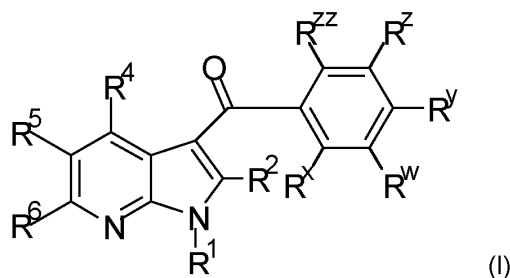


Claims

1. A compound having formula (I)



wherein

R^1 is H or alkyl;

R^2 is H or alkyl;

R^4 is H, or alkyl;

R^6 is H, or alkyl;

R^w is $-NR^{10}SO_2R^{12}$;

R^{10} is H, alkyl, or phenylalkyl;

R^{12} is H, alkyl, or phenylalkyl, wherein the phenyl group is optionally substituted with 1 or 2 groups independently selected from alkyl and halogen;

R^x , R^y , R^z and R^{zz} are selected from:

a) R^x and R^y are F and R^z and R^{zz} are H; and

b) R^x , R^y and R^{zz} are independently halogen and R^z is H;

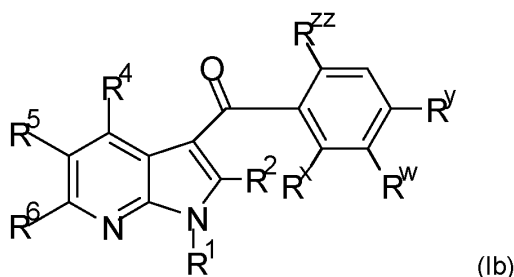
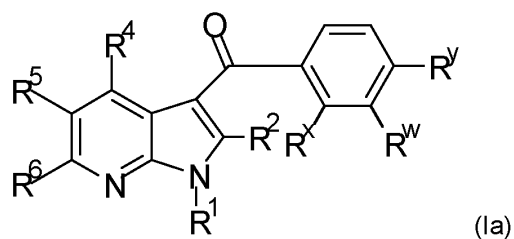
R^5 is selected from

(a) phenyl which is substituted with 1, 2 or 3 groups independently selected from
-POdi(alkyl), and
hydroxyalkyl-ONH-CO-;

(c) pyrimidinyl which is substituted with 1, 2 or 3 groups independently selected from
alkyl,
cycloalkyl,
alkoxy, and
alkylsulfanyl,

and a pharmaceutically acceptable salt, solvate and optical isomer thereof.

2. A compound of claim 1, wherein R⁵ is phenyl which is substituted with 1 or 2 groups independently selected from -POdi(alkyl), and hydroxyalkyl-ONH-CO-; and a pharmaceutically acceptable salt, solvate and optical isomer thereof.
- 5 3. A compound of claim 1, wherein R⁵ is pyrimidinyl which is substituted with 1 or 2 groups independently selected from alkyl, cycloalkyl, alkoxy, and alkylsulfanyl; and a pharmaceutically acceptable salt, solvate and optical isomer thereof.
4. A compound of claim 3, wherein the pyrimidinyl is bound in 5-position to the 1H-pyrrolo[2,3-b]pyridine and is substituted in 2-position with alkyl, cycloalkyl, or alkoxy and optionally substituted in 4-position with alkyl or alkylsulfanyl; and a pharmaceutically acceptable salt, solvate and optical isomer thereof.
- 10 5. A compound of claim 4, wherein the pyrimidinyl is bound in 5-position to the 1H-pyrrolo[2,3-b]pyridine and is substituted in 2-position with cycloalkyl or alkyl, and optionally substituted in 4-position with a group independently selected from alkyl and alkylsulfanyl, and a pharmaceutically acceptable salt, solvate and optical isomer thereof.
- 15 6. A compound of any one of the preceding claims having formula (Ia) or (Ib)
- 20

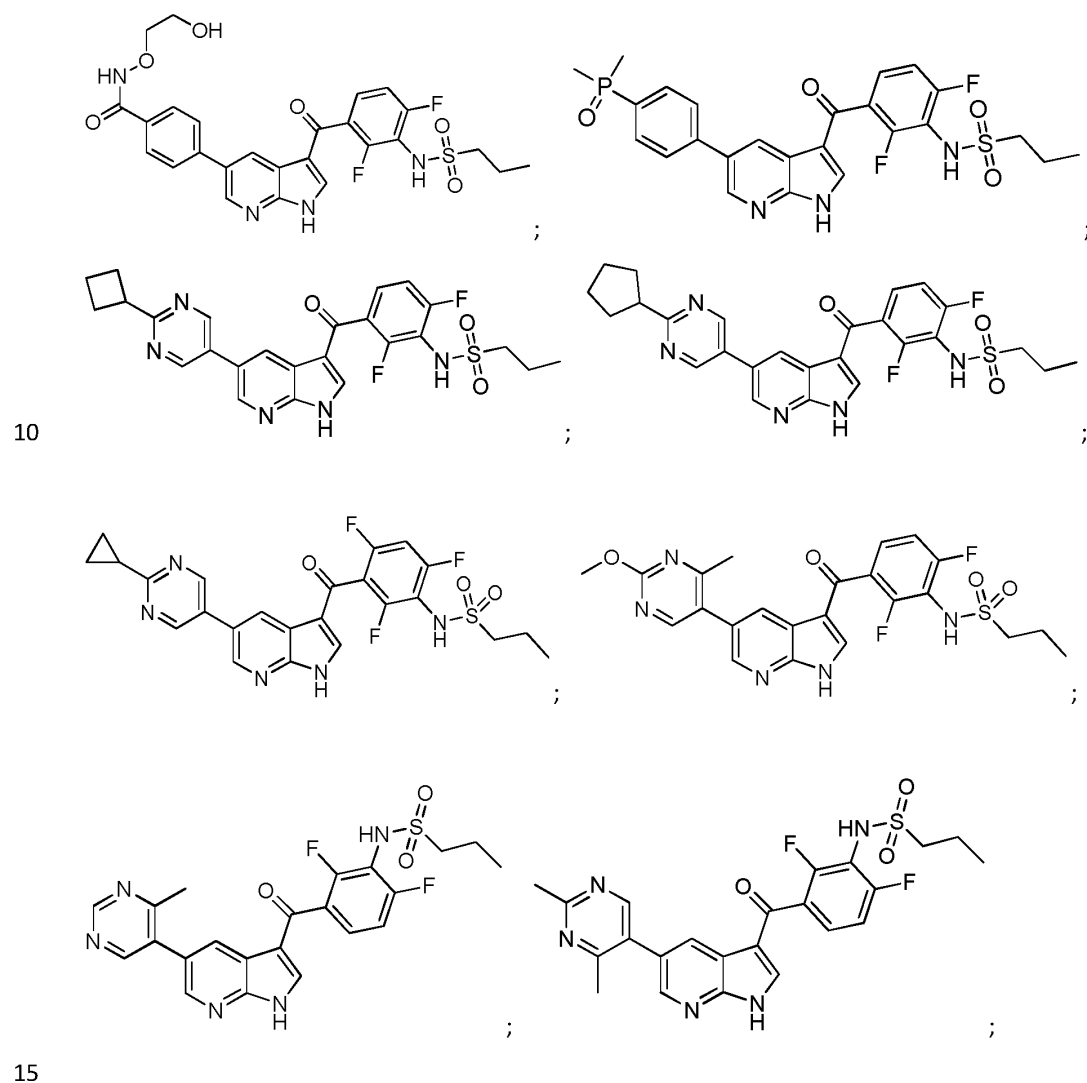


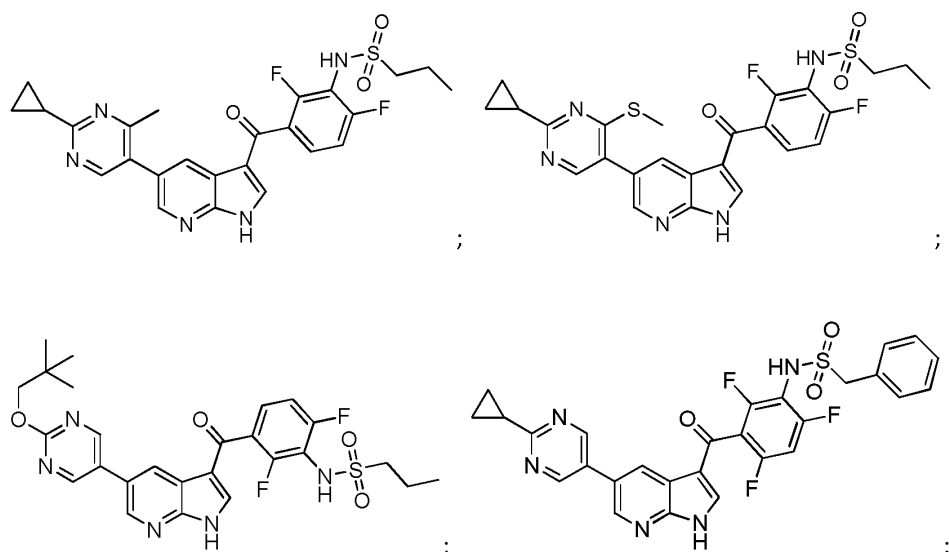
- and a pharmaceutically acceptable salt, solvate and optical isomer thereof.
- 25 7. A compound of any one of the preceding claims, wherein R¹, R², R⁴ and R⁶ are H,

and a pharmaceutically acceptable salt, solvate and optical isomer thereof.

8. A compound of any one of the preceding claims, wherein, if R^x , R^y , and/or R^{zz} stand for halogen, the halogen is F, Cl or Br, preferably F or Cl and in particular F,
5 and a pharmaceutically acceptable salt, solvate and optical isomer thereof.

9. A compound of claim 1 selected from





5 and a pharmaceutically acceptable salt, solvate and optical isomer thereof.

10. A pharmaceutical composition comprising a compound of any one of claims 1 to 9 or a pharmaceutically acceptable salt, solvate and optical isomer thereof.

10 11. A compound or a pharmaceutically acceptable salt, solvate and optical isomer thereof according to any one of claims 1 to 9 or a pharmaceutical composition according to claim 10 for use in selectively inhibiting protein kinase MKK4 over protein kinases JNK1 and MKK7.

12. A compound and the pharmaceutically acceptable salts, solvates and optical isomers thereof according to any one of claims 1 to 9 or a pharmaceutical composition according to claim 10 for use in promoting liver regeneration or preventing hepatocyte death.

13. A compound and the pharmaceutically acceptable salts, solvates and optical isomers thereof according to any one of claims 1 to 9 or a pharmaceutical composition according to claim 10 for use in the treatment of acute, acute-on-chronic or chronic liver disease.

14. A compound and the pharmaceutically acceptable salts, solvates and optical isomers thereof according to any one of claims 1 to 7 or a pharmaceutical composition according to claim 10 for use in treating

25

acute and chronic or acute on chronic liver diseases such as acute and chronic viral hepatitis like hepatitis B, C, E, hepatitis caused by Epstein-Barr virus, cytomegalovirus, herpes

simplex virus and other viruses, all types of autoimmune hepatitis, primary sclerosing hepatitis, alcoholic hepatitis;

5 metabolic liver diseases such as metabolic syndrome, fatty liver like non-alcoholic fatty liver (NAFL), non-alcoholic steatohepatitis (NASH), alcoholic steatohepatitis (ASH), Morbus Wilson, hemochromatosis, alpha1-antitrypsin deficiency, glycogen storage diseases;

10 all types of liver cirrhosis, such as primary biliary cirrhosis, ethyl toxic liver cirrhosis, cryptogenic cirrhosis;

acute (fulminant) or chronic liver failure such as toxic liver failure like acetaminophen (paracetamol) induced liver failure, alpha-amanitin induced liver failure, drug induced hepatotoxicity and liver failure caused, for example, by antibiotics, nonsteroidal anti-inflammatory drugs, anticonvulsants, acute liver failure induced by herbal supplements (kava, 15 ephedra, skullcap, pennyroyal etc.), liver disease and failure due to vascular diseases such as Budd-Chiari syndrome, acute liver failure of unknown origin, chronic liver disease due to right heart failure;

20 galactosemia, cystic fibrosis, porphyria, hepatic ischemia perfusion injury, small for size syndrome after liver transplantation, primary sclerosing cholangitis or hepatic encephalopathy.

15. A method of selectively inhibiting protein kinase MKK4 over protein kinases JNK1 and MKK7, promoting liver regeneration or preventing hepatocyte death, the treatment of acute, 25 acute-on-chronic or chronic liver disease, or for treating

acute and chronic or acute on chronic liver diseases such as acute and chronic viral hepatitis like hepatitis B, C, E, hepatitis caused by Epstein-Barr virus, cytomegalovirus, herpes simplex virus and other viruses, all types of autoimmune hepatitis, primary sclerosing 30 hepatitis, alcoholic hepatitis;

35 metabolic liver diseases such as metabolic syndrome, fatty liver like non-alcoholic fatty liver (NAFL), non-alcoholic steatohepatitis (NASH), alcoholic steatohepatitis (ASH), Morbus Wilson, hemochromatosis, alpha1-antitrypsin deficiency, glycogen storage diseases;

all types of liver cirrhosis, such as primary biliary cirrhosis, ethyl toxic liver cirrhosis, cryptogenic cirrhosis;

- acute (fulminant) or chronic liver failure such as toxic liver failure like acetaminophen (paracetamol) induced liver failure, alpha-amanitin induced liver failure, drug induced hepatotoxicity and liver failure caused, for example, by antibiotics, nonsteroidal anti-inflammatory drugs, anticonvulsants, acute liver failure induced by herbal supplements (kava, ephedra, skullcap, pennyroyal etc.), liver disease and failure due to vascular diseases such as Budd-Chiari syndrome, acute liver failure of unknown origin, chronic liver disease due to right heart failure;
- 10 galactosemia, cystic fibrosis, porphyria, hepatic ischemia perfusion injury, small for size syndrome after liver transplantation, primary sclerosing cholangitis or hepatic encephalopathy,
- 15 which comprises administering an effective amount of a compound or a pharmaceutically acceptable salt, solvate and optical isomer thereof or a composition according to any one of claims 1 to 10 to a subject in need thereof.