# Activating the patient's immune system to fight cancer

2Q 2019

22 August 2019

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# 1

# Intro & Highlights

2. Melanoma data
3. Financials



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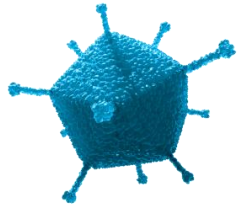
Targovax focus

# ONCOS ONCOLYTIC VIRUS

## Adenovirus Serotype 5



- Genetically engineered to **selectively infect cancer cells**
- Turns cold **tumors hot**

- One of the **furthest developed** oncolytic viruses
- Strong **single agent and combination data**
- **Four ongoing** clinical trials

- **Combination** with both **checkpoint inhibitors** and **chemotherapy**
- **Rich news flow** over the next 6-12 months

*Activates the immune system*

*Triggers patient-specific immune responses*

*No need for individualization*



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# 1H 2019 HIGHLIGHTS

**R&D**

- Treated the first patient in the dose expansion cohort in **melanoma** trial
- Completed enrollment of ONCOS-102 trial in **mesothelioma**
- Finalized first development stage for **new viruses**, filed patents on three viruses
- Published in vivo demonstration of abscopal effect of ONCOS-102 and Keytruda combination in the Journal of Medical Virology

**Post-period**

- Validated clinical responses in three out of nine patients (33% ORR) and immune activation in all nine patients in part 1 of **melanoma** trial
- Completed dose escalation part of **peritoneal malignancies** trial in combo with CPI Imfinizi. The expansion part opened for patient enrollment

**Corporate**

- Raised NOK 74m in a private placement, with a subsequent repair issue
- Made a strategic decision to **fully focus** the company's resources and efforts on the ONCOS program



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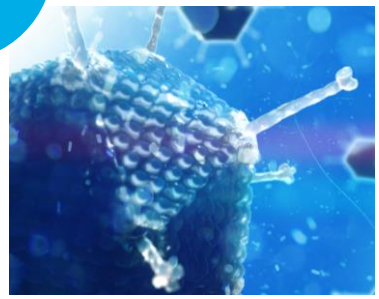
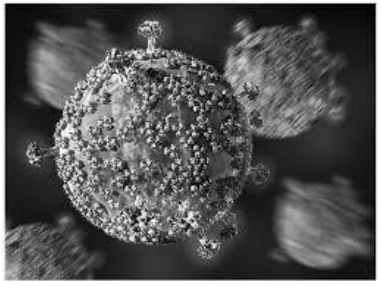
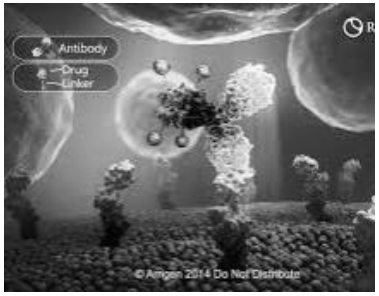
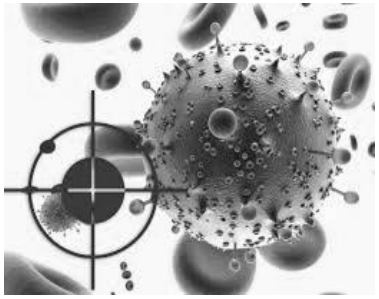
# ONCOLYTIC VIRUSES IN THE FUTURE CANCER THERAPY LANDSCAPE

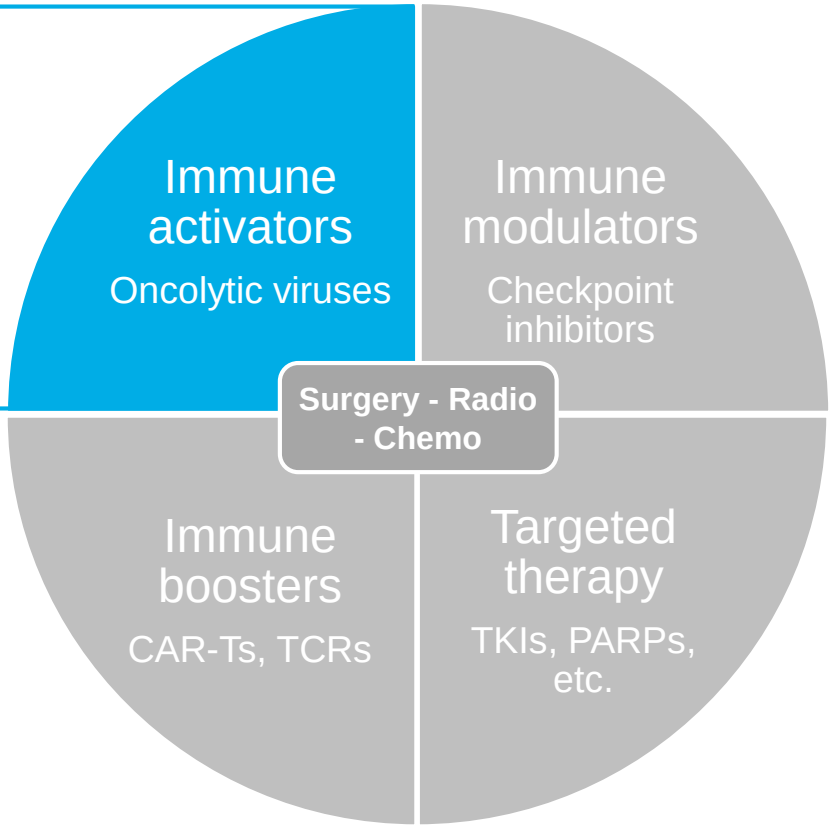
**Targovax focus**









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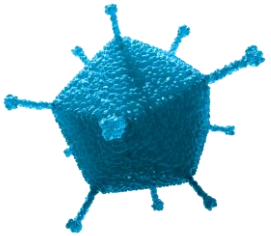
# BENEFITS OF ONCOS-102 ADENOVIRUS

*Triggers patient-specific immune responses*



**Highly immunogenic**, TLR-9 agonist, turning cold tumors hot


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

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

# 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<br>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 non-systemic IV | 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, IT only | Phase II |
| NCOLYTICS 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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- One of the furthest developed oncolytic viruses
- Strong single agent data
- Encouraging ORR in anti-PD1 refractory melanoma

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



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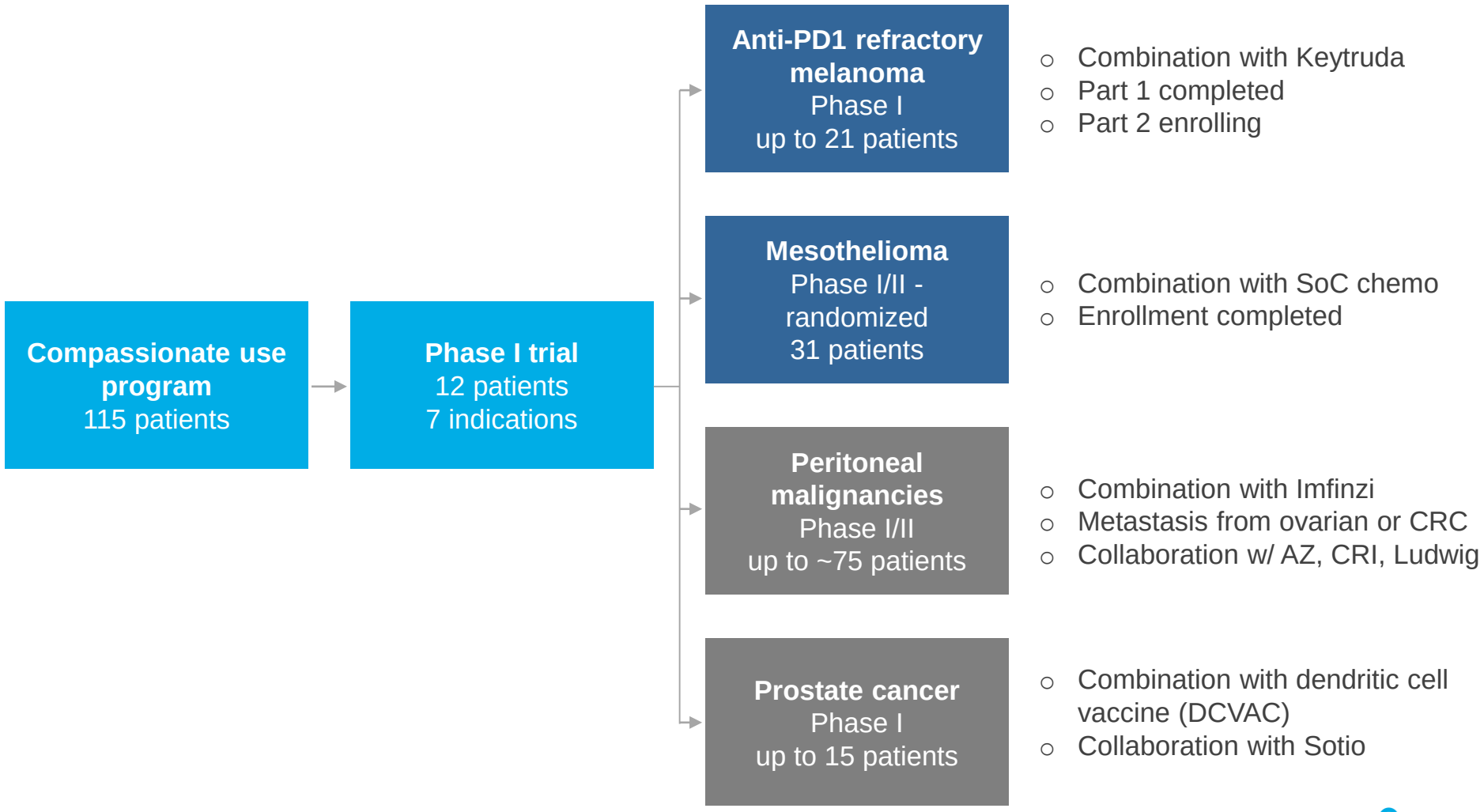
# THERE HAS BEEN A NUMBER OF TRANSACTIONS IN THE OV SPACE IN 2018-2019

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

# ONGOING ONCOS-102 PHASE I IN MELANOMA



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# 2

# Melanoma data

3. 2Q 2019 Financials

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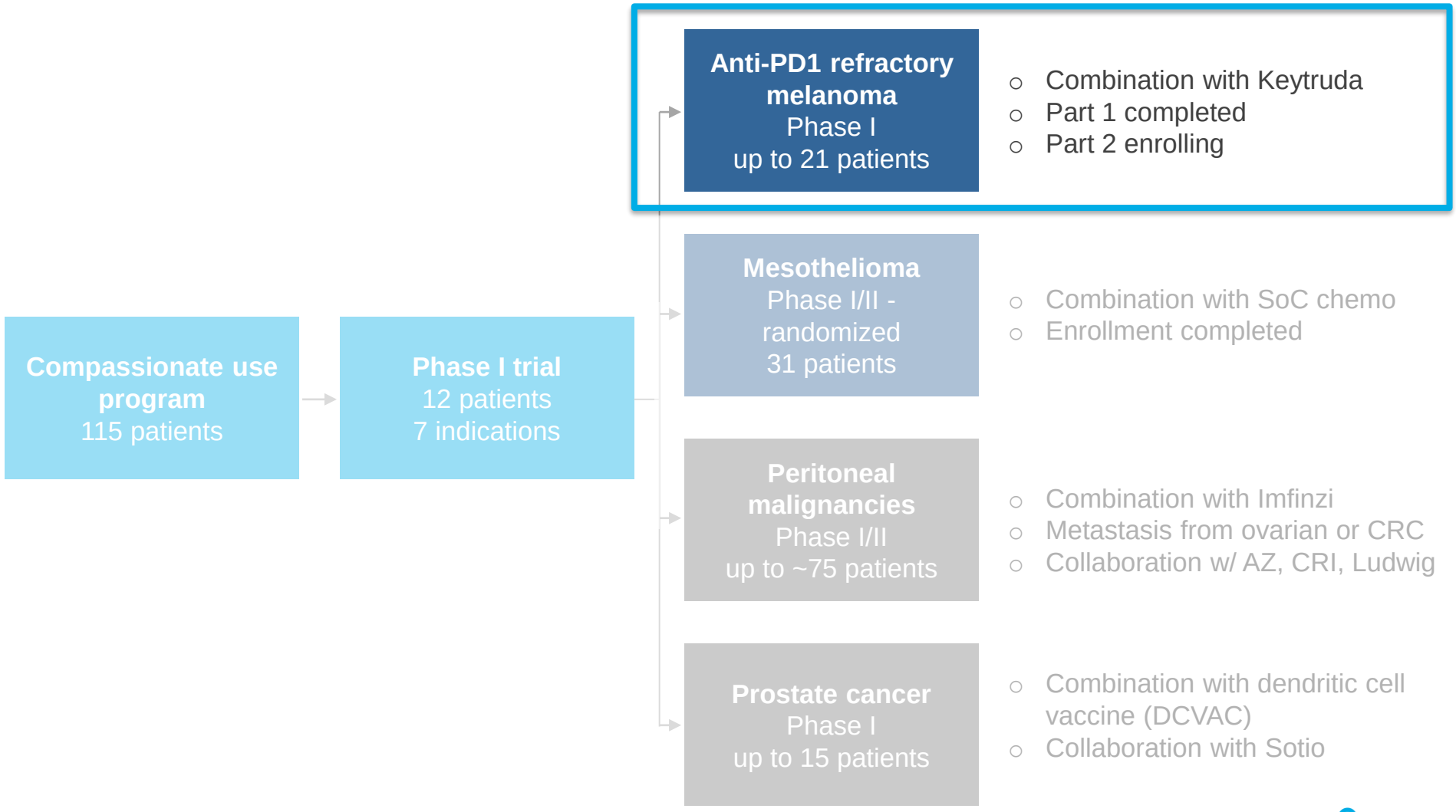
# ONGOING ONCOS-102 PHASE I IN MELANOMA



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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)**
- Poor prognosis, with **few treatment alternatives**

**Treatment regime**

- **3 ONCOS-102 injections** followed by 6 months of Keytruda (8-9 cycles)

**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**
  - Systemic increases i pro-inflammatory cytokines (9/9 patients)
  - Increased infiltration of CD8+ T-cells in tumor (8/9 patients)
  - T-cell infiltration into non-injected lesions (2/3 patients)
  - Generation of systemic tumor specific T-cells (4/9 patients)

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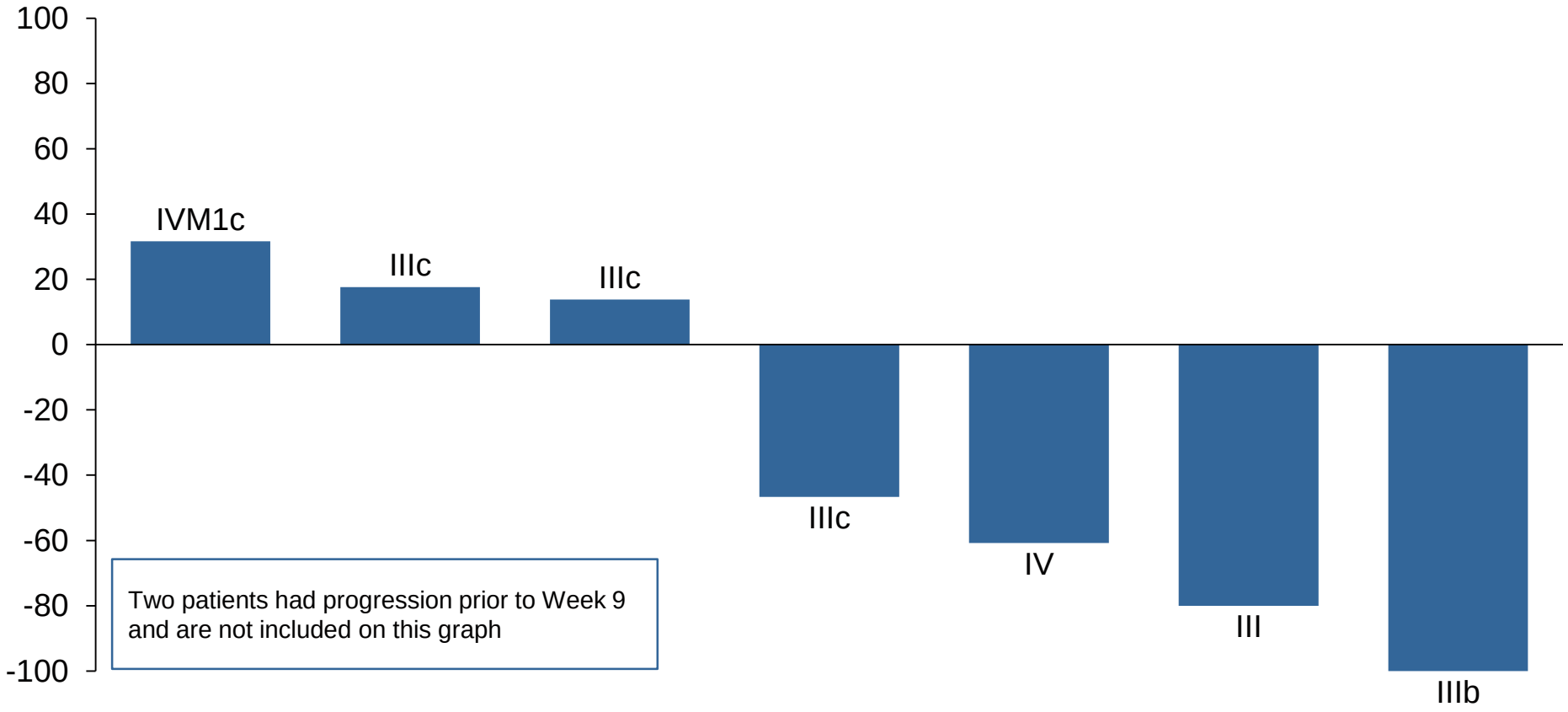
ONCOS-102 anti-PD1 refractory melanoma

# BEST PERCENTAGE CHANGE IN TUMOR BURDEN OF TARGET LESIONS




N=9
Letters and numbers indicating disease stage
Preliminary data

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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 | Week 3 | Week 9 |
|---|---|---|
|  |  |  |
| *Progression on Keytruda* | *Visible tumor regression after 3x ONCOS-102 injections* | *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**

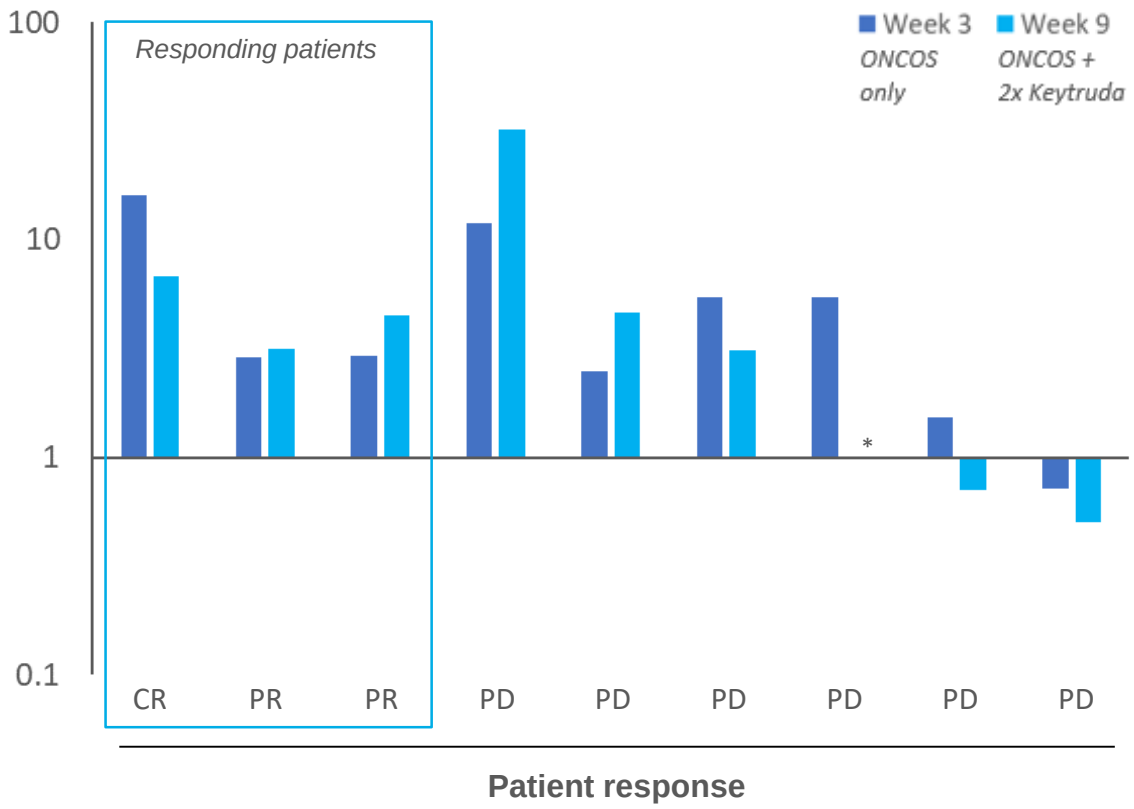
- Increase in systemic IFNg expression (8/8 pts)
- Systemic increase of the relative level of cytotoxic CD8+ and PD1+ CD8+ T-cells (9/9 pts)

**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

# POTENT INCREASE IN CD8+ T-CELL TUMOR INFILTRATION OBSERVED IN MOST PATIENTS

**CD8+ T-cell tumor infiltration**, -fold change from baseline




Unpublished company data
- Week 9 analysis not available

PD: Progressive disease



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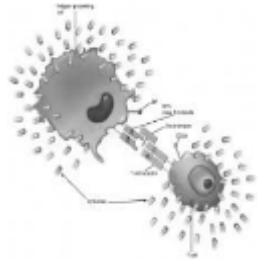
# ONCOS-102 + KEYTRUDA MELANOMA TRIAL

## 1
### Safety

- ✓ **Safety reviews completed with no concerns**
- ✓ ONCOS-102 and Keytruda combination is well-tolerated

## 2
### Innate immune activation

- ✓ **Systemic increase of pro-inflam-matory cytokines** (IFNg, TNFa, ++ 9/9 patients)
- ✓ Most patients develop fever /chills as a clinical sign



## 3
### Adaptive immune activation

- ✓ **Increased CD8+ T-cell infiltration** in 8/9 patients
- ✓ **Tumor-specific T cells** in 4/9 patients
- ✓ **Activation in non-injected lesions**

## 4
### Clinical efficacy

- ✓ **ORR 33%** in nine patients with one CR (very rare)
- ✓ **Best clinical response (CR) had the strongest immune response**



Preliminary data.

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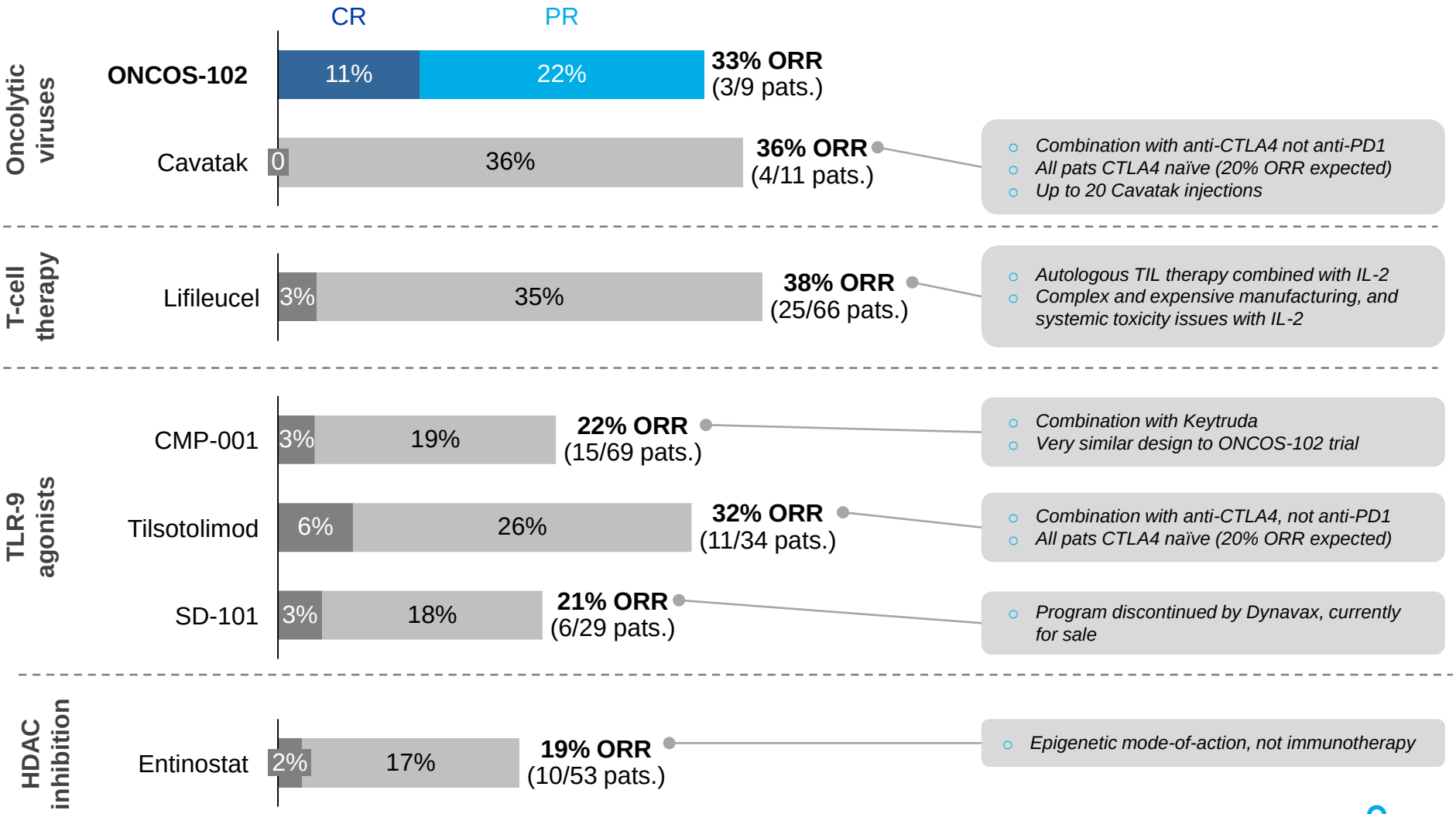
# ONCOS-102 + KEYTRUDA DATA IN CONTEXT

## Anti-PD1 refractory melanoma benchmark data

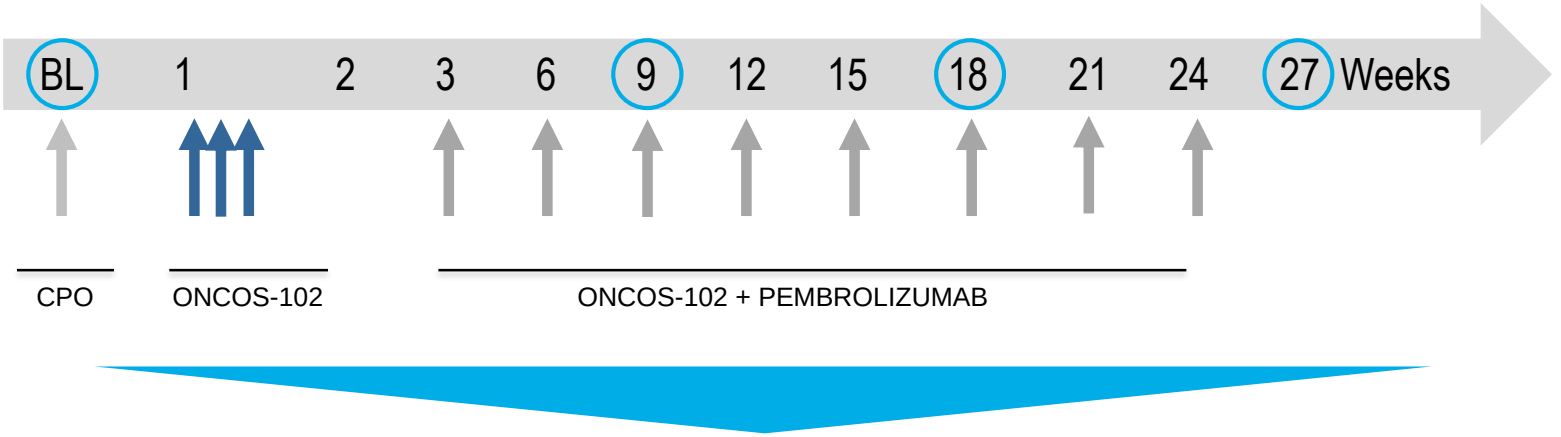



SOURCE: Targovax market analysis, August 2019

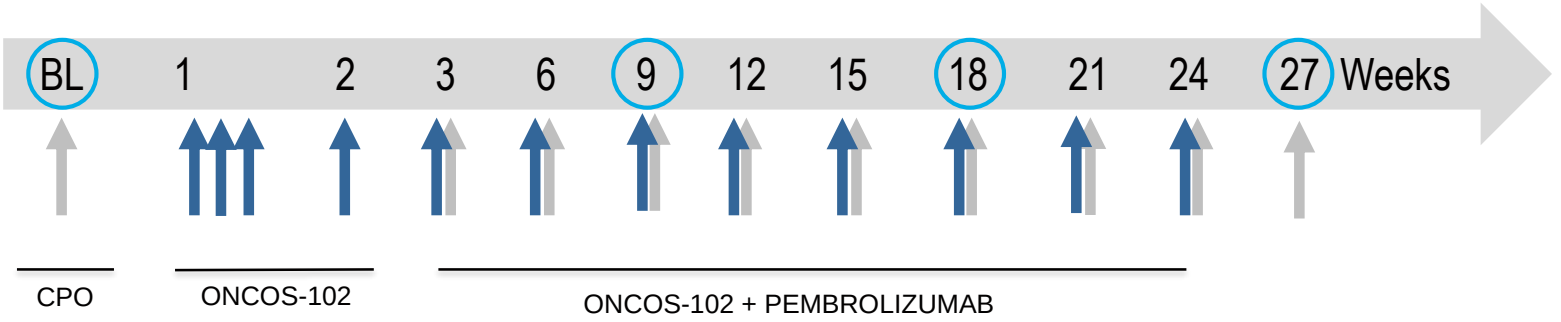
# MELANOMA PART 2 IS RECRUITING

up to 12 patients: 12 ONCOS-102 injections combined with 6 months Keytruda

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




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




○ *Imaging*

*CPO: Cyclophosphamide*



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# 3 Financials

# PROFIT AND LOSS

| NOK m | 2Q18 | 3Q18 | 4Q18 | 1Q19 | 2Q19 |
|---|---|---|---|---|---|
| **Total revenue** | **0** | **0** | **0** | **0** | |
| External R&D expenses | -14 | -17 | -21 | -19 | -22 |
| Payroll and related expenses | -15 | -12 | -14 | -14 | -18 |
| Other operating expenses | -7 | -5 | -7 | -7 | -5 |
| **Total operating expenses** | **-37** | **-34** | **-42** | **-40** | **-45** |
| Operating loss | -37 | -34 | -42 | -40 | -45 |
| Net financial items | -0 | -1 | 1 | -1 | -1 |
| Loss before income tax | -37 | -35 | -41 | -41 | -46 |
| Net change in cash | -28 | -27 | -22 | -46 | 30 |
| **Net cash EOP** | **201** | **173** | **151** | **105** | **135** |



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# TARGOVAX FINANCIAL POSITION

## Operations

Cash end of 2Q

**135 / 15**

**NOK million** **USD million**

Net cash flow - total 2Q

**30 / 3**

**NOK million** **USD million**

Annual run rate - last four quarters

**132 / 13**

**NOK million** **USD million**

## The share

Market Cap - at share price NOK ~5

**317 / 35**

**NOK million** **USD million**

Daily turnover - rolling 6 month avg.

**2.9 / 0.3 / 0.9%**

**NOK million** **USD million**

Analyst coverage

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



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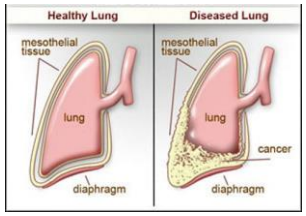
# ONCOS DEVELOPMENT STRATEGY

## 1

**Path-to-market**
Orphan indication

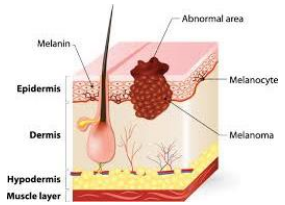



### Target launch indication

- **Mesothelioma**
- Orphan drug status
- Combo with SoC chemo
- Randomized phase II, 31 patients
- Enrollment completed

## 2

**Proof-of-concept**
Re-activating CPIs




### CPI refractory cancers

- **PD1 refractory melanoma**
- Combo with Keytruda
- Phase I, ~20 patients
- First 9 patients completed
- Second cohort initiated

## 3

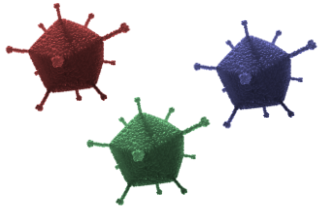
**Proof-of-concept**
New CPI indication

### Indications with no/ limited effect of CPIs

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

## 4

**Next generation**
oncolytic viruses



### Platform expansion with new targets

- 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**<br>Combination w/ pemetrexed/cisplatin | | | | **New year 2019-20**<br>Randomized data |
| | **Melanoma**<br>Combination w/Keytruda | | | | **1H 2020**<br>Part 2 data |
| | **Peritoneal metastasis**<br>Collaborators: Ludwig, CRI & AZ<br>Combination w/Imfinzi | | | | *Update by collaborator* |
| | **Prostate**<br>Collaborator: Sotio<br>Combination w/DCvac | | | | *Update by collaborator* |
| Next-gen ONCOS | **3 new viruses**<br>Double transgene | | | | **2H 2019**<br>First pre-clinical data |



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26

# 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 combination trials

Several upcoming data points next six to twelve months

## Innovative pipeline

Next generation oncolytic viruses in pre-clinical testing