



# ACTIVATING THE PATIENT'S IMMUNE SYSTEM TO FIGHT CANCER

2Q 2021

18 August 2021



targovax

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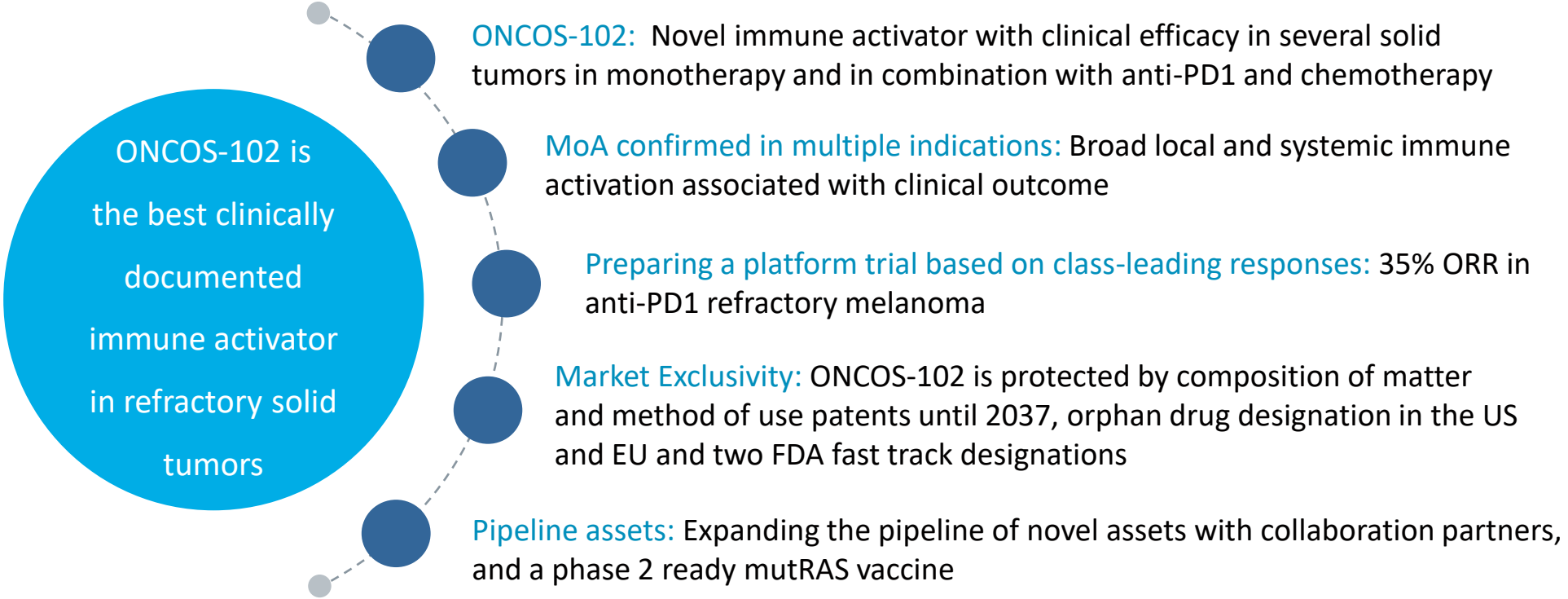
There are a number of factors that could cause actual results and developments to differ materially from those expressed or implied in these forward-looking statements. These factors include, among other things, risks or uncertainties associated with the success of future clinical trials; risks relating 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 and highlights

2. Melanoma
3. Finance
4. Summary

# TARGOVAX AT A GLANCE



ONCOS-102 is  
the best clinically  
documented  
immune activator  
in refractory solid  
tumors

**ONCOS-102:** Novel immune activator with clinical efficacy in several solid tumors in monotherapy and in combination with anti-PD1 and chemotherapy

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**Market Exclusivity:** ONCOS-102 is protected by composition of matter and method of use patents until 2037, orphan drug designation in the US and EU and two FDA fast track designations

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# FIRST HALF 2021 HIGHLIGHTS

## Trials

- Reported **class-leading median overall survival** in Targovax's ONCOS-102 trial in mesothelioma at the 24-month follow-up
- **Completed enrollment** of the phase 1/2 trial with ONCOS-102 in combination with durvalumab in patients with advanced colorectal cancer

## Pipeline

- Entered a research collaboration with **Papyrus Therapeutics** to develop novel ONCOS viruses with receptor tyrosine kinase (RTK) inhibitor functionality

## People

- Announced **Dr Lone Ottesen** as Chief Development Officer and **Dr Sonia Quaratino** as a new Board member

## FDA

- Received **Fast-Track** designation from the US FDA for ONCOS-102 in malignant pleural mesothelioma
- Received **Fast-Track** designation for ONCOS-102 in PD-1-refractory advanced melanoma as well as Scientific Advice for further development

# FAST TRACK DESIGNATION

## Requirements

Fast track designation is given for new treatments that:

- Are aimed at **serious medical conditions**
- Have demonstrated **potential to address the unmet medical need**

## Benefits

FDA commits to expedite development and review by:

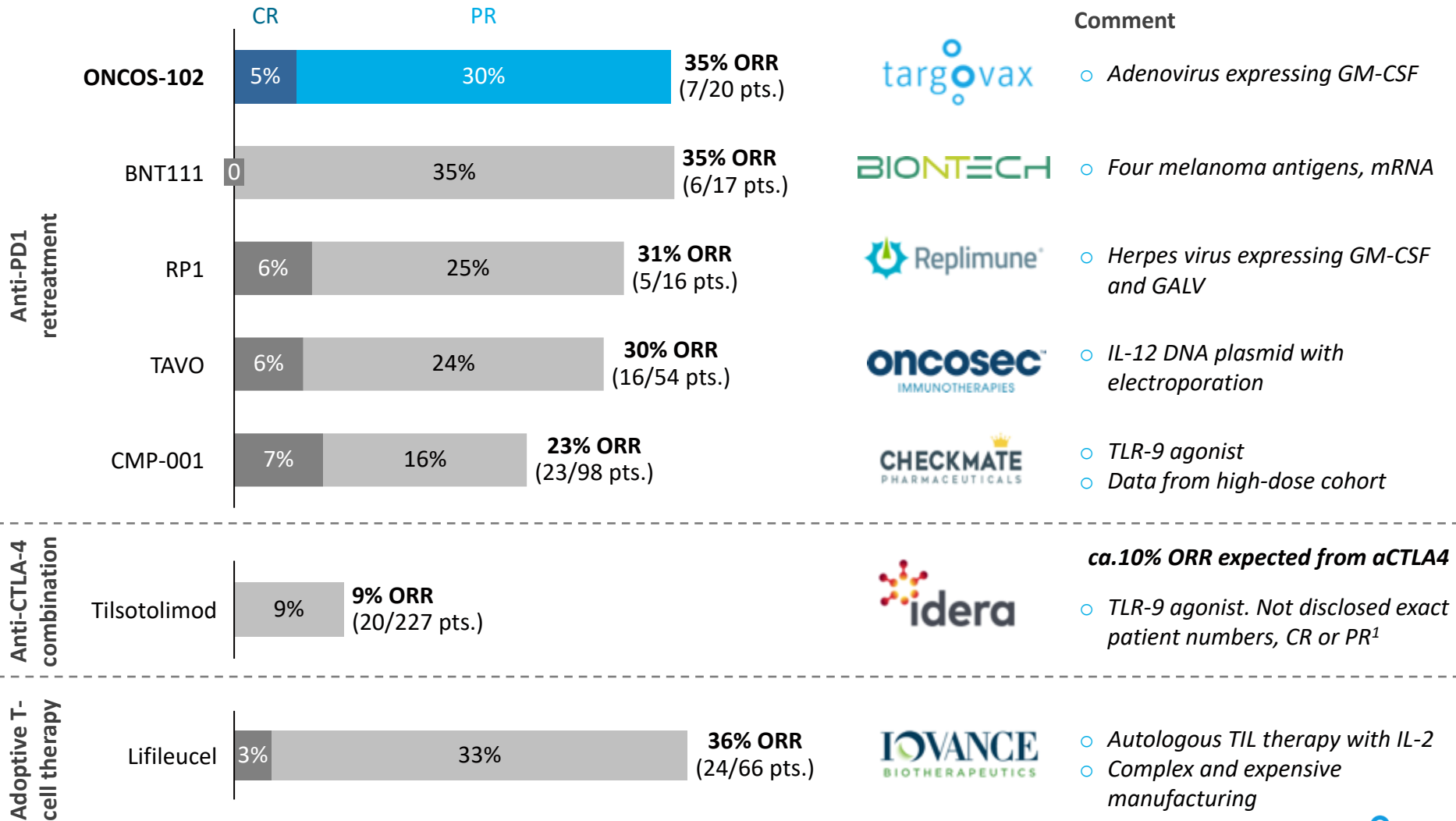
- Giving opportunities for **frequent interactions** with the review team
- Allowing for **rolling review** for a faster approval process
- Considering the option for **priority review**

# 2

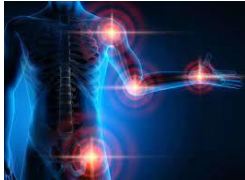
## Melanoma

3. Finance
4. Summary

# ONCOS-102 HAS DEMONSTRATED CLASS-LEADING EFFICACY IN PD1-REFRACTORY MELANOMA

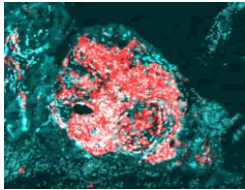


# WHAT CHARACTERIZES A GREAT IMMUNE ACTIVATOR?



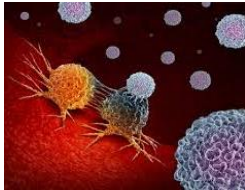
## Activate pro-inflammatory signalling pathways

- Trigger danger signalling, e.g. through TLR9 activation
- Stimulate release of cytokines and chemokines



## Drive increased tumor immune cell infiltrate

- Break down tumor entry barriers
- Recruit T-cells, NK-cells, dendritic cells, macrophages



## Facilitate priming of anti-tumor immune response

- Enhance processing of tumor antigens
- Stimulate maturation of antigen-presenting cells (APCs)



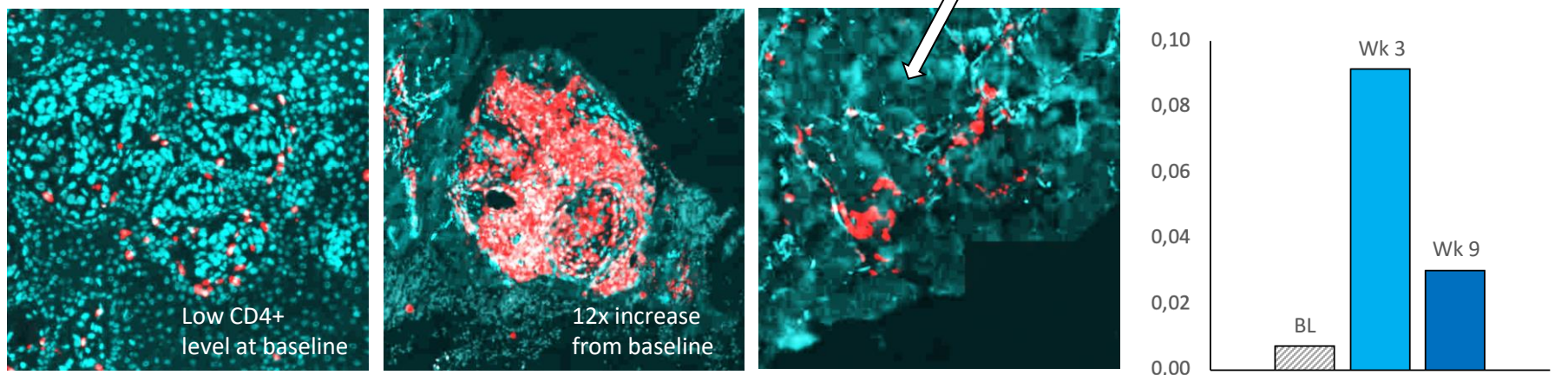
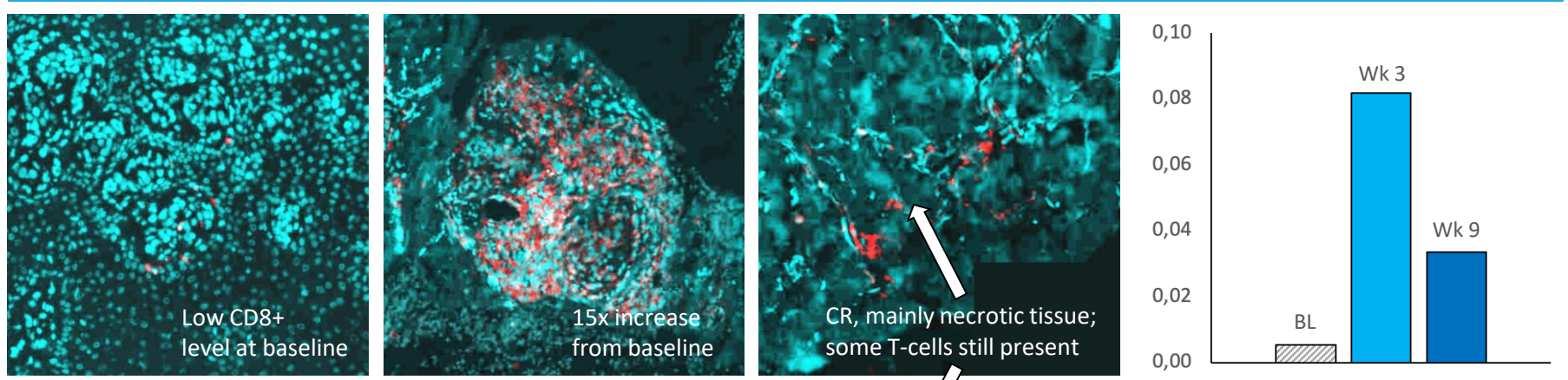
## Counteract inhibitory molecular pathways and cell subsets

- Prevent T-cell exhaustion/anergy
- Diminish inhibitory cell subsets, e.g. T<sub>regs</sub>, M2 macrophages

# ONCOS-102 INCREASES TUMOR T-CELL INFILTRATION

## COMPLETE RESPONSE MELANOMA PATIENT CASE EXAMPLE

### T-cell tumor infiltrate



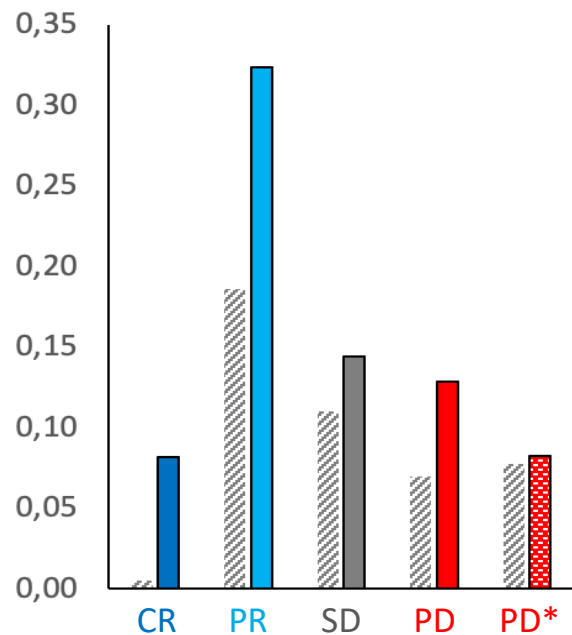
Progression on pembrolizumab

3x ONCOS-102 only

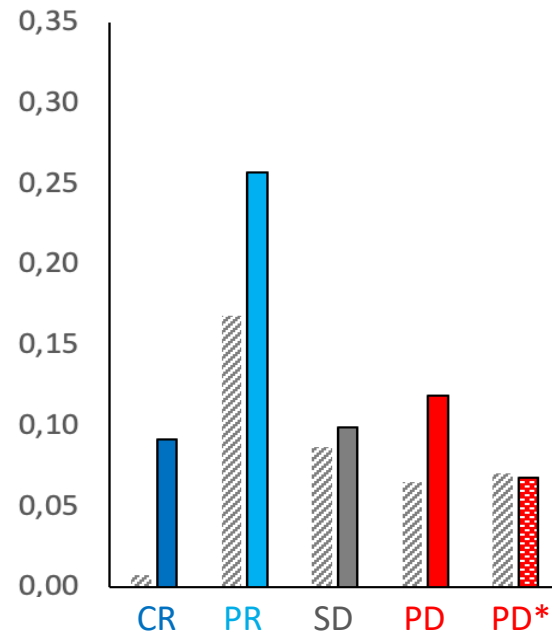
3x ONCOS-102 & 2x pembrolizumab



# INCREASED T-CELL INFILTRATION FOLLOWING ONCOS-102 MONOTHERAPY IS CONSISTENT WITH MELANOMA PATIENT OUTCOMES

**CD8+ T-cell infiltration**  
Average level by tumor response



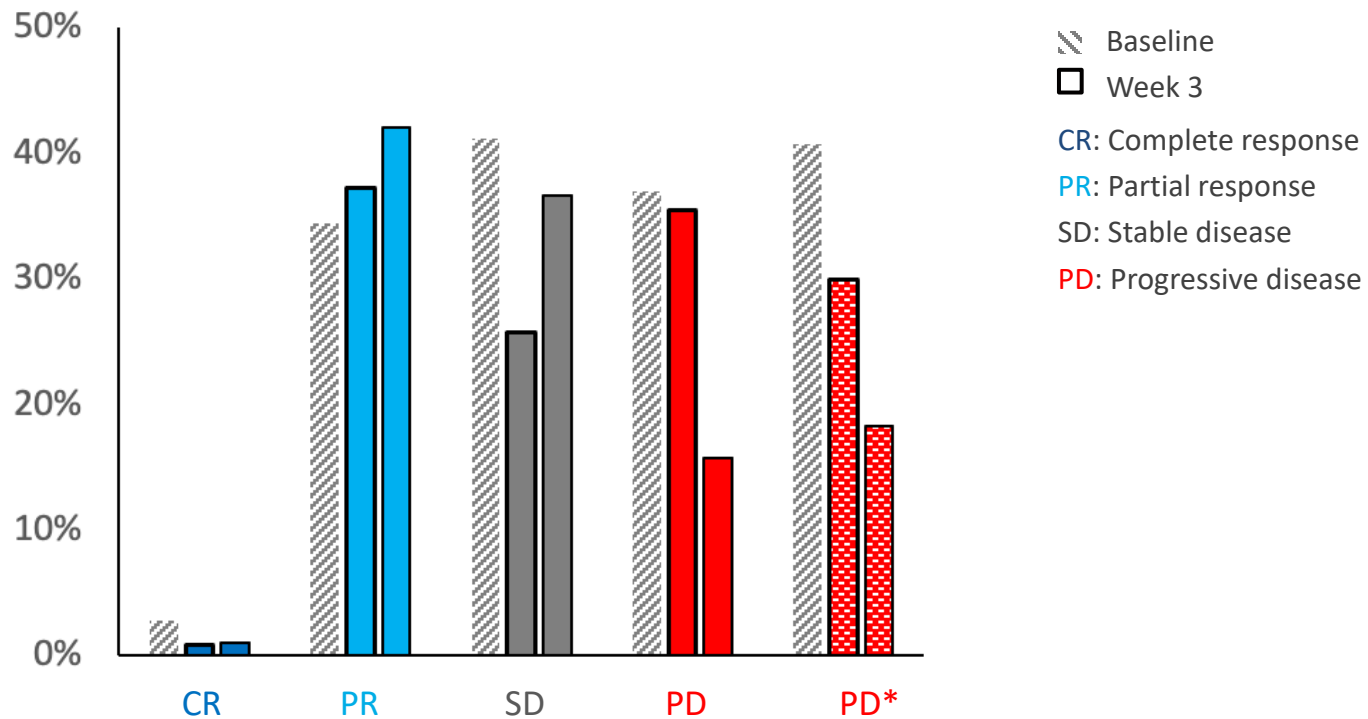
**CD4+ helper T-cell infiltration**  
Average level by tumor response



 Baseline  
 Week 3  
 CR: Complete response  
 PR: Partial response  
 SD: Stable disease  
 PD: Progressive disease

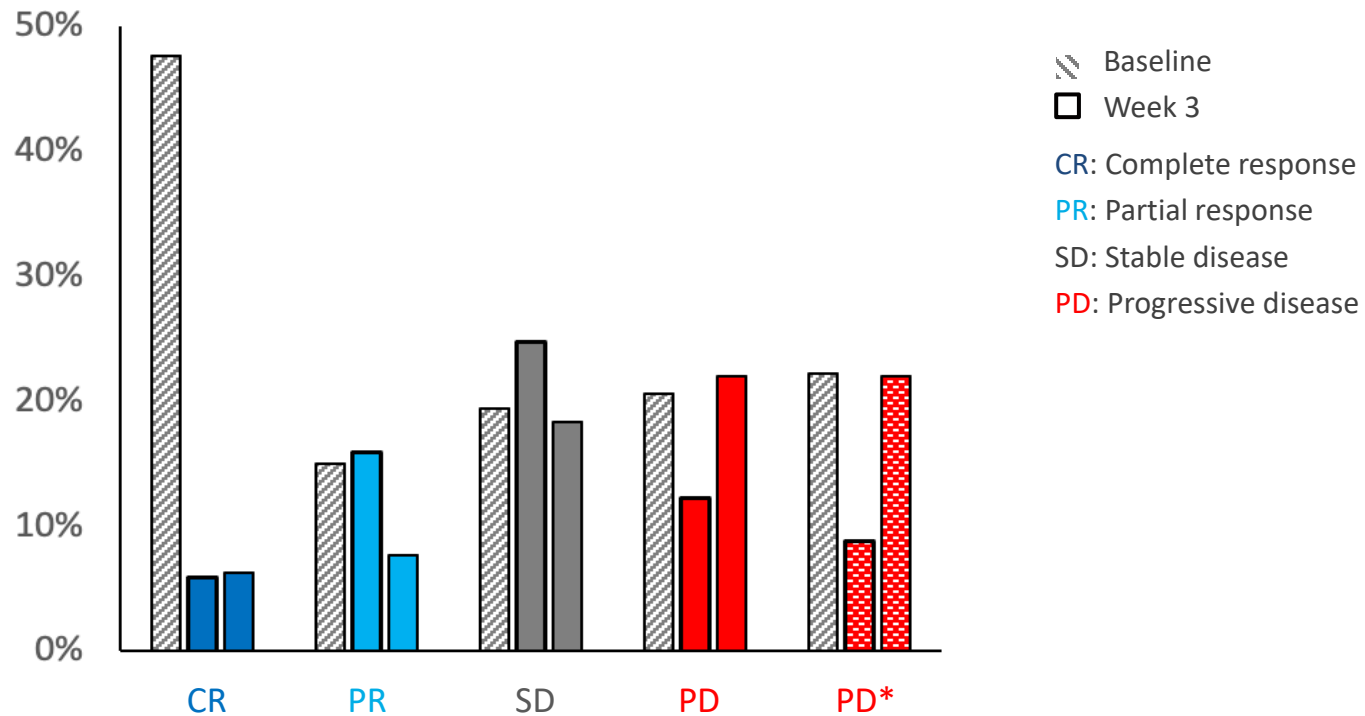
# HIGH RATIO OF ACTIVE CYTOTOXIC CD8+ T-CELLS INDICATE A “HOT” TUMOR MICROENVIRONMENT

GRB+ CD8+ T-cell infiltration; % of total CD8+ population



# CONVERSELY, INHIBITORY T<sub>REGS</sub> ARE DOWN-REGULATED IN RESPONDING MELANOMA PATIENTS

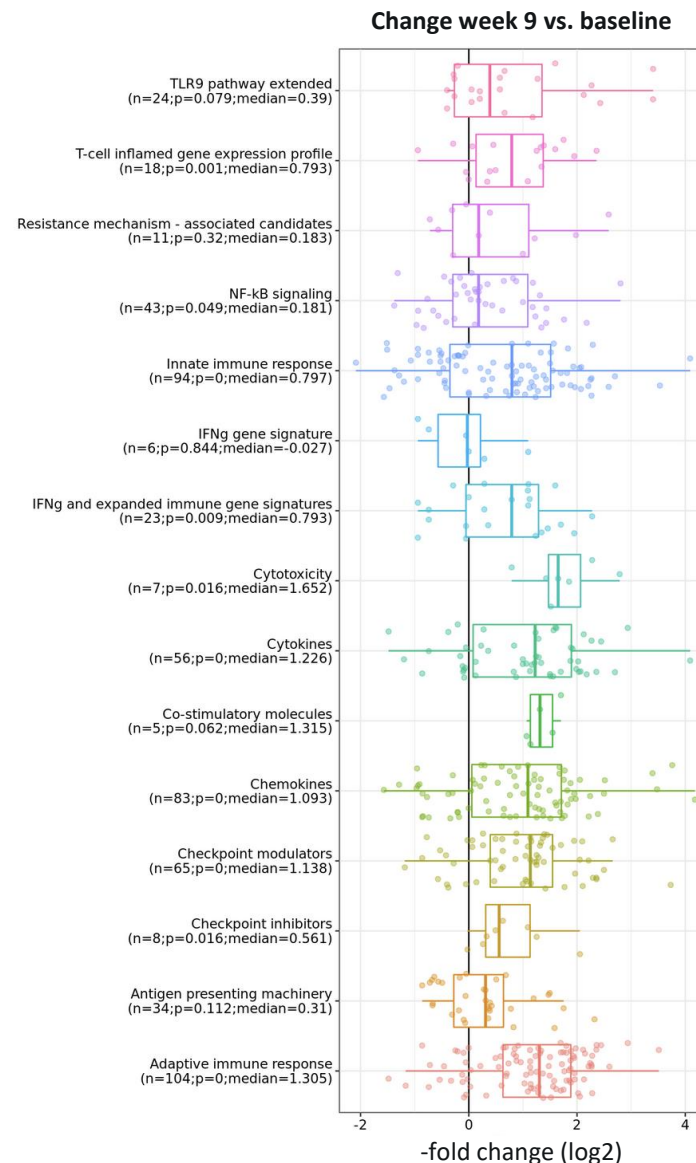
Regulatory T-cell infiltration; FOXP3+ % of total CD4+ population



# GENE EXPRESSION DATA CONFIRMS IHC\* OBSERVATIONS AND DETAILS BROAD PRO-INFLAMMATORY TUMOR RE-PROGRAMING

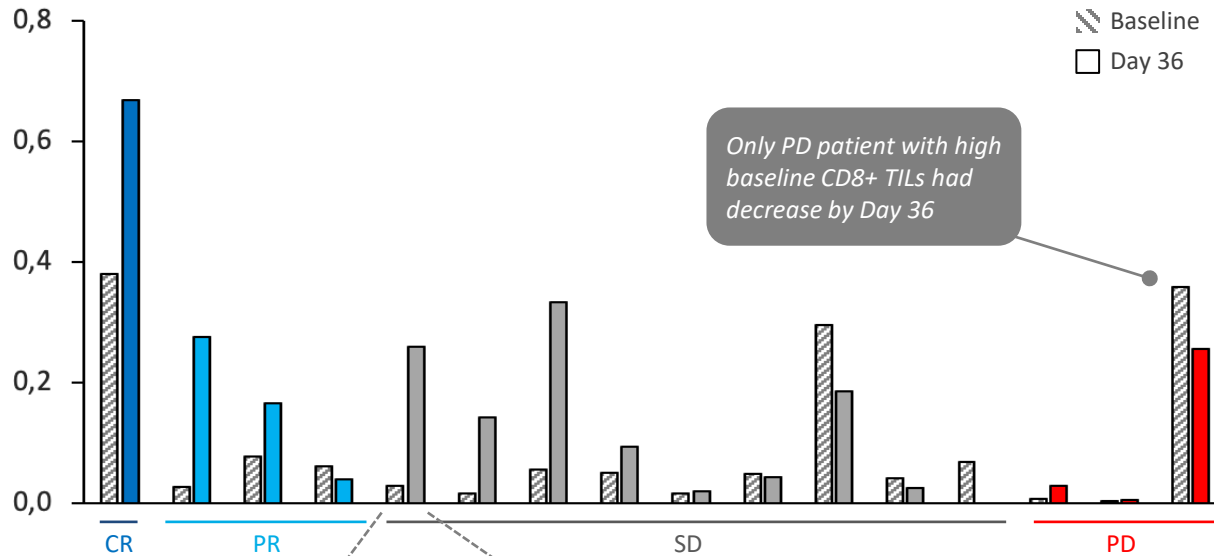
## RNAseq gene expression provides further insights:

- **Pro-inflammatory “hot” tumor remodeling** through multiple pathways and molecular mechanisms
- Increased expression of chemokines and cytokines **explain higher immune cell infiltrate**
- Strong upregulation of cytotoxic machinery **explains tumor shrinkage**
- Upregulation of immunomodulatory molecules present **targets for novel combinations beyond anti-PD1**
- **”Hot” tumor remodeling persists** at least until week 9
- **Potential genetic biomarker for patient selection identified** through additional DNA sequencing

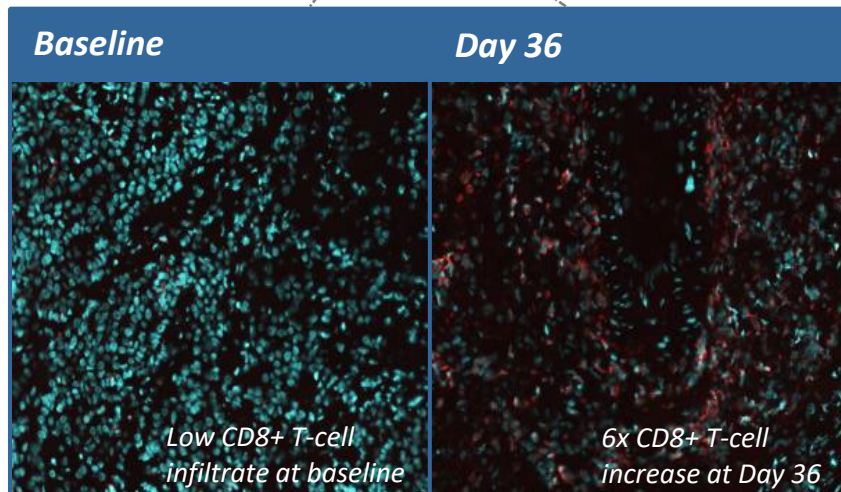
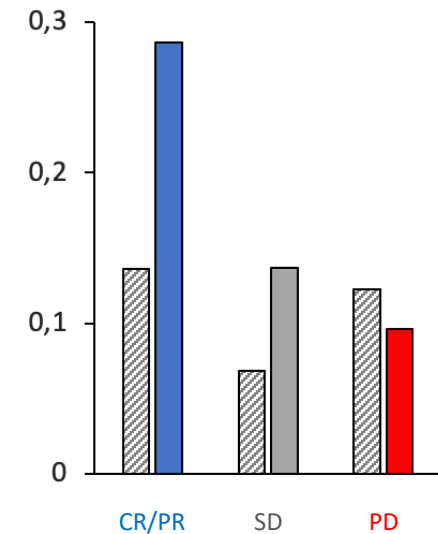


# IMPORTANTLY, THESE OBSERVATIONS ARE CONSISTENT ACROSS TUMOR TYPES – MESOTHELIOMA EXAMPLE

CD8+ T-cell infiltrate (TIL) for individual patients; tumor mIHC



Avg. CD8+ TILs Day 36 vs. BL

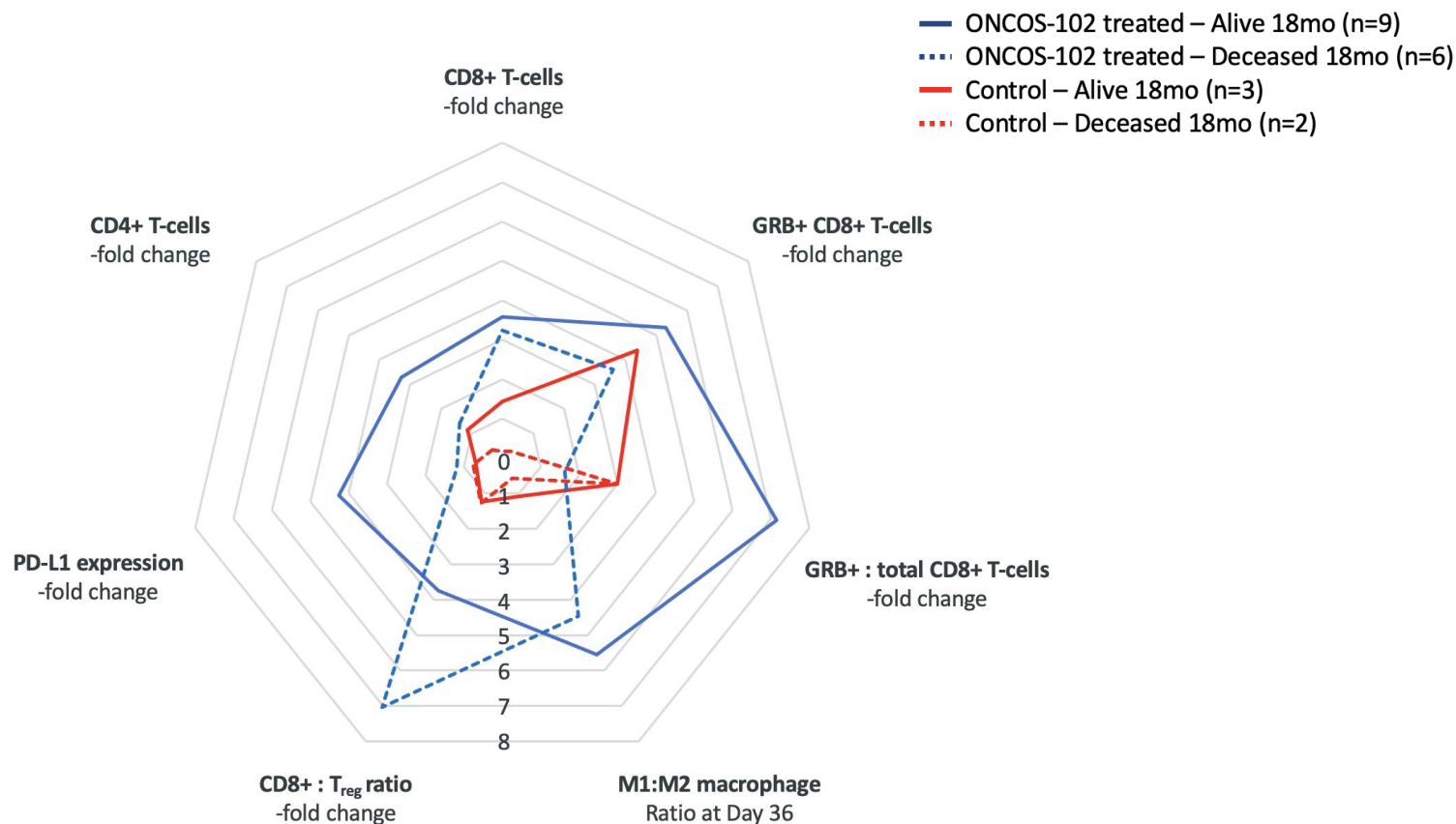


## Patient case example Day 36 vs. Baseline:

- 6x increase in total CD8+ T-cell infiltrate
- 16x increase in GrB+/CD8+ T-cells
- 3x increase in total CD4+ T-cell infiltrate
- 4x increase in CD8+ : T<sub>reg</sub> ratio
- 20x increase in PD-L1 expression
- 3x increase in M1 macrophages
- Patient still **alive** at 24 month follow-up

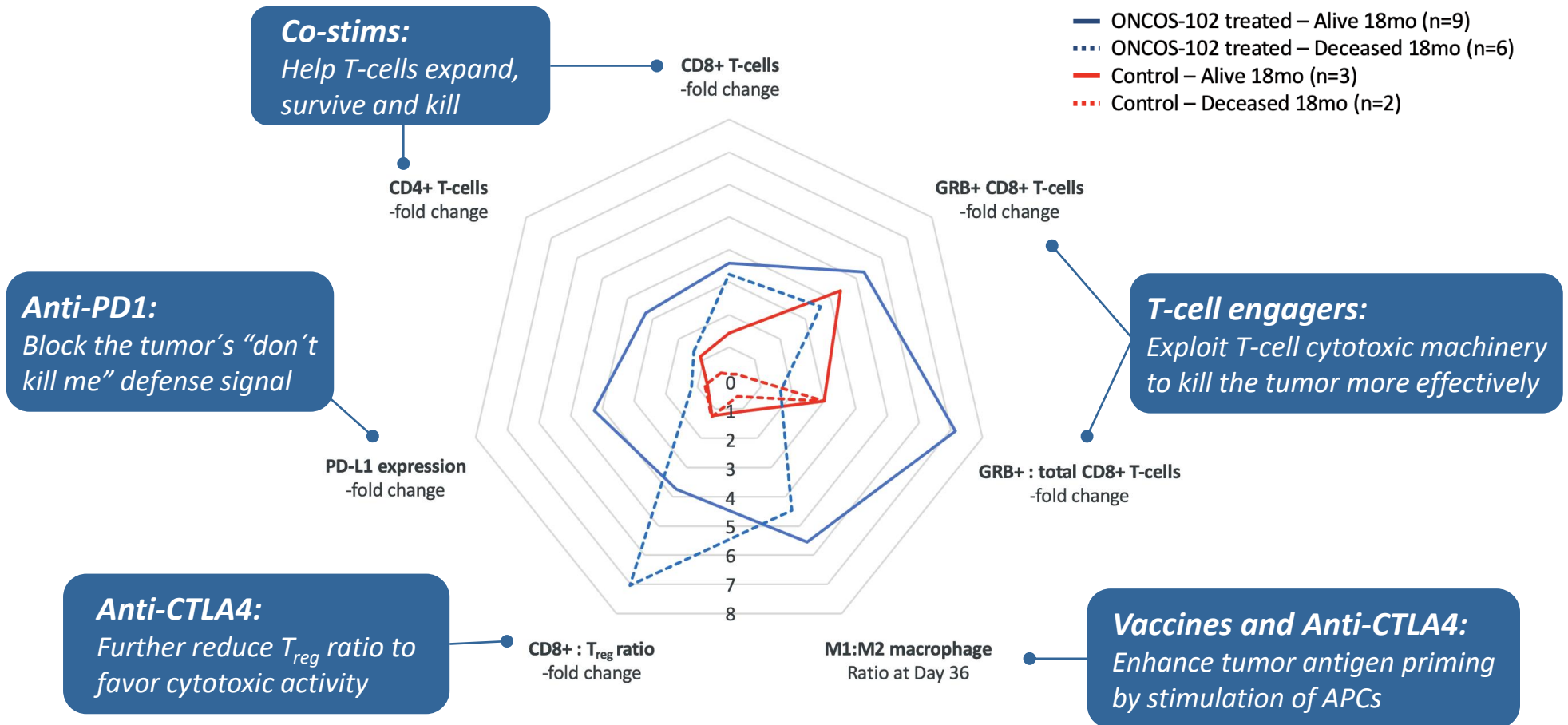
# IMMUNE MARKER DATA BUILD STRONG BIOLOGICAL RATIONALE FOR SEVERAL NEW COMBINATIONS WITH ONCOS-102

Immuno-modulation in tumor tissue; Mesothelioma, Day 36 vs. baseline



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# STRENGTH AND BREADTH OF ONCOS-102 CLINICAL DATA PACKAGE OPENS BROAD OPPORTUNITIES



## **Class-leading efficacy**

*ONCOS-102 drives meaningful clinical benefit, competitive with leading drug candidates*

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## **Highly consistent**

*ONCOS-102 data package is highly consistent across tumor types, survival, clinical response, immune cell infiltration and gene expression*

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## **Novel combinations**

*Mechanistic data provides strong biological rationale for combinations beyond anti-PD1 blockade*

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## **Biomarker selection**

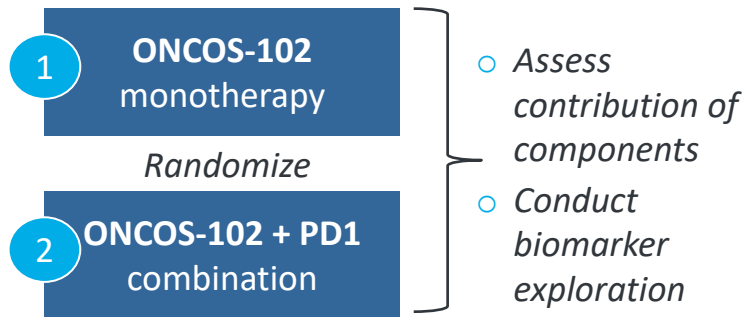
*Potential genetic biomarkers for patient selection identified in tumor biopsy NGS data set*

# PLANNING A MELANOMA PHASE 2 PLATFORM TRIAL TO EXPLORE MULTIPLE ONCOS-102 COMBINATIONS

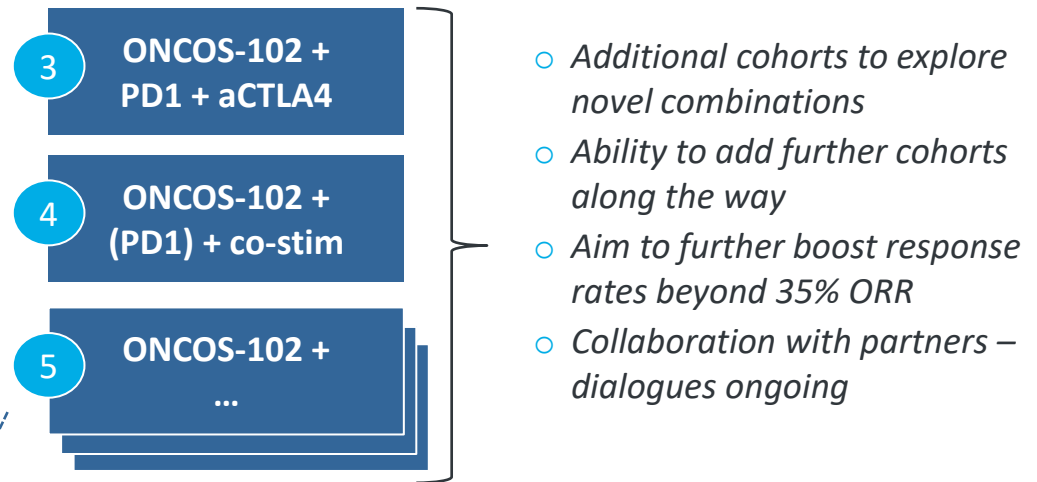
## Part 1 – run-in

Population:

Anti-PD1 refractory melanoma



## Part 2 – multi-cohort extension



**Several opportunities:**  
vaccine, bi-specifics, T-cell engagers, etc...

*Cohorts 2 onward can independently form the basis for a subsequent registrational trial*

# CLINICAL AND PRECLINICAL PIPELINE

Product candidate	Preclinical	Phase 1	Phase 2	Phase 3	Next expected event
ONCOS-102	Refractory Melanoma Platform trial				<b>1H 2022</b> First patient in
	Mesothelioma Combination w/pemetrexed/cisplatin				<b>2H 2021</b> Survival update
	Metastatic Colorectal cancer Combination w/anti PDL1				<b>1H 2022</b> Clinical data
Next Gen viruses					<i>Preclinical data and selection of candidates</i>
Novel mutRAS concepts					<i>Preclinical data and selection of candidates</i>

# 3

## Finance

### 4. Summary

# 2Q FINANCIAL SNAPSHOT

## Key figures

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Net cash flow in 2Q

**-24 / -2.7**

NOK million

USD million

Cash at end of 2Q

**71 / 8.4**

NOK million

USD million

Market cap

**630 / 71**

NOK million

USD million

Daily value traded

Average last 12 months

**3.1 / 0.35**

NOK million

USD million

## Shareholder base<sup>1</sup>

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Ownership by professional institutions, e.g.

- *HealthCap, Nordea, Radforsk, AP4, Arctic Aurora, MP Pension*

**31%**

Largest shareholder

- *HealthCap*

**14%**

Ownership by top 20 shareholders

**48%**

No of shareholders (approx.)

**5600**

## SECOND QUARTER OPEX IN LINE WITH PREVIOUS QUARTERS

NOK m	2Q20	3Q20	4Q20	1Q21	2Q21
<b>Total revenue</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>	<b>0</b>
External R&D expenses	-14	-9	-8	-9	-9
Payroll and related expenses	-11	-9	-12	-11	-13
Other operating expenses	-5	-4	-3	-2	-3
<b>Total operating expenses</b>	<b>-30</b>	<b>-22</b>	<b>-23</b>	<b>-23</b>	<b>-25</b>
Operating loss	-30	-22	-23	-23	-25
Net financial items	-4	-1	-3	1	-1
Loss before income tax	-33	-23	-26	-22	-26
Net change in cash	-34	-24	45	-27	-24
<b>Net cash EOP</b>	<b>101</b>	<b>78</b>	<b>122</b>	<b>95</b>	<b>71</b>

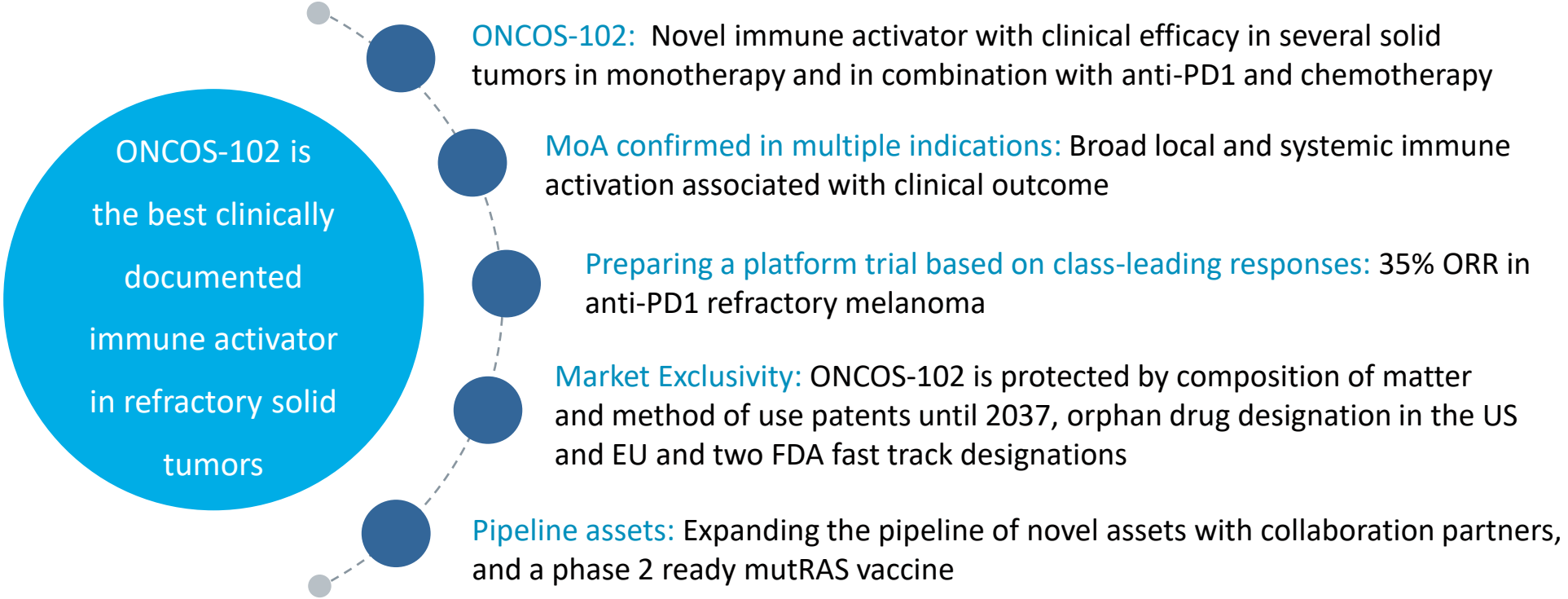
1 Including patent cost

2 Including depreciation

# 4

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## Upcoming conferences / events

- 7 Sep 2021:** Next Gen Cancer Vaccine Development Summit
- 17-21 Sep 2021:** European Society for Medical Oncology (ESMO)
- 26 Oct 2021:** Oncolytic Virotherapy Summit
- 26-29 Oct 2021:** 5th Annual Next Gen IO Conference EU edition

## Upcoming data milestones

- 2H 2021:** ONCOS-102 in combination with chemotherapy in unresectable malignant pleural mesothelioma – *Survival update*
- 1H 2022:** ONCOS-102 in combination with durvalumab in colorectal cancer with peritoneal carcinomatosis – *Clinical data*

## Financial Calendar 2021

- 4 Nov 2021:** Third Quarter presentation
- 17 Feb 2022:** Fourth Quarter presentation