



ACTIVATING THE PATIENT'S IMMUNE SYSTEM TO FIGHT CANCER

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targovax

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Introduction

2. Mesothelioma
3. Melanoma
4. Peritoneal malignancies
5. Pipeline and Newsflow

GROWING NEED FOR IMMUNE ACTIVATORS

Checkpoint inhibitors are revolutionizing cancer therapy...

...but minority of patients respond...

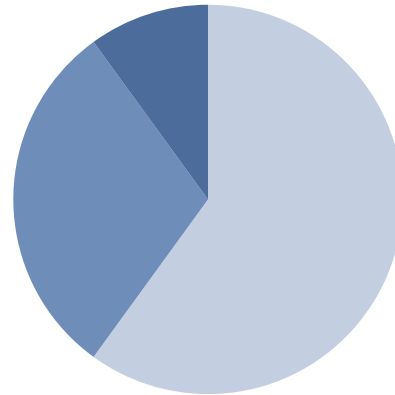
...leading to a high medical need for immune activators

22 bn USD

Global CPI market¹

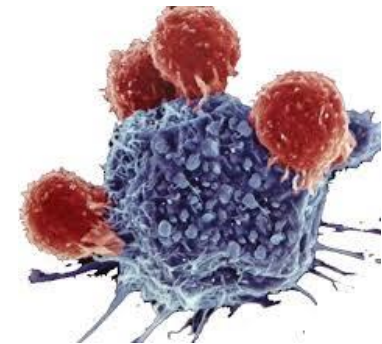
44 %

Patients eligible for CPI²:



10 - 40 %











Responders



¹ Immune Checkpoint Inhibitors Markets Report, 2020 January, ResearchAndMarkets.com

² Estimation of the Percentage of US Patients With Cancer Who Are Eligible for and Respond to Checkpoint Inhibitor Immunotherapy Drugs, JAMA Netw Open. 2019 May; 2(5), Haslam A., Prasad V.

SEVERAL SIGNIFICANT TRANSACTIONS IN THE ONCOLYTIC VIRUS SPACE IN 2018-2020

Acquirer	Target	Type of deal	Deal value
		Strategic collaboration Co-development of multiple vaccinia viruses, Pre-clinical	USD 120m near-term USD >900m total value
		M&A RNA virus, Phase II	USD 400m cash acquisition
		M&A Herpes virus, Pre-clinical	USD 140m up-front USD 1b total value
		M&A VSV virus, Pre-clinical	USD 250m cash acquisition
		R&D partnership Co-development of novel vaccinia viruses, Pre-clinical	USD 10m up-front Unknown total value

ACTIVATING THE IMMUNE SYSTEM TO FIGHT CANCER



ONCOS-102 lead clinical asset

- Oncolytic adenovirus platform targeting hard-to-treat **solid tumors**
- One of the **furthest developed** OV's with >200 patients treated to date
- Combination trials in **several indications** ensuring **rich news flow**



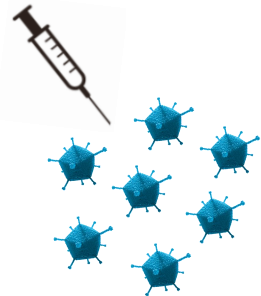
Clinical efficacy demonstrated and platform validation

- Strong clinical and immune data in **single agent, and in combinations with checkpoint inhibitor and chemotherapy**
- Platform endorsement through pharma and biotech collaborations

IMMUNE ACTIVATION STIMULATING T-CELLS

THAT CAN RECOGNIZE AND KILL CANCER

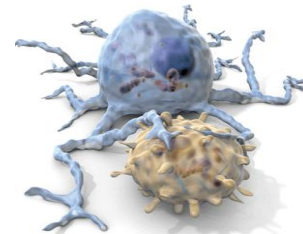
1 Virus injection
Local delivery



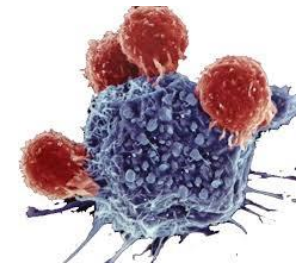
2 Oncolysis
Immune activation



3 Antigen processing
T-cell activation



4 T-cell response
Anti-tumor immunity



- Intratumoral or intra-peritoneal injection
- Tumor cell infection

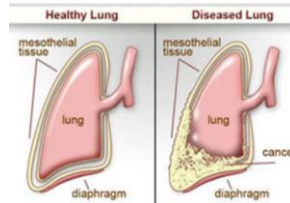
- Lysis of tumor cells
- Inflammatory response
- Tumor antigen release

- Antigen processing
- T-cell activation in lymph nodes

- T-cell tumor infiltration
- Tumor cell killing
- Synergy with checkpoint inhibitors

DEVELOPMENT STRATEGY WITH CPI COMBINATIONS

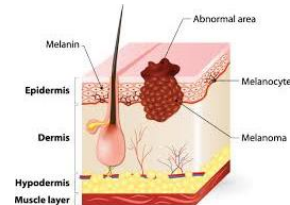
1 Establish path-to-market



Mesothelioma

- ~15.000 patients
- Limited competition, potential for first line

2 Activate refractory tumors



Anti-PD1 refractory melanoma

- Few alternatives for ~50.000 patients
- Competitive indication, serving as benchmarking arena for immune activators

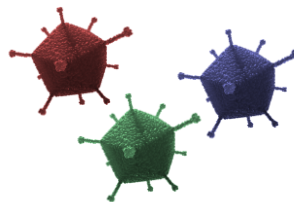
3 Expand CPI indications



Peritoneal malignancies

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

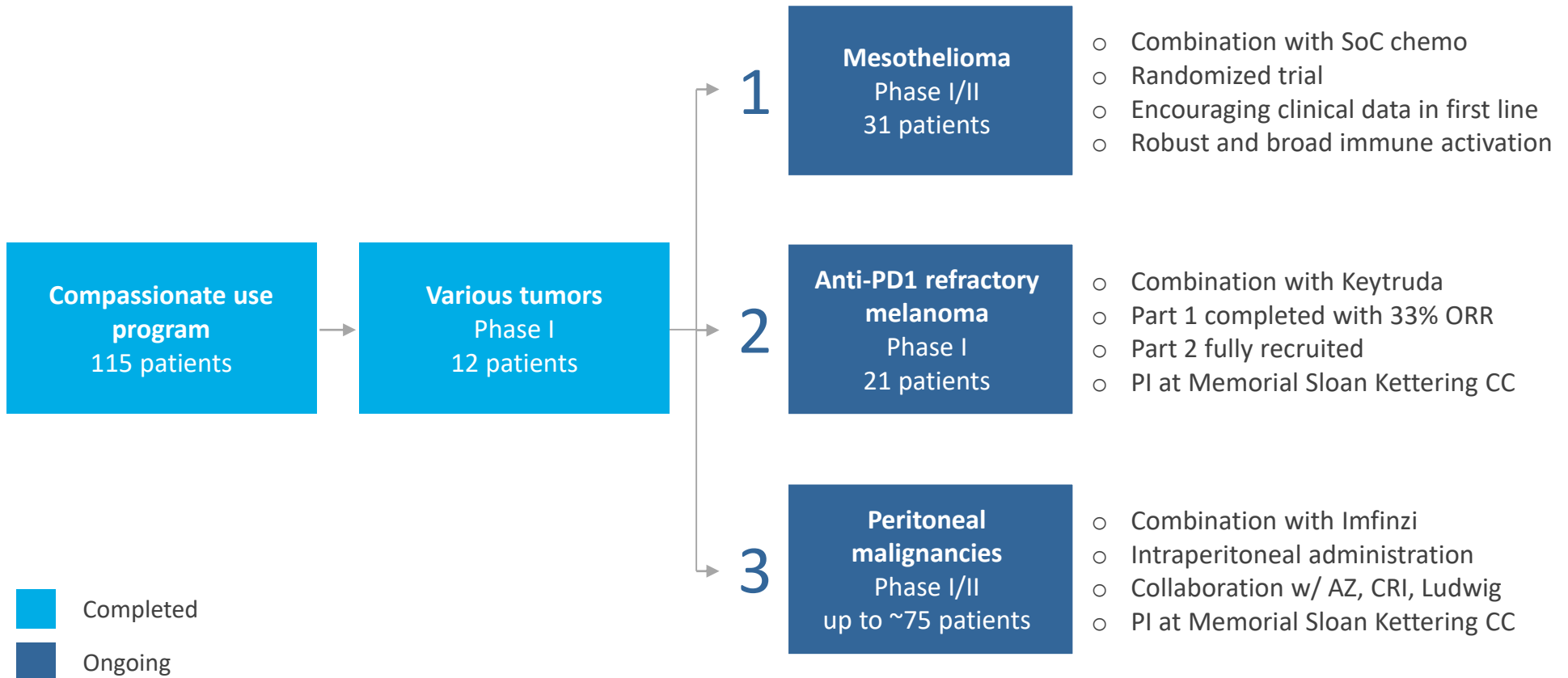
4 Expand platform



Next generation oncolytic viruses

- Double transgenes
- Novel targets and modes of action

CLINICAL DEVELOPMENT PROGRAM



SoC: Standard of Care. ORR: Overall Response Rate. PI: Principal Investigator.

Targovax is also involved in an ongoing combination trial in Prostate cancer where ONCOS-102 is combined with a dendritic cell vaccine (DCVAC).

This trial is sponsored by Sotio, a Czech biotech company

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Mesothelioma

3. Melanoma
4. Peritoneal malignancies
5. Pipeline and Newsflow

HIGH NEED FOR NEW TREATMENT APPROACHES IN MALIGNANT PLEURAL MESOTHELIOMA



Surgery

Only 10% of patients suitable for resection

Often diagnosed too late for surgery

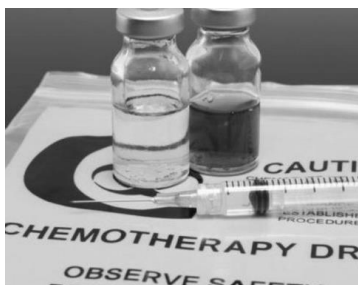
Technically challenging

Radiotherapy

Rarely effective due to tumor shape

Hard to focus radiation

Mainly palliative care



Chemotherapy

Standard of care (SoC) with limited efficacy

Only approved option is pemetrexed/cisplatin

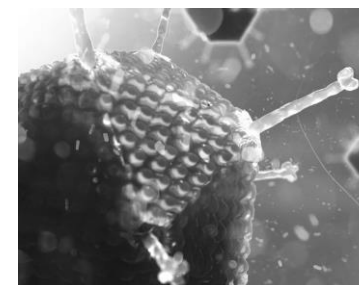
6 months mPFS and 12 months mOS in 1st line

Immunotherapy

Mixed signals from early CPI trials

CPIs included in NCCN guidelines as 2nd line option

Possible frontline therapy with orphan drug designation



ADVANCED MALIGNANT PLEURAL MESOTHELIOMA PHASE I/II TRIAL IN COMBINATION WITH CHEMO

Trial design

- First and second (or later) line
- Standard of Care (SoC) Chemo: Pemetrexed and cisplatin, 6 cycles
- ONCOS-102: 6 intra-tumoral injections

Safety lead-in
n=6

ONCOS-102
plus SoC Chemo

Randomized

Experimental group

n=14

ONCOS-102 plus
SoC Chemo

Control group

n=11

SoC Chemo only

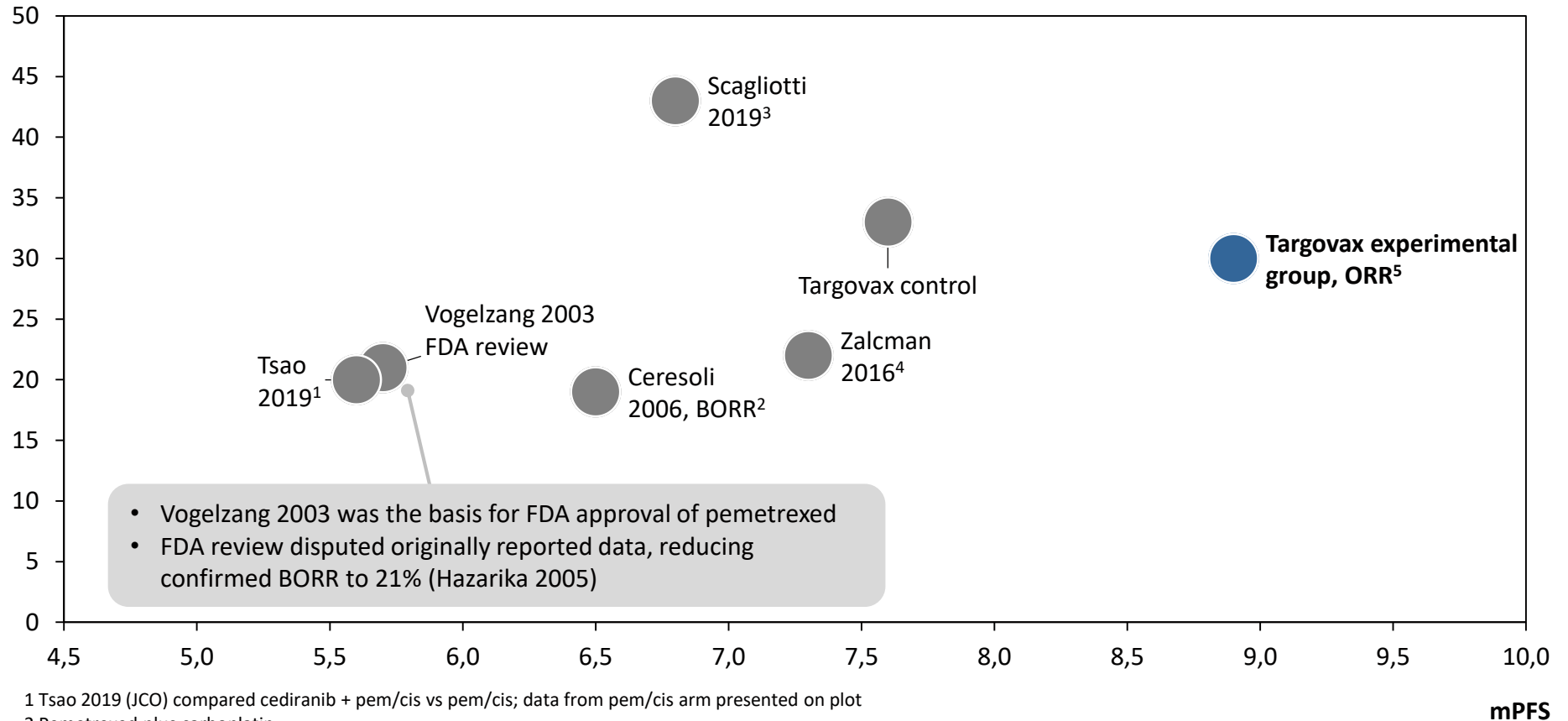
12-MONTH DATA ONCOS-102 MESOTHELIOMA PHASE I/II COMBINATION WITH SOC

PATIENT CHARACTERISTICS AND OUTCOMES

ITT: N = 31 (20+11) PP: N = 30 (19+11)	Experimental n= 20	Control n= 11	Comments
Tumor and disease characteristics at enrollment			
- Number of lesions	4.3	3.5	<i>Generally more advanced disease in the experimental group</i>
- Tumor burden mm (RECIST 1.1)	87	46	
- Stage III	30%	27%	
- Stage IV	60%	46%	
First line patients	11	6	<i>No previous chemotherapy</i>
Disease control rate (DCR)	90%	83%	<i>CR, PR & SD</i>
Median Progression Free Survival (mPFS)	8.9 months	7.6 months	
12-month survival rate	64%	50%	
Second (or later) line patients	9	5	<i>Received previous chemotherapy</i>
Disease control rate (DCR)	67%	80%	<i>CR, PR & SD</i>
Median Progression Free Survival (mPFS)	4.5 months	8.5 months	
12-month survival rate	44%	60%	

FIRST LINE ORR AND PFS DATA COMPARE FAVORABLY TO HISTORICAL CONTROL

ORR / BORR



1 Tsao 2019 (JCO) compared cediranib + pem/cis vs pem/cis; data from pem/cis arm presented on plot

2 Pemetrexed plus carboplatin

3 Scagliotti 2019 (Lancet) compared nintedanib + pem/cis vs pem/cis; data from pem/cis arm presented on plot

4 Zalcman 2016 (Lancet) compared bevacizumab + pem/cis vs pem/cis; data from pem/cis arm presented on plot. Not specified if ORR or BORR.

5 mPFS may change: Experimental group 11 patients (3 censored)

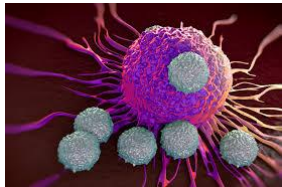
mPFS

ONCOS-102 DRIVES BROAD AND POWERFUL IMMUNE ACTIVATION ACROSS KEY PARAMETERS



Innate immune activation

- Clinical symptoms (fever), Cytokines, Macrophages, Gene expression



Adaptive immune activation

- Anti-tumor immunity, T-cell increase, Cytotoxicity, Gene expression



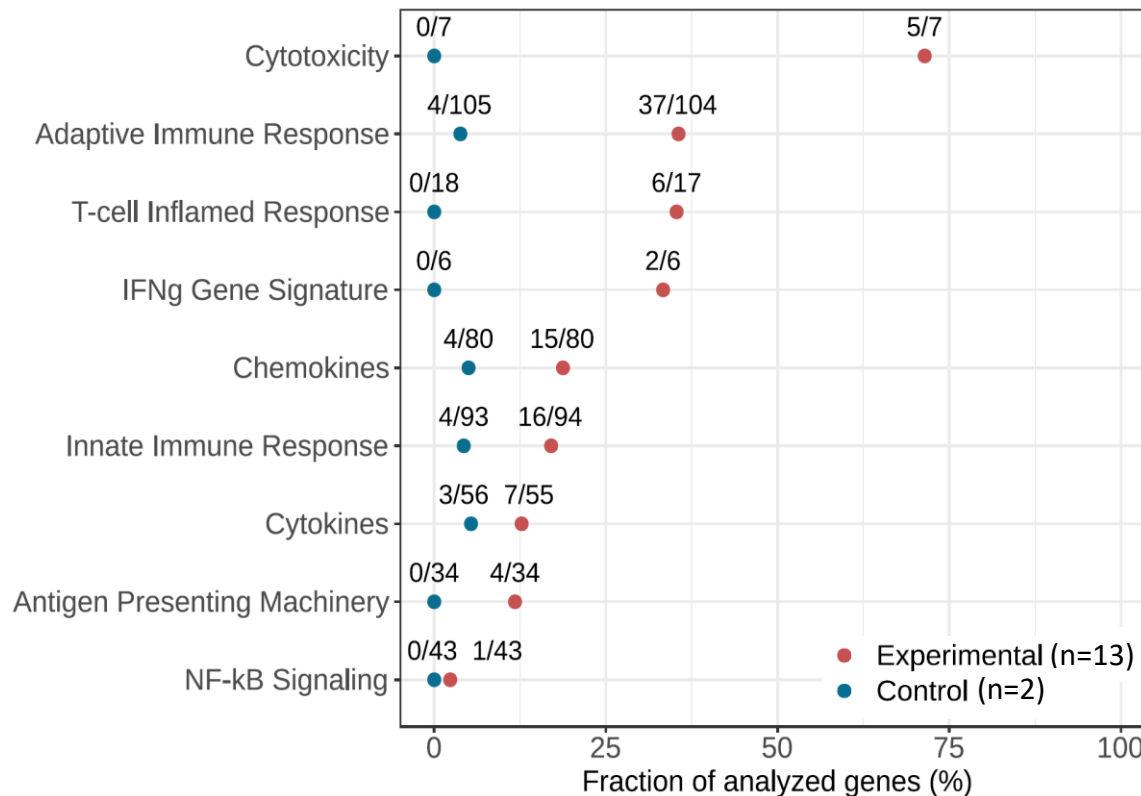
Remodeling of the tumor microenvironment

- Inflammation, M1:M2 Macrophage ratio, PD-L1 expression



CLEAR DIFFERENCE IN ONCOS-102-INDUCED IMMUNE ACTIVATION COMPARED TO CHEMOTHERAPY ONLY

ONCOS-102 treated vs. control patients, Fraction of modulated genes¹, Day 36 vs Baseline (%)



Innate immune activation



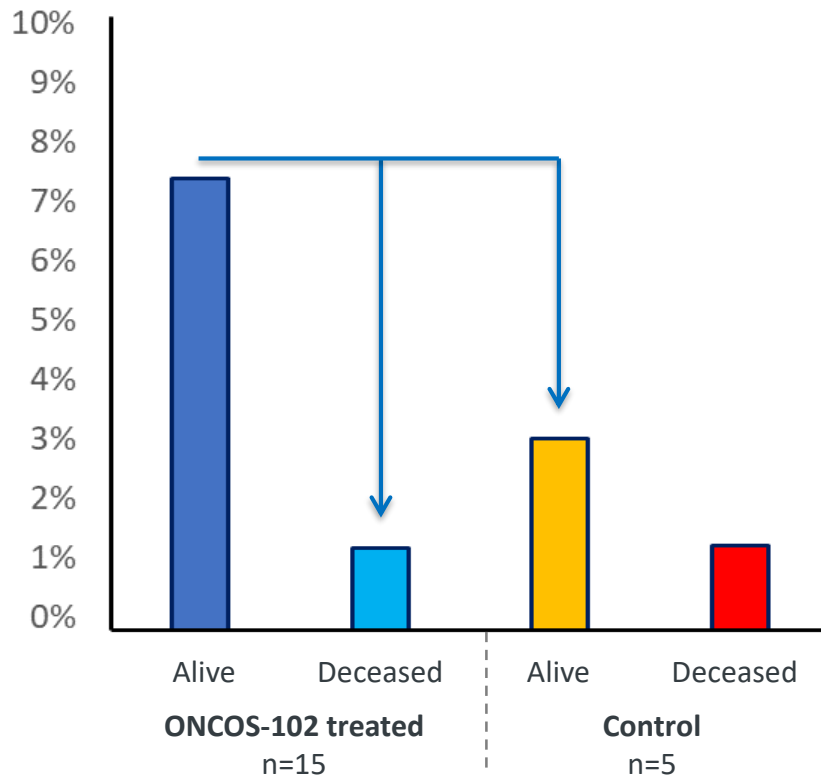
Adaptive immune activation



THE FRACTION OF CYTOTOXIC CD8+ T-CELLS IS CLEARLY HIGHEST IN RESPONDING ONCOS-102 TREATED PATIENTS

Relative level of cytotoxic CD8+ T-cells¹

Alive vs. deceased at 12 months²



Adaptive immune activation



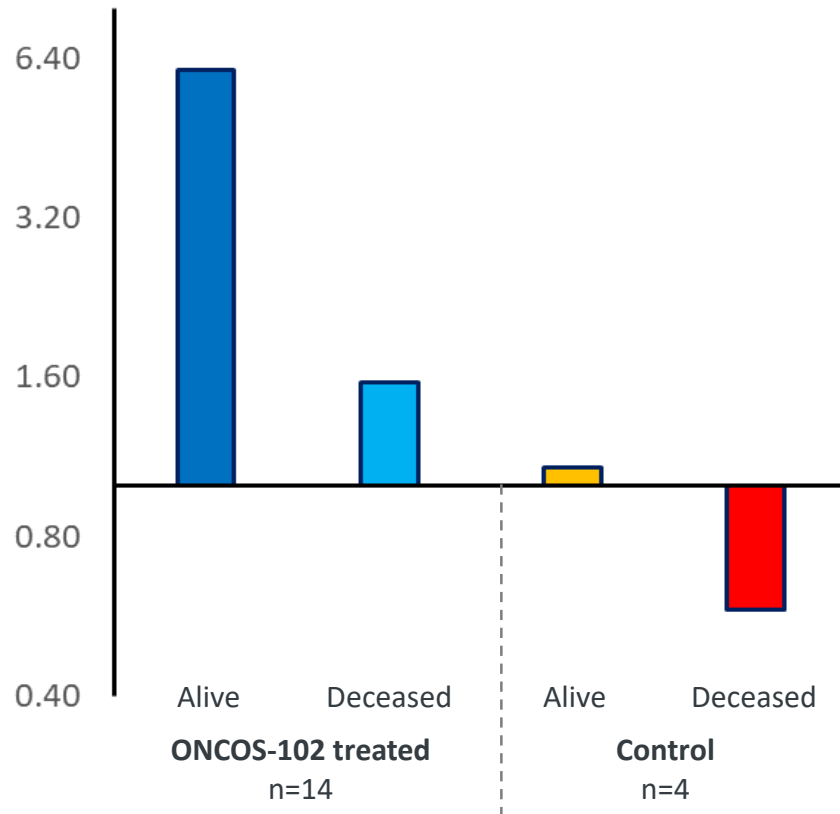
Remodeling of the tumor microenvironment



INCREASED M1:M2 MACROPHAGE RATIO CONFIRMS FAVORABLE REMODELLING OF THE TUMOR MICROENVIRONMENT

M1 vs. M2 macrophage ratio in tumor

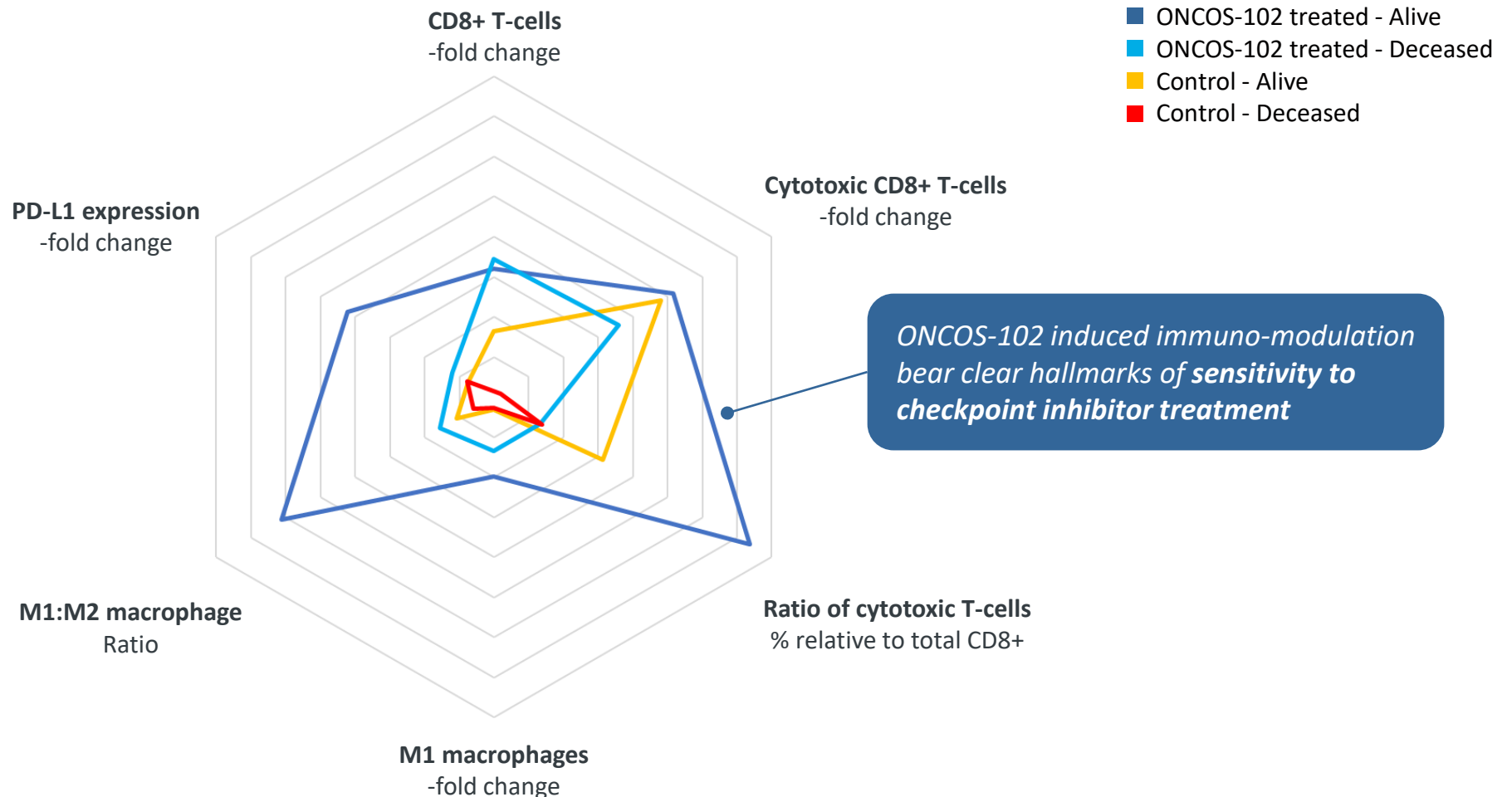
Alive vs. deceased at 12 months¹



Remodeling of the tumor microenvironment



A DISTINCT IMMUNE ACTIVATION PATTERN IS APPARENT IN RESPONDING ONCOS-102 TREATED PATIENTS



ONCOS-102 induced immuno-modulation bear clear hallmarks of sensitivity to checkpoint inhibitor treatment

CLINICAL AND IMMUNE DATA SUPPORT TRIPLE COMBINATION WITH CHECKPOINT INHIBITOR



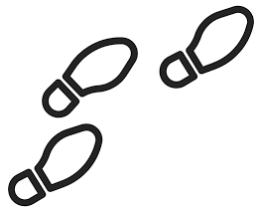
Excellent safety profile confirmed

- ONCOS-102 and SoC chemotherapy **combination is well-tolerated**



Clear clinical activity

- **Favorable mPFS of 8.9 months** in first line ONCOS-102 treated patients
- ONCOS-102 **mode-of-action confirmed** in mesothelioma
- **Powerful immune activation** associated with **clinical benefit**
- Remodeling of the tumor microenvironment indicates that **ONCOS-102 may induce sensitivity to checkpoint inhibition**



Next steps defined

- **First line** identified as **target population** for further development
- Strong rationale for **combination with anti-PD1/L1 checkpoint inhibitor and SoC chemotherapy** - advanced collaboration discussions with pharma partner

NEXT TRIAL: TRIPLE COMBINATION WITH ONCOS-102, CHEMO AND CPI IN FIRST LINE MESOTHELIOMA

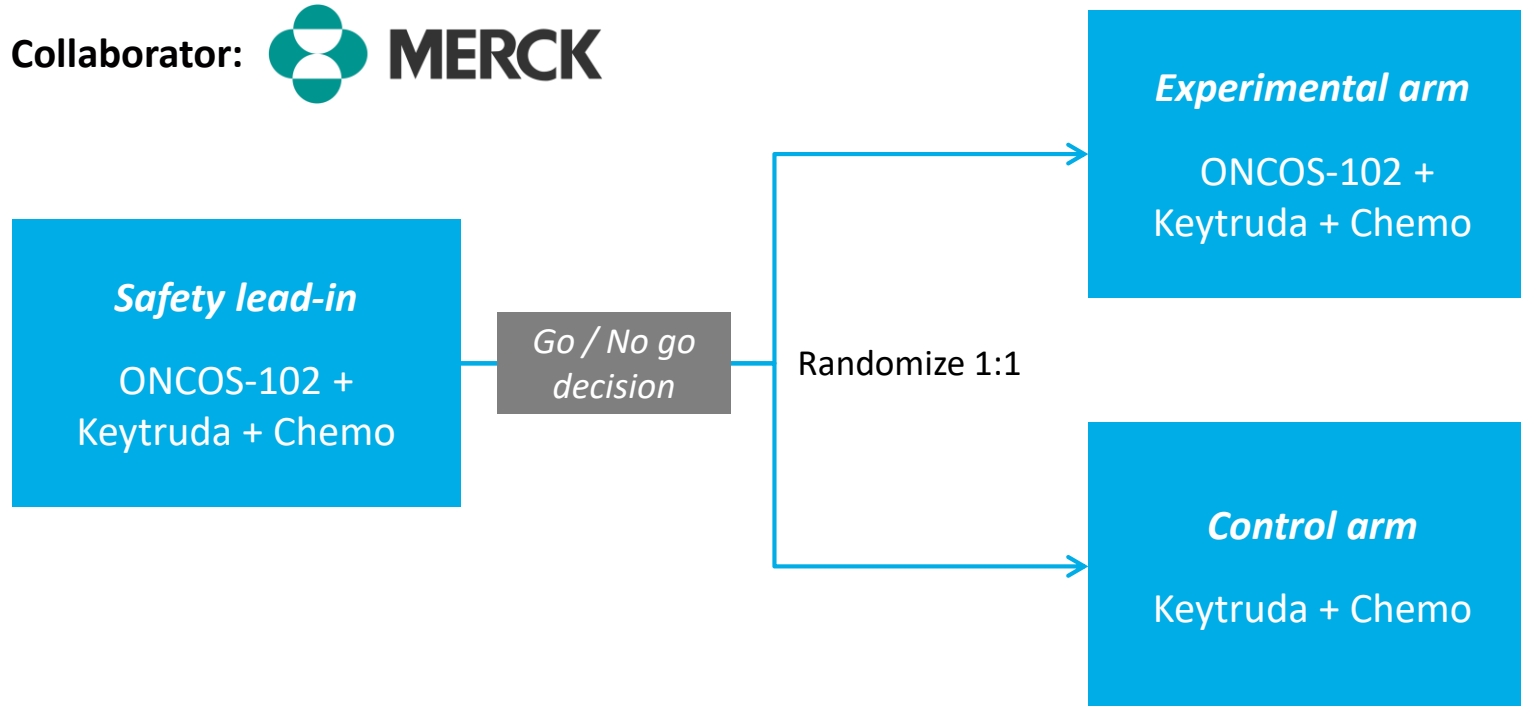
Study population: First line, unresectable, advanced and/or metastatic disease

Primary endpoint: median PFS

Size: Approx. 100 patients

Geography: the US and EU

Collaborator:  **MERCK**



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Melanoma

- 3. Peritoneal malignancies
- 4. Pipeline and Newsflow

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**
- Part 1: 9 patients. Part 2: 12 patients (ongoing, fully recruited)

Treatment regime

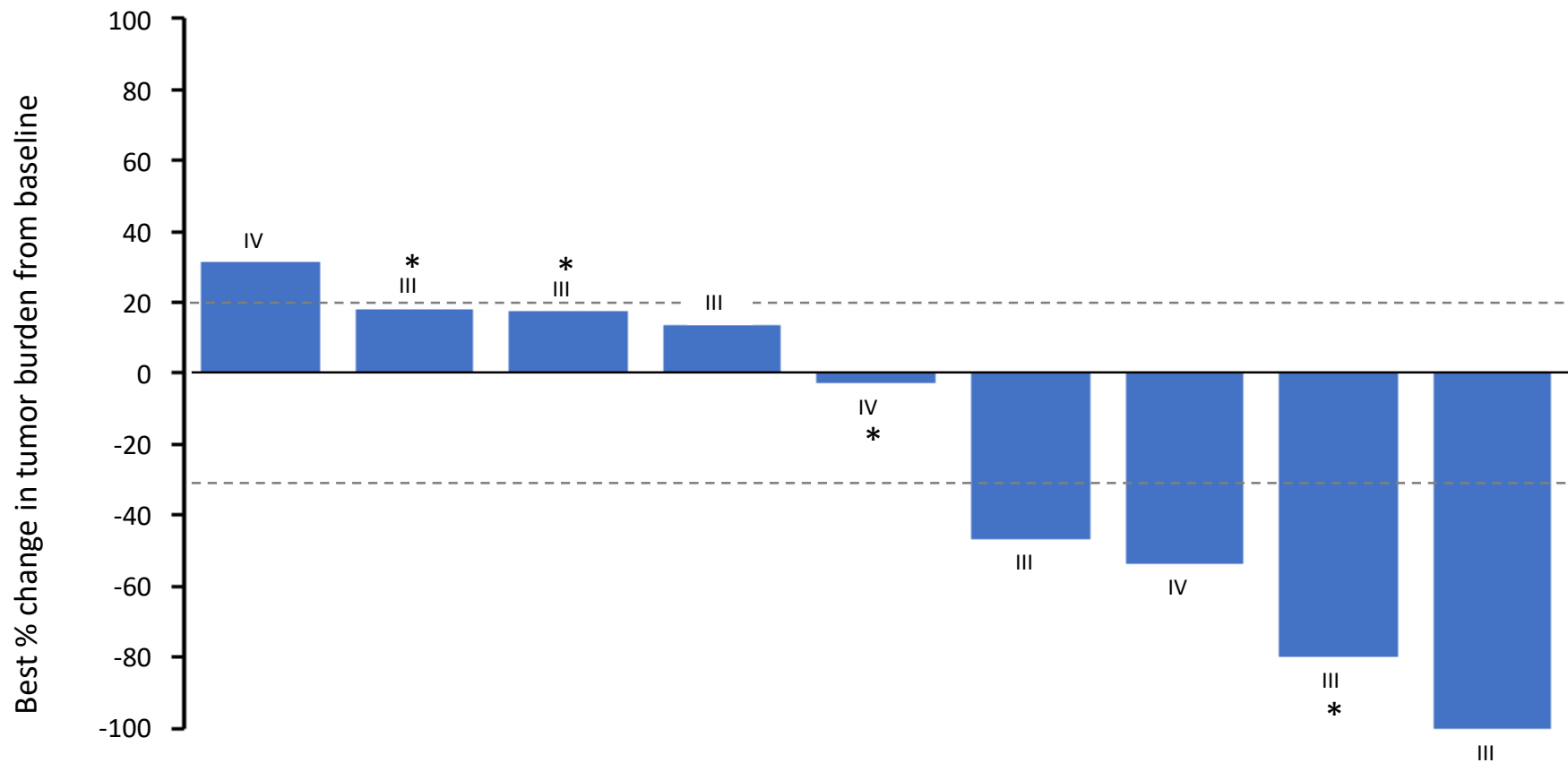
- **Part 1: 3 ONCOS-102 injections** followed by 5 months of Keytruda
- Part 2: 12 ONCOS-102 injections - priming and concomitantly

Clinical data

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

PART 1

BEST PERCENTAGE CHANGE IN TARGET LESIONS



* Progressive Disease due to non target progression

Letters and numbers indicating disease stage

Preliminary data

PART 1

CASE EXAMPLE: EARLY AND LASTING 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
T4a, N2b, M0

Prior therapies:

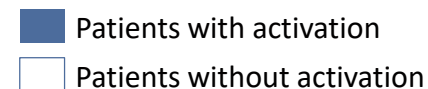
Surgery (x3)
Ipilimumab
Dabrafenib + Trametinib
Keytruda

RECIST 1.1:




CR, week 9-27

PART 1

ROBUST LOCAL AND SYSTEMIC IMMUNE ACTIVATION







Inflammatory response and innate immune activation




- Pro-inflammatory cytokine increase: IL-6 and / or TNFa 
- Increase in systemic IFN γ expression 
- Fever/chills 

Adaptive immune activation

T-cell tumor infiltration

- Increase in CD8+ T-cell infiltration 
- Increase in activated¹ CD8+ T-cells 
- PD1+/CD8+ T-cells in treated lesions 
- T-cells in non-treated lesions on Week 3 

Tumor specific activation

- Systemic increase in tumor specific T-cells, NY-ESO-1 and/or MAGE-A1 
- Increase in PD-L1 expression in tumor 
- Melanoma specific cancer markers strongly reduced 

4





Peritoneal malignancies

5. Pipeline and Newsflow

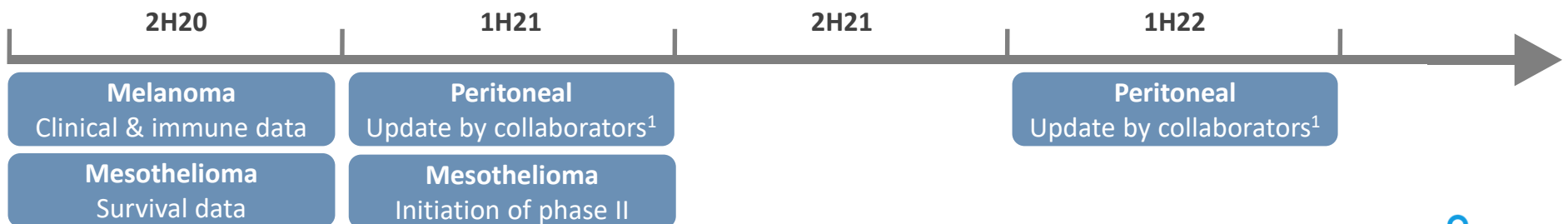
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Pipeline and Newsflow

PIPELINE WITH RICH NEAR-TERM NEWS FLOW

Product	Preclinical	Phase I	Phase II	Collaborator
ONCOS-102	Mesothelioma			
	Melanoma			
	Ovarian and colorectal			
	Prostate			
ONCOS-200 series	Next Gen viruses			
Novel mutRAS concepts				

Indicative timelines



ACTIVATING THE IMMUNE SYSTEM TO FIGHT CANCER

CLINICALLY PROVEN

One of the furthest developed unencumbered oncolytic viruses

Encouraging clinical data associated with strong immune activation

STRONG BACKING

Platform endorsement through pharma and biotech collaborations

Seasoned team with both experience and entrepreneurial drive

VALUE TRIGGERS

Ongoing combination trials ensuring rich news flow of clinical data

Pipeline of innovative pre-clinical ONCOS viruses