A lipid nanoparticle is typically spherical with the size of around 80 nm in diameter which is much smaller than the commercial cationic liposome-based transfection reagent (several hundred nm). Another notable clinical program is ALN-VSP from Alnylam which is composed of LNPs containing two different siRNAs targeting vascular endothelial growth factor A (VEGF-A; for inhibiting tumor angiogenesis) and kinesin spindle protein (KSP; for inhibiting tumor mitosis). An siRNA drug, ARC-520, developed by Arrowhead Research, which contains hepatocyte-tropic cholesterolconjugated siRNAs targeting HBV coagulation factor VII and is delivered by Dynamic Poly Conjugate technology, has shown promising result in a Phase I clinical trial and has just entered a Phase II clinical trial. TKM-PLK1, an LNP formulated siRNA therapy from Tekmira, is in early clinical trials for adrenocortical carcinoma, gastrointestinal neuroendocrine tumors and hepatocellular carcinoma. In a Phase I clinical trial for ALN-VSP, promising results showed that siRNAs were delivered into the tumor and siRNA-mediated mRNA cleavage of VEGF-A and regression of liver metastases were observed in some patients. Patisiran, composed of synthetic siRNAs targeting TTR gene and delivered by LNPs, led to knockdown of serum TTR protein levels of up to 96% in a Phase II clinical trial. In particular, Alnylam and Tekmira, two leading RNAi therapeutic companies, have developed new generations of LNPs that are exceedingly efficient for delivering siRNAs into liver cells by intravenous administration. TKM-Ebola is a mixture of three siRNAs targeting three Ebola genes (delivered by LNPs) and has shown 100% protection of monkeys from deadly Ebola infections. Patisiran is the first FDA approved siRNA drug in the market in 2018.

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