targovax

Next generation immune activators for solid tumors

Dr. Erik Digman Wiklund - CEO

DNB Nordic Healthcare Conference

15 December 2022

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 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.

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 Targovax'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.

The Immuno-Oncology revolution

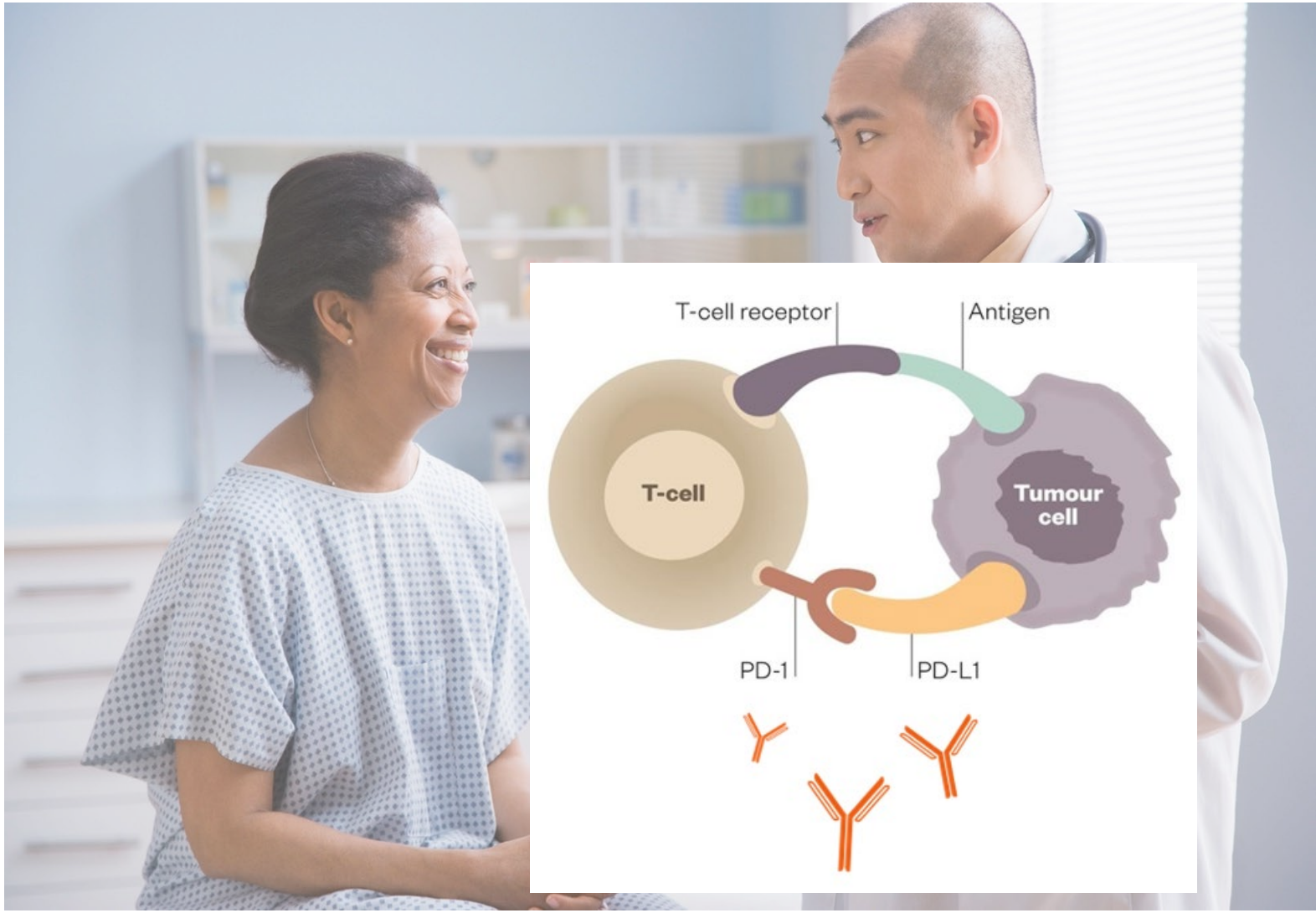
>500,000 patients treated per year

>4,000 ongoing clinical trials

>40% of US cancer patients eligible

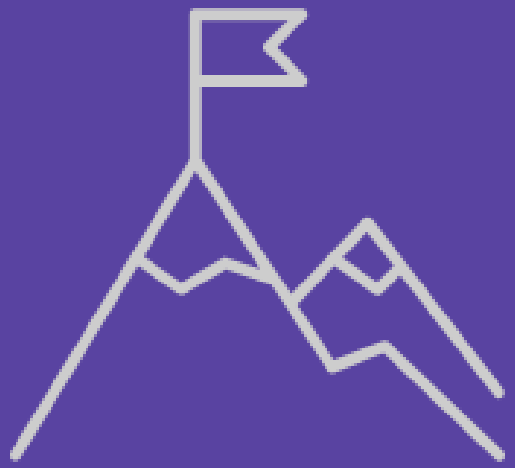
First generation immunotherapy: Checkpoint inhibitors

- **Cornerstone** of current cancer treatment
- **Deep and durable** responses
- **$30b** annual sales globally
- **8 products** approved to date, many more in development



THE CHALLENGE:

Make checkpoint inhibitors work for more patients

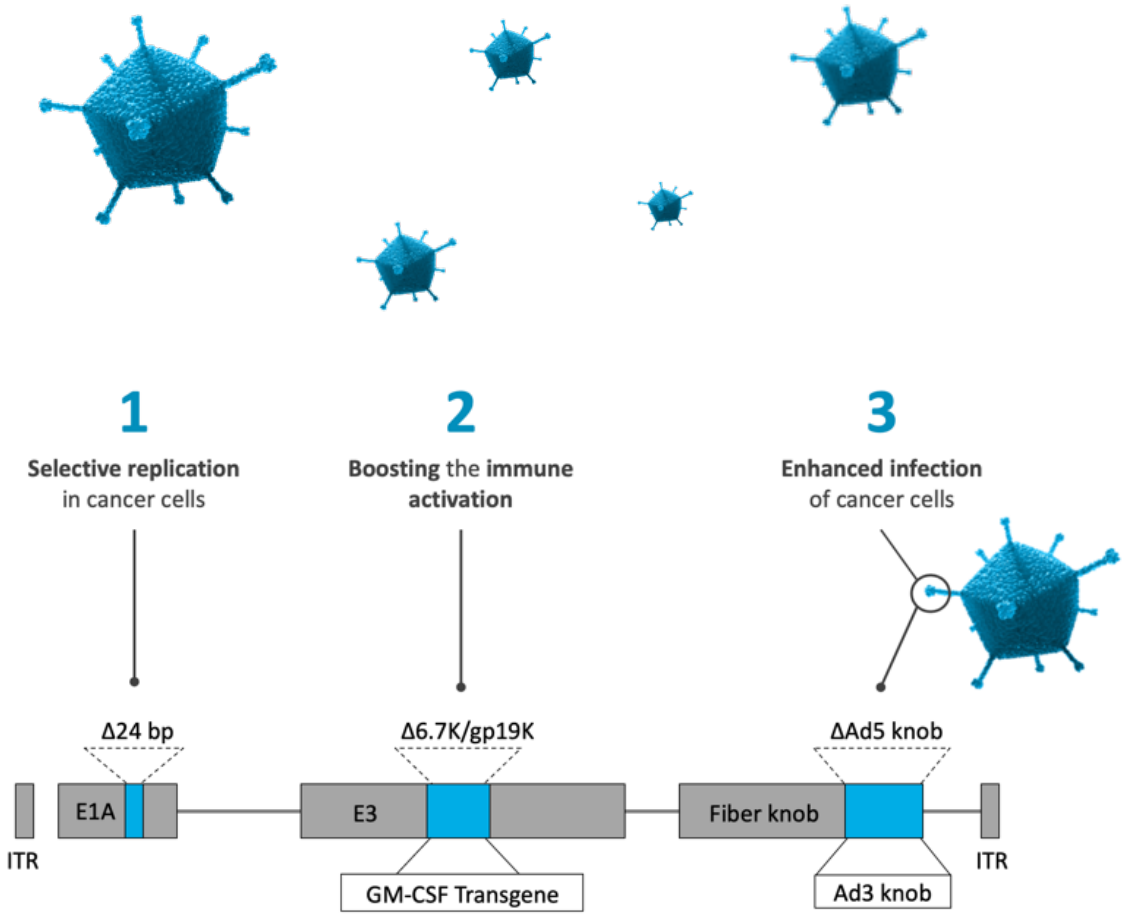


0-40% of treated patients respond

>50% of responding patients relapse

1 PD-1 checkpoint inhibitor monotherapy not sufficient

ONCOS-102 is an oncolytic immunotherapy based on a genetically modified adenovirus



Reverses immuno-suppressive defence mechanisms in the tumor

Primes anti-cancer T-cell responses

Delivers immune stimulatory payloads

Targovax development pipeline

Product candidate	Preclinical		Clinical			Milestones
	Discovery	IND-enabling	Phase 1	Phase 2	Phase 3 / pivotal	
ONCOS-102	**PD-1 Resistant Melanoma** Re-challenge combination w/anti PD-1					**1H 2023** Initiation of phase 2 trial (USA)
	Mesothelioma Combination w/Standard-of-Care (SoC)					**1H 2023** Publication in oncology journal
Mutant KRAS	Multiple Myeloma TG01 / QS-21					**2H 2022** Initiation of trial (Norway)
	Pancreatic cancer TG01 / QS-21 +/- anti-PD-1					**2H 2022** Initiation of trial (USA)
circular RNA						**2H 2022** Technical proof-of-concept data

Trials run and financed by collaboration partners

TG program update 15 December 2022: New collaborative trial in pancreatic cancer announced

Product candidate	Preclinical: Discovery	Preclinical: IND-enabling	Clinical: Phase 1	Clinical: Phase 2	Clinical: Phase 3 / pivotal	Milestones
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circular RNA						**2H 2022** Technical proof-of-concept data

Trials run and financed by collaboration partners

ONCOS-102 program: PD-1 resistant melanoma

Product candidate	Preclinical: Discovery	Preclinical: IND-enabling	Clinical: Phase 1	Clinical: Phase 2	Clinical: Phase 3 / pivotal	Milestones
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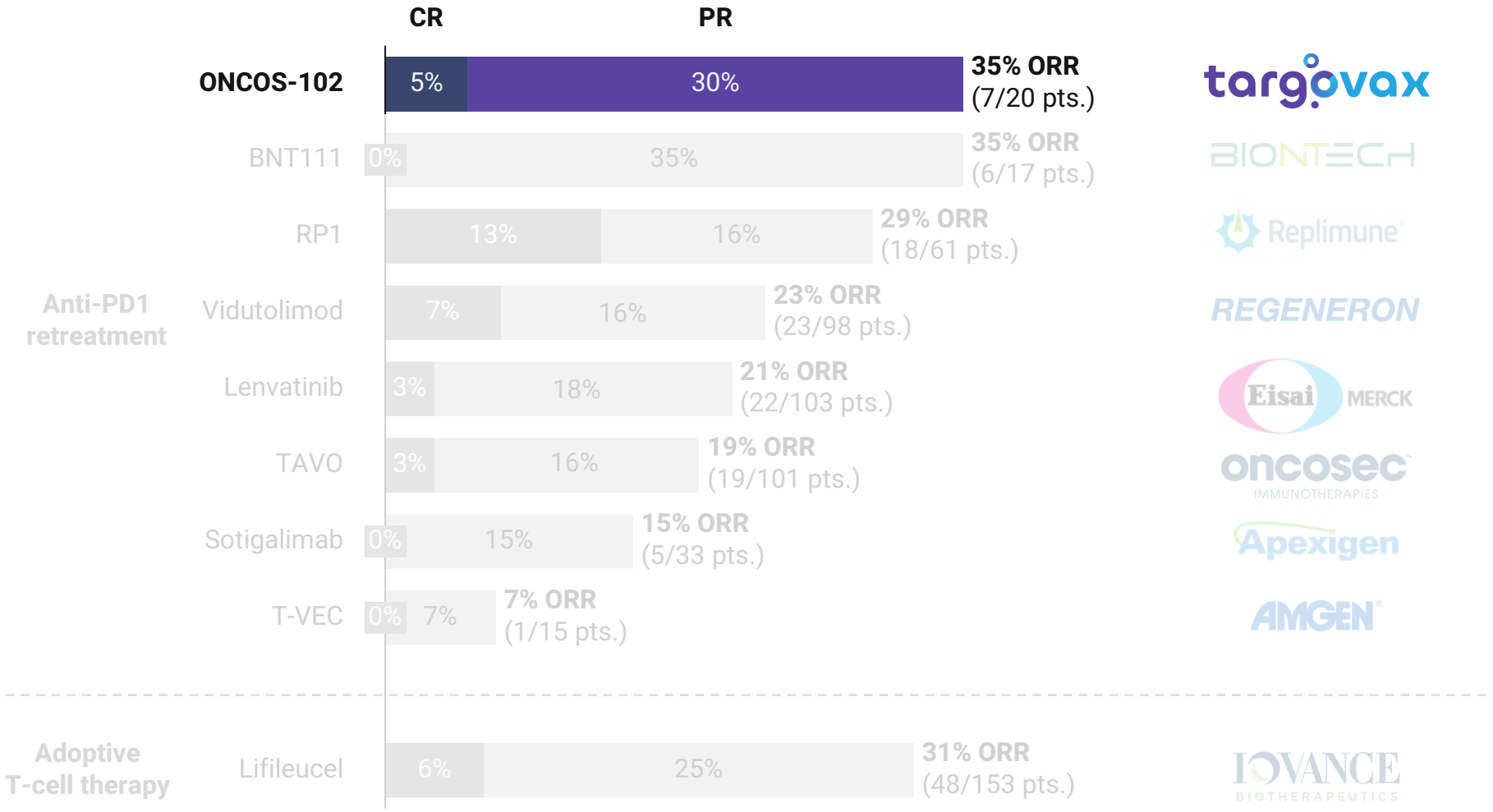
Trials run and financed by collaboration partners

There is a major and growing unmet medical need in PD-1 resistant melanoma

Incidence	Total **~50,000 patients per year** diagnosed with unresectable advanced malignant melanoma globally
PD-1 resistance	~50% of cases become PD-1 resistant Total **~25,000 patients per year**
Addressable	**Estimated 10,000 – 20,000 patients per year** addressable with intra-tumoral therapies
Other PD-1 resistance	*>100,000 patients per year lung cancer* *>50,000 patients per year head and neck*

ONCOS-102 has demonstrated a highly competitive ORR of 35% in PD-1 resistant melanoma

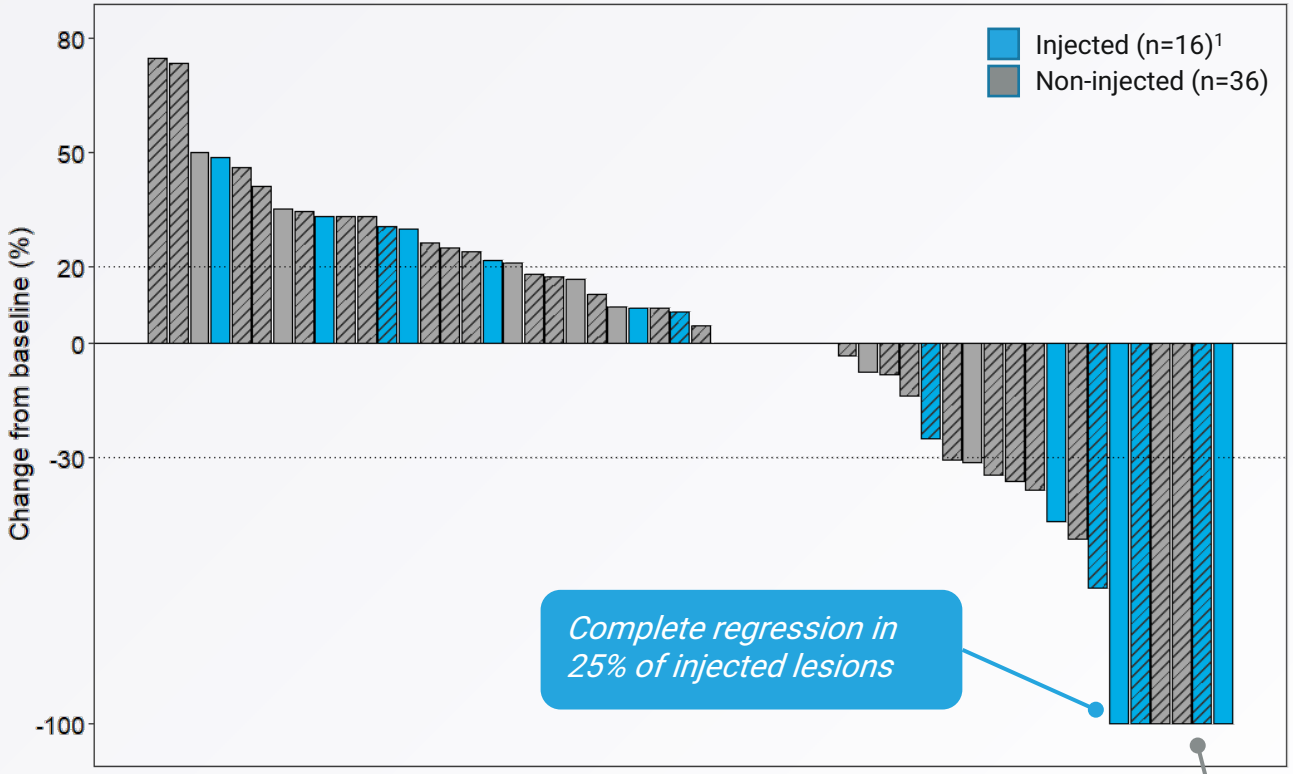


Targovax assessment, December 2022

Multiple examples of systemic (abscopal) effect, including complete regression in non-injected lesions

Response in individual tumors

% change from baseline; injected and non-injected target lesions



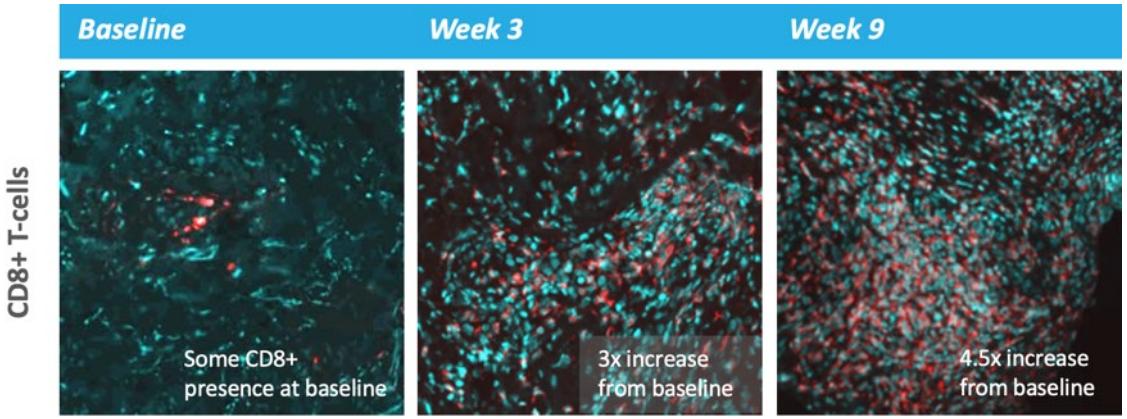
Observed systemic effect:

- **12 of 36 (33%)** non-injected target lesions reduced in size
- **8 of 15 (53%) patients** had reduction in non-injected target lesions
- **6 of 15 patients (40%)** with abscopal objective response (PR) according to RECIST 1.1 30% tumor shrinkage criteria

1: 8 patients had non-injected target lesions only, incl 2 patients with PR

ONCOS-102 drives strong and consistent T-cell infiltration in responding patients

CD8+ T-cell tumor infiltration
Tumor biopsy IHC, patient case example



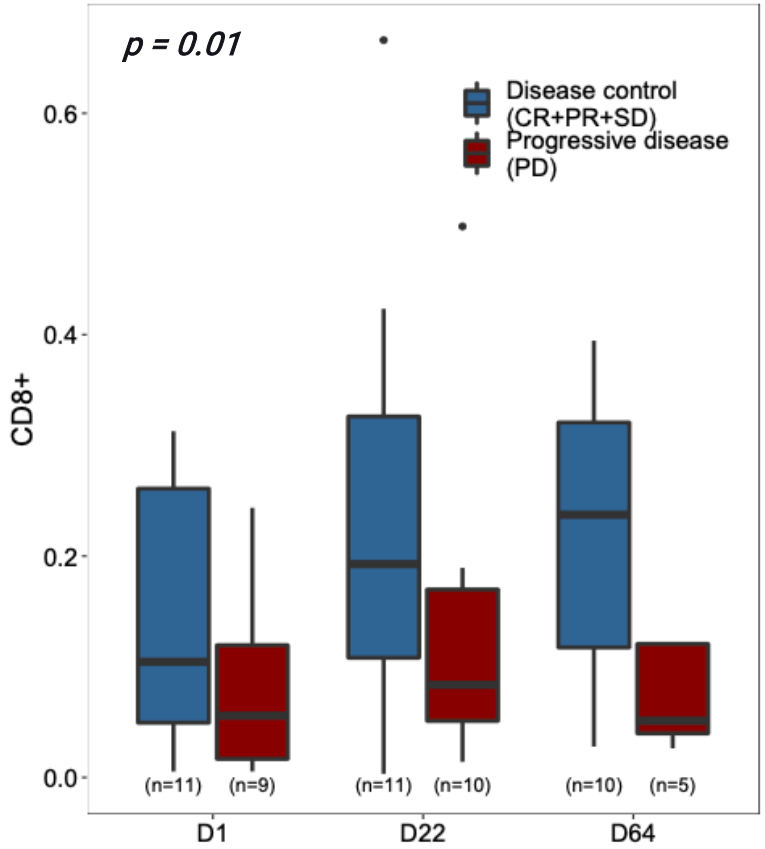
Progression on pembrolizumab

3x ONCOS-102 only monotherapy

6x ONCOS-102
2x pembrolizumab

Prior therapies:	T-vec (oncolytic virus)	**Disease stage:**	T4a-M1
	Ipilimumab (aCTLA-4)	**Outcome**	PR RECIST 1.1
	Pembrolizumab (aPD-1)		Week 9 - EoS

CD8+ T-cell infiltration increased over time in patients with clinical benefit (CR+PR+SD)



Next step ONCOS-102: multi-cohort Phase 2 trial with PD-1 and CTLA-4 checkpoint inhibitor combination

Part 1 – higher dose exploration run-in

1 **ONCOS-102** monotherapy high dose[1]

Randomize

2 **ONCOS-102 + balstilimab** low[2] → high dose

- *Confirm safety*
- *Select dose for expansion*

Part 2 – multi-cohort extension

2 **ONCOS-102 + balstilimab**
- *Expand to n=37*

3 **ONCOS-102 + botensilimab**
- *Initially n=18*
- *Expand to n =37*

4 **ONCOS-102 + balstilimab + botensilimab**
- *Initially n=18*
- *Expand to n =37*

Collaboration partner: agenus

Balstilimab: anti-PD-1
Botensilimab: Fc-enhanced anti-CTLA-4

The phase 2 trial is designed to enable future out-licensing and address regulatory requirements

- ✓ **Opportunity to achieve best-in-class data** in PD-1 resistant melanoma setting
- ✓ **Differentiated combinations vs. competitors**, with strong scientific and strategic rationale
- ✓ Design and size to **enable licensing decisions for big pharma partners**
- ✓ Confirm **ONCOS-102 high dose** and address FDA requirements for **contribution of components**
- ✓ **Support future expansion** of combinations into earlier lines of melanoma

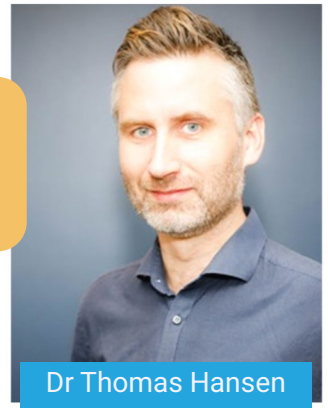
Pipeline development : Targovax is a pioneer in the emerging field of circular RNA (circRNA)

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 Kjems

The circRNA discoverers work for Targovax



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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

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.

BIOTECH

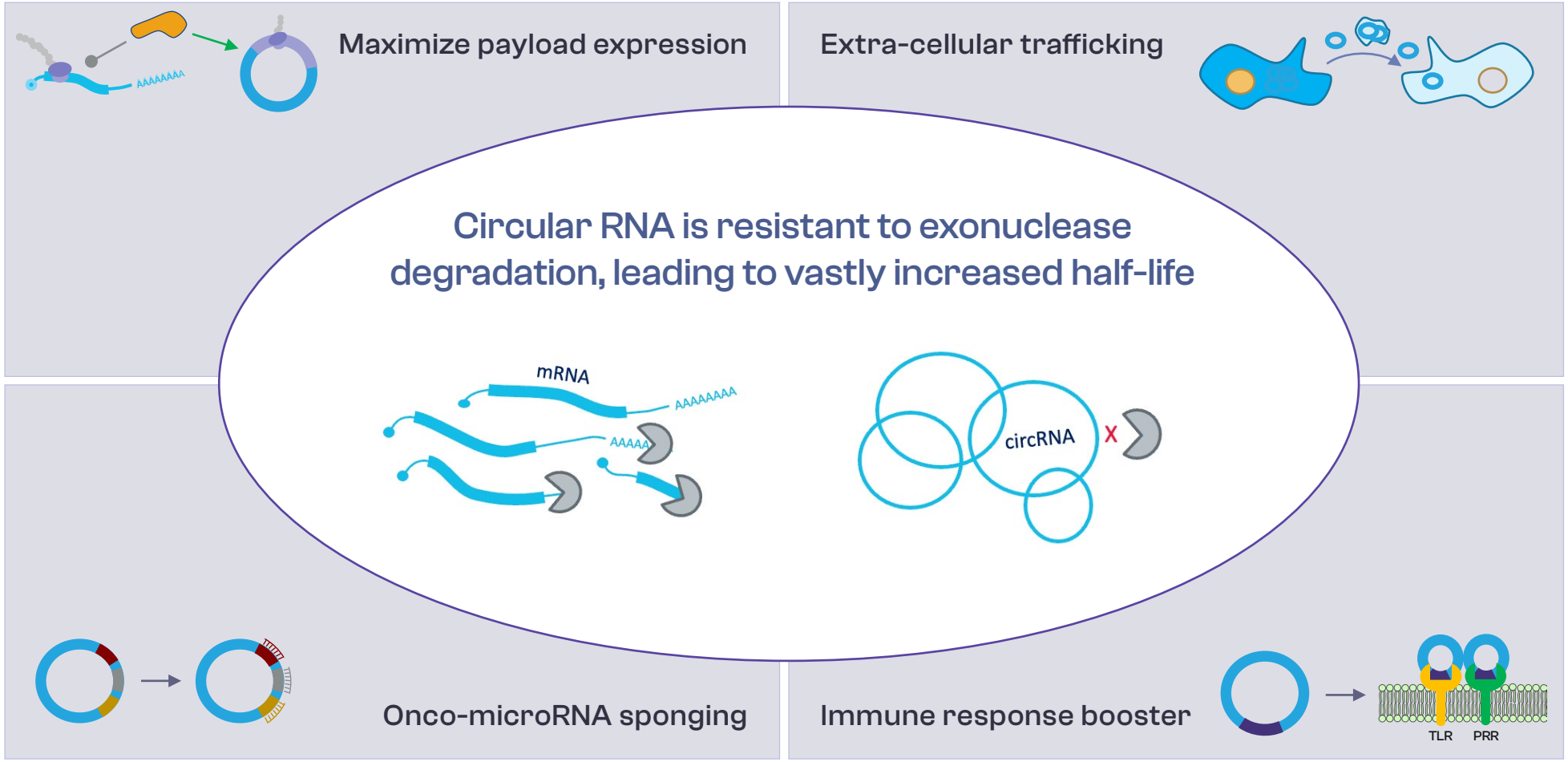
Merck bets big on circular RNA, paying $150M to work with Orna

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.

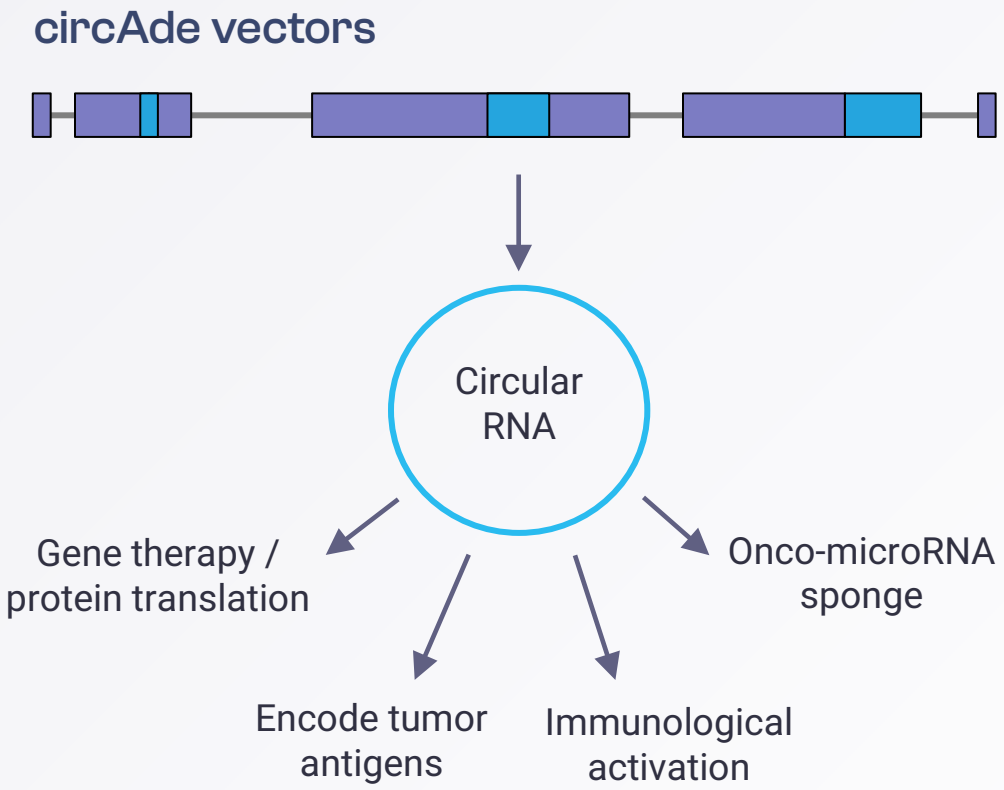
moderna

Flagship Pioneering

circRNA provides a toolbox to create a novel class of medicines



circAde – Targovax´s in-house vector system for circRNA delivery to solid tumors



2022 objectives for the Targovax circAde program:

- Establish technical proof-of-concept (PoC) for circAde approach
- Optimize vector expression constructs and circRNA structural design
- Explore and validate advantages of circRNA vs. mRNA delivery

Highly versatile – Multi-modal MoA – Excellent stability

Initial focus on oncology applications, with plans to expand platform into vaccines and rare disease

	Delivery	**Application** – leveraging circRNA to enhance existing medical toolbox	
1 **Oncology** Solid tumors	*circAde vector I*	• Delivery of immuno-stimulatory payloads against **validated targets that face systemic toxicity issues** • High-potency **neoantigen immunization** • Long-lasting supply of payloads that **target key cancer signalling and metabolic pathways**	*Core initial focus for in-house development*
2 **Vaccines** Infectious diseases	*circAde vector II*	• **Combine key benefits** of proprietary vector with circRNA-based vaccine approach • **Improved shelf-life and stability over mRNA**	*Expansion and partnering opportunities*
3 **Enzyme replacement** Rare diseases	*circAde vector III*	• Novel delivery tool for enzyme replacement therapy at **reduced cost and complexity over gene therapy** • Expand into **non-immunogenic circRNA applications**	

Targovax has a unique edge in the emerging circRNA field

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

- Led by circRNA pionéer Dr. Thomas Hansen

Unique circAde vector system for circRNA delivery to solid tumors

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

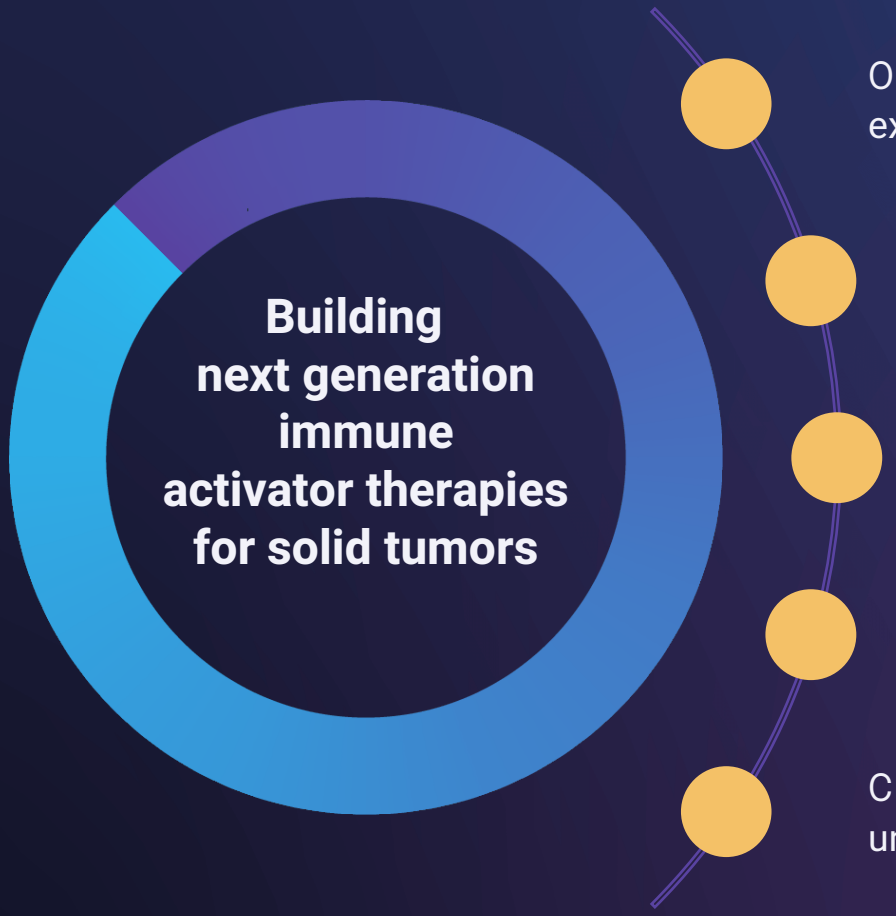
GMP manufacturing at scale using commercially available equipment

- 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 executive summary



ONCOS-102: oncolytic immunotherapy with demonstrated clinical efficacy and excellent safety profile in multiple solid tumors and treatment combinations

Highly competitive response rate: 35% ORR in anti-pd-1 resistant melanoma, responses in non-injected lesions and deep mechanistic analyses

KRAS immunotherapy: Clinical-stage polyvalent mutant KRAS vaccine with high-profile collaboration network and KRAS IO concepts in discovery phase

Circular RNA: Emerging pipeline in novel RNA biology leveraging 10 years of academic research, unique delivery approach for solid tumors

Company Financials: OSE listed since 2016, raised >USD 100M in total, cash runway until mid-2023