circio

The leader in circular RNA expression systems

Company presentation
2Q 2026

Circular RNA – a new generation of RNA medicines

circular RNA

- Naturally occurring
- Resistant to degradation
- Engineerable & versatile

Bristol Myers Squibb™ → ORBITAL THERAPEUTICS

M&A $1.5b

Lilly → ORNA

M&A $2.4b

circio → **First listed circRNA biotech**
USD 35m raised in 2026

Human circRNA was first described by Circio scientists

Dr Thomas B Hansen

Dr Erik D Wiklund

nature — 8,200 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 — 1,200 citations

CURRENT ISSUE ABOUT INFORMATION ARCHIVE ALERTS SUBMIT

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

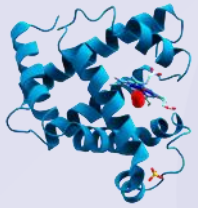
Eoghan O'Leary, Yanyi Jiang, Lasse S. Kristensen, Thomas B. Hansen & Jørgen Kjems

Nature Reviews Genetics (2025) | Cite this article

Circio has developed a powerful circular RNA alternative to the central dogma of molecular biology

The novel circVec alternative:



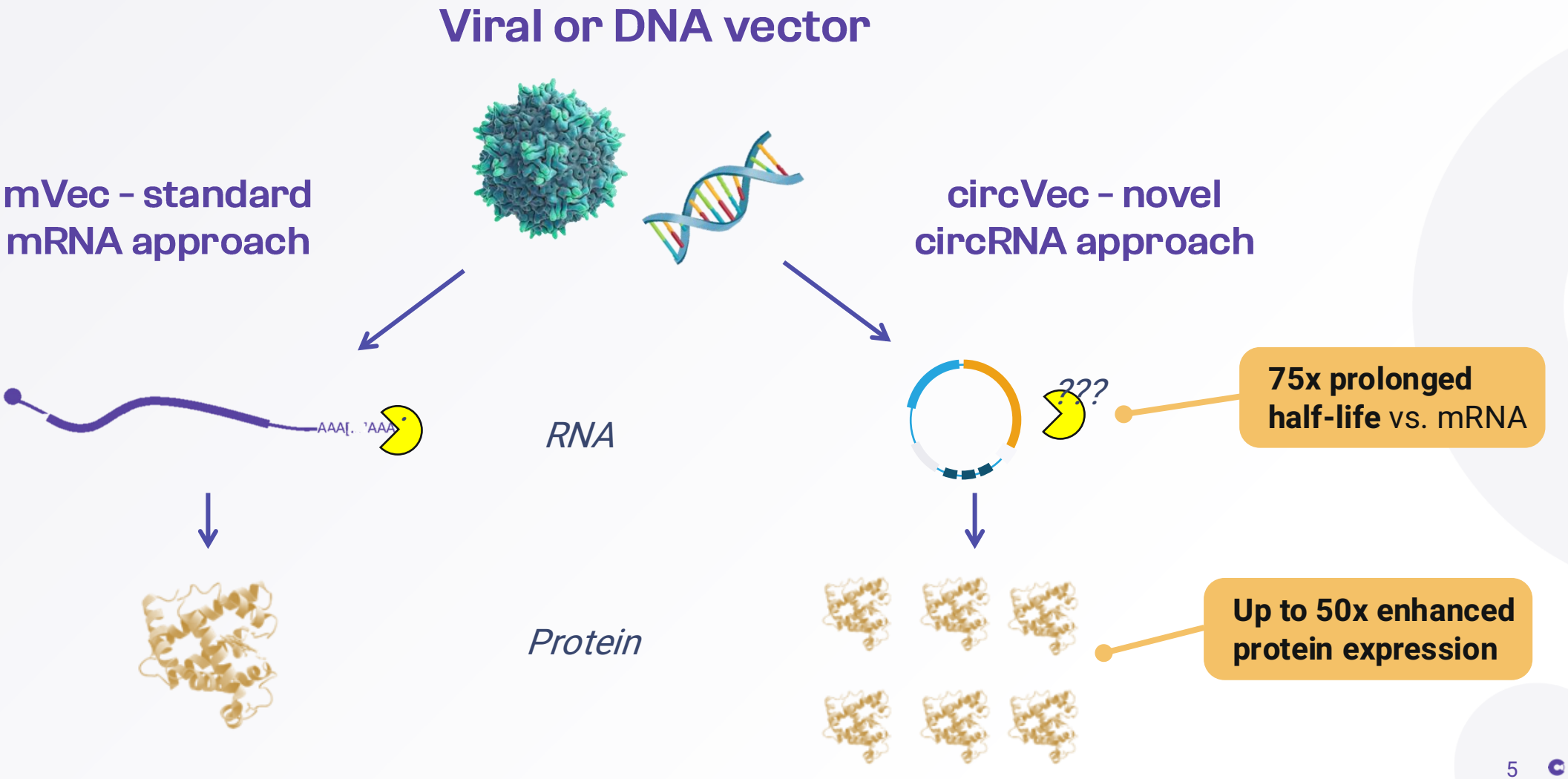


DNA → **circular RNA** → **Protein**

- **circVec** is a platform technology for vector-based gene delivery
- **circVec** enables enhanced and prolonged gene expression
- **Circio** has unique IP & know-how in circRNA gene expression

circVec

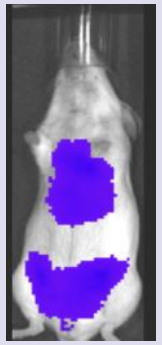
Circio´s unique and proprietary circRNA-based gene expression platform technology



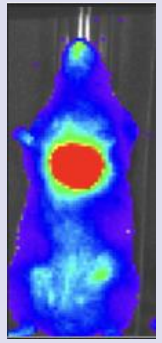
Circio is deploying the circVec technology to enhance conventional gene and cell therapy

Enhanced expression

Gene therapy



AAV benchmark

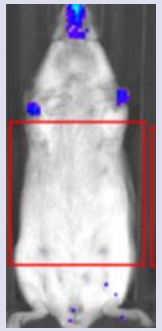


AAV circVec

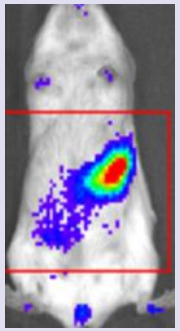
- **Up to 50x increased gene expression** for circRNA- vs. mRNA-based AAVs
- **Enhanced, safer and lower cost AAV gene therapy**

Improved durability

In vivo cell therapy



LNP:DNA benchmark



LNP:DNA circVec

- **>6 month durability for circRNA-** vs. <3 weeks for mRNA-based vectors
- **Durable and re-dosable in vivo CAR-T cell therapy**

Recent deal activity highlights substantial commercial opportunities in Circio areas

AAV gene therapy

Lilly → MEIRAGTx

Licensing, November 2025

$75m up-front

+ $400m milestones

AAV gene therapy for genetic eye disease

- AAV engineering platform, targeted capsids
- Phase 1, novel therapeutic candidate for vision loss

In vivo cell therapy

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
- Pre-clinical, CD19 CAR-T
- LNP w/o active T-cell targeting

Bristol Myers Squibb™ → ORBITAL THERAPEUTICS

M&A, October 2025

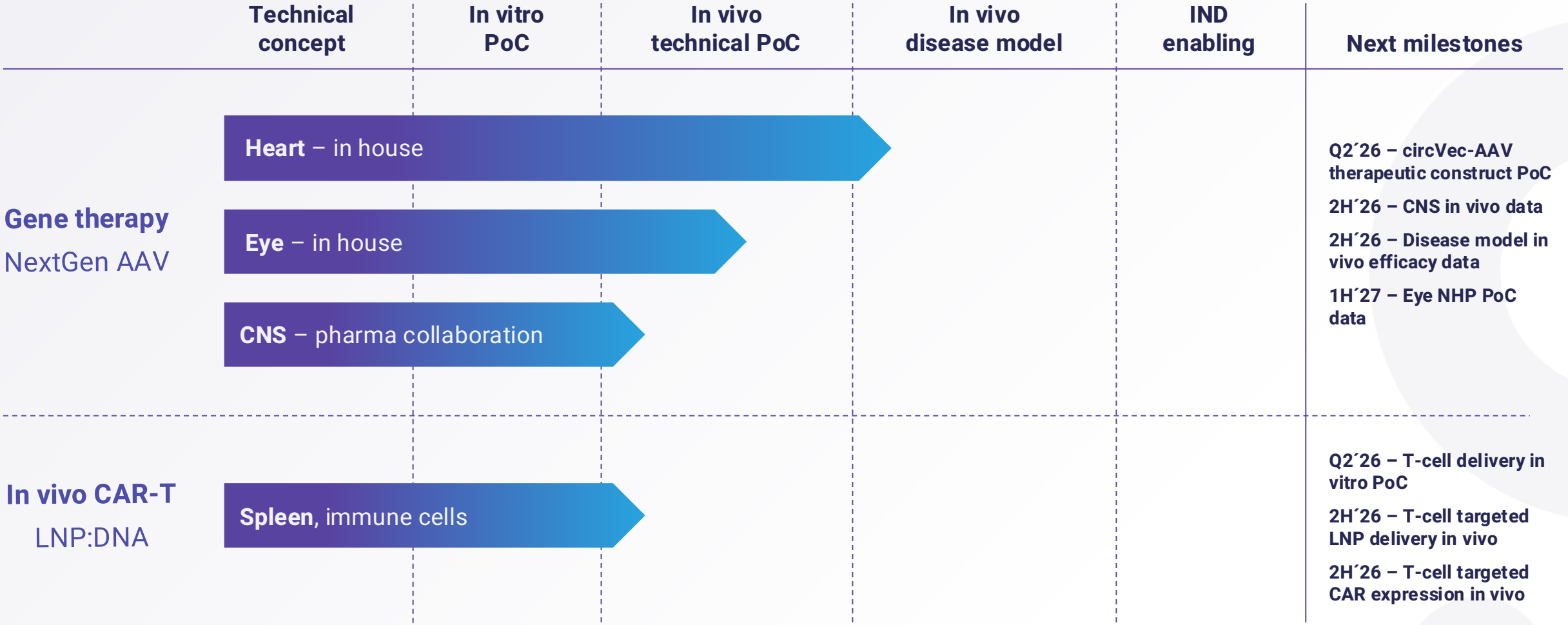
$1.5b

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

Circio pre-clinical circVec development pipeline



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

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

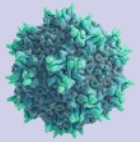
Gene therapy

Heart, eye and CNS genetic disease

1 mill. patients in target diseases

Enhanced, safer and lower cost AAVs

Ongoing 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 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:

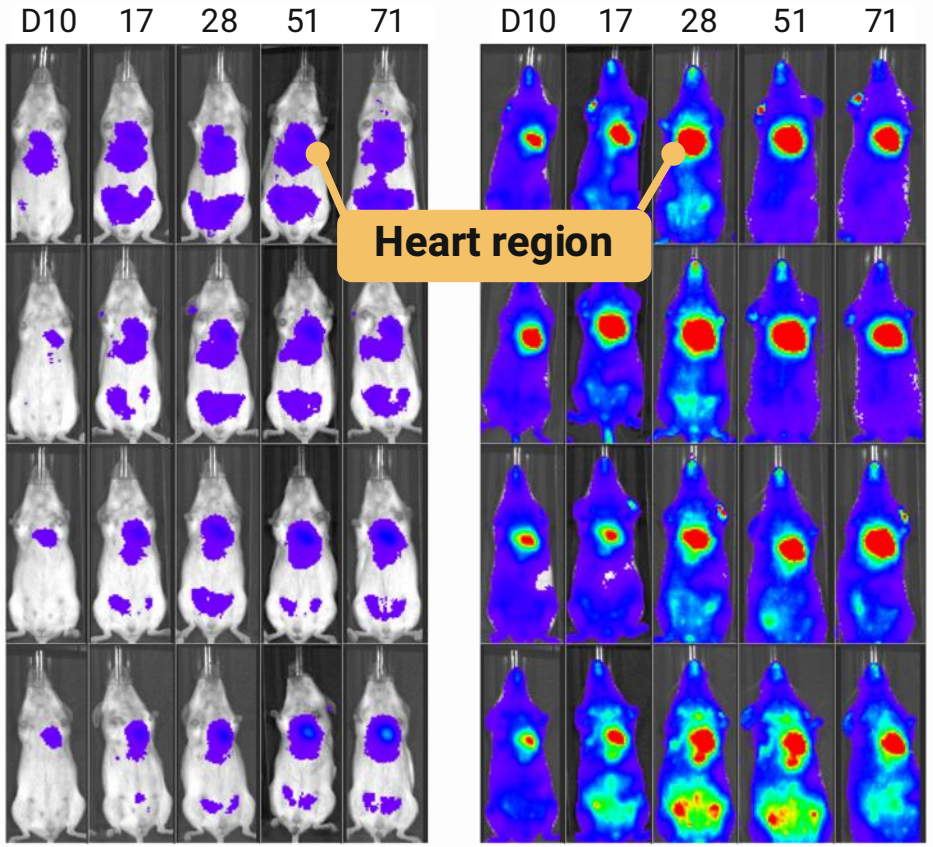
- Clinical benefit demonstrated, but too high dose
- ➢ **Severe adverse events, incl. risk of death**

Circio´s circVec technology can unlock:

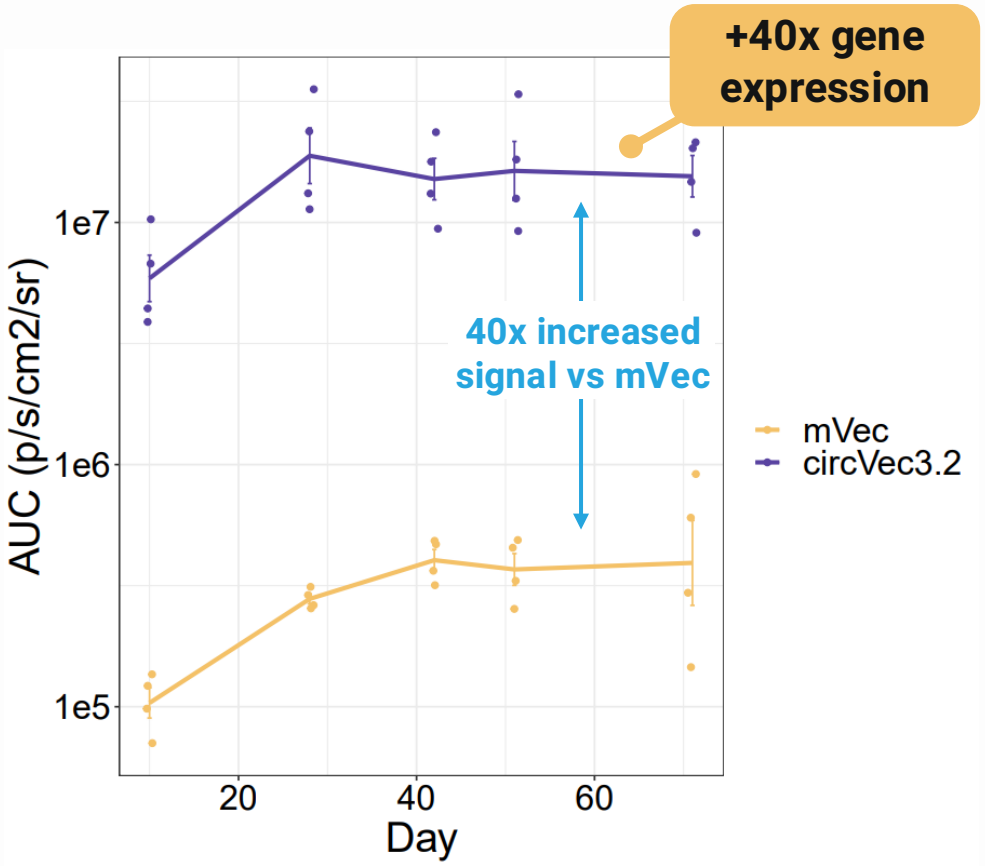
- Lower dose with same clinical benefit
- ➢ **Better, safer and lower cost AAV gene therapy**

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

AAV-mVec **AAV-circVec 3.2**

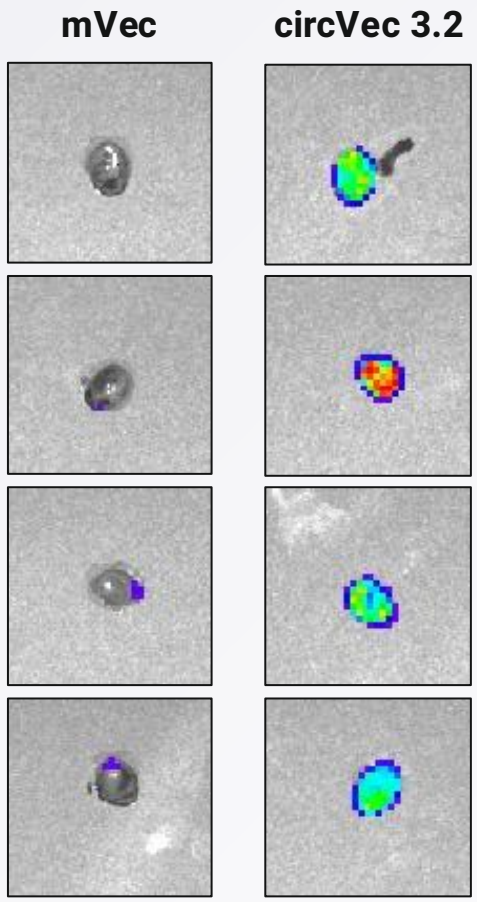


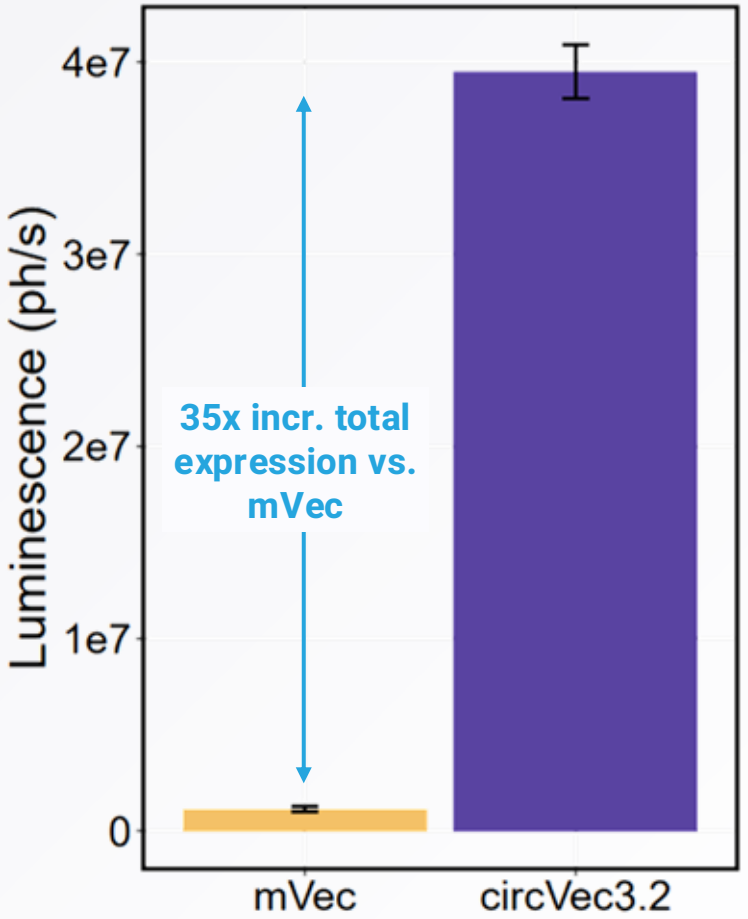
Gene expression quantification, f-luc IVIS signal



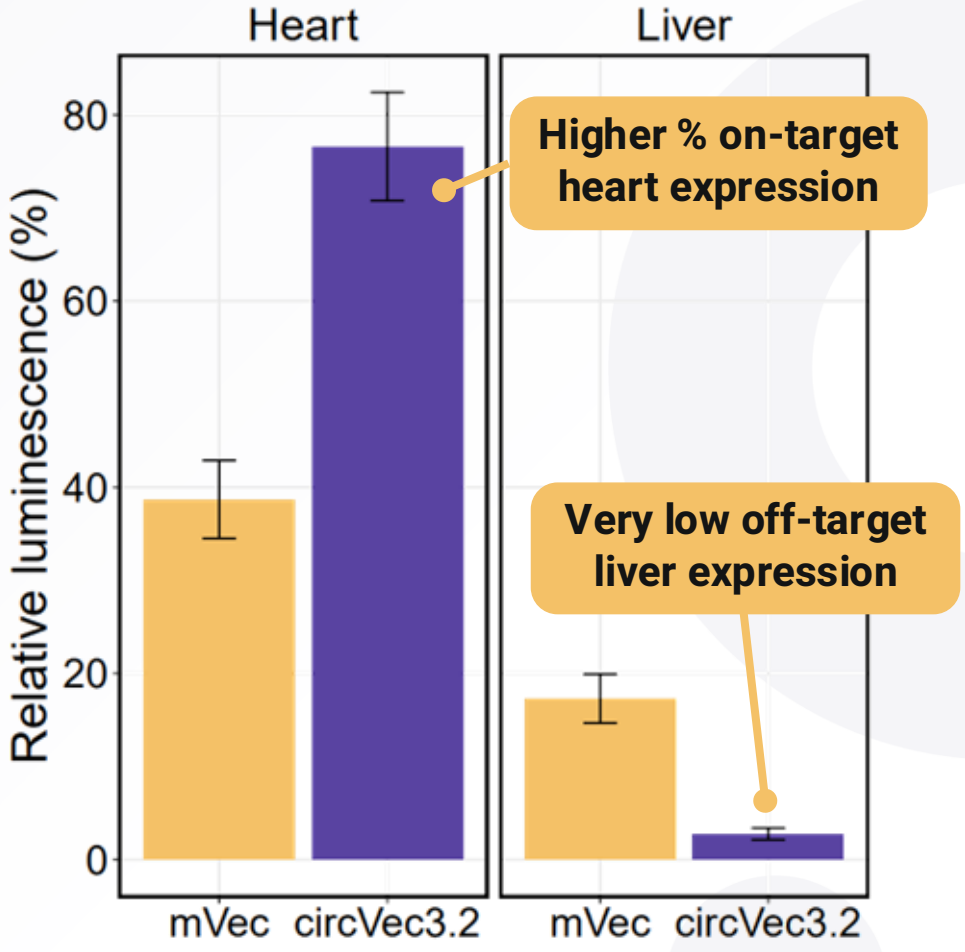
circVec shows increased on-target heart activity and substantially reduced off-target liver expression

Increased expression in heart, ex vivo tissue analysis week 10



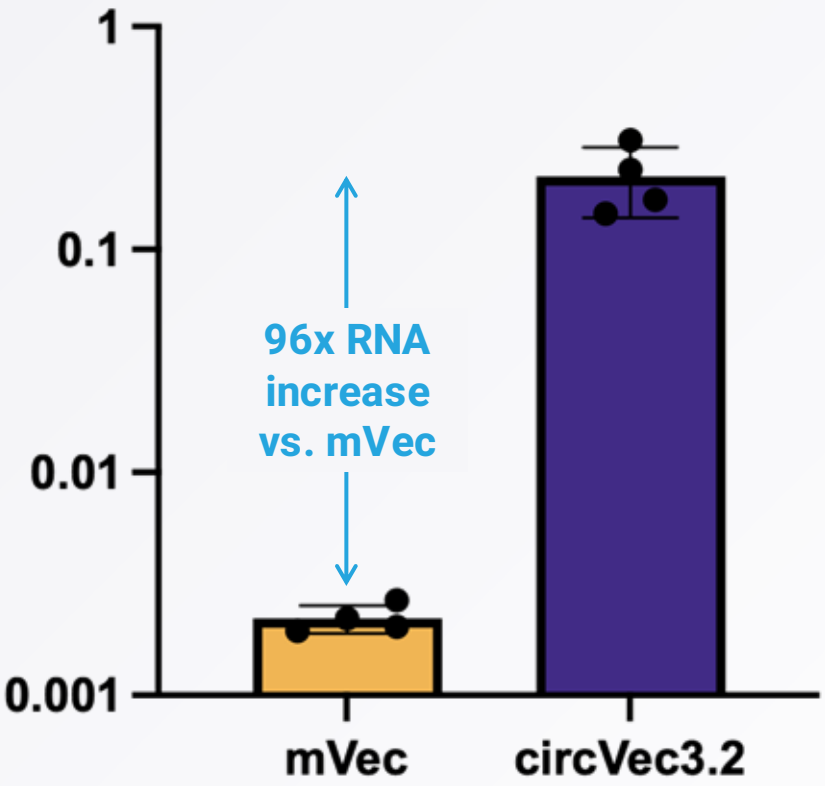


...and reduced off-target liver expression

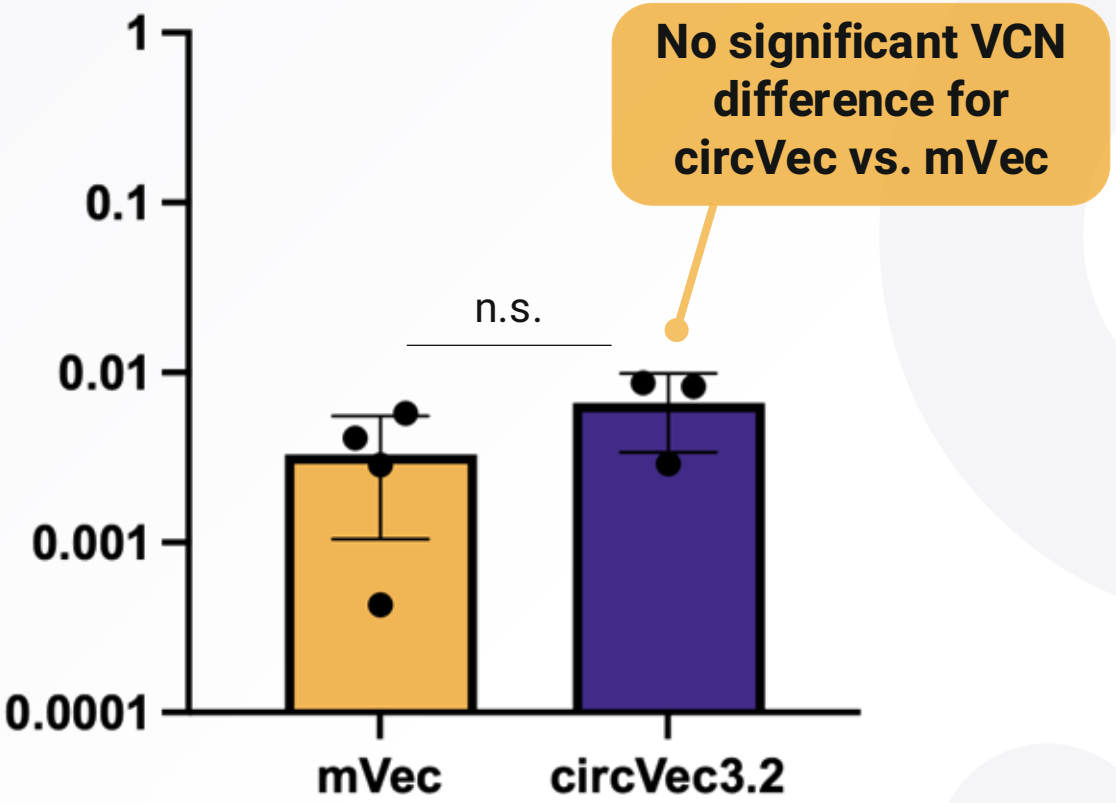


circVec advantage is driven by RNA transcript level, not AAV transduction or vector copy number

RNA expression in heart tissue, RT-qPCR



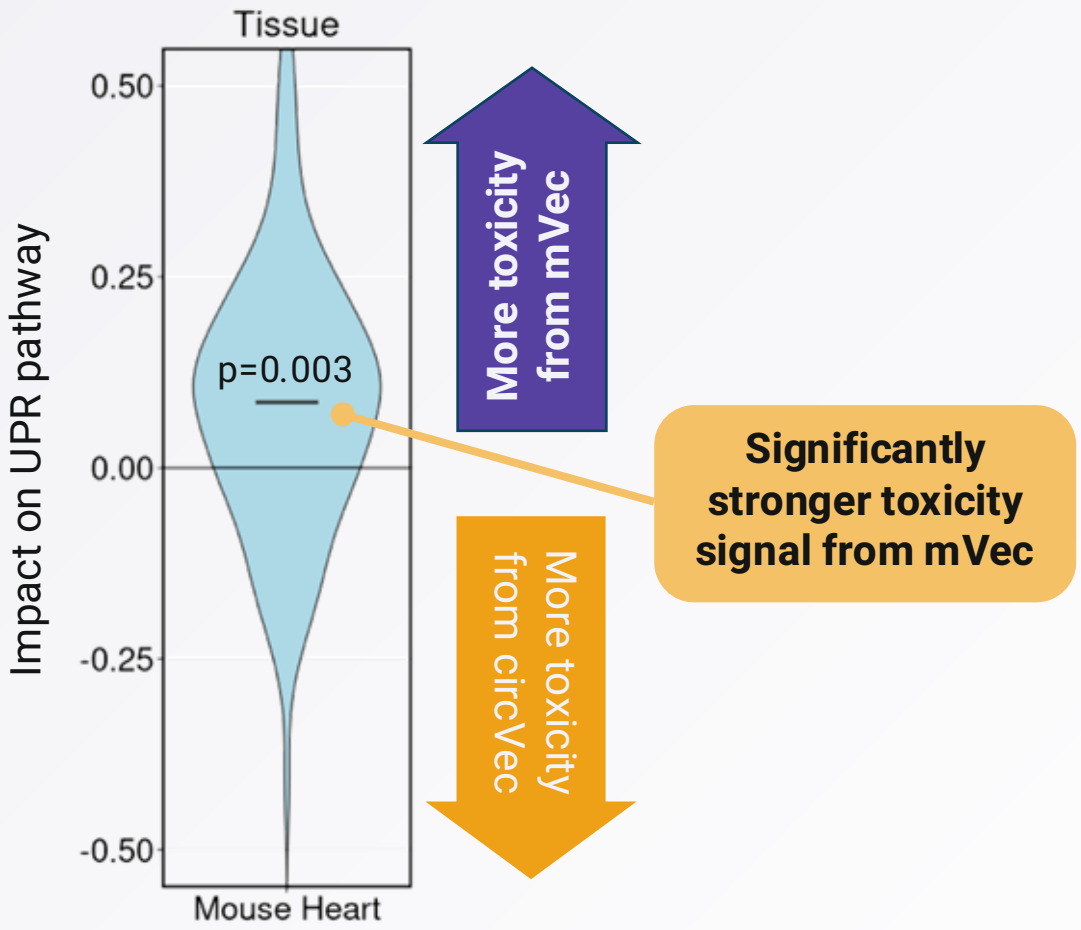
Vector Copy Number (VCN) in heart tissue, qPCR



**Data from repeat study

Reduced toxicity of circVec-AAV in heart, despite 40-fold higher gene expression

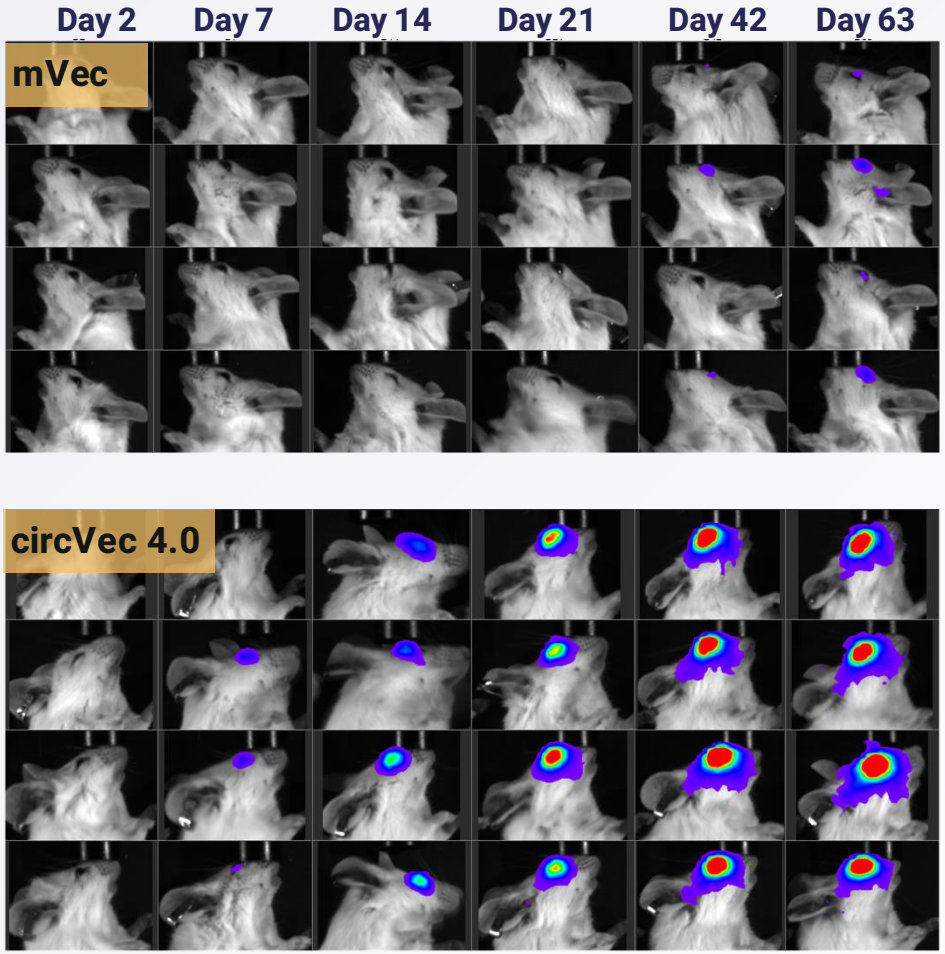
Cellular stress response, UPR pathway activation



- **Unfolded Protein Response** (UPR) activation is a **major contributor to AAV toxicity** in patients
- AAV-circVec shows **less activation of UPR pathway in heart** than AAV-mVec at **same dose**
  - Despite 40x increased gene expression
  - Confirmed in various cell lines

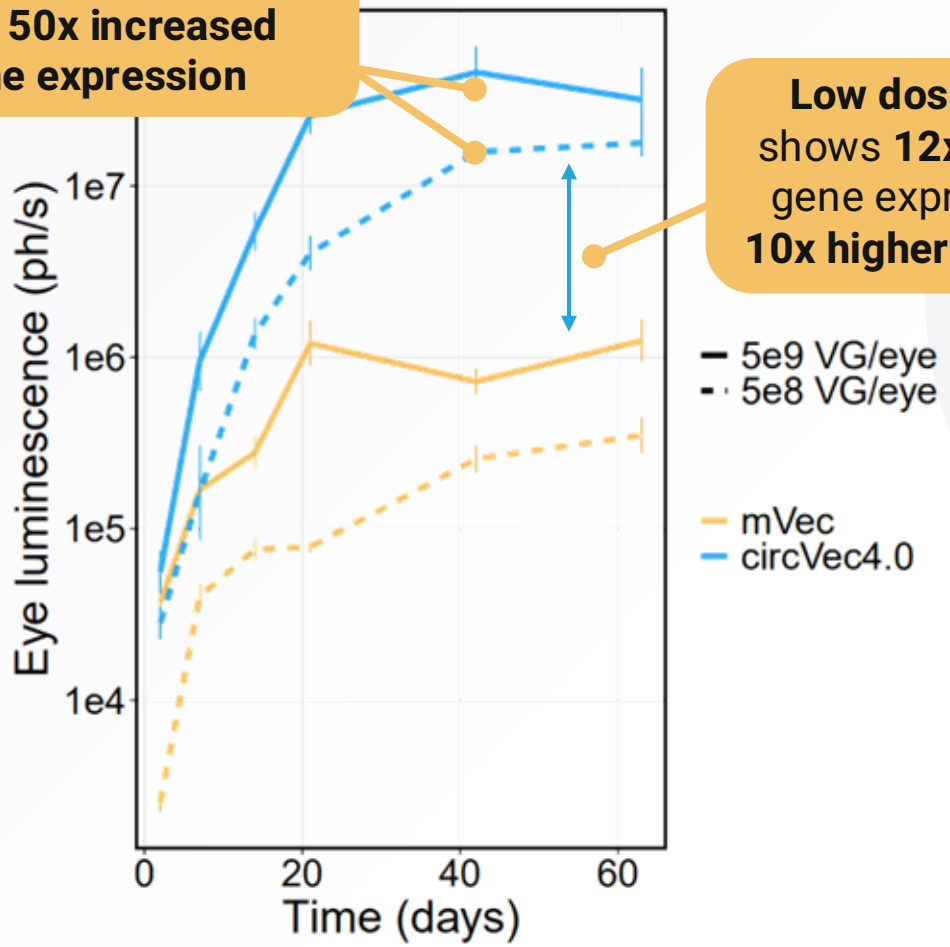
Ophthalmology: local delivery of AAV circVec 4.0 enhances gene expression by up to 50x in eye

IVIS images, low dose mice (5e8 VG/eye)



Expression over time, intra-vitreal inj. of AAV2-circVec vs. -mVec

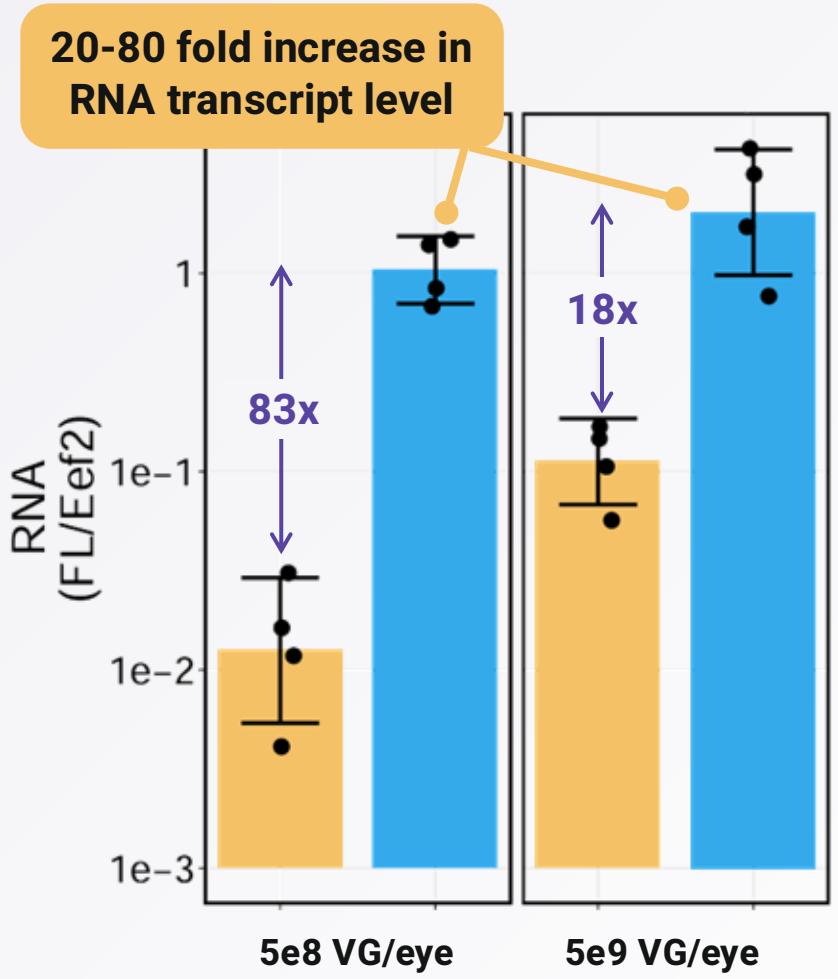
AAV-circVec vs. -mVec: **up to 50x increased gene expression**



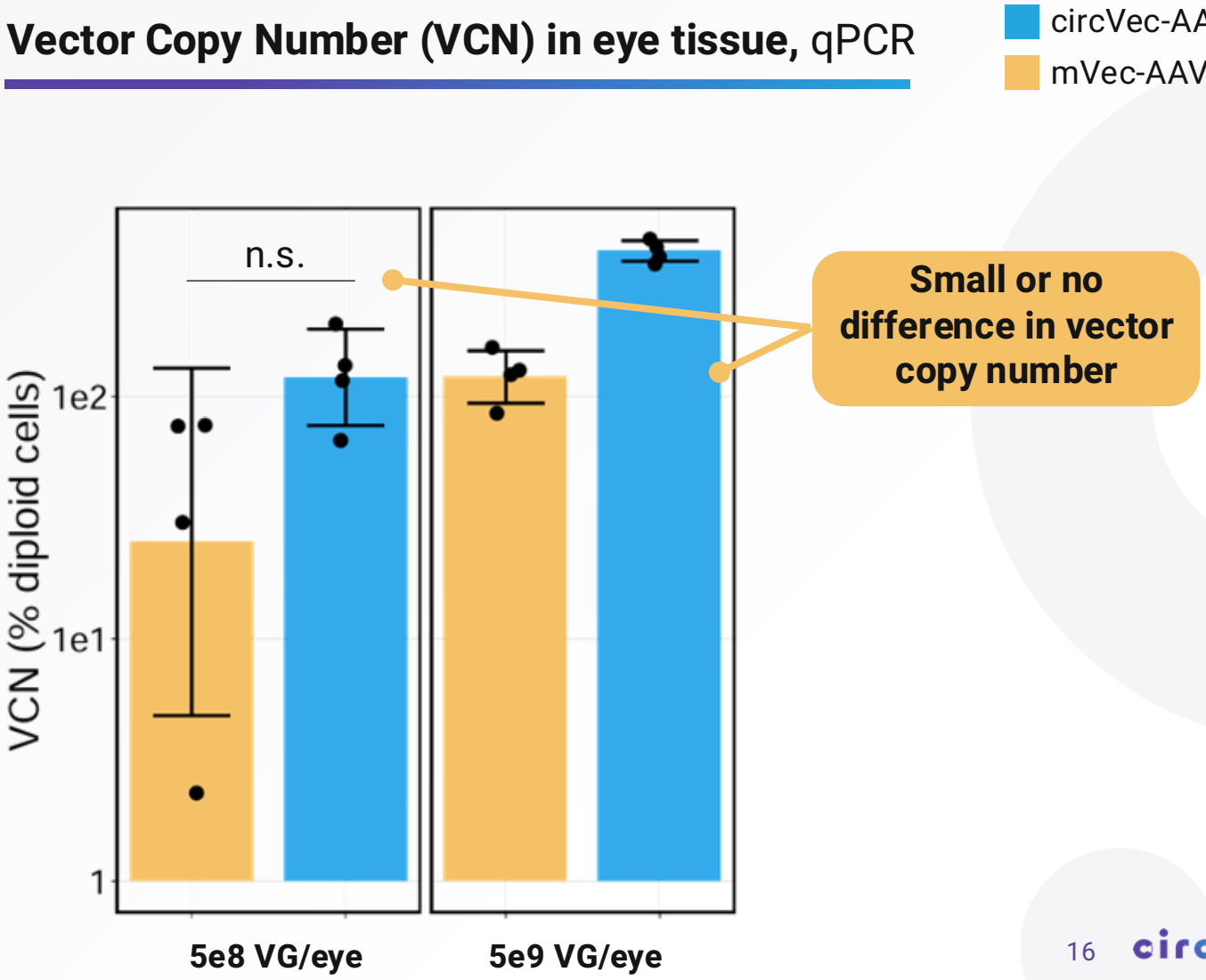
Low dose circVec shows **12x** increased gene expression vs. **10x higher dose mVec**

The circVec advantage is driven by increased circRNA transcript level also in the eye

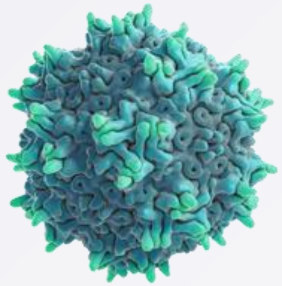
RNA expression in eye tissue, RT-qPCR



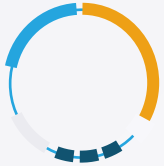
Vector Copy Number (VCN) in eye tissue, qPCR



Summary : AAV-circVec confers three major advantages

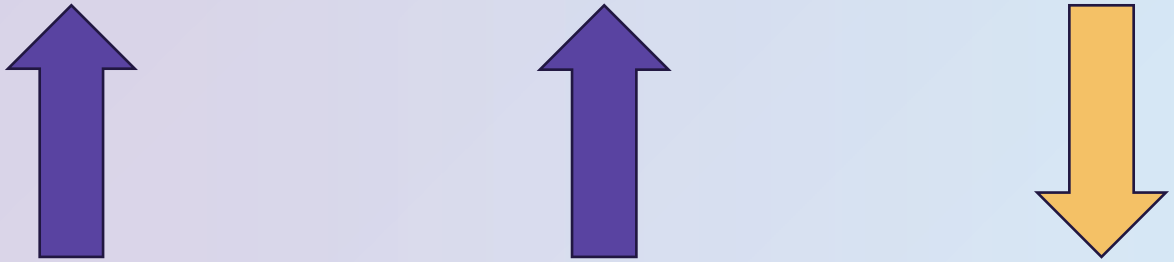


mVec

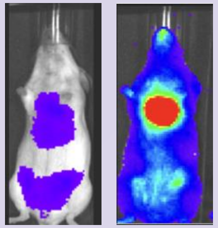


circVec

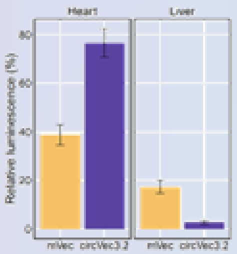
circVec-AAV compared to benchmark mVec-AAV:



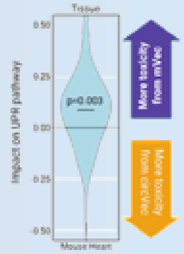
Expression



Specificity



Toxicity



AAV-circVec pre-clinical program in heart, eye and CNS

	Heart 	Eye 	CNS 
In vivo results	**Up to 40x increased expression**	**Up to 50x increased expression**	**>4x increased activity** for circVec 2.1
Next milestone	**In vivo heart disease model data**	**Validate expression in larger animal**	**In vivo data from top 5 pharma collaboration**
Market opportunities	**Arrhythmic cardiomyopathy** n = 50-70,000	**wetAMD** n = 7-8 million	**Neurodegenerative diseases** out-licensing

High unmet medical need and substantial commercial opportunities in Circio focus areas

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

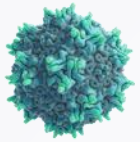
Gene therapy

Heart, eye and CNS genetic disease

1 mill. patients in target diseases

Enhanced, safer and lower cost AAVs

Ongoing collaboration with global pharma



Next Gen AAV

Cell therapy

Cancer, autoimmune disease

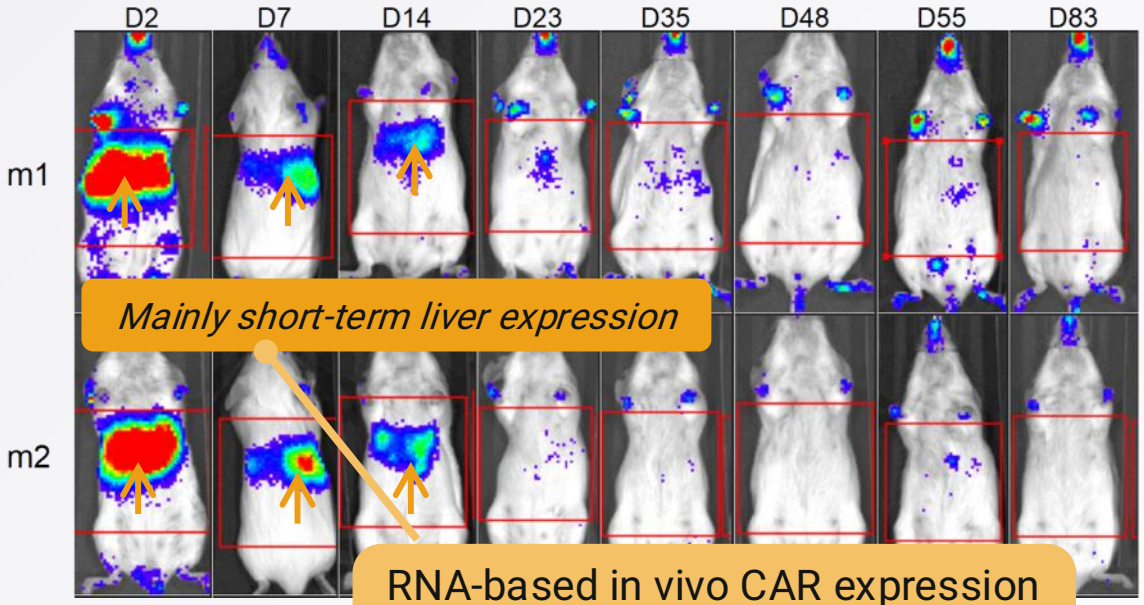
LNP: DNA format, redosable

Very large patient population, only autologous options available today

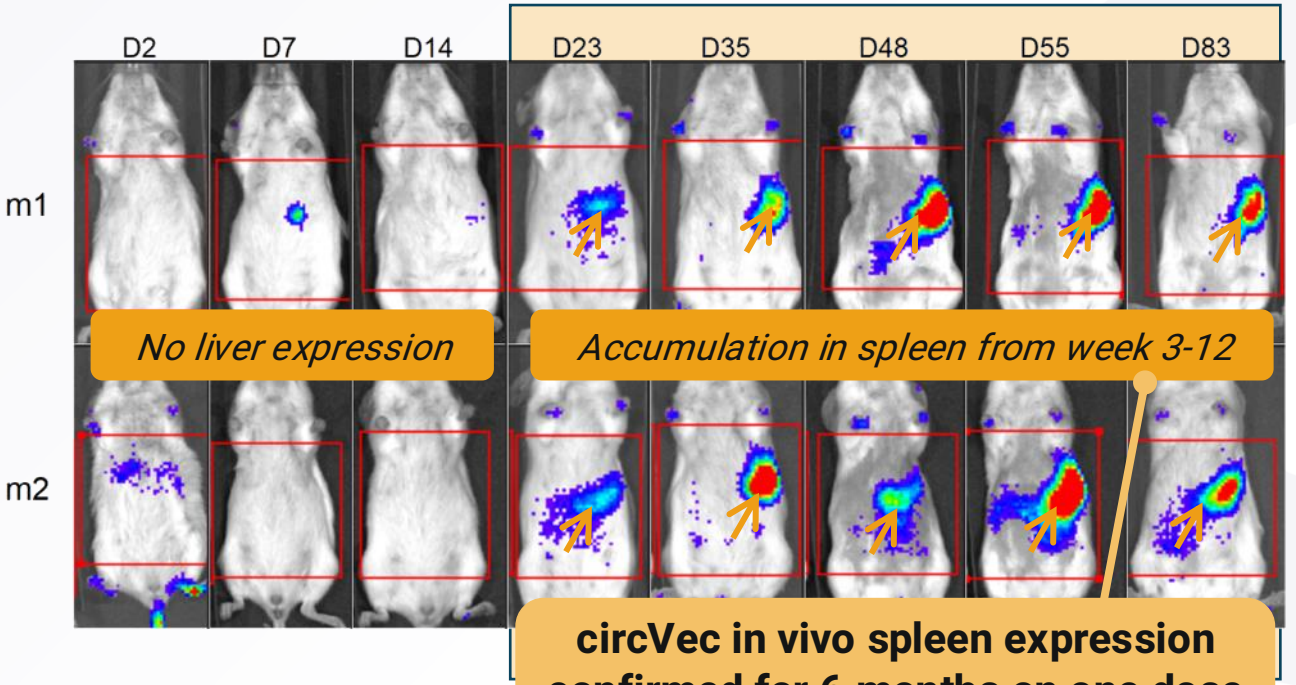
In vivo CAR

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

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

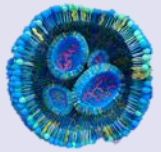


LNP-circVec (circRNA), luminescence
Systemic I.V. delivery, single dose on Day 0



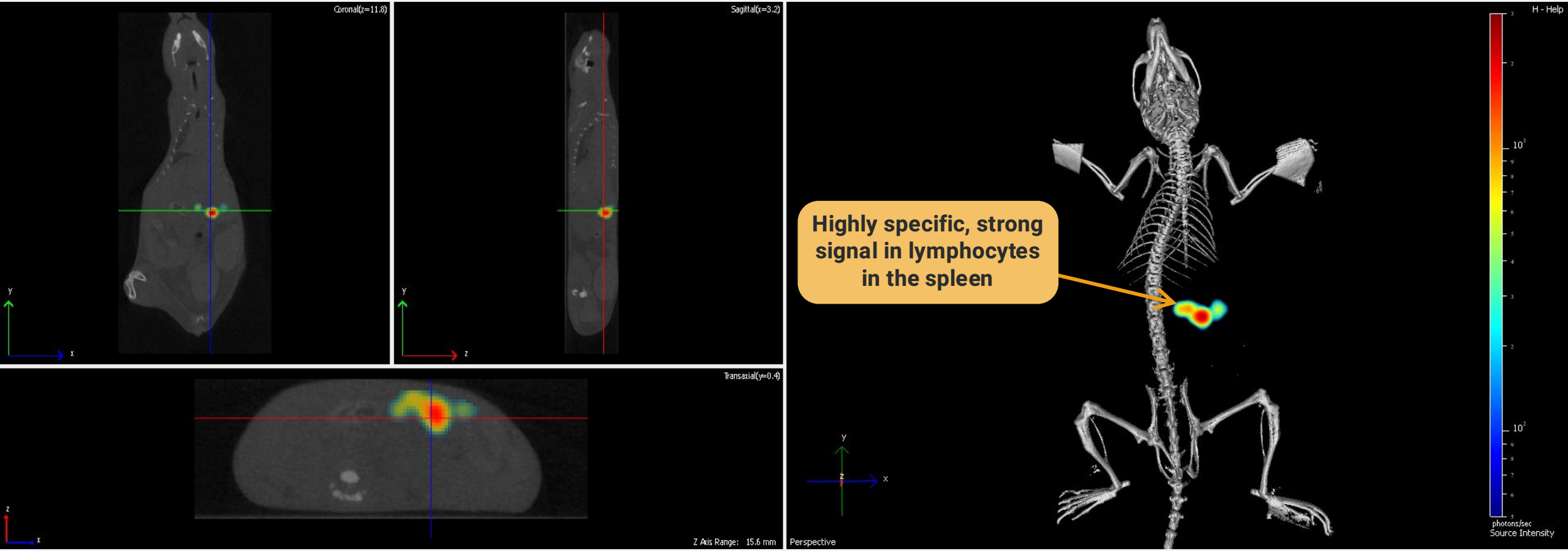
Non-viral synthetic dsDNA vector format

circVec 2.1



LNP delivery, non-targeted

circVec expression emanates from immune cells in spleen



Example animal, spleens harvested for cellular and molecular analyses

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

In vivo CAR modalities – duration

mRNA & circRNA ← **circVec-DNA opportunity** → Lentiviral

circVec-DNA benefits

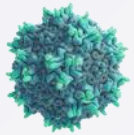
- **Non-genome integrating**
- **> 6 months duration of expression on single dose**
- **Redosable**

Therapeutic opportunity:

- **Opening up cancer indications to redosable in vivo CAR-T cell therapy**

- Ex vivo CAR-T effective, but too complex
- Lentiviral risk of secondary malignancies
- RNA in vivo CAR not sufficient duration

circVec is a first-in-class, industry-leading circRNA expression system: Take-home messages



- **AAV-circVec outperforms** conventional gene therapy on **expression (up to 50x), specificity and toxicity**

- **In vivo cell therapy** approach with **new and differentiated window-of-opportunity** in area of very high deal activity

- **Rich pipeline** of R&D milestones with **multiple shots on goal**
- **High unmet medical need** and **deal activity** in focus areas

In-house

circVec in vivo validation in relevant tissues and disease models

- ***Next step:*** *Heart and eye disease model testing of circVec-AAV*

Partnering

Entered first partnership with global pharma company in Q4´25

- ***Next step:*** *Additional partnerships in other disease areas*

Full team in place with strong blend of expertise to build and capitalize on Circio´s platform

Dr Erik D Wiklund

CEO

Overall strategy and execution

CV:

- *PhD Molecular Biology*
- *circRNA co-discoverer*
- *Biotech CFO & CBO*
- *McKinsey & Company*

Dr Lubor Gaal

CFO & CBO

Securing financing and partnering deals

CV:

- *PhD Neuroscience*
- *Big pharma BD*
- *Biotech executive*
- *Investment banking*

Dr Thomas B Hansen

CTO

Building technology platform and IP

CV:

- *PhD Molecular Biology*
- *circRNA co-discoverer and scientific pioneer*
- *Big data analysis*

Dr Victor Levitsky

CSO

Leading immunology and virology expert

CV:

- *PhD Virology*
- *Big pharma R&D*
- *Biotech executive*
- *Top academic centers*

Ola Melin

COO

Operational execution

CV:

- *BSc Chem. Eng*
- *Big pharma and biotech manufacturing, clinical and commercial*

Continued broad coverage of Circio in life science media

nature reviews genetics

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

Drug TARGET REVIEW

Circular RNA technology: the future of gene therapy

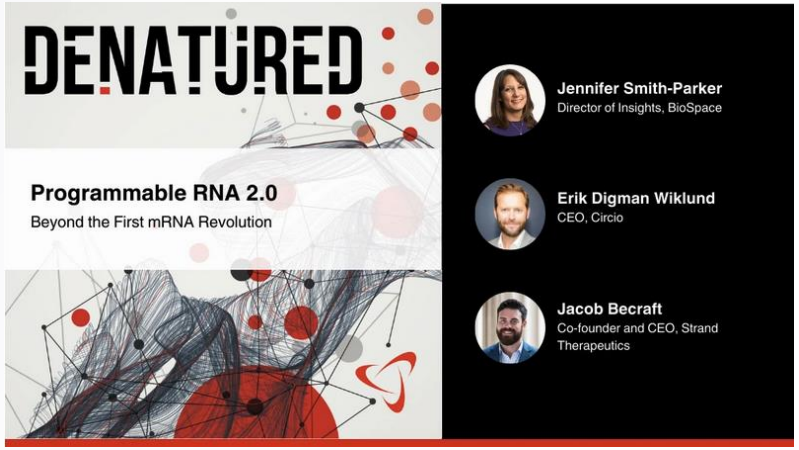
Posted: 13 November 2025 | Drug Target Review | No comments yet

Pioneering circular RNA could redefine what the future of gene therapy looks like. Erik Digman Wiklund, CEO of Circio, shares how his company's platform is enhancing gene expression and tackling toxicity challenges through smarter design and scientific collaboration.

CITELINE a norstella company

Circio's Vision For Long-Lasting Nucleic Acid Therapeutics

BioSpace



Opinion: Circular RNA Will Soon Replace mRNA in Biopharma

BIOTECH TV

Takes | BiotechTV U | Company News | Bright Minds | Shows | Tech + Tour

4 days ago

ASGCT 2026: Circio's circular RNA work has been advancing and is furthest along in cardiology indications. $35M in new funding will also help accelerate plans to for the eye, CNS, and in vivo CAR-T

Erik Wiklund describes the advantages of circular RNA, and the progress the company has been making since last year's ASGCT. With partnerships and additional funding in hand since then, the company is accelerating its work in multiple dimensions.