



CircVec – A novel Payload Expression Platform Based on Circular RNA Biogenesis: Features and Opportunities

Biologics World Nordics
Stockholm, Sweden
March 5th, 2025

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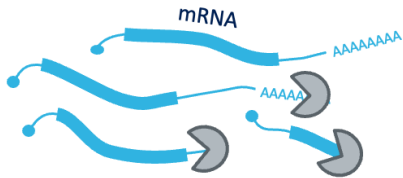
circRNA introduction

- 2. circVec platform
- 3. circVec lead program
- 4. Summary & team

circRNA increases durability and expression level to enhance the potency of nucleic acid medicines

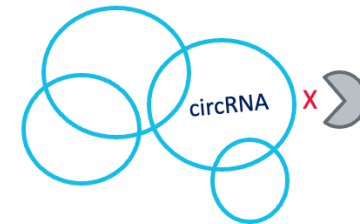
Extended RNA durability

70x half-life vs. mRNA in vivo



Higher protein expression

15x protein expression vs. mRNA in vivo



**circRNA will
outcompete linear
mRNA due to its
enhanced stability**

Reduced toxicity

Dose sparing for improved safety

Modular & multi-functional

Add'l 'remove & replace' MoA

Human circRNA was first described by Circio scientists



Dr Thomas B Hansen

Dr Erik D Wiklund



nature

7,400 citations

Published: 27 February 2013

Natural RNA circles function as efficient microRNA sponges

[Thomas B. Hansen](#), [Trine I. Jensen](#), [Bettina H. Clausen](#), [Jesper B. Bramsen](#), [Bente Finsen](#), [Christian K. Damgaard](#) & [Jørgen Kjems](#)

THE EMBO JOURNAL | EMBOpress | 30 September 2011 | 1,000 citations

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miRNA-dependent gene silencing involving Ago2-mediated cleavage of a circular antisense RNA

[Thomas B Hansen](#), [Erik D Wiklund](#), [Jesper B Bramsen](#), [Sune B Villadsen](#), [Aaron L Statham](#), [Susan J Clark](#), [Jørgen Kjems](#)

nature reviews genetics | January 2025

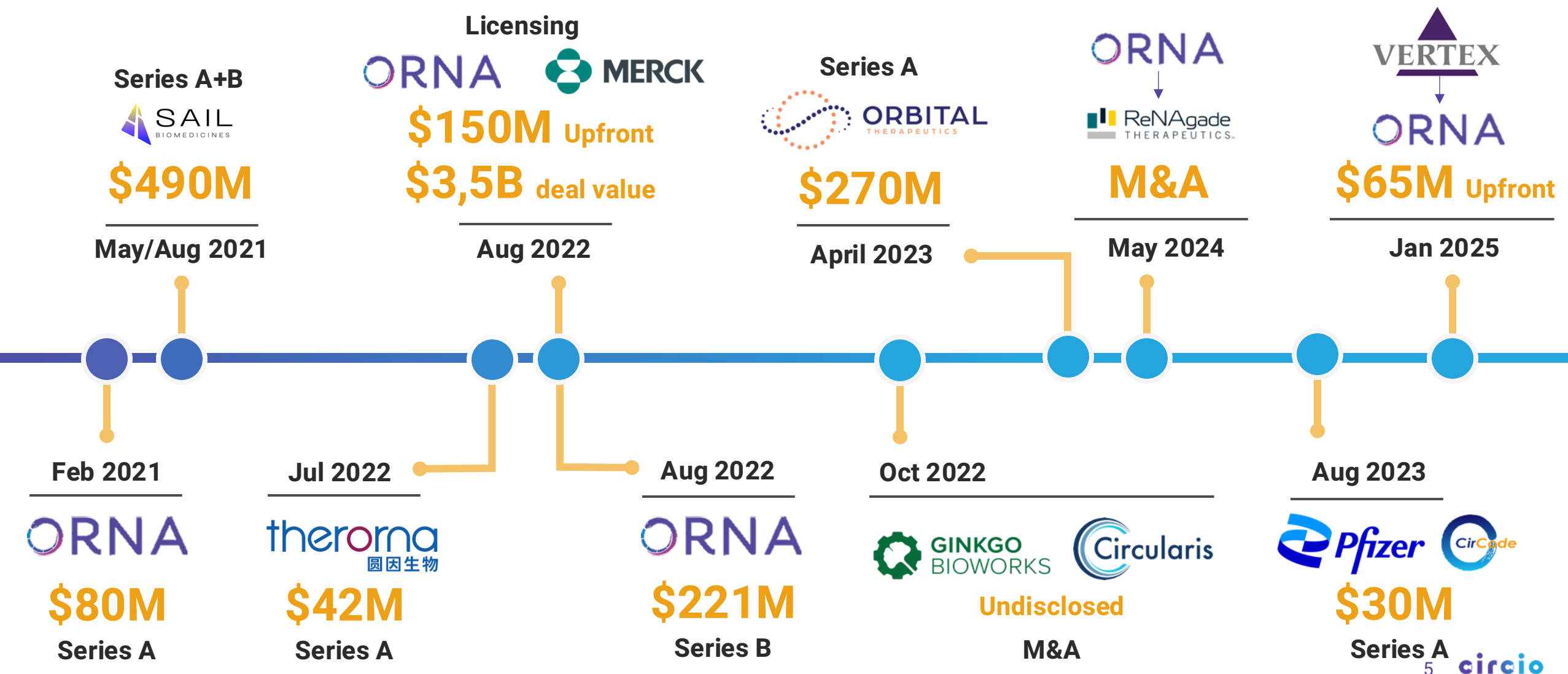
Review Article | Published: 09 January 2025

The therapeutic potential of circular RNAs

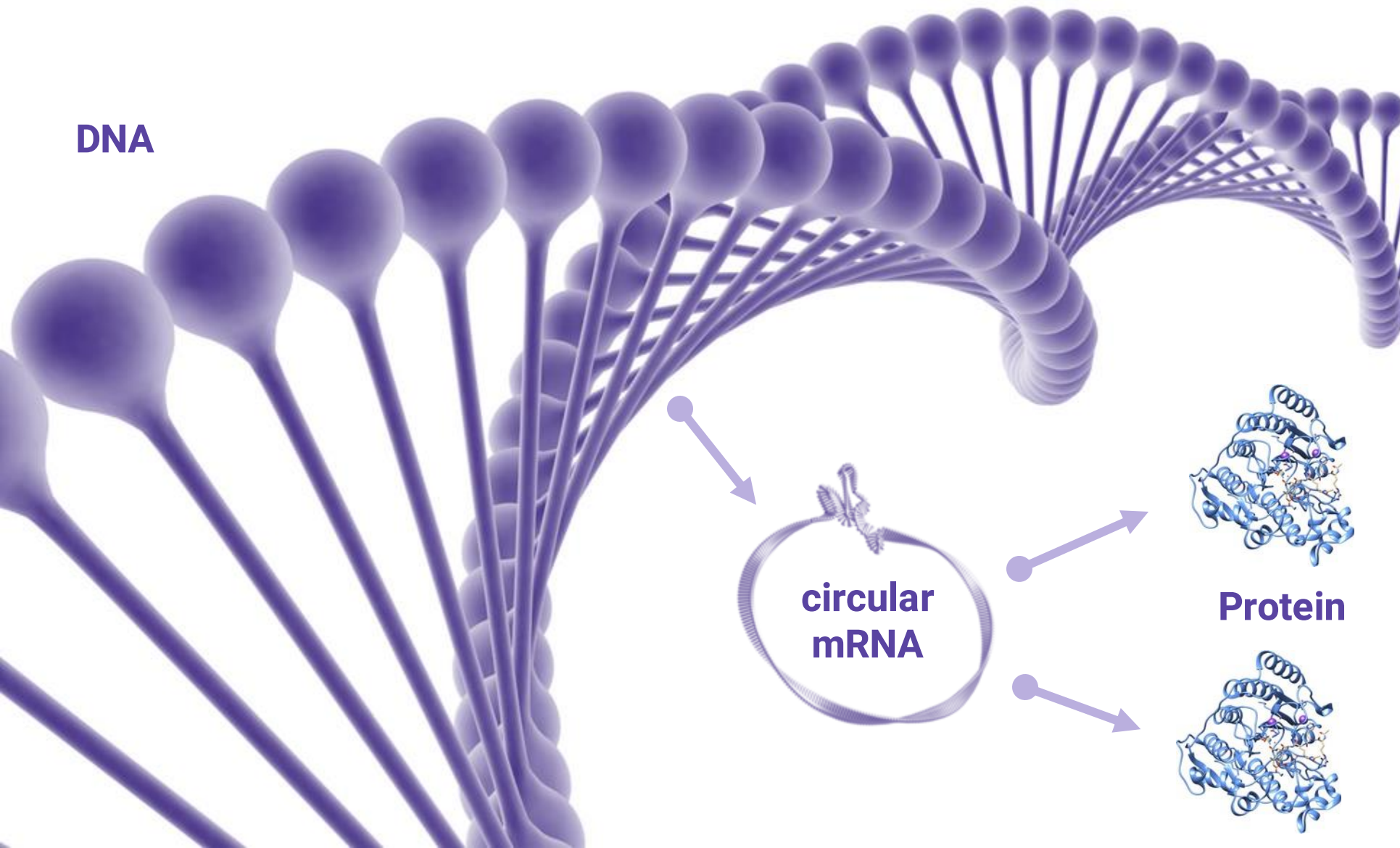
[Eoghan O'Leary](#), [Yanyi Jiang](#), [Lasse S. Kristensen](#), [Thomas B. Hansen](#) & [Jørgen Kjems](#)

[Nature Reviews Genetics](#) (2025) | [Cite this article](#)

These advantages drive high deal activity in circular RNA, competitors all focus on synthetic IVT circular RNA



The unique circVec expression system: Turning the patient's cells into circRNA factories



circVec
DNA or viral
vector






Inject

circRNA
biogenesis

Potent and durable
protein expression

circio

The circVec platform is technologically differentiated and creates novel opportunities for circRNA

		<i>Expression durability</i>	<i>Main opportunity in vaccines</i>	<i>Suitable for gene therapy</i>	<i>Delivery system</i>	<i>Existing CDMO manufacturing</i>
	circVec vector approach	months to years	✓ VLP-format	✓	Viral or DNA-LNP	✓
 	Synthetic circRNA	7-10 days	✓	✗	circRNA-LNP	✗
 	Synthetic mRNA	2-3 days	✓	✗	mRNA-LNP	✓

Circio is being recognized internationally as a leader with unique technology in the circRNA field

BIOCENTURY

ARTICLE | PRODUCT DEVELOPMENT

Emerging circular RNA field split on what to deliver and how to deliver it

The rising therapeutic modality is more durable than linear mRNA, promising efficacy and manufacturing advantages

BY DANIELLE GOLOVIN, BIOPHARMA ANALYST

August 17, 2023 11:34 PM UTC



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News > Drug Development

Opinion: Circular RNA Will Soon Replace mRNA in Biopharma

July 31, 2024 | 5 min read | Erik Digman Wiklund



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ARTICLE

Enhancing gene therapy with Circio

In this Q&A, Erik Wiklund, CEO of Circio, explains the key findings of their circVec circular RNA platform technology, why they chose AAV-based gene therapy for AATD as the lead programme, and their plans for the future to enhance the potency and reduce the cost of current gold-standard gene therapy.



IN VIVO
CITELINE COMMERCIAL

In Vivo >> Market Intelligence

Circio's Vision For Long-Lasting Nucleic Acid Therapeutics

16 Dec 2024 • By [David Wild](#)

Circular RNA has several advantages, but the field is young. Scandinavian startup Circio Holdings believes its version of the technology will prove the most robust.

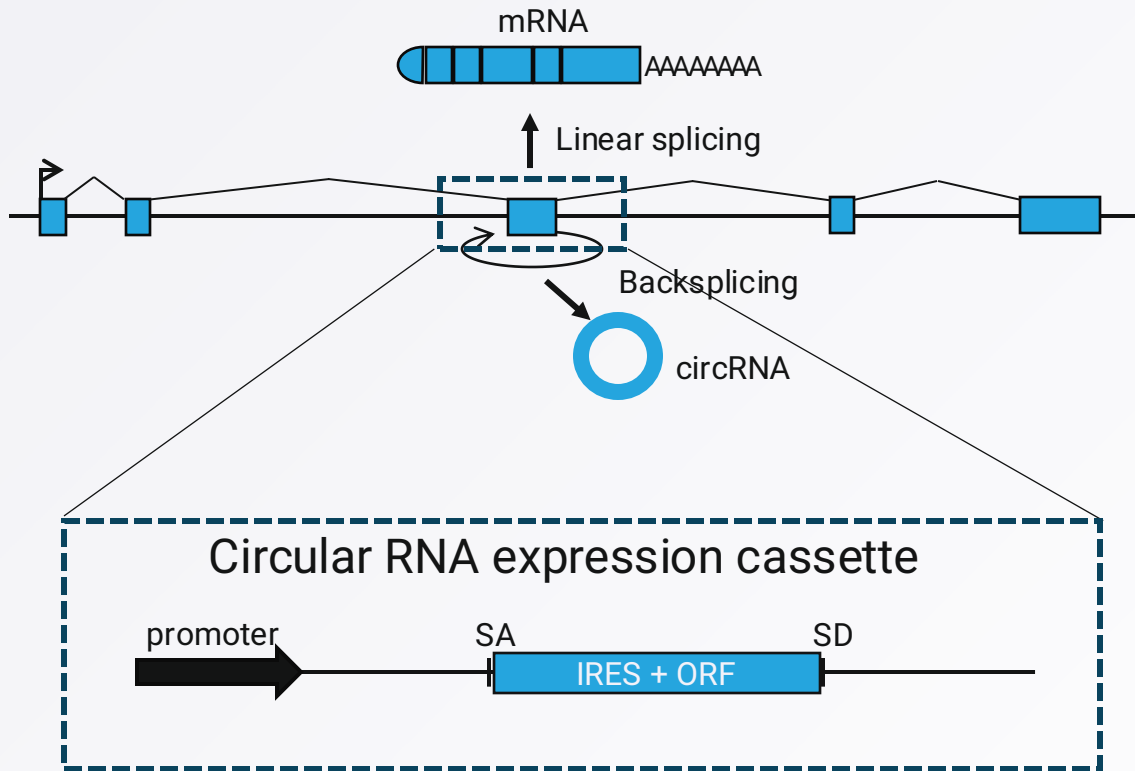


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circVec platform

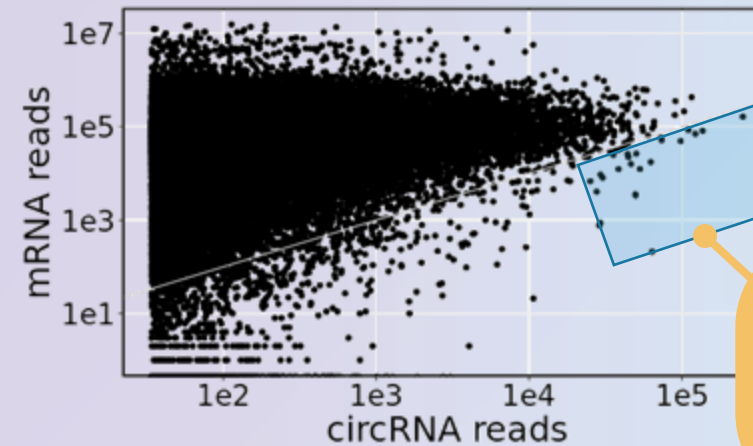
- 3. circVec lead program
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The starting point for the circVec construct is based on nature's best design



Expression of human endogenous circRNA

NGS analysis of 300+ RNAseq datasets

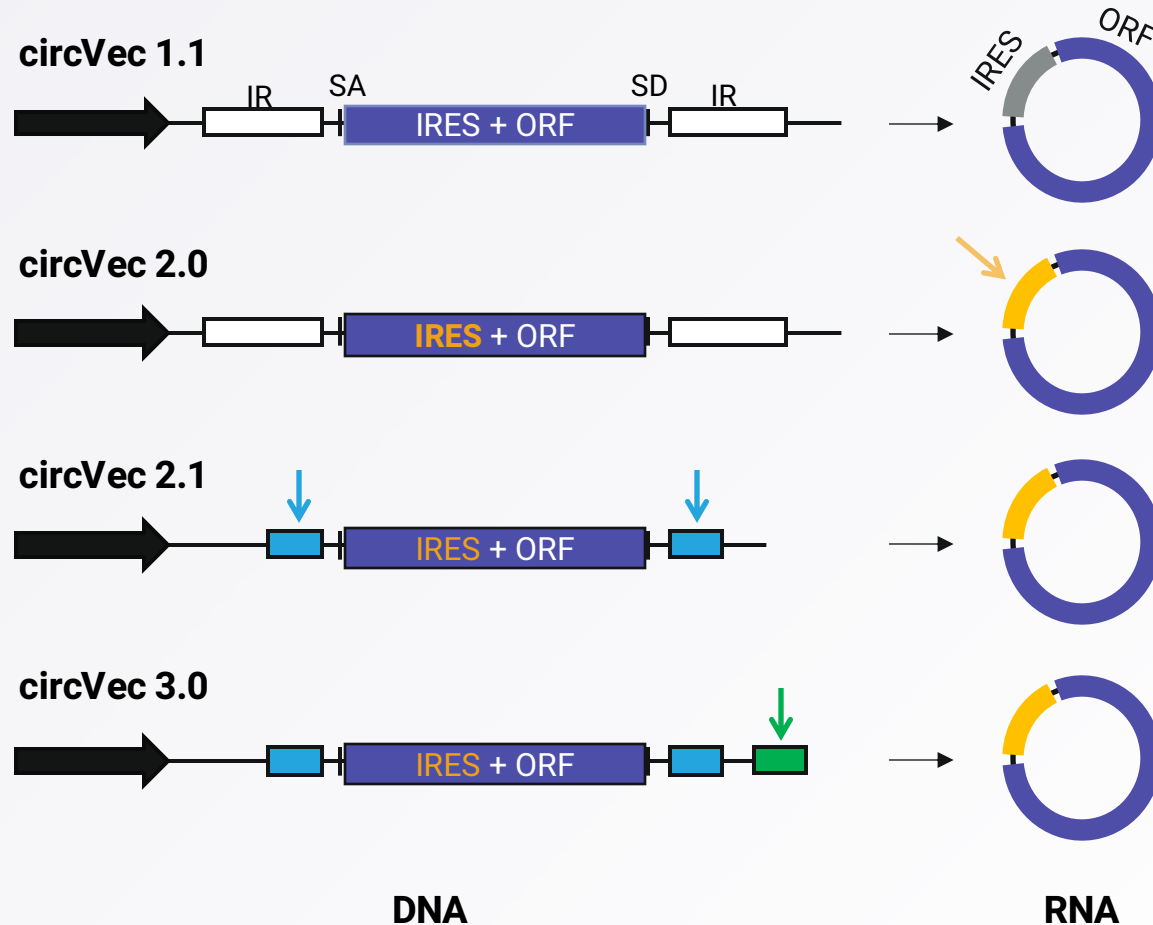


**Maximum
biogenesis-rate
of endogenous
circRNA**

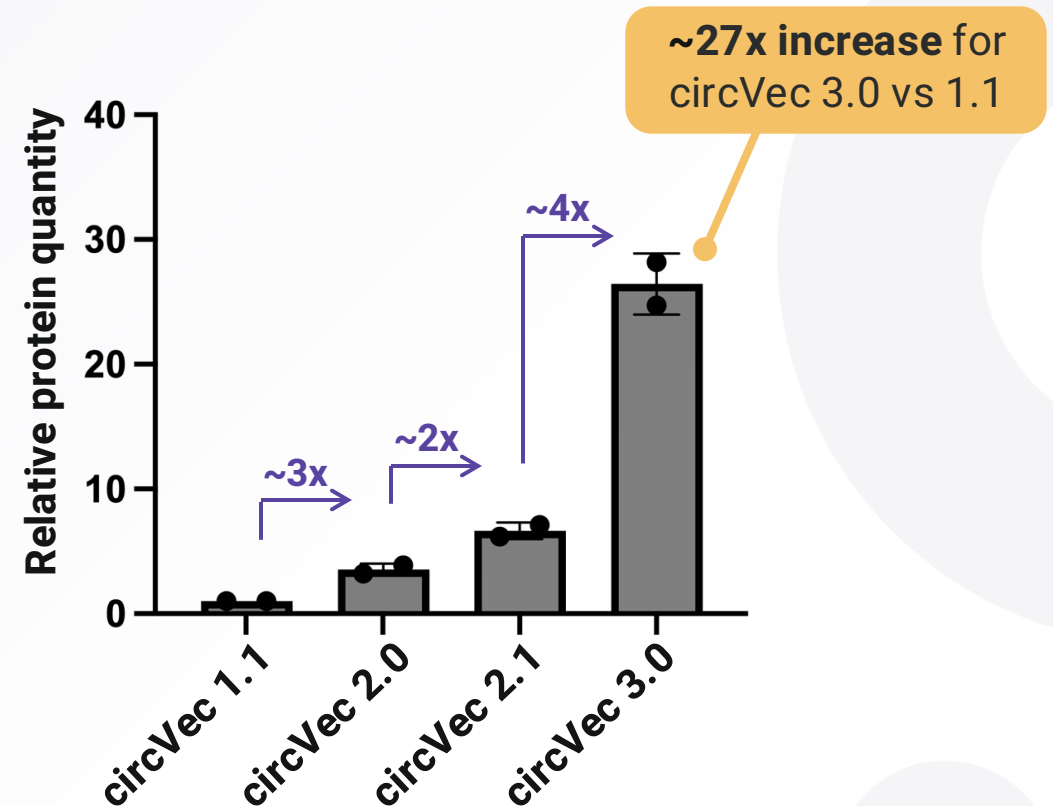
Screen and optimize the most effective loci in the human genome
→ **circVec 1st generation**

Optimizing nature's best design to build circVec 3.0

circVec generation 1.X – 3.X, design schematics



circVec protein quantification, Western blot



circVec substantially outperforms the expression level and durability of mRNA-based systems in cells

Increased expression level

Prolonged durability

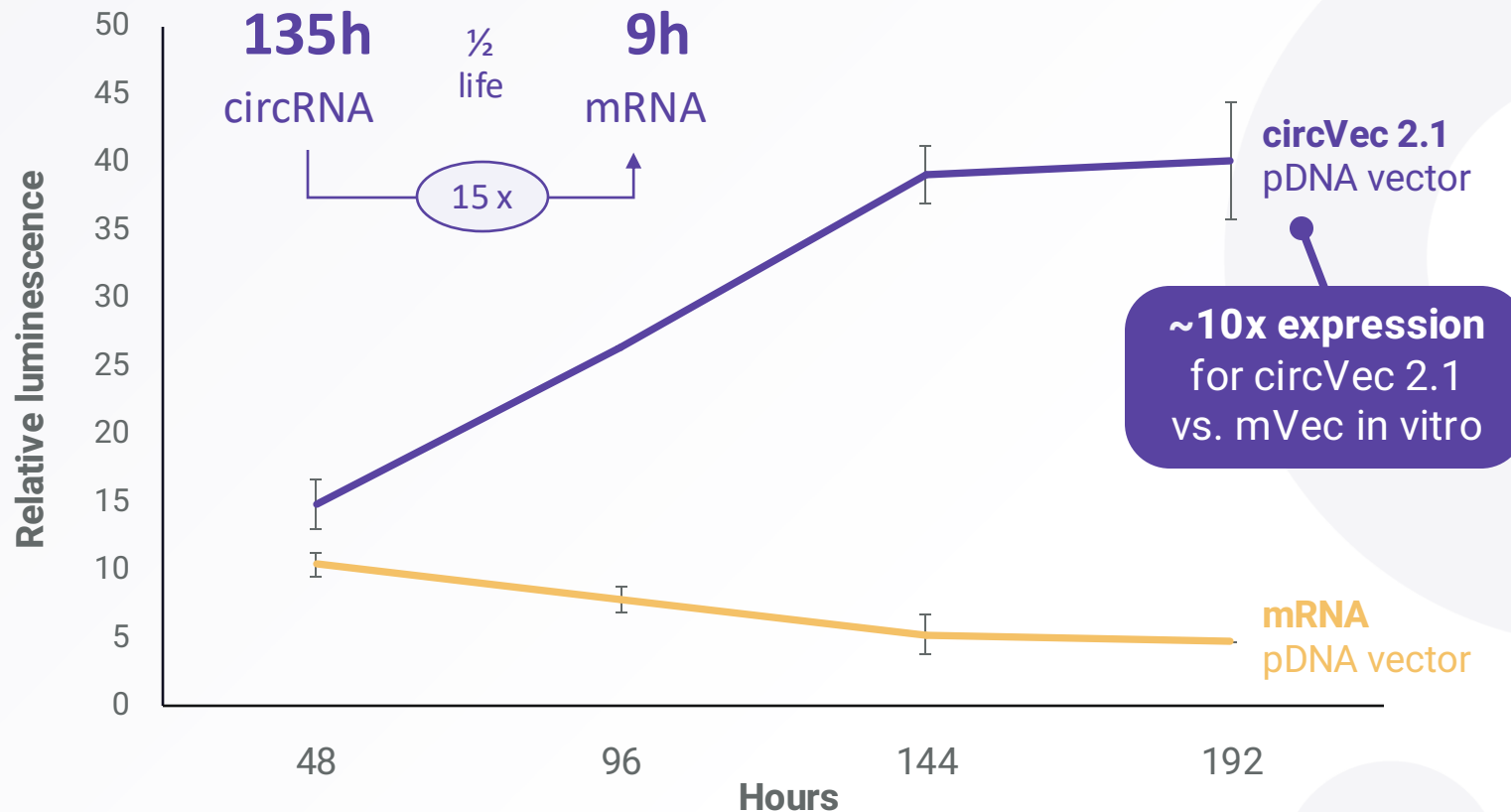
→ *Enhanced therapeutics*

“Due to its significant advantages, circRNA systems can be expected to replace mRNA-based expression for DNA format therapeutics in the future – just as synthetic circRNA can be expected to replace current mRNA formats”

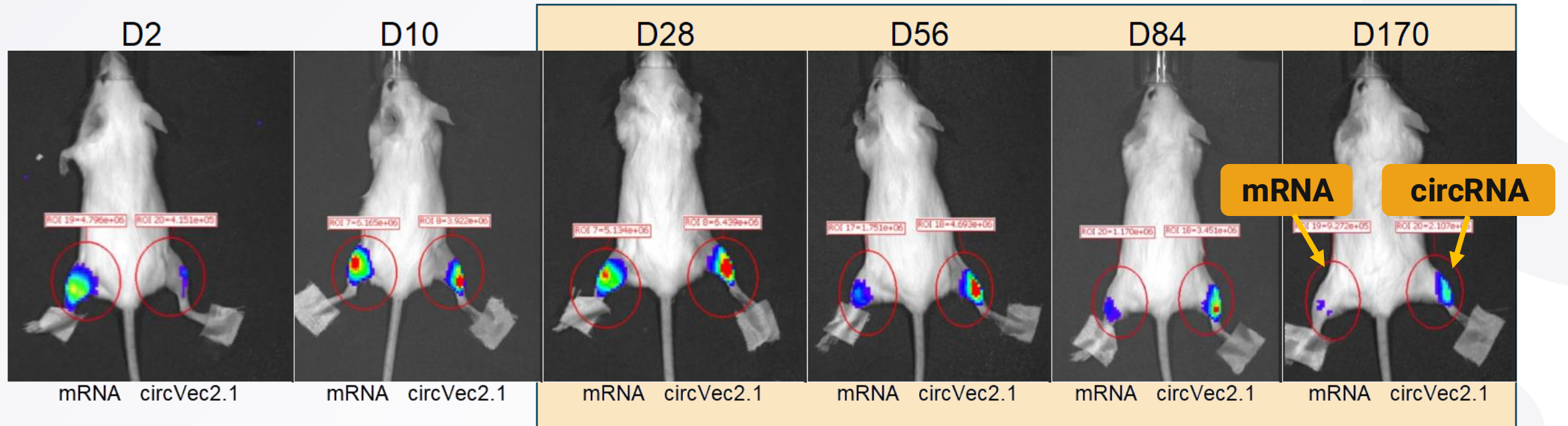
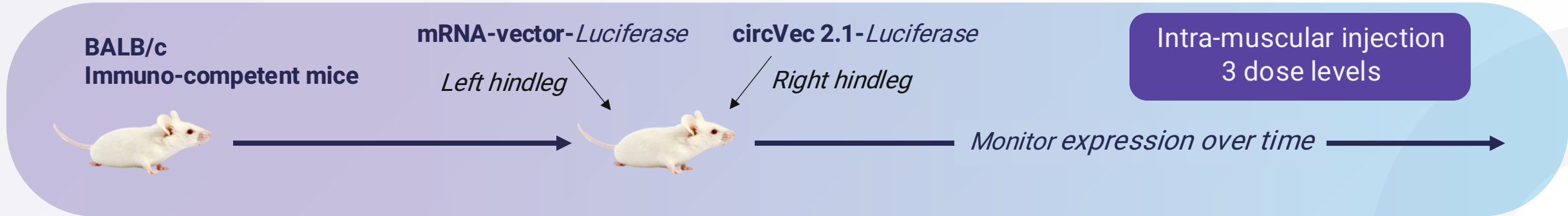
Dr. Alex Wesselhoeft

Scientific founder
oRNA Therapeutics

circVec 2.1 vs. mVec (mRNA) luciferase reporter expression; in vitro



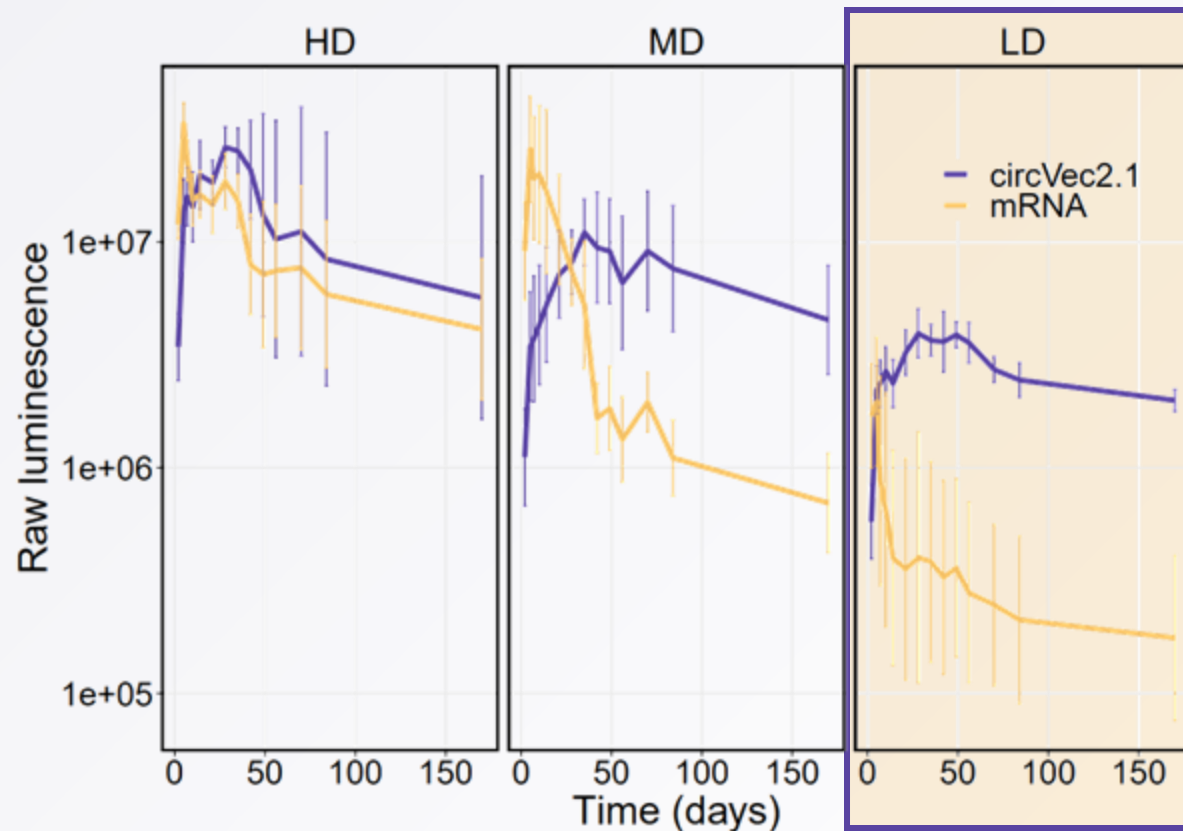
circVec 2.1 achieves > 6 month expression durability on one single injection in immuno-competent mouse muscle



circVec 2.1 dose response in vivo - strongest advantage vs. mRNA observed at low dose, high therapeutic relevance

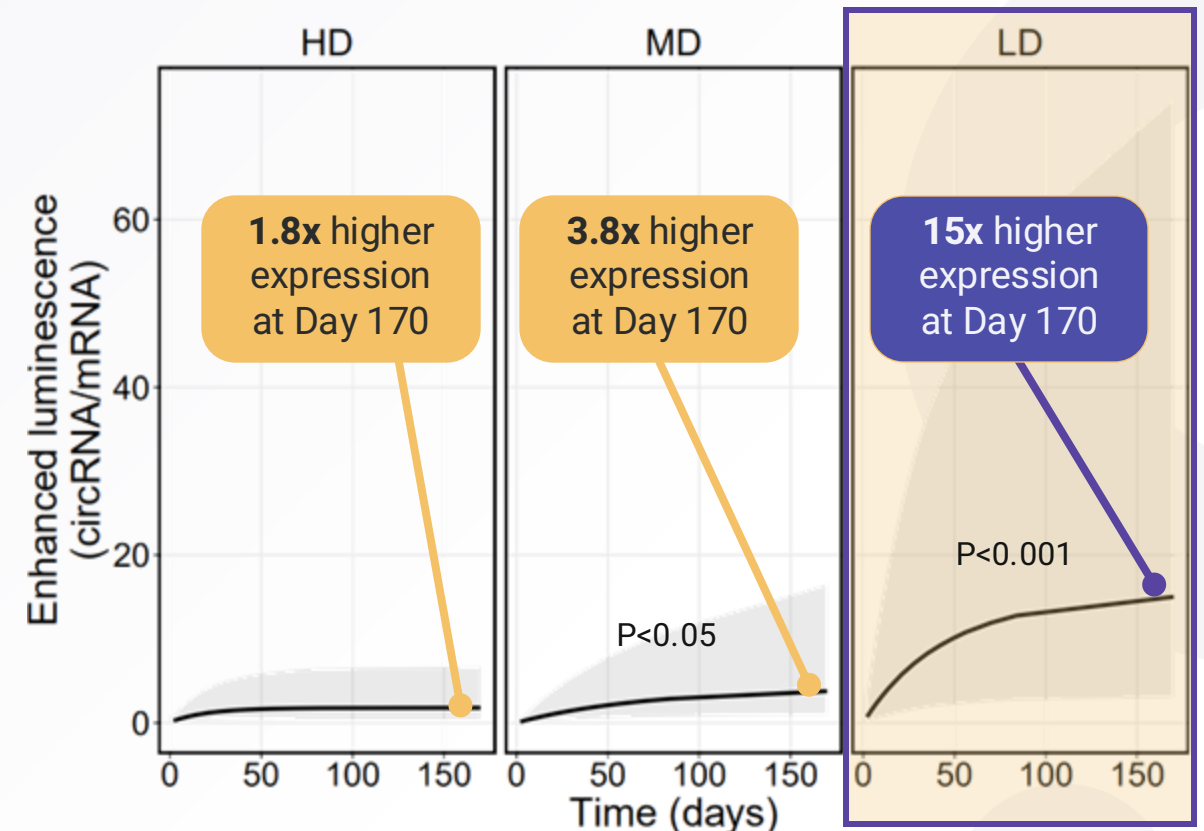
Absolute expression (luminescence)

circVec 2.1 vs. mRNA pDNA vector expression



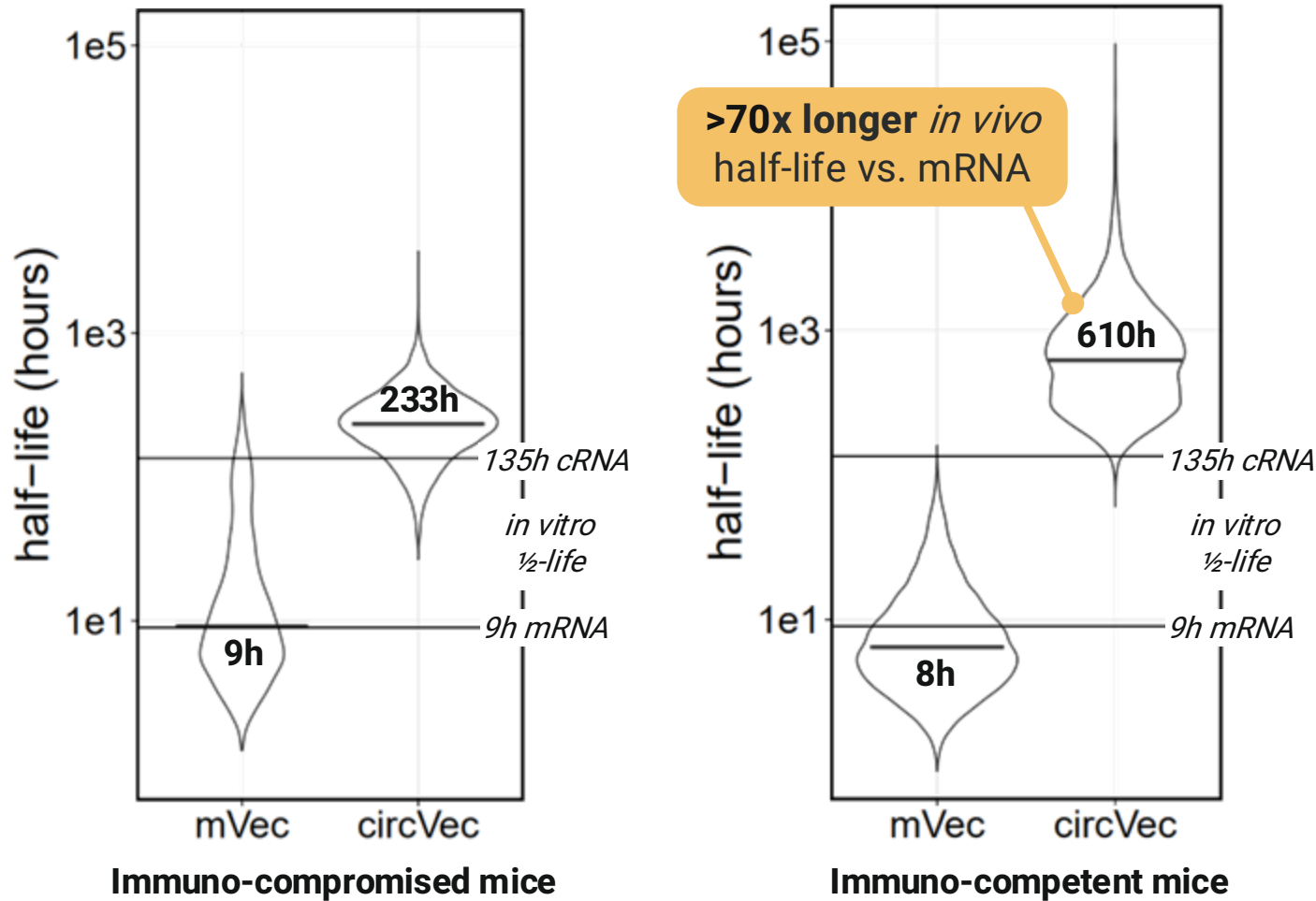
Relative expression (luminescence)

-fold change circVec 2.1 vs. mRNA expression

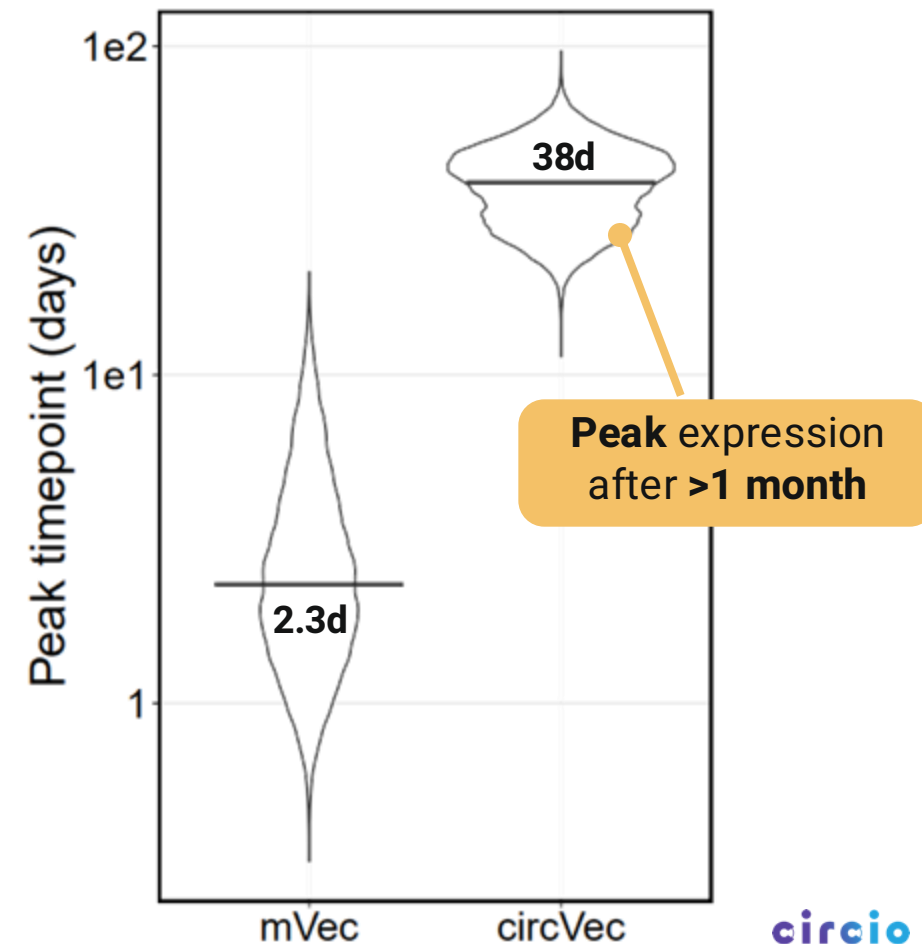


Bioinformatic analysis of circVec 2.1 in vivo data indicates over 70 times increased half-life of circRNA vs. mRNA

Inferred in vivo RNA half-life (hours), bioinformatic modelling

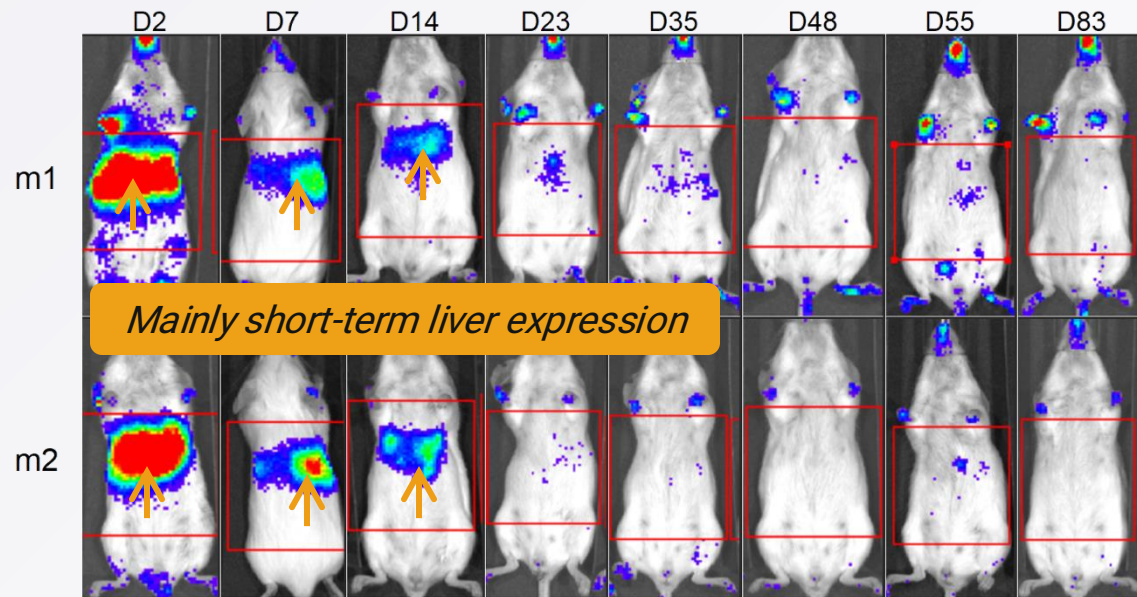


Inferred in vivo peak expression (days)

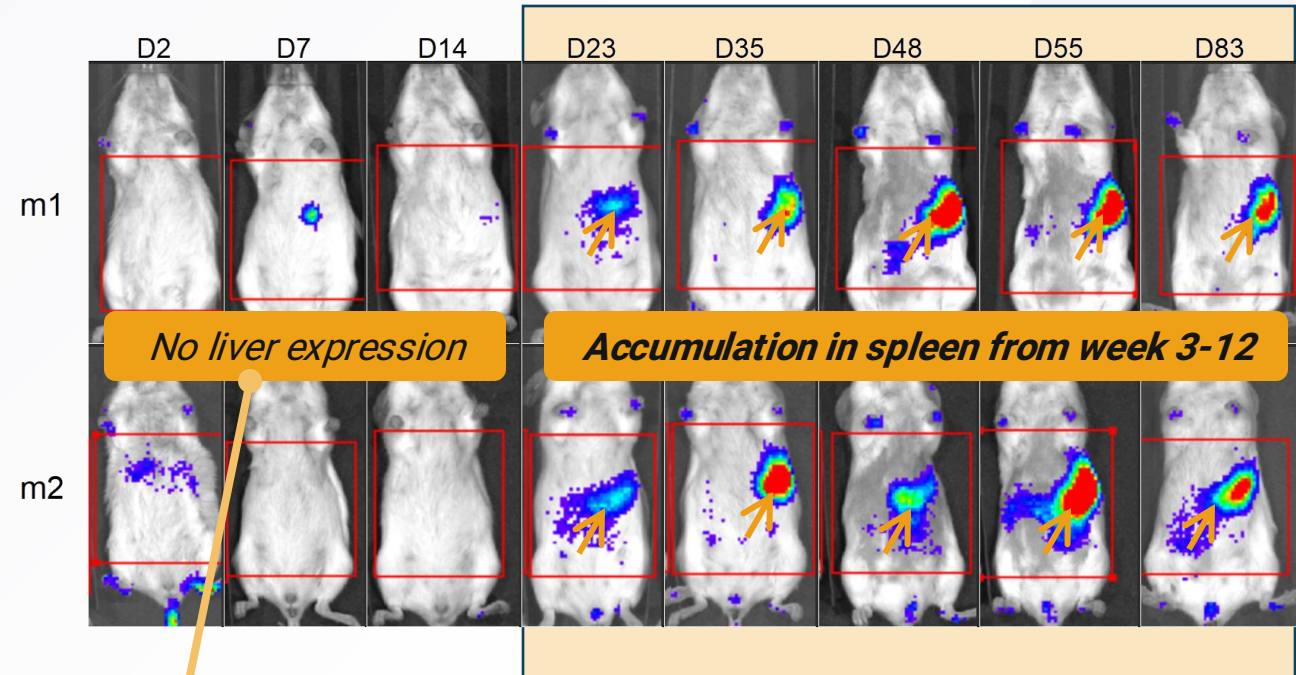


LNP-formulated circVec 2.1 accumulates in spleen with >12 week durability, minimizes liver expression

LNP-mVec (mRNA), luminescence
Systemic I.V. delivery, single dose on Day 0

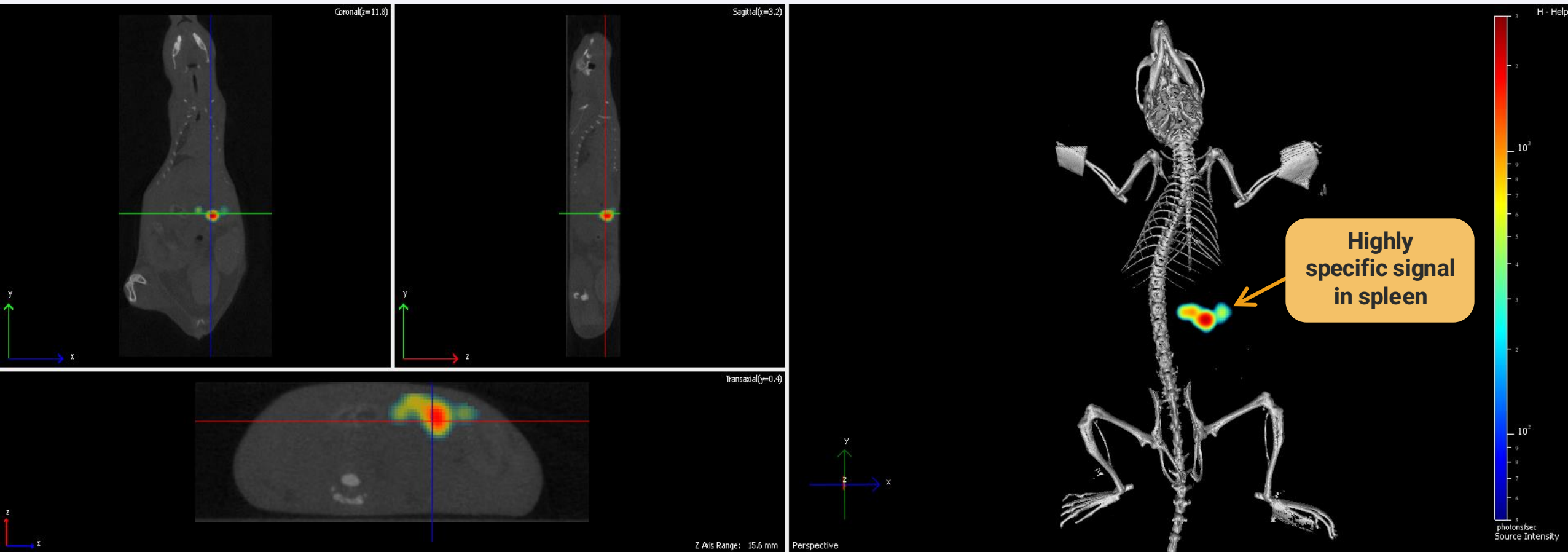


LNP-circVec 2.1 (circRNA), luminescence
Systemic I.V. delivery, single dose on Day 0



**circRNA durability adv.
does not apply in liver**

3D bioluminescence imaging + CT confirm spleen-specific circVec expression





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circVec lead program

4. Summary & team

The circVec platform can be deployed in multiple disease areas and therapeutic settings

**Lead program,
in house focus**

**Gene
therapy**



Genetic muscular dystrophies

Enhanced and durable expression

‘Remove & Replace’ concept

AAV and DNA format

**Next step /
partnership**

**Cell
therapy**



Auto-immune disease

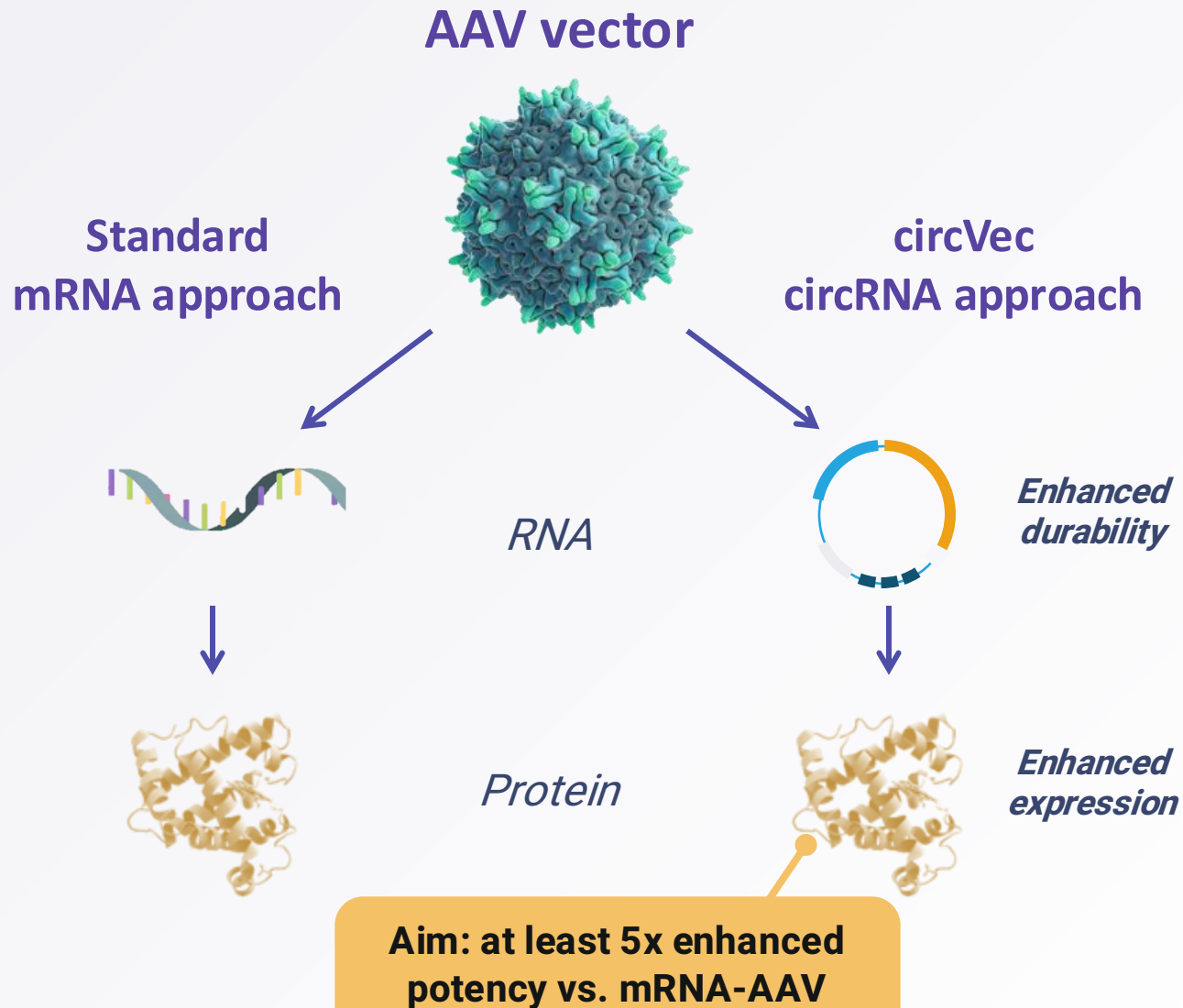
Non-integrating transduction

In vivo and ex vivo approach

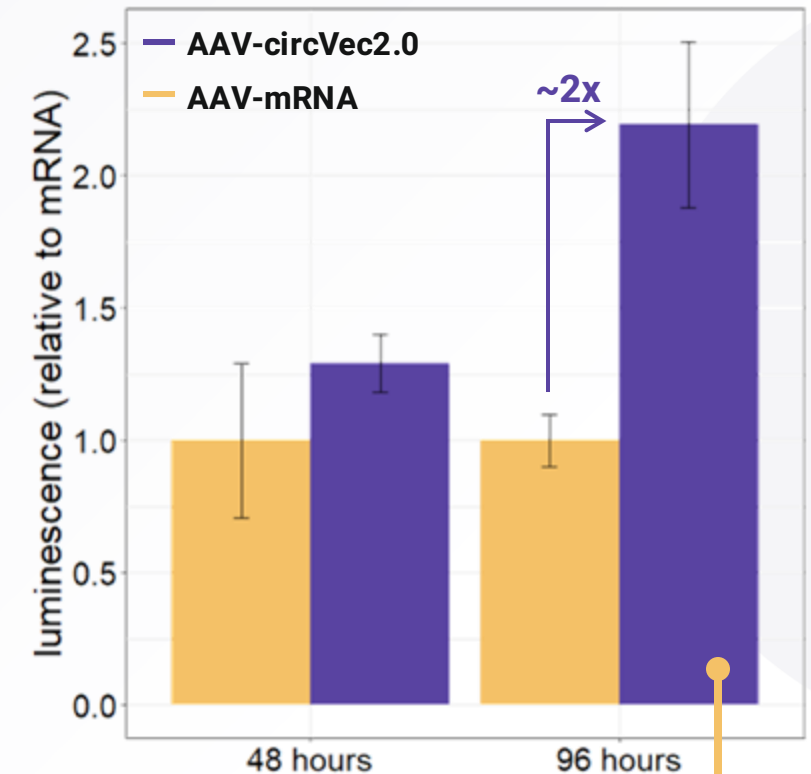
DNA and VLP format

Target, therapeutic format and disease to be prioritized based on data from ongoing in vivo program

circVec is a potentially disruptive novel expression technology for AAV gene therapy



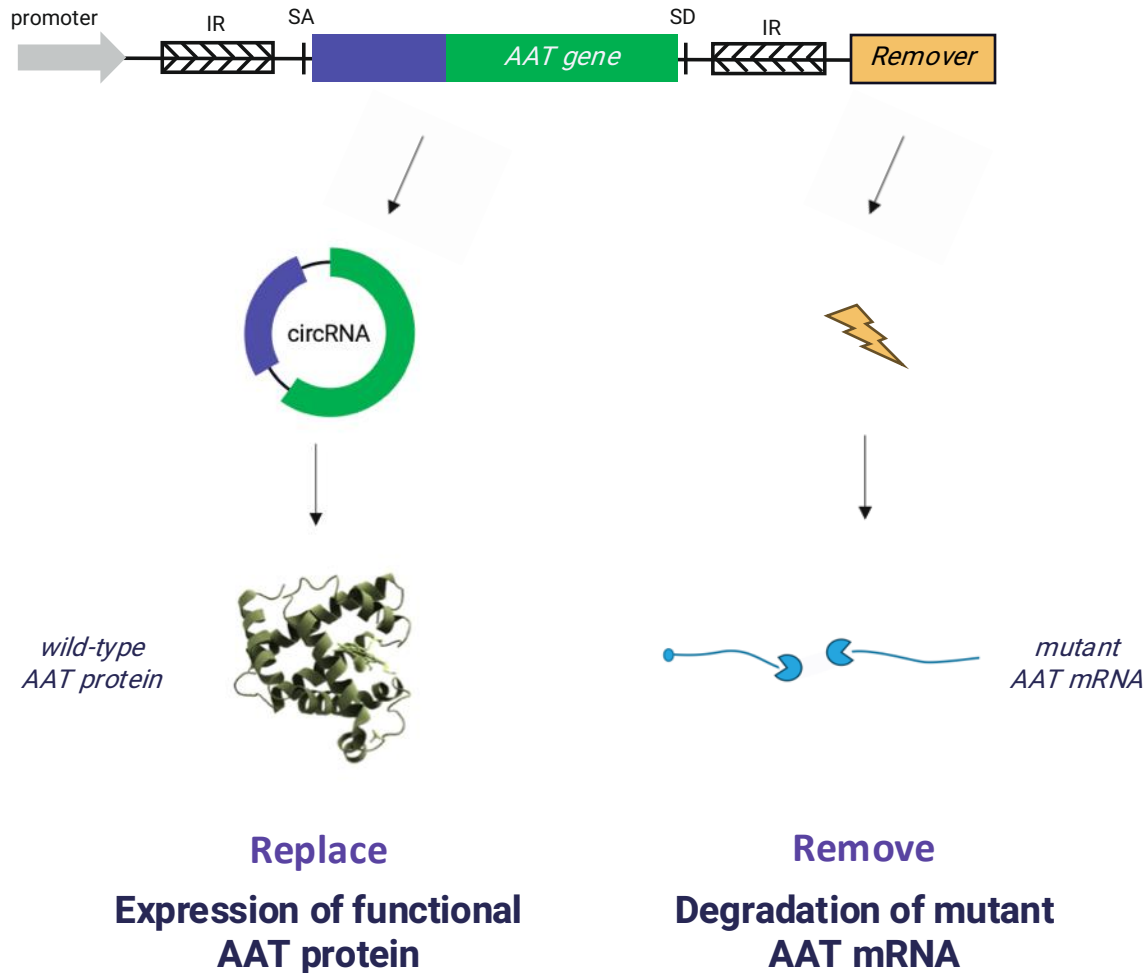
AAV protein expression, *in vitro* f-Luc



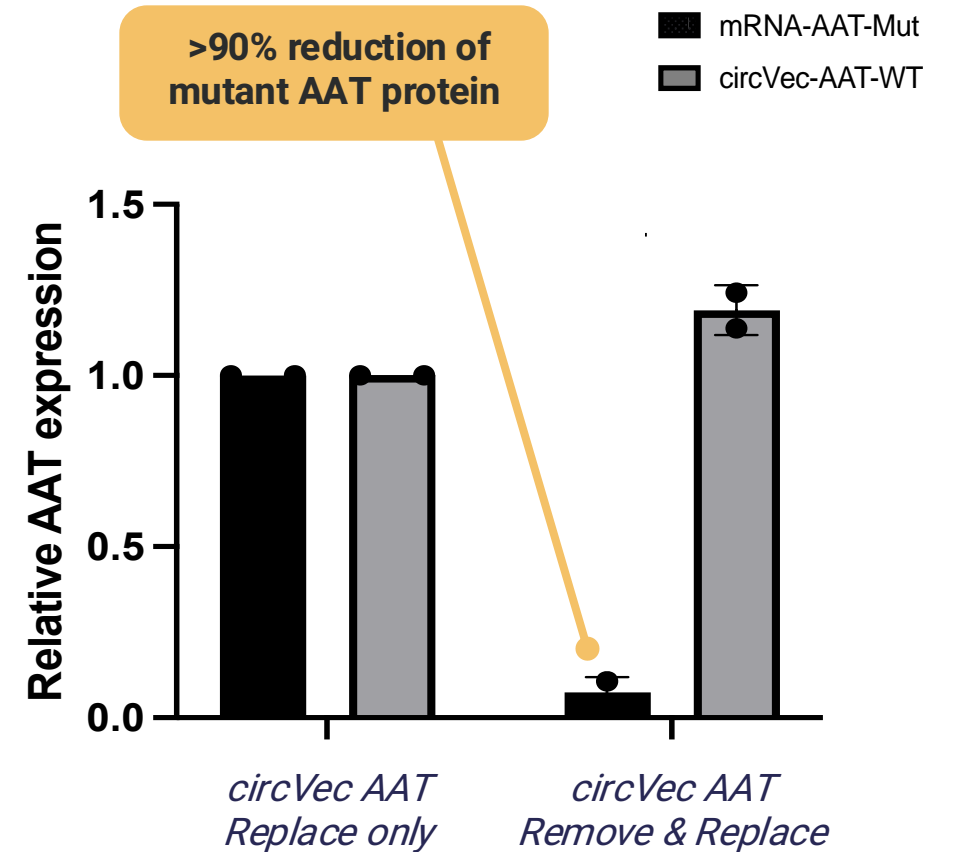
circVec-AAV feasibility validated, testing and optimization of constructs ongoing

circVec 'Remove-&Replace' gene therapy concept, AATD case example

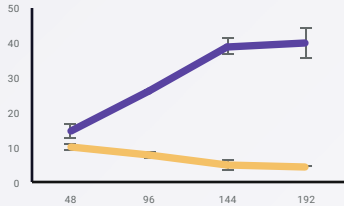
circVec AATD R&R design



Remove-&replace *in vitro* PoC

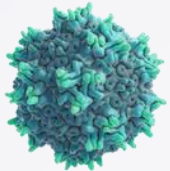


Circio is the leader in circRNA for genetic medicine, take-home messages:



**Best-in-class
durability**

The circVec technology delivers **70x durability** and **15x protein expression advantage** over conventional mRNA-based expression



**First-in-class
circRNA
gene therapy**

circVec brings the advantages of circRNA to genetic medicine, which is **not feasible with synthetic circRNA** (such as oRNA, Orbital, Therorna, etc..)



**True
platform potential**

New **circVec 3.0 generation** expected to further strengthen and solidify advantages → in vivo testing ongoing

Applicable for any **AAV and DNA format therapeutics**

Broad opportunities for **future partnering/licensing**