

A further aim of the present invention is to provide starting and/or intermediate compounds suitable in methods for the synthesis of the new compounds.

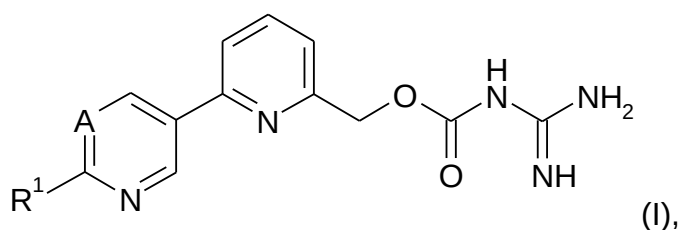
Further aims of the present invention become apparent to the one skilled in the art by the description hereinbefore and in the following and by the examples.

### Object of the Invention

Within the scope of the present invention it has now surprisingly been found that the new compounds of general formula (I) as described hereinafter exhibit an inhibiting activity with regard to AOC3.

According to the present disclosure it has been found that the new compounds of general formula (I) as described hereinafter exhibit an inhibiting activity with regard to AOC3.

The present disclosure provides a compound of general formula



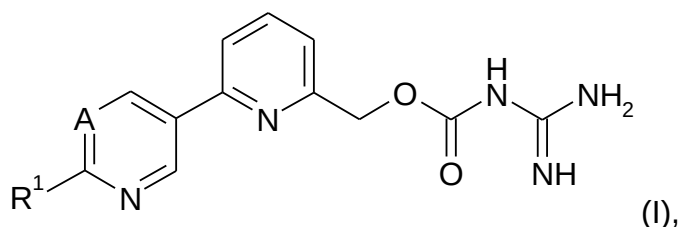
wherein

A is selected from the group A-G1 consisting of: N and CH;

R<sup>1</sup> is selected from the group R<sup>1</sup>-G1 consisting of:  
C<sub>1-6</sub>-alkyl, C<sub>3-6</sub>-cycloalkyl, heterocyclyl, -O-R<sup>2</sup>, -S-R<sup>2</sup>, -NH-R<sup>2</sup> and -N(R<sup>2</sup>)<sub>2</sub>,

wherein each R<sup>2</sup> is independently selected from the group R<sup>2</sup>-G1 consisting of C<sub>1-6</sub>-alkyl, C<sub>3-6</sub>-cycloalkyl, heterocyclyl, -(C<sub>1-2</sub>-alkyl)-(C<sub>3-6</sub>-

In one aspect the present disclosure relates to a compound of formula (I)



5 wherein

A is N or CH;

10 R<sup>1</sup> is selected from the group consisting of C<sub>1-6</sub>-alkyl, C<sub>3-6</sub>-cycloalkyl, heterocyclyl, -O-R<sup>2</sup>, -S-R<sup>2</sup>, -NH-R<sup>2</sup> and -N(R<sup>2</sup>)<sub>2</sub>,

wherein each R<sup>2</sup> is independently selected from the group consisting of C<sub>1-6</sub>-alkyl, C<sub>3-6</sub>-cycloalkyl, heterocyclyl, -(C<sub>1-2</sub>-alkyl)-(C<sub>3-6</sub>-cycloalkyl), -(C<sub>1-2</sub>-alkyl)-heterocyclyl, -(C<sub>1-2</sub>-alkyl)-aryl, -(C<sub>1-2</sub>-alkyl)-heteroaryl and -(C<sub>1-2</sub>-alkyl)-C≡CH;

15 wherein each heterocyclyl of R<sup>1</sup> and R<sup>2</sup> is a 4- to 7-membered saturated carbocyclic group, in which 1 or 2 CH<sub>2</sub>-moieties are independently of each other replaced by an atom or group selected from the group consisting of NH, O, S, -S(=O)-, -S(=O)<sub>2</sub>- and -C(=O)-; and

20 wherein each aryl is selected from the group consisting of phenyl and naphthyl; and

25 wherein each heteroaryl is a 5- or 6-membered heteroaromatic ring which contains 1, 2 or 3 heteroatoms independently selected from the group consisting of =N-, -NH-, -O- and -S-, wherein in heteroaromatic groups containing a -CH=N- unit, this group is optionally replaced by -NH-C(=O)-; and

wherein each of the alkyl, cycloalkyl, heterocyclyl, aryl and heteroaryl groups of R<sup>1</sup> and R<sup>2</sup> is optionally independently substituted with one or more substituents independently selected from the group consisting of F, Cl, CN, OH, C<sub>1-3</sub>-alkyl, -O-(C<sub>1-3</sub>-alkyl), -C(=O)-(C<sub>1-3</sub>-alkyl) and -C(=O)-(C<sub>3-7</sub>-cycloalkyl);

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wherein each of the above-mentioned alkyl groups may be linear or branched and is optionally substituted by one or more F;

or a salt thereof.

10

The present disclosure also relates to processes for preparing a compound of general formula (I) and to new intermediate compounds in these processes.

5 The disclosure also relates to a salt of the compounds of general formula (I) according to this invention, in particular to a pharmaceutically acceptable salt thereof. In another aspect the present disclosure relates to a pharmaceutically acceptable salt of a compound as defined herein.

10 In a further aspect this disclosure relates to a pharmaceutical composition, comprising one or more compounds of general formula (I) or one or more pharmaceutically acceptable salts thereof according to the disclosure, optionally together with one or more inert carriers and/or diluents.

15 This disclosure also relates to a method for treating diseases or conditions which are mediated by inhibiting the activity of AOC3 in a patient in need thereof characterized in that a compound of general formula (I) or a pharmaceutically acceptable salt thereof is administered to the patient.

20 According to the disclosure, there is provided a method for treating NASH (non-alcoholic steatohepatitis), pulmonary fibrosis, retinopathy or nephropathy in a patient in need thereof characterized in that a compound of general formula (I) or a pharmaceutically acceptable salt thereof is administered to the patient.

25 According to the disclosure, there is provided the use of a compound of the general formula (I) or a pharmaceutically acceptable salt thereof for the manufacture of a medicament for a therapeutic method as described above or hereinafter. According to another aspect the present disclosure relates to use of a compound as defined herein or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of NASH (non-alcoholic steatohepatitis), pulmonary  
30 fibrosis, retinopathy, nephropathy, chronic obstructive pulmonary disease (COPD) or diabetic retinopathy.

According to the disclosure, there is provided a compound of the general formula (I) or a pharmaceutically acceptable salt thereof for use in a therapeutic method as described above or hereinafter. According to another aspect the present disclosure relates to the compound as defined herein or a pharmaceutically acceptable salt thereof for use as a medicament. According to another aspect the present disclosure relates to the compound as defined herein or a pharmaceutically acceptable salt thereof for use in the treatment of NASH (non-alcoholic steatohepatitis), pulmonary fibrosis, retinopathy, nephropathy or chronic obstructive pulmonary disease (COPD).

This disclosure also relates to a method for treating a disease or condition mediated by the inhibition of AOC3 in a patient that includes the step of administering to the patient in need of such treatment a therapeutically effective amount of a compound of the general formula (I) or a pharmaceutically acceptable salt thereof in combination  
5 with a therapeutically effective amount of one or more additional therapeutic agents.

This disclosure also relates to a use of a compound of the general formula (I) or a pharmaceutically acceptable salt thereof in combination with one or more additional therapeutic agents for the treatment or prevention of diseases or conditions which  
10 are mediated by the inhibition of AOC3.

In a further aspect this disclosure relates to a pharmaceutical composition which comprises a compound according to general formula (I) or a pharmaceutically acceptable salt thereof and one or more additional therapeutic agents, optionally  
15 together with one or more inert carriers and/or diluents.

Other aspects of the disclosure become apparent to the one skilled in the art from the specification and the experimental part as described hereinbefore and hereinafter.

## 20 **Detailed Description**

Unless otherwise stated, the groups, residues, and substituents, particularly A, R<sup>1</sup> and R<sup>2</sup>, are defined as above and hereinafter. If residues, substituents or groups occur several times in a compound, as for example R<sup>2</sup>, they may have the same or different meanings. Some preferred meanings of individual groups and substituents  
25 of the compounds according to the invention will be given hereinafter. Any and each of these definitions may be combined with each other.

### **A:**

#### **A-G1:**

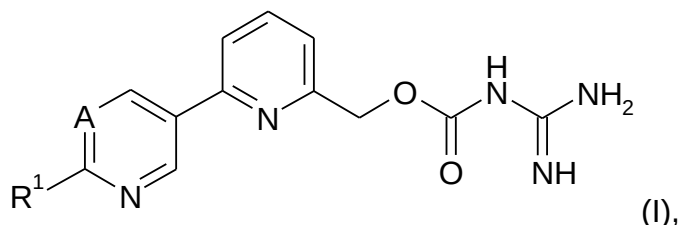
30 The group A is preferably selected from the group A-G1 as defined above.

#### **A-G2:**

## Claims

1. A compound of formula (I)

5



wherein

A is N or CH;

10

R<sup>1</sup> is selected from the group consisting of C<sub>1-6</sub>-alkyl, C<sub>3-6</sub>-cycloalkyl, heterocyclyl, -O-R<sup>2</sup>, -S-R<sup>2</sup>, -NH-R<sup>2</sup> and -N(R<sup>2</sup>)<sub>2</sub>,

15

wherein each R<sup>2</sup> is independently selected from the group consisting of C<sub>1-6</sub>-alkyl, C<sub>3-6</sub>-cycloalkyl, heterocyclyl, -(C<sub>1-2</sub>-alkyl)-(C<sub>3-6</sub>-cycloalkyl), -(C<sub>1-2</sub>-alkyl)-heterocyclyl, -(C<sub>1-2</sub>-alkyl)-aryl, -(C<sub>1-2</sub>-alkyl)-heteroaryl and -(C<sub>1-2</sub>-alkyl)-C≡CH;

20

wherein each heterocyclyl of R<sup>1</sup> and R<sup>2</sup> is a 4- to 7-membered saturated carbocyclic group, in which 1 or 2 CH<sub>2</sub>-moieties are independently of each other replaced by an atom or group selected from the group consisting of NH, O, S, -S(=O)-, -S(=O)<sub>2</sub>- and -C(=O)-; and

25

wherein each aryl is selected from the group consisting of phenyl and naphthyl; and

wherein each heteroaryl is a 5- or 6-membered heteroaromatic ring which contains 1, 2 or 3 heteroatoms independently selected

from the group consisting of =N-, -NH-, -O- and -S-, wherein in heteroaromatic groups containing a -CH=N- unit, this group is optionally replaced by -NH-C(=O)-; and

5

wherein each of the alkyl, cycloalkyl, heterocyclyl, aryl and heteroaryl groups of R<sup>1</sup> and R<sup>2</sup> is optionally independently substituted with one or more substituents independently selected from the group consisting of F, Cl, CN, OH, C<sub>1-3</sub>-alkyl, -O-(C<sub>1-3</sub>-alkyl),  
10 -C(=O)-(C<sub>1-3</sub>-alkyl) and -C(=O)-(C<sub>3-7</sub>-cycloalkyl);

wherein each of the above-mentioned alkyl groups may be linear or branched and is optionally substituted by one or more F;

15

or a salt thereof.

2. The compound of formula (I) according to claim 1, wherein R<sup>1</sup> is C<sub>1-4</sub>-alkyl, C<sub>3-5</sub>-cycloalkyl, heterocyclyl, -O-R<sup>2</sup>, -S-R<sup>2</sup>, -NH-R<sup>2</sup> or -N(R<sup>2</sup>)<sub>2</sub>;

20

wherein each heterocyclyl is a 4- to 6-membered saturated carbocyclic group, in which 1 or 2 CH<sub>2</sub>-moieties are replaced by a heteroatom selected from the group consisting of NH, O and S; and

25

wherein each of the alkyl, cycloalkyl and heterocyclyl groups is optionally independently substituted with 1 to 5 F and / or 1 to 3 substituents independently selected from the group consisting of Cl, CN, OH, C<sub>1-2</sub>-alkyl, -O-(C<sub>1-2</sub>-alkyl), -C(=O)-(C<sub>1-2</sub>-alkyl) and -C(=O)-(C<sub>3-4</sub>-cycloalkyl); and

30

wherein R<sup>2</sup> is as defined in claim 1;

or a salt thereof.

3. The compound of formula (I) according to claim 2, wherein R<sup>1</sup> is C<sub>1-2</sub>-alkyl, C<sub>3-4</sub>-cycloalkyl, heterocyclyl, -O-R<sup>2</sup>, -NH-R<sup>2</sup> or -N(R<sup>2</sup>)<sub>2</sub>;

wherein each heterocyclyl is selected from the group consisting of azetidiny, piperidiny, tetrahydrofurany, tetrahydropyrany and morpholiny; and

wherein each of the alkyl, cycloalkyl and heterocyclyl groups is optionally independently substituted with 1 to 3 F or one substituent selected from the group consisting of CN, OH, CH<sub>3</sub>, -O-CH<sub>3</sub>, -C(=O)-CH<sub>3</sub> and -C(=O)-cyclopropyl; and

wherein R<sup>2</sup> is as defined in claim 1;

or a salt thereof.

4. The compound of formula (I) according to any one of claims 1 to 3, wherein R<sup>2</sup> is selected from the group consisting of C<sub>1-4</sub>-alkyl, C<sub>3-5</sub>-cycloalkyl, heterocyclyl, -(C<sub>1-2</sub>-alkyl)-(C<sub>3-5</sub>-cycloalkyl), -(C<sub>1-2</sub>-alkyl)-heterocyclyl, -(C<sub>1-2</sub>-alkyl)-aryl, -(C<sub>1-2</sub>-alkyl)-heteroaryl and -(C<sub>1-2</sub>-alkyl)-C≡CH;

wherein each heterocyclyl is a 4- to 6-membered saturated carbocyclic group, in which 1 or 2 CH<sub>2</sub>-moieties are replaced by a heteroatom selected from the group consisting of NH, O and S; and

wherein each aryl is selected from the group consisting of phenyl and naphthyl; and

wherein each heteroaryl is a 5- or 6-membered heteroaromatic ring which contains 1, 2 or 3 heteroatoms independently selected from the group consisting of =N-, -NH-, -O- and -S-; and

wherein each of the alkyl, cycloalkyl, heterocyclyl, aryl and heteroaryl groups is optionally independently substituted with one or more substituents

independently selected from the group consisting of F, Cl, CN, OH, C<sub>1-2</sub>-alkyl, -O-(C<sub>1-2</sub>-alkyl), -C(=O)-(C<sub>1-2</sub>-alkyl) and -C(=O)-(C<sub>3-7</sub>-cycloalkyl);

or a salt thereof.

5

5. The compound of formula (I) according to any one of claims 1 to 3, wherein R<sup>2</sup> is selected from the group consisting of: C<sub>1-4</sub>-alkyl, -CH<sub>2</sub>-(C<sub>3-4</sub>-cycloalkyl), -CH<sub>2</sub>-heterocyclyl, -CH<sub>2</sub>-heteroaryl and -CH<sub>2</sub>-CH<sub>2</sub>-C≡CH;

10

wherein each heterocyclyl is selected from the group consisting of tetrahydrofuranyl and piperidinyl; and

wherein each heteroaryl is selected from the group consisting of isoxazolyl, thiazolyl and thiadiazolyl; and

15

wherein each of the alkyl, cycloalkyl, heterocyclyl, aryl and heteroaryl groups is optionally independently substituted with one or more substituents independently selected from the group consisting of F, CN, CH<sub>3</sub>, -OCH<sub>3</sub>, -C(=O)-CH<sub>3</sub> and -C(=O)-cyclopropyl;

20

or a salt thereof.

6. The compound of formula (I) according to any one of claims 1 to 5, wherein A is N;

25

or a salt thereof.

7. The compound of formula (I) according to claim 1, wherein

A is N; and

30

R<sup>1</sup> is selected from the group consisting of cyclopropyl, heterocyclyl and -O-R<sup>2</sup>;

wherein  $R^2$  is selected from the group consisting of  $C_{1-6}$ -alkyl,  $-(C_{1-2}\text{-alkyl})-(C_{3-6}\text{-cycloalkyl})$ ,  $-(C_{1-2}\text{-alkyl})\text{-heteroaryl}$  and  $-(C_{1-2}\text{-alkyl})\text{-C}\equiv\text{CH}$ ;

5 wherein each heterocyclyl is selected from the group consisting of azetidiny, piperidiny, tetrahydrofuranyl, tetrahydropyranyl and morpholinyl; and

10 wherein each heterocyclyl group is optionally independently substituted with one substituent selected from the group consisting of F, CN, OH,  $\text{CH}_3$  and  $-\text{O}-\text{CH}_3$ ; and

wherein each heteroaryl is selected from the group consisting of isoxazolyl, thiazolyl and thiadiazolyl; and

15 wherein each of the alkyl, cycloalkyl, heterocyclyl and heteroaryl groups is optionally independently substituted with one or more substituents independently selected from the group consisting of F, CN,  $\text{CH}_3$ ,  $-\text{OCH}_3$ ,  $-\text{C}(=\text{O})-\text{CH}_3$  and  $-\text{C}(=\text{O})\text{-cyclopropyl}$ ;

20 wherein each of the above-mentioned alkyl groups may be linear or branched and is optionally substituted by one or more F;

or a salt thereof.

25 8. The compound of formula (I) according to claim 1, wherein

A is N;

$R^1$  is selected from the group consisting of cyclopropyl, heterocyclyl and  $-\text{O}-R^2$ ;

30 wherein  $R^2$  is selected from the group consisting of  $C_{1-4}$ -alkyl,  $-\text{CH}_2-(C_{3-4}\text{-cycloalkyl})$ ,  $-\text{CH}_2\text{-heteroaryl}$  and  $-\text{CH}_2\text{-CH}_2\text{-C}\equiv\text{CH}$ ;

wherein each heteroaryl is selected from the group consisting of isoxazolyl, thiazolyl and thiadiazolyl;

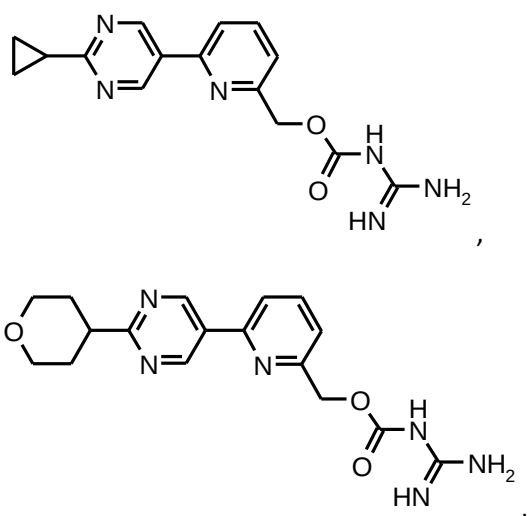
5 wherein each of the alkyl, cycloalkyl, aryl and heteroaryl groups is optionally independently substituted with one or more substituents independently selected from the group consisting of F, CN and -OCH<sub>3</sub>.

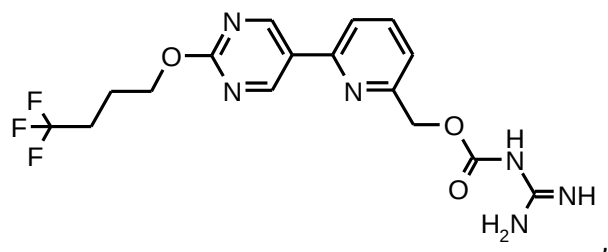
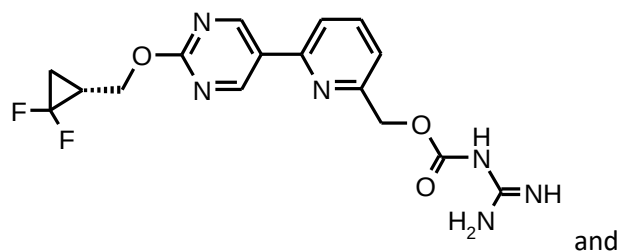
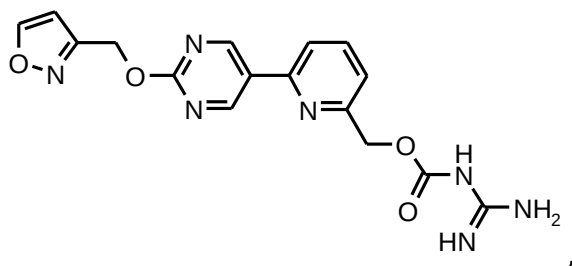
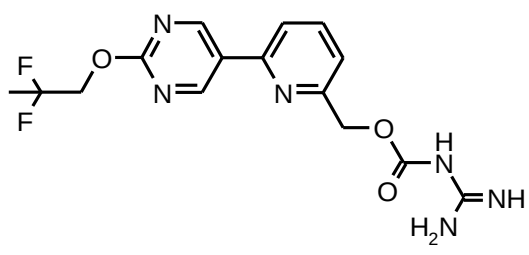
10 wherein each heterocyclyl is selected from the group consisting of azetidiny, piperidiny, tetrahydrofuranyl, tetrahydropyranyl and morpholinyl; and

15 wherein each heterocyclyl group is optionally independently substituted with one substituent selected from the group consisting of F, CN, OH, CH<sub>3</sub> and -O-CH<sub>3</sub>;

or a salt thereof.

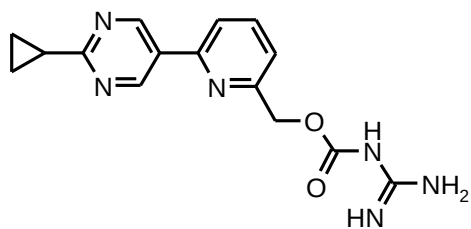
9. The compound of formula (I) according to claim 1 selected from the group  
20 consisting of:



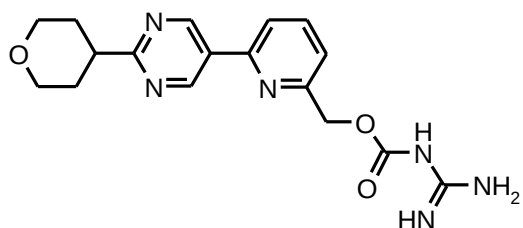


5 or a salt thereof.

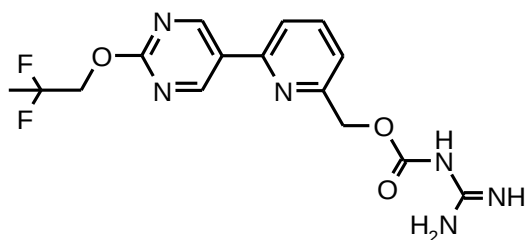
10. The compound of formula (I) according to claim 9 having the structure:



10 11. The compound of formula (I) according to claim 9 having the structure:

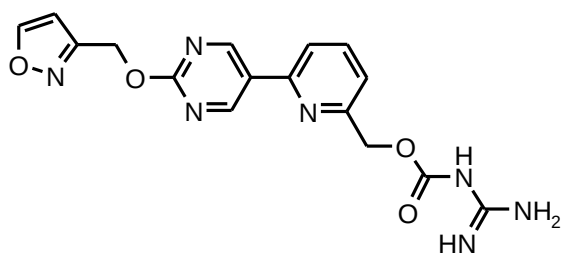


12. The compound of formula (I) according to claim 9 having the structure:

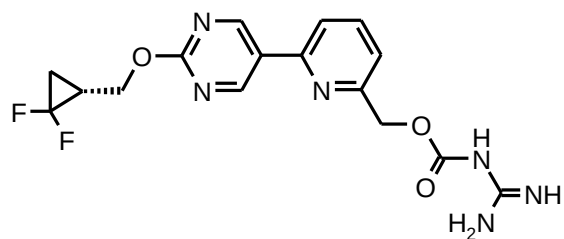


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13. The compound of formula (I) according to claim 9 having the structure:

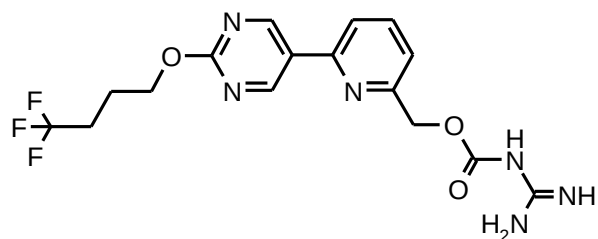


14. The compound of formula (I) according to claim 9 having the structure:



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15. The compound of formula (I) according to claim 9 having the structure:



16. A pharmaceutically acceptable salt of a compound according to any one of claims 1 to 15.

17. The compound according to any one of claims 1 to 15 or a pharmaceutically acceptable salt thereof for use as a medicament.

18. The compound according to any one of claims 1 to 15 or a pharmaceutically acceptable salt thereof for use in the treatment of NASH (non-alcoholic steatohepatitis), pulmonary fibrosis, retinopathy, nephropathy or chronic obstructive pulmonary disease (COPD).

19. The compound for use according to claim 18, wherein the retinopathy is diabetic retinopathy.

20. A pharmaceutical composition comprising a compound according to any one of claims 1 to 15 or a pharmaceutically acceptable salt thereof, optionally together with one or more inert carriers and/or diluents.

21. Use of a compound according to any one of claims 1 to 15 or a pharmaceutically acceptable salt thereof in the manufacture of a medicament for the treatment of NASH (non-alcoholic steatohepatitis), pulmonary fibrosis, retinopathy, nephropathy, chronic obstructive pulmonary disease (COPD) or diabetic retinopathy.

22. A pharmaceutical composition comprising one or more compounds according to any one of the claims 1 to 15 or a pharmaceutically acceptable salt thereof, and one or more additional therapeutic agents, optionally together with one or more inert carriers and/or diluents.