evOX THERAPEUTICS

30 August, 2024

Evox mission

Uniting two powerful natural mechanisms – exosomes & genome editors – to transform the lives of people living with severe diseases

Backed by leading investors and partners

Uniquely **experienced leadership team**

An **unrivalled foundational IP estate**

Backed by **leading investors and partners** committed to the future of **exosome-enabled genome editors**

Exosomes are the ultimate carrier for genome editing technologies

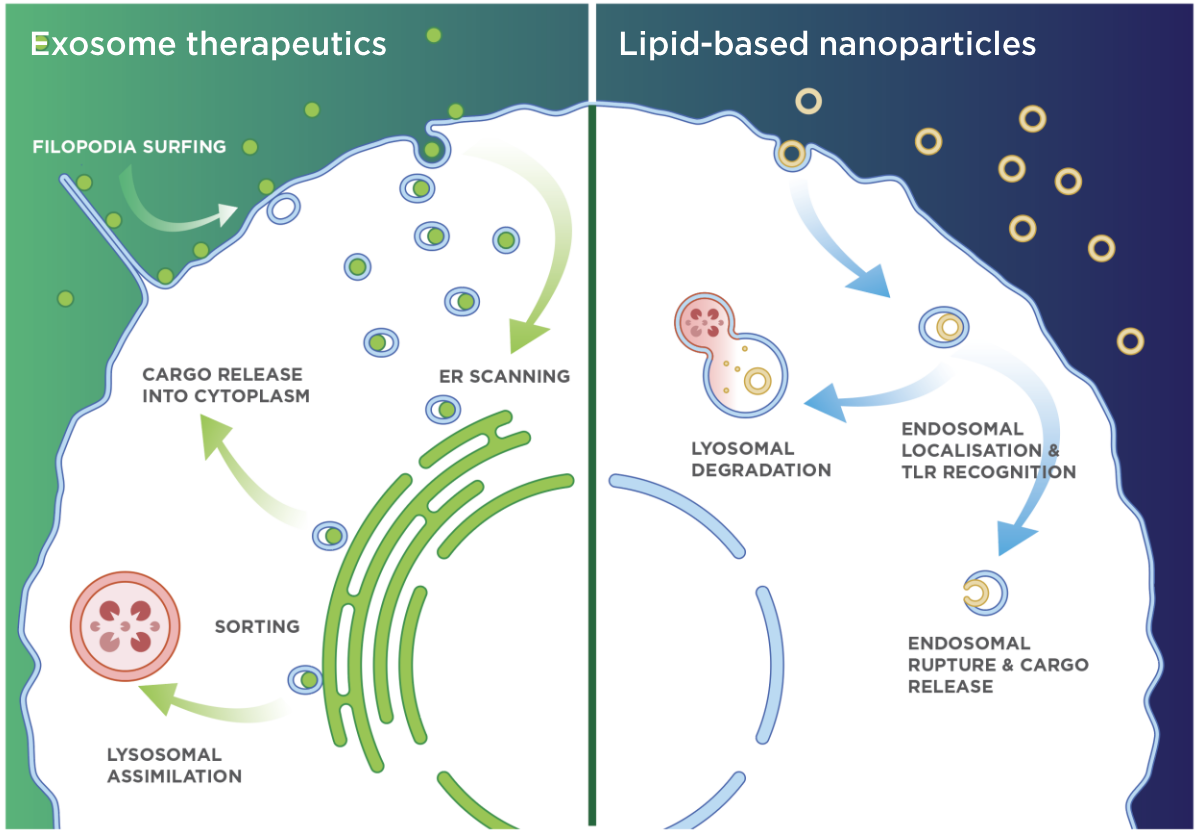
What
Natural nano-sized vesicles with unique delivery mechanism vs artificial lipid-based vehicles

Function
Body's delivery and communication system for a variety of complex payloads, delivered without immune recognition

Precision engineering
Engineering of the exosome machinery enables precise and highly efficient loading of genome editors

Strong safety indicators
Numerous exosome clinical trials run over 20+ years; blood transfusions contain large amounts of allogeneic exosomes

Opportunity
Engineered exosomes are a safe and potent modality for precision delivery of genome editing technologies



Exosome uptake into cells is distinct from other lipid-based nanoparticles

Adapted from Heusermann et al., (2016) *J. Cell Biol.* 213:173-184

Overcoming the challenges of genome editing

Delivery, delivery, delivery

Clinical progress in the editing space is limited to *ex vivo* cell therapies and hepatic delivery

Extrahepatic tissues are hard to address with current technologies and/or require repeated dosing for sufficient coverage

Safe edits & safe delivery

Current *in vivo* delivery technologies are:

(i) liver-centric (e.g. LNPs), or
(ii) has significant safety and tolerability concerns (e.g. AAVs)

In addition, off-target edits and double-stranded breaks are significant safety concerns, especially when persistently expressed over a long period of time (e.g. when using AAV)

Precise targeting, precision medicine

Targeted delivery remains the holy grail of drug delivery and is especially key for genome editors

Cell-type specific delivery is potentially needed to provide an added layer of specificity and safety

Combining a proprietary pipeline with strategic partnerships

Proprietary pipeline

- Proprietary **CNS-focused pipeline**
- 1st program targeting **genetically driven central nervous system disease**

Strategic partnerships

- **Opportunity to partner** within and outside the CNS
- **Validated extrahepatic delivery** technology using targeted exosomes

Driving the future of medicine through precision gene editing

Leveraging our proprietary **exosome engineering technology,** we are developing cutting-edge therapeutics based on exosome encapsulated **genome editing effectors** for safe, natural and targeted delivery to novel cell types and tissues for the treatment of **genetic diseases**

A CRISPR-Cas9 based reporter system for single-cell detection of exosome-mediated functional transfer of RNA

nature communications

Identification of a novel scaffold protein for efficient and precise engineering of extracellular vesicles

Molecular Therapy

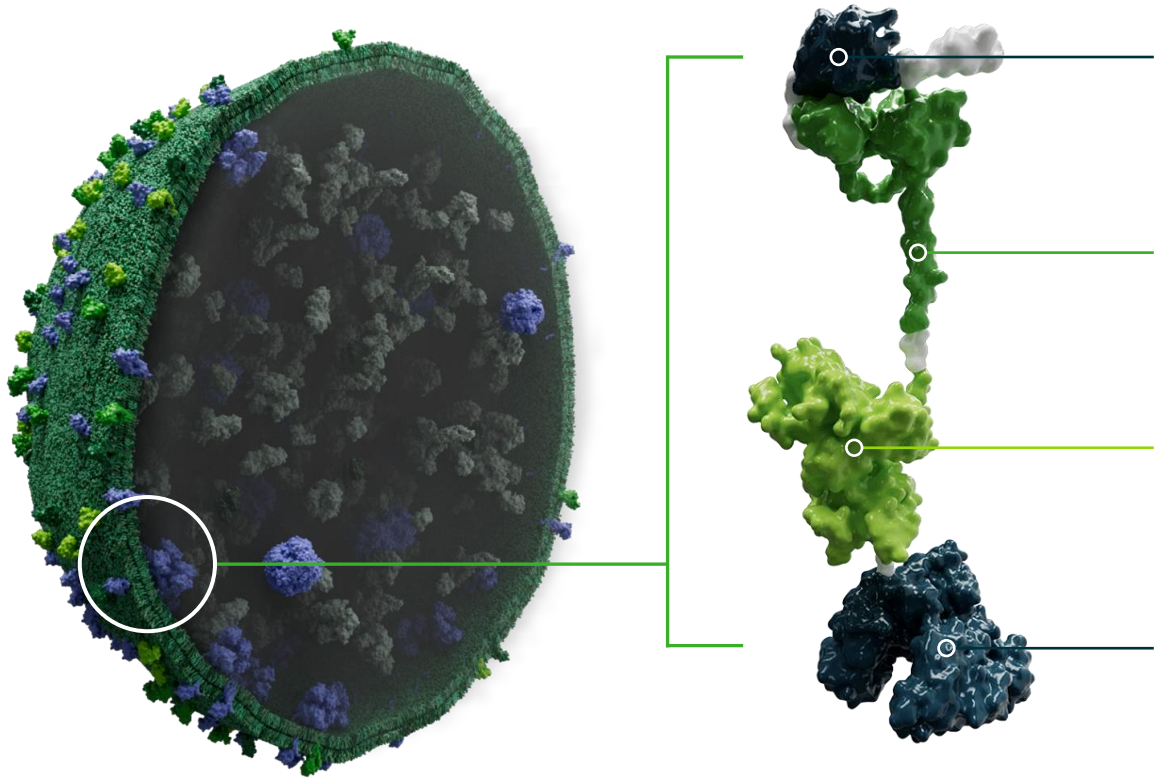
Bioengineering of exosomes to enable efficient drug cargo loading

Exosome therapeutics are the next precision medicine

Engineered exosomes are uniquely placed to enable and transform CNS & extrahepatic editing

	Exosome therapeutics	Lipid nanoparticles (LNPs)	Adeno-associated virus
Safety	Naturally occurring and non-immunogenic	Tolerability issues driven by both the LNP and the mRNA	Long-term expression increases risk of off-target edits and unspecific DSBs
Drug cargo	Nuclease + gRNA	mRNA + gRNA	Viral genome
Pharmacodynamics	Transient editing	Transient editing	Sustained long-term expression, except in cases of immune-mediated removal of transduced cells
Repeat dosing	Yes	Yes	No
Bioactivity	Intrinsic intracellular access, broad organ distribution, and targetable	Significant tolerability issues in the CNS; limited extrahepatic exposure	AAV tropism dependent

Our ExoEdit™ platform effectively shields and delivers intact ribonucleoproteins



Targeting moiety to enable cell-specific & precise delivery **on a broad biodistribution background**

Exosome loading scaffold adapted to loading & delivery of transient PD effects via RNPs

Luminal release technology ensures rapid RNP release & clearance

Flexible engineering technology for multiple RNPs to maximize strategic optionality

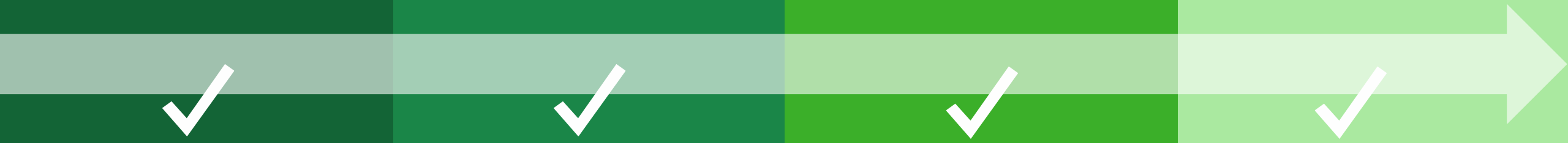
Engineered exosomes are a versatile platform for multiple generations of editing technologies

Meganucleases

CRISPR Cas9/Cas12

Base editors

Prime editors



Scalable & proprietary ExoEdit™ manufacturing process

Internal large-scale upstream capabilities

Genetically engineered human suspension GMP cell line encoding for editor RNP

In-house manufacturing capabilities up to 200L and experience scaling to 2,000L

Conventional & scalable downstream

Scalable downstream process seamlessly connecting R&D and GMP manufacturing

Conventional methods used in biologics and viral vector manufacture

Unrivalled single-particle analytics

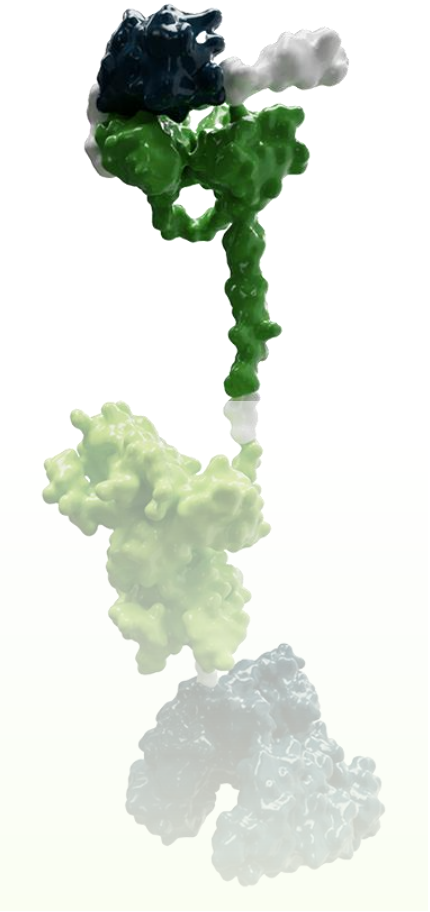
Unique single-particle analytics for product characterization and release

Strong analytics key to development

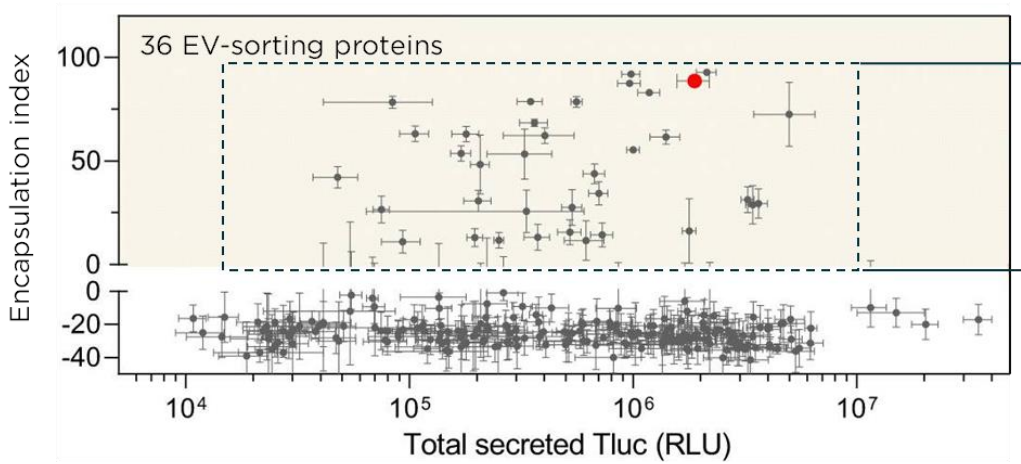
Evox pipeline

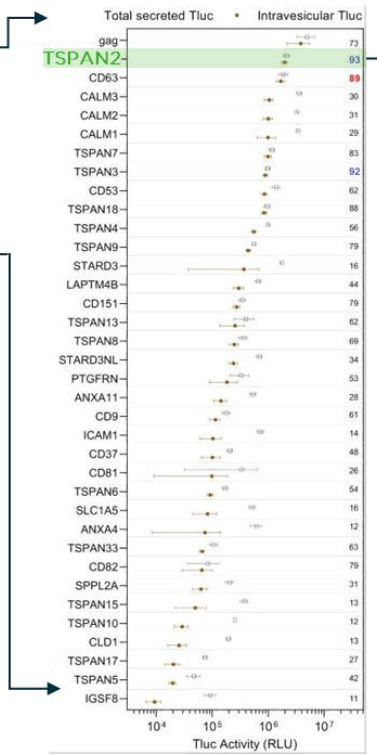
	Discovery	Preclinical	CTA/IND-enabling	Clinical
Proprietary				
CNS indication (undisclosed)				
CNS indication (undisclosed)				
Partnership opportunities				
CNS indications				
Extrahepatic indications				

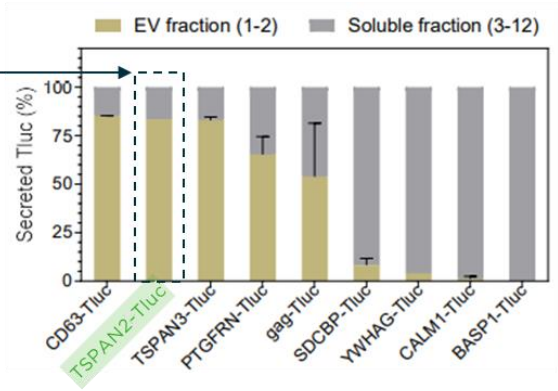
Evox platform enables precise and efficient drug loading



Screen for total payload expression and specificity of encapsulation into exosomes



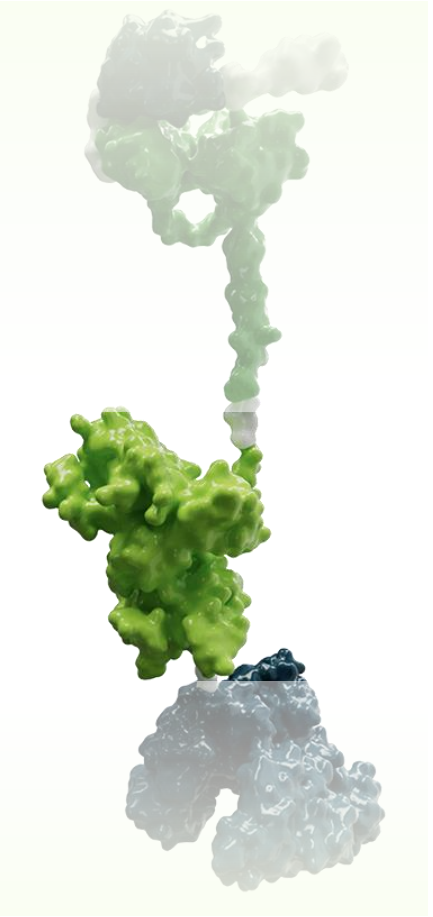




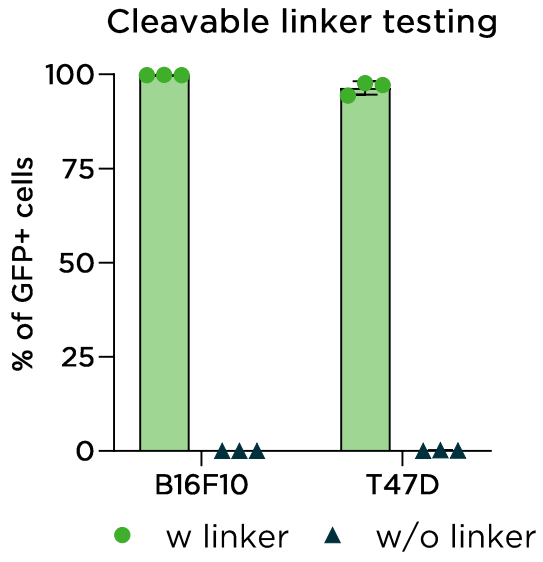
244 constructs screened – 36 robustly loaded into EVs

TSPAN2 was integrated into the Evox platform due to its superior EV localization and efficient cargo-loading capabilities

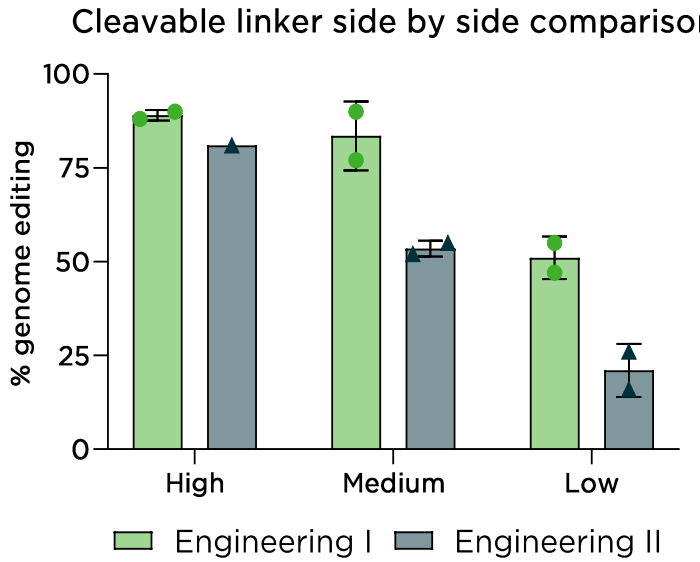
Proprietary cleavable linker system drives RNP release & delivery



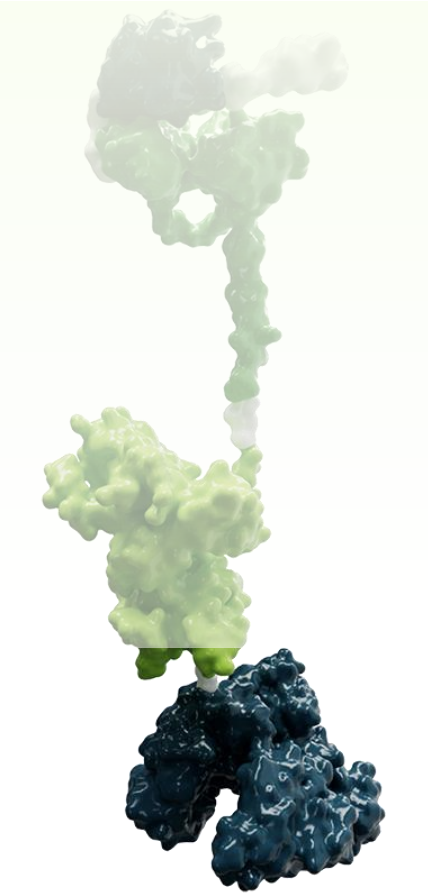
The cleavable linker is required for the release of cargo within the recipient cell



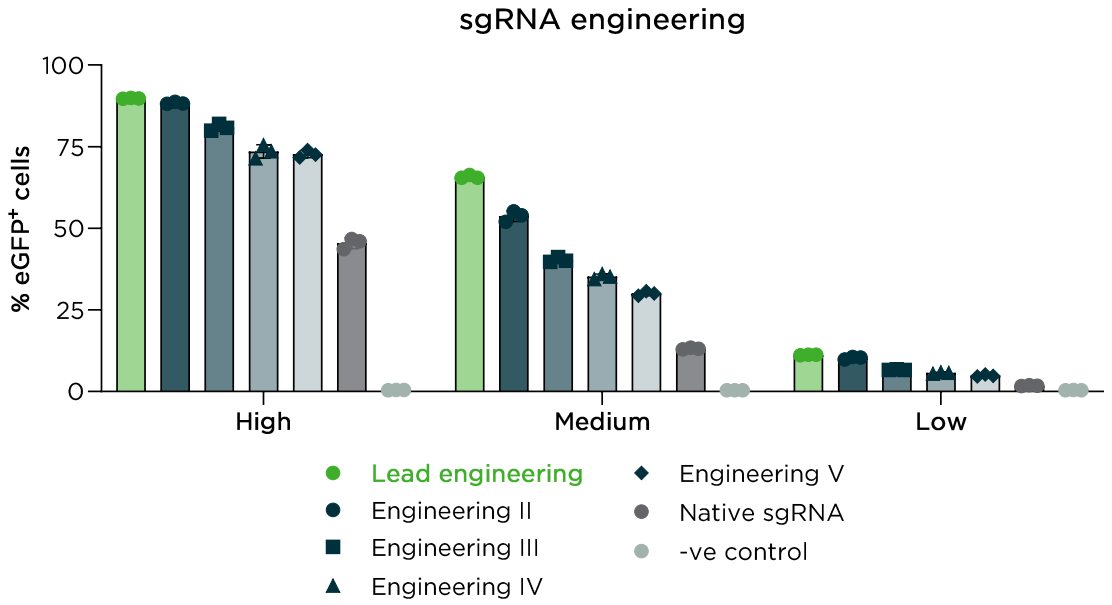
Two new variants were developed for improved efficiency



Proprietary sgRNA engineering enhances editing efficiency



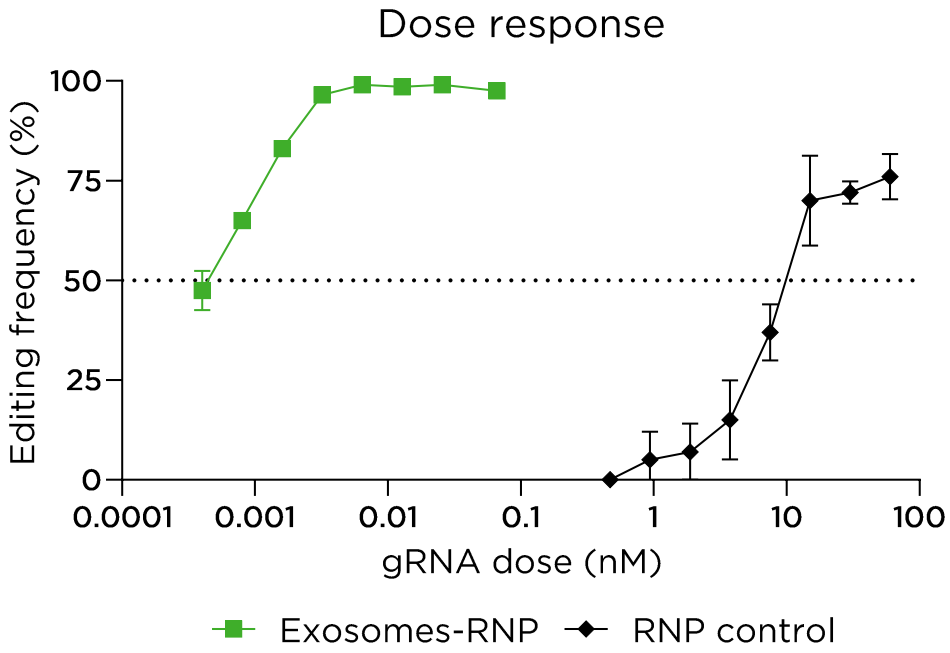
Scaffold gRNA modifications designed to improve potency and stability of gRNA



Our ExoEdit™ engineering technology drives improved potency compared to original sgRNAs

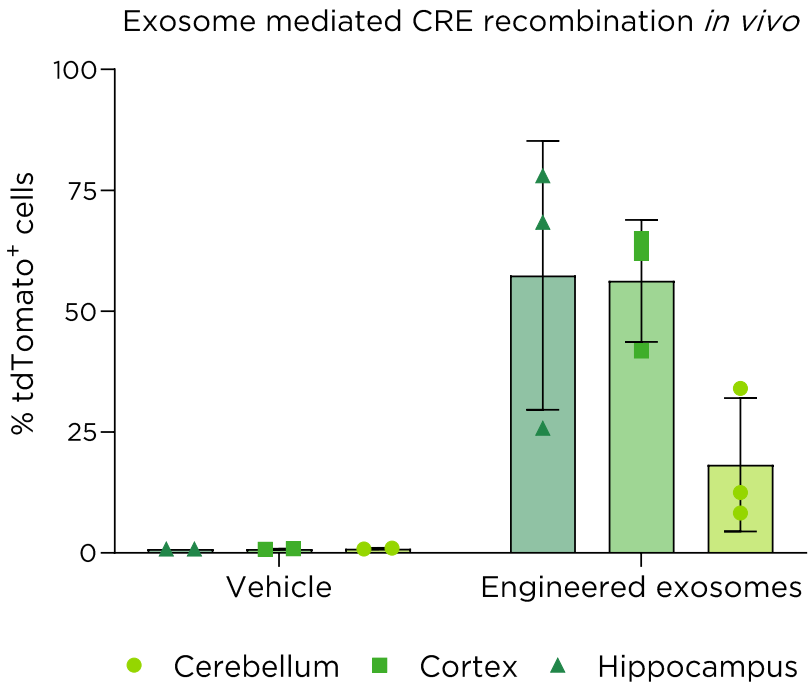
Exosome-mediated gene editing drives high-efficiency editing

- RNP potency with transfection reagent delivery as the gold standard for CRISPR/Cas9 delivery *in vitro* was compared to exosome-mediated delivery
- ExoEdit™ potency is **4-log superior** in EC50 compared to *in vitro* gold standard RNP control
- While RNP showed 0% editing <1nM, exosome-mediated delivery was still 50% editing in the pM range



Effective exosome-mediated *in vivo* gene recombination

- Exosomes **distributed** across both hemispheres of the brain
- Therapeutic potential in **hard-to-reach brain regions**



60% recombination observed, using lead engineering of Cre-delivering exosomes

Advancing exosome-enabled genome editors

Our ExoEdit™ exosome engineering platform allows for delivery of all main genome editing technologies, to the central nervous system and to other tissues

The unparallelled safety and delivery advantages of natural nanoparticles such as exosomes have enabled us to build a **CNS-focused pipeline of exosome-enabled editors**

Our versatile platform and unique R&D capabilities enables **strategic partnerships in key areas**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