Supplementary information

**Supplementary Figure 1. Organoid differentiation protocols**

Simplified schematic of the protocols used to generate A) Cerebral organoid (COs, Lancaster et al 2014), B) Dual SMAD organoid (DSO, Qian et al 2016) and C) engineered cerebral organoid (enCOR, Lancaster et al 2017) protocols.

***Supplementary Figure 2. Sanger sequencing of gene edited iPSC lines.***

iPSC cells with the following genotypes were used in this study: Wild type, Intron 10+16 C>T, monoallelic (red box), Intron 10+16 C>T, bilallelic (red box) and a double mutant line with the Intron 10+16 C>T, bilallelic (red box) C>T and a biallelic P301S mutation (purple dashed box).

***Supplementary Figure 3. qPCR of enCORs, total tau and 4R tau normalised to MAP2.***

cDNA from enCORs with WT, 10+16m, 10+16bi and 10+16bi/P301Sbi genotypes at 50, 100, 200 and 300 DIVwas analysed by qPCR for 4R tau and total tau. MAP2 expressoion was used to generated mean normalised expression (MNE) values. Prism software was used for statistical analysis by way of one-way ANOVA with Tukey’s post hoc test: \*p < 0.05, \*\* = < 0.01, \*\*\* = < 0.001. n=3 for all samples, except 300 DIV WT, where n=2.