# ACTIVATING THE PATIENT'S IMMUNE SYSTEM TO FIGHT CANCER

Øystein Soug, CEO

December 2019

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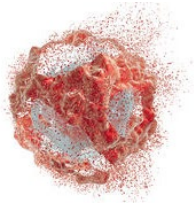
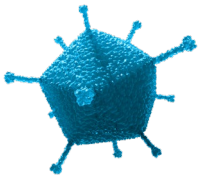
# ACTIVATING THE IMMUNE SYSTEM

## TO FIGHT CANCER



### Growing need for immune activators

- Immune activators can enhance the efficacy of checkpoint inhibitors
- ONCOS oncolytic adenovirus platform targets 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 ensuring **rich news flow** in 2020

### Encouraging clinical efficacy demonstrated

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

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### Listed on Oslo Stock Exchange

- Ticker: **TRVX**
- All assets unencumbered

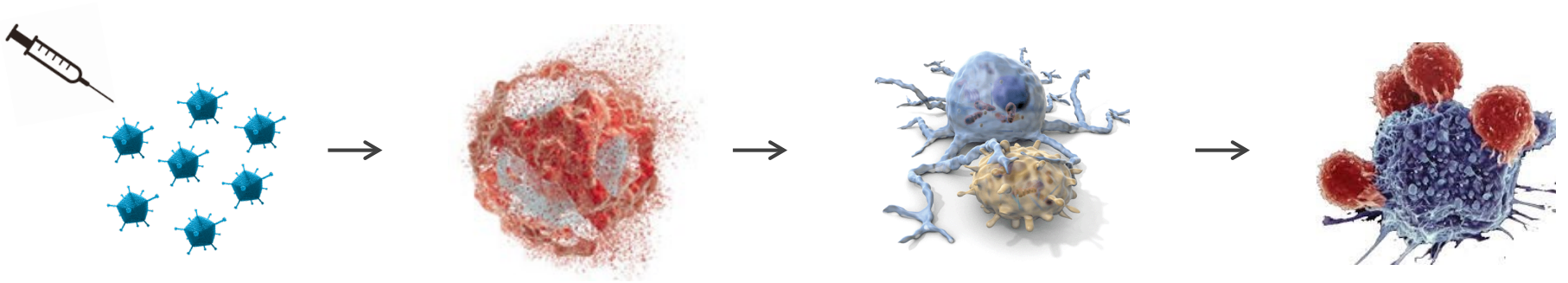
# ONCOS-102 MODE OF ACTION

**1 Virus injection**
Local delivery

**2 Oncolysis**
Immune activation

**3 Antigen processing**
T-cell activation

**4 T-cell response**
Anti-tumor immunity



- Intra-tumoral or intra-peritoneal injection
- Tumor cell infection

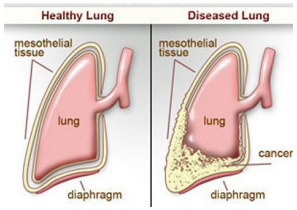
- Lysis of tumor cells
- Inflammatory response
- Tumor antigen release

- Antigen processing
- T-cell activation in lymph nodes

- T-cell tumor infiltration
- Tumor antigen recognition

# ONCOS DEVELOPMENT STRATEGY

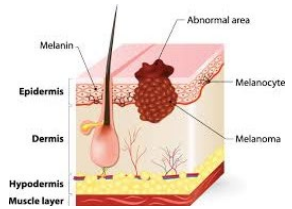
## 1 Establish path-to-market




**Mesothelioma**

- ~15.000 patients
- Potential for first line, limited competition

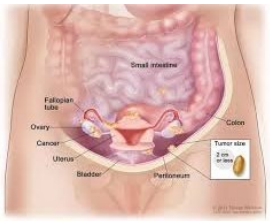
## 2 Activate refractory tumors




**Anti-PD1 refractory melanoma**

- Few alternatives for ~50.000 patients
- Benchmarking arena for immune activators

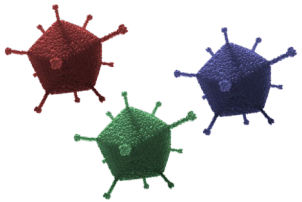
## 3 Expand CPI indications




**Peritoneal malignancies**

- Metastases from ovarian and colorectal cancers
- >100.000 patients not responding to CPIs

## 4 Expand platform



**Next generation oncolytic viruses**

- Double transgenes
- Novel targets and modes of action



Patient numbers are yearly incidence in EU5, US and Japan, Company estimates based on Global Data

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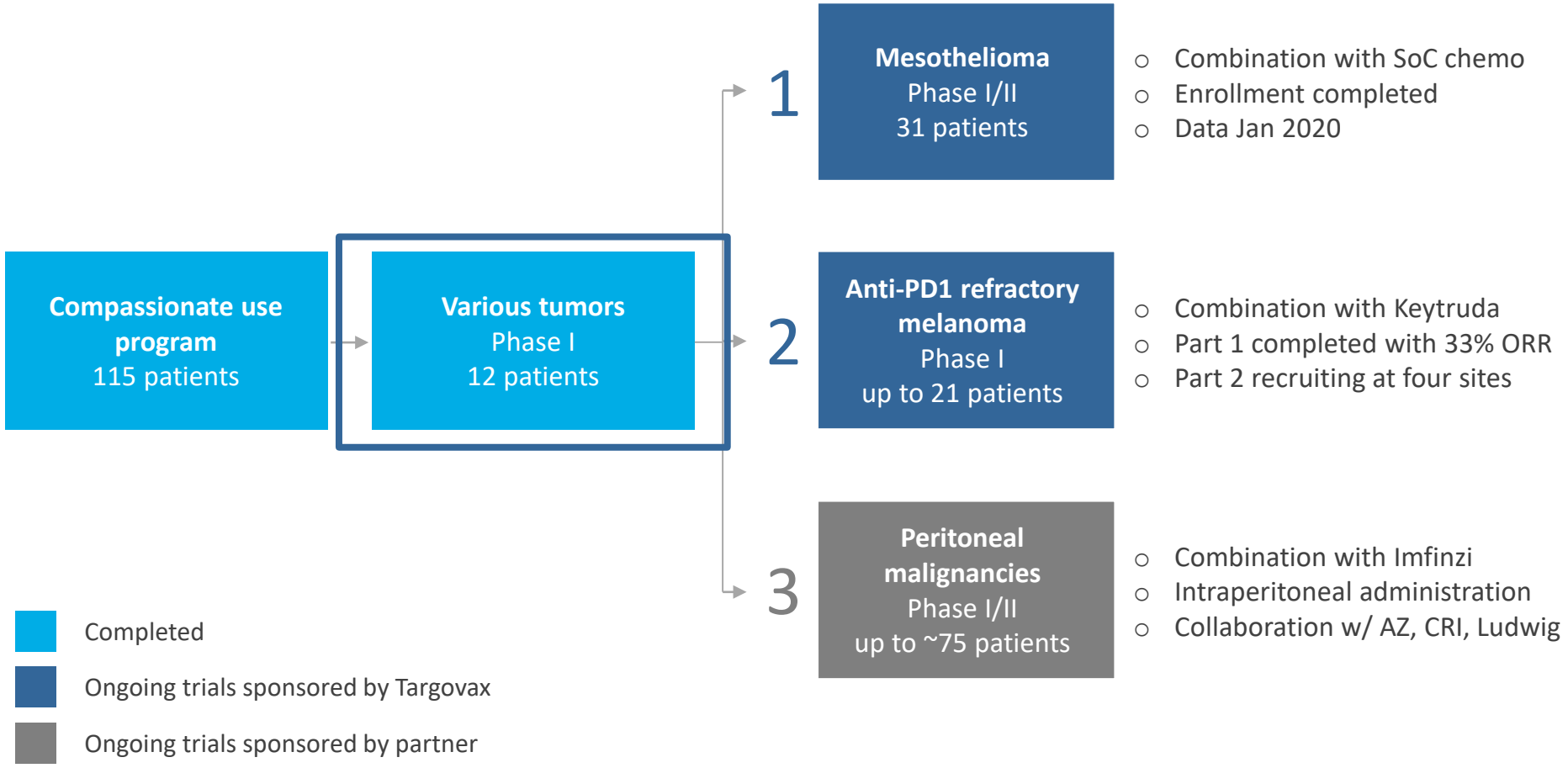
# ONCOS-102 CLINICAL DEVELOPMENT PROGRAM






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

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ONCOS-102

PHASE I SINGLE AGENT PROOF-OF-CONCEPT

# IMMUNE ACTIVATION DEMONSTRATED

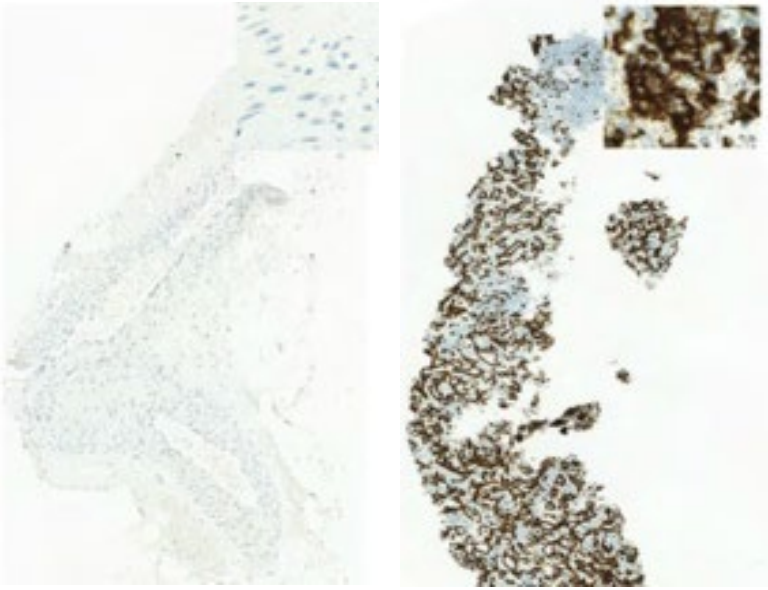
**ONCOS-102 Phase I trial design:**

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

**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



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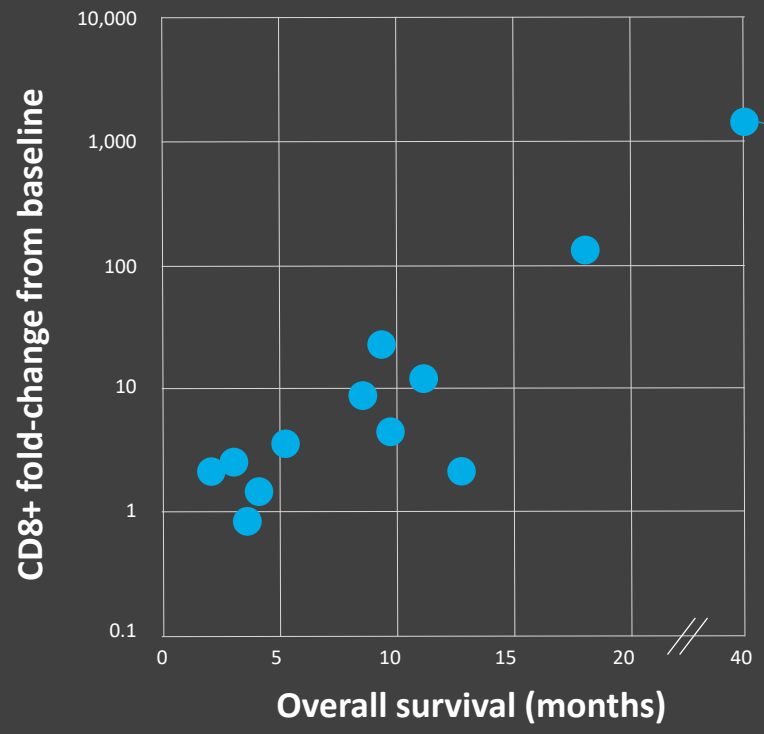
ONCOS-102

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 – 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

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



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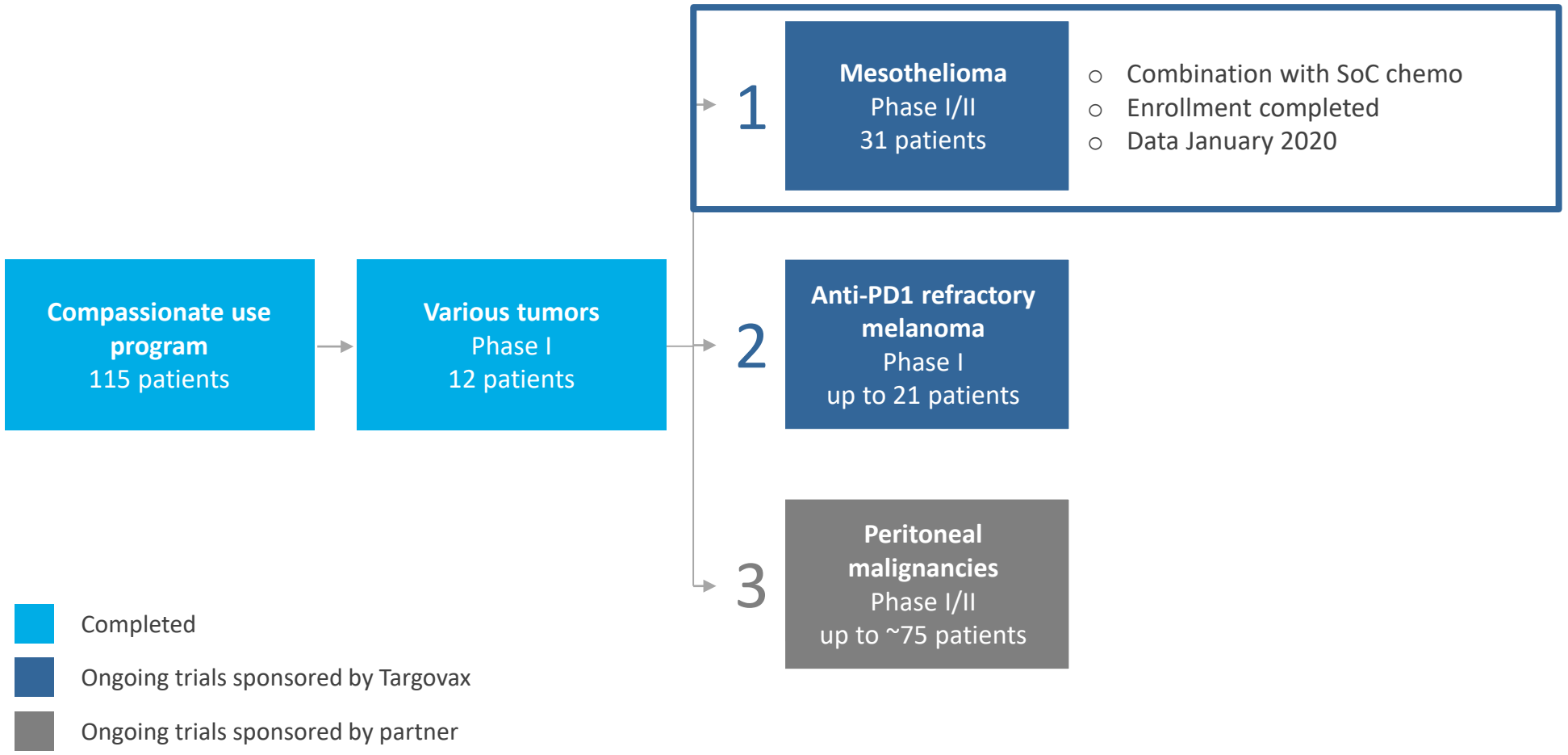
# ONCOS-102 CLINICAL DEVELOPMENT PROGRAM



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# RATIONALE FOR ONCOS-102 GO-TO-MARKET STRATEGY IN MESOTHELIOMA

**Become frontline therapy**

- Data so far indicate activity in mesothelioma
- Ongoing randomized trial combining with chemo
- Good safety profile

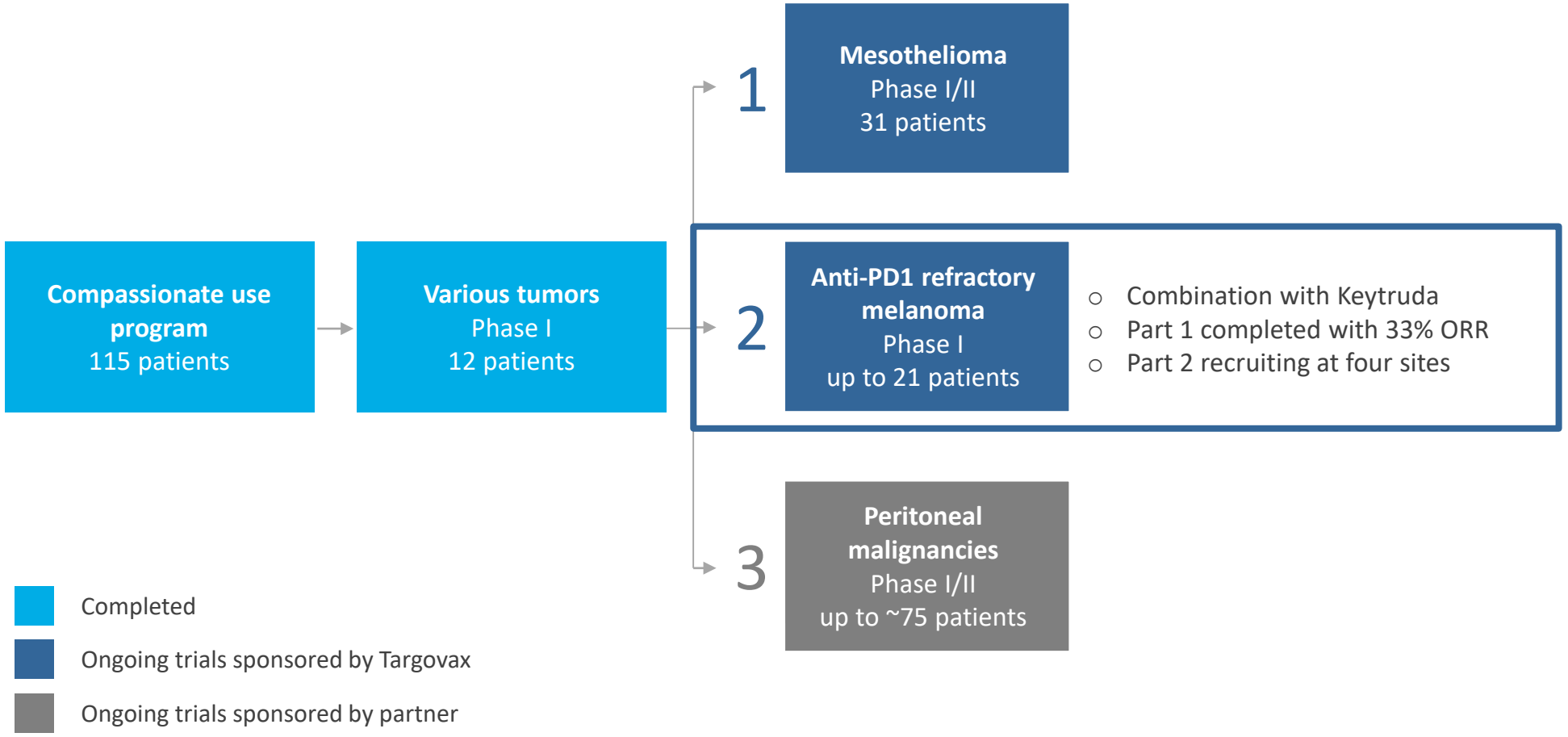
**Orphan Drug Designation**

- High unmet medical need; orphan drug designation
- 7-10 year market exclusivity
- Opportunity for accelerated regulatory routes to market

**Limited competition**

- Few other viruses in development
- ONCOS-102 most advanced
- CPIs are potential combinations

# ONCOS-102 CLINICAL DEVELOPMENT PROGRAM



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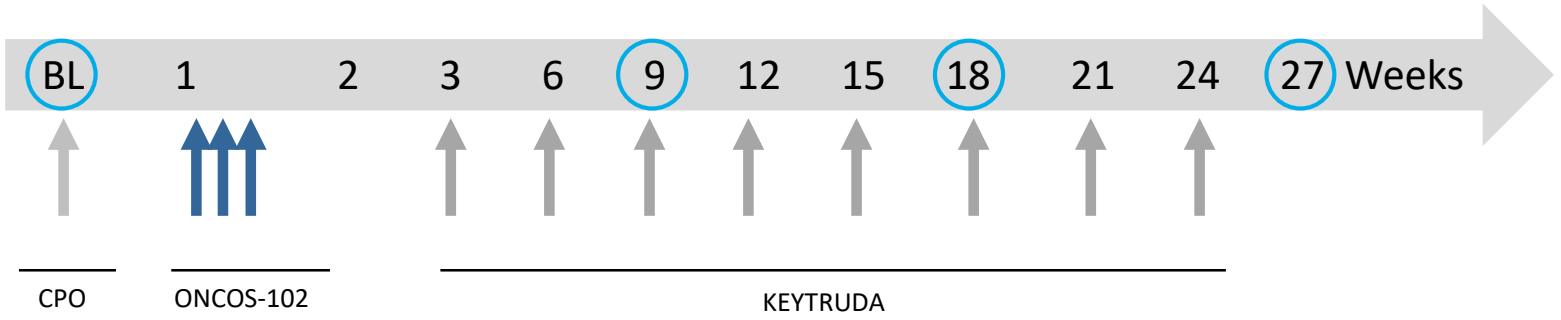
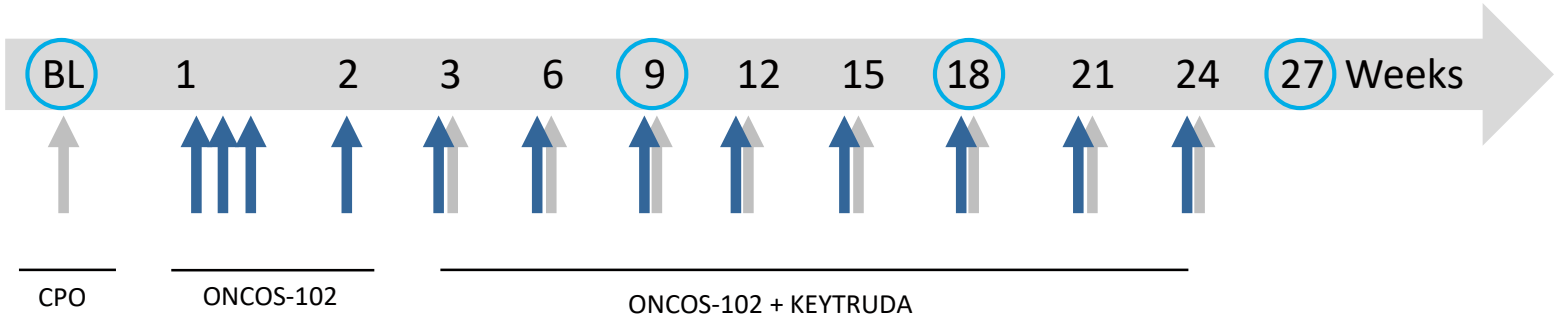
# MELANOMA PHASE I TRIAL DESIGN

## 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*



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ONCOS-102 ANTI-PD1 REFRACTORY MELANOMA PART 1

# 33% ORR AND ROBUST IMMUNE ACTIVATION

**Patient population**

- Advanced, unresectable **melanoma**
- Disease **progression** following prior treatment with anti-PD1
- Poor prognosis, with **few treatment alternatives**

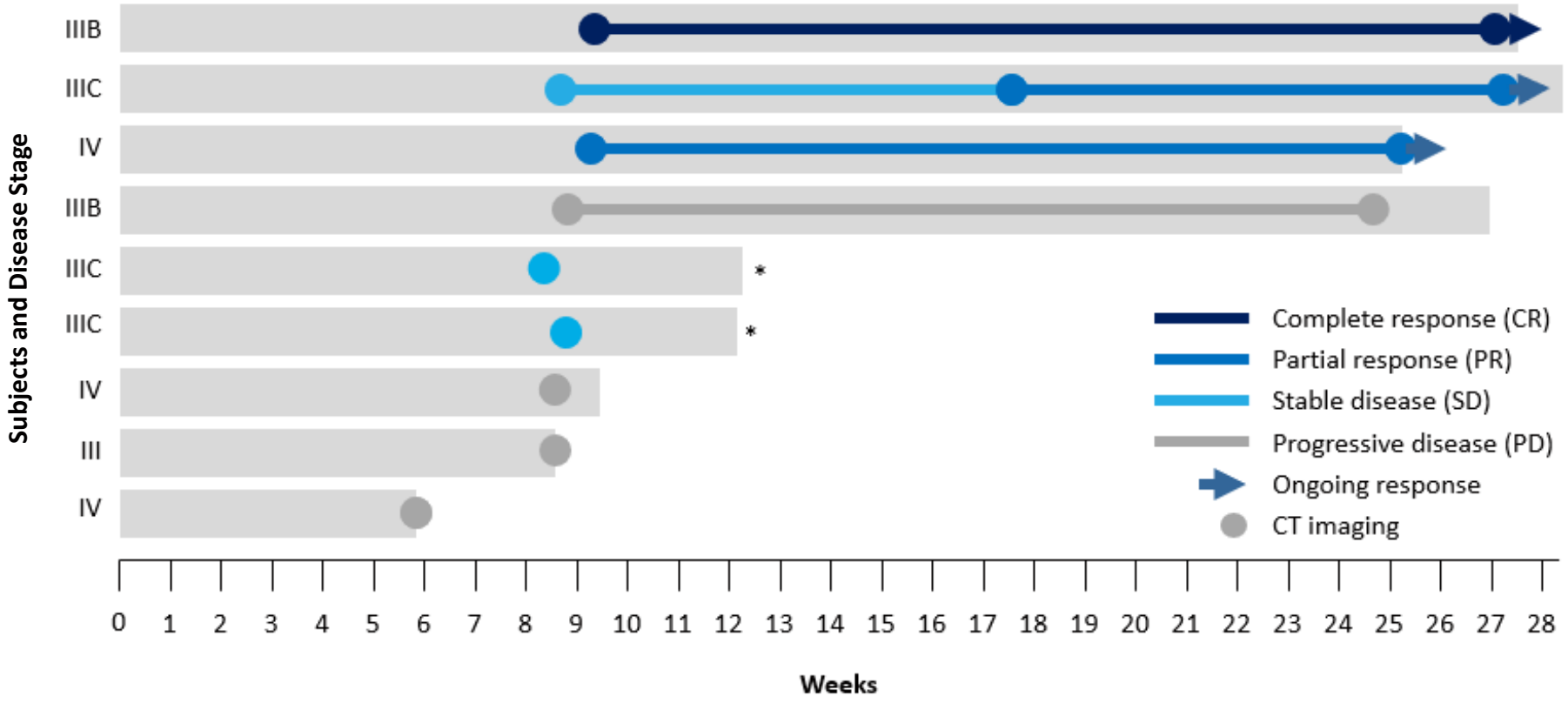
**Treatment regime**

- **3 ONCOS-102 injections** followed by 5 months of Keytruda

**Clinical data**

- Well tolerated, no major concerns
- **33% ORR** after 6 months by RECIST 1.1 and irRECIST
  - 1 Complete Response (CR)
  - 2 Partial Responses (PR)
- Robust systemic and local **immune activation**

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




∗ Withdrawn due to clinical PD

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



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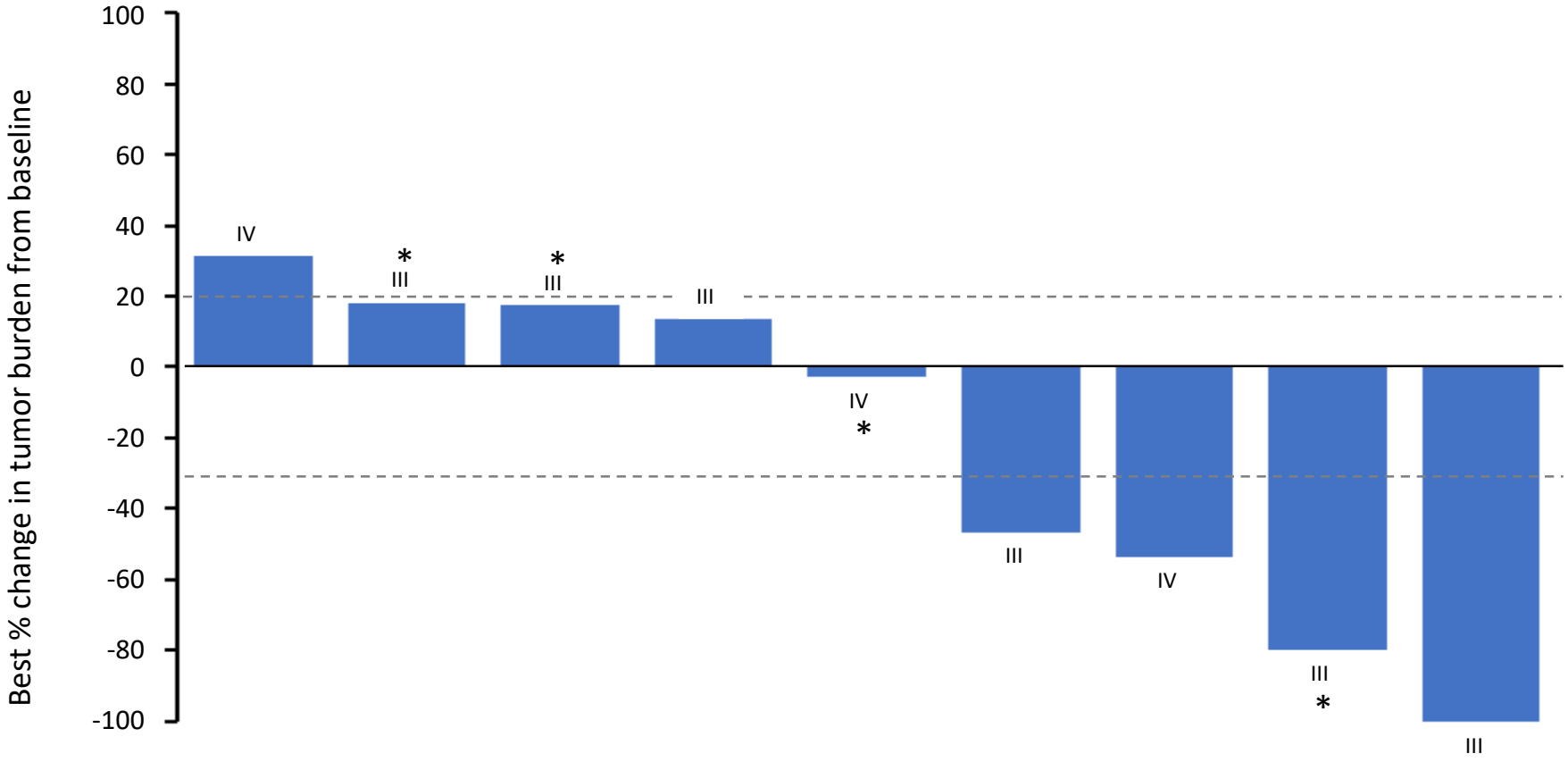
# BEST PERCENTAGE CHANGE IN TARGET LESIONS




* Progressive Disease due to non target progression

Letters and numbers indicating disease stage

Preliminary data



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# CASE EXAMPLE: PATIENT WITH COMPLETE RESPONSE

## Patient characteristics

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

**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 |



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# CASE EXAMPLE: PATIENT WITH PARTIAL RESPONSE

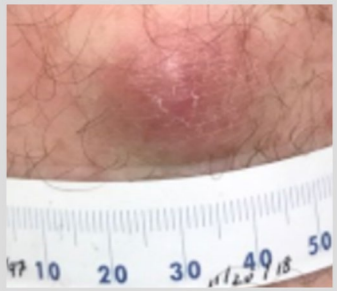
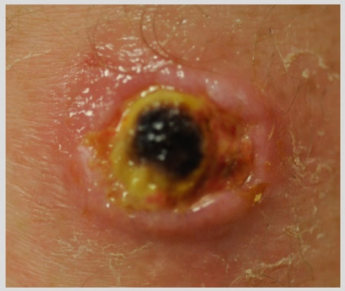
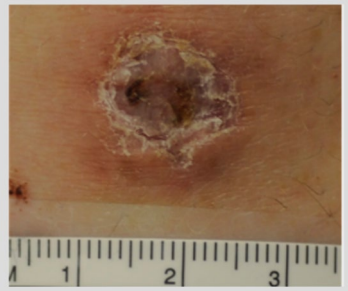
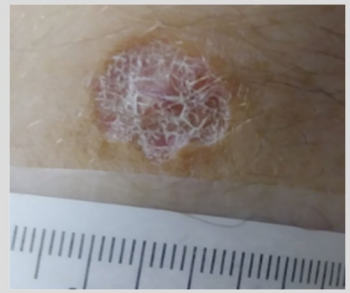
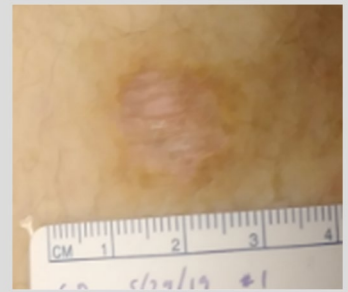
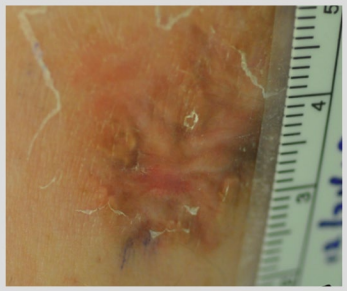
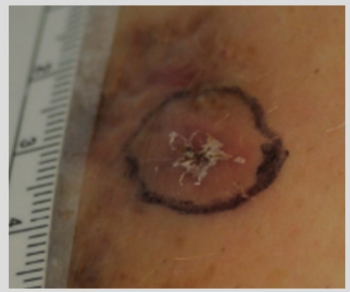
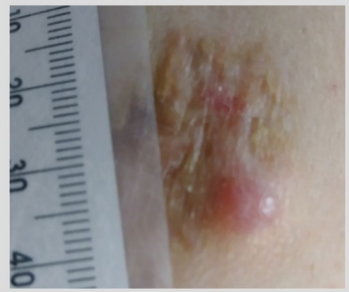
## Patient characteristics

**Tumor stage at enrollment:** **IV**
T4a, N1b, M1

**RECIST 1.1:** **PR**, week 9-27

**Prior therapies:**
Surgery
Talimogene-laherparepvec (T-vec)
Ipilimumab
Keytruda

**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 |



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# ROBUST LOCAL AND SYSTEMIC IMMUNE ACTIVATION

## Inflammatory response and innate immune activation

- Pro-inflammatory cytokine increase: IL-6 (8/8 pts), TNFa (7/8 pts)
- Increase in systemic IFNγ expression (8/8 pts)
- Fever/chills (7/9 pts)

## Adaptive immune activation

### T-cell tumor infiltration

- Increase in CD8+ T-cell infiltration (8/9 pts)
- Increase in activated[1] CD8+ T-cells (9/9 pts)
- PD1+/CD8+ T-cells in treated lesions (6/7 pts)
- T-cells in non-treated lesions (2/3 pts) on Week 3

### Tumor specific activation

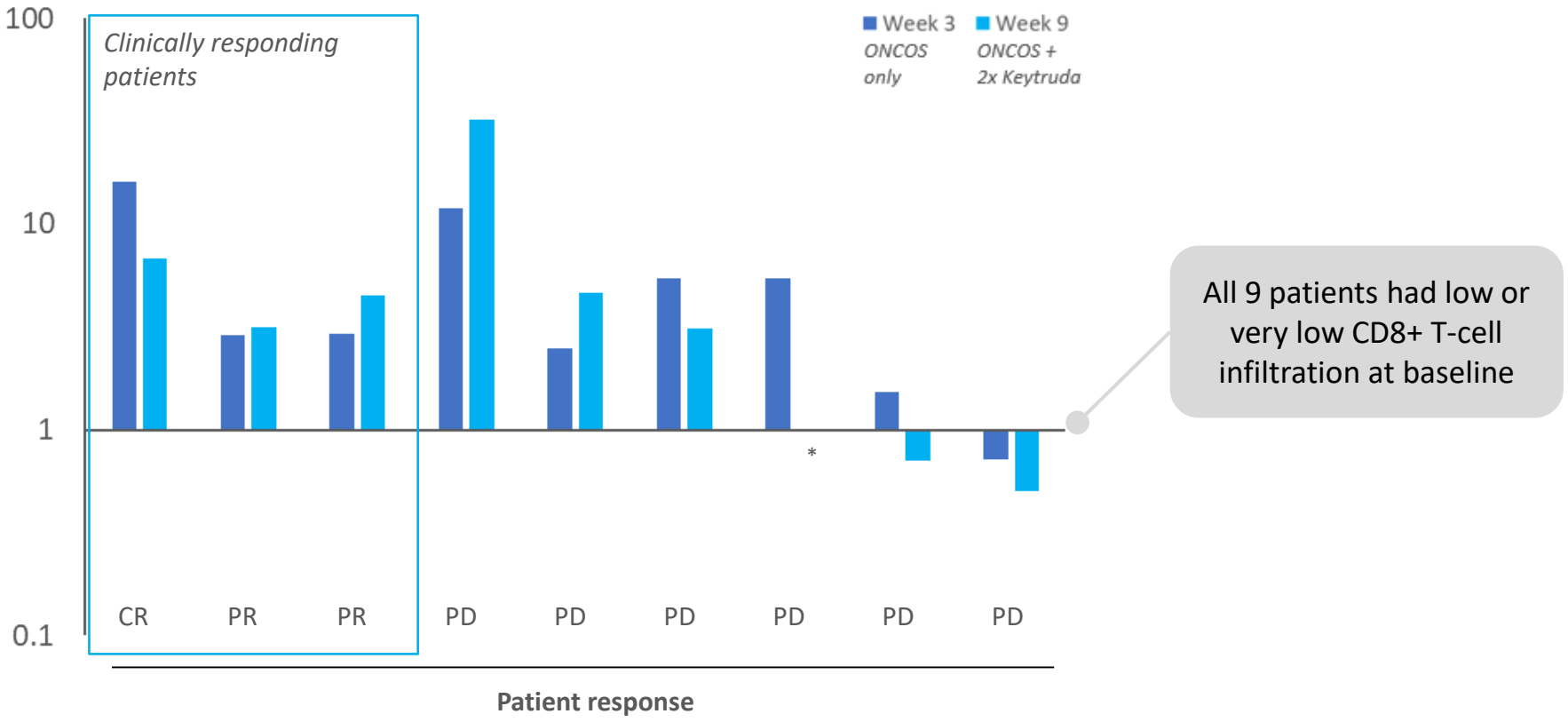
- Systemic increase in tumor specific T-cells (4/9 pts, NY-ESO-1 and/or MAGE-A1)
- Increase in PD-L1 expression in tumor (6/9 pts)
- Melanoma specific cancer markers strongly reduced in 2 of 3 responders



1 Defined as GRZB+/CD8+ T-cells
Unpublished company data

# 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




Do not post, unpublished company data

- Week 9 analysis not available

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



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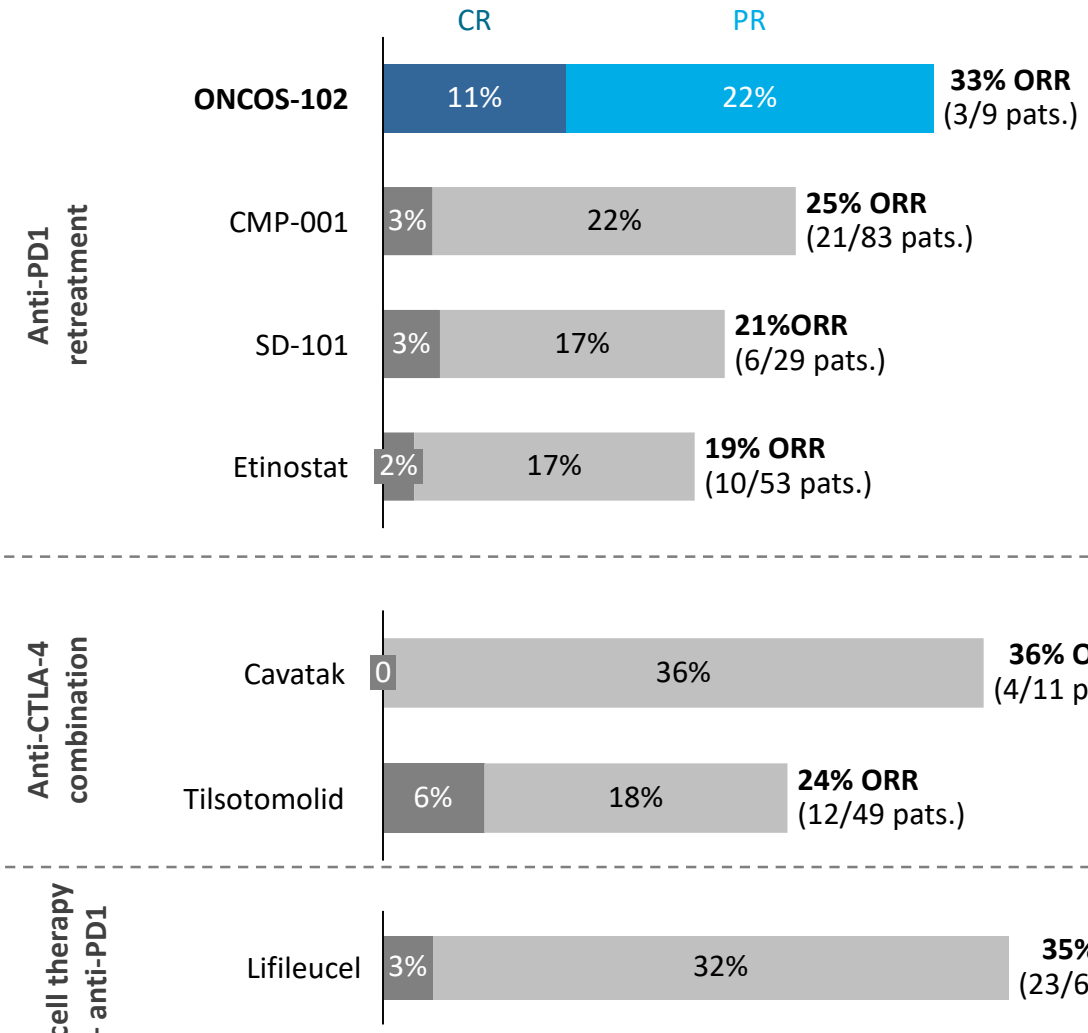
# ONCOS-102 + KEYTRUDA DATA IN CONTEXT

## 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, November 2019

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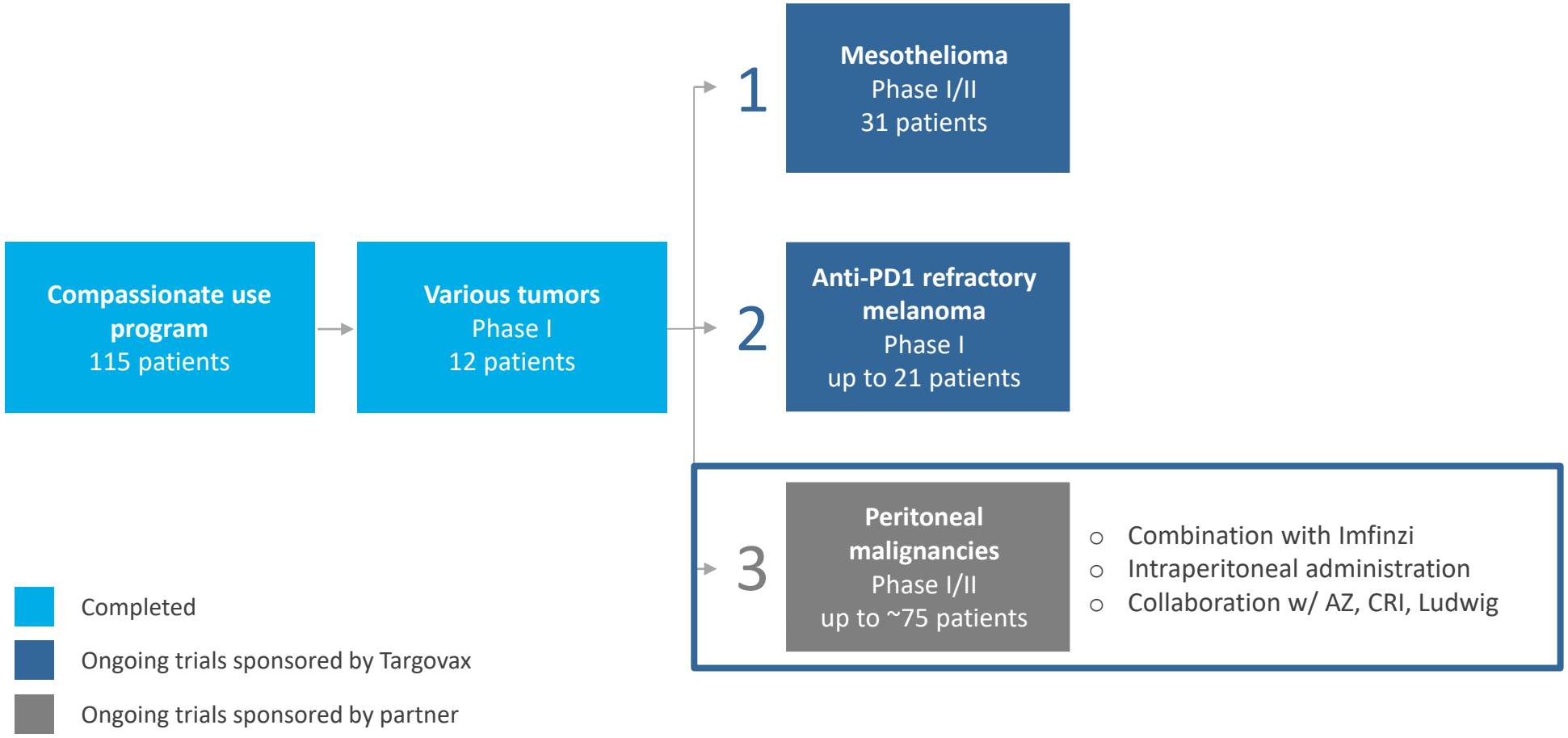
# ONCOS-102 CLINICAL DEVELOPMENT PROGRAM

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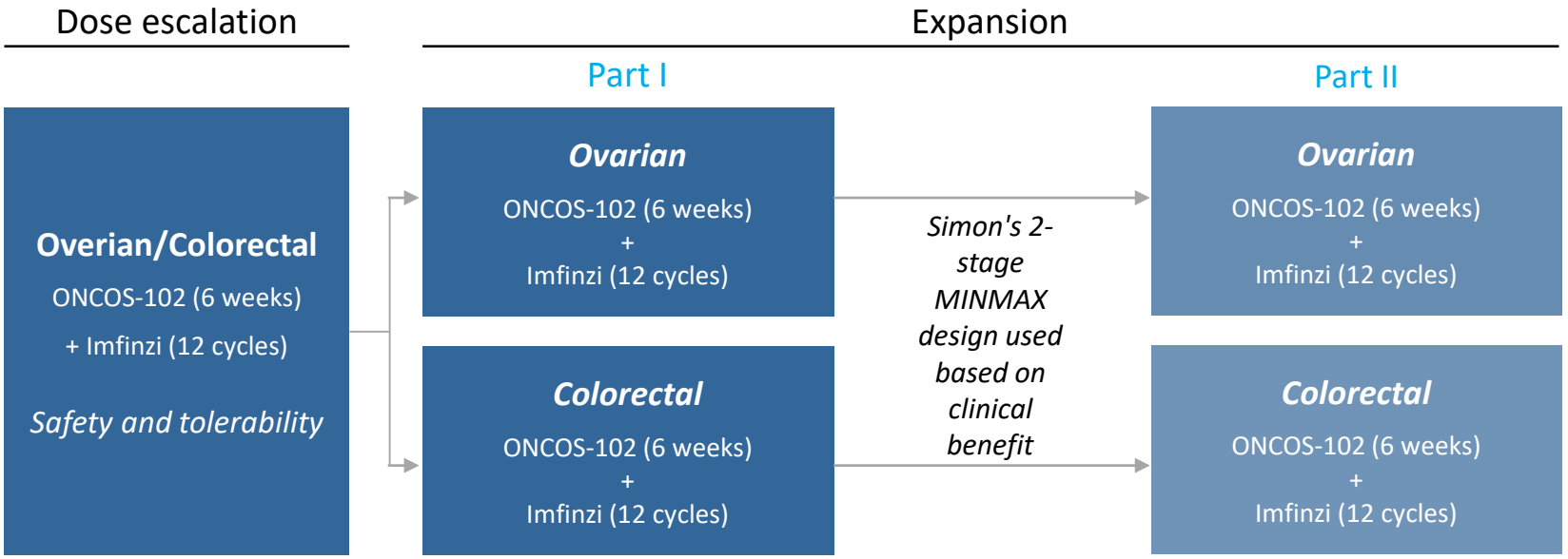
ONCOS-102 IN PERITONEAL MALIGNANCIES

# PHASE I/II TRIAL IN COMBINATION WITH IMFINZI

Collaboration with US-based Cancer Research Institute,
Ludwig Cancer Research (trial sponsor) and AstraZeneca

**Patient population**: peritoneal disease who have failed prior standard chemotherapy and have histologically confirmed platinum-resistant or refractory epithelial ovarian cancer or colorectal cancer



# 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>Clinical and immune activation data |
| | **Melanoma**<br>Combination w/Keytruda | | | | **1H 2020**<br>Clinical and immune activation data |
| | **Peritoneal malignancies**<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 |



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# ACTIVATING THE IMMUNE SYSTEM

## TO FIGHT CANCER

### CLINICALLY PROVEN

One of the furthest developed oncolytic viruses

Strong single agent data

Activation of anti-PD1 refractory tumors

### INNOVATIVE PIPELINE

Next generation virus platform in pre-clinical testing

### RICH NEWS FLOW

Clinical and immune activation from mesothelioma and melanoma trials in 1H 2020