CLAIMS

What is claimed is:

1. Use of a pharmaceutical composition in manufacturing a medicament for treating a disease or condition in a subject in need thereof, wherein the disease or condition is associated with a deficient amount or activity of the Nav1.1 protein encoded by the *SCN1A* gene in the subject, wherein the pharmaceutical composition comprises:

   an antisense oligomer, and

   a pharmaceutically acceptable excipient;

   wherein the antisense oligomer binds to a targeted portion of a pre-mRNA that contains a non-sense mediated RNA decay-inducing exon (NMD exon) and that encodes Nav1.1 protein, whereby the antisense oligomer promotes exclusion of the NMD exon from the pre-mRNA that contains the NMD exon and encodes Nav1.1, thereby increasing the level of processed mRNA encoding the Nav1.1 protein, and increasing the expression of the Nav1.1 protein in a cell having the pre-mRNA, when the cell is treated with the antisense oligomer, as compared to a corresponding control cell not treated with the antisense oligomer,

   wherein the NMD exon is located at a region from GRCh37/hg19: chr2:166,863,740 to GRCh37/hg19: chr2:166,863,803.

2. The use according to claim 1, wherein the disease or condition is associated with haploinsufficiency of the *SCN1A* gene.

3. The use according to claim 1, wherein the disease or condition is Dravet Syndrome (DS); severe myoclonic epilepsy of infancy (SMEI)-borderland (SMEB; also known as borderline SMEI); Febrile seizure (FS); epilepsy, generalized, with febrile seizures plus (GEFS+); cryptogenic generalized epilepsy; cryptogenic focal epilepsy; myoclonic-astatic epilepsy; Lennox-Gastaut syndrome; West syndrome; idiopathic spasms; sudden unexpected death in epilepsy (SUDEP); autism; malignant migrating partial seizures of infancy; or Alzheimer's Disease.

4. The use according to claim 1, wherein the disease or condition is Dravet Syndrome.

5. The use according to claim 1, wherein the disease or condition is associated with a mutation of the SCN1A gene that encodes the Nav1.1 protein.

6. The use according to claim 1, wherein the targeted portion:

   (i) is within an intron sequence flanking the NMD exon;

   (ii) at least partially overlaps with the NMD exon; or

   (iii) is within the NMD exon.

7. The use according to claim 1, wherein the targeted portion is within an intron sequence flanking the NMD exon.

8. The use according to claim 1, wherein the targeted portion at least partially overlaps with the NMD exon.

9. The use according to claim 1, wherein the targeted portion is within the NMD exon.

10. The use according to claim 1, wherein the targeted portion comprises a sequence with at least about 95% sequence identity to a region comprising at least 8 contiguous nucleic acids of SEQ ID NOs: 10, 7, 8, or 9.

11. The use according to claim 1, wherein the antisense oligomer comprises a sequence that is at least 80%, at least 85%, at least 90%, at least 95%, or 100% complementary to the targeted portion.

12. The use according to claim 1, wherein the antisense oligomer comprises a sequence that is at least about 80% identity to any one of SEQ ID NOs: , 21-61, 64-67, 210-250, 253-256, and 304-379.

13. The use according to claim 1, wherein the antisense oligomer is a sequence selected from the group consisting of SEQ ID NOs: 21-61, 64-67, 210-250, 253-256, and 304-379.

14. The use according to claim 1, wherein the antisense oligomer is SEQ ID NO: 42 or 231; 54 or 243; 306 or 344; 307 or 345; 308 or 346; or 330 or 368.

15. The use according to claim 1, wherein the antisense oligomer consists of from 12 to 50 nucleobases, or from 12 to 20 nucleobases.

16. The use according to claim 1, wherein the antisense oligomer comprises a backbone modification, a modified sugar moiety or a combination thereof.

17. The use according to claim 1, wherein each nucleotide of the antisense oligomer comprises a 2'-O-methoxyethyl moiety.

18. The use according to claim 1, wherein the pharmaceutical composition is formulated for intrathecal injection or intracerebroventricular injection.

19. The use according to claim 1, wherein the antisense oligomer is conjugated with a moiety that comprises an abasic nucleotide, a polyether, a polyamine, a polyamide, a peptide, a carbohydrate, a lipid, a polyhydrocarbon compound, or an antibody, optionally an antibody to transferrin receptor.

20. The use according to claim 1, wherein the pharmaceutical composition is to be administered to the subject by intrathecal injection or intracerebroventricular injection.

21. Use of a pharmaceutical composition in manufacturing a medicament for treating a disease or condition in a subject in need thereof, wherein the disease or condition is associated with a deficient amount or activity of the Nav1.1 protein encoded by the *SCN1A* gene in the subject, wherein the pharmaceutical composition comprises a viral vector encoding an antisense oligomer, wherein the

antisense oligomer binds to a targeted portion of a pre-mRNA that contains a non-sense mediated RNA decay-inducing exon (NMD exon) and that encodes Nav1.1 protein, whereby the antisense oligomer promotes exclusion of the NMD exon from the pre-mRNA that contains the NMD exon and encodes Nav1.1, thereby increasing a level of processed mRNA encoding the Nav1.1 protein, and increasing the expression of the Nav1.1 protein in a cell having the pre-mRNA, when the viral vector is introduced into the cell, as compared to a corresponding control cell that is not treated with the viral vector, wherein the NMD exon is located at a region from GRCh37/hg19: chr2:166,863,740 to GRCh37/hg19: chr2:166,863,803.

22. The use according to claim 21, wherein the antisense oligomer comprises a sequence selected from the group consisting of SEQ ID NOs: 21-61, 64-67, 210-250, 253-256, and 304-379.

23. The use according to claim 21, wherein the disease or condition is Dravet Syndrome (DS); severe myoclonic epilepsy of infancy (SMEI)-borderland (SMEB; also known as borderline SMEI); Febrile seizure (FS); epilepsy, generalized, with febrile seizures plus (GEFS+); cryptogenic generalized epilepsy; cryptogenic focal epilepsy; myoclonic-astatic epilepsy; Lennox-Gastaut syndrome; West syndrome; idiopathic spasms; sudden unexpected death in epilepsy (SUDEP); autism; malignant migrating partial seizures of infancy; or Alzheimer's Disease.

24. The use according to claim 21, wherein the disease or condition is Dravet Syndrome.

25. The use according to claim 21, wherein the targeted portion:

    (i) is within an intron sequence flanking the NMD exon;

    (ii) at least partially overlaps with the NMD exon; or

    (iii) is within the NMD exon.

26. The use according to claim 21, wherein the antisense oligomer is SEQ ID NO: 42 or 231; 54 or 243; 306 or 344; 307 or 345; 308 or 346; or 330 or 368.

27. The use according to claim 21, wherein the pharmaceutical composition is to be administered to the subject by intrathecal injection or intracerebroventricular injection.

28. An antisense oligomer that has a sequence selected from the group consisting of SEQ ID NOs: 32-35, 39, 40, 42-45, 49-51, 54-59, 66, 221-224, 228, 229, 231-234, 238-240, 243-248, 255, 304-308, 312-316, 318-324, 326-335, 337-346, 350-354, 356-362, 364-373 and 375-379.

29. The antisense oligomer of claim 28, wherein the antisense oligomer is SEQ ID NO: 42 or 231; 54 or 243; 306 or 344; 307 or 345; 308 or 346; or 330 or 368.

30. The antisense oligomer of claim 28 or 29, wherein the antisense oligomer comprises a backbone modification, a modified sugar moiety or a combination thereof.

31. The antisense oligomer of claim 28 or 29, wherein the antisense oligomer comprises a phosphorothioate linkage.

32. The antisense oligomer of claim 28 or 29, wherein the antisense oligomer comprises a phosphorodiamidate linkage.

33. The antisense oligomer of claim 28 or 29, wherein the antisense oligomer comprises at least one modified sugar moiety.

34. The antisense oligomer of claim 28 or 29, wherein the antisense oligomer comprises a 2'-O-methyl moiety, a 2'-Fluoro moiety, or a 2'-O-methoxyethyl moiety.

35. The antisense oligomer of claim 28 or 29, wherein at least one nucleotide of the antisense oligomer comprises a 2'-O-methoxyethyl moiety.

36. The antisense oligomer of claim 28 or 29, wherein each nucleotide of the antisense oligomer comprises a 2'-O-methoxyethyl moiety.

37. The antisense oligomer of claim 28 or 29, wherein the antisense oligomer is conjugated with a moiety that comprises an abasic nucleotide, a polyether, a polyamine, a polyamide, a peptide, a carbohydrate, a lipid, a polyhydrocarbon compound, or an antibody, optionally an antibody to transferrin receptor.