circio

The leader in circular RNA expression systems

R&D webcast

27 November 2026

1

R&D update
Gene therapy program

2. Business development update
3. Q&A session

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

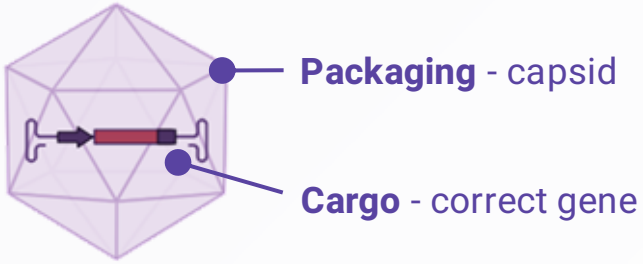
70%

of rare diseases **begin in childhood**

Only 5%

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

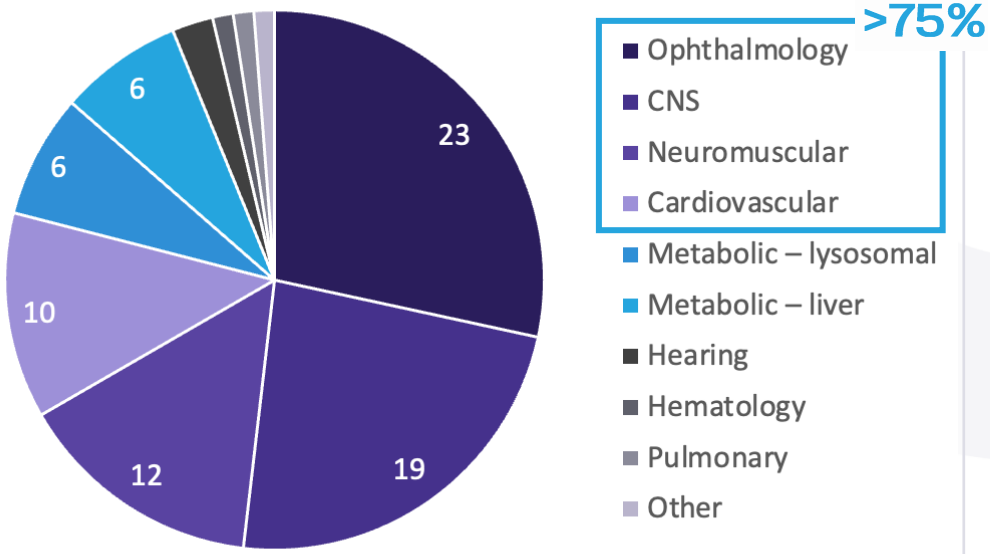
Currently the best solution



AAV: Adeno-Associated Virus
the gene therapy workhorse

- Tissue-specific delivery
- Long durability, single dose
- Clinically proven
- Eight FDA approvals

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

May 27, 2025

By **Alex Philippidis**



The FDA ordered a clinical hold on the Phase II trial after the adverse event was first disclosed.

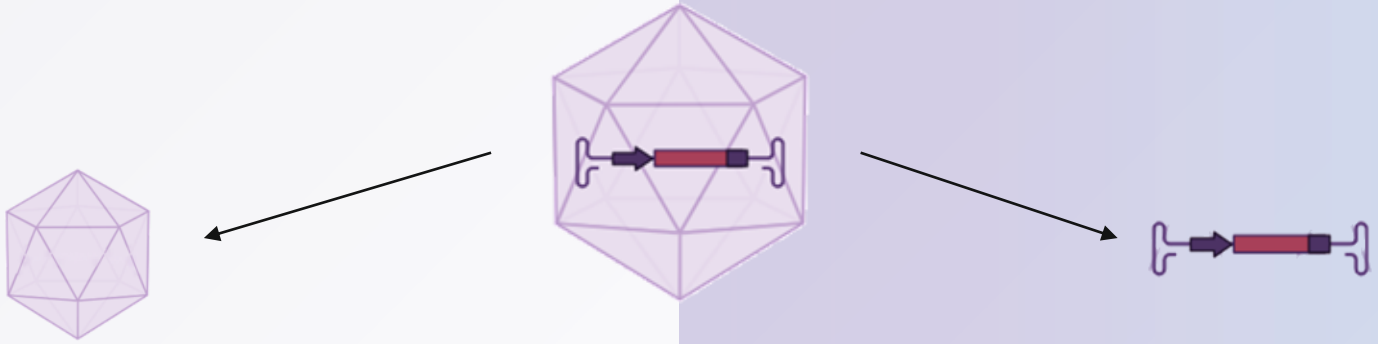
AAV gene therapy for Danon disease:

- Clinical benefit demonstrated, but at 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**

Engineering the next generation of AAV gene therapies for enhanced precision and dosing – and reduced cost



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 · 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

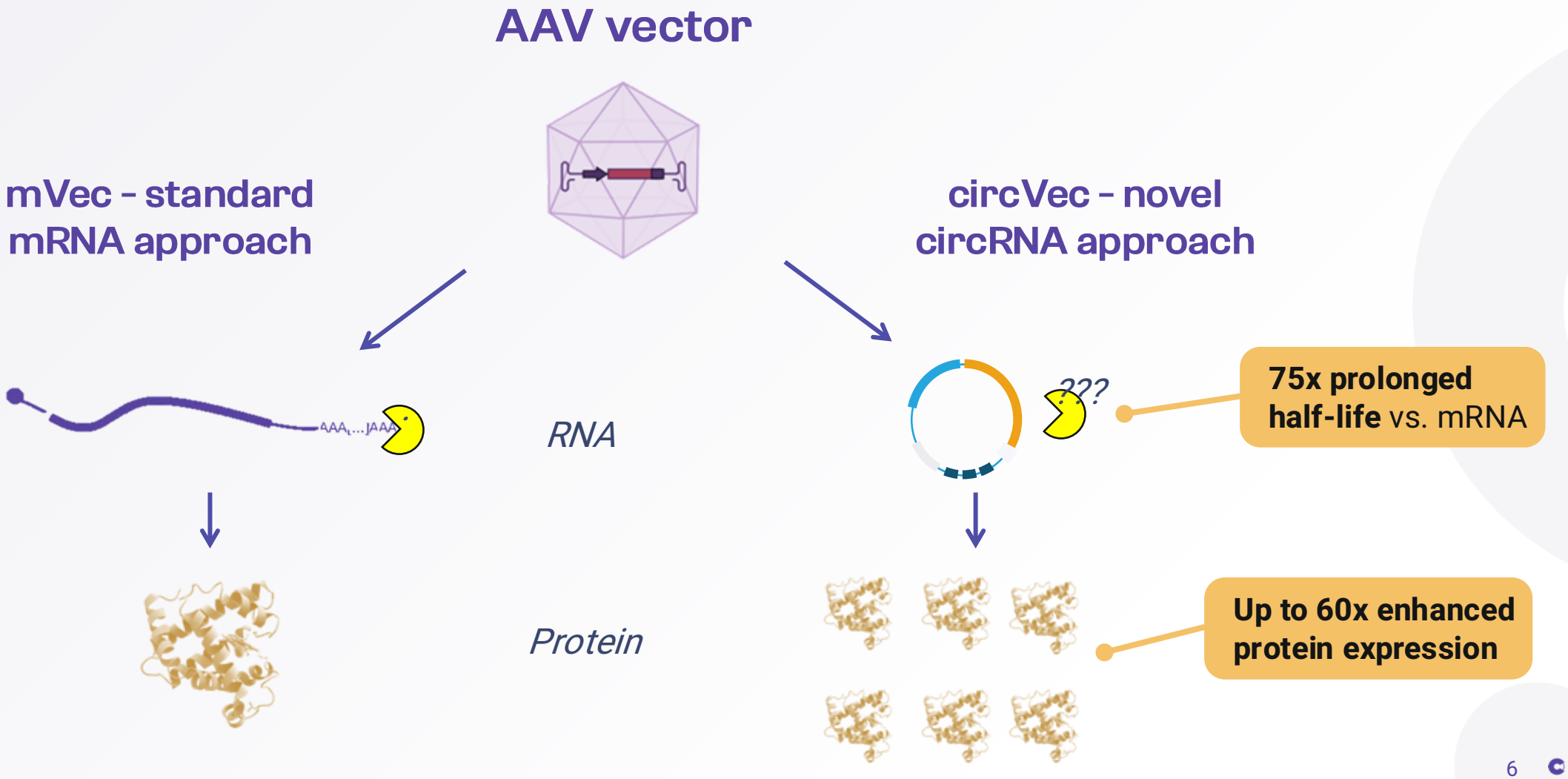
circio

Circio's approach is vector-agnostic

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

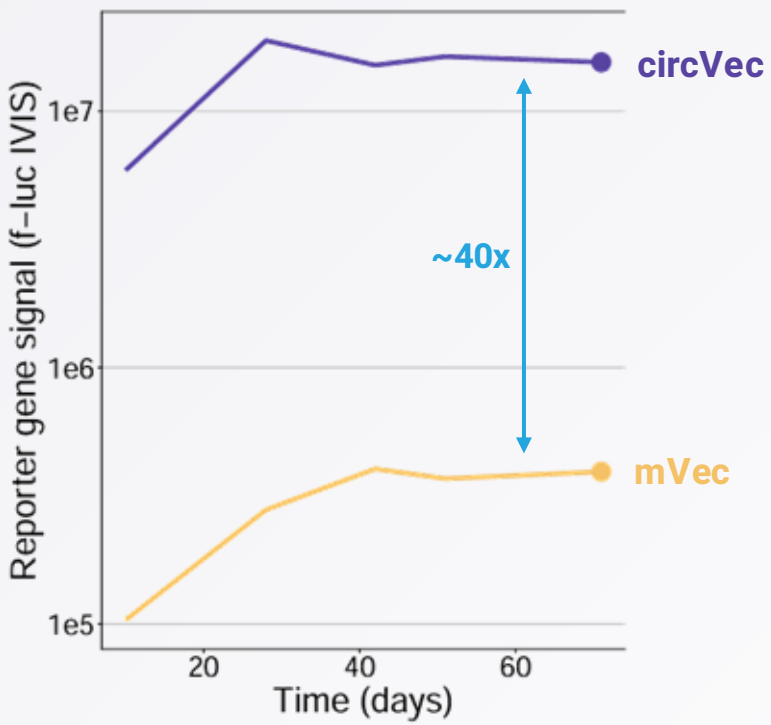
circVec

Circio's proprietary circRNA-platform to boost AAV-based gene expression

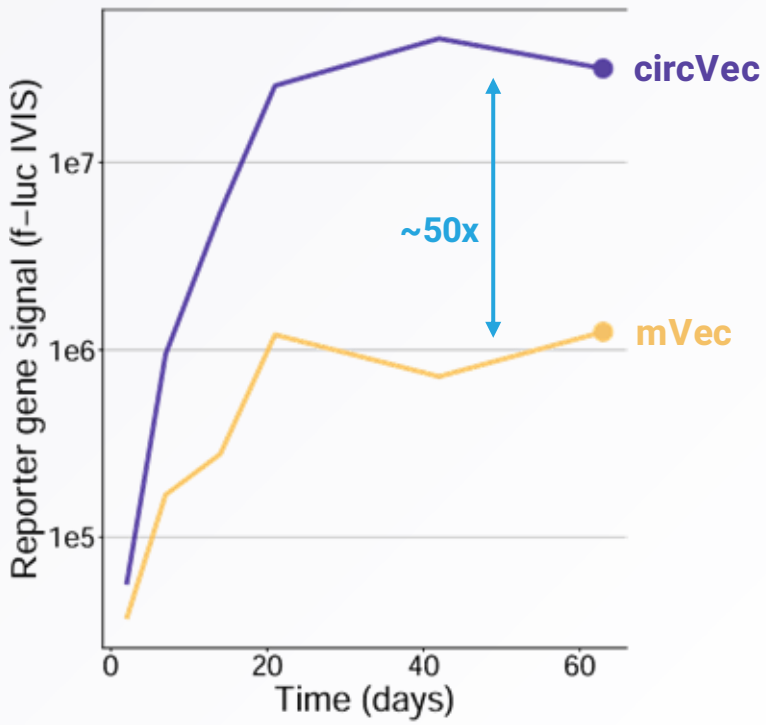


circVec consistently enhances conventional AAV vectors targeting heart, eye and CNS tissue in vivo

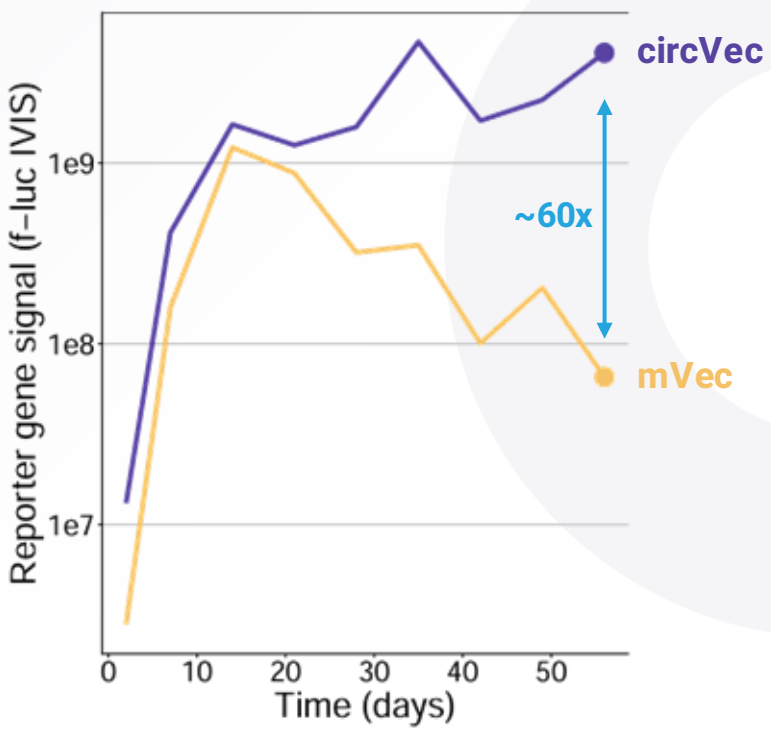
Heart AAV9-circVec 3.2 vs. mVec
Systemic delivery, IVIS signal



Eye AAV2-circVec 4.0 vs. mVec
Intra-vitreal injection, IVIS signal



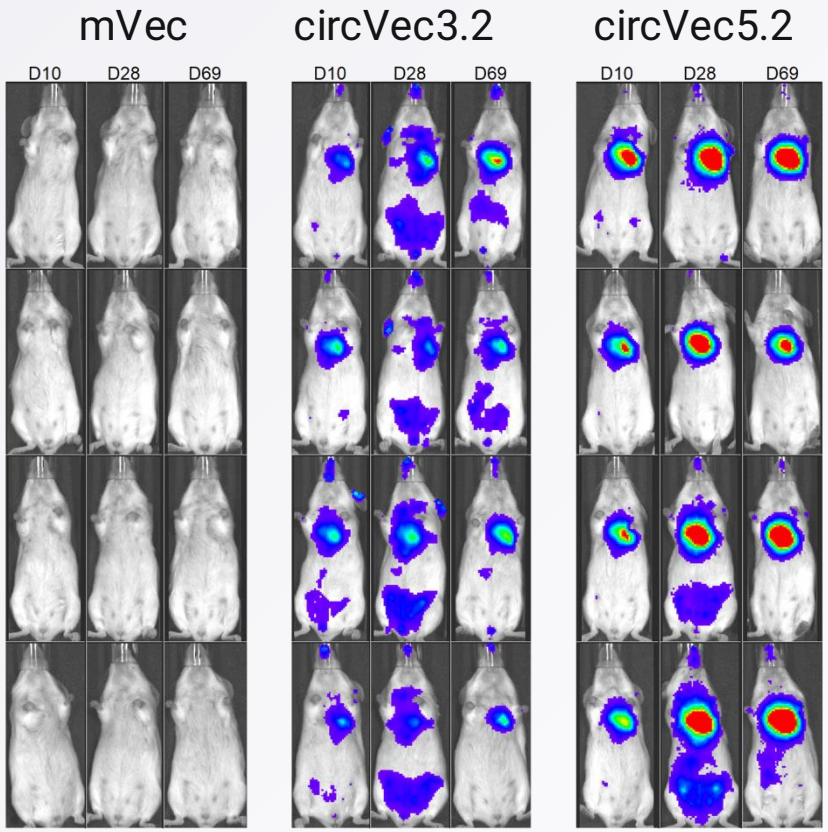
CNS AAV9-circVec 3.2 vs. mVec
Intra-thecal injection, IVIS signal



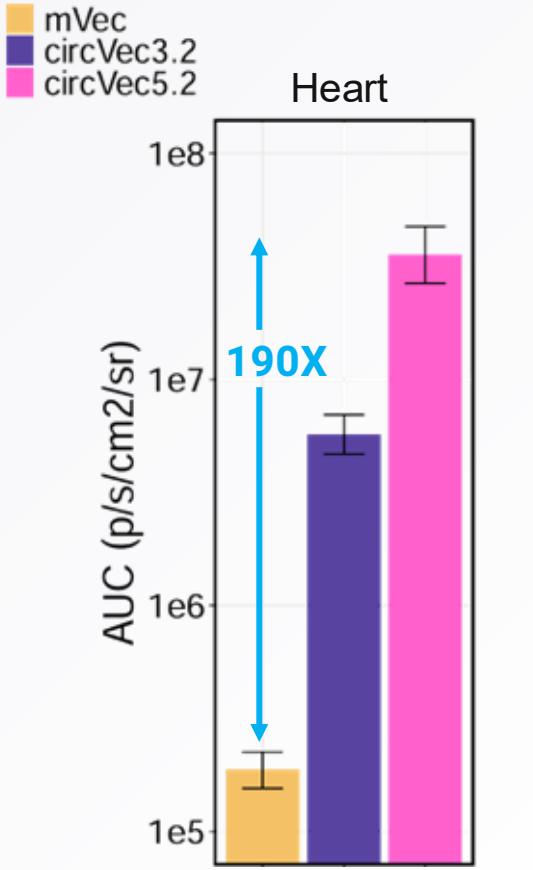
Consistent circVec performance observed across AAVs, tissues and delivery routes

ESGCT 2026: Heart-targeted circVec 5.2 outperforms circVec 3.2 on both expression level and specificity

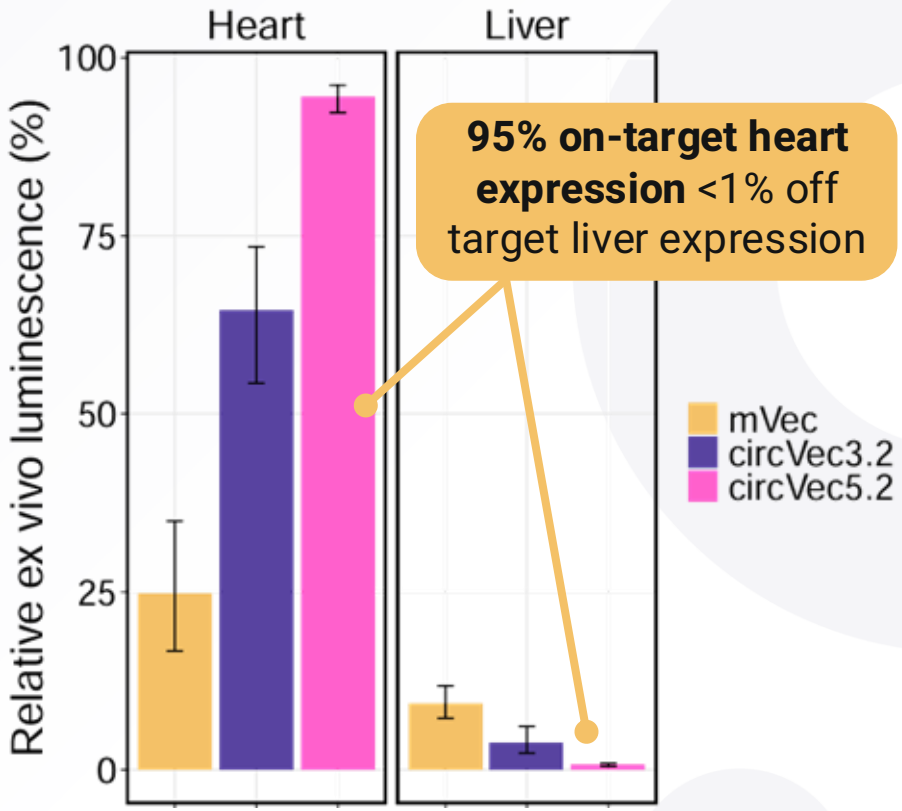
Reporter signal, systemic delivery, 5e12 vg/kg



Quantification, Heart signal



Ex Vivo signal, relative expression in tissues



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	**wet AMD** 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

Heart organoids – closest pre-clinical in vitro model of human heart tissue

2D heart organoid model setup



2D human heart-simulating in vitro testing system



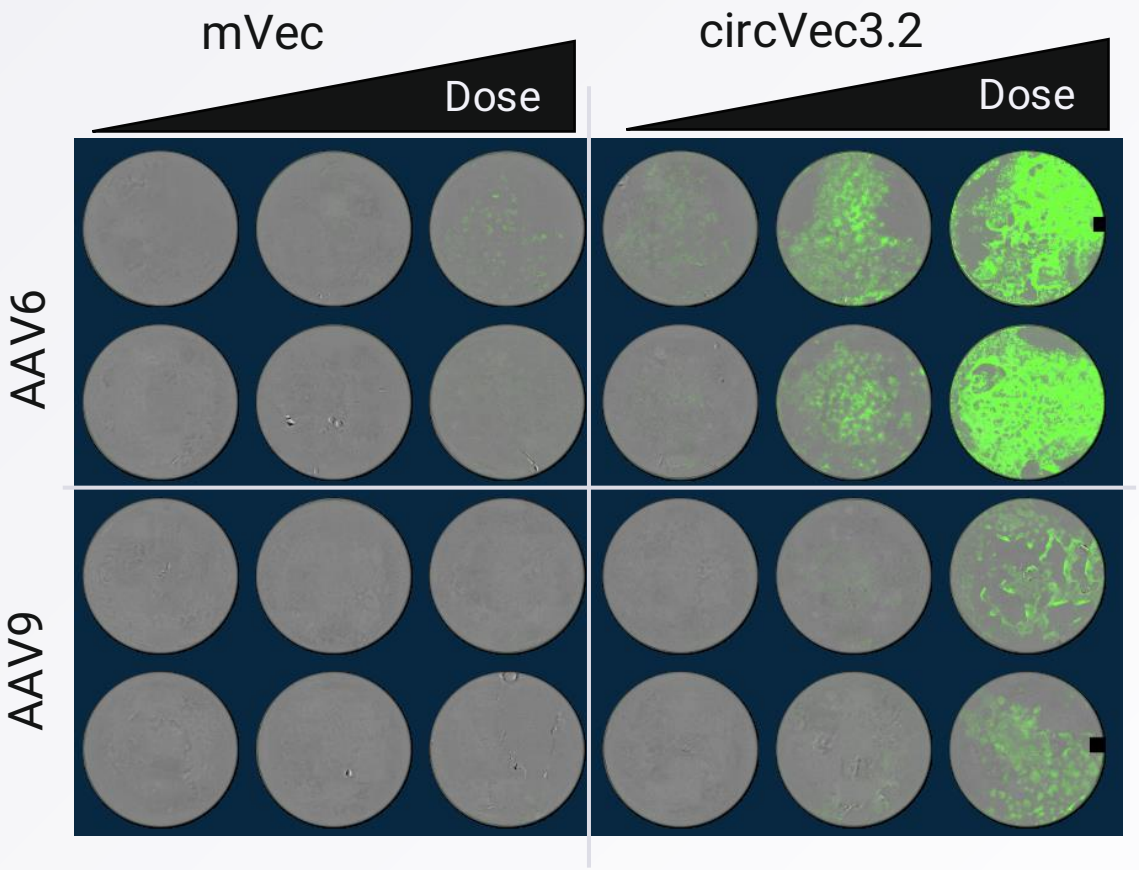
2D organoid transduced with AAV-circVec

Organoids for pre-clinical development

- Organoids enable **early screening** in **primary human cells**
- **Powerful combination with mouse in vivo data** as bridge to NHP and later clinical studies
- **Mitigates difference in mouse vs. human heart metabolism,** organoids respond to drugs more like human myocardium
- **Active FDA and EMA regulatory push** for new organoid methodologies to **reduce animal use**

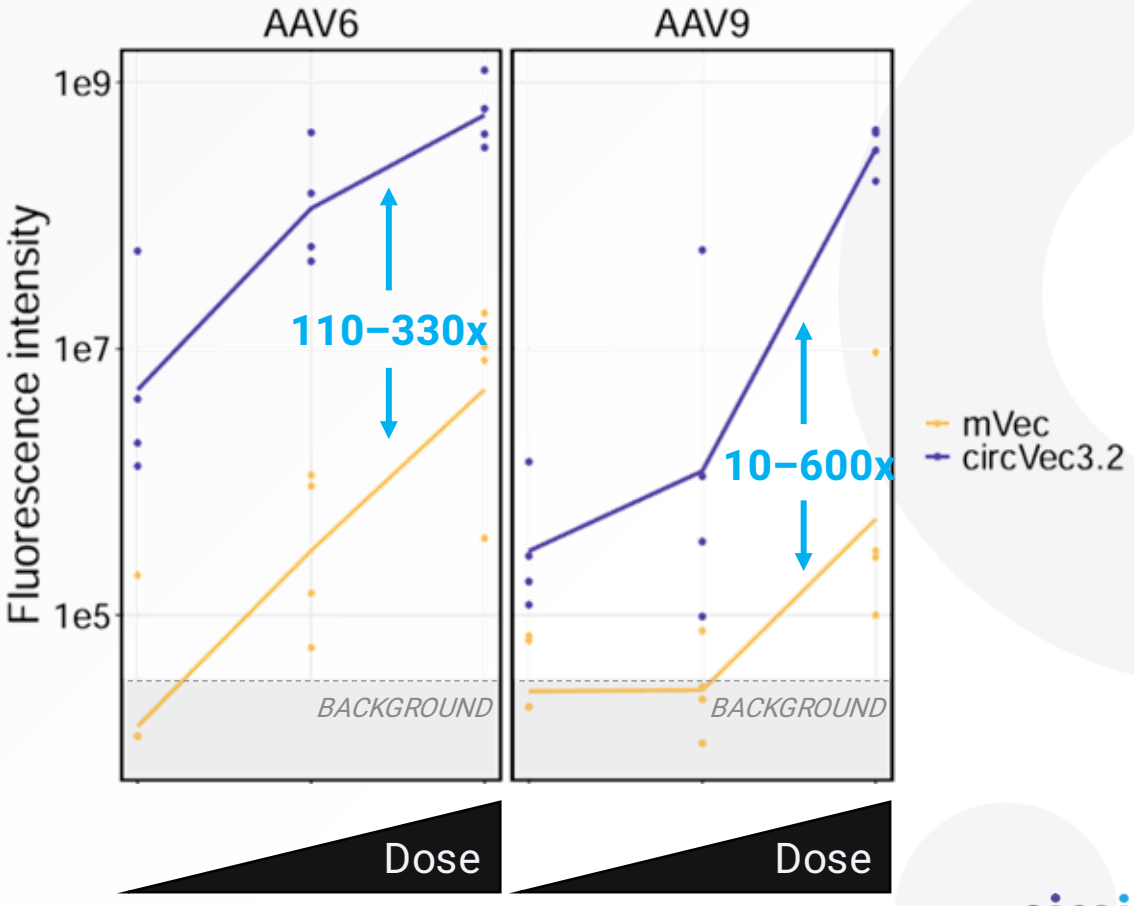
AAV-circVec 3.2 significantly outperforms mVec in human cardiac organoid model

Organoid microscopy analysis, GFP fluorescence
Two AAV serotypes, Three dose levels

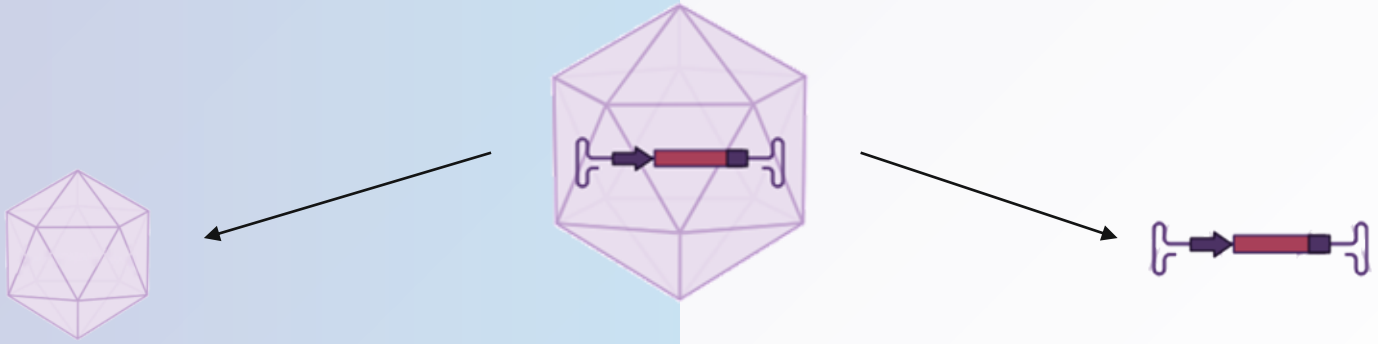


2D iPSC-derived human heart organoid, 96-well format

Signal quantification, GFP fluorescence
circVec vs. mVec performance



Engineering the next generation of AAV gene therapies for enhanced precision and dosing – and reduced cost



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Improve AAV gene expression

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Circio's approach is vector-agnostic

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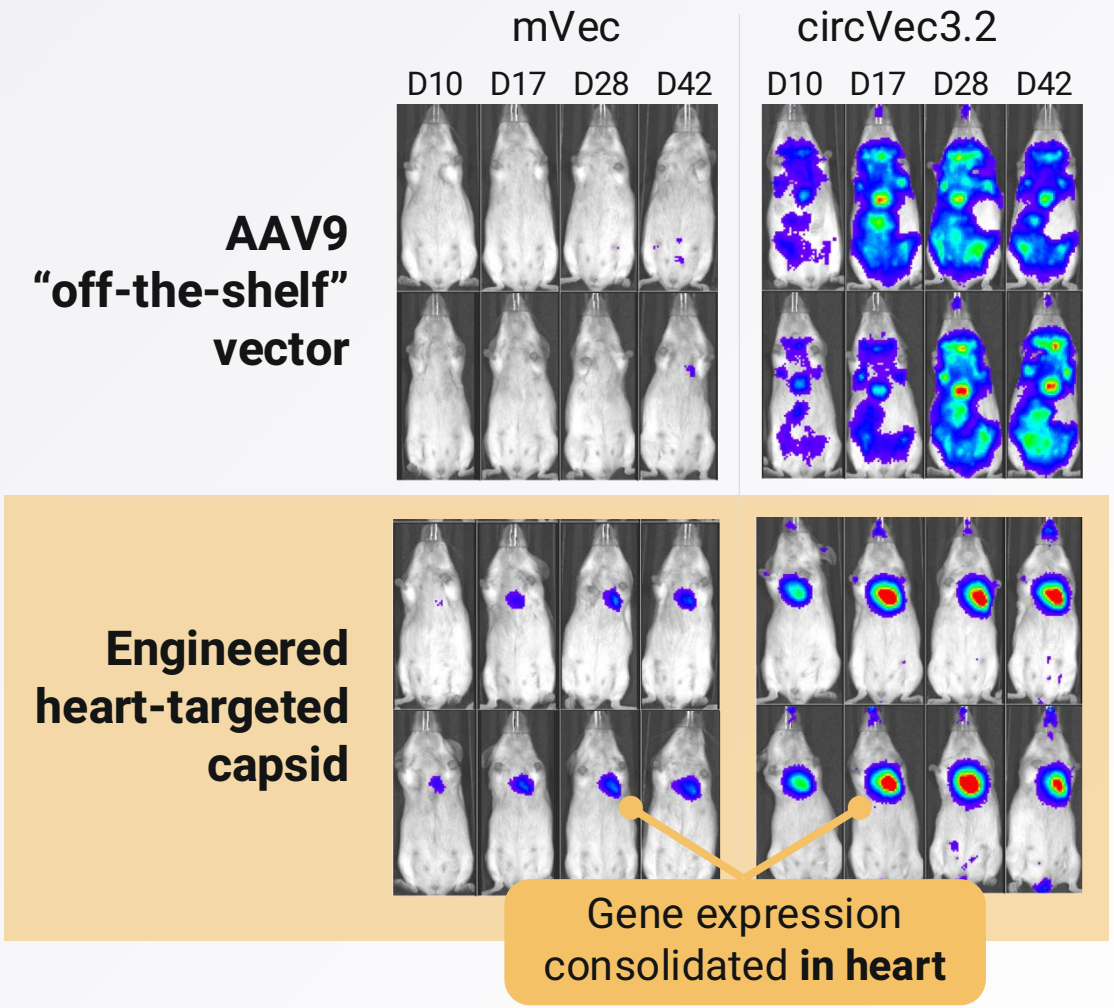
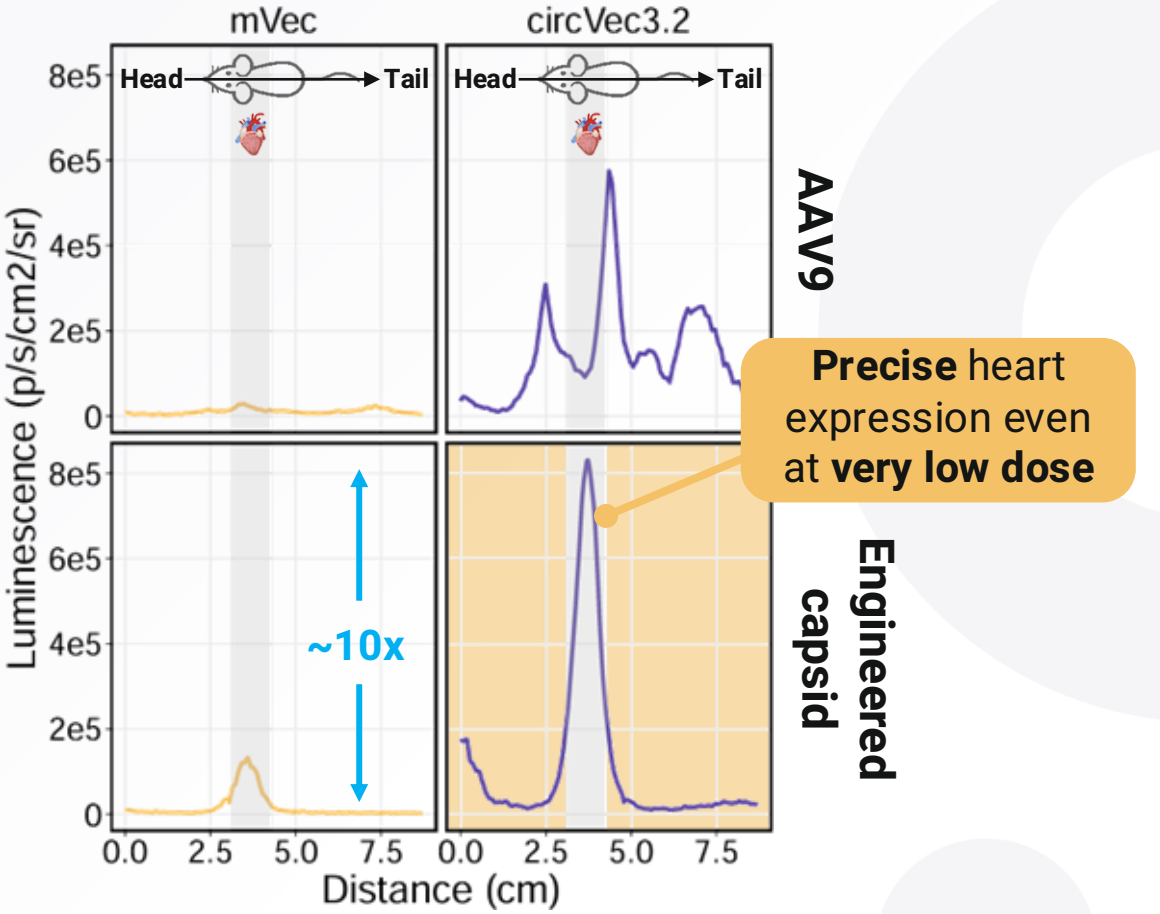
Engineered capsid + circVec shows precise and efficient cardiac expression at very low-dose

Reporter signal, IVIS f-luc, systemic delivery 1e12vg/kg

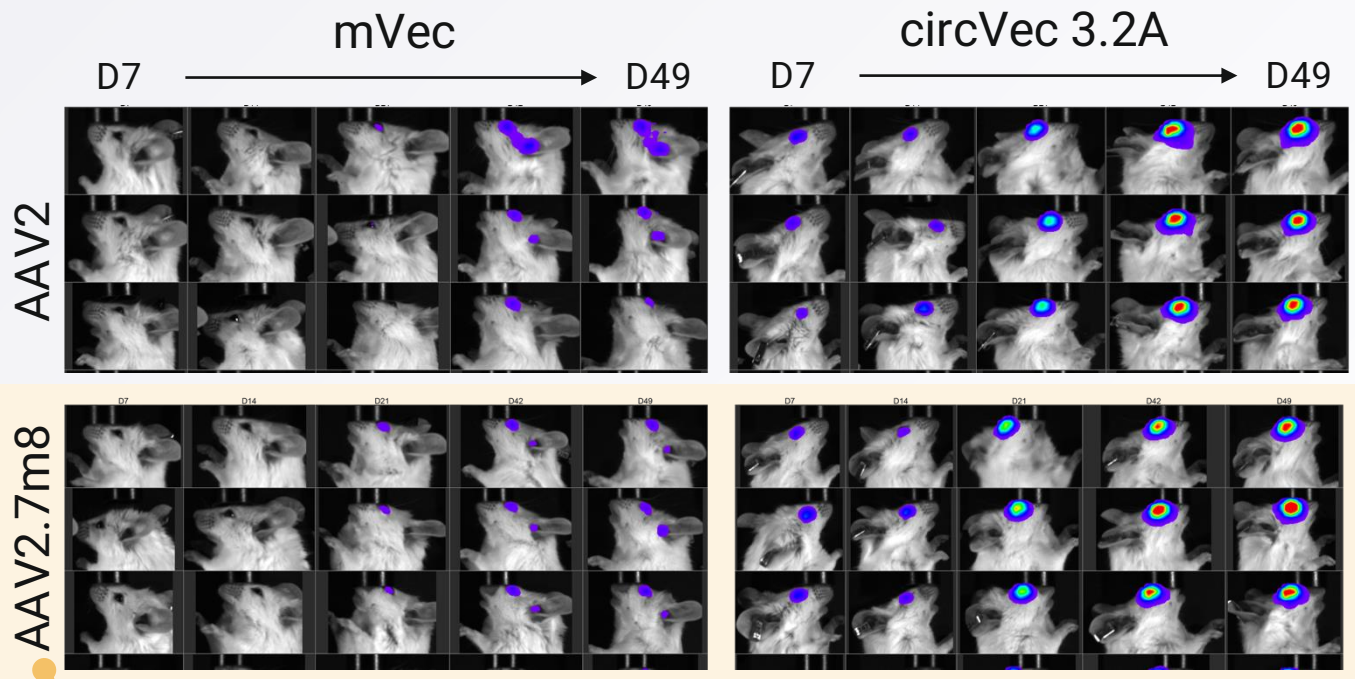


Signal distribution, vertical expression profile Day 42



Engineered capsid + circVec performance validated in whole eye, analyses ongoing at cellular level

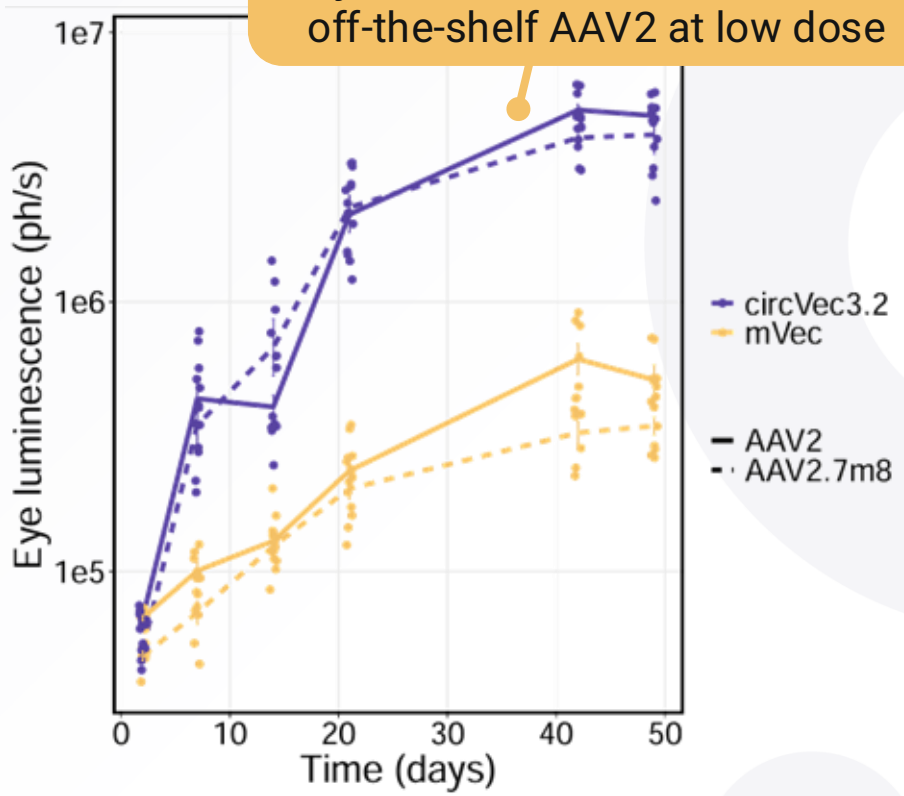
Reporter signal, IVIS f-luc, intra-vitreal delivery, 5e8 vg/kg



Engineered capsid for enhanced **pan-retinal penetrance**

Quantification, reporter signal in eye

Consistent performance in **whole eye** for **circVec AAV2.7m8** vs. off-the-shelf AAV2 at low dose



Next step: evaluating AAV-circVec expression profile at cellular level by scSEQ

circVec AAV summary: pre-clinical development under expansion both internally and externally

Engineered capsids



- circVec maintains **significant advantage** in combination with **engineered AAV capsids** for heart and eye transduction
- **Potent heart-specific expression** observed from circVec3.2 at very low AAV dosage (1e12 vg/kg)
- **circVec enhancement** observed for **eye-targeted AAV2.7m8** capsid, penetrance at cellular level being tested

Organoids



- **2D organoid model** established to mimic drug behavior in human-specific myocardium
- circVec outperforms mVec at **unprecedented levels** using two different AAV capsids

Next steps



- **In vivo disease model testing,** heart and eye models being set up
- **Single-cell analysis for eye AAV,** mouse (ongoing) and pig (2027)
- **Validation of heart AAV in NHPs,** under planning, start Q2'27

2

Business development update

3. Q&A session

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Circio is pursuing a broad BD strategy

Gene therapy

12 **R&D collaborations established**

- **Top 5 pharma** fully funded feasibility study
- **Engineered capsids** enhancement & new areas
- **Therapeutic co-development** with biotechs
- **Novel** / alternative gene therapy **applications**

Status:

- **Big pharma collaboration** in vivo stage ongoing
- **Engineered capsid testing** ongoing in heart, eye, CNS and muscle

Cell therapy

11 **R&D collaborations established**

- Testing **novel DNA vector formats**
- Screening **T-cell LNP delivery** systems
- **Alternative delivery or novel applications** collaborations

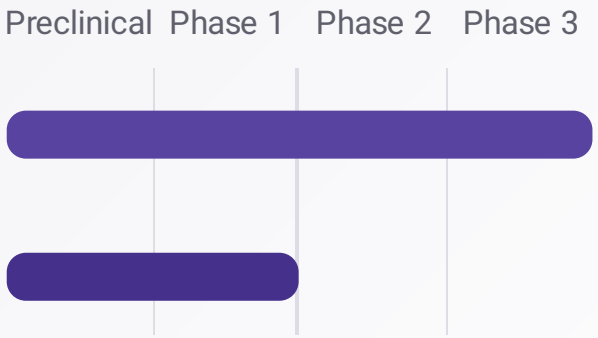
Status:

- **T-cell targeted LNP-screen ongoing in vitro and in vivo**
- **ssDNA testing starting Dec'26**

Heart gene therapy collaboration with Solid Biosciences

SOLID BIOSCIENCES **Nasdaq: SLDB**

Pipeline



SGT-003
Duchenne muscular dystrophy

SGT-212
Friedreich's ataxia

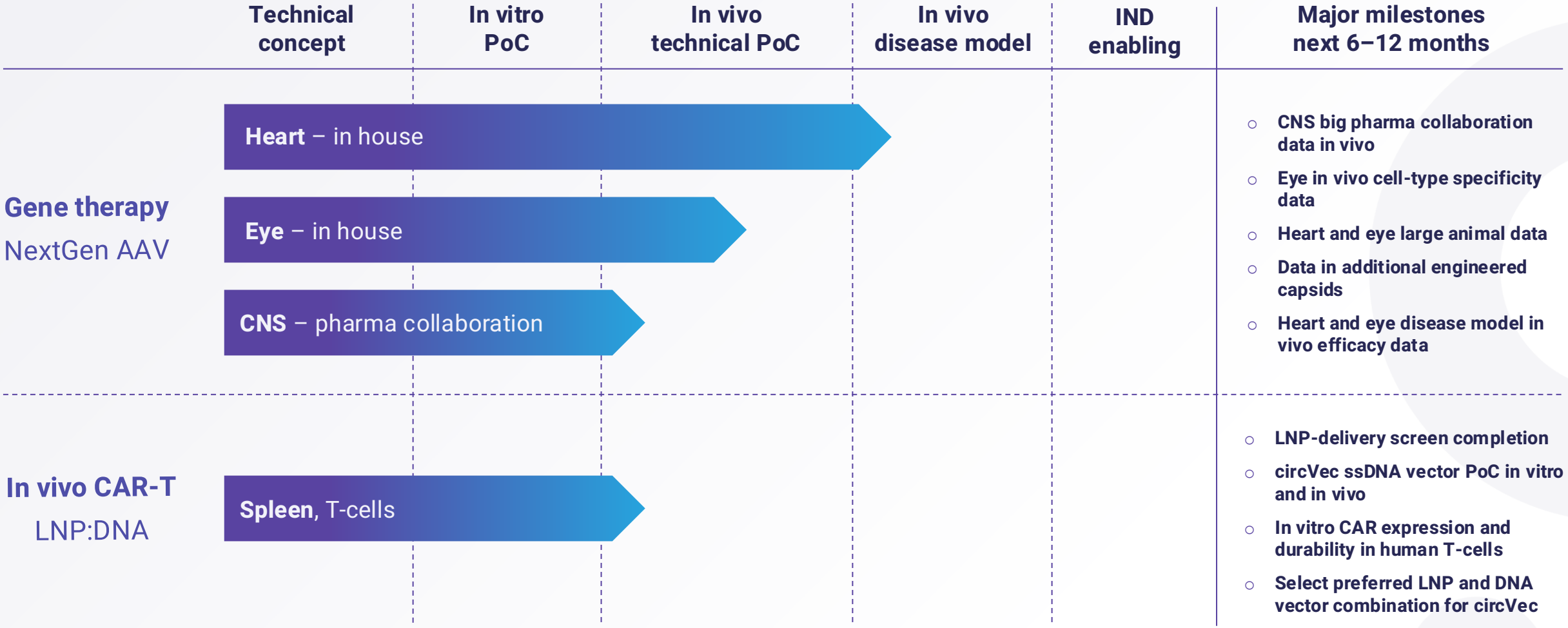
POLARIS-101™

- **Enhanced skeletal and cardiac tropism**, reduced liver biodistribution
- **Delivery capsid for SGT-003** in Phase 3 IMPACT DUCHENNE, excellent reported safety profile
- **50+ agreements and licenses** with companies and academic labs

Circio – Solid collaboration

- Establishing **circVec** expression constructs in **targeted POLARIS-101 capsid**
- **In vitro and in vivo testing** of circVec-POLARIS-101 by **both parties**
- Evaluate applications in **genetic heart and muscle diseases**
- **First in vivo milestone** expected in **mid-2027**
- **Next steps to be discussed** based on experimental outcome of in vitro and in vivo studies

Circio has a broad pipeline with expected rich news flow



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



- **Consistent 40–60x AAV-circVec 3.2 advantage in heart, eye & CNS**
- New **organoid** data show that **circVec outperforms in human cells**
- circVec advantage **validated for therapeutic genes**
- circVec advantage **validated for targeted engineered capsids**
- **circVec 5.2** shows significantly **enhanced potency and precision**

Business development



- **New strategic heart-AAV collaboration with Solid Biosciences**
- **In vivo stage ongoing for top 5 pharma R&D collaboration**
- **20+ active R&D collaborations** with biotechs and academia

Financing



- **NOK 820 million in new capital raised during 2026**
- **Cash runway secured** through to first clinical data in **2030**

Circio merchandise now available



Hat

NOK 250



Sports T-shirt

NOK 300



Water bottle

NOK 200

Order by email: contact@circio.com