

Evox Therapeutics  
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## Engineering exosomes to create transformational drugs

**Evox Therapeutics is harnessing the natural delivery capabilities of extracellular vesicles to develop an entirely novel class of biotherapeutics.**

Exosomes, nano-sized extracellular vesicles secreted by all cells, are a fundamental part of the human body's internal communication machinery, safely and efficiently transporting proteins and nucleic acids around the body. Evox Therapeutics, a privately held biotechnology company based in Oxford, UK, is leading the way in exploiting this natural mechanism to create transformative biotherapeutics.

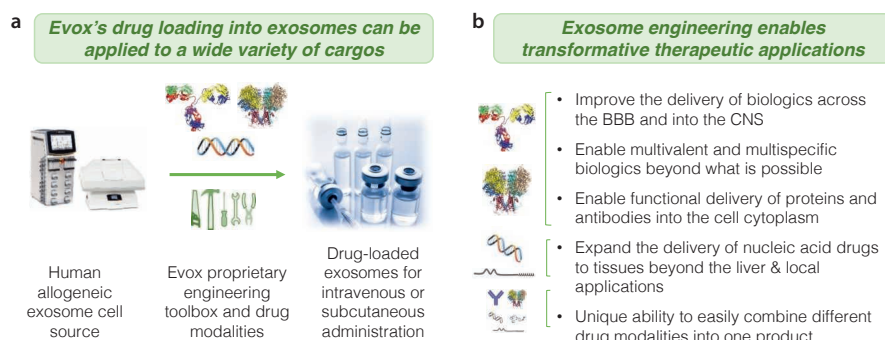
Evox is engineering exosomes—lipid-membrane-containing nanoparticles constitutively produced by cells—and loading them with protein therapeutics or nucleic-acid-based agents (Fig. 1). Production and loading of many of these drugs into exosomes can be hardwired into the cells making the exosomes themselves, or exosomes can be purified beforehand and loaded with drugs off the shelf. "Our proprietary technology enables us to routinely and homogeneously load hundreds to thousands of copies of drugs per exosome, which is one to two orders of magnitude more than what has been described by others," said Tony de Fougères, Evox's CEO.

Moreover, by also engineering different ligands onto the exosome surface, Evox is able to preferentially target delivery of the drug-laden exosomes to particular cells and tissues, many of which are currently inaccessible to conventional drugs. By crossing the blood-brain barrier, for instance, Evox's exosomes can improve the delivery of drugs to the central nervous system (CNS) by up to 20-fold. "Our tissue-targeted exosomes enable the intracellular and extrahepatic delivery of a wide variety of drugs, including RNA therapeutics and protein biologics or potentially even gene-editing modalities, to previously inaccessible tissues and compartments," explained de Fougères.

Successful delivery of exosomes with different payloads has been demonstrated in vivo in multiple preclinical disease models using a variety of protein and nucleic acid drug payloads, and, in nonhuman primates, drug-loaded engineered exosomes appear to be extremely well tolerated even upon repeated administration. "As exosomes are present in all biological fluids—a unit of blood, for example, contains  $10^{13}$ —we suspected our engineered exosomes would prove similarly safe," added de Fougères. "They seem to have none of the toxicity associated with man-made nanoparticles."

### Rare life-threatening diseases pipeline

The company's internal exosome pipeline is focused on rare, life-threatening diseases with significant unmet need. Its lead product is in preclinical development for Niemann–Pick disease type C, a disorder in



**Fig. 1 | Evox's exosomes.** **a**, Evox's exosomes are engineered to enable loading of a variety of cargos. **b**, Applications and advantages of engineered exosomes. BBB, blood-brain barrier; CNS, central nervous system.

which a defective cholesterol transporter Niemann–Pick type C1 (NPC1) results in cholesterol accumulation inside cells with devastating consequences. Traditional enzyme-replacement therapy does not work because the transmembrane NPC1 protein needs to be in a membrane to retain activity. But Evox has engineered the fully functional transporter into exosome membranes, which, when taken up by cells, can restore cholesterol conveyance; clinical trials are planned to begin in 2020. Following quickly behind this program, Evox is also advancing a number of treatments for other rare metabolic and lysosomal diseases that leverage the unique ability of exosomes to deliver drug payloads into target cells and into areas such as the CNS.

Based on groundbreaking exosome technology from Oxford University and the Karolinska Institute, Evox has developed an unparalleled biomolecular engineering toolbox, tailored targeting technology, proprietary manufacturing and purification methods, and the most comprehensive intellectual property estate in the exosome therapeutics space. Since its inception in 2016, Evox has raised approximately £45 million in equity financing from leading life sciences venture capital groups.

In 2019, the company won £1.5 million from Innovate UK to develop an exosome therapy to treat a rare urea cycle disorder and, in late 2018, it won £655,000 in funding from Duchenne UK to explore the exosome-mediated delivery of dystrophin in preclinical models of Duchenne muscular dystrophy, a highly debilitating, progressive muscle-wasting disorder caused by the lack of functional dystrophin protein. It also secured an undisclosed amount of funding from the Bill & Melinda Gates Foundation to expand its work on cell-targeted delivery of nucleic acid-based drugs, and was

identified by *The Sunday Times* as one of the top ten emerging UK companies in its Fast Track 100 'Disruptors to Watch.'

### Partnering

Evox, which can develop drugs ready for preclinical testing in as little as several months and have an investigational new drug (IND) in 18–24 months, has already formed several pharmaceutical collaborations to exploit the use of exosome-based therapeutics for the treatment of a wide variety of diseases. The company is open to partnerships with those interested in maximizing the enormous upside of this broadly applicable, highly versatile platform. "Exosome-based drugs have the potential to revolutionize the pharma industry by enabling delivery of protein biologics and nucleic-acid-based therapies to cells and tissues that are currently out of reach using other drug delivery technologies, and to also truly enable more targeted delivery of small molecules," said de Fougères. "As such, Evox is transforming the treatment of a broad range of severe/life-threatening diseases, with what we hope will be a profound positive impact on patients and their families."

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