NOs: 21, 25, 28, 36, or 63. In some embodiments, the subject is a human. In some embodiments, the subject is a non-human animal. In some embodiments, the subject is a fetus, an embryo, or a child. In some embodiments, the therapeutic agent is administered by intrathecal injection, intracerebroventricular injection, intraperitoneal injection, intramuscular injection, subcutaneous injection, intravitreal, or intravenous injection of the subject. In some embodiments, the method further comprises administering a second therapeutic agent to the subject. In some embodiments, the second therapeutic agent is a small molecule. In some embodiments, the second therapeutic agent is an ASO. In some embodiments, the ASO comprises a sequence that is at least about 80%, 85%, 90%, 95%, 97%, or 100% complimentary to any one of SEQ ID NOs: 115-161. In some embodiments, the second therapeutic agent corrects intron retention. In some embodiments, the disease or condition is Alzheimer's Disease, SCN2A encephalopathy, SCN8A encephalopathy, or SCN5A arrhythmia. In some embodiments, the disease or condition is Alzheimer's Disease, SCN2A encephalopathy, SCN8A encephalopathy, or SCN5A arrythmia. In some embodiments, the cells are *ex vivo*.

[0004a] In some embodiments, disclosed herein is a pharmaceutical composition comprising an antisense oligomer that comprises a sequence selected from the group consisting of SEQ ID NOs: 21-61, 64-67, 210-250, 253-256 and 304-379, and a pharmaceutically acceptable excipient.

[0004b] In some embodiments, disclosed herein is a composition comprising 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 mRNA) and that encodes Nav1.1 protein, whereby the antisense oligomer promotes exclusion of the NMD exon from the NMD exon mRNA encoding Nav1.1.

INCORPORATION BY REFERENCE

[0005] All publications, patents, and patent applications mentioned in this specification are herein incorporated by reference to the same extent as if each individual publication, patent, or patent application was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0006] The novel features of the invention are set forth with particularity in the appended claims. A better understanding of the features and advantages of the present invention will be obtained by reference to the following detailed description that sets forth illustrative embodiments, in which the principles of the invention are utilized, and the accompanying drawings of which:

[0007] FIG. 1 depicts a schematic representation of a target mRNA that contains a non-sense mediated RNA decay-inducing exon (NMD exon mRNA) and therapeutic agent-mediated

exclusion of the nonsense-mediated mRNA decay-inducing exon to increase expression of the full-length target protein or functional RNA. **FIG. 1A** shows a cell divided into nuclear and cytoplasmic compartments. In the nucleus, a pre-mRNA transcript of a target gene undergoes splicing to generate mRNA, and this mRNA is exported to the cytoplasm and translated into target protein. For this target gene, some fraction of the mRNA contains a nonsense-mediated mRNA decay-inducing exon (NMD exon mRNA) that is degraded in the cytoplasm, thus leading to no target protein production. **FIG. 1B** shows an example of the same cell divided into nuclear and cytoplasmic compartments. Treatment with a therapeutic agent, such as an antisense

CLAIMS

What is claimed is:

1. A pharmaceutical composition comprising an antisense oligomer that comprises a sequence selected from the group consisting of SEQ ID NOs: 21-61, 64-67, 210-250, 253-256 and 304-379, and a pharmaceutically acceptable excipient.

2. The pharmaceutical composition of claim 1, wherein the antisense oligomer comprises a sequence selected from the group consisting of SEQ ID NOs: 21-61 and 64-67.

3. The pharmaceutical composition of claim 1, wherein the antisense oligomer comprises a sequence selected from the group consisting of SEQ ID NOs: 210-250 and 253-256.

4. The pharmaceutical composition of claim 1, wherein the antisense oligomer comprises a sequence selected from the group consisting of SEQ ID NOs: 304-379.

5. The pharmaceutical composition of 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.

6. The pharmaceutical composition of claim 1, wherein the antisense oligomer comprises a 2'-O-methoxyethyl moiety.

7. The pharmaceutical composition of claim 6, wherein each nucleotide of the antisense oligomer comprises a 2'-O-methoxyethyl moiety.

8. The pharmaceutical composition of claim 1, wherein the antisense oligomer consists of from 8 to 50 nucleobases.

9. The pharmaceutical composition of claim 1, wherein the antisense oligomer consists of from 12 to 20 nucleobases.

10. The pharmaceutical composition of claim 1, wherein the pharmaceutical composition is formulated for intrathecal injection or intracerebroventricular injection.

11. The pharmaceutical composition of claim 1, wherein the antisense oligomer comprises a backbone modification, a modified sugar moiety or a combination thereof.

12. A composition comprising 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 mRNA) and that encodes Nav1.1 protein, whereby the antisense oligomer promotes exclusion of the NMD exon from the NMD exon mRNA encoding Nav1.1.

13. The composition of claim 12, wherein the antisense oligomer comprises a sequence selected from the group consisting of SEQ ID NOs: 21-67, 210-256 and 304-379.

14. The composition of claim 12, 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.

15. The composition of claim 12, wherein the antisense oligomer comprises 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.

16. The pharmaceutical composition of claim 1, wherein the antisense oligomer comprises 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.

17. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 32 or 221.

18. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 33 or 222.

19. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 42 or 231.

20. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 43 or 232.

21. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 44 or 233.

22. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 51 or 240.

23. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 54 or 243.

24. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 55 or 244.

25. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 56 or 245.

26. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 57 or 246.

27. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 58 or 247.

28. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 59 or 248.

29. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 304 or 342.

30. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 305 or 343.

31. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 306 or 344.

32. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 307 or 345.

33. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 308 or 346.

34. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 312 or 350.

35. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 313 or 351.

36. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 314 or 352.

37. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 315 or 353.

38. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 316 or 354.

39. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 318 or 356.

40. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID

NO: 319 or 357.

41. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 320 or 358.

42. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 321 or 359.

43. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 322 or 360.

44. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 323 or 361.

45. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 324 or 362.

46. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 326 or 364.

47. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 327 or 365.

48. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 328 or 366.

49. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 329 or 367.

50. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 330 or 368.

51. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 331 or 369.

52. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 332 or 370.

53. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 333 or 371.

54. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 334 or 372.

55. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 335 or 373.

56. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 337 or 375.

57. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 338 or 376.

58. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 339 or 377.

59. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 340 or 378.

60. The pharmaceutical composition of claim 1, wherein the antisense oligomer is SEQ ID NO: 341 or 379.

61. The pharmaceutical composition of any one of claims 16-60, wherein the antisense oligomer comprises a 2'-O-methoxyethyl moiety.

62. The pharmaceutical composition of any one of claims 16-60, wherein each nucleotide of the antisense oligomer comprises a 2'-O-methoxyethyl moiety.