



## **Carnegie Nordic Healthcare Conference**

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5 December 2017

# 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 future and which, by their nature, will have an impact on the results of operations and the financial condition of Targovax. 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.

# Immunotherapy has the potential to cure cancer

*Patient example – Yervoy® checkpoint inhibitor trial*



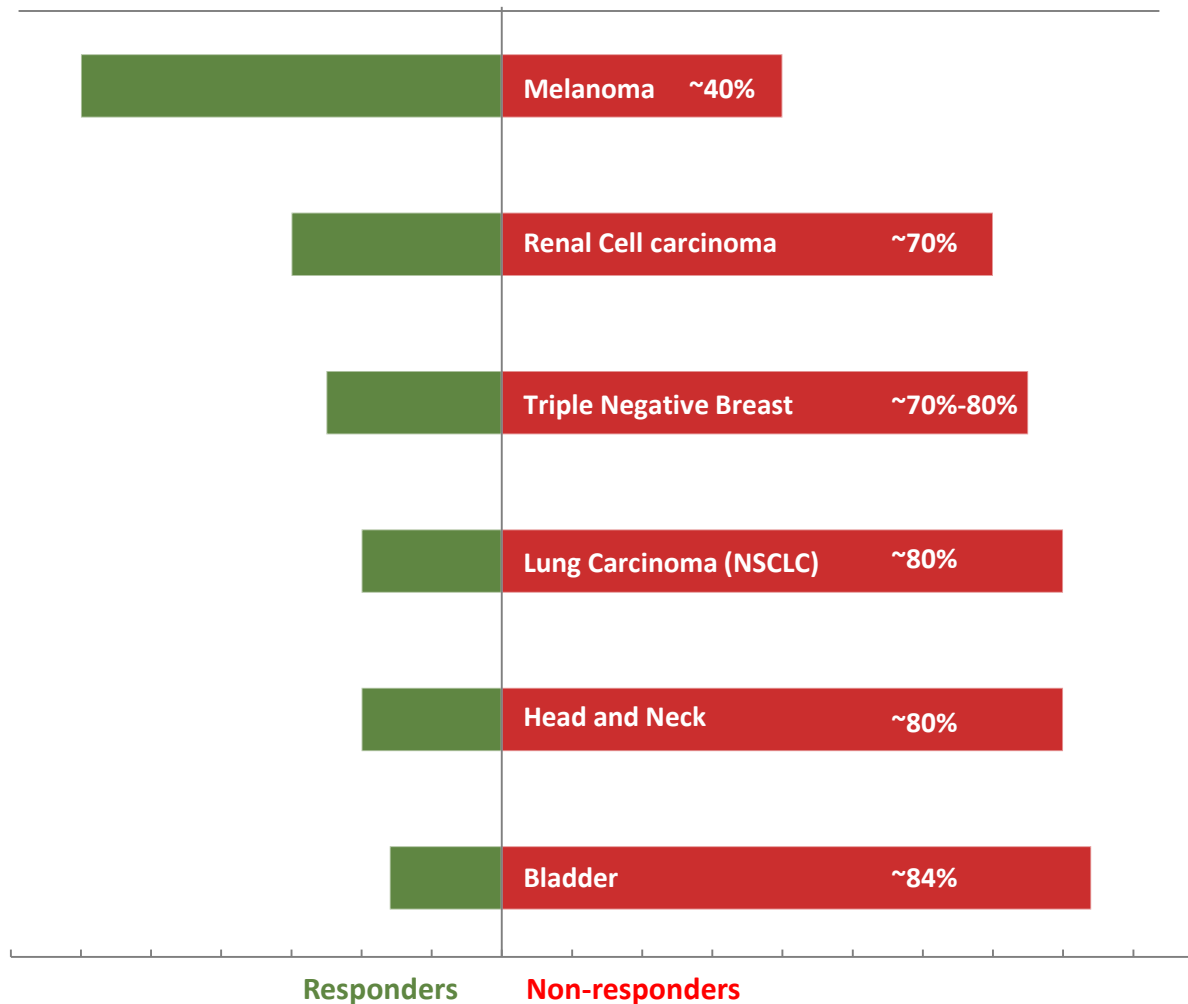
*Prior to Yervoy®*



*1 year after*

# Most patients do not respond to currently available immunotherapies

*Response rate to checkpoint inhibitors (CPIs)*

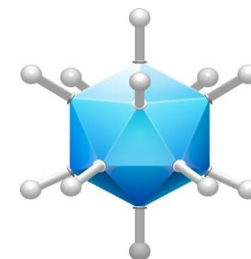


*Boosting T-cells in tumors may make checkpoint inhibitors effective in more patients*

# Targovax has two immuno-oncology programs in clinical development

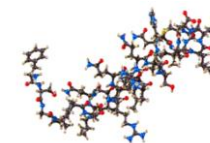
## ONCOS Oncolytic virus

- Genetically **designed adenovirus**
- Makes **cancer antigens** visible to immune system
- **Induces T-cells** specific to patients' tumor



## TG RAS neoantigen vaccine

- Cocktail of **synthetic peptides**
- Mimics cancer causing **RAS neoantigens**
- **Induces T-cells** specific to **RAS mutations**



# Agenda

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○ **ONCOS oncolytic virus platform**

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○ TG mutRAS neoantigen vaccine platform

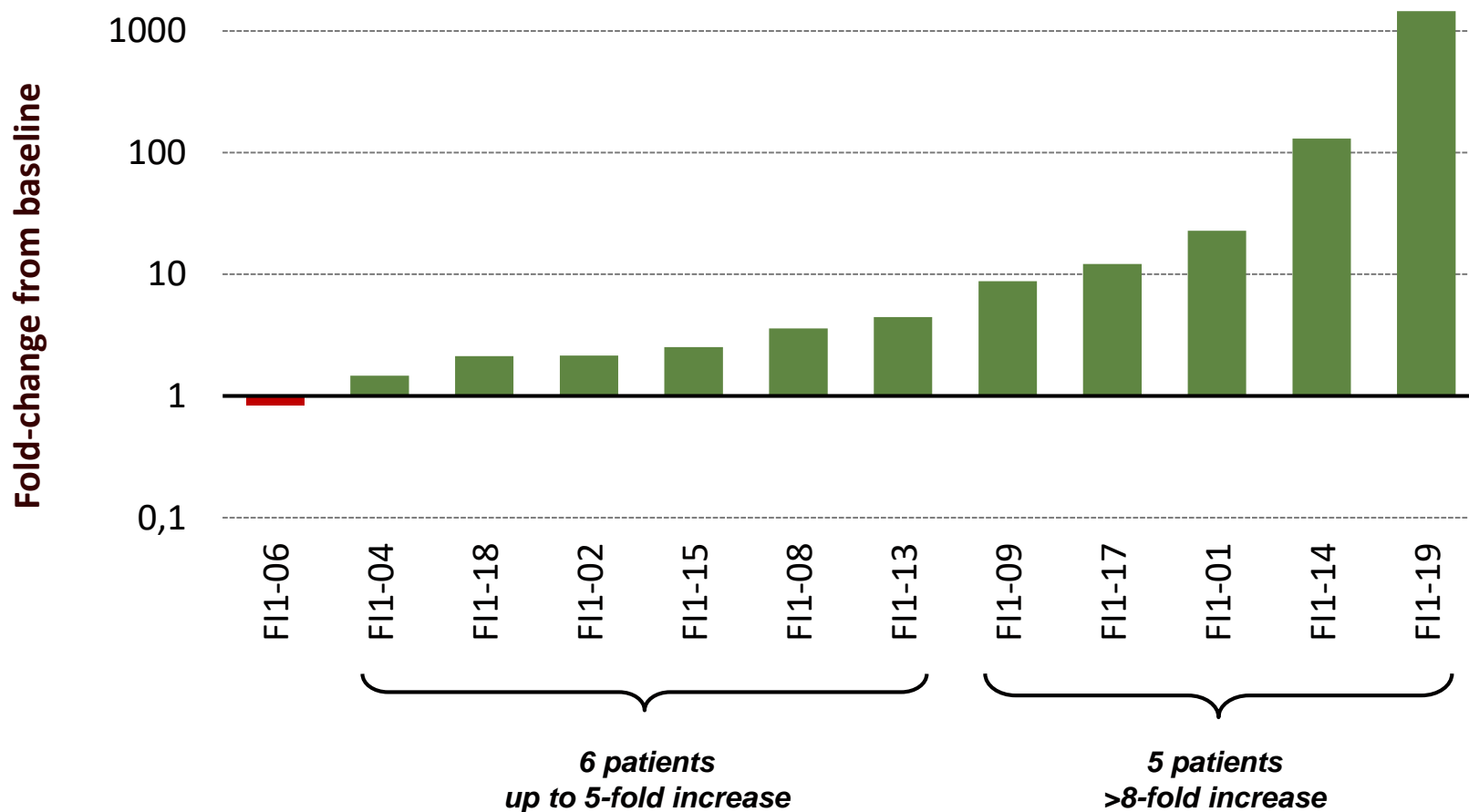
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○ Targovax clinical program overview

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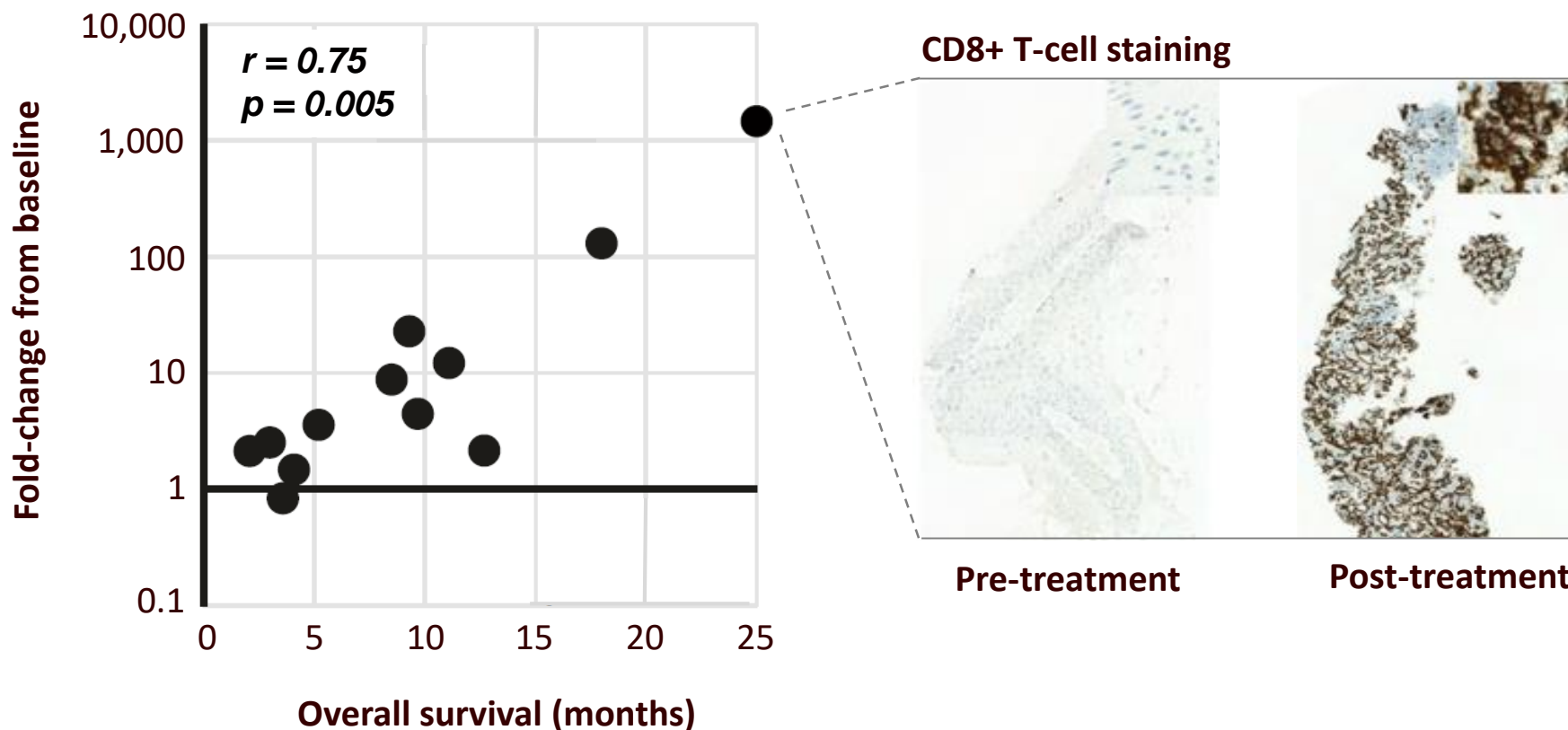
# ONCOS-102 can increase T-cell count in tumors

Phase I trial data: change in CD8+ T-cell count after treatment with ONCOS-102



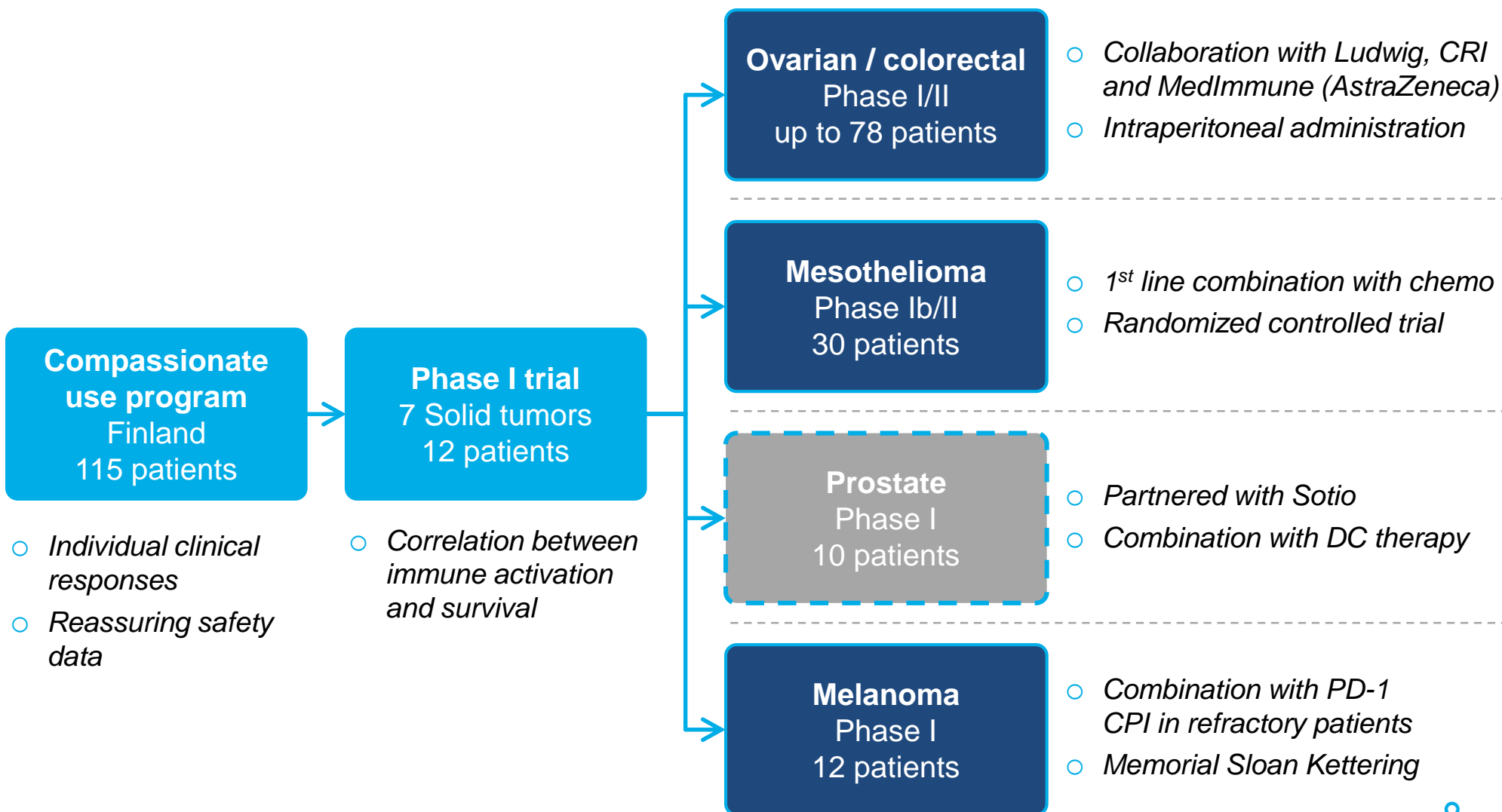
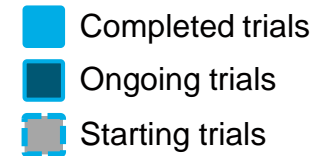
# The T-cell increase correlates with survival

## Phase I trial data: Fold-change CD8+ T-cell count vs. survival



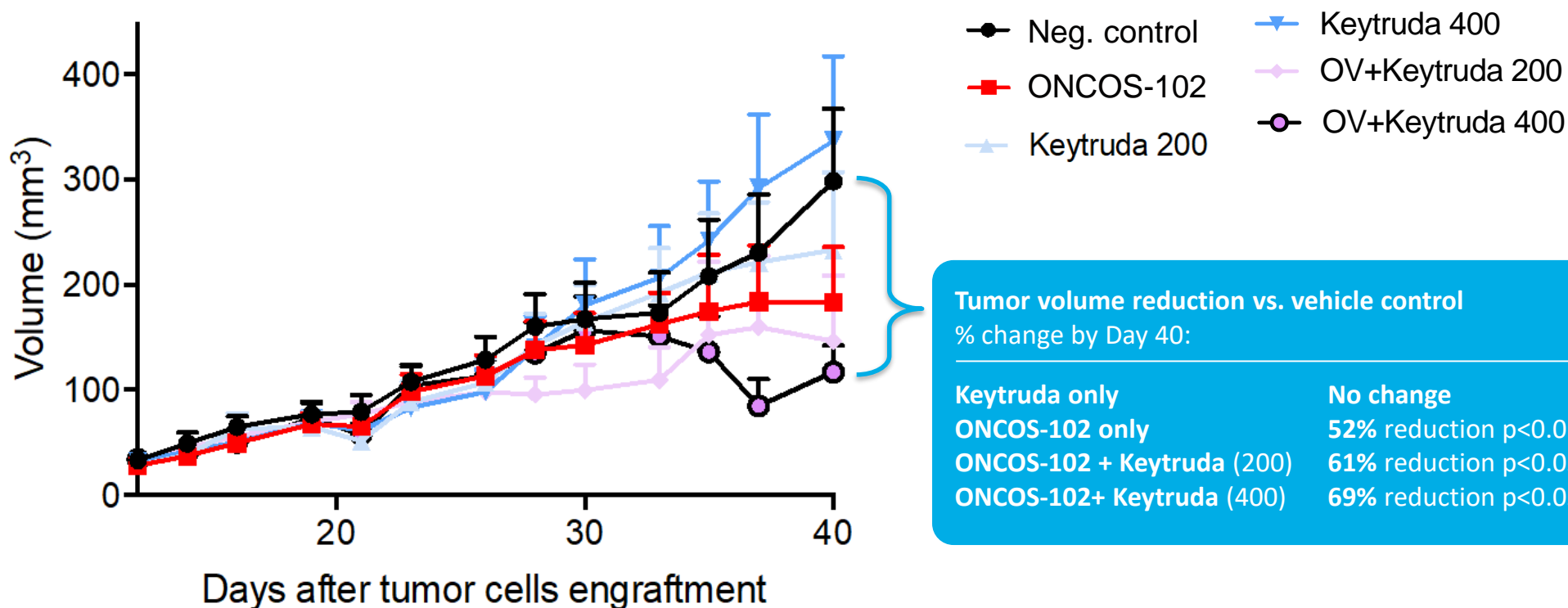


# Clinical trial program overview



# 70% reduction in tumor volume with CPI combination in mouse melanoma model

Effect of ONCOS-102 and Keytruda in humanized mouse melanoma model, change in tumor volume



# Agenda

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○ ONCOS oncolytic virus platform

○ **TG mutRAS neoantigen vaccine platform**

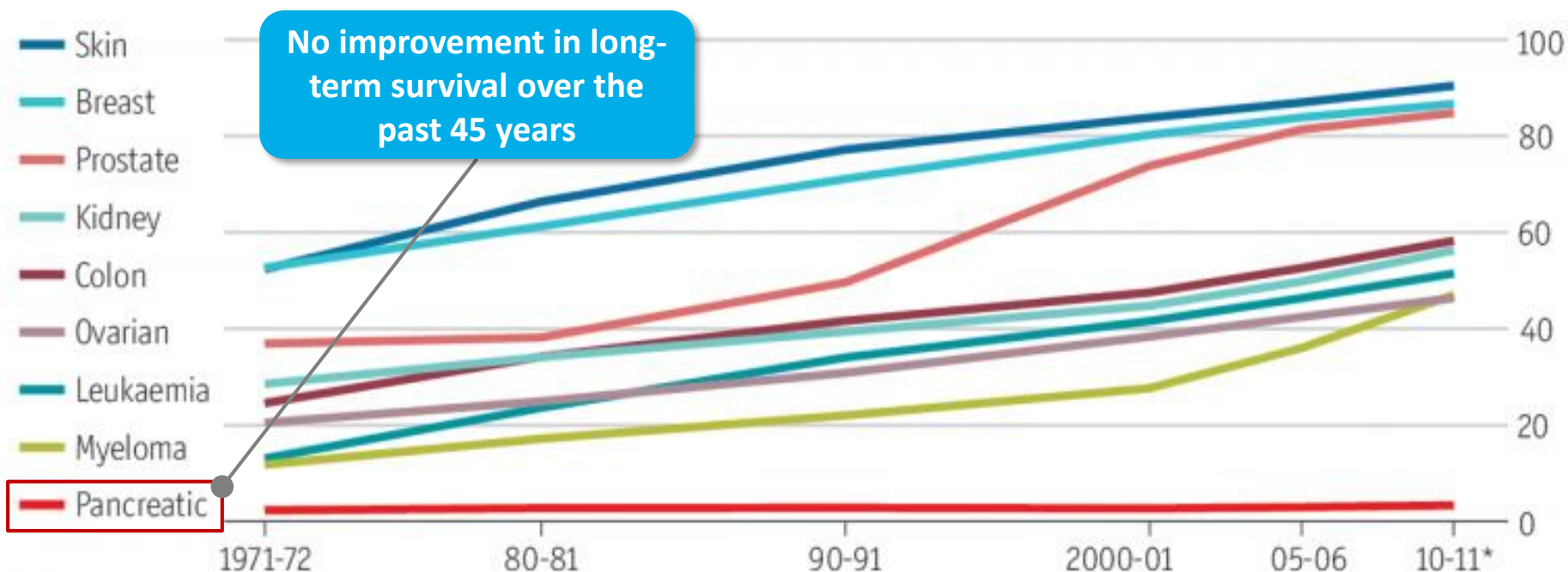
○ Targovax clinical program overview

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# The five year survival rate for pancreatic cancer patients has not improved since the 1970s

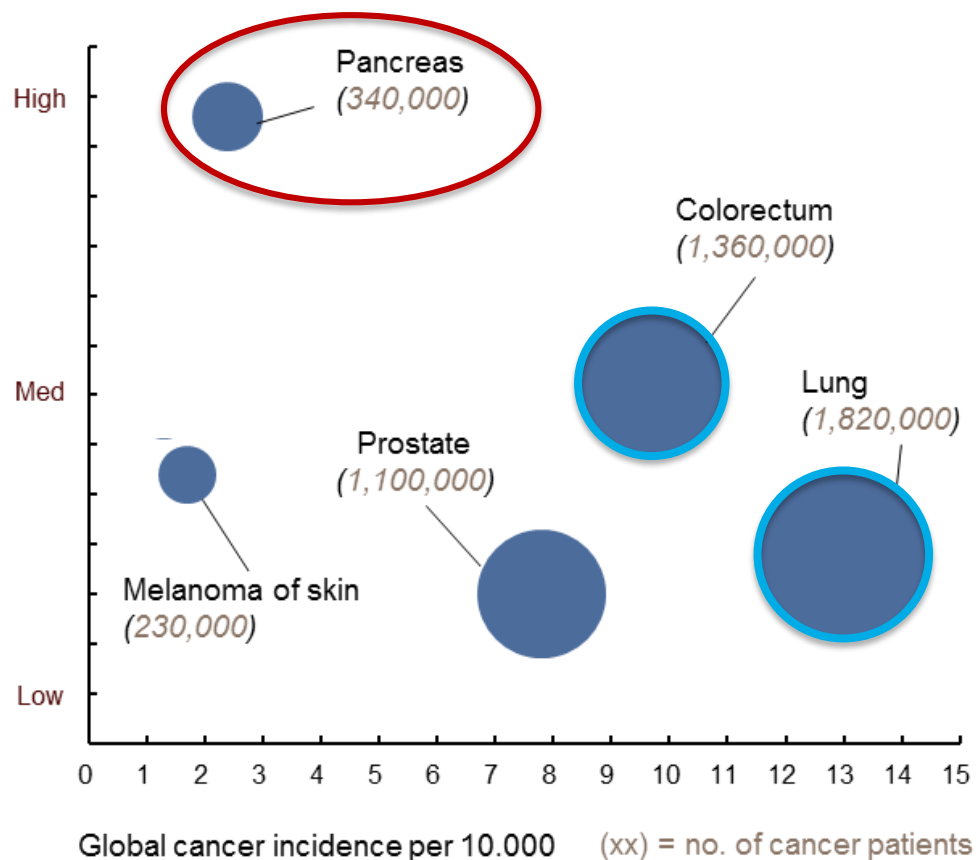
## Living longer

England and Wales, five-year relative survival rate by type of cancer, %



# The RAS gene is mutated in 90% of pancreatic cancer patients, making it an ideal target

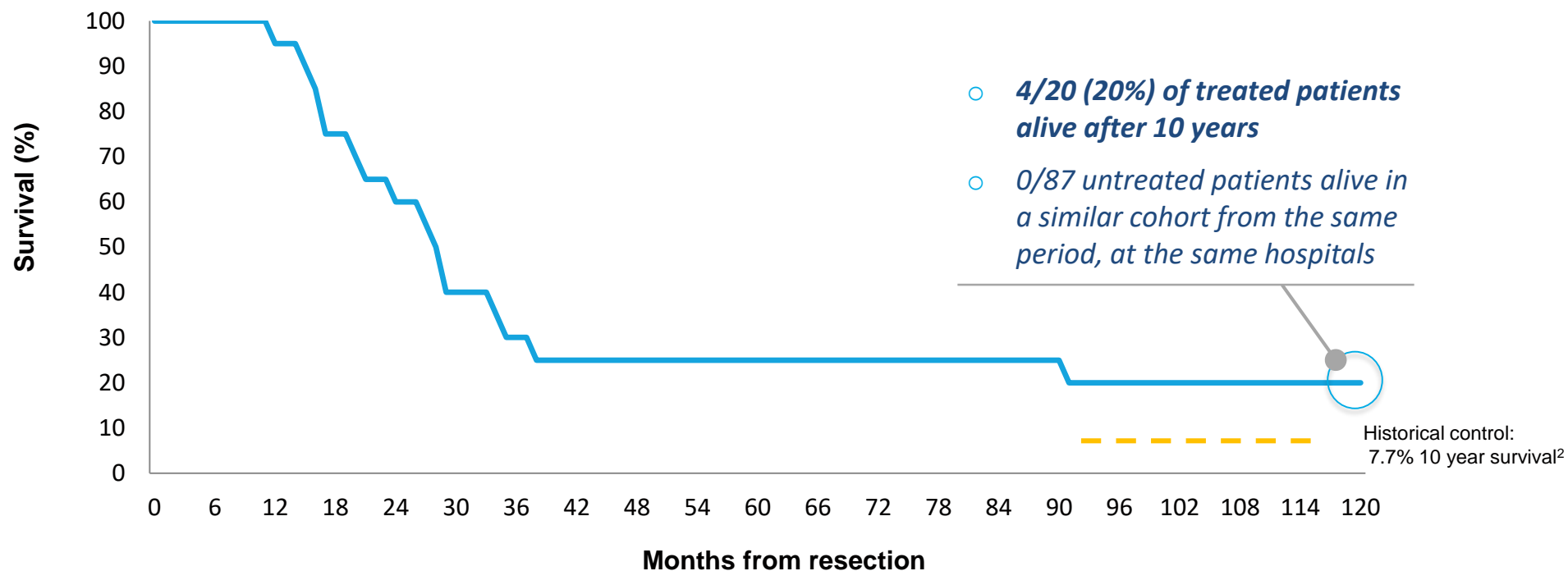
## Frequency of RAS mutations



- RAS mutations result in **uncontrolled cell division**
- **There are no existing therapies** targeting RAS
- Targovax has developed a unique **vaccine against mutant RAS**

# In previous trials in resected pancreatic cancer, TG vaccination has shown 20% 10 year survival

## 10 year survival in historical TG trials in resected pancreatic cancer (n=20, TG monotherapy)



<sup>1</sup> Wedén et al., 2011

<sup>3</sup> Oettle H et al., JAMA 2013, vol 310, no 14

# These promising results are now being validated in an ongoing phase I/II trial with adjuvant chemotherapy

## 1<sup>st</sup> cohort (19 patients)

- **Median survival 33.1 months vs. 27.6 for historical control**
- **13 of 19 patients (68%) alive 2 years after surgery, vs. 30-53% in historical controls**

## 2<sup>nd</sup> cohort (13 patients)

- **13 of 13 patients (100%) alive 1 year after surgery**

## mutRAS immune response (1 yr)

- **90% of patients (29/32) had RAS-specific immune activation**

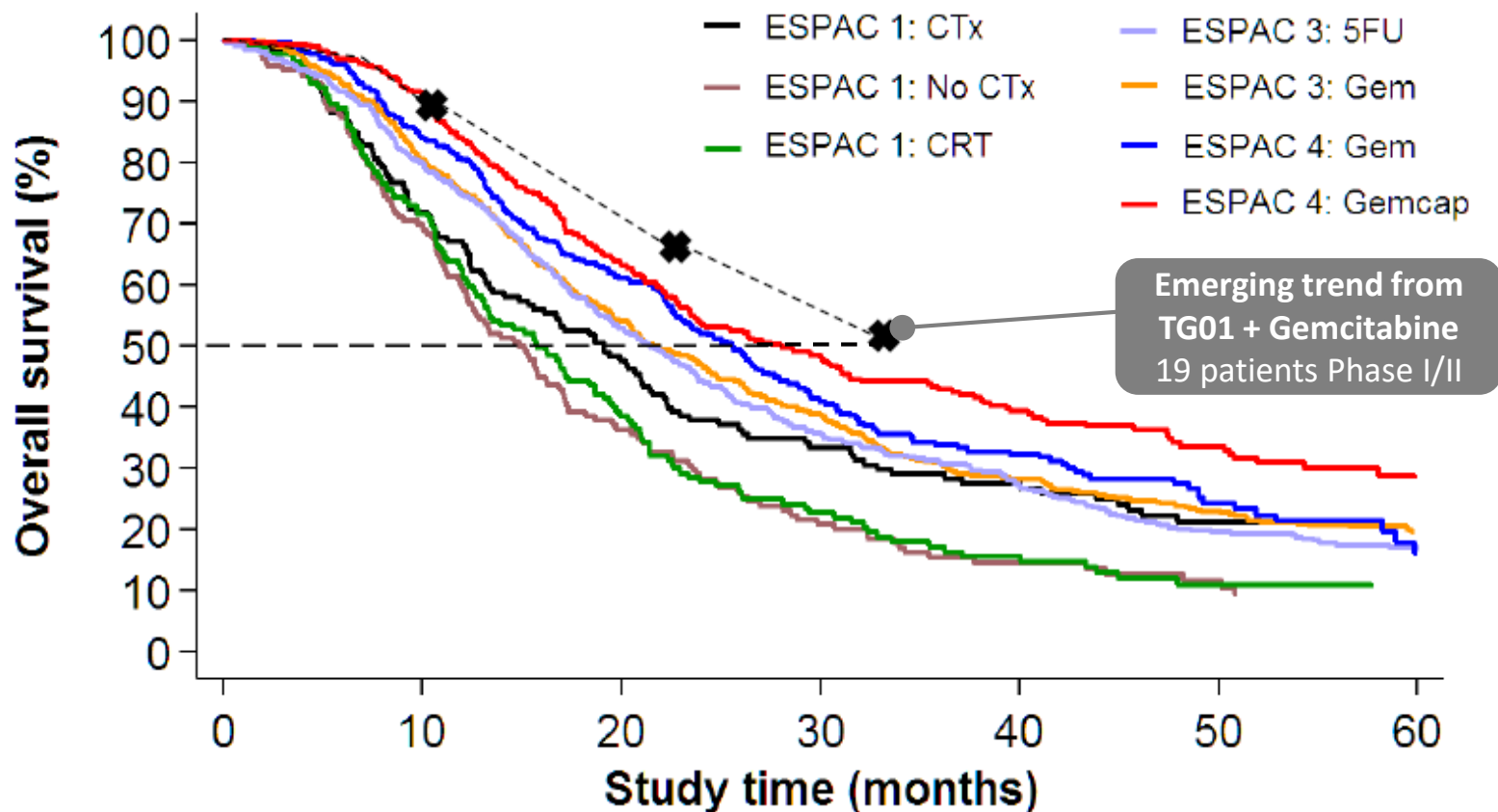
## Safety

- **TG01 and gemcitabine combination treatment is well-tolerated**
- **Four allergic reactions reported in 1<sup>st</sup> cohort, none in 2<sup>nd</sup> cohort (up to 1 year)**

# TG01 data in context

As presented by TG01 PI Prof. Daniel Palmer, London, June 2017

## Comparative survival rates across trials in resected pancreatic cancer



NOTE: Relative survival curves across studies (ESPAC), meant for indicative comparisons only. No Kaplan Meier analysis has been done of the TG01 study data. Instead 1 and 2 year survival as well as median OS have been plotted.



# Why TG may succeed where others have failed

## Lessons Learned

*Target often poorly defined and not cancer specific*

## The TG approach

✓ Mutated **RAS** is a **well-defined neo-antigen**, and a driving cause of cancer

*Insufficient immune activation of CD4+ helper and CD8+ killer T-cells*

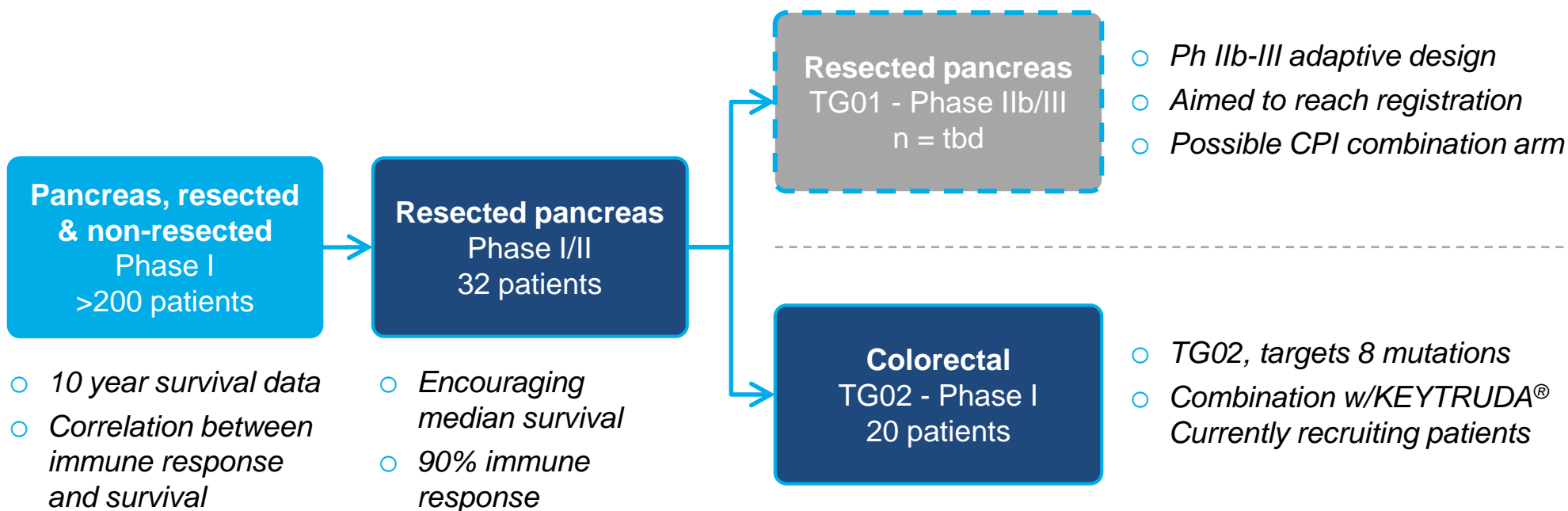
✓ TG peptides are **proven** to induce both **CD4+ and CD8+ mutRAS T-cells**

*Most clinical trials have been done in advanced disease*

✓ Initial focus on **resected patients, with stronger immune system**

- Completed trials
- Ongoing trials
- Planned trials

# Clinical trial program overview



# Resected pancreatic cancer is the lead indication, but all RAS mutated cancers are potential TG targets



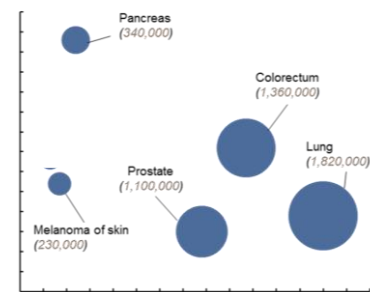
- **TG01 lead indication**
- Completing phase I/II
- Planning phase IIb/III
- **40.000 patients**



- **TG02 lead indication**
- Phase I trial recruiting
- 50% RAS mutated
- **Up to 500.000 patients**



- **TG02 potential future indication**
- 30% RAS mutated
- **Up to 500.000 patients**



- **TG02 + TG03 ultimate long-term potential**
- 30% of all cancers
- **Up to 30% of all cancer patients**

# Agenda

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○ ONCOS oncolytic virus platform

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○ TG mutRAS neoantigen vaccine platform

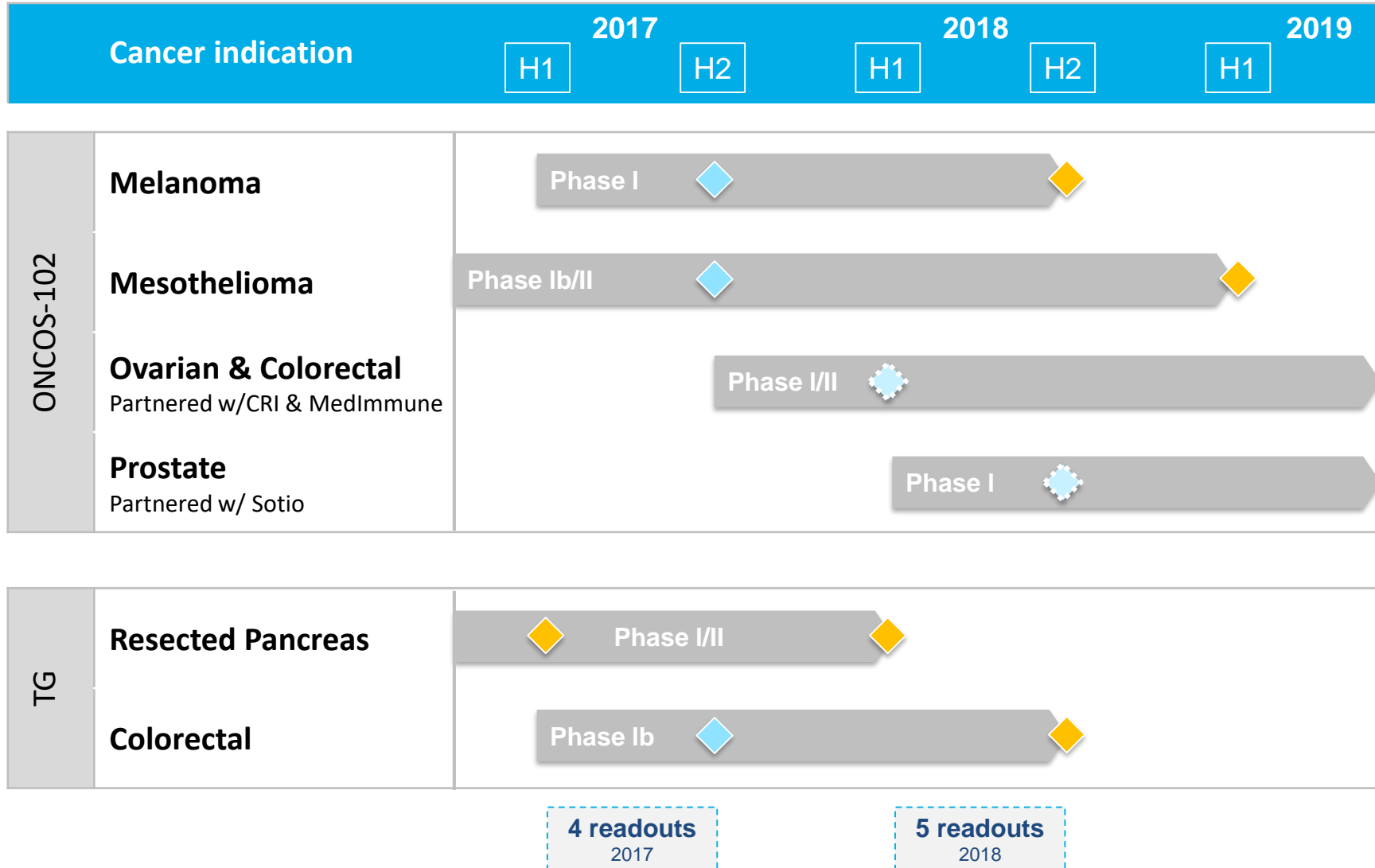
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**○ Targovax clinical program overview**

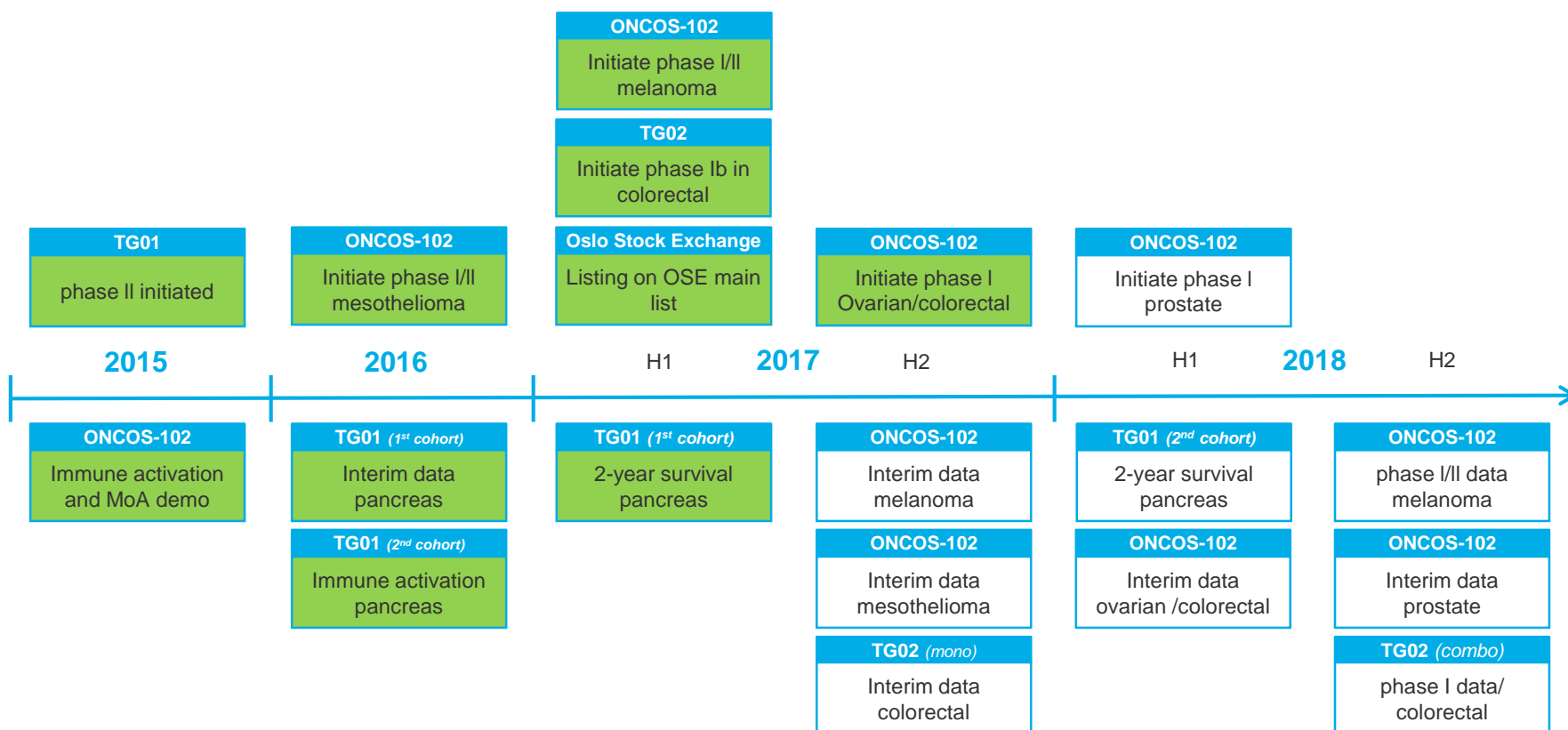
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# Overview of Targovax' full clinical program

-  Interim data
-  Interim data, partnered trials
-  Clinical, immune and safety data



# Strong upcoming news flow, with multiple near term value inflection points



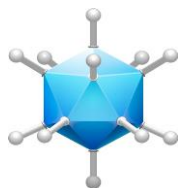
# Arming the patient's immune system to fight cancer

## Broad clinical program



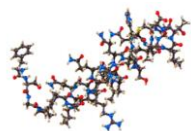
- ✓ Six shots on goal
- ✓ Several upcoming data points

## ONCOS



- ✓ Demonstrated ability to increase T-cell count
- ✓ Potential to make CPIs effective in more indications

## TG



- ✓ Unique approach for targeting RAS mutations
- ✓ Potential to benefit up to 1/3 of all cancer patients

# BACKUP



# Targovax has a sound financial position, with cash to complete the planned clinical program into 2019

Raised NOK 206 million in private placement June/July 2017  
10,000,000 new shares @ NOK 20 per share

Operations			
Cash end of Q3	NOK 286m	USD 36m	Sep 30 <sup>th</sup> 2017
Net cash flow	NOK -24m	USD -3m	Total Q3
Annual run rate	NOK 106m	USD 13m	Last four quarters

The share	OSE: TRVX		
Market Cap	NOK 930m	USD ~120m	At share price NOK ~17.5
Daily turnover	NOK 5m	USD 0.6m	Rolling 6 month avg.
Analysts	DNB, ABG Sundal Collier, Arctic, Edison, Redeye, Norske Aksjeanalyser,		

# The shareholder base is strong, with Swedish Biotech VC HealthCap as the major owner

Shareholder	Estimated ownership		
	Shares m	Relative	
HealthCap	Sweden	12,4	23,6 %
Nordea	Norway	4,7	8,9 %
RadForsk	Norway	4,4	8,4 %
KLP	Norway	1,9	3,7 %
Statoil	Norway	1,2	2,2 %
Thorendahl Invest AS	Norway	0,9	1,7 %
Danske Bank (nom.)	Denmark	0,8	1,5 %
Euroclear Bank (nom.)	Belgium	0,8	1,4 %
Timmuno	Norway	0,7	1,4 %
Prieta AS	Norway	0,7	1,4 %
Sundt AS	Norway	0,6	1,1 %
Yngve S. Lillesund	Norway	0,3	0,6 %
NHO - P665AK	Norway	0,3	0,5 %
The Bank of NY Mellon (nom.)	Belgium	0,2	0,5 %
The Bank of NY Mellon (nom.)	Belgium	0,2	0,4 %
Tobech Invest AS	Norway	0,2	0,4 %
Istvan Molnar	Norway	0,2	0,4 %
Danske Bank (nom.)	Denmark	0,2	0,3 %
Kristian Falnes AS	Norway	0,2	0,3 %
Spar Kapital Investor AS	Norway	0,2	0,3 %
<b>Top 20</b>		<b>31,0</b>	<b>59,0 %</b>
<i>Other shareholders (4160)</i>		21,6	41,0 %
<b>Total</b>		<b>52,6</b>	<b>100,0 %</b>

## Key international investors participating in PP 2017

- Nyenburgh (NL)
- Trium (UK)
- Millenium Capital Partners (UK)
- Interogo (SWE)
- AP3 (SWE)
- Aramea AM (DE)

## Shares and options

- **56.2m shares fully diluted**
  - Average strike price on options ~NOK 21
  - Total dilutive effect of options is 6.3%
- **52.6m ordinary shares**
  - Management ownership: 1.7%
  - >4,800 shareholders

# There is strong IP and market protection for the TG program overall

## Product patents

- **TG02 peptide mixture**; US patent granted, expires 2034

## Method of use patents

- **Therapeutic use of TG01 and TG02** in combination with anti-metabolite chemotherapy; US patent granted, expires 2035

## Orphan drug status

- **US FDA orphan drug status granted for TG01 in pancreatic cancer**, 7 years exclusivity from date of marketing approval
- **EU EMA orphan drug status granted for TG01 in pancreatic cancer**, 10 years exclusivity

# IP situation and market protection for the ONCOS program

## Products patents

- **ONCOS-102**; US, EPO, China, several other countries; patent granted, expires 2029

## Method of use patents

- **Therapeutic use of ONCOS-102**, also in combination with limited chemotherapy; EPO, China, several other countries, expires 2029
- **Applications; ONCOS-102** in combination with **chemotherapeutic agents**, (priority date 2016) and **check-point inhibitors** (priority date 2016)

## Orphan drug status

- **US FDA orphan drug status granted for ONCOS-102**  
7 years exclusivity from date of marketing approval
- **EU EMA orphan drug status granted for ONCOS-102**  
10 years exclusivity
  - 1) malignant mesothelioma
  - 2) ovarian cancer
  - 3) soft-tissue sarcoma

# ONCOS-102 makes tumors visible to the immune system

## 1. Activate immune system:

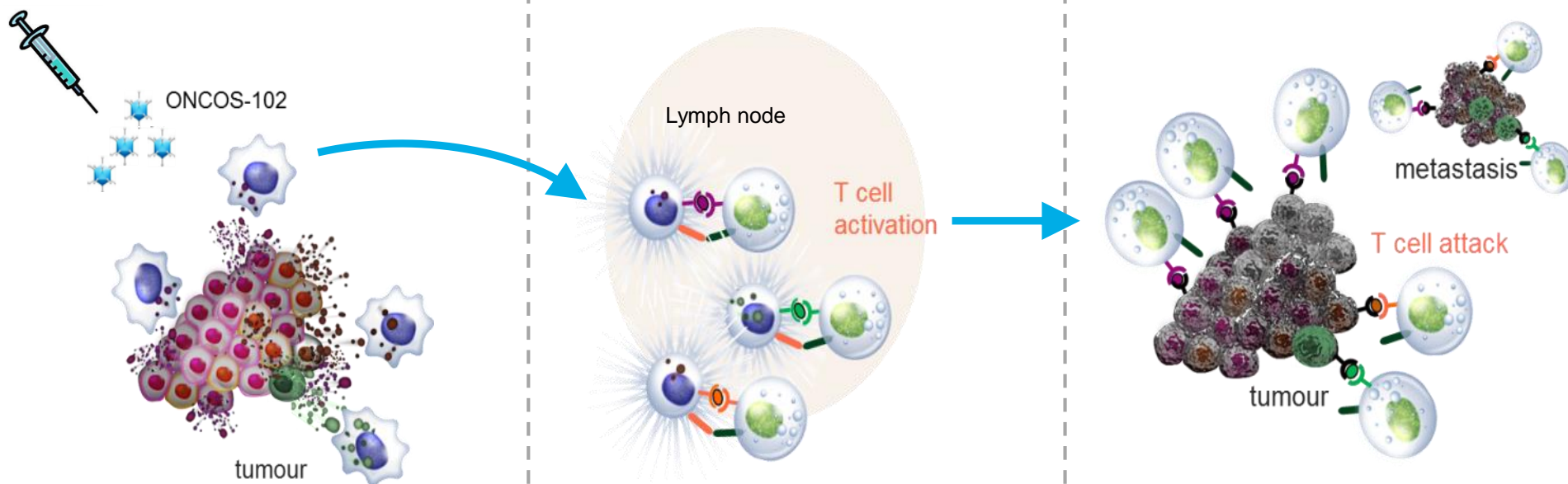
- Virus injected **directly into the tumor**
- Infected cells lyse and **release cancer-specific antigens**

## 2. Induce T-cells:

- APCs bring the cancer-specific **antigens to lymph nodes**
- Induction of **tumor specific T-cells**

## 3. Attack the cancer:

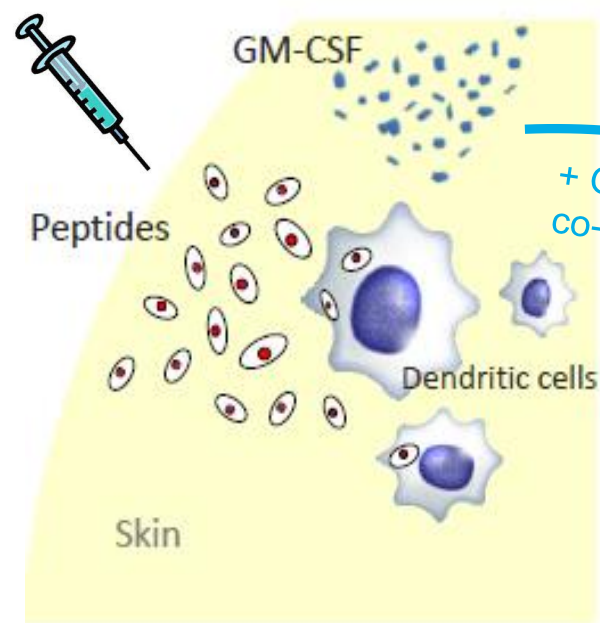
- Tumor specific T-cells **identify and destroy cancer cells**
- **Cold tumors become hot**



# Targovax' TG vaccine gears the immune system to recognize and destroy RAS mutated cancer cells

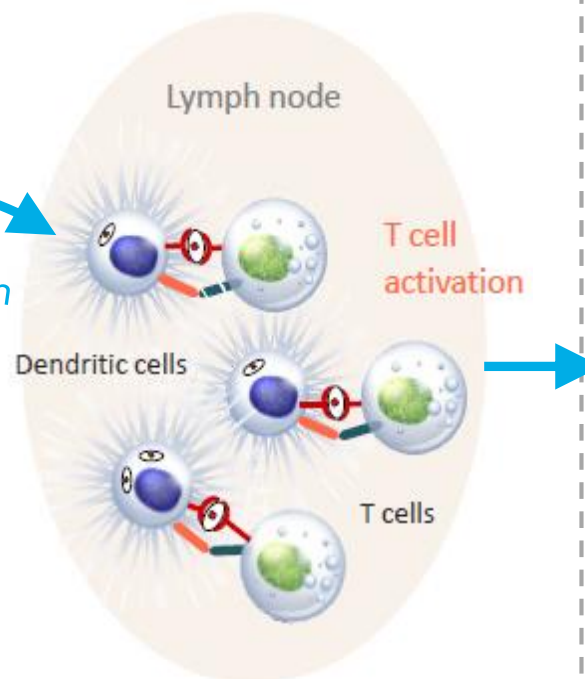
## 1. Activate immune system

- 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**

