



Next generation immune activators for solid tumors

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ABGSC Norwegian Oncology Lunch Seminar

23 November 2022

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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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The Immuno-Oncology revolution

>500,000 patients treated per year

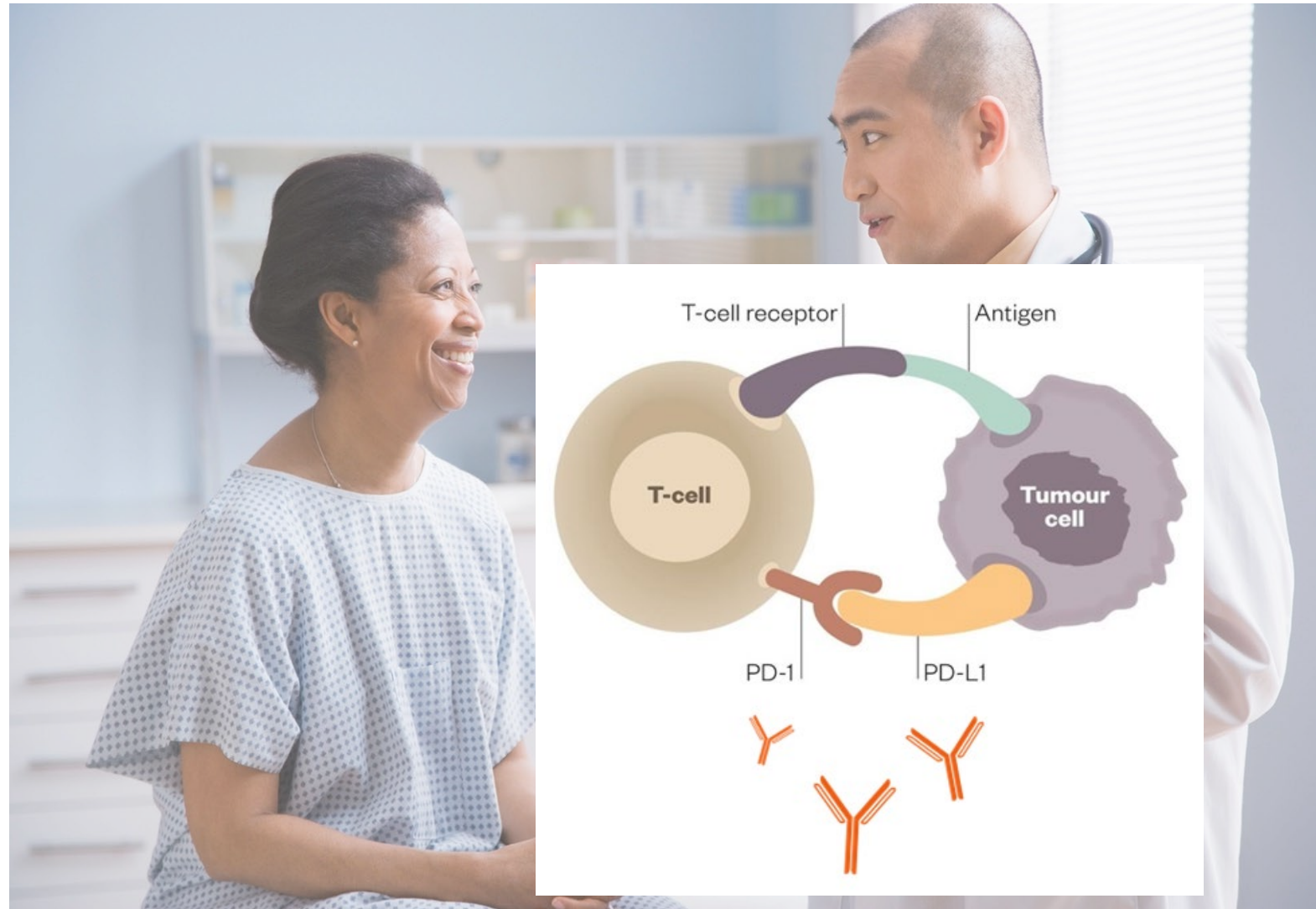
>4,000 ongoing clinical trials

>40% of US cancer patients eligible



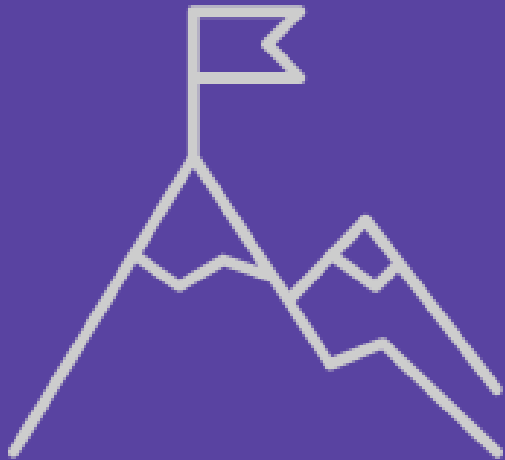
First generation immunotherapy: Checkpoint inhibitors

- 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

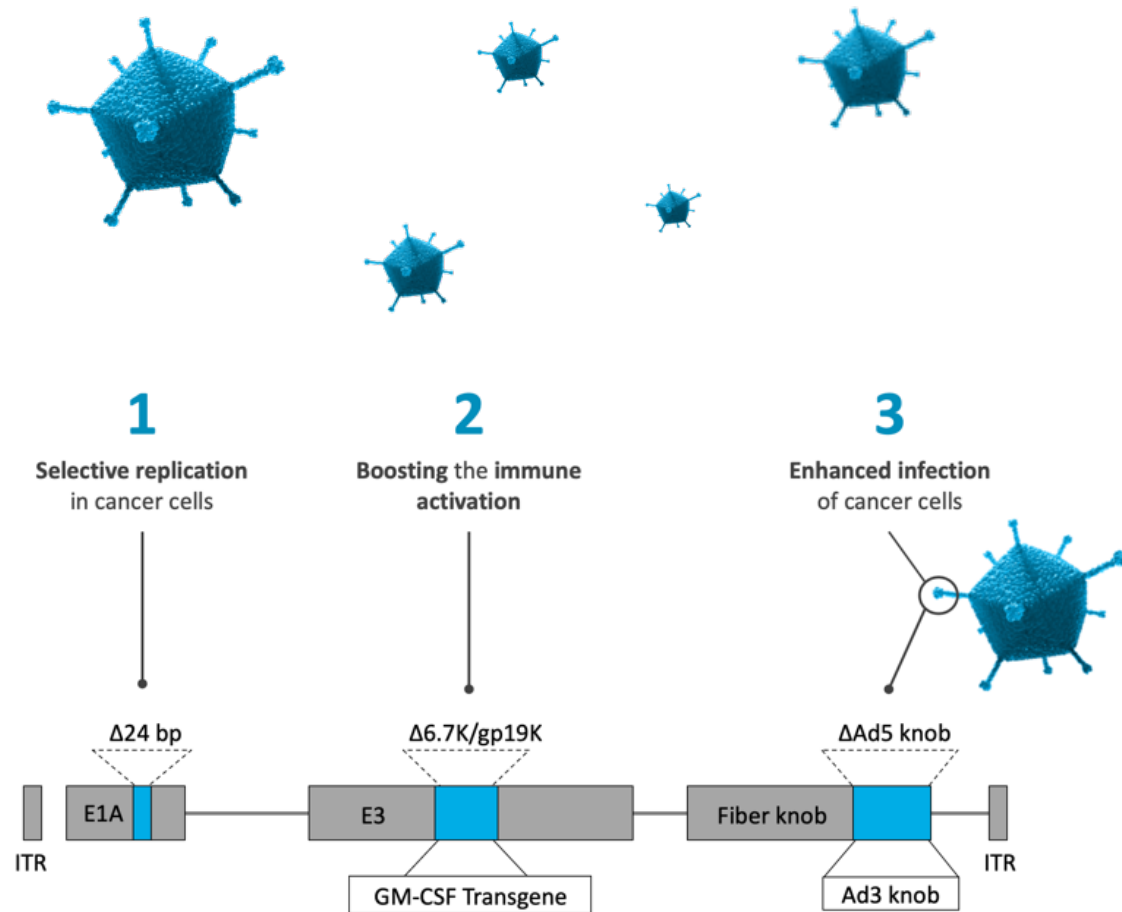
>50%

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

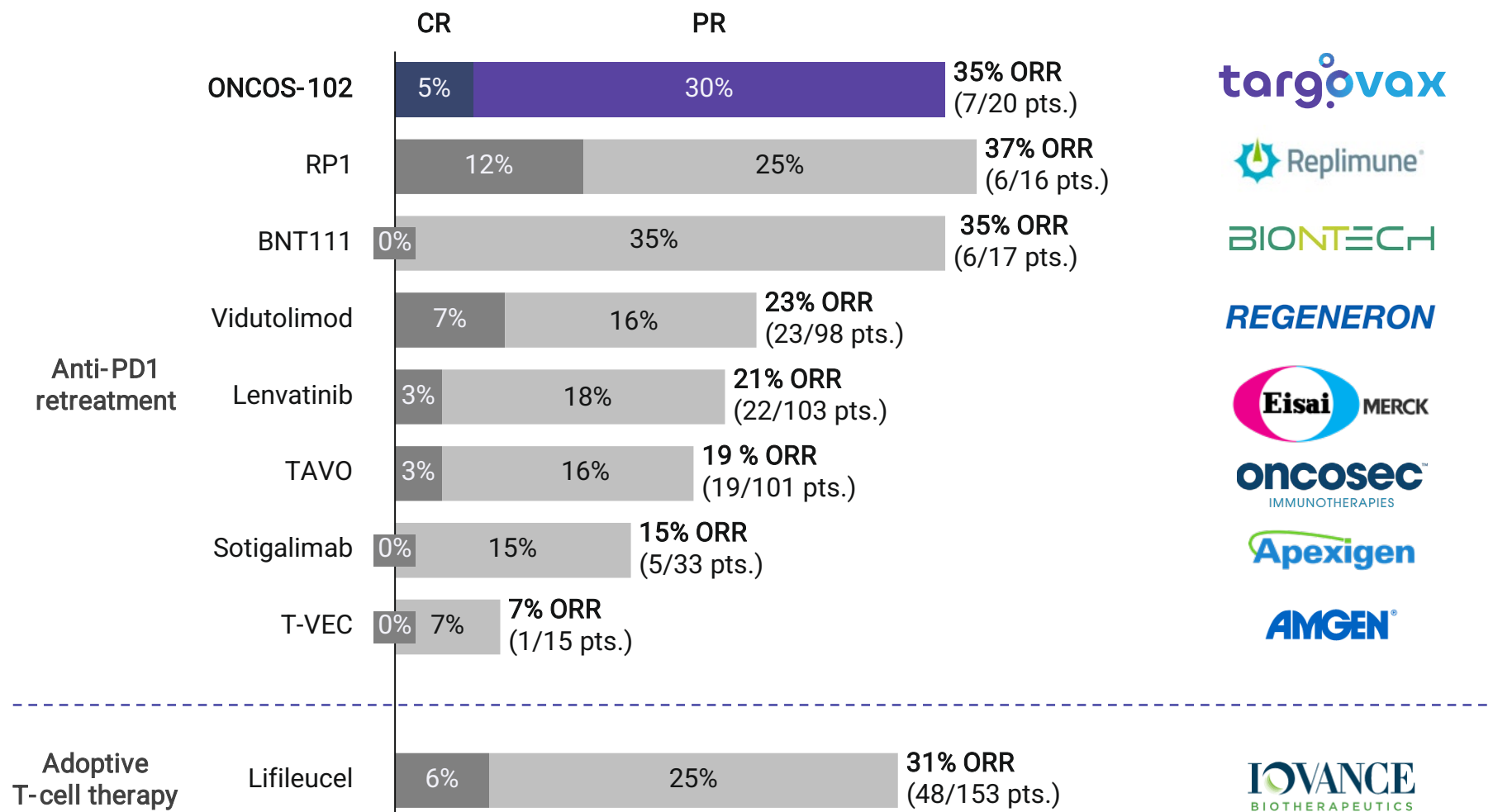
Product candidate	Preclinical		Phase 1	Clinical		Milestones
	Discovery	IND-enabling		Phase 2	Phase 3 / pivotal	
ONCOS-102	PD-1 Resistant Melanoma Re-challenge combination w/anti PD-1					1H 2023 Initiation of phase 2 trial (USA)
	Mesothelioma Combination w/Standard-of-Care (SoC)					1H 2023 Publication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

■ 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
<i>Other PD-1 resistance</i>	<i>>100,000 patients per year lung cancer >50,000 patients per year head and neck</i>

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



targovax

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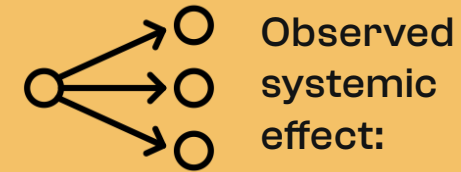
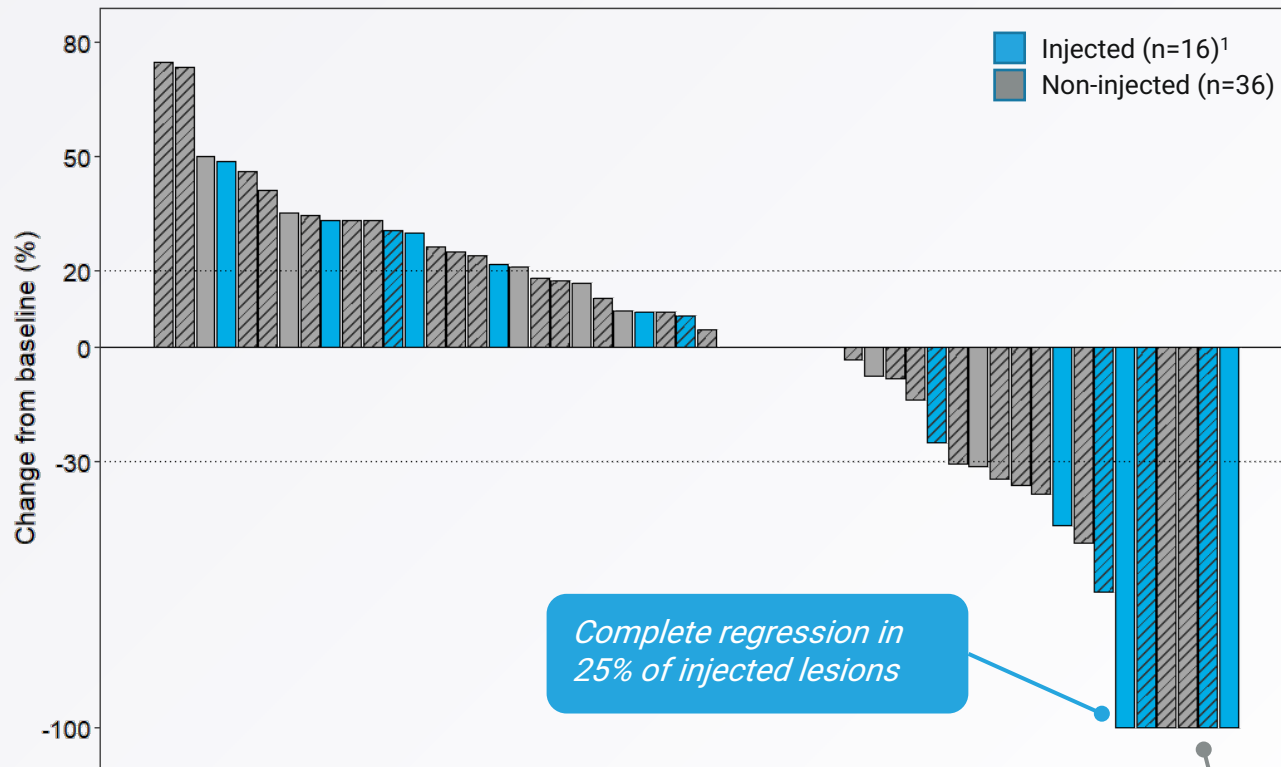
AMGEN®

IOVANCE
BIOTHERAPEUTICS

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

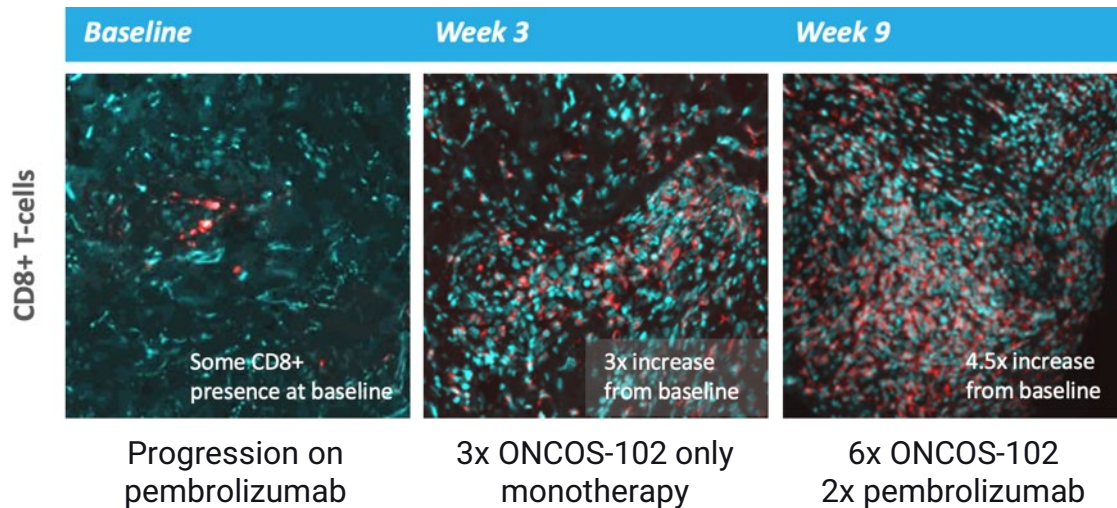


- 12 of 36 (33%) non-injected target lesions reduced in size
- 8 of 15 (53%) patients had reduction in non-injected target lesions
- 6 of 15 patients (40%) with abscopal objective response (PR) according to RECIST 1.1 30% tumor shrinkage criteria

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

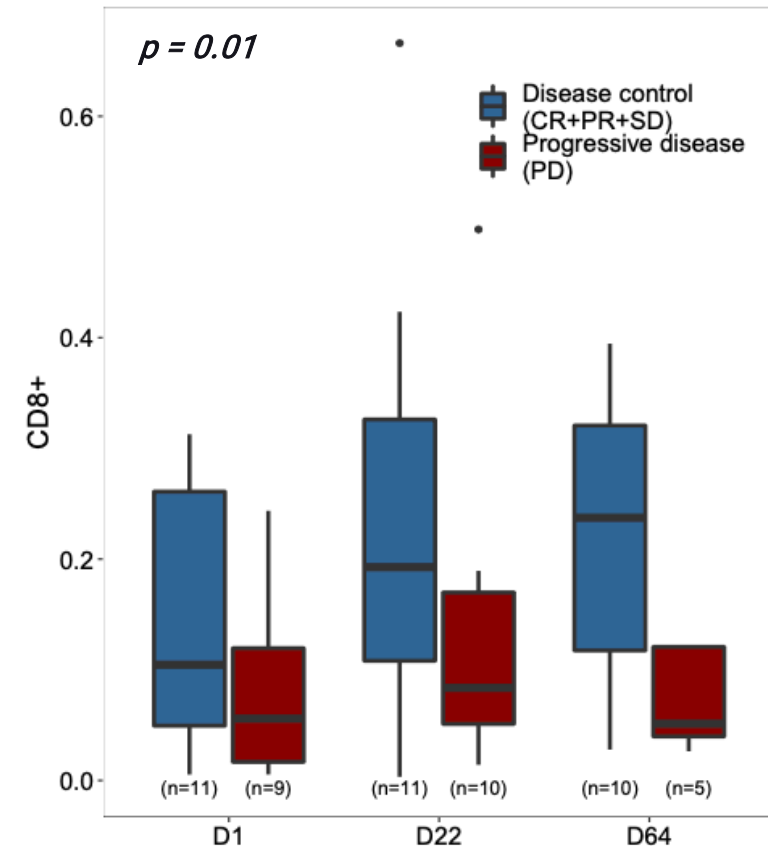
ONCOS-102 drives strong and consistent T-cell infiltration in responding patients

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



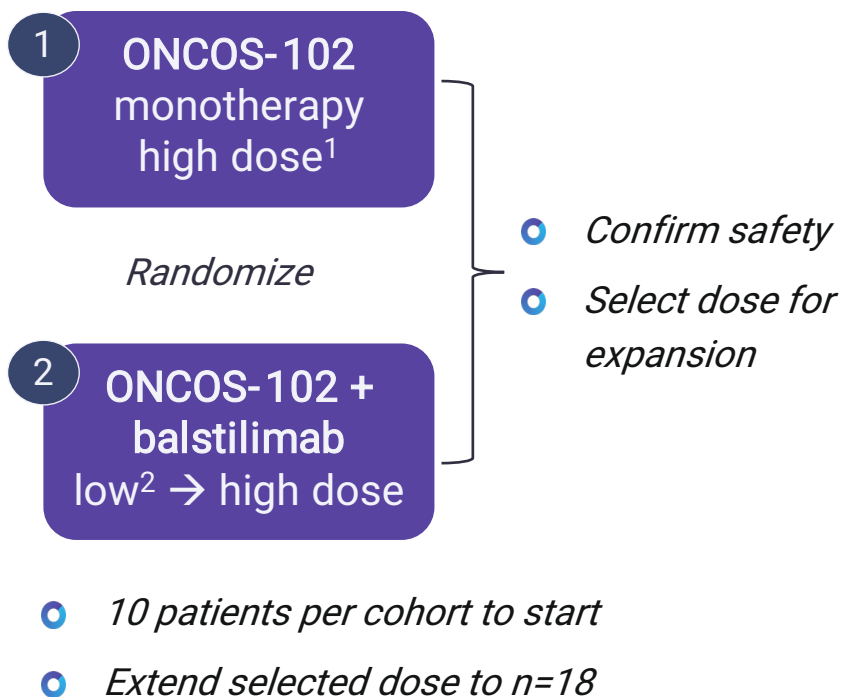
Prior therapies:	T-vec (oncolytic virus)	Disease stage:	T4a-M1
	Ipilimumab (aCTLA-4)	Outcome	PR RECIST 1.1
	Pembrolizumab (aPD-1)		Week 9 - EoS

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

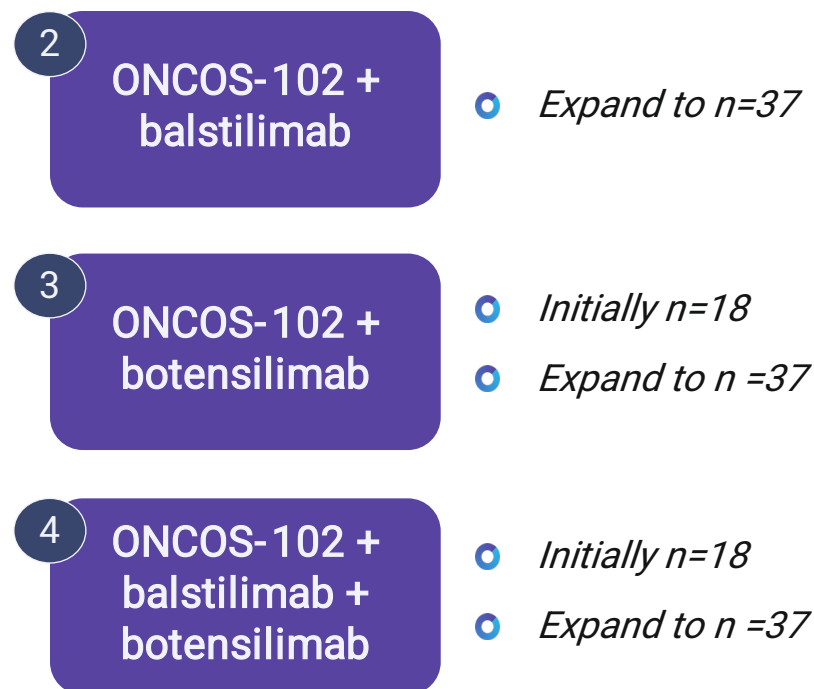


Next step ONCOS-102: multi-cohort Phase 2 trial with PD-1 and CTLA-4 checkpoint inhibitor combination

Part 1 – higher dose exploration run-in



Part 2 – multi-cohort extension



1: High dose: 1×10^{12} viral particles (VP)
2: Low dose 3×10^{11} VP
3: High dose expected selection for Part 2

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

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 Kjems

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

100k Accesses | 4746 Citations | 130 Altmeteric | [Metrics](#)



Dr Thomas Hansen



Dr Erik D Wiklund

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.



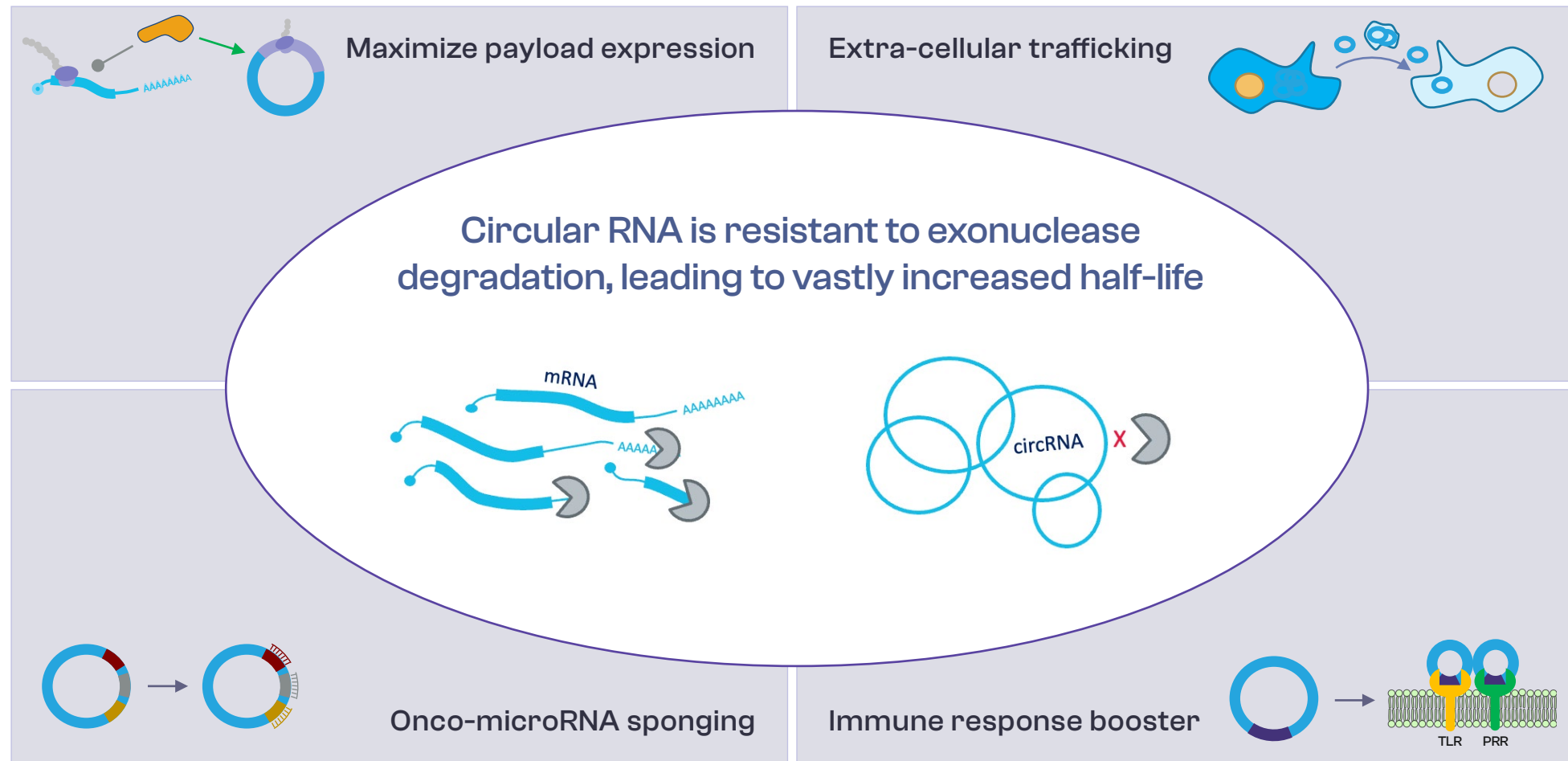
Merck bets big on circular RNA, paying \$150M to work with Orna

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.

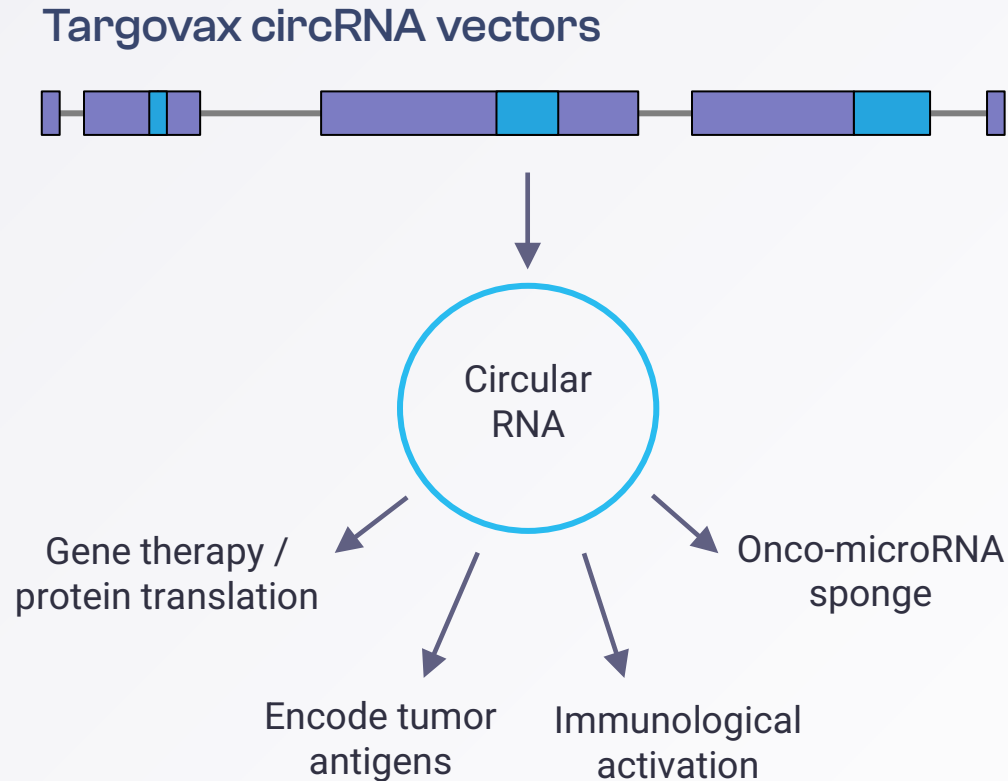
moderna

**Flagship
Pioneering**

circRNA provides a toolbox to create a novel class of medicines



Targovax is deploying an in-house vector system for circRNA delivery



2022 objectives for the Targovax circRNA program:

- Establish technical proof-of-concept (PoC) for circRNA vector 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

Approach		
1	Oncology Solid tumors	<ul style="list-style-type: none">• Activate validated immuno-stimulatory targets that face systemic toxicity issues• Modulate key cancer signalling and metabolic pathways• Immunize against tumor neoantigens
2	Vaccines Infectious disease	<ul style="list-style-type: none">• Enhance potency, durability and logistics over mRNA vaccines
3	Enzyme replacement Rare disease	<ul style="list-style-type: none">• Enzyme replacement therapy at reduced cost and complexity over gene therapy

Core initial focus for in-house development

Expansion and partnering opportunities

Targovax has a unique edge in the emerging circRNA field



World-leading circRNA experts in-house with deep technical experience

- Led by circRNA pion  r Dr. Thomas Hansen



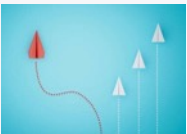
Unique vector system for circRNA delivery to solid tumors

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



GMP manufacturing at scale using commercially available equipment

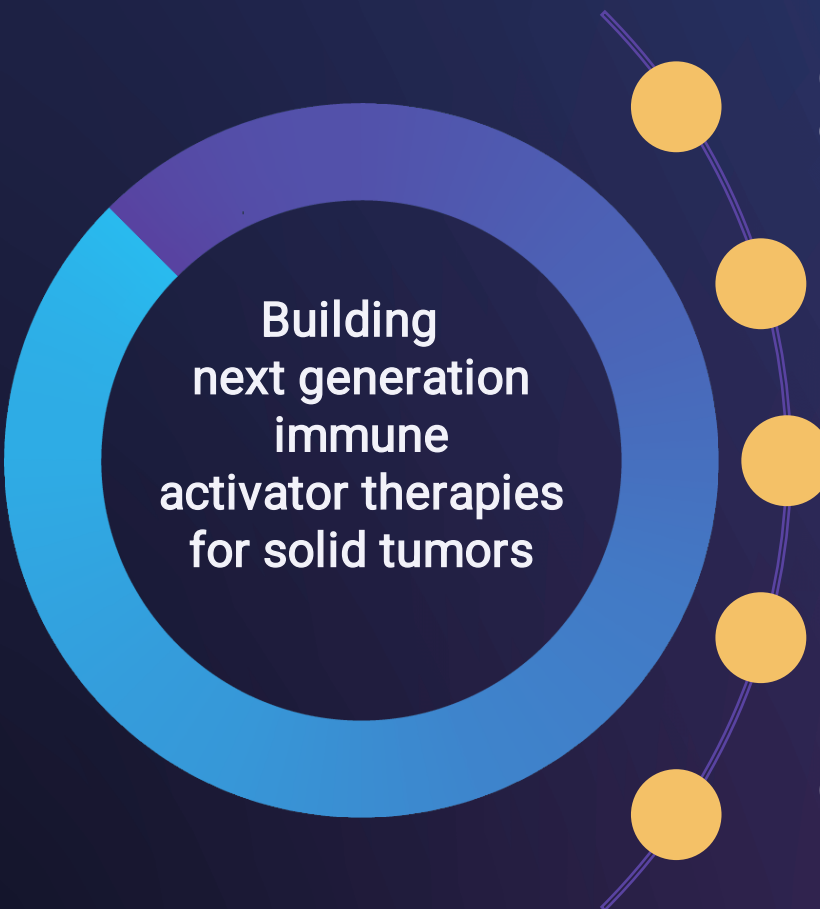
- circRNA GMP manufacturing at scale faces unresolved issues



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



**Building
next generation
immune
activator therapies
for solid tumors**

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