Dealmaking delivers for nucleic-acid-based drugs

The promise of accessing tissues beyond the liver is driving deals between pioneers in the field of nucleic-acid-based drugs and companies developing delivery platforms.

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Biopharma Dealmakers

In the past decade, nucleic-acid-based drugs have become firmly established as a therapeutic modality. Drugs in two classes have now reached the market for multiple diseases—antisense oligonucleotides (ASOs) and small-interfering RNAs (siRNAs)—both of which act by targeting RNA to specifically modulate expression of a particular gene. Furthermore, gene-editing strategies that use guide RNAs to determine the sites at which gene editing occurs are progressing in the clinic, as are messenger RNA (mRNA) therapeutics, which have been boosted by the success of mRNA vaccines for COVID-19.

However, achieving efficient drug delivery remains a key challenge to realizing the potential of all of these therapeutic classes, particularly delivery to organs and tissues other than the liver. Consequently, companies developing technologies that could enable nucleic-acid delivery to other tissues are attracting interest as partners for pioneering companies in the field of nucleic-acid-based drugs, including Ionis, Alnylam, Sarepta and Moderna (Table 1).

Two general types of delivery platform for nucleic-acid-based therapies that have proved effective already in marketed agents are bioconjugation and nanoparticle encapsulation.

In the first type, the nucleic-acid component is conjugated to a carrier that promotes targeting and uptake to particular cells. Several recent deals involve technologies of this type, such as Alnylam's $2.2 billion pact with PeptiDream to develop siRNA–peptide conjugates that can reach tissues outside the liver, and Ionis' $1.4 billion deal with Aro Biotherapeutics to develop conjugates of ASOs and small proteins, Centryins, that facilitate cell- and tissue-specific delivery.

In the second type, the nucleic-acid component is encapsulated in a nanoparticle, such as a lipid nanoparticle—also used for mRNA-based COVID-19 vaccines. Such platforms have driven deals for gene-editing therapies, including Moderna's potential $455 million deal with Vertex to develop RNA-based therapies for cystic fibrosis, and deals that Sarepta has signed with GenEdit and Genevant.

Table 1 | Selected deals for nucleic-acid delivery technologies with disclosed financial terms

Date	Licensor, licensee	Summary
Feb 2022	GenEdit, Sarepta Therapeutics	Sarepta enters partnership with GenEdit to apply GenEdit's polymeric nanoparticle platform, known as NanoGalaxy, to develop gene-editing therapies for up to four neuromuscular disease indications chosen by Sarepta. Under the terms of the deal, Sarepta will pay GenEdit up to $57 million in the near term for access to the NanoGalaxy platform.
Jan 2022	Entos Pharmaceuticals, Lilly	Lilly acquires exclusive rights to Entos' Fusogenix platform for the delivery of nucleic acids to central and peripheral nervous system targets. Lilly will be responsible for selecting proteo-lipid vehicles generated and optimized by Entos for clinical development and commercialization. Lilly will pay $50 million to Entos, including an equity investment in the company, and Entos is eligible to receive up to $400 million in milestone payments for each program in the collaboration, as well as sales royalties.
Jul 2021	PeptiDream, Alnylam	Alnylam and PeptiDream agree to collaborate on the discovery and development of peptide–siRNA conjugates for delivery to tissues outside the liver. PeptiDream will receive an undisclosed upfront payment and research funding and is eligible for milestone payments potentially totaling up to $2.2 billion and royalties on the sales of resultant products.
Jul 2021	Bicycle Therapeutics, Ionis	Ionis signs a deal to gain exclusive rights to Bicycle Therapeutics' bicyclic peptide technology to deliver oligonucleotides to tissues that express transferrin receptor protein 1 (Tfr1). Ionis will pay $45 million upfront, including an $11 million equity investment, as well as undisclosed milestone payments and sales royalties for each program developed through the partnership.
Jan 2021	Genevant Sciences, Sarepta Therapeutics	Genevant and Sarepta announce a collaboration to use Genevant's LNP-based delivery platform and Sarepta's gene-editing technology to develop therapeutics for up to four neuromuscular disease indications, including Duchenne muscular dystrophy. Genevant will receive up to ~$50 million in near-term payments and is eligible for undisclosed milestone payments and royalties on future product sales.
Sep 2020	Moderna, Vertex Pharmaceuticals	Moderna and Vertex partner on the development of mRNA-based gene-editing therapies delivered using LNPs to treat cystic fibrosis. Under the terms of the deal, Moderna will receive an upfront payment of $75 million and is eligible for milestone payments worth up to $380 million and royalties on resultant product sales.
Jan 2020	Aro Biotherapeutics, Ionis	Aro Biotherapeutics and Ionis collaborate to apply Aro's Centyrin technology for the cell- and tissue-specific delivery of ASOs to identify ASO–Centyrin conjugates for further development. Aro will receive an upfront cash payment, funding and milestone payments worth up to $1.4 billion, as well as royalties on sales.

ASO, antisense oligonucleotide; LNP, lipid nanoparticle; mRNA, messenger RNA; siRNA, small-interfering RNA.