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(54) Title: COMPOSITIONS AND METHODS FOR ALTERING A NUCLEOBASE IN A TRANSTHYRETIN POLYNU-
CLEOTIDE

(57) Abstract: Compositions for modifying or editing a polynucleotide (e.g., a gene) and methods of using the same to treat or prevent
conditions associated with the extracellular deposition in various tissues of amyloid fibrils formed by the aggregation of misfolded
transthyretin (TTR) proteins. Such conditions include, but are not limited to, polyneuropathy due to hereditary transthyretin amyloidosis
(hATTR-PN) and hereditary cardiomyopathy due to transthyretin amyloidosis (hATTR-CM), both associated with autosomal dominant
mutations of the *TTR* gene, and an age-related cardiomyopathy associated with wild-type TTR proteins (ATTRwt), also known as senile
cardiac amyloidosis are disclosed. Compositions and methods for editing TTR polynucleotides using base editor systems are disclosed.



WO 2025/159966 A1