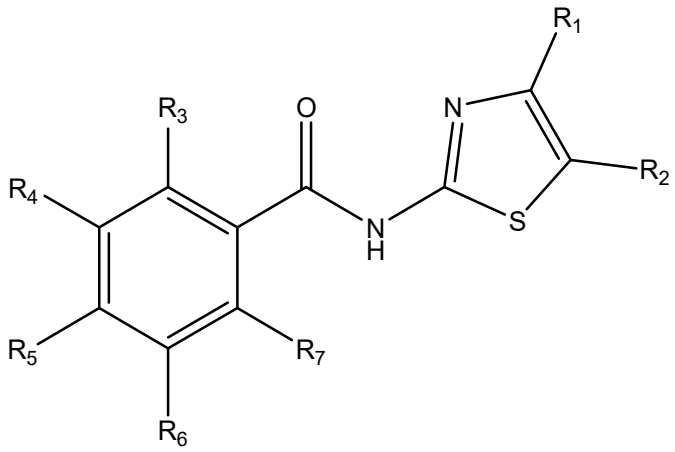
CLAIMS

1. A combination product comprising:

(i) a compound

of formula (I):



(I)

or a pharmaceutical acceptable salt thereof, in which:

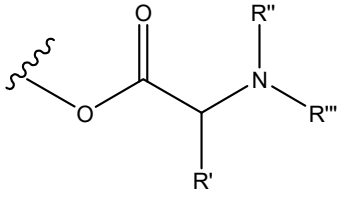
R1 represents a hydrogen atom (H), a deuterium atom (D), a halogen atom, a (C6-C14)aryl group, a heterocyclic group, a (C3-C14)cycloalkyl group, a (C1-C6)alkyl group, a sulfonyl group, a sulfoxyde group, a (C1-C6)alkylcarbonyl group, a (C1-C6)alkyloxy, a carboxylic group, a carboxylate group, a nitro group (NO2), an amino group (NH2), a (C1-C6)alkylamino group, an amido group, a (C1-C6)alkylamido group, a (C1-C6)dialkylamido group.

R2 represents a hydrogen atom, a deuterium atom, a NO2 group, a (C6-C14)aryl group, a heterocyclic group, a halogen atom, a (C1-C6)alkyl group, a (C3-C14)cycloalkyl group, a (C2-C6)alkynyl group, a (C1-C6)alkyloxy group, a (C1-C6)alkylthio group, a (C1-C6)alkylcarbonyl group, a (C1-C6)alkylcarbonylamino group, a (C6-C14)arylcarbonylamino group, a carboxylic or carboxylate group, an amido group, a (C1-C6)alkylamido group, a (C1-C6)dialkylamido group, a NH_2 group, a (C1-C6)alkylamino group,

or R1 and R2, together with the carbon atoms to which they are attached, form a substituted or unsubstituted 5- to 8- membered cycloalkyl, heterocyclic or aryl group,

R3, R4, R5, R6, and R7, identical or different, represent a hydrogen atom, a deuterium atom, a halogen atom, a hydroxyl group, a (C1-C6)alkylcarbonyl group, an (C1-C6)alkyl group, an (C1-C6)alkyloxy group, an (C1-C6)alkylthio group, an (C1-C6)alkylcarbonyloxy group, an (C6-C14)aryloxy group, a (C6-C14)aryl group, a heterocyclic group, a (C3-C14)cycloalkyl group, a NO2 group, a sulfonylaminoalkyle group, an NH2 group, an amino(C1-C6)alkyl group, an (C1-C6)alkylcarbonylamino group, a carboxylic group, a carboxylate group, or a R9 group;

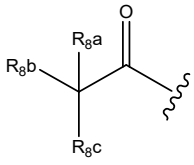
R9 represents a O-R8 group or an amino-acid selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine, or a moiety of formula (A):



(A)

wherein R' represents an (C1-C6)alkyl group, an (C2-C6)alkenyl group, an (C2-C6)alkynyl group, a (C3-C14)cycloalkyl group, (C3-C14)cycloalkylalkyl group, a (C3-C14)cycloalkyl(C2-C6)alkenyl group, a (C3-C14)cycloalkenyl group, a (C3-C14)cycloalkenyl(C1-C6)alkyl group, a (C3-C14)cycloalkenyl(C2-C6)alkenyl group, a (C3-C14)cycloalkenyl(C2-C6)alkynyl group; R'' and R''', independently, represent hydrogen atom, an (C1-C6)alkyl group, or a nitrogen protecting group;

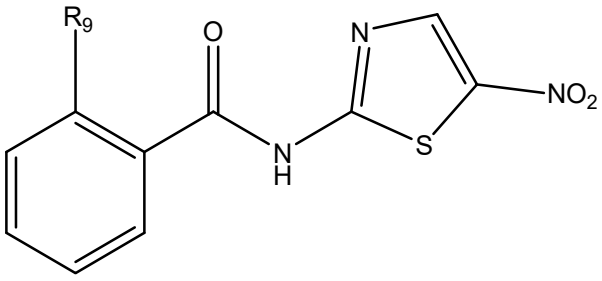
R8 represents a hydrogen atom, a deuterium atom, a glucuronidyl group, or a



group wherein, R8a, R8b and R8c, identical or different, represent a hydrogen atom or a deuterium atom; and

(ii) a compound selected in the group consisting of GS-0976, GS-4997 (Selonsertib), GKT-831 (formerly GKT137831), KD-025, Cenicriviroc (CVC), Aramchol, and Tropifexor (LJN-452) or a pharmaceutically acceptable salt thereof.

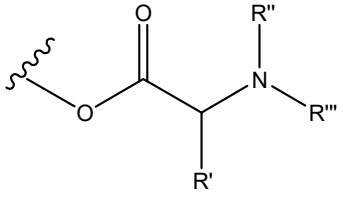
2. The combination product of claim 1, wherein component (i) is a compound of formula (II):



(II)

or a pharmaceutically acceptable salt thereof, in which R9 represents a hydrogen atom, a deuterium atom, a O-R8 group, or an aminoacid selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine,

isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine, or a moiety of formula (A):



(A);

wherein R' represents an (C1-C6)alkyl group, an (C2-C6)alkenyl group, an (C2-C6)alkynyl group, a (C3-C14)cycloalkyl group, (C3-C14)cycloalkyl(C1-C6)alkyl group, a (C3-C14)cycloalkyl(C1-C6)alkenyl group, a (C3-C14)cycloalkenyl group, a (C3-C14)cycloakenyl(C1-C6)alkyl group, a (C3-C14)cycloalkenyl(C2-C6)alkenyl group, a (C3-C14)cycloalkenyl(C2-C6)alkynyl group; R'' and R''', independently, represent a hydrogen atom, an (C1-C6)alkyl group, or a nitrogen protecting group
or a pharmaceutically acceptable salt thereof.

3. The combination product according to 1 or 2, wherein component (i) is selected from nitazoxanide, tizoxanide, [(5-nitro-1,3-thiazol-2-yl)carbamoyl]phenyl (d3)ethanoate, 2-[(5-nitro-1,3-thiazol-2-yl)carbamoyl]phenyl (d2) ethanoate, 2-[(5-nitro-1,3-thiazol-2-yl)carbamoyl]phenyl (d1) ethanoate, 2-(5-nitrothiazol-2-ylcarbamoyl)phenyl 2-amino-3,3-dimethylbutanoate, 2-(5-nitrothiazol-2-ylcarbamoyl)phenyl 2-amino-3-methylpentanoate, 2-(5-chlorothiazol-2-ylcarbamoyl)phenyl 2-amino-3,3-dimethylbutanoate, 2-(5-chlorothiazol-2-ylcarbamoyl)phenyl 2-amino-3-methylpentanoate or a pharmaceutically acceptable salt thereof.

4. The combination product according to any one of claims 1 to 3, wherein component (i) is nitazoxanide or a pharmaceutically acceptable salt thereof.

5. The combination product according to any one of claims 1 to 4, wherein the combination product is a composition comprising components (i) and (ii) and a pharmaceutically acceptable carrier.

6. A kit of parts comprising components (i) and (ii) as defined according to any one of claims 1 to 4, for sequential, separate or simultaneous use.

7. The combination product according to any one of claims 1 to 6, 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 oinment, a cream, a patch, or means of galenic forms for a prolonged and/or slow release.

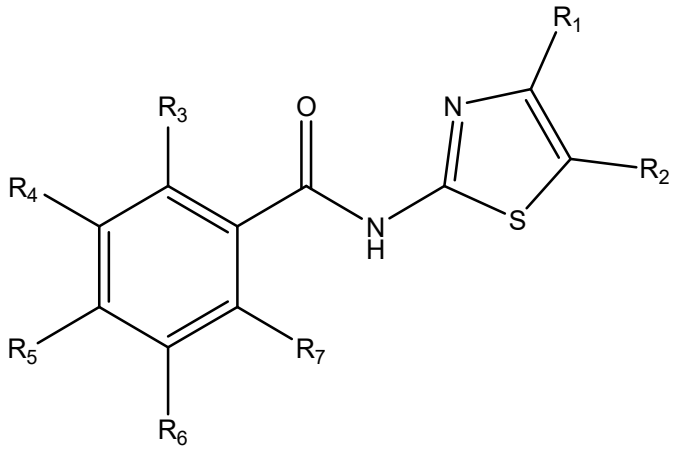
8. The combination product according to any one of claims 1 to 7, for use as a medicament.

9. The combination product according to any one of claims 1 to 7, for use in a method for treating a fibrotic disease.

10. The combination product for use according to claim 9, wherein the fibrotic disease is selected in the group consisting of liver, kidney, skin, epidermis, endodermis, muscle, tendon, cartilage, heart, pancreas, lung, uterus, nervous system, testis, penis, 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, in particular liver, gut, lung, heart, kidney, muscle, skin, soft tissue, bone marrow, intestinal, eye and joint fibrosis.

11. The combination product for use according to claim 9, wherein the fibrotic disease is selected in the group consisting of non-alcoholic steatohepatitis (NASH), pulmonary fibrosis, idiopathic pulmonary fibrosis, skin fibrosis, eye fibrosis (such as capsular fibrosis), endomyocardial fibrosis, mediastinal fibrosis, myelofibrosis, retroperitoneal fibrosis, progressive massive fibrosis (a complication of coal workers' pneumoconiosis), proliferative fibrosis, neoplastic fibrosis, lung fibrosis consecutive to chronic inflammatory airway disease (COPD, asthma, emphysema, smoker’s lung, tuberculosis), alcohol or drug-induced liver fibrosis, liver cirrhosis, infection-induced liver fibrosis, radiation or chemotherapeutic-induced fibrosis, nephrogenic systemic fibrosis, Crohn's disease, ulcerative colitis, keloïd, old myocardial infarction, scleroderma/systemic sclerosis, arthrofibrosis, some forms of adhesive capsulitis, chronic fibrosing cholangiopathies such as Primary Sclerosing Cholangitis (PSC) and Primary Biliary Cholangitis (PBC), biliary atresia, familial intrahepatic cholestasis type 3 (PFIC3), peri-implantational fibrosis and asbestosis

12. Use of a combination product comprising (i) a compound
of formula (I):



(I)

or a pharmaceutical acceptable salt thereof, in which:

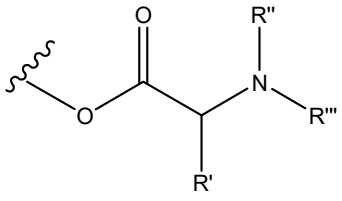
R1 represents a hydrogen atom (H), a deuterium atom (D), a halogen atom, a (C6-C14)aryl group, a heterocyclic group, a (C3-C14)cycloalkyl group, a (C1-C6)alkyl group, a sulfonyl group, a sulfoxyde group, a (C1-C6)alkylcarbonyl group, a (C1-C6)alkyloxy, a carboxylic group, a carboxylate group, a nitro group (NO2), an amino group (NH2), a (C1-C6)alkylamino group, an amido group, a (C1-C6)alkylamido group, a (C1-C6)dialkylamido group.

R2 represents a hydrogen atom, a deuterium atom, a NO2 group, a (C6-C14)aryl group, a heterocyclic group, a halogen atom, a (C1-C6)alkyl group, a (C3-C14)cycloalkyl group, a (C2-C6)alkynyl group, a (C1-C6)alkyloxy group, a (C1-C6)alkylthio group, a (C1-C6)alkylcarbonyl group, a (C1-C6)alkylcarbonylamino group, a (C6-C14)arylcarbonylamino group, a carboxylic or carboxylate group, an amido group, a (C1-C6)alkylamido group, a (C1-C6)dialkylamido group, a NH_2 group, a (C1-C6)alkylamino group,

or R1 and R2, together with the carbon atoms to which they are attached, form a substituted or unsubstituted 5- to 8- membered cycloalkyl, heterocyclic or aryl group,

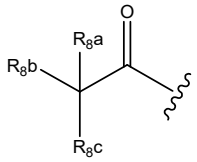
R3, R4, R5, R6, and R7, identical or different, represent a hydrogen atom, a deuterium atom, a halogen atom, a hydroxyl group, a (C1-C6)alkylcarbonyl group, an (C1-C6)alkyl group, an (C1-C6)alkyloxy group, an (C1-C6)alkylthio group, an (C1-C6)alkylcarbonyloxy group, an (C6-C14)aryloxy group, a (C6-C14)aryl group, a heterocyclic group, a (C3-C14)cycloalkyl group, a NO2 group, a sulfonylaminoalkyle group, an NH2 group, an amino(C1-C6)alkyl group, an (C1-C6)alkylcarbonylamino group, a carboxylic group, a carboxylate group, or a R9 group;

R9 represents a O-R8 group or an amino-acid selected from the group consisting of alanine, arginine, asparagine, aspartic acid, cysteine, glutamine, glutamic acid, glycine, histidine, isoleucine, leucine, lysine, methionine, phenylalanine, proline, serine, threonine, tryptophan, tyrosine, valine, or a moiety of formula (A):



(A)

wherein R' represents an (C1-C6)alkyl group, an (C2-C6)alkenyl group, an (C2-C6)alkynyl group, a (C3-C14)cycloalkyl group, (C3-C14)cycloalkylalkyl group, a (C3-C14)cycloalkyl(C2-C6)alkenyl group, a (C3-C14)cycloalkenyl group, a (C3-C14)cycloalkenyl(C1-C6)alkyl group, a (C3-C14)cycloalkenyl(C2-C6)alkenyl group, a (C3-C14)cycloalkenyl(C2-C6)alkynyl group; R'' and R''', independently, represent hydrogen atom, an (C1-C6)alkyl group, or a nitrogen protecting group;



R8 represents a hydrogen atom, a deuterium atom, a glucuronidyl group, or a group wherein, R8a, R8b and R8c, identical or different, represent a hydrogen atom or a deuterium atom; and

(ii) GS-0976, GS-4997 (Selonsertib), GKT-831 (formerly GKT137831), KD-025, Cenicriviroc (CVC), Aramchol, and Tropifexor (LJN-452) or a pharmaceutically acceptable salt thereof.