Activating the patient's immune system to fight cancer

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Pareto Securities Conference

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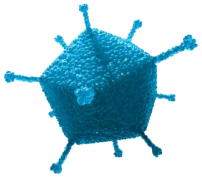
TARGOVAX HIGHLIGHTS

Oncolytic viruses

- Targovax develops **oncolytic adenoviruses**
- Oncolytic viruses promise to **turn cold tumors hot** and **complement other treatments**



ONCOS-102

- One of the **furthest developed** OVs **with >180 patients treated** to date
- Four ongoing combination trials with **data read-outs in 2019 and 2020**

Encouraging data

- Strong **single agent** data
- **33% ORR in PD-1 refractory melanoma** in combination with Keytruda
- **Encouraging interim data in mesothelioma** in combination with chemotherapy

OSLO BØRS

Listed on Oslo Stock Exchange

- Ticker TRVX
- All assets unencumbered

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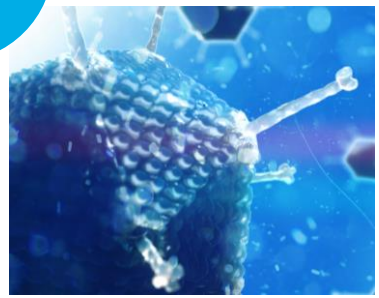
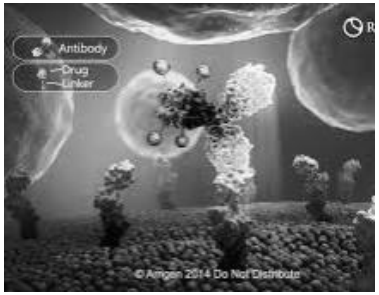
ONCOLYTIC VIRUSES IN THE FUTURE CANCER THERAPY LANDSCAPE

Targovax focus

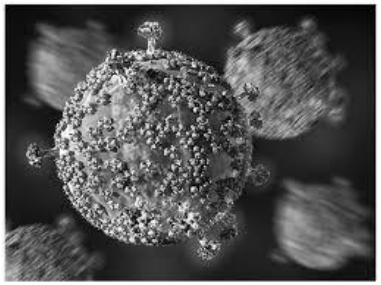


Immune activators
Oncolytic viruses

Immune modulators
Checkpoint inhibitors

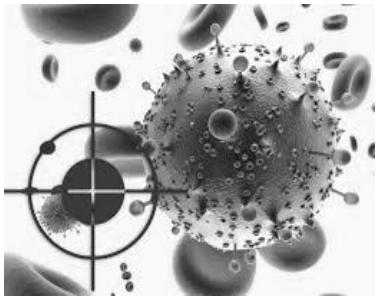


Surgery - Radio - Chemo



Immune boosters
CAR-Ts, TCRs

Targeted therapy
TKIs, PARPs, etc.



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THERE HAS BEEN A NUMBER OF TRANSACTIONS IN THE OV SPACE IN 2018-2019

Acquirer	Target	Type of deal	Deal value
Boehringer Ingelheim	ViraTherapeutics	**M&A** Pre-clinical VSV virus	**USD 250m** up-front cash
MERCK	Viralytics Developers of Oncolytic Immunotherapies	**M&A** Phase II RNA virus	**USD 400m** up-front cash
janssen PHARMACEUTICAL COMPANIES OF Johnson & Johnson	BeneVir	**M&A** Pre-clinical Herpes virus	**USD 140m** up-front cash **Up to USD 1b** total value
AstraZeneca	transgene	**R&D partnership** Co-development of novel vaccinia viruses Pre-clinical	**USD 10m** upfront payment Unknown potential total value

THE OV DEVELOPMENT LANDSCAPE

Overview of most relevant OVs in current development

Company		Asset/ Program	MoA	Highest Phase
AMGEN	H	Imlygic	HSV with GM-CSF transgene, IT only	Approved 2015 as mono Phase III PD1 combo
transgene	V	Pexa-Vec	Vaccinia virus with GM-CSF and beta-galactosidase transgenes, IT focus	Phase II
MSD	R	Cavatak	Coxsackievirus, non gene modified, IT focus, IV and IP trial ongoing	Phase II
DNAtrix	A	DNX-2401	Chimeric Ad5/3, no transgene, IT and intra-arterial	Phase II
targovax	A	ONCOS-102	Chimeric Ad5/3 with GM-CSF transgene, IT and IP administration	Phase II
Cold Genesys	A	CG0070	Ad5 with GM-CSF transgene, intravesical	Phase II
ONCOLYTICS BIOTECH INC	R	Reolysin	Reovirus, non gene modified, IV only	Phase II
PsiOxus THERAPEUTICS	A	Enadenotucirev	Chimeric Ad5, no transgene, IV only	Phase I/II
Replimune	H	RP1	HSV with GM-CSF, GALV, and ipilimumab transgenes, IT only	Phase I/II
LOKON	A	LOAd703	Chimeric Ad5/35 with TMZ-CD40L and 4-1BBL transgenes, IT only	Phase I/II
VYRIAD	R	Voyager V1	VSV virus with NIS and human interferon beta transgenes, IV only	Phase I
WESTERN ONCOLYTICS	R	Ad-MAGEA3	Maraba virus with MAGEA3 transgene, IV and IT	Phase I
Boehringer Ingelheim	R	VSV-GP	Chimeric VSV virus, IV only	Pre-clinical
TURNSTONE BIOLOGICS	V	WO-12	Vaccinia virus armed with TRIF and HPGD transgenes, IV only	Pre-clinical
Oncorus	H	oHSV	Herpes virus with multiple transgenes (PD1, CTLA4 ++), IT only	Pre-clinical

A *Adenovirus* H *Herpes virus* V *Vaccinia virus* R *RNA virus*

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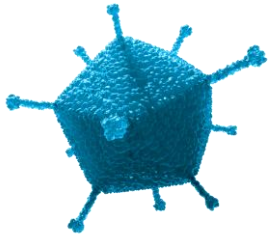
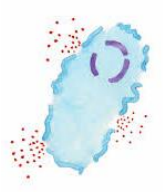
BENEFITS OF ONCOS-102 ADENOVIRUS





Selectively kills cancer cells, induces oncolysis

Highly immunogenic, TLR-9 agonist, stimulates inflammation

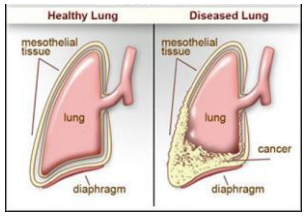
Well-characterized, well-tolerated and few safety concerns

Versatile DNA backbone, ability to carry multiple transgenes

ONCOS DEVELOPMENT STRATEGY

1

Path-to-market as orphan drug

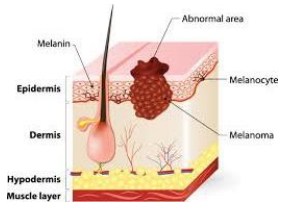


Target launch indication

- **Mesothelioma**
- Combo with SoC chemo
- Randomized phase II
- Enrollment of 31 patients completed

2

Activating CPI refractory tumors

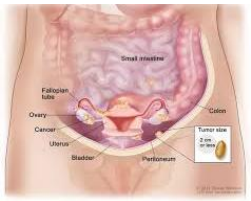


Proof of concept

- **Anti-PD1 refractory melanoma**
- Combo with Keytruda
- Phase I, ~20 patients
- First 9 patients completed
- Part 2 initiated

3

Expanding CPI indications

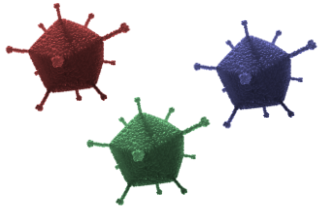


Proof of concept

- **Ovarian and colorectal cancers metastasized to peritoneum**
- Combo with Imfinzi
- Collaboration with AZ, CRI, & Ludwig
- Phase I/II, ~75 patients

4

Next generation



Platform expansion in solid tumors

- **Intratumoral**
- Double transgenes
- Novel targets and mode-of-action
- Ongoing *in vivo* testing

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RICH NEAR-TERM NEWS FLOW

ONCOS program pipeline overview

Product candidate	Preclinical	Phase I	Phase II	Phase III	Next expected event
ONCOS-102	**Mesothelioma** Combination w/ pemetrexed/cisplatin				**New year 2019-20** Randomized data
	Melanoma Combination w/Keytruda				**1H 2020** Part 2 data
	Peritoneal metastasis Collaborators: Ludwig, CRI & AZ Combination w/Imfinzi				*Update by collaborator*
	Prostate Collaborator: Sotio Combination w/DCvac				*Update by collaborator*
Next-gen ONCOS	**3 new viruses** Double transgene				**2H 2019** First pre-clinical data

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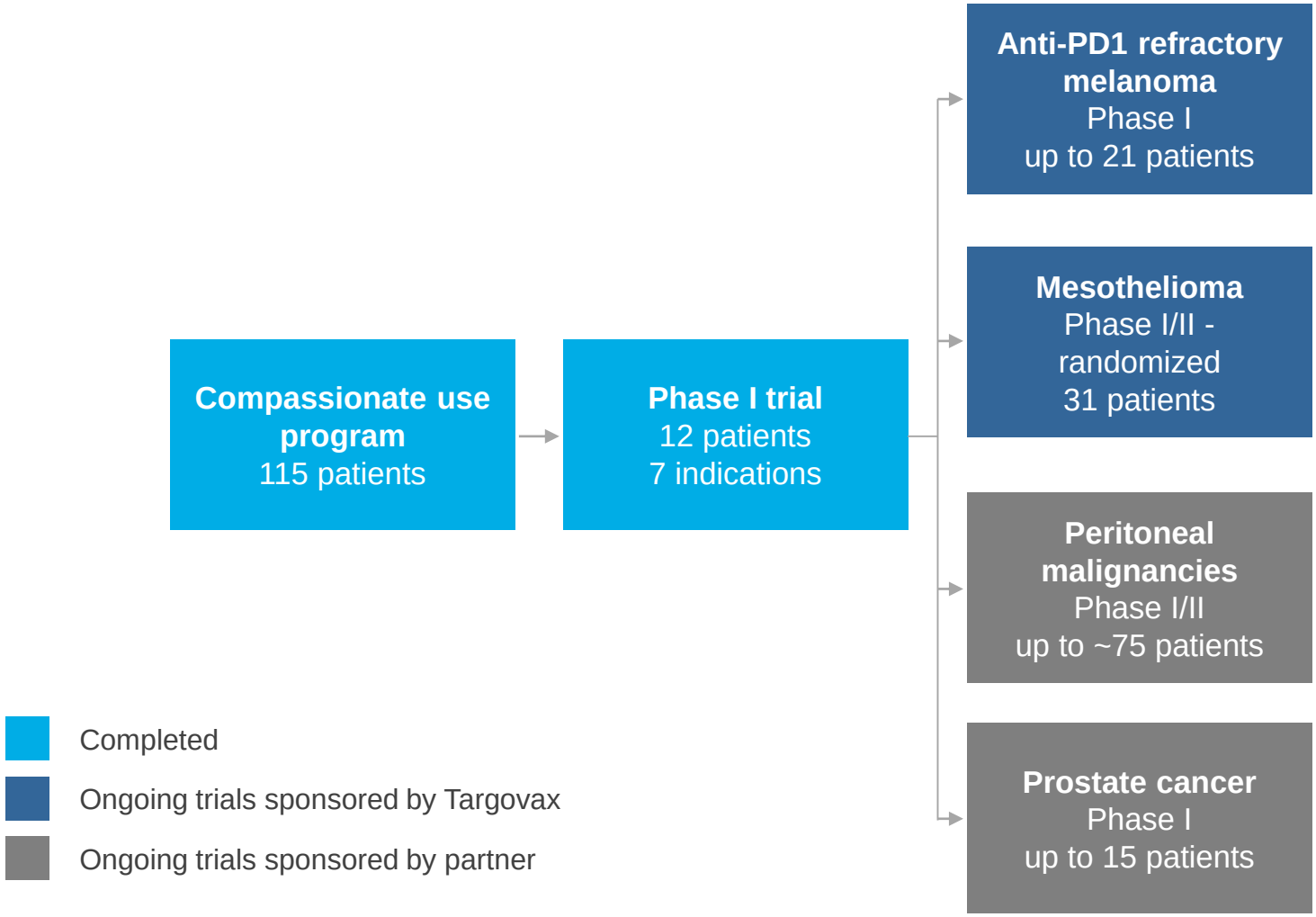
ONCOS-102 CLINICAL DEVELOPMENT PROGRAM



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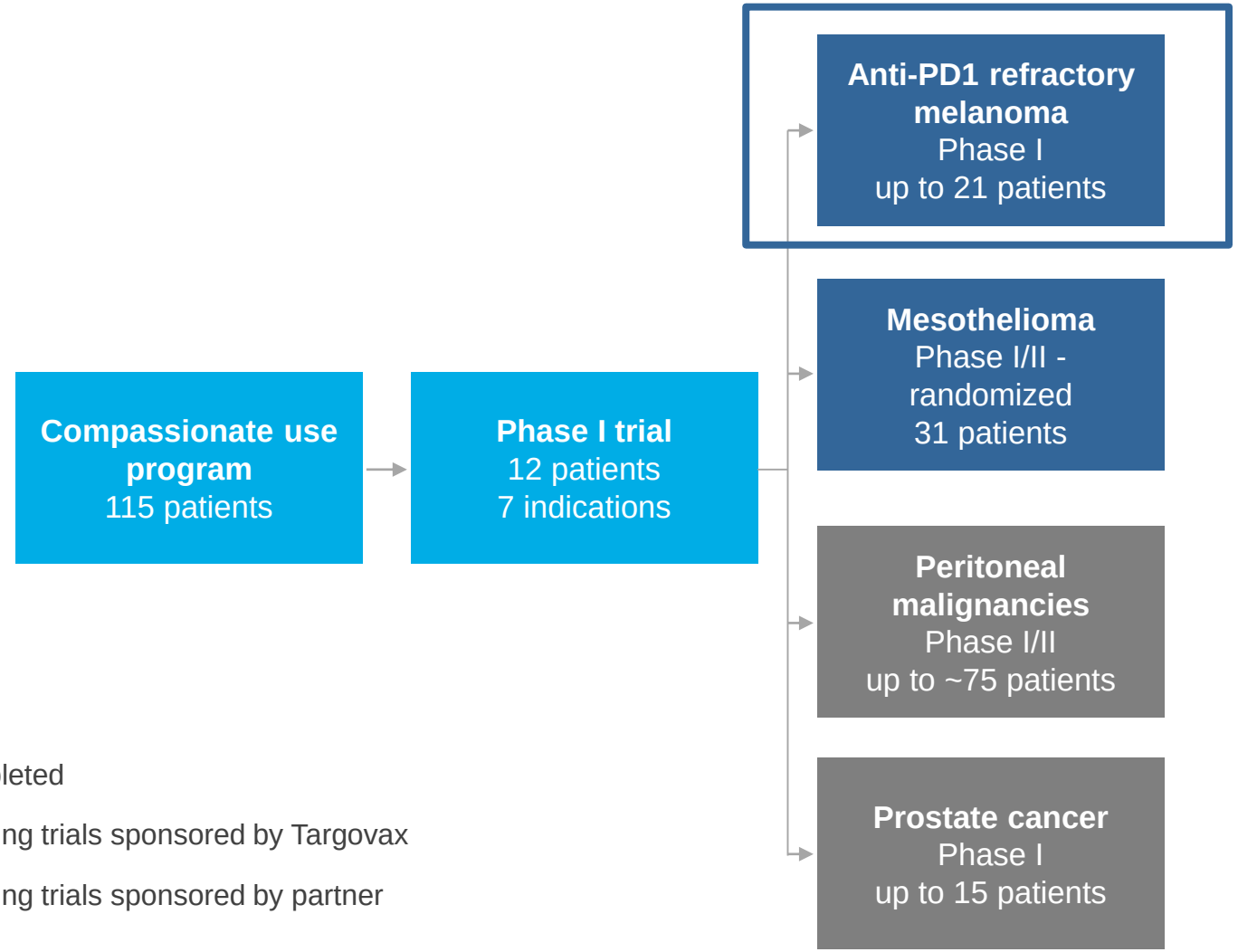
ONCOS-102 CLINICAL DEVELOPMENT PROGRAM



- Completed
- Ongoing trials sponsored by Targovax
- Ongoing trials sponsored by partner

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ONCOS-102 melanoma part 1 summary (n=9)

33% ORR AND ROBUST IMMUNE ACTIVATION

Patient population

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

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**

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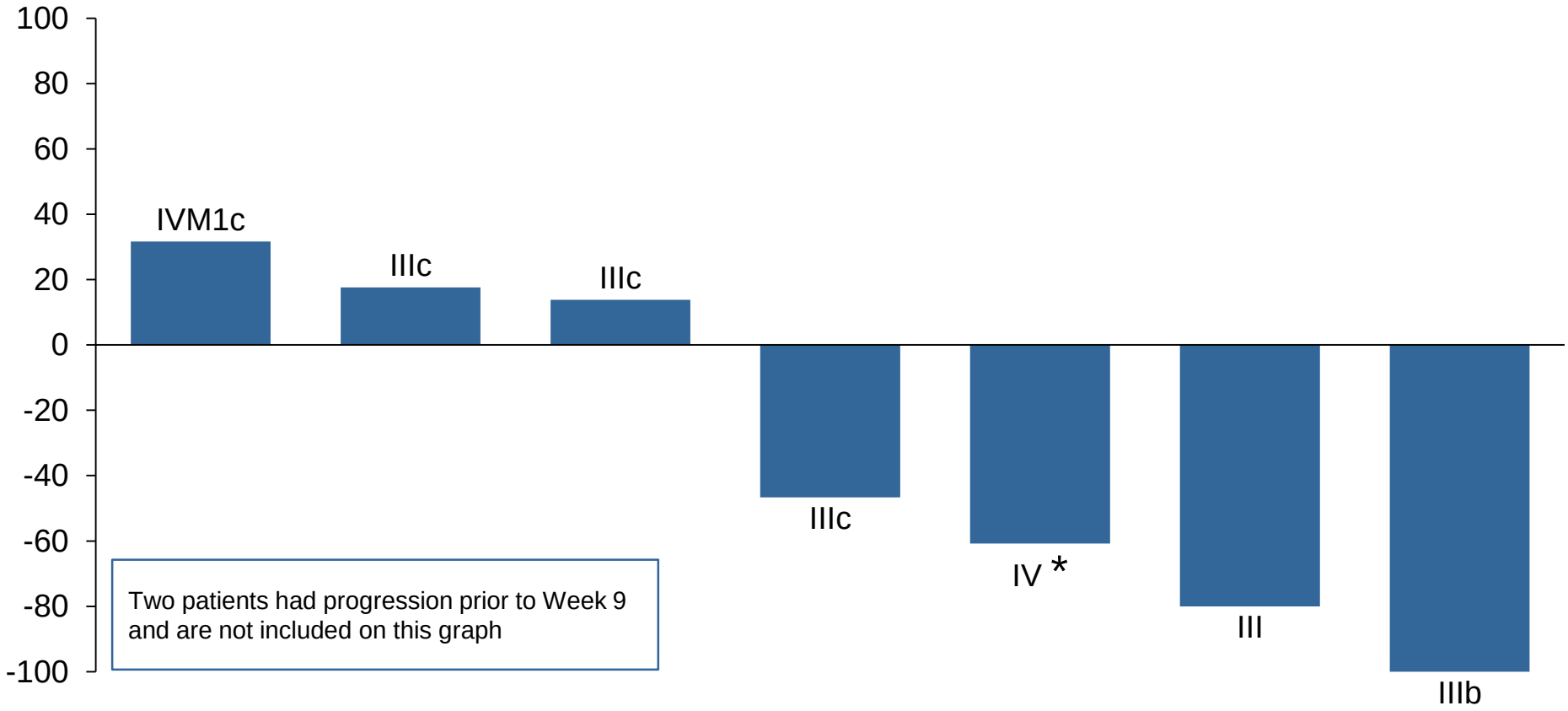
ONCOS-102 anti-PD1 refractory melanoma

BEST PERCENTAGE CHANGE IN TUMOR BURDEN OF TARGET LESIONS



n=9
Letters and numbers indicating disease stage
Preliminary data

* Unconfirmed tumor measurement

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COMPLETE RESPONSE IN ONE OF NINE PATIENTS

following ONCOS-102 and Keytruda combination treatment

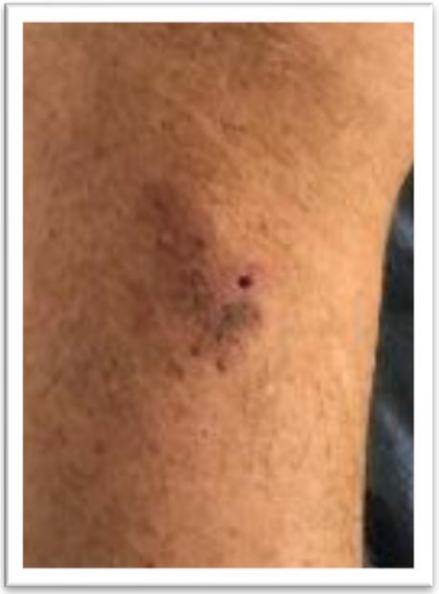
Stage IIIb (T4a, N2b, M0)

Prior therapies: Surgery x 3 Yervoy, Tafinlar + Mekinist, Keytruda

Baseline

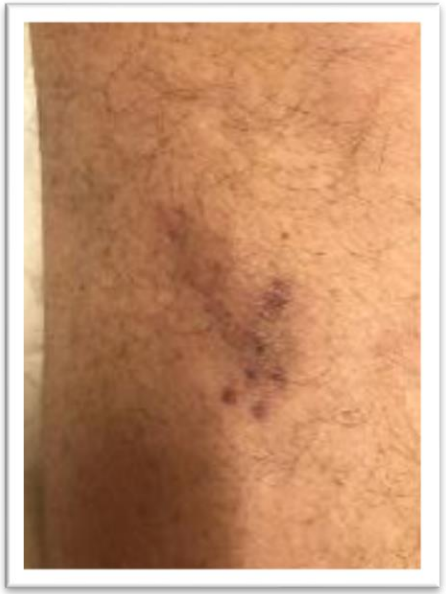
Progression on Keytruda

Week 3



Visible tumor regression after 3x ONCOS-102 injections

Week 9



Complete response after 3x ONCOS-102 injections & 2x Keytruda infusions

Immune data

Baseline (BL)	Week 3 (from BL)	Week 9 (from BL)
CD8+ TILs: Low	16x	7x
Activated CD8+: Low	5x	2x
PD1 CD8+ TILs: Low	20x	2x
MAGE-A1: Detectable	2x	3x

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BROAD AND ROBUST IMMUNE ACTIVATION

Innate immune activation

- Pro-inflammatory cytokine increase: IL-6 (8/8 pts), TNFa (7/8 pts)
- Fever/chills (7/9 pts)

Adaptive immune activation

T-cell infiltration

- CD8+ T-cells in treated lesions (8/9 pts)
- Activated CD8+ T-cells in treated lesions (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

Systemic T-cells

- Increase in systemic IFNg expression (8/8 pts)
- Systemic increase of the relative level of cytotoxic CD8+ and PD1+ CD8+ T-cells (9/9 pts)

Tumor specific activation

- Increase in tumor specific T-cells against NY-ESO-1 and/or MAGE-A1 (4/9 pts)
- Increasing levels of tumor specific T-cells throughout the treatment (4/4 pts)
- PD-L1 expression on tumor cells increased in 6/9 pts
- Melanoma specific cancer marker reduced in 2 of 3 responders

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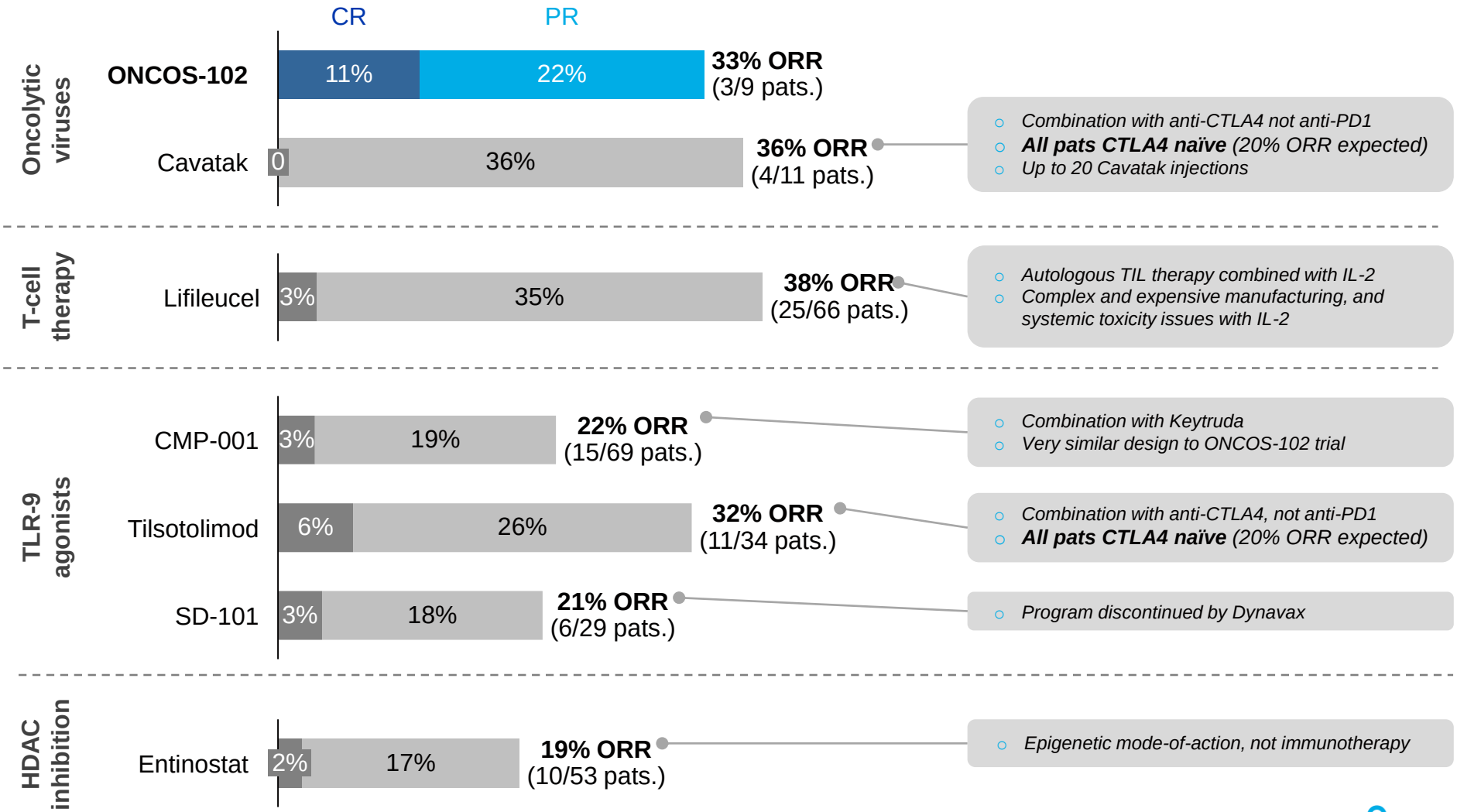
ONCOS-102 + KEYTRUDA DATA IN CONTEXT

Anti-PD1 refractory melanoma benchmark data



SOURCE: Targovax market analysis, August 2019

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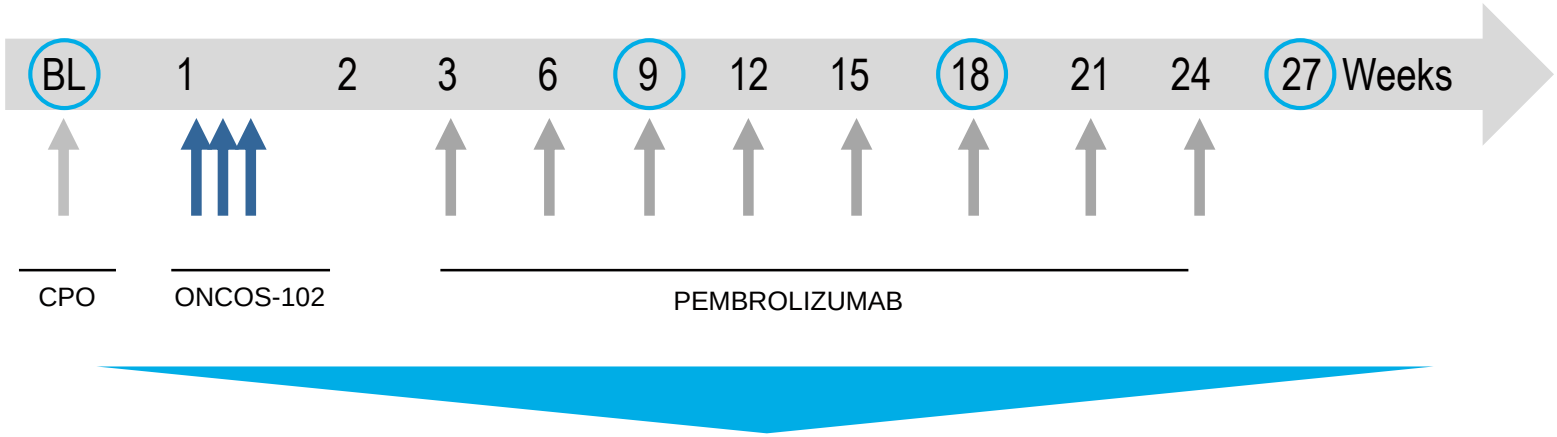
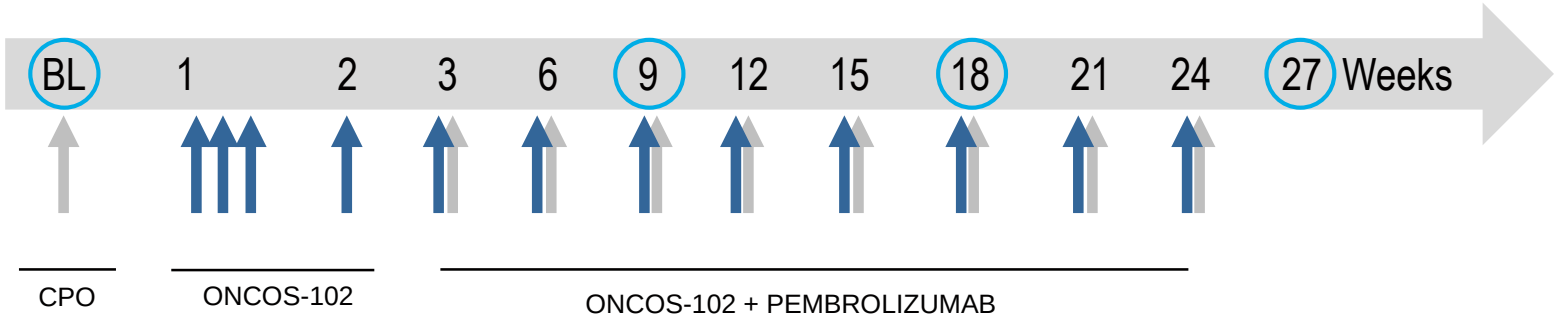
MELANOMA PART 2 IS RECRUITING

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

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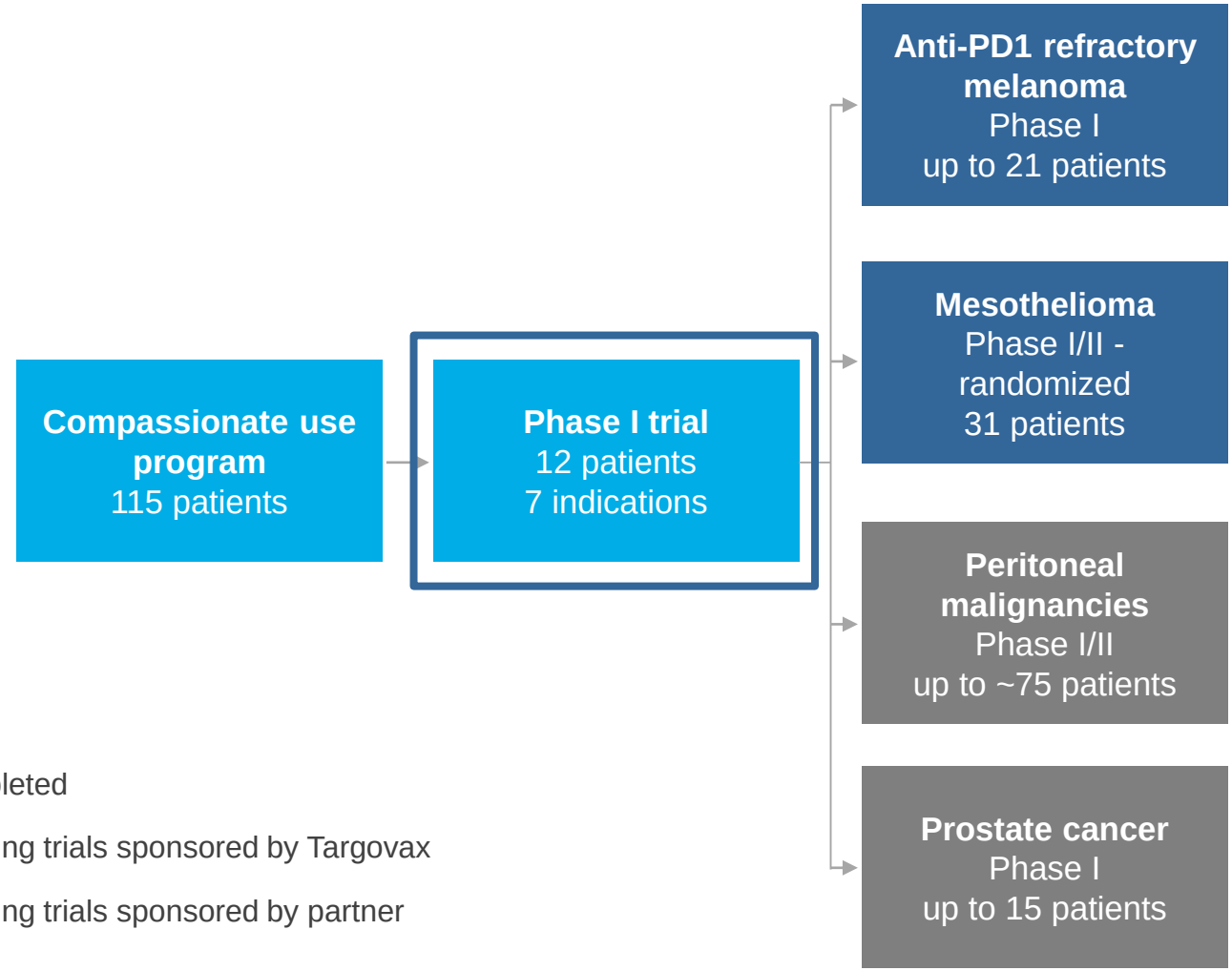
ONCOS-102 CLINICAL DEVELOPMENT PROGRAM



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ONCOS-102
Phase I single agent proof-of-concept

IMMUNE ACTIVATION DEMONSTRATED

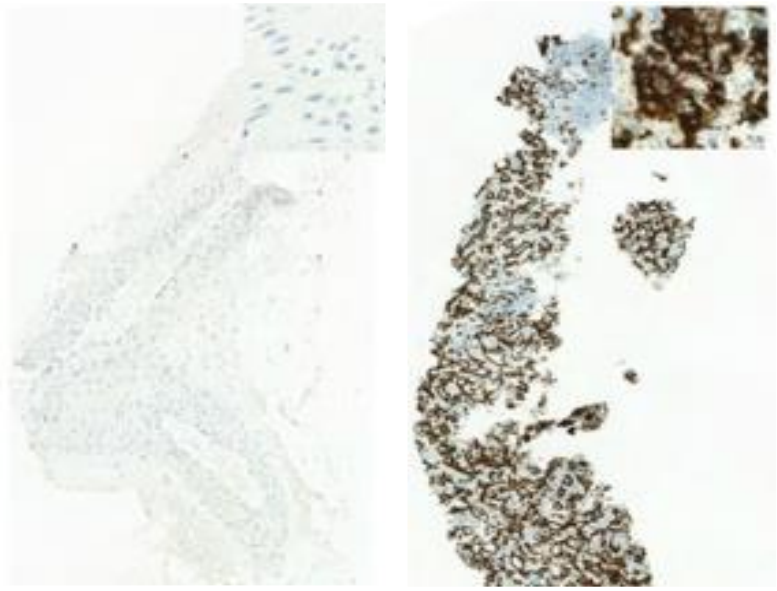
ONCOS-102 Phase I trial design:

- **12 patients**, 7 different solid tumors
- All **refractory to multiple lines** of therapy
- Treatment: **ONCOS-102 monotherapy**
  - 9 injections over 5 months

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

Cold tumor turned hot, CD8+ T-cell staining



Pre-treatment
Baseline

Post-treatment
Week 8

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

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ONCOS-102 MONOTHERAPY IN MESOTHELIOMA

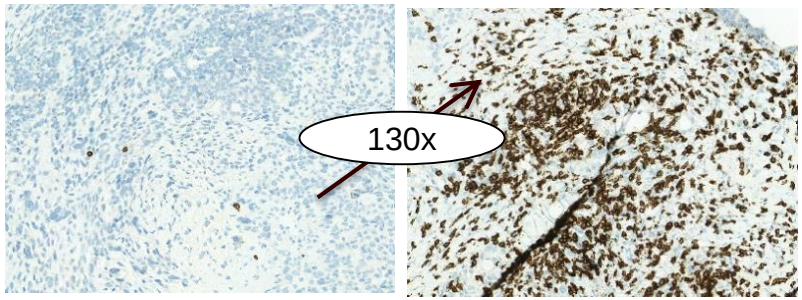
turning cold tumors hot

CD8+ T-cells in tumor
Tumor biopsy staining

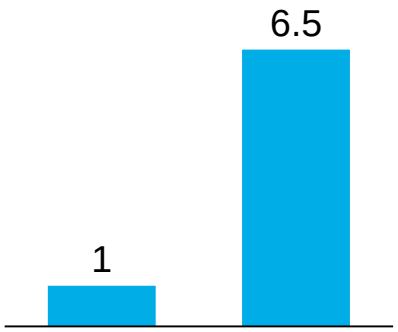
CD4+ T-cells in tumor
Fold change

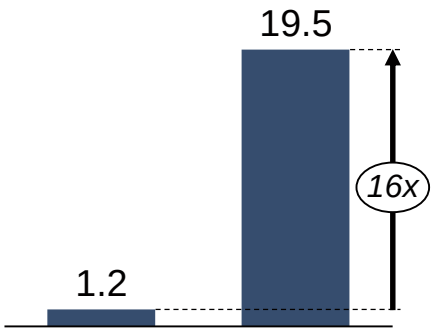
PD-L1 positive tumor cells
% of total

***Mesothelioma** – Phase I, patient 14*

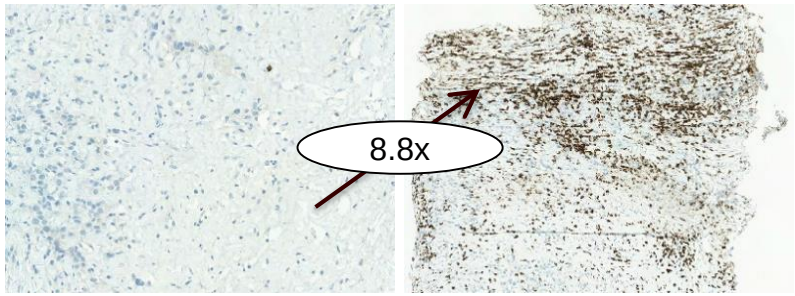


Baseline Week 5

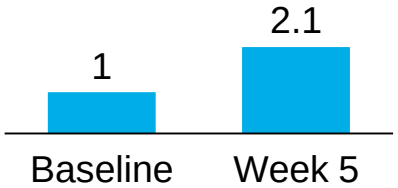


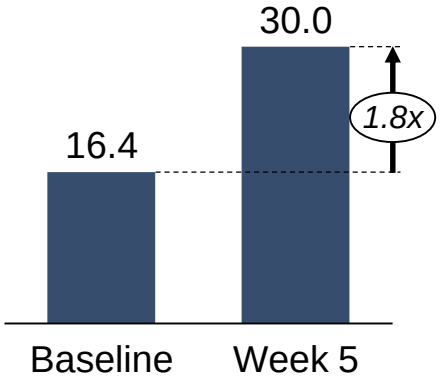


***Mesothelioma** – Phase I, patient 9*



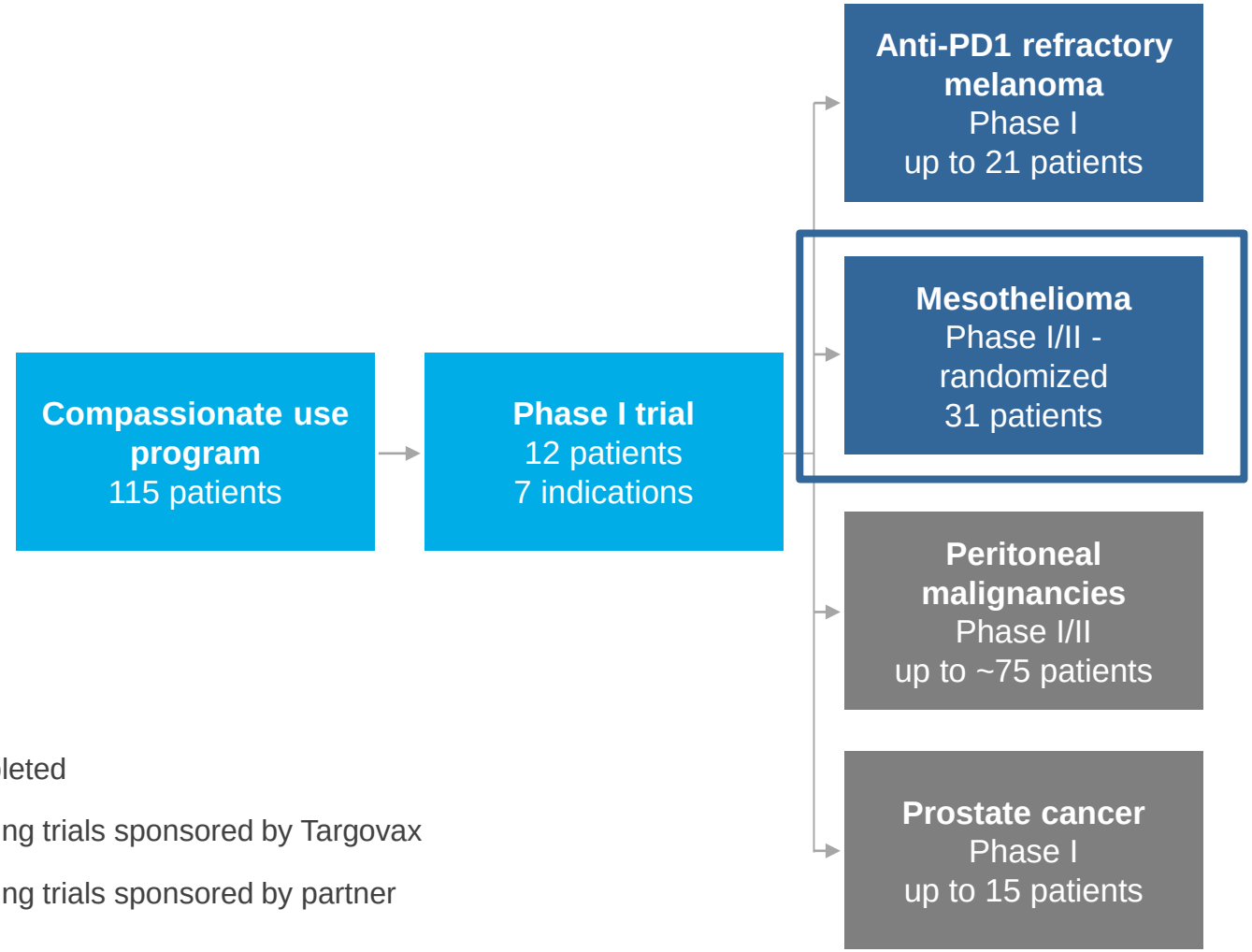
Baseline Week 5





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

ONCOS-102 CLINICAL DEVELOPMENT PROGRAM



- Completed
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MESOTHELIOMA IS THE SHORTEST PATH-TO-MARKET

Rationale for ONCOS-102 go-to-market strategy in mesothelioma:

Become frontline therapy

- **Preclinical data and phase I results**
- **Ongoing randomized phase I/II trial**
- **Good safety profile**

Orphan Drug Designation

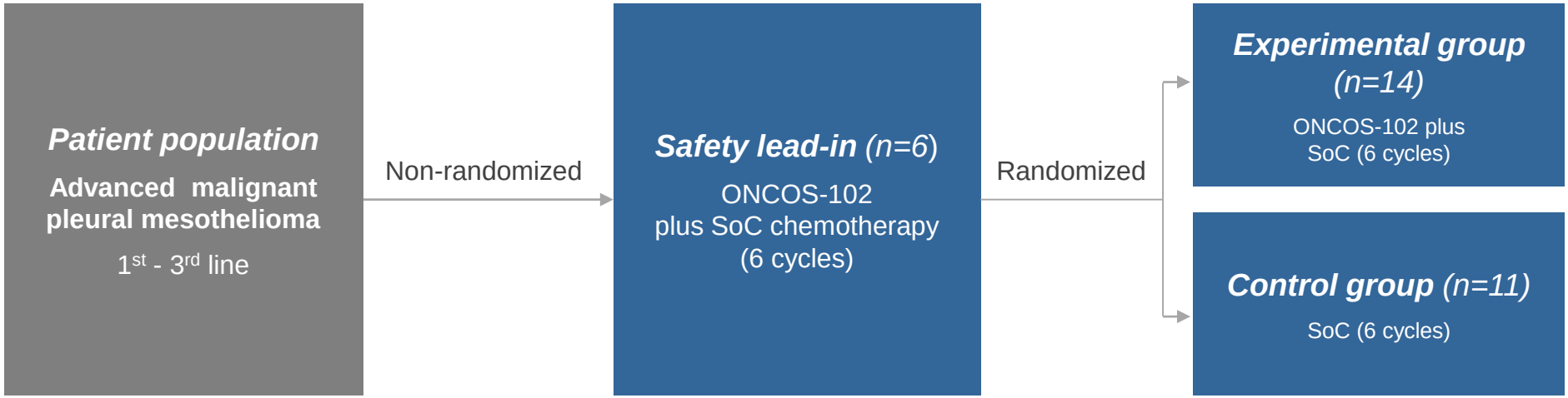
- High unmet medical need
- 7 year **market exclusivity** in the US and 10 years in the EU
- Opportunity for priority regulatory review, and **quick route-to-market**

Limited competition

- CPIs are **potential ONCOS-102 combinations**, rather than competitors
- **No competing viruses** and few other options in current clinical development

ONCOS-102 in malignant pleural mesothelioma

PHASE I/II STUDY DESIGN IN COMBINATION WITH SoC



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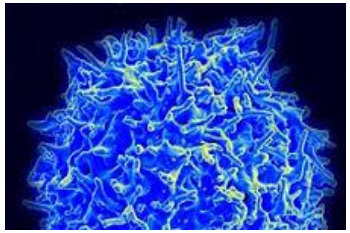
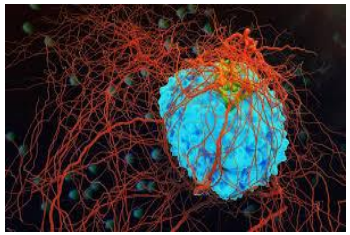
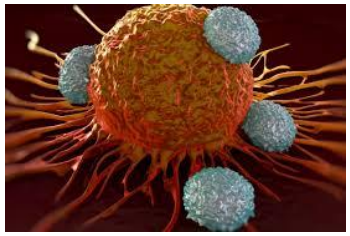
NEXT GENERATION ONCOS VIRUSES HAVE DOUBLE TRANSGENES AND DISTINCT MODE OF ACTIONS

	Target tumors	Development status
 **ONCOS-211** *Counteract immune-suppressive tumor microenvironment*	○ "Cold" immune suppressive tumors	○ *In vitro* testing completed ○ *In vivo* testing ongoing
 **ONCOS-212** *Inhibition of tumor growth and vascularization*	○ Highly invasive or metabolic tumors	○ *In vitro* testing completed ○ First *in vivo* testing completed
 **ONCOS-214** *Enhanced cell killing properties*	○ Rapidly growing or large size tumors	○ *In vitro* testing completed ○ *In vivo* testing ongoing

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SUFFICIENTLY FUNDED TO ADVANCE CLINICAL PROGRAM BEYOND VALUE INFLECTION POINTS

The company

Cash end of 2Q

135 / 15

NOK million **USD million**

Annual run rate - last four quarters

132 / 14

NOK million **USD million**

Analyst coverage

DNB, ABG Sundal Collier, Arctic, Redeye, HC Wainwright, Edison

The shareholders

	Estimated ownership	
Shareholder	**Shares, million**	**Ownership**
HealthCap	12,4	19,6 %
RadForsk	4,4	7,0 %
Nordea	3,6	5,6 %
KLP	1,5	2,4 %
Thorendahl Invest	1,4	2,2 %
Danske Bank (nom.)	0,9	1,4 %
Prieta	0,7	1,1 %
Timmuno	0,7	1,1 %
J.P. Morgan Bank	0,7	1,1 %
Sundt	0,7	1,0 %
10 largest shareholders	**26.8**	**42.3 %**
Other shareholders (4 341)	36.6	57.7%
Total shareholders	**63.4**	**100.0 %**

targovax

ACTIVATING THE PATIENT'S IMMUNE SYSTEM

Clinically proven

One of the furthest developed oncolytic viruses

Strong single agent data

Encouraging data in anti-PD1 refractory melanoma

Rich news flow

Four ongoing trials

Several upcoming data points

Innovative pipeline

Next generation oncolytic viruses in pre-clinical testing