**Supplementary Material**

**Calcilytic NPS 2143 Reduces Amyloid Secretion and Increases sAβPPα Release from PSEN1 Mutant iPSC-Derived Neurons**



**Supplementary Figure 1**. Comparative expression of CaSR. A) Lysates of human neuroblastoma SH-SY5Y transiently transfected with the HA-tagged human CaSR were immunoblotted with an anti-HA tag antibody or with an anti-CaSR antibody (ADD clone). Both antibodies recognized similar bands which validated specificity of CaSR protein. B) CaSR expression in SH-SY5Y overexpressing the HA-tagged human CaSR, NPCs, neurons at 4 and 6 weeks (week=W) of differentiation and human kidney tissue.



**Supplementary Figure 2**. NPS 2143 does not act as a γ-secretase inhibitor. A) Representative western blot analysis of Ctrl-1 and fAD-1 lysates showing the levels of AβPP full-length and AβPP C-terminal fragment upon treatment with vehicle (0.1% DMSO) or with 1 µM calcilytic for 48 h; No evident changes were induced by NPS 2143 as demonstrated by densitometric analyses showed in B).



**Supplementary Figure 3**. CaSR and PSEN1 expressed in the intracellular fractions. FT fractions relative bands of CaSR and PSEN1 were normalized to GAPDH and presented as a percent of the vehicle. No significant changes were observed. Western blot measurements were performed as biological triplicates.



**Supplementary Figure 4**. ADAM10 and BACE1 expression in biotinylated samples treated with NPS 2143. Representative western blot bands representing ADAM10 and BACE1 present in the “flow-through” (FT) and in the “Eluate” (E) fractions of biotinylated samples ± treatment with 1 µM NPS 2143 for 48 h.