



Circular RNA expression systems for enhanced gene and cell therapies

1H 2025 report and R&D update
Webcast - 28 August 2025

Important notice and disclaimer

This report contains certain forward-looking statements based on uncertainty, since they relate to events and depend on circumstances that will occur in the future and which, by their nature, will have an impact on the results of operations and the financial condition of Circio Holding ASA and the Circio Group. Such forward-looking statements reflect the current views of Circio and are based on the information currently available to the company. Circio cannot give any assurance as to the correctness of such statements.

There are a number of factors that could cause actual results and developments to differ materially from those expressed or implied in these forward-looking statements. These factors include, among other things, risks or uncertainties associated with the success of future clinical trials; risks relating to personal injury or death in connection with clinical trials or following commercialization of the company's products, and liability in connection therewith; risks relating to the company's freedom to operate (competitors patents) in respect of the products it develops; risks of non-approval of patents not yet granted and the company's ability to adequately protect its intellectual property and know-how; risks relating to obtaining regulatory approval and other regulatory risks relating to the development and future commercialization of the company's products; risks that research and development will not yield new products that achieve commercial success; risks relating to the company's ability to successfully commercialize and gain market acceptance for Circio's products; risks relating to the future development of the pricing environment and/or regulations for pharmaceutical products; risks relating to the company's ability to secure additional financing in the future, which may not be available on favorable terms or at all; risks relating to currency fluctuations; risks associated with technological development, growth management, general economic and business conditions; risks relating to the company's ability to retain key personnel; and risks relating to the impact of competition.



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Highlights & market update

- 2. R&D update
- 3. Corporate update

First half year 2025 highlights

Financing

- **Number of outstanding convertible bonds substantially reduced**
- **Extended financing commitment with Atlas, securing access to funding until end of 2025**

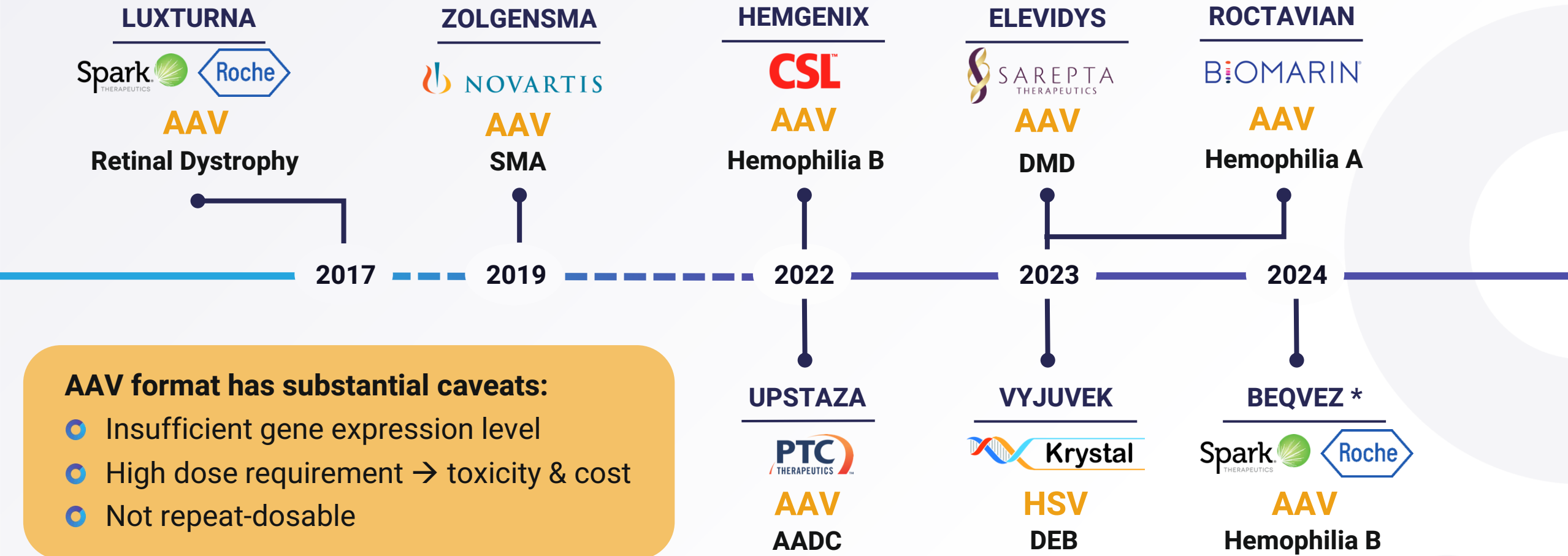
Business development

- **Entered 7 R&D collaborations with international partners** for circVec DNA delivery, novel DNA formats and protein production
- **4basebio, Certest, Entos, Neoregen, Lonza** (+ 2 confidential)

circVec R&D

- **Showed in vivo PoC with robust circVec advantage for AAV gene therapy and in vivo cell therapy**
- **Published circular RNA review in Nature Reviews Genetics**
- **Presented circVec gene and cell therapy data at ASGCT, the leading global conference in the field**

The AAV vector is the main gene therapy format today, 7 approved products to date



The circVec technology platform can address major challenges of current gold-standard AAV gene therapy



Danon Disease Patient Dies in Rocket Gene Therapy Trial

May 27, 2025

By Alex Philipp



BIOTECH

Sarepta LGMD trials all hit by FDA hold amid newly surfaced safety concerns over gene therapy

By Gabrielle Masson

Jul 21, 2025 11:36am

Rocket Pharm
a patient in a

disease gene therapy candidate RP-A501, a study that the FDA has placed on clinical hold.

Challenges for AAV gene therapy:

- Very high AAV dose level required (= high tox & cost)
- Co-administration of immune suppressive medication
- **Severe adverse events (SAEs), incl. risk of death**

Circio's circVec technology can unlock:

- >10-fold reduction of AAV dose level (= lower tox & cost)
- Reduction of immune suppressive medication
- **Elimination of most severe adverse events (SAEs)**

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

Lead program,
in house focus

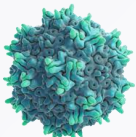
Gene
therapy



Muscle, cardiac and other genetic
disease

Tissue-specific, enhanced potency AAV

>150,000 patients in target diseases,
with no approved therapies



Next Gen AAV

Next step /
partnership

Cell
therapy



Auto-immune disease, oncology

LNP: DNA format, redosable

Very large patient population, only
autologous options available today



In vivo CAR



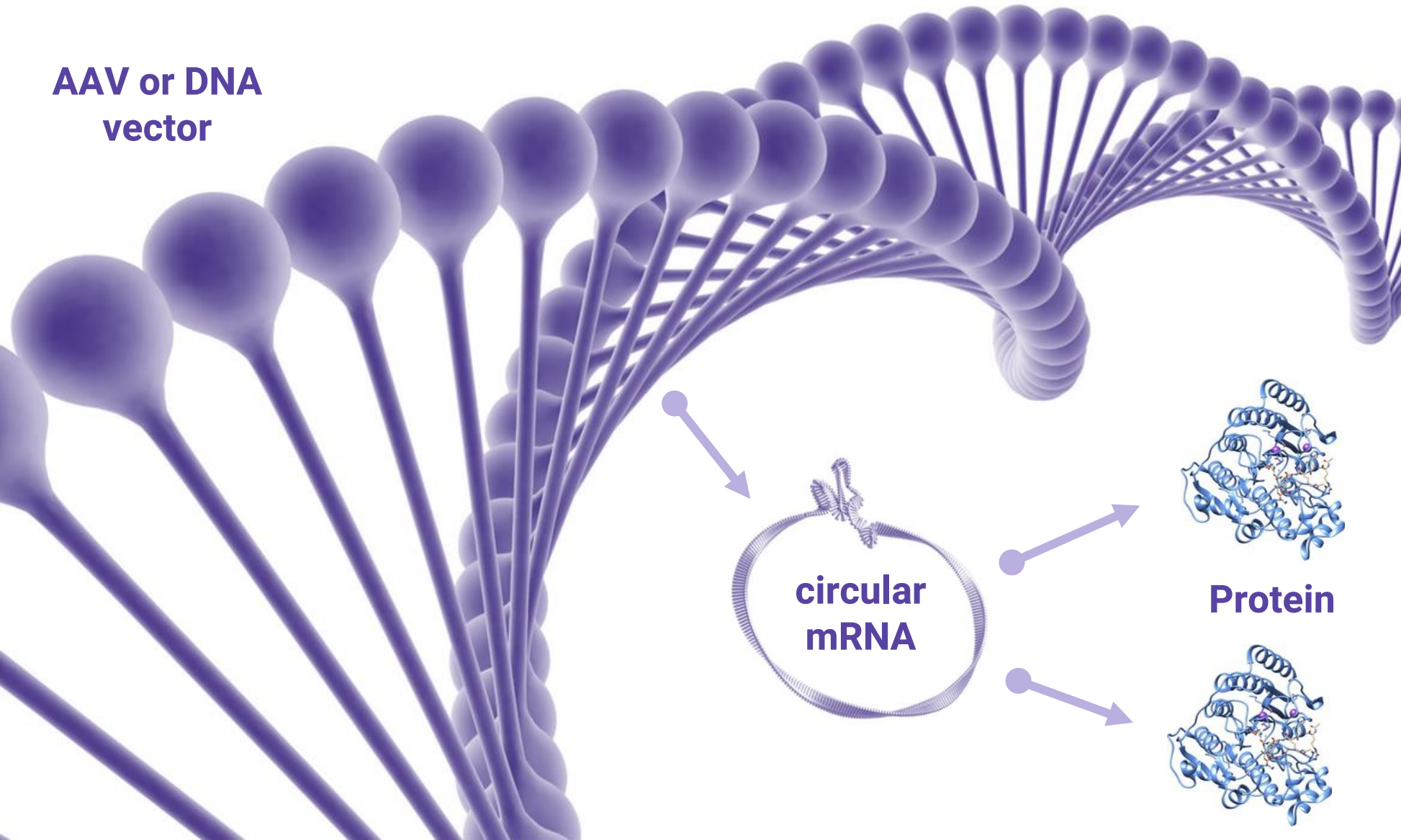
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R&D update

3. Corporate update

Circio's unique circVec expression system: Enhanced potency and durability by circular RNA

AAV or DNA
vector



circular
mRNA

Protein

circVec AAV or
DNA vector
therapeutic

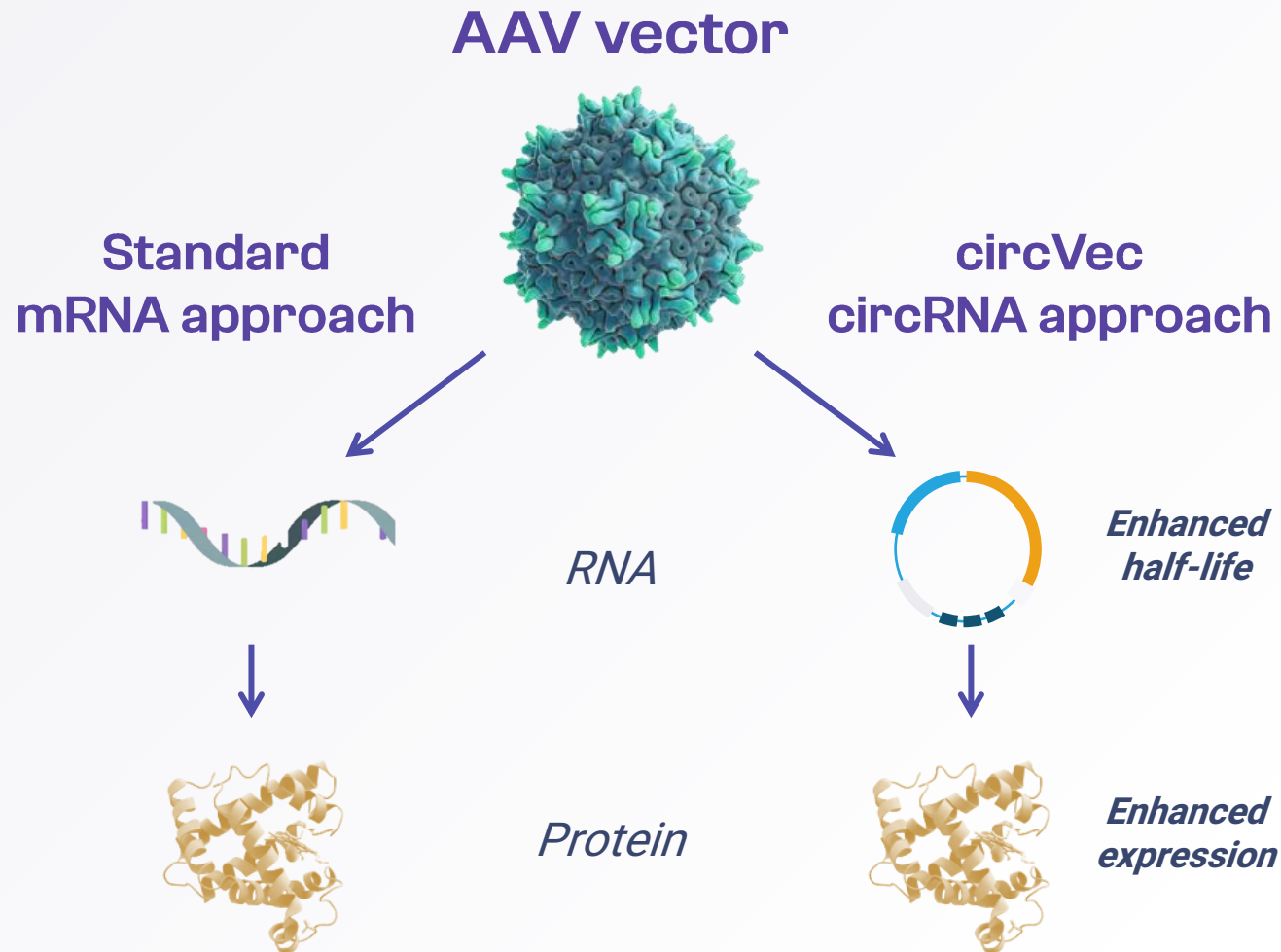
Inject

circRNA
expression in
patient cells

Higher and more
durable protein
expression

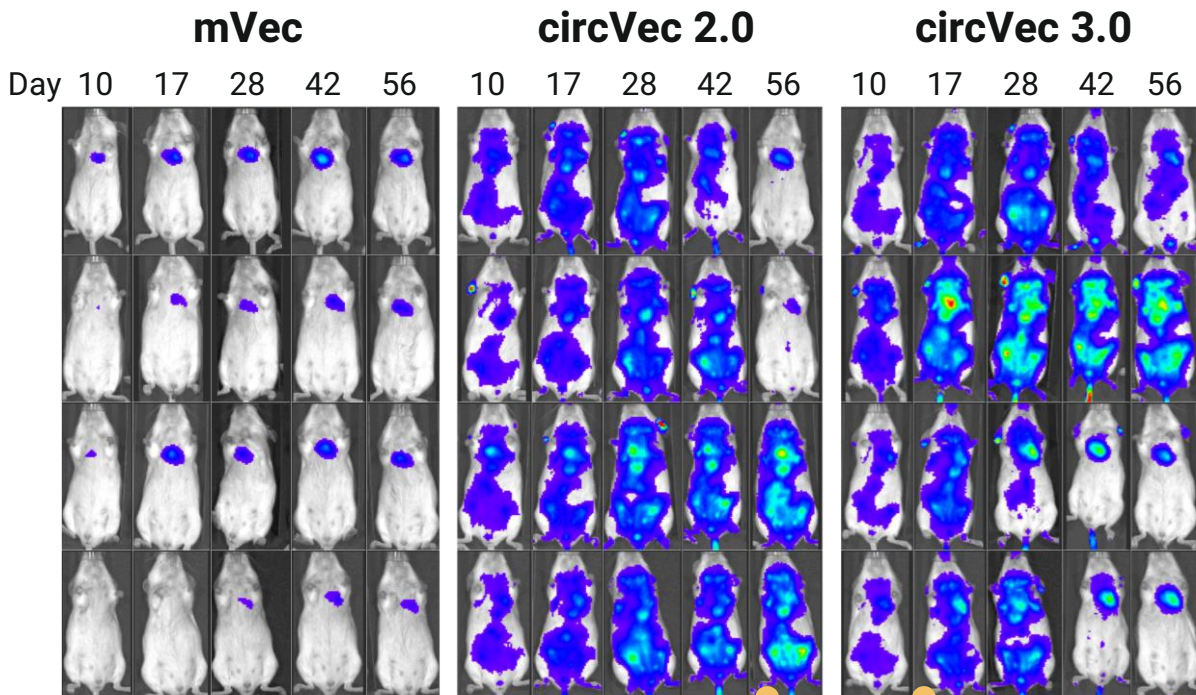
circio

Boosting the activity of AAVs by circVec expression



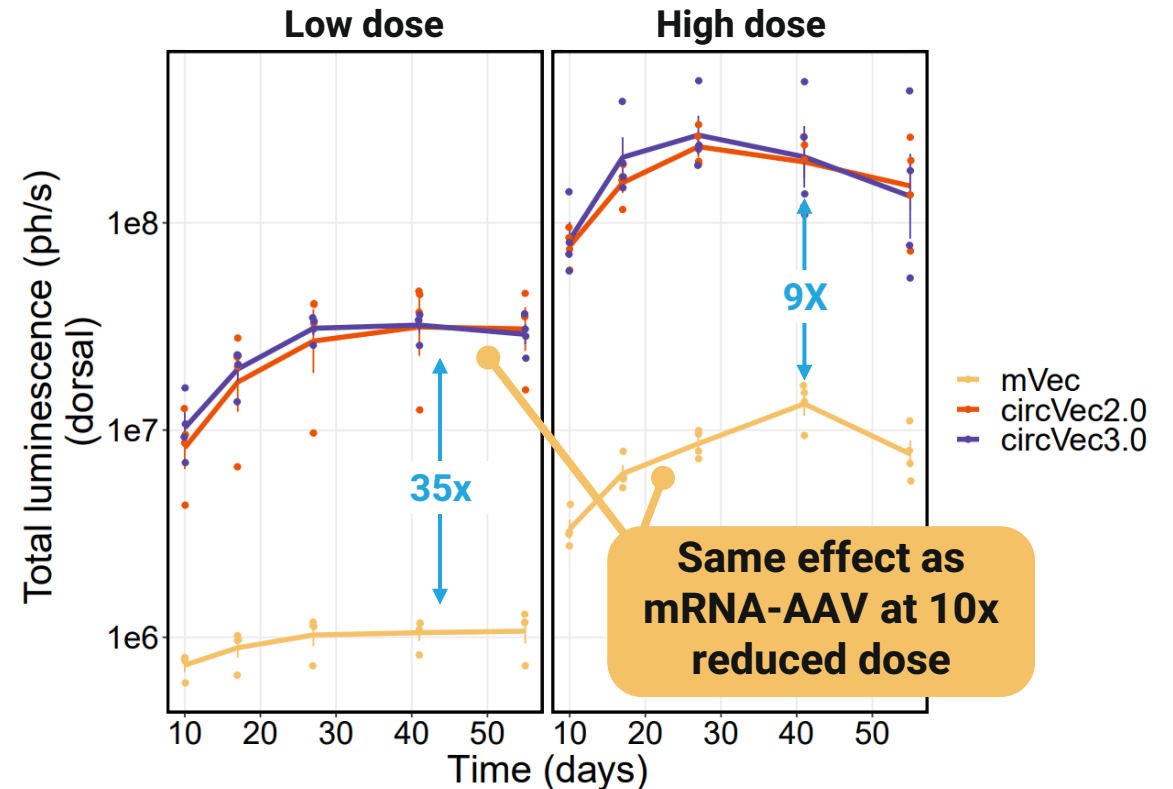
Data from May 2025: >10x advantage of circVec 2nd and 3rd generation vs. mVec-AAV in heart

AAV circVec, heart specific – two AAV designs
Quantification of signal (luminescence), high dose

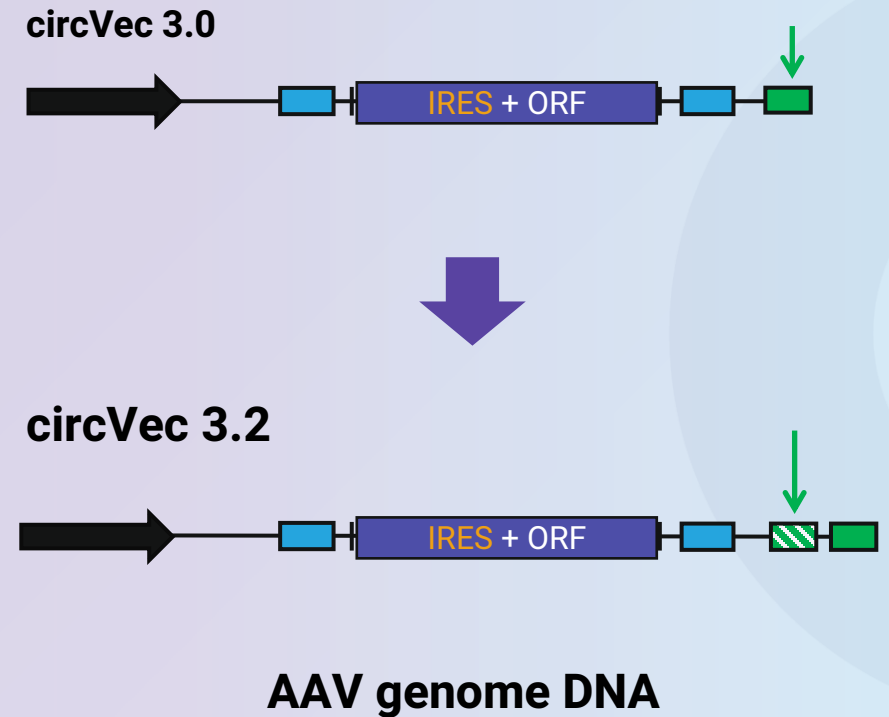
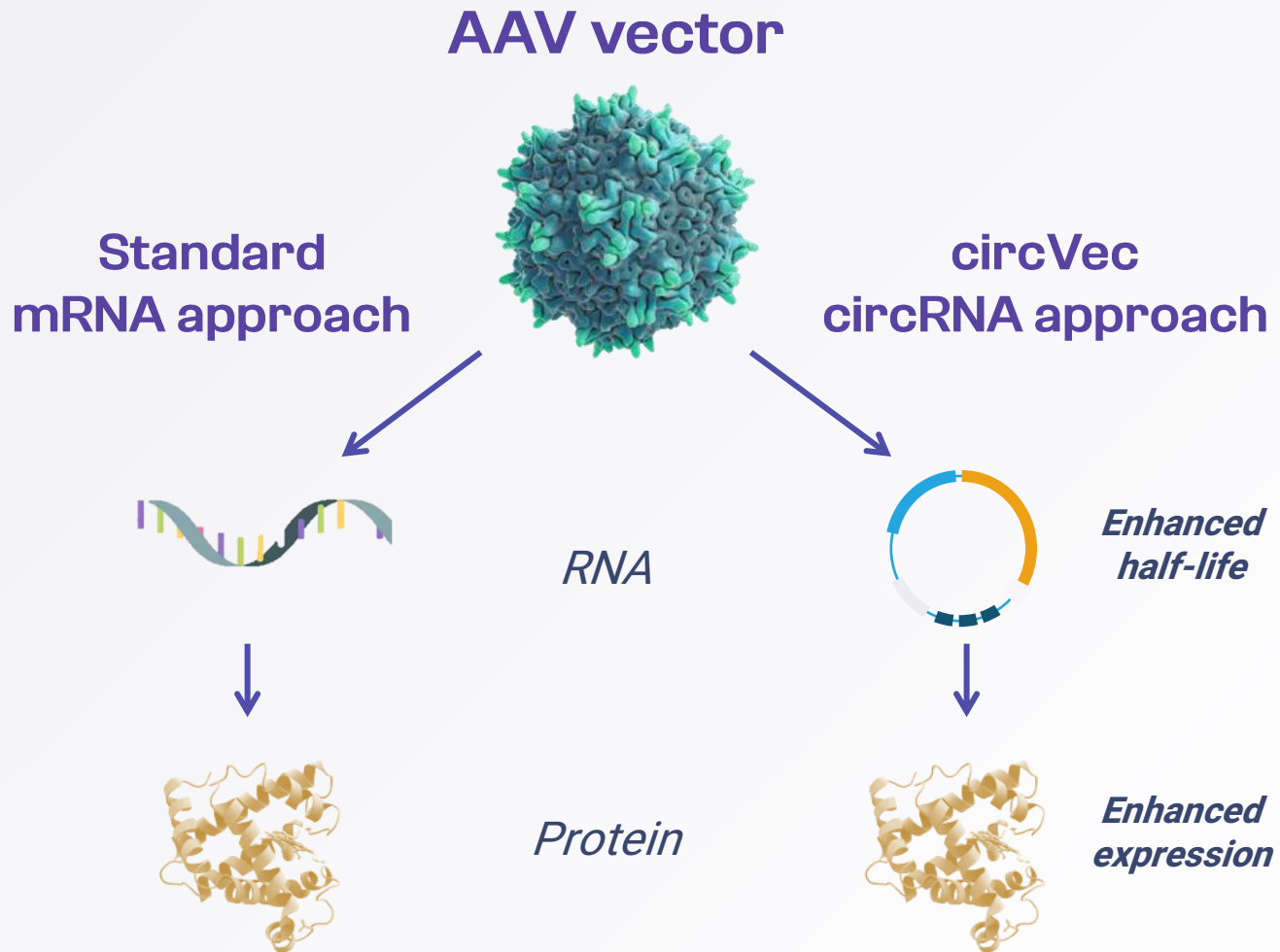


**Similar performance for circVec
2.1 and 3.0 in AAV format**

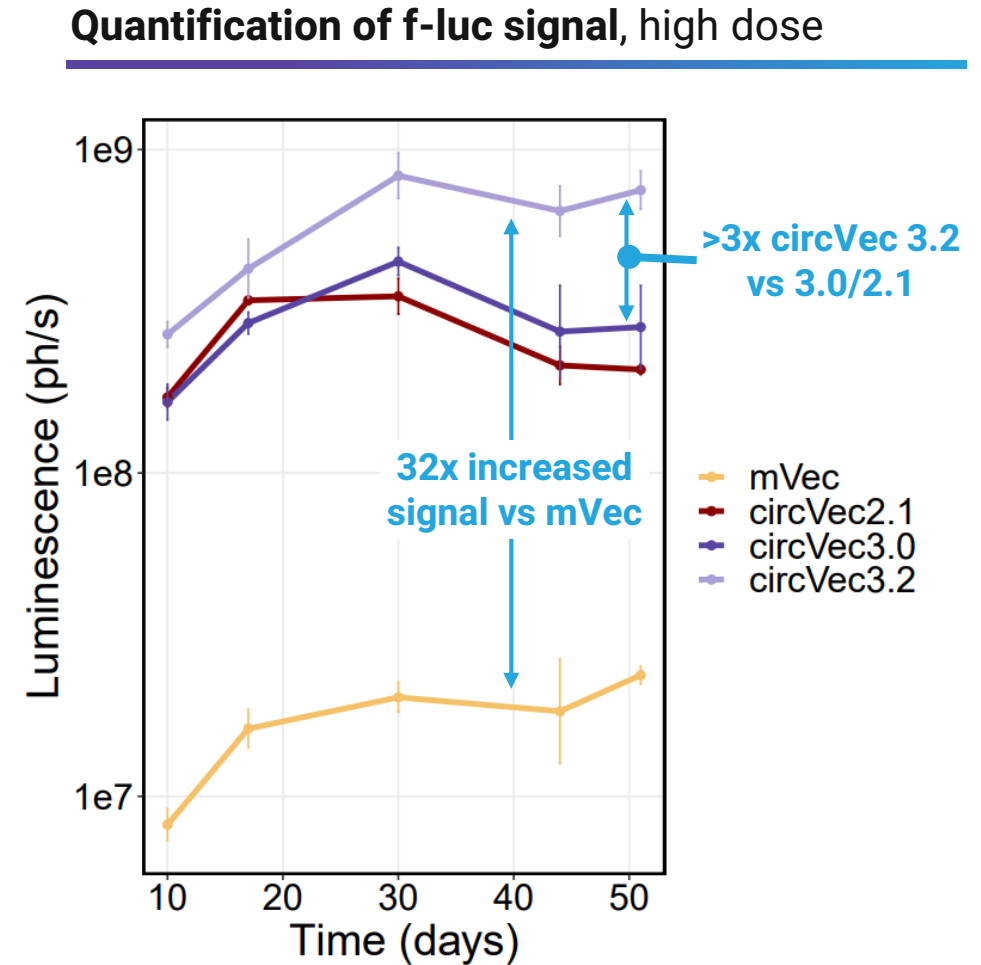
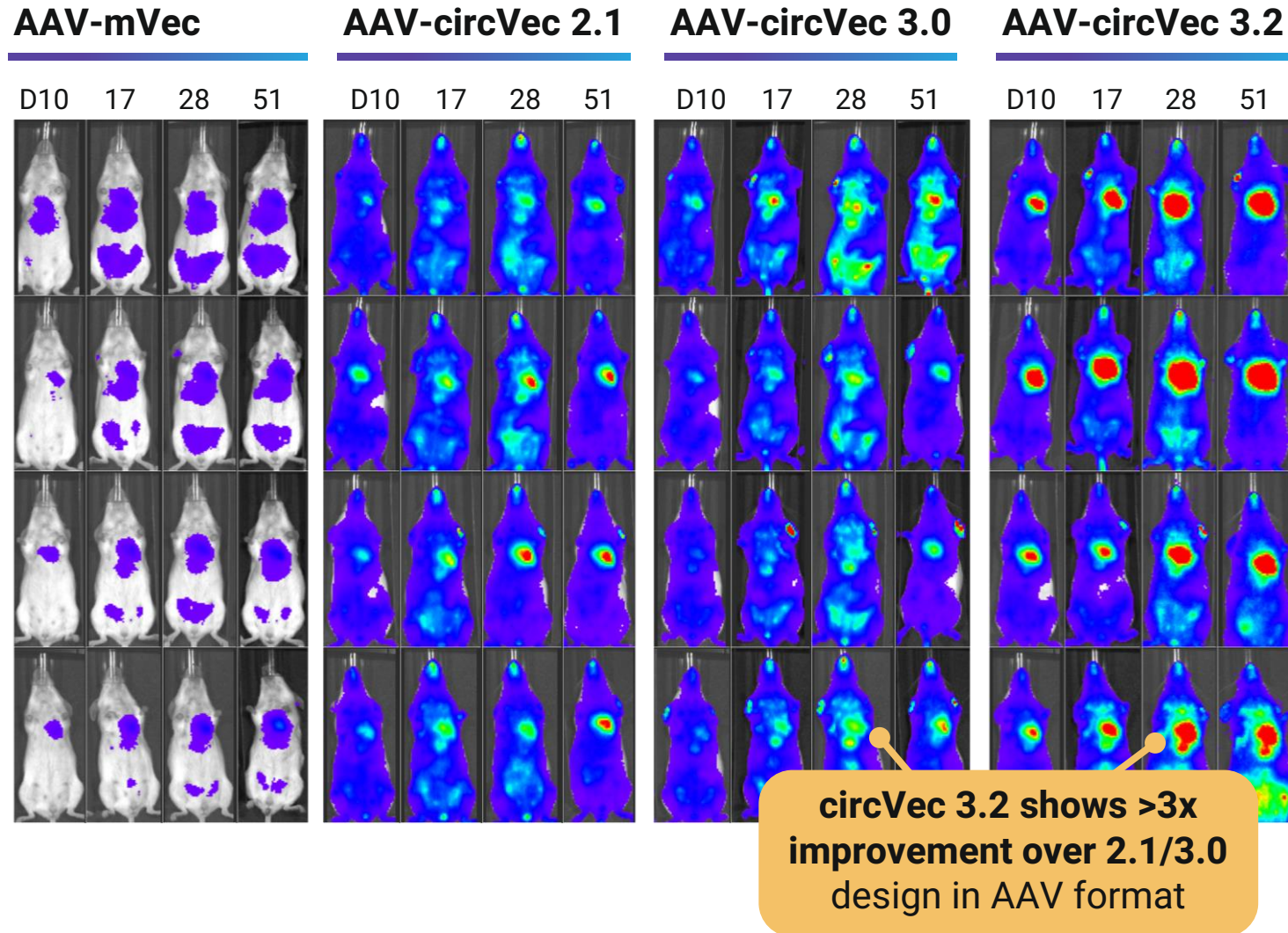
AAV-circVec, heart specific – two AAV designs
Quantification of signal, high/low dose comparison



Novel AAV-specific circVec 3.2 design identified

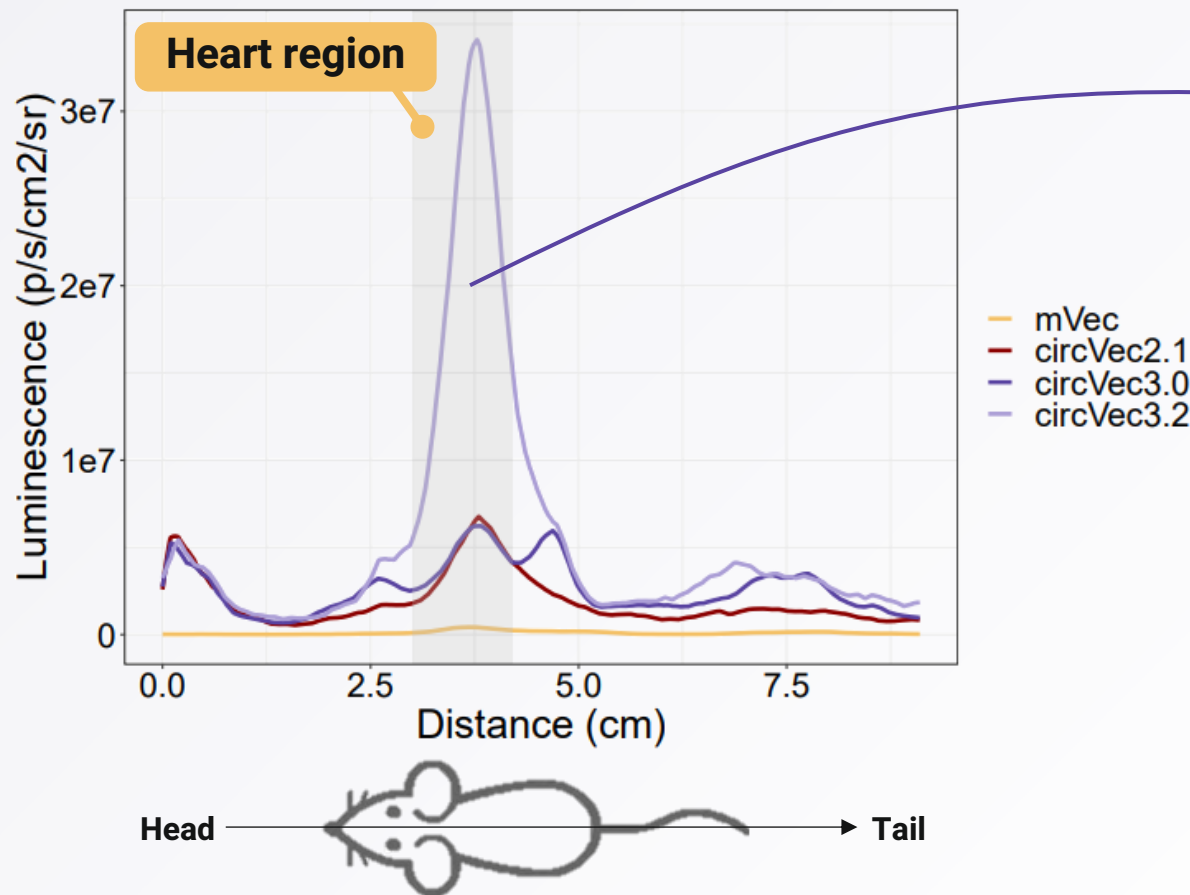


AAV-circVec 3.2 outperforms previous designs, increases advantage to >30x vs. mVec-AAV

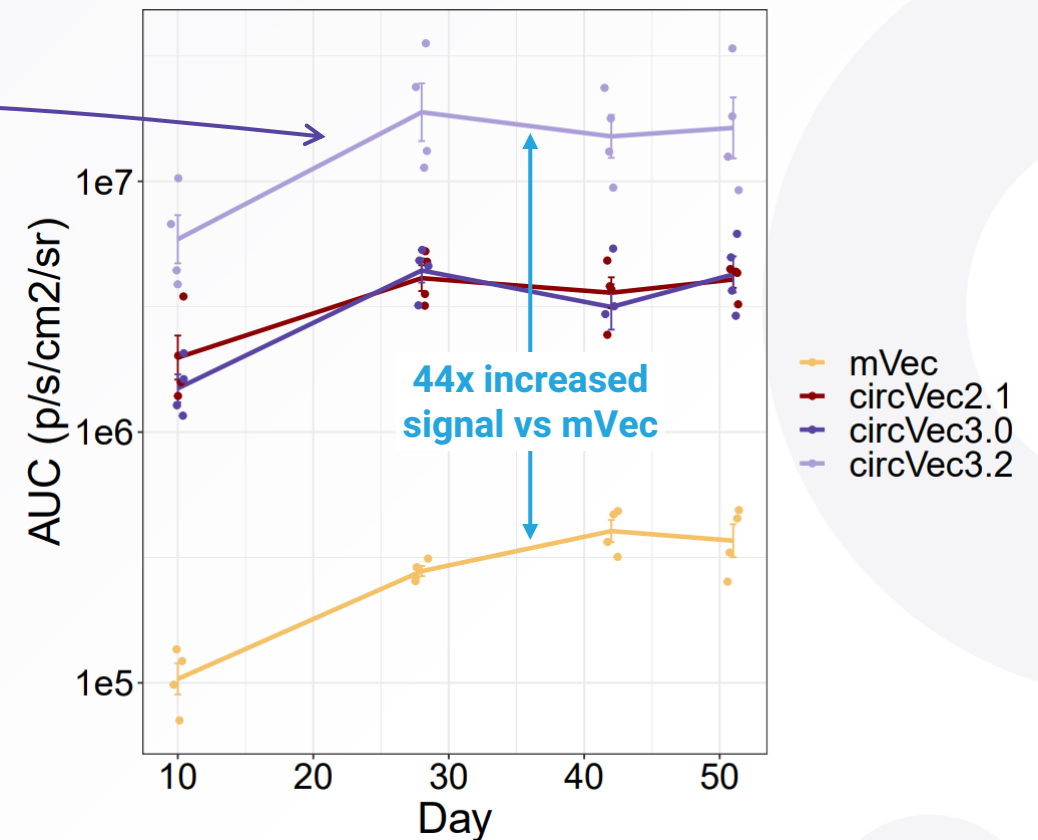


>40x circVec 3.2 advantage vs mVec in heart region

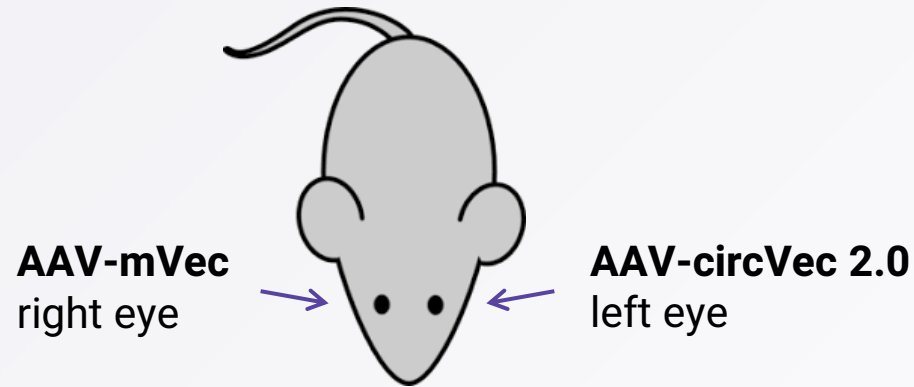
AAV f-luc signal profile from head to tail



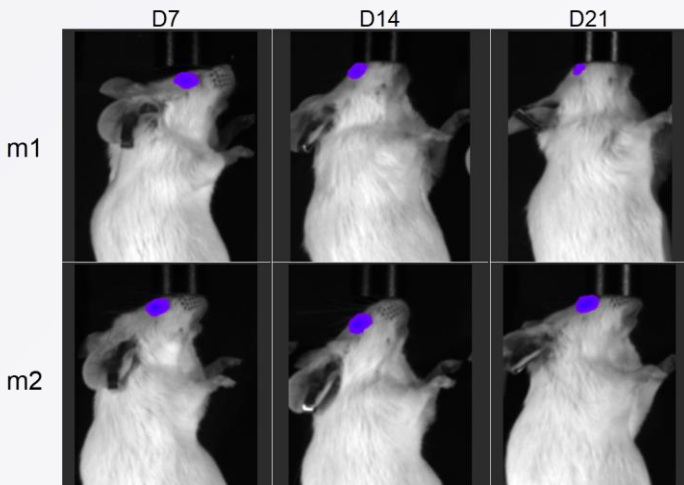
F-luc signal quantification, heart region



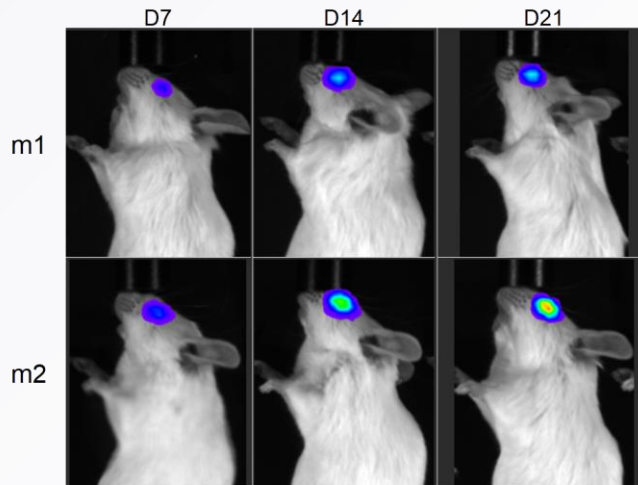
Robust AAV-circVec 2.0 advantage also shown in eye



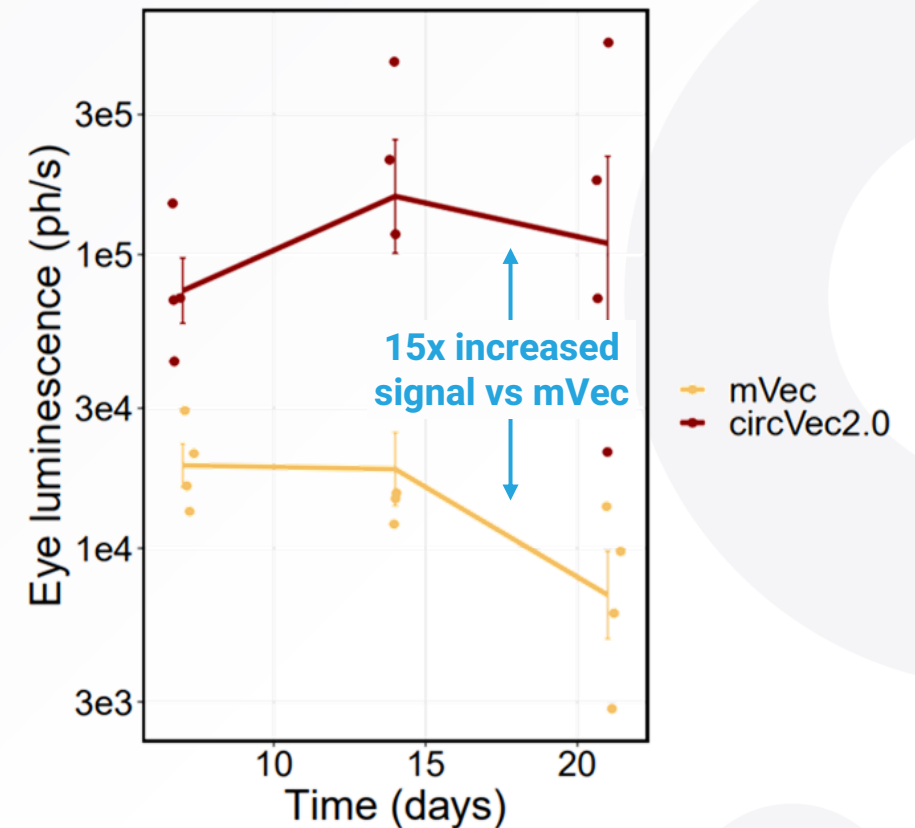
AAV-mVec, IVIS scan Day 7-21*



AAV-circVec, IVIS scan Day 7-21*



F-luc signal quantification in eye, Day 7-21*



* Ongoing experiment, high dose group

Take-home messages: transforming AAV gene therapy



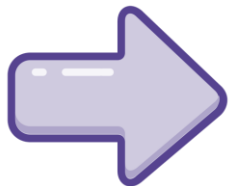
- **AAV-circVec** consistently **outperforms** conventional **AAV-mVec** designs by **10-40x**



- **AAV-circVec advantage** observed in **multiple tissues** using different **AAV variants and promoters**

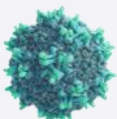



- **Novel AAV-specific circVec 3.2 design drives 3x enhancement** in vivo vs. prior generation 2 and 3 constructs



- **Transformative potential in AAV gene therapy: current data suggests circVec platform can unlock >10x dose reduction**
 - Improved safety profile, reduced toxicity
 - Lower cost

Development plan – Rich pipeline of R&D milestones

	Technical concept	In vitro PoC	In vivo technical PoC	In vivo disease model	IND enabling	Target milestones 2H 2025
 circVec-AAV	Heart & muscle			<i>In vivo testing of circVec 3.2 ongoing</i>		<ul style="list-style-type: none"> Fully implement circVec 3.2 design In vivo data secreted protein (eye) In vivo disease model data External H2H testing w/AAV partner
	CNS & eye			<i>In vivo testing of circVec 2 gen ongoing</i>		
 In vivo CAR-T	Spleen			<i>Identifying optimal vector and LNP combo</i>		<ul style="list-style-type: none"> Validate in vivo spleen delivery w/ novel vector and LNP systems Ex vivo T-cell CAR transduction External testing w/in vivo CAR partner

Continuous platform development: circVec generation 4, vector and delivery optimization



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Corporate update

Financial overview 1H 2025



Equity Financing

- **Warrant funds and Atlas facility** were the source of financing through 1H 2025
- **Ongoing discussion with investors** for new capital



Extended runway

- **Agreement with Atlas extends financing commitment until end of 2025**, with option for further extension
- **Continued tight cost control**, focus on R&D value creation



Reduced risk

- **Outstanding bonds reduced** from NOK 35m to NOK 9.5m*
- **Strengthened cap table with new investors**
- **Significantly strengthened data package reduces technical risk**, attracting partners and new investors

* As of 30.06.2025 (Nok 19m as of 28.08.2025)

1H 2025 accounts – continued tight cost control

NOK m	1H24	2H24	1H25 ¹	
Total revenue	0	0	0	
R&D expenses ²	-7	-4	-6	High number of ongoing in vivo projects
Payroll and related expenses	-10	-12	-10	Lean and efficient R&D team
Other operating expenses ³	-5	-3	-4	
Total operating expenses	-23	-20	-20	Cost control continues
Operating loss	-23	-20	-20	
Net financial items	65	35	-2	Waiver of ONCOS-102 R&D loans (2024)
Profit/loss before income tax	42	16	-22	
Net change in cash	-19	15	-12	
Net cash EOP	3	18	6	Drawing Atlas funds on a strict need-to basis

¹ Unaudited numbers

² Including patent costs

³ Including depreciation and impairment

Pursuing various options to strengthen the shareholder base and financial outlook



Financing

- **Continuously exploring multiple financing options**, building on recent strong AAV-circVec data
- **Market conditions remain challenging**, but improving slowly



Atlas facility

- **Financing commitment extended until end of 2025**
- Good relationship, **option for extension on mutual agreement**
- **Reliable access to capital** during tough market conditions



Business development

- **Continue to establish novel technology collaborations**
- **AAV gene therapy program most likely for short-term deal**
- **Monetize technology in non-core or complex areas**

Seven BD collaborations initiated in 2025



circVec
DNA DT*

- Entos PLV technology for DNA-circVec delivery
- Entos to drive and fund next stage of evaluation



circVec
DNA DT*

- Novel LNP formulation for spleen delivery of DNA-circVec
- Results showed specific and prolonged spleen expression



circVec
DNA DT*

- Neoregen CPP technology for DNA-circVec delivery
- Neoregen to fund next stage of in vivo evaluation



circVec
DNA format

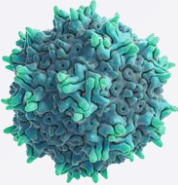


- Explore 4basebio DNA format for circVec
- 4basebio in house testing ongoing



Novel
Use

- Apply circVec to enhance protein manufacturing yield
- Ongoing testing of circVec in Lonza's proprietary system

circVec: next milestones and BD activities

		Next milestone	BD activities
	AAV gene therapy	<ul style="list-style-type: none">○ Test circVec 3.2 performance in multiple tissues○ CNS and eye in vivo data	<ul style="list-style-type: none">○ Active discussions with AAV gene therapy companies○ External circVec AAV testing
	DNA cell therapy	<ul style="list-style-type: none">○ Test new delivery systems○ circVec CAR expression○ Ex vivo T cell experiments	<ul style="list-style-type: none">○ Early discussions with cell therapy companies○ External circVec DNA testing
	DNA delivery	<ul style="list-style-type: none">○ Test additional LNP formulations○ Test other delivery systems○ Validate w/new DNA format	<ul style="list-style-type: none">○ Several ongoing collaborations○ Certest, Entos, 4BB + others, data during 2H'2025

Circio is the leader in circular RNA expression systems for gene and cell therapy – take-home messages:



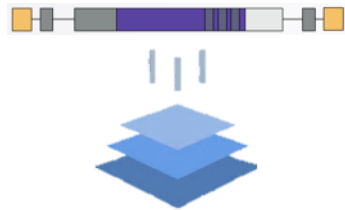
Durability

circVec offers **70x durability** and **15x protein expression advantage** over conventional mRNA-based expression
→ **transformative potential in gene and cell therapy**



Versatility

circVec **significantly improves** both **AAV and DNA vectors**
→ **Up to 40x enhanced activity of AAVs**, enabling dose reduction
→ **Novel LNP:DNA approach for in vivo CAR-T cell therapy**



Platform potential

circVec is a first-in-class, industry-leading circRNA expression system with **platform potential in multiple disease areas**

“Due to its significant advantages, circRNA systems can be expected to replace mRNA-based expression for DNA format therapeutics in the future – just as synthetic circRNA can be expected to replace current mRNA formats”

Dr. Alex Wesselhoeft
Scientific founder
oRNA Therapeutics

circio

Q & A Session

