



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

June 2017

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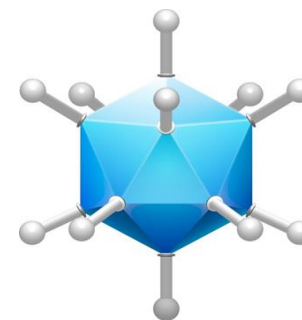
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# Targovax is developing two novel proprietary immunotherapy platforms, with promising phase I/II data

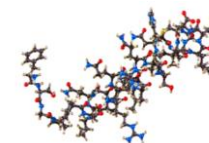
## ONCOS-102 Oncolytic virus

- Genetically tailored 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, thus generating tumor specific T-cells

## Activate immune system:

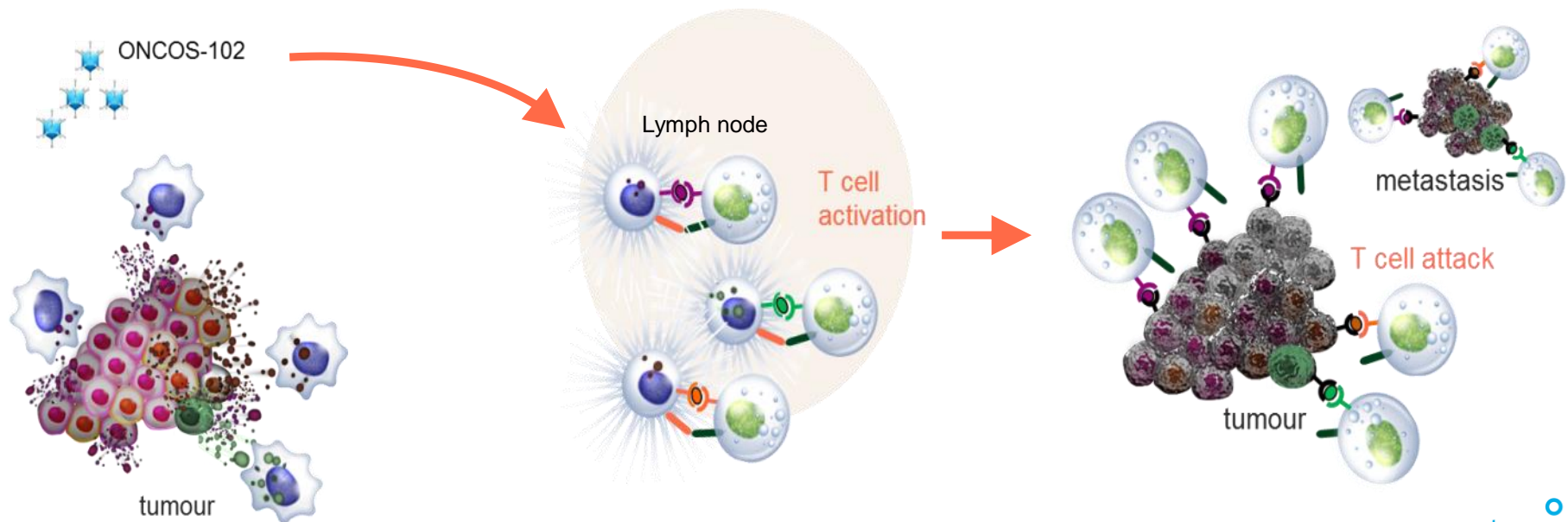
- Virus injected directly into the tumor / peritoneum
- Infected cells lyse and release cancer-specific antigens
- Immune system picks up antigens

## Train T-cells:

- APCs present tumor specific antigens at lymph nodes
- Production of tumor specific T-cells

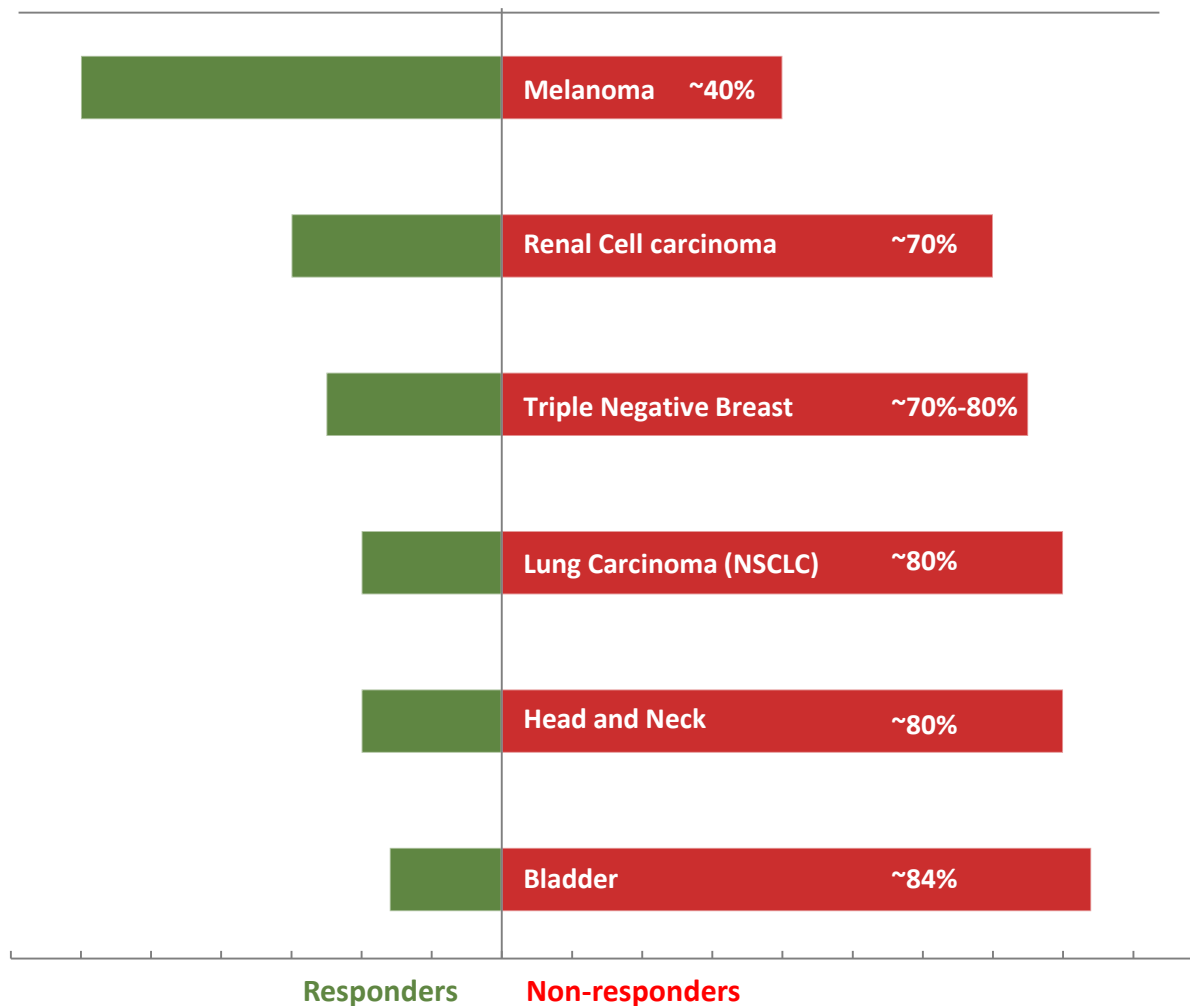
## Attack the cancer:

- Tumor specific T-cells circulate in the body
- Identify lesions and kill the cancer cells



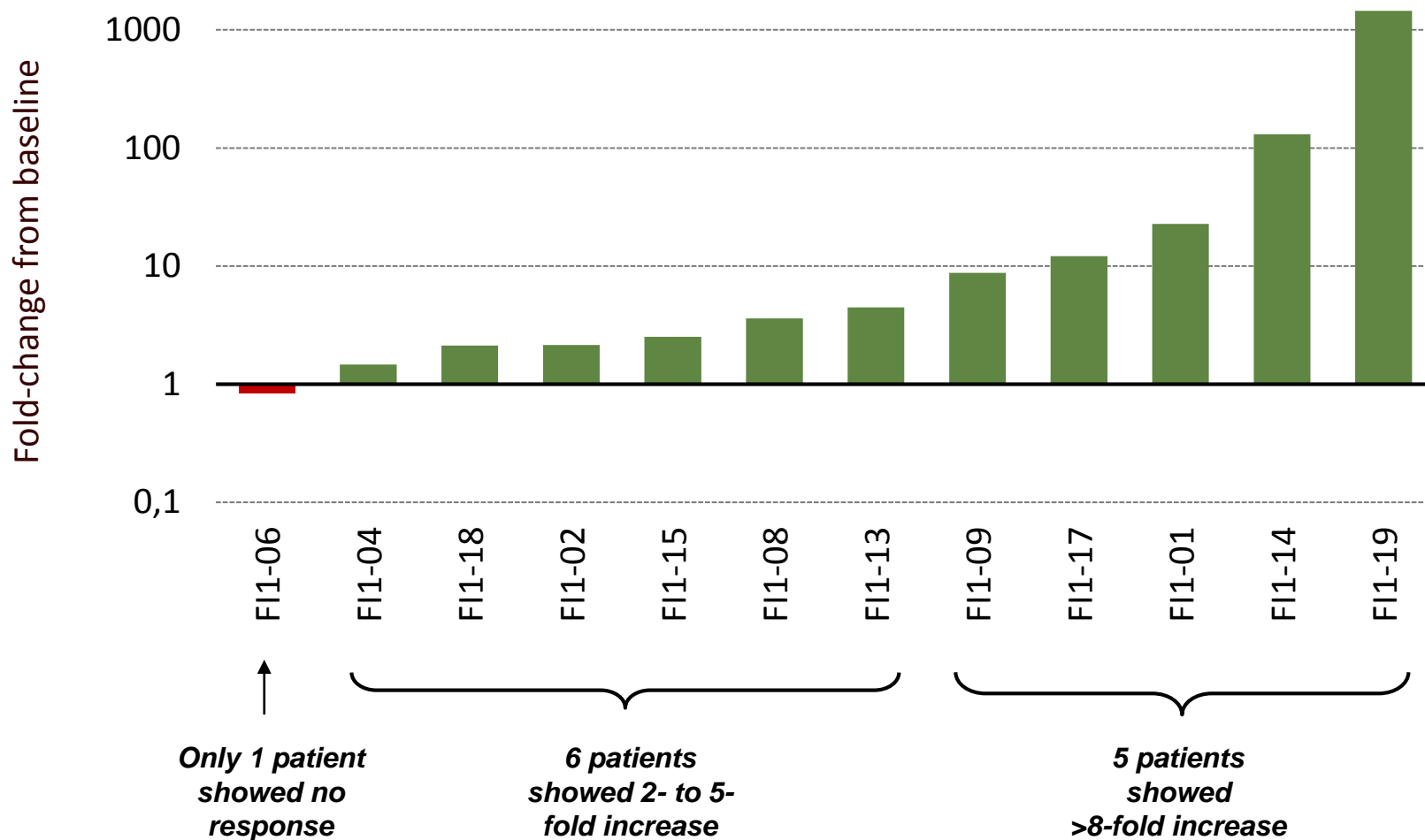
# Most patients do not respond to check point inhibitors (CPIs), due to lack of T-cells in the tumor microenvironment

*Response rate to checkpoint inhibitors (CPIs)*



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

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



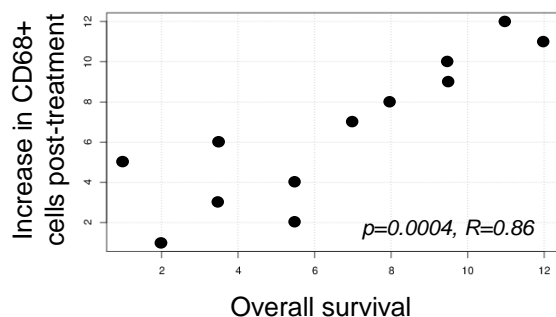
# In the initial Phase I ONCOS-102 trial tumor specific and systemic immune response was observed

## Evidence that immune system recognizes tumor threat

### Innate Immune System (biopsy)

- Induction of proinflammatory cytokines + fever (all patients)
- Infiltration of innate immune cells into tumors in 11 out of 12 patients

Scatterplot of ranks



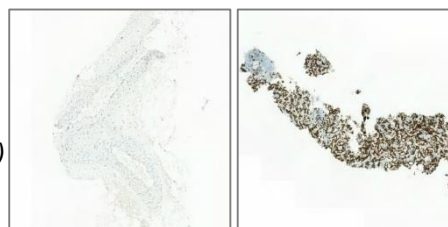
**Correlation between post-treatment increase in innate immune cells and OS**

## Evidence that T-cells find the tumor and are cell killing

### Adaptive immune system (biopsy)

- Increase in T-cell infiltration into tumors (including CD8+ killer T-cells) in 11 out of 12 patients
- Observation in one non-injected distant metastasis

OvCa.  
patient  
(F11-19)



**Correlation between post-treatment increase in CD8+ T-cells and OS**

## Evidence of production of tumor antigen specific T-cells

### Anti-tumor immune response (blood)

- Systemic induction of tumor-specific CD8+ T-cells

#### **Ovarian patient:**

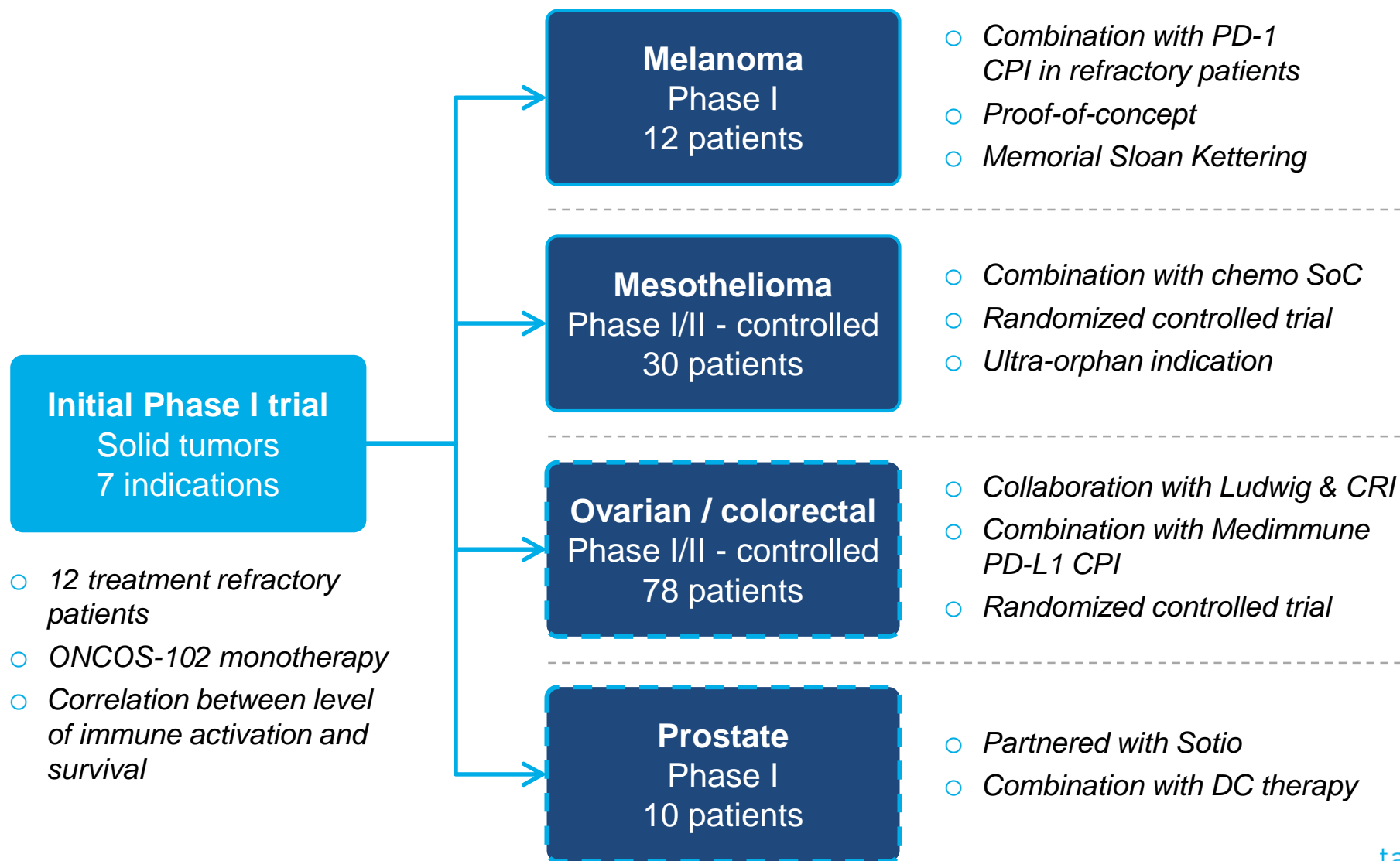
*NY-ESO-1, MAGE-A1, MAGE-A3, and Mesothelin specific CD8+ cells*

#### **Mesothelioma patient:**

*MAGE-A3 specific CD8+ cells*

**Associated with clinical benefit**

# The encouraging Phase I results have triggered the initiation of a broad ONCOS-102 clinical program consisting of four new trials





# Melanoma trial – will CPI refractory patients start responding after immune-priming with ONCOS-102?

## 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

## Proof-of-concept

- *Will CPI refractory melanoma patients start responding to Keytruda after challenge by ONCOS-102?*

# Agenda

- Introduction to immunotherapy
- 

- ONCOS-102 oncolytic virus platform
- 

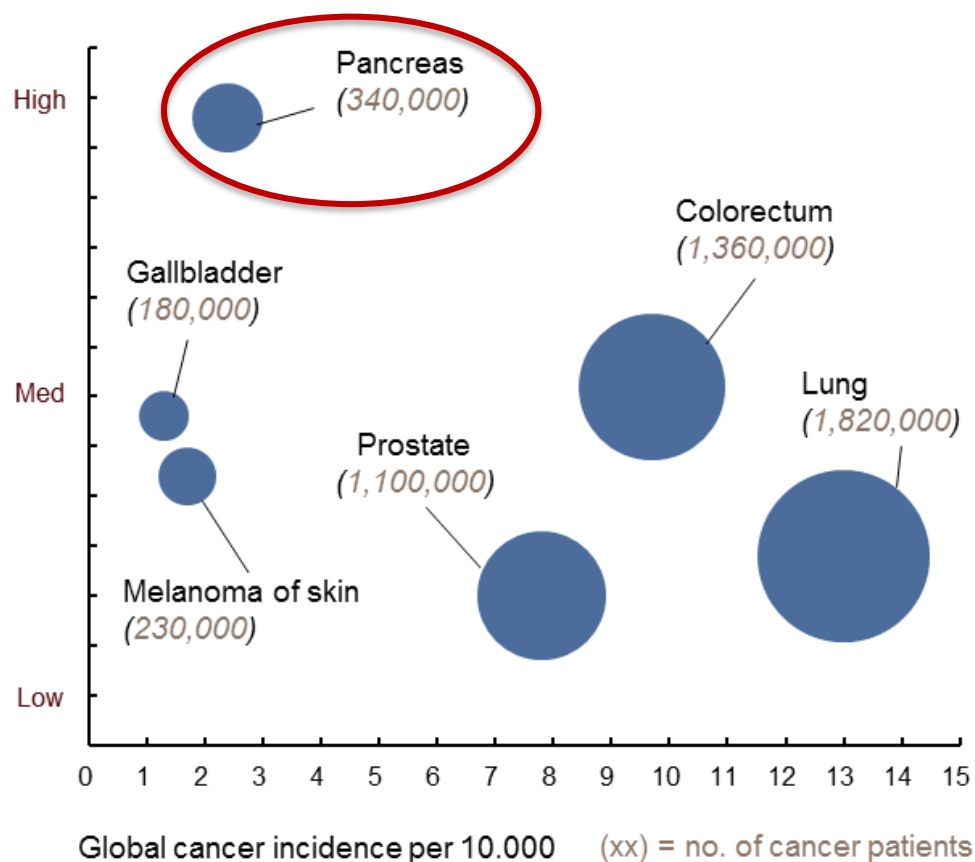
- **TG RAS-peptide vaccine platform**
- 

- Targovax clinical program overview
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- Financial highlights

**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

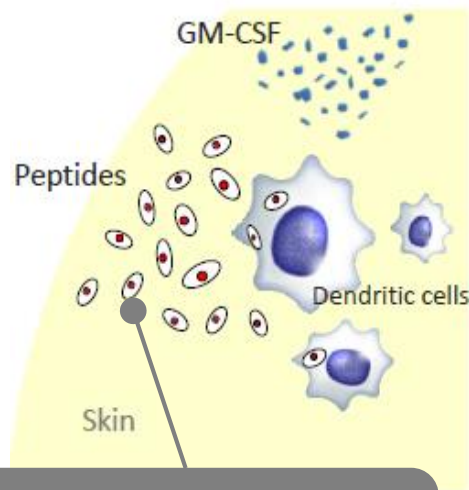


- One of the **most common mutations** in cancer
- RAS is one of the most **well-defined neoantigens**
- Results in **cell division permanently switched on**
- **No existing therapies** targeting RAS
- Occurs in **>85% of pancreatic cancer** patients

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

## *Activate immune system:*

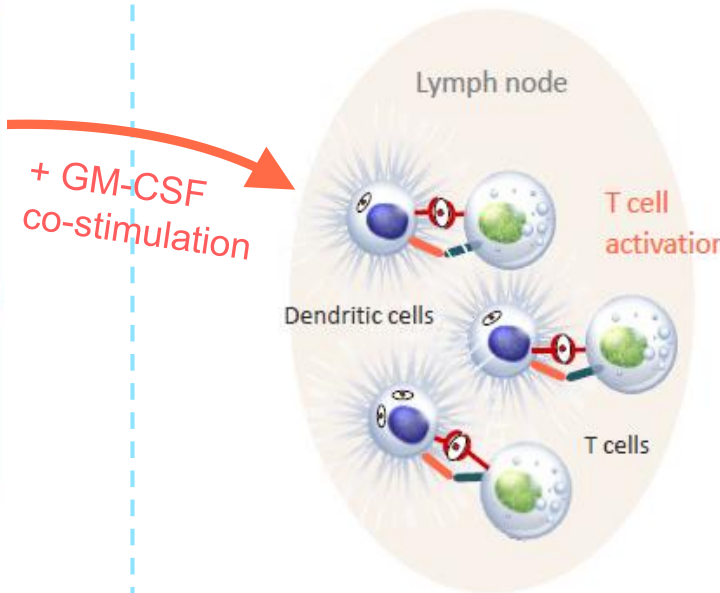
- TG peptides injected into the skin with GM-CSF adjuvant
- APCs pick up the TG RAS antigens



Cocktail of 7 peptides covering all relevant RAS mutations in pancreas

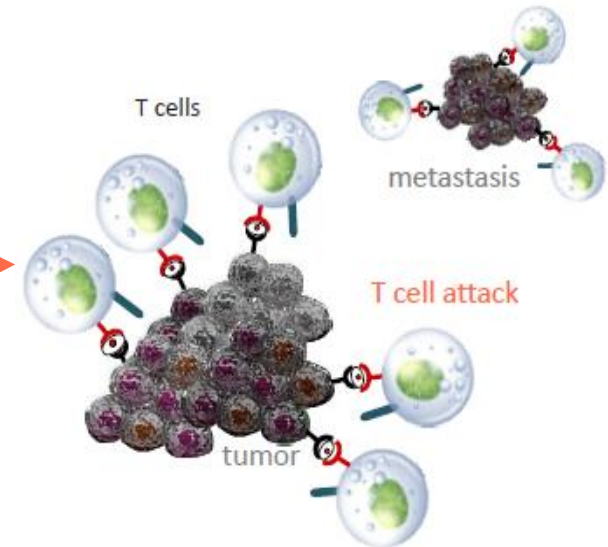
## *Train T-cells:*

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

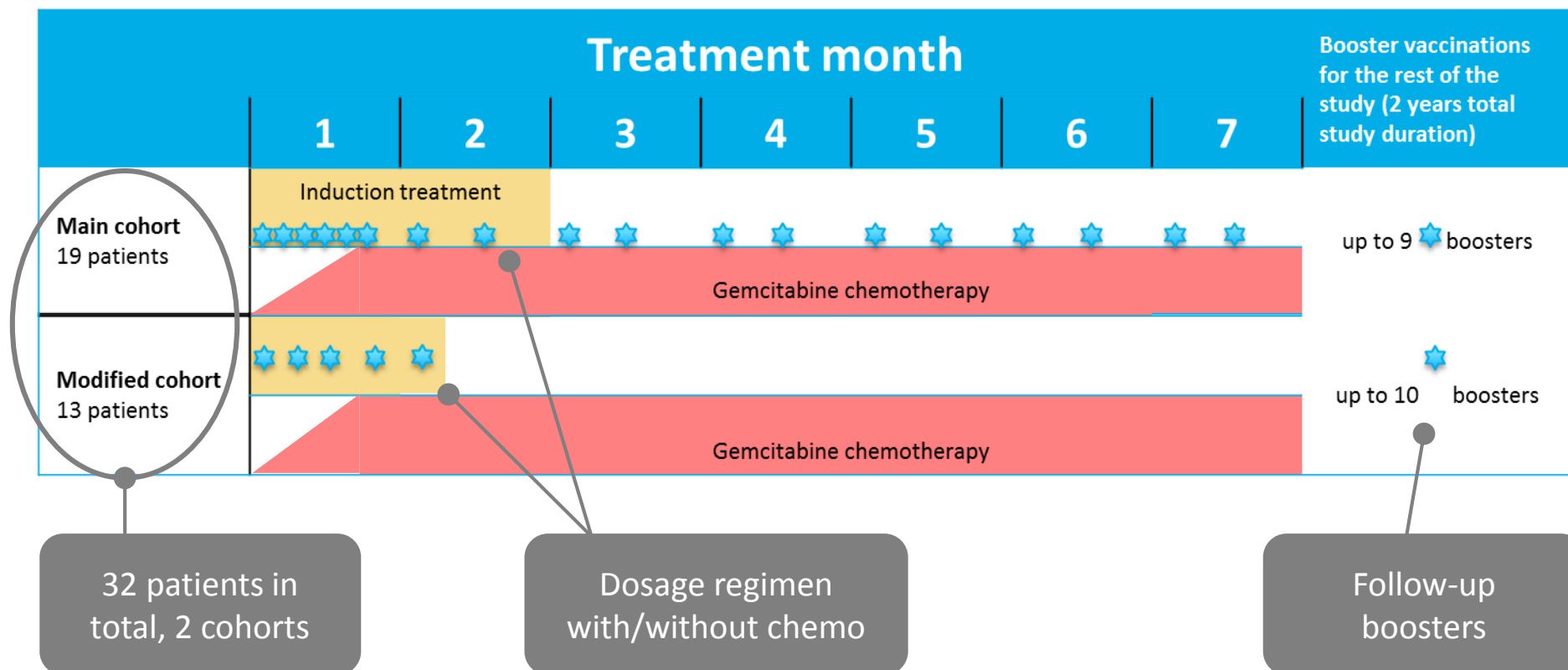


## *Attack the cancer:*

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



# 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: Signal of clinical efficacy

## 2 year OS

- **13 of 19 patients (68%) alive 2 years after surgery**
- Historical control 2 year OS range from 30-53%<sup>1</sup>

## Median survival

- **33.1 months**
- 27.6 months for SoC (Gemcitabine) in ESPAC-4 study<sup>2</sup>

## Immune response

- **16/18 patients (89%) showed TG specific immune sensitivity (DTH)** (analysis lacking for one patient)

## Resection status

- **R0: 32 % (6/19 patients) R1: 68% (13/19 patients)**
- Historical comparisons range from ca. 35-60% R1 patients

## Safety

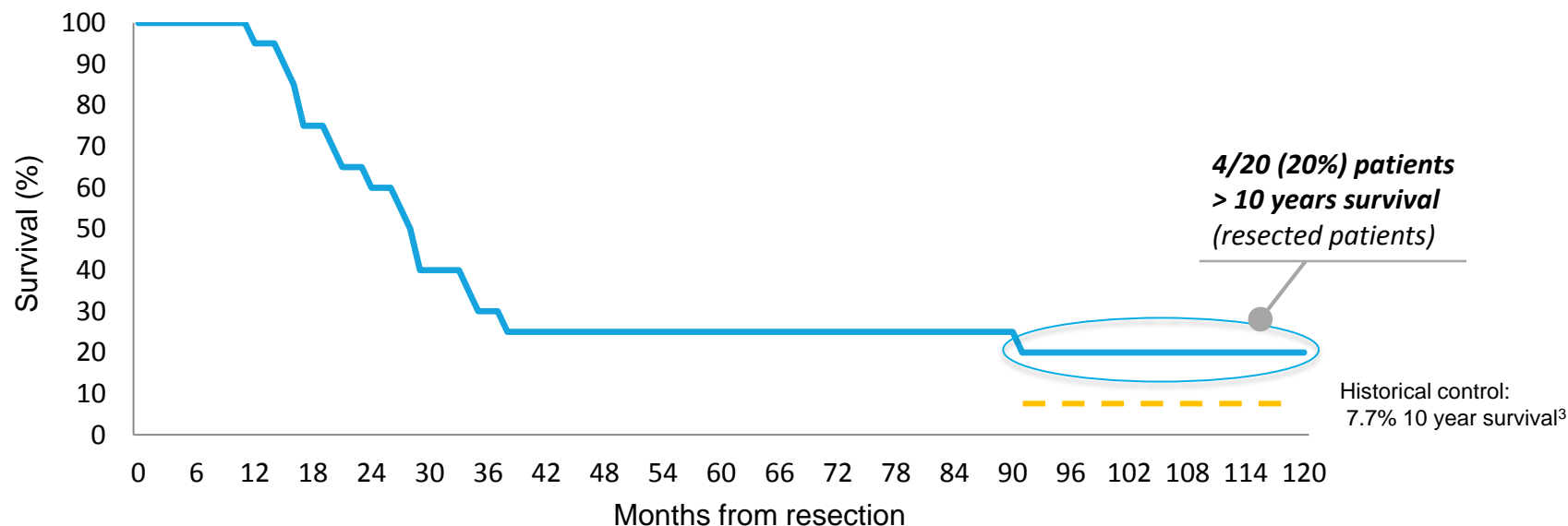
- **Treatment regimen generally well-tolerated**
- Some manageable allergic reactions were seen

1: Relevant historical control trials, not including ESPAC-4, which did not report 2 year OS

2: Based on ESPAC-4 reported 25.5 months median OS from randomisation, adding median time from surgery to randomization of 64 days (2.1 months)

# These results are backed by encouraging 10 year survival data and immune response correlation from earlier trials

## Long-term data from earlier TG mono-therapy trials – resected pancreatic cancer



Advanced pancreatic cancer TG01/GM-CSF (mono-therapy)	Evaluable patients	Median survival (from 1 <sup>st</sup> vaccination)	1 year survival (from 1 <sup>st</sup> vaccination)
Detected immune response	14 / 25 (56%)	156 days	3 (21%)
Not detected Immune response	11 / 25 (44%)	109 days	1 ( 9%)

**Significantly better outcome for patients with immune response (non-resected)**

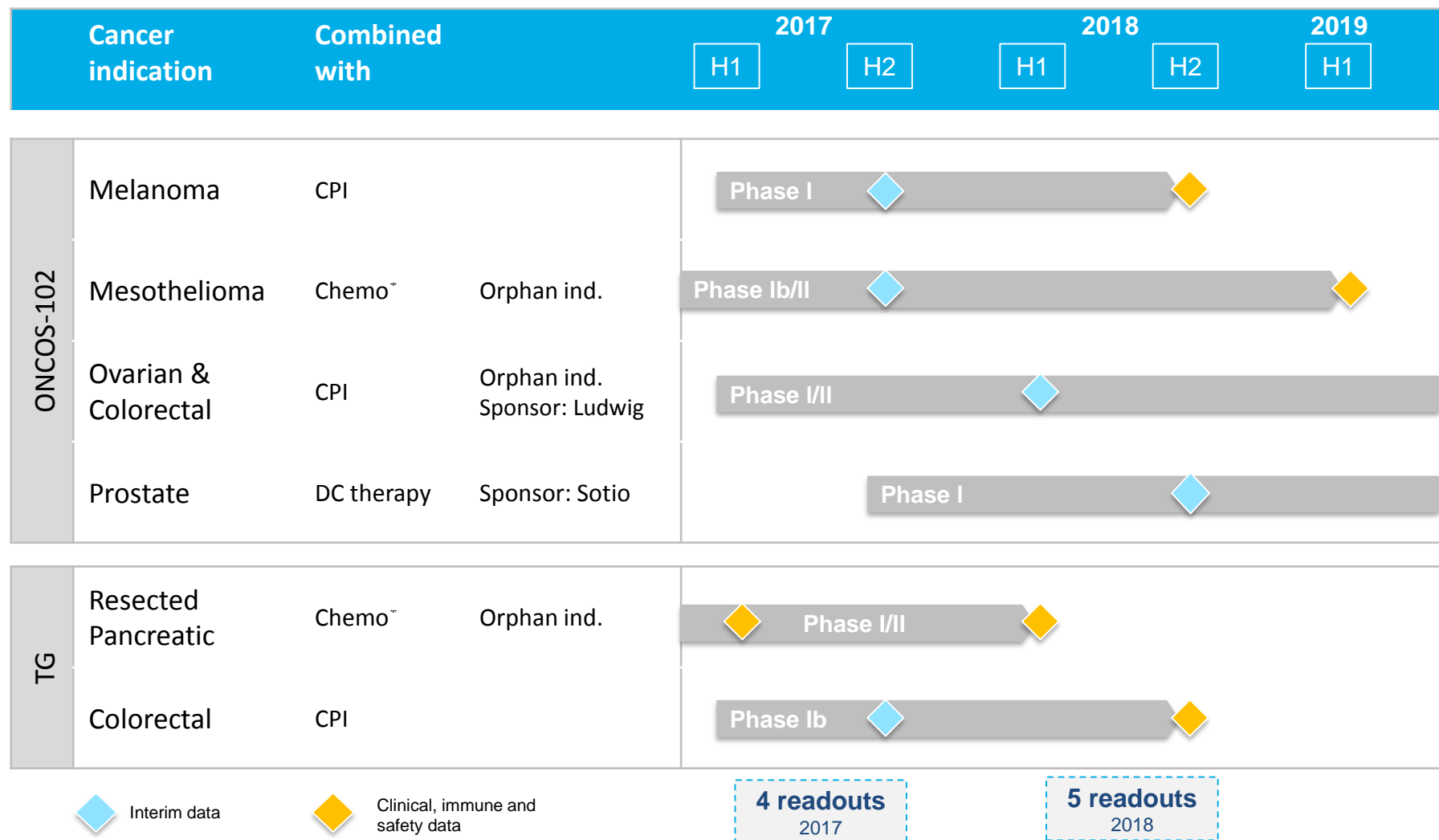
(Clinical study report CTN RAS 98010 on file)

<sup>1</sup> Wedén et al., 2011

<sup>2</sup> Oettle H et al., JAMA 2007, vol 297, no 3

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

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





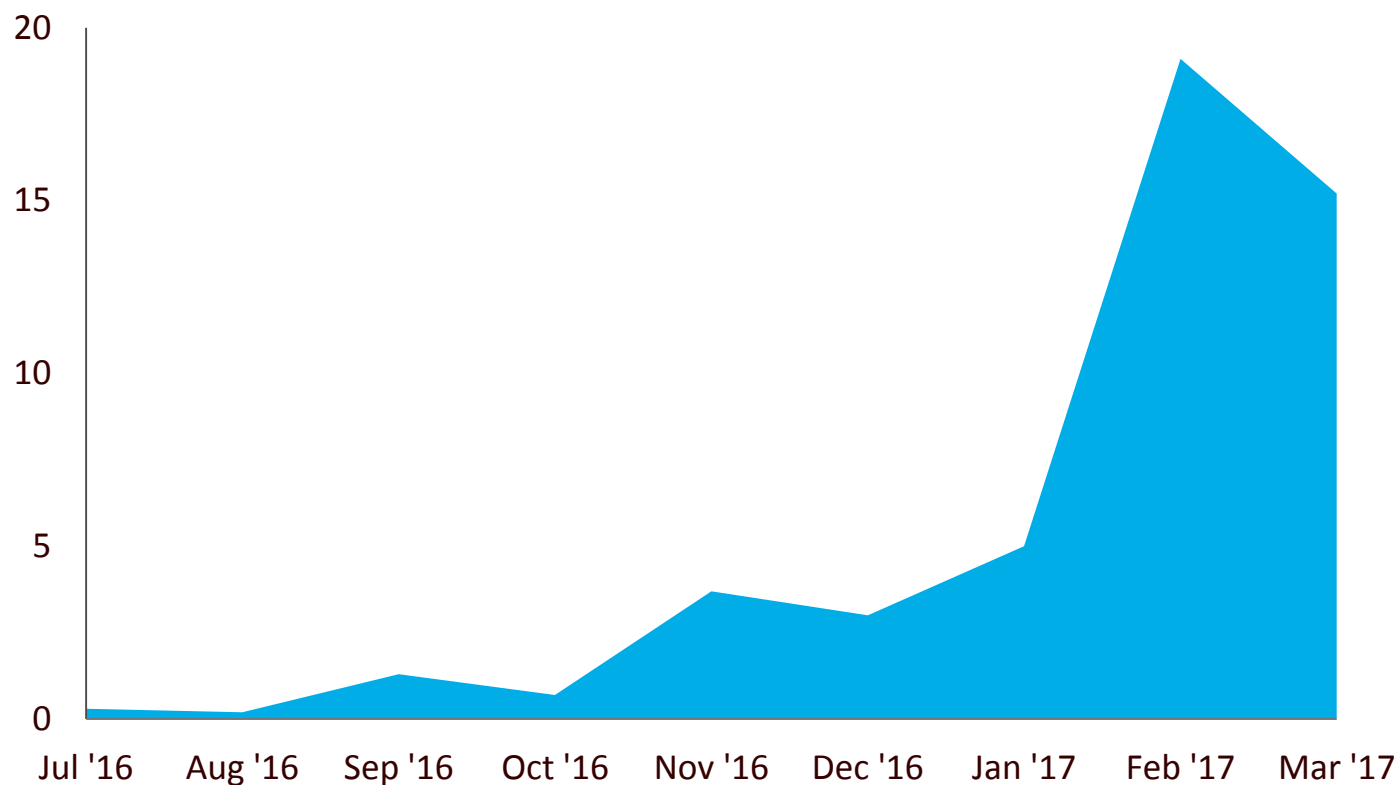
# Financial summary – end of Q1 2017

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 was upgraded to the main list on OSE in March, and has showed a positive trend in share turnover in 2017

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



- **NOK ~1.2b** 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 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>
<i>Other shareholders (3566)</i>		<i>14,4</i>	<i>34,1 %</i>
<b>Total</b>		<b>42,2</b>	<b>100,0 %</b>

## 42.2m ordinary shares

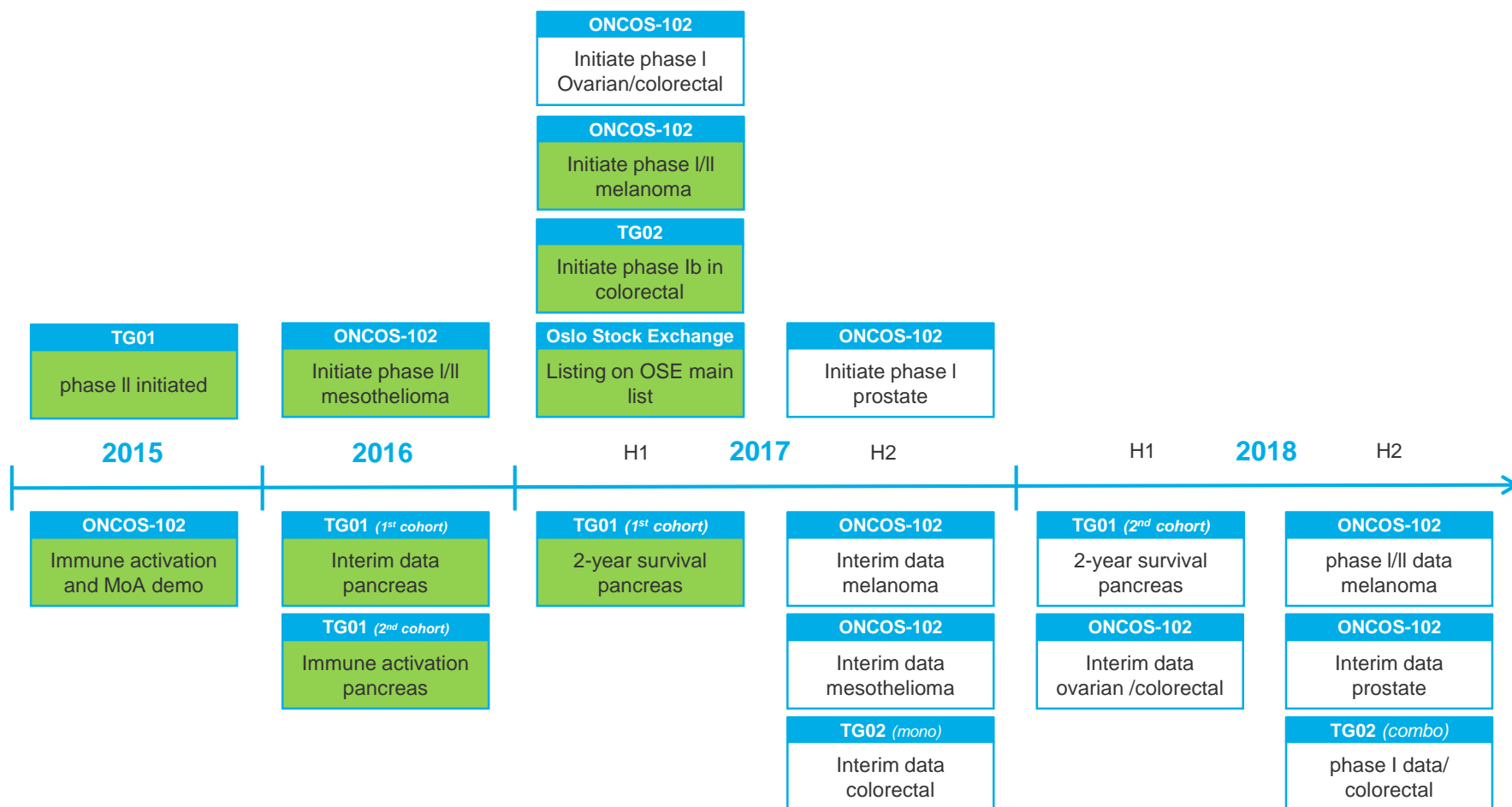
- Management ownership: 2.1%
- 3,586 shareholders

## 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



# 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

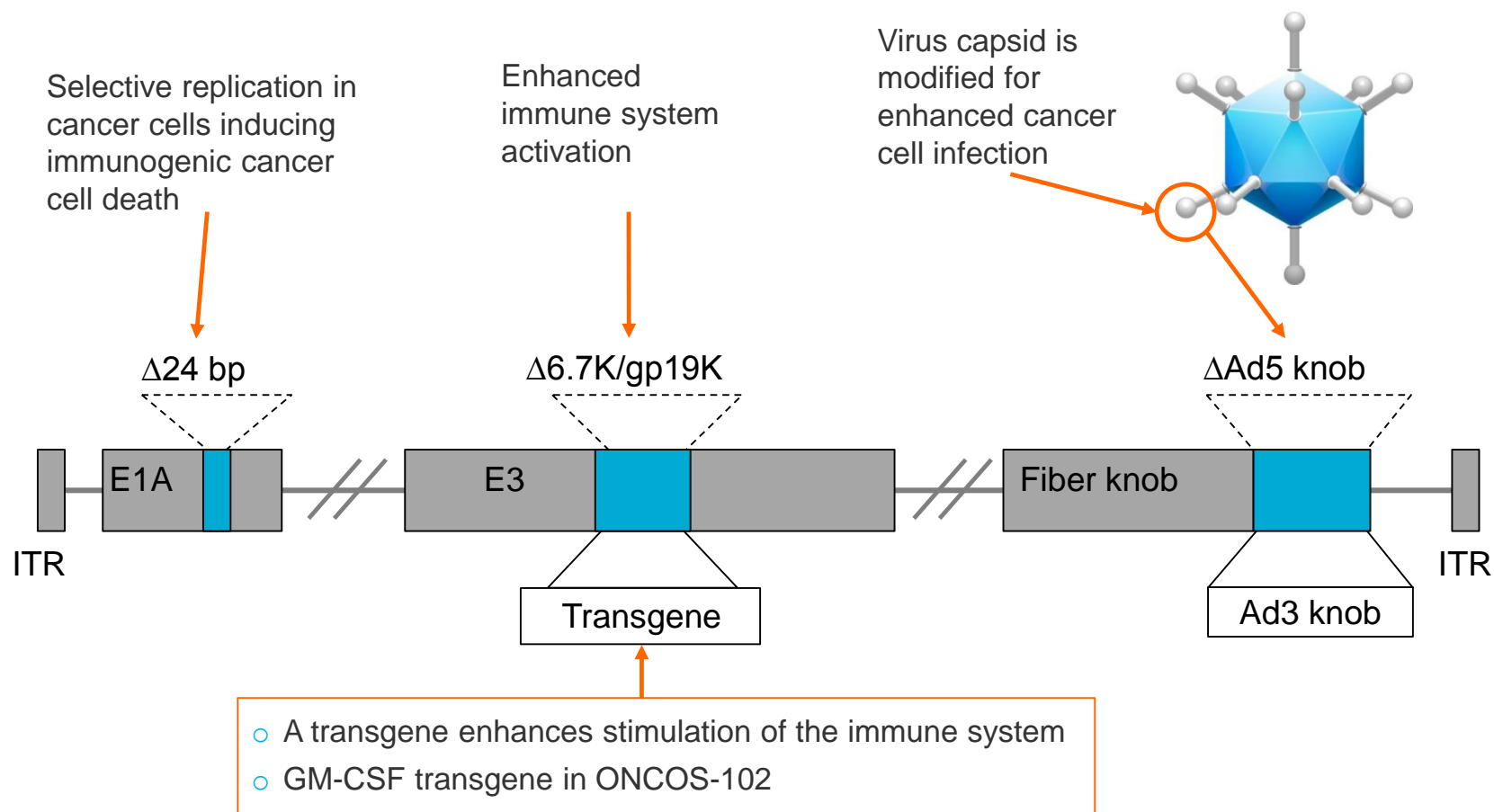
③

Clinical trials

- ✓ Six shots on goal, and steady news flow

# Appendix

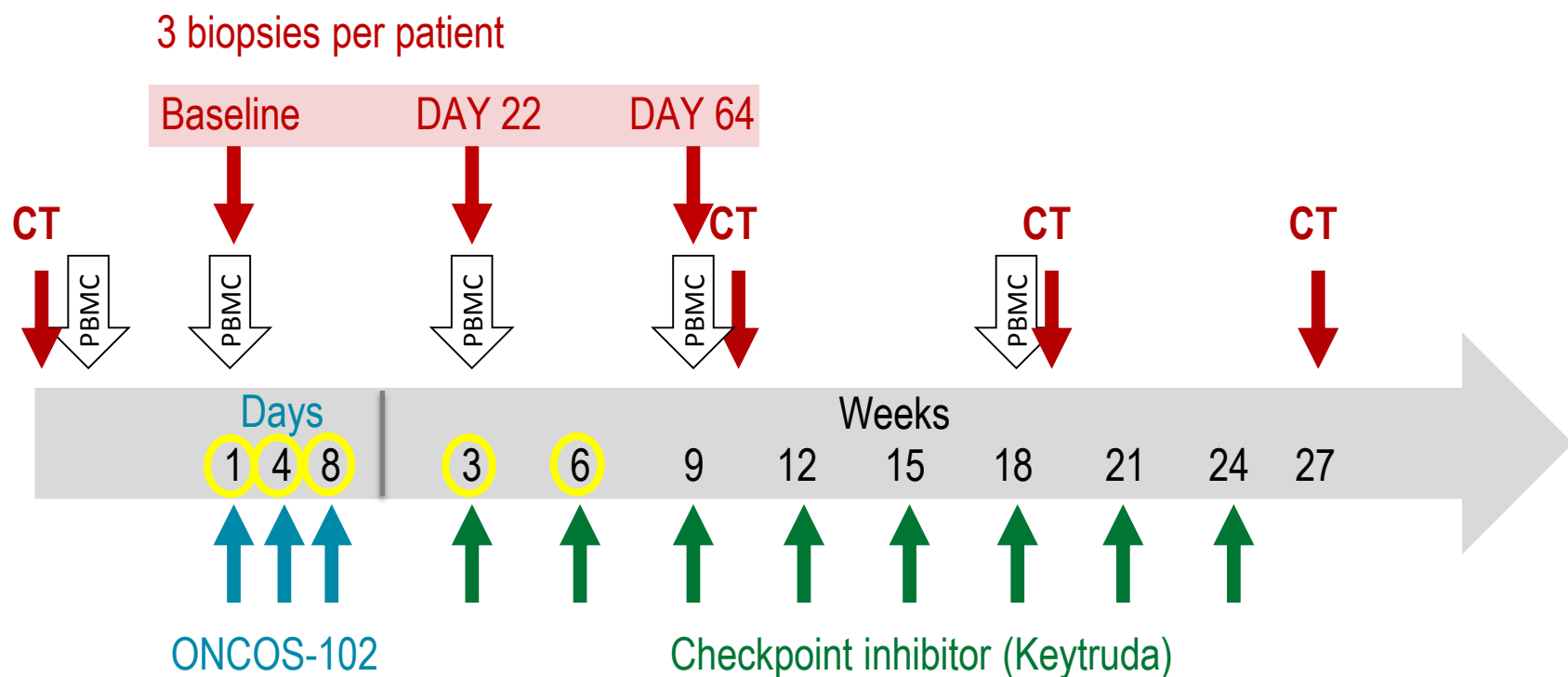
# ONCOS-102: An adenovirus armed with different immune stimulating transgenes



# ONCOS-102: CPI refractory melanoma trial details

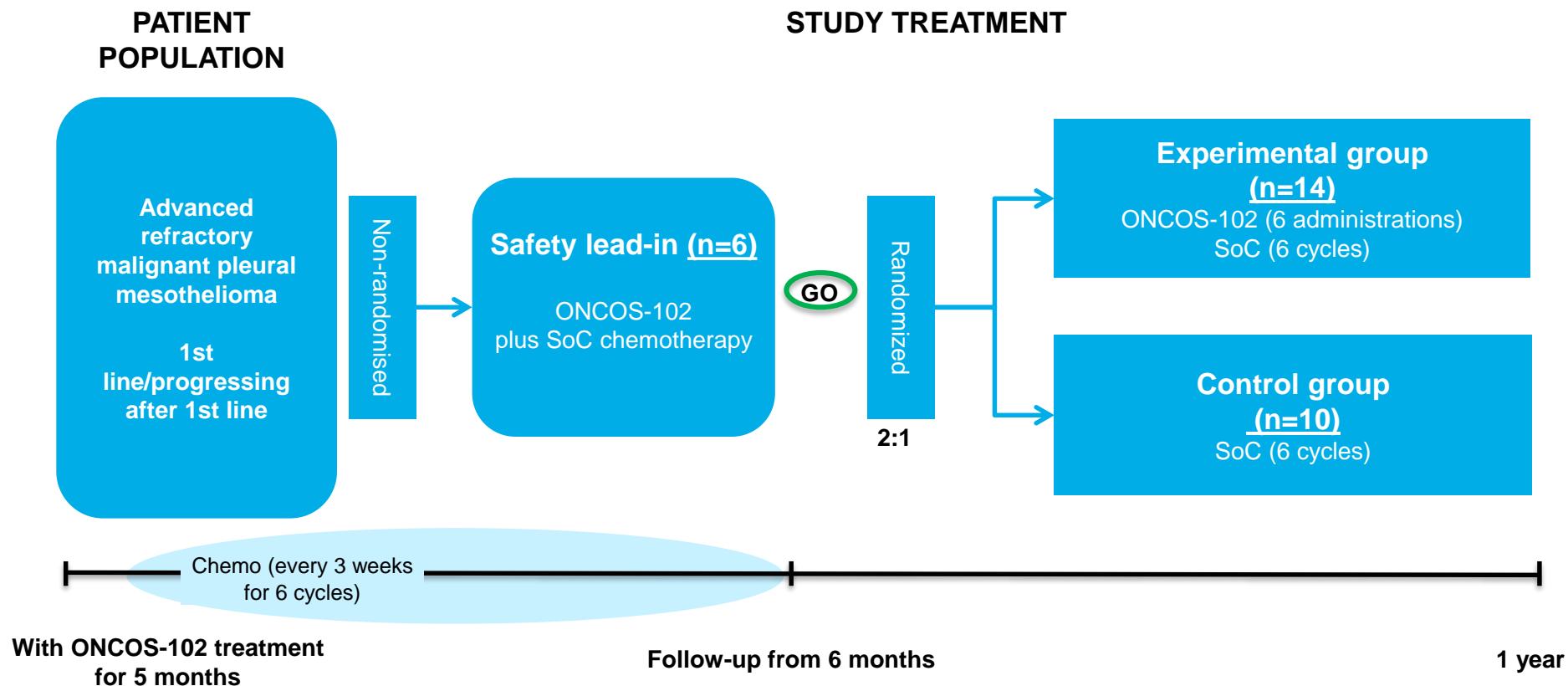
Open-label Phase I trial

- ONCOS-102: 3 injections at day 1, 4 & 8
- CPI (Keytruda) at day 22, then every 3 weeks for 5 months

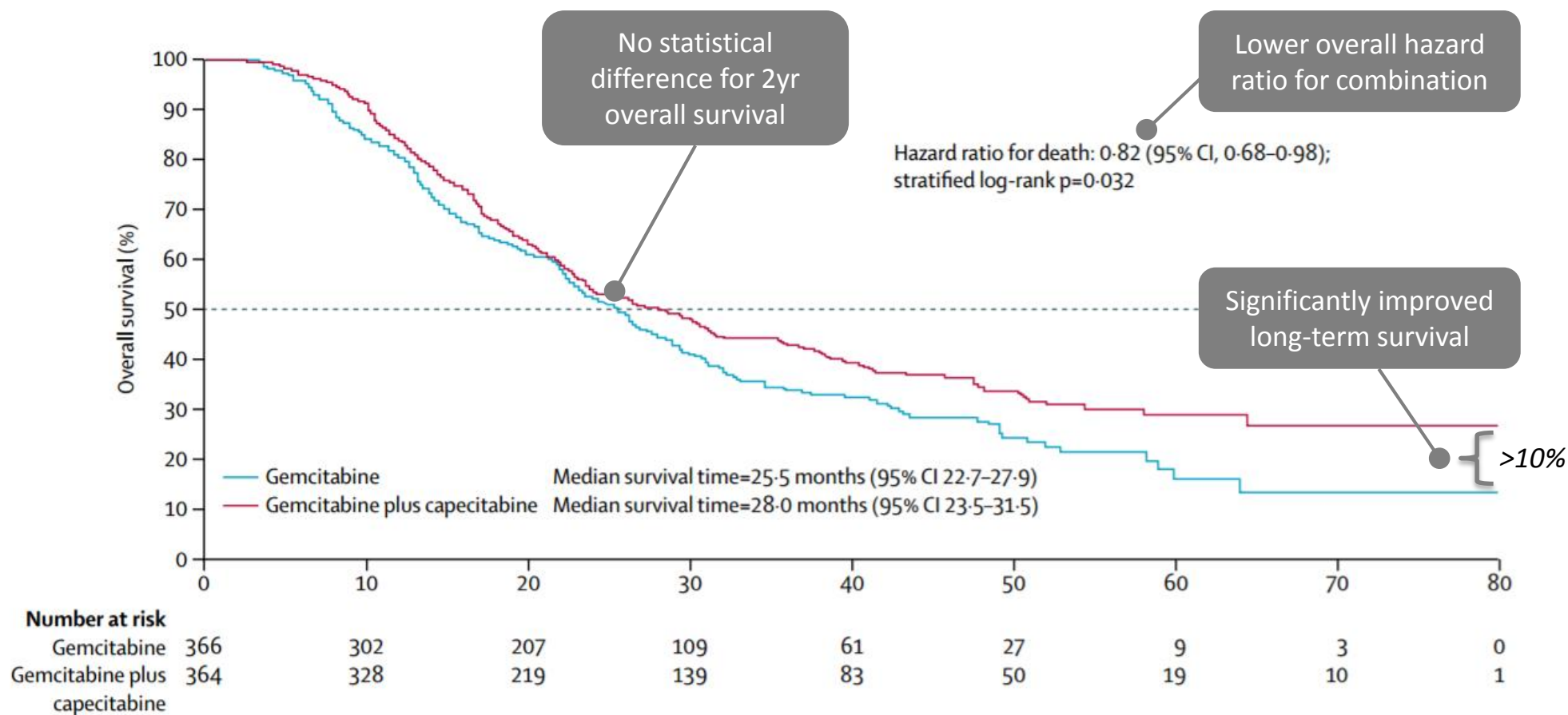




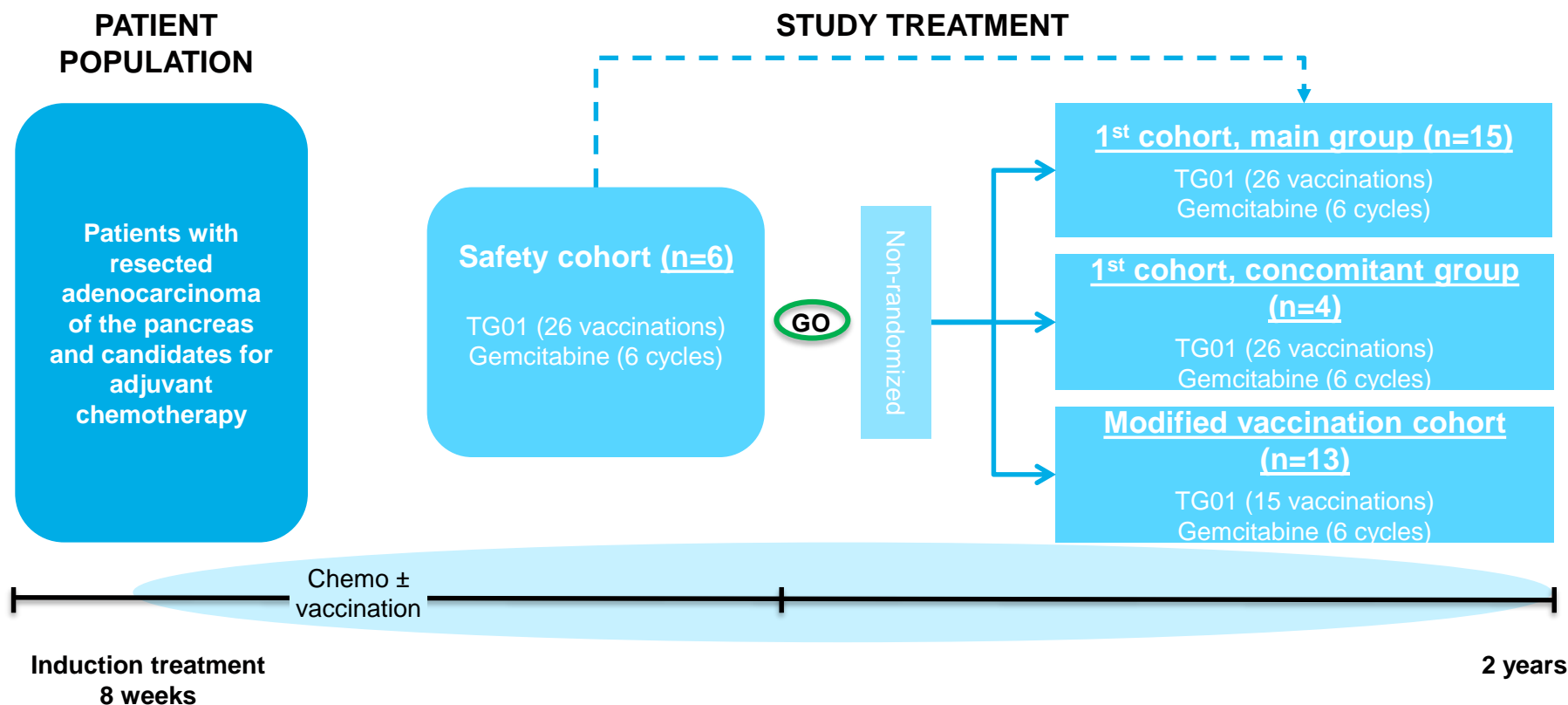
## ONCOS-102 in Mesothelioma – Phase I/II study design (NCT02879669)



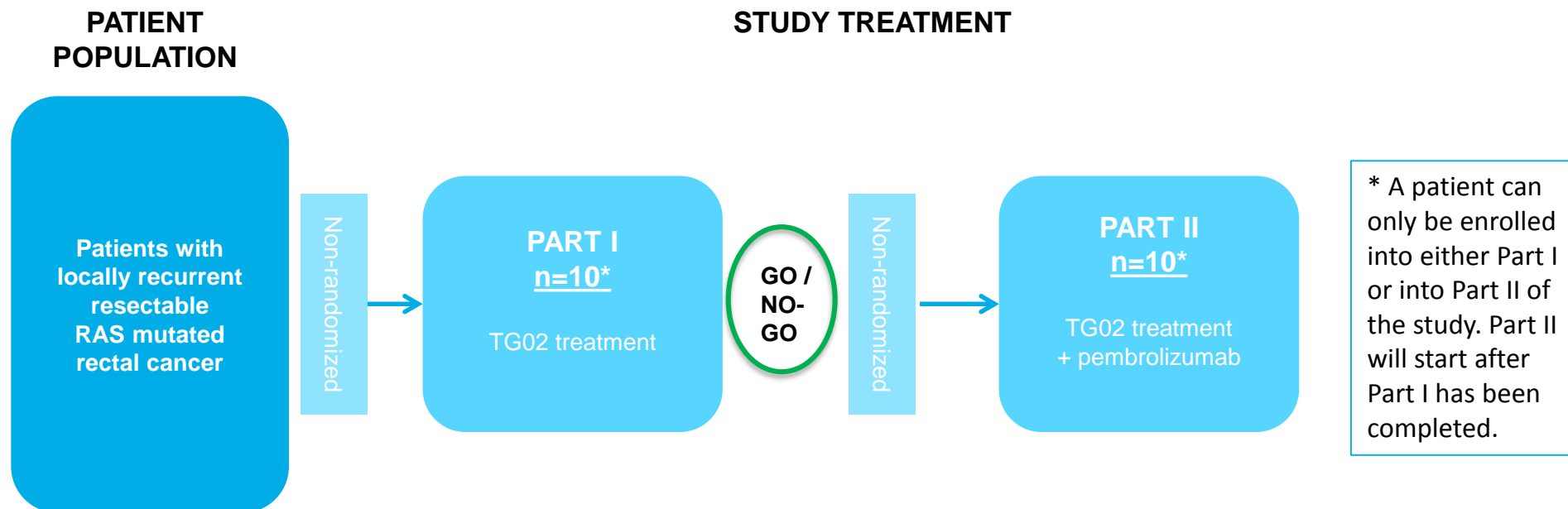
# Resected pancreatic cancer patients only have chemotherapy as a treatment option, and long term survival is poor



## TG01 in Resected Pancreatic Cancer – Phase I/II study design (NCT02261714)



## TG02 in Colorectal Cancer – Phase I study design (NCT02933944)



Study plan →

1. Baseline biopsy and immune assay when patients enter the clinical trial.
  - Induction treatment with TG02 for the patients in Part I
  - Induction treatment with TG02 in combination with pembrolizumab for the patients in Part II
2. Surgery 8 to 14 weeks after initiation of treatment. Immune assay of resected tumor.

# The results are being supported by 10 year long-term survival data from earlier TG trials

## Historical 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
- Correlation between immune response and clinical outcome

## 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

<sup>1</sup> Wedén et al, 2011 and Clinical trial reports

# 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>

# Highly experienced senior management team



## **Øystein Soug, CEO**

Joined as CFO in April 2015 before being appointed CEO in November 2016. Before joining Targovax Øystein 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



## **Dr. Magnus Jaderberg, CMO**

More than 25 years in various R&D functions and previously CMO at Bristol Meyers Squibb (Europe). Led development of Yervoy.



## **Erik Digman Wiklund, CFO**

Former consultant in the Pharma & Healthcare practice of McKinsey & Company, combined with a PhD in cancer research. Experience from management consulting, as well as commercial and operational roles in the biotechnology industry



## **Jon Amund Eriksen, CTIO**

35 years of R&D experience from pharmaceutical and biotech industry, 25 years within immuno-oncology. Co-founder of Targovax



## **Berit Iversen, VP, CMC**

More than 25 years of experience within Research & Development in the pharmaceutical and biotech industry. Berit is a Chemist by training



## **Tina Madsen, VP, Quality Assurance**

More than 20 years of experience within Research & Development and commercial manufacturing in the pharmaceutical and biotech industry, including quality assurance, process development and formulation



## **Anne-Kirsti Aksnes, VP, Clinical Development**

More than 20 years of experience within clinical research and development in the pharmaceutical and biotech industry and 10 years of experience working in clinical physiology.



## **Tiina Hakonen, Site Manager Helsinki**

More than 20 years of experience within clinical research and development in the pharmaceutical and biotech industry. Tiina has a Master of Science (Statistics) degree from the University of Oulu, Finland



## **Peter Skorpil, VP, Business Development**

Extensive experience in licensing, commercial assessments, business intelligence and partnering and previously Commercial Director at Pronova BioPharma

# Board of Directors



## **Jónas Einarsson, MD**

- CEO of Radiumhospitalets Forskningsstiftelse
- On the board of several Norwegian Biotech companies, and was one of the initiators behind Oslo Cancer Cluster and the Oslo Cancer Cluster Innovation



## **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



## **Eva-Lotta Allan**

- Currently 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)



## **Lars Lund-Roland**

- CEO of Bringwell AB
- Previously MD of MSD Norway (Merck & Co Inc. subsidiary) and has more than twenty-five years' experience from various executive positions within marketing and sales
- Chairman of the Board of PI Innovation and has served as board member of Infodoc and Health Tech



## **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®