DTx Pharma
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Creating next-generation RNA-targeting therapeutics

DTx Pharma's next-generation, fatty acid ligand-conjugated oligonucleotides enable efficient delivery of RNA-based therapeutics to cells and tissues throughout the body. With three disease franchises—ocular, neuromuscular and central nervous system (CNS), DTx is seeking partners to realize the potential of its platform.

DTx Pharma, Inc., a privately held biotechnology company located in San Diego, CA, and founded in 2018, has developed a proprietary technology platform to enable the delivery of novel RNA-based therapeutics to a wide range of tissues and cell types throughout the body. Using this platform, dubbed FALCON (Fatty Acid Ligand Conjugated OligoNucleotide), DTx has shown cellular uptake and broad activity of oligonucleotides in the retina, muscle, heart, neurons, T cells and many other specialized cell types.

Over the past decade, short interfering RNA (siRNA) or antisense oligonucleotide (ASO)-based gene knockdown therapeutics have been developed for a multitude of target disease genes in tissues throughout the body, but their application has been limited by poor biodistribution and rapid clearance. With the exception of *N*-acetylgalactosamine (GalNAc), which mediates liver targeting, there are no safe and effective means of delivering oligonucleotide drugs to other relevant target cells and tissues. DTx has created a technology platform that is analogous to GalNAc but can go beyond the liver.

DTx has developed a collection of novel motifs containing long chain fatty acids that improve biodistribution and allow for targeted and efficient uptake of siRNA and ASO by many different cell types and tissues in vivo. The company has several preclinical programs for neurodegenerative disorders of the eye, central nervous system (CNS) and peripheral neuromuscular system in development. DTx's most advanced preclinical program targets retinal neurons—the photoreceptors—in retinitis pigmentosa (RP), a rare progressive neurodegenerative disease that results in blindness.

DTx is seeking innovative strategic partners with therapeutic area expertise in neurodegenerative, ocular and neuromuscular disorders and for application of the company's technology to new targets of interest.

Harnessing the FALCON's acuity

Therapeutic oligonucleotide delivery has quickly evolved over the past decade from chemically modified molecules—rapidly cleared by the kidney and with minimal if any cellular uptake—and lipid nanoparticles—improved cellular uptake but mostly constrained to liver and with narrow therapeutic indices—to GalNAc-modified oligonucleotides—receptor-mediated uptake and improved therapeutic indices but limited to liver—and antibody-conjugated oligonucleotides—capable of targeting additional defined cell types, but costly and slow to develop.

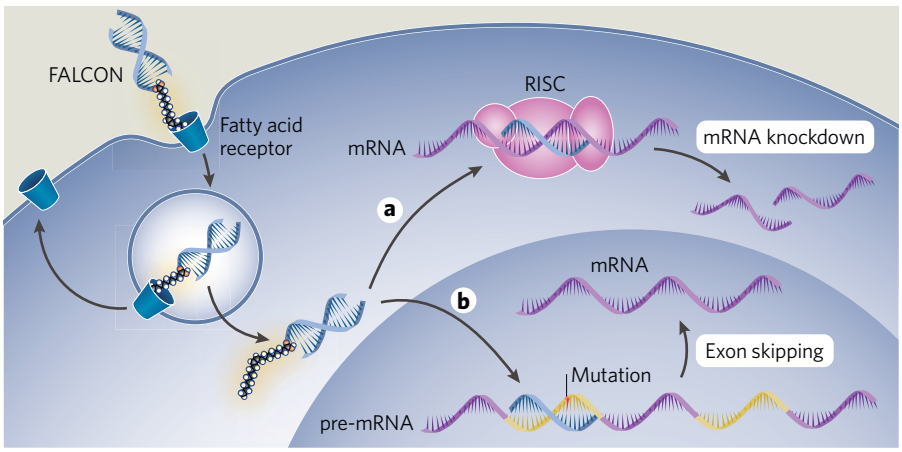

Fig. 1 | DTx Pharma's fatty acid ligand-conjugated oligonucleotides enable efficient delivery of RNA-based therapeutics to cells and tissues. RISC, RNA-induced silencing complex.

DTx's FALCON platform offers receptor-mediated uptake across most relevant cell types at a substantially lower cost than antibody-conjugated oligonucleotides and with comparatively shorter development timelines.

DTx conjugates its proprietary fatty acid motifs directly to the siRNA or ASO facilitating cellular entry via receptor-mediated uptake. Once in the cell, DTx's molecules can act in the cytoplasm to knockdown a targeted mRNA for gene suppression, or in the nucleus to impact exon skipping—splicing of a targeted pre-mRNA to restore function (Fig. 1). The DTx conjugates are highly soluble in aqueous solutions, improving biodistribution and avoiding toxicities associated with nanoparticle delivery. And, as is the case with a number of approved fatty acid-conjugated peptide and small protein therapeutics, the DTx conjugates exhibit prolonged half-life and increased safety profiles.

Deploying the DTx FALCONry

DTx has a broad pipeline of preclinical programs in neurodegenerative diseases. The company's lead candidate in RP is designed to reduce expression of a novel gene target, slowing or even preventing photoreceptor loss and preserving visual function. RP is caused by any one of more than 300 primary genetic defects described so far, making the development of specific therapies for each of the possible mutations highly unlikely. The approach taken by DTx is mutation-agnostic and could benefit patients with RP with varying underlying genetic etiologies.

DTx also has advanced preclinical programs in degenerative CNS and peripheral nerve disorders. In CNS, the company is focused on disorders characterized by abnormal accumulation of the tau protein—one uses siRNA to target tau mRNA, the other uses siRNA against a novel target gene involved in tau-mediated neuronal damage. In the peripheral neuromuscular system, DTx is addressing Charcot–Marie–Tooth disorder, which is caused by gene duplication of peripheral myelin protein 22 (*PMP22*), and impacts Schwann cell survival and function.

"Because of their modular nature and homology-based high specificity, RNA medicines are poised to dominate the next generation of novel drugs," said Jeff Friedman, COO of DTx. "We believe DTx's delivery technology is going to be an essential part of deploying these medicines to multiple tissues beyond the liver, and we're looking for partners with strong franchises in ophthalmic, CNS and neuromuscular disorders so that we can bring these promising candidates to patients sooner."

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