grey) flanked by 3′ and 5′ splice sites (underlined sequence). Inclusion of this exon leads to a frameshift and the introduction of a premature termination codon in exon 21 rendering the transcript a target of NMD. Figure discloses SEQ ID NO: 1100.

[0014] **FIG. 2** shows a study design timeline for monitoring wild type (WT) and Dravet Syndrome (DS) mice as well as a Kaplan-Meier curve showing DS and WT littermate mice monitored to 14 weeks for survival.

[0015] **FIG. 3** shows an experimental design for the EEG seizure monitoring study in DS mice and their WT littermates.

[0016] **FIGs. 4A-4E** show the results of monitoring seizure in mice administered with ASO-22 or PBS**. FIG. 4A** shows exemplary ECG recordings in DS mice. **FIG. 4B** shows the number of seizures occurring in various regions of the brain in the two mice groups. *Indicates $p<0.05$. **FIG. 4C** summarizes total number of spontaneous seizures (generalized and focal) recorded between P22 and P46 in DS mice dosed with PBS (n=21) or ASO-22 (n=21). *Indicates $p<0.05$. **FIG. 4D** shows the number of mice that had a number of seizures in each group. **FIG. 4E** shows effect of ASO-22 on the latency to the first recorded seizure between P22 and P46 in DS mice dosed with PBS (n=21) or ASO-22 (n=21).

[0017] **FIGs. 5A-5G** show that a single ICV injection of 20 μg ASO-22 at P2 results in reduced SUDEP incidence and increased $Na_V1.1$ protein expression in DS mice. **FIG. 5A** is a schematic for the experimental design. **FIGs. 5B, 5C, 5D, 5E, 5F, and 5G** illustrate the ASO-22 exposure, *Scn1a* expression, and $Na_V1.1$ expression in brain tissues at 7 weeks or 14 weeks after a single ICV injection of ASO-22 (20 μg) or PBS on P2, respectively.

[0018] **FIGs. 6A-6B** show the percent survival of DS and WT mice after a single ICV injection of ASO-22 (60 μg) or PBS on P14.

[0019] **FIGs. 7A-7F** show the ASO-22 exposure, *Scn1a* expression, and $Na_V1.1$ expression in brain tissues at P35 and P90 after a single ICV injection of ASO-22 (60 μg) or PBS on P14, respectively.

[0020] **FIG. 8** shows the experimental conditions and numbers of monkeys used per group.

[0021] **FIGs. 9A-9B** show the levels of ASO-22 in the cynomolgus monkey brain on study day 3 and 29.

[0022] **FIGs. 10A-10B** show the levels of $Na_V1.1$ protein in cynomolgus monkey brain regions on Day 3 and Day 29.

[0023] **FIGs. 11A-11B** show the percentages of productive *SCN1A* gene to total *SCN1A* gene as an evaluation of target engagement in cynomolgus monkeys on day 3 and day 29.

[0024] **FIG. 12A** shows the Plasma pharmacokinetics in cynomolgus monkey after Intrathecal Administration of ASO-22. **FIG. 12B** shows the levels of ASO-22 in the cynomolgus monkey cerebrospinal fluid (CSF) on study day 3 and 29.

[0025] **FIGs. 13A-13D** depict identification of an alternative splicing event in *SCN1A* that results in NMD. **FIG. 13A** shows *SCN1A* splicing isoforms with or without inclusion of the alternative exon in ReNcells as demonstrated by RT-PCR. **FIG. 13B** shows evaluation of the alternative splice event of the *SCN1A* gene in cerebral cortex from 4 species. **FIG. 13C** shows TBE PAGE of RT-PCR products corresponding to *Scn1a* productive (lower bands, 498bp) and non-productive transcript (upper bands, 562bp) amplified from total RNA extracted from WT C57BL/6J mouse brains from P0 to P20 and at 10 months. Mouse *Gapdh*