



**Fig. S1.** Effect of  $\delta$ -secretase inhibitor 11 on body weight and AEP activity. **a** Chemical structure of  $\delta$ -secretase inhibitor 11. **b** Body weight records of SAMP8 and SAMR1 mice over the treatment period.  $n = 9$  mice per group. **c** The enzymatic activity of AEP in the liver tissues of SAMP8 and SAMR1 mice was measured for 45 min. Mice had been treated with  $\delta$ -secretase inhibitor 11 (10 mg/kg) for 3 months. **d** AEP activity was obtained at 45 min after the substrate cleavage reaction.  $n = 6$  mice per group. **e, f** Measurement of AEP activity in

kidney tissues of SAMP8 and SAMR1 mice.  $n = 6$  mice per group.