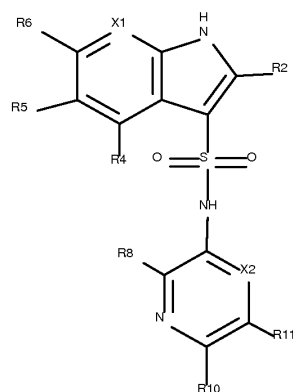


Claims

1. A compound of formula I

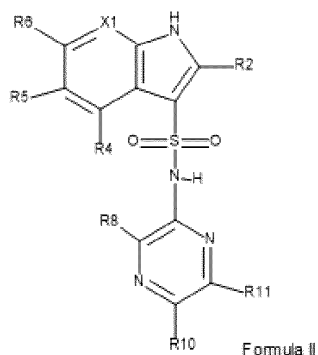


- 5 wherein
- X1 is N or C(R7),
- R2 and R4 are independently selected from hydrogen or fluoro,
- R5 is hydrogen or halogen,
- R6 is selected from halogen, cyano, C₃₋₅ cycloalkyl, C₃₋₅ cycloalkylmethoxy,
- 10 phenyloxy, benzyloxy, benzylmethoxy, pyridinylmethoxy, C₁₋₃ alkoxy and C₁₋₃ alkyl,
- wherein each cycloalkyl, benzyl, pyridinyl, alkyl and alkoxy can be substituted with
- one or more substituent selected from halogen, cyano, C₁₋₂alkoxy and fluoroC₁₋
- ₂alkoxy, or
- R6 together with R7 and the C-atoms to which they are attached form a five or six-
- 15 membered aromatic or non-aromatic ring which may comprise one or two ring
- forming heteroatoms, wherein said ring is unsubstituted or substituted with one to
- three residues R13,
- R7, if present, is selected from hydrogen, halogen, cyclopropyl, cyclopropyloxy, C₁₋
- ₃ alkoxy, and C₁₋₃ alkyl, wherein each alkyl and alkoxy can be substituted with one
- 20 or more substituent selected from halogen, C₁₋₂ alkoxy, fluoro(C₁₋₂)alkoxy and
- cyano, or R7 forms a ring together with R6 as described above,
- R8 is selected from hydrogen, halogen, methoxy, ethoxy, fluoromethoxy and
- fluoroethoxy,
- R10 is selected from hydrogen, cyano, halogen, C₃₋₅ cycloalkyl, C₃₋₅ cycloalkyloxy,
- 25 C₃₋₅ cycloalkylmethoxy, C₁₋₄ alkoxy, and C₁₋₄ alkyl, wherein each cycloalkyl,
- cycloalkyloxy, alkyl and alkoxy can be substituted with one or more substituent
- selected from halogen, C₁₋₃ alkoxy, fluoro(C₁₋₃)alkoxy and cyano,
- R11 is selected from hydrogen, fluoro and methoxy,

- X2 is N or C(R12),
R12 is selected from hydrogen, methoxy and halogen,
R13, in each occurrence, is independently selected from halogen, hydroxy, cyano,
methyl, methoxy, fluoromethyl and fluoromethoxy,
5 and pharmaceutically acceptable salts, solvates, isotopes and co-crystals thereof.
2. A compound according to claim 1, wherein
X1 is N or C(R7),
R2 is hydrogen or fluoro,
10 R4 is hydrogen or fluoro,
R5 is hydrogen or halogen,
R6 is selected from halogen, cyano, cyclopropyl, benzyl, benzyloxy,
pyridinylmethoxy, C₁₋₂ alkoxy and C₁₋₂ alkyl, wherein each cyclopropyl, benzyl,
pyridinyl, alkyl and alkoxy can be substituted with one or more substituent selected
15 from halogen, cyano, C₁₋₂ alkoxy and fluoroC₁₋₂alkoxy, or
R6 together with R7 and the C-atoms to which they are attached form a pyridyl
ring, such that the pyridyl together with the bicyclic ring system to which it is
annulated forms a 1H-pyrrolo[3,2-h]quinoline, wherein the pyridyl ring is
substituted with one or two residues R13 or is, preferably, unsubstituted,
20 R7, if present, is selected from hydrogen, halogen, cyclopropyl, cyclopropyloxy, C₁₋₃
alkoxy, and C₁₋₃ alkyl, wherein each alkyl and alkoxy can be substituted with one
or more substituent selected from halogen, C₁₋₂alkoxy, fluoro(C₁₋₂)alkoxy and
cyano, or
R7 forms a ring together with R6 as described above,
25 R8 is selected from hydrogen, halogen, methoxy, ethoxy, fluoromethoxy and
fluoroethoxy,
R10 is selected from hydrogen, cyano, halogen, C₃₋₅ cycloalkyl, C₃₋₅ cycloalkyloxy,
C₃₋₅ cycloalkylmethoxy, C₁₋₄ alkoxy, and C₁₋₄ alkyl, wherein each cycloalkyl,
cycloalkyloxy, alkyl and alkoxy can be substituted with one or more substituent
30 selected from halogen, C₁₋₃ alkoxy, fluoro(C₁₋₃)alkoxy and cyano,
R11 is selected from hydrogen, fluoro and methoxy,
X2 is N or C(R12),
R12 is selected from hydrogen, methoxy and halogen,
R13, in each occurrence, is independently selected from fluoro, chloro, cyano,
35 hydroxy, methyl, methoxy, fluoromethyl and fluoromethoxy,
and pharmaceutically acceptable salts, solvates, isotopes and co-crystals thereof.

3. A compound according to anyone of the preceding claims, wherein R2, R4 and R5 are all hydrogen and R6 is selected from halogen, cyano, fluoromethoxy and fluoromethyl.
- 5
4. A compound according to anyone of the preceding claims, wherein R8 is selected from fluoro and methoxy.
- 10
5. A compound according to anyone of the preceding claims, wherein R10 is selected from halogen cyclopropyl, and C₁₋₂ alkoxy, wherein the alkoxy can be optionally substituted with one or more substituent selected from fluoro, methoxy, ethoxy and fluoro C₁₋₂ alkoxy.
- 15
6. A compound according to anyone of the preceding claims, wherein R10 is selected from halogen, methoxy, ethoxy, fluoromethoxy, fluoroethoxy and fluoromethoxyethoxy.
- 20
7. A compound according to anyone of the preceding claims, wherein R11 is hydrogen or fluoro, preferably fluoro.
- 25
8. A compound according to anyone of the preceding claims, wherein R2, R4, and R5 are all hydrogen, R6 is selected from chloro, cyano, methyl, methoxy, fluoromethoxy and fluoromethyl, X1 is N or C(R7), R7, if present, is selected from hydrogen and fluoro, R8 is selected from fluoro and methoxy, R10 is selected from chloro, bromo, cyclopropyl and C₁₋₂ alkoxy, wherein the alkoxy is substituted with either up to three fluoro atoms or with one substituent selected from methoxy, fluoromethoxy and fluoroethoxy, R11 is hydrogen or fluoro, X2 is N or C(R12), R12, if present, is hydrogen or fluoro, preferably hydrogen, and pharmaceutically acceptable salts, solvates, isotopes and co-crystals thereof.
- 30
- 35

9. A compound according to anyone of claims 1 to 8, wherein X2 is N, thus having Formula II, wherein all substituents are as described in the preceding claims, and pharmaceutically acceptable salts, solvates, isotopes and co-crystals thereof



5

10. A compound according to claim 9, wherein

X1 is N or C(R7)

10

R2, R4 and R5 are all hydrogen

R6 is chloro or fluoromethyl,

R7, if present, is selected from hydrogen, fluoro, chloro, cyclopropyloxy and fluoromethyl,

R8 is selected from fluoro and methoxy,

15

R10 is selected from chloro, bromo, methoxy, fluoromethoxy, fluoroethoxy, fluoromethoxyethoxy and fluoroethoxymethoxy,

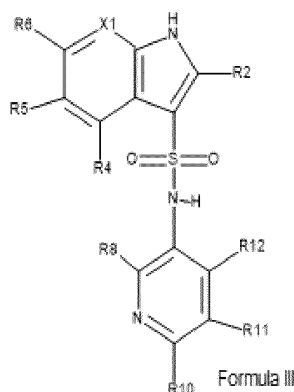
R11 is fluoro,

X2 is N or C(R12),

and R12, if present, is hydrogen.

20

11. A compound according to anyone of claims 1 to 8, wherein X2 is -C(R12)-, thus having formula III



wherein all substituents are as described in claims 1 to 8, and pharmaceutically acceptable salts, solvates, isotopes and co-crystals thereof.

5

12. A compound according to claim 11, wherein

R2, R4, and R5 are all hydrogen,

10 R6 is selected from halogen, cyano, methyl, isopropyl, methoxy, fluoromethoxy, fluoromethyl and benzyloxy,

X1 is N or C(R7),

R7, if present, is selected from hydrogen, halogen, fluoromethoxy and fluoromethyl,

R8 is selected from hydrogen, fluoro, C₁₋₂alkoxy and fluoroC₁₋₂alkoxy

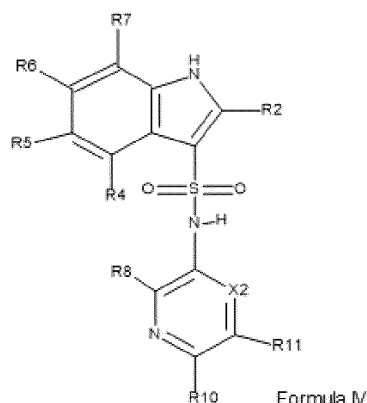
15 R10 is selected from halogen, cyclopropyl, C₁₋₂alkyl and C₁₋₂alkoxy, wherein the cyclopropyl, alkyl and alkoxy can each be optionally substituted with one or more substituent selected from fluoro, methoxy and fluoro C₁₋₂alkoxy,

R11 is selected from hydrogen, methoxy and fluoro,

R12 is selected from hydrogen and fluoro,

20 and pharmaceutically acceptable salts, solvates, isotopes and co-crystals thereof

13. A compound according to any one of claims 1 to 8, wherein X1 is -C(R7)-, thus having formula IV,



wherein all substituents are as described in claims 1 to 8, and pharmaceutically ^
acceptable salts, solvates, isotopes and co-crystals thereof.

5

14. A compound according to claim 13, wherein

R2, R4, and R5 are all hydrogen,

R6 is selected from halogen, cyano, methyl, isopropyl, methoxy, fluoromethoxy,
fluoromethyl and benzyloxy,

10

R7 is selected from hydrogen, halogen, fluoromethoxy and fluoromethyl,

X2 is N or C(R12),

R8 is selected from hydrogen, fluoro, C₁₋₂ alkoxy and fluoroC₁₋₂ alkoxy

R10 is selected from halogen, cyclopropyl, C₁₋₂ alkyl and C₁₋₂ alkoxy, wherein the
cyclopropyl, alkyl and alkoxy can each be optionally substituted with one or more
substituent selected from fluoro, methoxy and fluoro C₁₋₂ alkoxy,

15

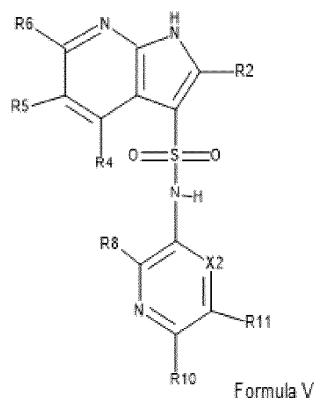
R11 is selected from hydrogen, methoxy and fluoro,

R12, if present, is selected from hydrogen, methoxy and fluoro,

and pharmaceutically acceptable salts, solvates, isotopes and co-crystals thereof.

20

15. A compound according to any anyone of claims 1-8, wherein X1 is N, thus having
formula V



wherein all substituents are as described in claims 1 to 8, and pharmaceutically acceptable salts, solvates, isotopes and co-crystals thereof.

5

16. A compound according to claim 15, wherein

R2, R4, and R5 are all hydrogen,

R6 is selected from halogen, cyano, methyl, isopropyl, methoxy, fluoromethoxy, fluoromethyl and benzyloxy,

X2 is N or C(R12),

R8 is selected from hydrogen, fluoro, C₁₋₂alkoxy and fluoroC₁₋₂alkoxy

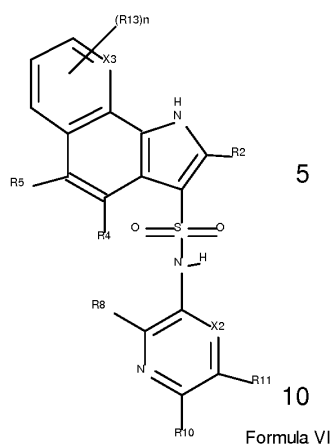
R10 is selected from halogen, cyclopropyl, C₁₋₂ alkyl and C₁₋₂ alkoxy, wherein the cyclopropyl, alkyl and alkoxy can each be optionally substituted with one or more substituent selected from fluoro, methoxy and fluoro C₁₋₂ alkoxy,

R11 is selected from hydrogen, methoxy and fluoro, preferably from hydrogen and fluoro,

R12, if present, is selected from hydrogen, methoxy and fluoro,

17. A compound according to claim 1 and having Formula VI:

25



wherein

n is 0 to 3, preferably 0 or 1,

X3 is CH or N,

15 R2 is hydrogen or fluoro,

R4 is hydrogen or fluoro,

R5 is hydrogen or halogen,

X2 is N or C(R12),

20 R8 is selected from hydrogen, halogen, methoxy, ethoxy, fluoromethoxy and fluoroethoxy,

R10 is selected from hydrogen, cyano, halogen, C₃₋₅ cycloalkyl, C₃₋₅ cycloalkyloxy, C₃₋₅ cycloalkylmethoxy, C₁₋₄ alkoxy, and C₁₋₄ alkyl, wherein each cycloalkyl, cycloalkyloxy, alkyl and alkoxy can be substituted with one or more substituent selected from halogen, C₁₋₃ alkoxy, fluoro(C₁₋₃)alkoxy and cyano,

25 R11 is selected from hydrogen, fluoro and methoxy,

R12 is selected from hydrogen, methoxy and halogen,

R13, in each occurrence, is independently selected from halogen, cyano, hydroxy, methyl, methoxy, fluoromethyl and fluoromethoxy,

and pharmaceutically acceptable salts, solvates, isotopes and co-crystals thereof.

30

18. A compound according to claim 17, wherein

n is 0

X3 is N or CH,

R2 and R4 are both hydrogen,

35 R5 is hydrogen or halogen, preferably hydrogen,

R8 is selected from hydrogen, fluoro and methoxy,

- R10 is selected from halogen, cyclopropyl, and C₁₋₂ alkoxy, wherein the alkoxy can be optionally substituted with one or more substituent selected from fluoro, methoxy, ethoxy, and fluoro C₁₋₂ alkoxy,
R11 is hydrogen or fluoro
5 X2 is N or C(R12), and
R12, if present, is selected from hydrogen, methoxy and fluoro
and pharmaceutically acceptable salts, solvates, isotopes and co-crystals thereof.
19. A compound selected from
- 10 6-chloro-N-[6-(2,2-difluoroethoxy)-2,5-difluoropyridin-3-yl]-1H-indole-3-sulfonamide
N-[6-(difluoromethoxy)-5-fluoro-2-methoxypyridin-3-yl]-1H-pyrrolo[3,2-h]quinoline-3-sulfonamide
N-[6-(2,2-difluoroethoxy)-5-fluoro-2-methoxypyridin-3-yl]-1H-pyrrolo[3,2-h]quinoline-3-sulfonamide
- 15 5-bromo-6-chloro-N-[6-(2,2-difluoroethoxy)-5-fluoro-2-methoxypyridin-3-yl]-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
6-chloro-N-[6-(2,2-difluoroethoxy)-5-fluoro-2-methoxypyridin-3-yl]-7-fluoro-1H-indole-3-sulfonamide
6-cyano-N-[6-(2,2-difluoroethoxy)-5-fluoro-2-methoxypyridin-3-yl]-1H-indole-3-sulfonamide
- 20 N-[6-(2,2-difluoroethoxy)-5-fluoro-2-methoxypyridin-3-yl]-6-(difluoromethoxy)-1H-indole-3-sulfonamide
N-[6-[2-(difluoromethoxy)ethoxy]-5-fluoro-2-methoxypyridin-3-yl]-6-(difluoromethyl)-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
- 25 6-chloro-N-[6-[2-(difluoromethoxy)ethoxy]-5-fluoro-2-methoxypyridin-3-yl]-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
N-[6-(2,2-difluoroethoxy)-5-fluoro-2-methoxypyridin-3-yl]-6-(difluoromethyl)-1H-indole-3-sulfonamide
6-chloro-N-(6-cyclopropyl-5-fluoro-2-methoxypyridin-3-yl)-1H-indole-3-sulfonamide
- 30 6-chloro-N-(5-fluoro-2-methoxypyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
N-[6-(difluoromethoxy)-5-fluoro-2-methoxypyridin-3-yl]-6-methoxy-1H-indole-3-sulfonamide
N-[6-(2,2-difluoroethoxy)-5-fluoro-2-methoxypyridin-3-yl]-6-methoxy-1H-indole-3-sulfonamide
- 35

- 6-chloro-N-[6-[2-(difluoromethoxy)ethoxy]-5-fluoro-2-methoxypyridin-3-yl]-1H-indole-3-sulfonamide
- N-[6-(difluoromethoxy)-5-fluoro-2-methoxypyridin-3-yl]-6-methyl-1H-indole-3-sulfonamide
- 5 6-cyano-N-[6-(difluoromethoxy)-5-fluoro-2-methoxypyridin-3-yl]-1H-indole-3-sulfonamide
- 6-(difluoromethyl)-N-(2,5-difluoro-6-methylpyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
- 6-(difluoromethyl)-N-(5-fluoro-2,6-dimethoxypyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
- 10 6-(difluoromethyl)-N-[5-fluoro-6-(2-fluoroethoxy)-2-methoxypyridin-3-yl]-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
- 6-chloro-N-(6-cyclopropyl-2,5-difluoropyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
- 15 6-chloro-N-[6-(2,2-difluoroethoxy)-5-fluoro-2-methoxypyridin-3-yl]-1H-indole-3-sulfonamide
- 6-chloro-N-(6-cyclopropyl-2,5-difluoropyridin-3-yl)-1H-indole-3-sulfonamide
- N-[6-(2,2-difluoroethoxy)-5-fluoro-2-methoxypyridin-3-yl]-6-(difluoromethyl)-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
- 20 6-chloro-N-[6-(2,2-difluoroethoxy)-5-fluoro-2-methoxypyridin-3-yl]-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
- N-[6-(2,2-difluoroethoxy)-2-methoxypyridin-3-yl]-6-(difluoromethyl)-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
- 6-chloro-N-[6-(2,2-difluoroethoxy)-2-methoxypyridin-3-yl]-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
- 25 N-[6-(2,2-difluoroethoxy)-2,5-difluoropyridin-3-yl]-6-(difluoromethyl)-1H-indole-3-sulfonamide
- 6-chloro-N-[6-(difluoromethoxy)-4-methoxypyridin-3-yl]-1H-indole-3-sulfonamide
- 6-chloro-N-[6-(2,2-difluoroethoxy)-2-methoxypyridin-3-yl]-1H-indole-3-sulfonamide
- 30 6-chloro-N-[2-(2,2-difluoroethoxy)-6-methoxypyridin-3-yl]-1H-indole-3-sulfonamide
- N-[6-(difluoromethoxy)-5-fluoro-2-methoxypyridin-3-yl]-6-(difluoromethyl)-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
- 6-chloro-N-[6-(difluoromethoxy)-2-methoxy-3-pyridyl]-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
- 35 N-(6-chloro-5-fluoro-2-methoxypyridin-3-yl)-6-(difluoromethyl)-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide

- 6-chloro-N-[6-(2-fluoroethoxy)-2-methoxypyridin-3-yl]-1H-indole-3-sulfonamide
 6-chloro-N-[5-fluoro-6-(2-fluoroethoxy)-2-methoxypyridin-3-yl]-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
 6-chloro-N-[5-fluoro-6-(2-fluoroethoxy)-2-methoxypyridin-3-yl]-1H-indole-3-sulfonamide
 N-[6-(difluoromethoxy)-5-fluoro-2-methoxypyridin-3-yl]-6-(difluoromethyl)-1H-indole-3-sulfonamide
 6-chloro-N-[6-(difluoromethoxy)-5-fluoro-2-methoxypyridin-3-yl]-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
 6-chloro-N-(5-chloro-3-methoxypyrazin-2-yl)-1H-indole-3-sulfonamide
 6-chloro-N-[6-(difluoromethoxy)-5-fluoro-2-methoxypyridin-3-yl]-1H-indole-3-sulfonamide
 N-(5-bromo-3-methoxypyrazin-2-yl)-6-chloro-1H-indole-3-sulfonamide
 6-chloro-N-(2,5-difluoro-6-methylpyridin-3-yl)-1H-indole-3-sulfonamide
 6-chloro-N-(5-fluoro-2,6-dimethoxypyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
 6-chloro-N-(6-chloro-5-fluoro-2-methoxypyridin-3-yl)-1H-pyrrolo[2,3-b]pyridine-3-sulfonamide
 6-chloro-N-(5-fluoro-2,6-dimethoxypyridin-3-yl)-1H-indole-3-sulfonamide
 6-chloro-N-(2,5-difluoro-6-methoxypyridin-3-yl)-1H-indole-3-sulfonamide
 6-chloro-N-(6-chloro-5-fluoro-2-methoxypyridin-3-yl)-1H-indole-3-sulfonamide
 6-chloro-N-(6-chloro-2,5-difluoropyridin-3-yl)-1H-indole-3-sulfonamide
 6-chloro-N-(6-iodopyridin-3-yl)-1H-indole-3-sulfonamide
 6-chloro-N-(6-chloro-4-fluoropyridin-3-yl)-1H-indole-3-sulfonamide
 and pharmaceutically acceptable salts, solvates, isotopes and co-crystals thereof.

20. A compound according to anyone of the preceding claims for use in therapy.
21. A compound according to anyone of the preceding claims for use in treating or preventing a demyelination disorder including, but not limited to multiple sclerosis.
22. Method of treating or preventing a demyelination disorder, including but not limited to multiple sclerosis, comprising administering to a patient in need thereof a therapeutically effective amount of a compound as defined in anyone of the preceding claims.

23. Therapeutic composition comprising a compound according to anyone of the preceding claims and a pharmaceutically acceptable carrier.