circio

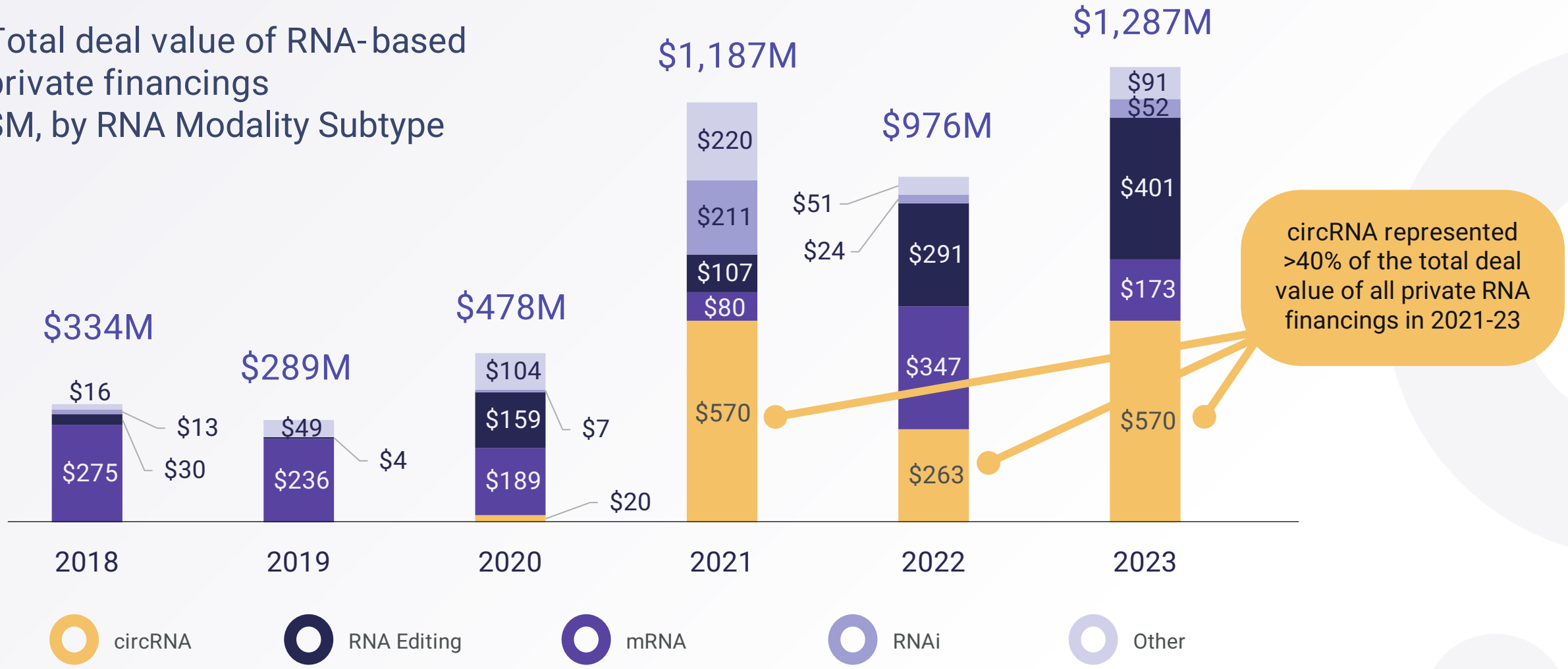
Disruptive circRNA technology for genetic medicine

Dr. Erik Digman Wiklund - CEO

BioSeed - London
22 January 2024

RNA financing has flowed from mRNA towards circular RNA during 2021-23

Total deal value of RNA-based private financings
$M, by RNA Modality Subtype



Source: BioEquity

Note: Other includes ASOs, saRNAs and tRNA private financing deals

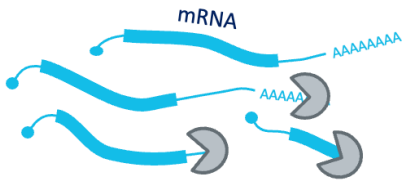
Circular RNA (circRNA) is a novel disruptive RNA format

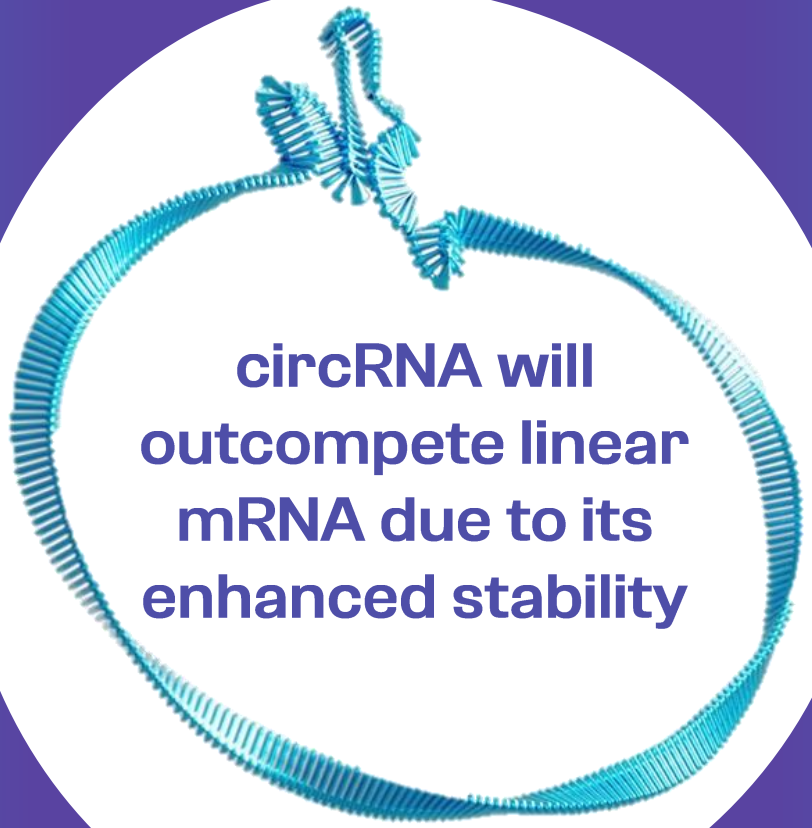
Extended RNA durability

15x half-life vs. mRNA

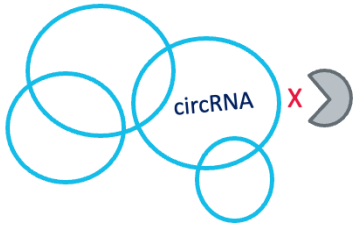
Higher protein expression

5x translation rate vs. mRNA





circRNA will outcompete linear mRNA due to its enhanced stability



microRNA sponging

mRNA is destabilized by microRNAs

Modular & multi-functional

Enables ´remove & replace´ strategy

The discoverers of circRNA are in the Circio leadership team

Dr Thomas B Hansen

Dr Erik D Wiklund

nature 6,373 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 922 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

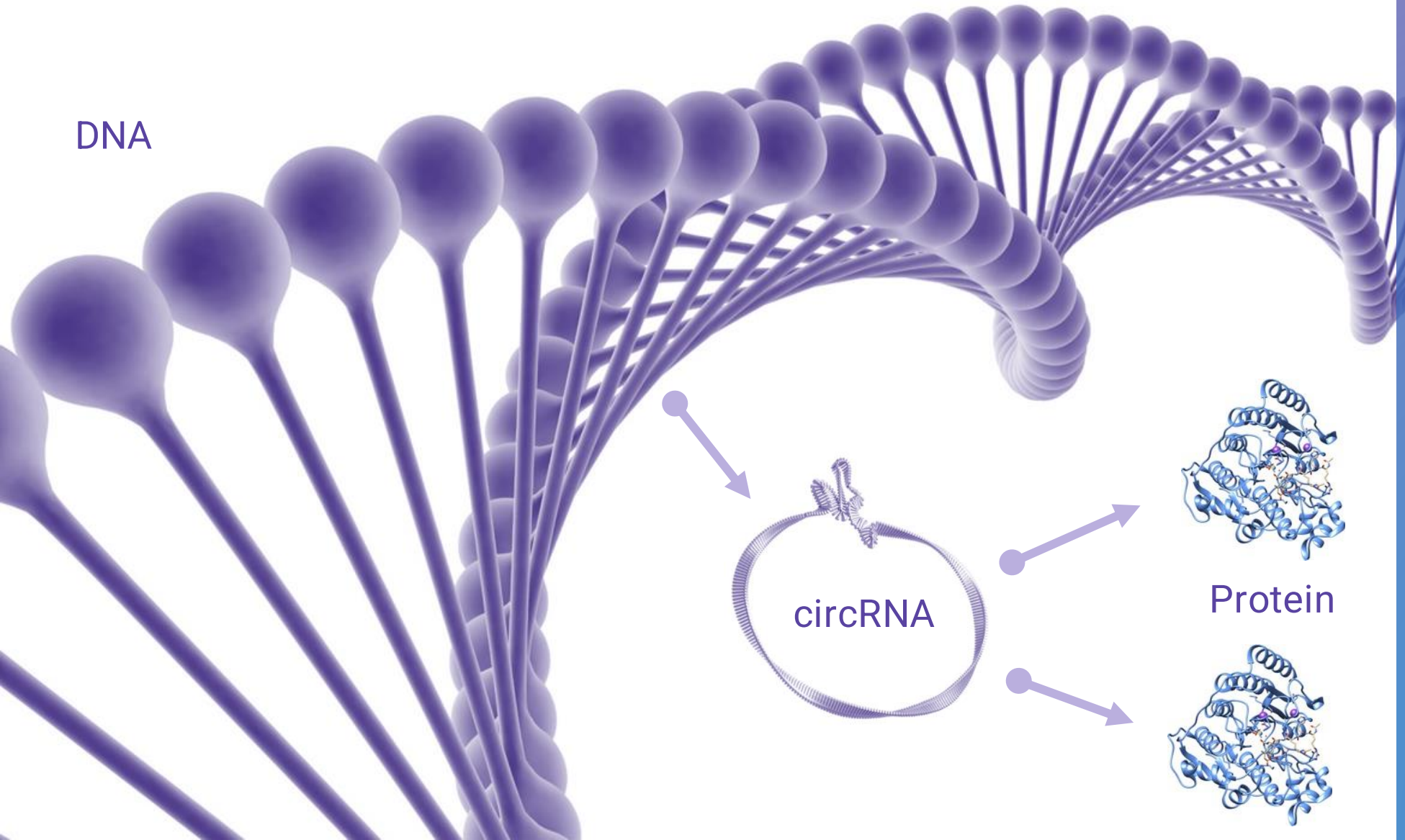
nature reviews genetics 2,291 citations

Review Article | Published: 08 August 2019

The biogenesis, biology and characterization of circular RNAs

Lasse S. Kristensen, Maria S. Andersen, Lotte V. W. Stagsted, Karoline K. Ebbesen, Thomas B. Hansen & Jørgen Kjems

The circVec expression system: making circRNA from a DNA starting point



circVec
DNA or viral
vector

Inject

circRNA
biogenesis

Intra-cellular
protein expression

circVec substantially outperforms the expression level and durability of mRNA-based systems

Increased expression level

Prolonged durability

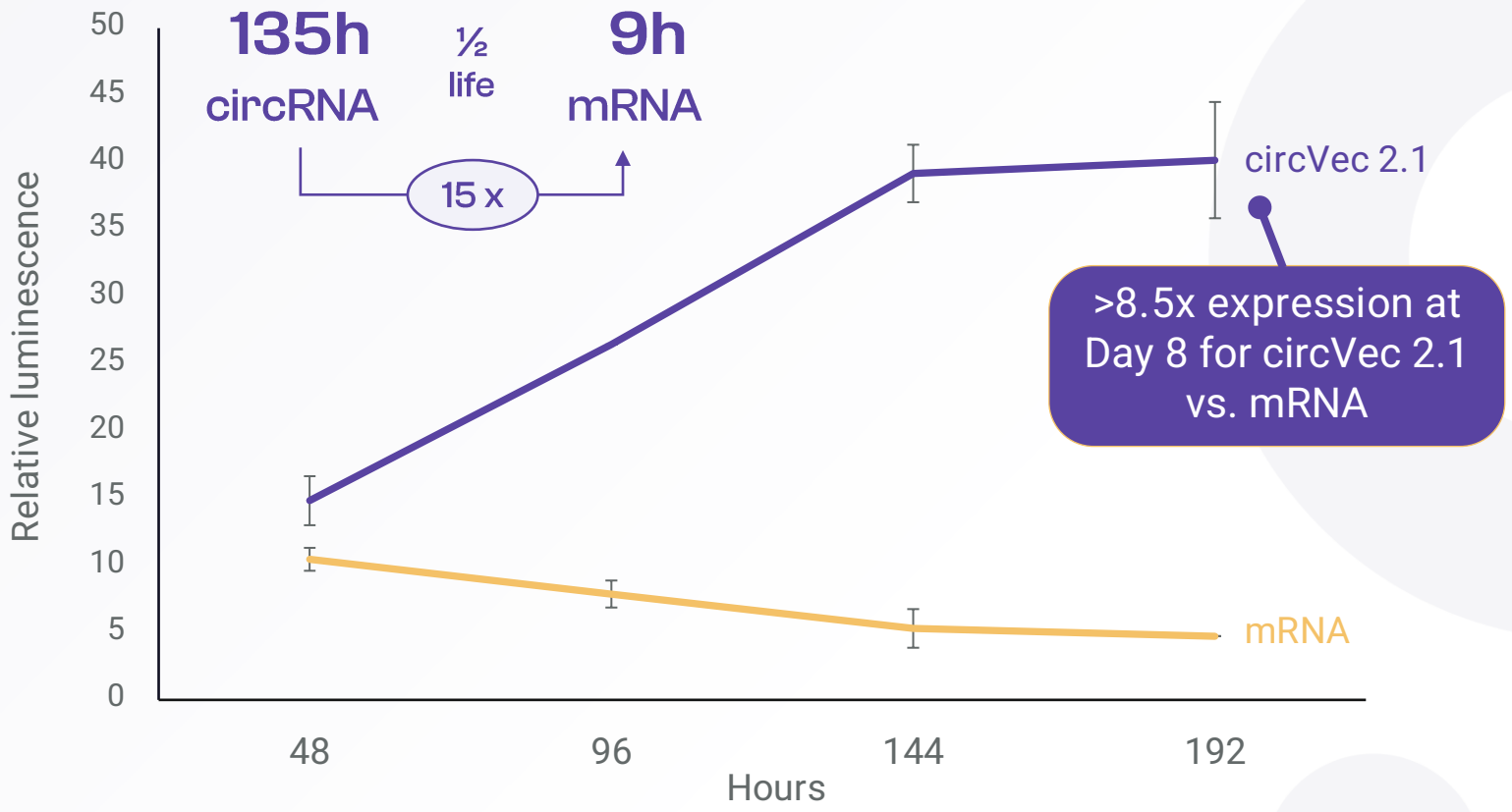
Enhanced therapeutic potency

"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

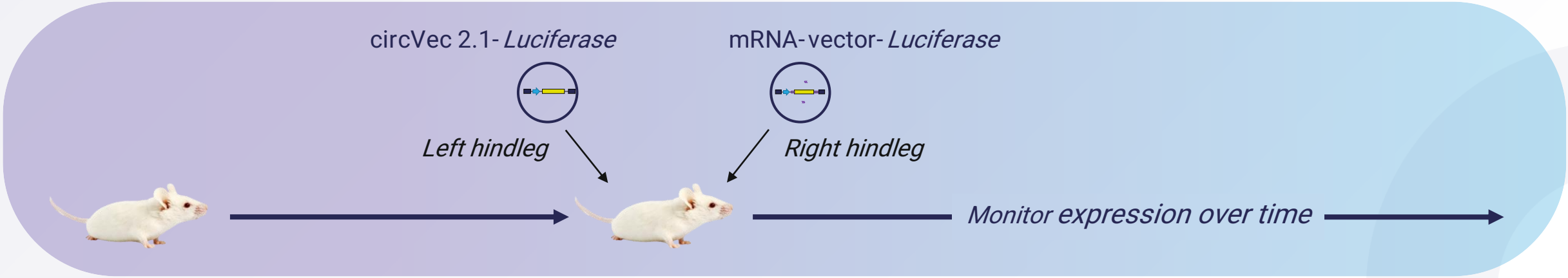
Scientific founder
oRNA Therapeutics

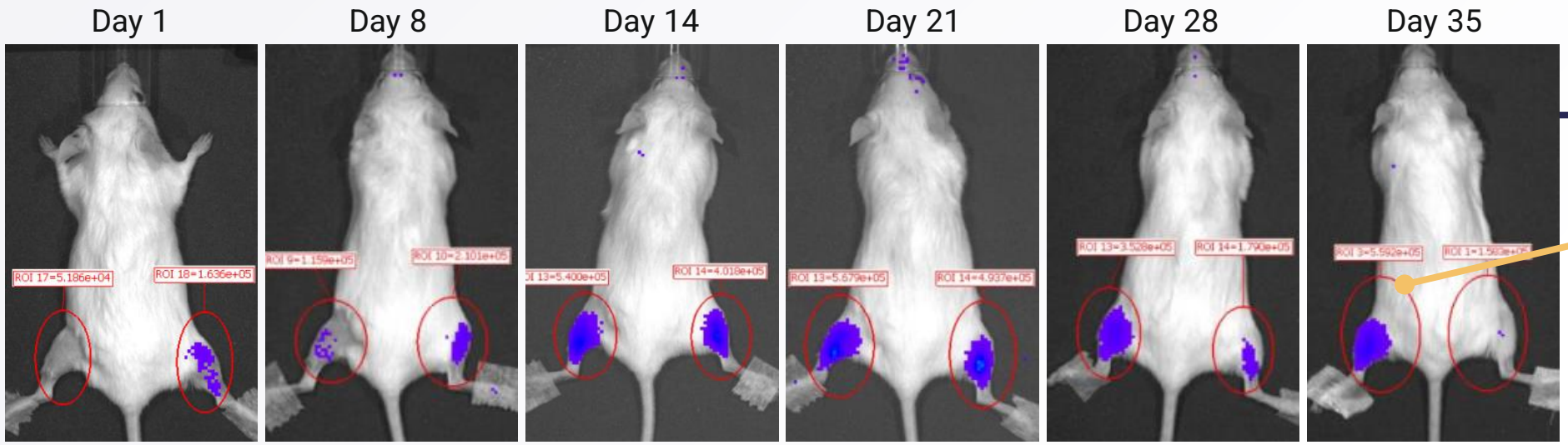
circVec vs. mRNA luciferase reporter expression; time course



circio

In vivo reporter pilot study: circVec 2.1 outperforms mRNA over time





Real-time monitoring ongoing

Increasing circVec expression: highest at Day 35, mRNA lowest at Day 35

Strategy to develop a new class of circRNA medicines and create value from unique circVec system

Build platform

- Test and validate applicability of circVec system
- Identify and select lead applications and targets
- Build robust IP portfolio

Demonstrate efficacy

- Demonstrate superiority of circVec system vs. gold standard for selected lead applications
- Design and test targeted circVec candidates *in vivo*
- Go / No Go for continued development or partnering

Strategic partnerships

- Capitalize on platform potential to partner early for specific applications (e.g. vaccines)
- Access complementary technology to address major unmet medical needs in genetic disease

Circio investment case – executive summary

Disruptive technology

- Circular RNA (circRNA) is a next generation mRNA format
- Potential to disrupt the genetic medicine and vaccine fields

Circio´s unique position

- Deep expertise: the discoverers of circRNA work for Circio
- Differentiated approach to circRNA, with substantially improved durability and unique ´remove & replace´ functionality
- Proprietary circVec expression system with platform potential

Value drivers

- Aiming to enter several partnering deals during 2024-2025
- Targeting to enter the clinic with first in-house candidate in 2026