evox THERAPEUTICS

Corporate presentation

2024 Q4

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

Leadership team uniquely **positioned to deliver on the promise of exosome-enabled editing technology**

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

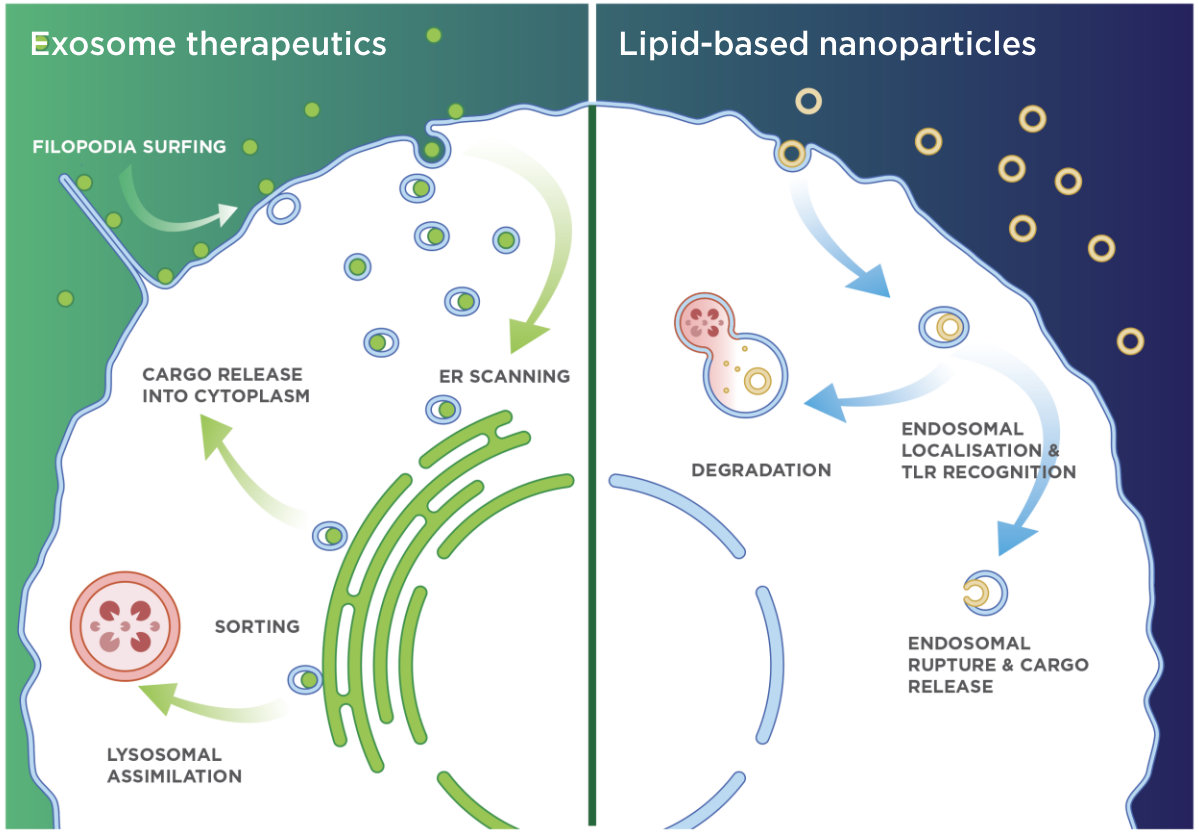
What
Natural nano-sized vesicles with differentiated delivery mechanism vs artificial lipid-based vehicles and viral delivery systems

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

Most targets for genome editing therapies are outside of the liver, but extrahepatic tissues are not adequately addressed using today's technology

Safe edits & safe delivery

Current *in vivo* delivery technologies:

(i) are liver-centric (e.g. LNPs) and unable to reach organs such as the brain, or
(ii) come with significant short-term toxicity and immunogenicity risks & long-term safety concerns (i.e. the risks of off-target edits increase upon sustained viral delivery)

Precise targeting, precision medicine

Efficient delivery to multiple cell types is key to unlocking the genome editing opportunity

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

Combining a proprietary pipeline with strategic partnerships

Proprietary pipeline

- Proprietary **CNS-focused pipeline**
- Internal programs targeting **genetically driven central nervous system diseases**

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

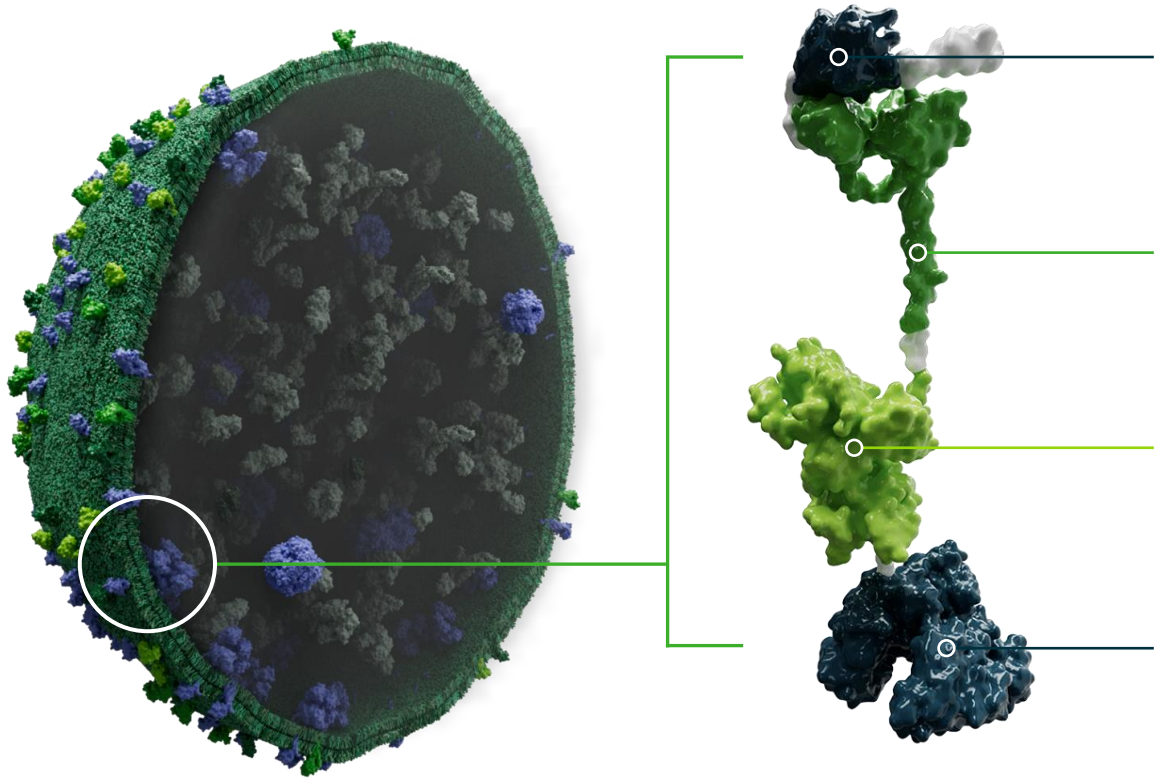
Bioengineering of exosomes to enable efficient drug cargo loading

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 edits via RNPs

Luminal release technology ensures rapid RNP release & clearance

Flexible engineering technology for multiple RNPs to maximize strategic optionality

Evox pipeline

	Target	Preclinical	CTA/IND-enabling	Clinical
Proprietary pipeline				
Spinocerebellar ataxia type 2	Ataxin 2			
Amyotrophic lateral sclerosis	Ataxin 2			
Partnership opportunities				
CNS indications	Multiple			
Extrahepatic indications	Multiple			

Editing of the ATXN2 gene for the treatment of SCA2 and ALS

One-and-done exosome-mediated delivery of CRISPR-Cas RNP leads to rapid knock-out of the ATXN2 gene and fast clearance of editing machinery for an excellent safety profile

	SCA2	ALS
	**- Autosomal dominant CAG repeat** expansions in the **ATXN2** gene **- 10-15 years** life expectancy after onset; **no disease-modifying** therapies	**- ATXN2 drives pathological TDP43 aggregation in ALS** - **2-5 years** life expectancy after onset and **highly limited therapeutic options**
	**- 2,000+** diagnosed patients (US, UK, EU4); reported **incidence 1 per 100,000** people	**- 47,000+** diagnosed patients (US, UK, EU4); reported **incidence 4.1-8.4 per 100,000** people
	**- No approved therapies** and limited competition	- A handful approved drugs; **increasing number of ATXN2 agents in development**

Multiple linked yet diversified near-term opportunities & significant expansion potential

SCA2 as a sentinel monogeneic disease program

One-and-done gene edit with the potential for re-dosing

Established safety profile, including in the CNS

Direct CNS RoA to maximize exposure

Significant unmet medical need & limited competition

ATXN2 knock-out has the potential to be a highly impactful treatment for ALS

Same product and same target

One-and-done edit with the potential for re-dosing

Severe, rapidly progressing neurodegenerative disease

ATXN2 increasingly recognized as an important driver of ALS

Further CNS & extrahepatic expansion

Compelling cellular tropism in local contexts, e.g. cardiomyocyte homing

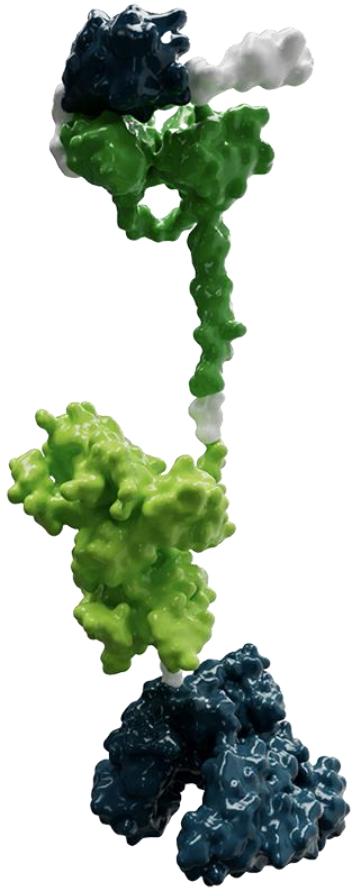
Systemic extrahepatic targeting

Further CNS & extrahepatic expansion

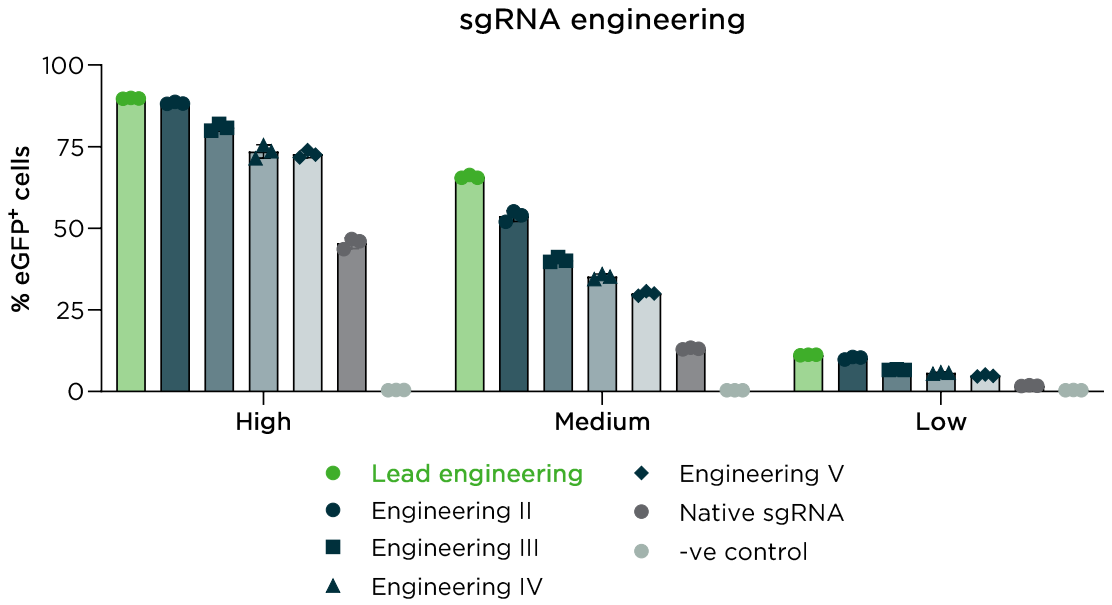
Indication expansion into large neurodegenerative disease

Sentinel program targeting a rare severe monogeneic CNS disease

Proprietary sgRNA engineering enhances editing efficiency after exosome delivery



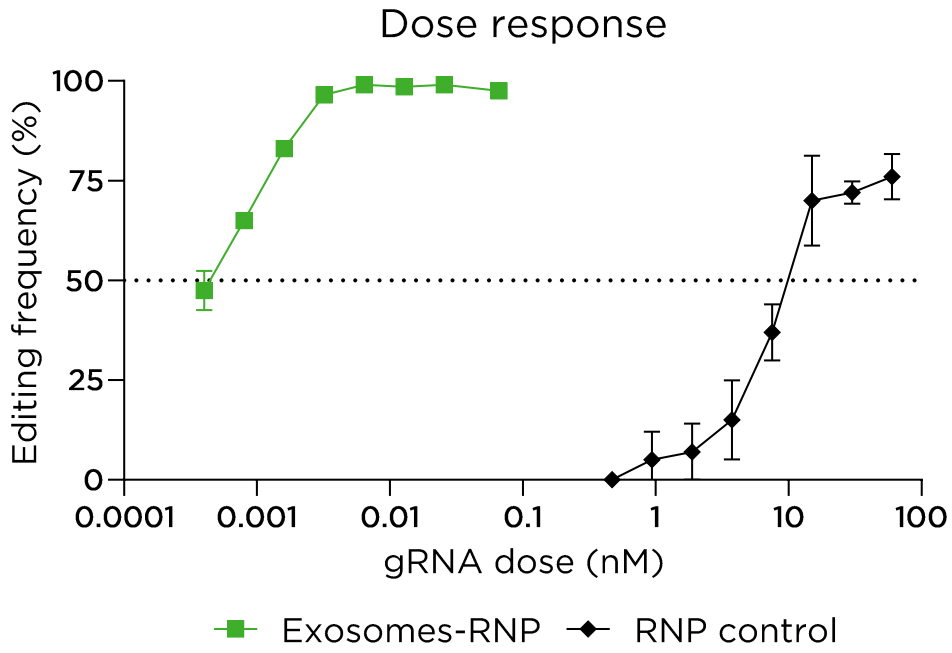
Scaffold gRNA modifications designed to improve potency and stability of gRNA



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

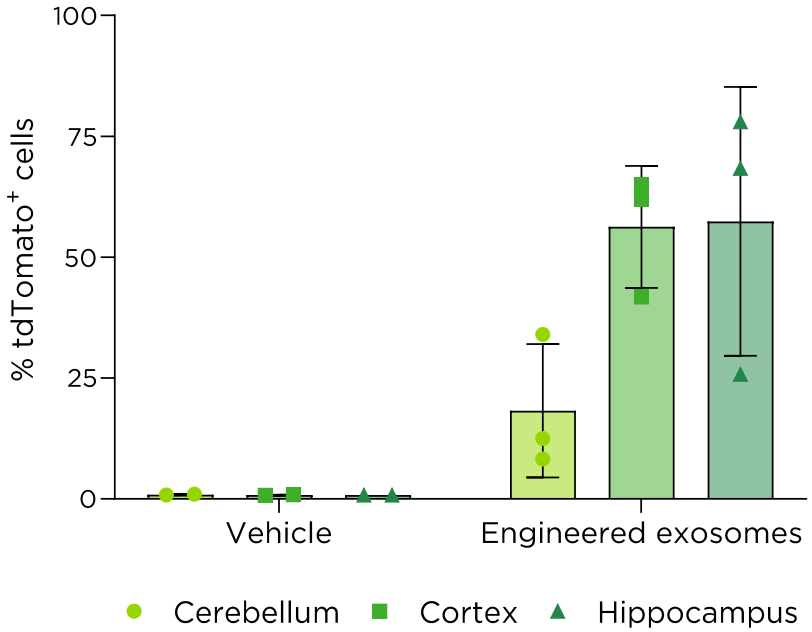
Exosome-mediated gene editing drives high-efficiency editing in relevant target cells

- Exosome-mediated potency is **4-log superior** in EC50 compared to gold standard RNP delivery vehicles
- While RNP showed 0% editing <1nM, exosome-mediated delivery was still 50% editing in the pM range



Our ExoEdit™ platform enables effective exosome-mediated gene recombination via Cre recombinase *in vivo*

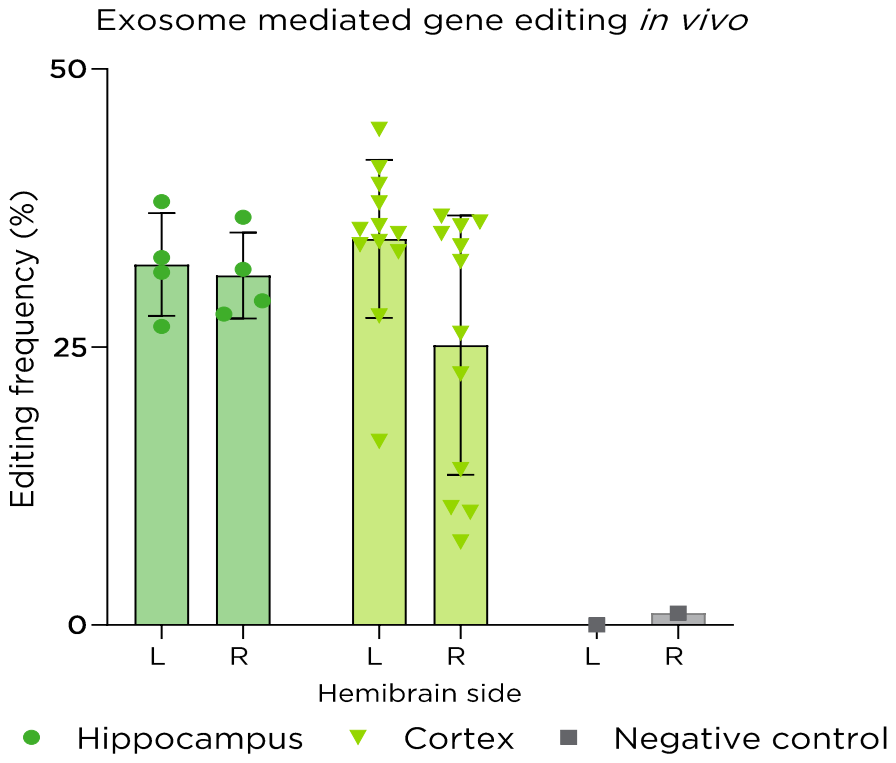
- Exosomes are **well tolerated in the CNS and in other tissues and distribute broadly** across both hemispheres of the brain
- Therapeutic potential in **hard-to-reach brain regions with broad cell type tropism**



60% recombination observed using Cre-delivering exosomes

Exosome-enabled CRISPR-Cas9 delivery into the CNS is well tolerated and exhibit unparallelled activity

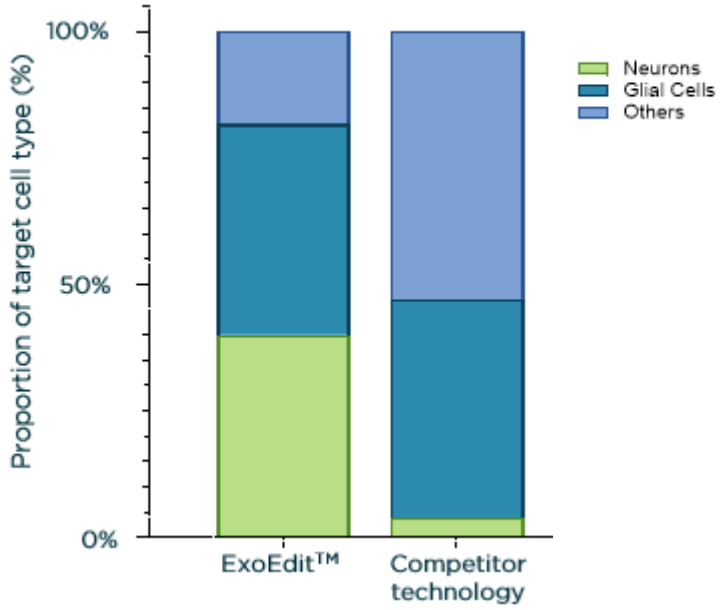
- Leading competitive non-viral delivery technologies show limited (~6.1%) editing in the CNS when delivered in P0 mice (newborns) (Banskota *et al.* 2022)
- Using early versions of our ExoEdit™ platform we achieve broad and potent delivery of CRISPR-Cas9 in adult rodent brains, with up to **40% editing**
- Editing observed on both the contralateral and ipsilateral sides, confirming **broad biodistribution**



Remarkable improvement in CNS editing compared to published state of the art

Broad cell-type tropism of our ExoEdit™ technology unlocks a plethora of disease targets across the brain

- Competitive non-viral delivery technologies typically result in insufficient neuronal exposure
- Evox's ExoEdit™ engineered exosomes show broad cell type tropism in the CNS, with extensive bioactive delivery to neurons
- The ability to repeatedly dose our engineered exosomes combined with broad neuronal delivery enables Evox to address major CNS diseases using a variety of genome editing modalities, including Cas9, Cas12 and base editors



Broad cell type tropism in the CNS

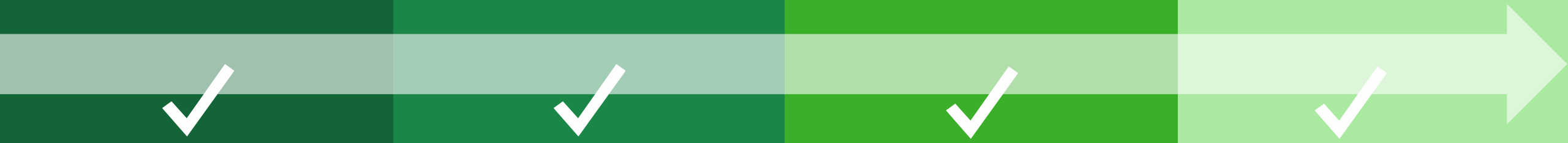
Engineered exosomes are a versatile platform for multiple generations of editing technologies

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

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 which is advancing rapidly toward the clinic**

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