

WHAT IS CLAIMED IS:

- 1 **1.** Use of a composition disrupting amyloid precursor protein (APP)
2 genomic sequence in the manufacture of a medicament for treating or reducing risk of an
3 amyloid pathology in a person in need thereof.
- 1 **2.** The use of claim 1, further comprising sequencing at least a portion of
2 the person's genome prior to administration of the medicament.
- 1 **3.** The use of claim 1, wherein the person's APP genomic sequence
2 comprises at least one mutation.
- 1 **4.** The use of claim 3, wherein the at least one mutation comprises a
2 Swedish mutation (K670N/M671L), a Florida mutation (I716V), a London mutation (V717I),
3 or any combination thereof.
- 1 **5.** The use of claim 4, wherein the at least one mutation comprises a
2 Swedish mutation (K670N/M671L).
- 1 **6.** The use of claim 1, wherein the amyloid pathology is Alzheimer's
2 Disease (AD), cerebral amyloid angiopathy, or Down Syndrome.
- 1 **7.** The use of claim 6, wherein the AD is familial AD or sporadic AD.
- 1 **8.** The use of claim 1, wherein the person has been diagnosed with AD,
2 or the person is not yet diagnosed with AD but has known risk factors for AD.
- 1 **9.** The use of claim 1, wherein the composition comprising an siRNA, a
2 microRNA, a miniRNA, a lncRNA, or an antisense oligonucleotide targeting the APP
3 genomic sequence.
- 1 **10.** The use of claim 1, wherein the composition comprising one or more
2 vectors encoding (1) an endonuclease guided by a small guide RNA (sgRNA) targeting a
3 location within the APP genomic sequence; and (2) the sgRNA.
- 1 **11.** The use of claim 1, wherein the sgRNA targets a region within the
2 APP genomic sequence comprising the at least one mutation or a β - or γ -secretase cleavage
3 site.

1 **12.** The use of claim 10, wherein the composition comprises one vector
2 encoding a Cas9 nuclease and one sgRNA, preferably a *Streptococcus pyogenes* Cas9
3 nuclease (SpCas9).

1 **13.** The use of claim 10 or 11, wherein the one or more vectors are one
2 viral vector, preferably an adeno-associated virus (AAV) vector.

1 **14.** The use of claim 1, wherein the medicament is to be administered by
2 subcutaneous, intramuscular, intravenous, intraperitoneal, or intracranial injection or by oral
3 or nasal administration.

1 **15.** The use of claim 13, wherein the medicament is to be administered in
2 the form of a solution, a suspension, a powder, a paste, a tablet, or a capsule.

1 **16.** A kit for treating or reducing risk of an amyloid pathology in a person
2 in need thereof, comprising a container containing a composition disrupting APP genomic
3 sequence.

1 **17.** The kit of claim 16, wherein the composition is formulated for
2 subcutaneous, intramuscular, intravenous, intraperitoneal, or intracranial injection, or for oral
3 or nasal administration.

1 **18.** The kit of claim 16, wherein the composition comprising an siRNA, a
2 microRNA, a miniRNA, a lncRNA, or an antisense oligonucleotide targeting the APP
3 genomic sequence.

1 **19.** The kit of claim 16, wherein the composition comprising one or more
2 vectors encoding (1) an endonuclease guided by a small guide RNA (sgRNA) targeting one
3 location within the APP genomic sequence; and (2) the sgRNA.

1 **20.** The kit of claim 19, wherein the sgRNA targets a region within the
2 APP genomic sequence comprising the at least one mutation or a β - or γ -secretase cleavage
3 site.

1 **21.** The kit of claim 16, wherein the composition comprises one vector
2 encoding a Cas9 nuclease and one sgRNA, preferably a *Streptococcus pyogenes* Cas9
3 nuclease (SpCas9).

1 **22.** The kit of any one of claims 19-21, wherein the one or more vectors
2 are one or more viral vectors, preferably an adeno-associated virus (AAV) vector.

1 **23.** The kit of claim 16, wherein the composition is to be administered by
2 subcutaneous, intramuscular, intravenous, intraperitoneal, or intracranial injection or by oral
3 or nasal administration.

1 **24.** The kit of claim 16, further comprising a second container containing
2 agents for sequencing at least a portion of the person's genome.

1 **25.** The kit of claim 16, further comprising an instruction manual for
2 administration of the composition.

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