

CLAIMS

1. Use of a therapeutically effective amount of tramiprosate, a pharmaceutically acceptable salt of tramiprosate, a tramiprosate prodrug, or an active tramiprosate metabolite in the manufacture of a medicament for treating Alzheimer's disease in an adult human subject who is determined to:

- i. comprise an APOE4/4, APOE3/4, or APOE2/APOE4 genotype,
- ii. be asymptomatic for Alzheimer's disease, and
- iii. have at least one of:
 - (1) a hippocampal volume below a threshold level; or
 - (2) cortical thickness below a threshold level; and

wherein for subjects comprising an APOE4/4 genotype, the threshold levels are

- the hippocampal volume is at least 5% lower than the baseline hippocampal volume and the baseline hippocampal volume is obtained within 12 months prior to selection,
- the hippocampal volume is at least 10% lower than the baseline hippocampal volume and the baseline hippocampal volume is obtained less than 24 months prior to selection,
- the hippocampal volume is less than 4.75 cm³,
- the cortical thickness is at least 3% less than the baseline cortical thickness and the baseline cortical thickness is obtained within 12 months prior to selection,
- the cortical thickness is at least 6% less than the baseline cortical thickness and the baseline cortical thickness is obtained within 24 months prior to selection, or
- the cortical thickness is less than 2.50 mm;

wherein for subjects comprising an APOE3/4 genotype, the subject is selected only if the subject is further determined to be positive for amyloid deposits in the brain, and the threshold levels are

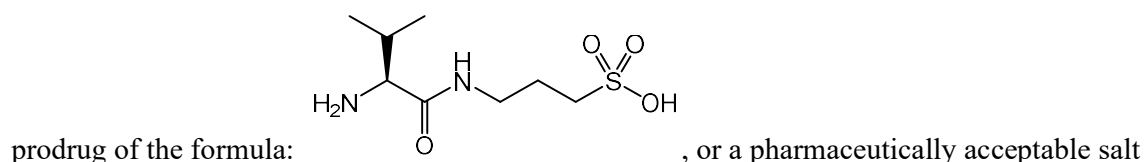
- the hippocampal volume is at least 5% lower than the baseline hippocampal volume and the baseline hippocampal volume is obtained within 12 months prior to the selection,

- the hippocampal volume is at least 10% lower than the baseline hippocampal volume and the baseline hippocampal volume is obtained less than 24 months prior to the selection,
- the hippocampal volume is less than 5.10 cm³,
- the cortical thickness is at least 3% less than the baseline cortical thickness and the baseline cortical thickness is obtained within 12 months prior to the selection,
- if the cortical thickness is at least 6% less than the baseline cortical thickness and the baseline cortical thickness is obtained within 24 months prior to the selection, or
- the cortical thickness is less than 2.50 mm;

wherein for subjects comprising an APOE2/4 genotype, the subject is selected only if the subject is further determined to be positive for amyloid deposits in the brain, and the threshold levels are

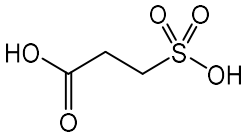
- the hippocampal volume is at least 4% lower than the baseline hippocampal volume and the baseline hippocampal volume is obtained within 12 months prior to the selection,
- the hippocampal volume is at least 7% lower than the baseline hippocampal volume and the baseline hippocampal volume is obtained less than 36 months prior to the selection,
- the hippocampal volume is less than 6.10 cm³,
- cortical thickness is at least 2% less than the baseline cortical thickness and the baseline cortical thickness is obtained within 12 months prior to the selection,
- the subject is selected if the cortical thickness is at least 4% less than the baseline cortical thickness, and the baseline cortical thickness is obtained within 36 months prior to the selection, or
- the cortical thickness is less than 2.50 mm.

2. The use of claim 1, wherein the human subject is to be administered a tramiprosate



thereof.

3. The use of claim 1, wherein the human subject is to be administered a tramiprosate

metabolite of the formula: , or a pharmaceutically acceptable salt thereof.

4. The use of any one of claims 1-3, wherein the subject is determined to be asymptomatic for Alzheimer's disease if the subject scores 28 or higher on a MMSE.

5. The use of any one of claims 1-4, wherein one or both of hippocampal volume and cortical thickness is measured by MRI.

6. The use of any one of claims 1-5, wherein amyloid deposits are detected by PET imaging or cerebral spinal fluid biomarkers.