circio

The leader in circular RNA expression systems

Investor Konferencen
November 25, 2026

Thomas Hansen, CTO



Circio: Platform company harnessing the power of circular RNA to enhance gene and cell therapy

circio

- First listed **circRNA** biotech
- USD **88m** raised in 2026
- Runway until **2030**
- Listed on OSE: **CRNA**
- Therapeutic focus on enhancing **cell and gene therapy**

Technology



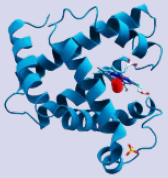
DNA

↓



Circular RNA

↓



Protein

Developed by circRNA pioneers

THE EMBO JOURNAL — EMBOpress — 30 September 2011 — 1,200 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 — 8,600 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

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

AAV gene therapy is the main tool available for treating inherited genetic diseases

The problem

300 million

people worldwide live with an inherited genetic disease,
4% of the global population

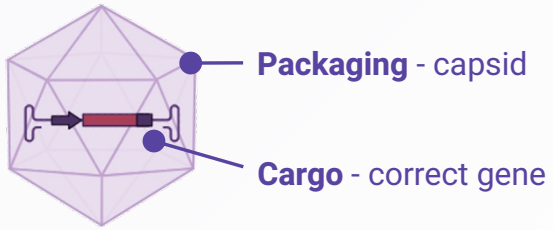
70 %

of rare diseases **begin in childhood**

Only 5 %

of rare diseases have an **approved, disease-modifying therapy**

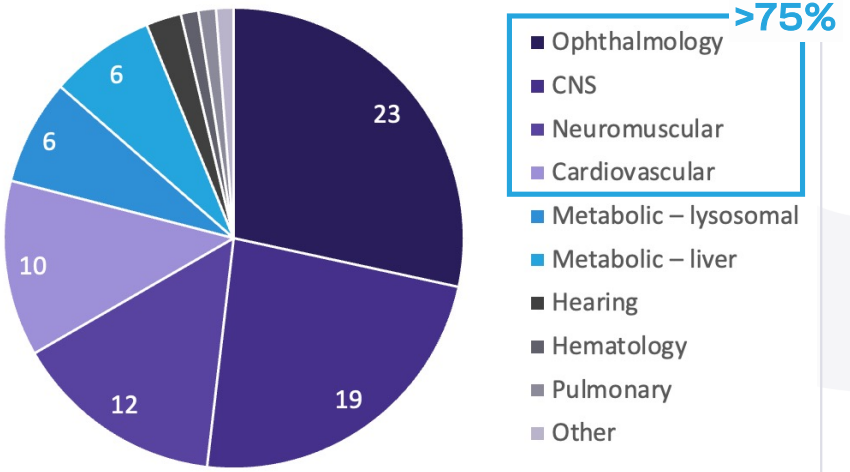
Currently the best solution



AAV: Adeno-Associated Virus
the gene therapy work horse

- Tissue-specific delivery
- Long durability, single dose
- Clinically proven

AAV gene therapy programs active in the clinic (total 81)



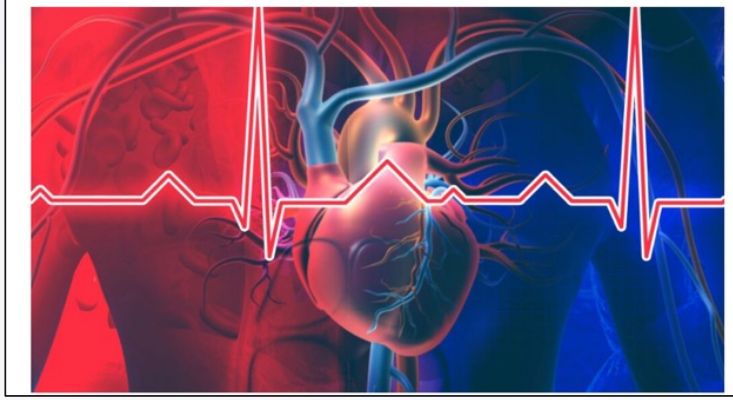
AAV gene therapy main challenge – reducing the dose

GEN Genetic Engineering & Biotechnology News

Danon Disease Patient Dies in Rocket Gene Therapy Trial

May 27, 2025

By **Alex Philippidis**



AAV gene therapy for Danon disease:

Clinical benefit demonstrated, but too high dose

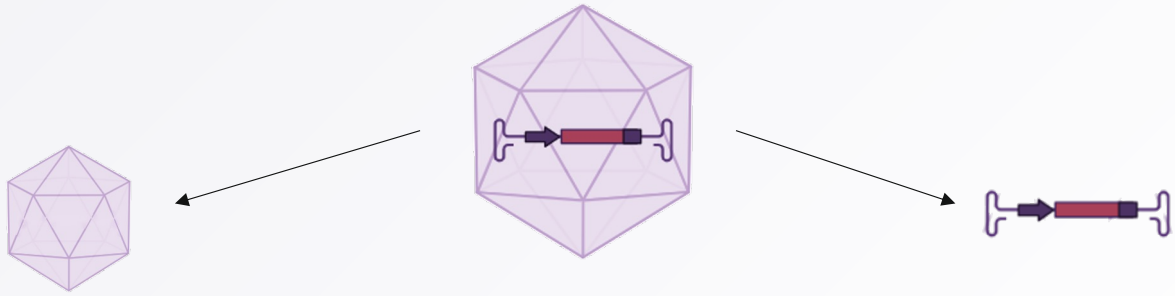
Severe adverse events, incl. risk of death

Solution to the toxicity issue:

Lower dose with same clinical benefit

Better, safer and lower cost AAV gene therapy

Engineering the next generation of AAV gene therapies



Improve AAV targeting

How effectively the AAV targets and enters the cells of interest, and avoids off-target tissues

SOLID BIOSCIENCES · AaviGen · GEMMABio · affinia THERAPEUTICS · rAAVen · CAPSIDA BIOTHERAPEUTICS · 4DMT · voyager therapeutics · ADVERUM · Dyne THERAPEUTICS · coave THERAPEUTICS

Improve AAV gene expression

How effectively the AAV expresses the therapeutic gene in the cells of interest

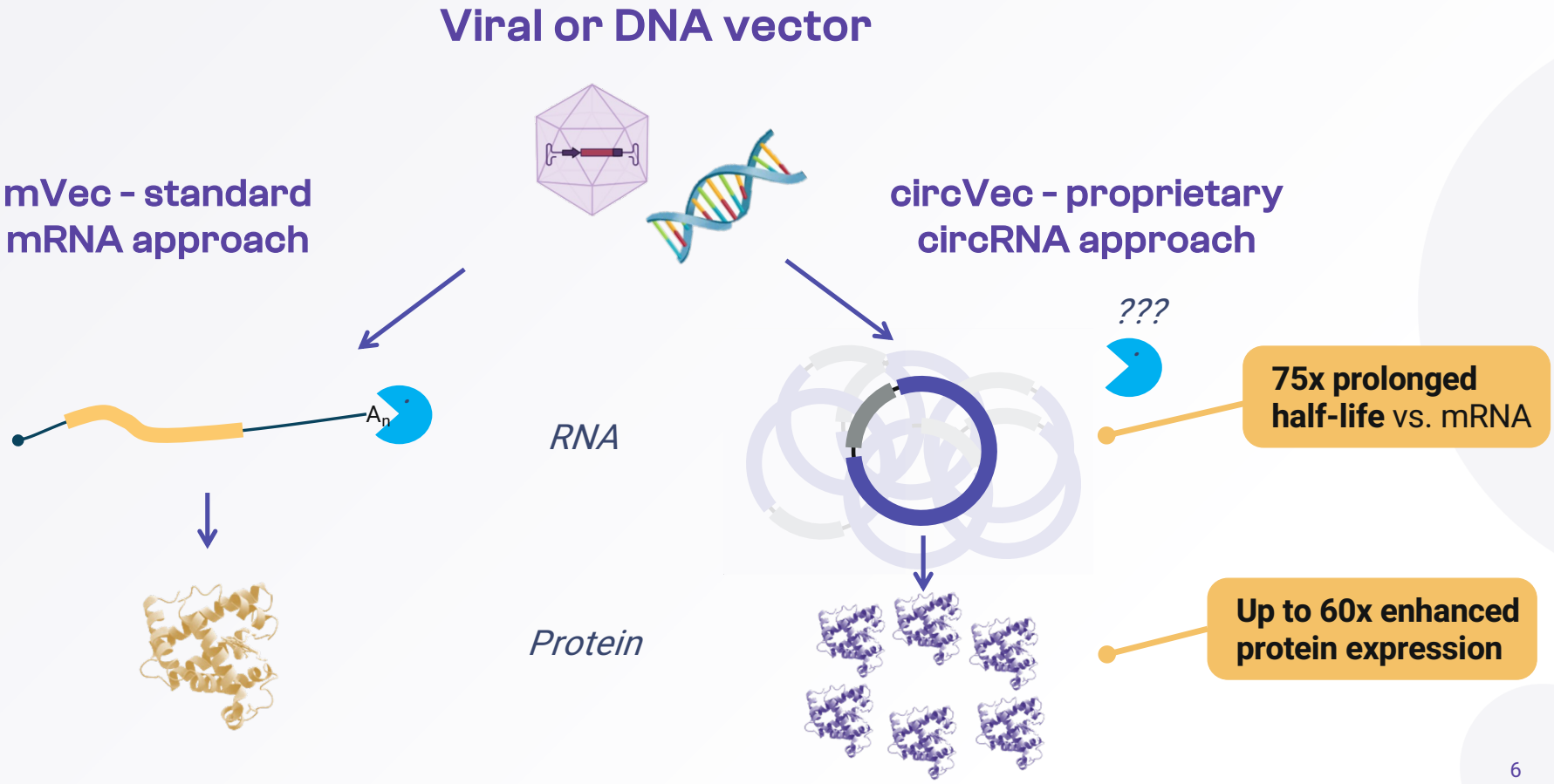
circio

Circio's approach is vector agnostic

- Compatible with **all DNA formats**
- AAV is simply a means of delivery

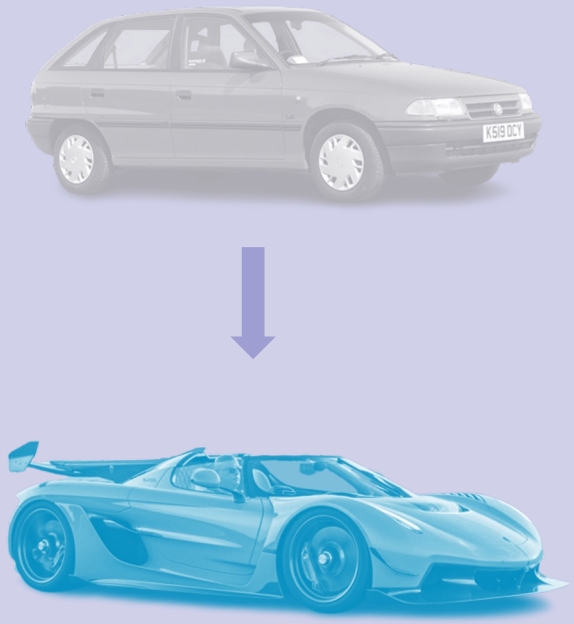
circVec

Circio´s unique and proprietary circRNA-based gene expression platform technology

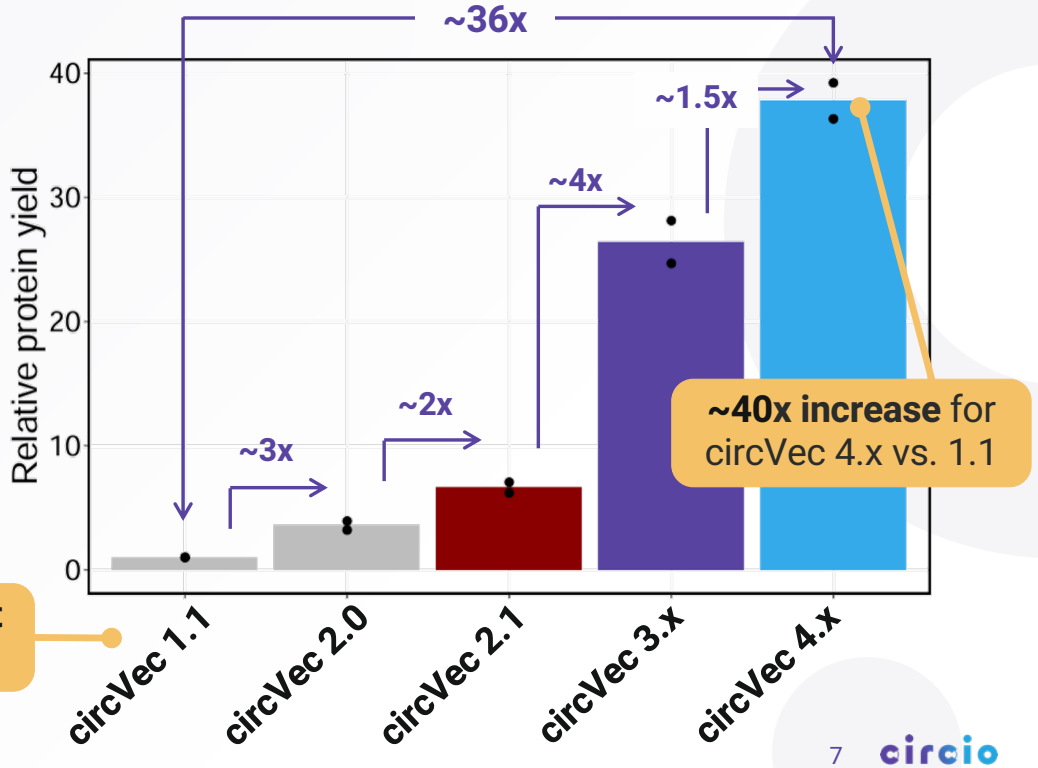


Optimizing circular RNA-based gene expression: circVec construct design and evolution from Gen 1 → 4

The circVec evolution



circVec protein quantification, Western blot



circVec: a first-in-class, industry-leading circRNA expression system with platform potential in several disease areas

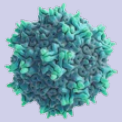
Gene therapy

Heart, eye and CNS genetic disease

1 mill. patients in target diseases

Enhanced, safer and lower cost AAVs

Research collaboration with global pharma



Next Gen AAV

Cell therapy

Cancer, autoimmune disease

LNP: DNA format, redosable

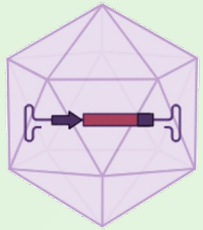
Very large patient population, only autologous options available today



In vivo CAR

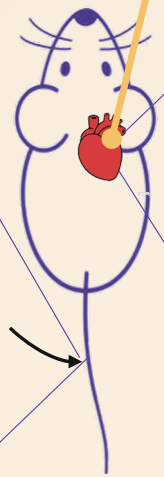
AAV-circVec for heart rare disease

AAV9 particle



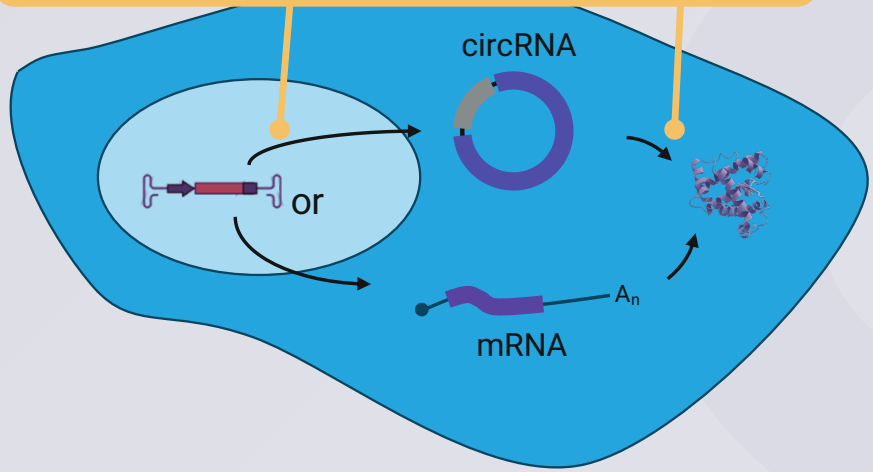
AAV9 formulation
ssDNA in an AAV particle

Heart targeting



AAV9 tropism
Using systemic delivery (tail vein)

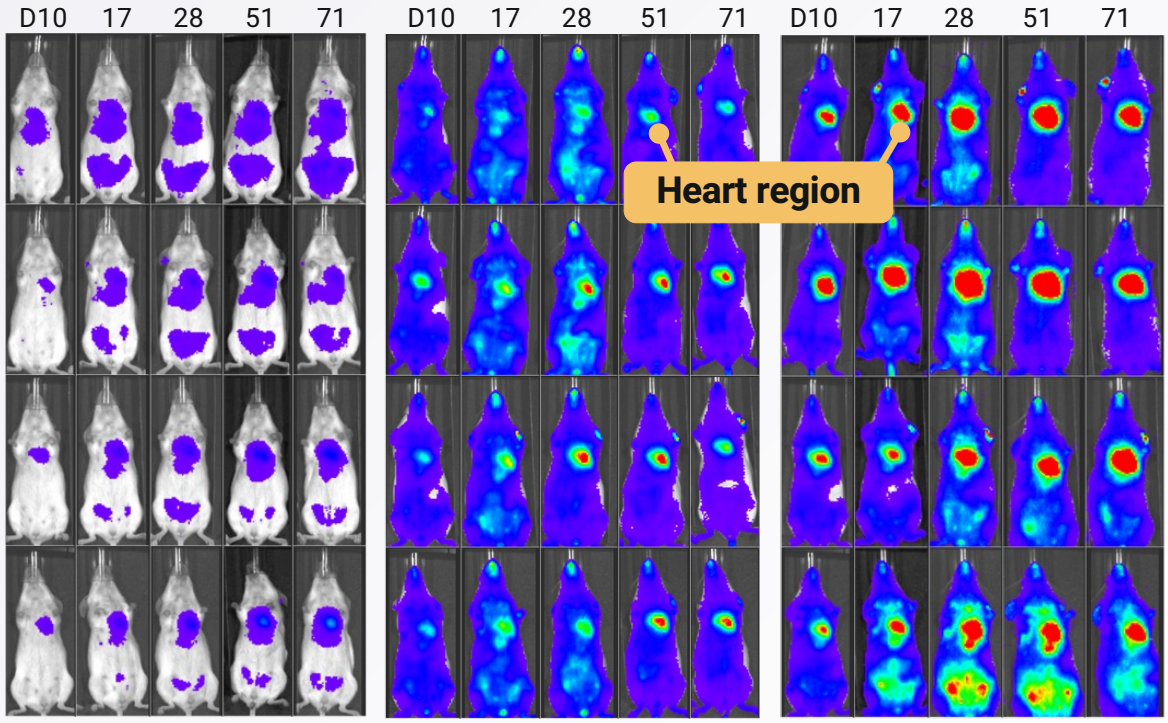
RNA biogenesis and translation



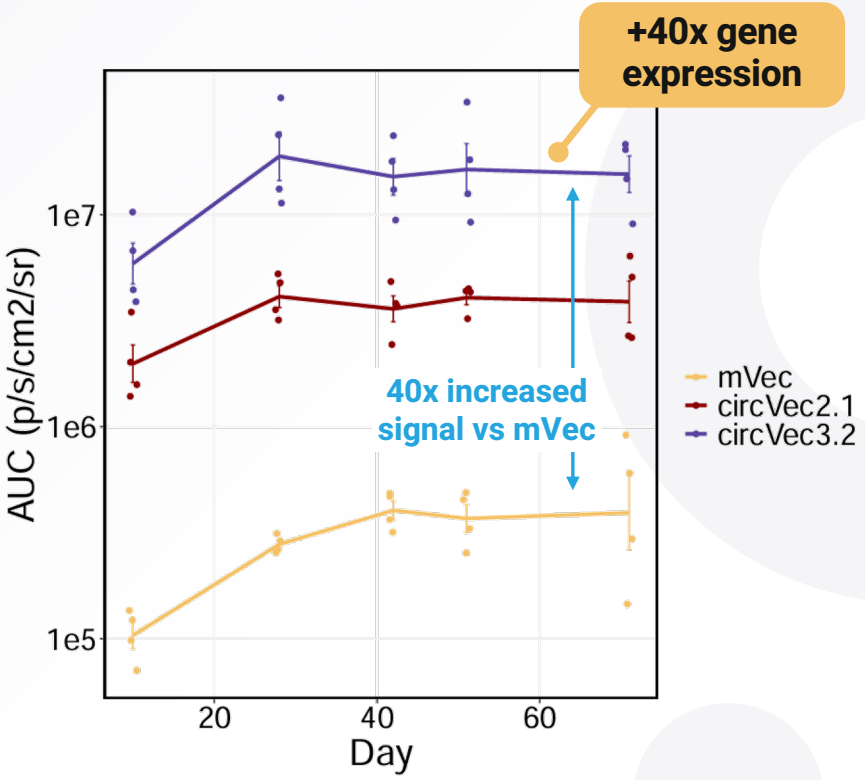
Gene expression kinetics in heart cells
Determined by production and decay-rates, and translational efficacy

40-fold enhanced expression in heart for circVec-AAV vs. conventional mRNA-based AAV

AAV-mVec | **AAV-circVec 2.1** | **AAV-circVec 3.2**



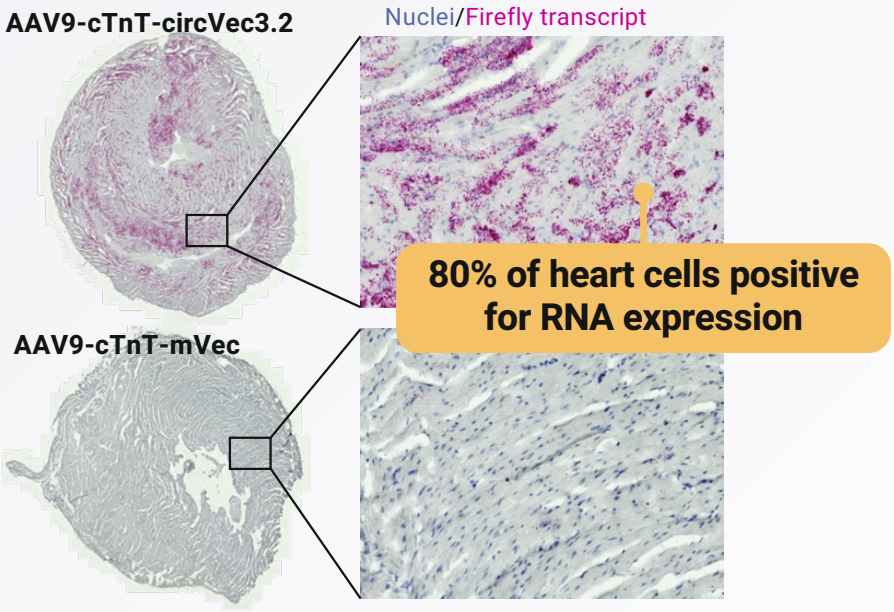
Gene expression quantification, Firefly IVIS signal



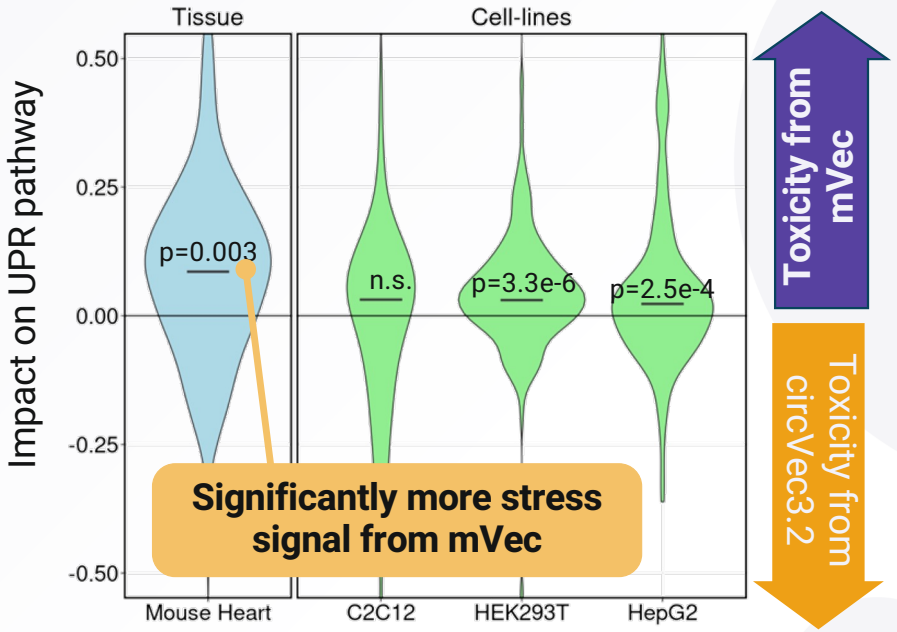
Systemic delivery, AAV9 vector, 5e12 vg/kg dose

circVec increases heart penetrance and reduces cellular stress response vs. conventional AAV

circVec increases RNA penetrance in heart
RNAscope analysis, circRNA vs. mRNA



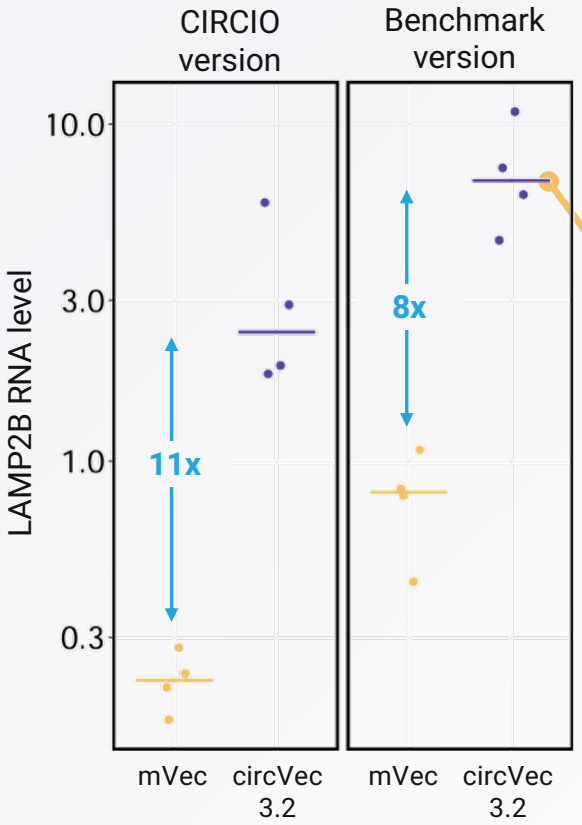
circVec reduces cellular stress response
UPR pathway activation, RNAseq analysis



circio

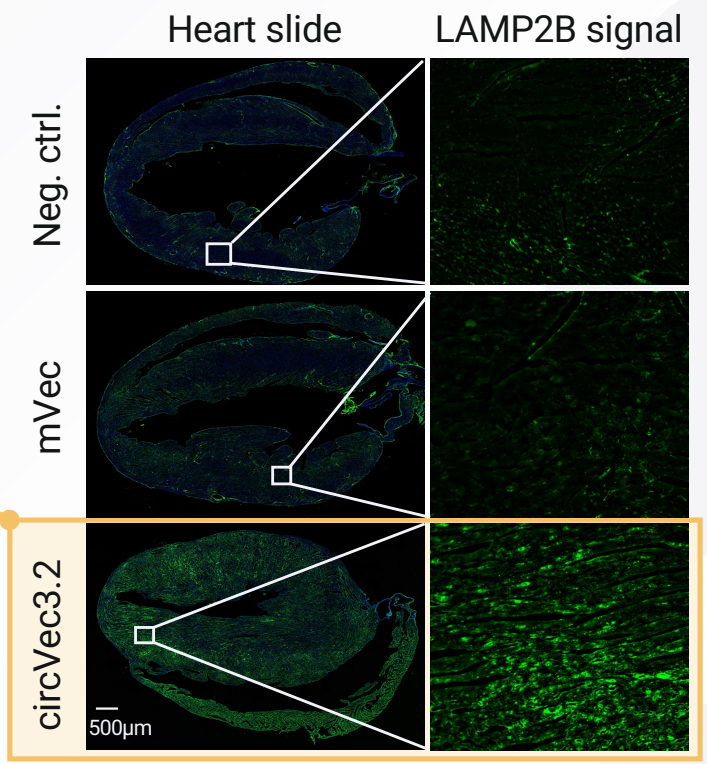
circVec expression advantage confirmed for the defective gene in Danon disease

Therapeutic gene, LAMP2B RNA, heart @ Day 57



Significant enhancement of Danon disease gene expression **by circVec**

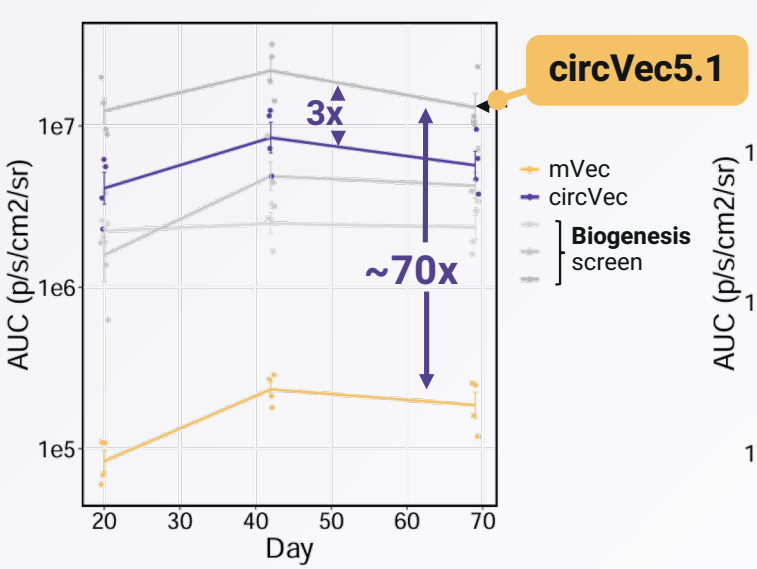
LAMP2B IHC staining, heart @ Day 57



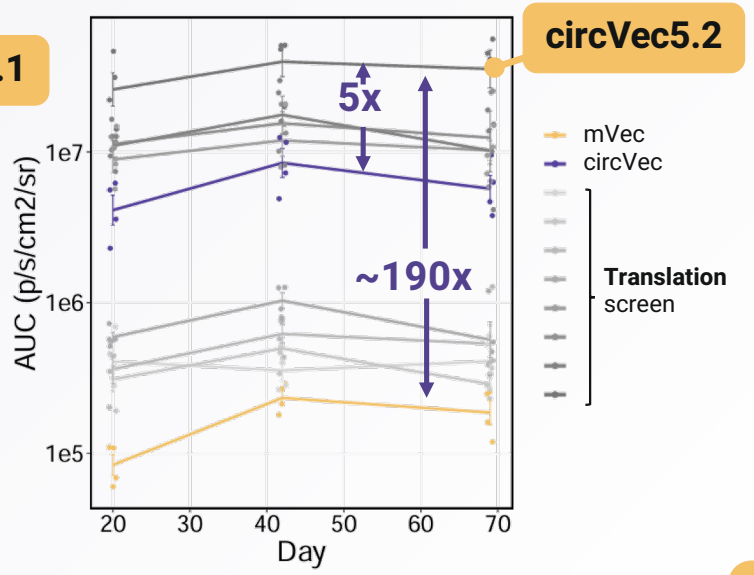
Circio version LAMP2B

circVec optimization for heart increases expression advantage to ~200-fold with 95% on-target specificity

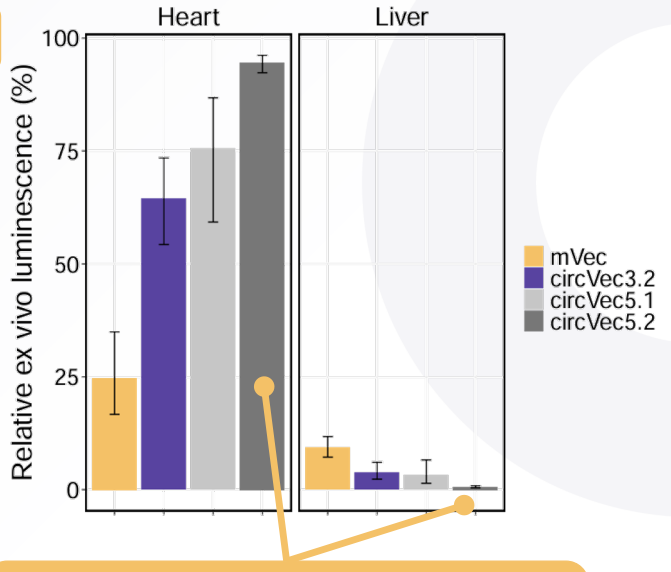
Enhancement of biogenesis in heart,
In vivo heart luminescence



Enhancement of translation in heart,
In vivo heart luminescence



Reduced off-target liver expression,
Ex vivo luminescence



95% on-target heart expression
<1% off target liver expression

Summary : AAV-circVec confers four major advantages for the treatment of genetic heart disorders

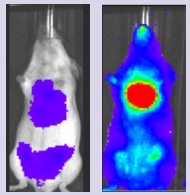




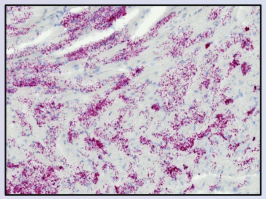
circVec

circVec-AAV compared to benchmark mVec-AAV:

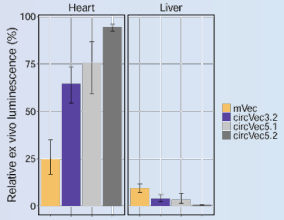
Expression



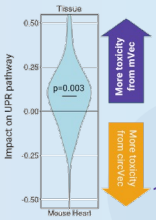
Penetrance



Specificity



Toxicity



circio

Consistent circVec performance across three major gene therapy areas

	Heart 	Eye 	CNS 
In vivo results	**Up to 40x increased expression**	**Up to 50x increased expression**	**Up to 60x increased expression**
Next milestone	**In vivo heart disease model data**	**Validate expression in larger animal**	**In vivo data from top 5 pharma collaboration**
Market opportunities	**Arrhythmic** (and other) **cardiomyopathies** n = up to 100,000	**wetAMD** n = 7-8 million out-licensing	**Neurodegenerative diseases** out-licensing

Further boost by circVec generation 5: potential to outperform conventional AAV by 200x or more

circVec: a first-in-class, industry-leading circRNA expression system with platform potential in several disease areas

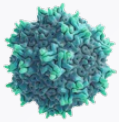
Gene therapy

Heart, eye and CNS genetic disease

1 mill. patients in target diseases

Enhanced, safer and lower cost AAVs

Research collaboration with global pharma



Next Gen AAV

Cell therapy

Cancer, autoimmune disease

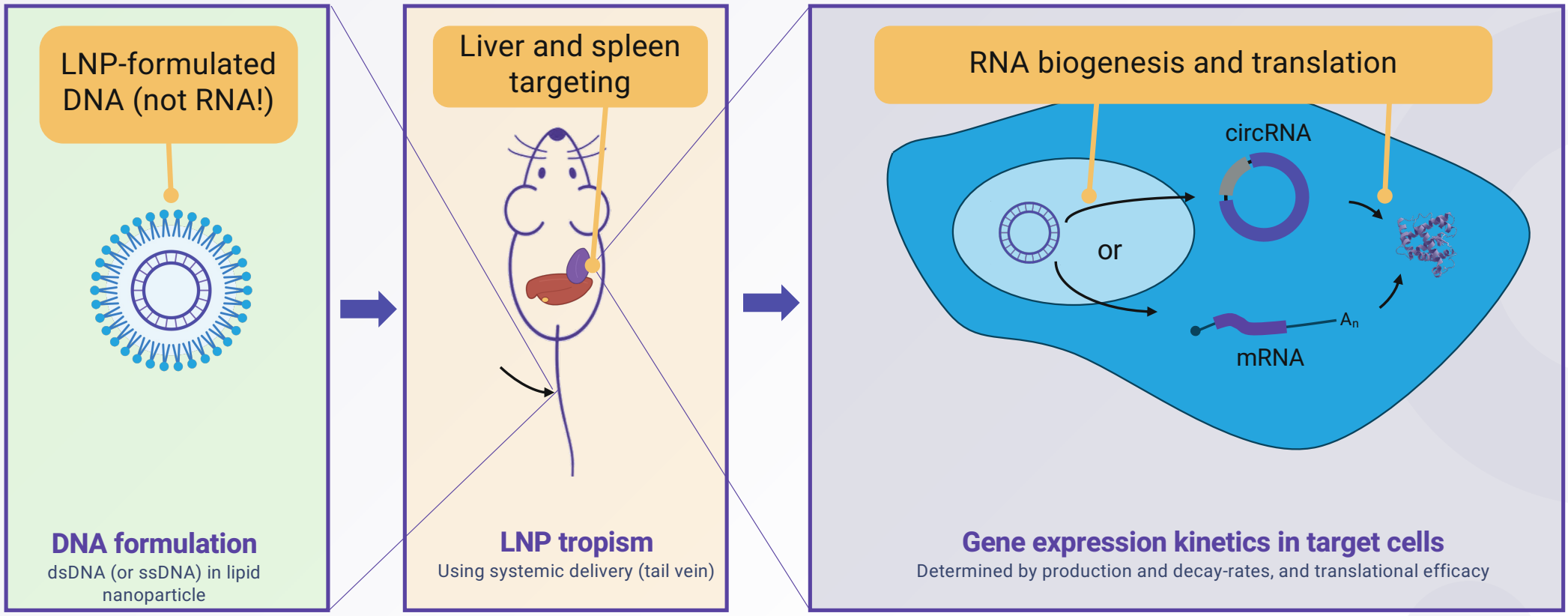
LNP: DNA format, redosable

Very large patient population, only autologous options available today



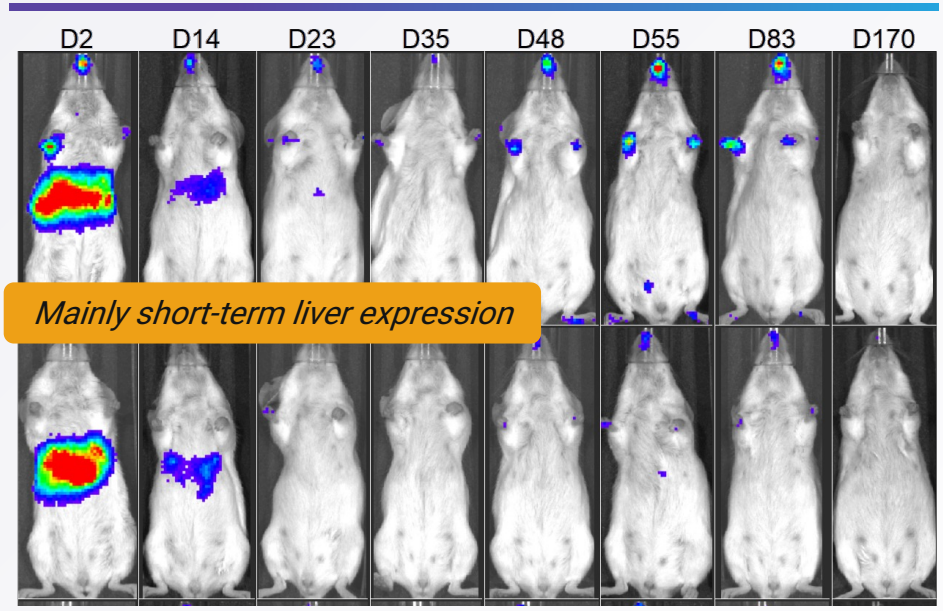
In vivo CAR

Non-viral circVec: LNP-formulated DNA for durable and redosable in vivo cell therapy

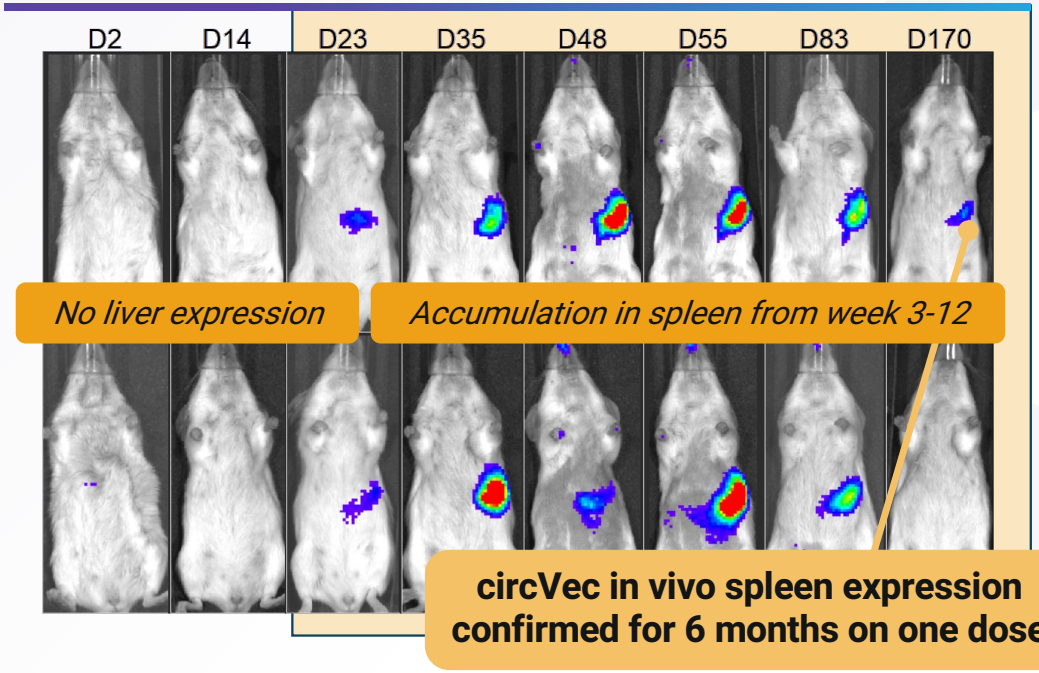


In vivo cell therapy: circVec expression duration up to 6 months vs. 2 weeks for mVec

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



LNP-circVec luminescence
Systemic I.V. delivery, single dose on Day 0

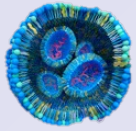




Non-viral DNA



circVec 2.1



LNP delivery, non-targeted

circVec offers a unique window of opportunity for in vivo cell therapy applications

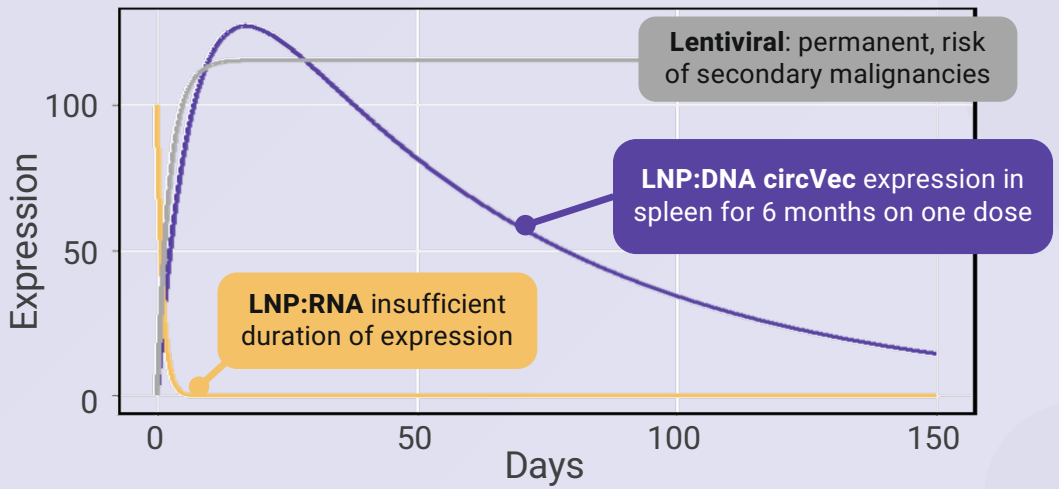
In vivo CAR modalities - duration

Days	Months	Permanent
mRNA & circRNA	**circVec therapeutic window**	Lentiviral

circVec benefits

- Non-genome integrating
- Up to **6 months** duration of expression on single dose
- Redosable

Therapeutic opportunity in oncology:



Major deal activity in hot in vivo CAR space

Bristol Myers Squibb → ORBITAL THERAPEUTICS

M&A, October 2025

$1.5b

cash buy out

In vivo CAR-T therapy for autoimmune disease

- LNP-delivered synthetic circular RNA platform
- Pre-clinical, CD19 CAR-T
- LNP w/ active T-cell targeting

Lilly → ORNA

M&A, February 2026

$2.4b

cash upfront + earn-out

In vivo CAR-T therapy for autoimmune disease

- LNP-delivered synthetic circular RNA platform
- Early clinical, CD19 CAR-T
- LNP w/o active T-cell targeting

J&J → SAIL BIOMEDICINES

M&A, July 2026

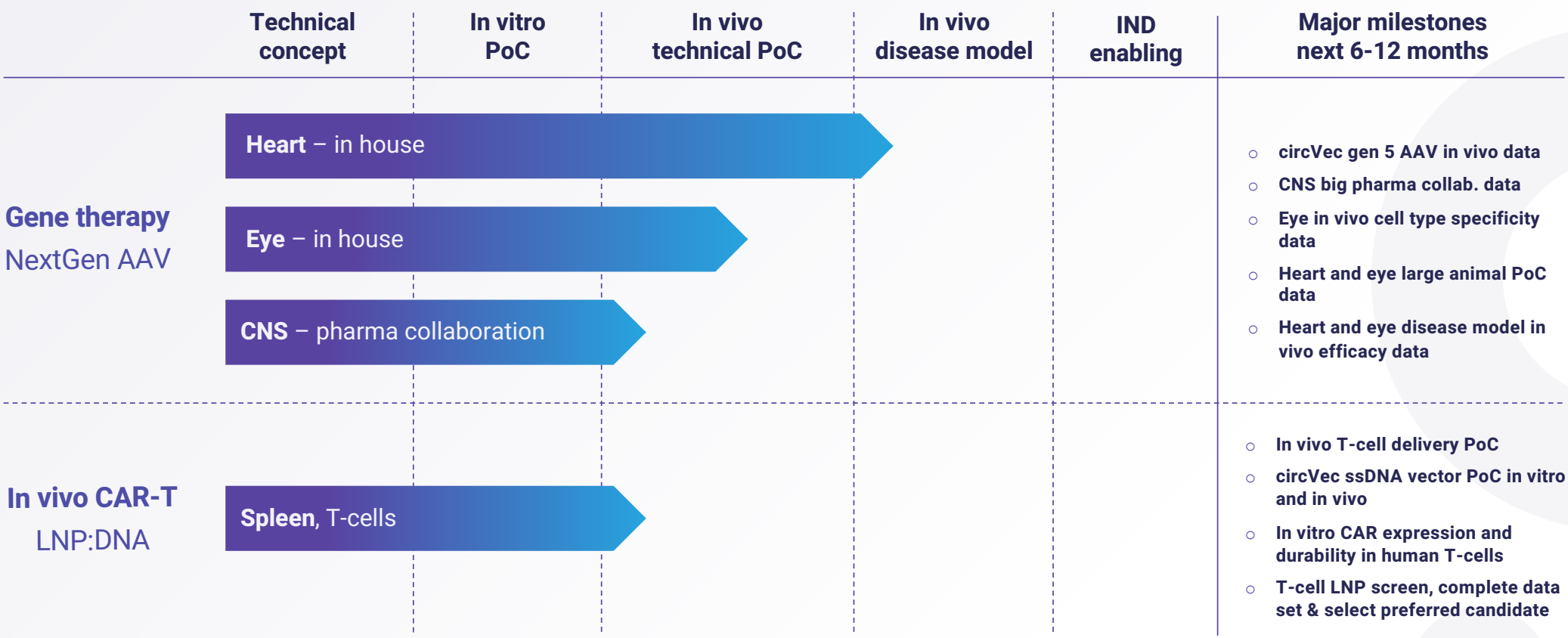
$2.5b

strategic transaction

In vivo CAR-T therapy for autoimmune disease

- LNP-delivered synthetic mRNA + circRNA RNA platform
- Pre-clinical, CD19 CAR-T
- LNP w/ active T-cell targeting

Circio has a broad pipeline with expected rich newsflow



Data & Timeline disclaimer: current best estimates - experiments have uncertain outcomes and may need to be repeated, impacting plans and timelines

PoC: proof of concept IND: investigational new drug LNP: lipid nanoparticle CAR: chimeric antigen receptor AAV: adeno-associated virus

Circio take-home messages: the leader in circular RNA gene expression systems

circVec R&D



- **40x gene therapy advantage in heart,** validated for therapeutic gene
- **Up to 60x gene** therapy advantage demonstrated **in CNS and eye**
- circVec generation 5 **potential to reach 200x or more advantage**
- **In vivo CAR-T approach** with novel, unique therapeutic window

Business development



- **Fully funded feasibility study ongoing with global top 5 pharmaco**
- **20+ active R&D collaborations with biotechs and academia**
- **Select and secure complementary technologies for in vivo CAR-T**

Financing



- **Strong circRNA and market momentum utilized for fundraising**
- **Circio is funded until clinical data in 2030**