

# Activating the patient's immune system to fight cancer

2Q & 1H 2018 Report

23 August 2018



targovax

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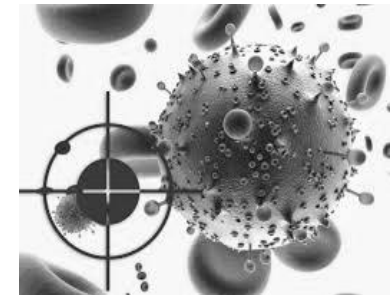
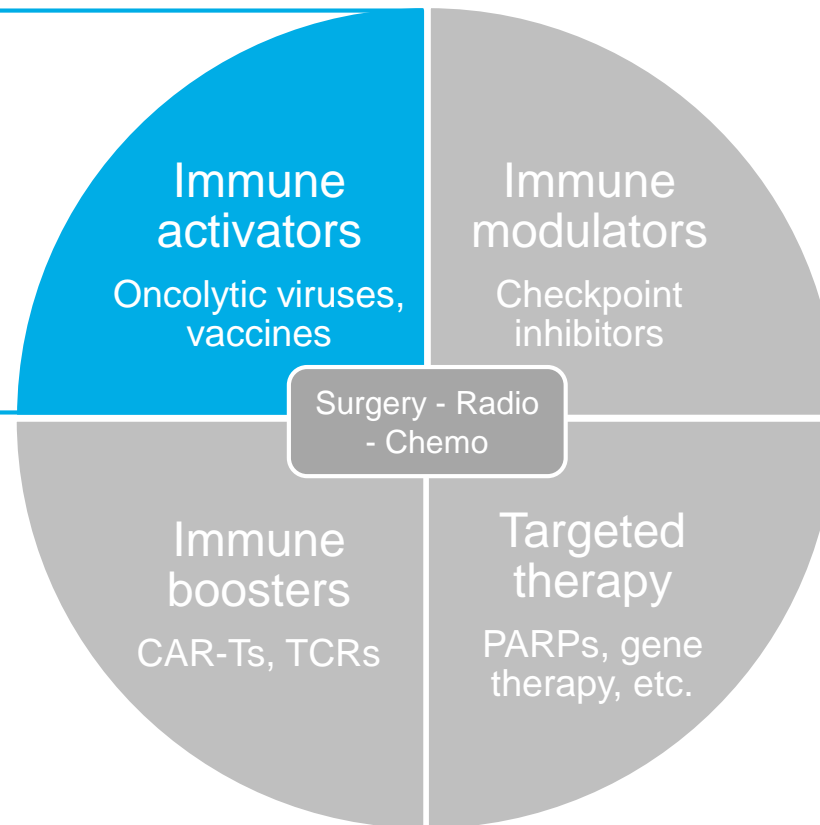
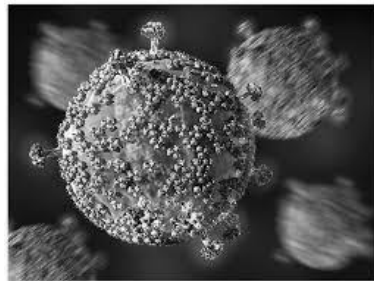
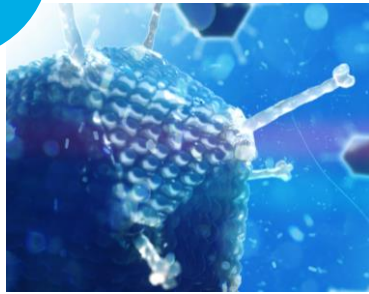
# 1

## Status & Highlights

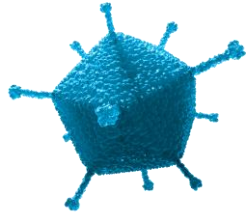
2. ONCOS oncolytic virus program update
3. 2Q & 1H 2018 Financials

# TARGOVAX AIM IS TO ACTIVATE THE PATIENT'S OWN IMMUNE SYSTEM TO FIGHT CANCER

Targovax focus



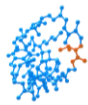
Targovax has two programs in clinical development, with an  
**ONCOLYTIC VIRUS LEAD PRODUCT CANDIDATE**



**ONCOS**  
Oncolytic virus

**Lead product candidate**

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



**TG**  
Neoantigen  
vaccine

**Pipeline product**

- **Shared neoantigen**, therapeutic cancer vaccine
- Triggers the immune system to **recognize mutant RAS cancers**

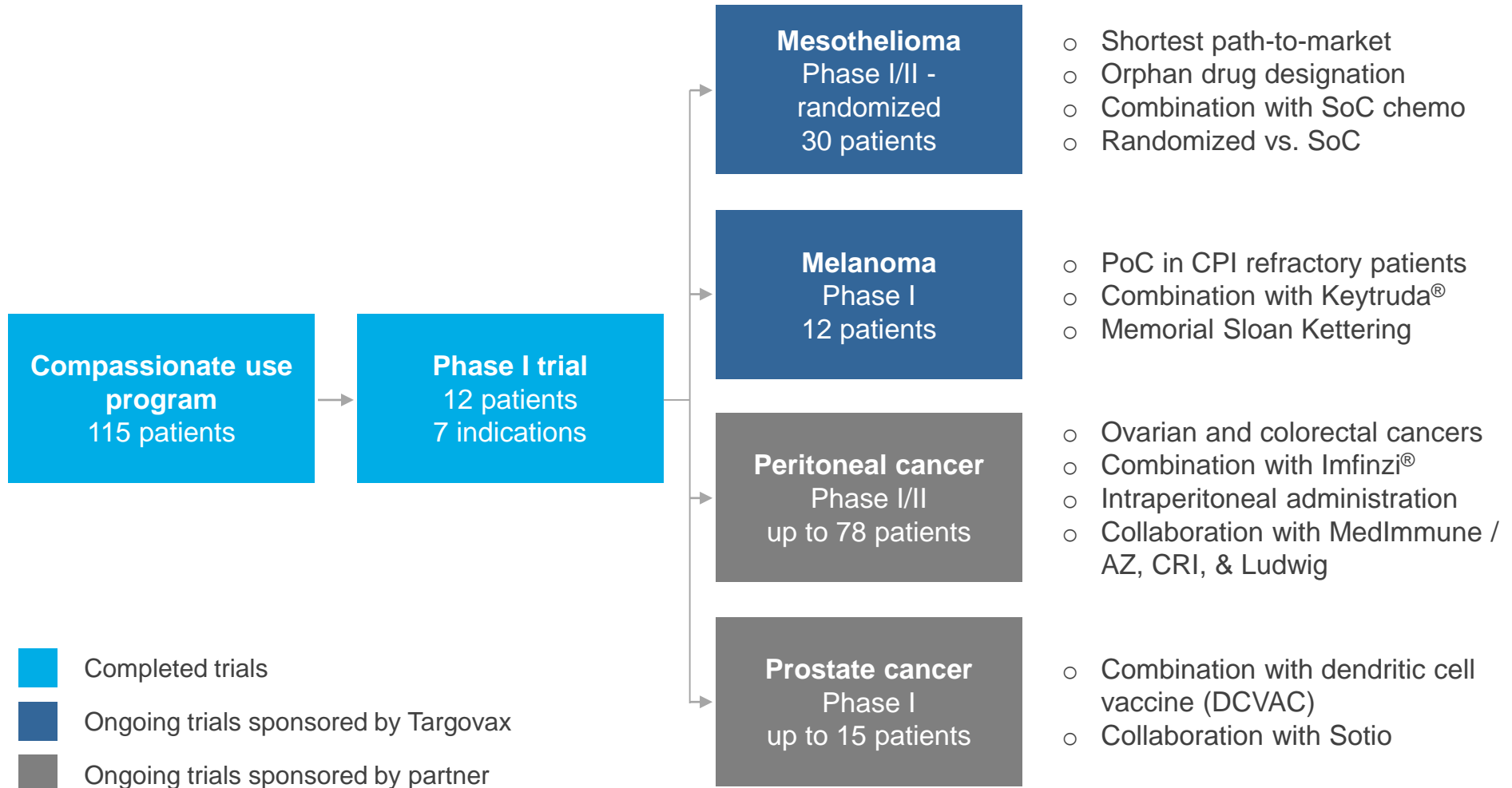
*Activates the  
immune system*

*Triggers patient-  
specific responses*

*No need for  
individualization*

# ONCOS

## CLINICAL PROGRAM OVERVIEW



# 1H 2018 HIGHLIGHTS

## During period

### **ONCOS-102 Mesothelioma phase I/II trial:**

- Six patient safety lead-in cohort completed without any concerns
- All patients were immune activated
- 50% disease control rate was observed after 6 months

### **ONCOS-102 Melanoma CPI refractory phase I trial:**

- ONCOS-102 generated both innate and adaptive immune activation in all of the first 4 patients treated

### **TG01 Resected pancreatic cancer phase I/II trial:**

- Encouraging 2-year and median overall survival data was reported

### **Corporate development:**

- Strengthened development focus on ONCOS as lead clinical program
- Targovax was granted a product patent in the EU for TG02
- Dr. Catherine Wheeler was elected to the Board of Directors

## Post-period

### **ONCOS-102 Peritoneal cancer phase I/II trial in combination w/ Imfinzi®:**

- Safety evaluation of first dose cohort completed without any concerns

### **ONCOS-102 Prostate cancer phase I trial in combination w/ DCVAC:**

- First patient has been dosed

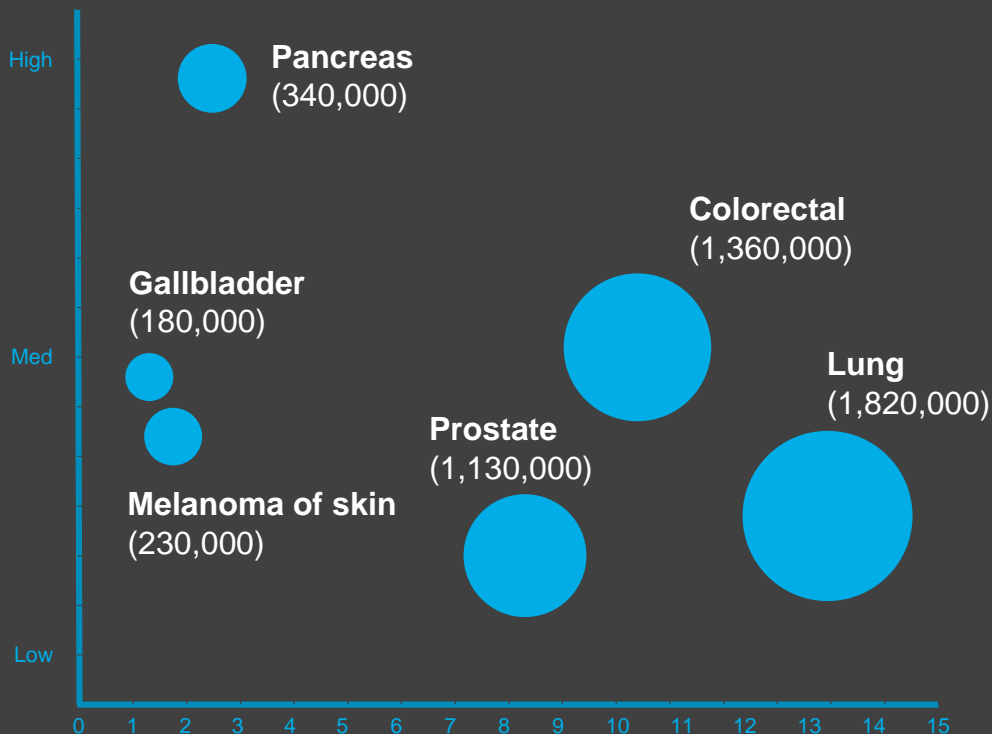


# The RAS gene is mutated in 90% OF PANCREATIC AND 50% OF COLORECTAL CANCERS

## Frequency of RAS mutations

Global cancer incidents per 10,000

(xx) = no. of cancer patients

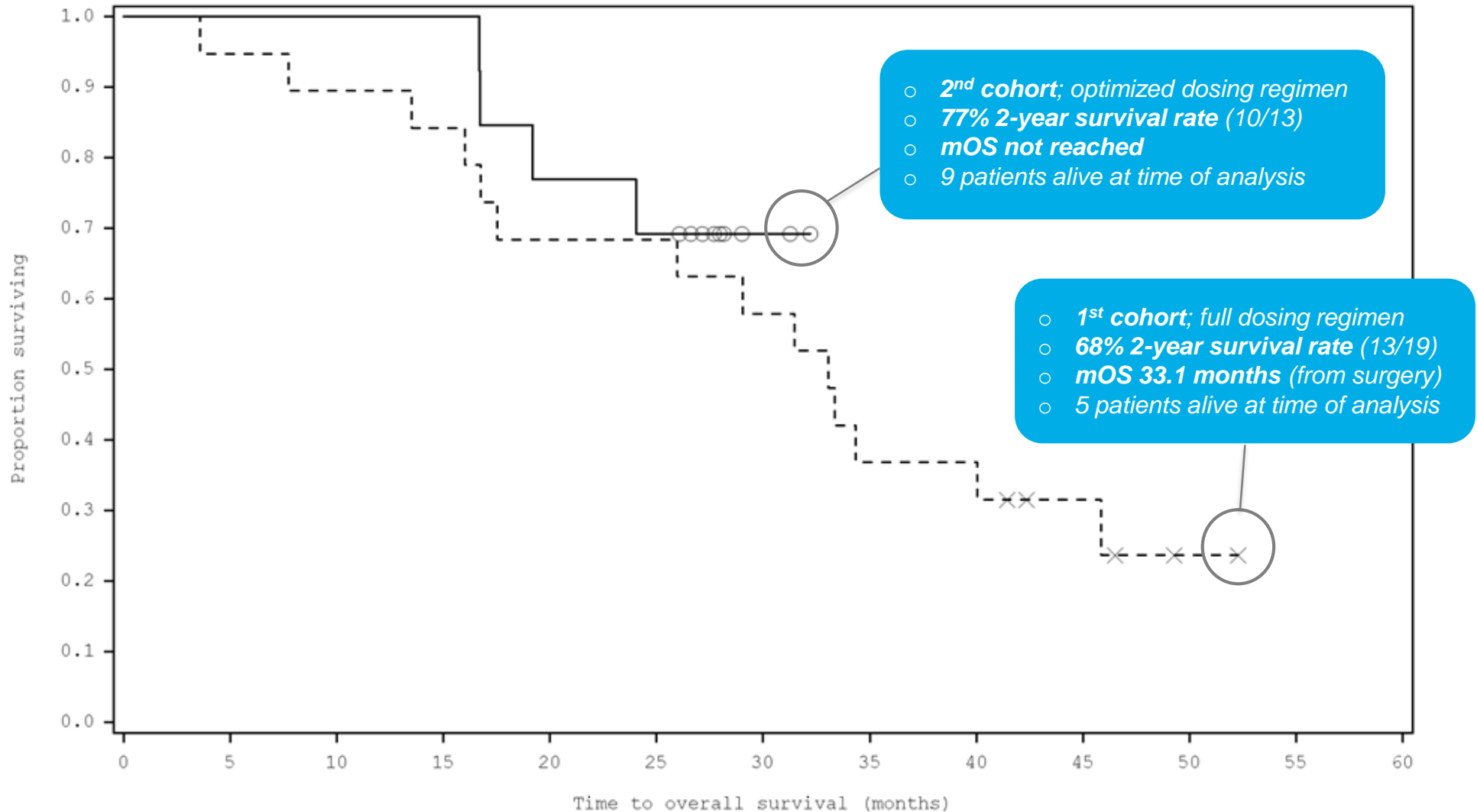


- RAS mutations are oncogenic and result in **uncontrolled cell division**
- There are **no existing therapies** targeting RAS mutations
- Targovax' TG program is a **unique vaccine approach for mutant RAS cancer**



# TG01 CURRENT KAPLAN-MAIER SURVIVAL CURVES

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



# 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 (preliminary, 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

**mutRAS immune activation**

**30 out of 32 patients (94%)** had **RAS-specific immune activation**

**Dosing and safety**

**Dosing regimen defined** and TG01 is **well-tolerated** in combination with chemotherapy

***PRODIGE trial***  
*Folfirinox now expected new standard of care*

***Phase III trial of adjuvant Folfirinox vs. Gemcitabine (n=493)<sup>1</sup>***

- ***ASCO 2018 late breaker, Investigator-led academic study***
- ***Median OS: 54.4 vs. 35.0 months***

# TG

## CLINICAL DEVELOPMENT STRATEGY

1

### Resected pancreatic cancer



#### TG01 indication

- Ph I/II completed
- Next steps being reassessed
- ~40 000 incidents

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### Colorectal cancer



#### TG02 lead indication

- Ph I trial ongoing
- 50% mutRAS
- ~0.5m incidents

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### Lung cancer (NSCLC)

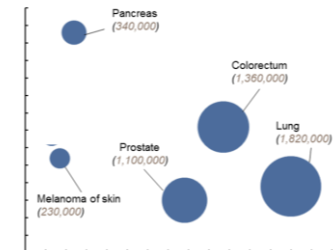


#### TG02 potential future indication

- 30% mutRAS
- ~0.5m incidents

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### All mutRAS cancers



#### TG02 + TG03 long-term potential

- Up to 30% of all cancer patients

# 2

## ONCOS oncolytic virus program update

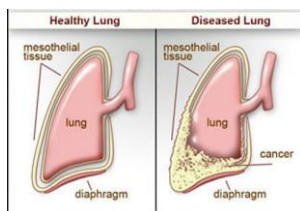
3. 2Q & 1H 2018 Financials

# ONCOS

## CLINICAL DEVELOPMENT STRATEGY

1

### Path-to-market Mesothelioma

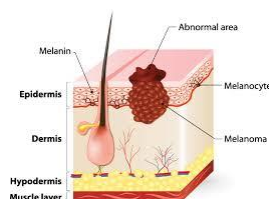


#### Target launch indication

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

2

### Proof-of-concept CPI refractory



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

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

3

### Proof-of-concept New CPI indication

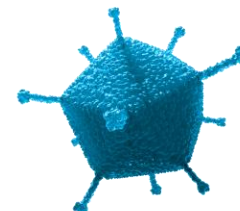


#### Peritoneal malignancies

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

4

### Next generation oncolytic viruses

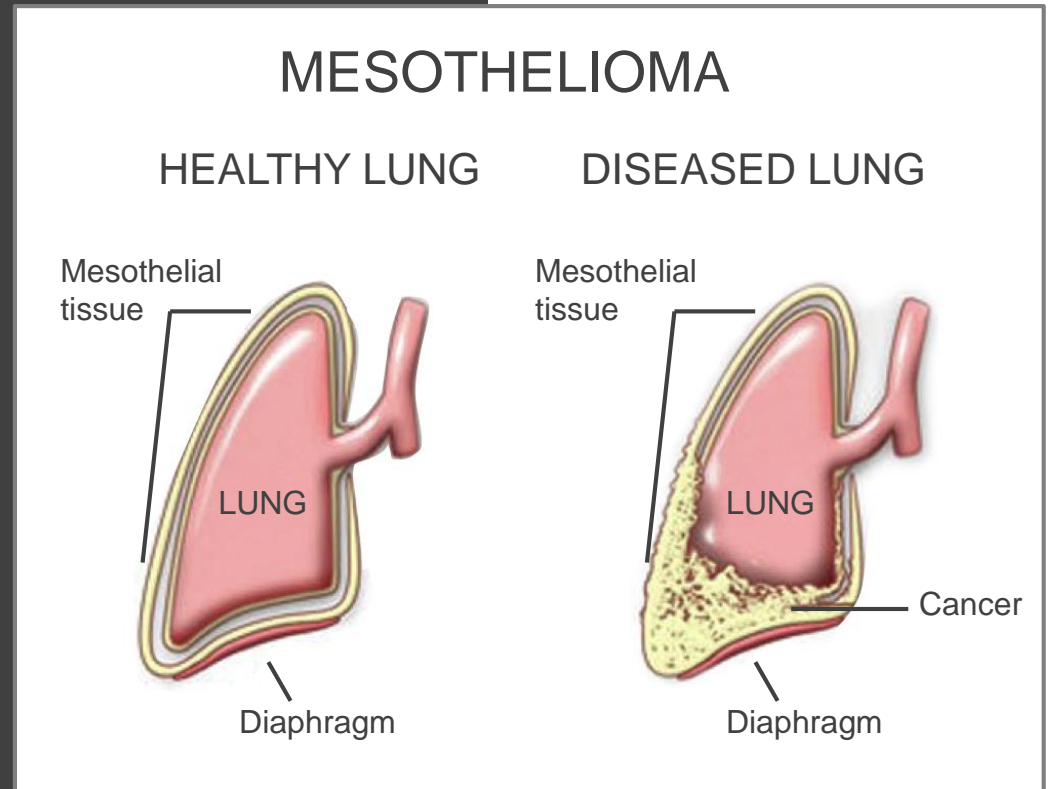


#### Double transgene adenoviruses

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

ONCOS-102 target  
launch indication  
**MALIGNANT  
PLEURAL  
MESOTHELIOMA**

- **Orphan disease**, estimated 15,000 new cases per year (EU, USA, Australia)
- **Incidence is increasing** and predicted to peak in 5-10 years
- Often **caused by asbestos** exposure, with a latency period of up to 40 years before diagnosis
- Aggressive cancer form with **median survival of 12 months**
- **No significant treatment advance** in the last decade



ONCOS-102 has the potential to become a breakthrough  
**MESOTHELIOMA IS SHORTEST PATH-TO-MARKET**

*Rationale for ONCOS-102 opportunity in mesothelioma:*

### Become frontline therapy

- **Preclinical data and phase I results** indicate potential of ONCOS-102 in mesothelioma
- **Ongoing randomized phase I/II trial** combining ONCOS-102 with SoC chemotherapy
- **Good safety profile**

### Orphan Drug Designation

- High unmet medical need, ONCOS-102 has **orphan drug designation**
- Opportunity for priority regulatory review, and **quick route-to-market**
- 7 year **market exclusivity** in the US and 10 years in the EU

### Limited competition

- CPIs show some early signs of efficacy, but are **potential ONCOS-102 combinations**, rather than competitors
- **No/few competing viruses** and vaccines in current clinical development in mesothelioma

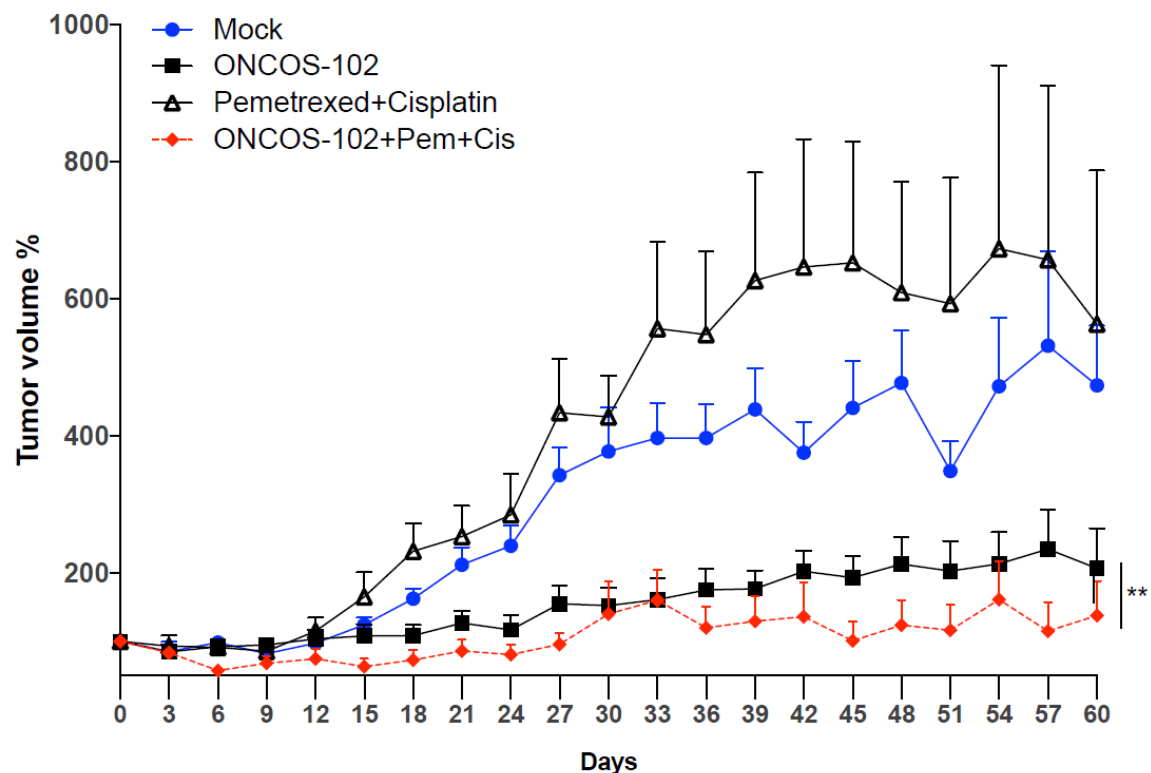


# SYNERGY BETWEEN ONCOS-102 AND CHEMOTHERAPY

demonstrated in mesothelioma mouse model

## Anticancer effect of ONCOS-102 and standard of care chemotherapy in xenograft mouse mesothelioma model

% change in tumor volume, 7 animals per group (14 tumors/group)



### Effects observed at Day 60:

#### ONCOS-102 vs. mock

56% tumor volume reduction  
 $p < 0.01$

#### ONCOS-102 vs. pem/cis

63% tumor volume reduction  
 $p < 0.01$

#### ONCOS-102+pem/cis vs. pem/cis

75% tumor volume reduction  
 $p < 0.001$

#### ONCOS-102+pem/cis vs. ONCOS-102

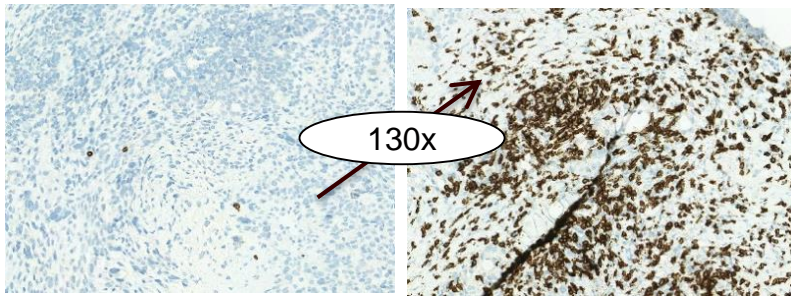
33% tumor volume reduction  
 $p < 0.01$

# ONCOS-102 CAN TURN MESOTHELIOMA HOT

demonstrated in 2 of 2 mesothelioma patients in phase I basket trial

**CD8+ T-cells in tumor**  
Tumor biopsy staining

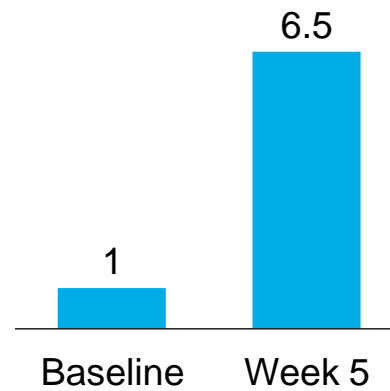
*Mesothelioma – hase I, patient 14*



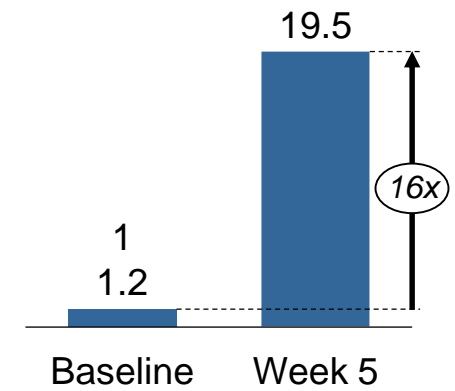
Baseline

Week 5

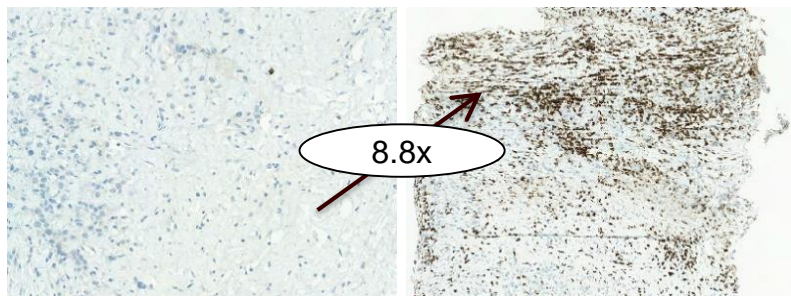
**CD4+ T-cells in tumor**  
Fold change



**PD-L1 positive tumor cells**  
% of total

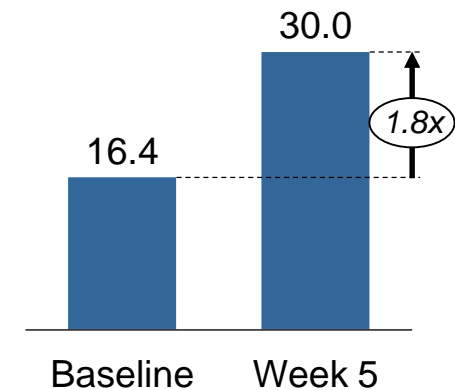
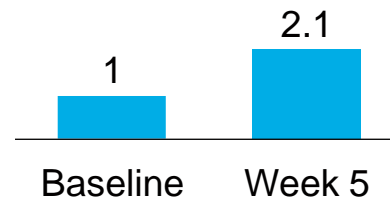


*Mesothelioma – Phase I, patient 9*



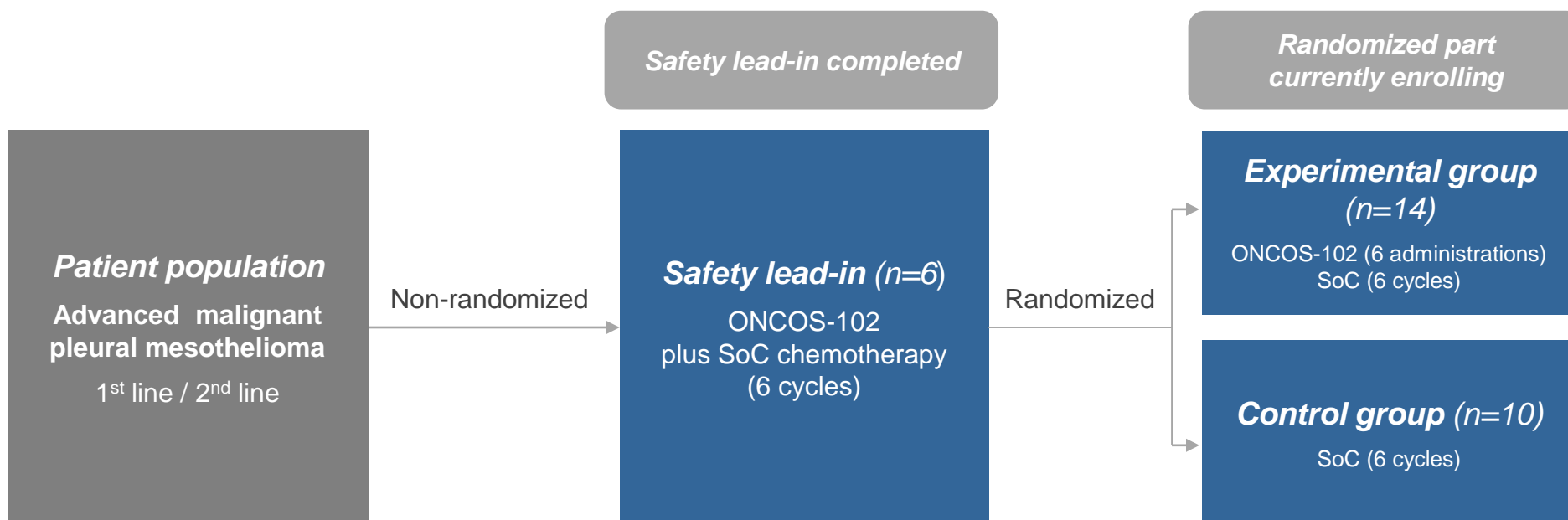
Baseline

Week 5



# ONCOS-102 in malignant pleural mesothelioma

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



# Ongoing ONCOS-102 malignant pleural mesothelioma Phase I/II trial

## SIGNAL OF EFFICACY IN THE FIRST 6 PATIENTS

1

### Safety

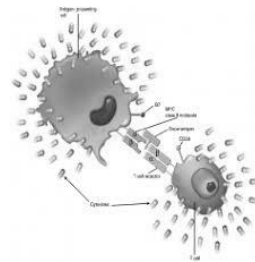
- ✓ ONCOS-102 **well-tolerated** in combination **with chemotherapy**



2

### Innate immune activation

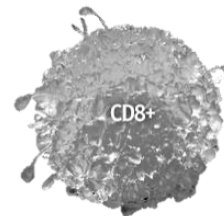
- ✓ **Systemic increase of pro-inflammatory cytokines** in 6/6 patients (IL-6, TNF $\alpha$  and IFN $\gamma$ )



3

### Adaptive immune activation

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



4

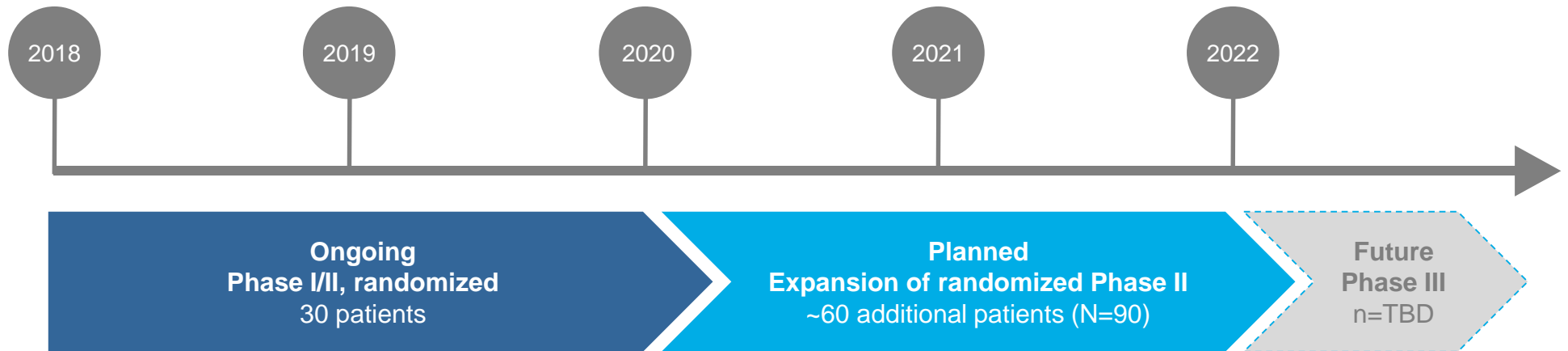
### Clinical activity

- ✓ **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



**Ongoing**  
Phase I/II, randomized  
30 patients

**Planned**  
Expansion of randomized Phase II  
~60 additional patients (N=90)

**Future**  
Phase III  
n=TBD

- 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

# WHY ONCOS-102?

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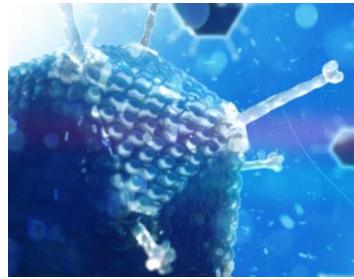
## In vivo efficacy



- **Efficacy shown** in both melanoma and mesothelioma models
- **Demonstrated synergy** with both CPIs and chemotherapy

2

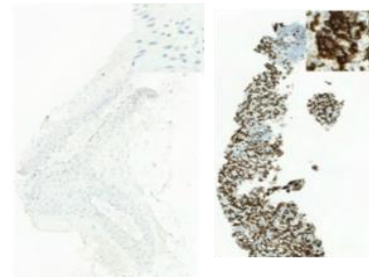
## Innate immune activation



- **Strong innate immune activation** as single agent, and in combinations, in nearly all injected patients

3

## CD8+ T-cell response



- Validated to induce **cancer specific CD8+ T-Cells** both clinically and *in vivo*
- Both **systemic and tumor-infiltrating** T-cells

4

## Well tolerated



- **>130 patients treated to date**
- **Well-tolerated** both as monotherapy and in combination with **CPIs and chemotherapy**

# 3

## 2Q & 1H 2018 Financials



# TARGOVAX HAS A SOUND FINANCIAL POSITION

with cash to complete the planned clinical program well into 2H 2019

## Operations

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Cash end of 2Q - Jun 30<sup>th</sup> 2018

**201 / 25**

NOK million    USD million

Net cash flow - total 2Q

**-28 / -3**

NOK million    USD million

Annual run rate - last four quarters

**109 / 13**

NOK million    USD million

## The share

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Market Cap - at share price NOK ~10

**600 / 70**

NOK million    USD million

Daily turnover - rolling 6 month avg.

**2.6 / 0.3 / 0.5**

NOK million    USD million    % of share capital

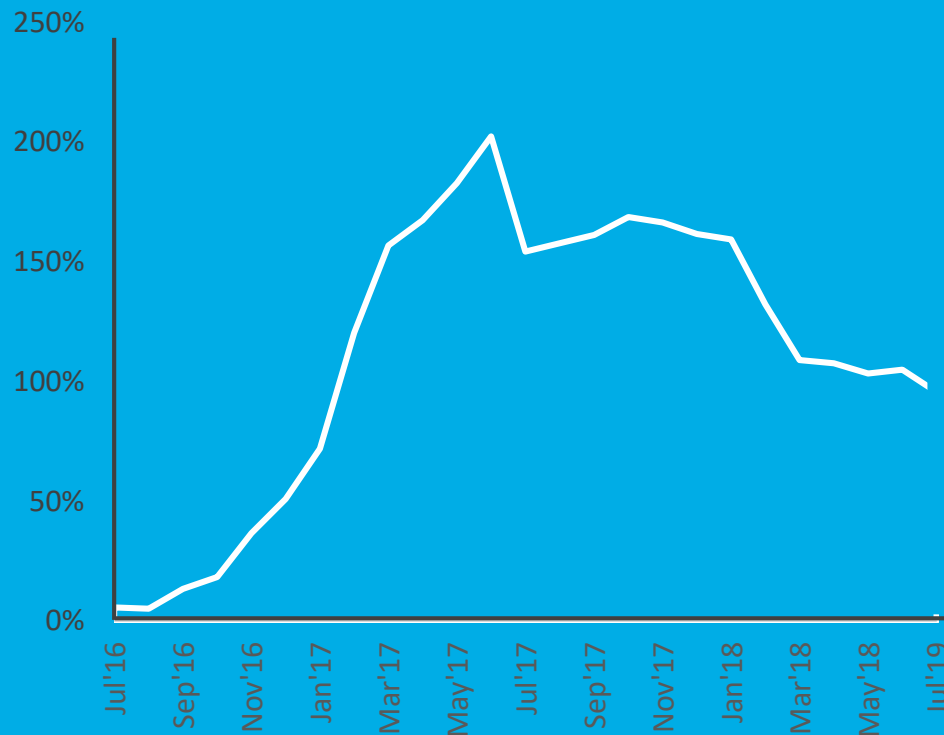
Analyst coverage

DNB, ABG Sundal Collier, Arctic,  
Redeye, Edison

# TARGOVAX IS LISTED ON THE OSLO STOCK EXCHANGE

and included in the OSEBX index as of December 2017

## TRVX share turnover (% of share capital, rolling 12 month)



- USD ~70 m market cap
- USD 0,3m avg. daily turnover in last 6 months
- USD 25m total turnover in 2Q
- 240k shares avg. daily volume in 2Q
- ~ 4,100 owners
- 52.6m shares (57.4 fully diluted)

# R&D PIPELINE OVERVIEW AND MILESTONES

Platform	Product candidate	Preclinical	Phase I	Phase II	Phase III	Last event	Next expected event
ONCOS	ONCOS-102 oncolytic adenovirus	Mesothelioma Comb. w/ pemetrexed/cisplatin <sup>1</sup>				Phase Ib safety lead-in cohort, incl. immune activation and ORR data (6 pts)	<b>1H 2020</b> Randomized ORR data 30 pts
		Melanoma Comb. w/KEYTRUDA®				First safety review, incl. immune activation (4 pts)	<b>2H 2018</b> Interim immune and ORR data
		Peritoneal cancers <sup>2,3</sup> Partner: Ludwig, CRI & AZ Comb. w/IMFINZI®				First dose escalation cohort safety review (4 pts)	<i>Update by partner, expected 2019</i>
		Prostate <sup>3</sup> Partner: Sotio Comb. w/DCVAC				First patient dosed	<i>Update by partner, expected 2019</i>
	Next-gen ONCOS	3 viruses undisclosed				Virus construct cloning and <i>in vitro</i> validation	<b>1H 2019</b> Target disclosure and <i>in vivo</i> data
TG	TG02 neo-antigen cancer vaccine	Colorectal cancer Proof-of-mechanism Comb. w/KEYTRUDA®				First safety review, incl. immune activation data (3 pts)	<b>1H 2019</b> Immune activation and mechanistic data
	TG01/02 neo-antigen cancer vaccine	CPI synergy TG + PD-1					<b>1H 2019</b> TG02 + PD-1 combination <i>in vivo</i> data

<sup>1</sup> Current standard of care chemotherapy for patients with unresectable malignant pleural mesothelioma

<sup>2</sup> Patients with advanced peritoneal disease, who have failed prior standard chemotherapy and have histologically confirmed platinum-resistant or refractory epithelial ovarian or colorectal cancer

<sup>3</sup> Partner sponsored trials

■ Ongoing partner sponsored trials

