



## **Arming the immune system to fight cancer**

**BioEquity**

**May 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 is revolutionizing the way we treat cancer, in some cases curing previously thought incurable patients

*Case example – Patient in a Yervoy checkpoint inhibitor trial*



*Prior to Yervoy\**



*4 weeks*



*8 weeks*



*20 weeks*



*8 months*



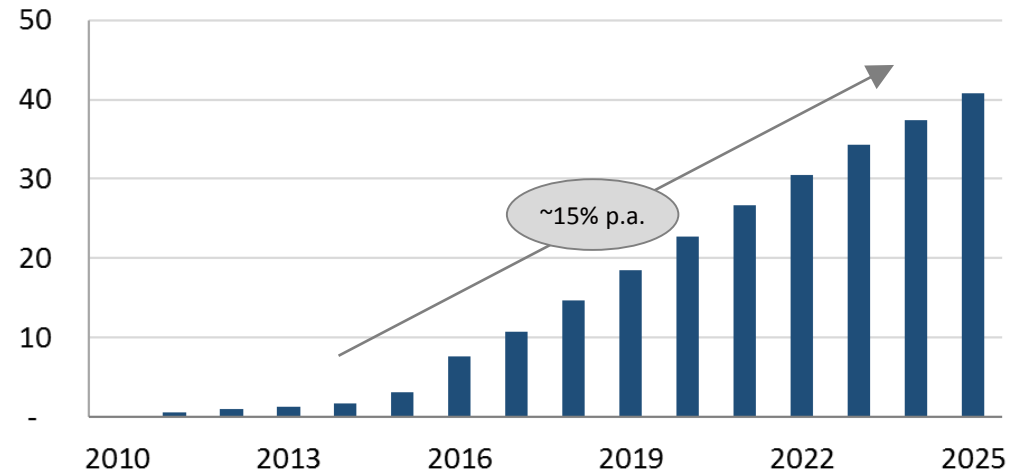
*1 year*

# Immunotherapy is considered to have enormous potential, and the market is expected to reach 30-50b USD by 2025



Science, December 2013

Estimated market size (\$Bn)\*

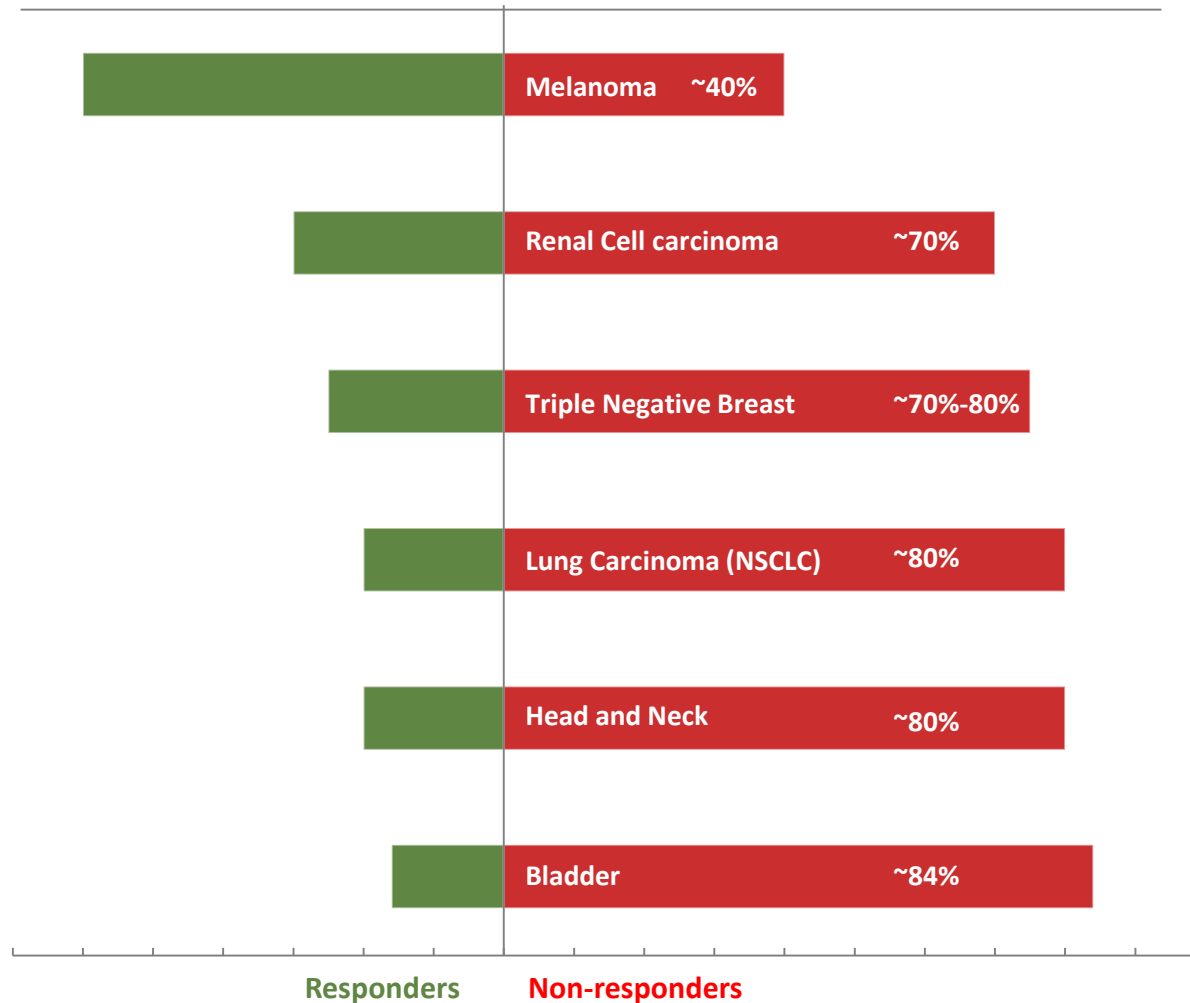


- Market estimated to reach 40b USD in 2025
- Estimated that 2/3 of cancers will be treated by immune therapy by 2025

\* Citi Research, Barclays Capital, Leerink Swann, BMO Capital Markets

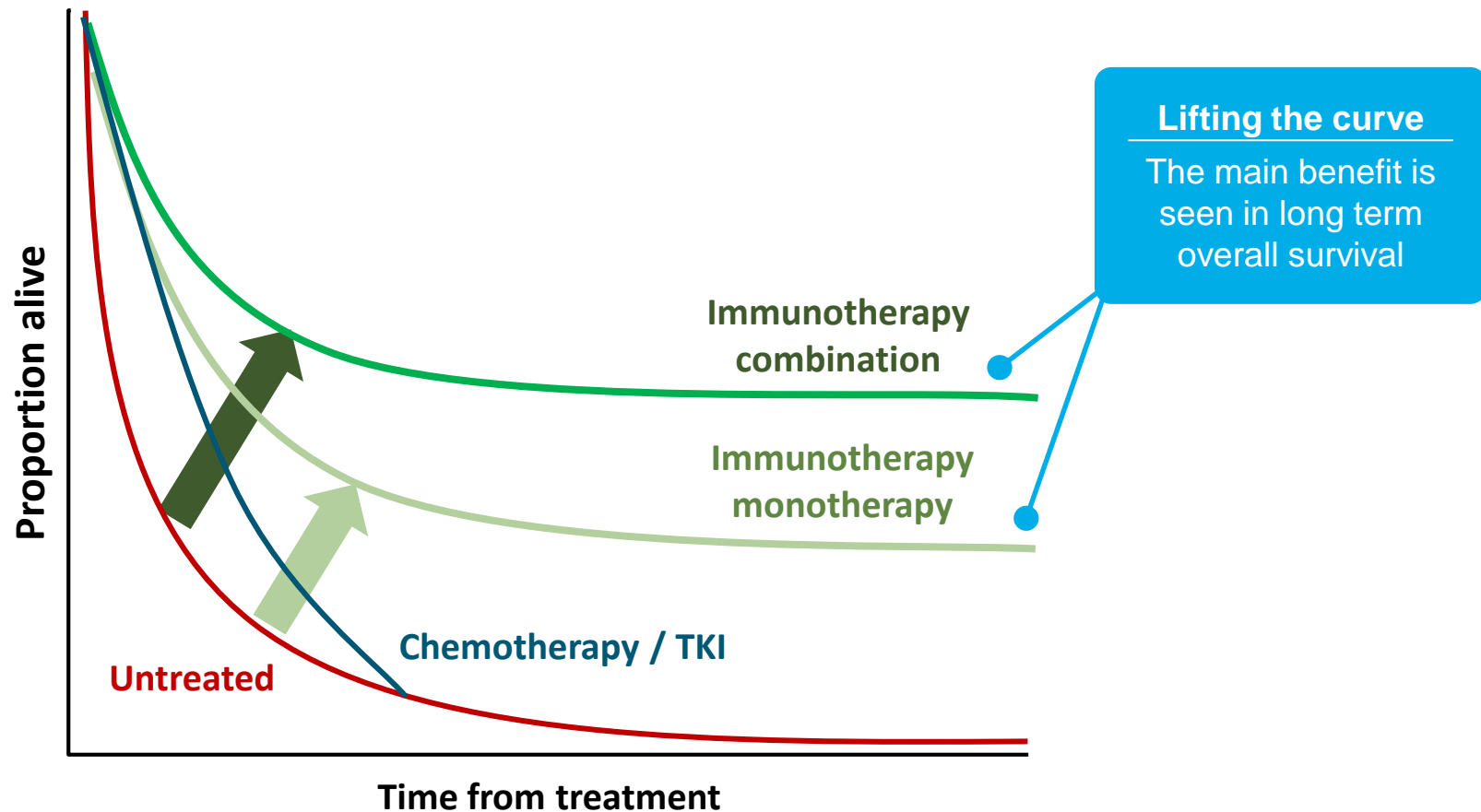
# However, most patients do not respond to check point inhibitors

*Response rate to checkpoint inhibitors (CPIs)*



*Complimentary  
immune priming  
medicines may make  
tumors **respond**  
better to checkpoint  
inhibitors*

# The goal is to turn cancer into a manageable chronic disease by combining immuno-oncology therapies

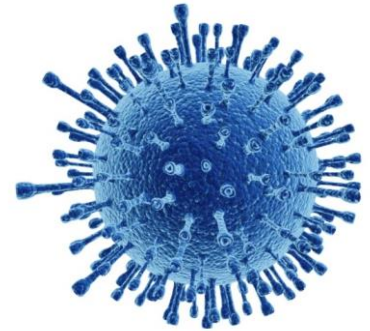


<sup>1</sup> Citi Research: "Immunotherapy - The Beginning of the End for Cancer", A. Baum, 22 May 2013

# Targovax is developing two novel proprietary immunotherapy platforms with promising phase I/II data

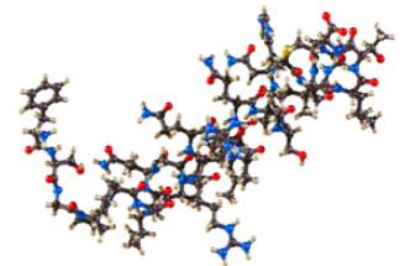
## ONCOS-102 Oncolytic virus

- Genetically optimized Adenovirus
- Selectively infects and lyses cancer cells
- Releases cancer antigens
- Triggers immune response

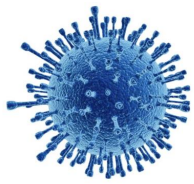


## TG01 Peptide vaccine

- Cocktail of 7 synthetic peptides mimicking clinically relevant RAS mutations
- Generates RAS-specific T-cells
- T-cells kill cancer cells displaying mutated RAS antigens on their surface







# ONCOS-102 works by making cancer antigens visible to the immune system

## *Activate immune system:*

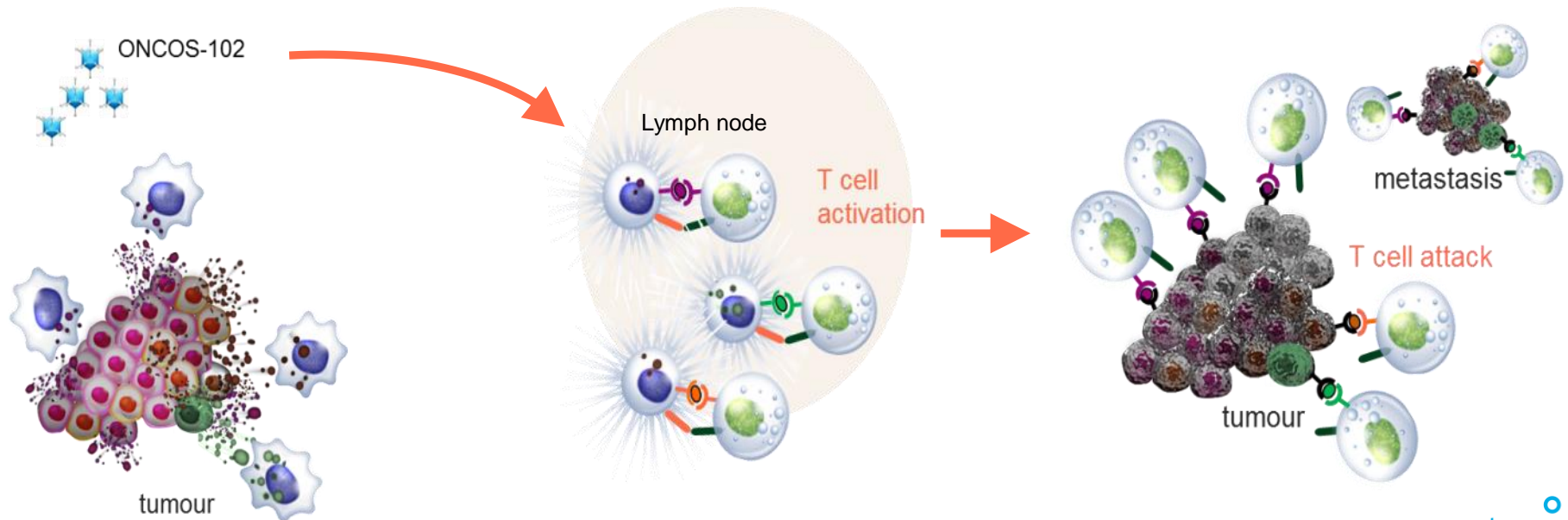
- Virus injected directly into the tumor / pleura
- Infected cells lyse and release cancer specific antigens
- Immune system picks up antigens

## *Train T-cells:*

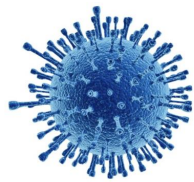
- APCs present tumor specific antigens
- Production of tumor specific T-cells

## *Attack the cancer:*

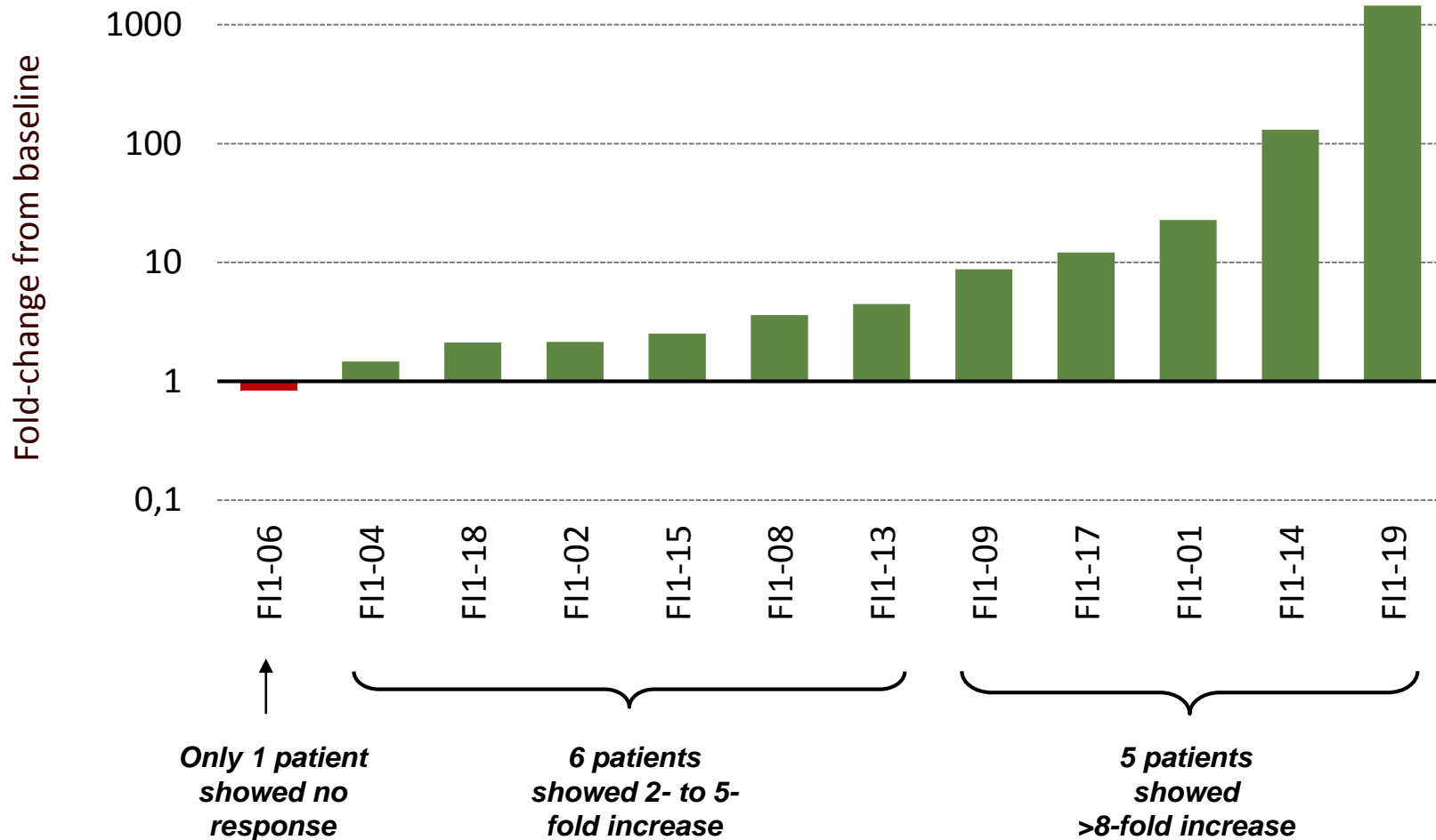
- Tumor specific T-cells identify lesions and kill the cancer cells

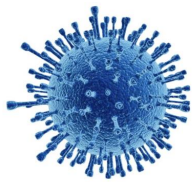






# ONCOS-102 increased tumor infiltrating CD8+ T-cells in 11 of 12 cancer patients with a range of solid tumors





# A Phase I ONCOS-102 trial initiated in CPI refractory melanoma to assess the immune activation potential

## Setting

- Advanced malignant melanoma patients not responding to CPIs
- Immune activate patients with ONCOS-102, then re-challenge with a CPI (Keytruda®)

## Site

- 12 patients
- Memorial Sloan Kettering Cancer Centre

## Key endpoints

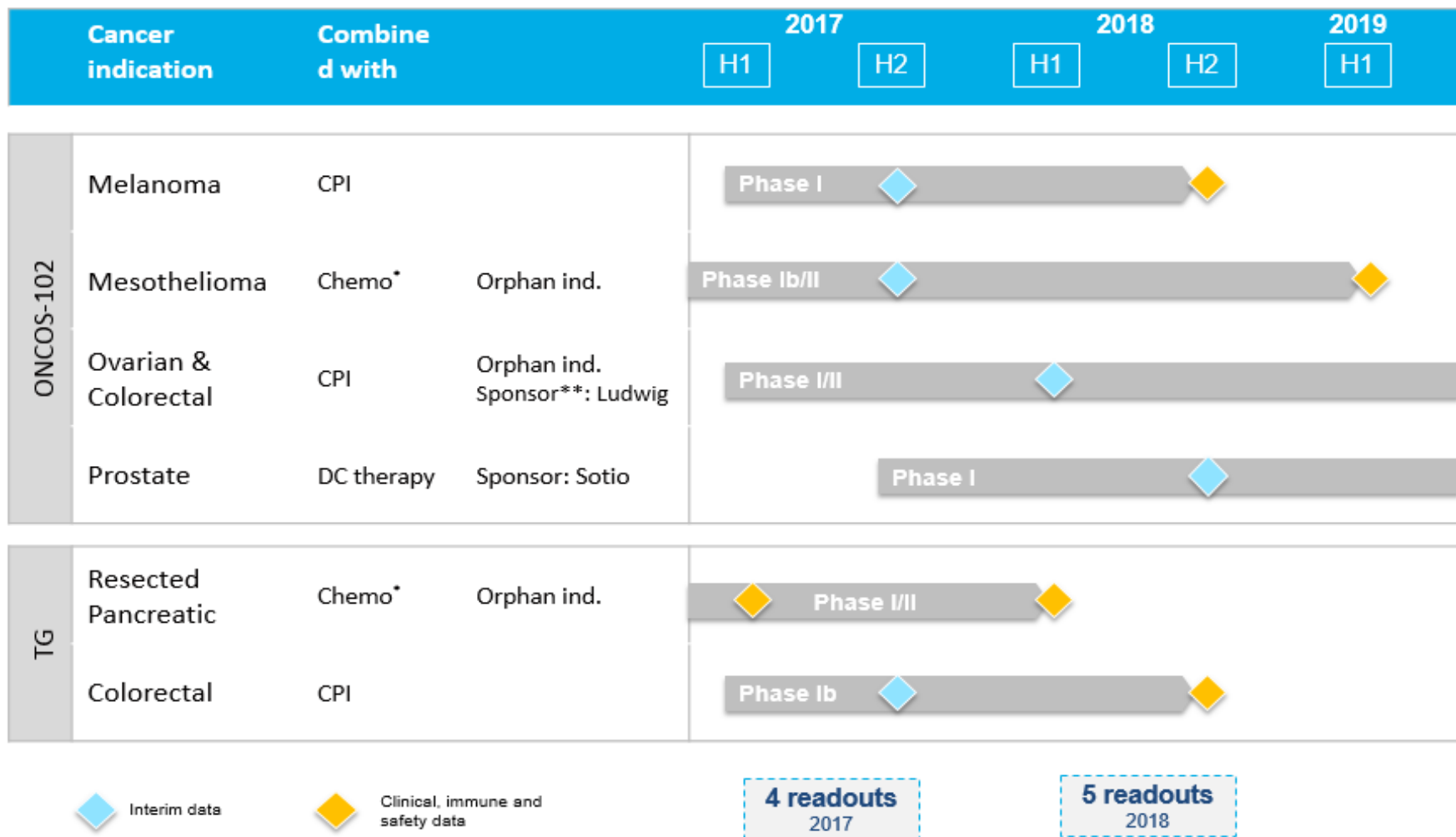
- Safety
- Immune activation
- Clinical response data

## Sequence

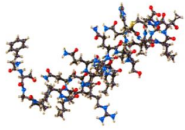
ONCOS-102 – 3 weeks

Keytruda – 5 months

# A comprehensive clinical development program has been initiated

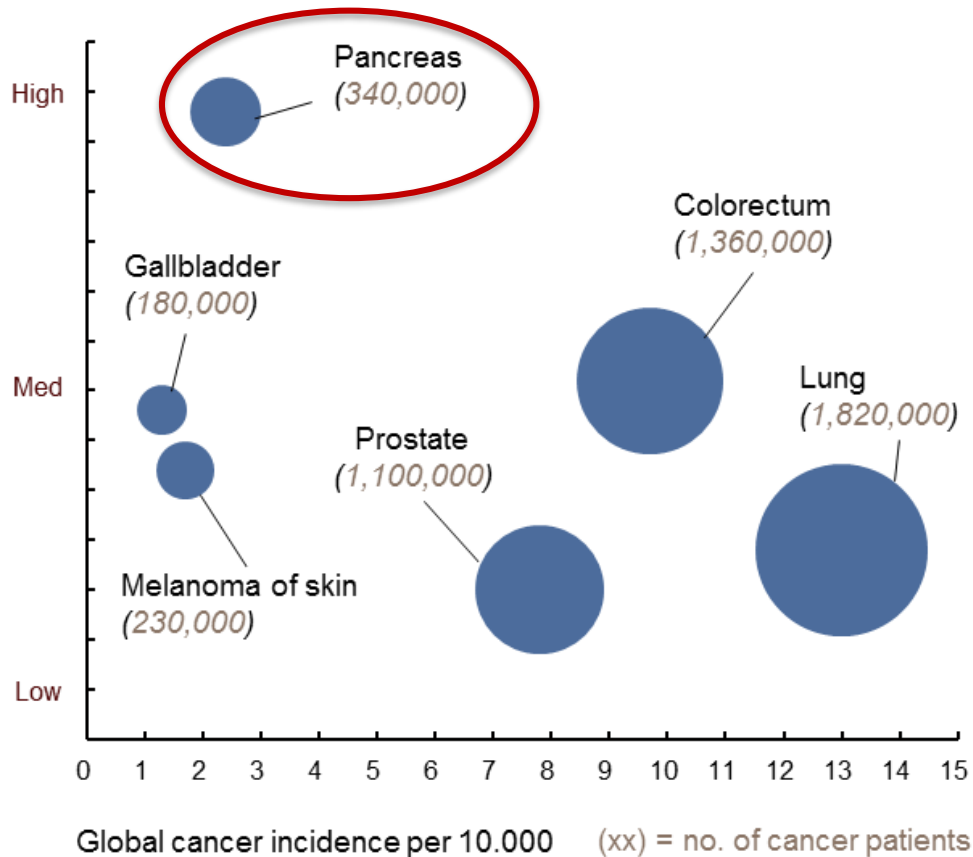


\* In combination with Standard of Care Chemotherapy. Pemetrexed/cisplatin for Mesothelioma and Gemcitabine for Resected Pancreatic  
 \*\* A sponsor is the company or institution that submits the application for a clinical study to the regulatory authorities and that is responsible for conducting and reporting the study in compliance with the regional regulatory legislations and guidelines.

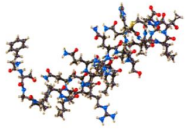


**RAS is a key regulator of cell cycle that is mutated in 20-30% of all cancer patients, and >85% of pancreatic cancers**

### Incidence of RAS mutations



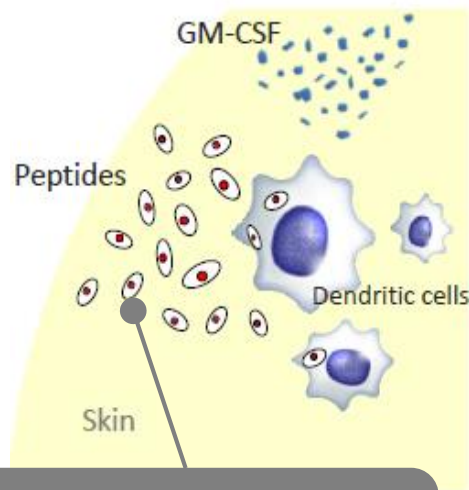
- RAS is one of the most **well-defined neoantigens**
- Results in **cell division being permanently switched on**
- **No existing therapies** targeting RAS
- One of the **most common mutations** in cancer
- Occurs in **>85% of pancreatic cancer** patients



# The TG peptides prime the immune system to recognize and destroy RAS mutated cancer cells

## Activate immune system:

- TG peptides injected into the skin with GM-CSF adjuvant
- APCs pick up the TG RAS antigens

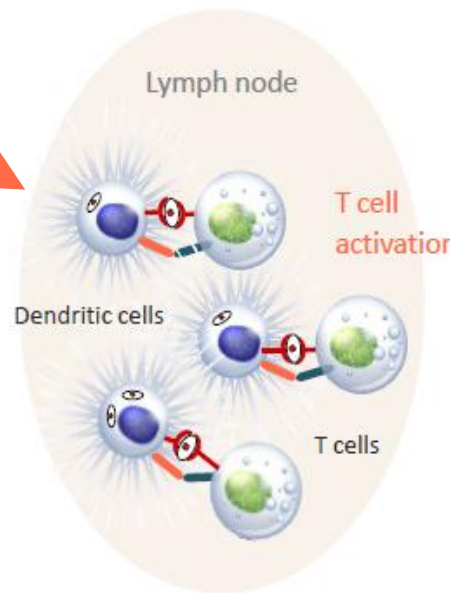


Cocktail of 7 peptides covering all relevant RAS mutations in pancreas

+ GM-CSF  
co-stimulation

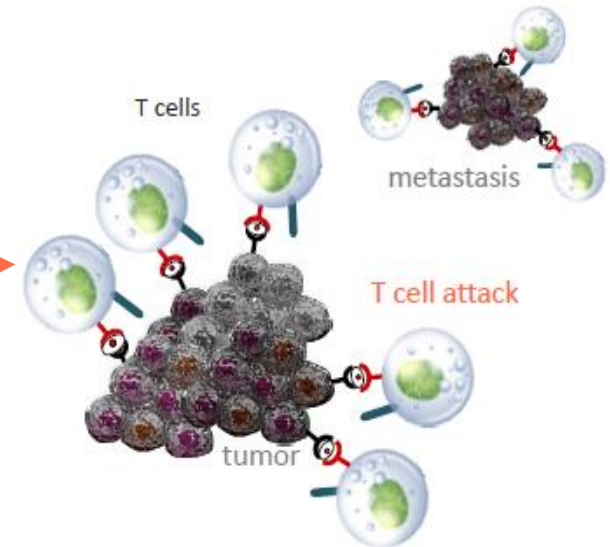
## Train T-cells:

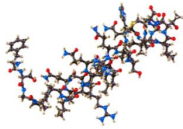
- APCs migrate to lymph nodes and present RAS specific antigens
- Production of RAS specific T-cells



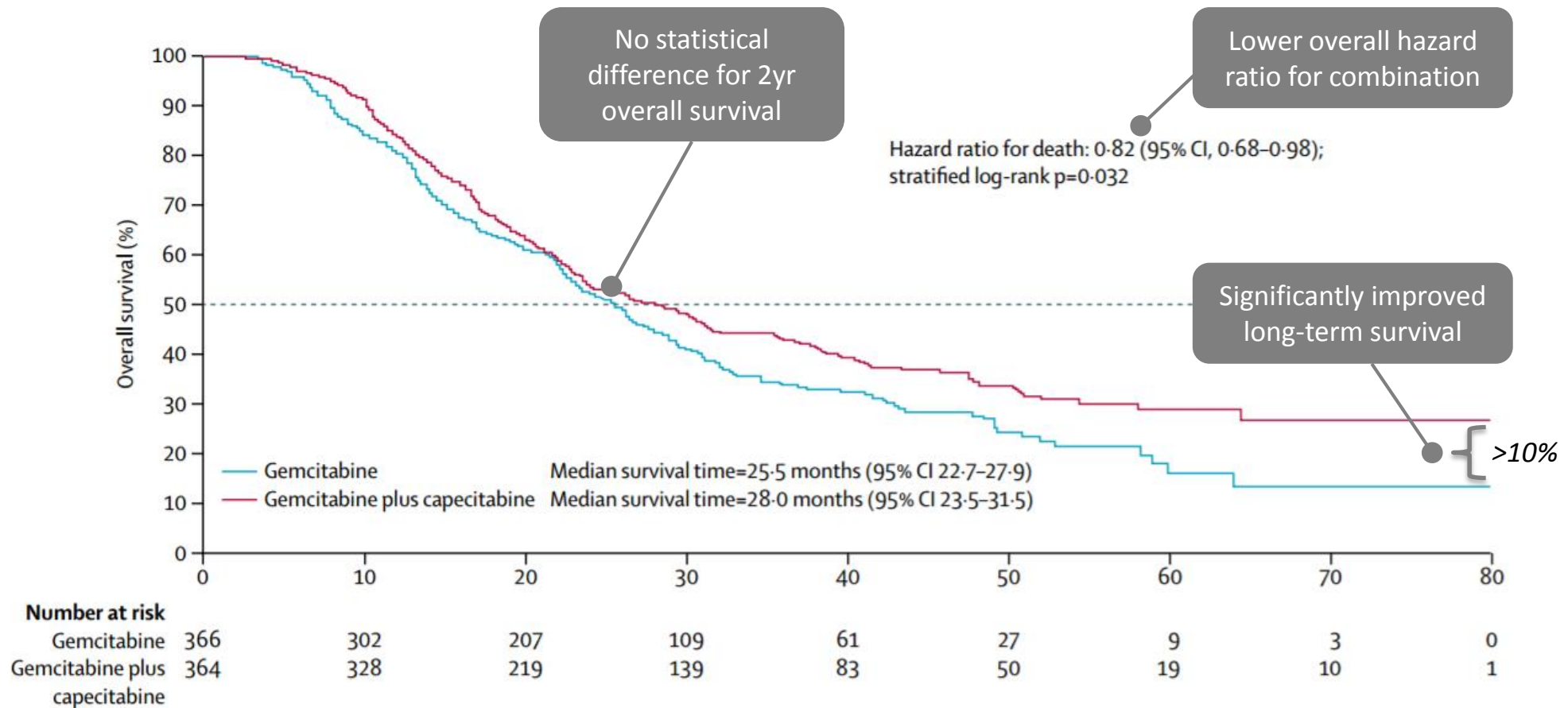
## Attack the cancer:

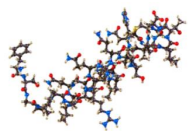
- RAS specific T-cells identify mutated RAS antigens on cancer cell surface
- Killer T-cells destroy the cancer cells



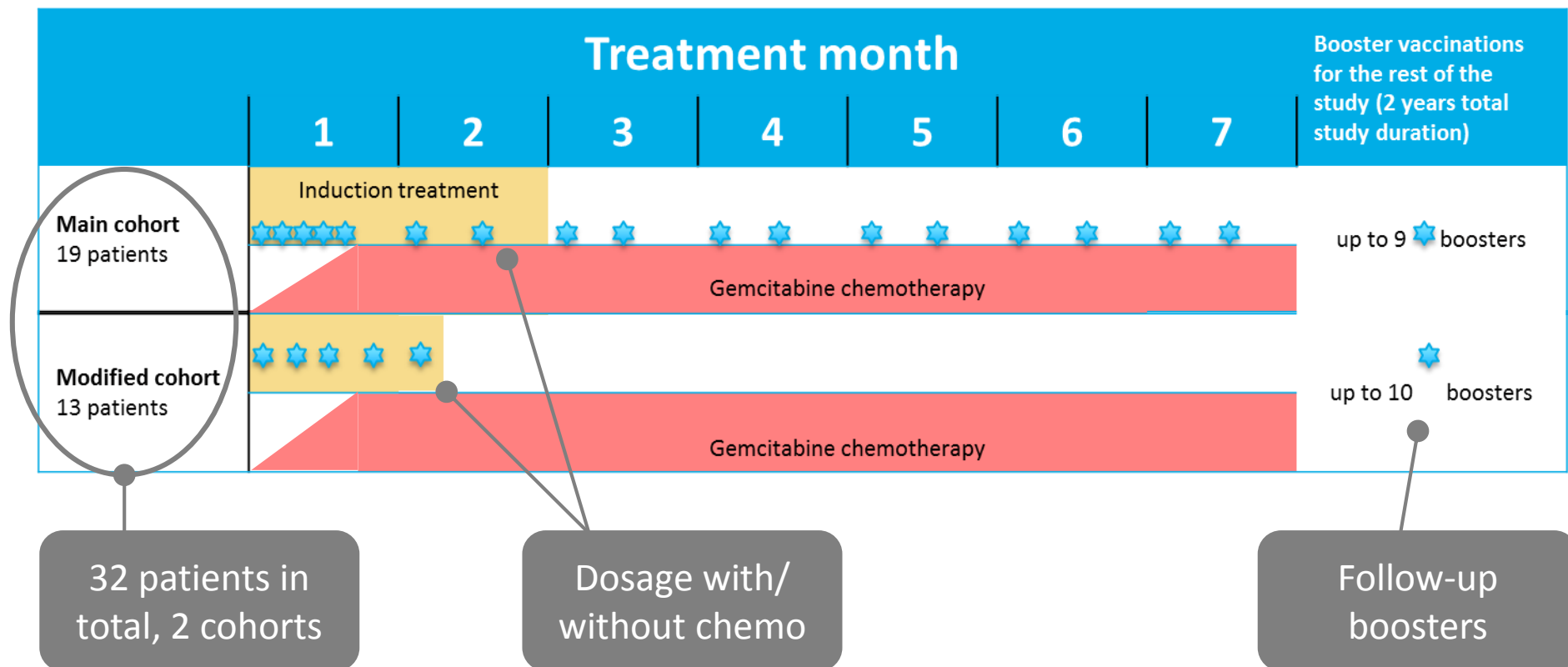


# Resected pancreatic cancer patients only have chemotherapy as a treatment option, and long term survival is poor

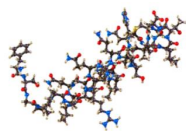




# A Phase I/II trial with TG01 in Resected Pancreatic Cancer is currently being completed







# Key results from TG01 Phase I/II trial in resected pancreatic cancer: 5 months longer median survival

## 2 year OS

- **13 of 19 patients (68%) alive 2 years after surgery**
- Historical SoC controls range from 30-50% 2 year OS

## Median OS

- **33.1 months**
- SoC (Gemcitabine) 27.6 months\*

## Immune response

- **16/18 patients (89%) showed TG specific immune sensitivity**
- DTH test at week 11

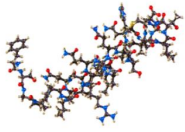
## Resection status

- **R0: 32 % (6/19 patients) R1: 68% (13/19 patients)**
- Historical data: R0: 67%; R1: 33%

## Safety

- **Treatment regimen generally well-tolerated**
- Some manageable allergic reactions were seen

\*ESPAC-4 counted OS from randomization which was 64 days on average after surgery



# The results are being supported by 10 year long-term survival data for previous trials

## Long-term data

### Long-term data available from previous trials

- 4 out of 20 patients (20%) alive after 10 years in similar trial on resected pancreatic cancer
- Compares to 5-10% expected survival based on historical data

## RAS target

### Highly specific and well-understood target

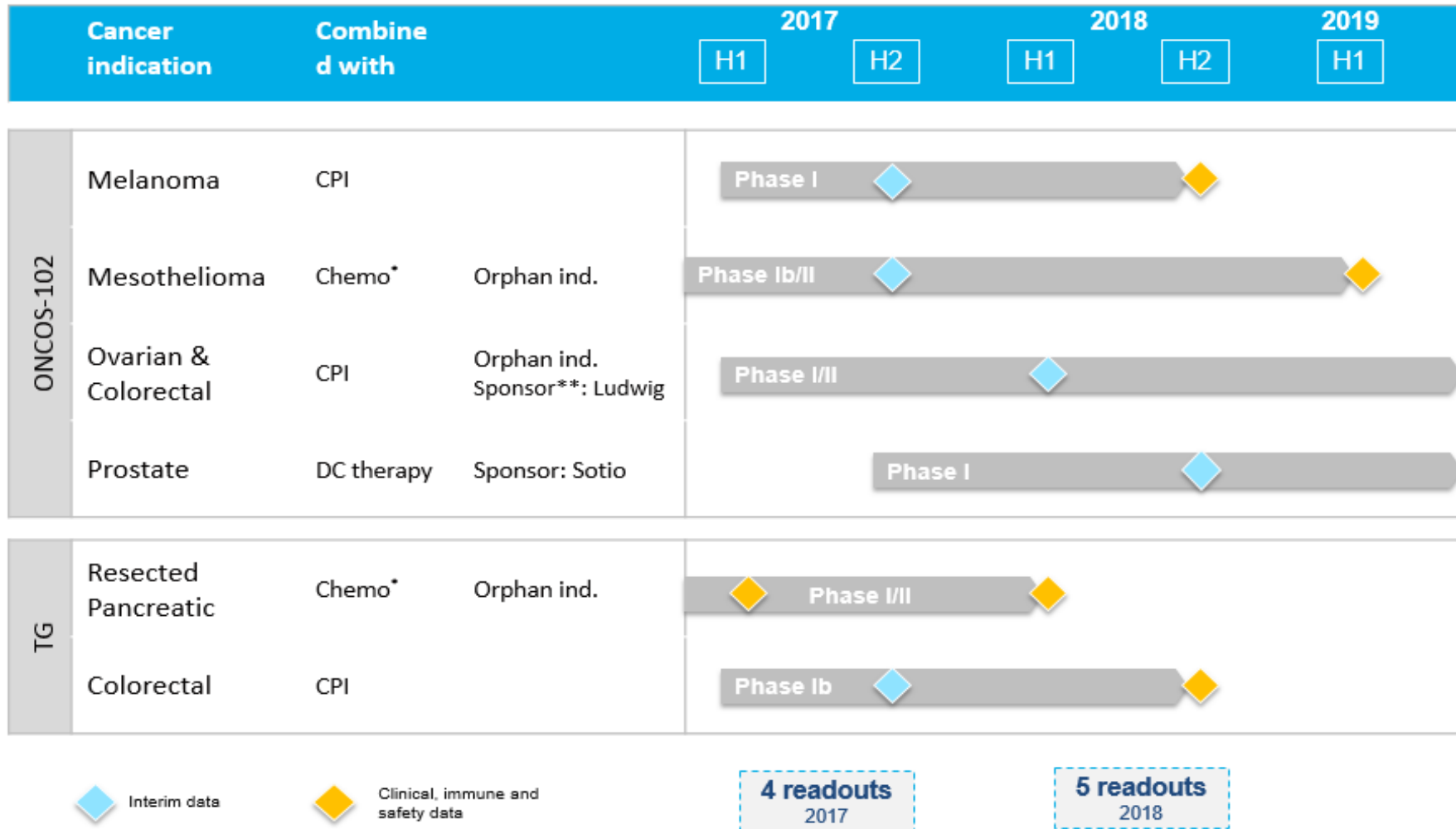
- RAS mutations are well-characterized neoantigens
- Exclusively found in cancer cells, and >85% of pancreatic cancers

## Antigen targeting

### Peptide design ensures full immune response

- 17 amino acid chain length activate both CD4+ and CD8+ T cells
- T-cells recognize mutated RAS antigens presented on the surface of cancer cells, with no need for intra-cellular targeting

# Two platforms and six clinical trials in total ensures a diversified program with frequent data readouts



\* In combination with Standard of Care Chemotherapy. Pemetrexed/cisplatin for Mesothelioma and Gemcitabine for Resected Pancreatic

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# Arming the patient's immune system to fight cancer

1	TG	✓ Encouraging median survival and top line two-year OS data in resected pancreatic cancer
2	ONCOS	✓ Important proof of concept trial in CPI refractory melanoma
3	Clinical trials	✓ Six shots on goal

# Financials

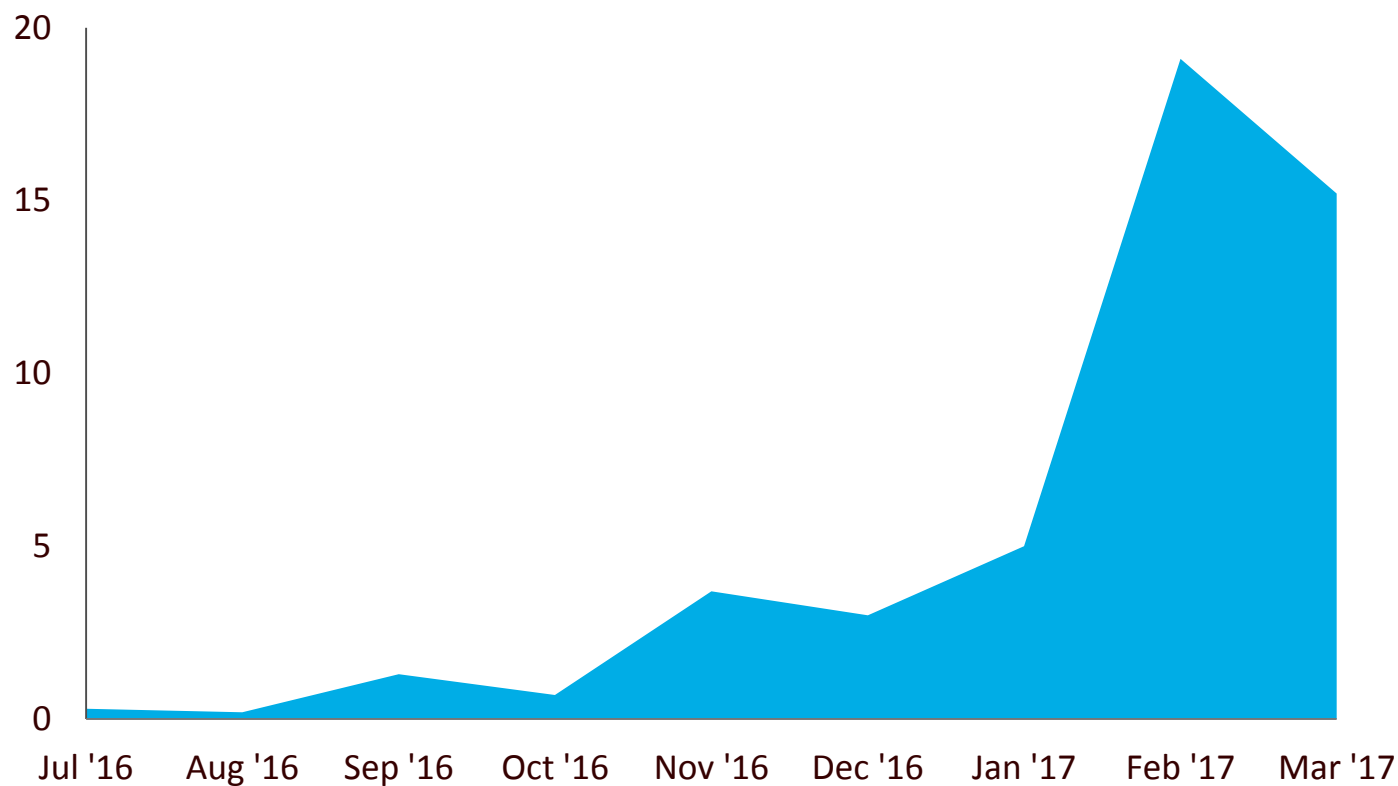
# Financial summary – end of Q1 2017

Operations			
Cash	NOK 147m	USD 17m	<i>End of Q1 2017</i>
Net cash flow	NOK -24m	USD -3m	<i>Total Q1</i>
Annual run rate	NOK 104m	USD 12m	<i>Last four quarters</i>
Annual opex	NOK 116m	USD 13m	<i>Last four quarters</i>

The share	OSE: TRVX		
Market Cap	NOK ~1bn	USD ~120m	<i>At share price NOK ~24</i>
Daily turnover	NOK 14m	USD 1.6m	<i>Last three months avg.</i>
Debt	NOK 43m	USD 5m	<i>EUR 6m conditional</i>
No. of shares	42.2m	<i>46.0m fully diluted per April 18</i>	
Analysts	DNB, ABG Sundal Collier, Arctic, Redeye, Norske Aksjeanalyser		

# TRVX upgraded to the main list on OSE, and showed a positive trend in share turnover

*Development in daily average share turnover (NOK million / day)*



- **NOK ~1b** market cap
- **NOK 14m** avg. daily turnover in last 3 months
- **NOK 850m** total turnover in Q1
- **560k shares** avg. daily volume in Q1
- **>3,500 owners**
- **42.2m shares** (46.0 fully diluted)



# Strong shareholder base as per April 18<sup>th</sup> 2017

Shareholder		Estimated ownership	
		Shares m	Relative
HealthCap	Sweden	11,2	26,4 %
RadForsk	Norway	4,1	9,7 %
Nordea	Norway	3,0	7,2 %
KLP	Norway	1,6	3,7 %
Nordnet Livsforsikring	Norway	1,4	3,3 %
Statoil	Norway	0,9	2,2 %
Danske Bank (nom.)	Denmark	0,8	1,8 %
Timmuno AS	Norway	0,7	1,7 %
Prieta AS	Norway	0,7	1,7 %
Rasmussengruppen	Norway	0,7	1,7 %
Nordnet Bank AB (nom.)	Sweden	0,7	1,5 %
Sundt AS	Norway	0,3	0,7 %
DNB	Norway	0,3	0,6 %
Avanza Bank AB (nom.)	Sweden	0,3	0,6 %
Thorendahl Invest AS	Norway	0,3	0,6 %
The Bank of NY Mellon (nom.)	Belgium	0,2	0,5 %
Netfonds Livsforsikring AS	Norway	0,2	0,5 %
Tobech Invest AS	Norway	0,2	0,5 %
Istvan Molnar	Norway	0,2	0,4 %
Danske Bank (nom.)	Denmark	0,2	0,4 %
<b>Top 20</b>		<b>27,8</b>	<b>65,9 %</b>
Other shareholders (3566)		14,4	34,1 %
<b>Total</b>		<b>42,2</b>	<b>100,0 %</b>

## 42.2m ordinary shares

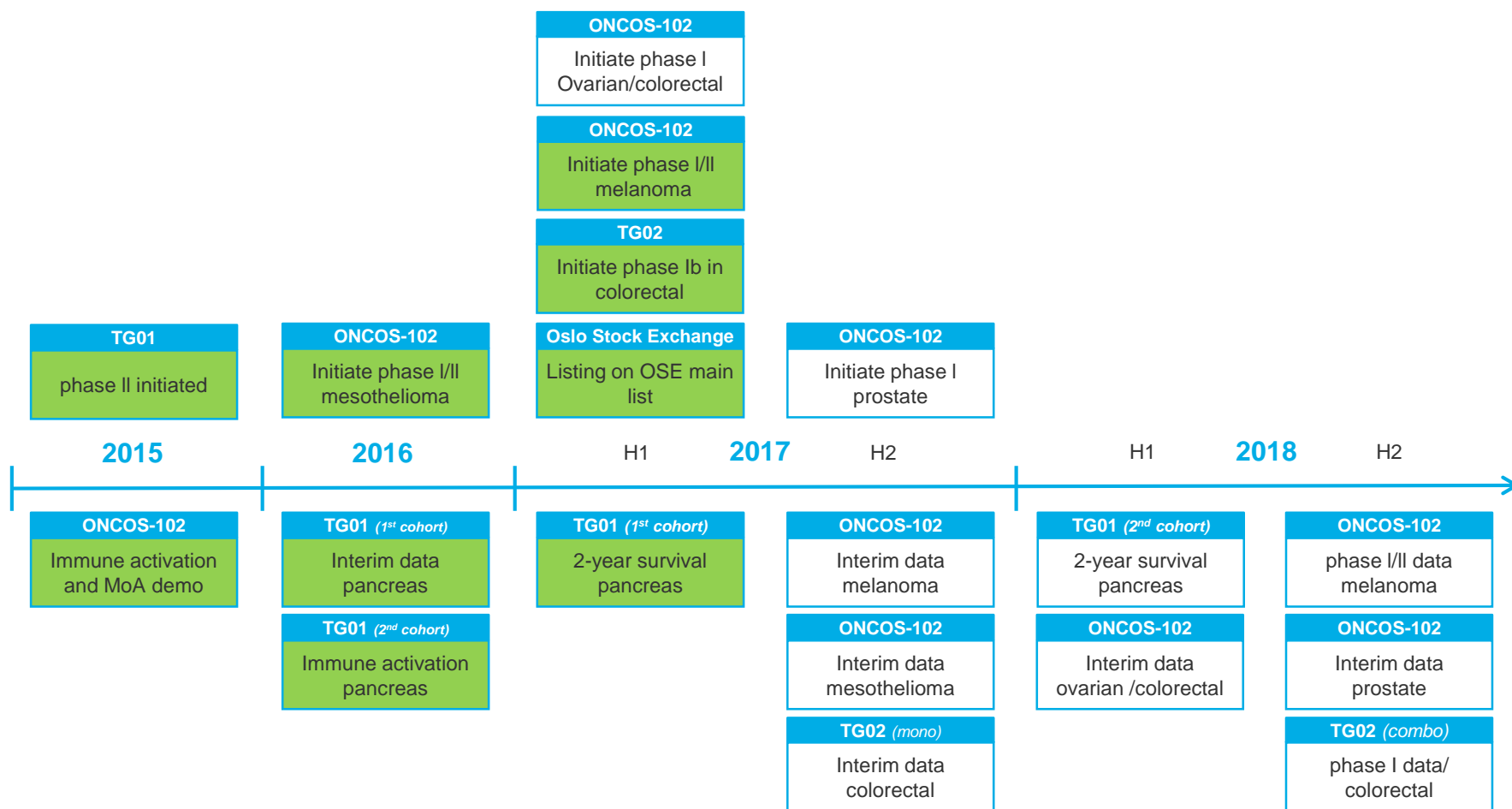
- Management ownership: 2.1%
- 3,586 shareholders

## 46.0m<sup>1</sup> shares fully diluted

- Average strike price on options ~NOK 21
- Total dilutive effect of options is 7.9%

<sup>1</sup> Includes outstanding options (3,634,263) and Restricted Stock Units (169,128) to Board members

# Multiple near term value inflection points



# Investment highlights

1	Core focus on immuno-oncology	<ul style="list-style-type: none"><li>✓ Two differentiated product platforms, oncolytic adenovirus (ONCOS-102) and RAS-peptide cancer vaccine (TG)</li><li>✓ Targeting refractory solid tumors with combination trials</li></ul>
2	Proprietary platforms and pipeline	<ul style="list-style-type: none"><li>✓ Promising Phase I/II data from both proprietary platform technologies, with clinically demonstrated immune activation and signal of efficacy</li></ul>
3	Multiple near term value inflection points	<ul style="list-style-type: none"><li>✓ Six combination trials started or about to start (phase I &amp; II)</li><li>✓ All six trials read out in 2017-2018</li></ul>
4	Corporate	<ul style="list-style-type: none"><li>✓ TRVX transferred to the OSE main list in Q1 2017</li><li>✓ Strong increase in share turnover</li><li>✓ Cash at approx. NOK 147m (USD 17m)</li></ul>