Dicerna invented GalXC™, a proprietary technology platform that advances the development of subcutaneously administered RNAi-based therapies designed to silence disease-driving genes in the liver across multiple therapeutic areas, including rare diseases, chronic liver diseases, cardiovascular disease and viral infectious diseases. In preclinical studies, GalXC compounds have demonstrated: potency that is on par with or better than comparable platforms; high specificity to their gene targets; long duration of action; and a convenient subcutaneous route of administration.

Each GalXC molecule is a chemically optimized, double-stranded RNA designed to potently induce RNAi. We attach N-acetyl galactosamine (GalNAc) sugars to one or more points on GalXC compounds, yielding multiple effective and proprietary conjugate delivery configurations. These molecules specifically bind to highly expressed asialoglycoprotein (ASGPR) receptors on the target cells, leading to internalization via endosomes and access to the RNAi machinery within the cells. Within the endosome, the ASGPR releases the GalXC and recycles to the cell surface, enabling delivery of the GalXC into the cytoplasm of the cell (hepatocytes in the liver).

Upon entering the cytoplasm, the GalXC molecule is bound by the Dicer enzyme, which unwinds the molecule and delivers the correct strand to the RNA-induced silencing complex (RISC). This results in the preferential incorporation of the RNA guide strand (also known as the antisense strand) into RISC, whereas the RNA passenger strand (also known as the sense strand) is released and degraded.

Dicer hands the guide strand to Ago2, the core component of RISC that mediates the destruction of the target mRNA.

Loaded RISC complex binds to intact target mRNA resulting in mRNA cleavage.

Intact mRNA

Cleaved target mRNA fragments, no protein produced