Activating the patient's immune system to fight cancer

Company overview

January 2019

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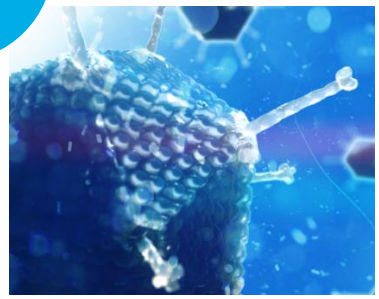
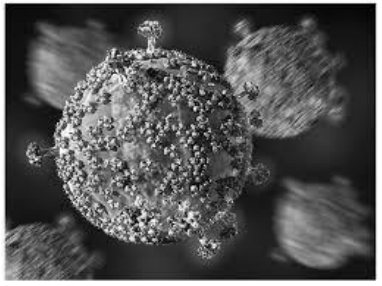
1 Introduction

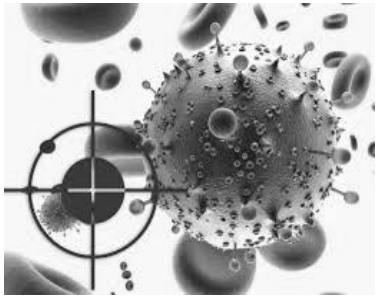
2. ONCOS oncolytic virus program
3. TG mutant RAS vaccine program
4. Corporate overview

TARGOVAX'S POSITION IN THE FUTURE CANCER THERAPY LANDSCAPE

Targovax focus







Immune activators
Oncolytic viruses, vaccines

Immune modulators
Checkpoint inhibitors

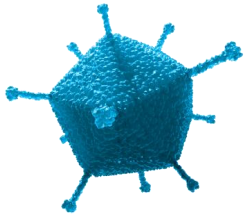
Surgery - Radio - Chemo

Immune boosters
CAR-Ts, TCRs

Targeted therapy
TKIs, PARPs, etc.

Targovax has two programs in clinical development, with an

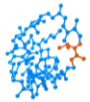
ONCOLYTIC VIRUS LEAD PRODUCT CANDIDATE



ONCOS
Oncolytic virus

Lead product candidate

- Genetically **armed adenovirus**
- Turns cold **tumors hot**
- Induces **tumor specific T-cells**
- Single agent **phase I completed**
- **4 ongoing combination trials**



TG
Neoantigen vaccine

Pipeline product

- **Shared neoantigen**, therapeutic peptide vaccine
- Triggers the **T-cell response** to oncogenic **RAS driver mutations**
- 32 patient **phase I/II trial completed**

Activates the immune system

Triggers patient-specific responses

No need for individualization

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PIPELINE OVERVIEW AND MILESTONES

Platform	Product candidate	Preclinical / Phase I / Phase II / Phase III	Last event	Next expected event
ONCOS oncolytic adenovirus	ONCOS-102	**Mesothelioma** Comb. w/ pemetrexed/cisplatin	Phase Ib safety lead-in cohort, incl. immune activation and ORR data (6 pts)	**1H 2020** Randomized ORR data 30 pts
		Melanoma Comb. w/Keytruda®	ORR and immune activation (6 pts), 1/6 CR	**1H 2019** ORR and immune data first cohort
		Peritoneal metastases[1] Collab: Ludwig, CRI & AZ Comb. w/Imfinzi®	First dose escalation cohort safety review (4 pts)	*Update by collaborator, expected 2019*
		Prostate Collab: Sotio Comb. w/DCVAC	First patient dosed	*Update by collaborator, expected 2019*
	Next-gen ONCOS	**3 viruses** undisclosed	Virus construct cloning and *in vitro* validation	**2H 2019** Pre-clinical data
TG neo-antigen cancer vaccine	**TG01**	**Pancreatic cancer** Comb. w/gemcitabine	mOS 33.4 months Demonstrated mutant RAS-specific immune activation	TBD
	TG02	**Colorectal cancer** Proof-of-mechanism Comb. w/Keytruda®	First safety review, incl. immune activation data (3 pts)	**1H 2019** Immune activation and mechanistic data (mono)
	TG02	**CPI synergy** TG + PD-1		**2H 2019** Pre-clinical data

[1] Patients with advanced peritoneal disease, who have failed prior standard chemotherapy and have histologically confirmed platinum-resistant or refractory epithelial ovarian or colorectal cancer

Ongoing collaborator sponsored trials

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ONCOS-102 CLINICAL DATA SUMMARY

	Patient population	Safety	Immune activation	Efficacy
Various solid tumors Phase I Monotherapy	○ End-stage patients, 3rd line and beyond ○ 7 different solid tumors ○ 12 patients	○ Well tolerated	○ Innate: 12/12 ○ Adaptive: 11/12	○ 40% DCR ○ 2 long-term survivors ○ Survival correlated with TIL increase

Mesothelioma
Phase I/II randomized
With SoC chemo
	○ Metastatic
	○ 1st and 2nd/3rd line
	○ 6 patients completed trial to date
		○ Well tolerated
		○ No added toxicity with chemo
			○ Innate: 6/6
			○ Adaptive: 3/4
				○ 50% DCR
				  ○ 1 PR
				  ○ 2 SD

Melanoma Phase I Combo with Keytruda®	○ PD-1 refractory advanced melanoma ○ 6 patients completed trial to date	○ Well tolerated ○ No safety issues	○ Innate: 6/6 ○ Adaptive: 4/4	○ 1 CR, w/supporting immune data ○ 3 with local effect, but with distal progression

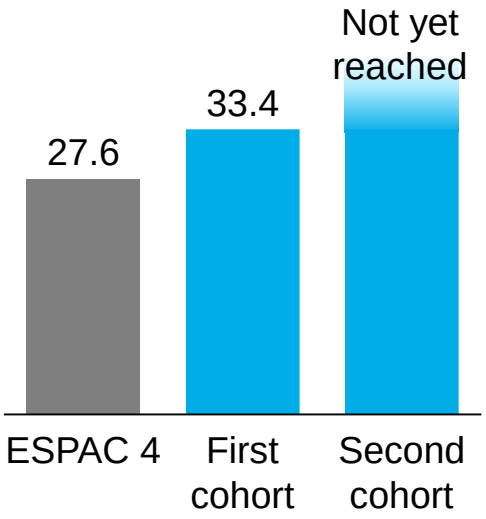
Completed

Ongoing trials sponsored by Targovax

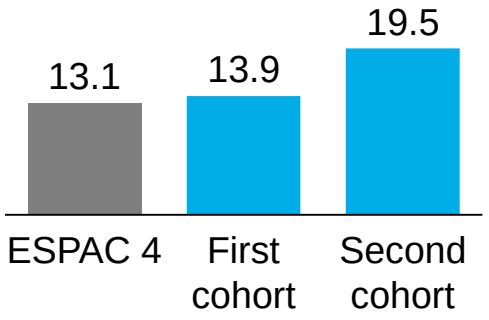
TG01 IN RESECTED PANCREATIC CANCER

EFFICACY SIGNAL SEEN IN PHASE I/II TRIAL

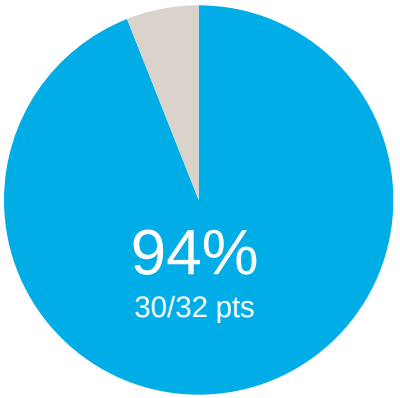
Median overall survival, months



Median disease free survival, months



RAS-specific immune activation



TG01 is well-tolerated - improved dosing regimen in second cohort

First cohort: 19 pts, Second cohort: 13 pts. Total 32 pts.
ESPAC4 trial for gemcitabine alone
DFS both cohorts: 16.1 months

2

ONCOS oncolytic virus program

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ONCOS-102 is a oncolytic adenovirus serotype 5 armed with a GM-CSF transgene

1

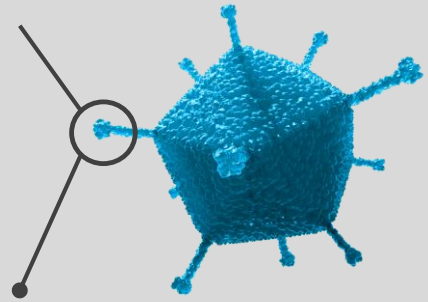
Selective replication
in cancer cells

2

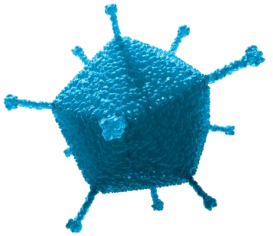
Boosting the **immune activation**

3

Enhanced infection
of cancer cells



BENEFITS OF ADENOVIRUS SEROTYPE 5 BACKBONE



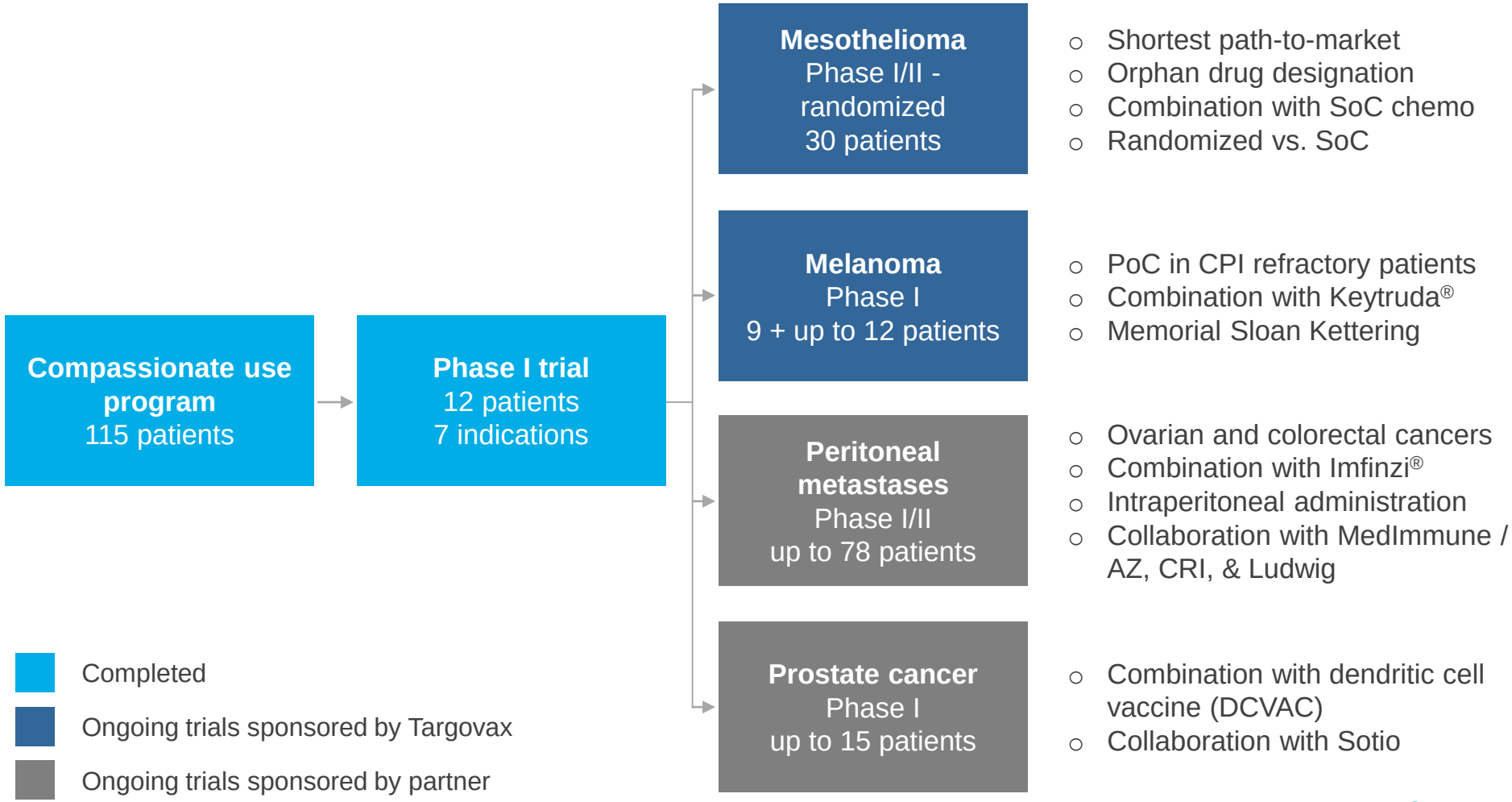
Highly immunogenic, Toll like receptor 9 (TLR9) agonist

Well-characterized, well-tolerated and few safety concerns

Double stranded DNA, possibility for transgenes, non-enveloped

Pre-existing immunity, reduced issue of immuno-dominance

ONCOS CLINICAL PROGRAM OVERVIEW



ONCOS-102
Phase I single agent

IMMUNE ACTIVATION DEMONSTRATED

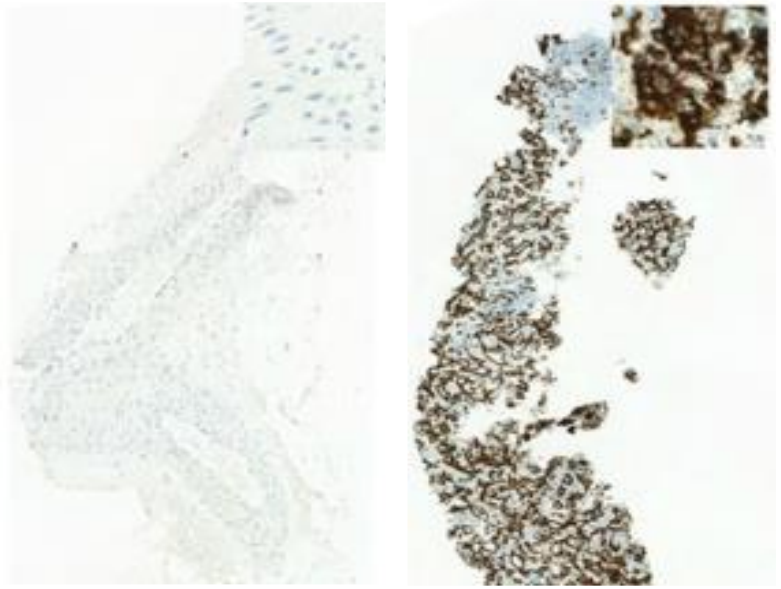
ONCOS-102 Phase I trial design:

- **12 patients**, 7 different solid tumors
- All **refractory to multiple lines** of therapy
- **ONCOS-102 monotherapy**
  - 9 injections over 5 months

Top-line results:

- **100% innate immune activation**
- **11/12 patients increase in CD8+ T-cells**
- **40% SD, 2 long-term survivors**
- **Abscopal effect** and lasting **systemic immune responses** observed

Cold tumor turned hot, CD8+ T-cell staining



Pre-treatment
Baseline

Post-treatment
Week 8

Ranki et al., Journal for Immunotherapy of Cancer 2016, 4(17)

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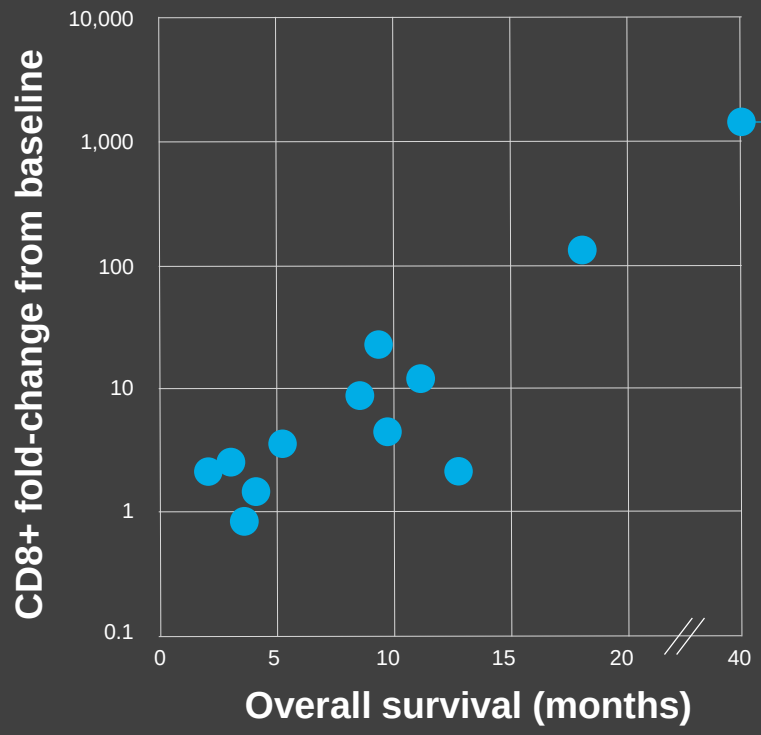
ONCOS-102
Phase I single agent

CD8+ T-CELL INFILTRATION CORRELATES WITH SURVIVAL

Fold-change CD8+ T-cell count vs. survival

r = 0.75 p = 0.005



Case example

- **Ovarian cancer,** 38yr old woman
- Failed on 5 types of chemotherapy
- **>1,000-fold increase** in TILs
- **Tumor specific T-cells detected** up to 2 years after treatment
- **Stable disease for 3 years**, survived for 3.5 years

Ranki et al., Journal for Immunotherapy of Cancer 2016, 4(17)

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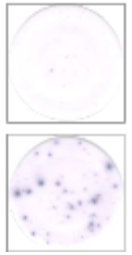
MELANOMA ONCOS-102 + KEYTRUDA COMBINATION

induction of tumor-specific T-cells

Tumor antigen specific T-cell response
IFN-γ ELISPOT analysis for tumor antigen activated T-cells

Patient 5
Previous Yervoy® & Keytruda

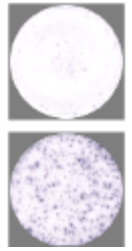
MAGE-A1
Week 3



Increased infiltration of MAGE-A1 tumor specific T-cells
- MAGE-A1 T-cells also detected at baseline

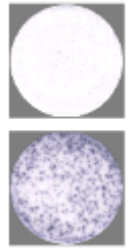
Patient 4
Previous Yervoy, Keytruda & Imlygic®

NY-ESO-1
Week 3



***De novo* induction of NY-ESO-1 tumor specific T-cells**
- Not present at baseline

MAGE-A1
Week 3



***De novo* induction of MAGE-A1 tumor specific T-cells**
- Not present at baseline

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MELANOMA ONCOS-102 + KEYTRUDA COMBINATION

one complete response by week 9

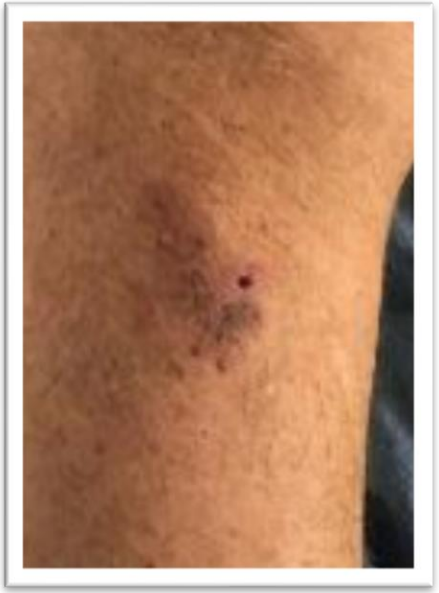
Patient 5

Previous Yervoy & Keytruda

Baseline

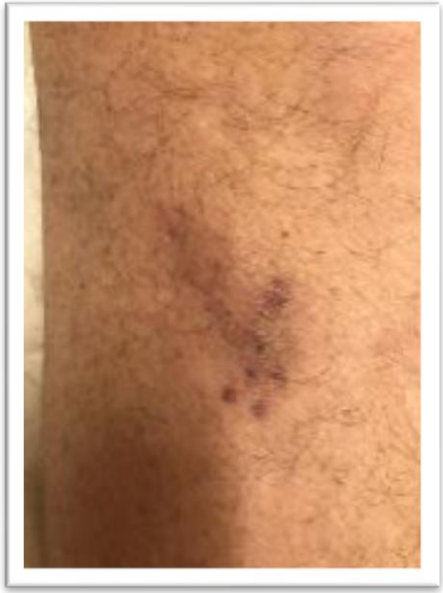
Progression on Keytruda

Week 3



Visible tumor regression after 3x ONCOS-102 injections

Week 9



Complete response after 3x ONCOS-102 injections & 2x Keytruda infusions

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ONCOS-102 + KEYTRUDA MELANOMA TRIAL

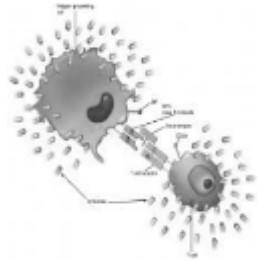
data summary first 6 patients

1 Safety

- ✓ **First safety review completed with no concerns**
- ✓ ONCOS-102 and Keytruda combination is well-tolerated

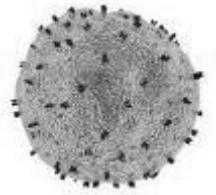
2 Innate immune activation

- ✓ **Systemic increase of pro-inflam-matory cytokines** (6/6 patients)
- ✓ All patients develop fever



3 Adaptive immune activation

- ✓ **Increase** in tumor **T-cell infiltration** (TILs, 3/4 patients)
- ✓ **Tumor-specific T cells** in 2/4 patients
- ✓ **Abscopal immune response** in one patient



4 Efficacy

- ✓ **Complete response** in 1/6 patients (very rare)
- ✓ **Transient regression** observed in 3 patients
- ✓ **Associated** with level of immune **activation**

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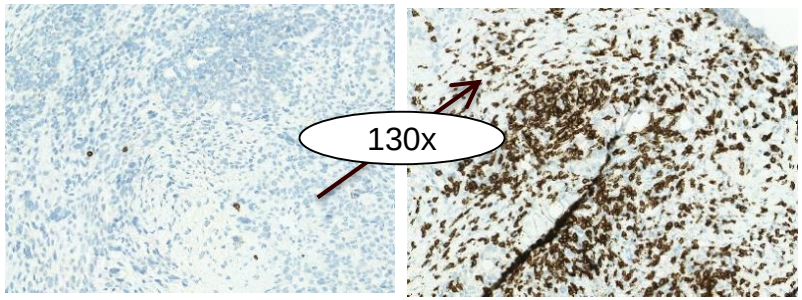
ONCOS-102 IN MESOTHELIOMA

turning cold tumors hot

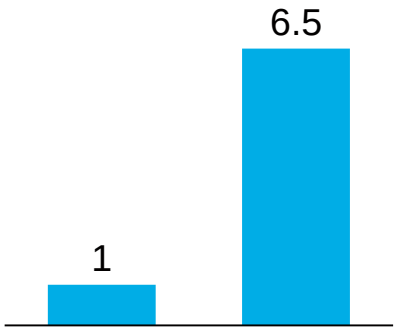
CD8+ T-cells in tumor
Tumor biopsy staining

Mesothelioma *– Phase I, patient 14*

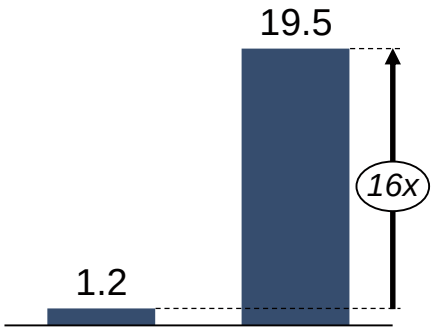


Baseline Week 5

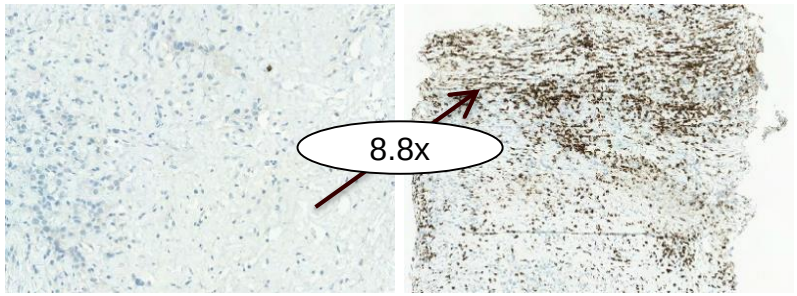
CD4+ T-cells in tumor
Fold change



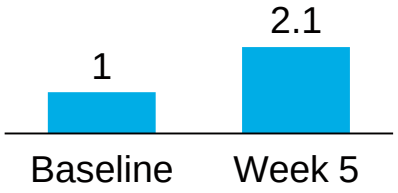
PD-L1 positive tumor cells
% of total

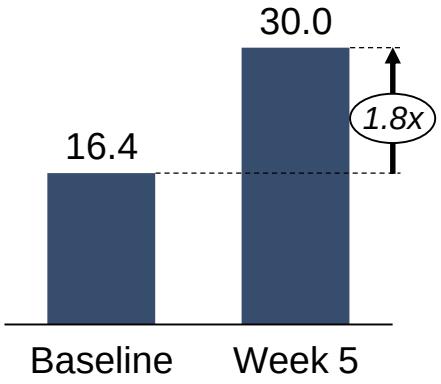


Mesothelioma *– Phase I, patient 9*



Baseline Week 5





Ranki et al., Journal for Immunotherapy of Cancer 2016, 4(17)

ONCOS-102 + SoC MESOTHELIOMA TRIAL

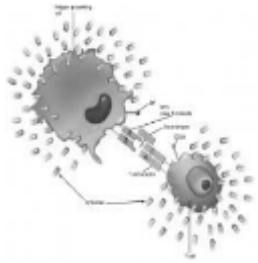
data summary first 6 patients

1
Safety

- ✓ ONCOS-102 **well-tolerated** in combination **with chemotherapy**

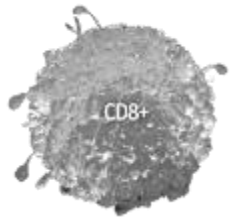
2
Innate immune activation

- ✓ **Systemic increase of pro-inflammatory cytokines** in 6/6 patients



3
Adaptive immune activation

- ✓ Increase in **tumor infiltration of CD4+ and CD8+ T-cells** in 3/4 patients
- ✓ **Tumor-specific T-cells** in 2/6 patients



4
Efficacy

- ✓ **One partial response** (PR) and two stable disease (SD)
- ✓ **50% disease control rate**

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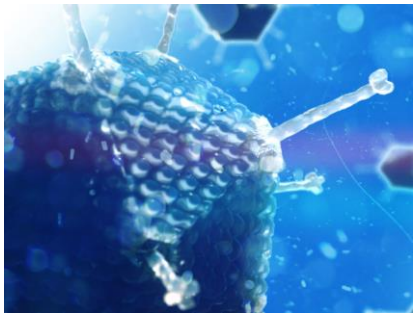
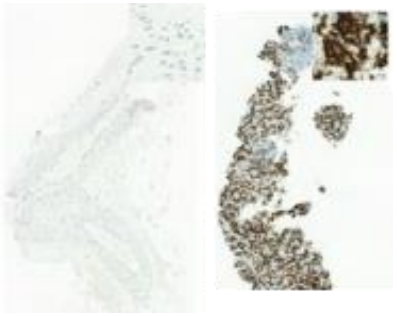
WHY ONCOS-102?

1 Innate immune activation

- **Strong innate immune activation** in nearly all injected patients
- **Correlation with clinical outcome**



2 Adaptive immune activation



- **Increase in T-cells** systemically and in tumor (TILs)
- **Tumor-specific T-cells** identified in several patients

3 In vivo efficacy

- **Anti-tumor effect**
- **Abscopal effect**
- **Tumor-specific immune responses**
- **Synergy** with both **CPIs and chemo**

4 Clinical efficacy

- **Complete response** seen in CPI refractory melanoma patient
- Outcome associated with immune activation
- **Well-tolerated,** >150 patients treated

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3

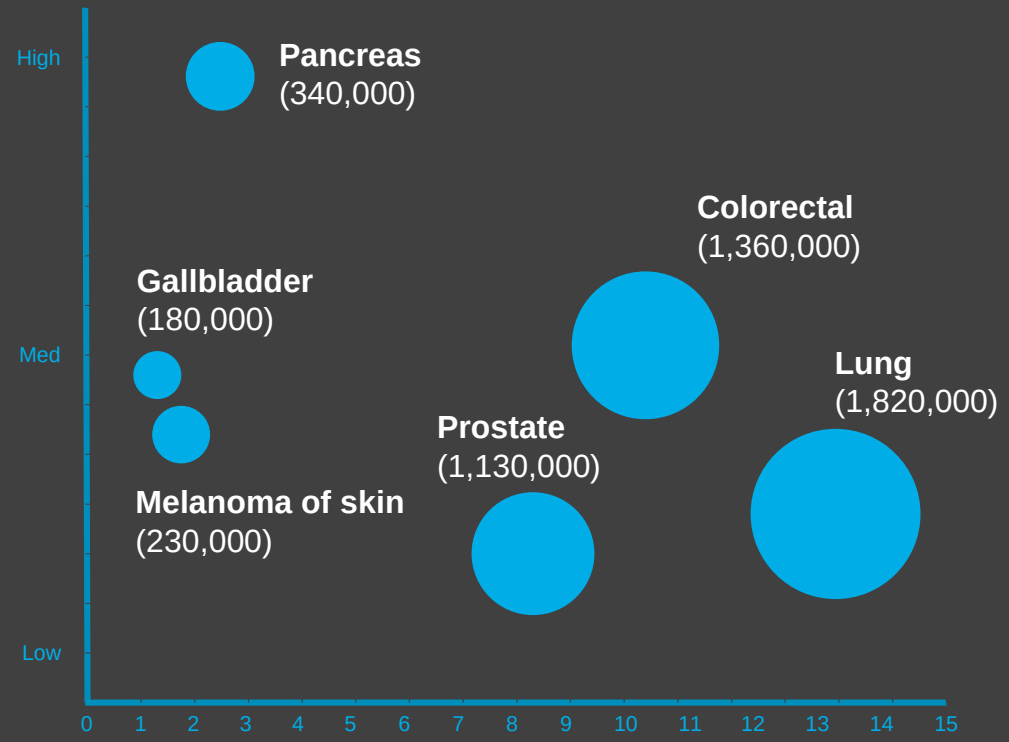
TG mutant RAS vaccine program

4. Corporate overview

The RAS gene is central in oncogenesis and is mutated in 90% OF PANCREATIC AND 50% OF COLORECTAL CANCERS

Frequency of RAS mutations

Global cancer incidents per 10,000
(xx) = no. of cancer patients



- RAS mutations are **trunk neoantigens** that **drive oncogenesis**
- **There are no existing therapies** targeting RAS mutations
- Targovax' TG program is a **unique vaccine approach for mutant RAS cancer**

Fernandez-Medarde; RAS in Cancer and Developmental Diseases; Genes & Cancer. 2011;2(3)

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The TG neo-antigen vaccine teaches the immune system to

RECOGNIZE AND KILL RAS MUTATED CANCER CELLS

1. Activate immune system

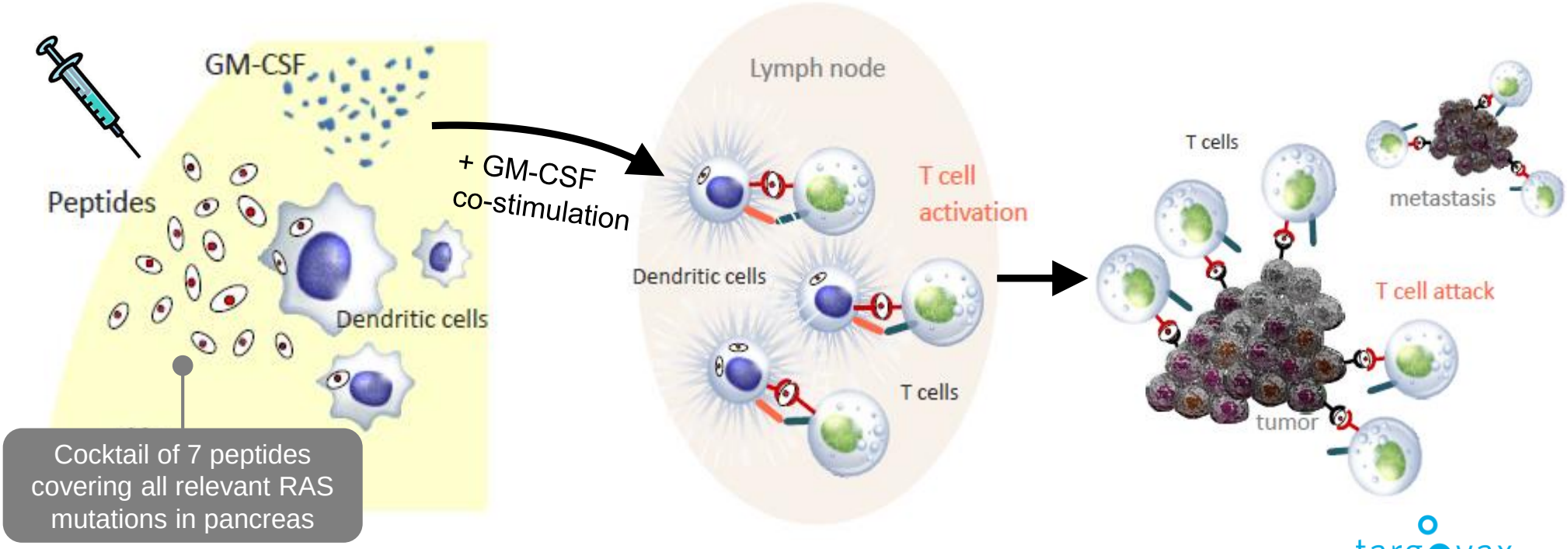
- TG vaccine **injected intradermally** and picked up by APCs

2. Induce mutRAS T-cells

- CD4+ and CD8+ **mut-RAS T-cells induced** in the lymph node

3. Attack the cancer

- mutRAS T-cells identify and **destroy RAS mutated cancer cells**



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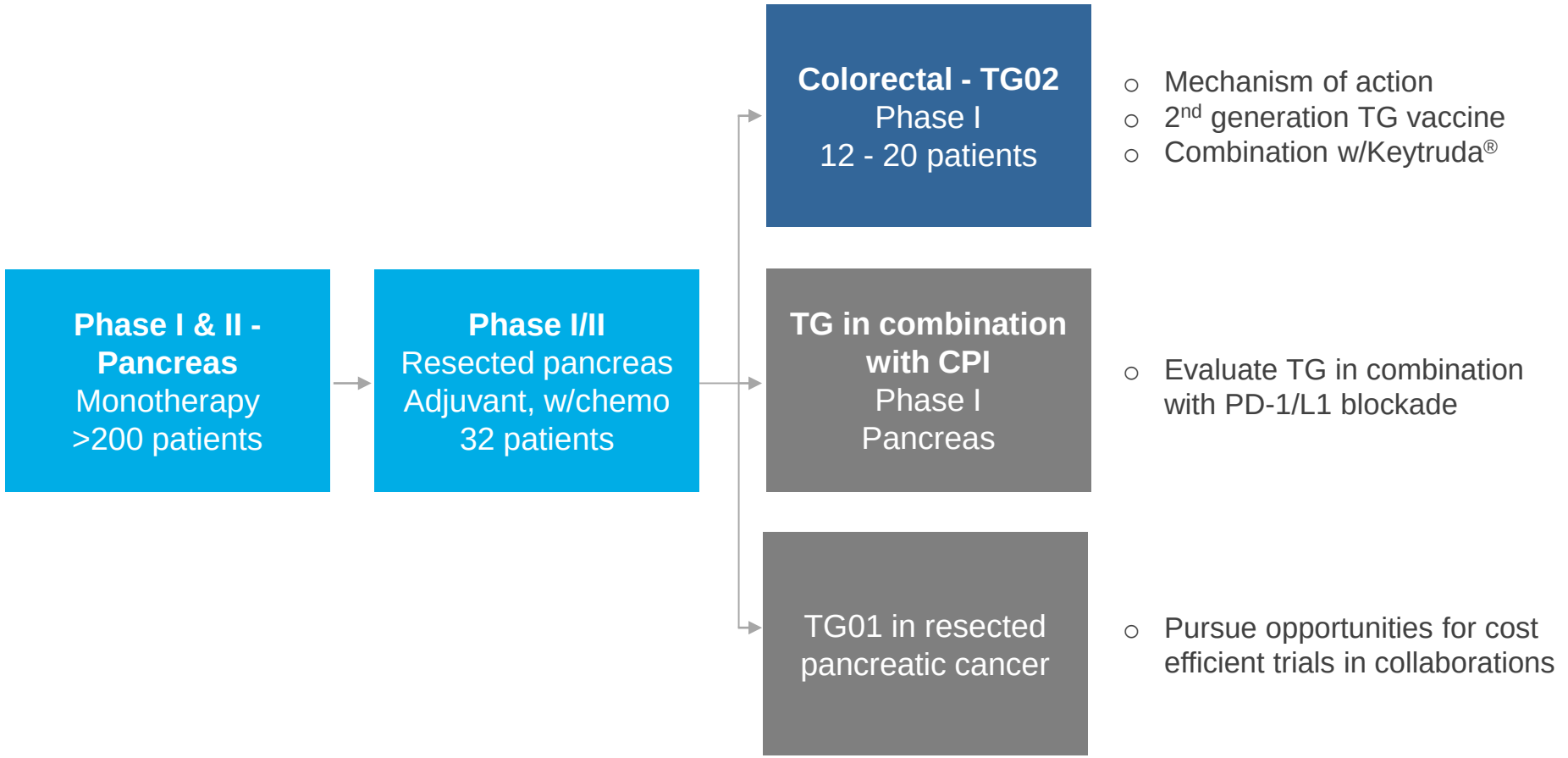
TG CLINICAL PROGRAM OVERVIEW

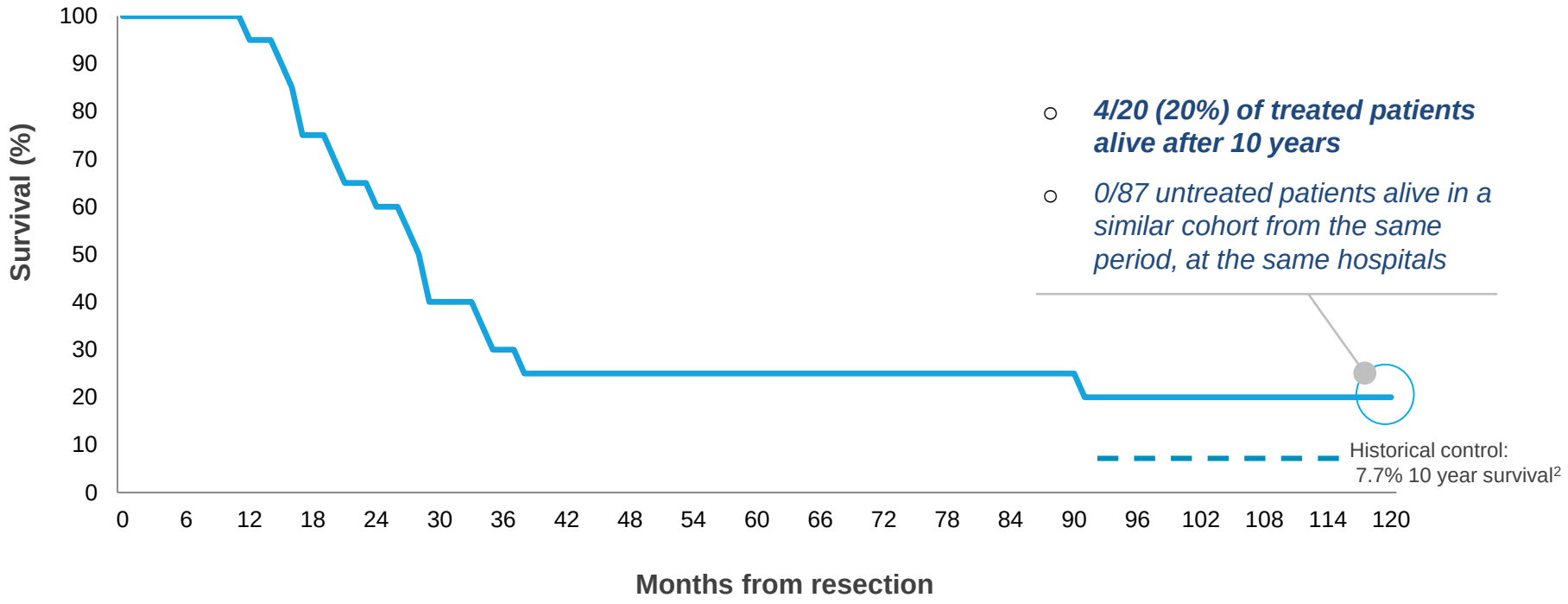


PHASE I MONOTHERAPY SURVIVAL DATA

TG vaccination showed 20% 10 year survival in resected pancreatic cancer

10 year survival in historical TG trials in resected pancreatic cancer[1]

n=20, resected patients from two clinical trials, TG monotherapy



[1] Wedén et al., 2011

[2] Oettle H et al., JAMA 2013, vol 310, no 14

TG01 IN PHASE I/II TRIAL

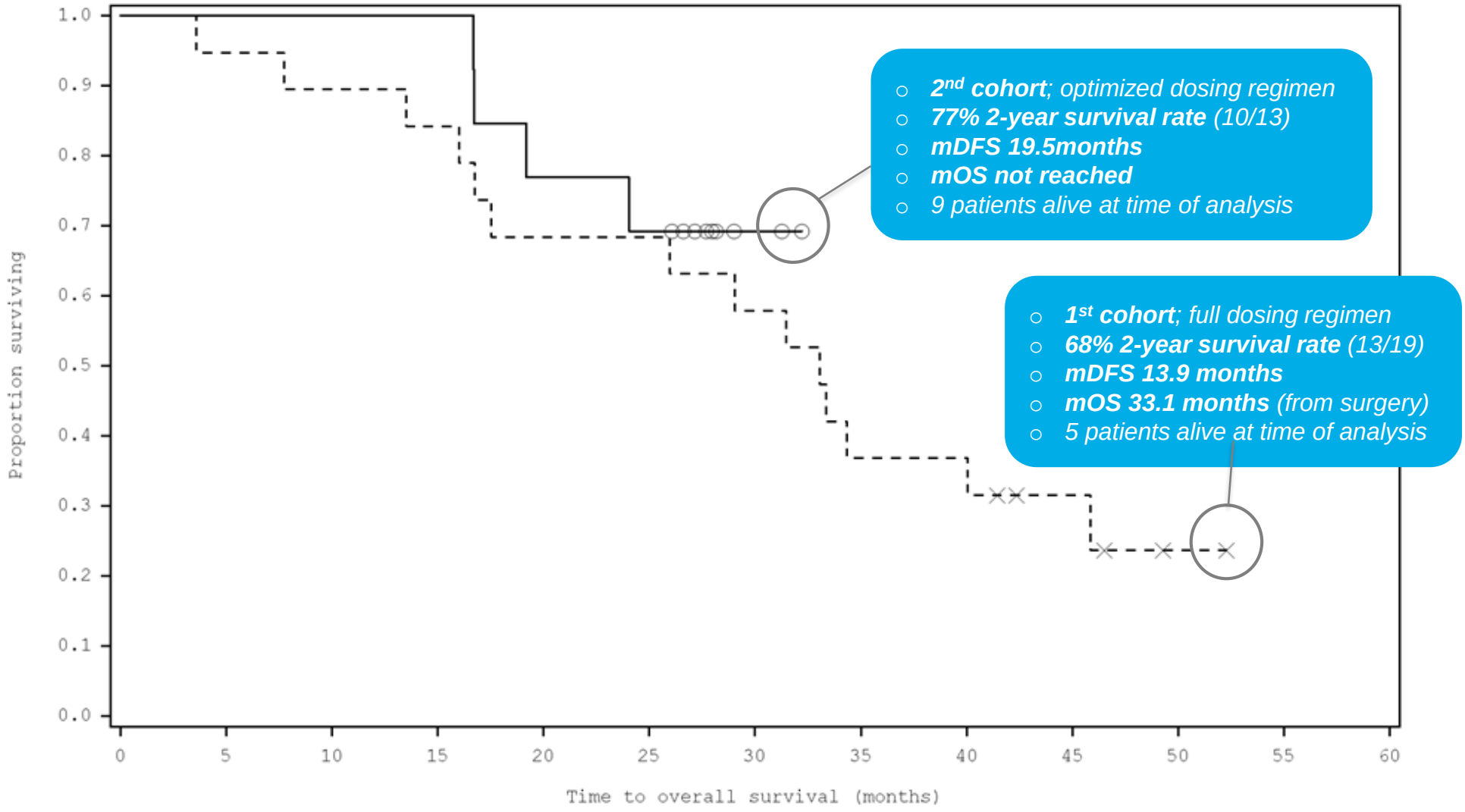
SIGNAL OF EFFICACY IN RESECTED PANCREATIC CANCER

Median overall survival	**33.4 vs. 27.6 months** reported in the ESPAC4 trial for gemcitabine alone (from time of surgery) ○ First cohort: 33.1 months ○ **Second cohort: not yet reached**
Median disease free survival	**16.1 vs. 13.1 months** reported in the ESPAC4 trial for gemcitabine alone (from time of surgery) ○ First cohort 13.9 months ○ **Second cohort 19.5 months**
mutRAS immune activation	**94%** (30 out of 32 patients) had **RAS-specific immune activation**
Dosing and safety	**Dosing regimen improved** and TG01 is **well-tolerated**

First cohort: 19 pts, Second cohort: 13 pts. Total 32 pts.

TG01 resected pancreas cancer trial survival - first vs. second patient cohorts

SECOND PATIENT COHORT PERFORMING BETTER



- ***2nd cohort**; optimized dosing regimen*
- ***77% 2-year survival rate** (10/13)*
- ***mDFS 19.5months***
- ***mOS not reached***
- *9 patients alive at time of analysis*

- ***1st cohort**; full dosing regimen*
- ***68% 2-year survival rate** (13/19)*
- ***mDFS 13.9 months***
- ***mOS 33.1 months** (from surgery)*
- *5 patients alive at time of analysis*

WHY THE TG APPROACH MAY WORK

where other cancer vaccines have failed

Historical lessons learned	*The TG approach*
Target often poorly defined and not cancer specific, mainly TAAs	Mutated **RAS is a well-defined, cancer-specific neo-antigen**, driving the cancer
No or insufficient immune activation of the adaptive immune system	TG peptides are **clinically proven** to induce both **CD4+ and CD8+ mutRAS T-cells**
Most clinical trials have been done in **progressive metastatic disease**	Initial focus on **earlier stage patients, with stronger immune system**

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4

Corporate overview

TARGOVAX HAS A SOUND FINANCIAL POSITION

with cash to complete the planned clinical program into 2020

Operations

Cash end of 3Q - Sep 30th 2018

173 / 21

NOK million **USD million**

Net cash flow - total 3Q

-27 / -3

NOK million **USD million**

Annual run rate - last four quarters

112 / 14

NOK million **USD million**

The share

Market Cap - at share price NOK ~7

370 / 42

NOK million **USD million**

Daily turnover - rolling 6 month avg.

2.5 / 0.3 / 0.5

NOK million **USD million** **% of share capital**

Analyst coverage

DNB, ABG Sundal Collier, Arctic, Redeye, Edison

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THE SHAREHOLDER BASE IS STRONG

with a mix of specialist, generalist and retail investors

		Estimated ownership	
	Shareholder	**No. of shares**	**Ownership**
1	HealthCap	12 405 584	23,6 %
2	Nordea	4 599 906	8,7 %
3	RadForsk	4 427 255	8,4 %
4	KLP	2 062 998	3,9 %
5	Thorendahl Invest AS	1 000 000	1,9 %
6	Danske Bank (nom.)	828 845	1,6 %
7	Timmuno AS	728 601	1,4 %
8	Prieta AS	720 000	1,4 %
9	Sundt AS	500 000	1,0 %
10	Meyerløkka AS	428 000	0,8 %
	Other shareholders (~4119)	24 915 259	47,4 %
	Total	**52 616 448**	**100,0 %**

Shares and options

57.4m shares fully diluted

- Average strike price on options ~NOK 20
- Total dilutive effect of options is 8.1%

52.6m ordinary shares

- Management ownership: 0.3%
- >4,000 shareholders

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SENIOR MANAGEMENT TEAM

Highly experienced

Øystein Soug, CEO

- Joined as CFO in April 2015 before being appointed CEO in November 2016.
- Before joining Targovax Oystein was CFO at Algeta, where he built up the functions of Finance, IR, Compliance, IT and HR, and oversaw its ultimate sale to Bayer for USDbn 2.9

Magnus Jäderberg, MD, CMO

- More than 30 years experience in various R&D functions
- Previously CMO at Bristol Meyers Squibb in Europe
- Involved in the clinical development of Yervoy

Anne-Kirsti Aksnes, PhD, VP Clin. Dev.

- More than 25 years of experience within clinical research and development in pharma/biotech
- Before joining Targovax, VP Clinical Development at Algeta and Director Clinical Development at Nycomed /Amersham Health/GE Healthcare
- PhD in medicine from Karolinska Institute

Erik D. Wiklund, PhD, CBO

- Former consultant in the Pharma & Healthcare practice of McKinsey & Company
- PhD in cancer research (molecular biology)
- Held several commercial and operational roles in biotech, including Algeta ASA

Berit Iversen, VP CMC

- More than 25 years of experience within R&D and Operations in the pharmaceutical and biotech industry, including CMC, Quality Assurance and Quality Control.
- Before joining Targovax, responsible for CMC and quality in Lytix Biopharma AS

Torbjørn Furuseth, MD, CFO

- Experienced executive with a broad background within life science
- Former consultant in the Pharma & Healthcare practice of McKinsey & Company
- Medical Doctor from Norwegian University of Science and Technology (NTNU)

32

INTERNATIONAL BOARD OF DIRECTORS

with broad expertise

Patrick Vink, Chairman

- More than 30 years' experience from senior roles at leading pharmaceutical and biotechnology companies
- On the board of several private and listed companies in the pharma and biotech space, including Santhera Pharmaceuticals, Concordia Healthcare and Spero Therapeutics

Eva-Lotta Allan

- Former Chief Business Officer at Immunocore
- More than 25 years of experience from the biotechnology and life science industry in both private and public companies
- Has held senior positions at e.g. Ablynx, Vertex Pharmaceuticals and Oxford Asymmetry (Evotec)

Johan Christenson, MD, PhD

- Partner of HealthCap
- Previously supervised the healthcare portfolio of SEB Företagsinvest
- Senior management experience from Astra Pain Control and AstraZeneca
- PhD in basic neuroscience
- Author of 17 scientific articles

Per Samuelsson

- Partner of HealthCap
- Prior to joining HealthCap in 2000, he gained over 15 years of investment banking experience, mainly with Aros Securities in Sweden
- Prior to this Mr. Samuelsson was head of Research, also at Aros Securities

Catherine Wheeler, MD

- Consultant, Former CMO of Acetylon Pharmaceuticals with 20 years of experience in senior clinical and business development roles.
- Significant drug development experience with a strong medical oncology focus from across academia and industry

Bente-Lill Romøren

- Board member of Radiumhospitalets Forskningsstiftelse and chairman of Farmastat and Photocure
- Previously employed by Novo Nordisk Scandinavia (1976-2012) in various positions, including position as CEO of the Norwegian unit (1983-2002, 2008-2012). Board member at Nordic Nanovector (2013-2014)

Robert Burns, PhD

- Consultant and advisor to companies developing immune based therapies in cancer
- Extensive experience in building biotechnology companies, previously CEO of 4-Antibody, Affitech and Celldex Therapeutics
- Previously Director at the Ludwig Cancer Research

Diane Mellett

- Consultant to biotech and medical device companies
- Qualified in both UK and US law
- Formerly General Counsel for Cambridge Antibody Technology (CAT)
- Led successful defence for CAT concerning a contractual dispute on Humira®

33