

# Activating the immune system to fight cancer

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New York City

Dr. Magnus Jäderberg - CMO  
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The logo for Targovax, featuring the word "targovax" in a lowercase, sans-serif font. The letter "o" is replaced by a stylized circular icon composed of three smaller circles arranged in a triangle. The background of the logo is a white circle.

targovax

# 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.

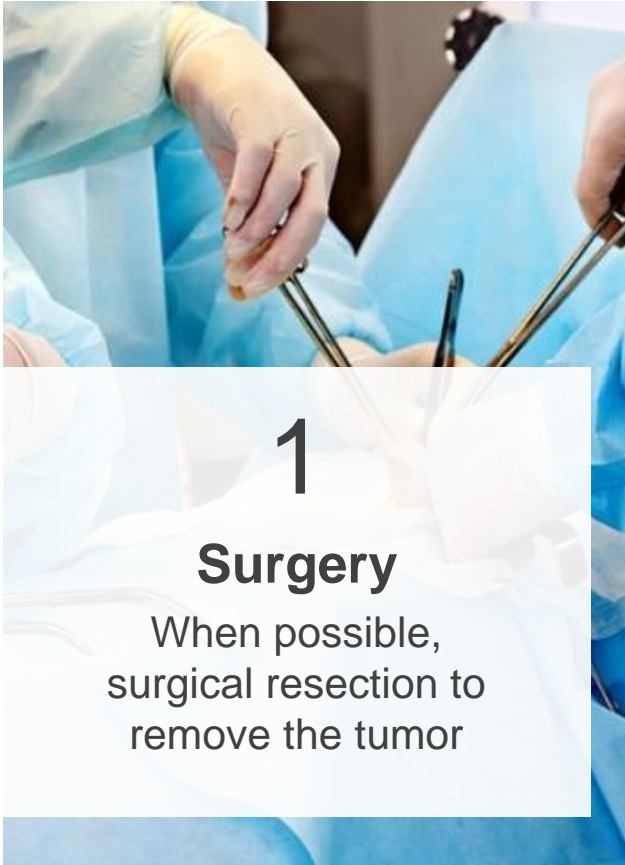
There are a number of factors that could cause actual results and developments to differ materially from those expressed or implied in these forward-looking statements. These factors include, among other things, risks or uncertainties associated with the success of future clinical trials; risks relating 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.

# 1

## Introduction

2. ONCOS oncolytic virus program
3. TG mutRAS neoantigen vaccine program
4. Targovax pipeline
5. Corporate overview

# From a sequential treatment strategy directly targeting the cancer...



1

## Surgery

When possible,  
surgical resection to  
remove the tumor



2

## Radiotherapy

Tumor irradiation  
to shrink  
tumor volume



3

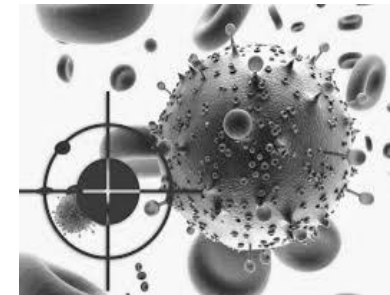
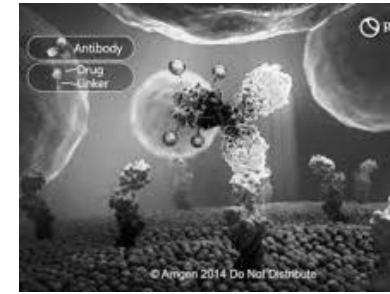
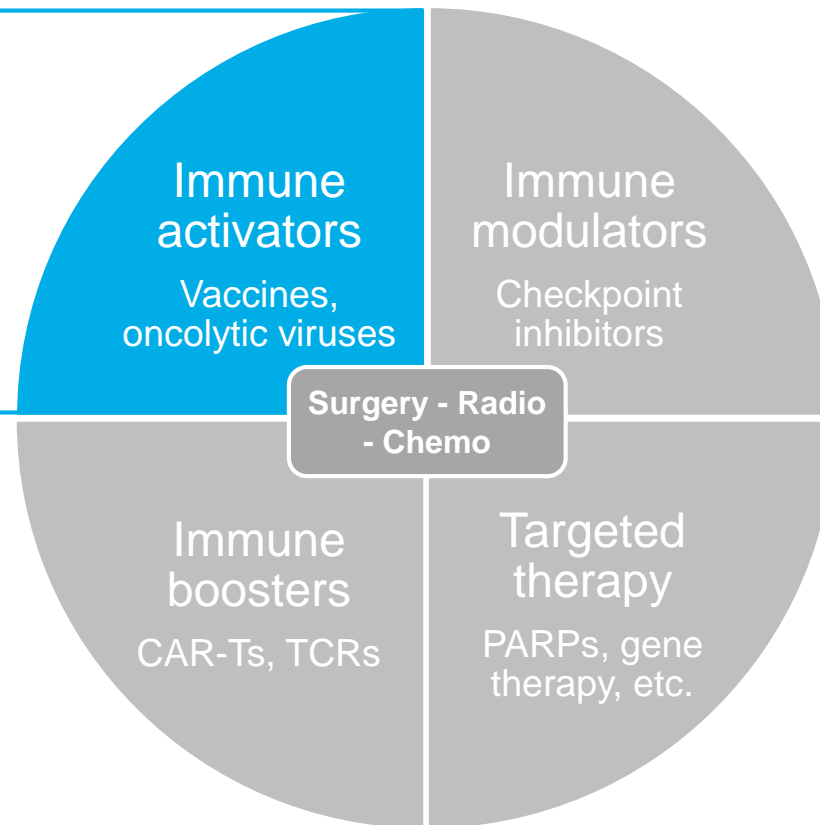
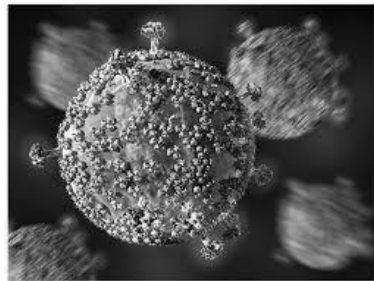
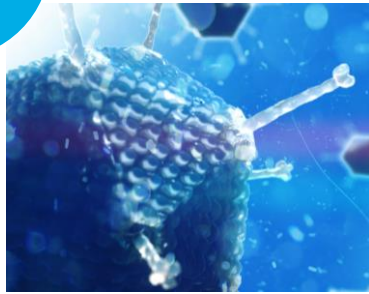
## Chemotherapy

Cornerstone treatment  
in most cancer forms

...to an integrated combination approach

# HARNESSING THE POWER OF THE PATIENT'S OWN IMMUNE SYSTEM

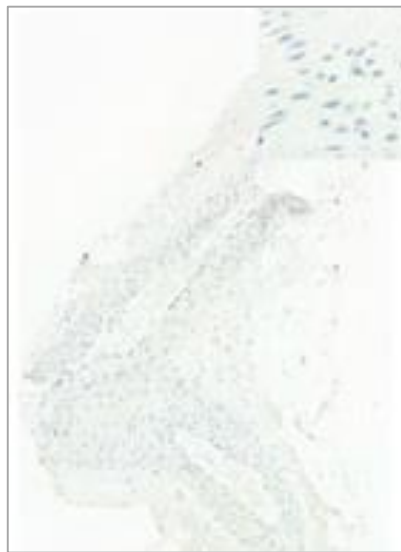
Targovax focus



Mode of action

# IMMUNE ACTIVATORS TURN COLD TUMORS HOT

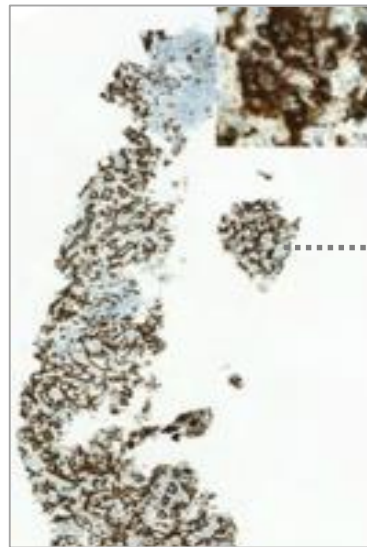
Example from Targovax Phase I trial – Ovarian cancer patient



**Before injection of  
oncolytic virus**

“Cold tumor”

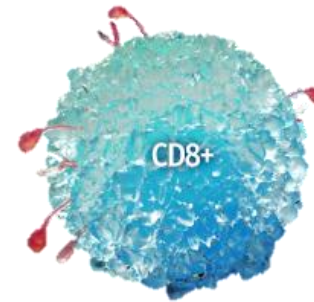
No T-cell infiltration



**After injection of  
oncolytic virus**

“Hot tumor”

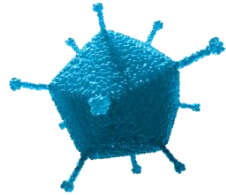
Full T-cell infiltration



**CD8+ T-cell**

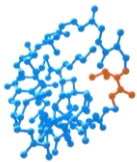
Recognizes  
and destroys  
cancer cells

# Targovax has two complementary programs in clinical development, **PROVEN TO ACTIVATE THE IMMUNE SYSTEM**



**ONCOS**  
Oncolytic virus

- Genetically **armed adenovirus**
- **Alerts the immune system** to the presence of cancer antigens
- **Induces T-cells** specific to patients' tumor



**TG**  
RAS neoantigen  
vaccine

- **Shared neoantigen**, therapeutic cancer vaccine
- Triggers the immune system to **recognize oncogenic, mutated RAS** neoepitopes
- Induces mutant **RAS-specific T-cells**

*Activates the  
immune system*

*Triggers patient-  
specific responses*

*No need for  
individualization*

# 2

## ONCOS oncolytic virus program

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# ONCOS-102

Phase I proof of concept

## IMMUNE ACTIVATION DEMONSTRATED

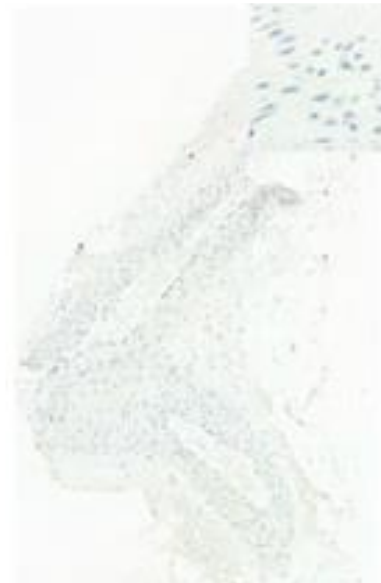
### ONCOS-102 Phase I trial design:

- **12 patients, 7 different solid tumors**
  - Ovarian, Mesothelioma, Colorectal, Sarcoma, Liver, Lung
- **No other treatment options left**
  - All chemotherapy refractory
- **ONCOS-102 monotherapy**
  - 9 injections over 5 months

### Top-line results:

- **100% innate immune activation**
- **11/12 patients increase in CD8+ T-cells**
- **40% stable disease**
- **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

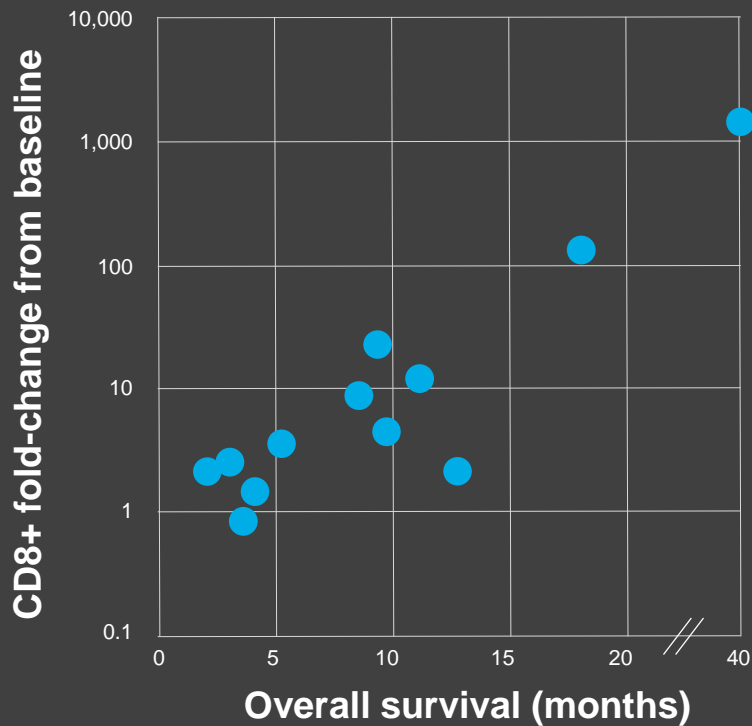
# ONCOS-102

Phase I proof of concept

## 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 CD8+ T-cell infiltration
- **Tumor specific T-cells detected** up to 2 years after treatment
- **Stable disease for 3 years**, survived for 3.5 years

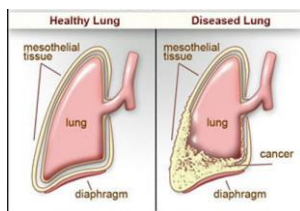
# ONCOS

## CLINICAL DEVELOPMENT STRATEGY

1

### Mesothelioma

Orphan disease



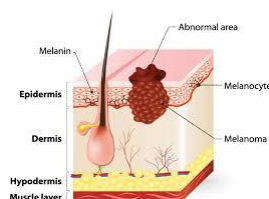
#### Target launch indication

- Orphan drug status
- Aim to become addition to SoC
- Ongoing Phase I/II
- 15,000 patients per year

2

### CPI synergy

Intra-tumoral



#### Indications with no/limited effect of CPIs

- Ongoing melanoma Phase I
- Combo w/PD-1
- >100,000 patients per year

3

### CPI synergy

Intra-peritoneal



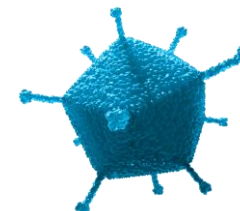
#### Peritoneal malignancies

- Ongoing Phase I/II in ovarian and colorectal
- Combo w/PD-L1
- >100,000 patients per year

4

### Next generation

ONCOS viruses

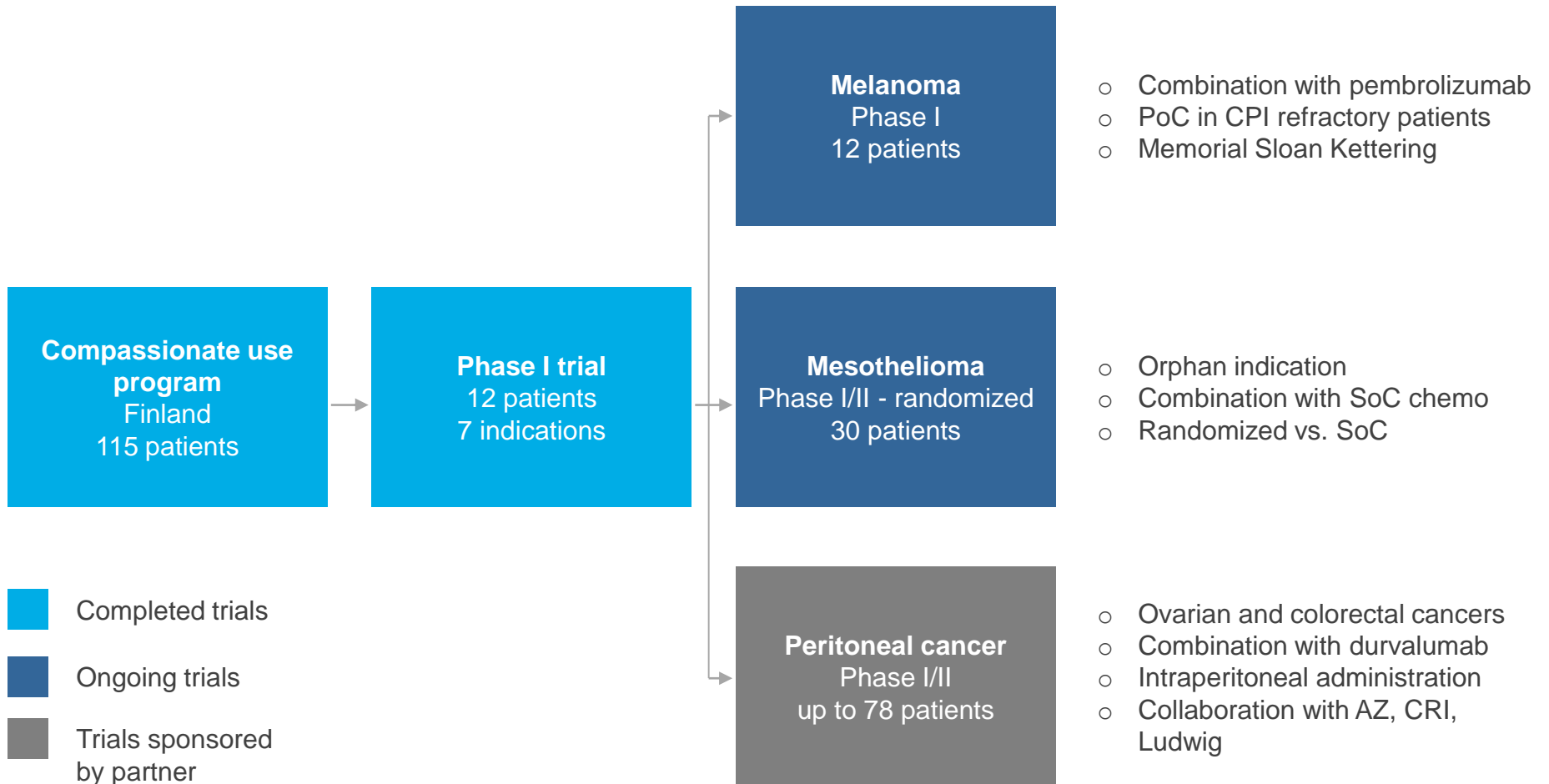


#### Double transgene adenoviruses

- Novel targets
- Ongoing *in vivo* testing
- Broad spectrum of solid tumors

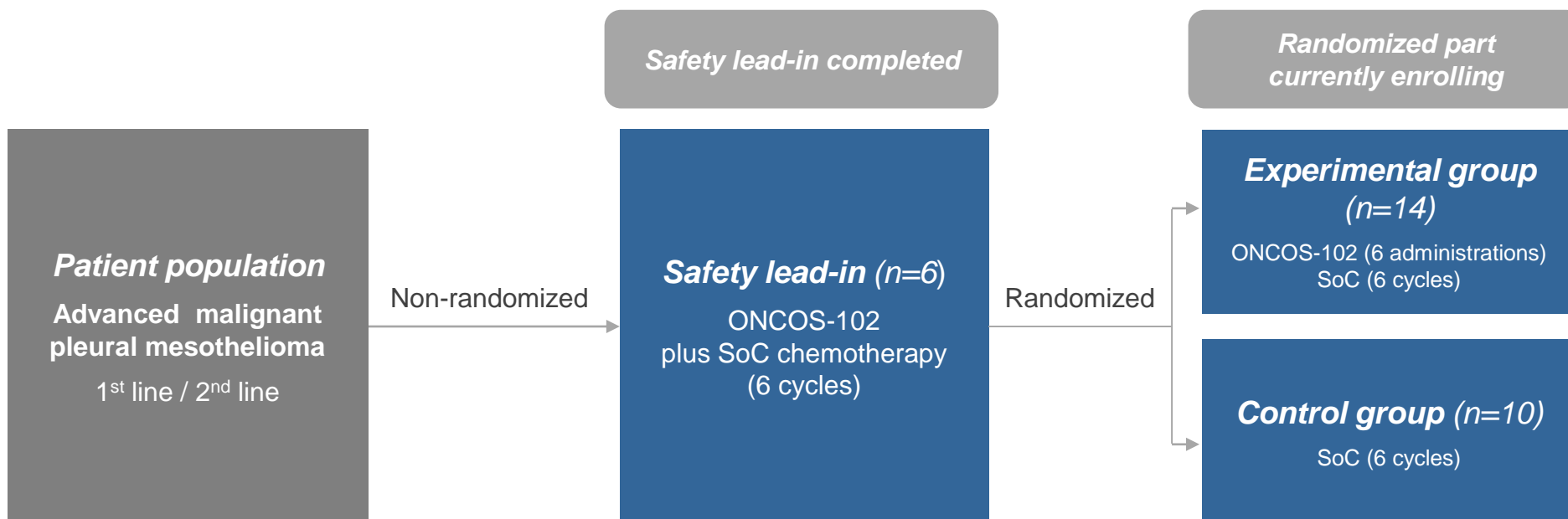
# ONCOS

## CLINICAL PROGRAM OVERVIEW



# ONCOS-102 in malignant pleural mesothelioma

## PHASE I/II STUDY DESIGN IN COMBINATION WITH SoC



# ONCOS-102 in malignant pleural mesothelioma

## SIGNAL OF EFFICACY IN THE FIRST 6 PATIENTS

1

### Safety

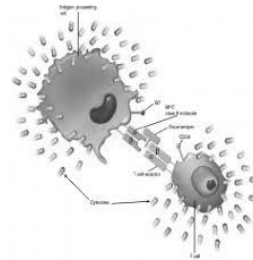
- ✓ ONCOS-102 **well-tolerated** in combination **with chemotherapy**



2

### Innate immune activation

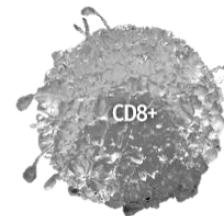
- ✓ **Systemic increase of pro-inflammatory cytokines** in 6/6 patients (IL-6, TNF $\alpha$  and IFN $\gamma$ )



3

### Adaptive immune activation

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



4

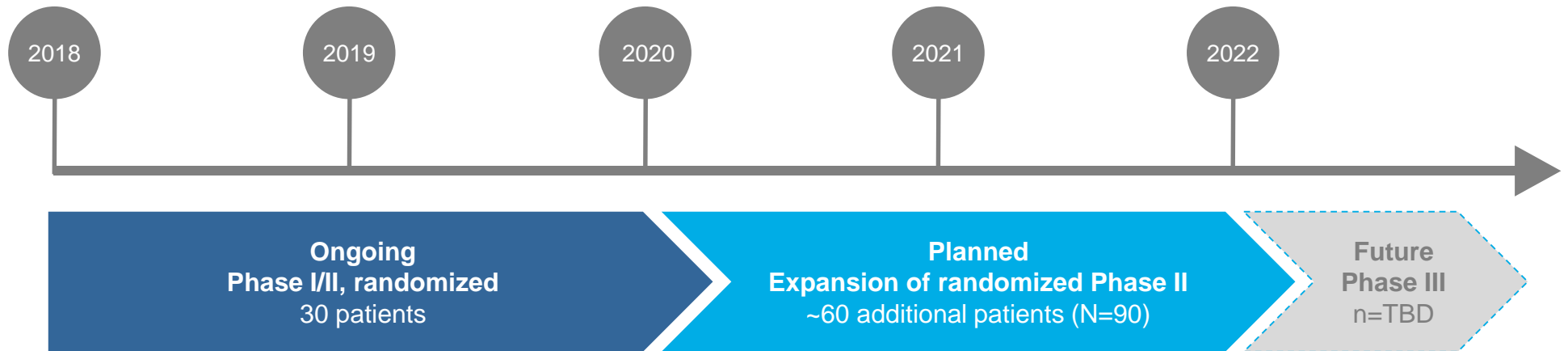
### Clinical activity

- ✓ **Clinical activity** seen in **3/6 patients** after 6 months
- ✓ **50% disease control rate**



# ONCOS-102 in malignant pleural mesothelioma

## DEVELOPMENT STRATEGY AND INDICATIVE TIMELINES



- Randomized ORR and OS data 30 patients
- Decide on possible CPI combination arm
- EMA & FDA advisory meetings

- Randomized ORR and OS data 90 patients
- Potentially use as basis for a submission for conditional approval
- Potentially start Phase III OS trial for full MAA

# 3

## TG mutRAS neoantigen vaccine program

4. Targovax pipeline
5. Corporate overview

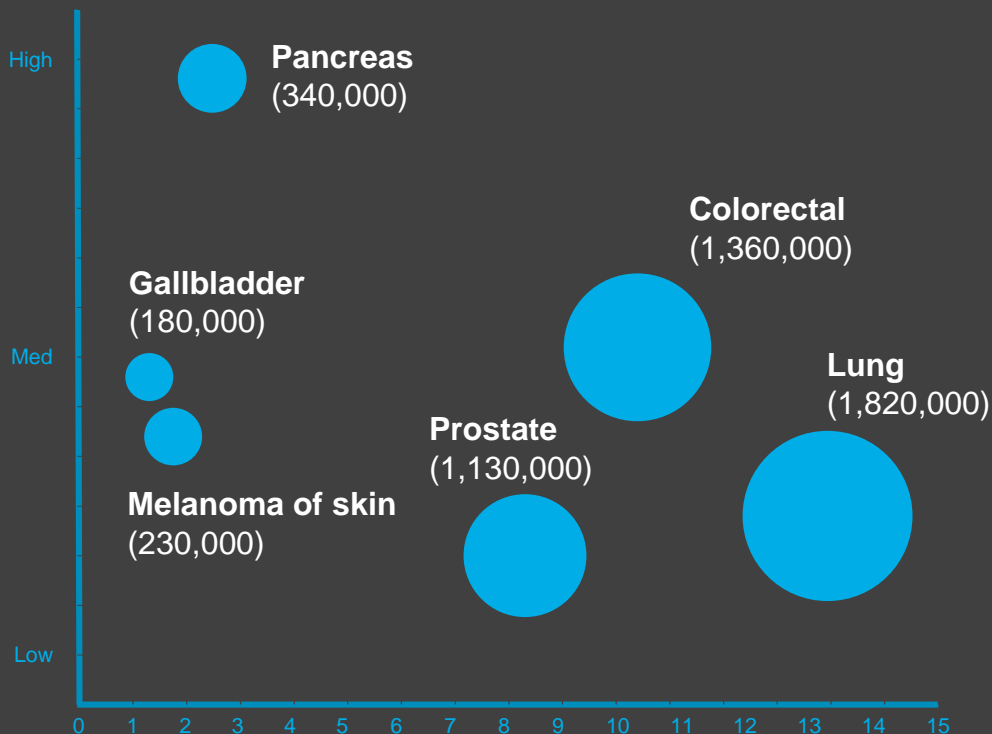


# The RAS gene is mutated in 90% OF PANCREATIC AND 50% OF COLORECTAL CANCERS

## Frequency of RAS mutations

Global cancer incidents per 10,000

(xx) = no. of cancer patients



- RAS mutations are oncogenic and result in **uncontrolled cell division**
- **There are no existing therapies** targeting RAS mutations
- Targovax' TG program is a **unique vaccine approach for mutant RAS cancer**

# WHY THE TG APPROACH MAY WORK

where other cancer vaccines have failed

## *Historical lessons learned*

**Target often poorly defined** and not cancer specific, mainly TAAs

**No or insufficient immune activation** of the adaptive immune system

Most clinical trials have been done in **advanced disease**

## *The TG approach*

Mutated **RAS** is a well-defined, cancer-specific neo-antigen, driving the cancer

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

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

# TG

## CLINICAL DEVELOPMENT STRATEGY

1

### Pancreatic cancer (resected)



#### TG01 lead indication

- Phase I/II completed
- Orphan drug status
- Up to 40,000 patients per year

2

### Colorectal cancer



#### TG02 lead indication

- Phase I trial ongoing
- 50% RAS mutated
- Up to 500,000 patients per year

3

### Lung cancer (NSCLC)

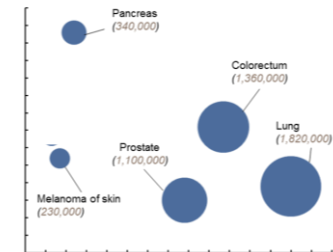


#### TG02 potential future indication

- 30% RAS mutated
- Up to 500,000 patients per year

4

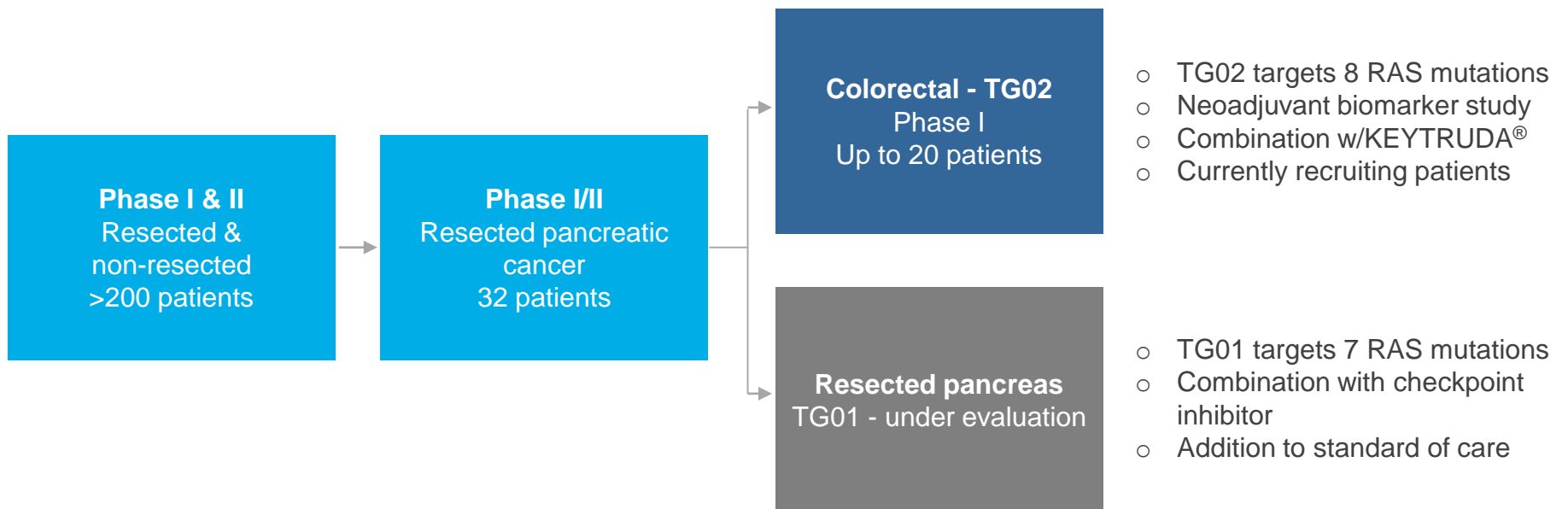
### All mutRAS cancers



#### TG02 + TG03 ultimate long-term potential

- 30% of all cancers
- Up to 30% of all cancer patients

# TG CLINICAL PROGRAM OVERVIEW



■ Completed trials ■ Ongoing trials ■ Planned trial

# TG01 IN RESECTED PANCREATIC CANCER

## SIGNAL OF EFFICACY DEMONSTRATED IN PHASE I/II TRIAL WITH ADJUVANT CHEMOTHERAPY

**Median overall survival (N=32)**

**33.4 vs. 27.6 months** reported in the ESPAC4 trial for gemcitabine alone (counting from time of surgery)

**2-year survival rate**

**23 out of 32 patients alive two years after surgery (72%)**, comparing to 30-53% two-year survival with gemcitabine alone

**1-year survival rate**

**30 out of 32 patients alive one year after surgery (94%)**

**mutRAS immune activation**

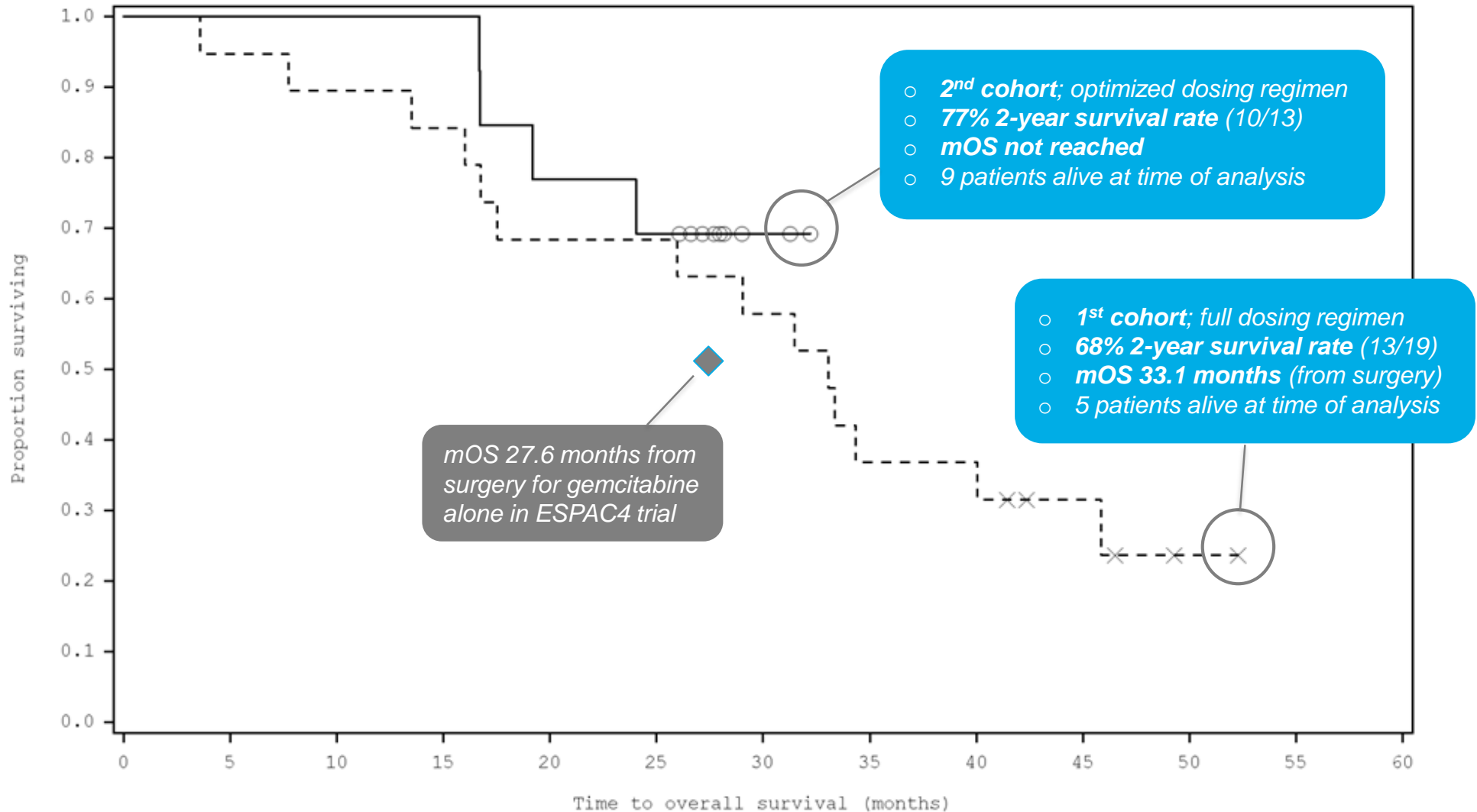
**29 out of 32 patients (90%)** had **RAS-specific immune activation** by one-year

**Dosing and safety**

**Optimized dosing regimen defined** for future development, and TG01 is well-tolerated in combination with chemotherapy

# TG01 CURRENT KAPLAN-MAIER SURVIVAL CURVES

First (n=19) and second (n=13) patient cohort

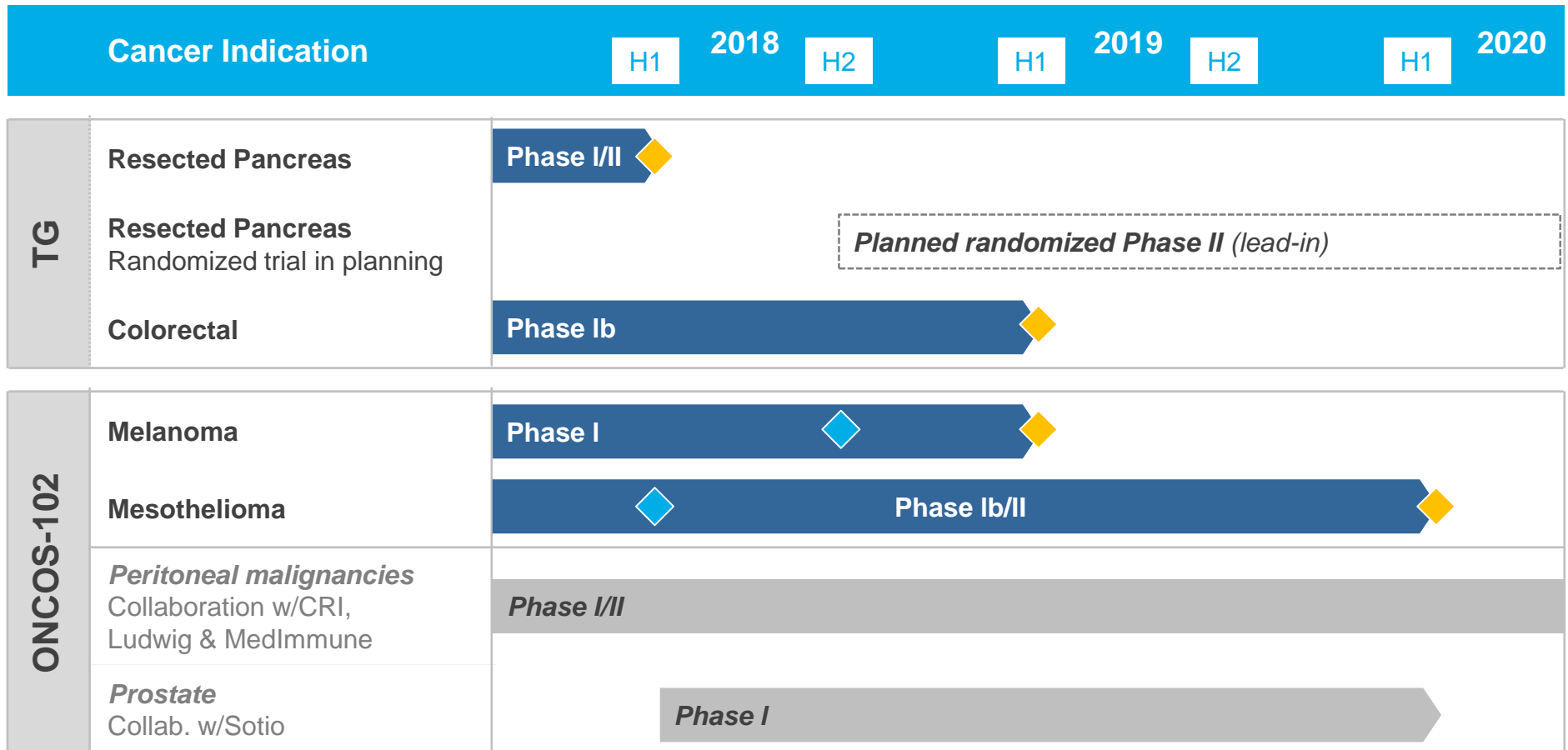


# 4

## Targovax pipeline

5. Corporate overview

# Targovax overall CLINICAL PROGRAM TIMELINES



◆ Interim data    
 ◆ Clinical, immune and safety data    
 ■ Ongoing clinical trials, Targovax sponsored    
 ■ Ongoing clinical trials, partner sponsored



# ACTIVATING THE PATIENT'S IMMUNE SYSTEM

to fight cancer

## Broad clinical program

Six shots on goal

Several upcoming data points

## Defined path to market

Aim to become frontline treatment in high unmet need cancers

Orphan status in mesothelioma and pancreas

## Innovative pipeline

Next gen double transgene viruses in testing

Systemic administration routes under evaluation

# 5

## Corporate overview

# TARGOVAX HAS A SOUND FINANCIAL POSITION

with cash to complete the planned clinical program well into 2019

## Operations

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Cash end of Q1 - Mar 31<sup>st</sup> 2018

**229 / 29**

NOK million    USD million

Net cash flow - total Q1

**-32 / -4**

NOK million    USD million

Annual run rate - last four quarters

**113 / 15**

NOK million    USD million

## The share

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Market Cap - at share price NOK ~17

**900 / 110**

NOK million    USD million

Daily turnover - rolling 6 month avg.

**3 / 0.4**

NOK million    USD million

Analyst coverage

DNB, ABG Sundal Collier, Arctic,  
Redeye, Norske Aksjeanalyser, Edison

# THE SHAREHOLDER BASE IS STRONG

with a mix of specialist, generalist and retail investors

| 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              | 2,1         | 4,0 %          |
| Statoil                          | Norway              | 1,2         | 2,3 %          |
| Thorendahl Invest                | Norway              | 1,0         | 1,9 %          |
| Danske Bank (nom.)               | Norway              | 0,8         | 1,6 %          |
| Timmuno                          | Norway              | 0,7         | 1,4 %          |
| Prieta                           | Norway              | 0,7         | 1,4 %          |
| Sundt                            | Norway              | 0,5         | 1,0 %          |
| Yngve S. Lillesund               | Norway              | 0,3         | 0,7 %          |
| NHO - P665AK                     | Norway              | 0,3         | 0,5 %          |
| DNB                              | Norway              | 0,2         | 0,4 %          |
| Tobech Invest                    | Norway              | 0,2         | 0,4 %          |
| Istvan Molnar                    | Norway              | 0,2         | 0,4 %          |
| Danske Bank (nom.)               | Norway              | 0,2         | 0,4 %          |
| Spar Kapital Investor            | Norway              | 0,2         | 0,3 %          |
| Peter Kenneth Zwilgmeyer         | Norway              | 0,2         | 0,3 %          |
| Rolf Arne Olsen                  | Norway              | 0,1         | 0,3 %          |
| Scott Paul Tønnessen             | Norway              | 0,1         | 0,3 %          |
| <b>Top 20</b>                    |                     | <b>30,6</b> | <b>58,3 %</b>  |
| <i>Other shareholders (4138)</i> |                     | <i>22,0</i> | <i>41,7 %</i>  |
| <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

### 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%
- >4,100 shareholders

Learn more at:  
[WWW.TARGOVAX.COM](http://WWW.TARGOVAX.COM)

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