

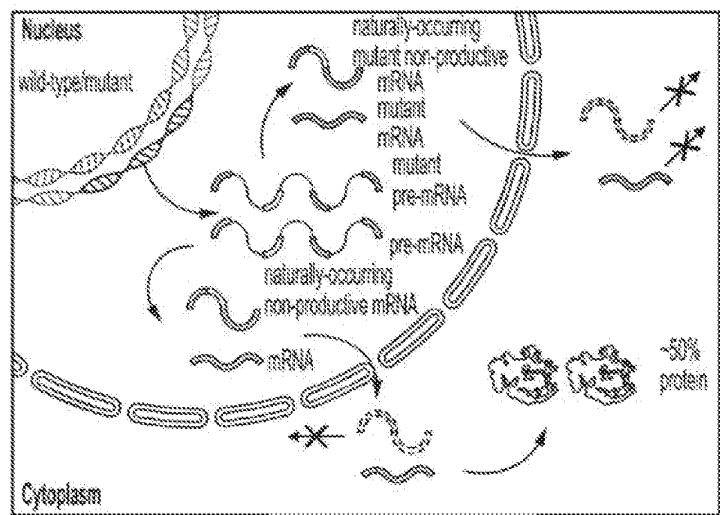


FIG. 1A

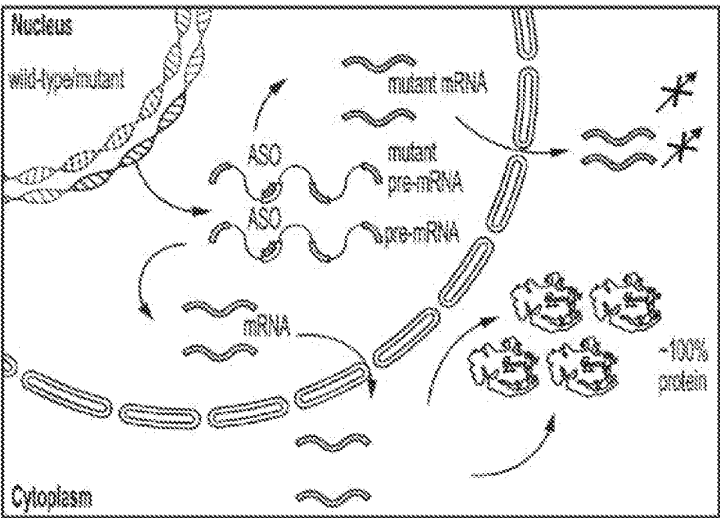


FIG. 1B

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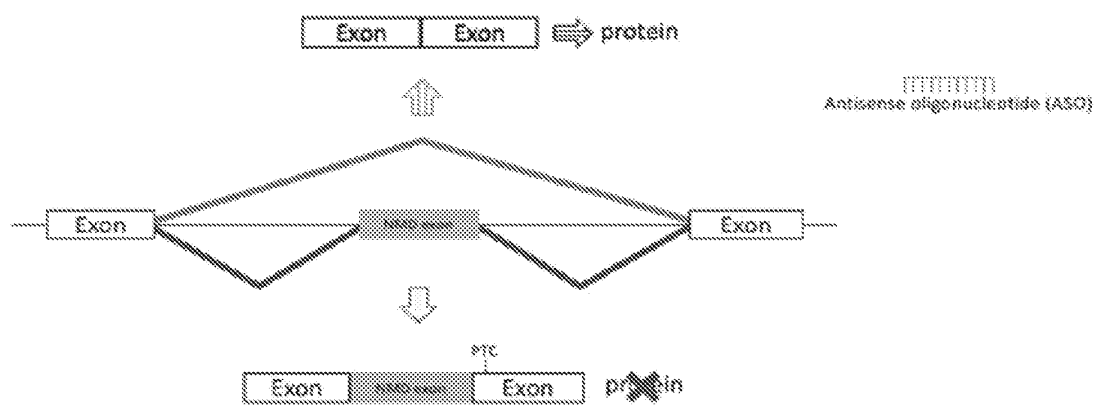


FIG. 1C

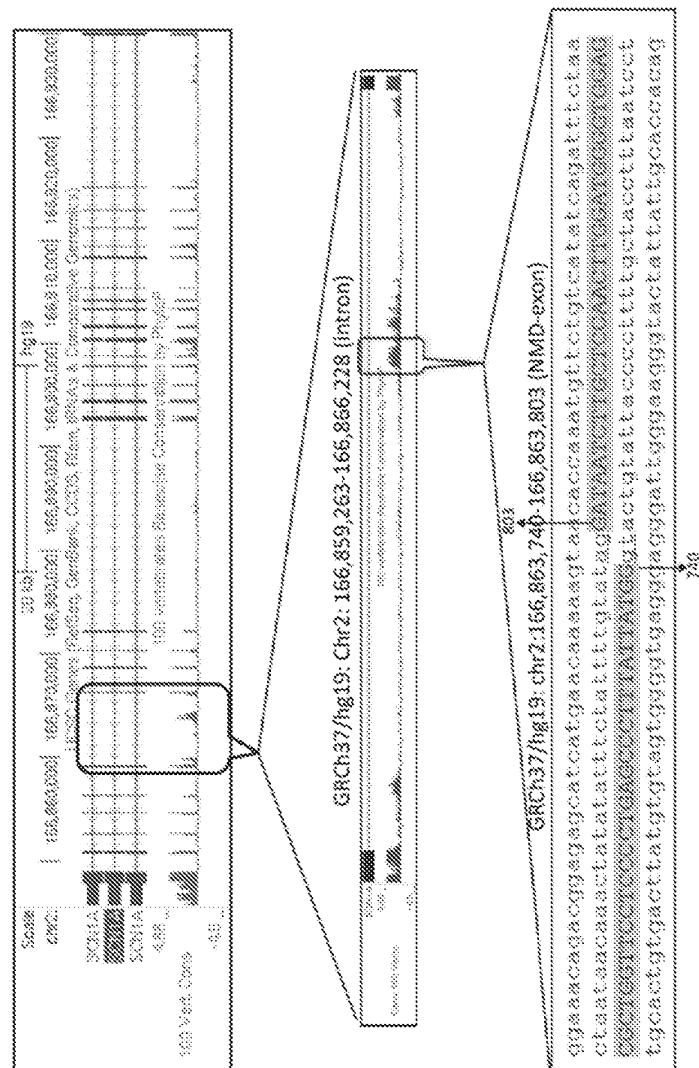


FIG. 1D

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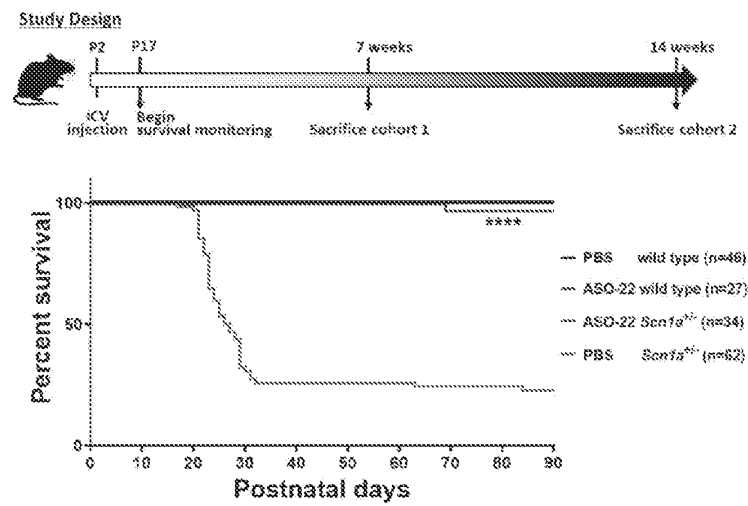


FIG. 2

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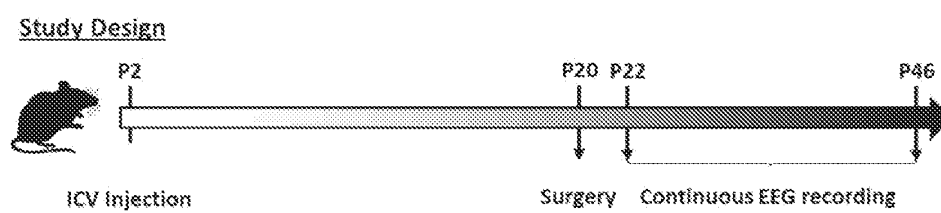


FIG. 3

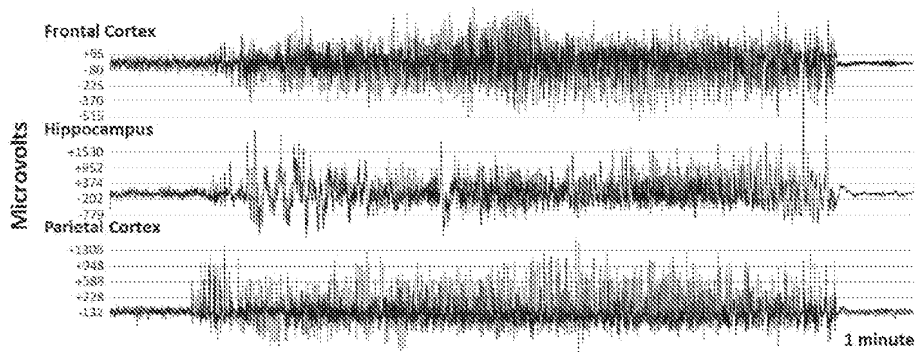


FIG. 4A

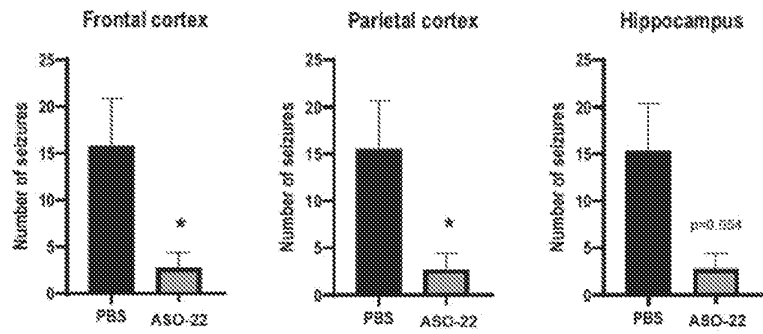


FIG. 4B

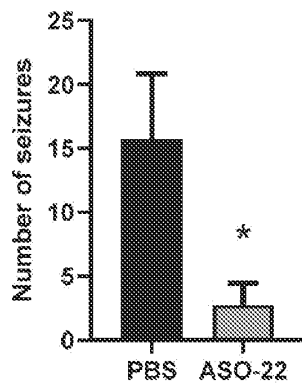


FIG. 4C

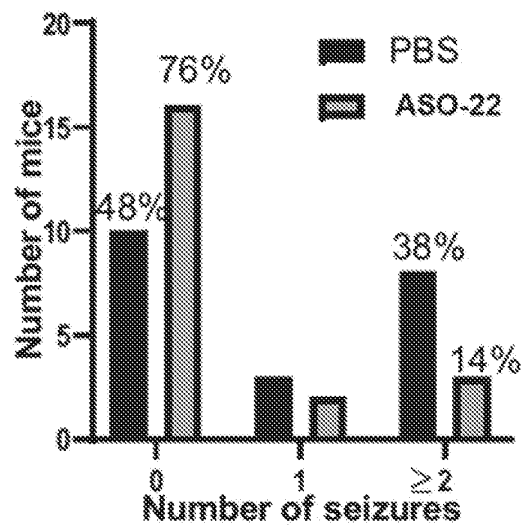


FIG. 4D

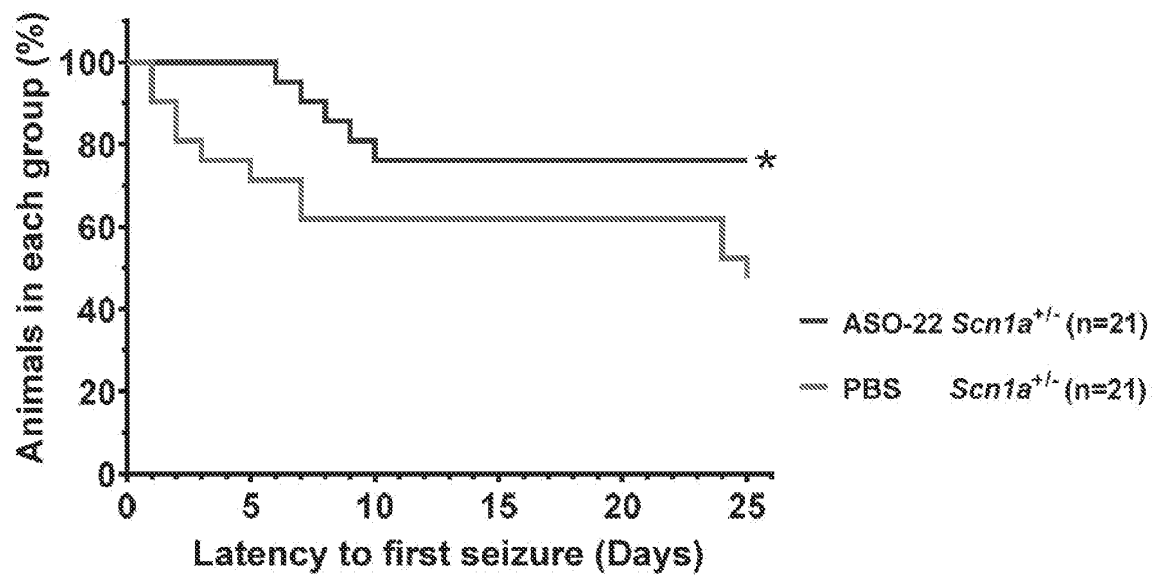


FIG. 4E

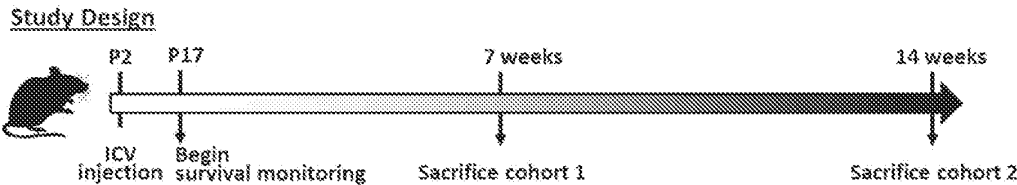


FIG. 5A

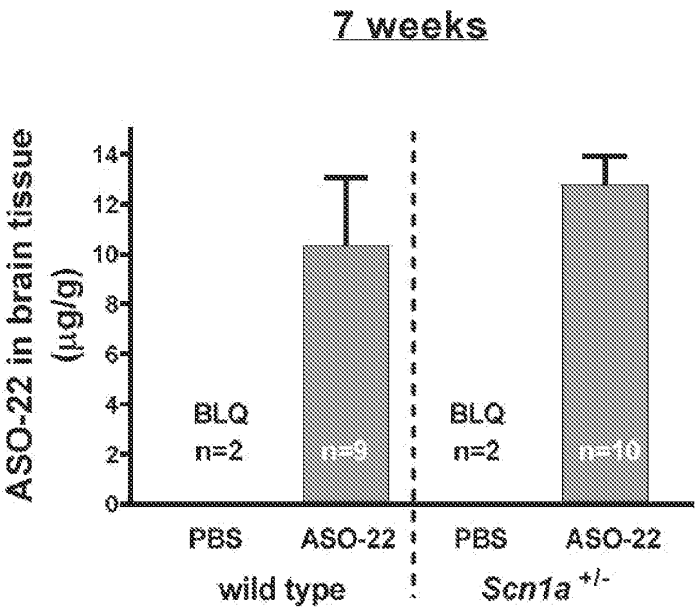


FIG. 5B

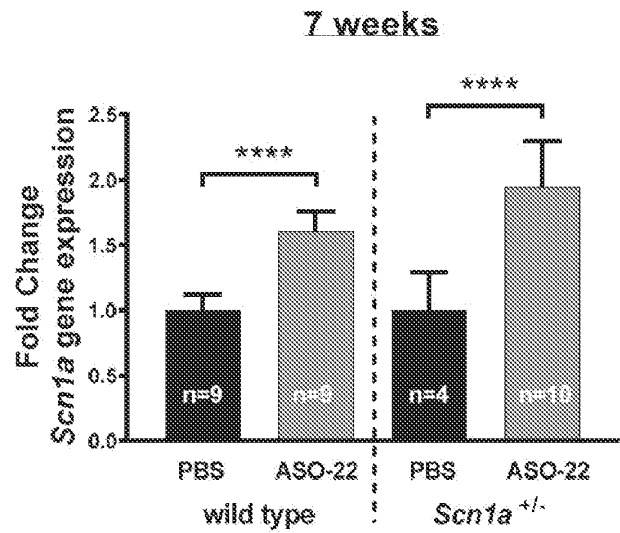


FIG. 5C

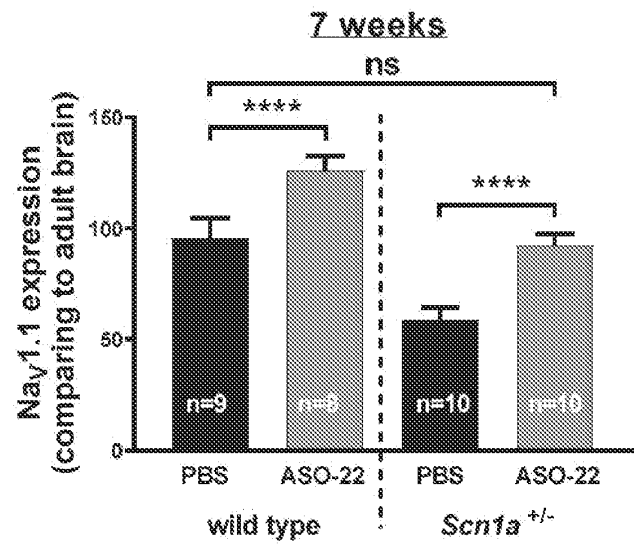


FIG. 5D

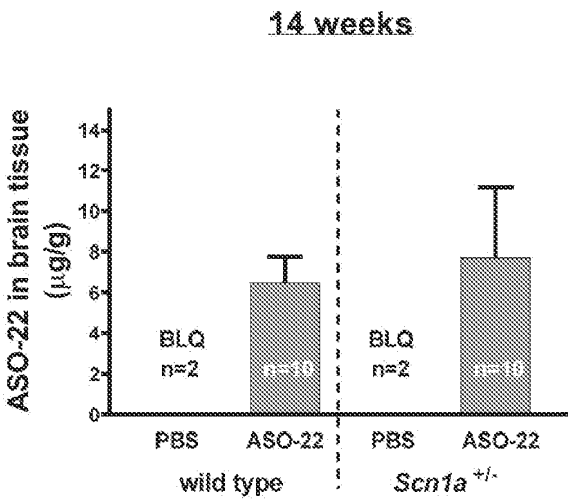


FIG. 5E

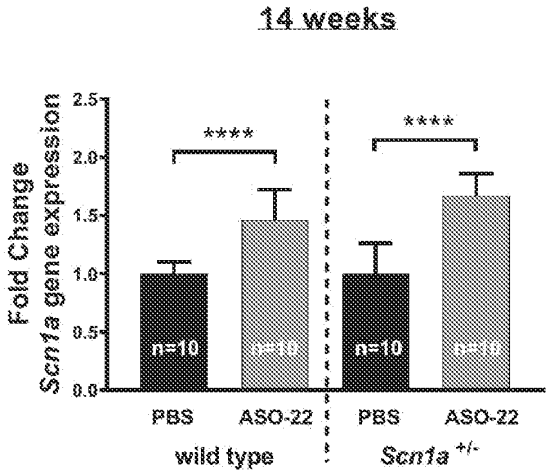


FIG. 5F

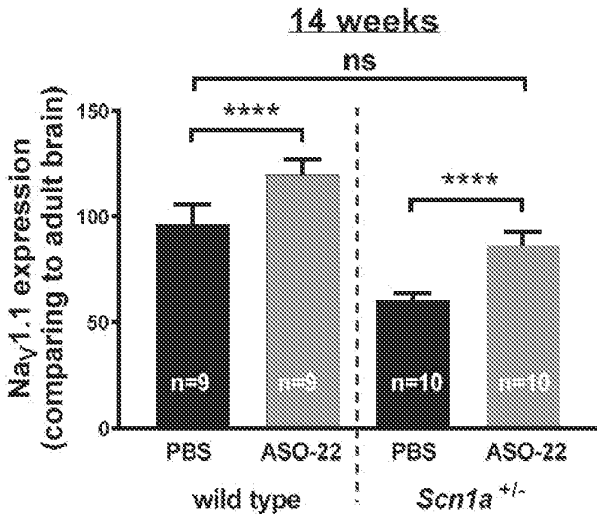


FIG. 5G

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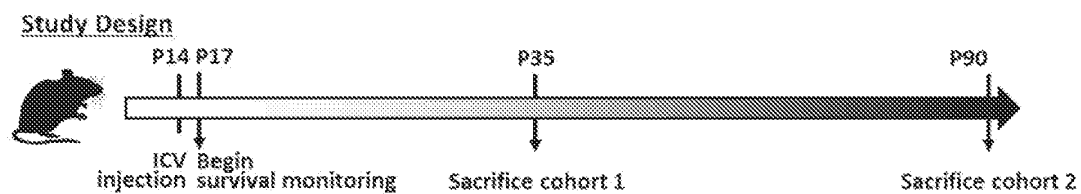


FIG. 6A

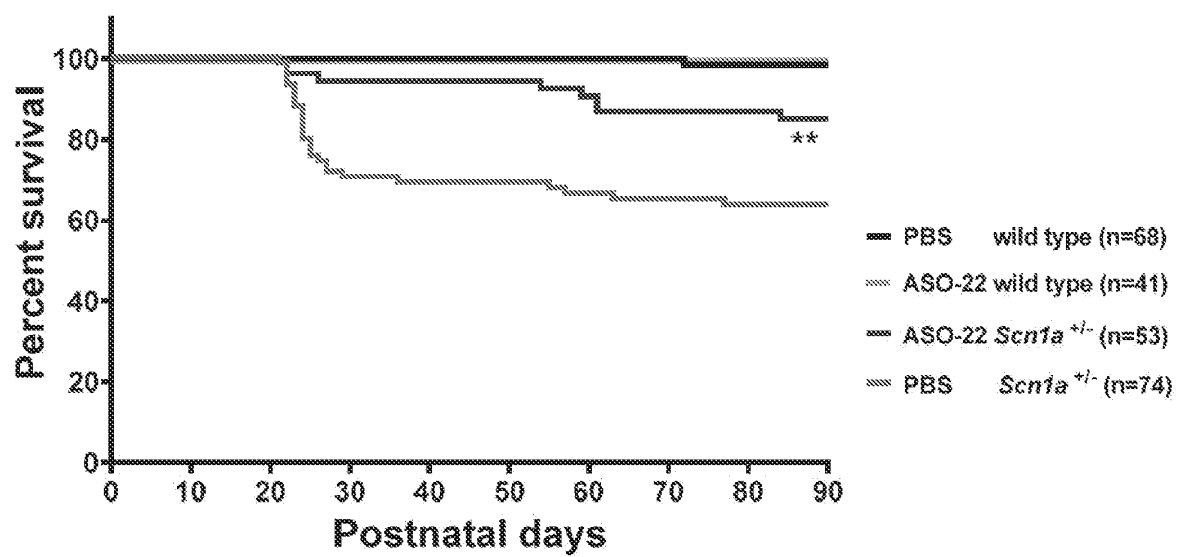


FIG. 6B

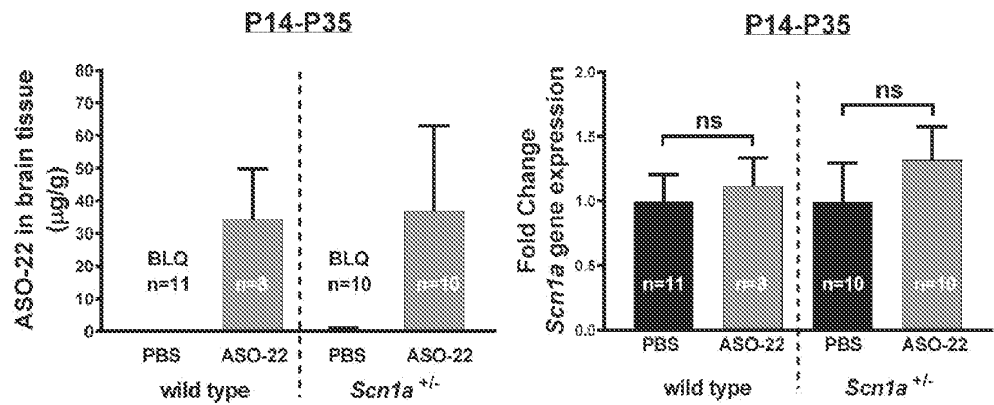


FIG. 7A

FIG. 7B

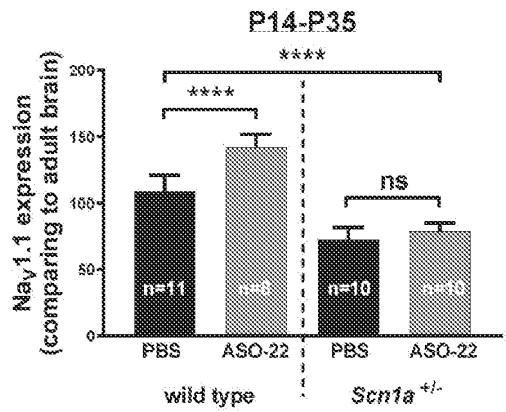


FIG. 7C

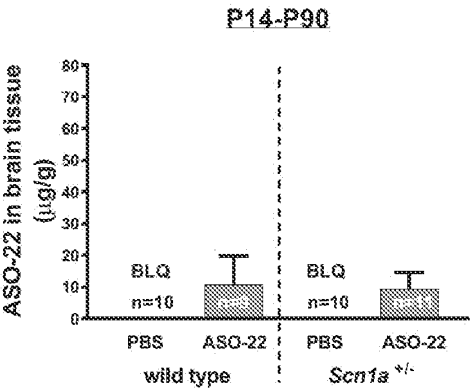


FIG. 7D

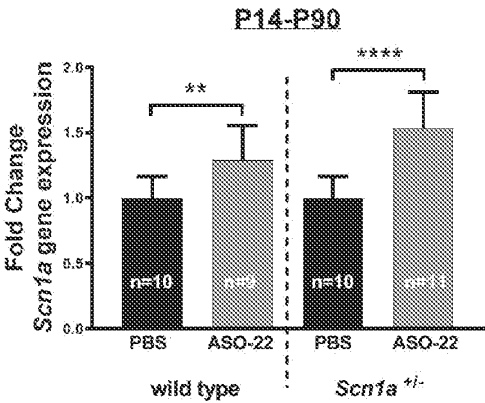


FIG. 7E

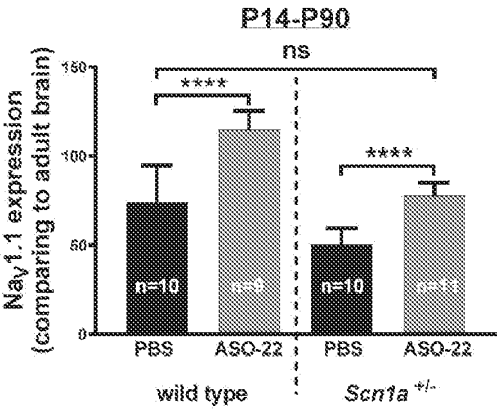


FIG. 7F

Treatment	Dose	Day 3 Necropsy	Day 29 Necropsy
Vehicle (aCSF)	na	2 Male	2 Male
ASO-22	Low	3 Male	3 Male
ASO-22	High	3 Male	3 Male

FIG. 8

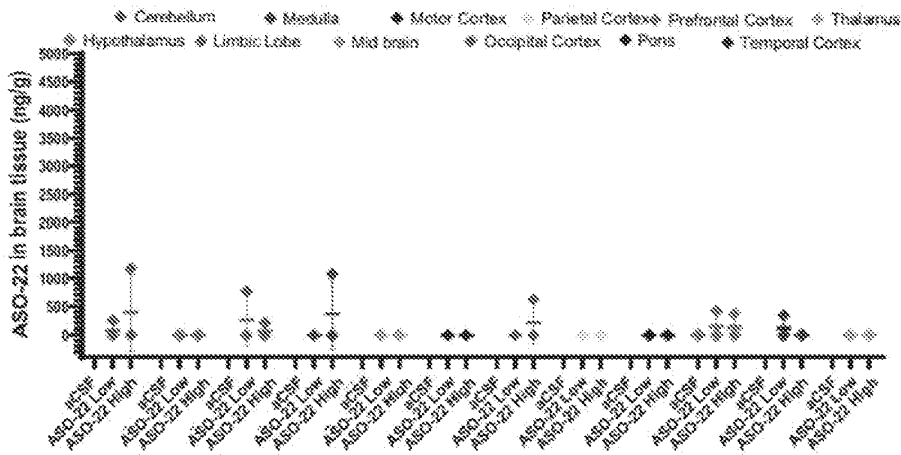


FIG. 9A

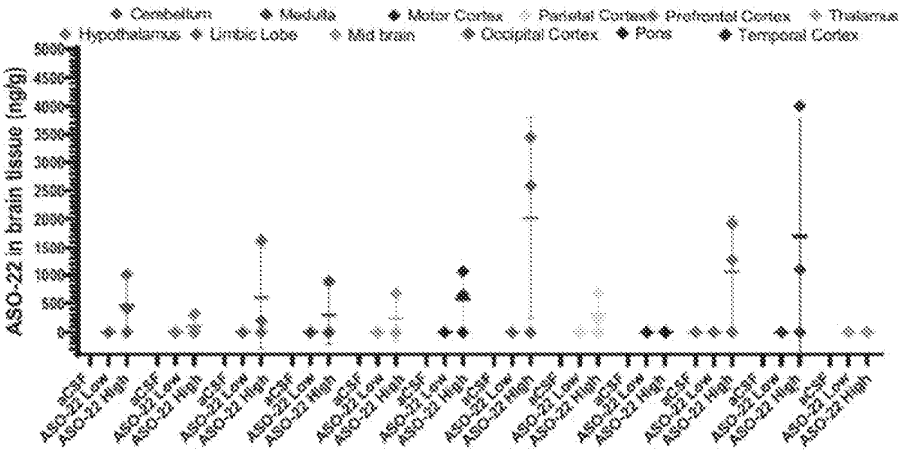


FIG. 9B

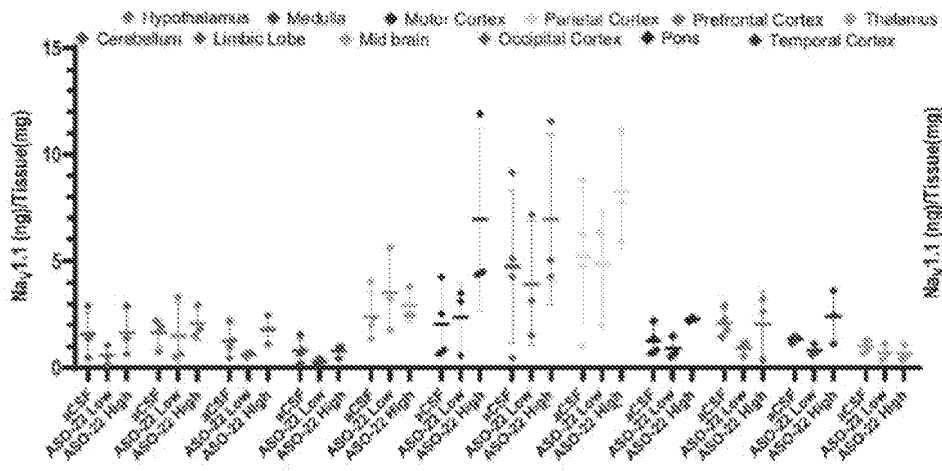


FIG. 10A

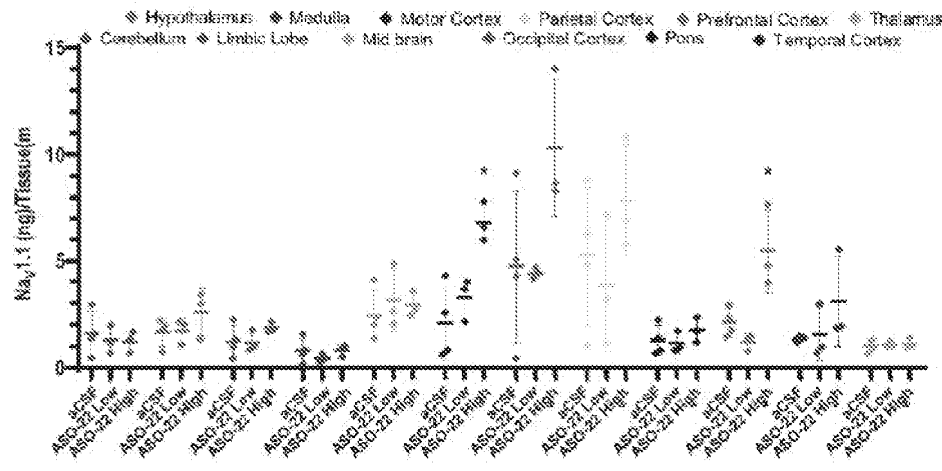


FIG. 10B

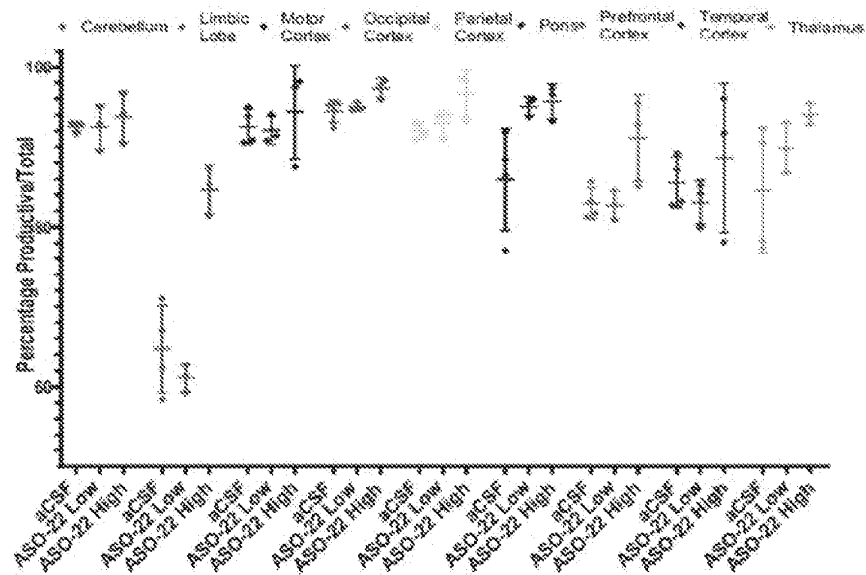


FIG. 11A

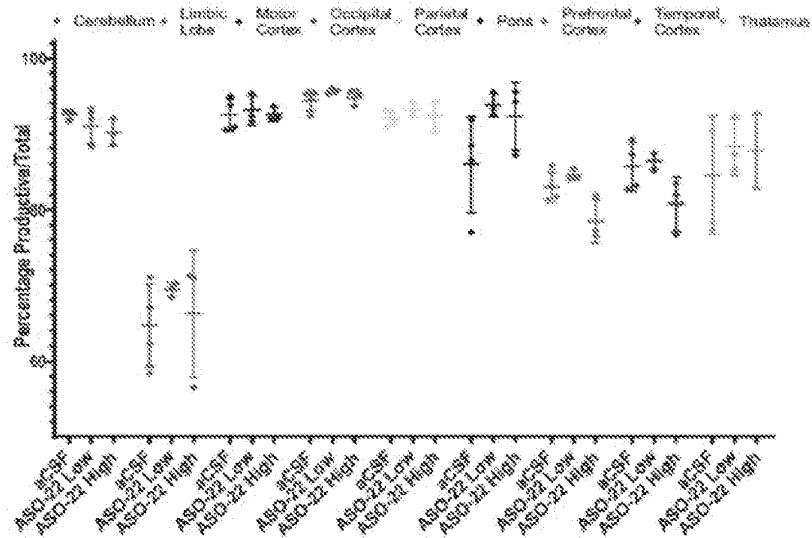


FIG. 11B

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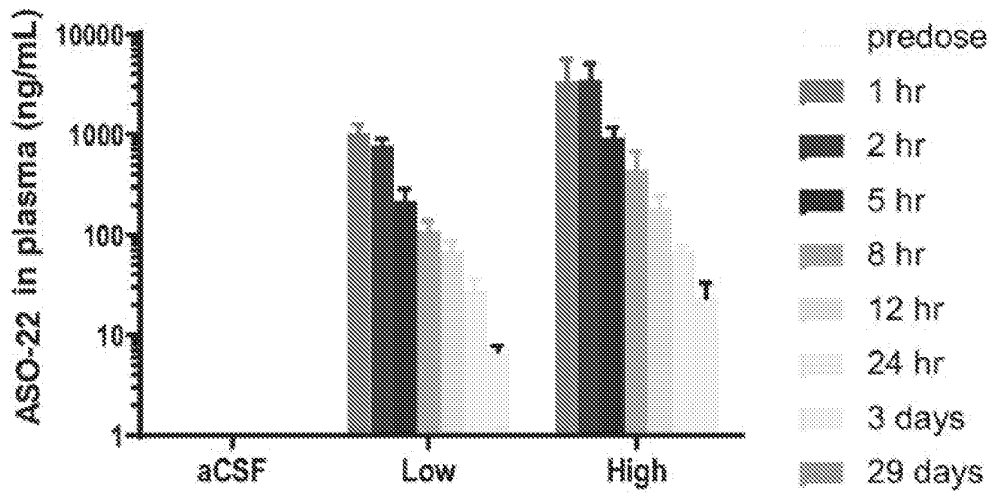


FIG. 12A

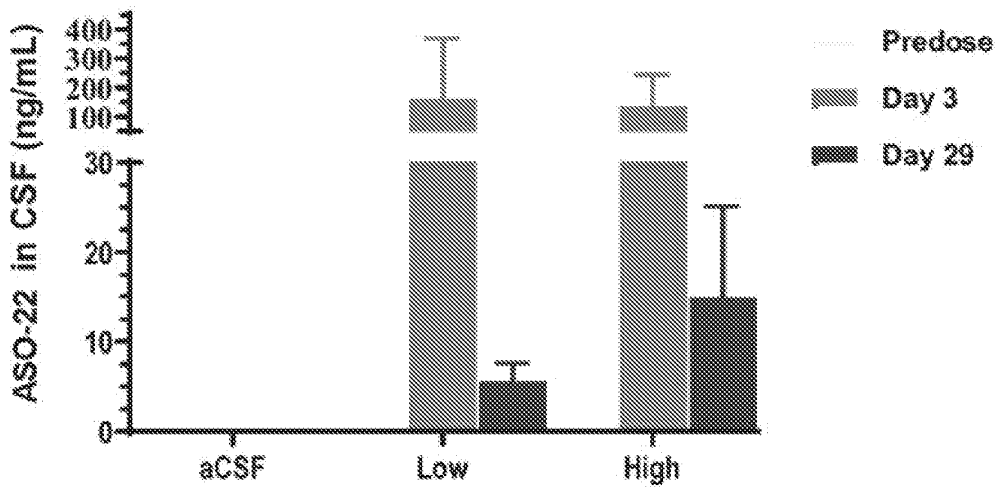


FIG. 12B

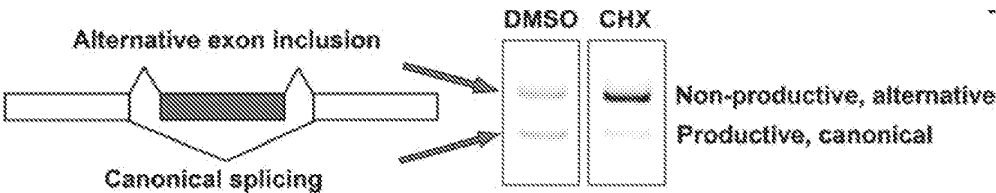


FIG. 13A

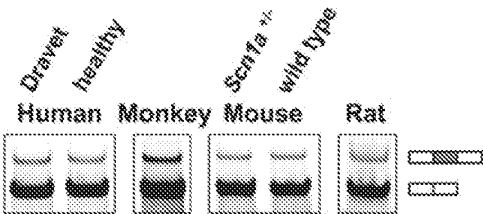


FIG. 13B

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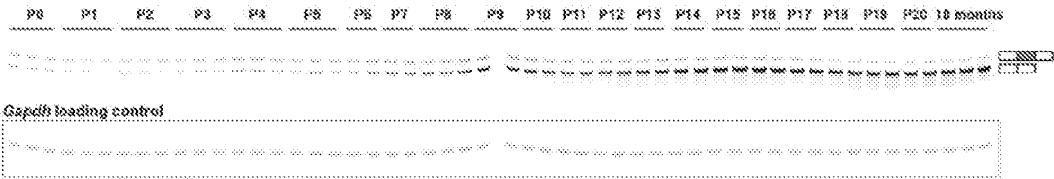


FIG. 13C

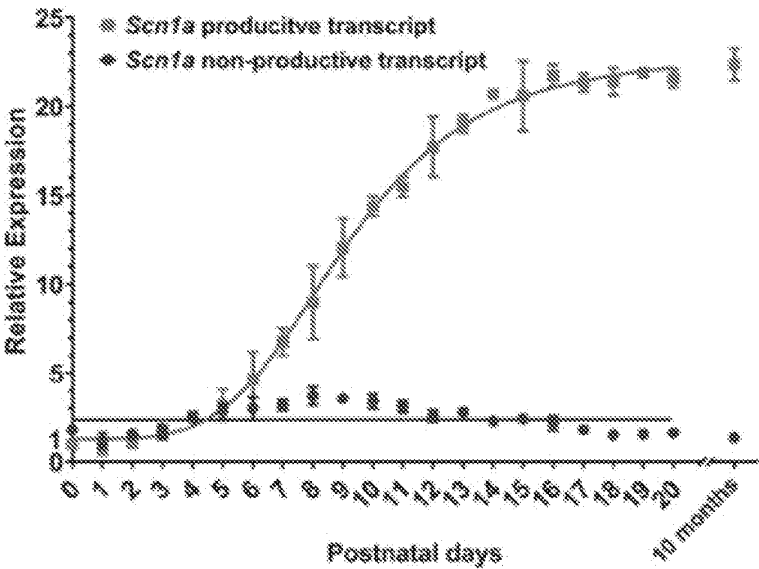


FIG. 13D

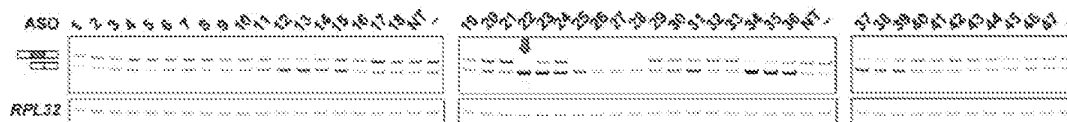


FIG. 14A

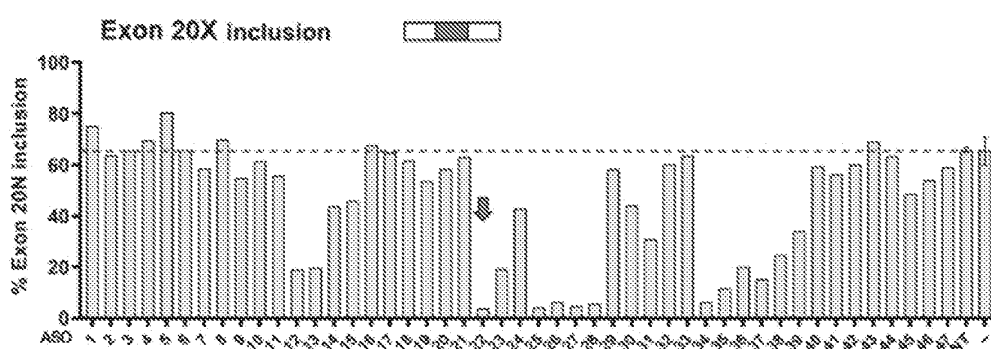


FIG. 14B

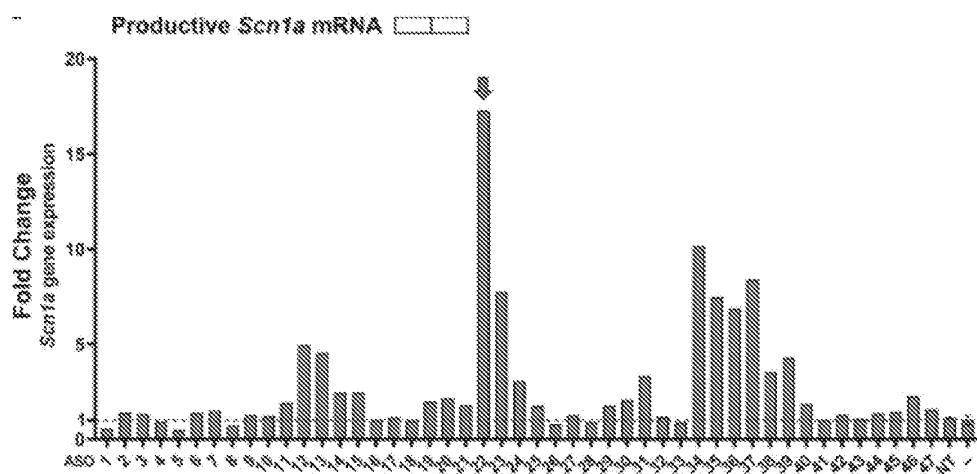


FIG. 14C

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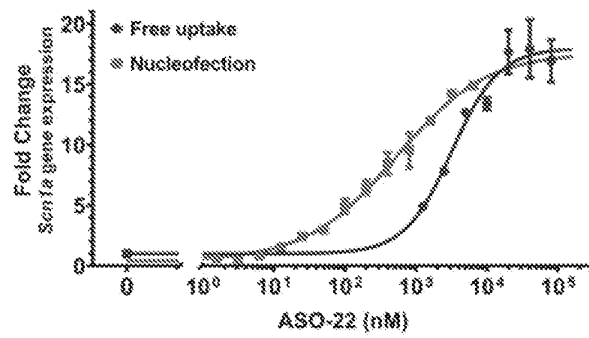


FIG. 14D

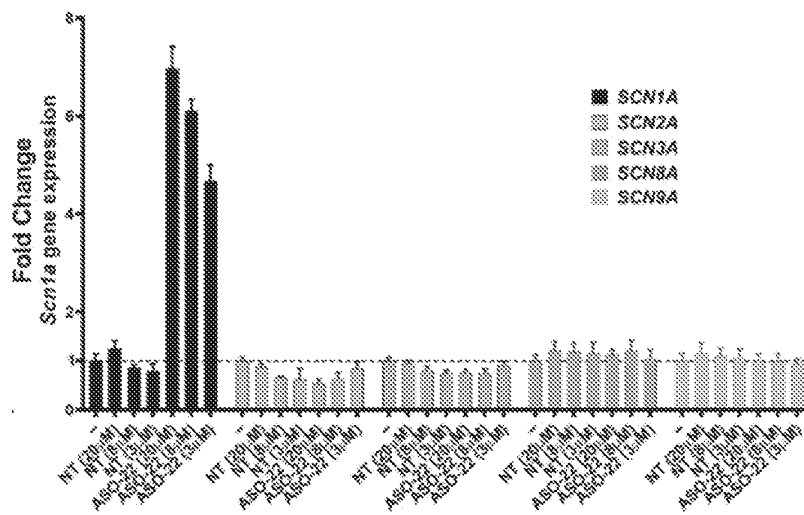


FIG. 14E

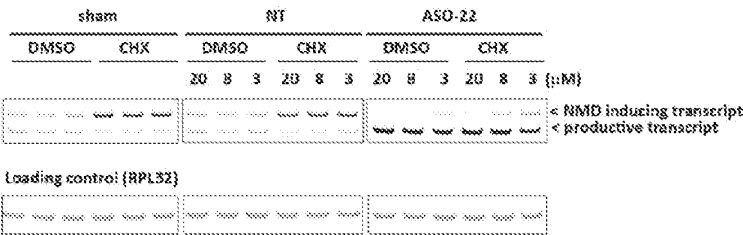


FIG. 15A

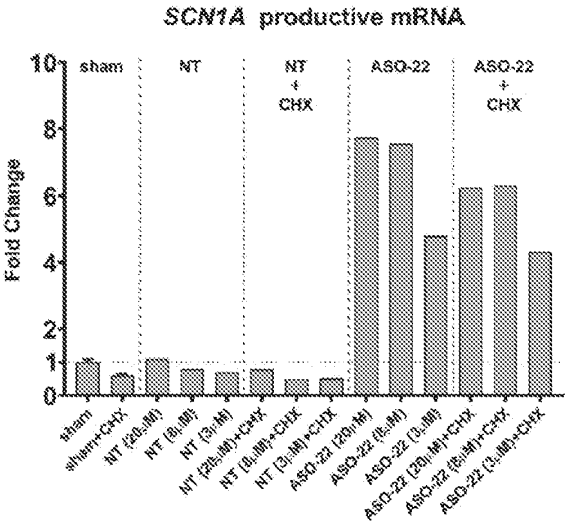


FIG. 15B

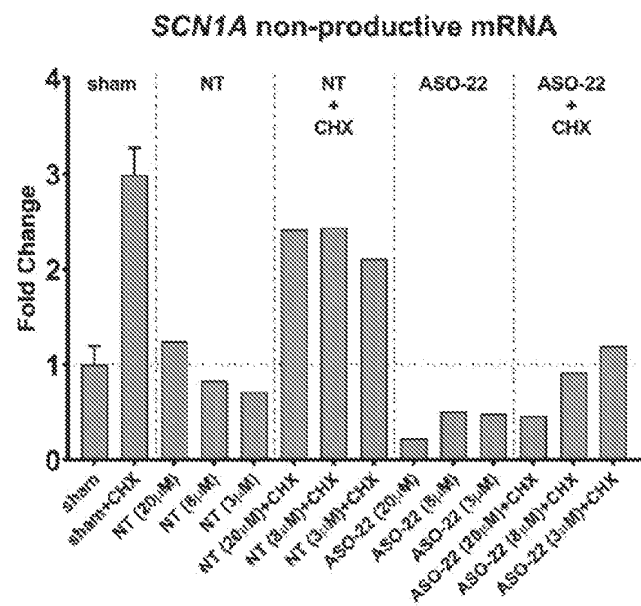


FIG. 15C

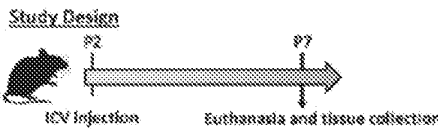


FIG. 16A

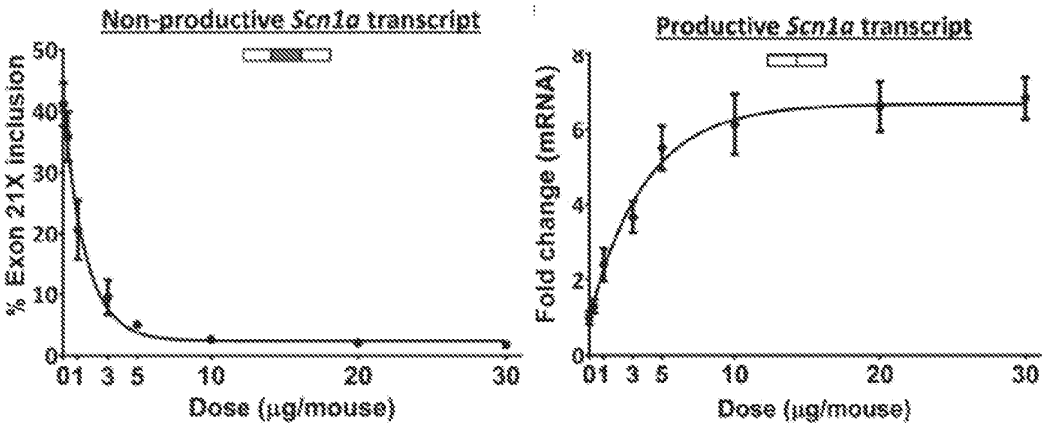


FIG. 16B

FIG. 16C

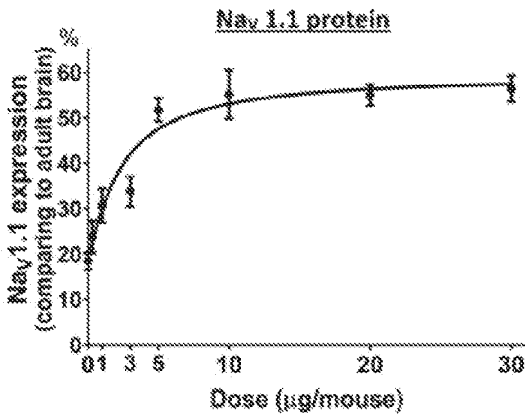
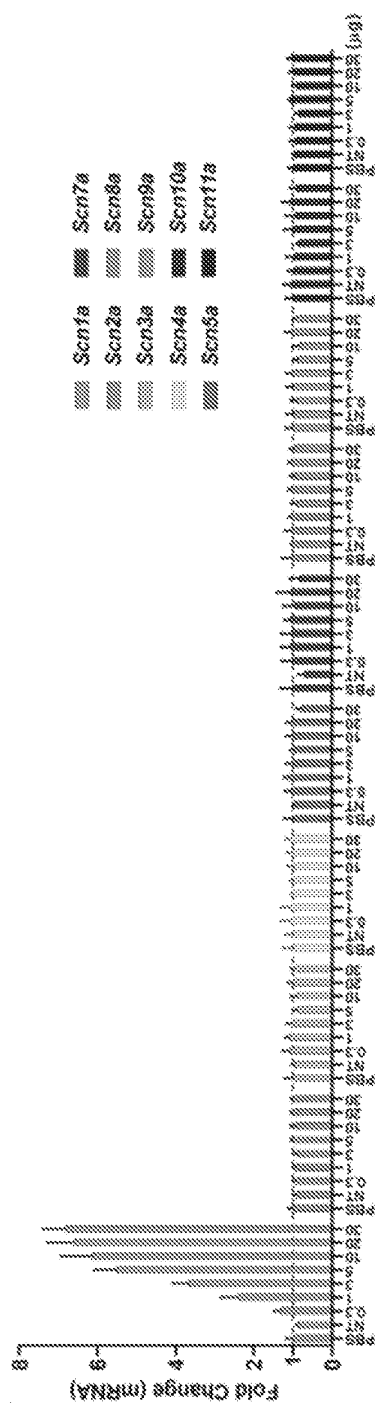


FIG. 16D



SE

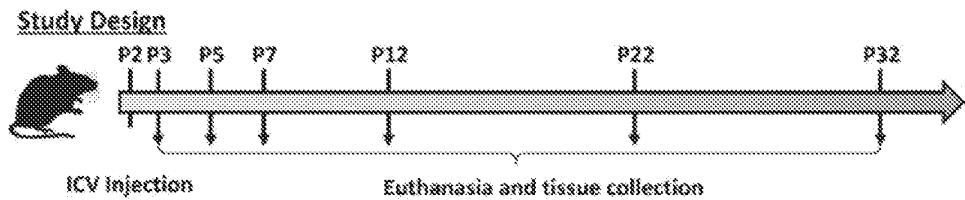


FIG. 16F

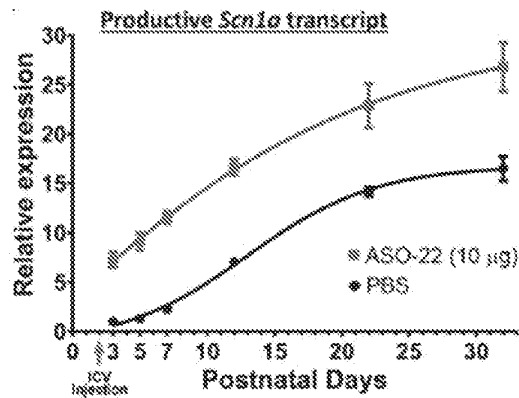


FIG. 16G

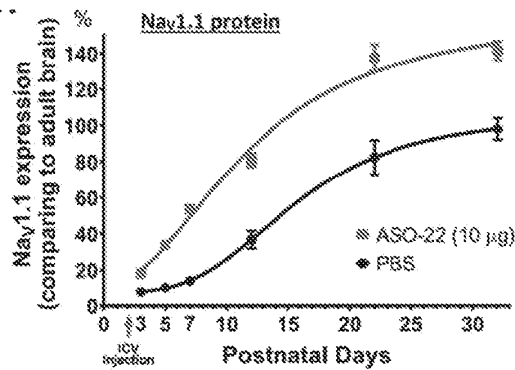


FIG. 16H

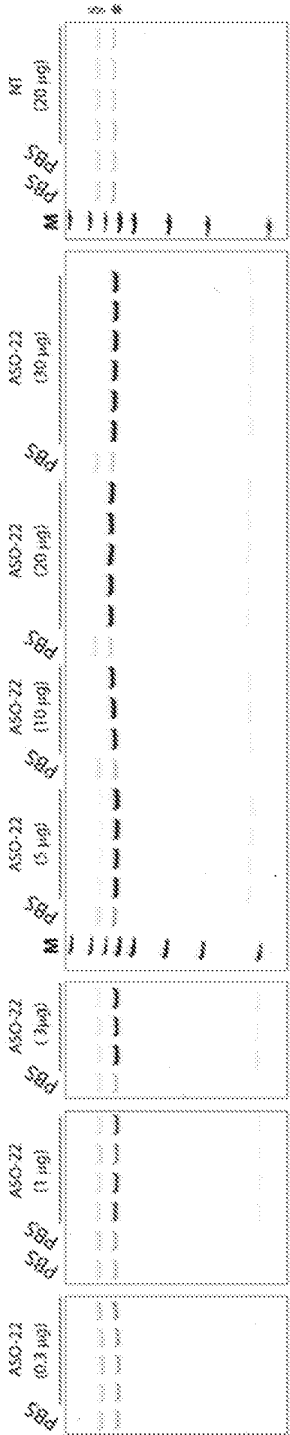


FIG. 17

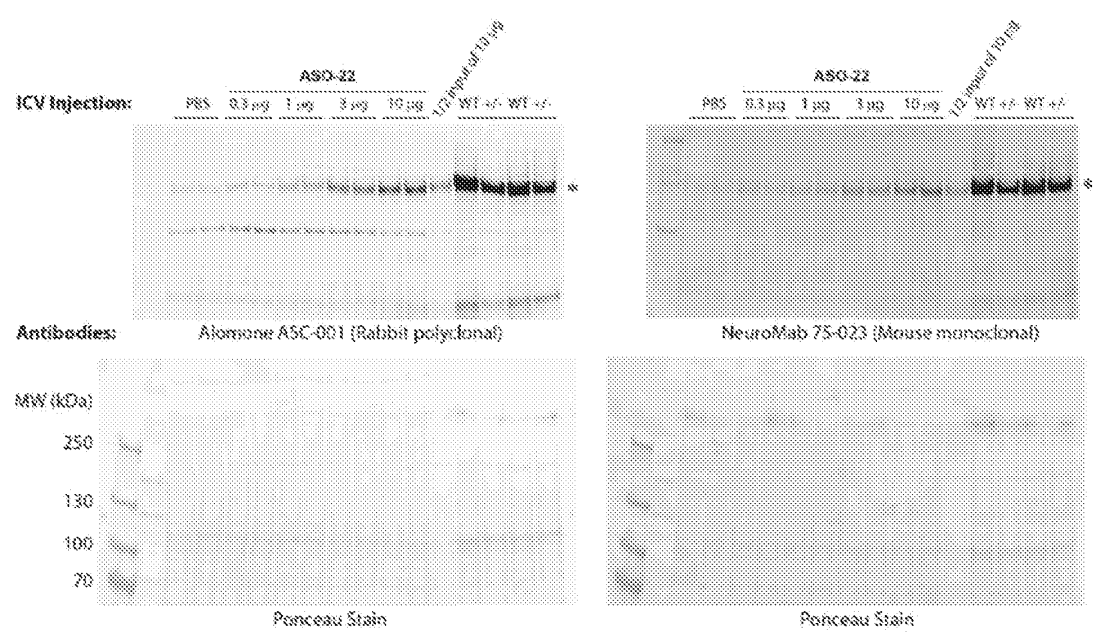


FIG. 18

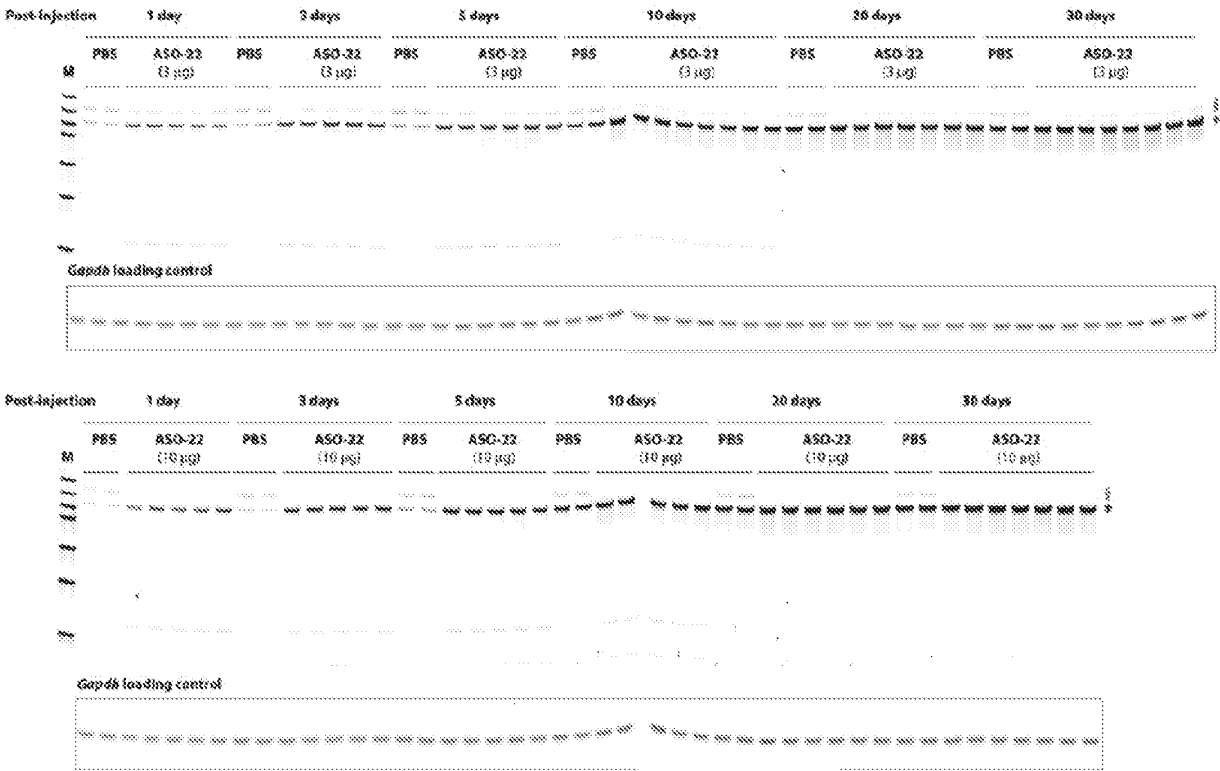


FIG. 19

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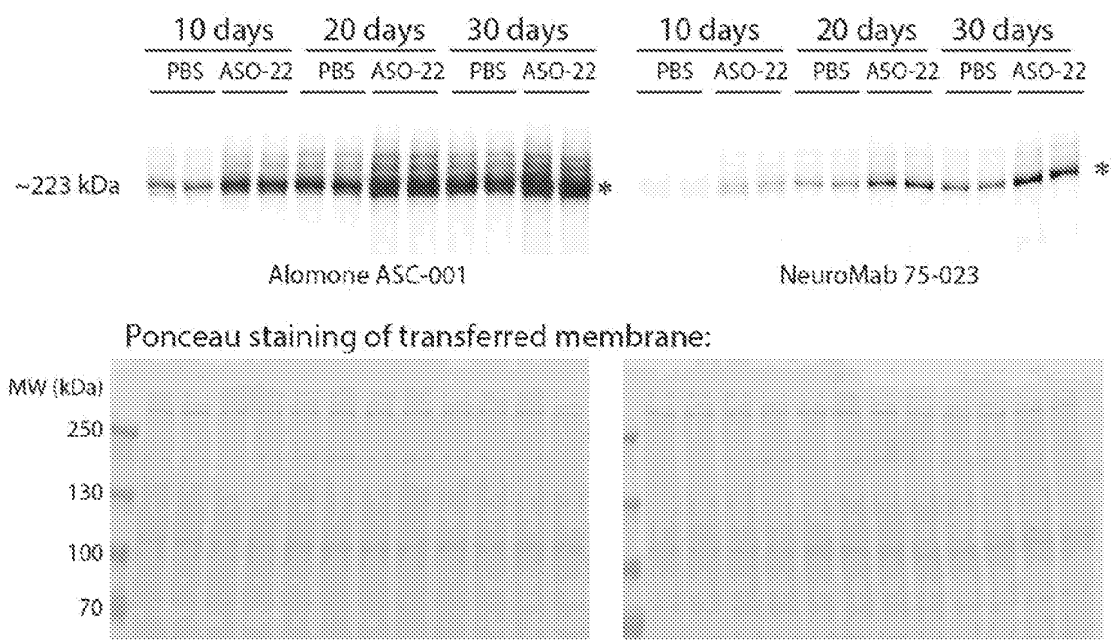


FIG. 20

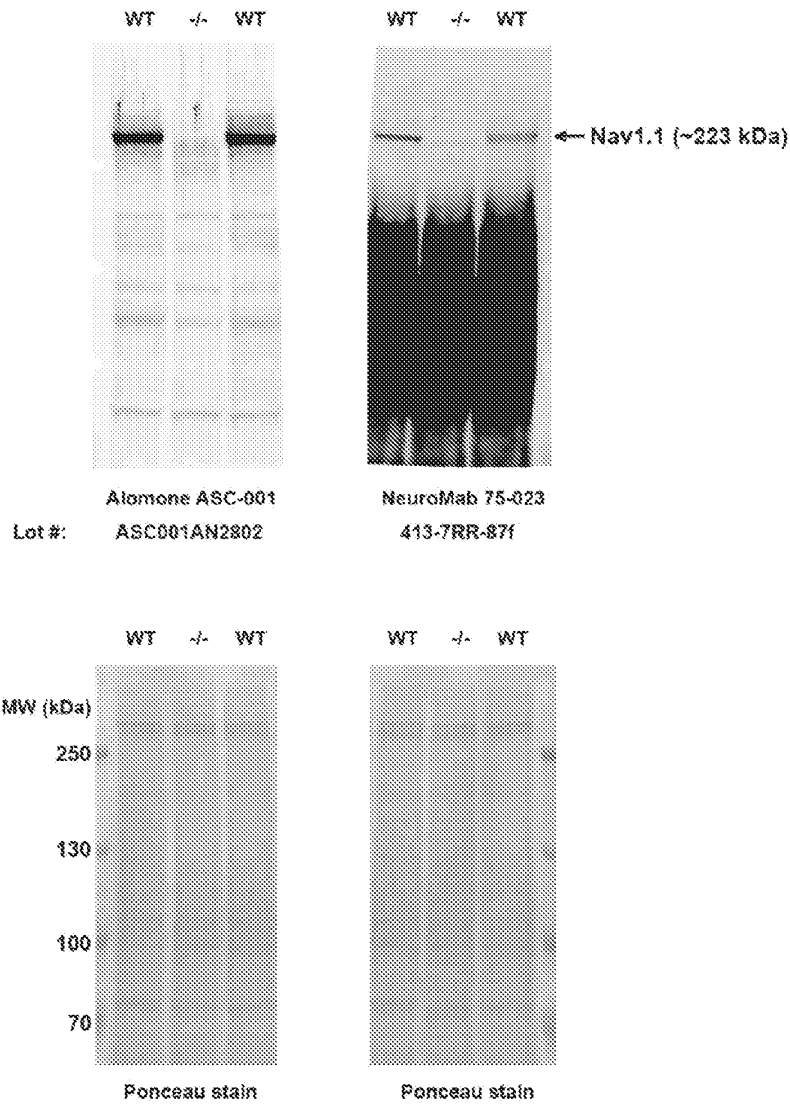


FIG. 21

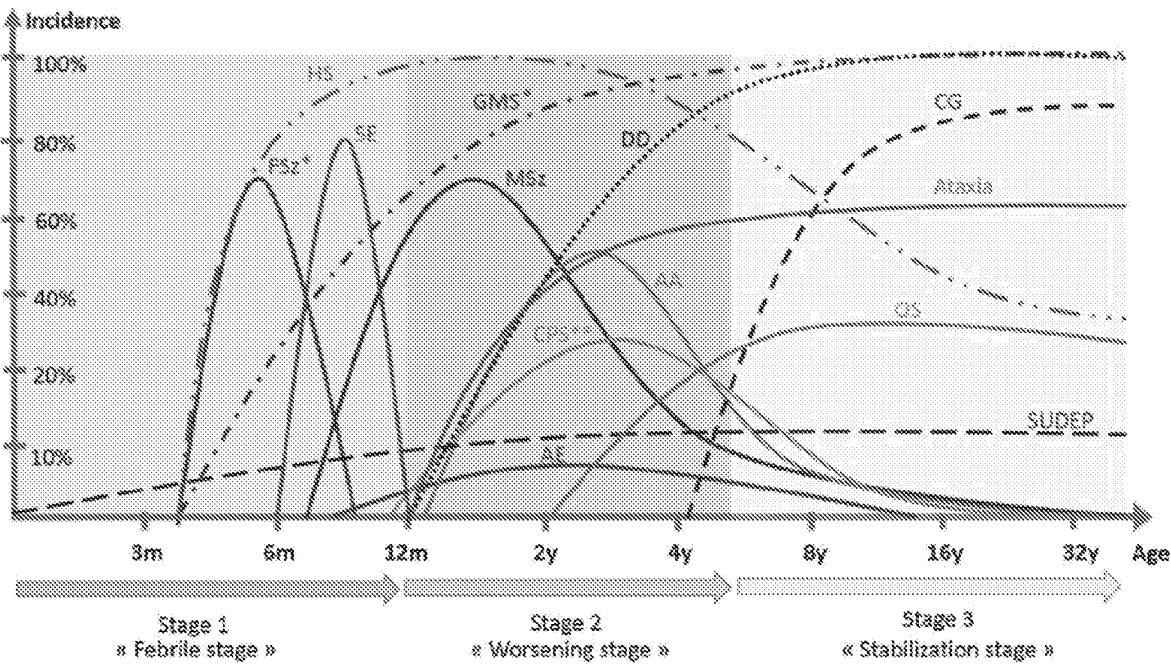


FIG. 22

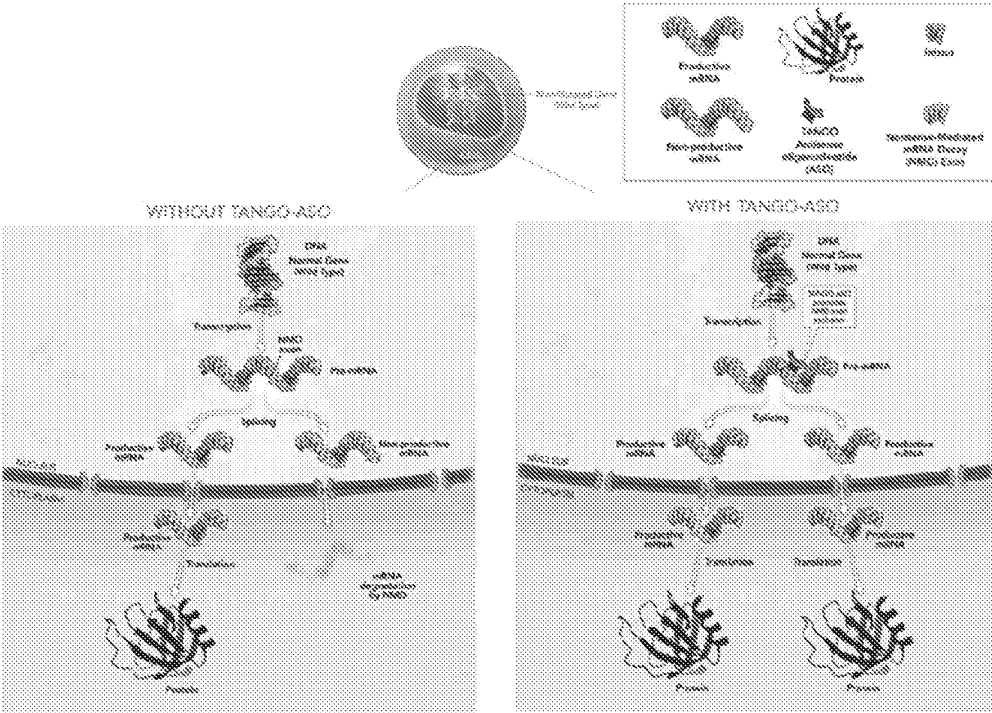


FIG. 23

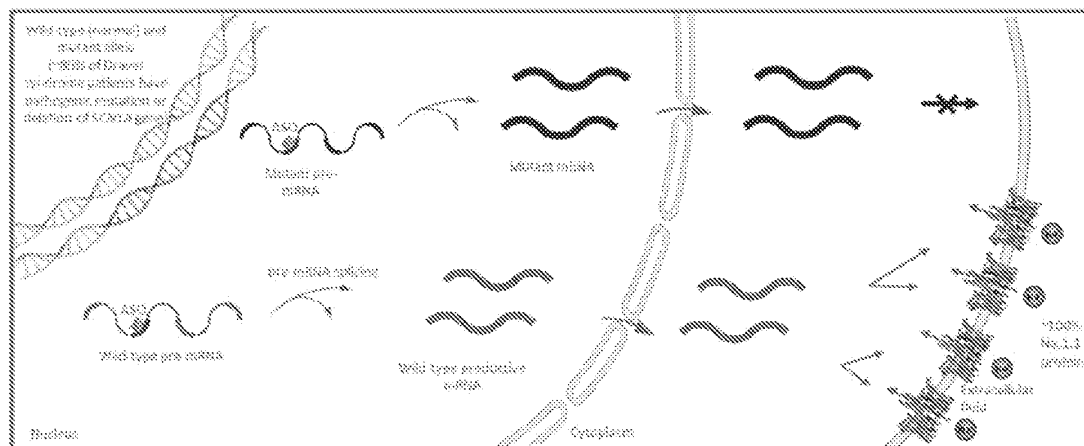


FIG. 24

Item	Proposed Amendment v3.0
Cohorts	Single and Multiple Ascending Doses (MAD)
Study duration	7-9 months / patient
Number of patients	<70

FIG. 25

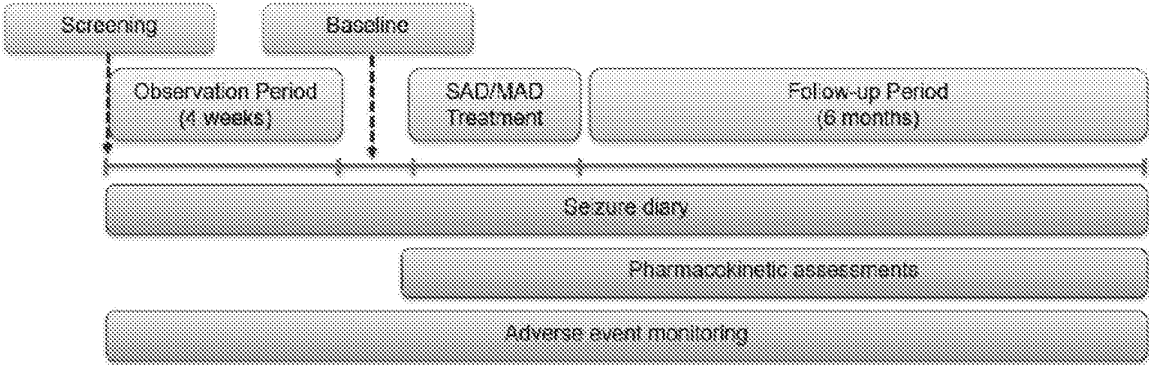


FIG. 26

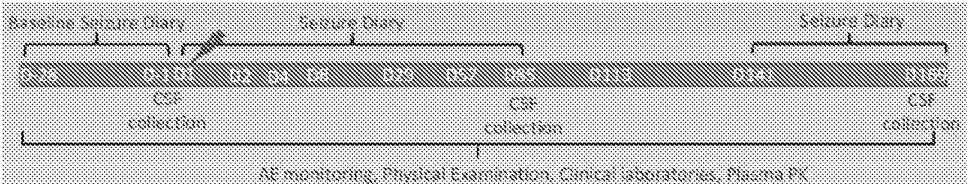
Inclusion Criteria	Exclusion Criteria
Aged 2-16 years (inclusive)	Known pathogenic mutation in another gene that causes epilepsy
DS onset <12 months of age with recurrent seizures (focal motor, hemiclonic, or generalized tonic-clonic) - No history of causal MRI lesion (MRI not required) - No other known etiology - Normal development at seizure onset	Currently being treated with an anti-epileptic drug acting primarily as a sodium channel blocker, as maintenance treatment
Documented pathogenic, likely pathogenic variant, or variant of uncertain significance in SCN1A	Clinically significant unstable medical condition(s) other than epilepsy
≥2 prior treatments for epilepsy that lacked adequate seizure control or had to be discontinued due to adverse events (AEs)	Clinically relevant symptoms or a clinically significant illness in the 4 weeks prior to screening or dosing on day 1, other than epilepsy
≥1 anti-epileptic drug (and any other treatments) at a stable dose for ≥4 weeks	Any other significant disease or disorder, in the investigator's opinion, that may put the patient at risk, influence the study results, or affect the patient's ability to participate in the study

FIG. 27

Primary Outcome Measures	
Safety assessments	• Adverse events
Pharmacokinetics	• Plasma concentrations of Compound-A
Cerebral spinal fluid (CSF)	• Compound-A levels
Secondary Outcome Measures	
Seizure frequency	• Measured by paper diary
Clinical status (caregiver)	• Caregiver Global Impression of Change (CaGIC): 7-level scale from very much improved to very much worse
Clinical Status (clinician)	• Clinical Global Impression of Change (CGIC) : 7-level scale from very much improved to very much worse
Quality of life	• EQ-5D-Y (patients ≥8 years will complete themselves [Self Complete version] if able): scale 0-100

FIG. 28

SAD Study Assessments



MAD Study Assessments

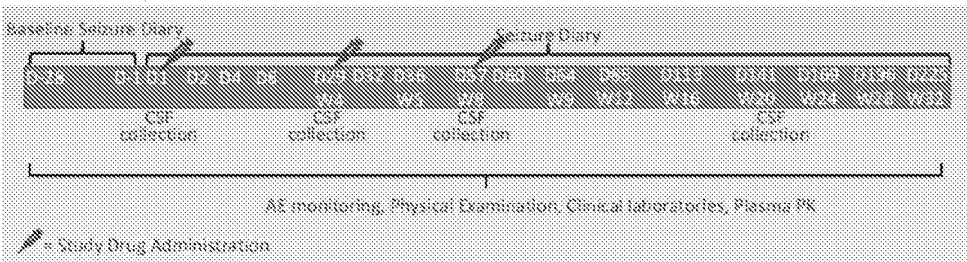


FIG. 29

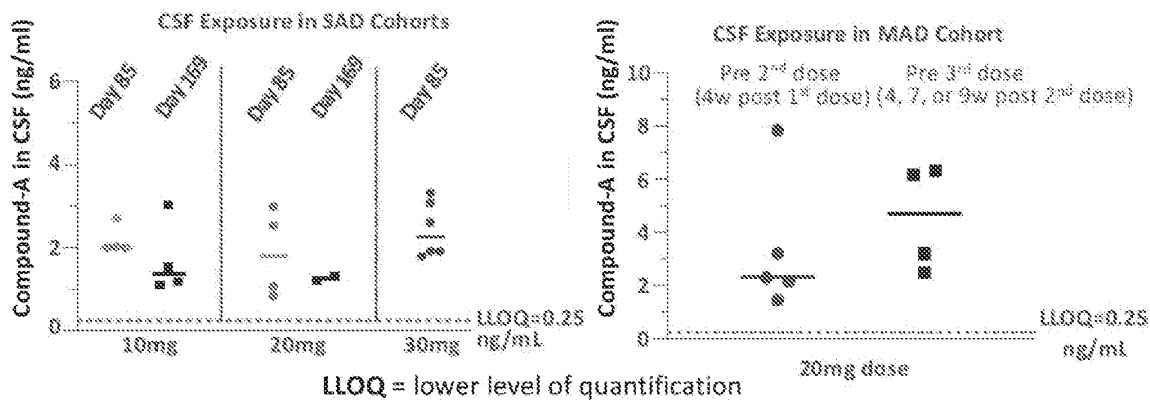


FIG. 30

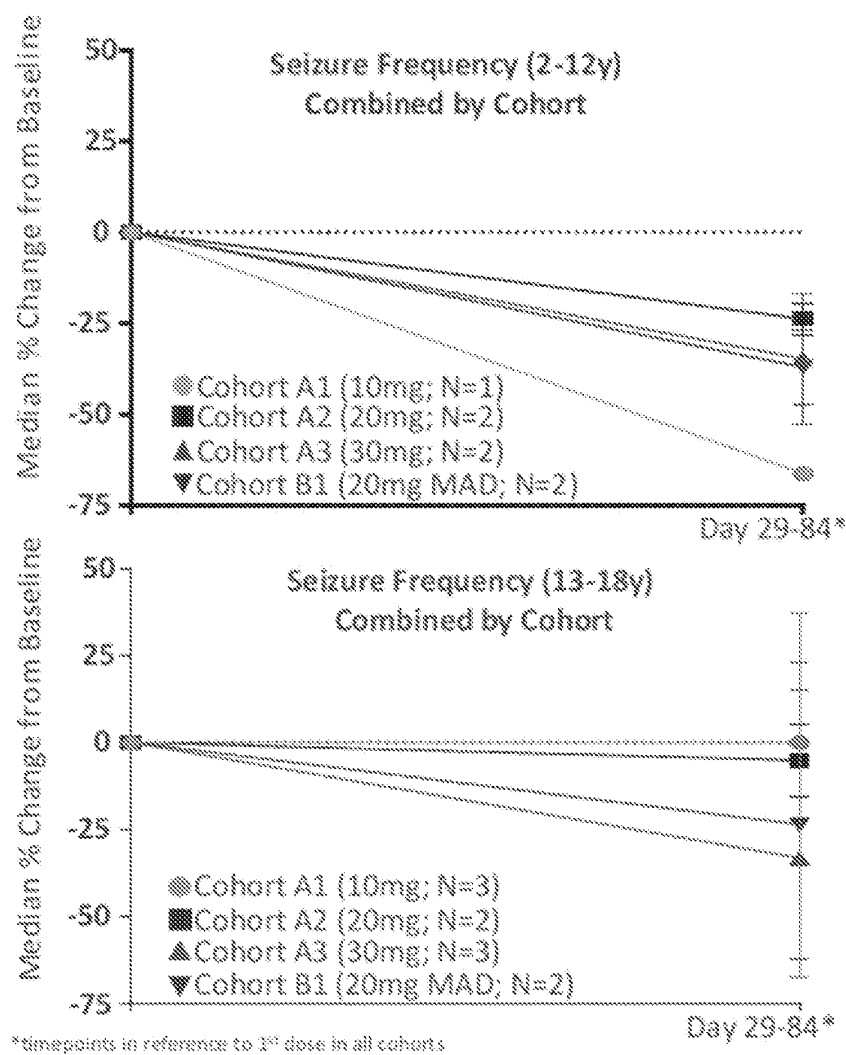


FIG. 31

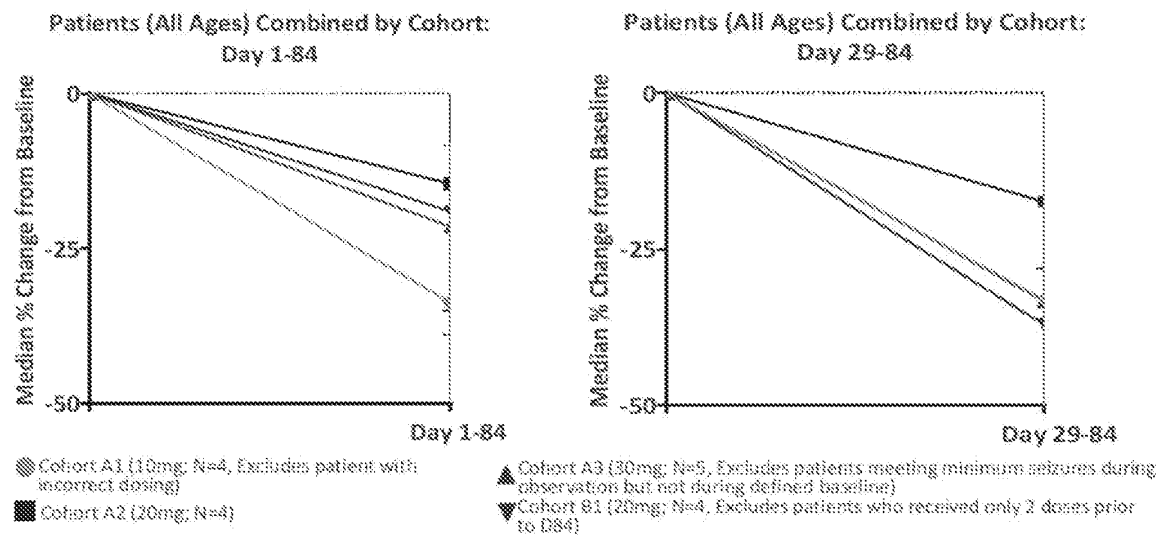


FIG. 32