ONCOS-102: from lab to patients

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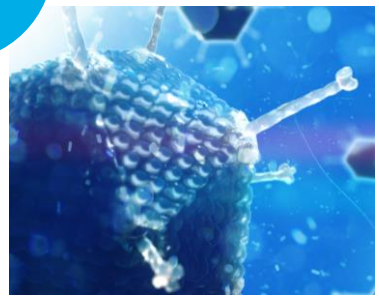
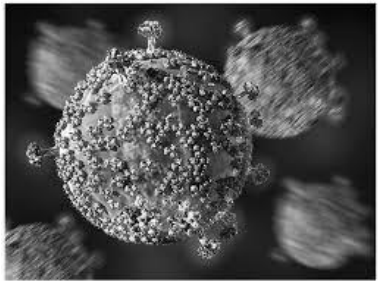
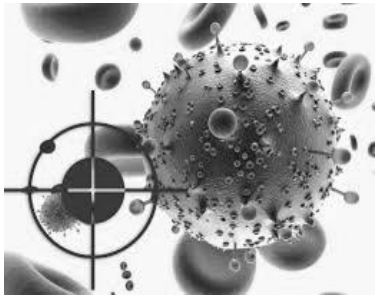
Chief Medical Officer

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

Targovax focus







Immune activators
Oncolytic viruses, vaccines

Immune modulators
Checkpoint inhibitors

Surgery - Radio - Chemo

Immune boosters
CAR-Ts, TCRs

Targeted therapy
PARPs, gene therapy, etc.

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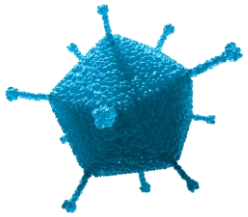
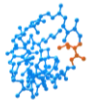


ONCOS
Oncolytic virus

Lead product candidate

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



TG
Neoantigen vaccine

Pipeline product

- Triggers the immune system to **recognize mutant RAS cancers**

Activates the immune system

Triggers patient-specific responses

No need for individualization

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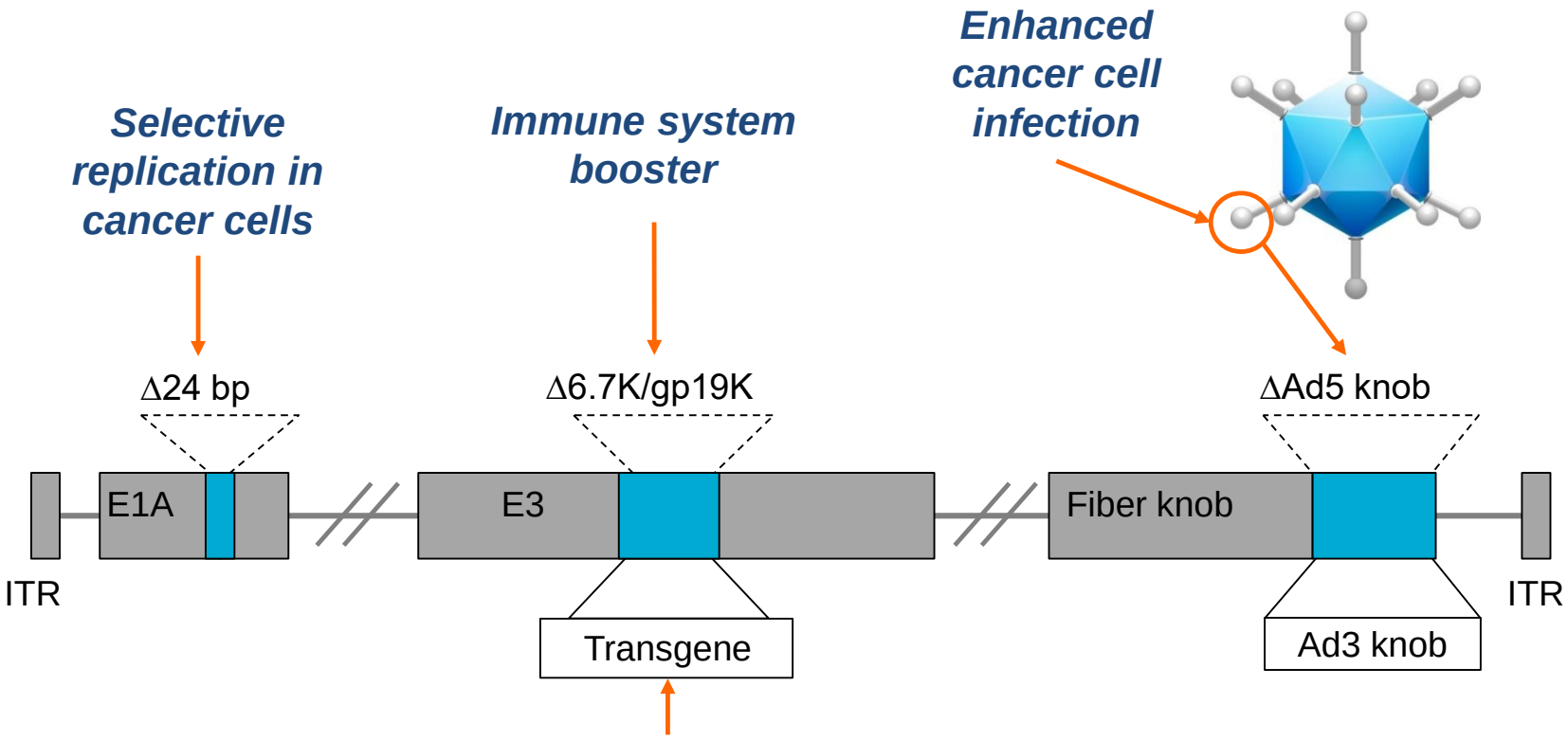
ONCOS-102 is a cancer targeting adenovirus armed with an immune stimulating transgene



- *GM-CSF transgene*
- *Triggers innate immune response and recruits APCs*

ONCOS-102 makes tumors visible to the immune system

1. Activate immune system:

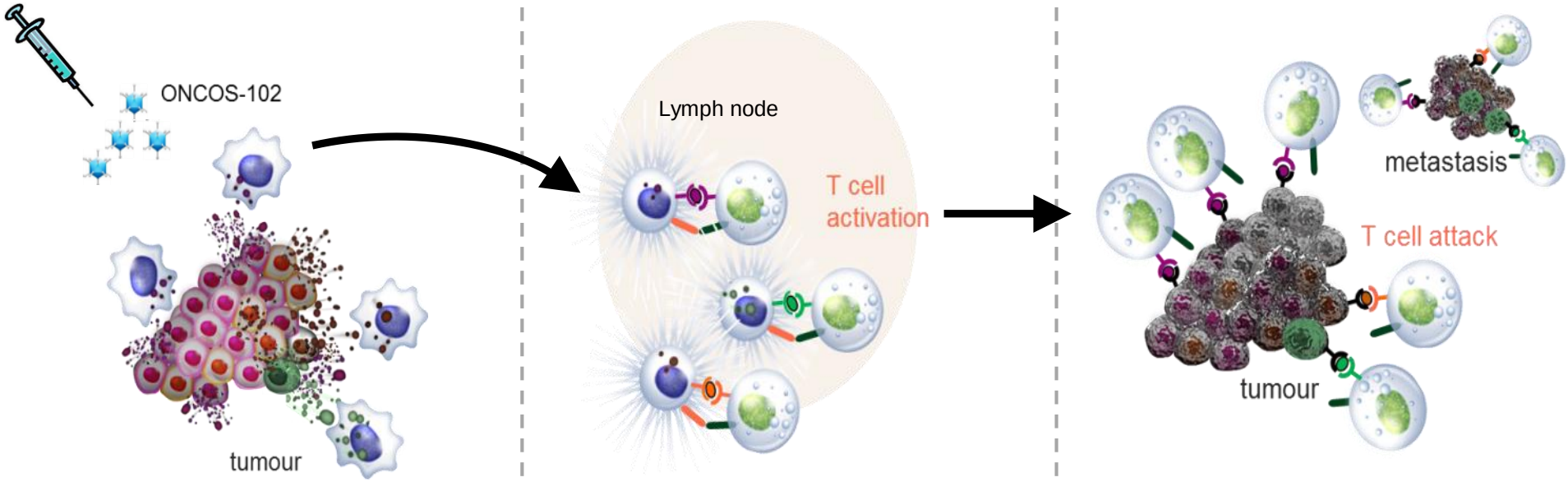
- Virus injected **directly into the tumor**
- Infected cells lyse and **release cancer-specific antigens**

2. Induce T-cells:

- APCs bring the cancer-specific **antigens to lymph nodes**
- Induction of **tumor specific T-cells**

3. Attack the cancer:

- Tumor specific T-cells **identify and destroy cancer cells**
- **Cold tumors become hot**

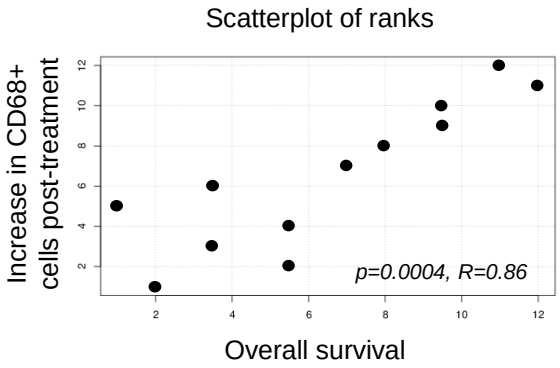


Phase I: ONCOS-102 triggers a cancer specific immune response

Innate immune response triggered

Innate Immune System (biopsy)

- Induction of proinflammatory cytokines + fever (all patients)
- Infiltration of innate immune cells into tumors in 11 out of 12 patients



Correlation between level of innate immune response and survival

CD8+ T-cells recruited to the tumor

Adaptive immune system (biopsy)

- Increase in T-cell infiltration into tumors (including CD8+ killer T-cells) in 11 out of 12 patients
- Observation in one non-injected distant metastasis

OvCa. patient (FI1-19)

Correlation between increase in CD8+ T-cells and survival

Cancer specific T-cells produced

Anti-tumor immune response (blood)

- Systemic induction of tumor-specific CD8+ T-cells

Ovarian patient:
NY-ESO-1, MAGE-A1, MAGE-A3, and Mesothelin specific CD8+ cells

Mesothelioma patient:
MAGE-A3 specific CD8+ cells

Long-lasting systemic anti-cancer effect

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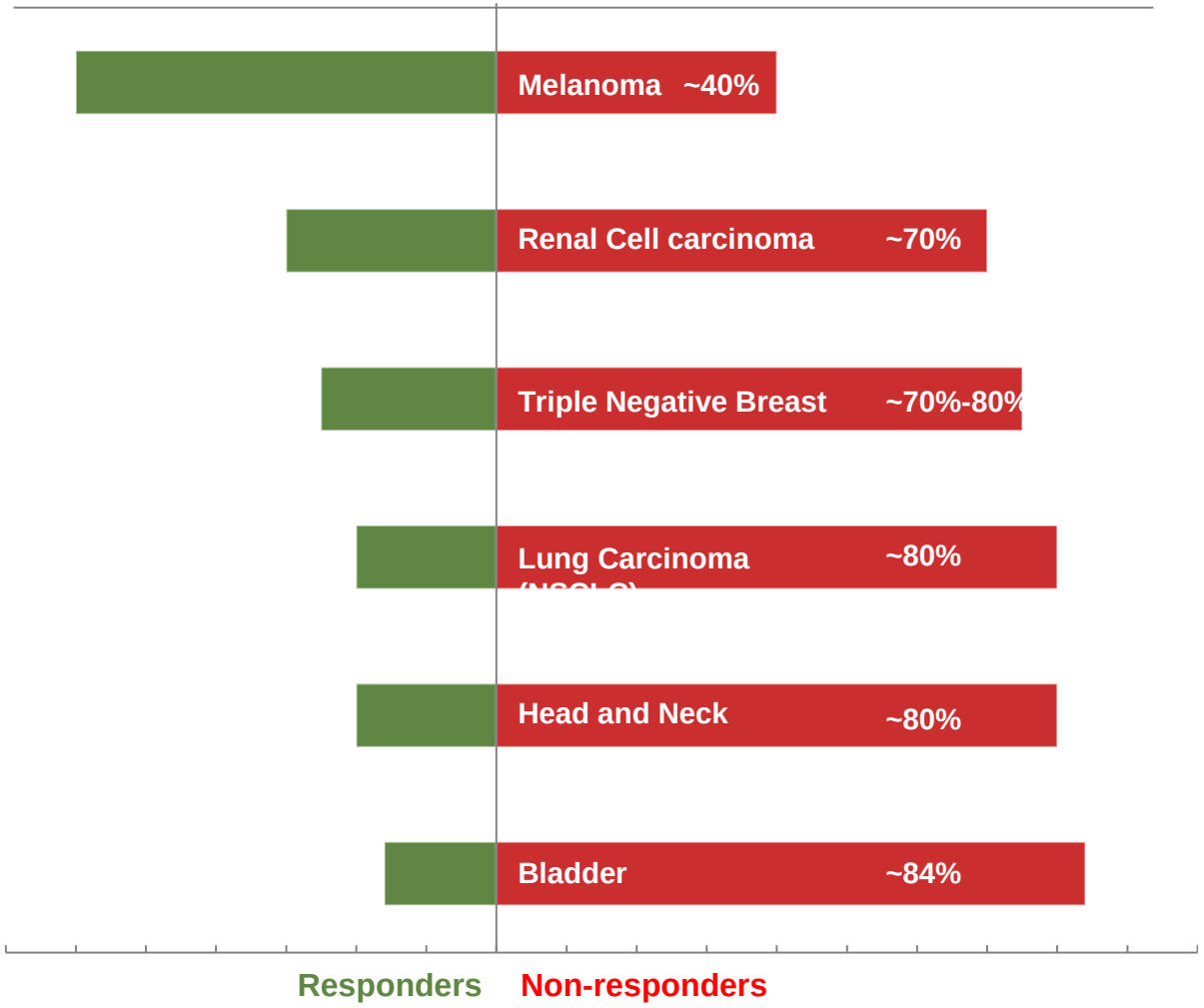
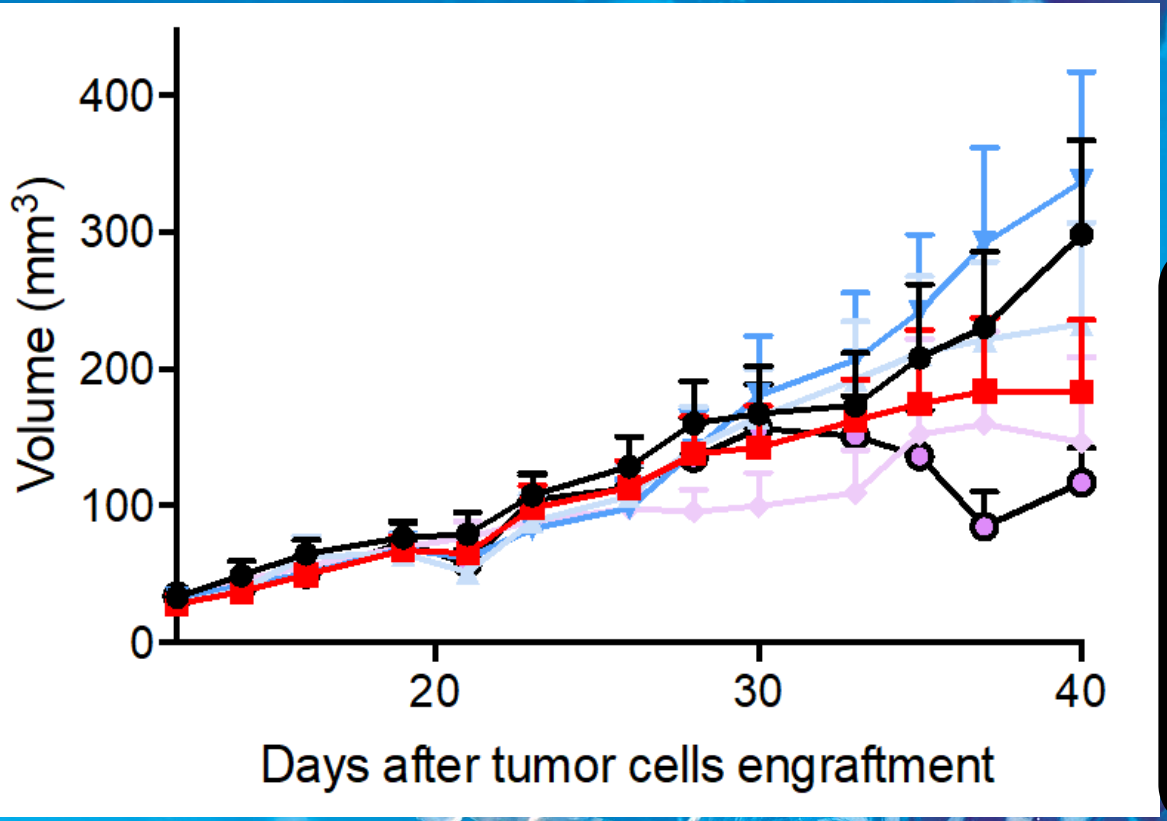
Most patients do not respond to check point inhibitors

Response rate to checkpoint inhibitors (CPIs)



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

70% reduction in tumor volume with ONCOS - CPI combination in humanized mouse melanoma model



Keytruda only	**No change**
ONCOS-102 only	**52%** reduction p<0.05
ONCOS-102 + Keytruda (200)	**61%** reduction p<0.05
ONCOS-102+ Keytruda (400)	**69%** reduction p<0.05

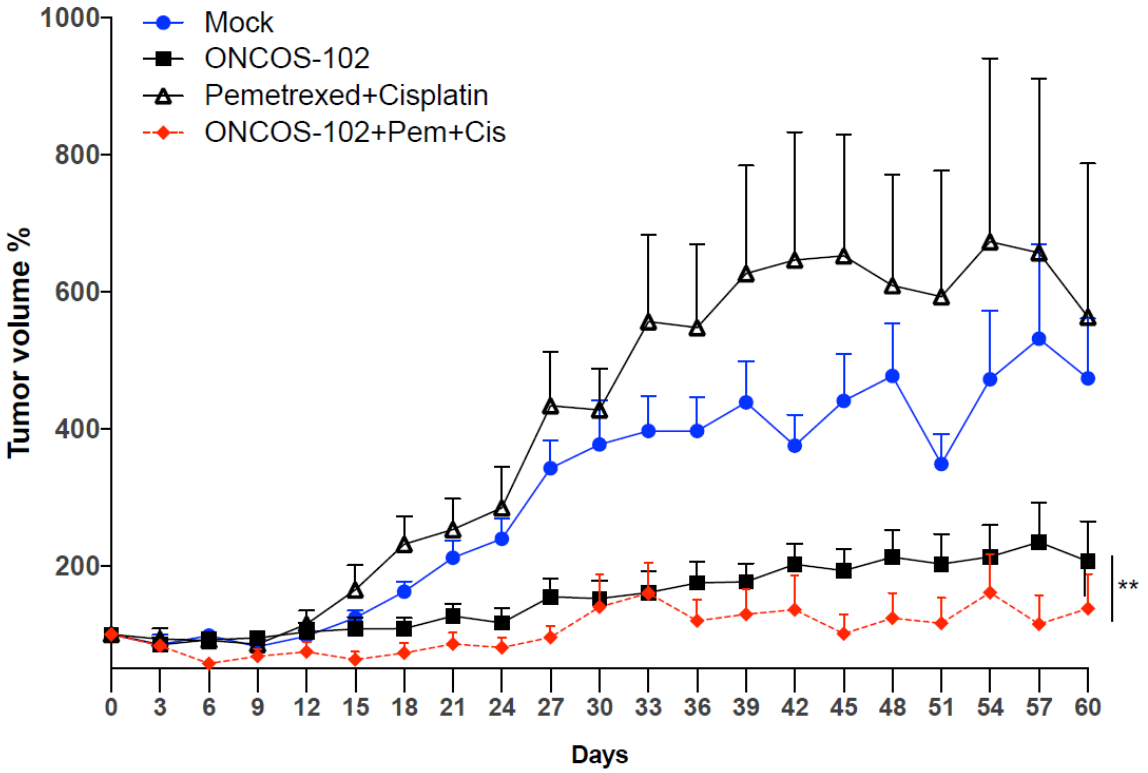
Source: Kuryk et al, ASGTC 2018

SYNERGY BETWEEN ONCOS 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

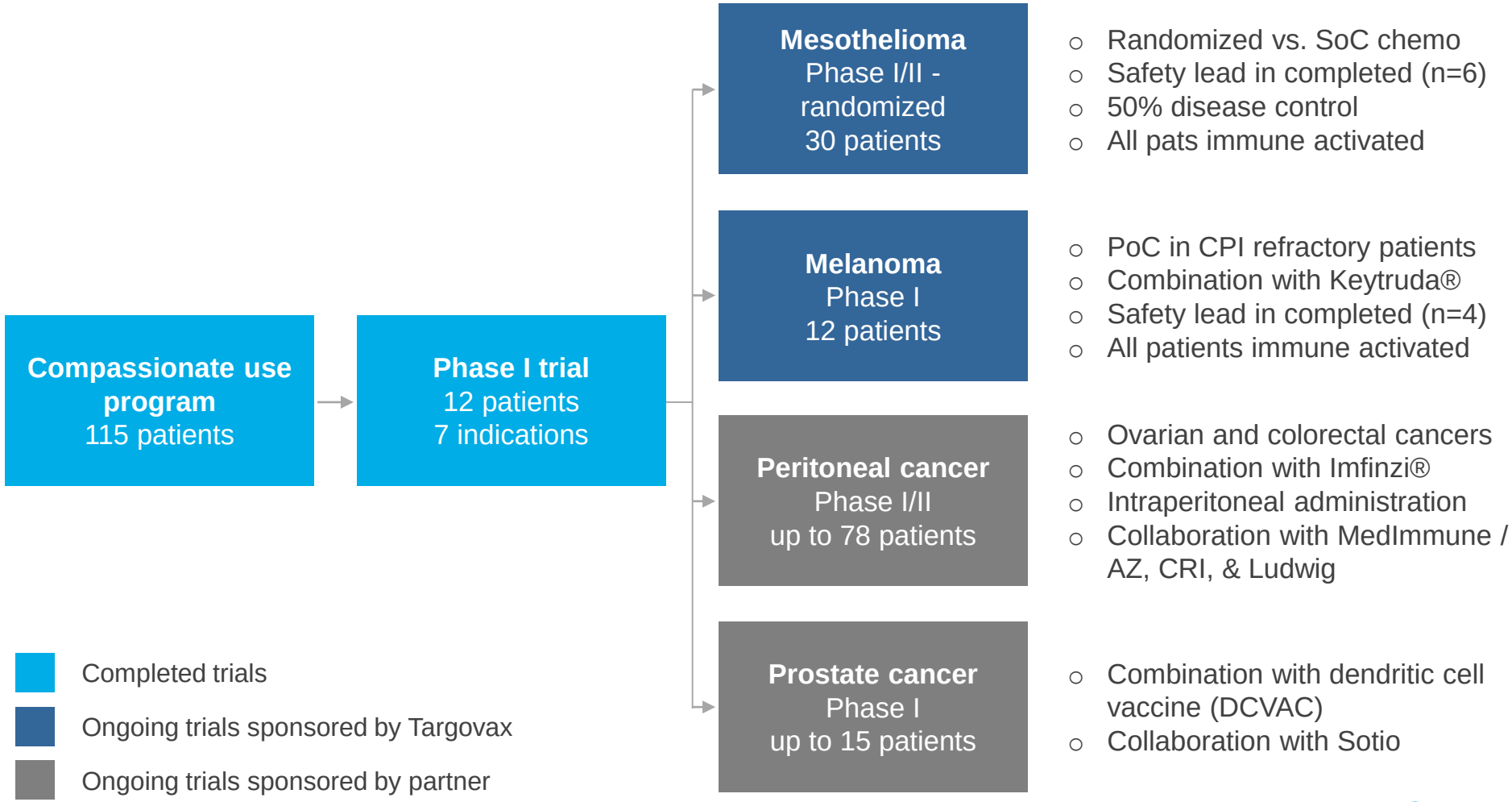
75% tumor volume reduction
p < 0.001

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

33% tumor volume reduction
p < 0.01

SOURCE: Kuryk et al., Int J Cancer, 10 June 2016

CLINICAL PROGRAM OVERVIEW

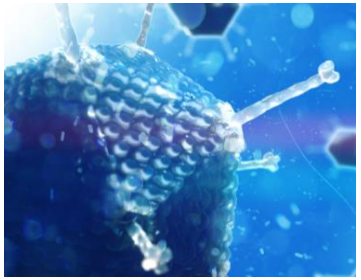


WHY ONCOS-102?

1
In vivo efficacy

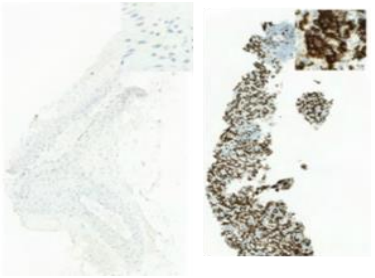
- **Efficacy shown** in both melanoma and mesothelioma models
- **Demonstrated synergy** with both CPIs and chemotherapy

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**

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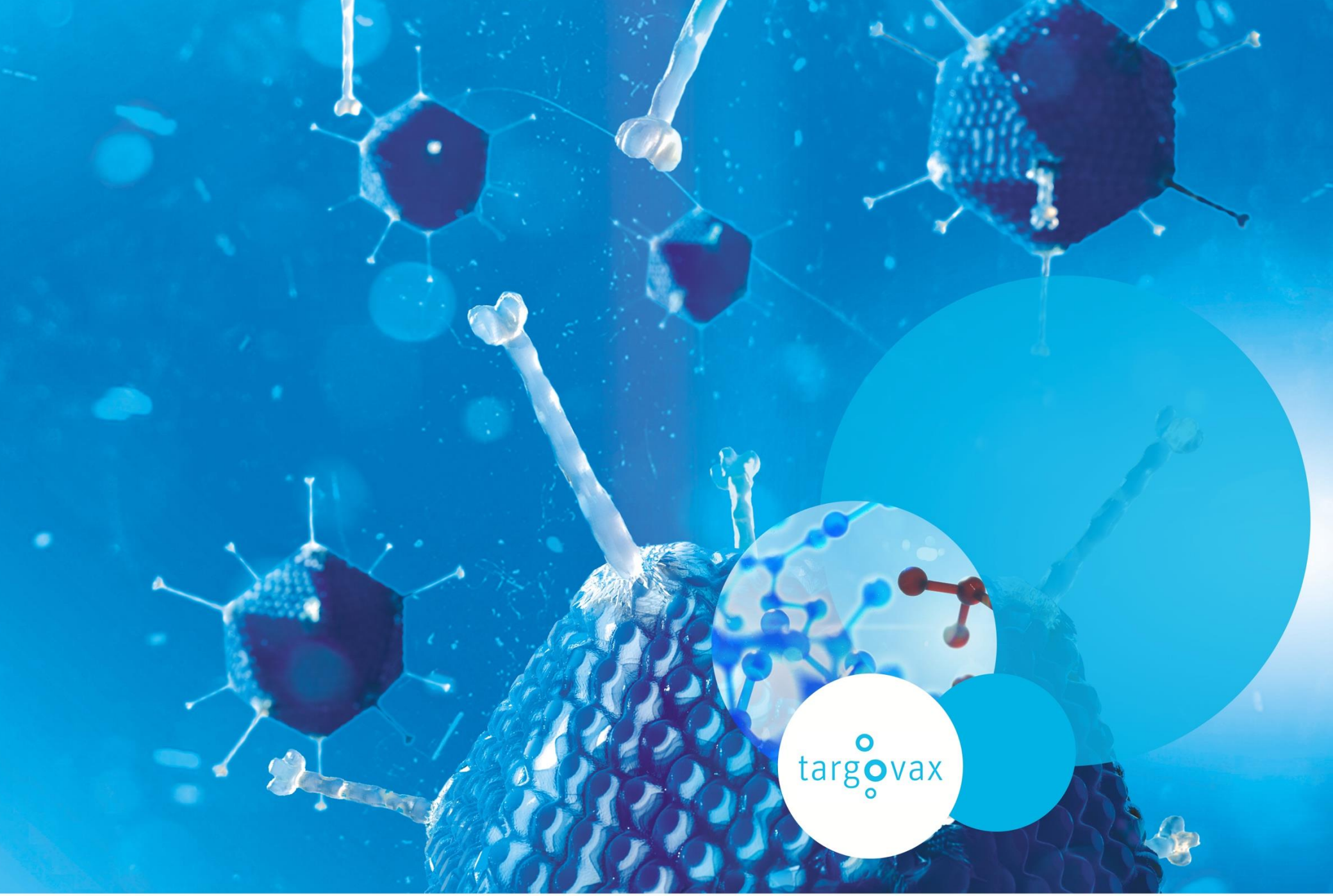
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