

WHAT IS CLAIMED IS:

1. A method of promoting remyelination in a subject in need thereof, comprising administering to the subject an effective amount of a steroid hormone and a Hedgehog signaling pathway modulator.
2. A method according to claim 1, wherein the steroid hormone is an androgen receptor ligand such as testosterone, a progesterone receptor ligand, such as progesterone or allopregnanolone, an estrogen receptor ligands such as estradiol, or is dehydroepiandrosterone.
3. A method according to claim 1, wherein the steroid hormone is a selective hormone receptor modulator such as a selective androgen receptor modulator, a selective estrogen receptor modulator, or a selective progesterone receptor modulator.
4. A method according to claim 1, wherein the steroid hormone is testosterone.
5. A method according to any one of the preceding claims, wherein the Hedgehog signaling pathway modulator is a Smoothened (Smo) agonist.
6. A method according to claim 5, wherein the Smo agonist is 3-Chloro-N-[trans-4-(methylamino)cyclohexyl]-N-[[3-(4-pyridinyl)phenyl]methyl]benzo[b]thiophene-2-carboxamide (SAG).
7. A method according to any one of the claims 1-4, wherein the Hedgehog signaling pathway modulator is a Hedgehog signaling pathway antagonist, such as a Gli antagonist.
8. A method according to claim 7, wherein the Hedgehog signaling pathway antagonist is 2,2'-[[Dihydro-2-(4-pyridinyl)-1,3(2H,4H)-pyrimidinediyl]bis(methylene)]bis[N,N-dimethylbenzenamine (GANT-61).
9. A method according to claims 1-4, wherein the method comprising administering both a Smo agonist and a Gli antagonist.
10. A method according to claim 9, wherein the Smo agonist is SAG.
11. A method according to any one of claims 9-10, wherein the Gli antagonist is GANT-61.

12. A method according to any one of the preceding claims, wherein the steroid hormone and the Hedgehog signaling pathway modulator are administered in separate compositions, substantially simultaneously or sequentially.
13. A method according to any one of the preceding claims, wherein the steroid hormone and the Hedgehog signaling pathway modulator are administered in the same composition.
14. A method according to any one of the preceding claims, wherein one or both of the steroid hormone and the Hedgehog signaling pathway modulator is administered intranasally in an intranasal pharmaceutical composition that further comprises: (a) at least one lipophilic or partly lipophilic carrier present in an amount of from about 60% to about 98% by weight of the formulation; (b) at least one compound having surface tension decreasing activity present in an amount of from about 1% to about 20% by weight of the formulation; and (c) at least one viscosity regulating agent present in an amount of from about 0.5% to about 10% by weight of the formulation.
15. A method according to claim 14, wherein the intranasal pharmaceutical composition comprises the steroid hormone.
16. A method according to claim 14, wherein the intranasal pharmaceutical composition comprises the Hedgehog signaling pathway modulator.
17. A method according to claim 14, wherein the intranasal pharmaceutical composition comprises the steroid hormone and the Hedgehog signaling pathway modulator.
18. A method according to claim 14, wherein the intranasal pharmaceutical composition comprises the steroid hormone, an Smo agonist, and a Gli antagonist.
19. A method according to any one of claims 1-13, wherein one or both of the steroid hormone and the Hedgehog signaling pathway modulator is administered intranasally in an intranasal pharmaceutical composition comprising a porous excipient, wherein the steroid hormone and/or the Hedgehog signaling pathway modulator is/are loaded onto a surface of the porous excipient located inside pores of the porous excipient.
20. A method according to claim 19, wherein the steroid hormone is loaded onto a surface of the porous excipient located inside pores of the porous excipient.

21. A method according to claim 19, wherein the Hedgehog signaling pathway modulator is loaded onto a surface of the porous excipient located inside pores of the porous excipient.
22. A method according to claim 19, wherein both the steroid hormone and the Hedgehog signaling pathway modulator are loaded onto a surface of the porous excipient located inside pores of the porous excipient.
23. A method according to claim 19, wherein the steroid hormone, an Smo agonist, and a Gli antagonist are loaded onto a surface of the porous excipient located inside pores of the porous excipient.
24. A method according to any one of the preceding claims, wherein the subject is a human, a non-human primate, a dog, a cat, a cow, a sheep, a horse, a rabbit, a mouse, or a rat.
25. A method according to any one of the preceding claims, wherein the subject is suffering from a demyelinating disease.
26. A method according to any one of the preceding claims, wherein the subject is suffering from a demyelinating disease of the central nervous system selected from multiple sclerosis, amyotrophic lateral sclerosis, Devic's disease, inflammatory demyelinating diseases, central nervous system neuropathy, central pontine myelinolysis, myelopathies, tabes dorsalis, syphilitic myelopathy, leukoencephalopathies like progressive multifocal leukoencephalopathy, Leukodystrophies, and Alzheimer's disease.
27. A method according to any of the preceding claims, wherein the subject is suffering from a demyelinating disease of the peripheral nervous system selected from Guillain-Barré syndrome, chronic inflammatory demyelinating polyneuropathy, Anti-MAG peripheral neuropathy, Charcot-Marie-Tooth disease, hereditary neuropathy with liability to pressure palsy, peripheral neuropathy, myelopathy, optic neuropathy, and progressive inflammatory neuropathy.
28. A steroid hormone and a Hedgehog signaling pathway modulator for use in a method of promoting remyelination in a subject in need thereof.

29. A steroid hormone and a Hedgehog signaling pathway modulator for use according to claim 28, wherein the steroid hormone is an androgen receptor ligand such as testosterone, a progesterone receptor ligand, such as progesterone or allopregnanolone, an estrogen receptor ligands such as estradiol, or is dehydroepiandrosterone.
30. A steroid hormone and a Hedgehog signaling pathway modulator for use according to claim 28, wherein the steroid hormone is a selective hormone receptor modulator such as a selective androgen receptor modulator, selective estrogen receptor modulator, or selective progesterone receptor modulator.
31. A steroid hormone and a Hedgehog signaling pathway modulator for use according to claim 28, wherein the Hedgehog signaling pathway modulator is a Smoothed agonist, such as 3-Chloro-N-[trans-4-(methylamino)cyclohexyl]-N-[[3-(4-pyridinyl)phenyl]methyl]benzo[b]thiophene-2-carboxamide (SAG).
32. A steroid hormone and a Hedgehog signaling pathway modulator for use according to claim 28, wherein the Hedgehog signaling pathway modulator is a Gli antagonist, such as 2,2'-[[Dihydro-2-(4-pyridinyl)-1,3(2H,4H)-pyrimidinediyl]bis(methylene)]bis[N,N-dimethylbenzenamine (GANT-61).
33. A steroid hormone and a Hedgehog signaling pathway modulator for use according to claim 28, wherein the Hedgehog signaling pathway modulator comprises both a Smo agonist, such as 3-Chloro-N-[trans-4-(methylamino)cyclohexyl]-N-[[3-(4-pyridinyl)phenyl]methyl]benzo[b]thiophene-2-carboxamide (SAG), and a Gli antagonist, such as 2,2'-[[Dihydro-2-(4-pyridinyl)-1,3(2H,4H)-pyrimidinediyl]bis(methylene)]bis[N,N-dimethylbenzenamine (GANT-61).
34. A steroid hormone and a Hedgehog signaling pathway modulator for use according to any one of claims 28-33, wherein the steroid hormone and the Hedgehog signaling pathway modulator are administered in separate compositions, substantially simultaneously or sequentially, or are administered in the same composition.

35. A steroid hormone and a Hedgehog signaling pathway modulator for use according to any one of claims 28-34, wherein one or both of the steroid hormone and the Hedgehog signaling pathway modulator is administered intranasally in an intranasal pharmaceutical composition that further comprises: (a) at least one lipophilic or partly lipophilic carrier present in an amount of from about 60% to about 98% by weight of the formulation; (b) at least one compound having surface tension decreasing activity present in an amount of from about 1% to about 20% by weight of the formulation; and (c) at least one viscosity regulating agent present in an amount of from about 0.5% to about 10% by weight of the formulation.
36. A steroid hormone and a Hedgehog signaling pathway modulator for use according to any one of claims 28-34, wherein one or both of the steroid hormone and the Hedgehog signaling pathway modulator is administered intranasally in an intranasal pharmaceutical composition comprising a porous excipient, wherein one or both of the steroid hormone and the Hedgehog signaling pathway modulator are loaded onto a surface of the porous excipient located inside pores of the porous excipient.
37. A steroid hormone and a Hedgehog signaling pathway modulator for use according to any one of claims 28-36, wherein the subject is suffering from a demyelinating disease.
38. Use of a steroid hormone and/or a Hedgehog signaling pathway modulator in the preparation of a medicament for treating demyelination in a subject in need thereof, wherein the method comprises administering the steroid hormone and the Hedgehog signaling pathway modulator to the subject.
39. The use according to claim 38, wherein the subject is suffering from a demyelinating disease.
40. A method of producing oligodendroglial cells, comprising culturing primary mixed glial cells in a medium comprising a steroid hormone and a Smoothened agonist.
41. A method according to claim 40, wherein the steroid hormone is testosterone.
42. A method according to any one of claims 40-41, wherein the Smoothened agonist is 3-Chloro-N-[trans-4-(methylamino)cyclohexyl]-N-[[3-(4-pyridinyl)phenyl]methyl]benzo[b]thiophene-2-carboxamide (SAG).

43. A method of differentiating oligodendroglial cells into myelin-producing cells, comprising incubating oligodendroglial cells in a medium comprising a steroid hormone and a Hedgehog signaling pathway antagonist.
44. A method according to claim 43, wherein the steroid hormone is testosterone.
45. A method according to any one of claims 43-44, wherein the Hedgehog signaling pathway antagonist is 2,2'-[[Dihydro-2-(4-pyridinyl)-1,3(2H,4H)-pyrimidinediyl]bis(methylene)]bis[N,N-dimethylbenzenamine (GANT-61).