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(54) Title: COMPOSITIONS AND METHODS FOR IN VIVO NUCLEASE-MEDIATED GENE TARGETING FOR THE TREATMENT OF GENETIC DISORDERS

(57) Abstract: A dual vector system for treating a genetic disorder is provided. The system includes (a) a gene editing vector comprising an expression cassette comprising a nucleic acid sequence encoding a nuclease and regulatory sequences that direct expression of the nuclease in a target cell comprising a PCSK9 gene; and (b) a donor vector comprising a nucleic acid sequence encoding an exogenous product for expression from the PCSK9 locus, wherein the inserted nucleic acid sequence does not encode PCSK9, wherein the system further comprises sequences that direct the nuclease to specifically targets the native PCSK9 gene locus; and wherein the native PCSK9 in the target cell is optionally ablated or reduced post-dosing with the dual vector system.

