circio

The leader in circular RNA expression systems

R&D and corporate update
26 February 2026

Human circRNA was first described by Circio scientists

Dr Thomas B Hansen

Dr Erik D Wiklund

nature 8,000 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 1,100 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

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

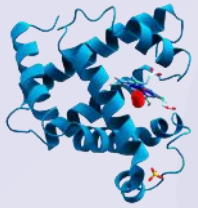
Lilly → ORNA

M&A $2.4b

RIBOX THERAPEUTICS → **First-in-man circRNA, March´25**

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 expertise, IP & know-how covering circVec

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

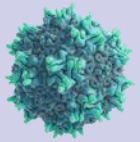
Gene therapy

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

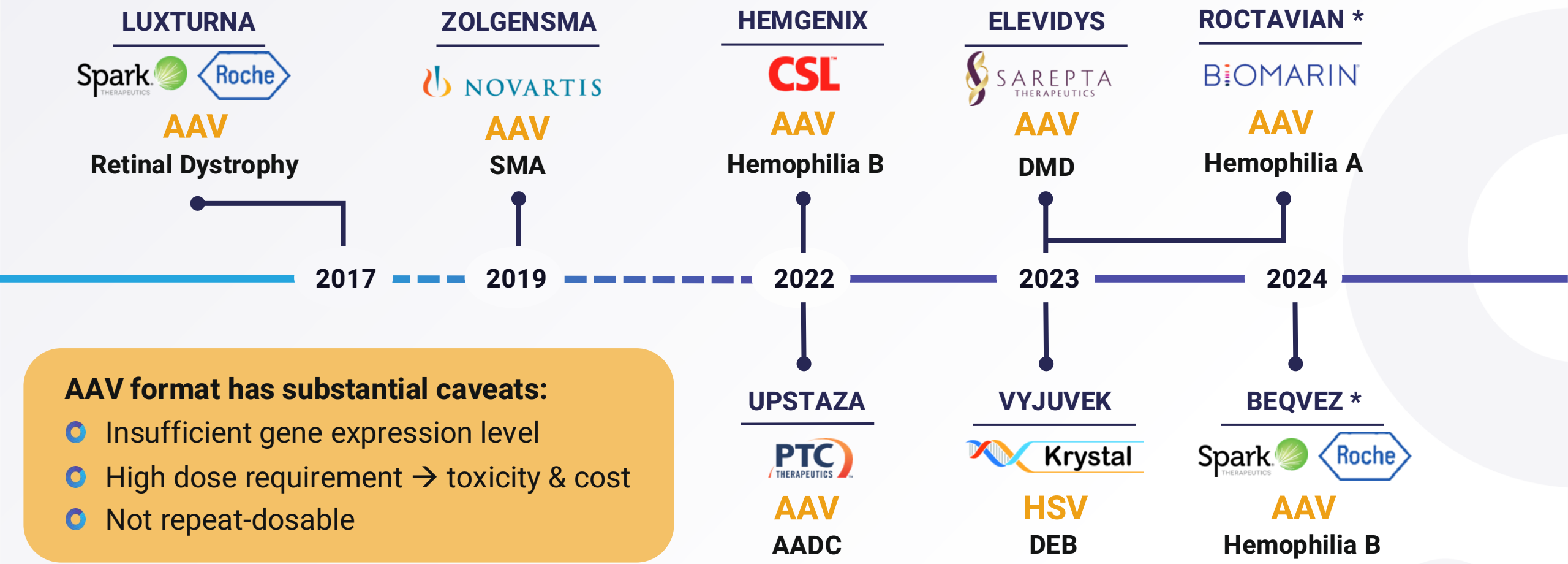
Cancer, autoimmune disease

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:

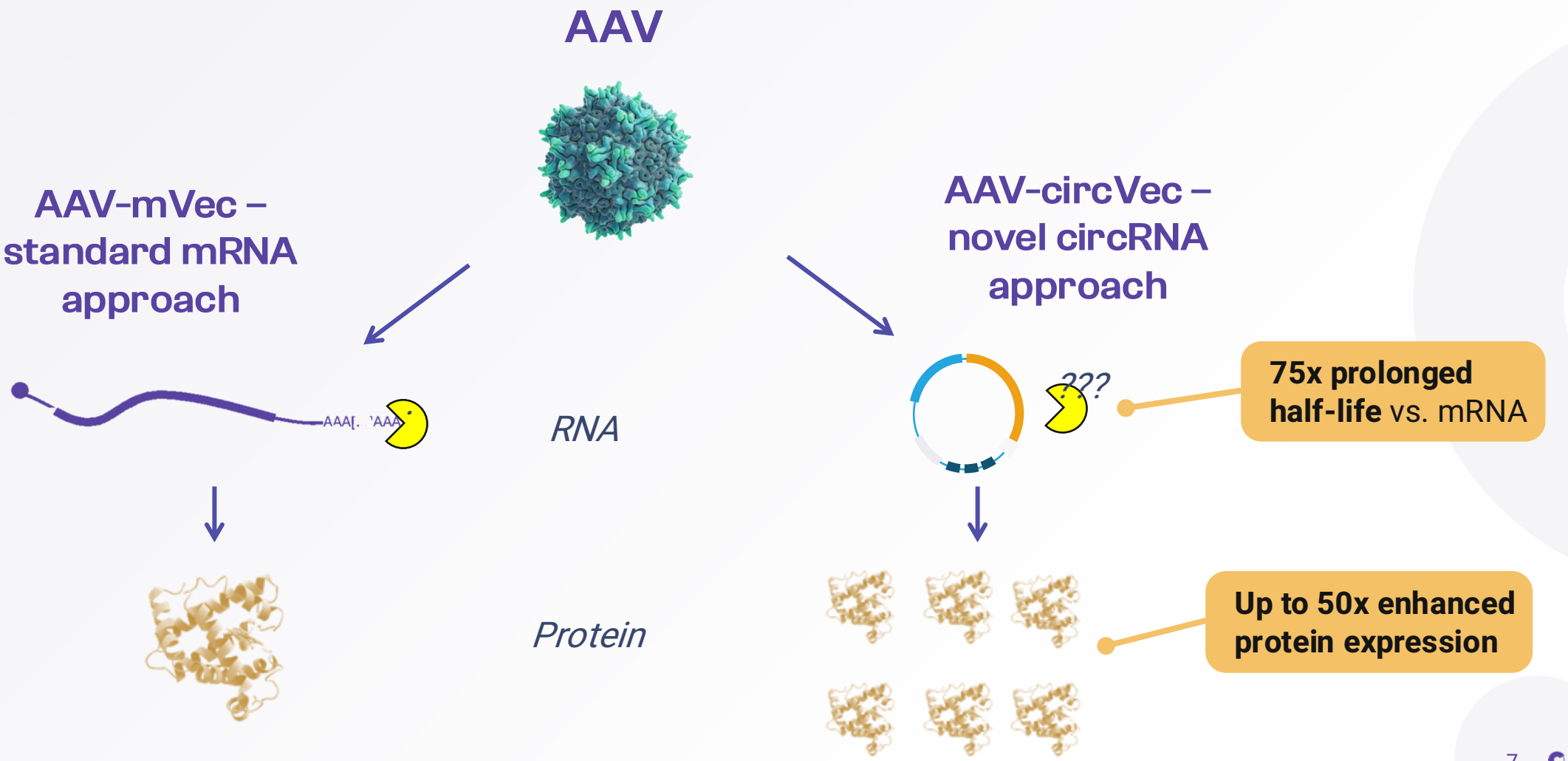
- Insufficient gene expression level
- High dose requirement → toxicity & cost
- Not repeat-dosable

AAV: Adeno-Associated Virus, currently best known vector for long-term protein expression in humans

* Not longer commercially available

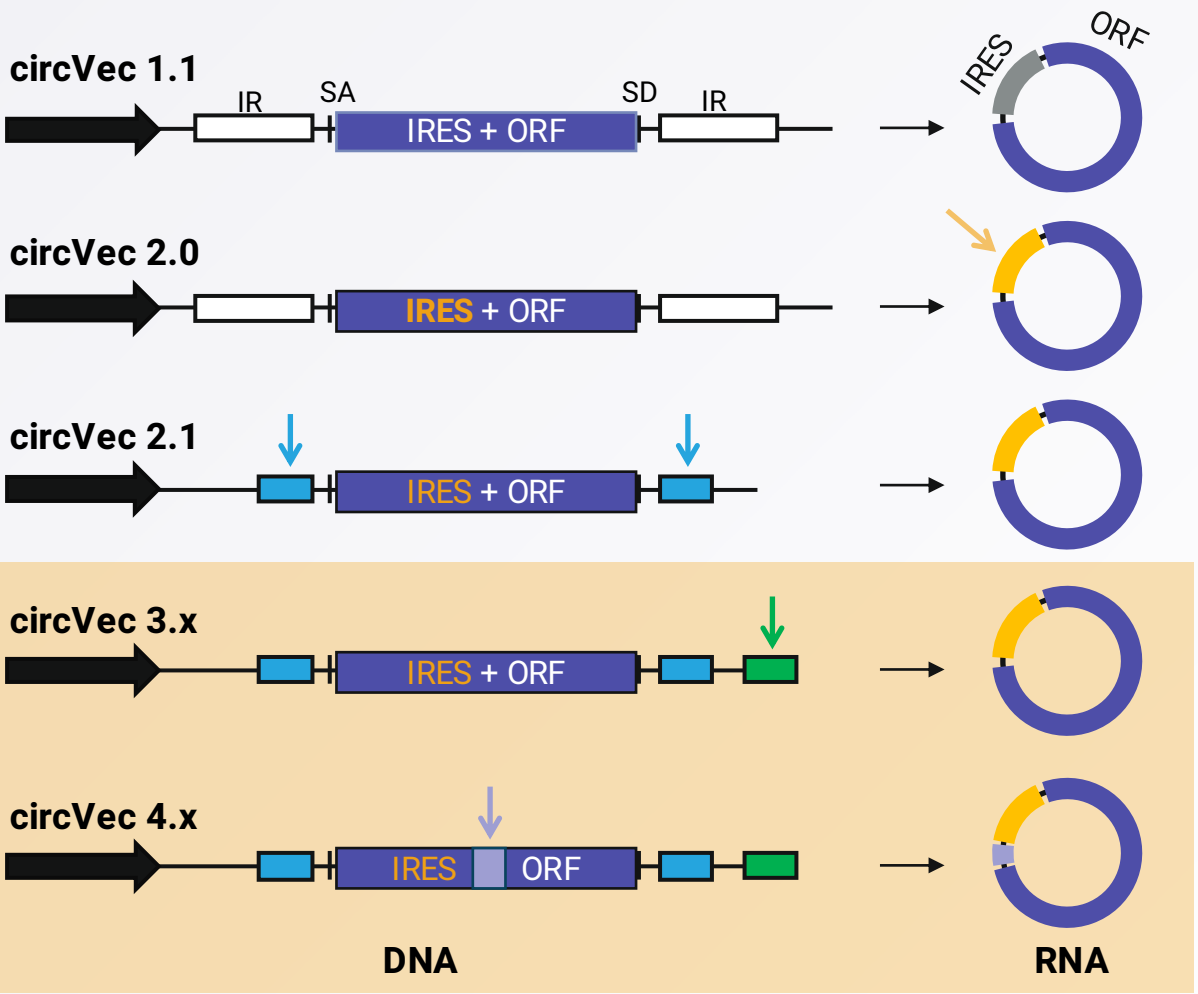
circVec

Circio´s unique circRNA-based gene expression platform can enhance AAVs

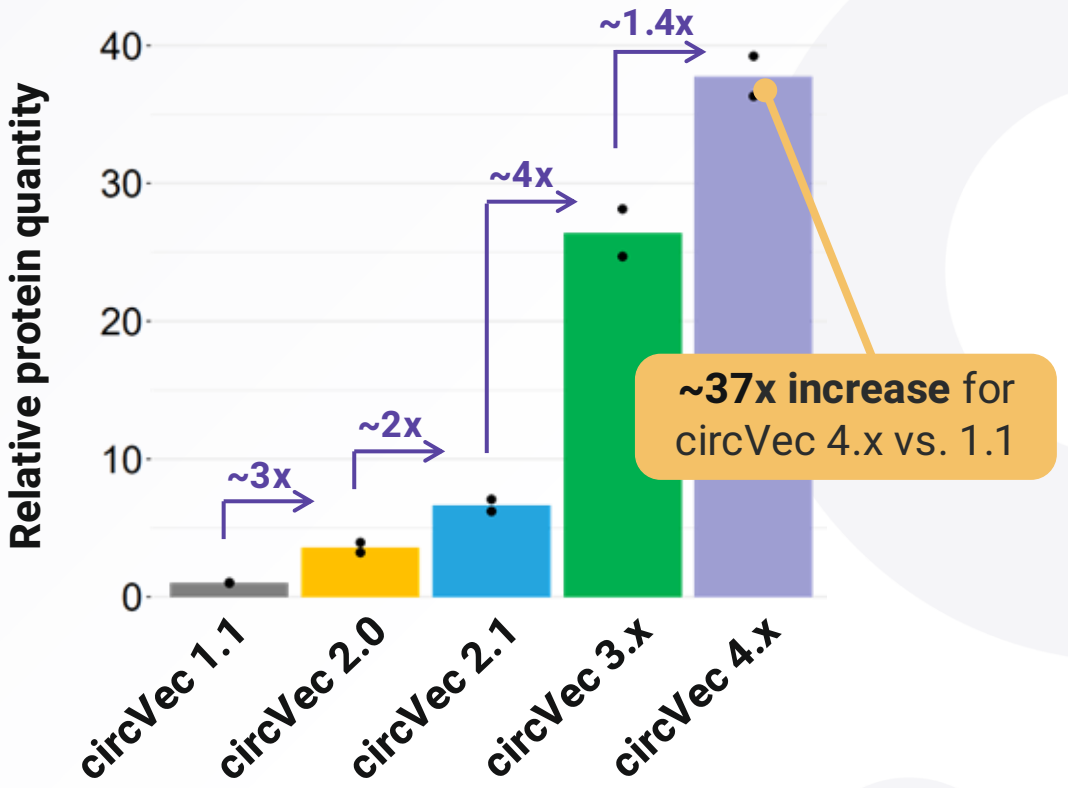


circVec construct design and evolution from Gen 1 → 4

circVec generation 1.X – 4.X, design schematics

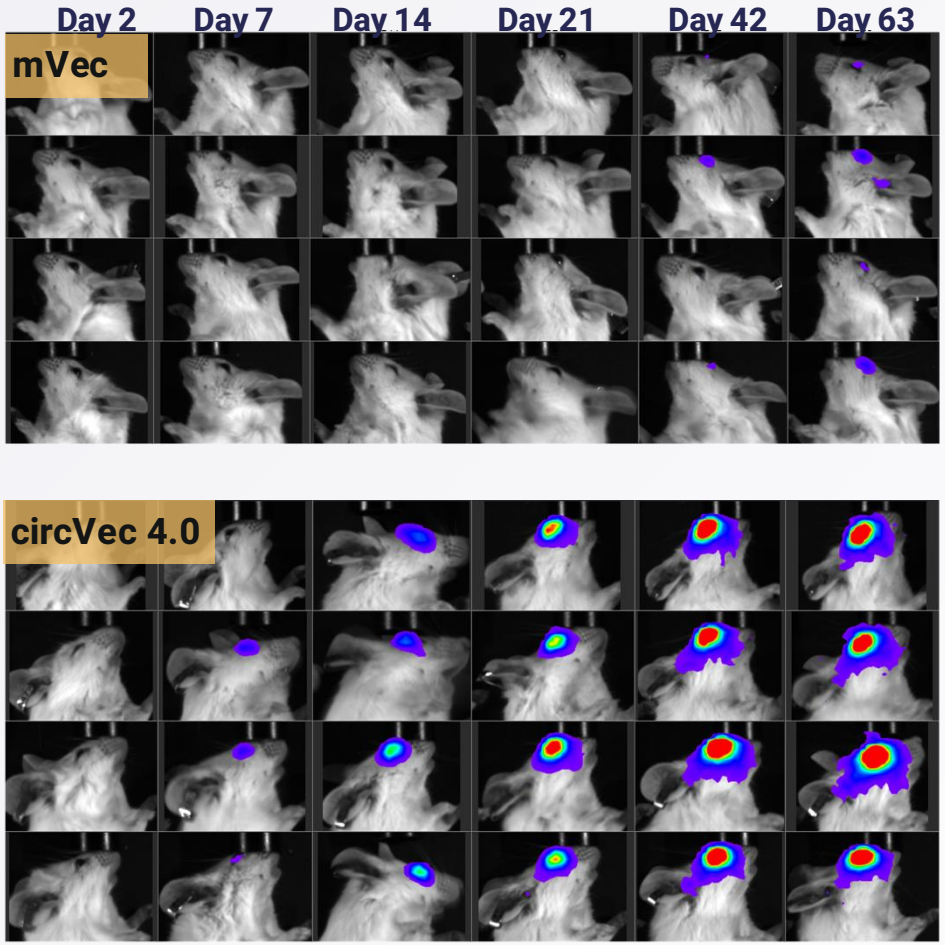


circVec protein quantification, Western blot



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

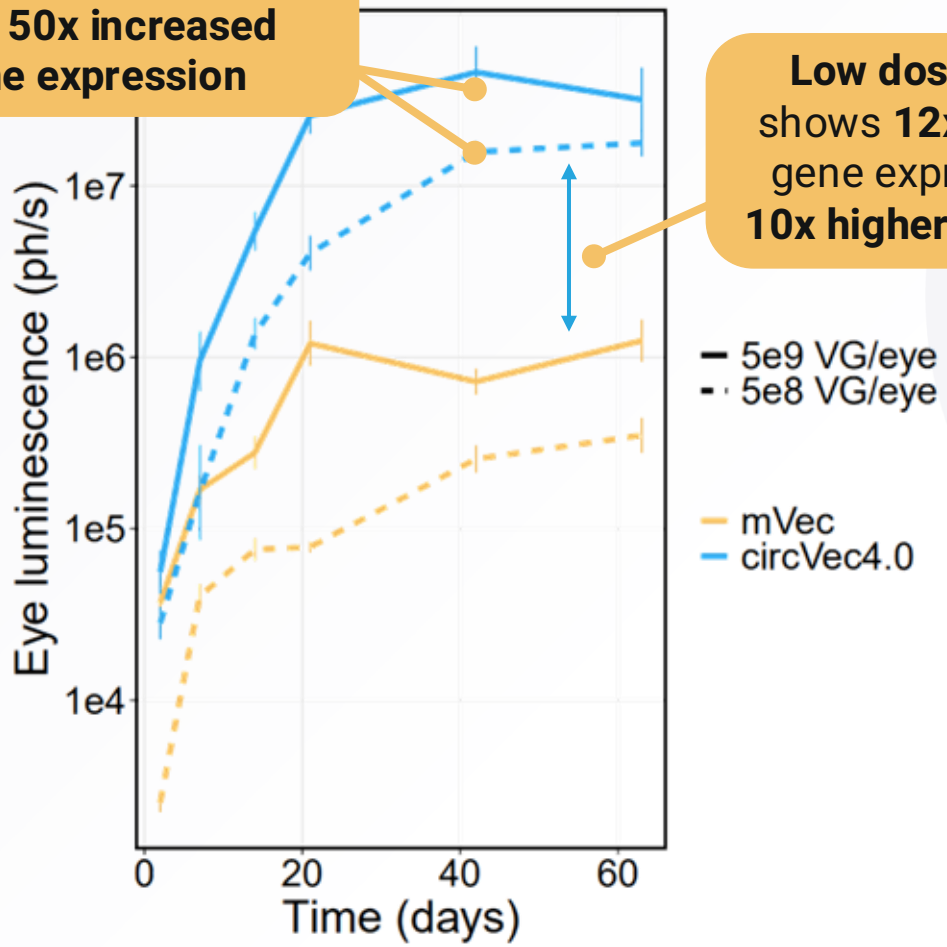
IVIS images, low dose mice (5e8 VG/eye)



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

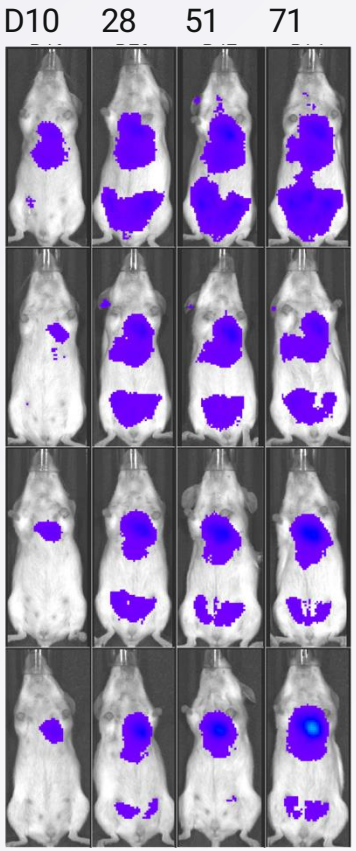
AAV-circVec vs. -mVec: **up to 50x increased gene expression**

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

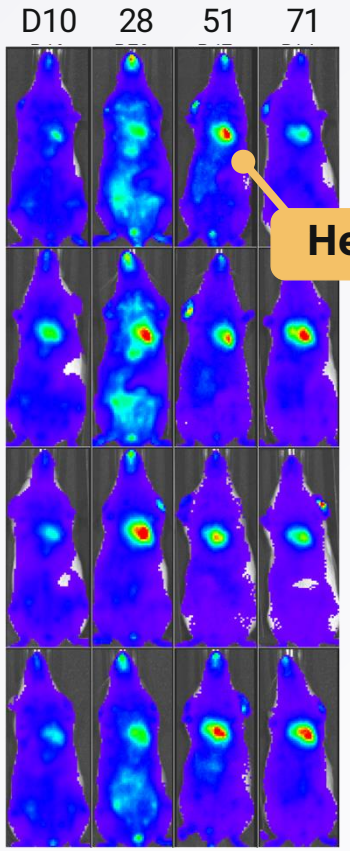


2025 RECAP: circVec 3.2 consistently shows 40x enhanced AAV gene expression in heart

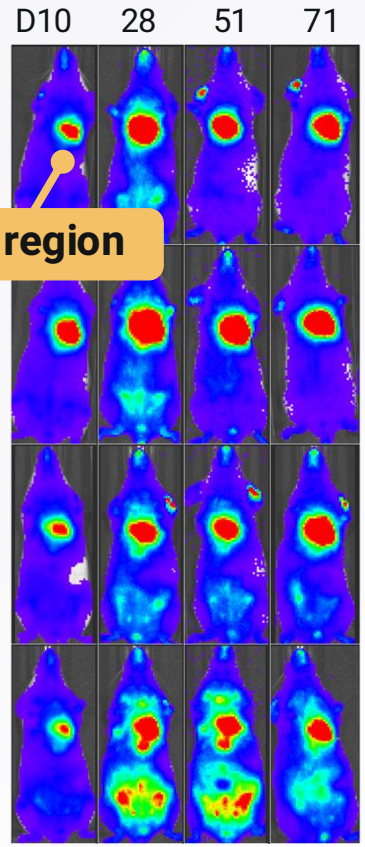
AAV-mVec



AAV-circVec 2.1

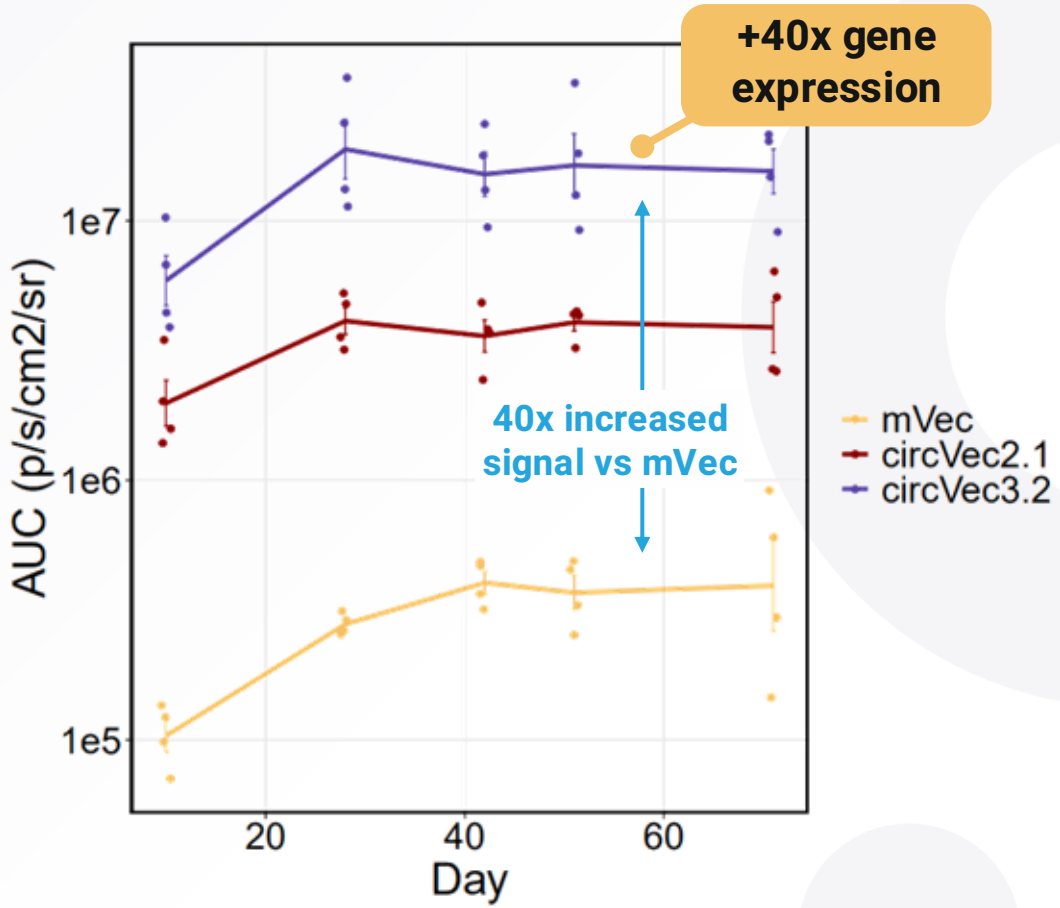


AAV-circVec 3.2



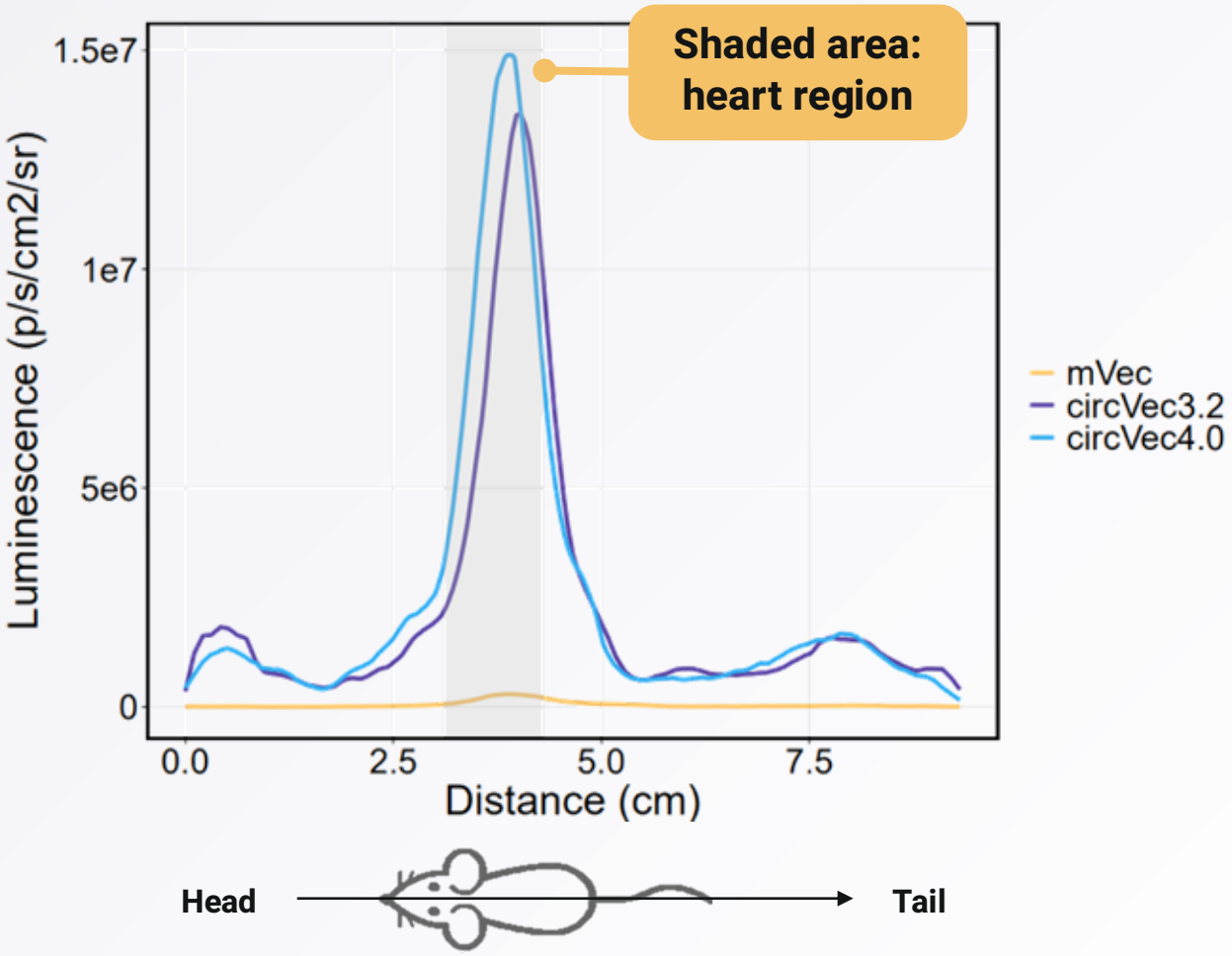
Heart region

Gene expression quantification, IVIS signal in heart

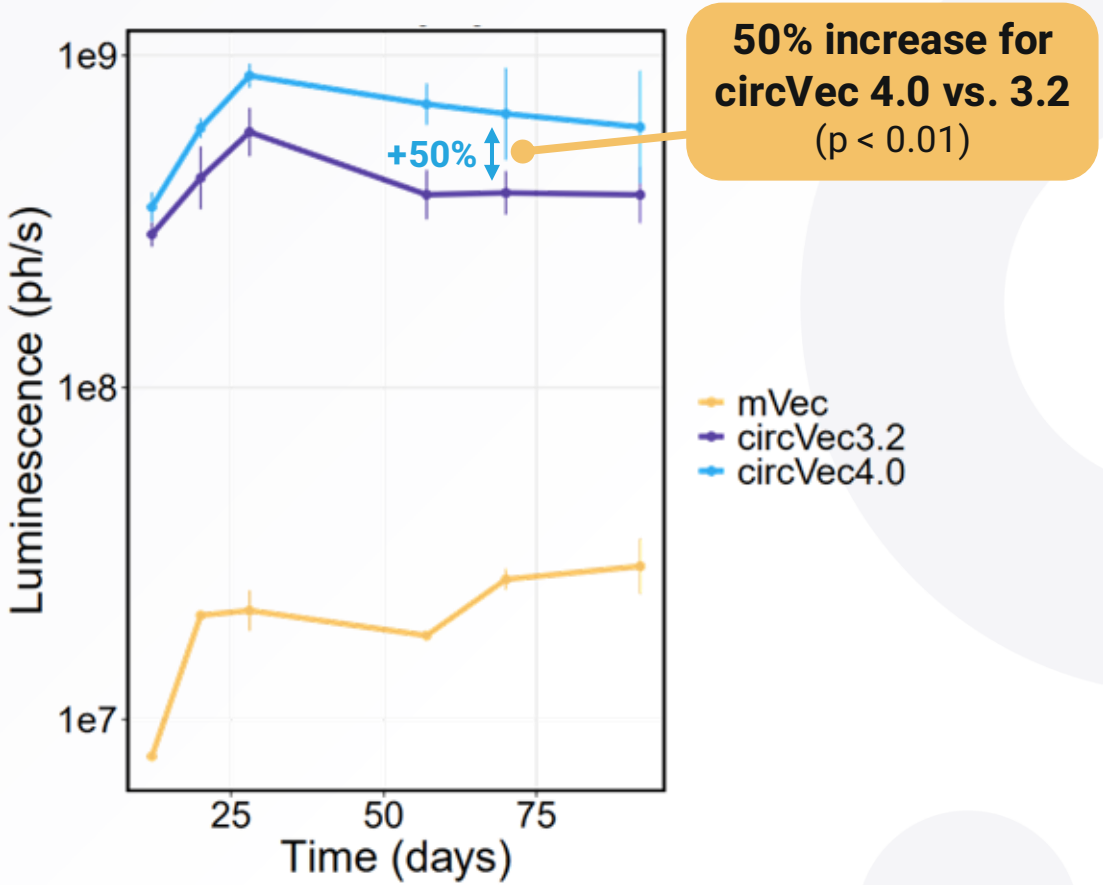


Heart data has been reproduced from scratch: consistent circVec 3.2 → 4.0 performance

Luminescence profile, across mouse body

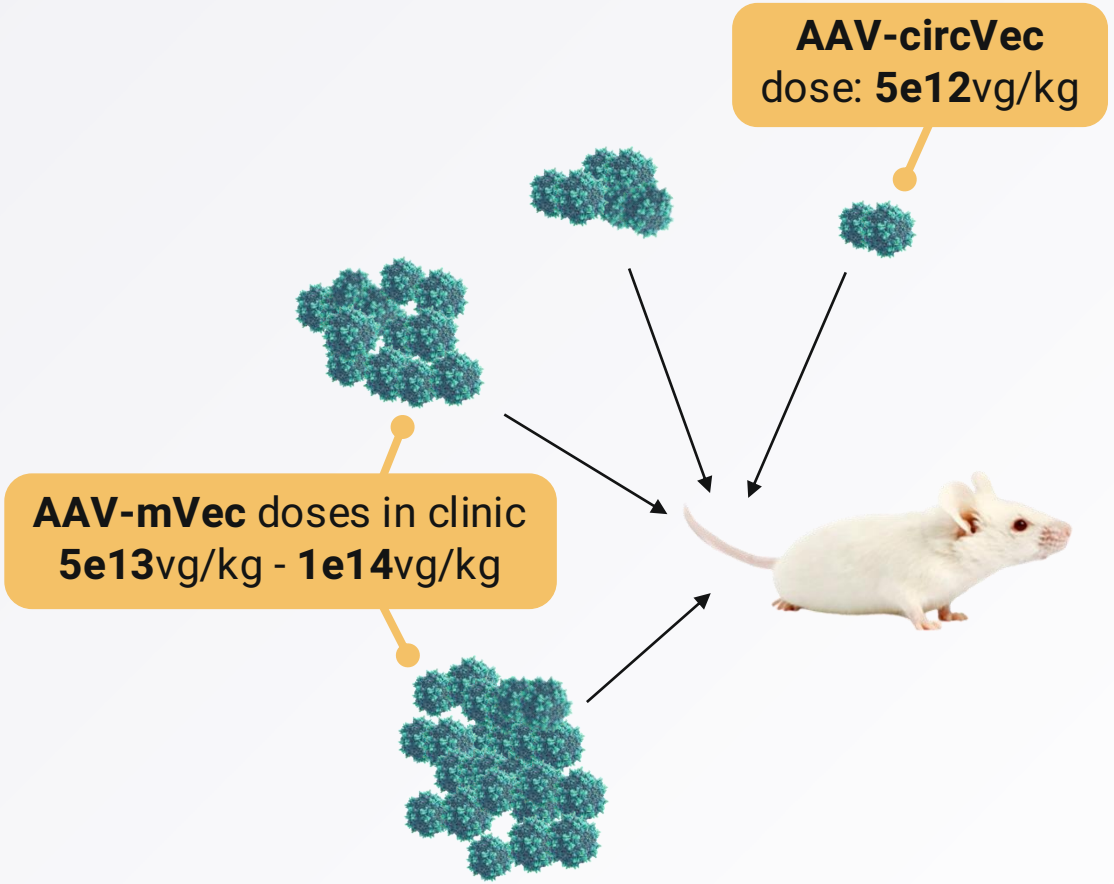


Quantification, body luminescence

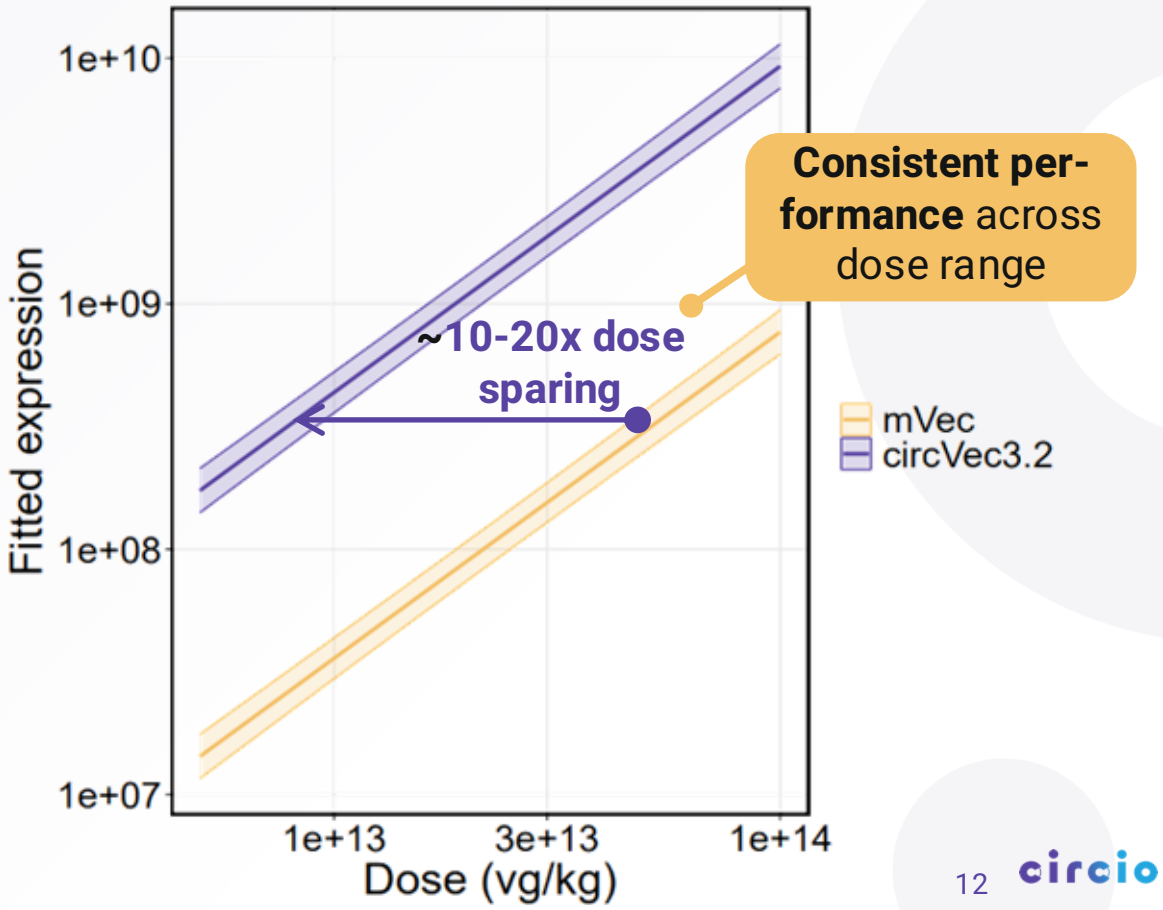


Dose-response: comparing the performance of circVec 3.2 and mVec across four dose levels

AAV circVec vs. mVec dose escalation study
Dose range from 5e12 to 1e14 vg/kg

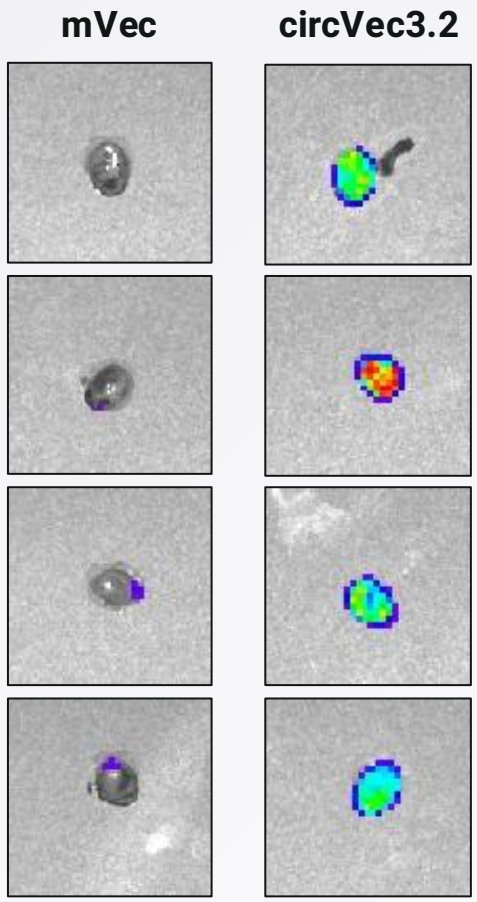


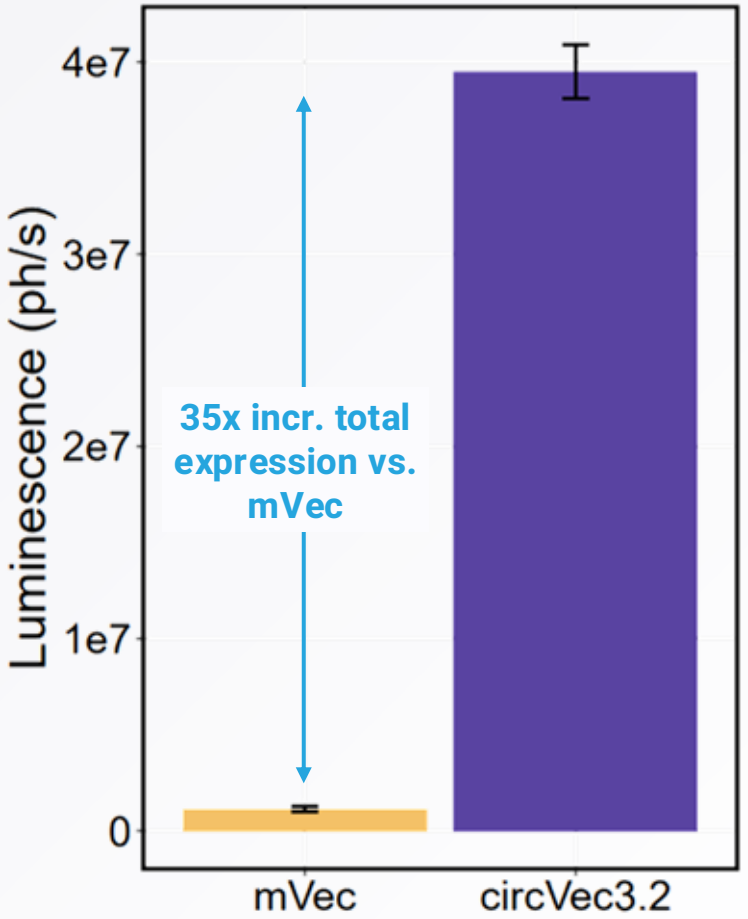
Gene expression level AAV circVec vs. mVec
Luminescence signal by dose, mixed model



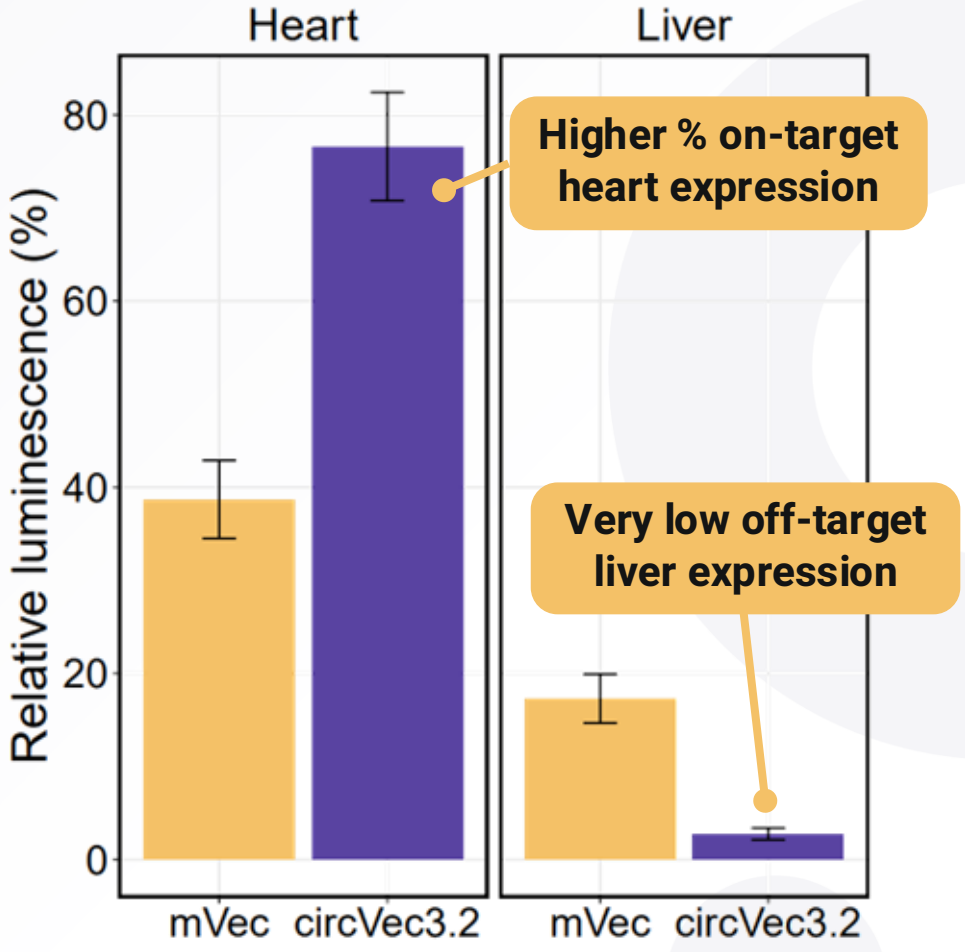
circVec shows increased on-target heart activity and substantially reduced off-target liver expression

Increased expression in heart, ex vivo tissue analysis week 10



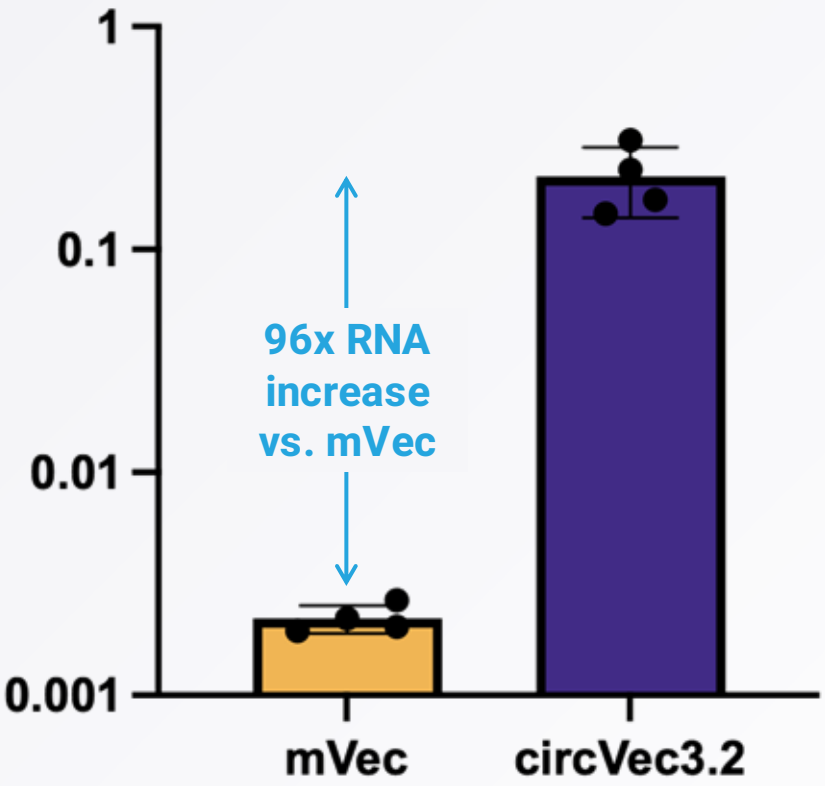


...and reduced off-target liver expression

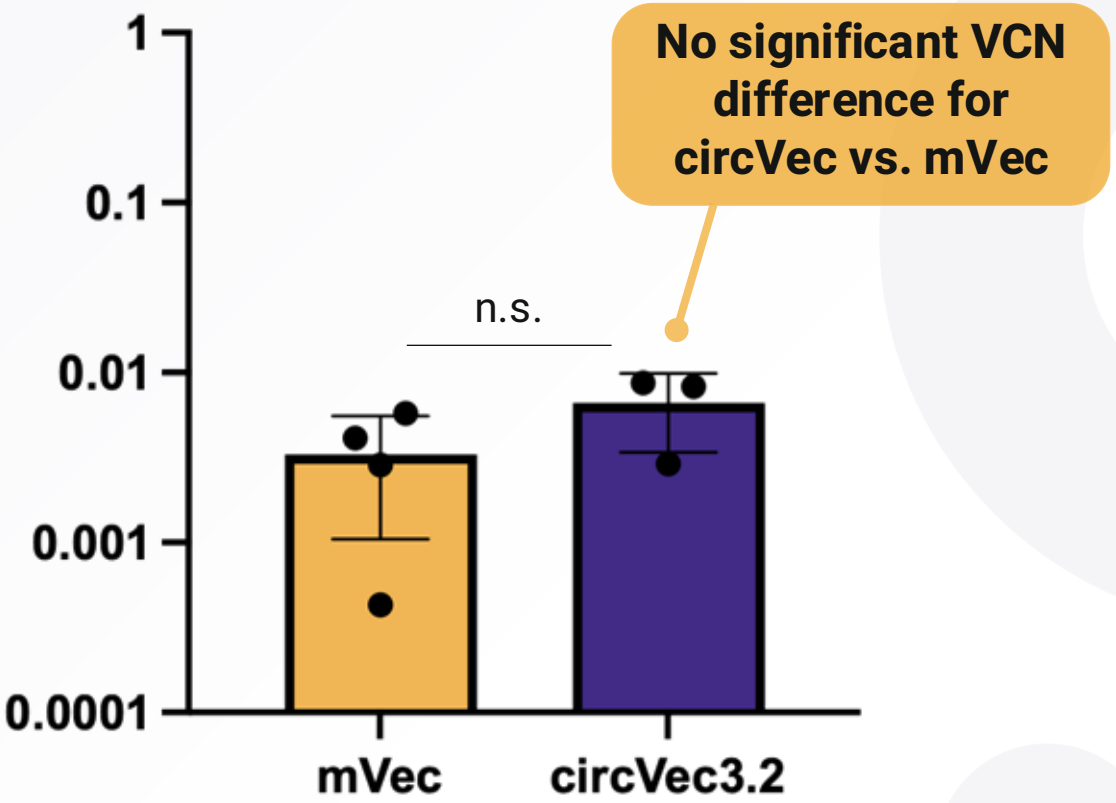


circVec advantage is driven by RNA transcript level, not AAV transduction or vector copy number

RNA expression in heart tissue, RT-qPCR



Vector Copy Number (VCN) in heart tissue, qPCR



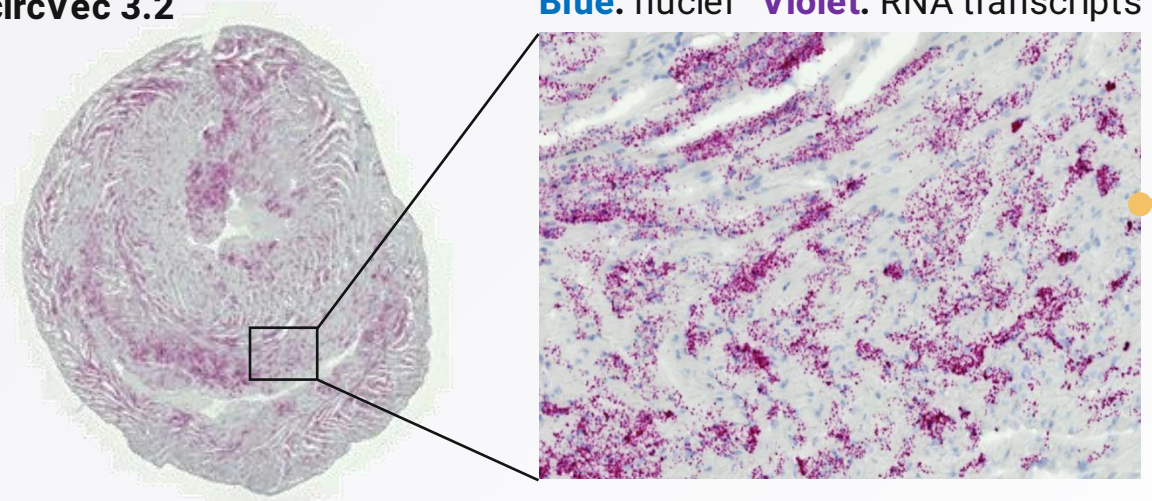
**Data from repeat study

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

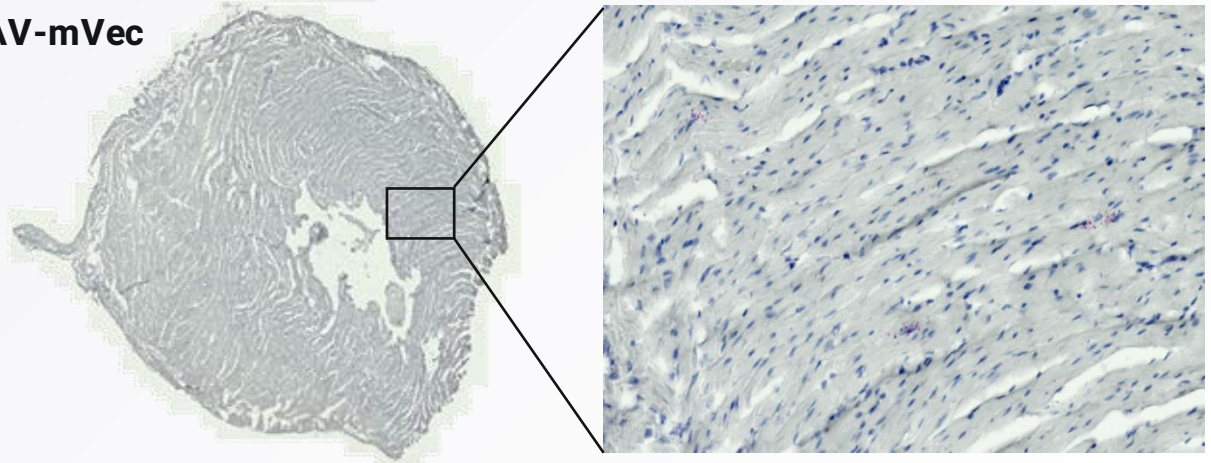
RNA expression in heart, RNAscope* microscopy ex vivo tissue section, low dose

AAV-circVec 3.2

Blue: nuclei **Violet:** RNA transcripts



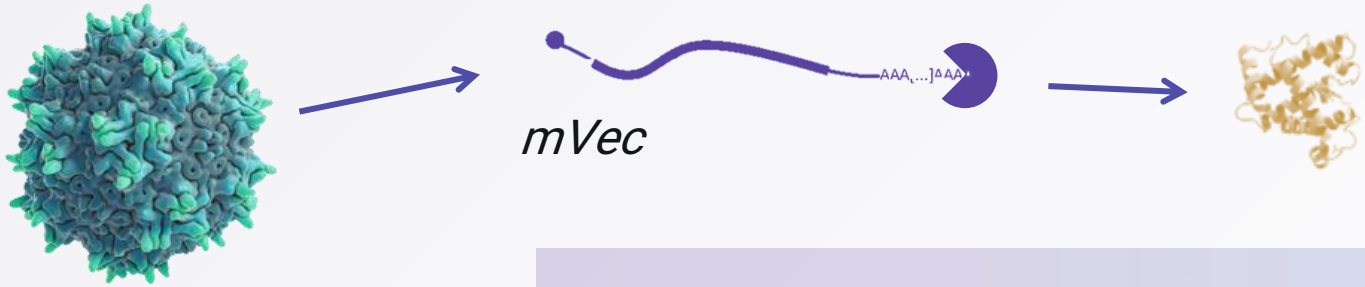
AAV-mVec



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

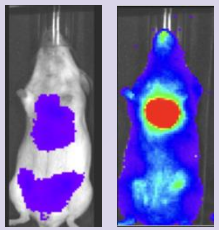
*** RNAscope:** single molecule detection of Firefly Luciferase RNA

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

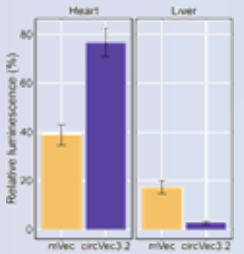


circVec-AAV compared to benchmark mVec-AAV:

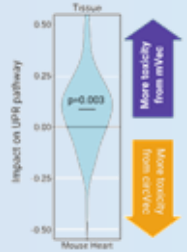
Expression



Specificity



Toxicity



circio

circVec can solve major caveats and improve the commercial viability of AAV gene therapy

GEN Genetic Engineering & Biotechnology News

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

Recent VC & BD deal activity emphasizes need for AAV-enhancing technologies

Lilly → MEIRAGTx

Licensing, November 2025

$75m up-front

+ $400m milestones

AAV gene therapy for genetic eye disease

- AAV engineering platform
- Targets specific eye cell types
- Phase 1, novel therapeutic candidate for vision loss

AAVANTGARDE

Series B, November 2025

$140 mill

AAV gene therapy for genetic eye disease, 2 programs

- Intein-based recombination
- Atlas Venture, Forbion, Schroders Capital ++
- IND / phase 1 stage

SPLICEBIO

Series B, June 2025

$135 mill

AAV gene therapy for genetic eye disease, 1 program

- Intein-based recombination
- EQT, Sanofi Ventures, Roche Ventures, NEA
- Phase 1 → phase 2 stage

NOVARTIS

M&A
Nov´24

KATE THERAPEUTICS

$1.1b
up-front + milestones

- AAV capsid engineering platform
- Muscular dystrophies
- Pre-clinical

circio

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

	Heart 	Eye 	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	1. **Arrhythmic cardiomyopathy** n = 50-70,000 2. **Dilated cardiomyopathy** n = 40-60,000 3. **Chronic heart failure** (non-genetic) n = >1 mill.	1. **Wet AMD** n = 7-8 mill. 2. **Retinitis pigmentosa** n = 200,000 3. **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

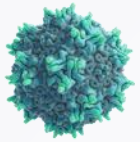
Gene therapy

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

circio

Big pharma is investing heavily into RNA-format in vivo CAR cell therapy

Lilly → ORNA

M&A, February 2026

$2.4b

in cash + 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

in 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

abbvie → capstan therapeutics

M&A, June 2025

$2.1b

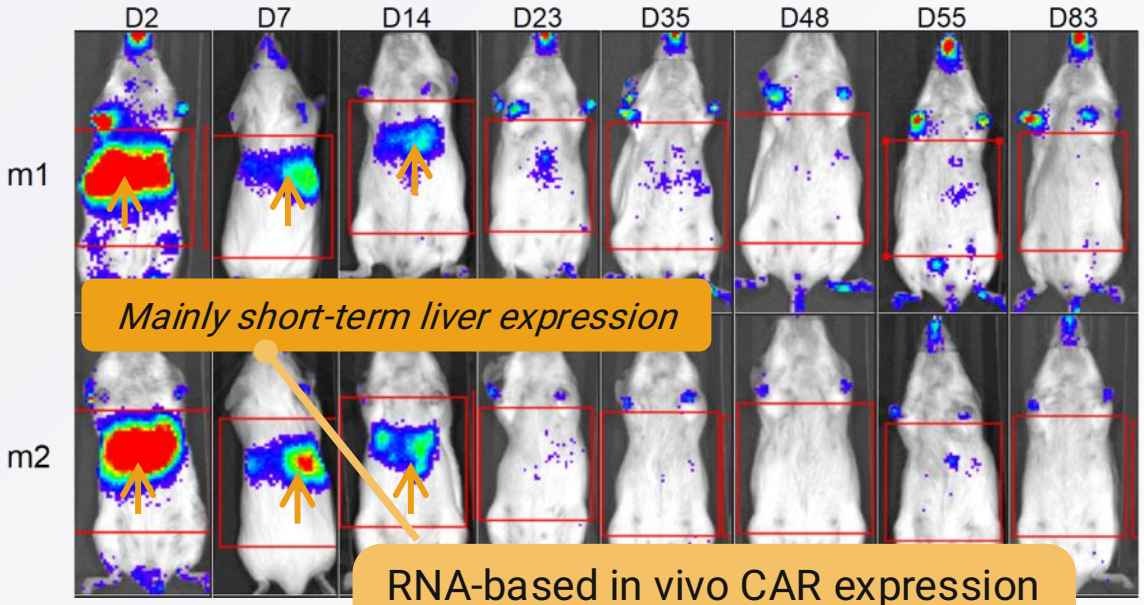
in cash buy out

In vivo CAR-T therapy for autoimmune disease

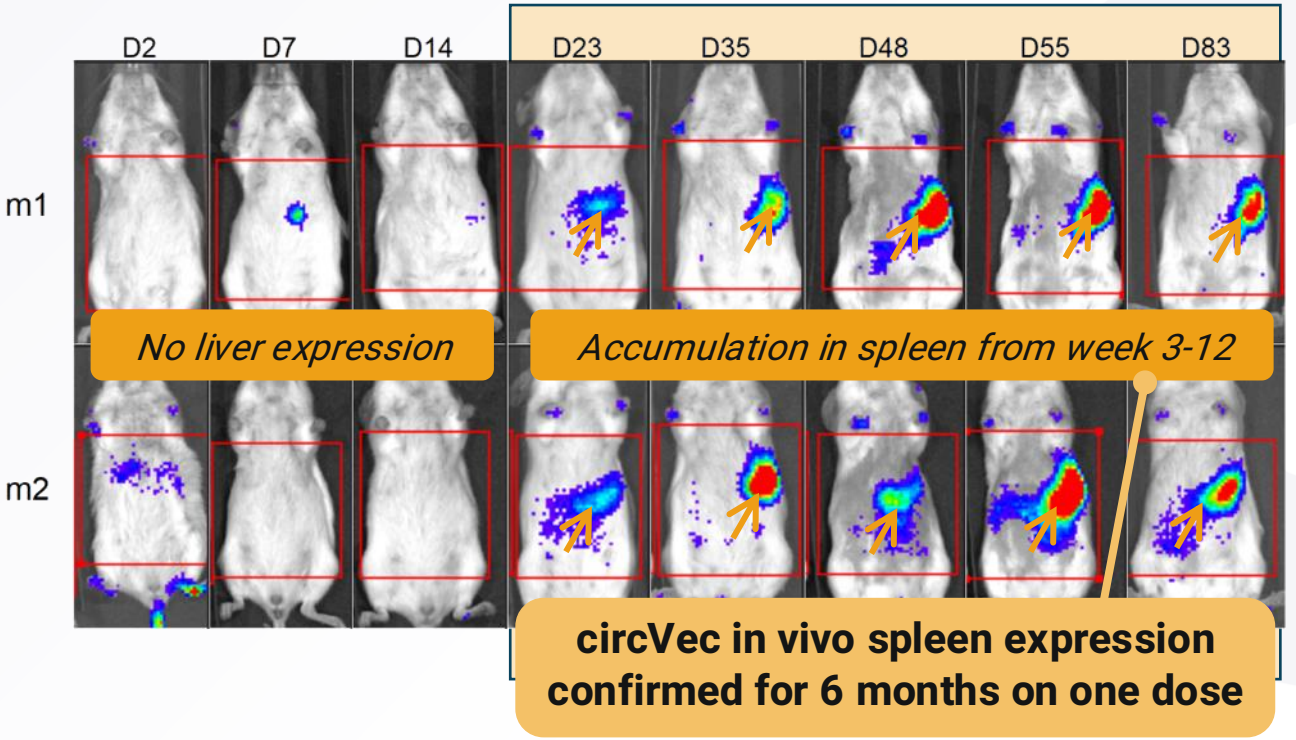
- LNP-delivered synthetic mRNA platform
- Phase 1-ready, CD19 CAR-T
- LNP w/ active T-cell targeting

In vivo cell therapy: DNA-circVec expression duration confirmed to over 6 months on single dose

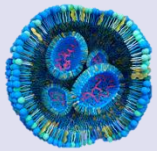
LNP-mVec (mRNA), luminescence
Systemic I.V. delivery, single dose on Day 0



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

Days	Months	Permanent
mRNA & circRNA	← **circVec-DNA opportunity** →	Lentiviral

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

Finance update & summary

Summary of highly successful rights issue targeting NOK 50 million in gross proceeds

Pre-subscriptions	NOK 24.2 mill (88%)
Total subscriptions	NOK 77.9 mill (156%)
No. of subscriptions	Approx. 1,000
% of orders >1 mill	32% of 77.9m (15 orders of total 25.2m)
Directed issue #1	NOK 15 mill
Directed issue #2	NOK 3.6 mill
Total gross proceeds	NOK 68.6 mill
Warrant coverage	67.7 mill warrants available in total, exercise 26 May - 9 June @ 20% discount to VWAP

12 month runway

Runway extension by 6-12 months*

* current estimate, depends on share price and investor demand

Business development update

Big pharma feasibility study

- Initiated a **fully funded feasibility study with a major global pharmaceutical corporation**
- Testing **circVec-AAV** gene therapy in **specific disease area**
- May lead to **subsequent circVec-licensing** if successful

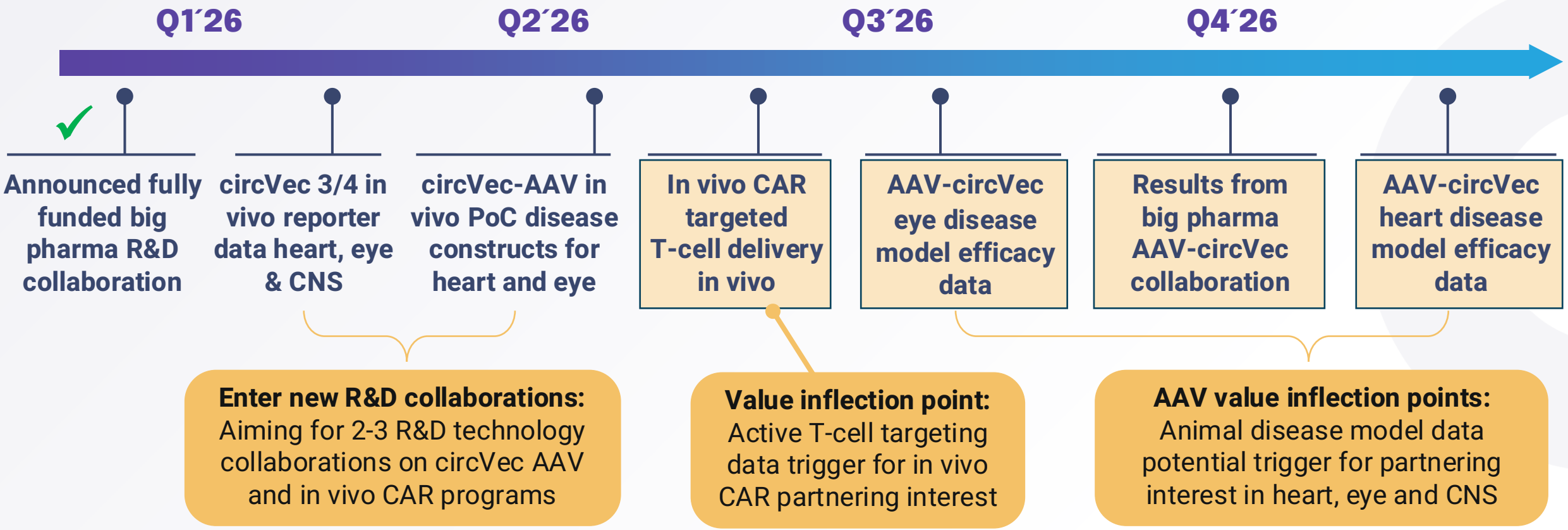
Active R&D collabo - rations

- **Several ongoing and new** 50:50 R&D collaborations
- Mainly for **circVec-DNA delivery and vector technology**
- Expected **market updates during 2026** from progressing collaboration projects

Seeking new partner - ships

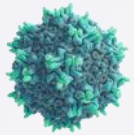
- **Big pharma R&D collaborations** in available disease areas
- In vivo cell therapy **T-cell targeted circVec-DNA delivery**
- **Engineered/targeted AAV capsids** for tissues of interest

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



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

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*

Further reading – Circio in industry and scientific press