nCage

A novel synthetic VLP platform for the development of next generation vaccines

Introduction

nCage Therapeutics Sp. z o.o.

WHO ARE WE?

nCage technology has the potential to improve vaccines

nCage

FOUNDED
2019

LOCATION
KRAKÓW, POLAND

- Development of a **novel technology for respiratory vaccines**
- Unique, **patent-protected TRAP-cage technology**
- Preclinical animal data have demonstrated **excellent efficacy** of our platform
- Team of leading **scientists** and globally experienced **biotech professionals**

The two segments of nCage's focus

nCage

We focus on implementing our technology in

Synthetic VLP Vaccines

Stronger & more durable vaccines against respiratory diseases

USD **29.4 bn**

Addressable market (2022)

8.6%

CAGR forecast (2023-2030)

Antibody Drug Conjugates (ADCs)

Enhancing safety profile of the blockbuster anti-cancer drugs

USD **7.8 bn**

Addressable market (2022)

11.2%

CAGR forecast (2023-2030)

HOW WE DO IT

nCage solution mimics the virus which leads to an increased immune response

Typical virus

~

Synthetic virus-like particle (VLP)

Variants have been tested by nCage and its competition

Very strong immune response already proven in clinical trials

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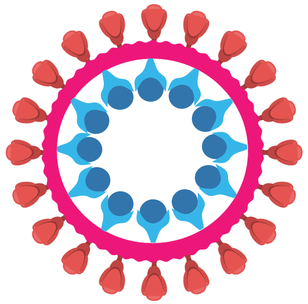
TRAP-cage

A specific synthetic VLP developed by nCage



Adding the **internally** mounted antigens creates a chance for **even stronger immune response**

Virus-like structure is **easily recognized** by the body and enables the delivery of a **large number of antigens close together** which increases the immune response.

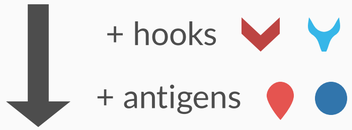
Synthetic VLPs, unlike viruses, are **non-infectious** because they contain no genetic material.

How does nCage make TRAP-cages?

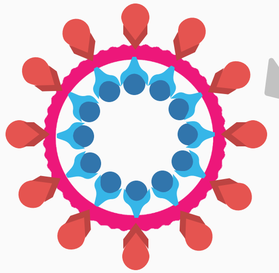
1. Protein cage **"the scaffold"**

TRAP Proteins connected by **gold links** ensuring high cage stability

2. **Add-ons**



3. Ready **synthetic VLP**

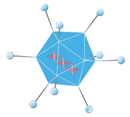


with antigens mounted both on the **interior** and **exterior** of the cage

Vaccination leading to a strong immune response

ADVANTAGES OF SYNTHETIC VLPs AS VACCINES

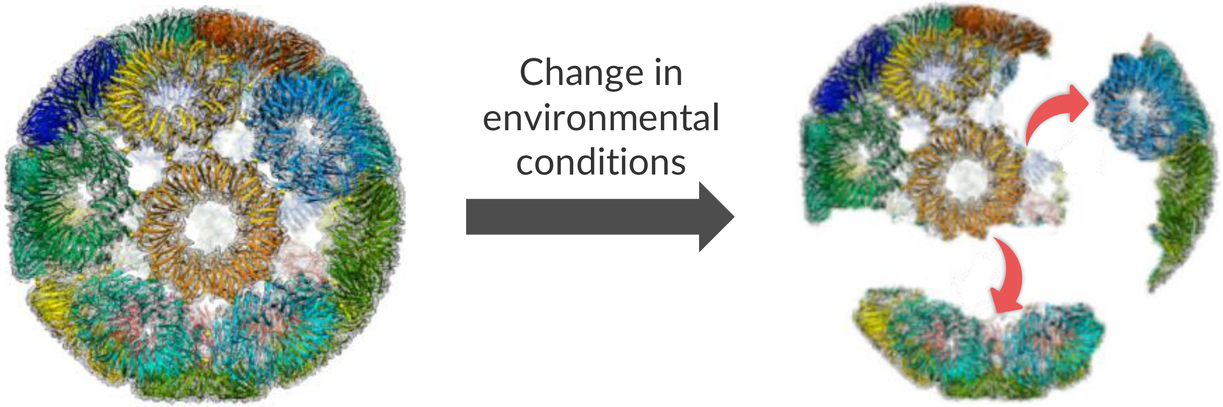
Synthetic VLPs have demonstrated competitive advantages versus current vaccines

	Viral Particles	Recombinant Protein	Viral Vectors	mRNA	Naturally occurring Virus-like Particles (VLPs)	Synthetic VLPs
Illustration						
Description	Inactivated viral particles	Adjuvanted protein subunit vaccine	Replication-incompetent viral vector vaccines that cause cells within the body to express antigen	Antigen encoded on genetic material and expressed by the body	Few cases where soluble antigen naturally forms a particle structure	Artificially designed and manufactured VLPs, applicable to all viruses
Pros	• Many examples of successful viral vaccine developments using this methodology	• Easy storage and transport • Strong efficacy in clinical trials	• Low cost • Easy manufacturing	• Strong efficacy in clinical trials (and real world) • Allows for 'programmable' vaccines	• Very good vaccines • Strong and durable responses • Considered best vaccines on the market	• Strong efficacy • Low side effects • Easy manufacturing • Easy storage and transport
Cons	• Supply issues due to scale-up problems	• Not as fast to develop as competitive technologies	• Question marks regarding the safety of adenovirus vaccines • Lower efficacy	• Complicated distribution due to cold storage supply • Side effect after multiple boosters	• Only possible for HPV and HepB • **To date, most viral antigens do not form a VLP structure**	• New technology – only one vaccine approved to date

PROGRAMMABLE CAGE OPENING

Unique aspect of nCage's technology – programmable opening of TRAP-cages

A unique aspect of nCage technology – **TRAP-cages can be programmed to open and close in certain environmental conditions,** such as the reducing conditions inside of a cell. This allows for **delivery of an antigen cargo**.



Better efficacy

The ability to deliver peptide antigens to the interior of cells provides an opportunity to further improve VLP vaccines providing a market leading technology

Trap-cages have the potential to increase **the immune response** of the body due to both high number of antigens on the outside of the cage and delivered antigens transported in the inside of the cage.

IN VIVO EXPERIMENTS

In vivo study confirming nCage's ability to produce effective respiratory vaccines

Study design

Mice used in the experiment

50 mice

- **10 mice** – PBS/Addavax (control group)
- **10 mice** – TRAP-cage/Addavax
- **10 mice** – TRAP-cage-RBD/Addavax
- **10 mice** – RBD/Addavax
- **10 mice** – TRAP-cage + unconjugated RBD/Addavax

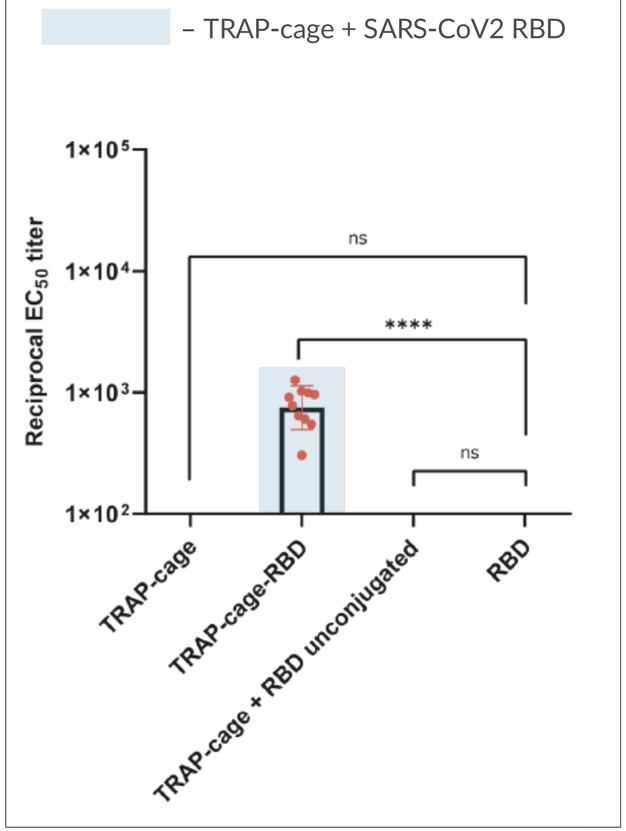
Key time points

25th May 2023 – 10th July 2023

Day -10	Day 0	Day 1	Day 14	Day 21	Day 35
mice arrived	1st vaccine dose	1st blood sample	2nd blood sample	2nd vaccine dose	final blood sample

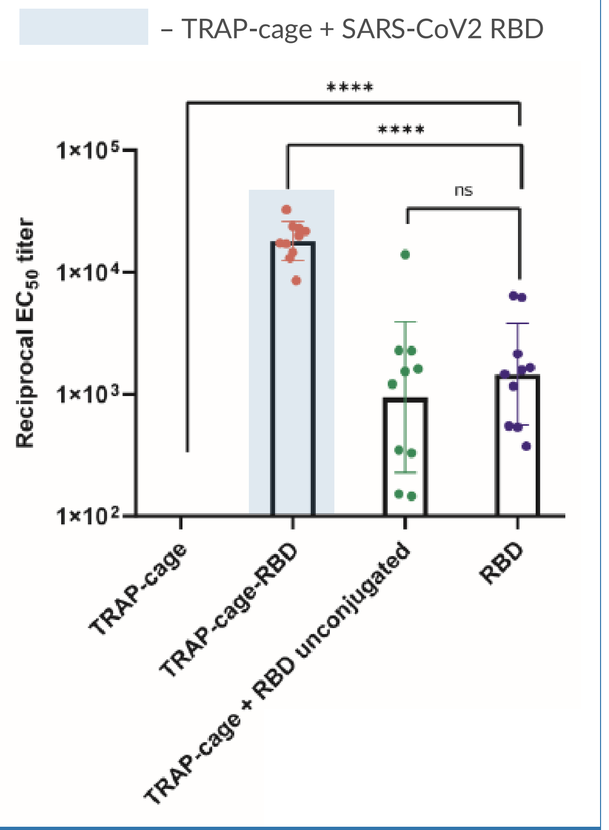
Results

Antibody response after 1st dose



ns – statistically not significant
**** - statistically significant, p<0.0001

Antibody response after 2nd dose



>10x increase in antibody response from TRAP-cage platform

SYNTHETIC VLP VACCINES

Acquisition of IcoSavax by AstraZeneca, demonstrates the marketplace recognition of the significant potential of synthetic VLP vaccines

About Icosavax

ICOSAVAX

- Icosavax a previously NASDAQ-listed company developing synthetic VLP vaccines – **the similar technology as nCage**
- Spin-off from the **University of Washington**
- **>USD 780m** market capitalization
- **>USD 400m** raised to date
- Lead candidate (RSV/hMPV combo vaccine) is currently in **Phase 2 clinical trial**

Icosavax to be acquired by AstraZeneca in Q1 2024

AstraZeneca

- **USD 838m equity value** (43% above market value on announcement date, 73% above 60-day VWAP*)
- **Additional c. USD 280m USD** payable upon achievement of specified regulatory and net sales milestones

> *This virus-like particle vaccine technology has the **potential to transform prevention against severe infectious diseases**, including RSV and hMPV.*
>
> Iskra Reic, Executive Vice President, Vaccines & Immune Therapies, AstraZeneca

Icosavax's funding timeline & key milestones

2017	2019	April 2021	July 2021	September 2021	June 2023	December 2023
Company foundation	**Series A** >USD 51m raised	**Series B** >USD 100m raised	**IPO** >USD 182m raised	**Phase 1** initiation (RSV/hMPV)	**Phase 2** initiation (RSV/hMPV)	**Acquisition** by AstraZeneca announced (USD 838m – 1.1bn)

** Volume-Weighted Average Price for the 60-day period preceding the transaction announcement date*

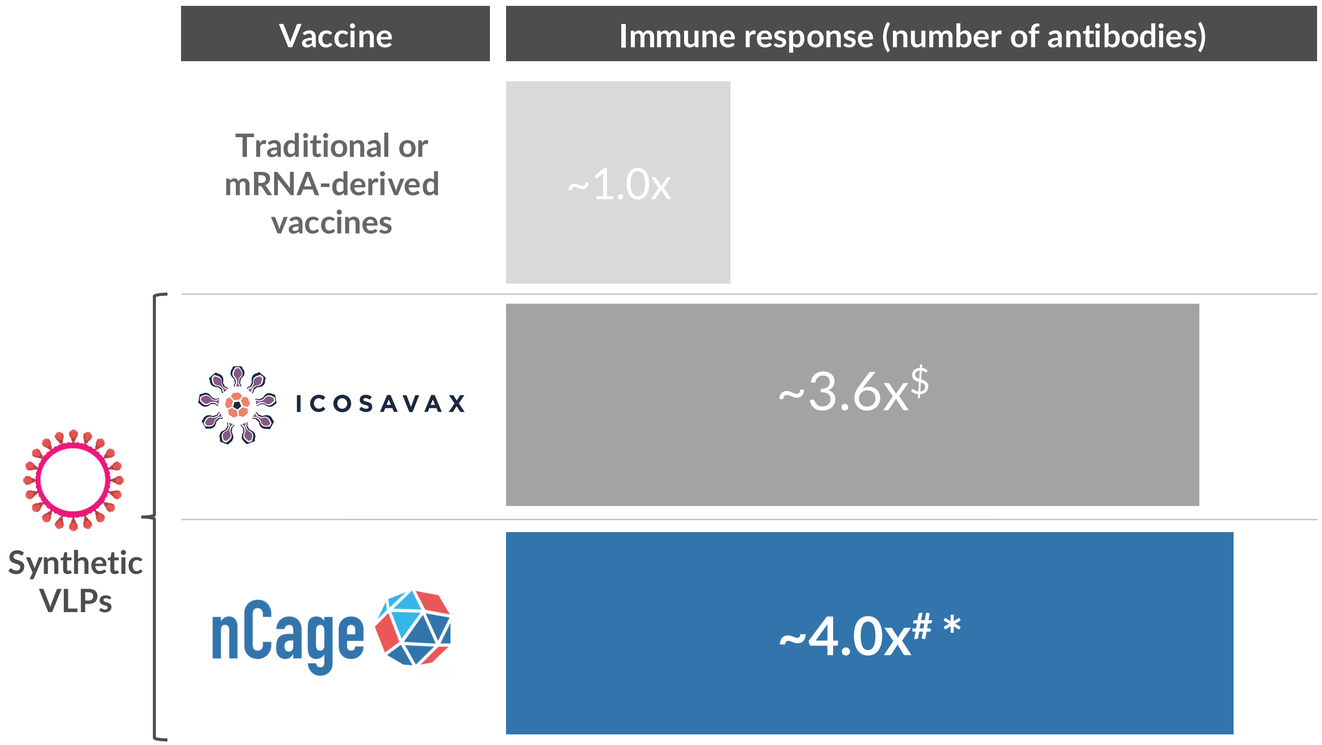
SYNTHETIC VLP VACCINES

Potential advantages of nCage TRAP-cages versus Icosavax's protein cages

Comparison of nCage's TRAP-cages and Icosavax's protein cages

	nCage	ICOSAVAX
Hyper Stable	✓	✓
Can Display External Antigens	✓	✓
Folded Antigen Display	✓	✓
Programmable Disassembly	✓	✗
Triggerable Disassembly	✓	✗
Plug and Play Platform	✓	✗
Internal Cargo	✓	✗
Display of Oligomeric Antigen	✓	✓
Cell Delivery	✓	✗

TRAP-cage immune response compared to traditional vaccine types and synthetic VLP vaccine market leader



Mounted antigen source: # ovalbumin, $ RSV

** nCage's in vivo experiment conducted in 2022 in collaboration with MSD*
Source: Data on File Merck Sharp & Dohme, nCage Therapeutics, Figure 4 C, Marcandalli et al. Cell 176, (2019): 1420- 1431

Respiratory viruses – a global health concern

Vaccines are the primary method of prevention from respiratory diseases. However, a significant number of people **refuse vaccination** because of:

- Adverse side effects
- Inconvenience due to numerous injections
- No coverage of new virus types by existing vaccines

New and existing respiratory viruses pose a serious threat to the elderly population

1. RSV

177k	14k
hospitalizations in the US a year	**deaths** in the US a year

2. Influenza

171k	12k
hospitalizations in the US a year	**deaths** in the US a year

3. hMPV

123k	13k
hospitalizations in the US a year	**deaths** in the US a year

SYNTHETIC VLP VACCINES

RSV & hMPV – emerging threat for elderly people

RSV (Respiratory syncytial virus)

1/3 of 75+ adults died within a year of an RSV-associated hospitalization

92% of all RSV hospitalizations in the EU were observed in elderly adults (65+)

hMPV (Human Metapneumovirus)

36% of YoY increase in HMPV-positive tests in March 23' (US)

40% of all HMPV-infected 50+ adults develop pneumonitis

RSV and hMPV may cause bronchitis and pneumonia, especially among children and **elderly adults**.

Source: https://journals.sagepub.com/doi/10.1177/1753466621995050#body-ref-bibr32-1753466621995050, https://www.healio.com/news/infectious-disease/20200729/rsv-linked-to-severe-morbidity-mortality-among-hospitalized-older-adults); https://www.news-medical.net/news/20230320/RSV-causes-160000-hospitalizations-every-year-in-the-EU-according-to-new-study.aspx; https://edition.cnn.com/2023/05/29/health/human-metapneumovirus-explainer-wellness/index.html)

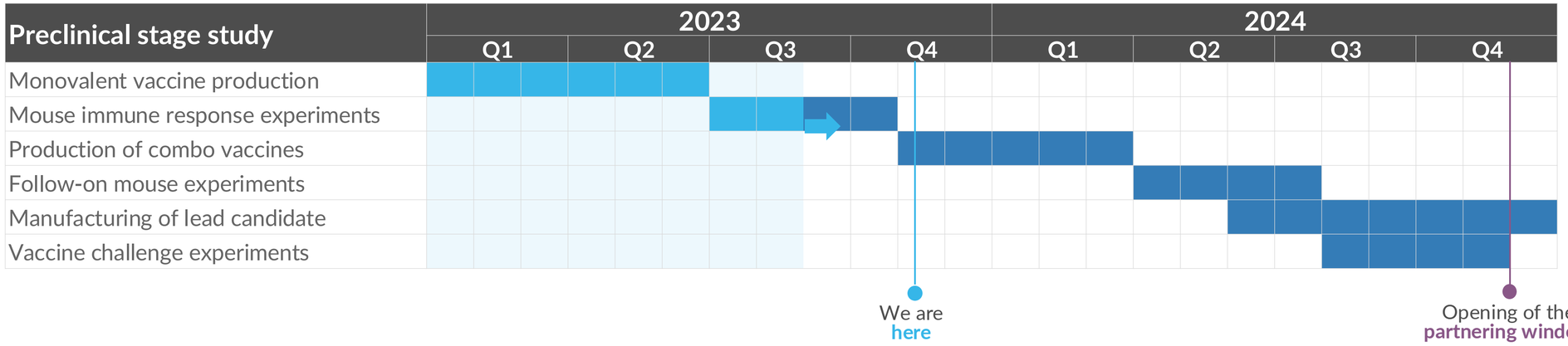
SYNTHETIC VLP VACCINES

Two nCage's combo vaccine candidates with potential to become best-in-class

Vaccine projects developed in collaboration with two major British academic centers

Product	Stage of development	Rationale for market entry	Phase I start date	Academic partner
Combo RSV/hMPV Vaccine	Antigen Production	• There are currently no vaccines for hMPV • RSV vaccines are yet to be trialed in large populations and limited options for patients	2025	THE UNIVERSITY of EDINBURGH
Combo Covid/Flu Vaccine	Selection of Antigens	• Elderly patients are recommended to have both Covid and Flu boosters • No combo option available	2026	The University of Nottingham

Development plans for the lead candidate – RSV/hMPV combo vaccine



At this point, nCage will have an RSV/hMPV combo vaccine candidate with **safety & efficacy proven in animal model**, ready for an IND enabling study.

The second candidate (Covid/Flu combo vaccine) will follow the same timetable **starting from Q1 2024**.

nCage Therapeutics

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