



# ACTIVATING THE PATIENT'S IMMUNE SYSTEM TO FIGHT CANCER

Company Presentation

February 2020



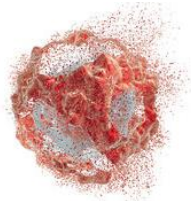
targovax

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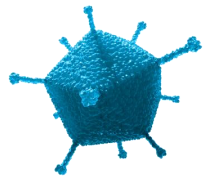
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# ACTIVATING THE IMMUNE SYSTEM TO FIGHT CANCER



## 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
- First data set with **encouraging clinical and immune data**

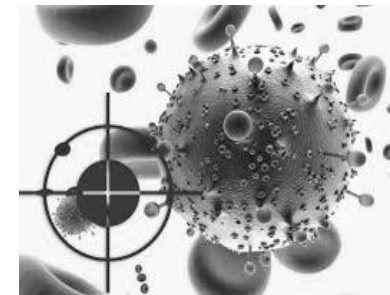
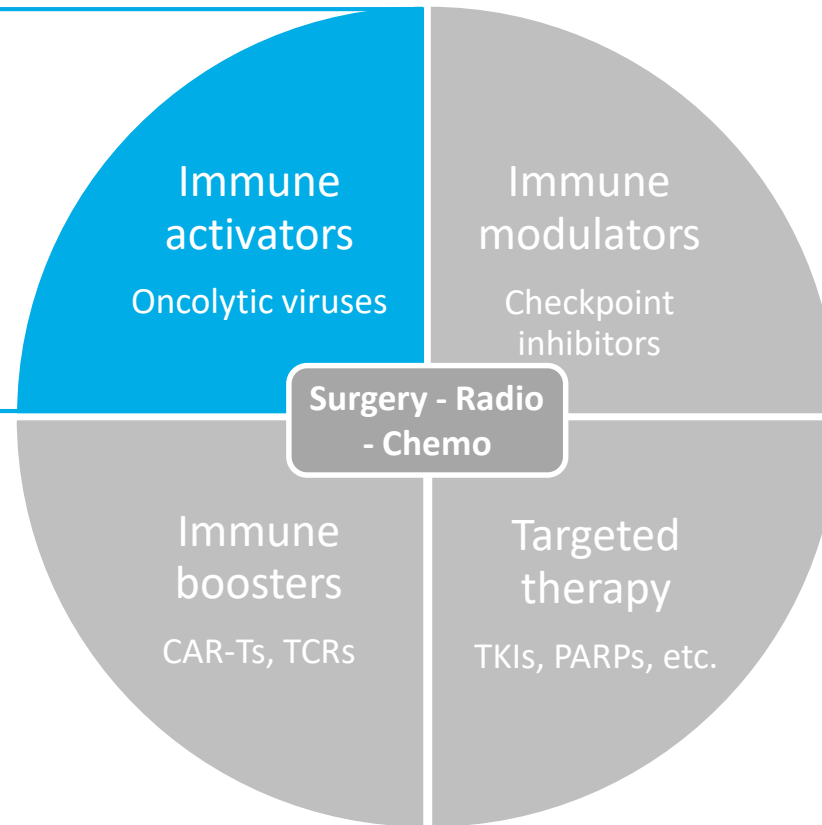
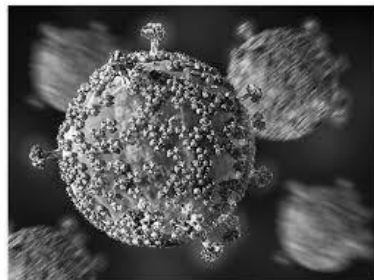
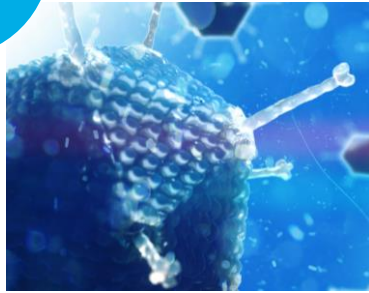


## Listed on Oslo Stock Exchange

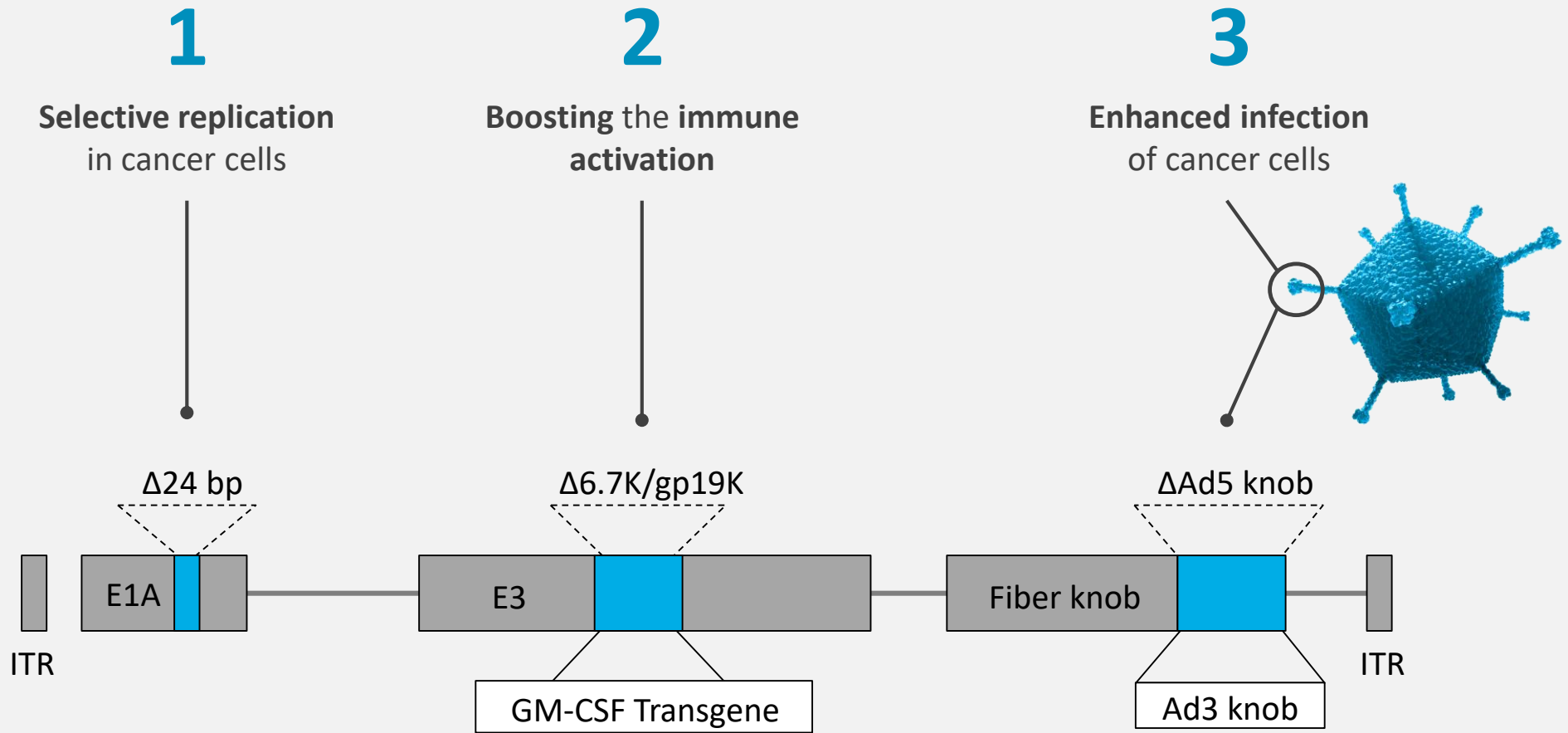
- Ticker: **TRVX**
- All virus assets unencumbered

# ONCOLYTIC VIRUSES INCREASINGLY IMPORTANT IN THE FUTURE CANCER THERAPY LANDSCAPE

Targovax  
focus

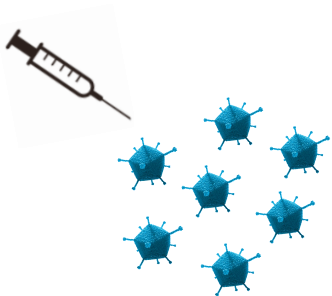


# ONCOS-102 IS AN ONCOLYTIC ADENOVIRUS SEROTYPE 5 ARMED WITH A GM-CSF TRANSGENE



# ONCOS-102 MODE OF ACTION

## 1 Virus injection Local delivery



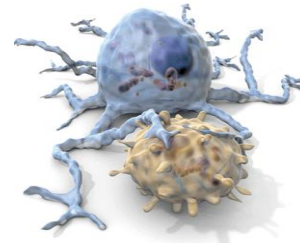
- Intra-tumoral or intra-peritoneal injection
- Tumor cell infection

## 2 Oncolysis Immune activation



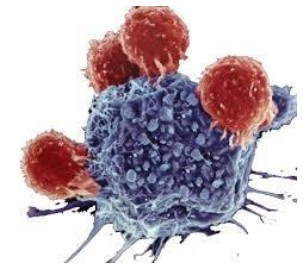
- Lysis of tumor cells
- Inflammatory response
- Tumor antigen release

## 3 Antigen processing T-cell activation



- Antigen processing
- T-cell activation in lymph nodes

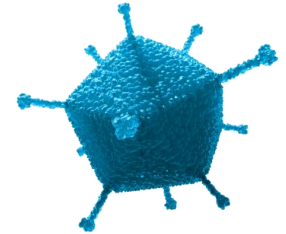
## 4 T-cell response Anti-tumor immunity



- T-cell tumor infiltration
- Tumor antigen recognition

# BENEFITS OF ONCOS-102 ADENOVIRUS

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













**Well-characterized**, well-tolerated and few safety concerns



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
















# SEVERAL SIGNIFICANT BD TRANSACTIONS IN THE ONCOLYTIC VIRUS SPACE IN 2018-2019

Acquirer	Target	Type of deal	Deal value
	 <small>Developers of Oncolytic Immunotherapies</small>	<b>M&amp;A</b> RNA virus, Phase II	<b>USD 400m</b> cash acquisition
 <small>PHARMACEUTICAL COMPANIES OF Johnson &amp; Johnson</small>		<b>M&amp;A</b> Herpes virus, Pre-clinical	<b>USD 140m</b> up-front <b>USD 1b</b> total value
		<b>M&amp;A</b> VSV virus, Pre-clinical	<b>USD 250m</b> cash acquisition
		<b>R&amp;D partnership</b> Co-development of novel vaccinia viruses, Pre-clinical	<b>USD 10m</b> up-front Unknown total value
		<b>Strategic collaboration</b> Co-development of multiple vaccinia viruses, Pre-clinical	<b>USD 120m</b> near-term <b>USD &gt;900m</b> total value



# THE OV DEVELOPMENT LANDSCAPE

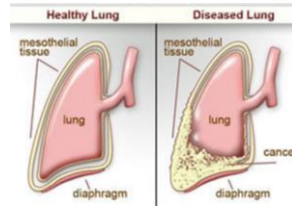
## OVERVIEW OF MOST RELEVANT OVS IN CURRENT DEVELOPMENT

Company		Asset/ Program	MoA	Highest Phase
	H	Imlygic	HSV with GM-CSF transgene, IT only	Approved 2015 as mono Phase III PD1 combo
	R	Cavatak	Coxsackievirus, non gene modified, IT focus, IV and IP trial ongoing	Phase II
	A	DNX-2401	Chimeric Ad5/3, no transgene, IT and intra-arterial	Phase II
	A	<b>ONCOS-102</b>	<b>Chimeric Ad5/3 with GM-CSF transgene, IT and IP administration</b>	<b>Phase II</b>
	A	CG0070	Ad5 with GM-CSF transgene, intravesical	Phase II
	R	Reolysin	Reovirus, non gene modified, IV only	Phase II
	A	Enadenotucirev	Chimeric Ad5, no transgene, IV only	Phase I/II
	H	RP1	HSV with GM-CSF, GALV, and ipilimumab transgenes, IT only	Phase I/II
	A	LOAd703	Chimeric Ad5/35 with TMZ-CD40L and 4-1BBL transgenes, IT only	Phase I/II
	R	Voyager V1	VSV virus with NIS and human interferon beta transgenes, IV only	Phase I
	R	Ad-MAGEA3	Maraba virus with MAGEA3 transgene, IV and IT	Phase I
	R	VSV-GP	Chimeric VSV virus, IV only	Pre-clinical
	V	RIVAL	Maraba and Vaccinia viruses armed with multiple transgenes, IV only	Pre-clinical
	V	Invir.IO	Vaccinia virus platform armed with CTLA-4 ++, solid tumors	Pre-clinical
	H	oHSV	Herpes virus with multiple transgenes (PD1, CTLA4 ++), IT only	Pre-clinical



# ONCOS DEVELOPMENT STRATEGY

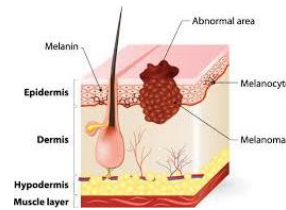
## 1 Path-to-market as orphan drug



### Mesothelioma

- ~15.000 patients<sup>1</sup>
- Focused market entry in niche indication
- Potential as frontline therapy, limited competition

## 2 Activating CPI refractory tumors



### Anti-PD1 refractory melanoma

- No/few alternatives for ~50.000 patients<sup>1</sup>
- Benchmarking arena for immune activators
- May release a large potential in other indications

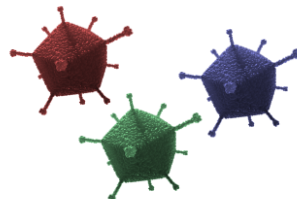
## 3 Expanding CPI indications



### Peritoneal malignancies

- Originating from ovarian and colorectal cancers
- >100.000 patients<sup>1</sup> with tumors not responding to CPIs
- Intraperitoneal administration may open new indications

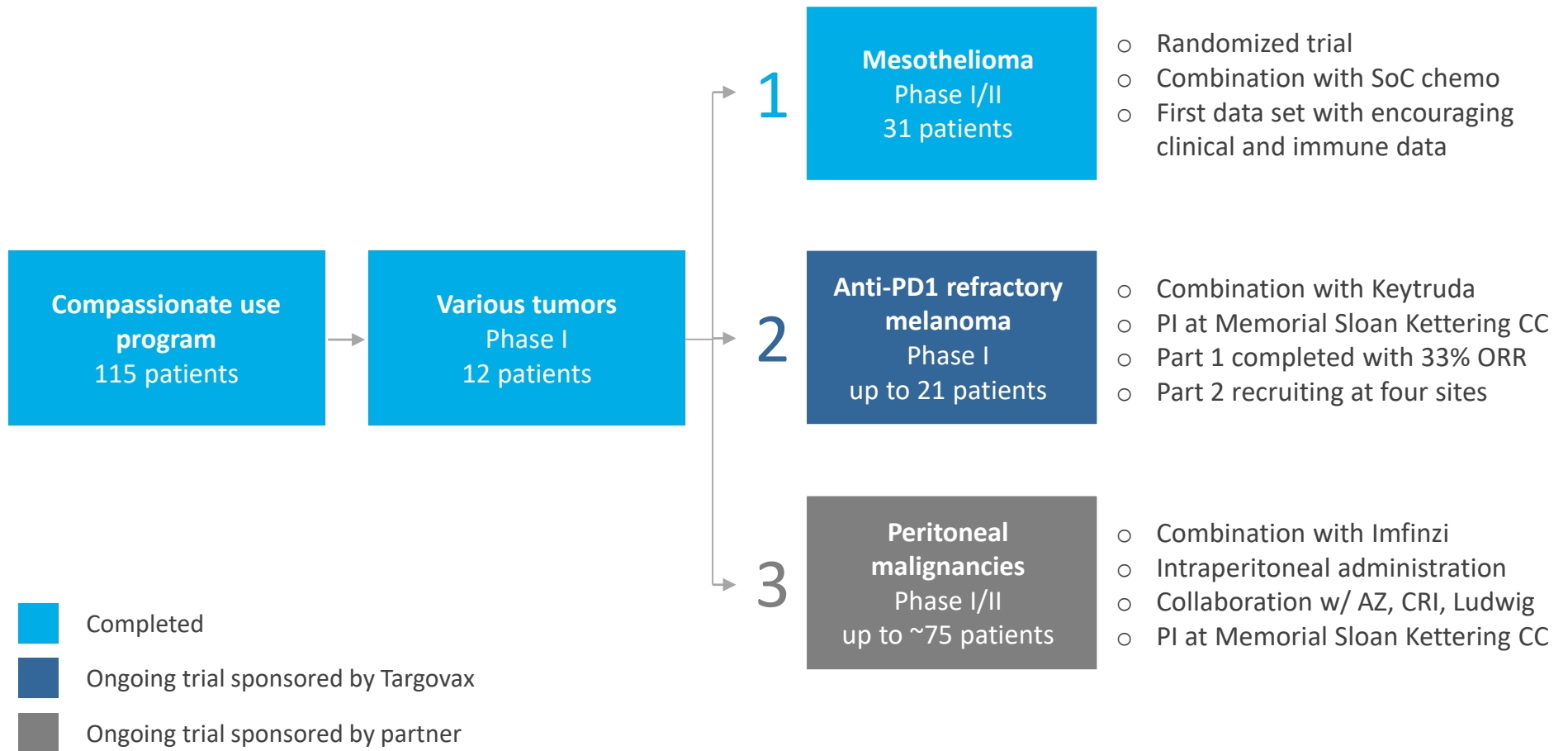
## 4 Next generation



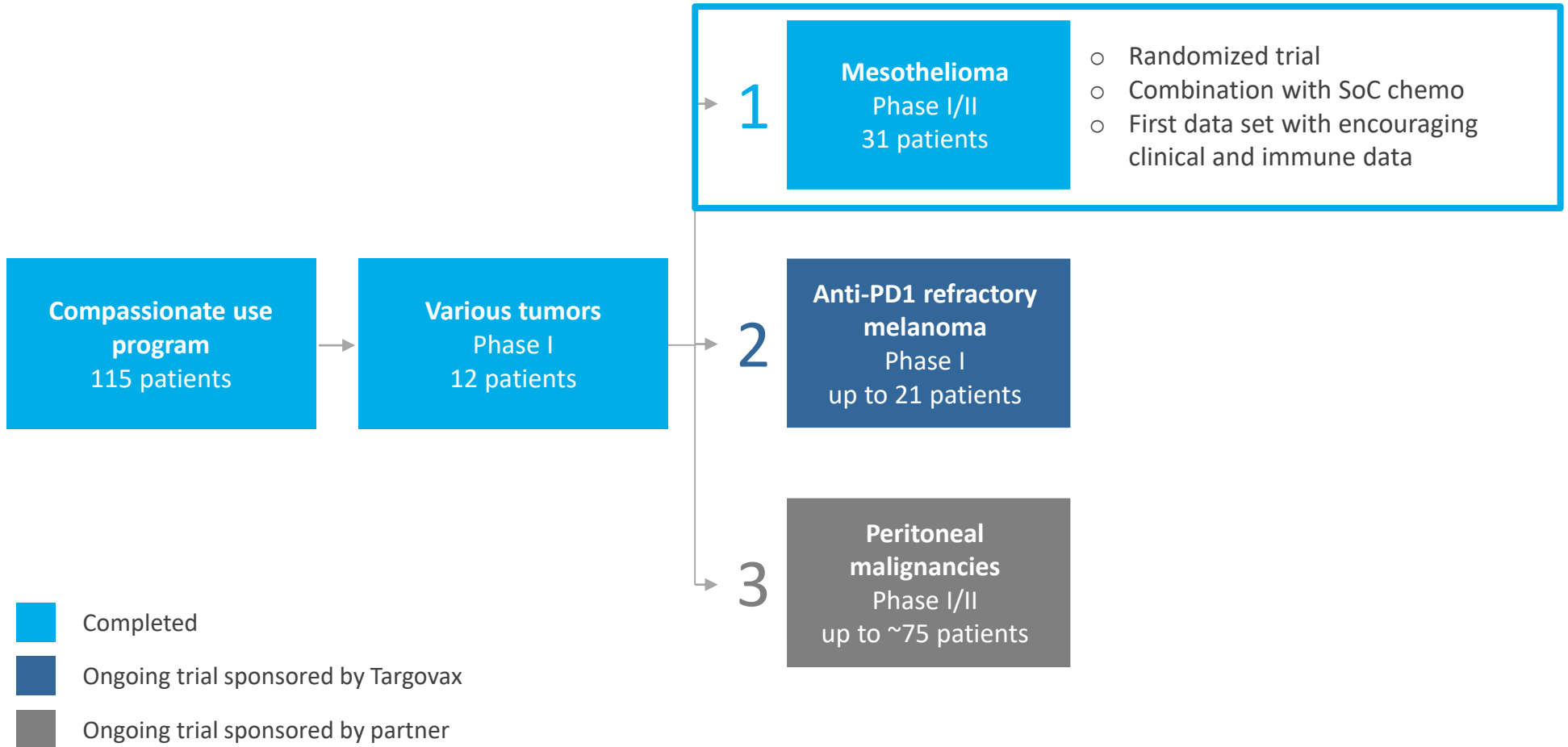
### Platform expansion in solid tumors

- Double transgenes
- Novel targets and modes of action
- Ongoing pre-clinical testing

# ONCOS-102 CLINICAL DEVELOPMENT PROGRAM



# ONCOS-102 CLINICAL DEVELOPMENT PROGRAM



# MALIGNANT PLEURAL MESOTHELIOMA

## HIGH NEED FOR NEW TREATMENT APPROACHES



### Surgery

**Only 10% of patients suitable for resection**

Technically challenging due to location

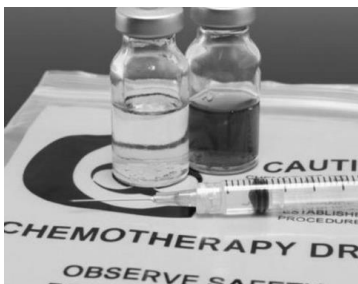
Diagnosis often too late for surgery

### Radiotherapy

**Rarely effective due to tumor shape**

Shape of tumors make them hard to target

Mainly palliative care



### Chemotherapy

**Standard of care (SoC) has limited efficacy**

Only approved SoC option is pemetrexed/cisplatin

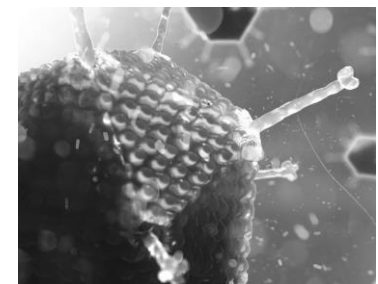
6 month PFS and 12 month median OS in 1<sup>st</sup> line

### Immunotherapy

**Mixed signals from early IO trials**

CPIs included in NCCN guidelines as 2<sup>nd</sup> line option

No/few other oncolytic viruses in development



# 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

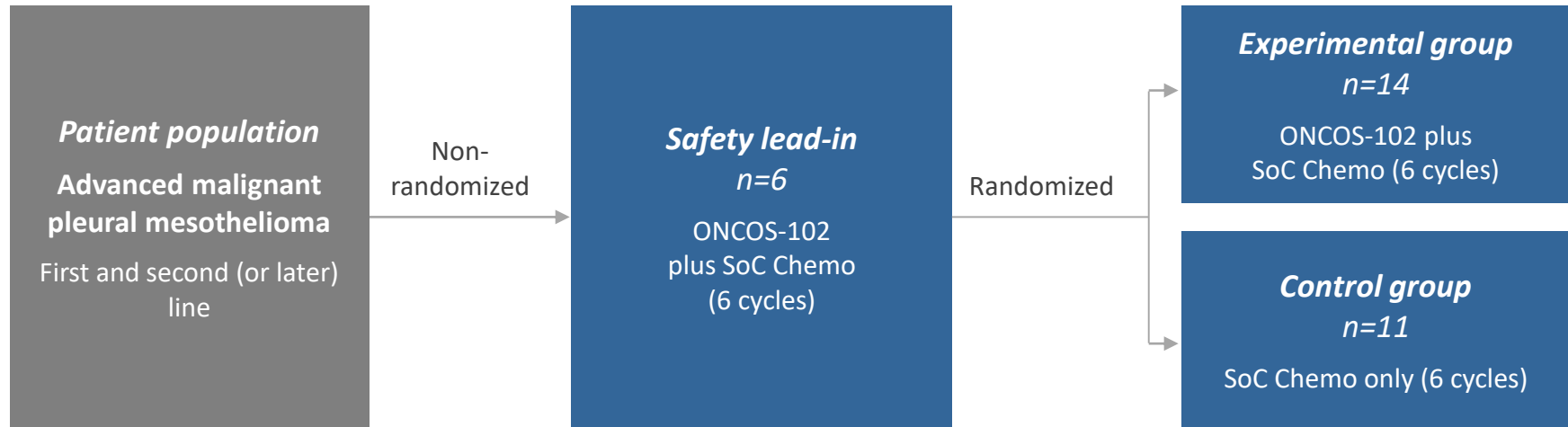
- High unmet medical need; orphan drug designation
- 7-10 year market exclusivity
- Opportunity for accelerated regulatory routes to market

## Limited competition

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

# ONCOS-102 MESOTHELIOMA PHASE I/II TRIAL IN COMBINATION WITH CHEMO

## STUDY DESIGN



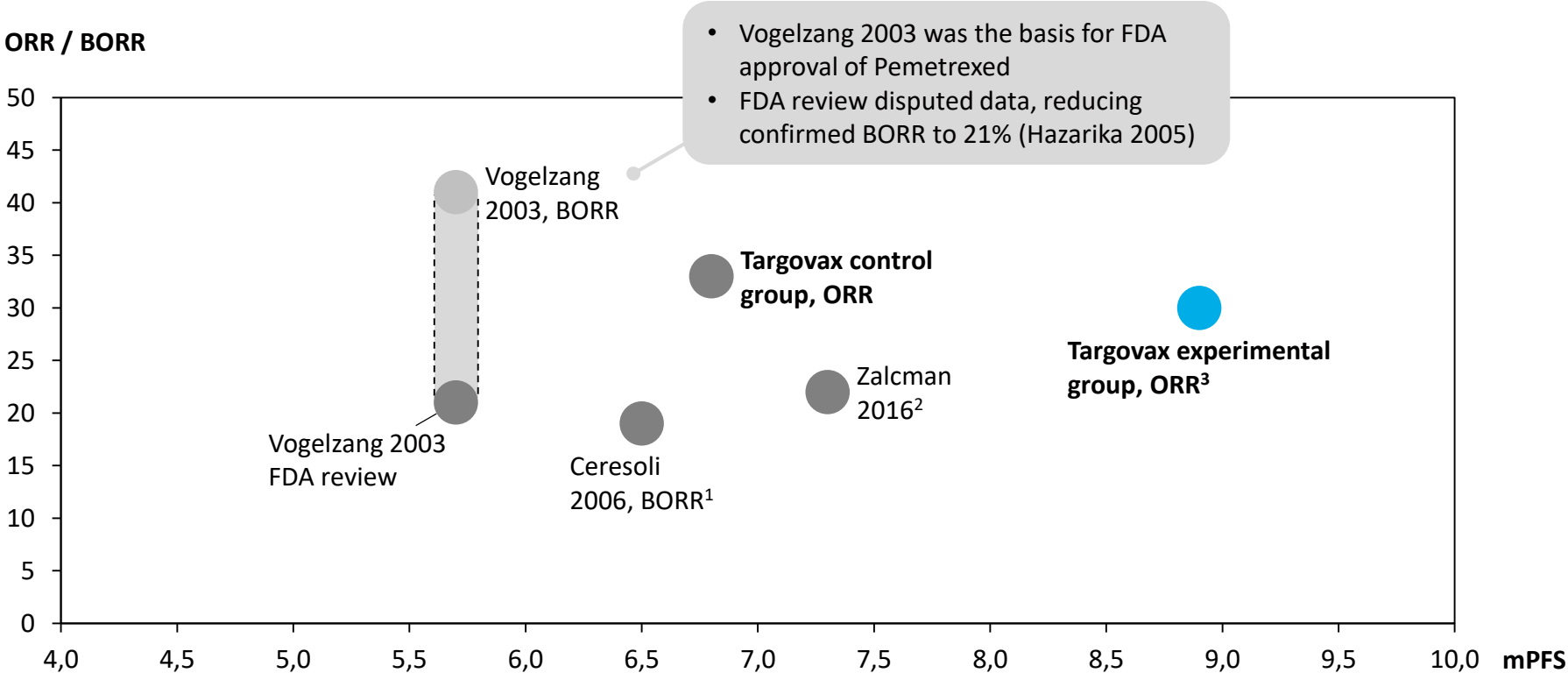
# ONCOS-102 MESOTHELIOMA PHASE I/II COMBINATION WITH SOC

## PATIENT CHARACTERISTICS AND OUTCOMES

ITT: N = 31 (20+11) PP: N = 30 (19+11)	Experimental n= 20	Control n= 11	Comments
<b>Tumor and disease characteristics at enrollment</b>			
- Number of lesions	4.3	3.5	<i>Generally more progressed disease in experimental group</i>
- Tumor burden mm (RECIST 1.1)	87	46	
- Stage III	30%	27%	
- Stage IV	60%	46%	
<b>First line patients (number)</b>	<b>11 of 20</b>	<b>6 of 11</b>	<i>No previous chemotherapy</i>
Median Progression Free Survival (mPFS)	8.9 months	6.8 months	<i>Early data, many patients censored</i>
Overall Response Rate (ORR, n=10 / n=6)	30%	33%	
Disease Control Rate (DCR, n= 10 / n=6)	90%	83%	
<b>Second (or later) line patients (number)</b>	<b>9 of 20</b>	<b>5 of 11</b>	<i>Received previous chemotherapy</i>
Median Progression Free Survival (mPFS)	4.5 months	ND	<i>Early data, many patients censored</i>
Overall Response Rate (ORR, n=9 / n=5)	11%	60%	
Disease Control Rate (DCR, n=9 / n=5)	67%	80%	



# FIRST LINE ONCOS-102 ORR AND EARLY PFS DATA COMPARE FAVORABLY TO HISTORICAL CONTROL



1 Pemetrexed plus carboplatin

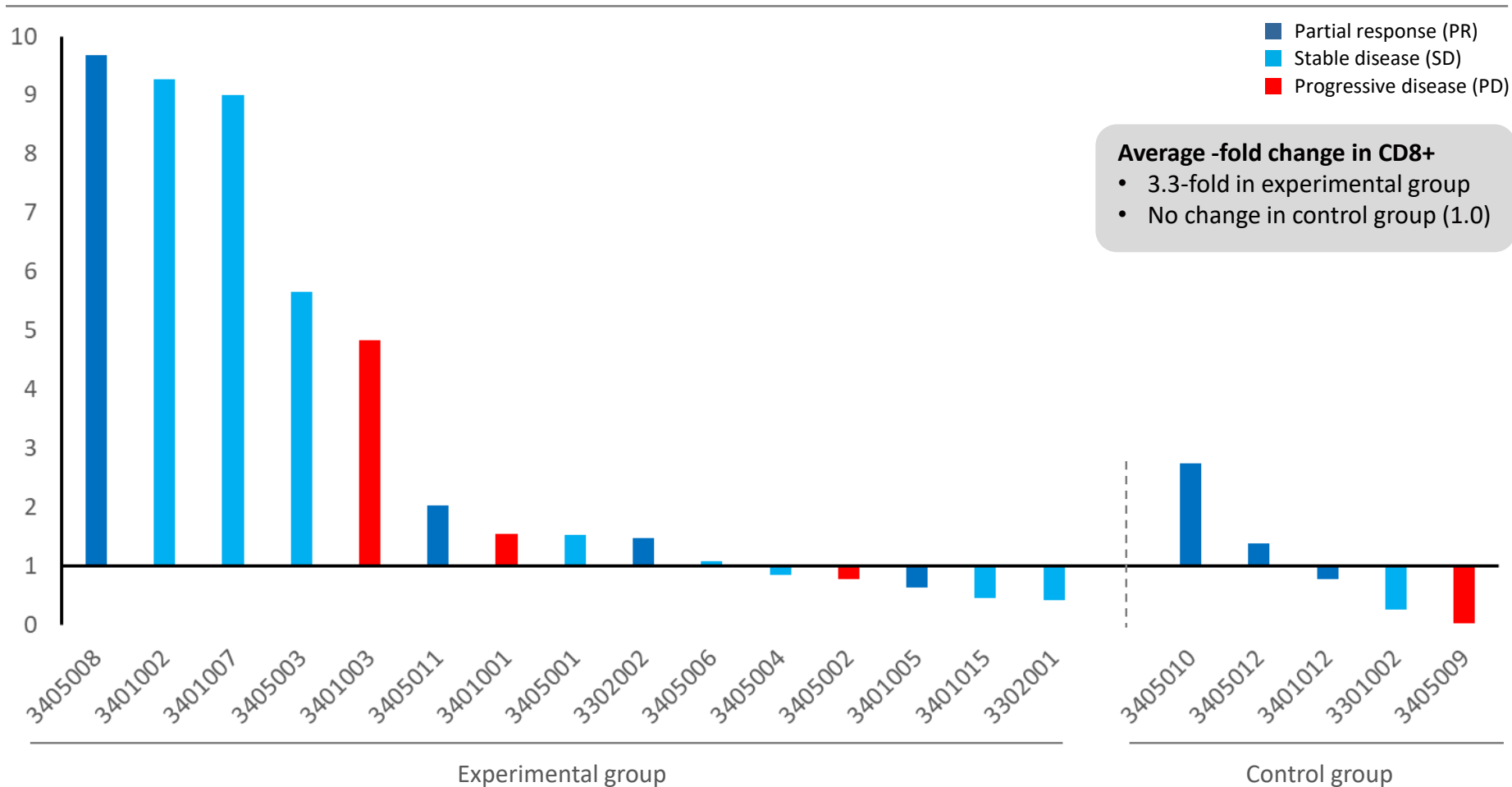
2 Zalcman 2016 (Lancet) compared bevacizumab + pem/cis vs pem/cis; data from pem/cis arm only presented on plot. Not specified if ORR or BORR.

3 mPFS in Targovax trial is early and will change: Control group 6 patients (3 censored), Experimental group 11 patients (7 censored)

# ONCOS-102 MESOTHELIOMA IMMUNE ACTIVATION

## INCREASED T-CELL INFILTRATION IN EXPERIMENTAL GROUP

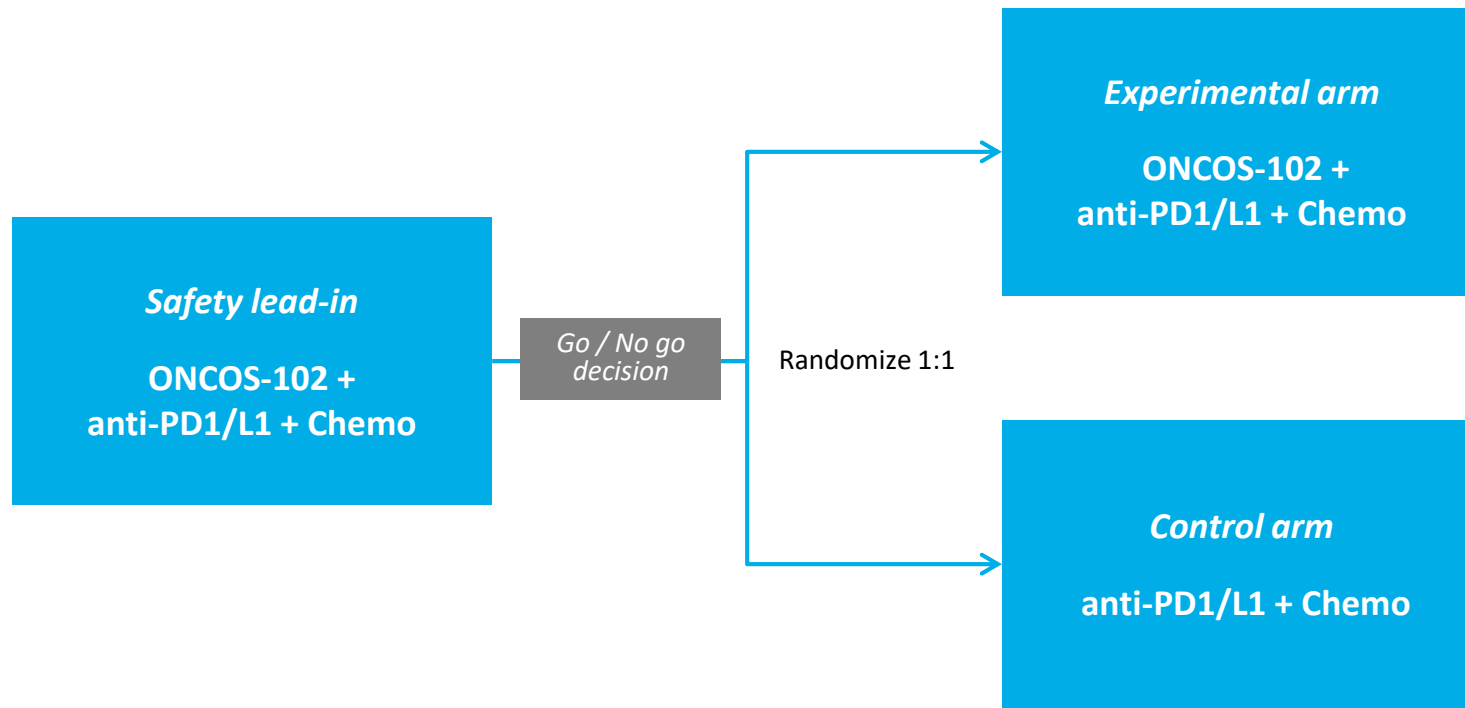
CD8+ T-cell infiltration -fold change from baseline to day 36 (n=20<sup>1</sup>)



# NEXT STEP: ONCOS-102 + ANTI-PD1/L1 + CHEMO TRIPLE COMBINATION IN FIRST LINE MESOTHELIOMA

## Study population – malignant pleural mesothelioma:

First line, unresectable, advanced and/or metastatic disease  
ca. 100 patients



# ONCOS-102 MESOTHELIOMA PHASE I/II TRIAL

## SUMMARY AND NEXT STEPS



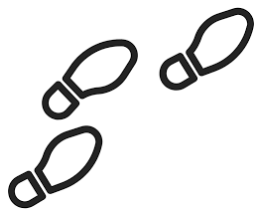
### Excellent safety profile

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



### Clinical activity observed

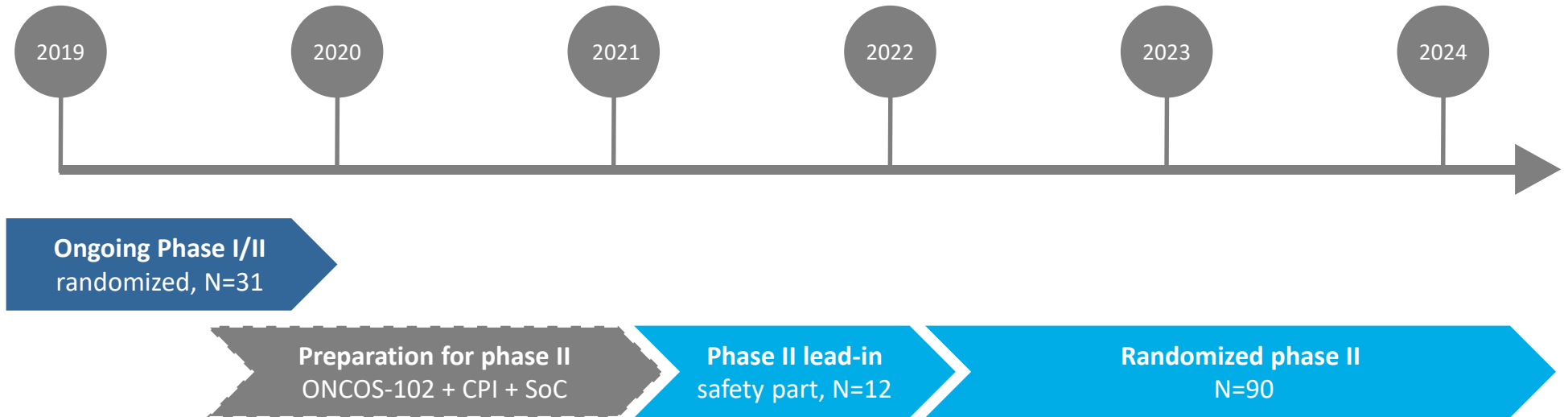
- Emerging data suggest **benefit for ONCOS-102 treated patients** and **compare favorably** to historical control
- Increased **T-cell infiltration** and **PD-L1 expression**
- Robust immune activation **associated with clinical benefit**



### Next steps defined

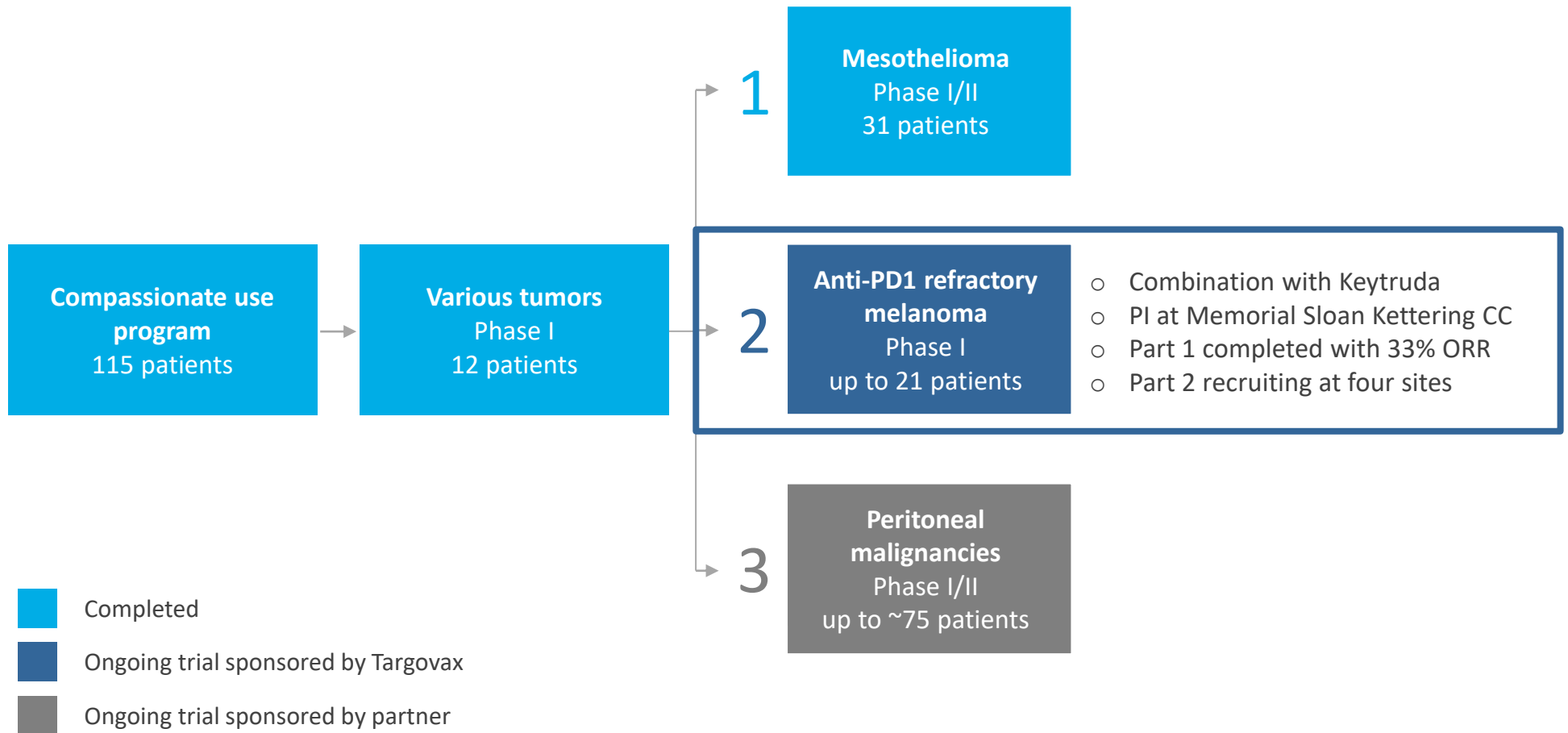
- **First line** identified as **target population** for follow-up trial
- **Strong rationale** for combination with anti-PD1/L1 CPI
- **Discussion ongoing with pharma partner** for trial collaboration

# ONCOS-102 DEVELOPMENT PATH IN MALIGNANT PLEURAL MESOTHELIOMA STRATEGY AND INDICATIVE TIMELINES



- Phase I/II trial of ONCOS-102 + SoC vs. SoC
- 1<sup>st</sup> and 2<sup>nd</sup> to 4<sup>th</sup> line
- Clinical and immune data Jan 2020
- Phase II trial of ONCOS-102 + CPI + SoC vs. CPI + SoC
- 1<sup>st</sup> line
- EU and US sites
- 45 patients per arm, plan to expand into registrational trial if data allow

# ONCOS-102 CLINICAL DEVELOPMENT PROGRAM



# ONCOS-102 ANTI-PD1 REFRACTORY MELANOMA PART 1

## 33% ORR AND ROBUST IMMUNE ACTIVATION

### Patient population

- Advanced, unresectable **melanoma** with **disease progression following prior treatment with anti-PD1**
- Typically treated with **2-3 immunotherapies prior to inclusion**
- **Median age 73 years (40-87)**
- Poor prognosis, with **few treatment alternatives**

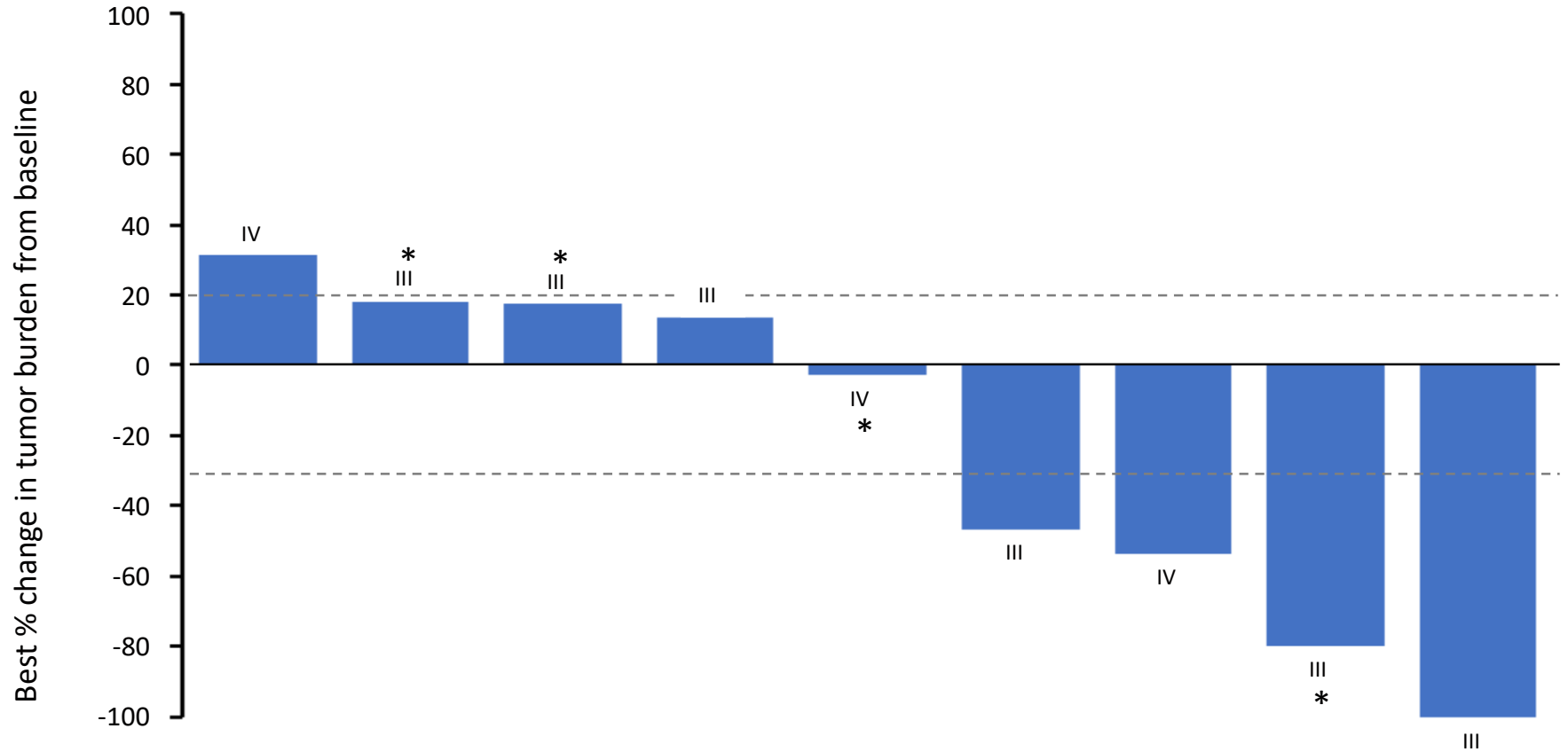
### Treatment regime

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

### Clinical data

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

# BEST PERCENTAGE CHANGE IN TARGET LESIONS



\* Progressive Disease due to non target progression

Letters and numbers indicating disease stage

Preliminary data



# 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**  
T4a, N2b, M0

**Prior therapies:**

Surgery (x3)  
Ipilimumab  
Dabrafenib + Trametinib  
Keytruda

**RECIST 1.1:**

**CR**, week 9-27

# 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 IFN $\gamma$  expression (8/8 pts)
- Fever/chills (7/9 pts)

## Adaptive immune activation

### T-cell tumor infiltration

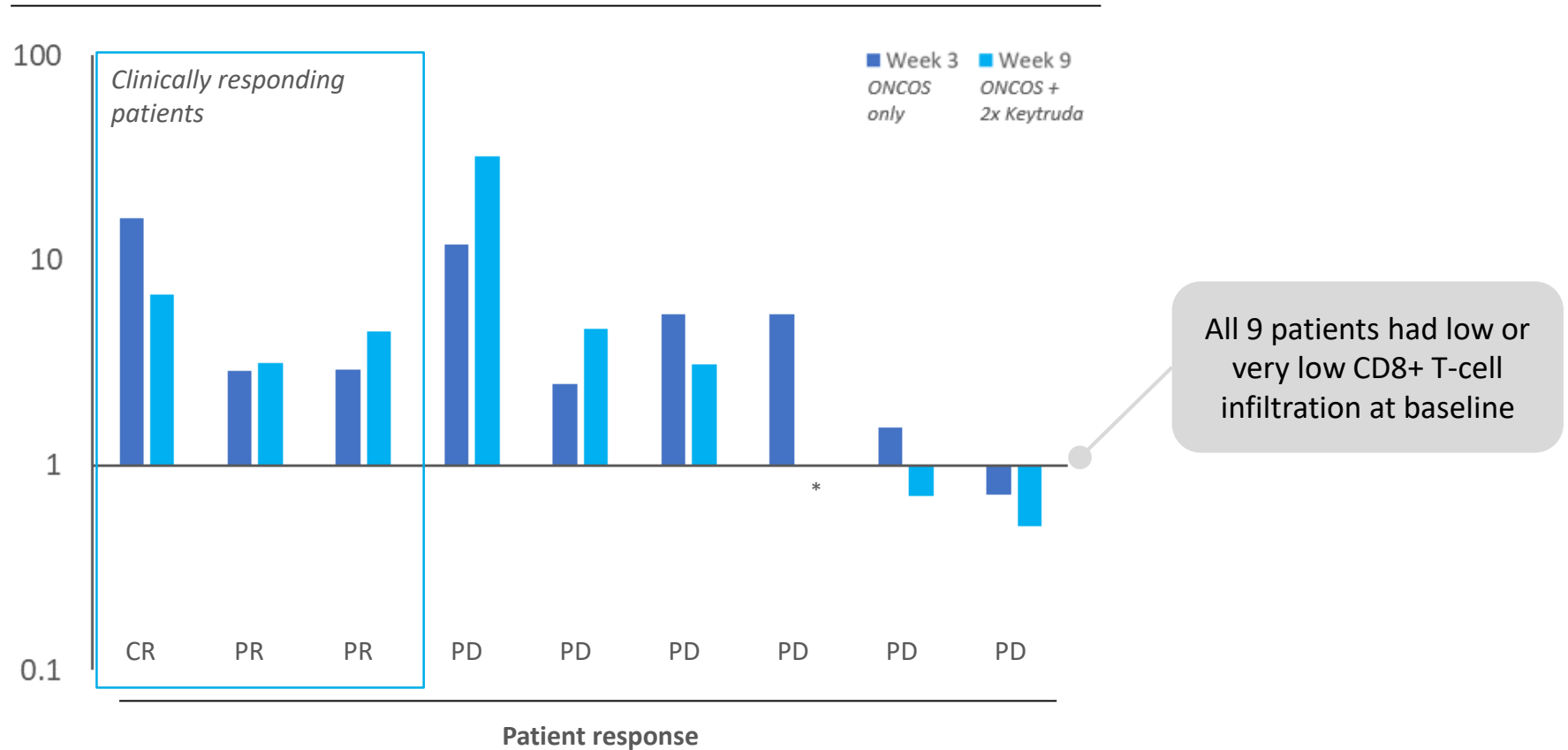
- Increase in CD8+ T-cell infiltration (8/9 pts)
- Increase in activated<sup>1</sup> CD8+ T-cells (9/9 pts)
- PD1+/CD8+ T-cells in treated lesions (6/7 pts)
- T-cells in non-treated lesions (2/3 pts) on Week 3

### 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

# 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

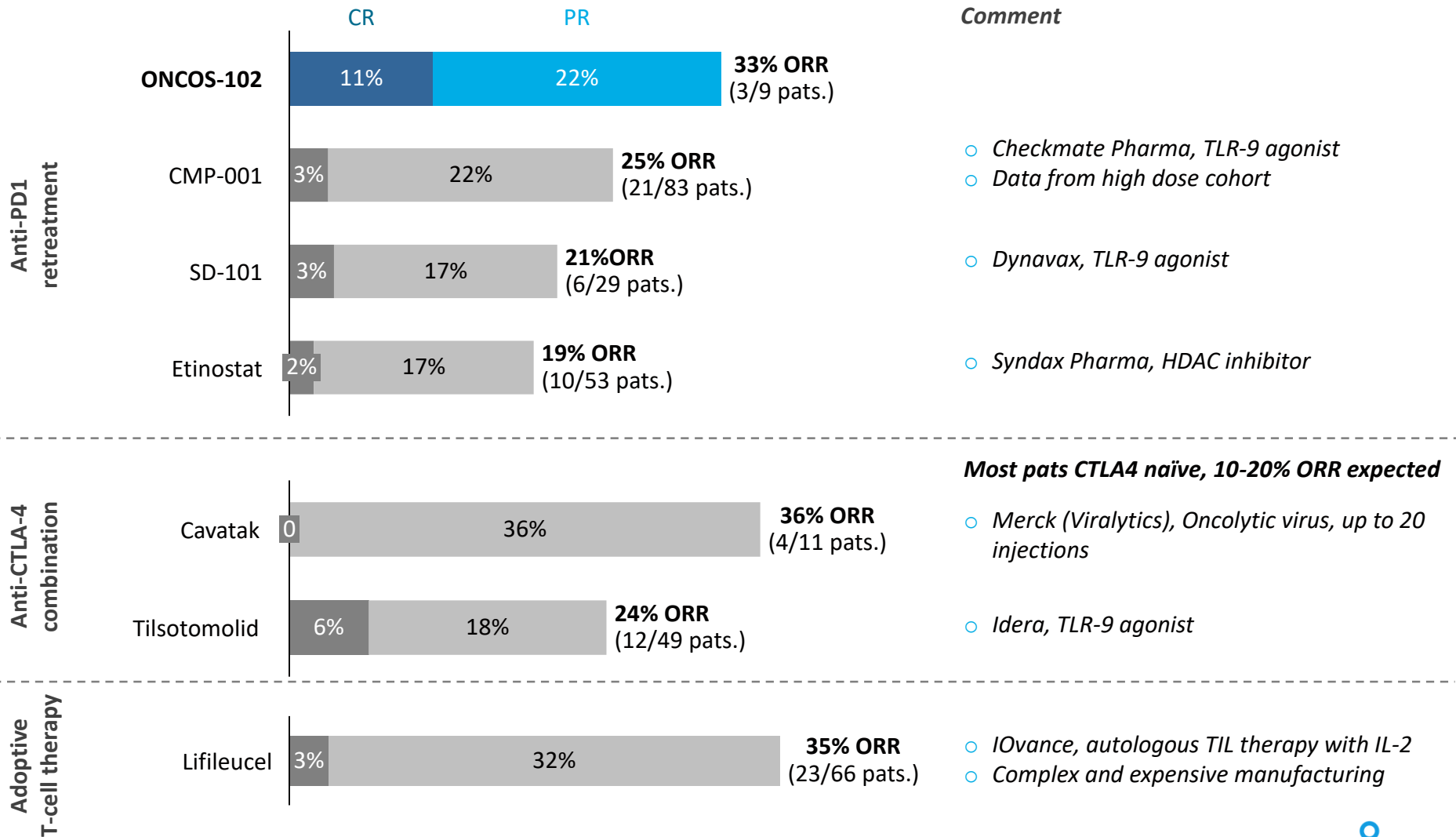
Do not post, unpublished company data

• Week 9 analysis not available

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

# ONCOS-102 + KEYTRUDA DATA IN CONTEXT

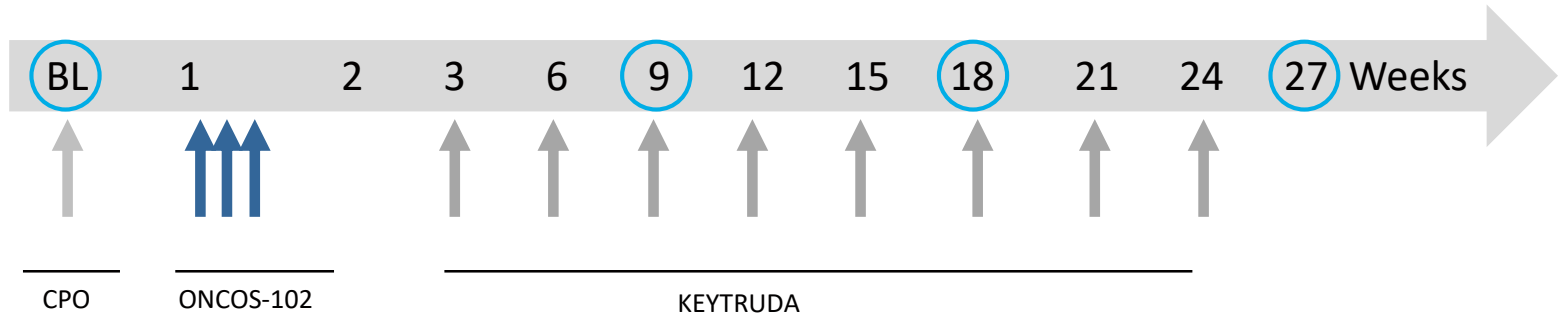
## ANTI-PD1 REFRACTORY MELANOMA BENCHMARK DATA



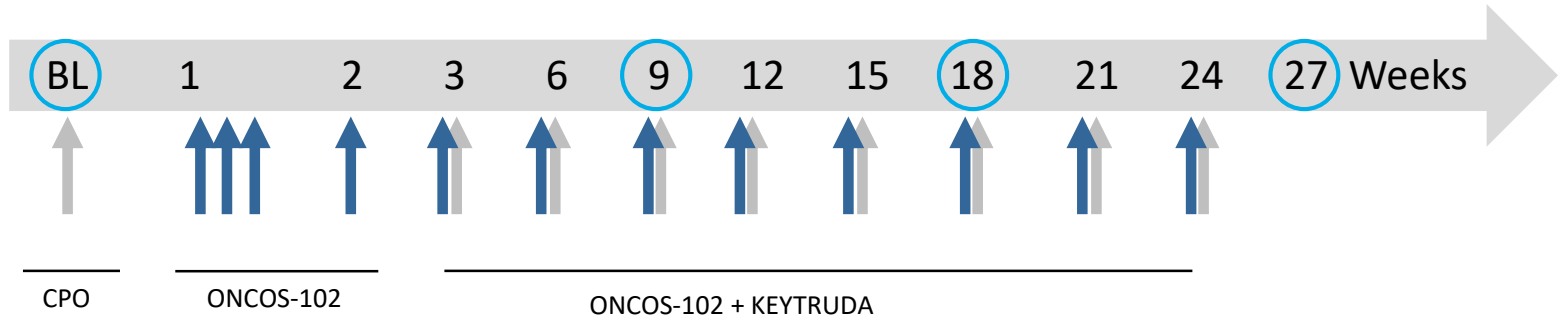
# MELANOMA PART 2 IS RECRUITING


UP TO 12 PATIENTS: 12 ONCOS-102 INJECTIONS COMBINED WITH 5 MONTHS KEYTRUDA

**Part 1:**  
3 ONCOS-102  
injections

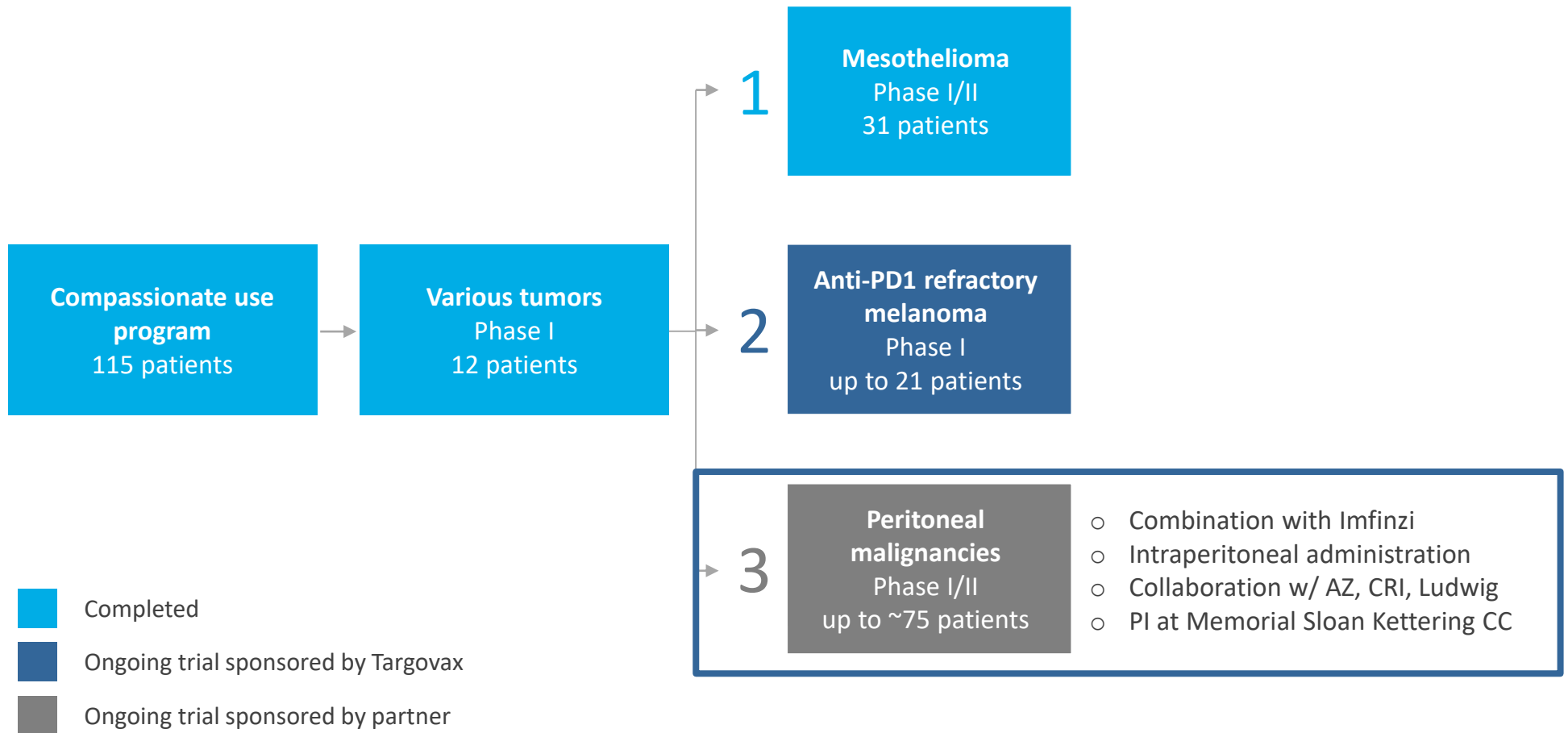


**Part 2:**  
12 ONCOS-102  
injections



 Imaging  
CPO: Cyclophosphamide

# ONCOS-102 CLINICAL DEVELOPMENT PROGRAM

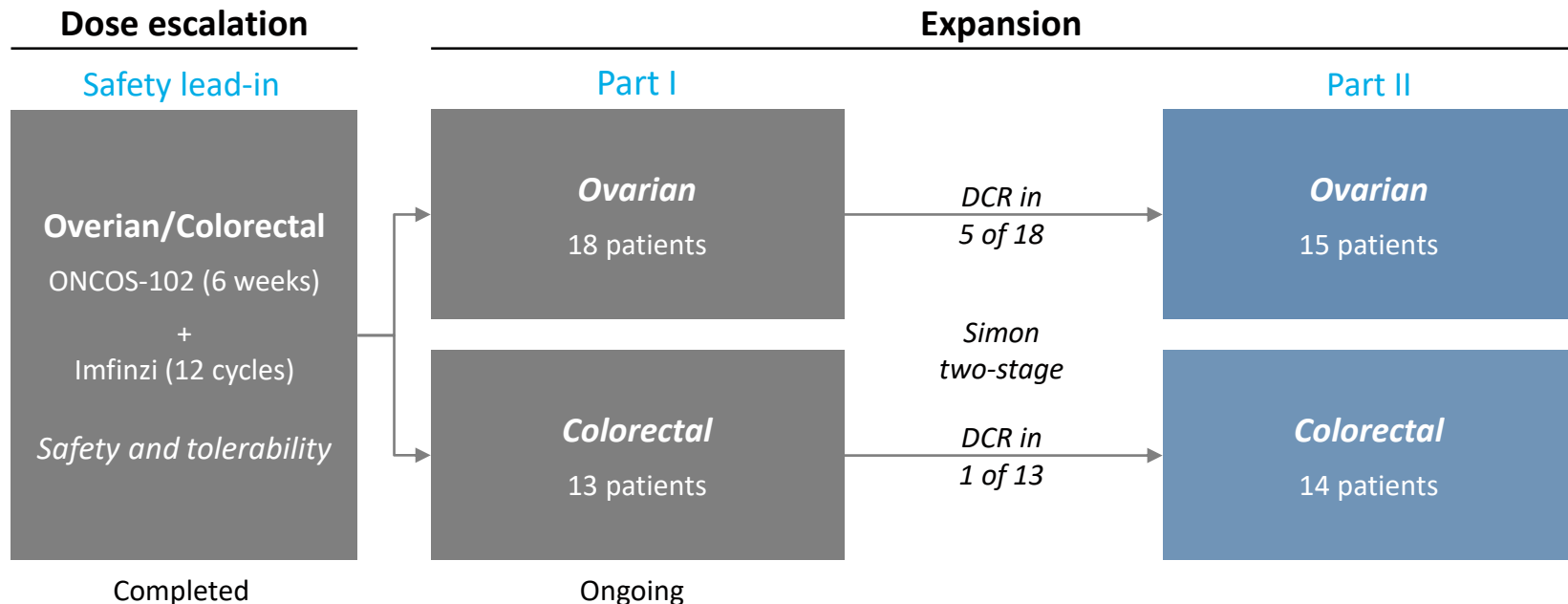


# ONCOS-102 IN PERITONEAL MALIGNANCIES

## 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

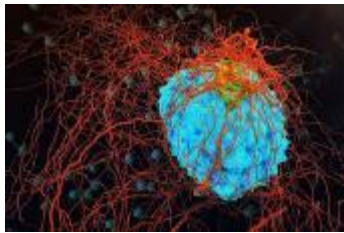
Product candidate	Preclinical	Phase I	Phase II	Phase III	Next expected event
ONCOS-102	<b>Mesothelioma</b> Combination w/ pemetrexed/cisplatin				<b>1H 2020</b> Updated clinical and immune data
	<b>Melanoma</b> Combination w/Keytruda				<b>1H 2020</b> Clinical and immune activation data
	<b>Peritoneal malignancies</b> Collaborators: Ludwig, CRI & AZ Combination w/Imfinzi				<i>Update by collaborator</i>
	<b>Prostate</b> Collaborator: Sotio Combination w/DCvac				<i>Update by collaborator</i>
Next-gen ONCOS	<b>3 new viruses</b> Double transgene				<b>1H 2020</b> Pre-clinical data



# NEXT GENERATION ONCOS VIRUSES HAVE DOUBLE TRANSGENES AND DISTINCT MODES OF ACTION

## Mode of action

## Target tumors

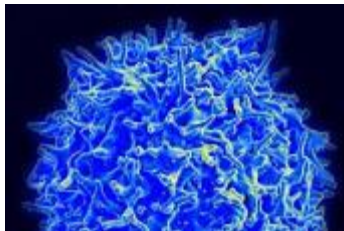


### ONCOS-210 & -212

*Inhibition of tumor growth and vascularization*

- Interfere with tumor's ability to break down surrounding tissue
- Induce cell cycle arrest
- Inhibit angiogenesis

- Highly invasive or metabolic tumors

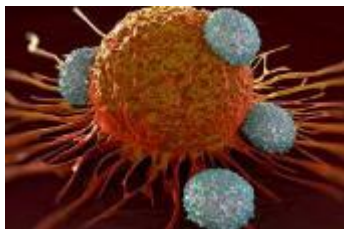


### ONCOS-211

*Counteract immune-suppressive tumor microenvironment*

- Decrease inhibitory factors from tumor microenvironment
- Activate T-cells

- "Cold" uninflamed tumors



### ONCOS-214

*Enhanced cell killing properties*

- Induce immunogenic cell death
- Extend cell killing ability to neighboring non-infected cells

- High-stroma tumors

# TG01/02 IOVAXIS OPTION AGREEMENT



**IOVAXIS THERAPEUTICS**

*Fighting Cancer with Your Own Weapons*

**CEO:** John Wang

**HQ:** Nantong, China

**Founded:** 2018

**R&D focus:** Shared and personalized cancer vaccines

## Topic

- **Exclusive option** to license TG01/02 vaccines for **Greater China and Singapore**
- **License option to be executed** upon approval to **start first clinical trial**
- **IOVaxis clinical trial sponsor** and responsible for local regulatory filings

## Terms

- **US\$250.000 option fee**
- **US\$3m up-front fee** upon option exercise
- **Up to US\$100m** total development and commercial **milestones**
- **Tiered royalties** on net sales up to **mid teens**

## Next steps

- **File for China IND**
- **Establish full license agreement**
- Define **regional development plan**
- **Initiate** one or more China and Singapore **TG clinical trials, incl. IO combinations**



# SUFFICIENTLY FUNDED TO ADVANCE CLINICAL PROGRAM BEYOND VALUE INFLECTION POINTS

## The company

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Cash end of 3Q

**104 / 11**

NOK million      USD million

Net cash flow - total 3Q

**-31 / -3**

NOK million      USD million

Market cap

**620      72**

NOK million      USD million

Analyst coverage

**DNB, H.C. Wainwright, Arctic, ABG Sundal Collier, Redeye, Edison**

## The shareholders

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Estimated ownership<sup>1</sup>

Shareholder	Shares, million	Ownership
HealthCap	12.4	19.6 %
RadForsk	4.4	7.0 %
Nordea	3.7	5.8 %
Thorendahl Invest	1.4	2.2 %
KLP	1.0	1.6 %
Danske Bank (nom.)	0.9	1.4 %
Prieta	0.7	1.1 %
J.P. Morgan Bank	0.7	1.1 %
Sundt	0.7	1.0 %
Morgan Stanley	0.6	0.9 %
<b>10 largest shareholders</b>	<b>26.4</b>	<b>41.6 %</b>
Other shareholders (4 288)	37.0	58.4%
<b>Total shareholders</b>	<b>63.4</b>	<b>100.0 %</b>



# 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

Potential readouts from  
peritoneal trial