

CLAIMS

1. ~~Use of a~~ CNNM4 inhibitor for use in the manufacture of a medicament for the
treatment of an acute or a chronic disease in a subject, wherein the disease is selected
5 from the group consisting of a liver disease, a kidney disease and a lung disease.

2. The ~~CNNM4 inhibitor for use~~ according to claim 1,
 - wherein said liver disease is selected from liver fibrosis, veno-occlusive
liver disease, drug-induced liver injury (DILI), steatosis, non-alcoholic
10 steatohepatitis (NASH), cirrhosis, hepatocellular carcinoma (HCC) and Budd-
Chiari syndrome, hepatitis;
 - wherein said kidney disease is selected from acute kidney injury (AKI),
chronic kidney disease, nephritis, nephrosis and renal fibrosis;
 - and wherein said lung disease is pulmonary fibrosis.

- 15 3. The ~~CNNM4 inhibitor for use~~ according to ~~any one of~~ claims 1 or 2, wherein
said inhibitor is selected from the group consisting of a neutralising antibody or
functional fragment thereof, an antagonist, a soluble binding protein, a soluble receptor
variant, a non-functional derivative, an antisense polynucleotide, a RNA interference
20 oligonucleotide, a phosphorodiamidate morpholino oligomer (PMO), miRNA, siRNA,
shRNA, sgRNA, antisense RNA, a dicer-substrate 27-mer duplex, an aptamer, a
DNAzyme, a ribozyme, a triplex forming oligonucleotide (TFO), a small molecule and
combinations thereof.

- 25 4. The ~~CNNM4 inhibitor for use~~ according to claim 3, wherein the small molecule
is 7-amino-2-phenyl-5H-thieno[3,2-c]pyridin-4-one or 2-[5-(4-Oxo-2-thioxo-
thiazolidin-5-ylidenemethyl)-furan-2-yl]-benzoic acid.

5. An *in vitro* method for diagnosing liver disease, kidney disease or lung disease
30 in a subject which comprises:
 - (a) determining the expression level of CNNM4 in a sample from said
subject, and

(b) comparing said level with a reference value,

wherein an increased expression level of CNNM4 in said sample with respect to the reference value is indicative that the patient suffers from a liver disease, a kidney disease or a lung disease.

5

6. The *in vitro* method according to claim 5, wherein the sample is a liver, kidney or lung biopsy.

7. The *in vitro* method according to any one of claims 5 or 6,

10

- wherein said liver disease is selected from liver fibrosis, veno-occlusive liver disease, drug-induced liver injury (DILI), steatosis, non-alcoholic steatohepatitis (NASH), cirrhosis hepatocellular carcinoma (HCC) and Budd-Chiari syndrome, hepatitis;

15

- wherein said kidney disease is selected from acute kidney injury (AKI), chronic kidney disease, nephritis, nephrosis and renal fibrosis;

- and wherein said lung disease is pulmonary fibrosis.

8. Use of reagents specific for determining the expression level of CNNM4, for *in vitro* diagnosing a liver disease, a kidney disease or a lung disease in a subject.

20

9. The use according to claim 8,

25

- wherein said liver disease is selected from liver fibrosis, veno-occlusive liver disease, drug-induced liver injury (DILI), steatosis, non-alcoholic steatohepatitis (NASH), cirrhosis hepatocellular carcinoma (HCC) and Budd-Chiari syndrome, hepatitis;

- wherein said kidney disease is selected from acute kidney injury (AKI), chronic kidney disease, nephritis, nephrosis and renal fibrosis;

- and wherein said lung disease is pulmonary fibrosis.

30

10. The use according to ~~any one of~~ claims 8 or 9, wherein the reagents specific for determining the expression level of CNNM4 are selected from the group consisting of a set of probes which specifically hybridize to the mRNA of CNNM4 and a set of primer

pairs which are capable of specifically amplifying the mRNAs of CNNM4, or wherein the reagent specific for determining the expression level of CNNM4 is an antibody which specifically binds to the CNNM4 polypeptide.

- 5 11. An *in vitro* method of reducing an induced disease or condition in a cell, wherein the induced disease or condition is a disease model for the study of DILI, steatosis, NASH, cirrhosis, HCC, liver fibrosis, kidney fibrosis or lung fibrosis, the method comprising contacting the cell with a specific CNNM4 inhibitor in an amount effective to decrease a CNNM4 activity, level or function in the cell.

10

12. An *in vitro* method for identifying a compound potentially useful for reducing an induced CNNM4-mediated disease or condition in a cell, the method comprising contacting the cell with a candidate compound in an amount effective to decrease a CNNM4 activity, level or function in the cell, or in an amount effective to reduce the relative lipid accumulation or to reduce the relative mitochondrial ROS with respect to a reference value, wherein a candidate compound that inhibits CNNM4 activity, reduces the relative lipid accumulation with respect to a reference value or reduces the relative mitochondrial ROS with respect to a reference value in an induced CNNM4-mediated disease or condition in a cell is identified as a compound potentially useful for treating and/or preventing a CNNM4-mediated liver, kidney and/or lung disease.
- 15
- 20

13. The *in vitro* method according to ~~any one of~~ claims 11 or 12, wherein said inhibitor or said compound is selected from the group consisting of a neutralising antibody or functional fragment thereof, an antagonist, a soluble binding protein, a soluble receptor variant, a non-functional derivative, an antisense polynucleotide, a RNA interference oligonucleotide, a phosphorodiamidate morpholino oligomer (PMO), miRNA, siRNA, shRNA, sgRNA, antisense RNA, a dicer-substrate 27-mer duplex, an aptamer, a DNAzyme, a ribozyme, a triplex forming oligonucleotide (TFO), a small molecule and combinations thereof.
- 25