



Arming the patient's immune system to fight cancer

3Q 2017 presentation

2 November 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 relating to the company's ability to retain key personnel; and risks relating to the impact of competition.



### **Agenda**

- O 3Q 2017 Highlights
- Program overview
- TG mutRAS neo-antigen cancer vaccine platform
- ONCOS-102 oncolytic virus platform
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### Highlights from the third quarter 2017

Initiation of the phase I/II trial with ONCOS-102 in combination **Clinical trials** with durvalumab for patients with ovarian and colorectal cancer Granted US patent for the therapeutic use of the TG products **Patents** in combination with anti-metabolite chemotherapy Three posters presented at the ESMO annual meeting in **Clinical data** Madrid - European Society of Molecular Oncology Raised NOK 6.4m (USD 0.8m) in a subsequent offering in July, **Financing** following the NOK 200m private placement in June Reported one-year data for the 2<sup>nd</sup> cohort in the TG01 ph I/II **trial** in resected pancreatic cancer – in line with the 1<sup>st</sup> cohort **Post-period** Granted US patent for the 2<sup>nd</sup> generation product from the TG platform, TG02



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#### Immunotherapy has the potential to cure cancer

Patient example - Yervoy® checkpoint inhibitor trial





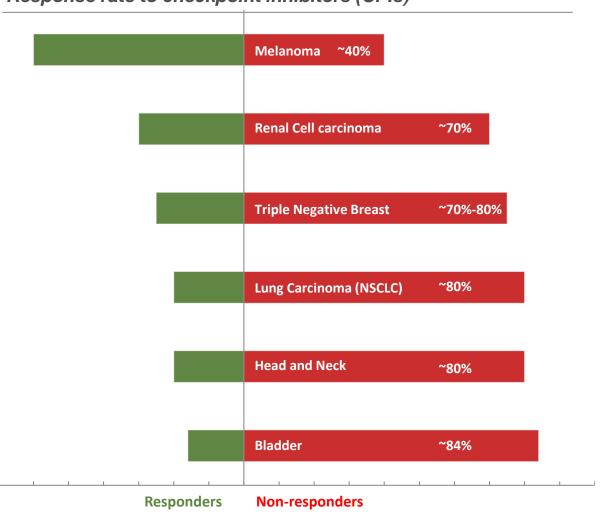
Prior to Yervoy®

1 year after



# Most patients do not respond to currently available immunotherapies

Response rate to checkpoint inhibitors (CPIs)



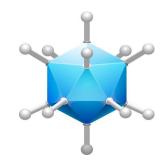
Complimentary
immune priming
medicines may make
tumors respond
better to checkpoint
inhibitors



# Targovax is developing two drugs to boost the effect of immunotherapy

### ONCOS-102 Oncolytic virus

- Genetically tailored oncolytic adenovirus
- Selectively infects and lyses cancer cells
- Triggers tumor specific immune response
- Phase I completed and 4 ongoing Phase I/II trials



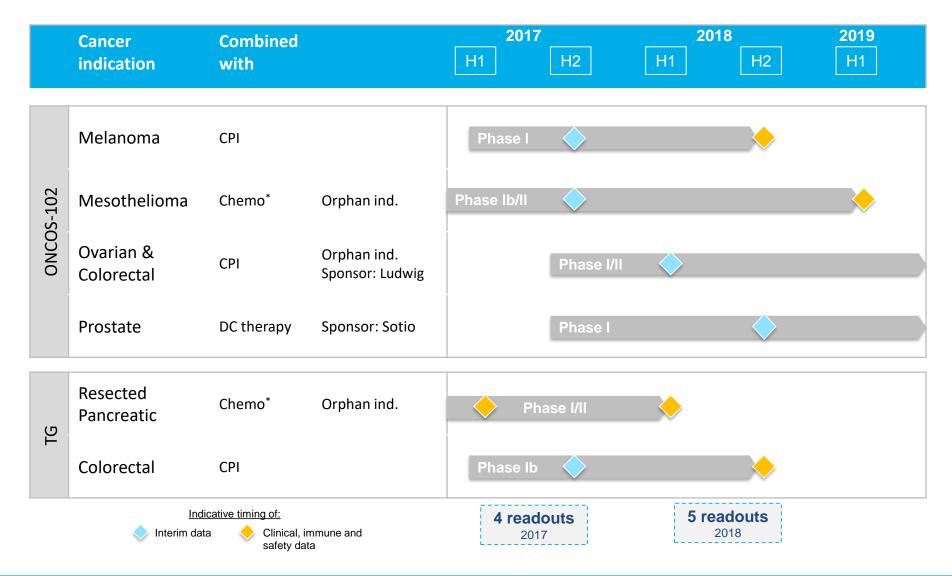
## **TG01**Neoantigen vaccine

- Cocktail of synthetic peptides targeting oncogenic RAS mutations
- Generates RAS-specific CD4+ and CD8+ T-cells
- T-cells circulate and identify cancer cells displaying mutated RAS epitopes
- Encouraging survival data from Phase I/II trials in pancreatic cancer





#### Clinical program and upcoming data read-outs

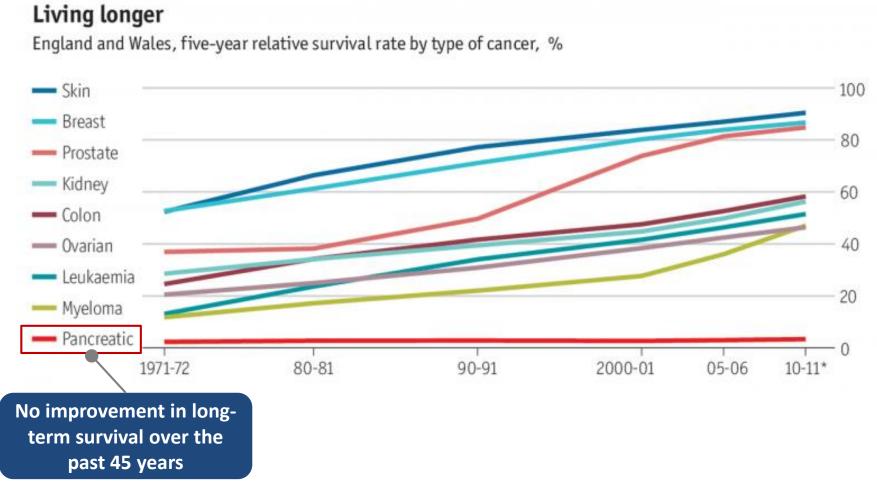


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# The five year survival rate for pancreatic cancer patients has not improved since the 1970s

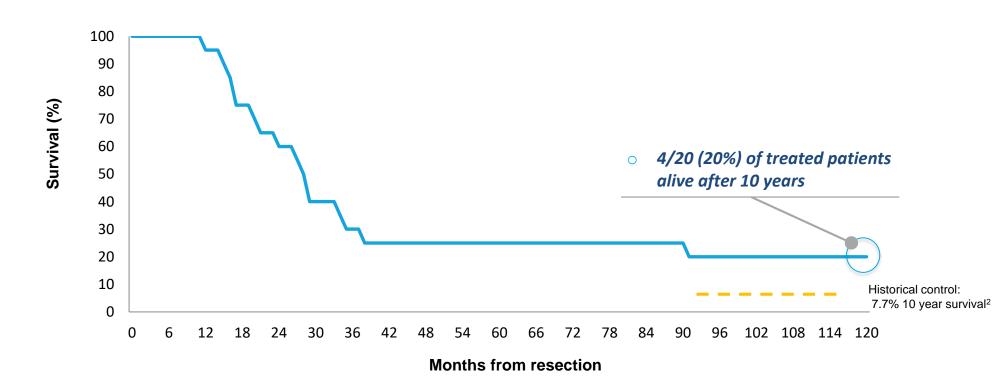




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# In earlier trials, TG vaccination has shown 20% 10-year survival in retrospective analyses

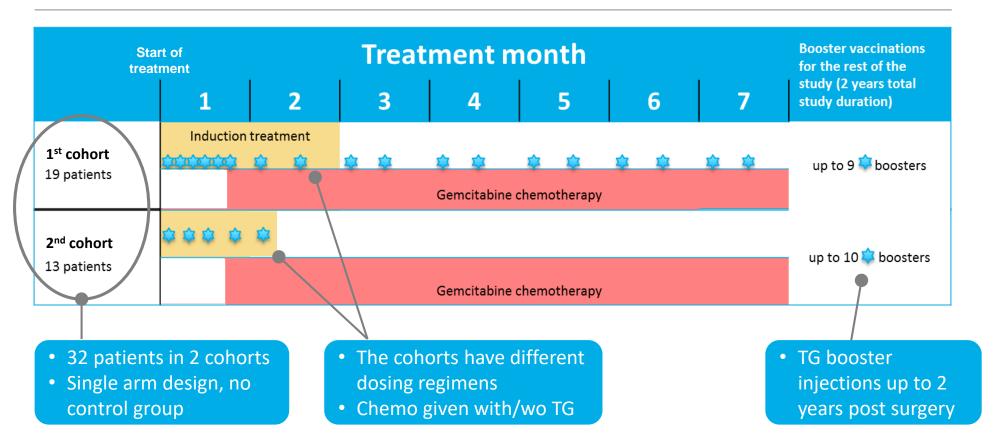
10 year survival in historical TG trials in resected pancreatic cancer (n=20, TG monotherapy)<sup>1</sup>





# Targovax was set up to validate the TG concept in a modern setting with adjuvant chemotherapy

Ongoing Phase I/II trial in resected pancreatic cancer with adjuvant Gemcitabine (SoC)





# Survival, immune activation and safety data from the ongoing TG trial is so far very encouraging

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

- Median survival 33.1 months vs. 27.6 for historical control<sup>1</sup>
- 13 of 19 patients (68%) alive 2 years after surgery, historical control 2 year OS range from 30-53%<sup>2</sup>

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

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

mutRAS immune response (1 yr)

- 1st cohort 18/19 patients (95%) had immune activation
- o 2<sup>nd</sup> cohort 11/13 patients (85%) had 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)



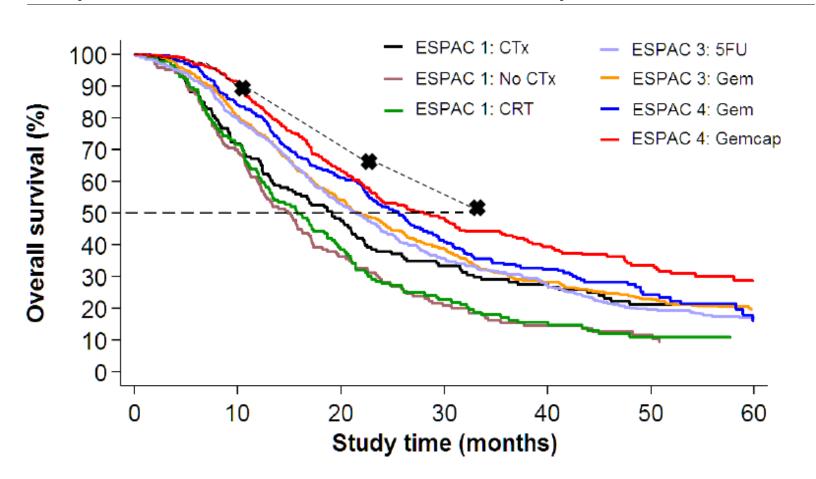
<sup>1:</sup> Based on ESPAC-4 reported 25.5 months median OS from randomisation, adding median time from surgery to randomization of 64 days (2.1 months)

<sup>2:</sup> Relevant historical control trials, not including ESPAC-4, which did not report 2 year OS

#### TG01 data in context

#### Ref. 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

# Immunological response (DTH) to TG01 is associated with increased survival in non-resectable pancreatic cancer

#### Observational study of 25 patients receiving 12 vaccinations during 1 year

Advanced pancreatic cancer TG01/GM-CSF (mono-therapy)	Evaluable patients	<b>Median survival</b> (from 1 <sup>st</sup> vaccination)	<b>1 year survival</b> (from 1 <sup>st</sup> vaccination)
Detected immune response	14 / 25 (56%)	5.2 months	3 (21%)
Not detected Immune response	11 / 25 (44%)	3.6 months	1 ( 9%)

Ref. ESMO 2017



Large safety database

### Clinical development overview for the TG program

**Planned / recruiting trials Historical trials Completing trial**  Ph IIb-III adaptive design Resected pancreas Aimed to reach registration TG01 - Phase IIb/III Currently seeking n = tbdPhase I Phase I/II collaboration opportunities Resected & Resected pancreatic cancer non-resected >200 patients 32 patients TG02, targets 8 mutations Colorectal - TG02 Combination w/KEYTRUDA® Phase I Encouraging median 10 year survival data Currently recruiting patients 20 patients survival Correlation between immune response and 3 year survival rate survival in 1H 2018



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# How TG is different from other peptide vaccine approaches, and 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 neoantigen, and a driving cause of cancer

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

TG peptides are designed and proven to induce both CD4+ helper and CD8+ killer mutRAS-specific T-cells

**Depot-forming adjuvants not suitable**, as activated T-cells return to depot instead of tumor site Non depot-forming immune modulator GM-CSF used as adjuvant to stimulate strong, systemic T-cell response



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#### Targovax has initiated a broad clinical program to test the clinical benefit of ONCOS-102

Compassionate use program **Finland** 115 patients

- Testing within ATAP EU program
- Individual clinical responses
- Reassuring safety data

**Initial Phase I trial** Solid tumors 7 indications

- 12 refractory patients
- Monotherapy
- Correlation between immune activation and survival

Melanoma Phase I 12 patients

- Combination with PD-1 CPI in refractory patients
- Proof-of-concept
- Memorial Sloan Kettering

Mesothelioma Phase I/II - controlled 30 patients

- Combination with chemo
- Randomized controlled trial
- Ultra-orphan indication

Ovarian / colorectal Phase I/II - controlled 78 patients

- Collaboration with Ludwig & CRI
- Combination with Medimmune's durvalumab (Imfinzi™)
- Randomized controlled trial

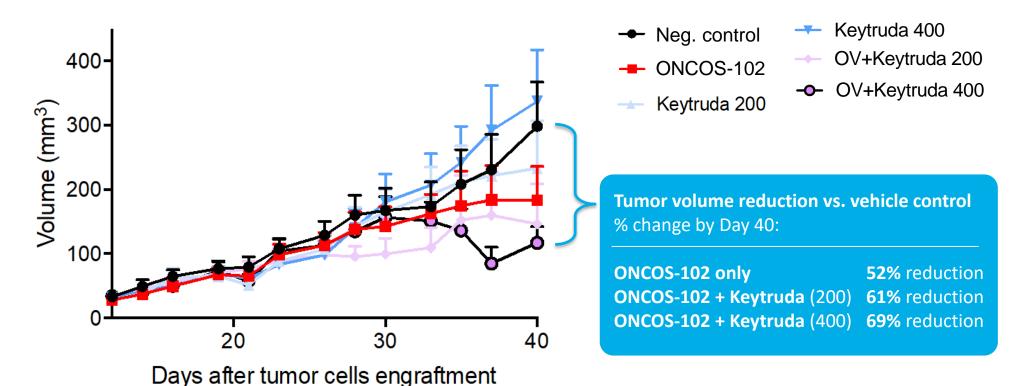
**Prostate** Phase I 10 patients

- Partnered with SOTIO
- Combination with DC therapy



## ONCOS-102 in melanoma – 70% reduction in tumor volume with KEYTRUDA® combination in mouse model

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





## The mouse data support the scientific rationale of the ongoing clinical melanoma study with ONCOS-102 and KEYTRUDA®

### Reduction in tumor volume

- ONCOS-102 + KEYTRUDA® (high) reduced volume by 69%
- ONCOS-102 alone reduced tumor volume by 51%
- KEYTRUDA® alone did not reduce tumor volume

### CD8+ T-cell infiltration

- ONCOS-102 + KEYTRUDA® >2-fold increase in CD8+ T-cell count in tumor (vs. neg. control and vs. KEYTRUDA® alone)
- KEYTRUDA® alone no change

#### **Conclusions**

- Synergistic anti-tumor effect of ONCOS-102 + KEYTRUDA®
- ONCOS-102 primes the immune system and enhances response to KEYTRUDA®



## In Q3, a large trial combining ONCOS-102 and the PD-L1 CPI durvalumab in ovarian and colorectal cancer was initiated

Indication

- Ovarian cancer 42 patients
- Colorectal cancer 36 patients
- Safety lead-in 6 patients

Route of administration

Intraperitoneal administration via catheter

**Combination** 

MedImmune's PD-L1 checkpoint inhibitor durvalumab (Imfinzi™)

Partners and sponsor

- Funded by Cancer Research Institute (CRI)
- Sponsored by Ludwig Cancer Research



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# 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

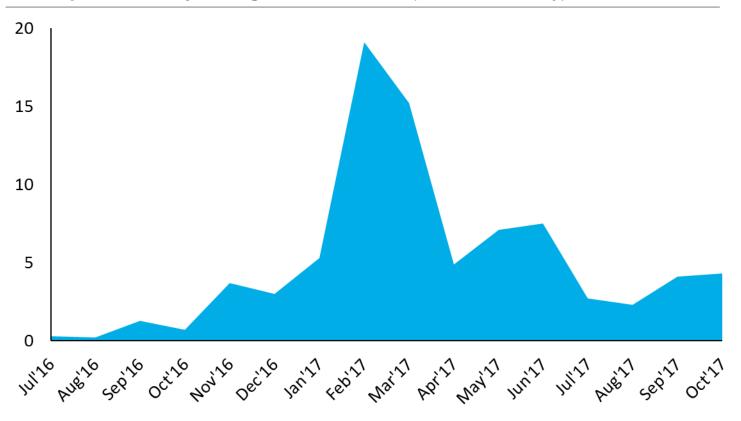
Operations			
Cash end of Q3	NOK 286m	USD 36m	Sep 30 <sup>th</sup> 2017
Net cash flow	NOK -24m	USD -3m	Total Q3
Annual run rate	NOK 106m	USD 13m	Last four quarters

The share	OSE: TRVX			
Market Cap	NOK 950m	USD ~120m	At share price NOK ~18	
Daily turnover	NOK 5m	USD 0.6m	Rolling 6 month avg.	
Analysts	DNB, ABG Sundal Collier, Arctic, Redeye, Norske Aksjeanalyser, Edison			



# Targovax is listed on the main board on the Oslo Stock Exchange, with average daily liquidity of NOK 3.5m

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



- NOK ~930 m market cap
- NOK 3.5m NOK avg. daily turnover in last 3 months
- NOK 197m total turnover in 3Q
- 160k shares avg. daily volume in 3Q
- >4,800 owners
- **52.6m shares**\* (56.2 fully diluted)

targovax

# The shareholder base is strong, with a mix of specialist, generalist and retail investors

Shareholder		<b>Estimated ownership</b>	
		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 %
Top 20		31,0	59,0 %
Other shareholders (4160)		21,6	41,0 %
Total		52,6	100,0 %

#### 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%
  - 4,180 shareholders



# Planned strong news flow with multiple near term value inflection points

