RNAi Therapeutics Targeting PCSK9 for LDLc Lowering in Hypercholesterolemia

**Abstract**

Recent advances in RNAi technologies have enabled the development of effective treatments for hypercholesterolemia. PCSK9 is a key regulator of low-density lipoprotein cholesterol (LDLc) production, making it an attractive target for intervention. In this study, we evaluated the efficacy of RNAi-based treatments targeting PCSK9 in animal models.

**Results**

We developed siRNA formulations that efficiently targeted PCSK9 in murine, rodent, and human systems. In vivo studies in NHPs demonstrated >50% reduction in LDLc levels without changes in HDLc at doses >0.1mg/kg. Additional dose-sparing paradigms were also investigated.

**Conclusions**

RNAi therapeutics targeting PCSK9 show promise for lowering LDLc levels, potentially offering a new class of treatments for hypercholesterolemia.