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(54) Title: IN VIVO NICKASE-BASED EDITING OF THE *LPA* GENE FOR TREATMENT OF CARDIOVASCULAR DISEASE

(57) Abstract: Provided herein are gene editing systems and compositions directed to effectuate *in vivo* edits in the *LPA* gene. Treatment or prevention of cardiovascular disease through disruption of the production of apo(a) through genetic editing and the reduction of the blood lipoprotein(a) [Lp(a)] concentration is disclosed herein. Disclosed are nickase-based gene editing systems designed to effectuate the installation of insertions and/or deletions (indel variants) and/or non-synonymous variants in the coding sequence of *LPA*. The nickase-based gene editing systems generally comprise one or more mRNAs that encode one or more nickases and a plurality of guide oligonucleotides (e.g., gRNAs) and may be delivered *in vivo* to a mammalian subject in need thereof via a suitable delivery system, such as lipid nanoparticles (LNPs) (with or without GalNAc targeting moieties) intravenously, or otherwise, administered to a patient as potentially a once-and-done therapeutic. The manufacturing, use, and formulation of the gene editing systems and compositions are also disclosed.