



circio

Building next generation RNA therapeutics

Company update
16 May 2023

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 Targovax 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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Company update Erik D Wiklund - CEO

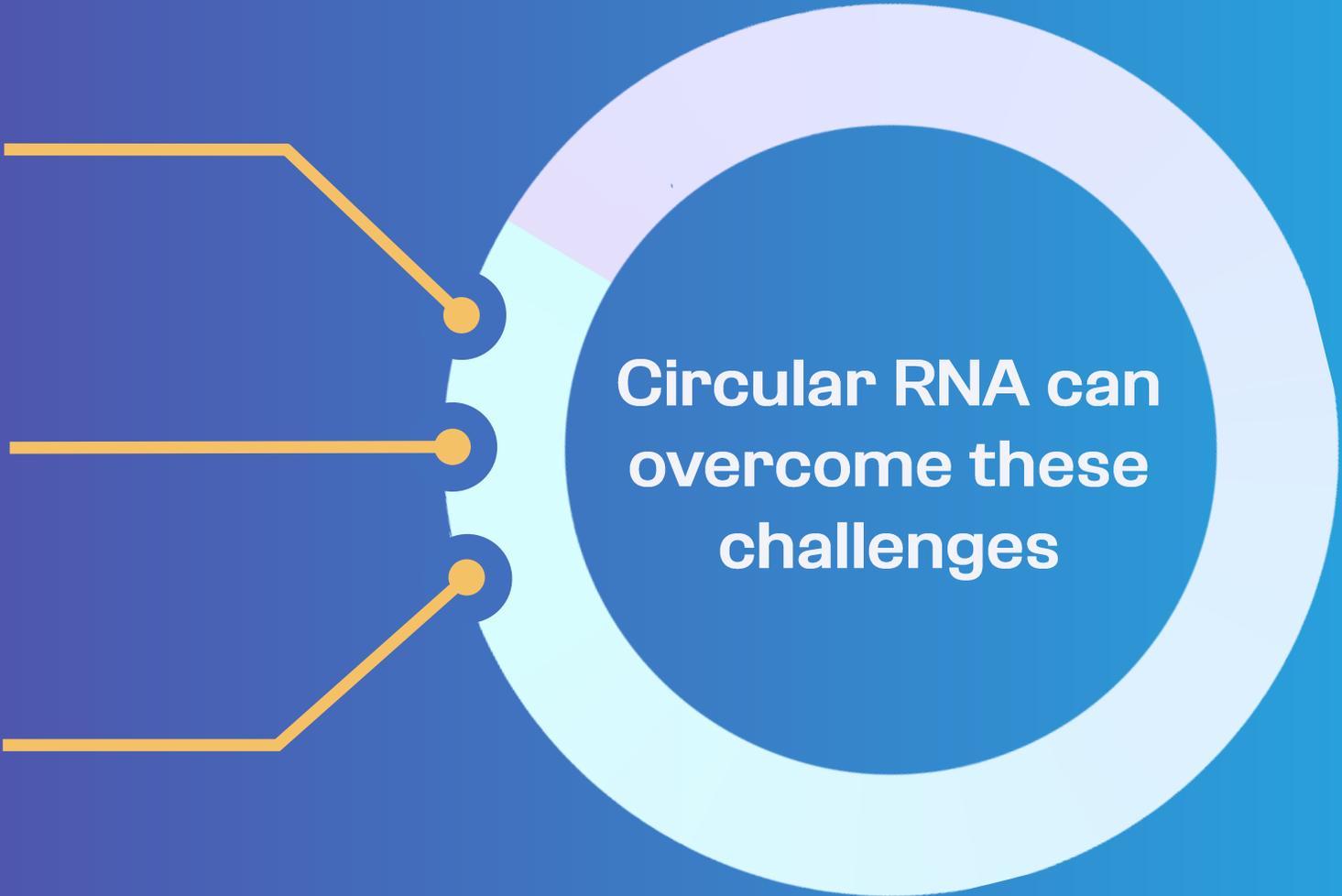
2. Corporate objectives & compensation
Thomas Falck, Chair of compensation committee
3. Board remuneration
Ludvik Sandnes, Chair of nomination committee
4. Q&A

mRNA has proven highly successful for COVID vaccines, but several challenges remain unsolved

RNA is chemically unstable – mRNA vaccines have required significant chemical modifications

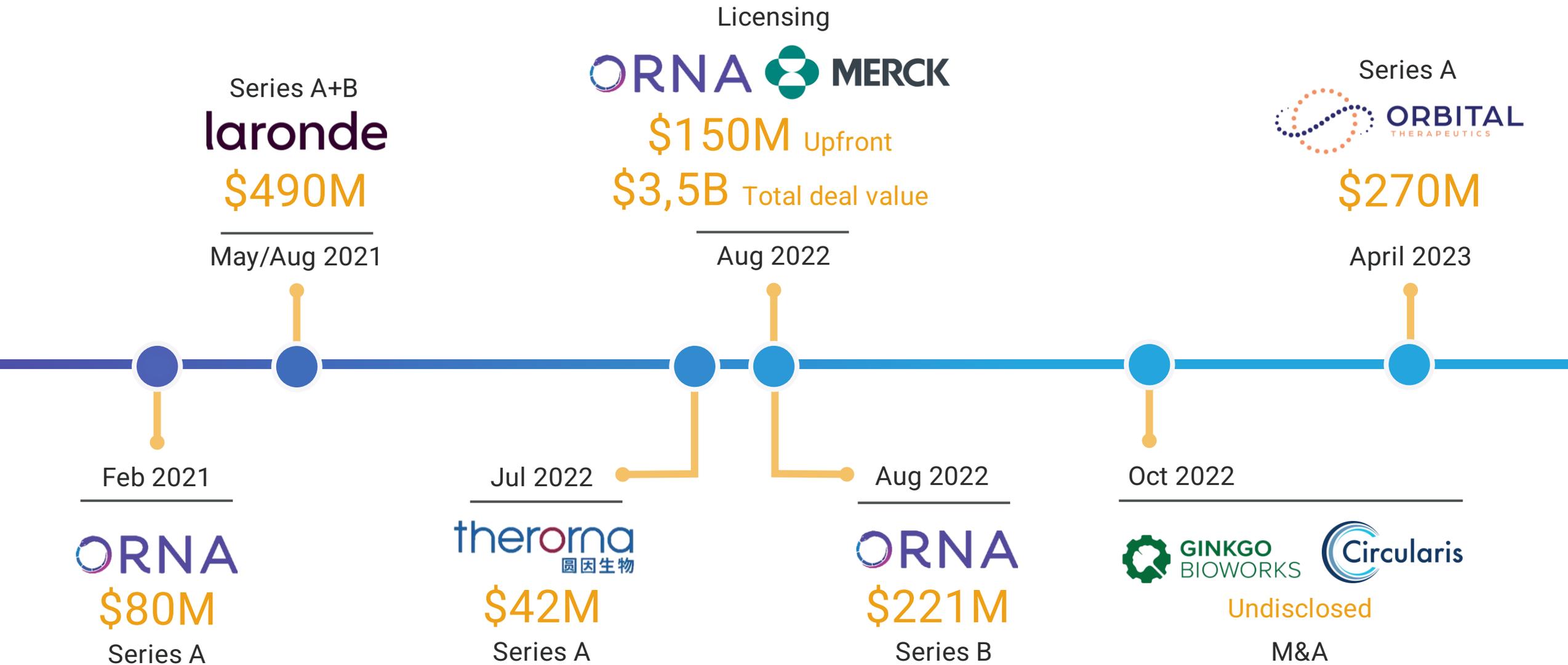
Efficient delivery of RNA therapeutics is currently limited to LNP-based systems for vaccines and liver targeting

mRNA has limited ability to deliver therapeutic protein payloads due to short half-life and immunogenicity

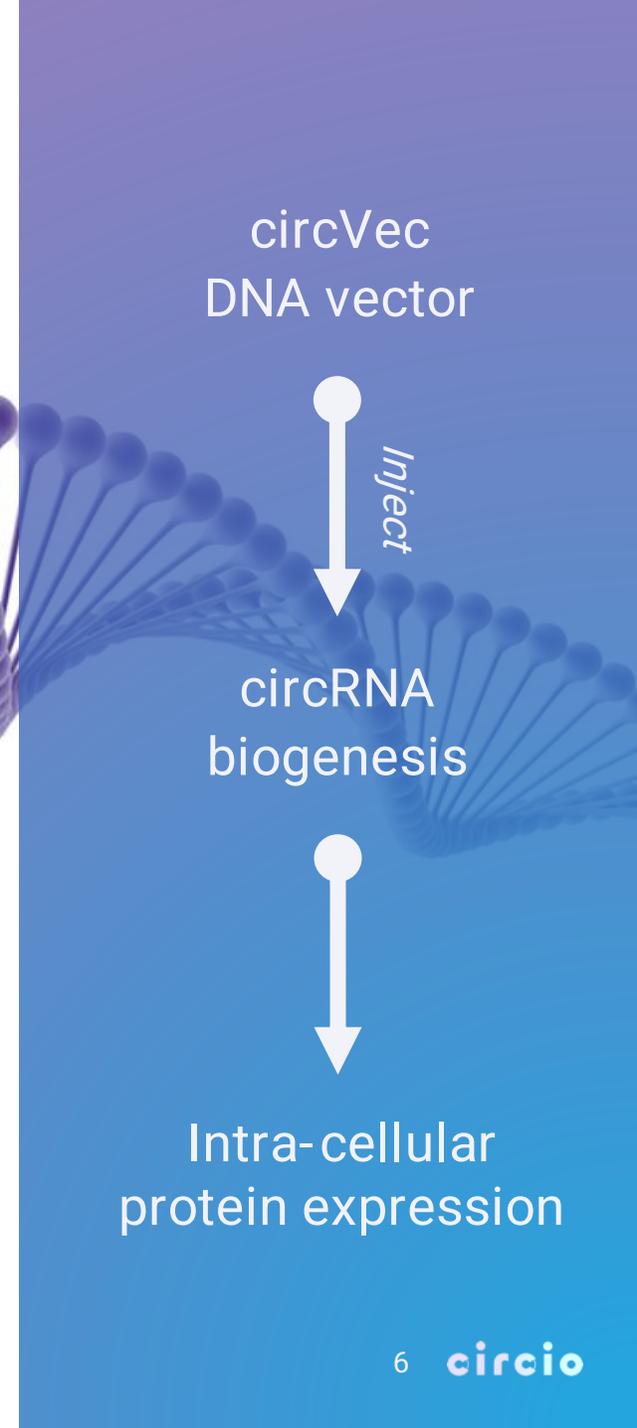
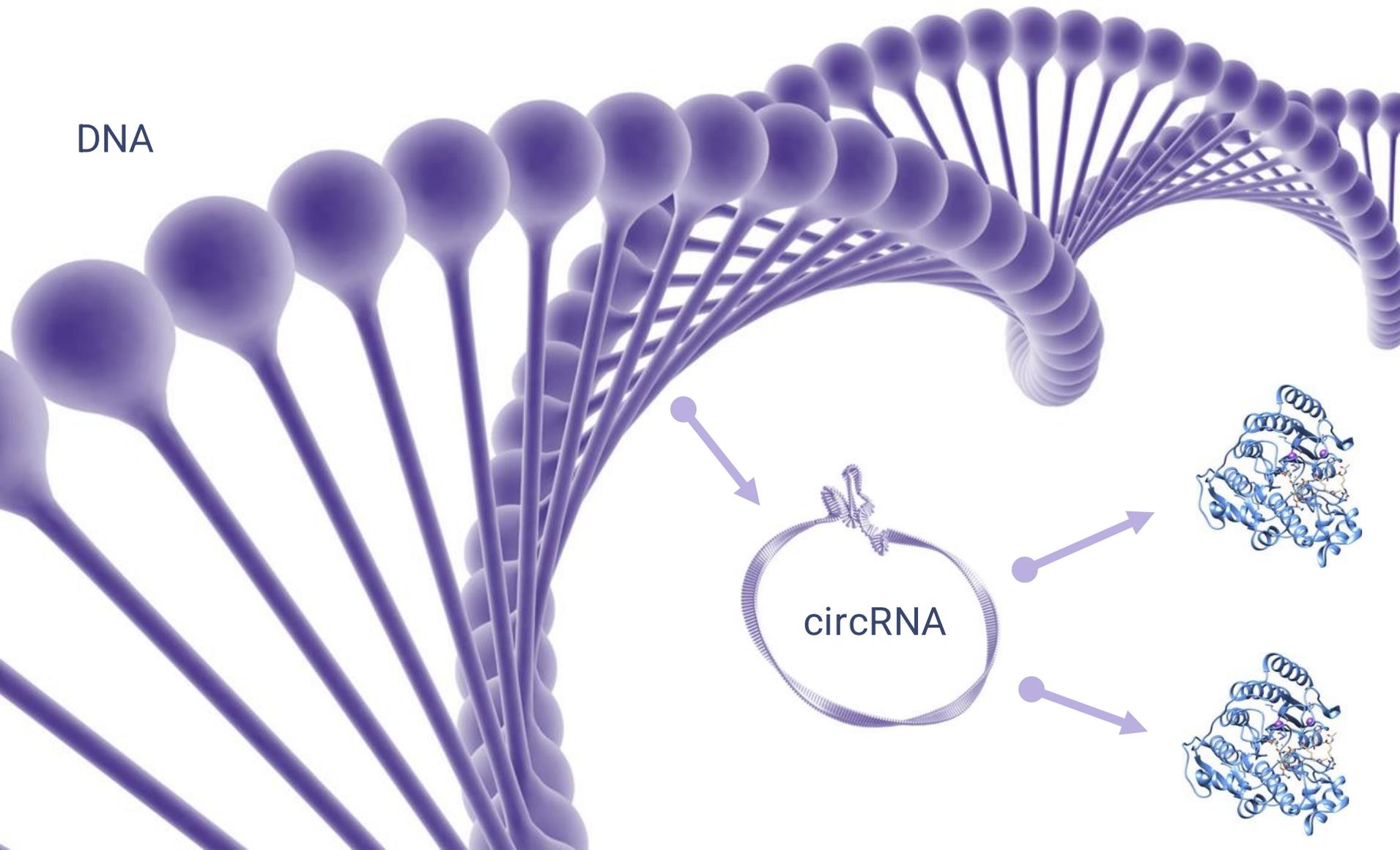


Circular RNA can overcome these challenges

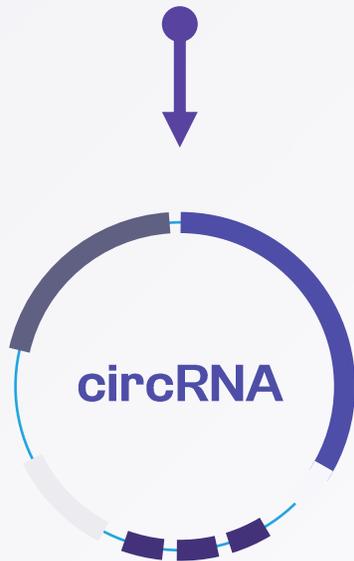
circRNA is rapidly gaining momentum as an enhanced mRNA format



circVec – Circio's proprietary vector system for intra-cellular protein expression



circVec is a modular genetic cassette for intracellular circRNA biogenesis and protein expression



Genetic cassette design

+

Multi-functional circRNA design

- Modular structure
- Efficient circRNA biogenesis
- Co-expression of siRNA for RNAi
- Core circVec design IP filed 4Q'22
- Vector agnostic – IP filed 1Q'23 for use in adenoviral vectors

- Long-half life
- Enhanced protein expression
- microRNA sponging
- Regulatory functionality

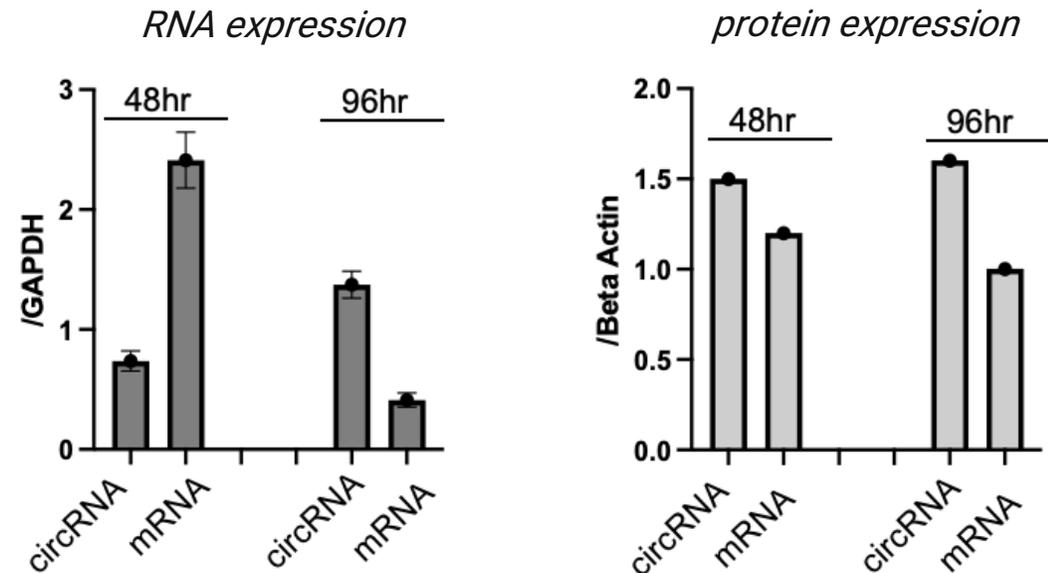
circVec achieves 15x prolonged circRNA half-life and increased protein expression vs. mRNA *in vitro*

circVec RNA stability
RT-qPCR, nascent vs. total RNA

135h vs. **9h**
circRNA mRNA

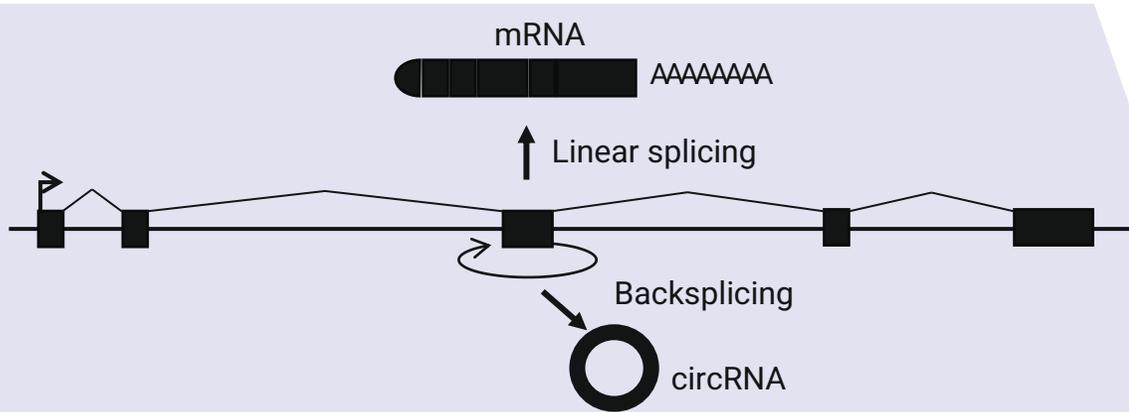


Accumulation of circVec circRNA and protein payload over time, RT-PCR and Western blot

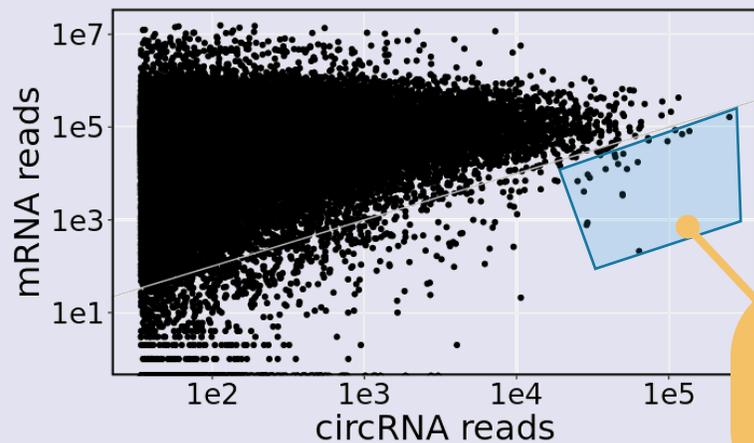


circVec v.1 outperforms mRNA in vitro – confirmatory in vivo experiments ongoing

circVec starting point is based on nature's best design

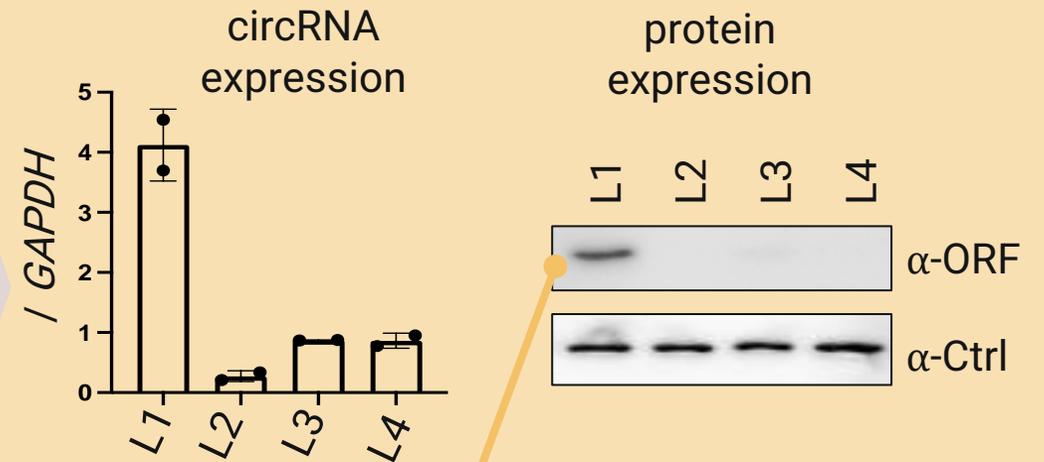


Expression of endogenous circRNA
NGS analysis of 300+ RNAseq datasets



Maximum
biogenesis-rate
of endogenous
circRNA

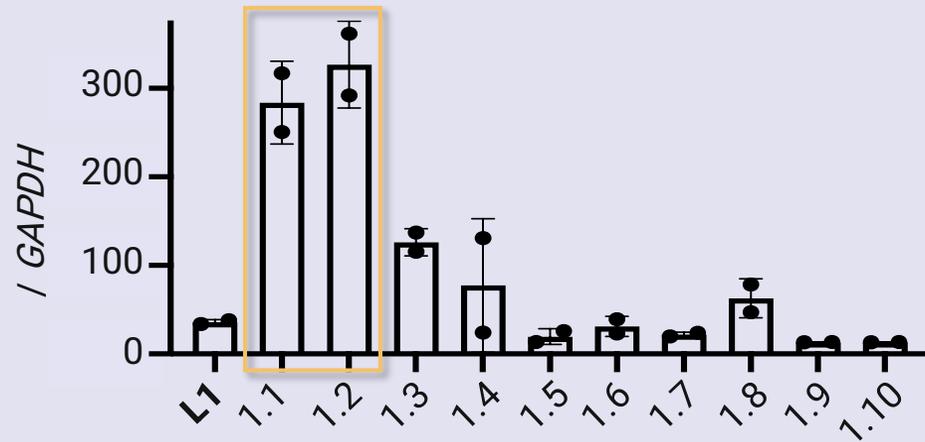
Screening of most effective circRNA-producing
sequences invented by nature



L1 cassette design
shows best circRNA
biogenesis

circVec design has been systematically optimized for circRNA biogenesis and protein expression

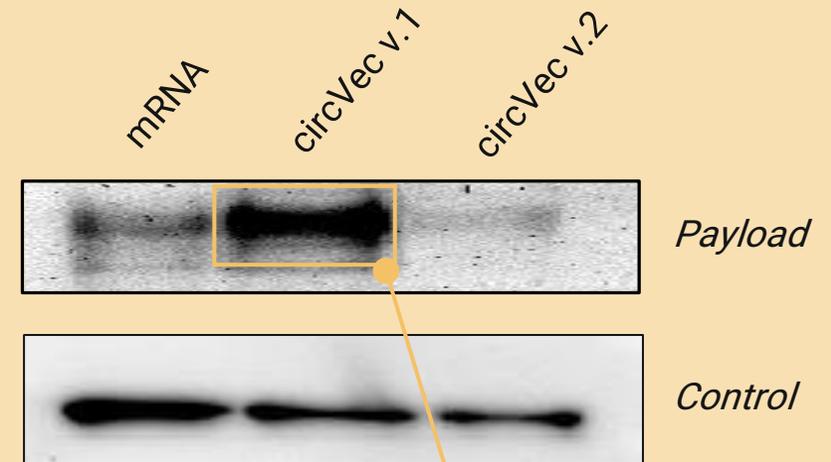
Design optimization for circRNA biogenesis
circRNA-specific RT-PCR



Design optimization for protein expression
Western blot, circRNA protein payload



Efficient circRNA designs outperform mRNA
Western blot, protein expression



circVec v.1 superiority over mRNA achieved by optimal combination of features

circVec can overcome limitations of linear RNA approaches and open new opportunities for circRNA

Oncology



Efficient, selective delivery and durable expression of therapeutic proteins in solid tumors

Vaccines



Enhanced potency, single dose vaccine concept with simplified administration

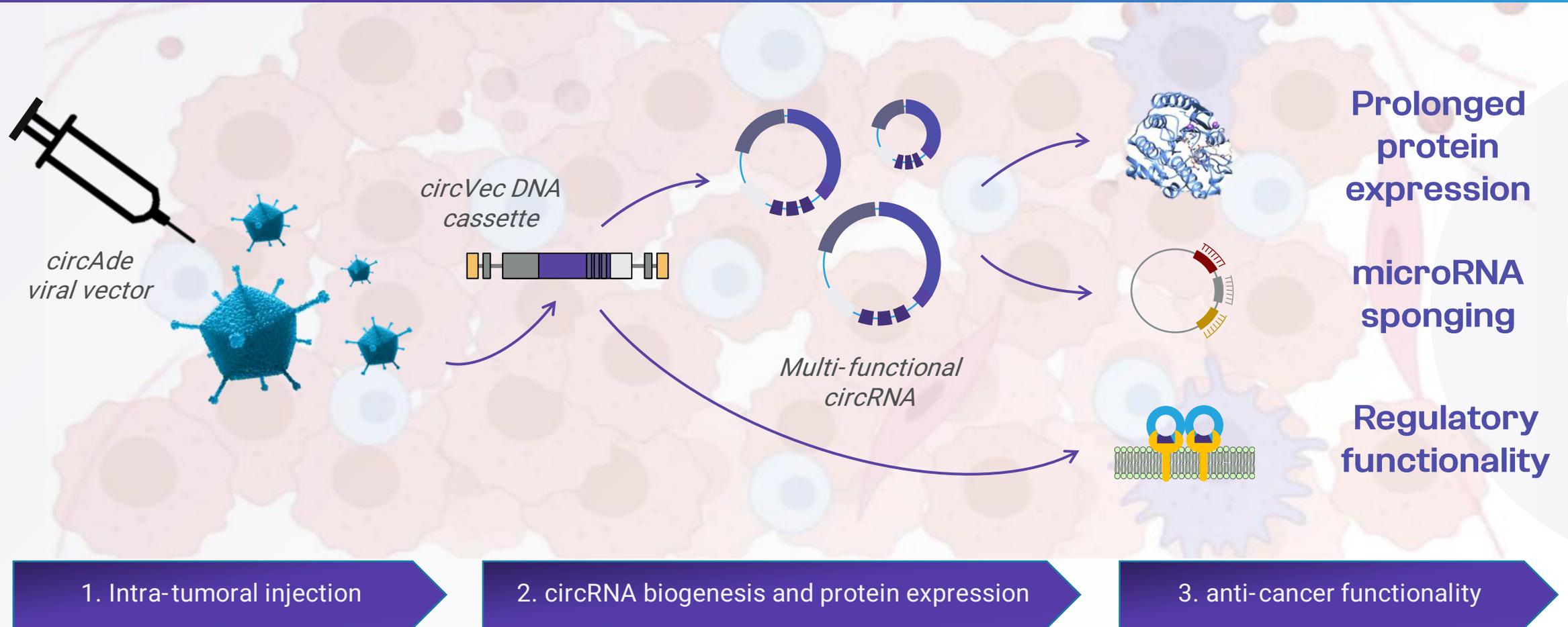
Rare disease



Durable protein replacement, without need for genome integration or LNP delivery

Designed for intra-cellular circRNA supply, durable protein expression and targeted regulatory functionality

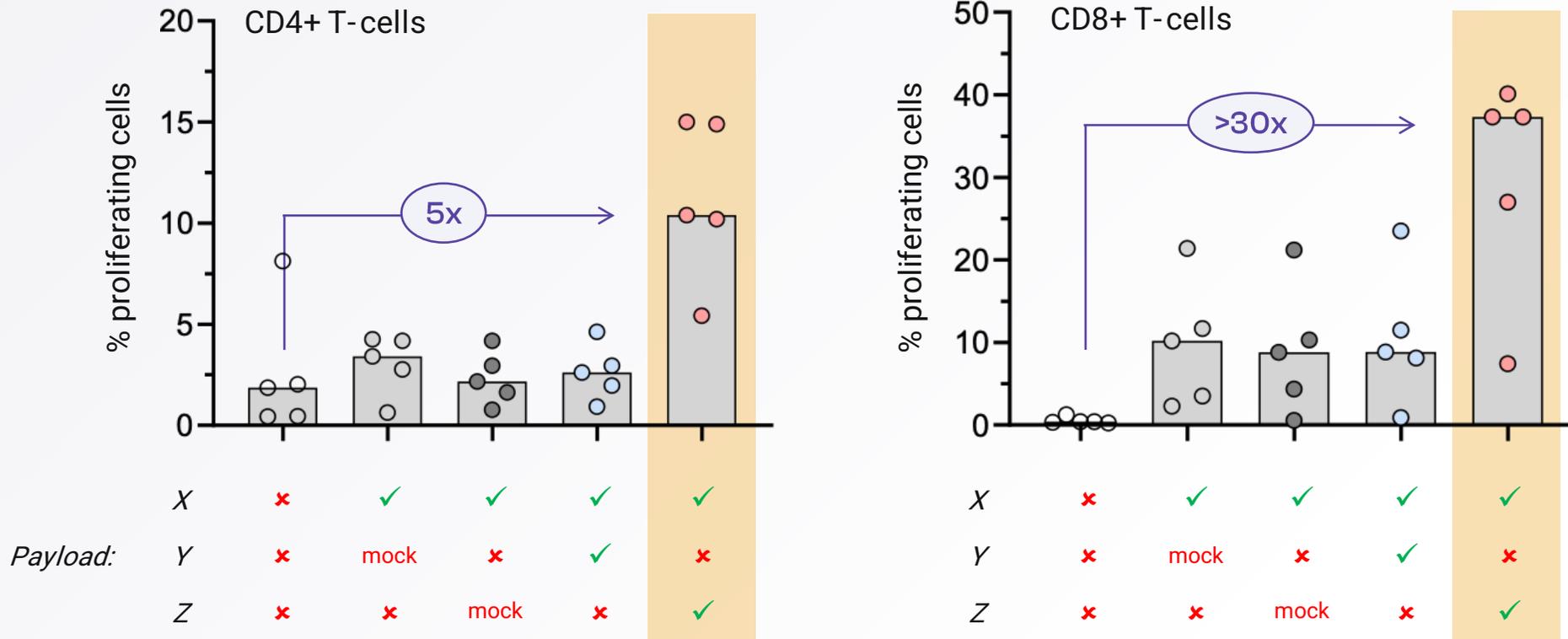
circAde concept for delivery to solid tumors: building on clinically validated in house adenoviral platform



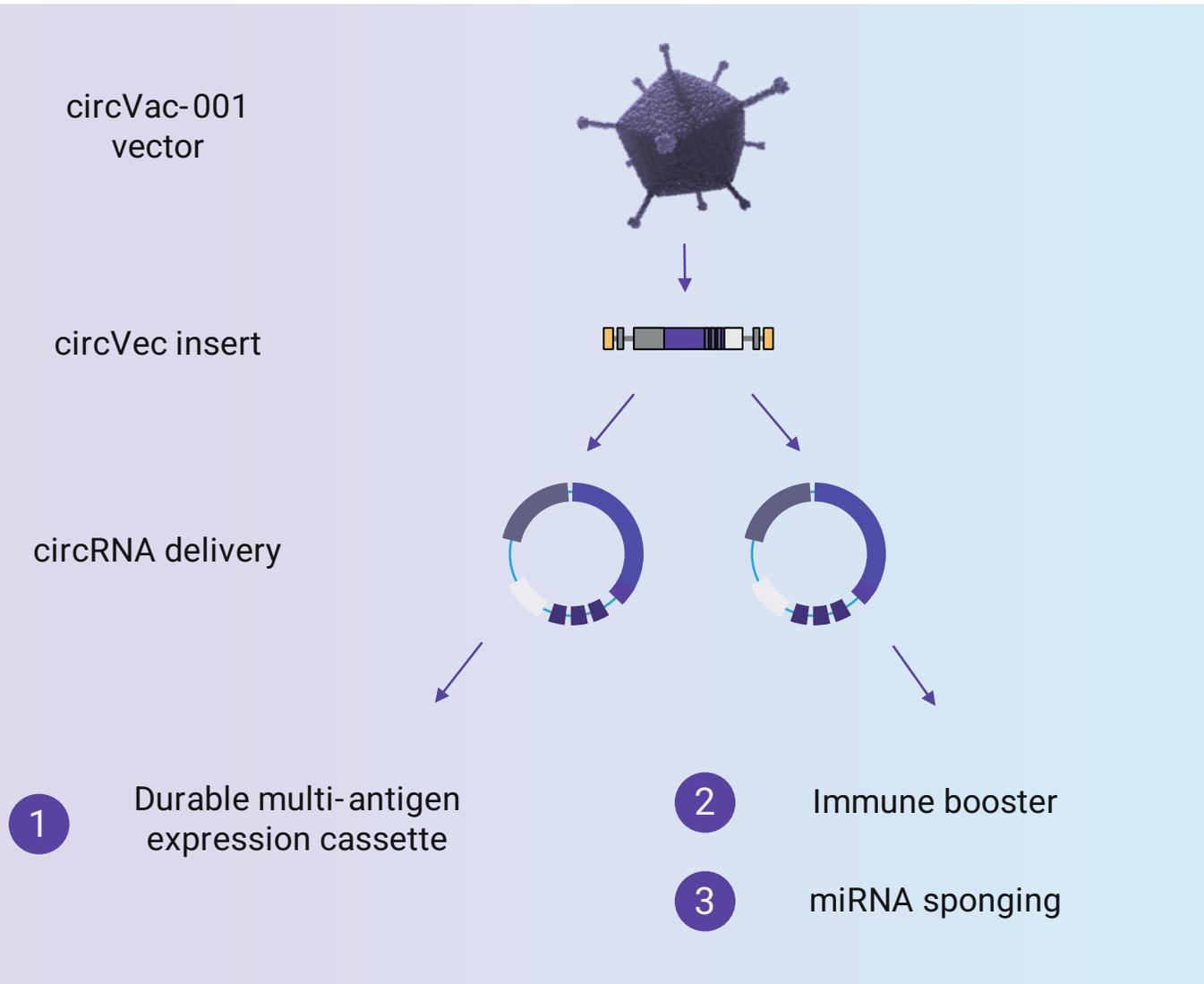
circAde payload screening has identified a potent combination for maximizing T-cell expansion

Ability of circAde payloads to drive T-cell expansion
T-cell proliferation assay, healthy donor lymphocytes

Selected payload combination



Vaccine project: Establishing circVac proof-of-concept with aim to out-license for clinical development



Development plan & target indication

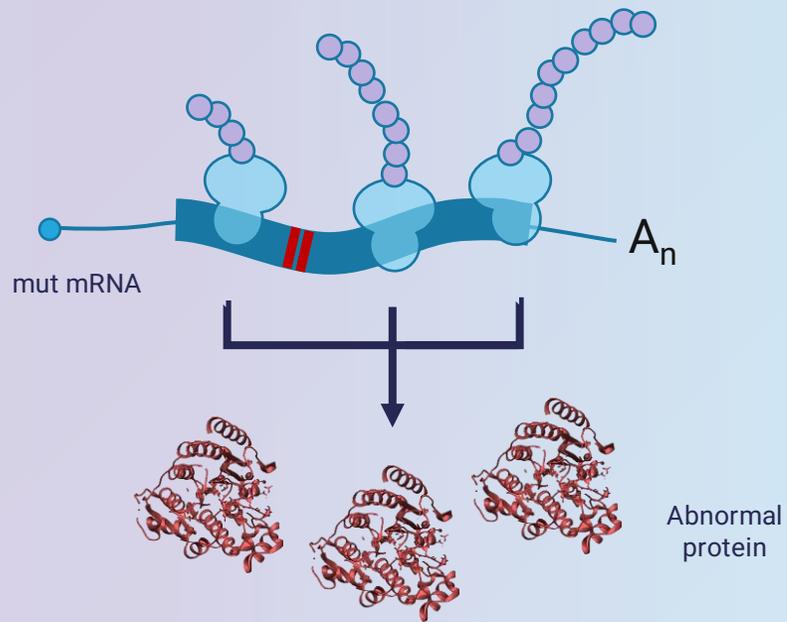
- Major infectious diseases where mRNA has had issues, e.g. influenza, shingles, malaria
- Out-license technical concept for clinical development following pre-clinical PoC

Project status

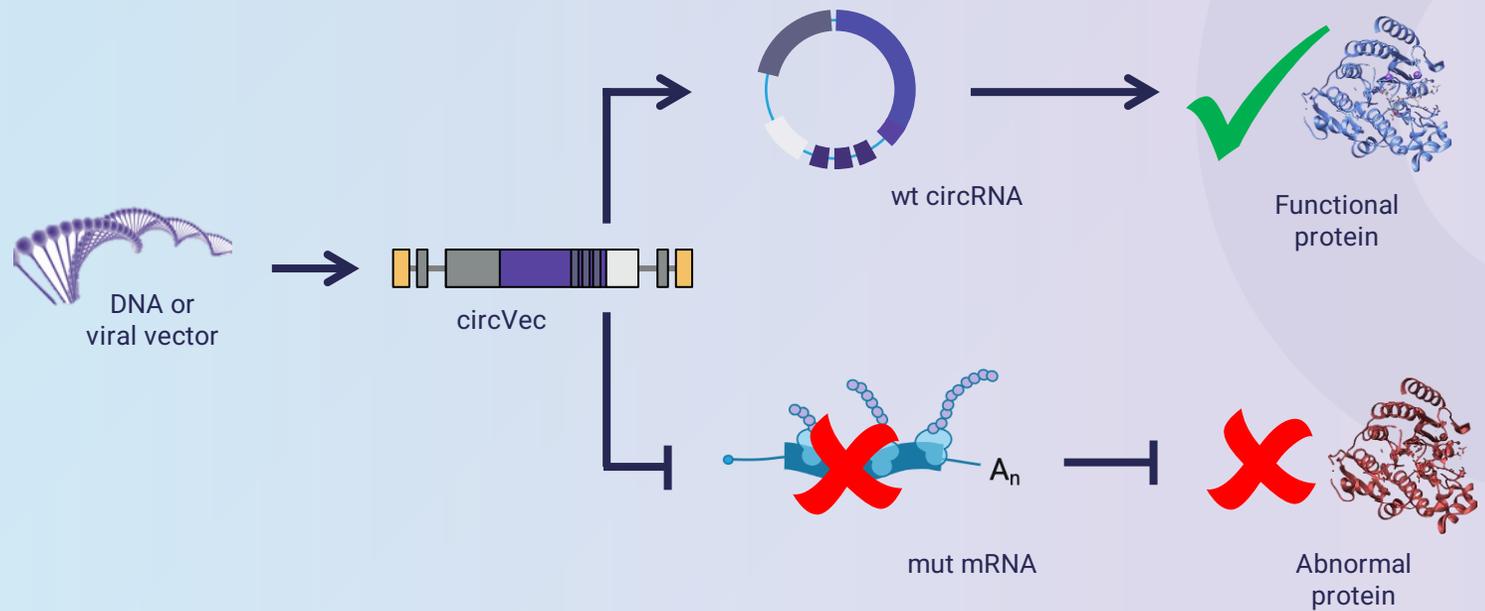
- Optimization of antigen expression level and durability for model antigens
- Comparative *in vivo* immunogenicity studies initiated
- Evaluation of immune booster options

"Remove-and-Replace" concept in monogenic disorders

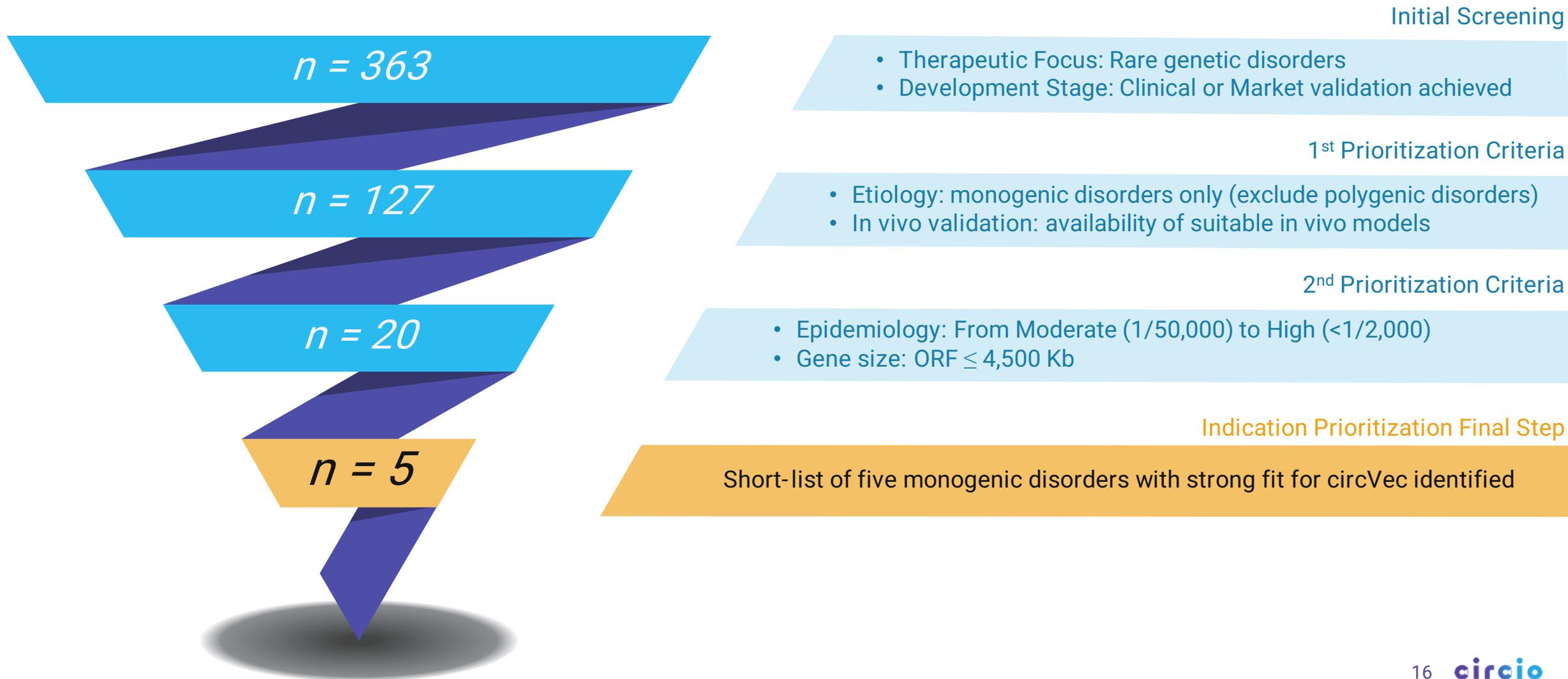
Mutations in the disease gene result in accumulation of abnormal protein in specific tissues



Depleting the mutant disease gene while replenishing with circRNA-encoded functional protein reverse toxic accumulation of abnormal protein and restores normal function



Screening and prioritization ongoing to identify target rare diseases suitable for circVec approach



Upcoming milestones for the three circVec programs

Oncology



In vivo circRNA expression and durability data in tumors, with comparison to mRNA

Vaccines



In vivo immunogenicity data, with comparison to mRNA

Rare disease



Disease and target selection, in vitro technical proof-of-concept

First *in vivo* studies initiated, read-out during 2H 2023

Circio has a unique edge in the emerging circRNA field



World-leading experts in-house with over 10 years experience in circRNA biology

- Led by circRNA discoverer and pioneer Dr. Thomas B Hansen



Differentiated vector delivery platform opening new therapeutic areas for circRNA

- Unique lead program in cancer, rapid expansion to vaccines and rare disease
- Efficient circRNA biogenesis and superiority vs. mRNA established in vitro
- In vivo PoC studies initiated – first validation of a vector-delivered circRNA



Circio aims to be first to clinic with a circRNA product already in 2025

- Leveraging clinical validation and existing manufacturing capability for in house AdV5 vector platform

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Corporate objectives & compensation

Thomas Falck – Chair of
compensation committee

3. Board remuneration
Ludvik Sandnes, Chair of nomination
committee

4. Q&A

Circio has attracted a strong international senior management team with broad experience



Dr Erik D Wiklund
Chief Executive Officer

Co-discoverer of circRNA, Pharma consultant at McKinsey & Co and various commercial and R&D roles in biotech, Previously CFO and CBO of Targovax

PhD Cancer epigenetics and non-coding RNA



Dr Lubor Gaal
Chief Financial Officer

BD and finance industry executive with 25 years experience from big pharma and biotech, incl. BMS, Bayer, Ammirall and Locust Walk

PhD Molecular and cell biology



Dr Lone Ottesen
Chief Medical Officer

Extensive experience across global oncology and immune-oncology drug development spectrum with nearly 20 years from AZ, GSK ++

MD, PhD



Dr Victor Levitsky
Chief Scientific Officer

Deeply experienced tumor immunology scientist from academia and industry, incl Karolinska Institute, John's Hopkins, Roche and Molecular Partners

MD, PhD Virology and tumor biology



Dr Thomas B Hansen
VP & Head of Research

World-leading pioneer and co-discoverer of circular RNA; 10 years as group leader at Aarhus University in RNA biology and bioinformatics

PhD Molecular Biology and Bioinformatics



Mr Ola Melin
VP & Head of Manufacturing

25 years experience in Biologics development, manufacturing, and supply, most recently as Director of Technical Operations at OxThera AB.

BS Biochemical engineering



Circio compensation policy

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**Base
salary**

**Competitive pay level for
Norway / Nordics**

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Bonus

**Short-term incentive,
operational objectives**

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Options

**Long-term retention,
strategic objectives**

Circio is competing for specialized competencies and talent in an international market

Corporate Objectives

Background:

- Defined and agreed with management during Q1 each year
- Specific and measurable
- Both strategic and operational
- Covers all corporate functions

How are they used?

- Rating is the basis for bonus payment to management and staff
- CEO bonus % is equal to total corporate objectives rating
- Other management rated 50% on corporate and 50% on function objectives
- 2022 total score: 90%
- 2021 total score: 72%

Category	Objectives ¹	Weight
Finance	Main goal: Secure financing through first data read-out from melanoma platform trial	25%
	Develop attractive and ambitious new investor pitch by end of February 2022	
	Execute US and EU road shows with specialist investors by Q3 2022	
	Secure financing to mid-2024	
Clinical development	Main goal: On track for first patient in for melanoma platform trial in Q1 2023	20%
	Request FDA type C meeting and provide briefing package by April 2022	
	Final protocol ready and signed-off in time to enable enrollment by Q1 2023	
	Provide all necessary Targovax documentation to enable successful IND/CTAs for TG clinical trials	
Pipeline development	Main goal: File first circRNA-ONCOS patent application	15%
	Generation and full in vitro testing of first round of circRNA constructs by Q3 2022	
	File first circRNA patent application by Q4 2022	
	Generation and first in vitro testing of constructs for 3 collaboration partner projects by Q4 2022	
Business development	Main goal: Secure supply collaboration for aPD1 + novel combination drug for melanoma platform trial	15%
	Secure anti-PD1 and anti-CTLA4 supply collaboration for ONCOS-102 platform trial by Q1 2022	
	Execute TG01 study contracts with Oslo University Hospital and Kansas University by Q2 2022	
	Enter at least one new pre-clinical research collaboration	
Manufacturing	Main goal: Keep ONCOS-102 scale-up process development and TG supply on track on cost and timelines	15%
	Execute ONCOS-102 manufacturing scale-up plan according to board approved budget and timeline	
	Complete TG01 DS and DP manufacturing in time for trial opening	
	Ensure on time ONCOS-102 and TG01/02 drug supply to all clinical trials and pre-clinical collaborations	
Corporate development	Main goal: Develop new equity story, company positioning and branding	10%
	Revamp visual profile and strengthen design/branding by Q3 2022	
	Enhance external visibility and communications locally and internationally (e.g. conferences, media, etc.)	
	Fill key vacancies to strengthen science and finance/BD teams and complete the organizational structure by Q2	

¹ Structure and examples of actual 2022 objectives

The option program is used as a tool for long-term incentives and employee retention



- New employees
- Annual performance grants
- Promotions
- ca. 60:40 split between management : staff

Delayed vesting incentivizes employees to stay, non-vested options are lost upon resigning

- Four years vesting period
- First vesting after 12 months
 - 1/4 of options after 12 months
 - Then 1/36 of options per mo. until fully vested after 4 years

- If vested options are “in-the-money” they can be settled by:
 - Cash payment
 - Transfer of own shares held by Circio (Targovax) ASA
 - Issuing new shares

The board requests an annual mandate from the AGM to settle existing options by issuing new shares – lowest cost settlement alternative for the company

3

Board remuneration

Ludvik Sandnes– Chair of
nomination committee

4. Q&A

Circio has established a strong, international Board covering key competencies



Damian Marron
Chairperson

Thomas Falck
Director, chair of comp. com.

Robert Burns
Director

Diane Mellett
Director

Sonia Quaratino
Director

Raphael Clynes
Director

Bente-Lill Romøren
Director



Biotech executive experience & financing

Finance, Norwegian board experience

Immunology, biotech executive experience

IP law and patenting

Clinical development

Pre-clinical development

RadForsk representative, Norwegian pharma

Remuneration policy for the Board of Directors

2023 compensation level

- Chairperson: NOK 535,000
- Director: NOK 320,000
- Committee chairs: NOK 40.000
- Committee members: NOK 20.000

Below average level for OSE listed companies

Payment options

- Each individual Director can select to receive the annual remuneration either as:
 - **Cash**
 - **Restricted Stock Units (RSUs)**
 - A **combination** of cash and RSUs

Over the past 3 years, 68% of total given as cash and 32% as RSUs
- RSUs reduce cash cost to the company

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Q&A
