

CLAIMS

1. A single stranded antisense oligonucleotide that suppresses the expression of a SYF2, wherein the antisense oligonucleotide has a nucleobase sequence that comprises at least 12 or 15 consecutive nucleobases of any of the nucleobase sequences of SEQ ID NOs: 1-121.
2. The antisense oligonucleotide of claim 1, wherein the antisense oligonucleotide has a nucleobase sequence of any one of SEQ ID NOs: 1-161.
3. The antisense oligonucleotide of claim 1 or 2, wherein the antisense oligonucleotide has 18 to 20 linked nucleosides.
4. The antisense oligonucleotide of any of the preceding claims, wherein at least one internucleoside linkage is a modified internucleoside linkage.
5. The antisense oligonucleotide of claim 4, wherein at least one modified internucleoside linkage is a phosphorothioate internucleoside linkage.
6. The antisense oligonucleotide of claim 4, wherein each modified internucleoside linkage is a phosphorothioate internucleoside linkage.
7. The antisense oligonucleotide of any of the preceding claims, wherein at least one internucleoside linkage is a phosphodiester internucleoside linkage.
8. The antisense oligonucleotide of claim 7, wherein at least one internucleoside linkage is a phosphorothioate linkage and at least one internucleoside linkage is a phosphodiester linkage.
9. The antisense oligonucleotide of any of the preceding claims, wherein at least one nucleoside comprises a modified nucleobase.
10. The antisense oligonucleotide of claim 9, wherein the modified nucleobase is a 5-methylcytosine.

11. The antisense oligonucleotide of any of the preceding claims, wherein at least one nucleoside of the antisense oligonucleotide comprises a modified sugar moiety.

12. The antisense oligonucleotide of claim 11, wherein the modified sugar moiety comprises a 2'-O-methoxyethyl group.

13. The antisense oligonucleotide of claim 11, wherein the modified sugar moiety comprises a 2'-F.

14. The antisense oligonucleotide of claim 11, wherein the modified sugar moiety comprises a 2'-O-hexadecyl.

15. The antisense oligonucleotide of any of the preceding claims, wherein the antisense oligonucleotide is a gapmer.

16. The antisense oligonucleotide of claim 15, wherein the antisense oligonucleotide comprises:

a gap segment consisting of 8 to 12 linked deoxynucleosides;

a 5' wing segment consisting of 3 to 5 linked nucleosides; and

a 3' wing segment consisting of 3 to 5 linked nucleosides,

wherein the gap segment is positioned between the 5' wing segment and the 3' wing segment and wherein a nucleoside of each wing segment comprises a modified sugar moiety.

17. The antisense oligonucleotide of claim 16, wherein each nucleoside of each wing segment comprises a modified sugar moiety.

18. The antisense oligonucleotide of claim 16, wherein the nucleosides making up each wing segment comprises at least two different modified sugar moieties.

19. The antisense oligonucleotide of claim 16, wherein the nucleosides making up each wing segment comprises the same modified sugar moiety.

20. The antisense oligonucleotide of claim 17, wherein the modified sugar moiety comprises a 2'-O-methoxyethyl group.

21. The antisense oligonucleotide of any of the preceding claims, wherein the antisense oligonucleotide comprises 15 to 50 nucleosides.

22. A pharmaceutical composition comprising the antisense oligonucleotide of any one of the preceding claims, and a pharmaceutically acceptable carrier, diluent and/or excipient.

23. The pharmaceutical composition of claim 22, wherein the pharmaceutical composition is formulated for parenteral delivery.

24. The pharmaceutical composition of claim 22, wherein the pharmaceutical composition is formulated for intracerebroventricular injection.

25. Use of a therapeutically effective amount of the antisense oligonucleotide of any one of claims 1 to 21 in the manufacture of a pharmaceutical composition for treating a neurological or neurodegenerative disease in a subject in need thereof.

26. The use of claim 25, wherein the neurological disease is associated with neuronal hyperexcitability.

27. The use of claim 25, wherein the neurological disease is associated with aberrant endosomal trafficking.

28. The use of claim 25, wherein the neurological disease is associated with aberrant lysosomal trafficking.

29. The use of claim 25, wherein the neurological disease is selected from the group consisting of familial and sporadic amyotrophic lateral sclerosis (ALS), familial and sporadic frontotemporal dementia (FTD), progressive supranuclear palsy, Alzheimer's disease, chronic traumatic encephalopathy, Parkinson's disease, Charcot Marie Tooth 2A and 4B,

Huntington's disease, dementia, transmissible spongiform encephalopathy, spinobulbar muscular atrophy, dentatorubral-pallidoluysian atrophy, spinocerebellar ataxias, and Creutzfeldt-Jakob disease.

30. An oligonucleotide consisting of 12 to 30 linked nucleosides and having a nucleobase sequence comprising at least 8, at least 9, at least 10, at least 11, at least 12, at least 13, at least 14, at least 15, at least 16, at least 17, at least 18, at least 19, or at least 20 consecutive nucleobases of any of the nucleobase sequences of SEQ ID NOs: 1-121.