



circio

The leader in circular RNA expression systems

Company presentation
1Q 2026

Circular RNA – a new generation of RNA medicines



circular RNA

- Naturally occurring
- Resistant to degradation
- Long half-life
- Engineerable & versatile

 Bristol Myers
Squibb™



 ORBITAL
THERAPEUTICS

M&A \$1.5b







M&A \$2.4b





First-in-man
circRNA, March '25

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

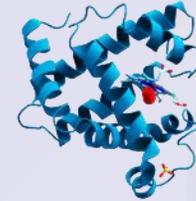
The novel circVec alternative:



DNA

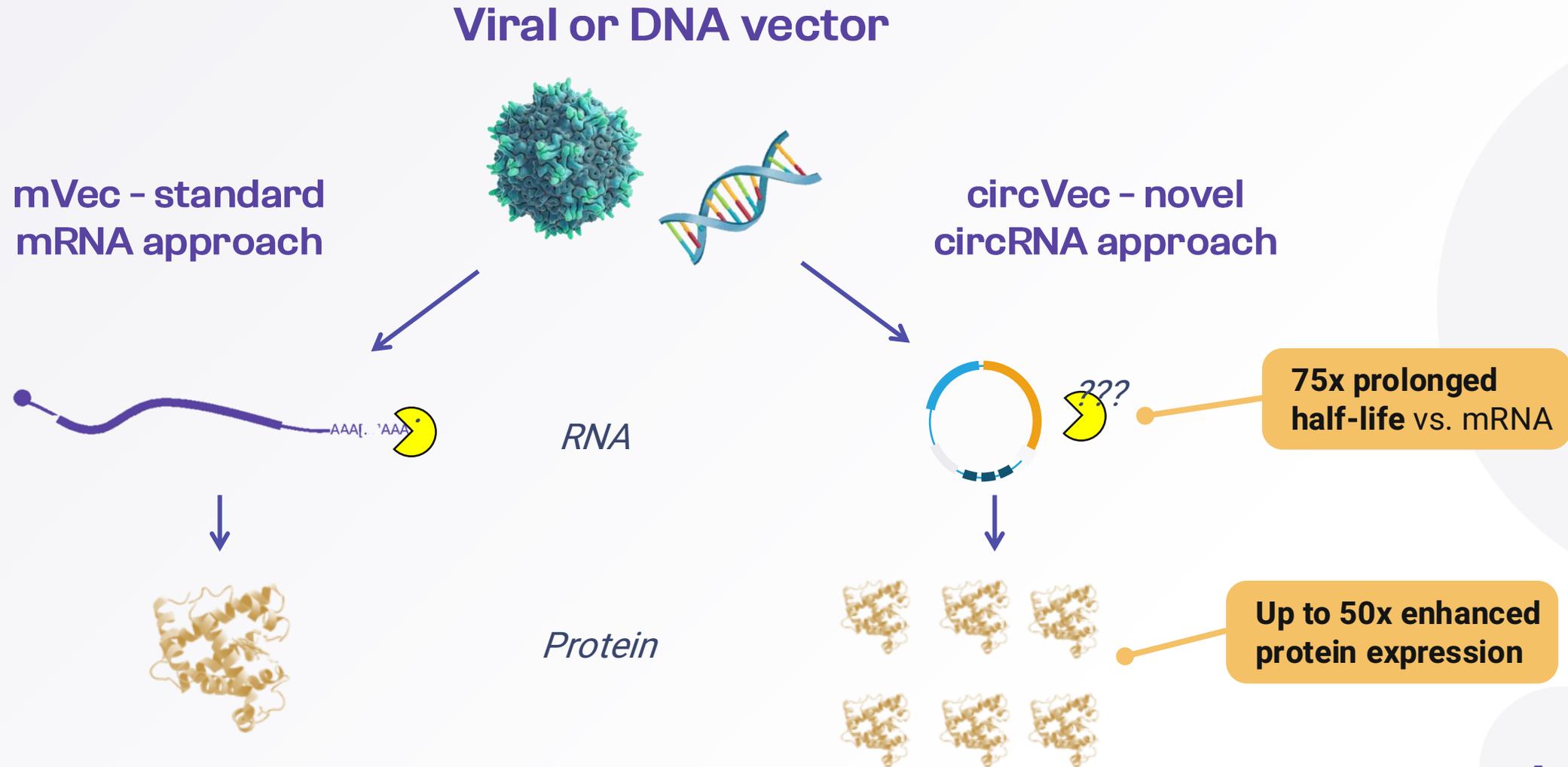


circular RNA



Protein

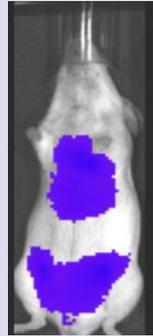
- **circVec** is a platform technology for vector-based gene delivery
- **circVec** enables enhanced and prolonged gene expression
- **Circio** has unique IP & know-how in circRNA gene expression



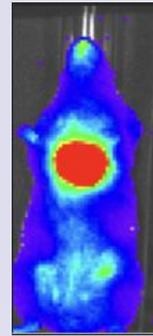
Circio is deploying the circVec technology to enhance conventional gene and cell therapy

Enhanced expression

Gene therapy



AAV
benchmark

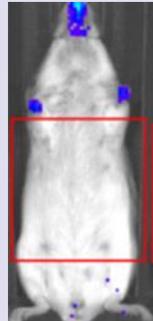


AAV
circVec

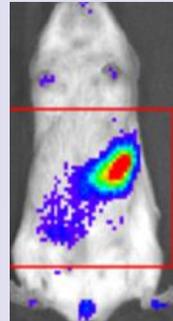
- Up to 50x increased gene expression for circRNA- vs. mRNA-based AAVs
- Enhanced, safer and lower cost AAV gene therapy

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



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

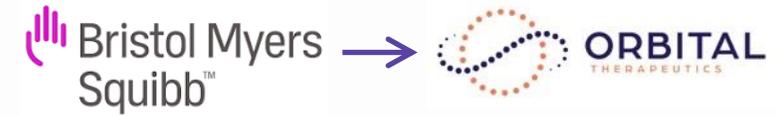


M&A, February 2026

\$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



M&A, October 2025

\$1.5b
cash buy out

In vivo CAR-T therapy for autoimmune disease

- LNP-delivered synthetic circular RNA platform
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circVec: a first-in-class, industry-leading circRNA expression system with platform potential in several disease areas

Gene therapy

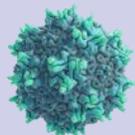


Heart, eye and CNS genetic disease

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

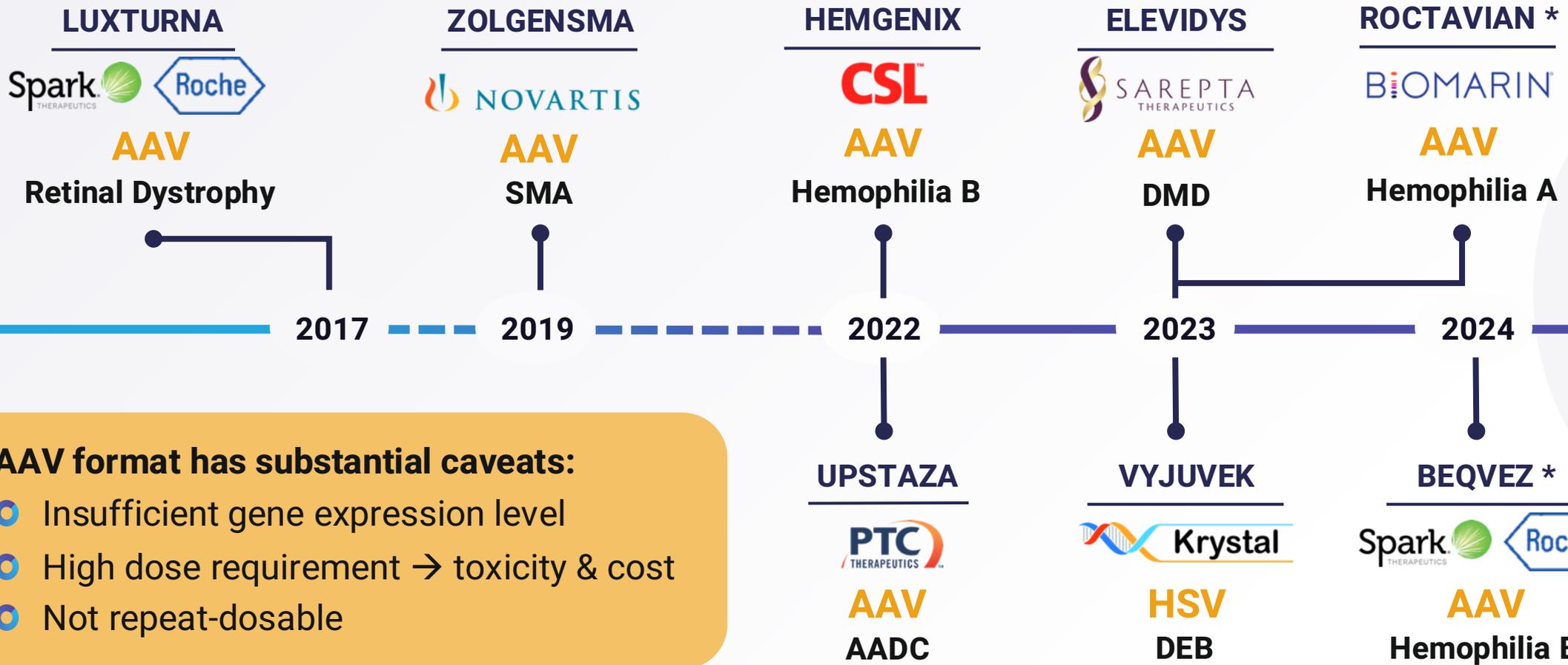
LNP: DNA format, redosable

Very large patient population, only autologous options available today



In vivo CAR

The AAV vector is the main gene therapy format today, however, high cost and toxicity remain major issues



AAV format has substantial caveats:

- Insufficient gene expression level
- High dose requirement → toxicity & cost
- Not repeat-dosable

circVec value proposition for AAV gene therapy: unlocking dose reduction to lower toxicity and cost



Danon Disease Patient Dies in Rocket Gene Therapy Trial

May 27, 2025

By Alex Philippidis



Rocket Pharmaceuticals acknowledged the death of a patient in a pivotal trial assessing its Danon disease gene therapy candidate RP-A501, a study that the FDA has placed on clinical hold.

AAV gene therapy for Danon disease:

- Clinical benefit demonstrated, but severe toxicity
- Very high AAV dose level required (= high tox & cost)
- **Severe adverse events, incl. risk of death**

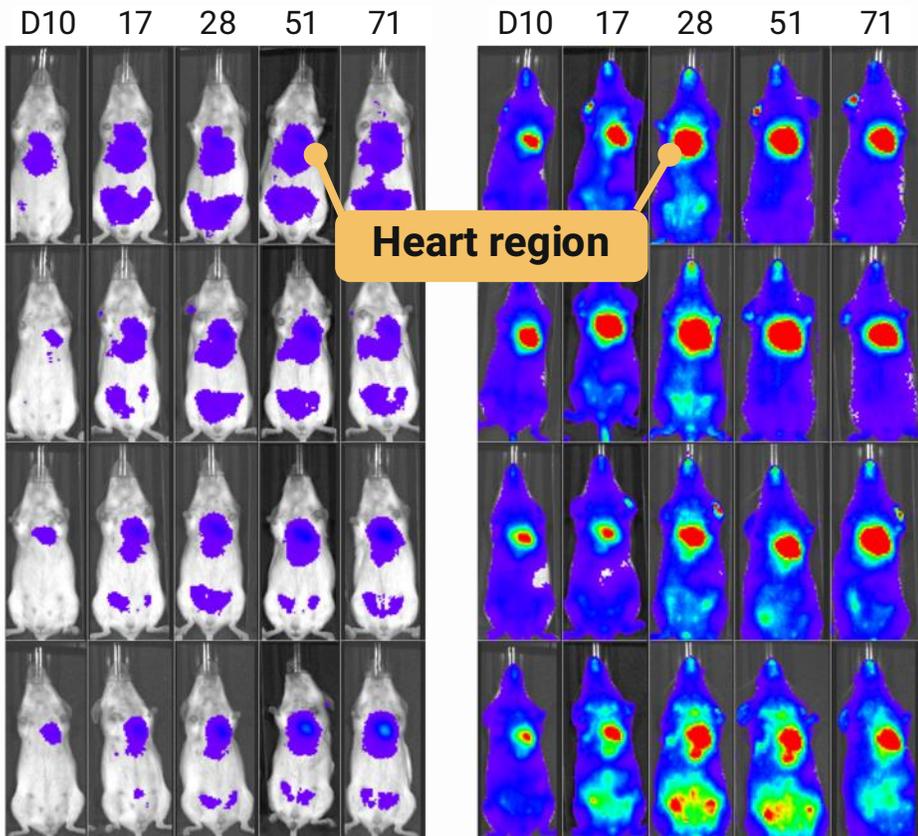
Circio's circVec technology can unlock:

- Significant AAV dose reduction with same clinical benefit
- Reduced toxicity and cost, better commercial viability
- **Better, safer and lower cost AAV gene therapy**

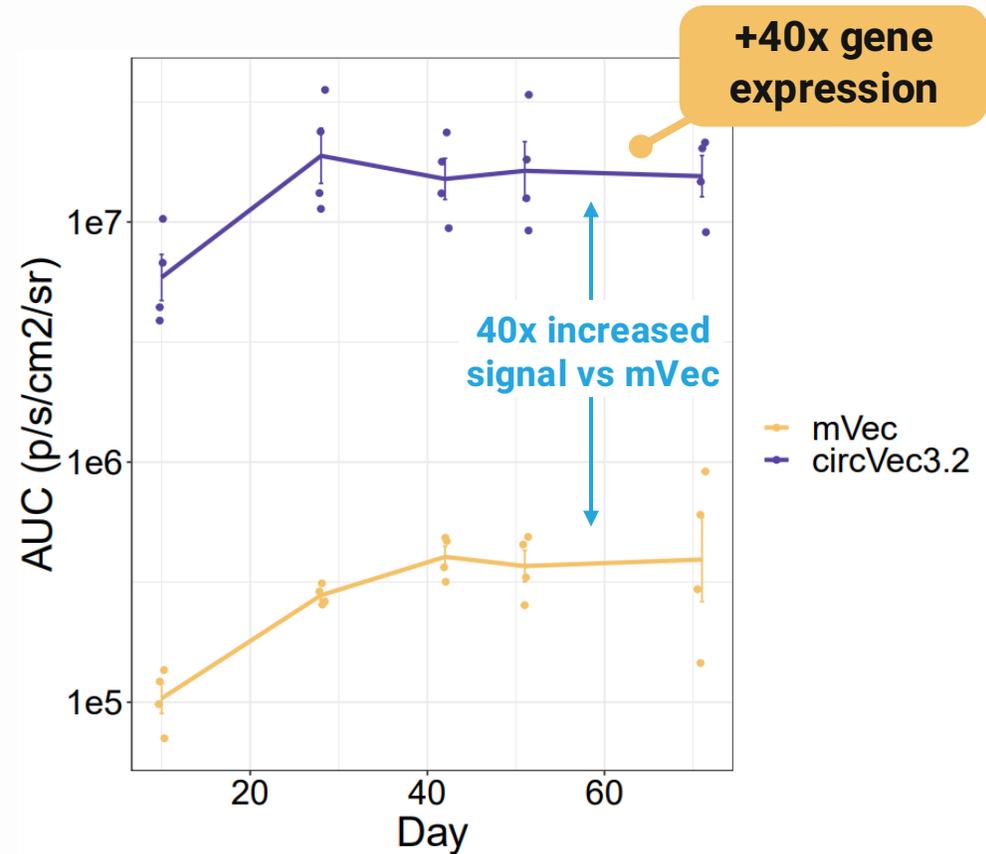
40-fold enhanced expression in heart for circVec-AAV vs. conventional mRNA-based AAV

AAV-mVec

AAV-circVec 3.2



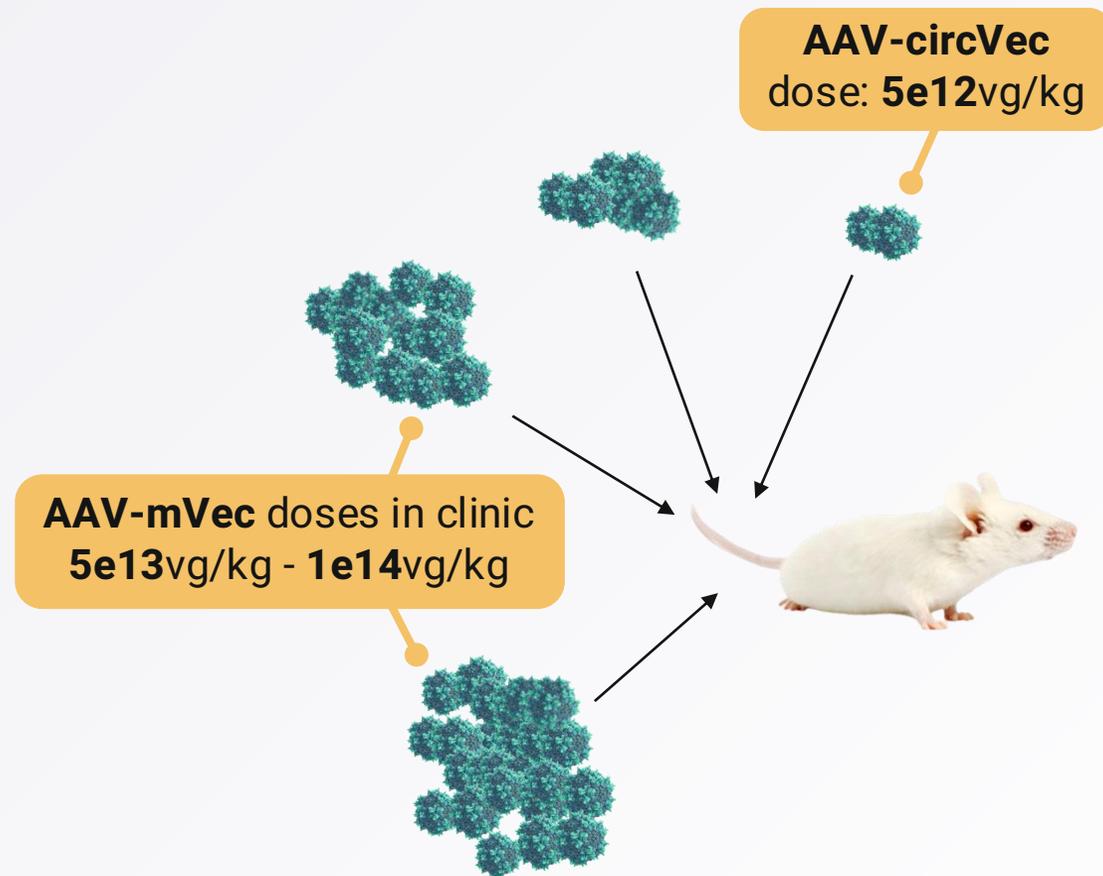
Gene expression quantification, f-luc IVIS signal



Dose-response: comparing the performance of circVec 3.2 and mVec across four dose levels

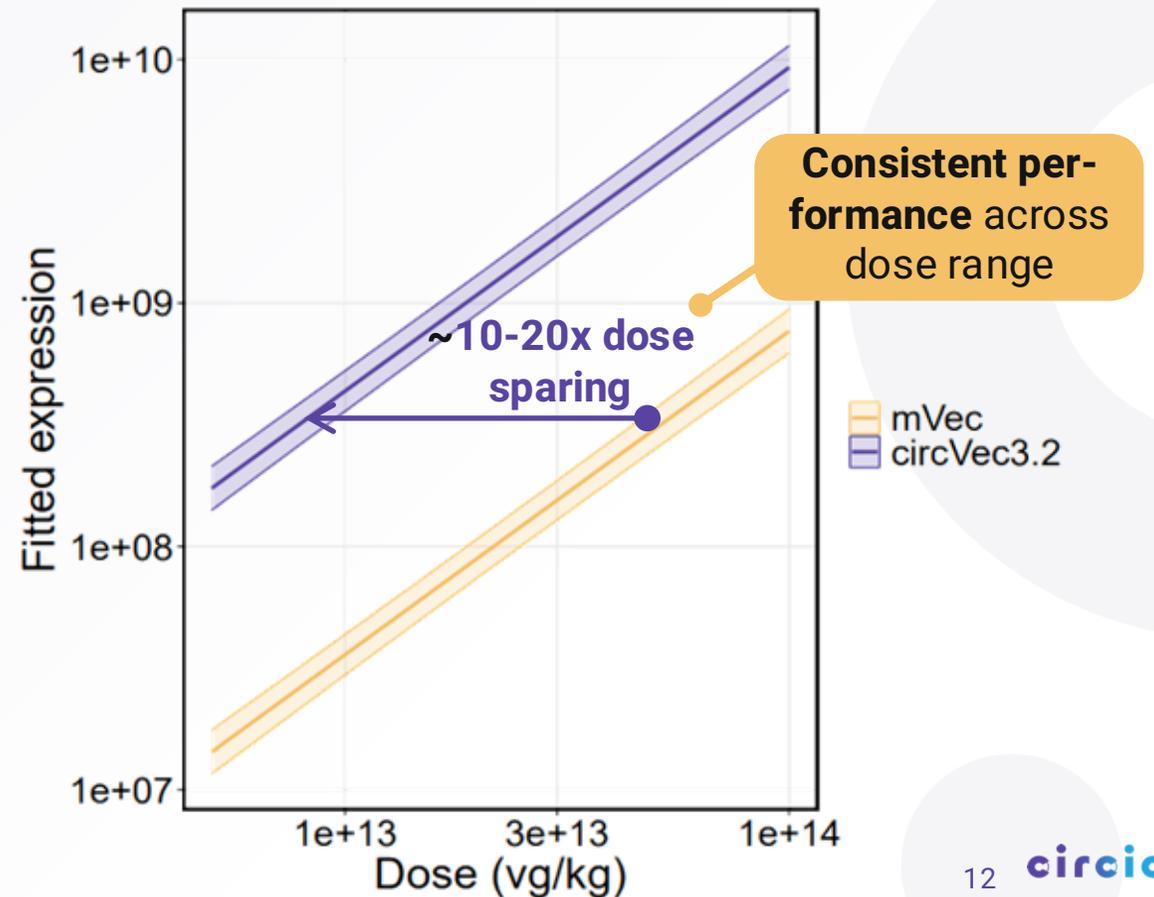
AAV circVec vs. mVec dose escalation study

Dose range from $5e12$ to $1e14$ vg/kg



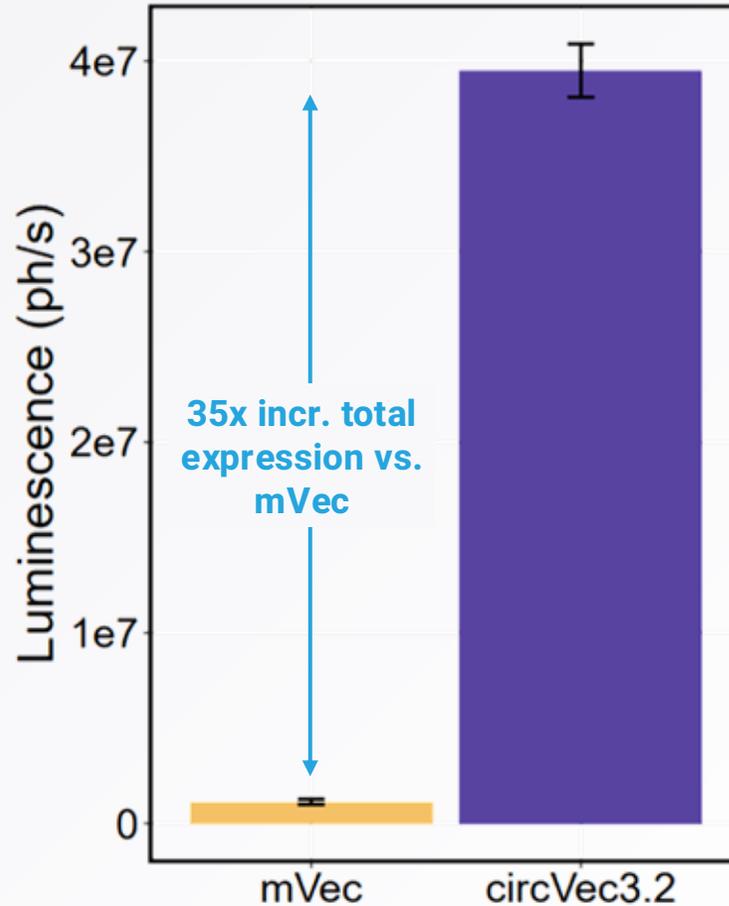
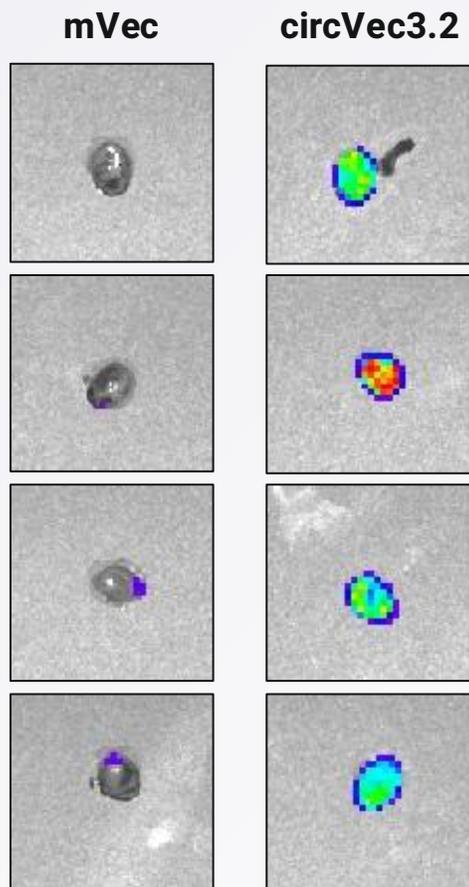
Gene expression level AAV circVec vs. mVec

Luminescence signal by dose, mixed model

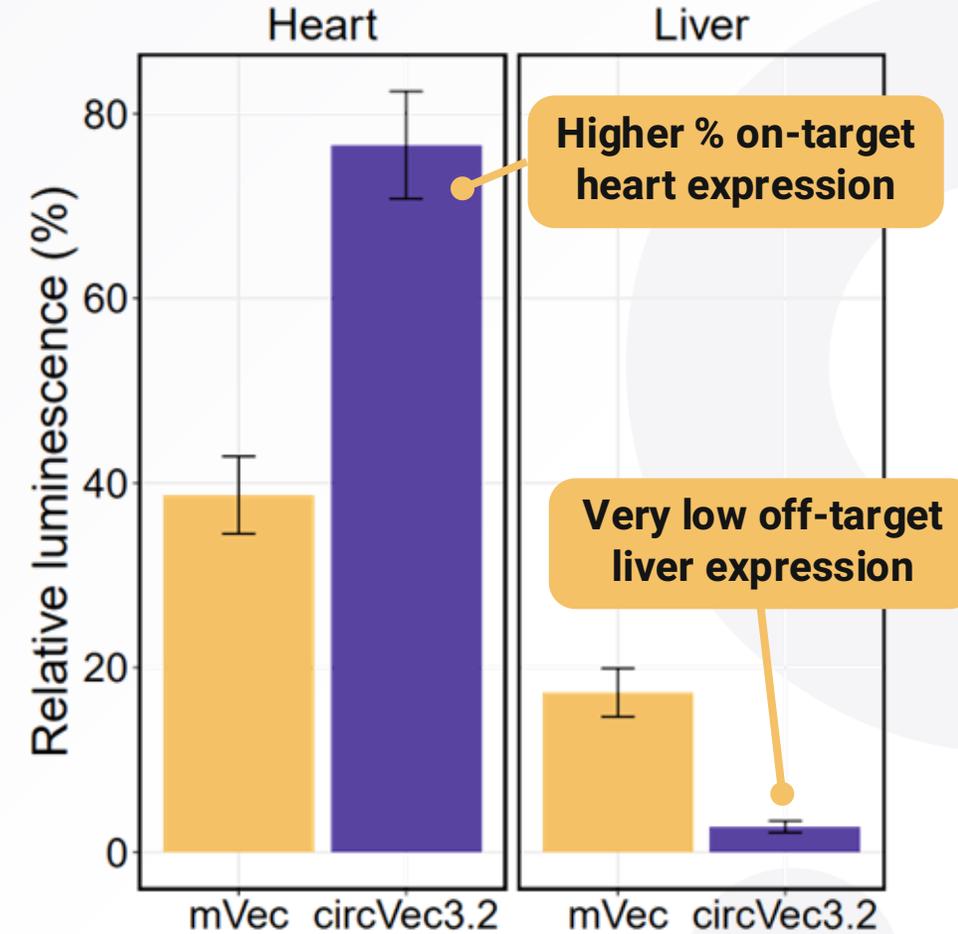


circVec shows increased on-target heart activity and substantially reduced off-target liver expression

Increased expression in heart, ex vivo tissue analysis week 10

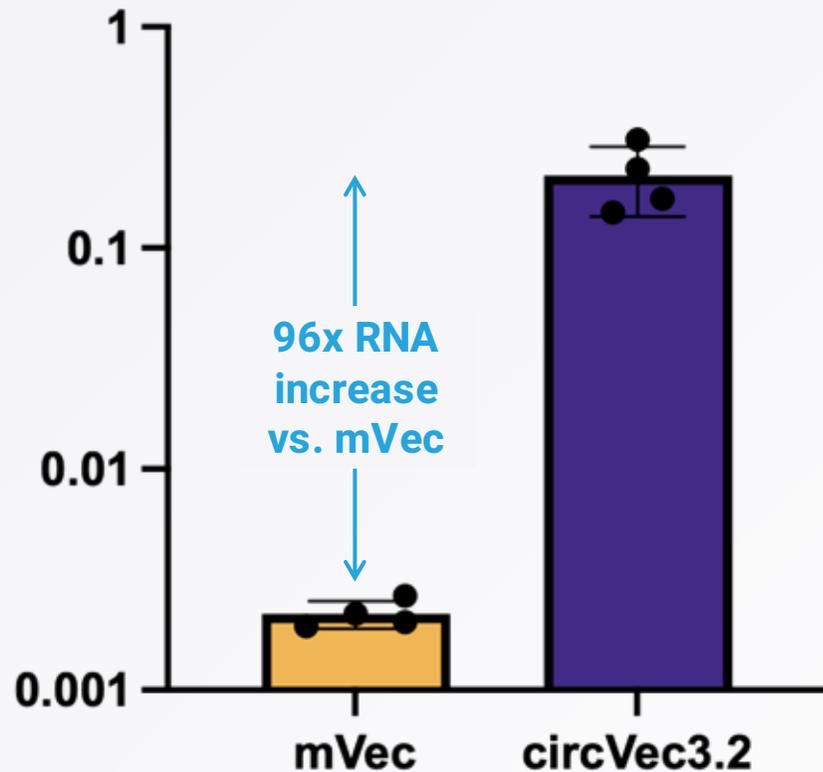


...and reduced off-target liver expression

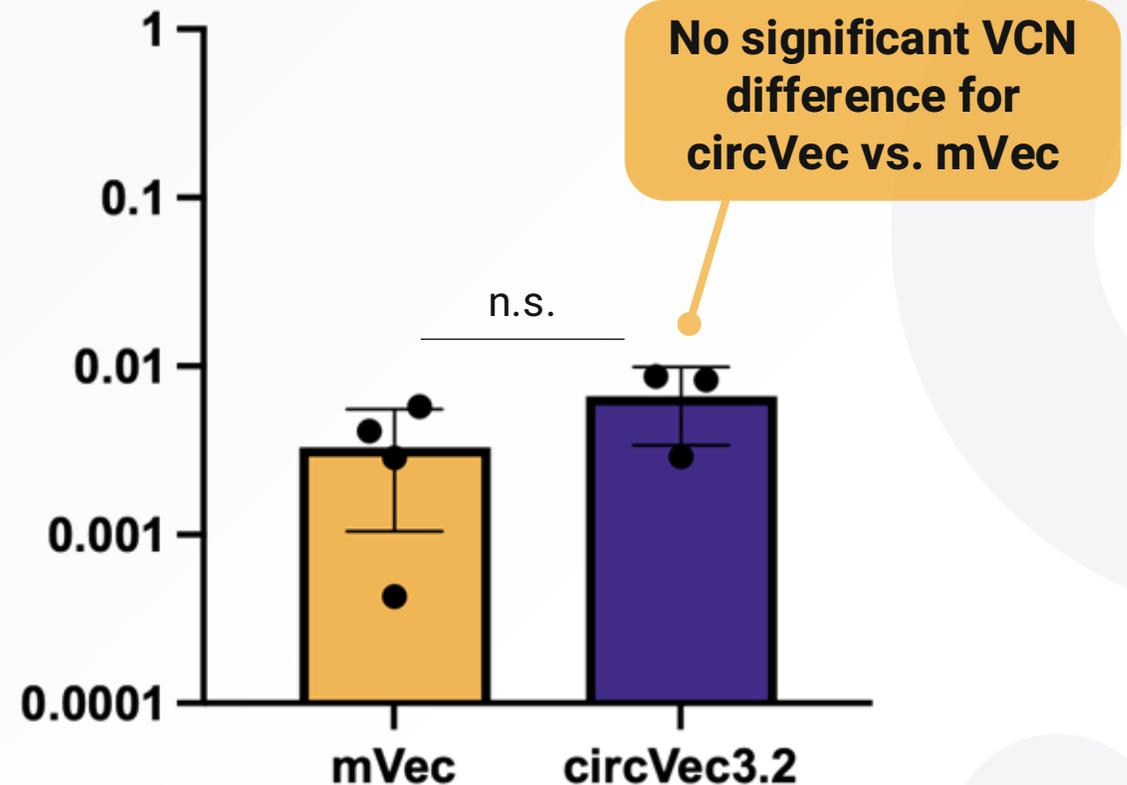


circVec advantage is driven by RNA transcript level, not AAV transduction or vector copy number

RNA expression in heart tissue, RT-qPCR



Vector Copy Number (VCN) in heart tissue, qPCR

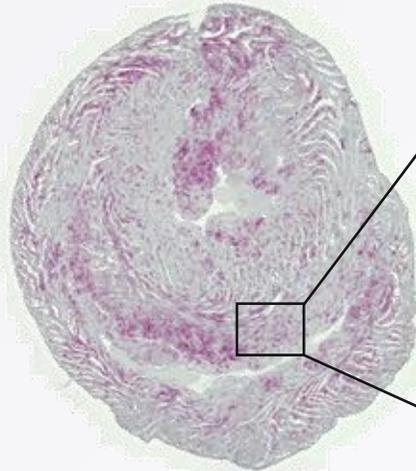


**Data from repeat study

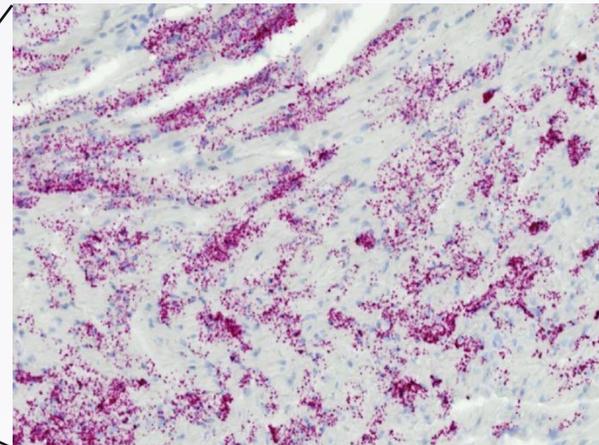
Low dose circVec-AAV achieves efficient circRNA expression in 80% of heart cells

RNA expression in heart, RNAscope* microscopy ex vivo tissue section, low dose

AAV-circVec 3.2

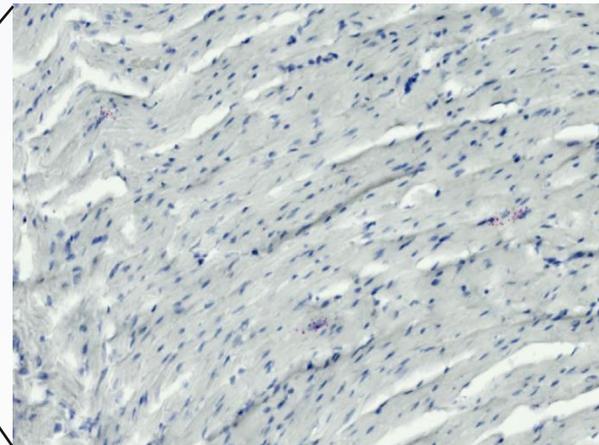
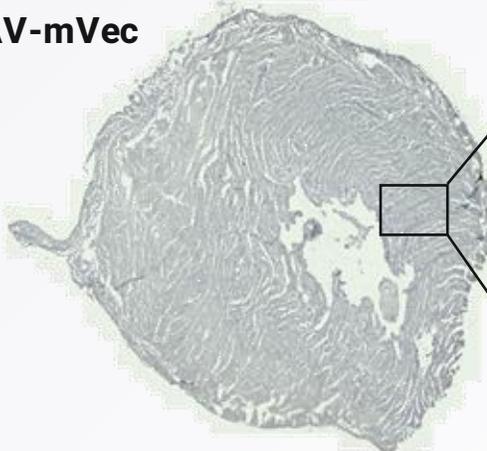


Blue: nuclei Violet: RNA transcripts



80% of heart cells positive for circRNA expression, substantial improvement vs. AAV benchmarks

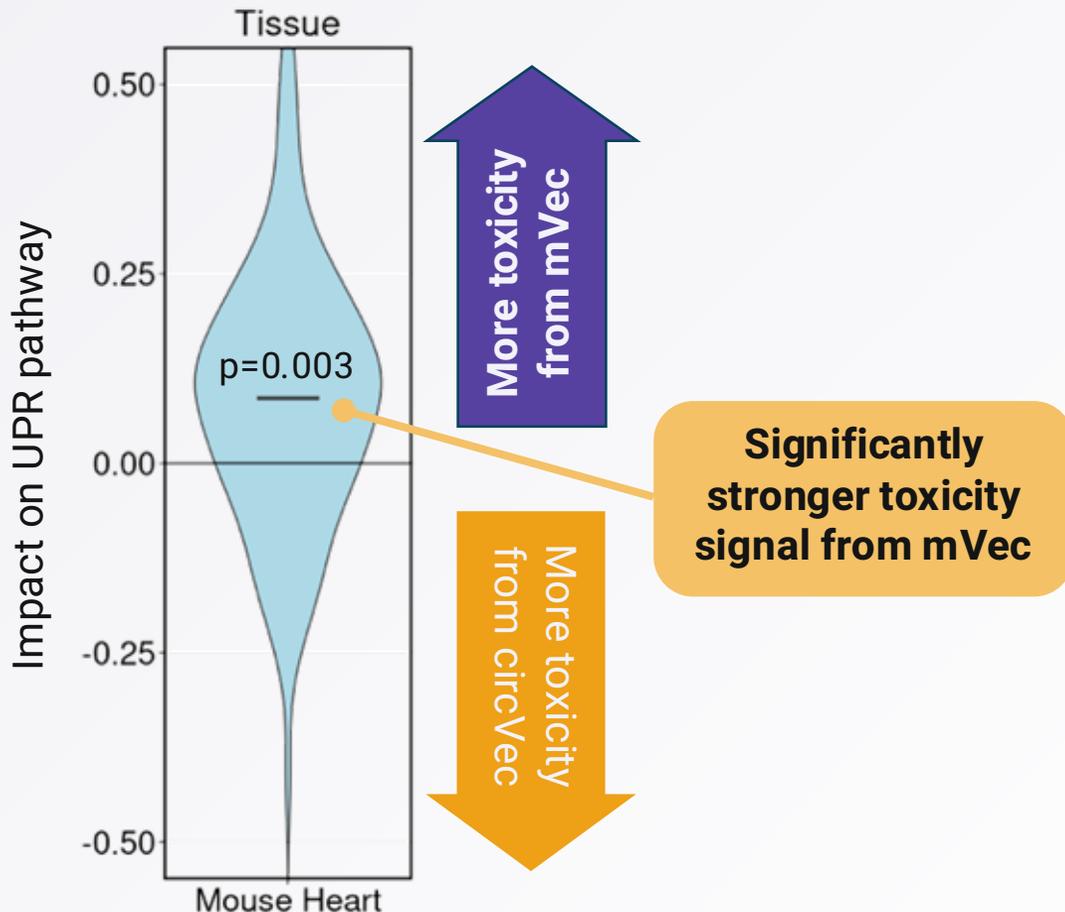
AAV-mVec



* RNAscope: single molecule detection of Firefly Luciferase RNA

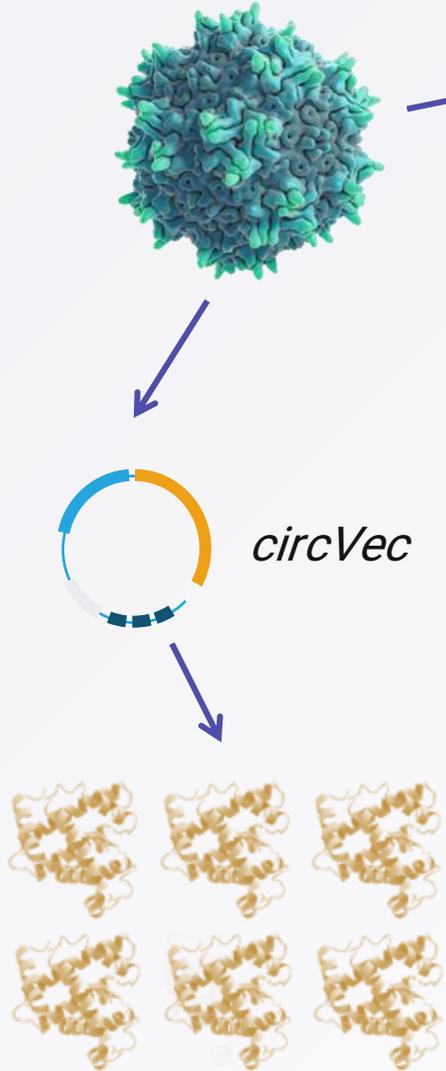
Reduced toxicity of circVec-AAV in heart, despite 40-fold higher gene expression

Cellular stress response, UPR pathway activation



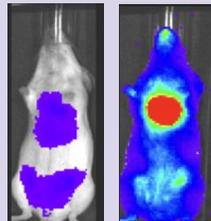
- **Unfolded Protein Response (UPR)** activation is a **major contributor to AAV toxicity** in patients
- AAV-circVec shows **less activation of UPR pathway in heart** than AAV-mVec at **same dose**
 - Despite 40x increased gene expression
 - Confirmed in various cell lines

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

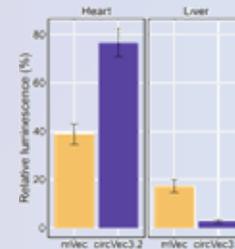


circVec-AAV compared to benchmark mVec-AAV:

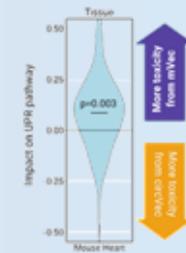
Expression



Specificity

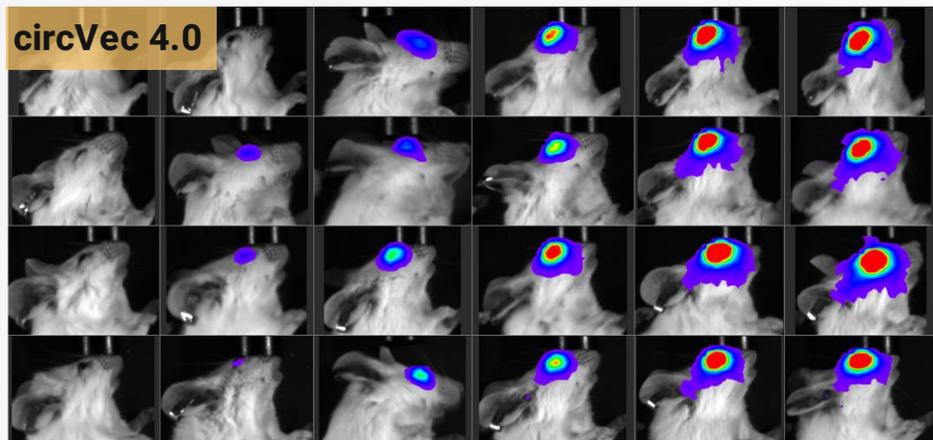
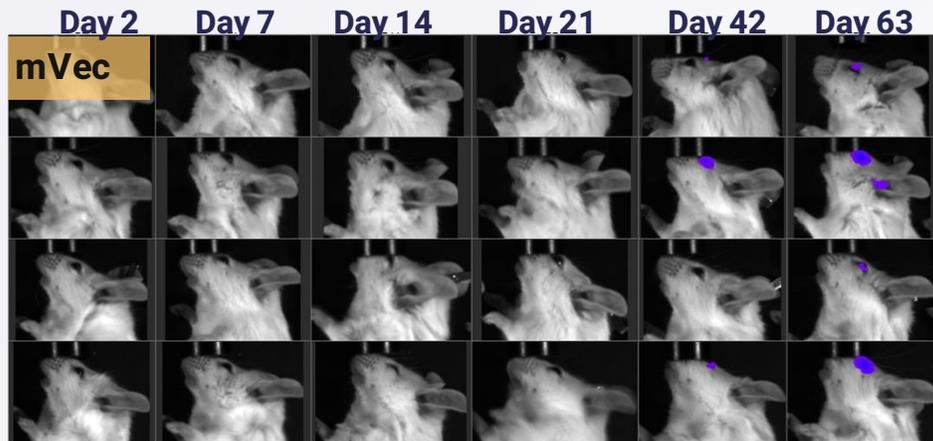


Toxicity



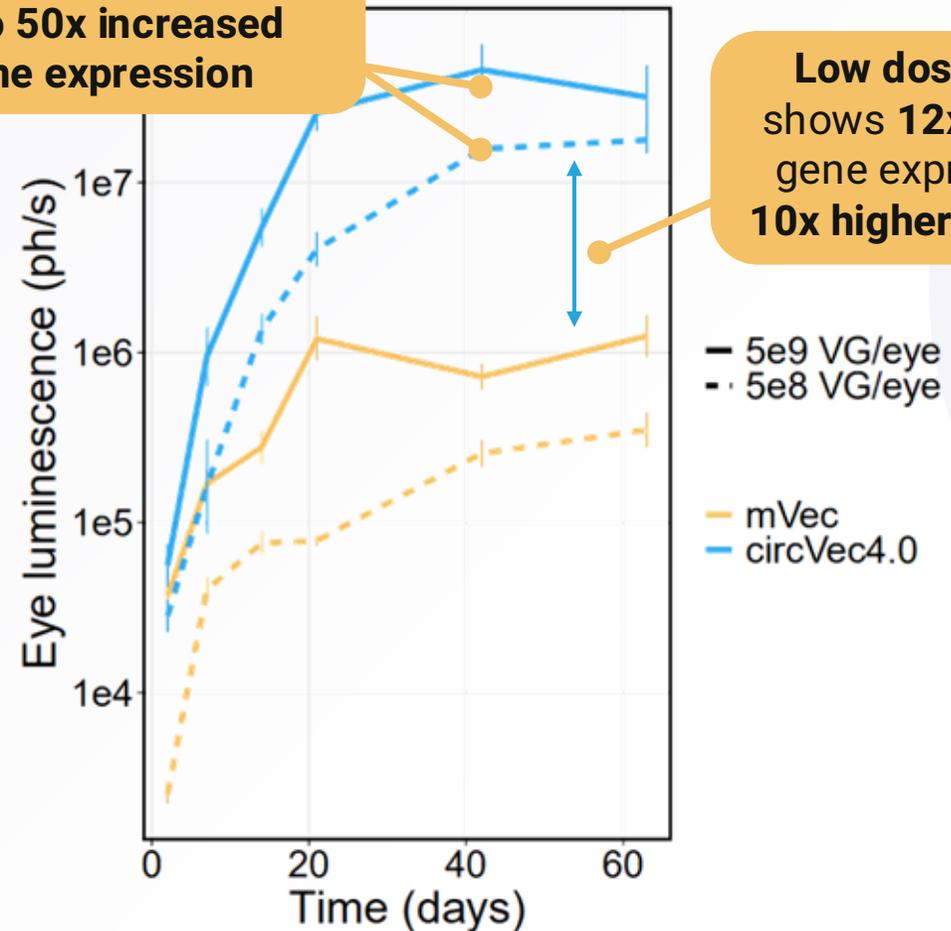
New in vivo data shows that circVec 4.0 can enhance AAV gene expression by up to 50x in eye

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



AAV-circVec approach is showing promising pre-clinical data in heart, eye and CNS



In vivo results

- Up to 40x increased activity for circVec 3.2/4.0
- 50% boost by circVec 4

- Up to 50x increased activity for circVec 4.0
- 3.2/4.0 testing ongoing

- >4x increased activity for circVec 2.1 (3.2/4.0 ongoing)
- 3.2/4.0 testing 1-2Q'26

Rationale

- Increase on-target expression
- Reduce systemic dose, → lower tox and cost

- Maximize local payload secretion
- Reduced local dose → less inflammation, cost

- Enhanced local CNS payload expression
- Open new AAV opportunities in challenging CNS diseases

Market opportunities

- Arrhythmic cardiomyopathy
n = 50-70,000
- Dilated cardiomyopathy
n = 40-60,000
- Chronic heart failure (non-genetic) n = >1 mill.

- Wet AMD
n = 7-8 mill.
- Retinitis pigmentosa
n = 200,000
- Best disease
n = 15-20,000

- Tay-Sachs, Krabbe Gaucher disease ++
- Neurodegenerative diseases
- Ongoing R&D collaboration with a big pharma

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

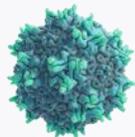


Heart, eye and CNS genetic disease

1 mill. patients in target diseases

Enhanced, safer and lower cost AAVs

Research collaboration with global pharma



Next Gen AAV

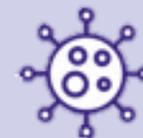
Cell therapy



Cancer, autoimmune disease

LNP: DNA format, redosable

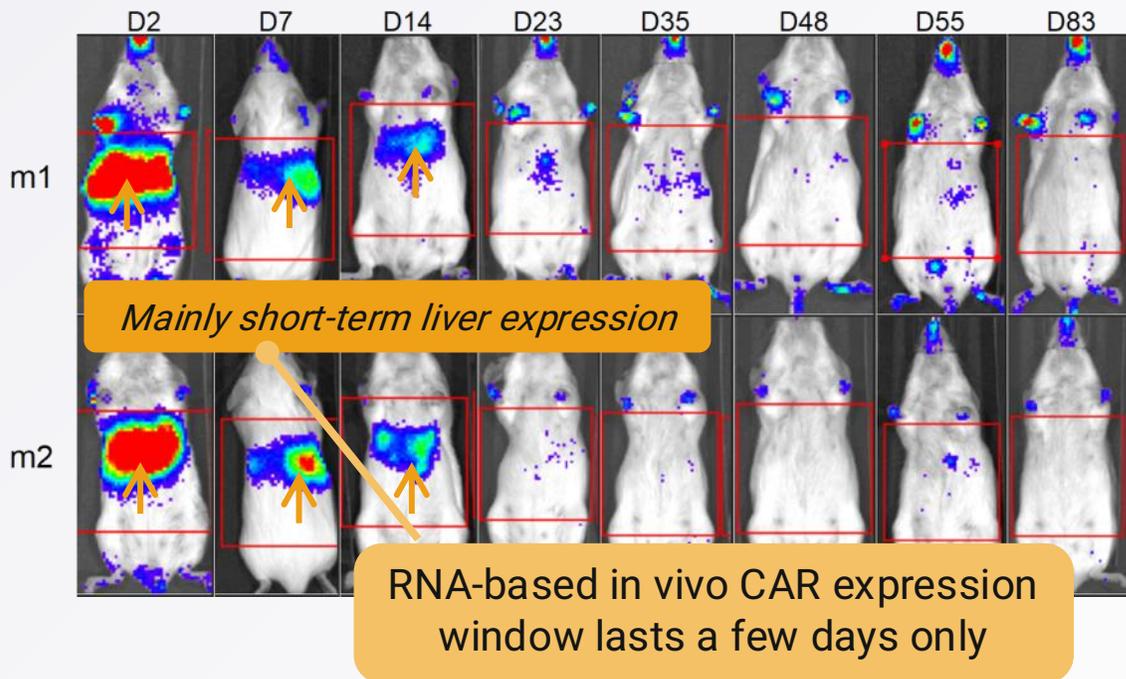
Very large patient population, only autologous options available today



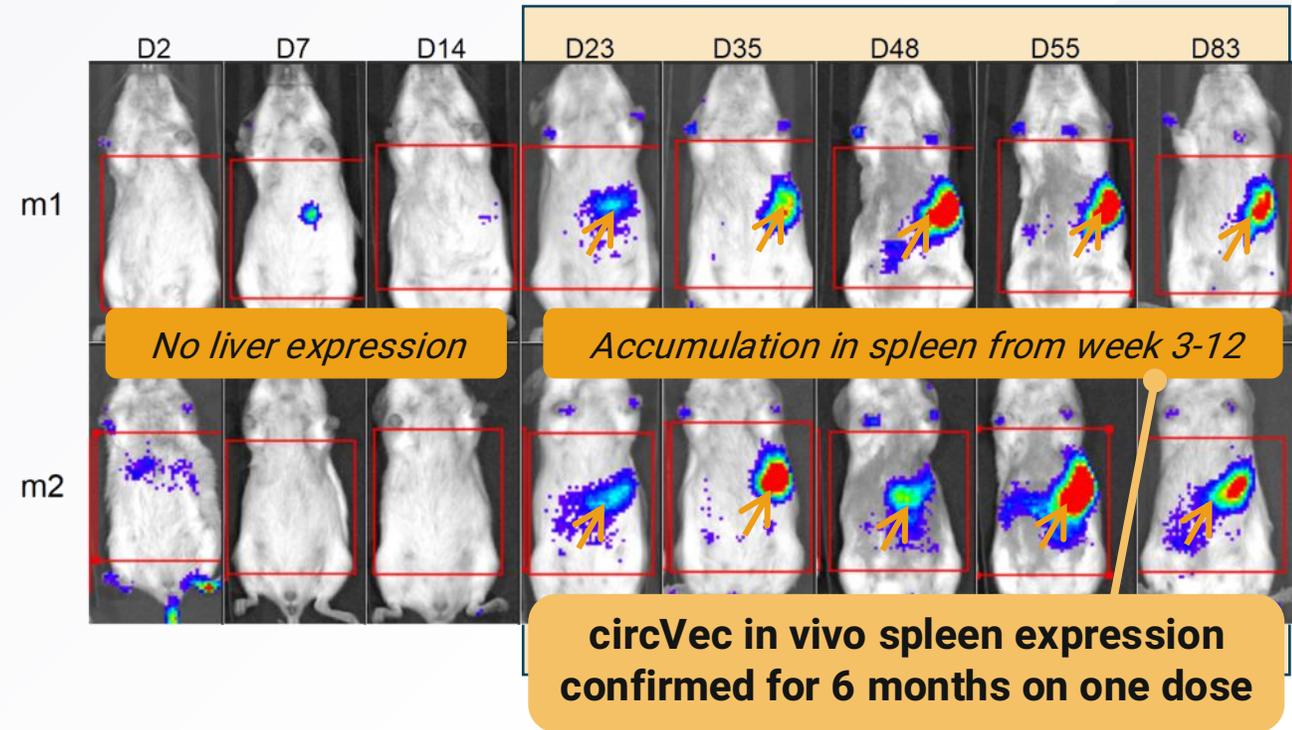
In vivo CAR

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

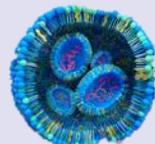
LNP-mVec (mRNA), luminescence
Systemic I.V. delivery, single dose on Day 0



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



Non-viral synthetic
DNA vector format



LNP-delivery
formulation



circVec 2.1

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

In vivo CAR modalities - duration



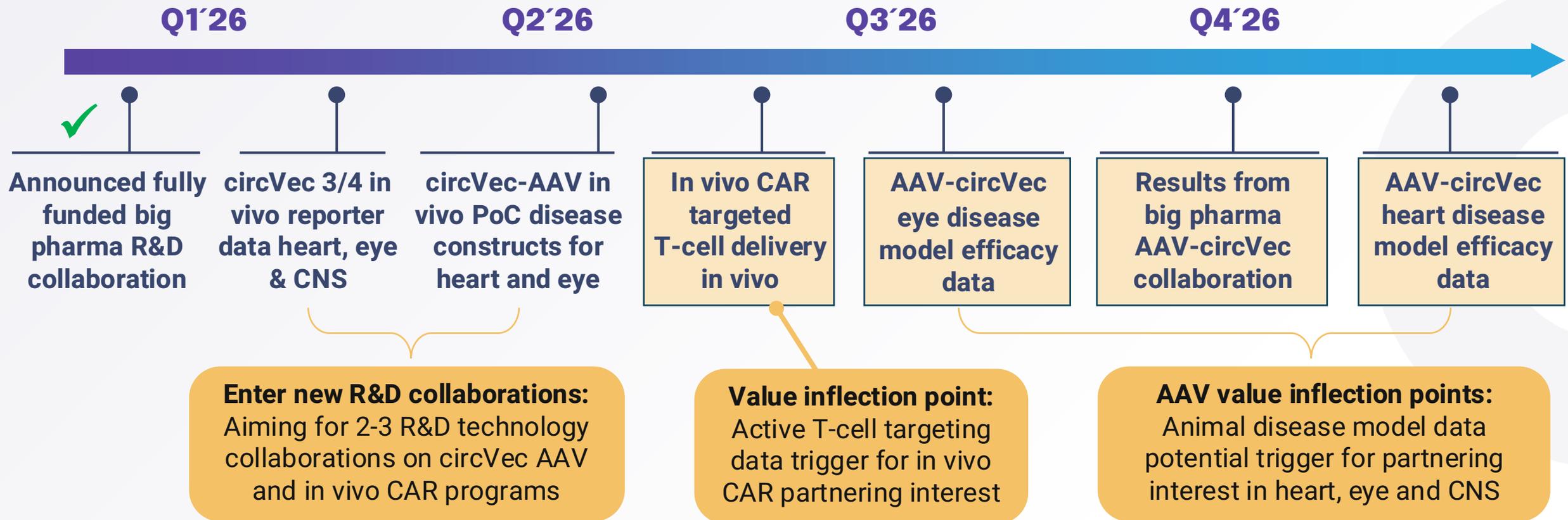
circVec-DNA benefits

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

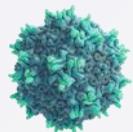
Therapeutic applications

- **Cancer**, e.g. lymphoma
 - Ex vivo CAR-T effective, but expensive
 - Lentiviral risk of secondary malignancies
 - RNA in vivo CAR not sufficient duration
- **Autoimmune disease**, e.g. Lupus
 - secondary opportunity

Rich pipeline of R&D and BD milestones next 12 months



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

Further reading – Circio in industry and scientific press

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](#)

Pivoting To RNA

with Circio's Dr. Erik Digman Wiklund

Ep. 217

Business of Biotech



CITELINE
a norstella company

IN VIVO

CITELINE COMMERCIAL

In Vivo >> Market Intelligence

Circio's Vision For Long-Lasting Nucleic Acid Therapeutics

16 Dec 2024 • By [David Wild](#)



DENATURED

Programmable RNA 2.0

Beyond the First mRNA Revolution

February 5, 2026 | 1 min read | Jennifer Smith-Parker, BioSpace Insights

- Jennifer Smith-Parker
Director of Insights, BioSpace
- Erik Digman Wiklund
CEO, Circio
- Jacob Becraft
Co-founder and CEO, Strand Therapeutics



Cell & Gene Bioprocessing Technology & Manufacturing

Bringing New Ideas to AAV Gene Therapy

As safety concerns and commercial doubts threaten the AAV gene therapy field, new technologies may offer a “well-rounded” solution.

By Erik Wiklund | 11/20/2025 | 3 min read | Discussion

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.

News > Drug Development

Opinion: Circular RNA Will Soon Replace mRNA in Biopharma

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