

targovax

# Biotech showcase

January 2023

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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 and the Targovax Group. Such forward-looking statements reflect the current views of Targovax and are based on the information currently available to the company. Targovax cannot give any assurance as to the correctness of such statements.

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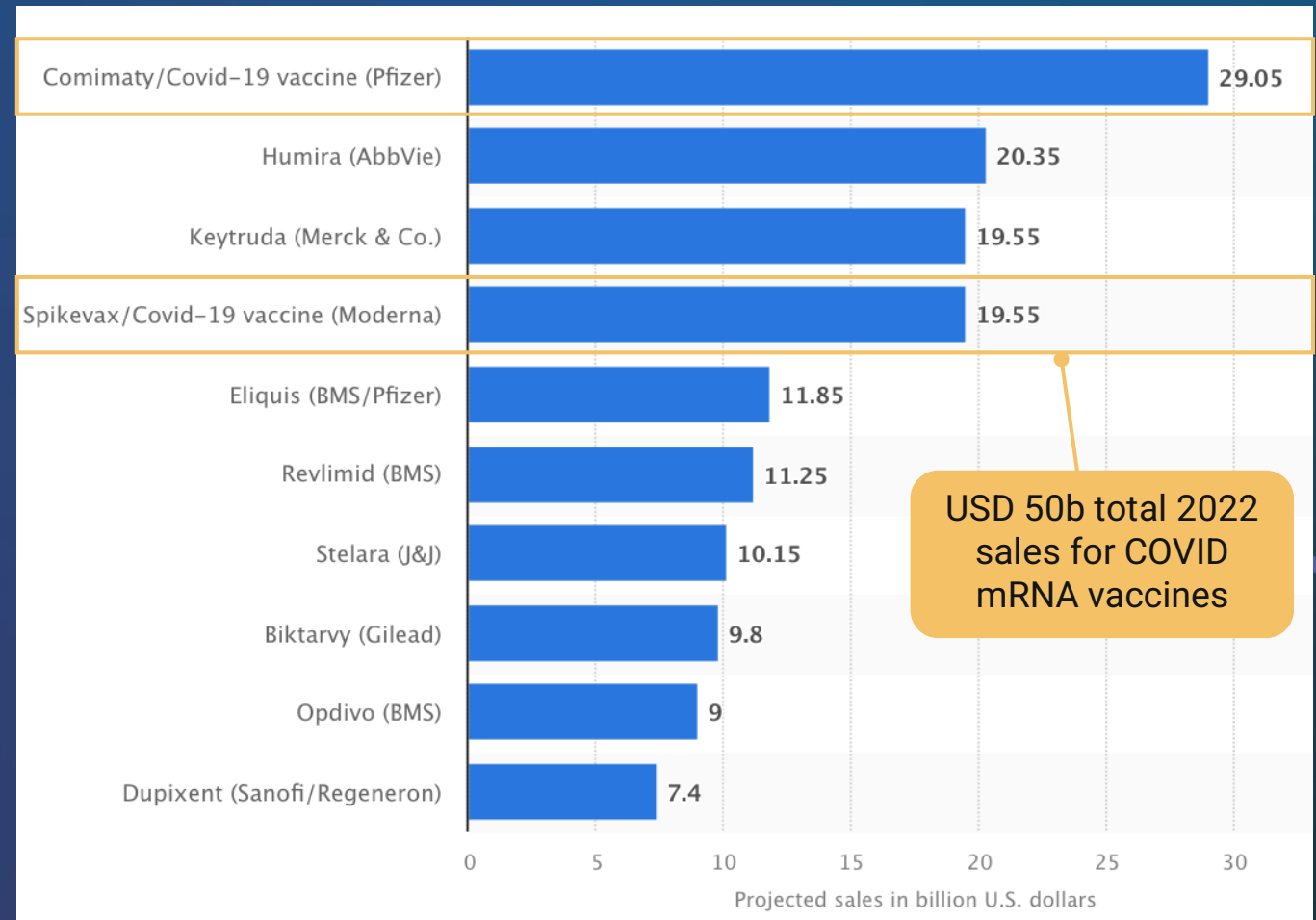
# mRNA was the top-selling drug class in 2022

*Remarkable success given first mRNA-based therapeutics were approved in 2020*

*mRNA outcompeted more established concepts in COVID vaccine race*

*However, challenges remain...*

## Top 10 drugs by 2022 projected sales



# RNA is a highly promising therapeutic class, Targovax aims to address unsolved challenges

*RNA is chemically unstable –  
mRNA vaccines have required  
heavy modifications*

*Efficient delivery of RNA  
therapeutics is currently limited to  
vaccines and liver disease*

*Challenging to achieve sufficient  
targeting and half-life in tumors*

- Circular RNA is resistant to intracellular RNA degradation mechanisms
- Expressing RNA from a DNA vector solves the stability issue
- Clinically validated DNA vector enabling delivery to solid tumors and beyond
- Clinically validated spread and persistence of vector in tumors

# Targovax is a pioneer in circular RNA (circRNA)

Article | 30 September 2011 | **FREE ACCESS**

## 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 Kiems

The circRNA discoverers work for Targovax



**nature**

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nature > letters > article

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 Kiems

Nature 495, 384–388 (2013) | Cite this article

100k Accesses | 4746 Citations | 130 Altmetric | Metrics

## As RNA remains hot, Flagship's Laronde raises \$440m for a new class of medicines

By Anissa Gardizy Globe Staff. Updated August 30, 2021, 6:30 a.m.



**MERCK**

BIOTECH

### Merck bets big on circular RNA, paying \$150M to work with Orna

Orna revealed a double dose of good news, taking the lid off an alliance with Merck worth \$150 million upfront and a \$221 million series B round.

laronde



# Targovax development pipeline

| Product candidate | Preclinical  |              | Clinical |   |                   | Milestones                                      |
|-------------------|--|--------------|----------|---|-------------------|---|
|                   | Discovery  | IND-enabling | Phase 1  | Phase 2                                   | Phase 3 / pivotal |   |
| ONCOS-102         | PD-1 Resistant Melanoma<br>Re-challenge combination w/aPD-1 & CTLA-4 |              |          |   | agenus            | 1H 2023<br>Initiation of phase 2 trial (USA)    |
|                   | Mesothelioma<br>Combination w/Standard-of-Care (SoC)                 |              |          |   |                   | 1H 2023<br>Publication in oncology journal      |
| Mutant KRAS       | Multiple Myeloma<br>TG01 / QS-21                                     |              | agenus   | Oslo University Hospital                  |                   | 1H 2023<br>First patient dosed (Norway)         |
|                   | Pancreatic cancer<br>TG01 / QS-21 +/- anti-PD-1                      |              | agenus   | THE UNIVERSITY OF KANSAS<br>CANCER CENTER |                   | 1H 2023<br>First patient dosed (USA)            |
| circular RNA      |  |              |          |   |                   | 1H 2023<br><i>In vivo</i> proof-of-concept data |

■ Trials run and financed by collaboration partners

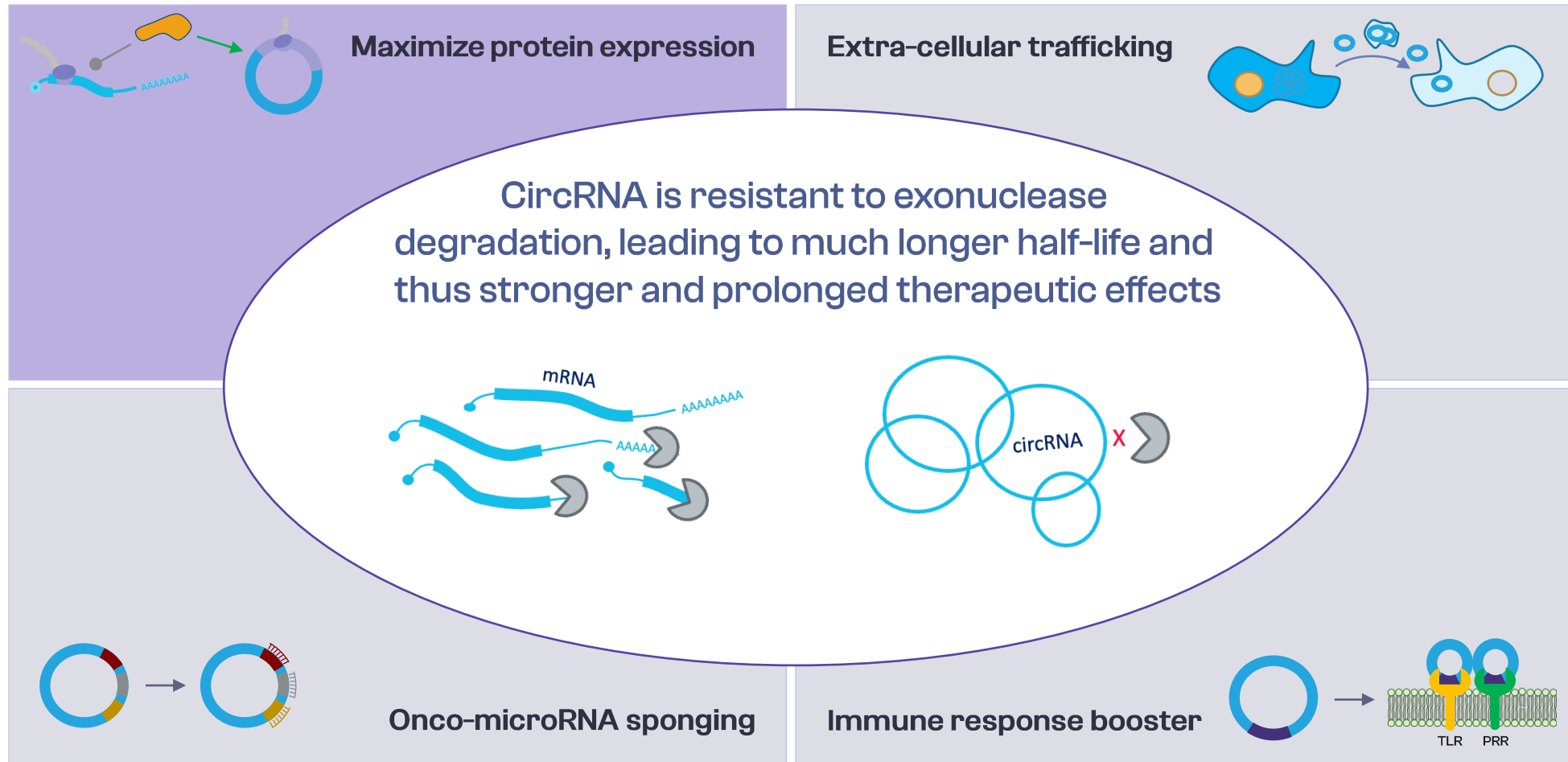
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## Circular RNA platform

2. Technical proof-of-concept data
3. Team
4. Summary

# circRNA provides a toolbox to create a novel class of medicines





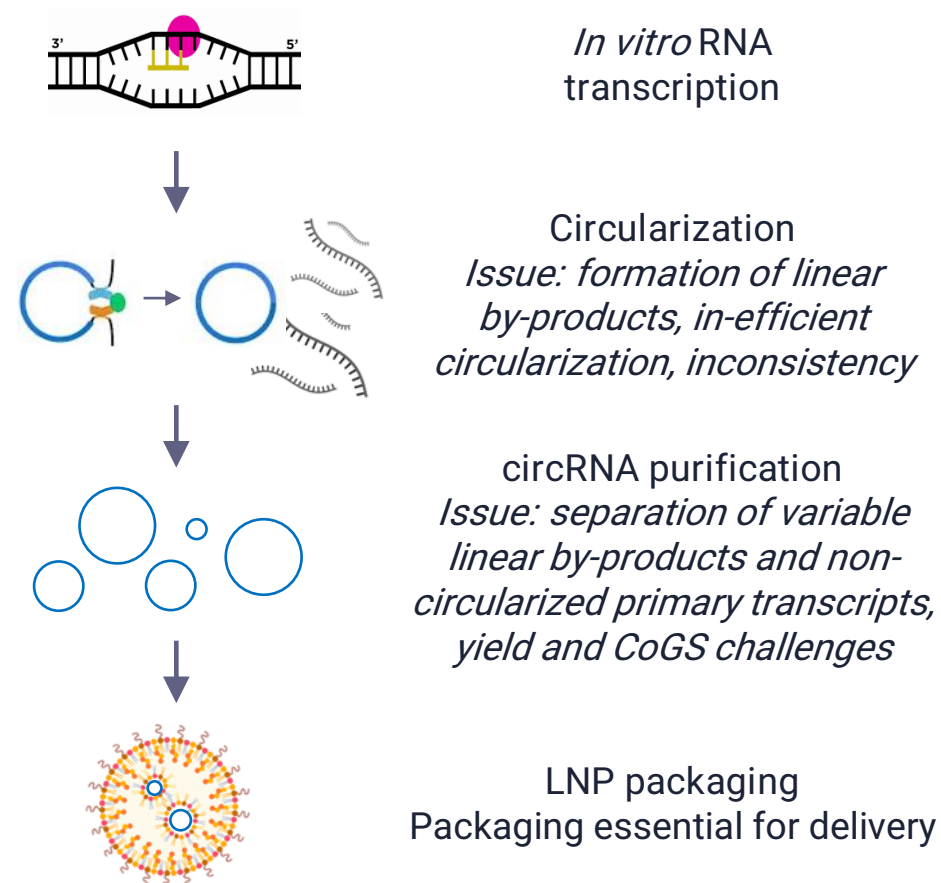
# Targovax's circAde vector system offers important advantages

|                   | <i>Enhanced intra-cellular stability</i> | <i>Does not require packaging</i> | <i>Delivery to liver</i> | <i>Vaccination platform</i> | <i>Delivery to solid tumors</i> | <i>Existing GMP manufacturing</i> |
|-------------------|--|-----------------------------------|--------------------------|-----------------------------|---------------------------------|-----------------------------------|
| Targovax circAde  | ✓  | ✓                                 | ✓                        | ✓                           | ✓                               | ✓                                 |
| Synthetic circRNA | ✓  | ✗                                 | ✓                        | ✓                           | ✗                               | ✗                                 |
| Synthetic mRNA    | ✗  | ✗                                 | ✓                        | ✓                           | ✗                               | ✓                                 |

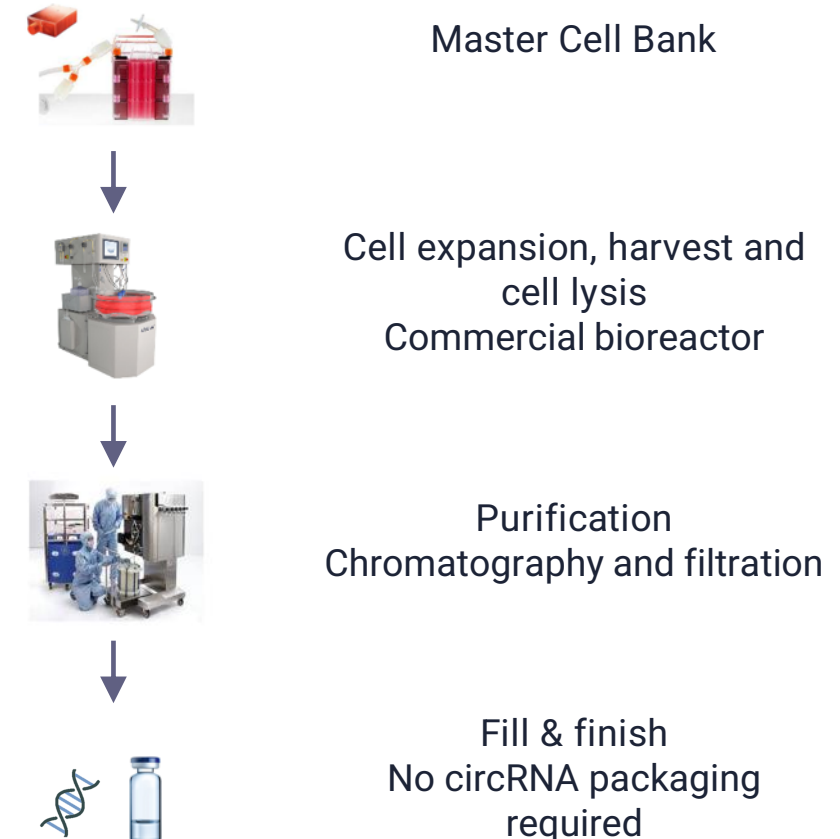
- Targovax has the only vector to deliver to solid tumors
- cGMP vector manufacturing available at scale

# CirAde - scalable, validated cGMP manufacturing process

Synthetic circRNA manufacturing process<sup>1</sup>  
Currently only small-scale, no commercial systems



Targovax manufacturing process  
Using commercially available equipment



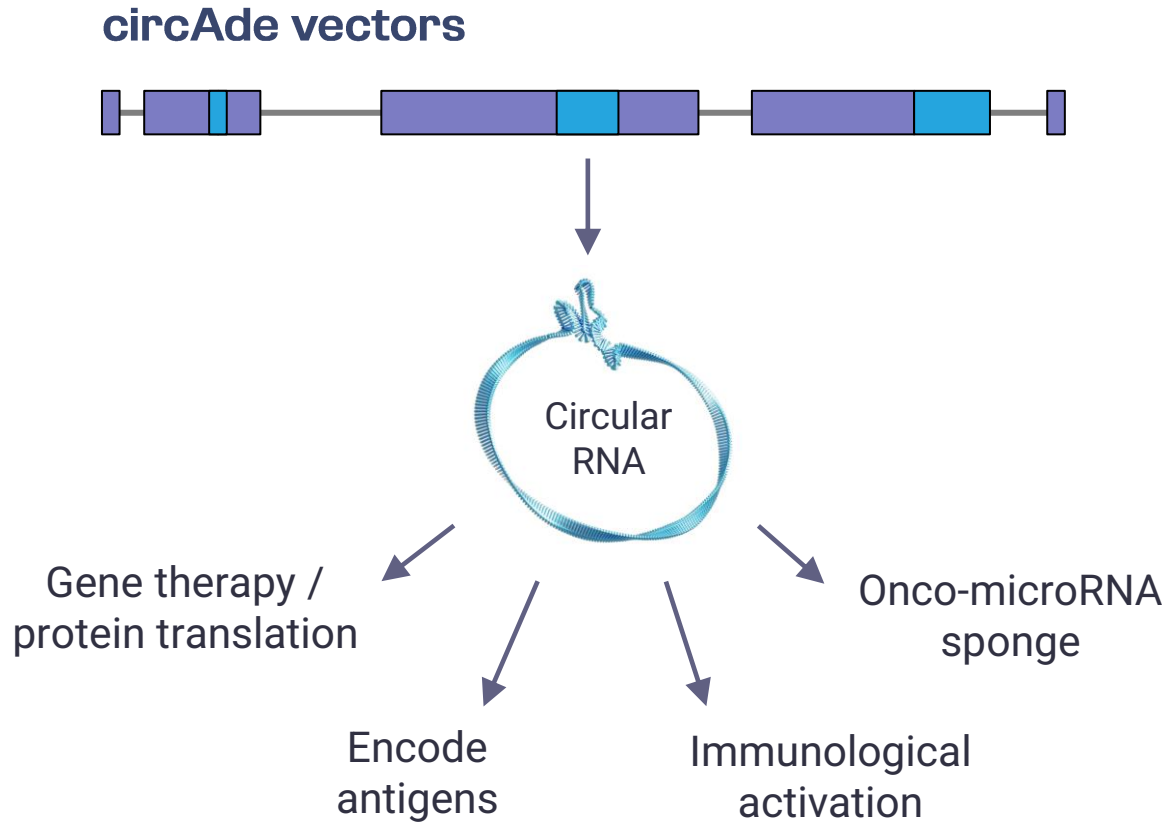
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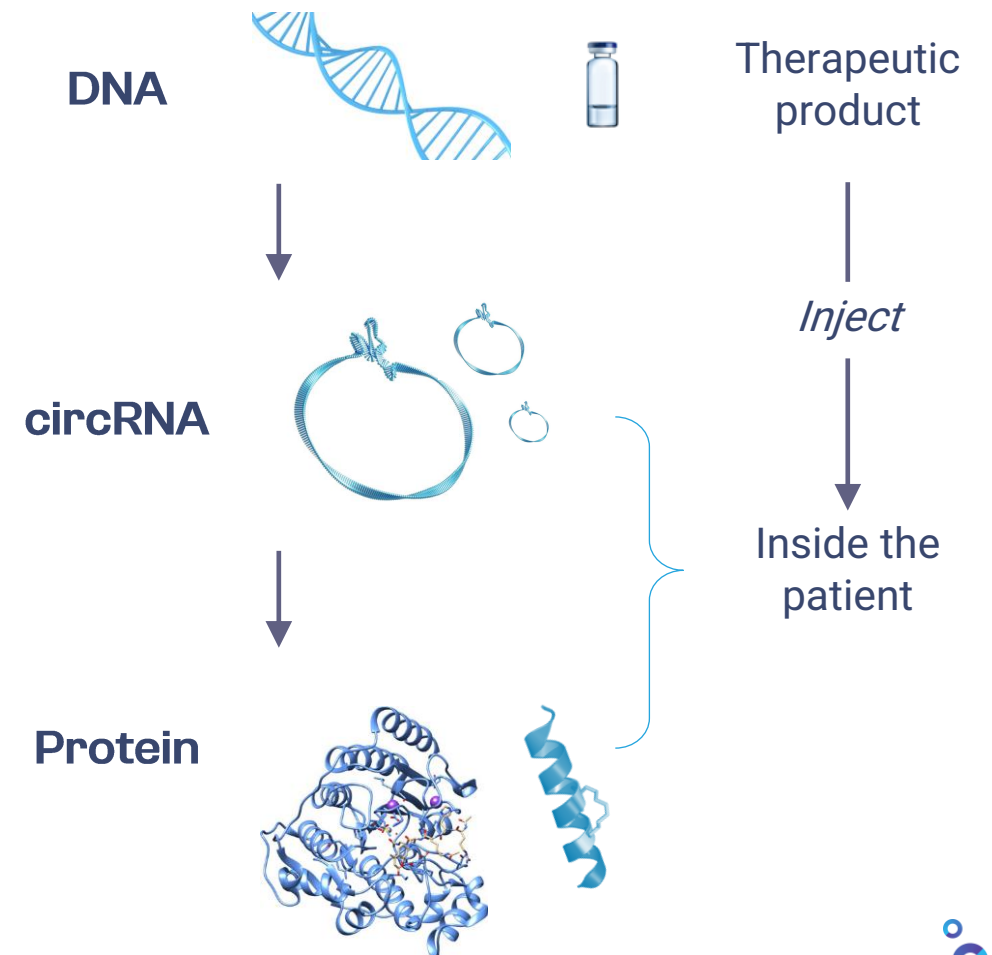
## Technical proof-of- concept data

3. Summary

# circAde – protein expression platform



*Highly versatile – Multi-modal MoA – Excellent stability*

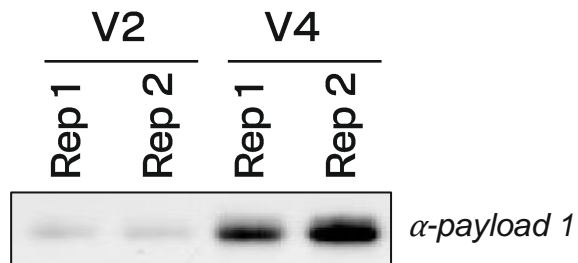


# circRNA vs. mRNA - Technical proof-of-concept

Functional vector established  
Payload expressed from vector-encoded circRNA

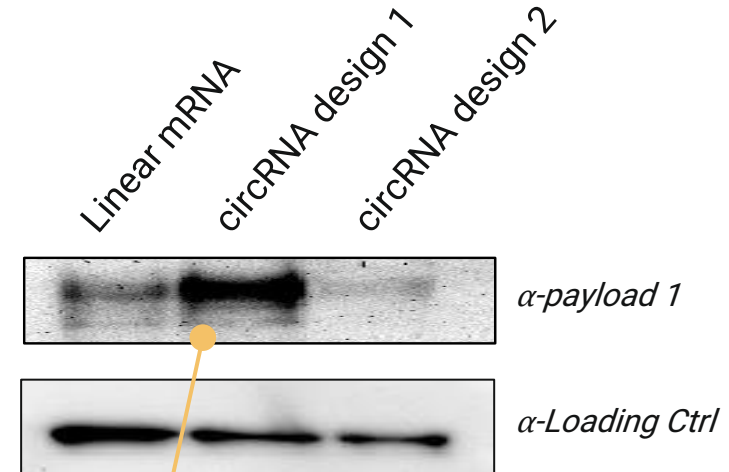
| Insertion strategy | Vector function |
|--------------------|-----------------|
| V1                 | ✗               |
| V2                 | ✓               |
| V3                 | ✗               |
| V4                 | ✓               |

Protein expression



- Insertion strategy is critical for effective vector design

Highly effective circRNA design identified  
Plasmid-expressed circRNA, transfected cells

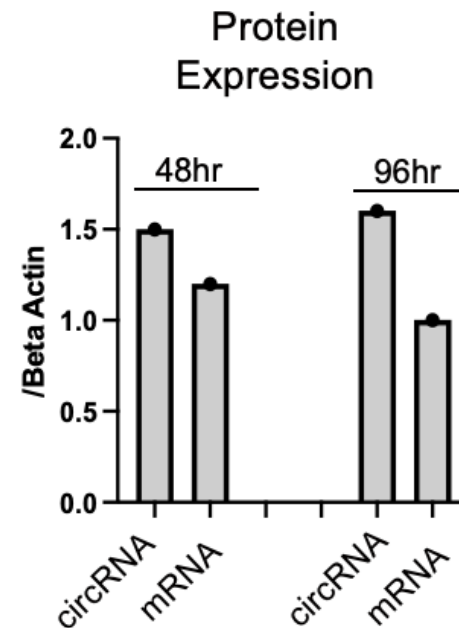
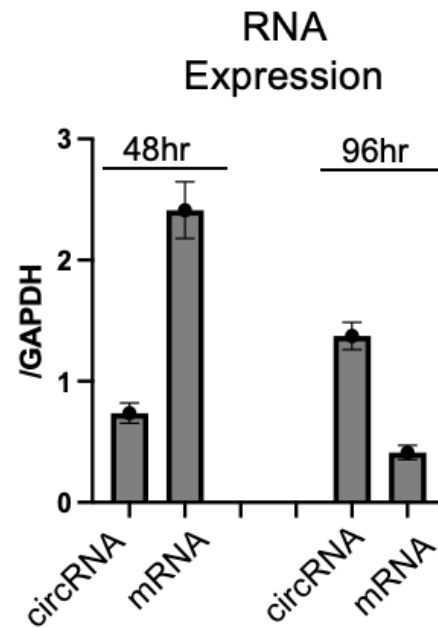


- circRNA design strategy is critical for output
- Superior protein output relative to linear mRNA, even at early time points

# circRNA level increases over time, and achieves higher and longer-lasting protein expression vs. mRNA

## Output quantification; circRNA and protein payload Plasmid-expressed circRNA, transfected cells

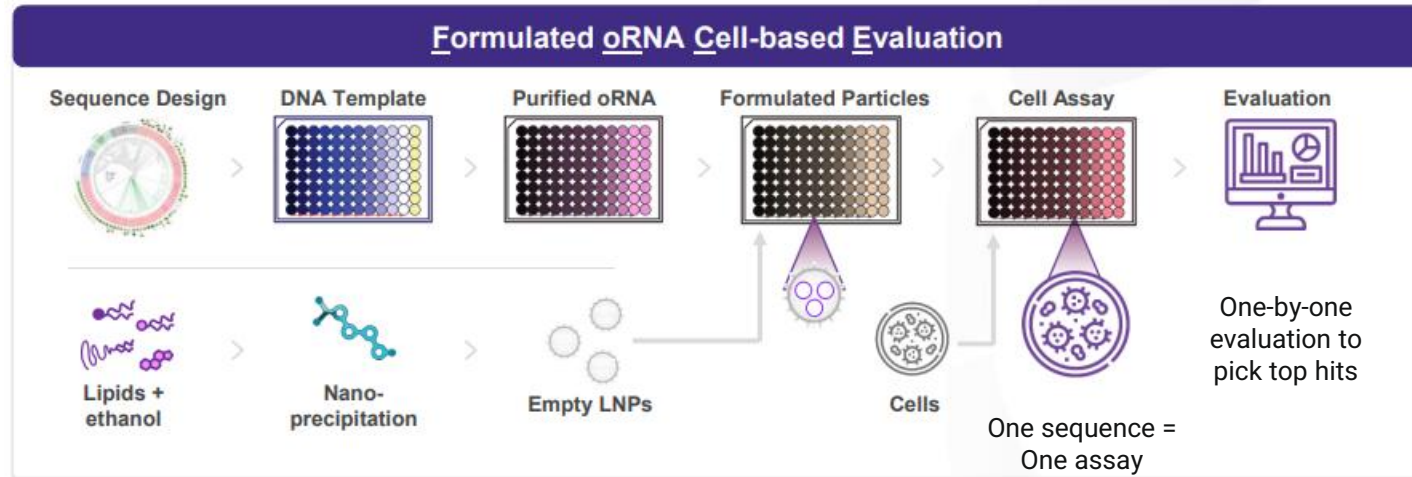
- Increase in circRNA level from 48 → 96h
- In same period, >80% drop in mRNA level



- circRNA expression higher, even at 48hr time point
- circRNA protein level builds from 48 → 96h, increasing difference to mRNA

# CircAde enables fast high-throughput screening

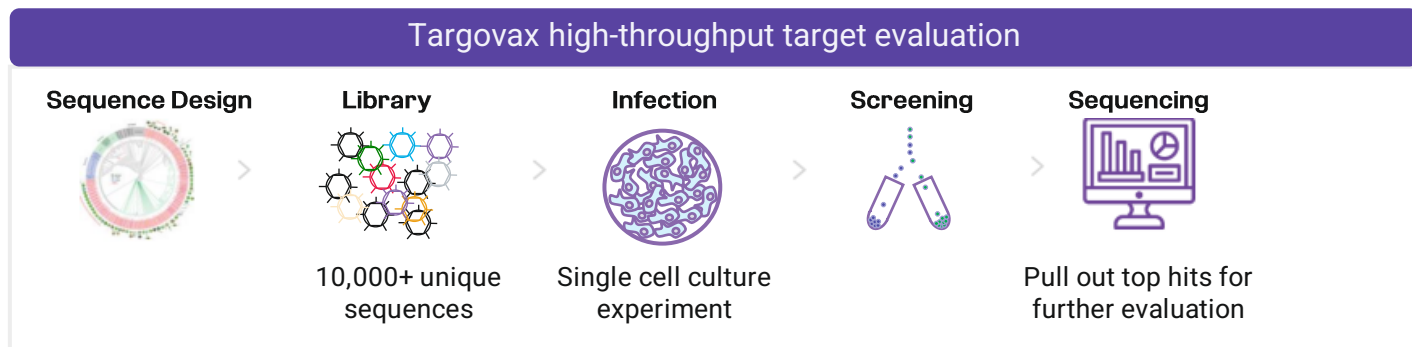
Synthetic circRNA: One circRNA per experiment – oRNA approach



- *Laborious approach*
- *Requires circRNA purification*
- *Sensitive to RNA yield, LNP formulation and transfection efficiencies*

*versus*

Vector-based circRNA: Parallel circRNA screening – Targovax approach



- *Ability to compare 10,000+ sequences in parallel*
- *Enables high throughput screening of biogenesis efficacy and IRES activity*
- *Simple to replicate in various cell types*



# Targovax achieved milestones

- ✓ Functional vector design established
- ✓ Superior circRNA design identified
- ✓ Extended circRNA half-life confirmed
- ✓ Enhanced and prolonged circRNA protein expression vs. mRNA

*In vivo PoC experiments being run in 1H 2023*



# Initial focus on oncology applications, expand to vaccines and rare disease

Oncology  
Solid tumors

*Vector I*

- High-potency neoantigen immunization
- Immuno-stimulatory payloads for validated targets with systemic toxicity issues
- Long-term supply of proteins or peptides to target key cancer signalling and metabolic pathways

*Focus for in-house development*

Vaccines  
Infectious diseases

*Vector II*

- Higher and long-lasting expression will lead to strong immune boosting response
- Improved shelf-life and stability over mRNA

*Expansion and partnering opportunities*

Rare diseases  
Enzyme replacement

*Vector III*

- Enzyme replacement therapy at reduced cost and complexity over gene therapy
- Expand to other circRNA applications in CNS, ERT, dermatology or cardiovascular

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Summary

# Targovax has a unique edge in the circRNA field



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

- Led by circRNA pion er Dr. Thomas Hansen



Unique circAde vector system for circRNA delivery to solid tumors

- Technical PoC established, vector turns cancer cells into circRNA factory



GMP manufacturing at scale using commercially available equipment

- circRNA GMP manufacturing at scale faces unresolved issues



No known competitors active in circRNA therapeutics for solid tumors

- Efficient delivery of synthetic RNA to solid tumors is an unresolved challenge



# targovax

## Want to learn more?

**CFO**      **Lubor Gaal**  
**Contact**      [lubor.gaal@targovax.com](mailto:lubor.gaal@targovax.com)

[www.targovax.com](http://www.targovax.com)

