# ACTIVATING THE PATIENT'S IMMUNE SYSTEM TO FIGHT CANCER

## ONCOS Program

Oncolytic Virotherapy Summit

Boston - 4 December 2019

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' 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

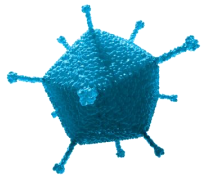
2. ONCOS-102 Phase I monotherapy data
3. ONCOS-102 Phase I PD1 refractory melanoma
4. ONCOS Program next steps

targovax

# TARGOVAX AT A GLANCE

## Immune activation by oncolytic viruses

- Addressing the growing need for **immune activators** to enhance efficacy in combination with other treatments, such as checkpoint inhibitors
- ONCOS clinical stage **adenovirus platform** targeting hard-to-treat solid tumors



## ONCOS-102 lead clinical asset

- One of the **furthest developed** OVs with >180 patients treated to date
- Four ongoing combination trials with **rich news flow** the next 3-12 months

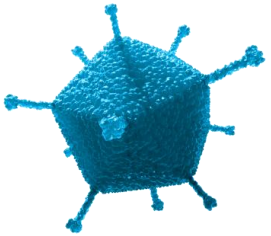
## Encouraging clinical efficacy demonstrated

- Strong **single agent** immune activation and clinical data
- **33% ORR** in anti PD-1 refractory melanoma in combination with Keytruda
- Promising interim data in mesothelioma in combination with chemotherapy

## Corporate highlights

- **All assets unencumbered**
- Listed on Oslo Stock Exchange: **TRVX**
- Market cap **USD ~40m**

# ONCOS IS BASED ON AN ADENOVIRUS SEROTYPE 5 BACKBONE



**Highly immunogenic**, TLR-9 agonist, stimulates inflammation

**Versatile DNA backbone**, ability to carry multiple transgenes


**Well-characterized** and well-tolerated, suitable for combinations

# ONCOS-102 IS THE LEAD CLINICAL STAGE ASSET

**1**

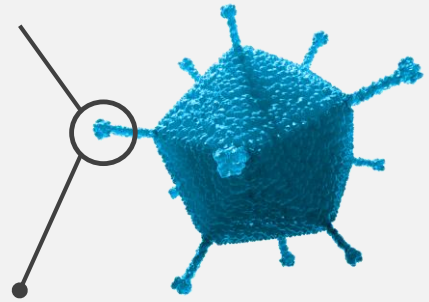
**Selective replication** in cancer cells

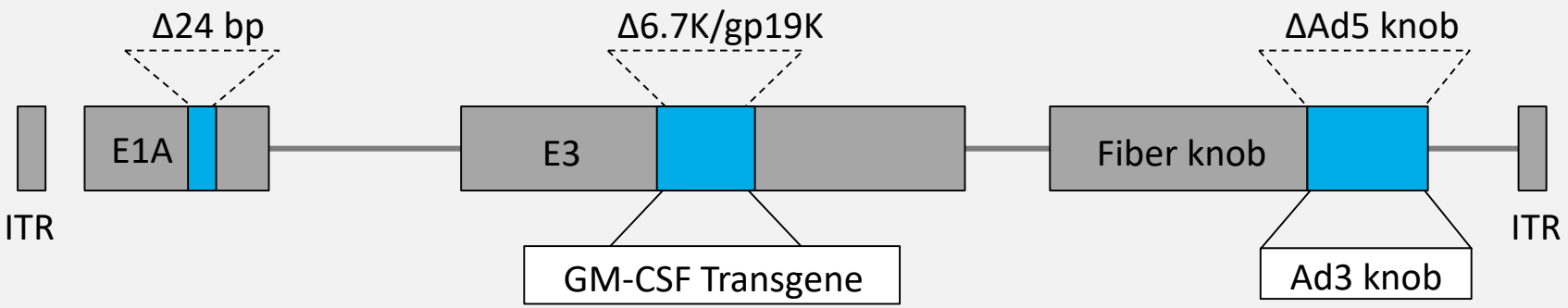
**2**

**Boosting** the **immune activation**

**3**

**Enhanced infection** of cancer cells






*Rb binding site in E1A removed*

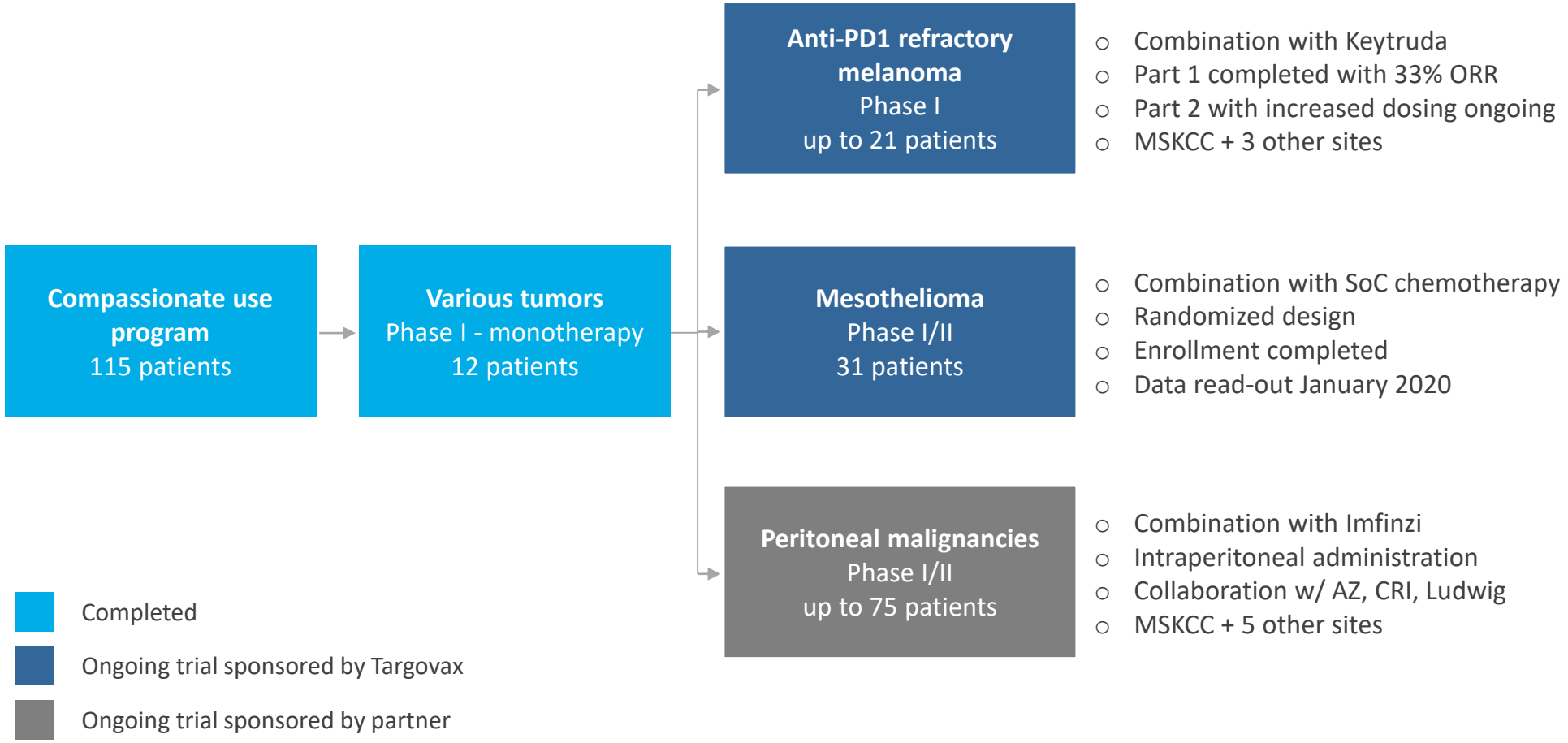
*Transgene insertion site, up to 4.5kb payload*

*Added infectivity via DSG2 and CD46 receptors*



targovax

# ONCOS-102 CLINICAL DEVELOPMENT PROGRAM






Targovax is also involved in an ongoing combination trial in Prostate cancer were ONCOS-102 is combined with a dendritic cell vaccine (DCVAC). This trial is sponsored by Sotio, a Czech biotech company

targovax

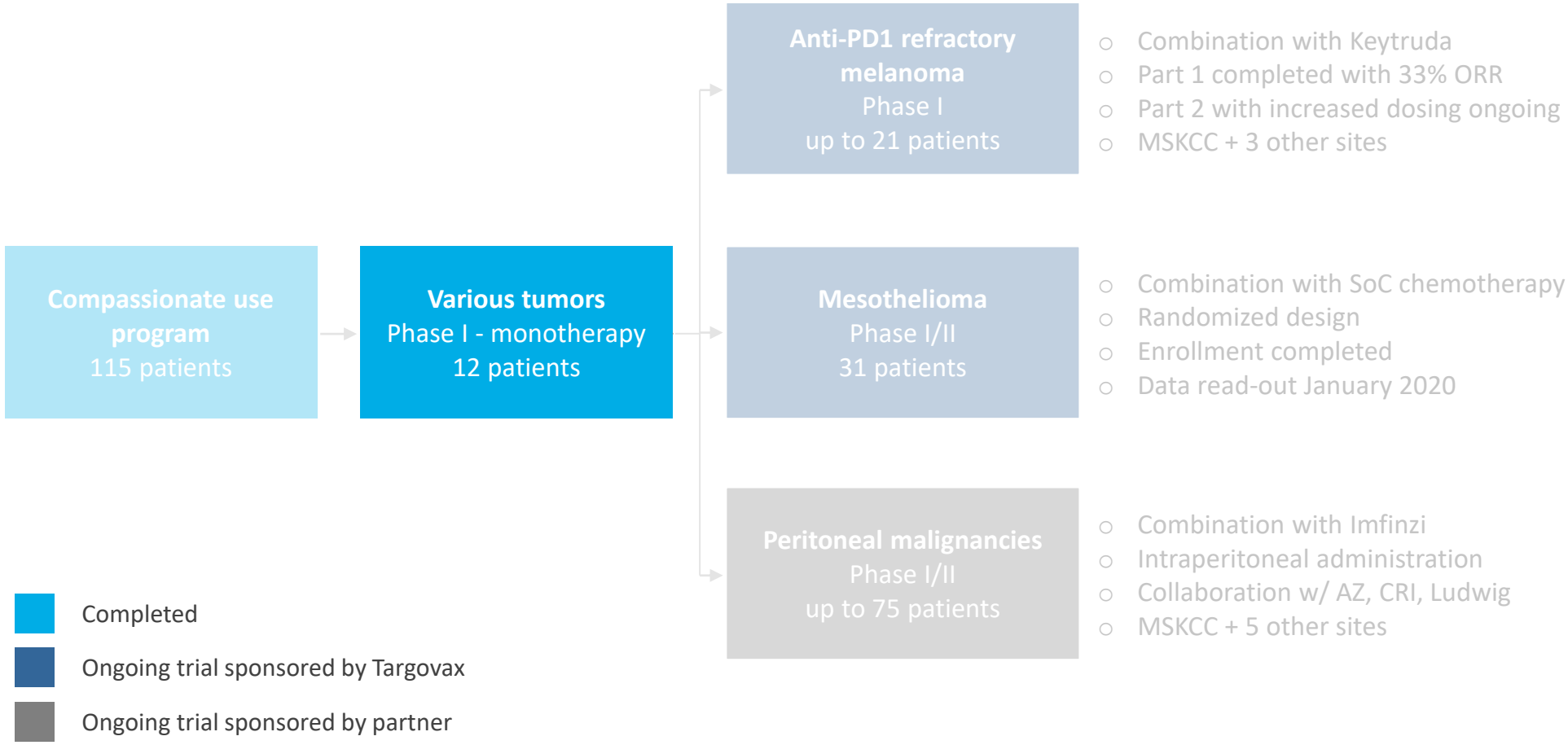
# 2

# ONCOS-102 Phase I monotherapy data

3. ONCOS-102 Phase I PD1 refractory melanoma
4. ONCOS Program next steps

targovax

# ONCOS-102 CLINICAL DEVELOPMENT PROGRAM






Targovax is also involved in an ongoing combination trial in Prostate cancer were ONCOS-102 is combined with a dendritic cell vaccine (DCVAC). This trial is sponsored by Sotio, a Czech biotech company

targovax

ONCOS-102

PHASE I SINGLE AGENT PROOF-OF-CONCEPT

# IMMUNE ACTIVATION DEMONSTRATED

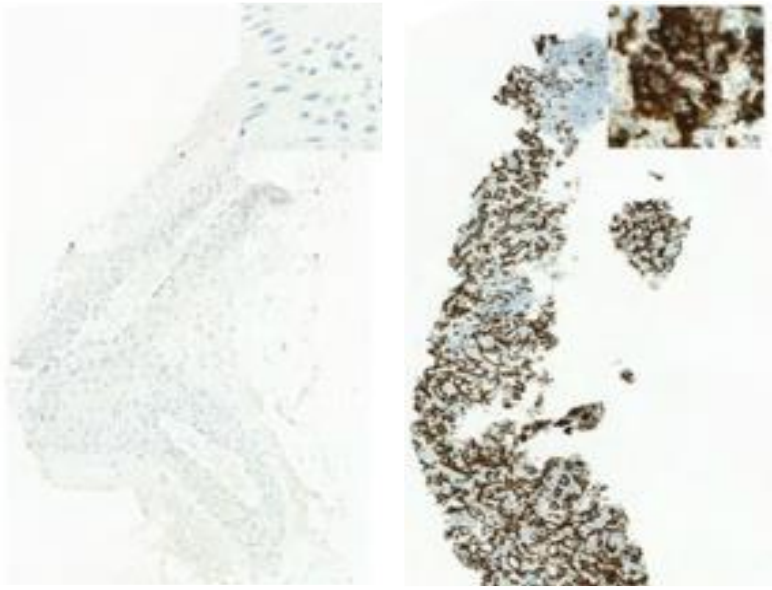
**ONCOS-102 Phase I trial design:**

- 12 patients, 7 different solid tumors
- All refractory to multiple lines of therapy
- Treatment: ONCOS-102 monotherapy
  - 9 injections over 5 months

**Top-line results:**

- 100% innate immune activation
- 11/12 patients increase in CD8+ T-cells
- 40% DCR after 3 months
- 2 long-term survivors
- Abscopal effect and lasting systemic immune responses observed
- Induction of tumor specific T-cells

**Cold tumor turned hot**, CD8+ T-cell staining



**Pre-treatment**
Baseline

**Post-treatment**
Week 8



targovax

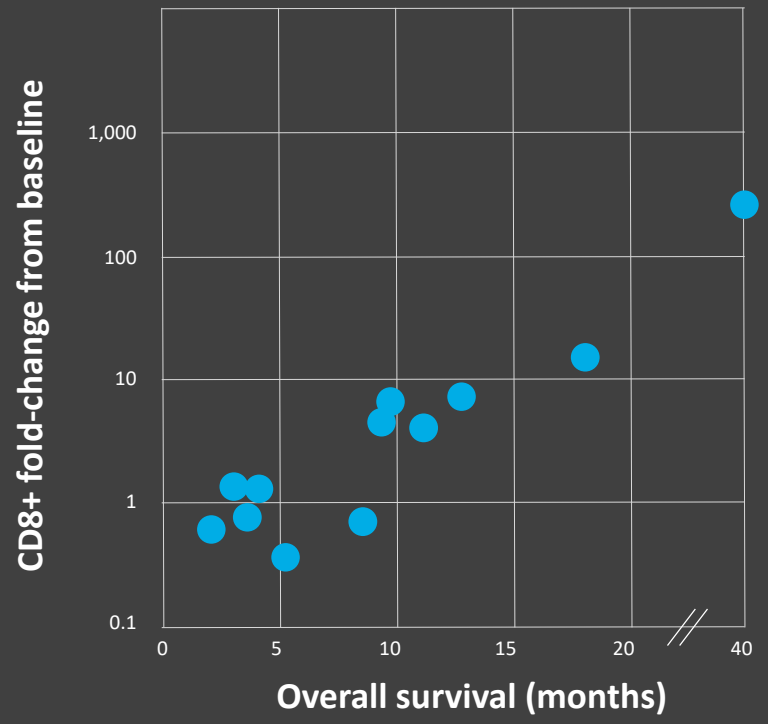
ONCOS-102

Phase I single agent proof-of-concept

# MACROPHAGE INFILTRATION CORRELATES WITH SURVIVAL

**Fold-change CD68+ macrophage count vs. survival**

*r = 0.75  p = 0.005*




***Potent inflammatory immune responses induced by ONCOS-102***

- **CD68+ macrophage tumor infiltration** increased in 8 out of 12 patients
- Highest fold-change in **longest surviving patients**
- Switch from **M2 to M1 phenotype**, indicative of type I immune response
- **All patients** had robust increases in systemic **pro-inflammatory cytokines**

Ranki et al., Journal for Immunotherapy of Cancer 2016, 4(17)



targovax

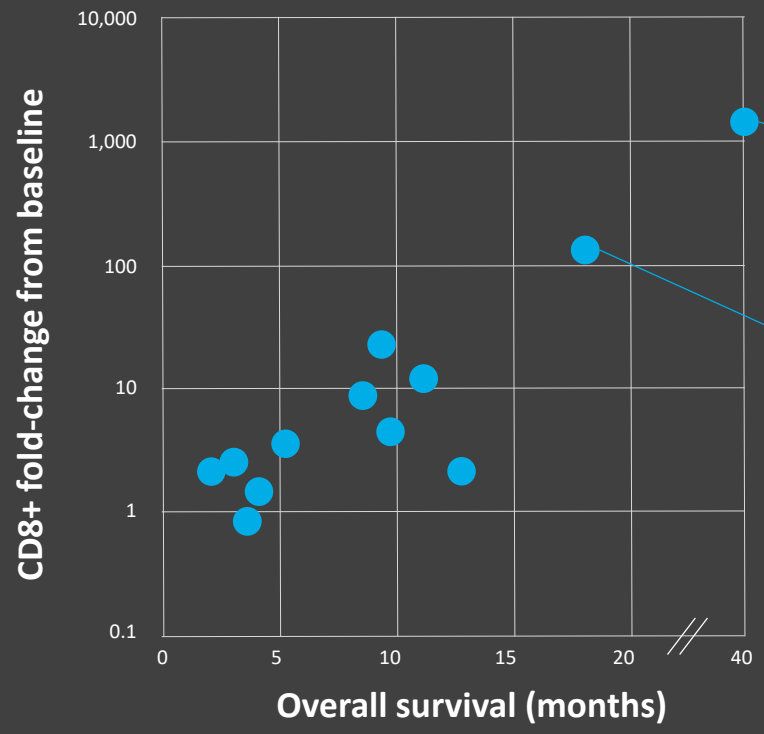
ONCOS-102

Phase I single agent 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 #1 – Ovarian cancer***

- Failed on 5 types of chemotherapy
- **>1,000-fold increase** in CD8+ T-cell infiltration
- **Stable disease for 3 years**, survived for 3.5 years

***Case example #2 – Mesothelioma***

- Radio- and chemotherapy refractory
- **130-fold increase** in CD8+ T-cell infiltration
- **47% reduction of tumor on PET** 6 weeks after last ONCOS-102 injection, survived 18 months



Ranki et al., Journal for Immunotherapy of Cancer 2016, 4(17)

targovax

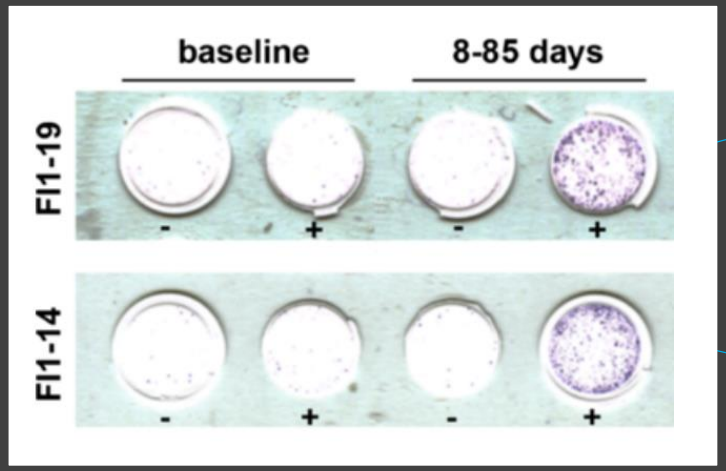
ONCOS-102

Phase I single agent proof-of-concept

# INDUCTION OF TUMOR-SPECIFIC T-CELL RESPONSES

***De novo* tumor-specific systemic CD8+ T-cell response**

IFNγ ELISPOT assays on T-cells isolated from PBMC




***Ovarian cancer patient** (FI1-19)*

- Example - anti-Mesothelin ELISPOT assay
- MAGE-A1, MAGE-A3 and NY-ESO-1 CD8+ T-cells also detected
- NY-ESO-1 still present at 17 month follow-up

***Mesothelioma patient** (FI1-14)*

- Example - anti-MAGE-A3 ELISPOT assay
- MAGE-A3 T-cells detected up to 6 months after start of treatment



Ranki et al., Journal for Immunotherapy of Cancer 2016, 4(17)

targovax

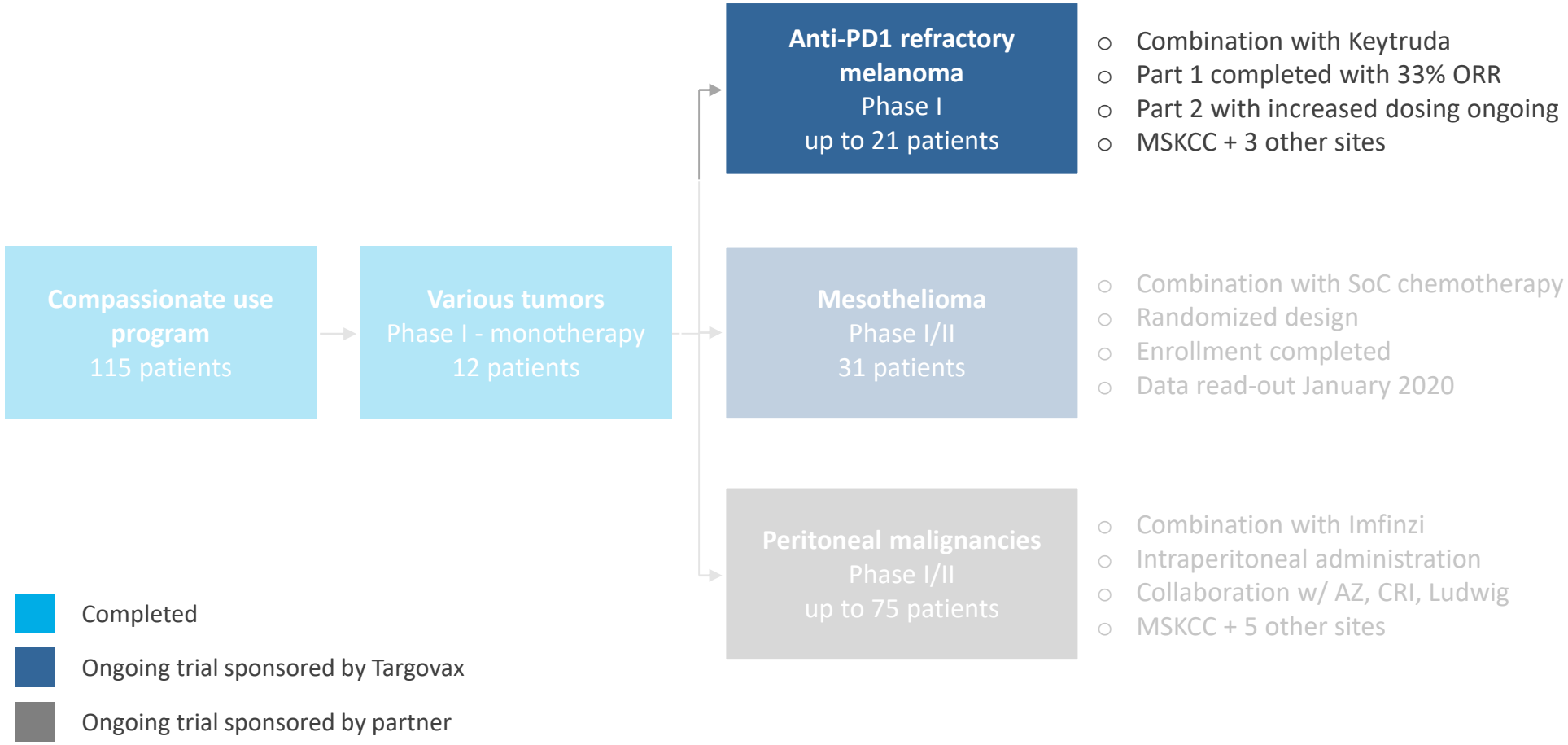
# 3

# ONCOS Phase I PD-1 refractory melanoma

4. ONCOS Program next steps

targovax

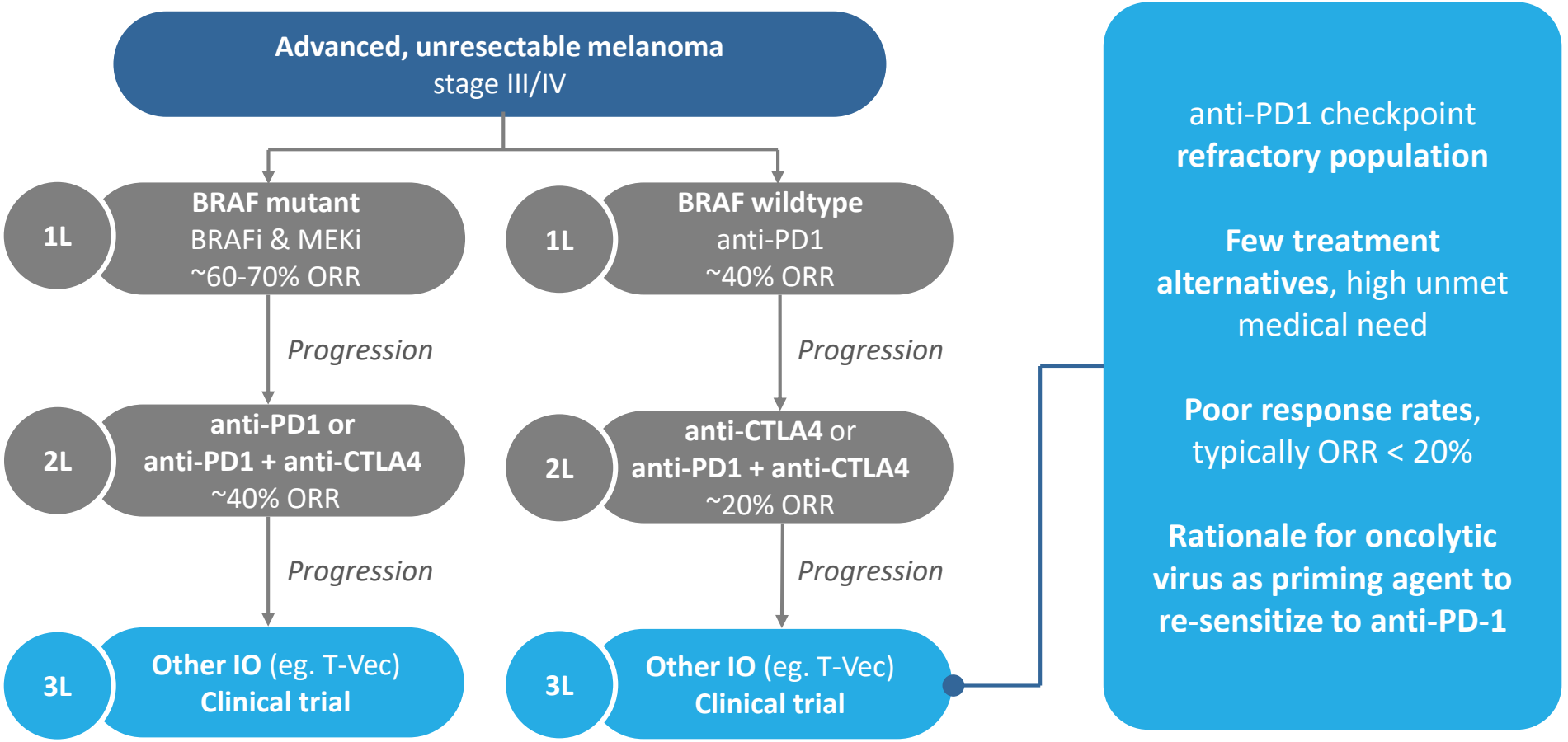
# ONCOS-102 CLINICAL DEVELOPMENT PROGRAM






Targovax is also involved in an ongoing combination trial in Prostate cancer were ONCOS-102 is combined with a dendritic cell vaccine (DCVAC). This trial is sponsored by Sotio, a Czech biotech company

# LIMITED TREATMENT OPTIONS FOR ANTI PD-1 REFRACTORY MELANOMA



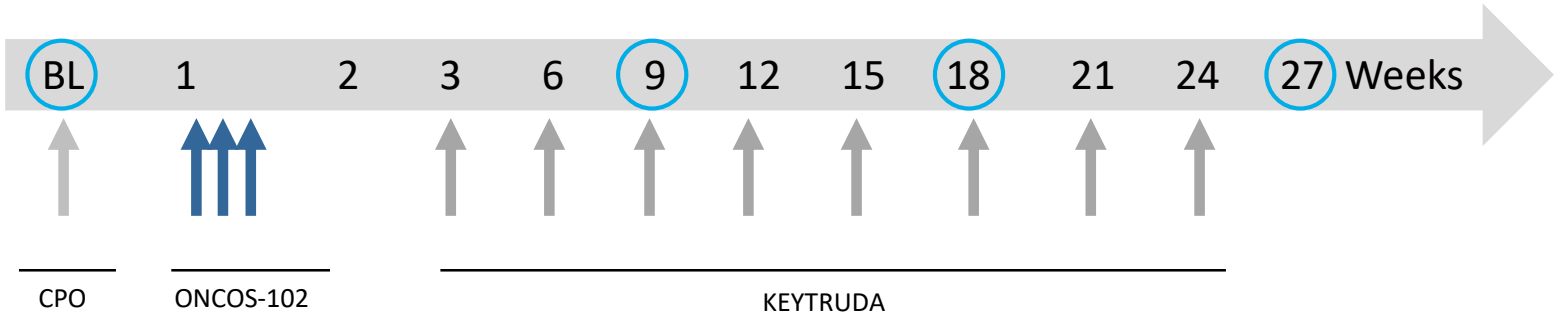



targovax

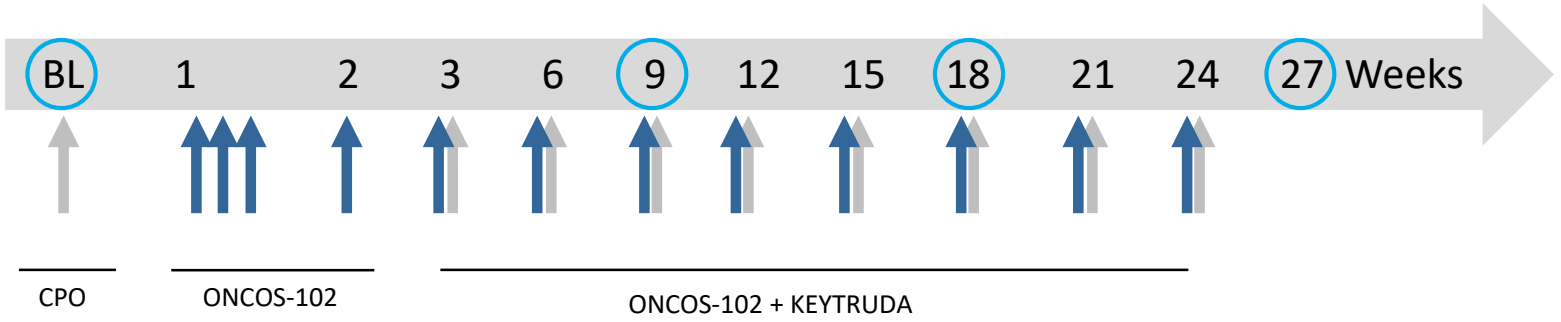
# MELANOMA PHASE I TRIAL DESIGN

## ONCOS-102 + KEYTRUDA COMBINATION IN ANTI-PD1 REFRACTORY MELANOMA

***Part 1** completed:*
*3x ONCOS-102 injections*
*Sequential treatment*




***Part 2** enrolling:*
*12x ONCOS-102 injections*
*Combination treatment*




○ *Imaging*

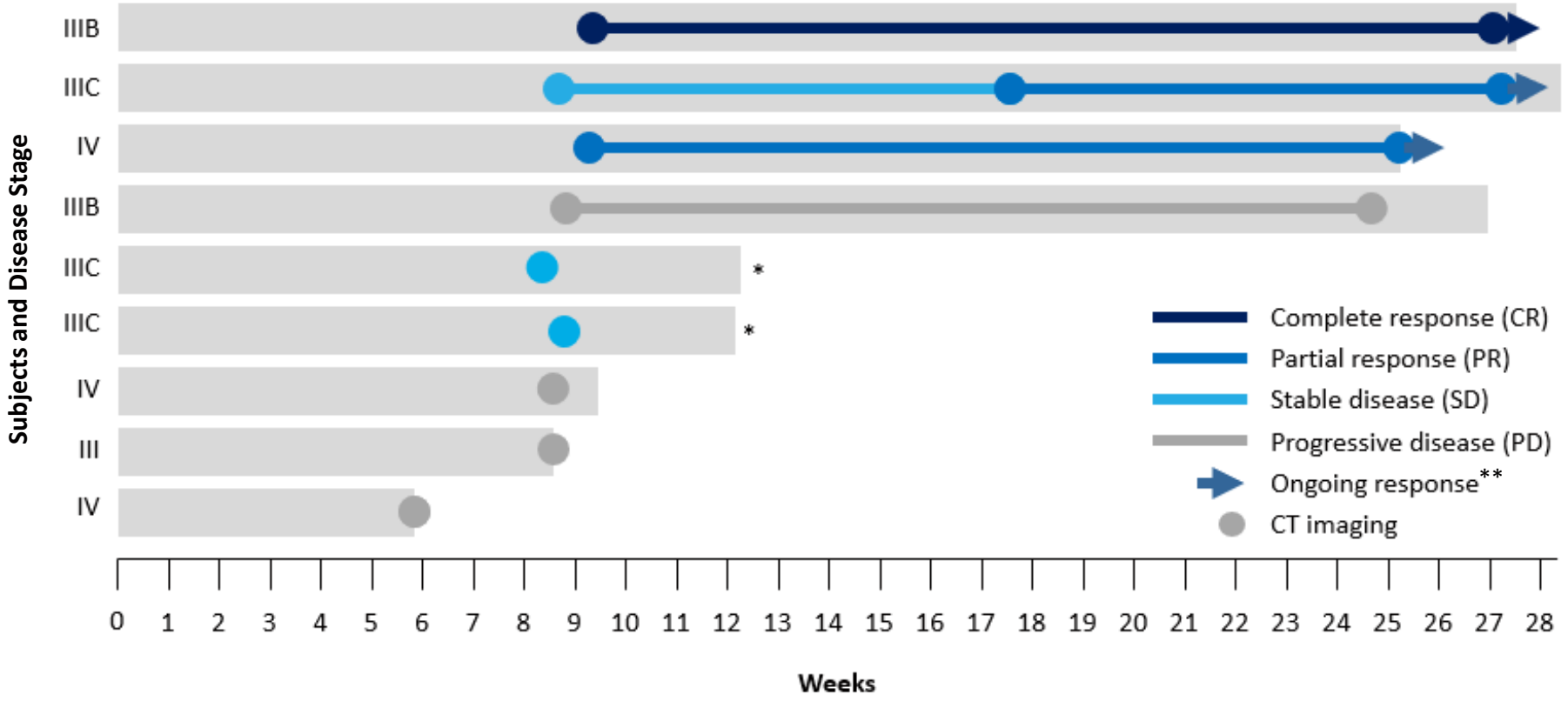
*CPO: Cyclophosphamide*



targovax

ONCOS-102 ANTI-PD1 REFRACTORY MELANOMA

# CLINICAL RESPONSE IN 3 OF 9 PATIENTS (33% ORR)




* Withdrawn due to clinical PD

** Response still ongoing at last CT scan

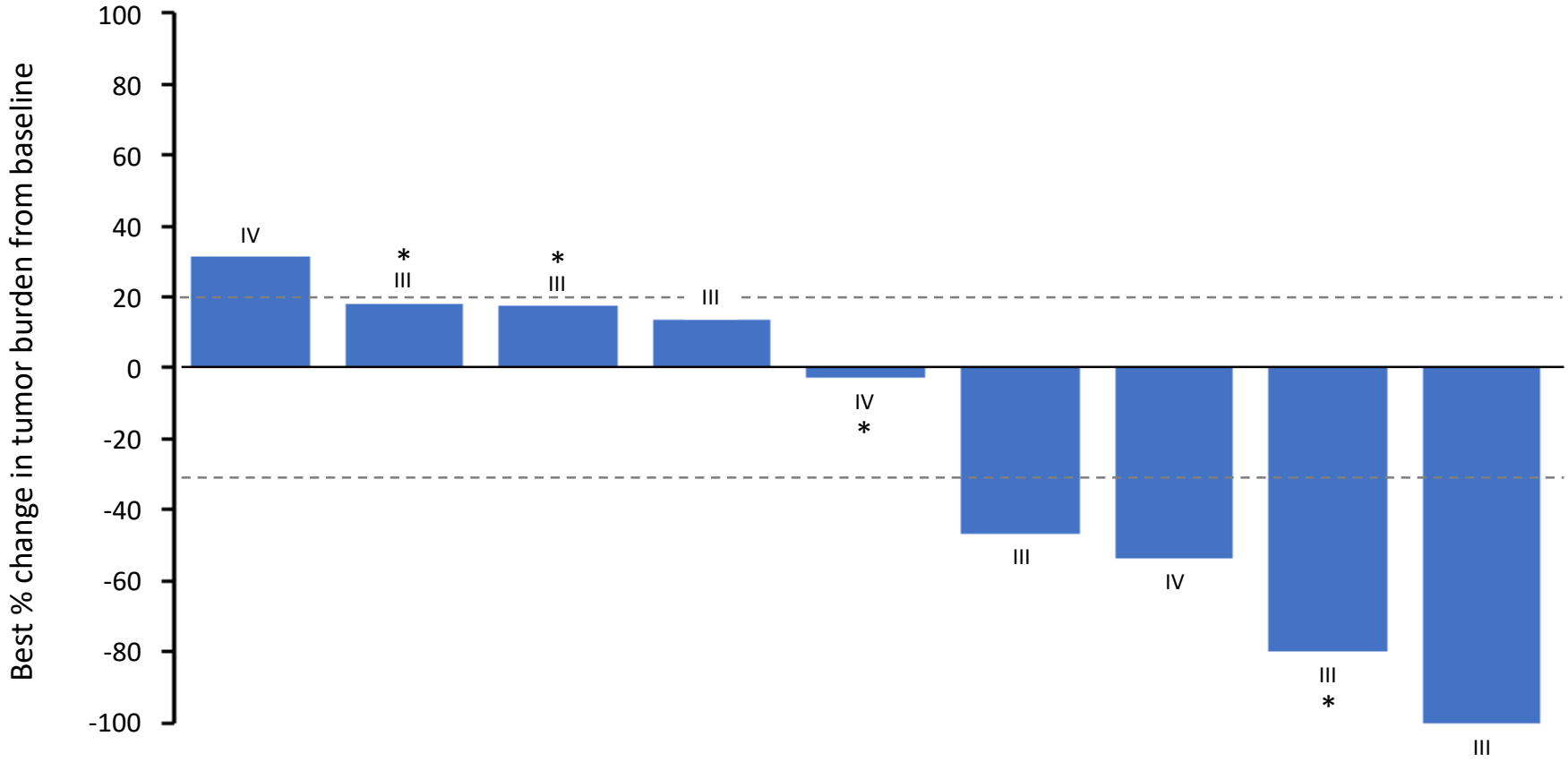
Length of grey bars indicate time from first ONCOS-102 injection to discontinuation/EoS



targovax

# ONCOS-102 ANTI-PD1 REFRACTORY MELANOMA

## BEST PERCENTAGE CHANGE IN TARGET LESIONS




∗ Non-target progression / new lesion (PD)

Letters and numbers indicating disease stage
Preliminary data



targovax

ONCOS-102 ANTI-PD1 REFRACTORY MELANOMA

# CASE EXAMPLE: PATIENT WITH COMPLETE RESPONSE

**Tumor response**, 1 of 1 injected lesion

| *Baseline* | *Week 3* | *Week 9* | *Week 18* | *Week 27 (EoS)* |
|---|---|---|---|---|
|  |  |  |  |  |
| Progression on Keytruda | 3x ONCOS-102 only | 3x ONCOS-102 & 2x Keytruda | 3x ONCOS-102 & 5x Keytruda | 3x ONCOS-102 & 8x Keytruda |

## Patient characteristics

| | | | |
|---|---|---|---|
| **Tumor stage at enrolment:** | **IIIb**<br>T4a, N2b, M0 | **Prior therapies:** | Surgery (x3)<br>Ipilimumab<br>Dabrafenib + Trametinib<br>Keytruda |
| **RECIST 1.1:** | **CR**, week 9-27 | | |

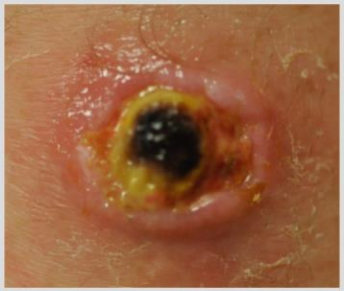
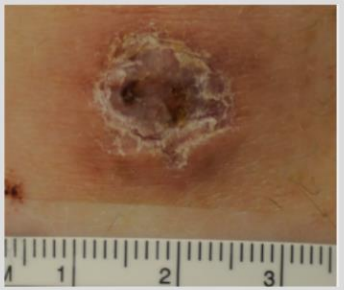
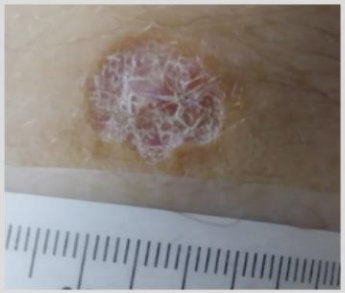
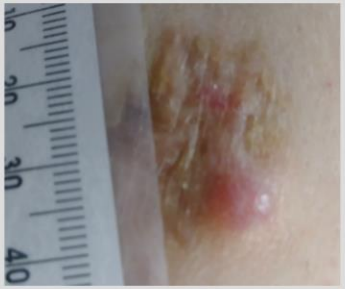


targovax

ONCOS-102 ANTI-PD1 REFRACTORY MELANOMA

# CASE EXAMPLE: PATIENT WITH PARTIAL RESPONSE

**Tumor response**, 2 of 2 injected lesions

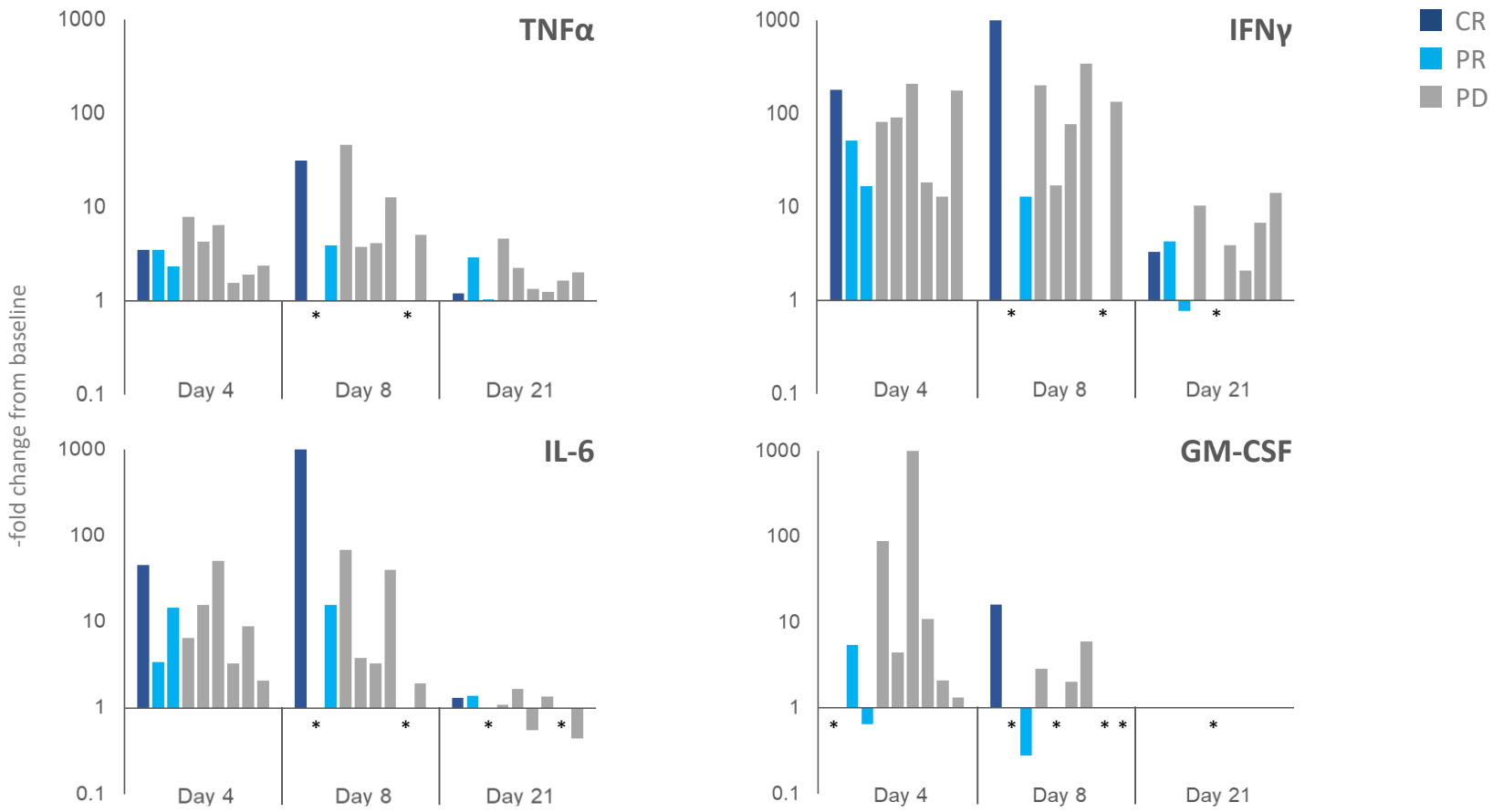
| | *Baseline* | *Week 3* | *Week 9* | *Week 18* | *Week 27 (EoS)* |
|---|---|---|---|---|---|
| Lesion 1 of 2 |  |  |  |  |  |
| Lesion 2 of 2 |  |  |  |  |  |
| | Progression on Keytruda | 3x ONCOS-102 only | 3x ONCOS-102 & 2x Keytruda | 3x ONCOS-102 & 5x Keytruda | 3x ONCOS-102 & 8x Keytruda |

## Patient characteristics

| | | | |
|---|---|---|---|
| **Tumor stage at enrolment:** | **IV**<br>T4a, N1b, M1 | **Prior therapies:** | Surgery<br>Talimogene-laherparepvec (T-vec)<br>Ipilimumab<br>Keytruda |
| **RECIST 1.1:** | **PR**, week 9-27 | | |

# BROAD UPREGULATION OF PRO-INFLAMMATORY CYTOKINES OBSERVED IN ALL PATIENTS

**Systemic expression of pro inflammatory cytokines**, -fold change from baseline





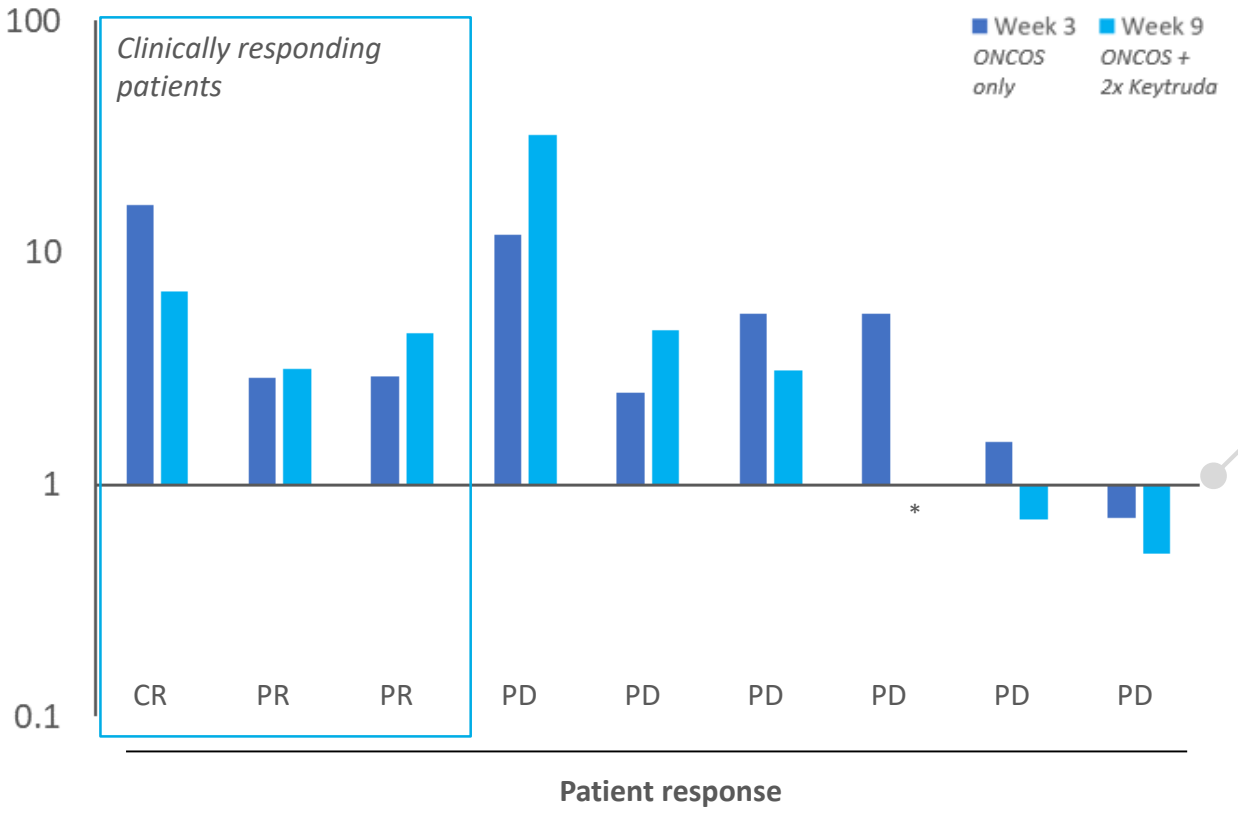

Unpublished company data

* Below detection limit (BDL); If baseline was BDL, then baseline set to BDL for reference

targovax

# INCREASE IN CD8+ T-CELL INFILTRATION APPEARS TO BE NECESSARY, BUT NOT SUFFICIENT, FOR RESPONSE

**CD8+ T-cell infiltration into injected lesions**, -fold change from baseline




All 9 patients had low or very low CD8+ T-cell infiltration at baseline

Do not post, unpublished company data

- Week 9 analysis not available

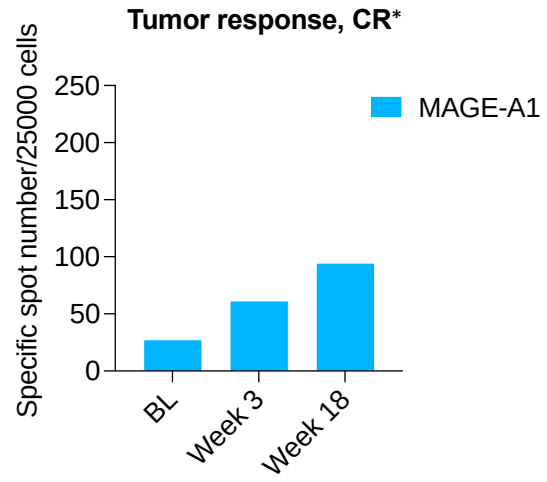
PD: Progressive disease PR= Partial response CR= Complete response

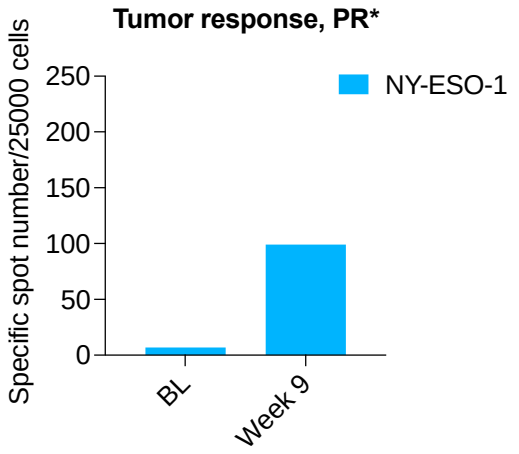


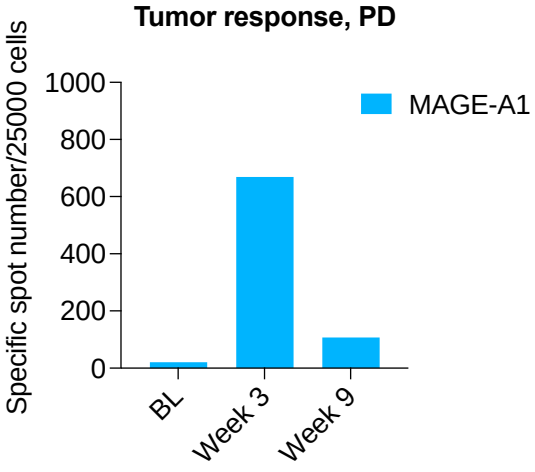
targovax

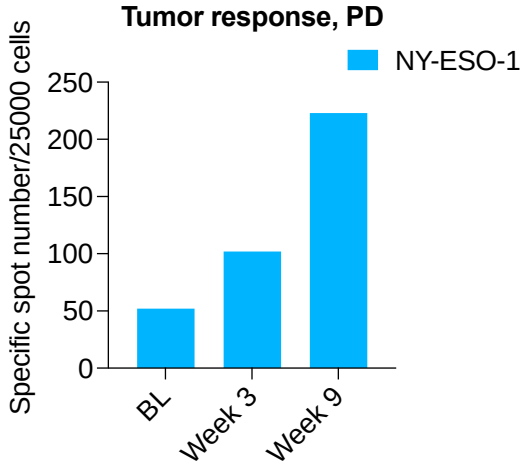
# SYSTEMIC INCREASE IN TUMOR SPECIFIC T-CELLS OBSERVED IN FOUR PATIENTS

**Presence of systemic tumor antigen specific T-cells**
IFNγ ELISPOT, spot number / 25,000 cells



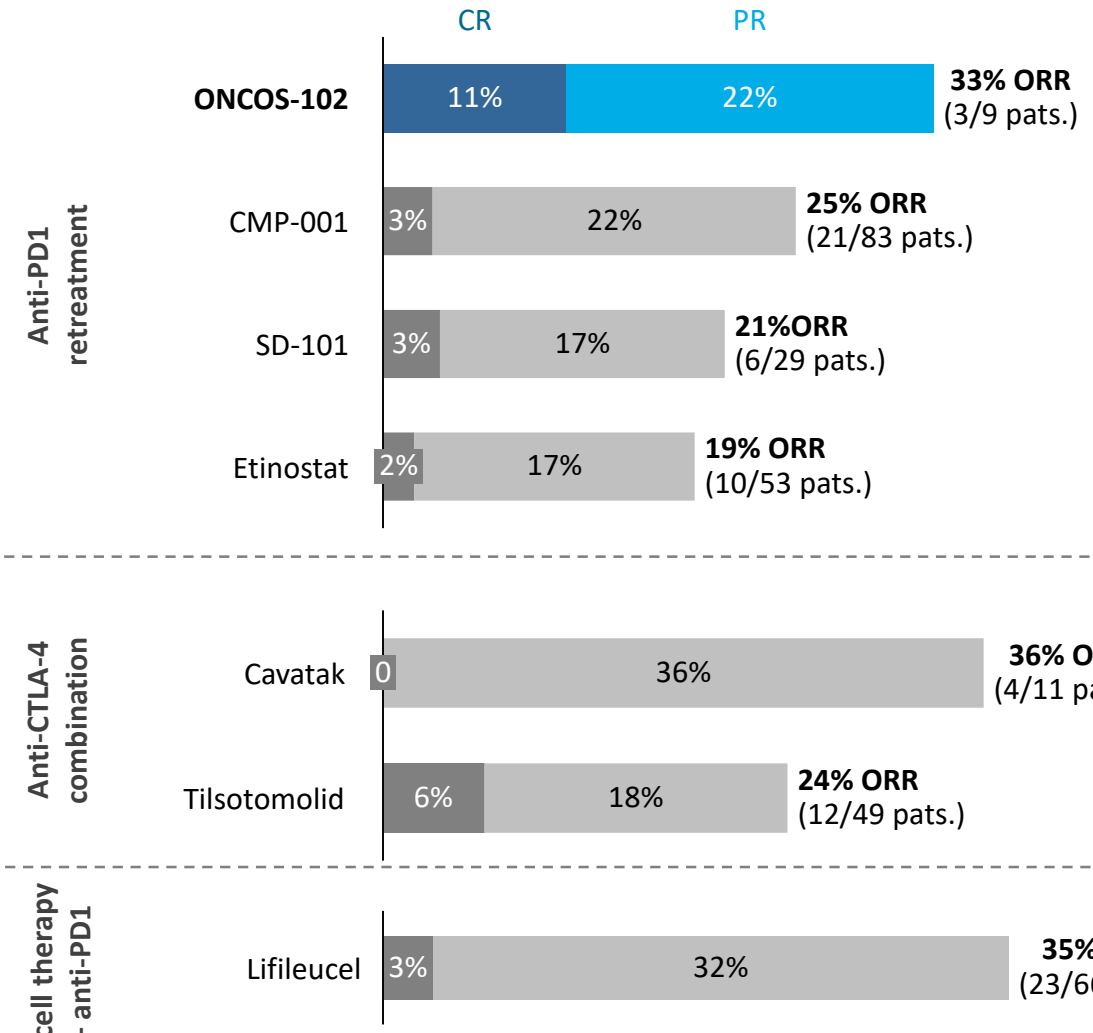



* Week 3/9 analysis not performed

targovax

# ONCOS-102 + KEYTRUDA DATA IN CONTEXT

## ANTI-PD1 REFRACTORY MELANOMA BENCHMARK DATA




***Comment***

- *Checkmate Pharma, TLR-9 agonist*
- *Data from high dose cohort*
- *Dynavax, TLR-9 agonist*
- *Syndax Pharma, HDAC inhibitor*

***Most pats CTLA4 naïve, 10-20% ORR expected***

- *Merck (Viralytics), Oncolytic virus, up to 20 injections*
- *Idera, TLR-9 agonist*
- *IOvance, autologous TIL therapy with IL-2*
- *Complex and expensive manufacturing*



SOURCE: Targovax market analysis, August 2019

targovax

# 4

# ONCOS Program
# Next Steps

targovax

# PIPELINE WITH RICH NEAR-TERM NEWS FLOW

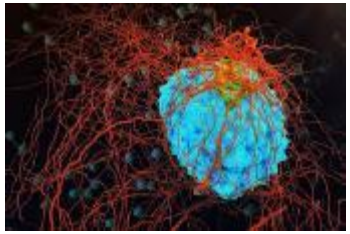
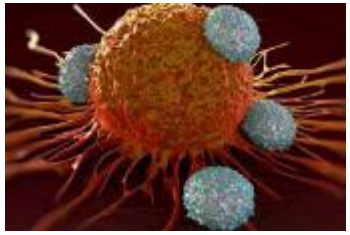
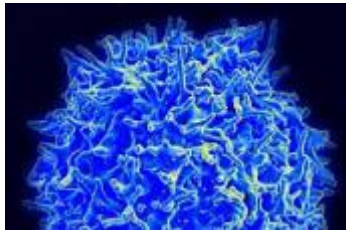
| Product candidate | Preclinical | Phase I | Phase II | Phase III | Next expected event |
|---|---|---|---|---|---|
| ONCOS-102 | **Mesothelioma**<br>Combination w/ pemetrexed/cisplatin | | | | **January 2020**<br>Randomized data |
| | **Melanoma**<br>Combination w/Keytruda | | | | **1H 2020**<br>Part 2 data |
| | **Peritoneal metastasis**<br>Collaborators: Ludwig, CRI & AZ<br>Combination w/Imfinzi | | | | *Update by collaborator* |
| | **Prostate**<br>Collaborator: Sotio<br>Combination w/DCvac | | | | *Update by collaborator* |
| Next-gen ONCOS | **3 new viruses**<br>Double transgene | | | | **1H 2020**<br>Pre-clinical data |



targovax

27

# ONCOS-200 SERIES VIRUSES HAVE DOUBLE TRANSGENES AND DISTINCT MODES OF ACTION

| | Mode of action | Target tumors |
|---|---|---|
|  **ONCOS-210 & -212** *Inhibition of tumor growth and metabolism* | ○ Interfere with tumor's ability to break down surrounding tissue<br>○ Induce cell cycle arrest<br>○ Inhibition of angiogenesis | ○ Highly invasive or metabolic tumors<br>○ e.g. bladder |
|  **ONCOS-214** *Enhanced cell killing properties* | ○ Immunogenic cell death<br>○ Extend cell killing ability to neighboring non-infected cells | ○ High-stroma tumors<br>○ e.g. pancreas |
|  **ONCOS-211** *Counteract immune-suppressive tumor microenvironment* | ○ Removal of immune suppressive molecules from tumor microenvironment<br>○ Activation of T-cells | ○ "Cold" uninflamed tumors<br>○ e.g. colorectal |



targovax

# ACTIVATING THE PATIENT'S IMMUNE SYSTEM

## TO FIGHT CANCER

### CLINICALLY PROVEN

One of the furthest developed oncolytic viruses

Strong single agent data

Activation of anti-PD1 resistant tumors

### RICH NEWS FLOW

Mesothelioma randomized data January 2020

Melanoma Part 2 data 1H 2020

### INNOVATIVE PIPELINE

Next generation virus platform in pre-clinical testing

Available for collaborations and partnering