

[00024a] Also provided herein is the anti-human A β_{pE3} antibody as described herein for use in therapy.

[00024b] Also provided herein is a use of the anti-human A β_{pE3} antibody as described herein in the manufacture of a medicament for treating a neurodegenerative disorder.

6. BRIEF DESCRIPTION OF THE DRAWINGS

[00025] FIG. 1 shows representative binding of AC-264713 to human A β_{pE3-42} fibrils. The binding of AC-264713 to human A β_{pE3-42} fibrils was assessed in direct binding ELISA. Plates coated with human A β_{pE3-42} fibrils (50 ng/well) were incubated with serially diluted AC-264713. The ELISA was repeated three times and a representative graph is shown. Plotted on the Y axis is Optical Density at 450 nm. The EC₅₀ value of AC-264713 binding to human A β_{pE3-42} fibrils is 0.7 nM.

[00026] FIG. 2 depicts plaque area bound by AC-264713 and a comparator antibody Ab1 in fresh frozen human AD tissue from frontal cortex. Tissue from 6 AD donors were analyzed and the data were expressed as mean $\pm$ SEM. AC-264713 bound plaques in AD brain tissue in a concentration-dependent manner. Lines represent fits to data for the 6 donors combined as described in Example 3.

[00027] FIG. 3 shows that AC-264713 stimulates amyloid plaque removal from unfixed APPPS1-21 brain tissue by hiPSC-derived phagocytes. hiPSC-derived phagocytes were co-cultured with APPPS1-21 brain tissue pre-incubated with different concentrations of AC-264713. The amyloid plaques remaining in the tissue were stained using thioflavin S and quantified. Data were expressed as mean $\pm$ SEM and analyzed with One-way ANOVA followed by Dunnett's multiple comparisons test *, $p < 0.05$.

[00028] FIG. 4 depicts dose dependent target binding of AC-264713 in APPPS1-21 mice 72 hours following single intraperitoneal administration. AC-264713 (Panel A) and comparator antibody Ab1 (Panel D) in the brain were detected using anti-hIgG immunohistochemistry. The total target A β_{pE3} on an adjacent section was stained using AC-264713 (Panel B) or comparator antibody Ab1 (Panel E). The % total target occupied by AC-264713 (Panel C) or comparator antibody Ab1 (Panel F) at increasing doses was then calculated and is presented on the y-axis. * $P < 0.05$ (Kruskal-Wallis followed by Dunn's multiple comparison test).

[00029] FIG. 5 shows the correlation of AC-264713 and comparator antibody Ab1 exposure in brain and dose-dependent target binding in APPPS1-21 mice 72 hours following single intravenous doses in female mice. Data (symbols) correlating individual animal brain exposure with A β_{pE3} occupancy is shown together with the Nonlinear Fits (lines).