



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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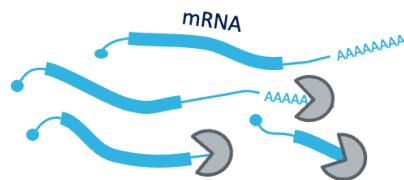
circRNA introduction

- 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

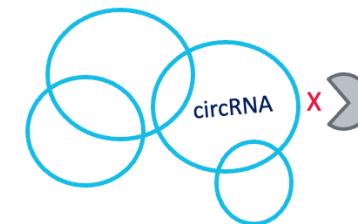
70x half-life vs. mRNA in vivo



circRNA will outcompete linear mRNA due to its enhanced stability

Higher protein expression

15x protein expression vs. mRNA in vivo



Reduced toxicity

Dose sparing for improved safety

Modular & multi-functional

Addt'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

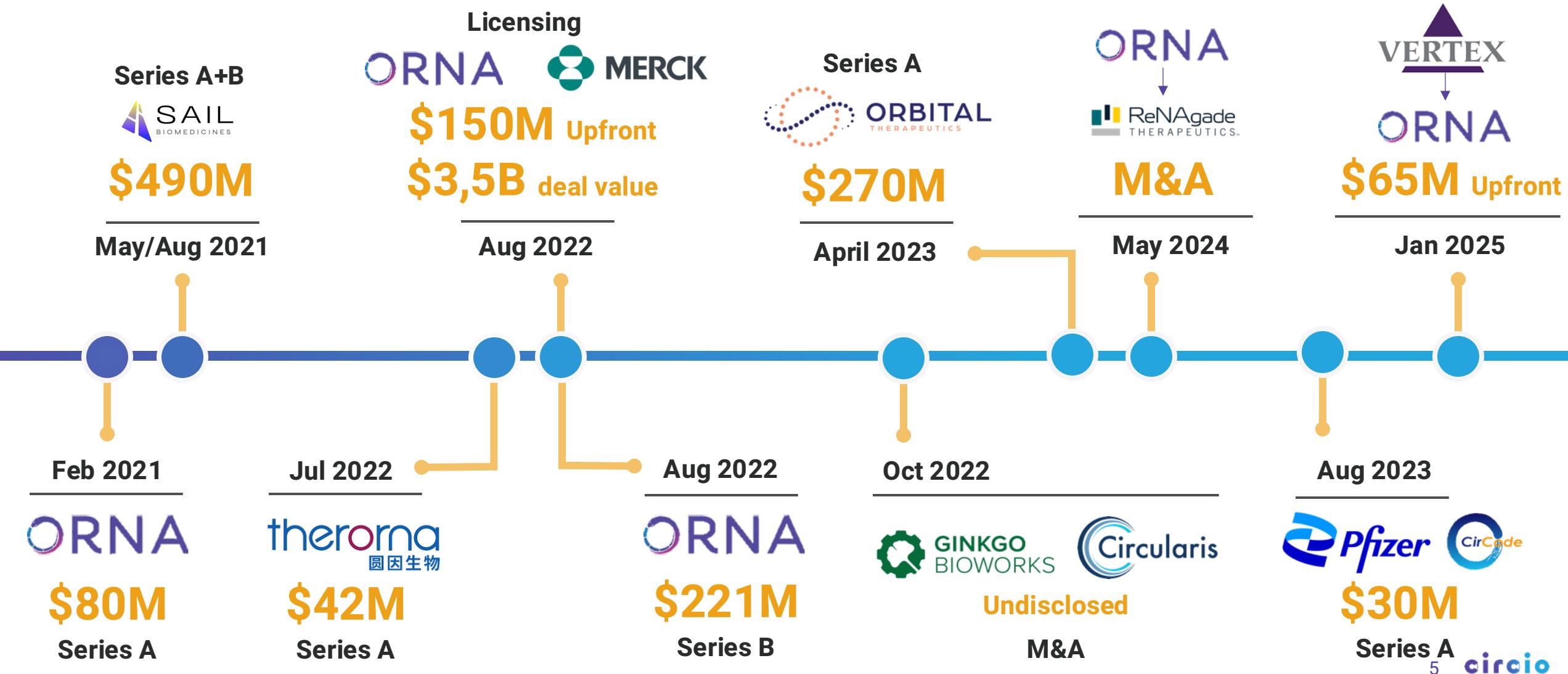
The therapeutic potential of circular RNAs

Eoghan O'Leary, Yanyi Jiang, Lasse S. Kristensen, Thomas B. Hansen & Jørgen Kjems

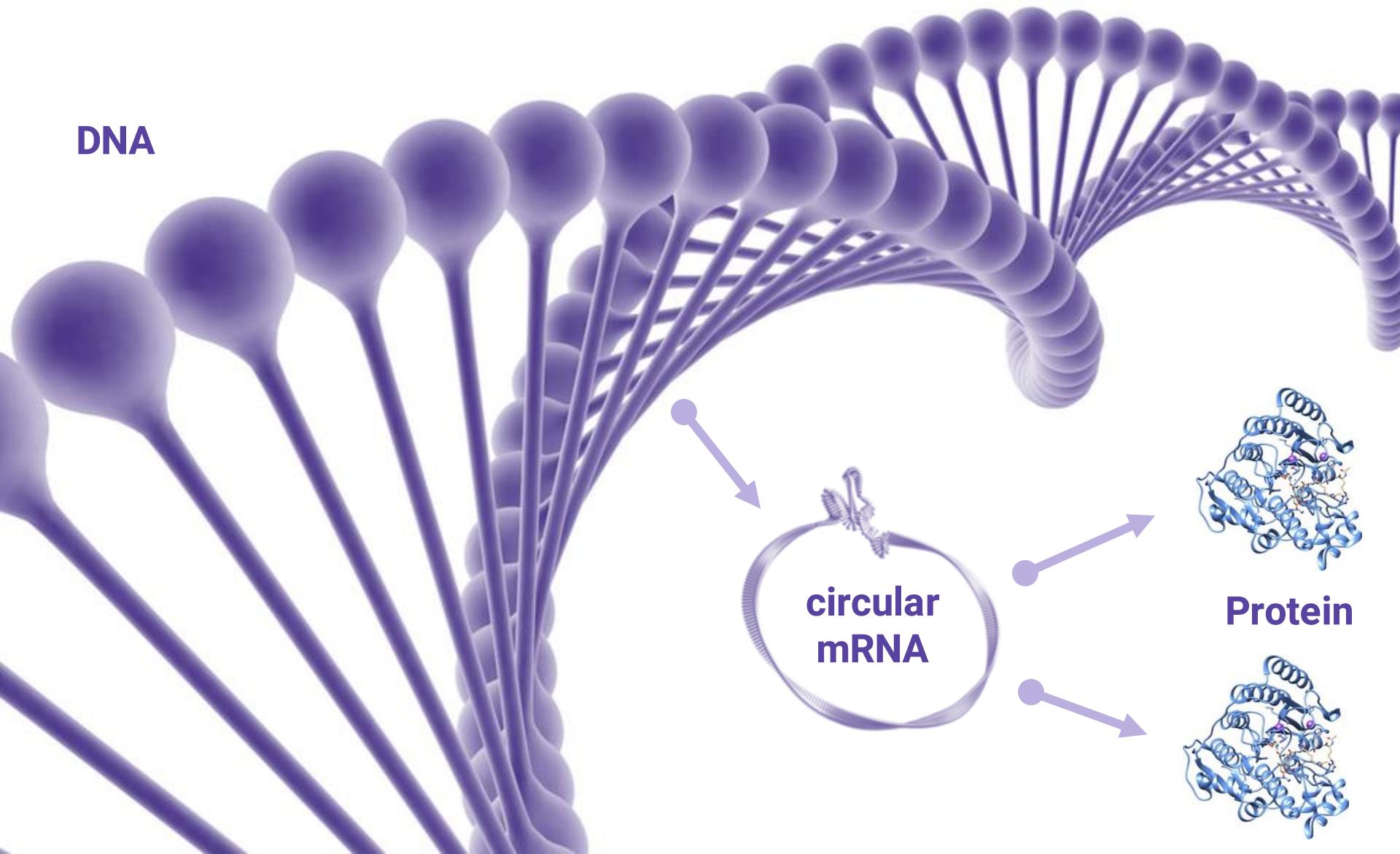
Nature Reviews Genetics (2025) | [Cite this article](#)

circio

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>
circio	circVec vector approach	months to years	✓ VLP-format	✓	Viral or DNA-LNP	✓
ORNA  	Synthetic circRNA	7-10 days	✓	✗	circRNA-LNP	✗
moderna BIONTECH	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

BioSpace

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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
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In Vivo >> Market Intelligence

Circio's Vision For Long-Lasting Nucleic Acid Therapeutics

16 Dec 2024 • By [David Wild](#)

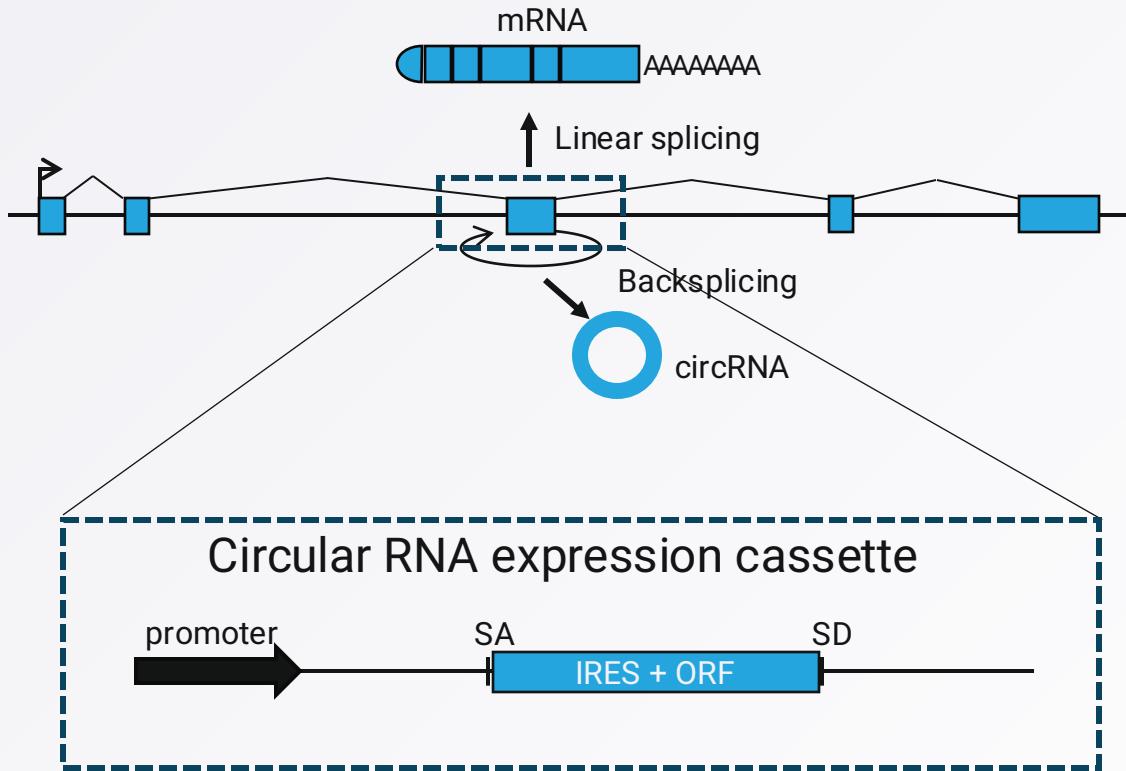
Circular RNA has several advantages, but the field is young. Scandinavian startup Circio Holdings believes its version of the technology will prove the most robust.

2

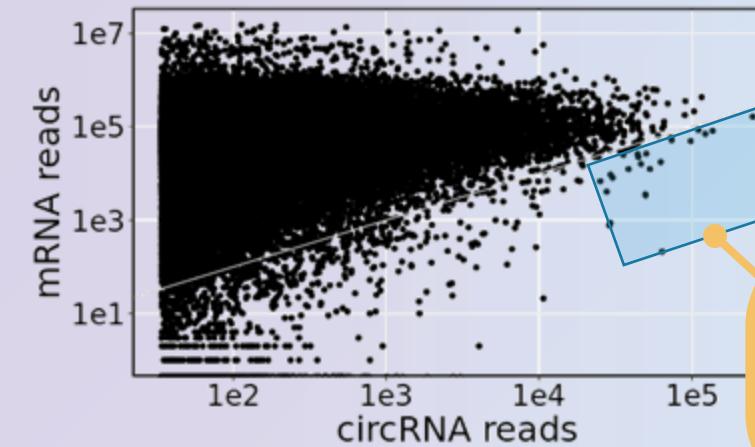
circVec platform

3. circVec lead program
4. Summary & team

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

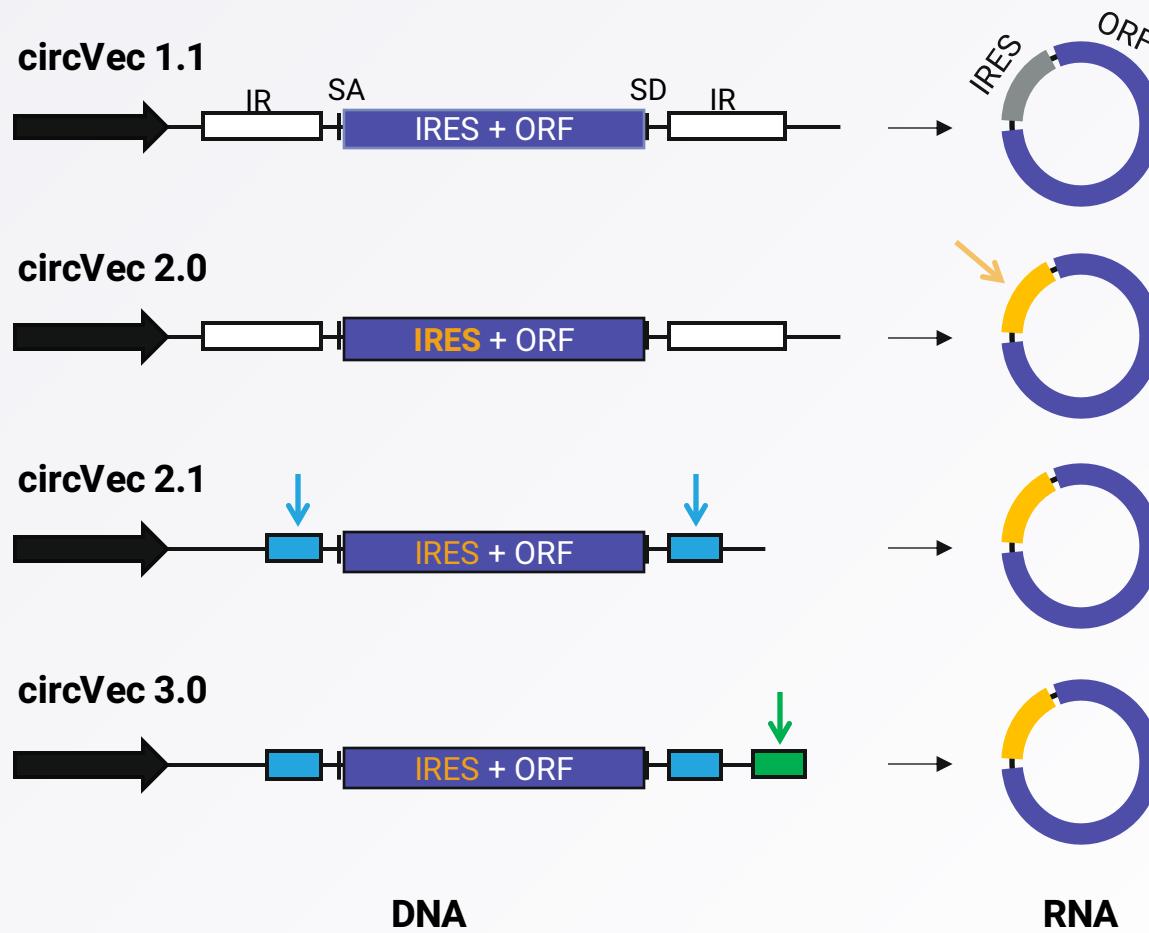


**Maximum
biogenesis-rate
of endogenous
circRNA**

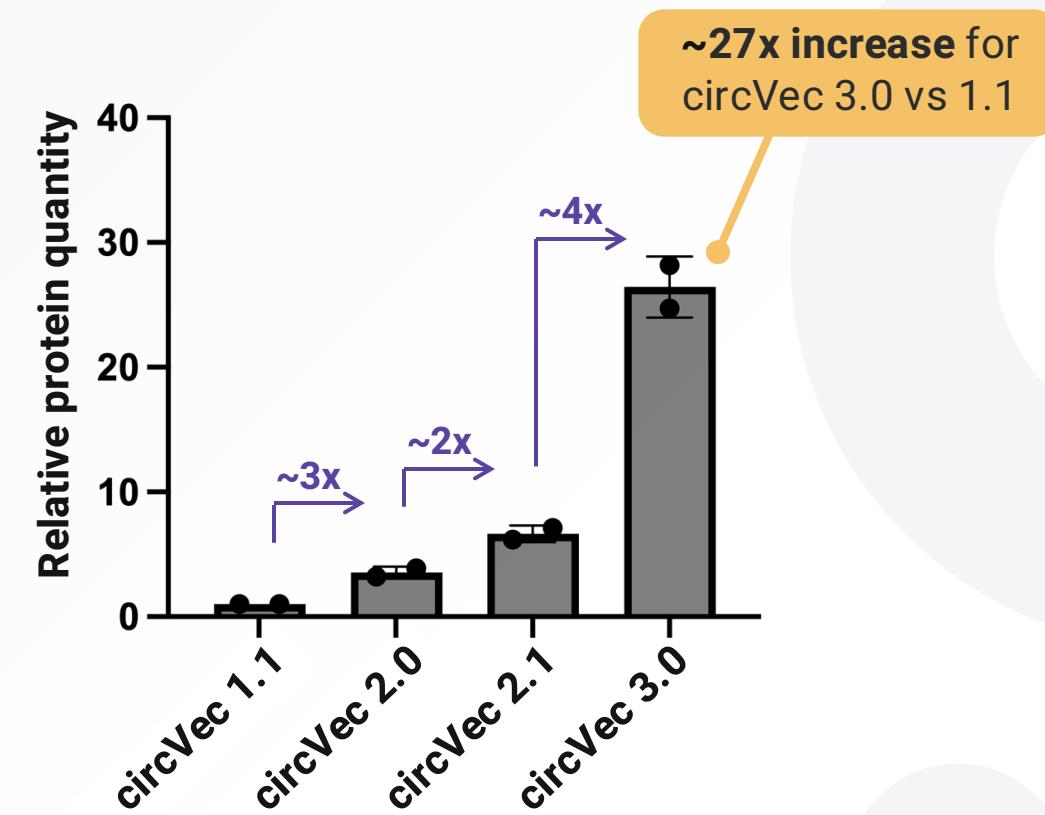
Screen and optimize the most
effective loci in the human genome
→ **circVec 1st generation**

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

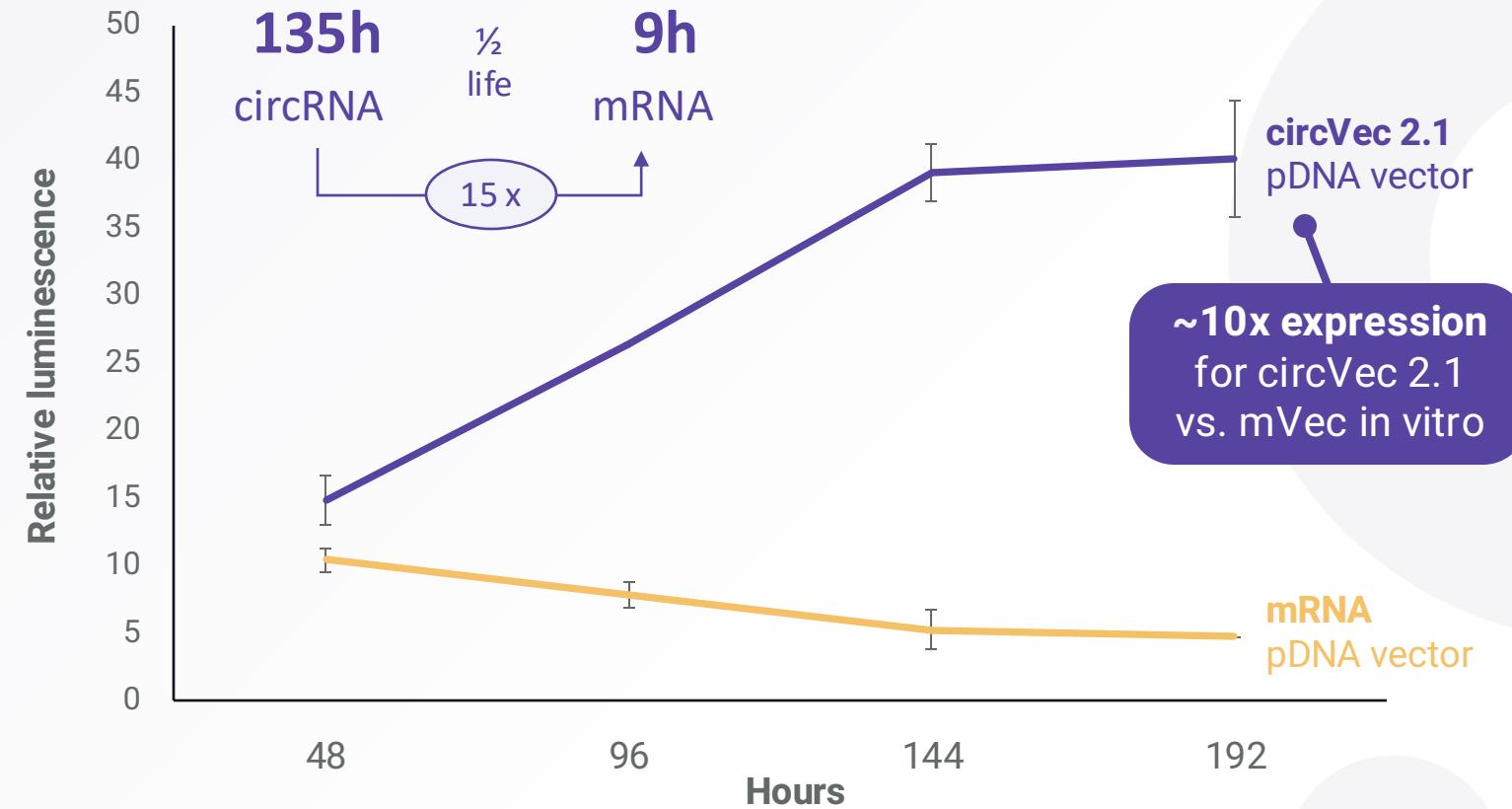
→ Enhanced therapeutics

“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”

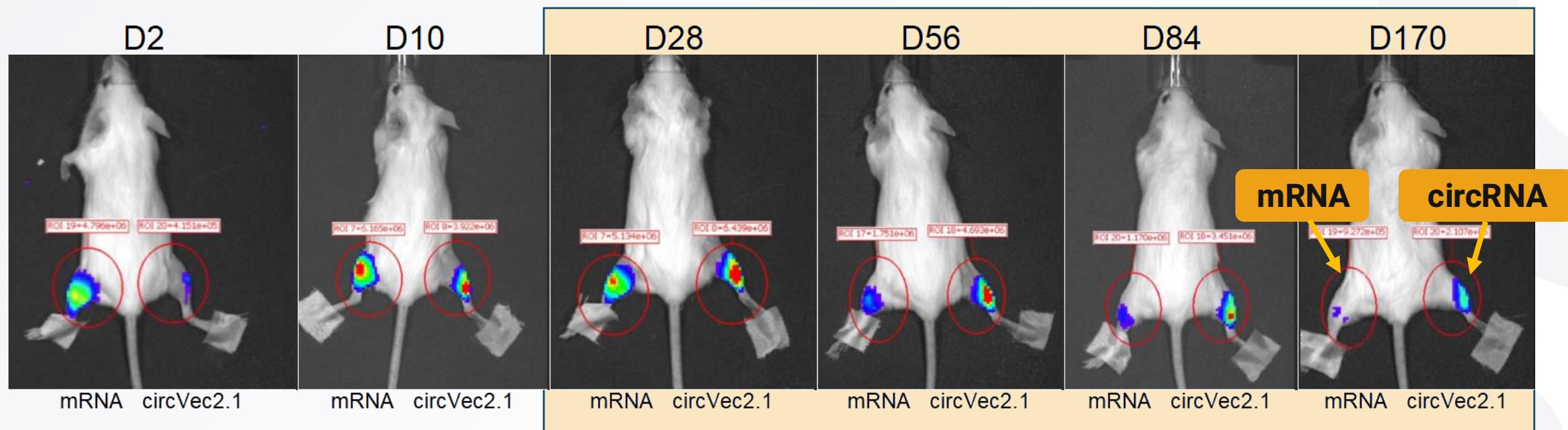
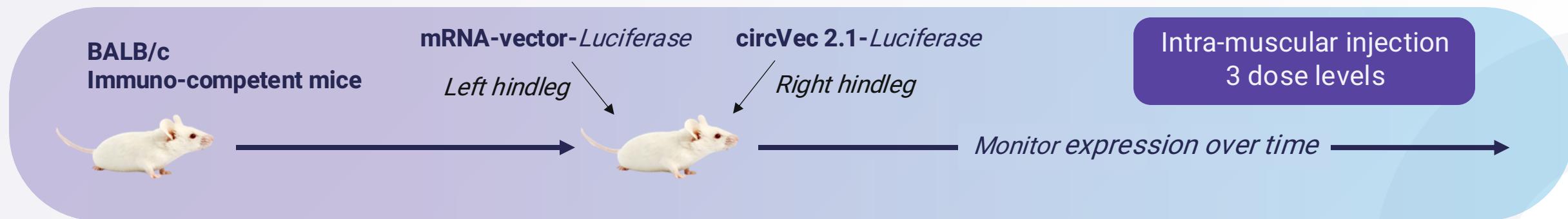
Dr. Alex Wesselhoeft

Scientific founder
oRNA Therapeutics

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



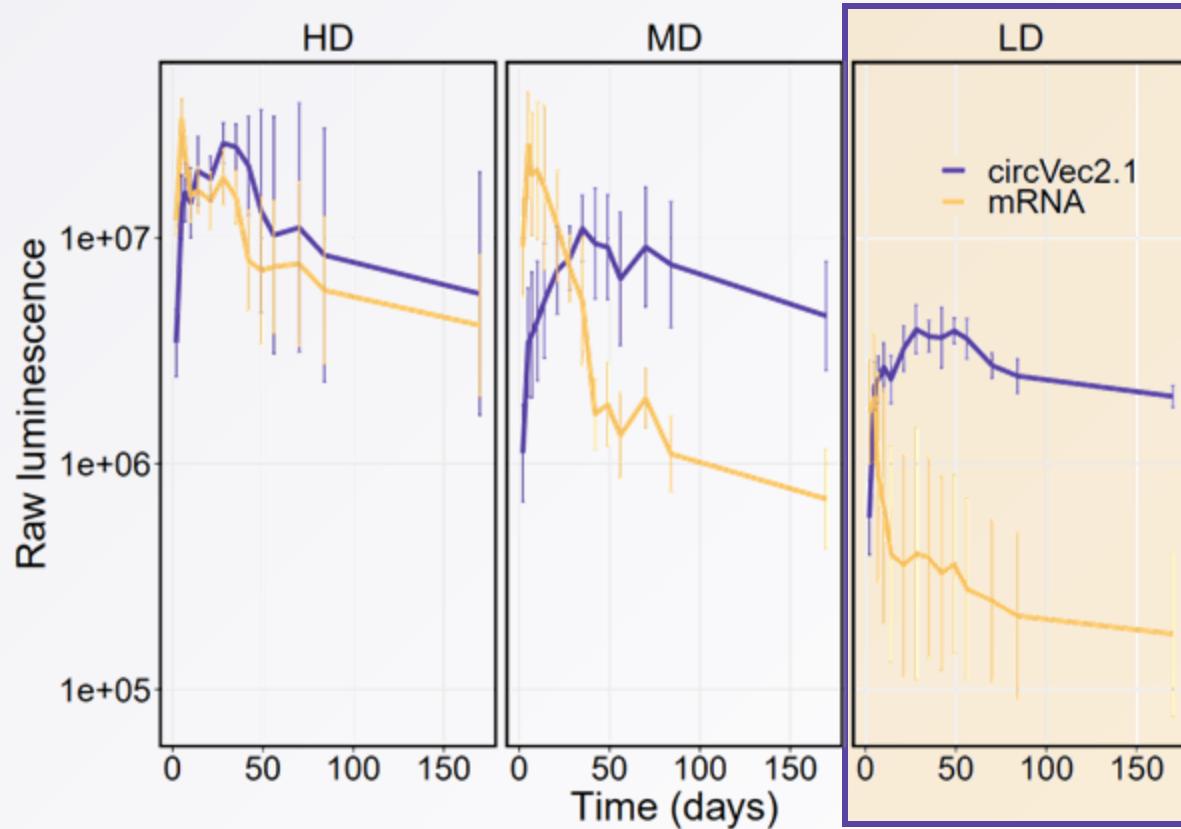
circVec 2.1 achieves > 6 month expression durability on one single injection in immuno-competent mouse muscle



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

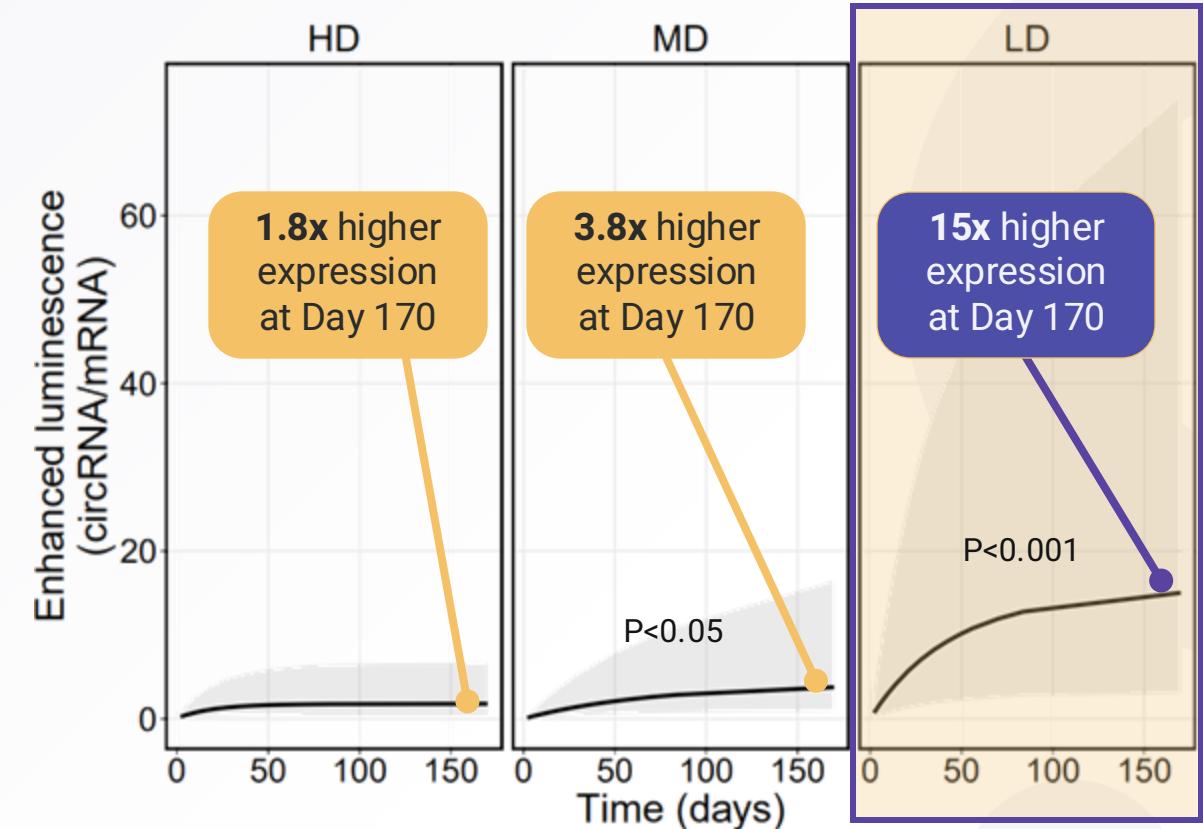
Absolute expression (luminescence)

circVec 2.1 vs. mRNA pDNA vector expression



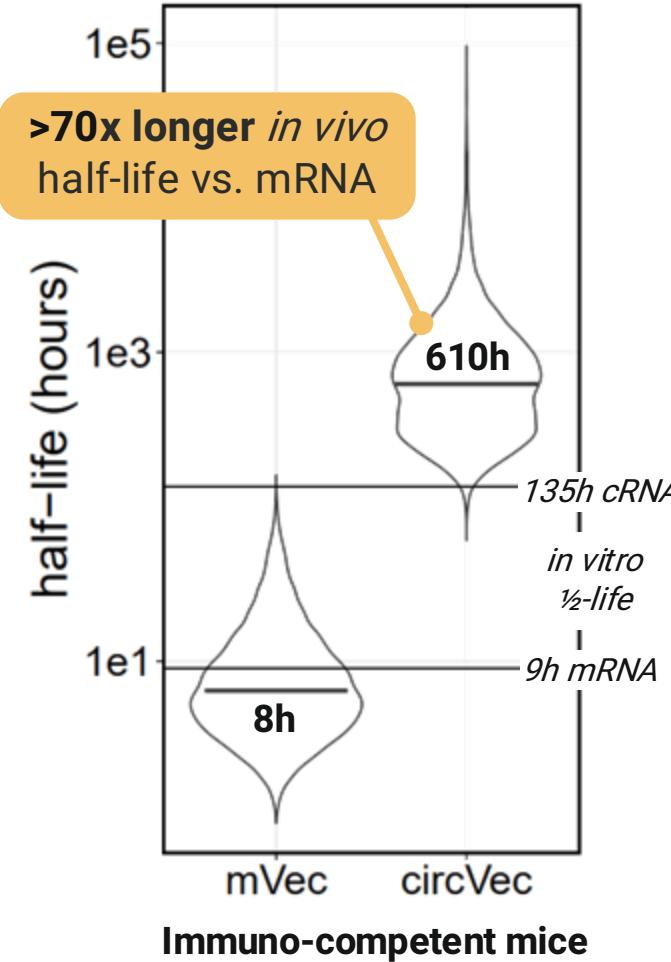
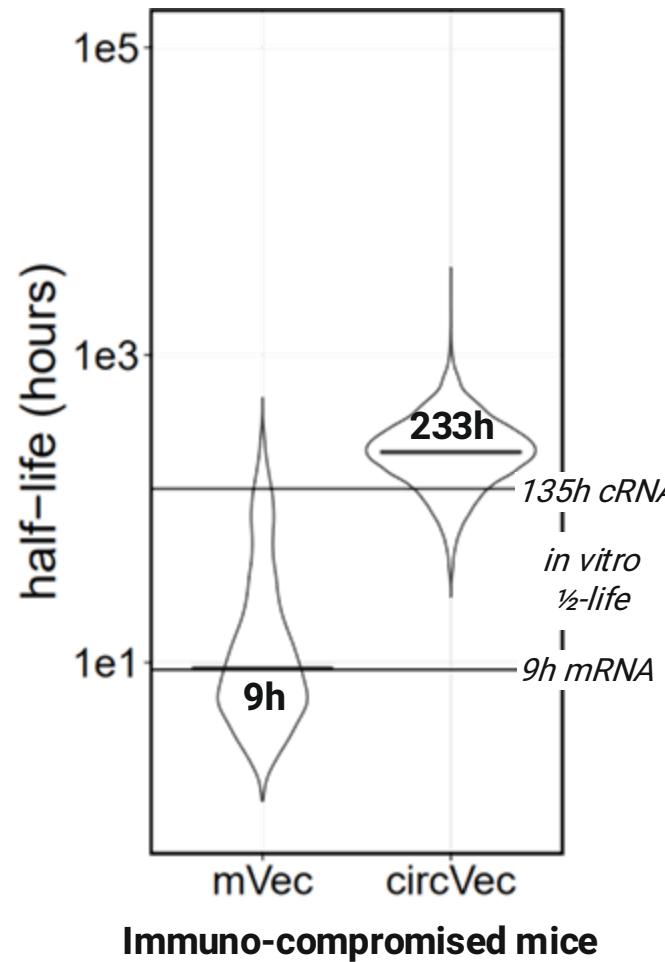
Relative expression (luminescence)

-fold change circVec 2.1 vs. mRNA expression

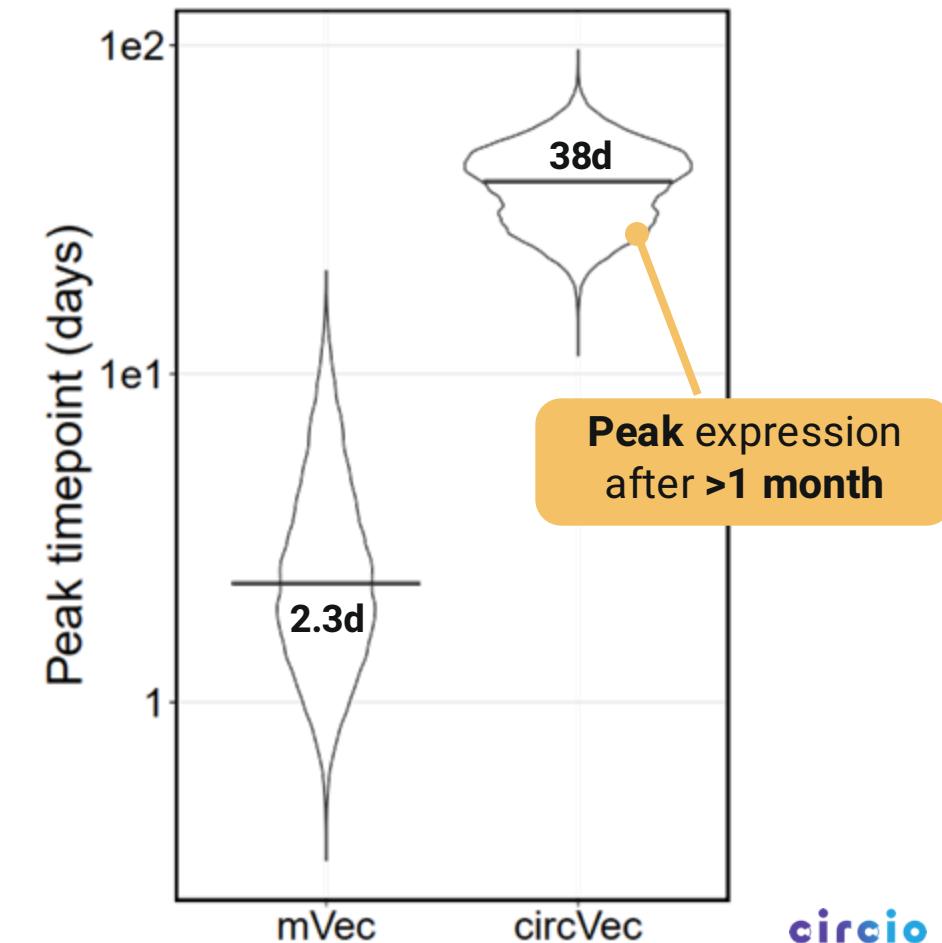


Bioinformatic analysis of circVec 2.1 in vivo data indicates over 70 times increased half-life of circRNA vs. mRNA

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

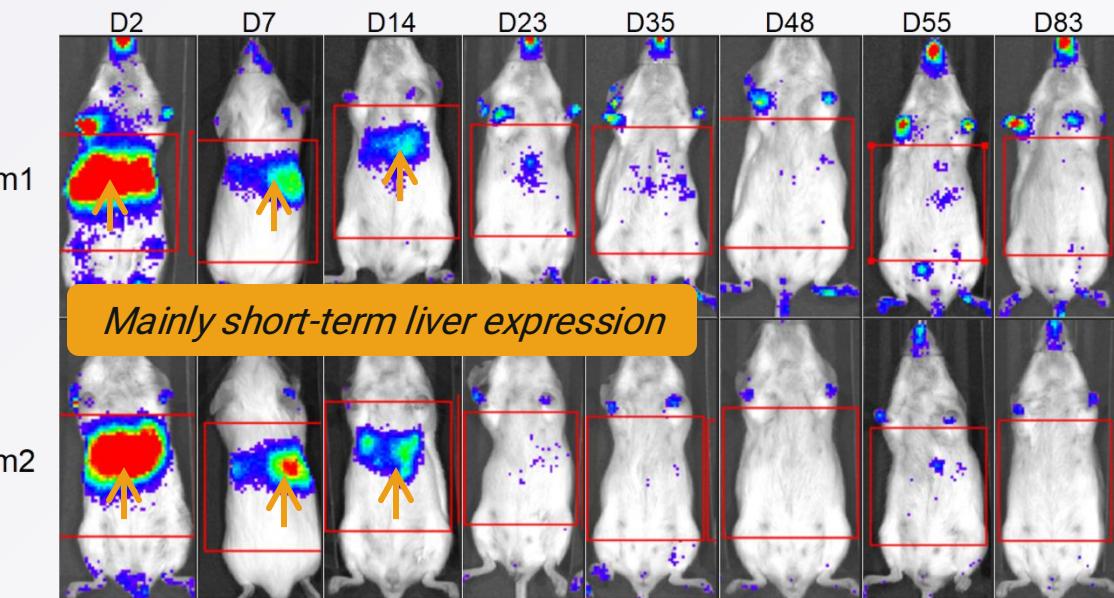


Inferred in vivo peak expression (days)

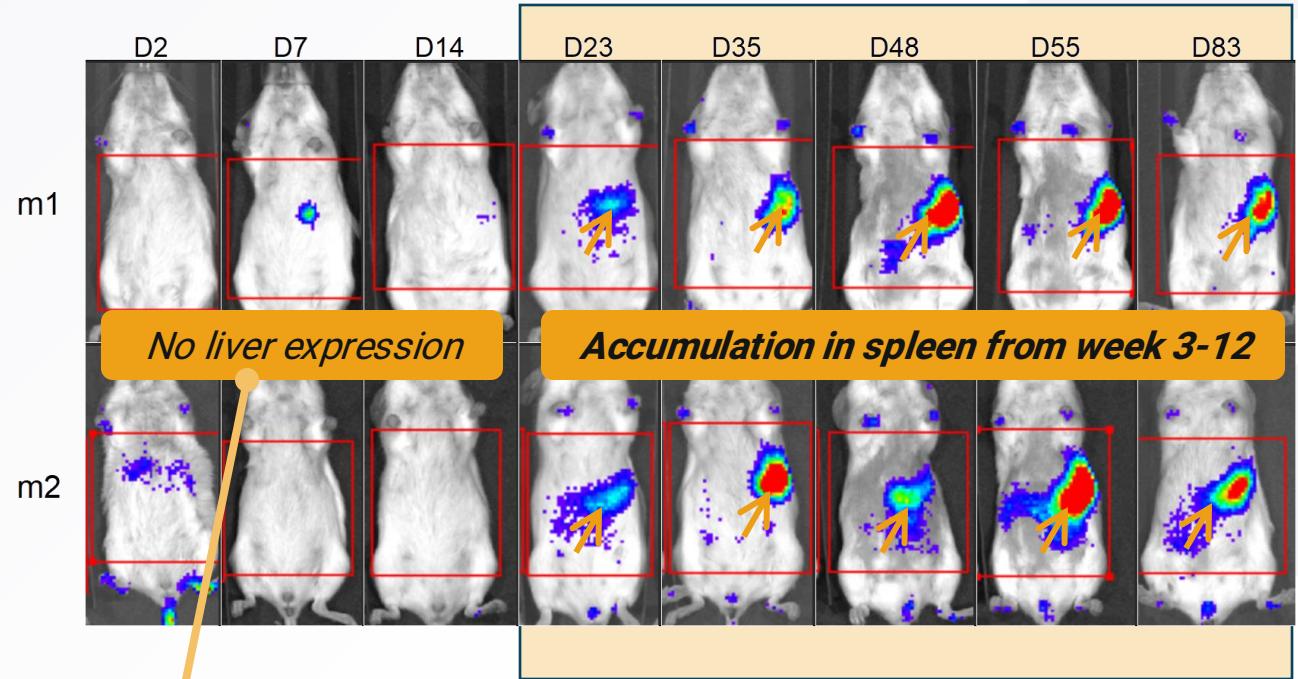


LNP-formulated circVec 2.1 accumulates in spleen with >12 week durability, minimizes liver expression

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

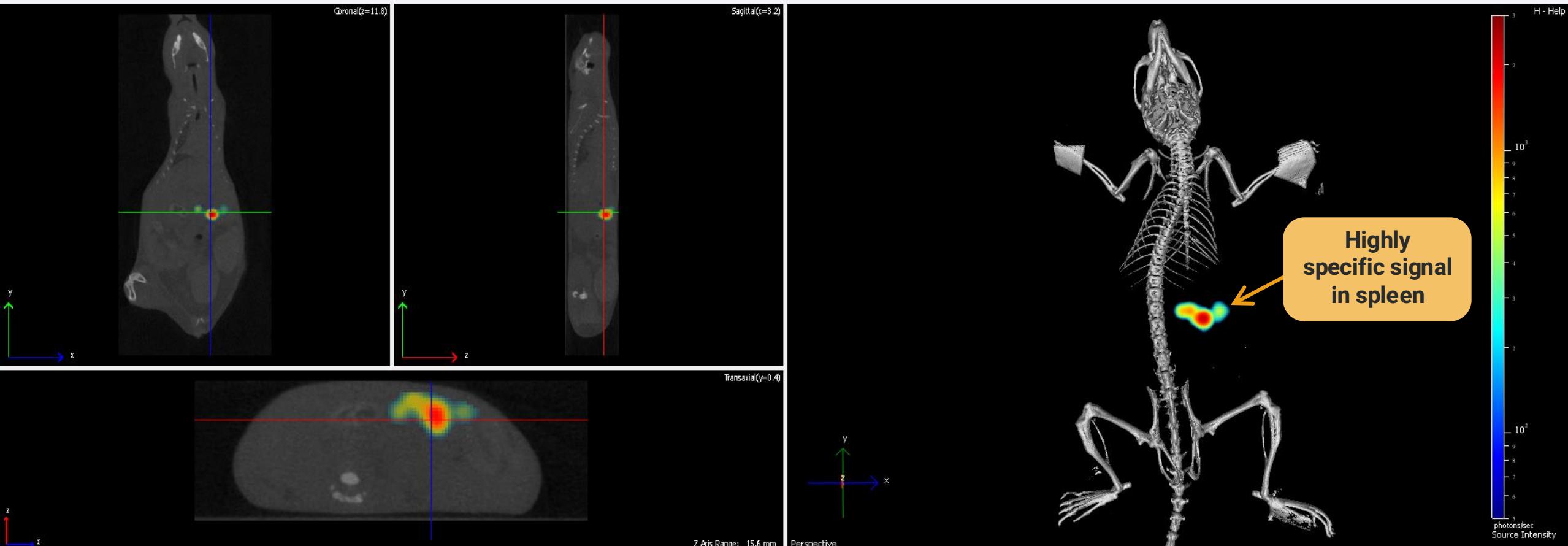


LNP-circVec 2.1 (circRNA), luminescence
Systemic I.V. delivery, single dose on Day 0



circRNA durability adv.
does not apply in liver

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



Ongoing in vivo experiment, example animal

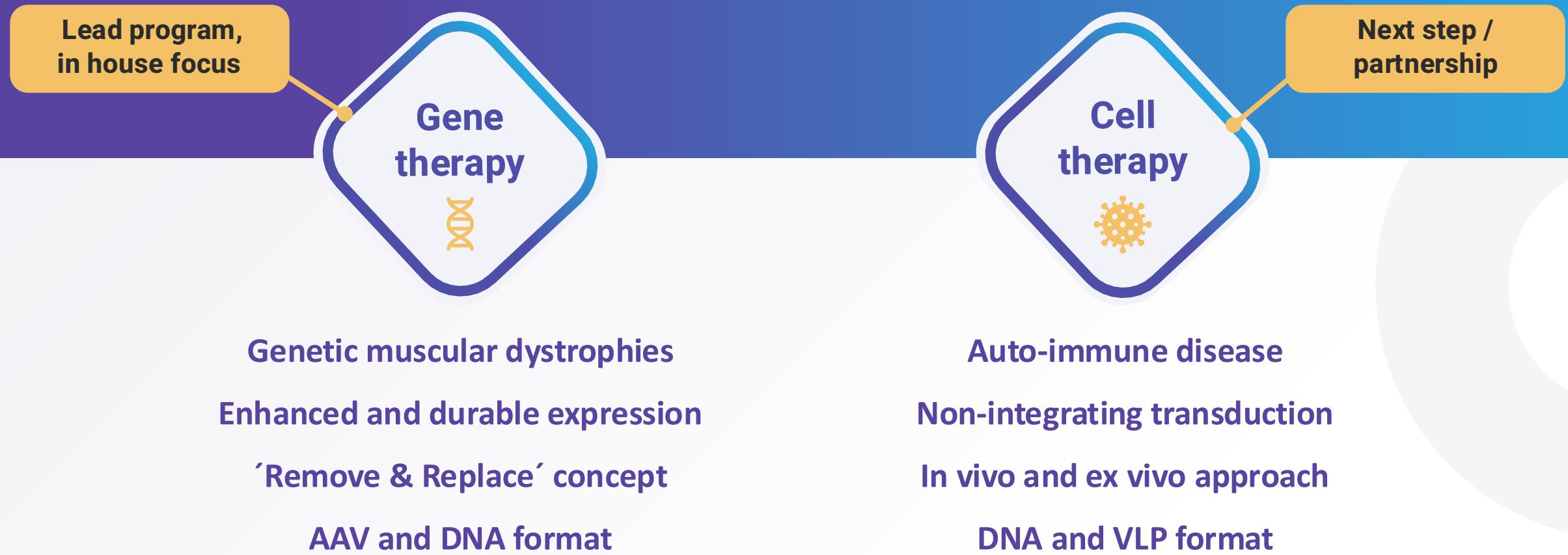


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circVec lead program

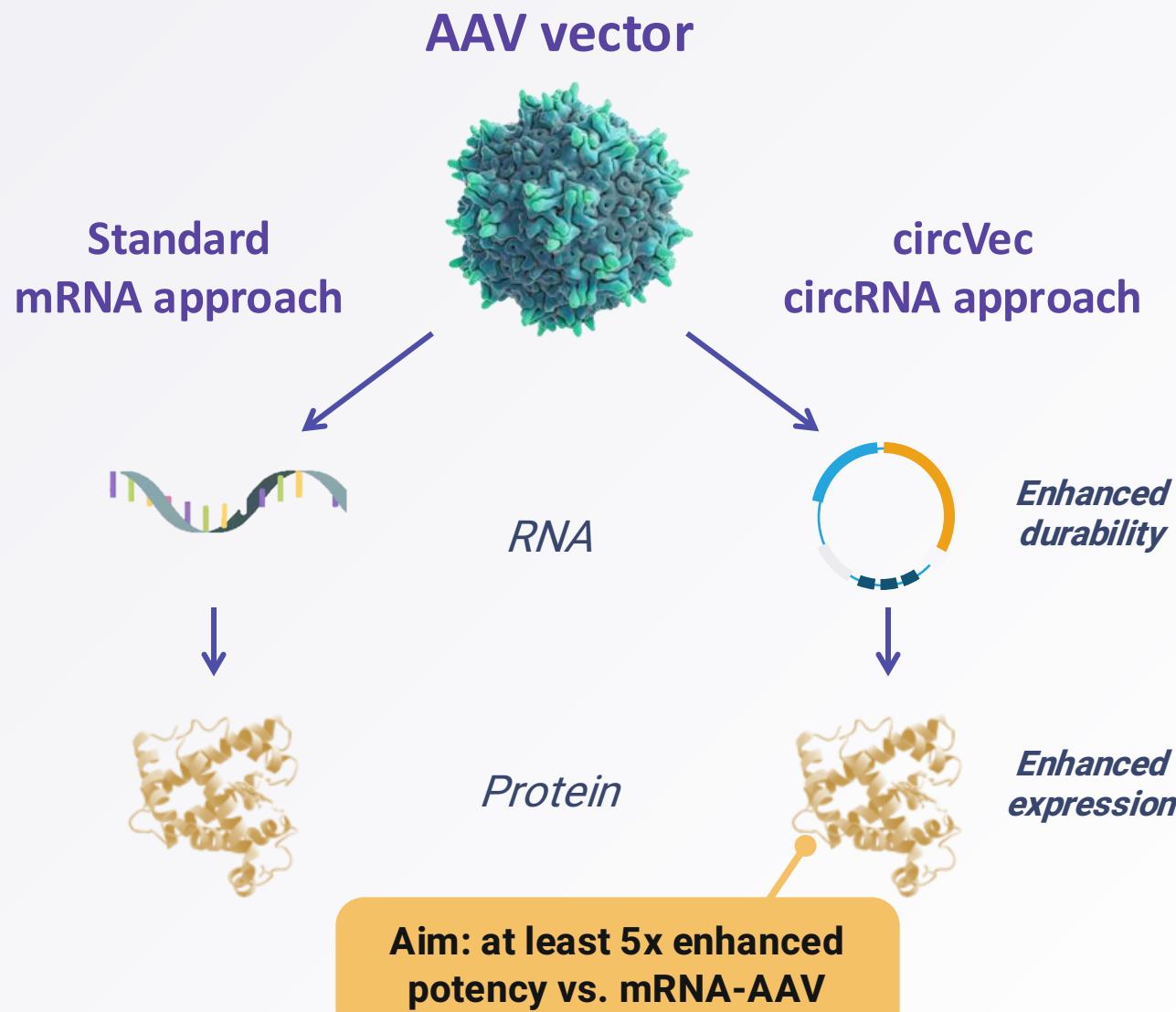
4. Summary & team

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

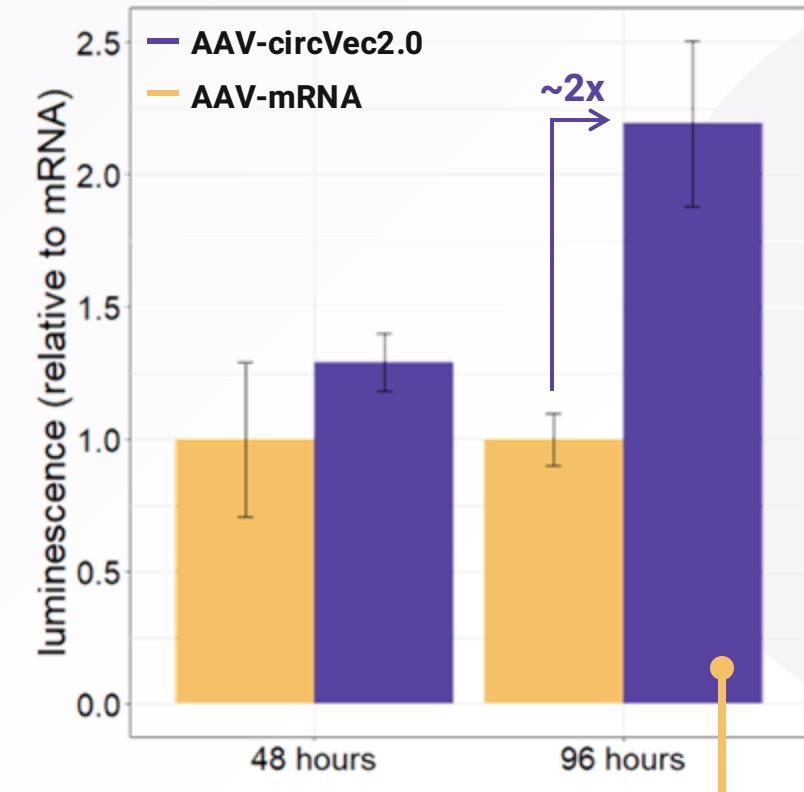


Target, therapeutic format and disease to be prioritized based on data from ongoing in vivo program

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



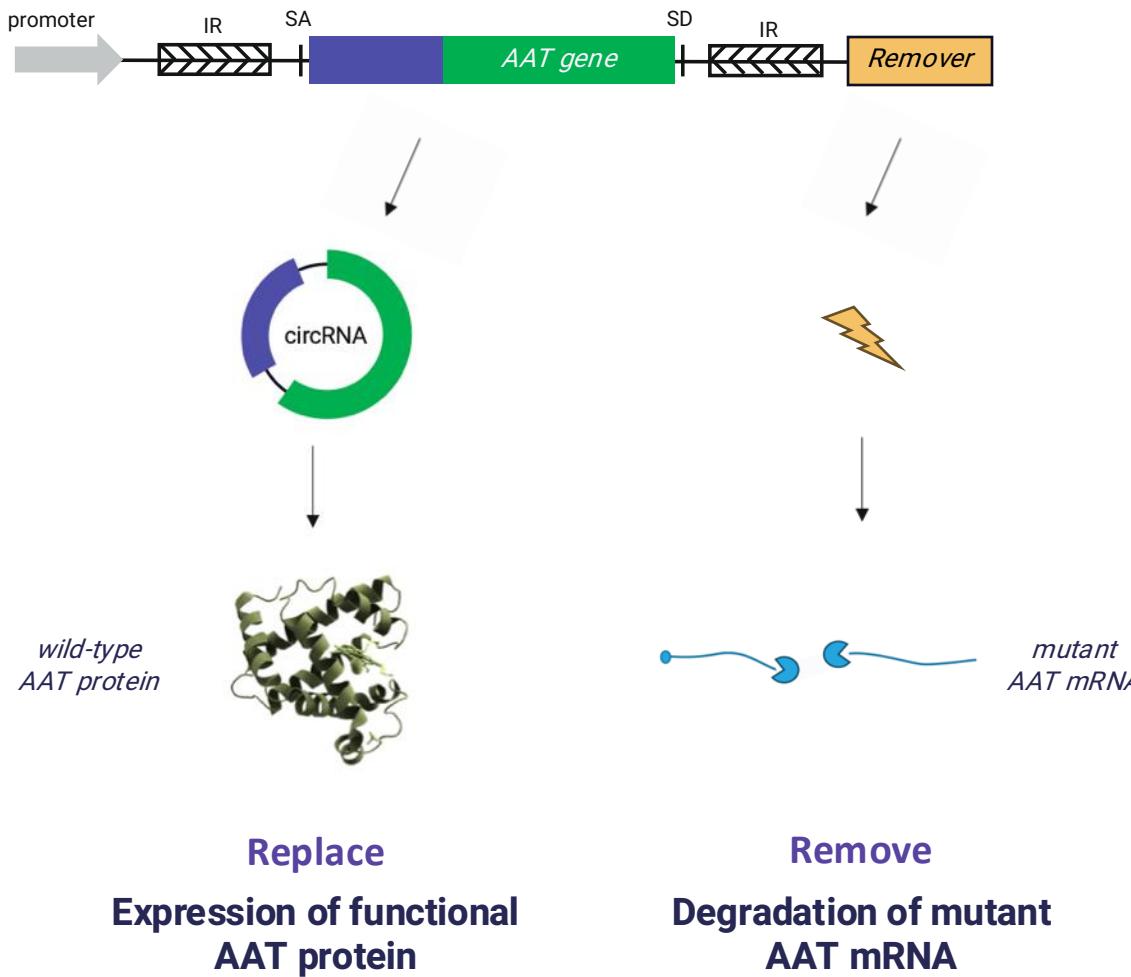
AAV protein expression, *in vitro* f-Luc



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

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

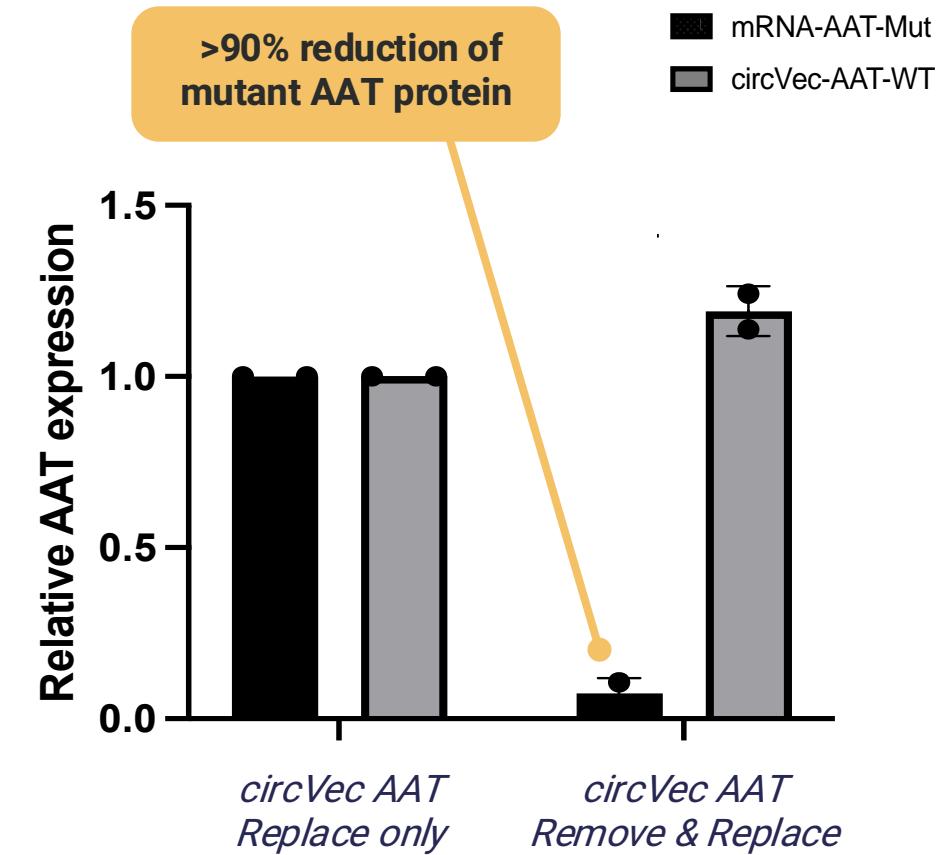
circVec AATD R&R design



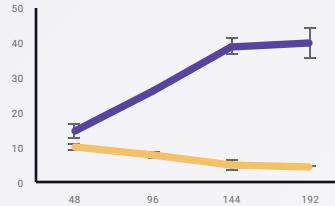
Replace
Expression of functional
AAT protein

Remove
Degradation of mutant
AAT mRNA

Remove-&-replace *in vitro* PoC

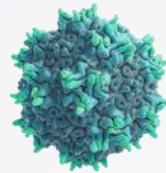


Circio is the leader in circRNA for genetic medicine, take-home messages:



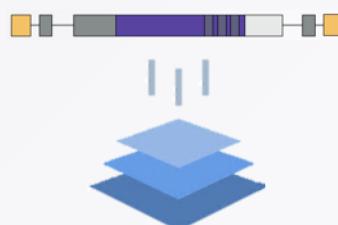
Best-in-class durability

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**