# ACTIVATING THE PATIENT'S IMMUNE SYSTEM TO FIGHT CANCER

Company presentation

February 2021

OSE:
TRVX

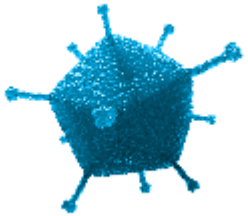
targovax

# IMPORTANT NOTICE AND DISCLAIMER

This report contains certain forward-looking statements based on uncertainty, since they relate to events and depend on circumstances that will occur in future and which, by their nature, will have an impact on the results of operations and the financial condition of Targovax. Such forward-looking statements reflect the current views of Targovax and are based on the information currently available to the company. Targovax cannot give any assurance as to the correctness of such statements.

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.

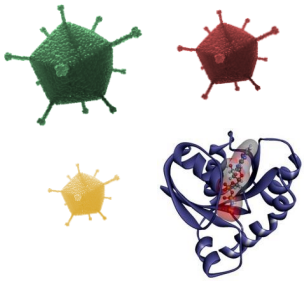
# TARGOVAX AT A GLANCE



**ONCOS-102**

**Lead product candidate**

- Class-leading data in monotherapy and combinations with chemo and aPD-1
- Powerful immune activation
- Ideal combination partner to aPD-1
- Path to market



**Pipeline**

- Novel virus approaches
- Novel payloads and modes of action
- Mutant RAS cancer vaccine concepts

**Vision:**
*Unlock greater clinical benefits in cancer patients by deploying multifunctional platforms to target key immune regulators and oncogenic drivers*



targovax

# HIGH AND GROWING MEDICAL NEED FOR IMMUNE ACTIVATORS

***CPIs are revolutionizing cancer therapy…***

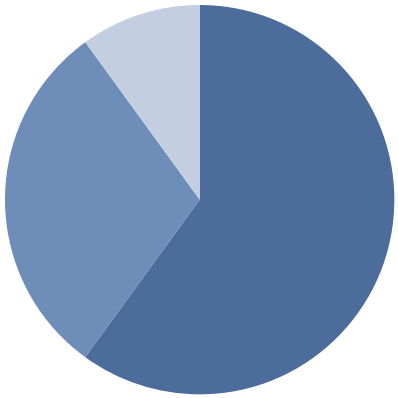
$25bn

**Global CPI market**

44%

**Patients eligible for CPI[2]:**

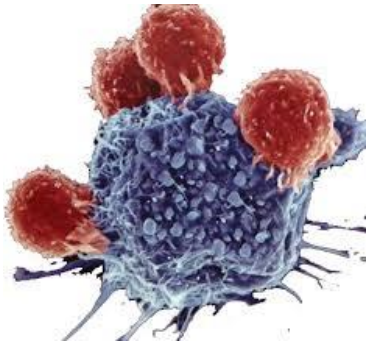
***…but most patients do not respond…***



60 - 90%

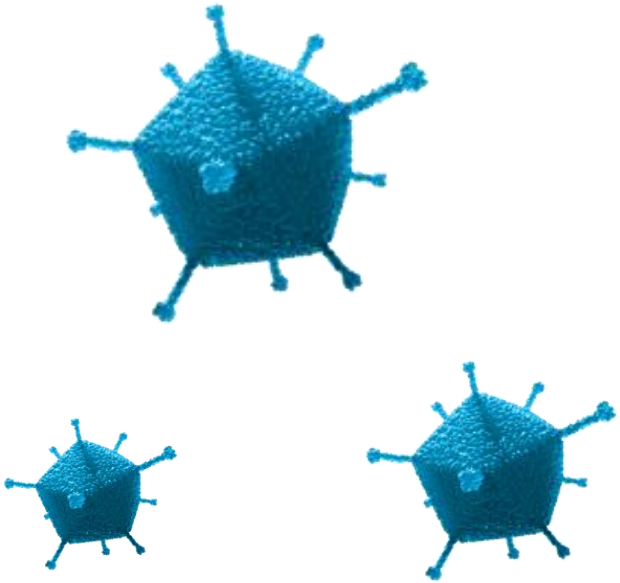
**Non-responders**

***…leading to a high medical need for immune activators***



1 Immune Checkpoint Inhibitors Markets Report, 2020 January, ResearchAndMarkets.com, Roth Capital Analyst Report
2 Estimation of the Percentage of U.S. 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.

# THE SOLUTION:
# ONCOS-102 IMMUNE ACTIVATION



**Activates** the body´s own T-cells against the cancer

**Unblinds** the tumor to the immune system

**Reverses** immunosuppresive defense mechanisms in the tumor

# ONCOS-102 IS AN ONCOLYTIC ADENOVIRUS SEROTYPE 5 ARMED WITH AN IMMUNE ACTIVATING TRANSGENE

**1**

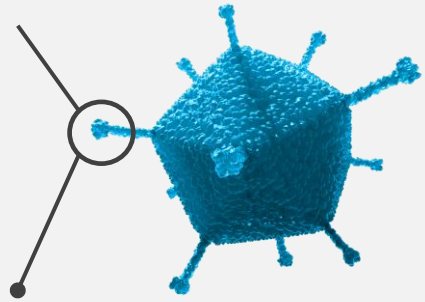
**Selective replication** in cancer cells

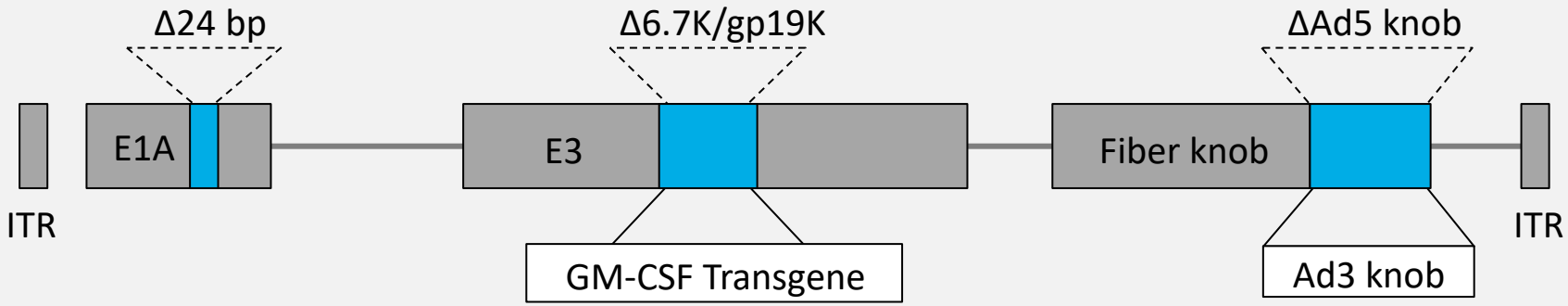
**2**

**Boosting** the **immune activation**

**3**

**Enhanced infection** of cancer cells








targovax

# EARLY-STAGE DEVELOPMENT SUCCESSFULLY COMPLETED – ENTERING LATE-STAGE DEVELOPMENT

**Early-stage development**

- ✓ Clinical data
- ✓ Immune activation
- ✓ Safety profile

**Late-stage development**

PD-1 refractory melanoma

**Expansion opportunities**

- Mesothelioma
- Colorectal cancer
- Other indications
- Other IO combinations
- Platform development



targovax

# CLINICAL AND PRECLINICAL PIPELINE

| Product candidate | Preclinical | Phase 1 | Phase 2 | Collaborator | Next expected event |
|---|---|---|---|---|---|
| ONCOS-102 | **Melanoma**<br>Combination w/anti PD1 | | | | **1H 2022**<br>First patient |
| | **Colorectal cancer**<br>Combination w/Imfinzi | | | AstraZeneca<br>CANCER RESEARCH INSTITUTE | *Updates by collaborator expected 1H22* |
| | **Mesothelioma**<br>Combination w/pemetrexed/cisplatin | | | MERCK | **1H 2021**<br>Survival update |
| ONCOS-200 series | **Next Gen viruses** | | | leidos<br>Papyrus | *Updates at conferences* |
| Novel mutRAS concepts | | | | VALO THERAPEUTICS<br>OBLIQUE THERAPEUTICS | |


All rights to ONCOS-102 retained

| Product candidate | Preclinical | Phase 1 | Phase 2 | Collaborator | Next expected event |
|---|---|---|---|---|---|
| **ONCOS-102** | **Melanoma**<br>Combination w/anti PD1 | | | | |
| | **Colorectal cancer**<br>Combination w/Imfinzi | | | | |
| | **Mesothelioma**<br>Combination w/pemetrexed/cisplatin | | | | |
| **ONCOS-200 series** | **Next Gen viruses** | | | | |
| **Novel mutRAS concepts** | | | | | |



targovax

ONCOS-102 ANTI-PD1 REFRACTORY MELANOMA

# 35% ORR AND SYSTEMIC EFFECT

**Patient population**

- Advanced, unresectable **melanoma**
- Disease **progression** despite prior treatment with anti-PD1
- Poor prognosis, with **few treatment alternatives**
- 20 patients, 11 stage III and 9 stage IV

**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**

- **35% ORR** by RECIST 1.1 and irRECIST
  - 1 Complete Response (CR)
  - 6 Partial Responses (PR)
- Multiple examples of **systemic effect**
- Robust systemic and local **immune activation**
- Well tolerated, no safety concerns

# PATIENT DEMOGRAPHICS – MORE ADVANCED DISEASE IN PART 2

| Parameters | Part 1 (n=8) | Part 2 (n=12) | Total (N=20) |
|---|---|---|---|
| Age (median) | 70.5y | 72y | 72y |
| Time from diagnosis to start of ONCOS-102 (median) | 6.9y | 2.9y | 4.5y |
| Number of treatments prior to study (average)<br>- Surgery (average)<br>- Treatments ex. surgery (average) | 5.3<br>2.1<br>3.1 | 5.9<br>1.9<br>3.9 | 5.6<br>2.0<br>3.6 |
| Time (months) from last anti-PD1 to study start (median) | 1.8m | 1.9m | 1.9m |
| Number of prior checkpoint treatment regimens (average) | 1.8 | 2.3 | 2.2 |
| Prior CTLA-4 treatment (number of patients, %) | 4 (50%) | 8 (67%) | 12 (60%) |
| Baseline number of lesions (median) | 4.0 | 8.5 | 7.0 |
| Baseline tumor burden RECIST1.1 (mm, median) | 37.5 | 73.5 | 55.0 |
| Tumor stage at enrollment<br>- Stage III<br>- Stage IV | <br>6<br>2 | <br>5<br>7 | <br>11<br>9 |

More advanced disease in Part 2

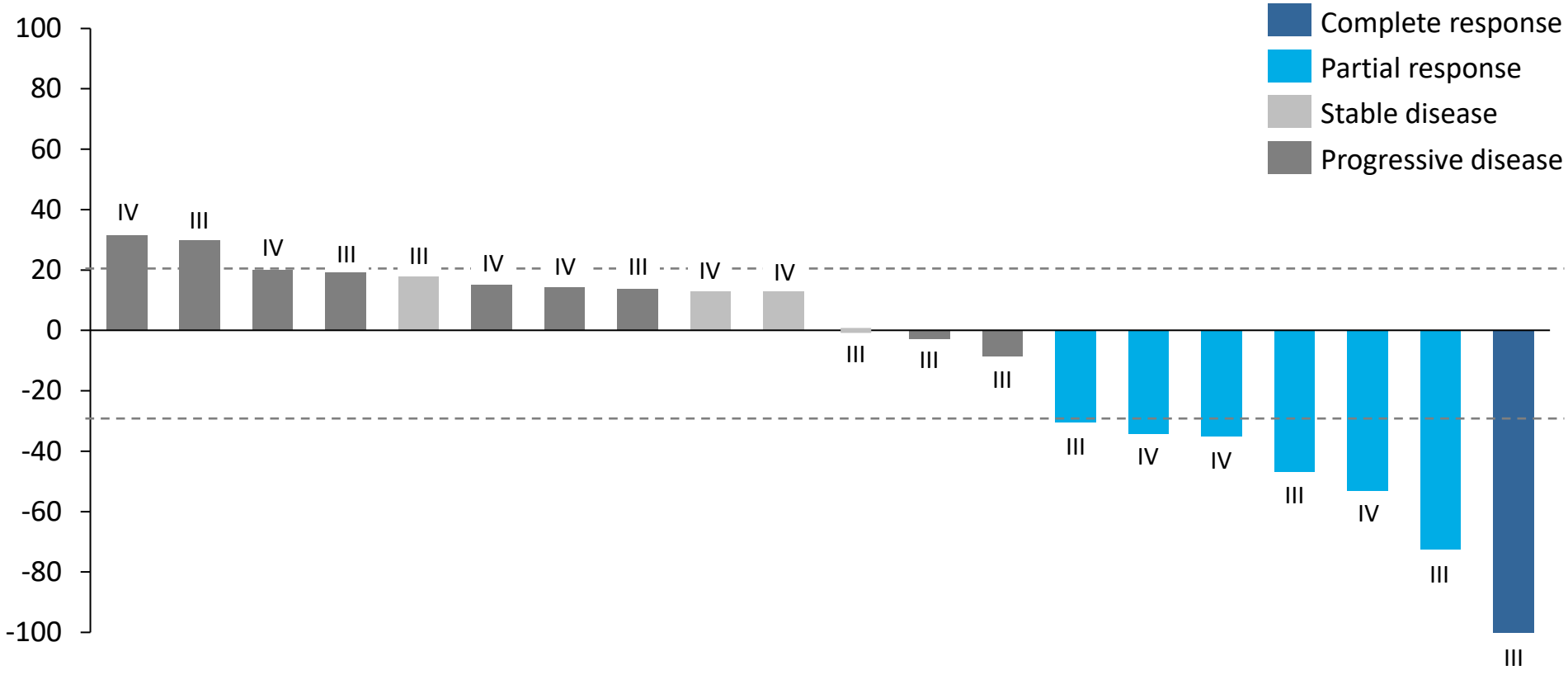
Preliminary data



targovax

# BEST-IN-CLASS RESPONSE RATE WITH ORR OF 35%

**Relative change (percent) in tumor burden from baseline to best response**

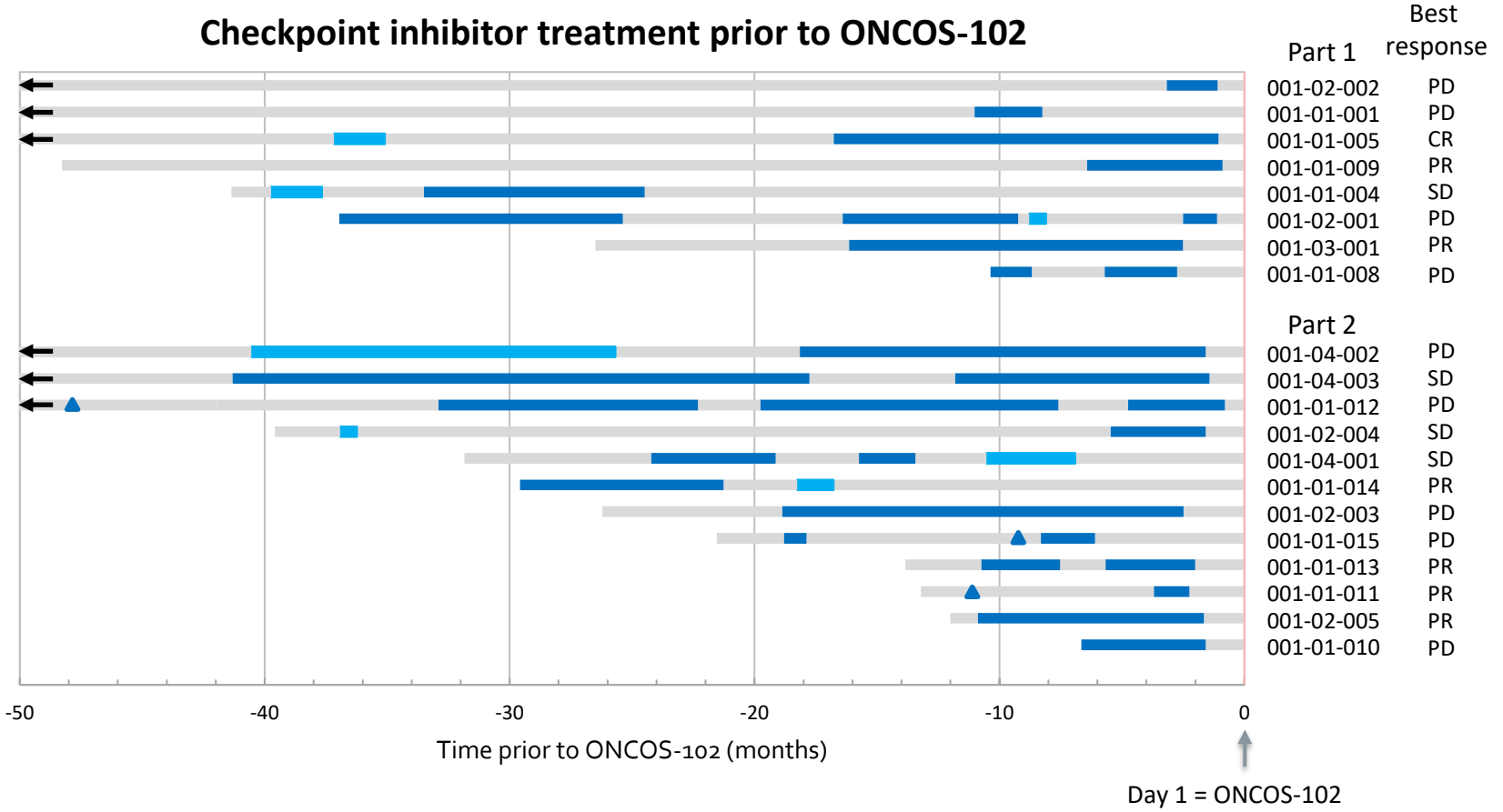



Stage at enrollment
Response evaluated by RECIST 1.1 in at least one CT scan



targovax

# 6 OF 7 RESPONDERS HAD LAST ANTI-PD1 TREATMENT LESS THAN 3 MONTHS PRIOR TO ENTERING THE TRIAL




**CPI treatment prior to trial inclusion:**

**15 / 20 patients** last aPD1 treatment < 3 months (6 / 7 PR/CR)

**3 / 20 patients** last aPD1 treatment > 6 months (no PR)

**2 / 20 patients** last treatment aCTLA4 monotherapy > 6 months (1 / 7 PR)

aPD1 mono or combos, e.g aCTLA4

aCTLA4 monotherapy

no/other treatment than CPI

Pts very first anti-cancer treatment > 50 months prior to ONCOS-102

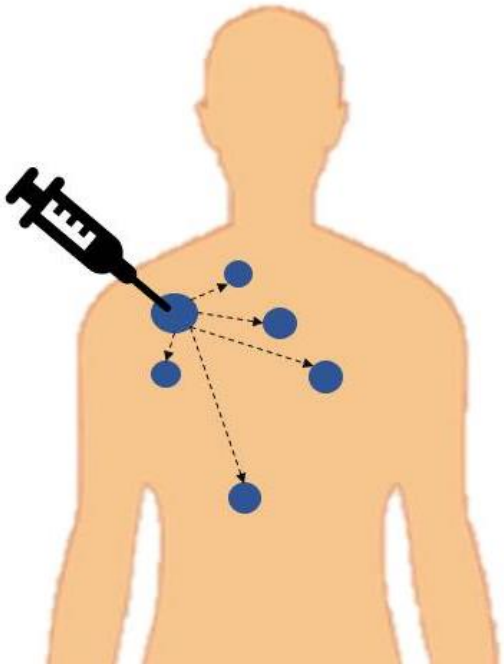
aPD1 +/- aCTLA4 one dose **or** UNK treatment period



targovax

# MULTIPLE EXAMPLES OF SYSTEMIC (ABSCOPAL) EFFECT

## TWO PATIENTS WHERE A NON-INJECTED LESION COMPLETELY DISAPPEARED



**Conservative definition of abscopal effect per lesion:**

- ≥30% tumor reduction from baseline
- ≥ 5mm absolute reduction

**Abscopal effect observed in 4 / 20 patients (20%)**

- 1 / 8 patients in Part 1 (12.5%)
- 3 / 12 patients in Part 2 (25%)

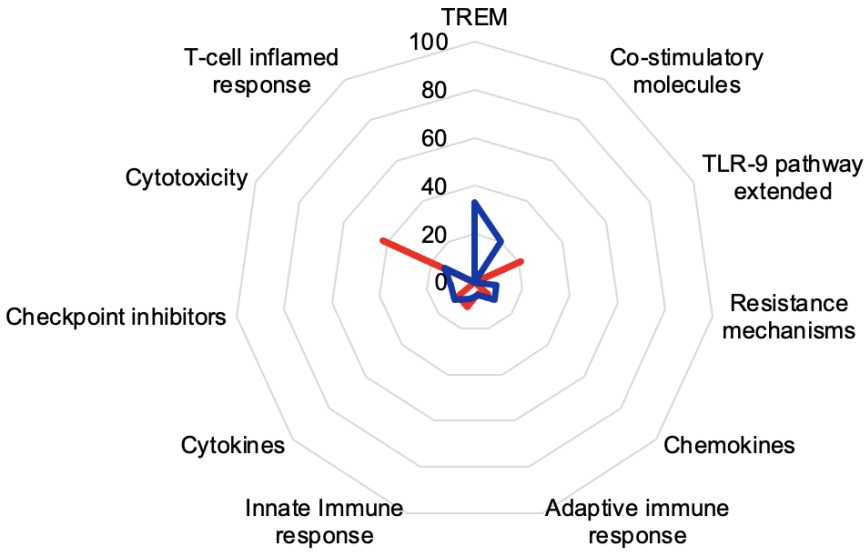
**Complete regression (100%) of a non-injected lesion observed in two patients**

1 Similar to RECIST 1.1 criteria for response

# GENE EXPRESSION DATA SHOWS RESHAPING OF THE TUMOR MICROENVIRONMENT

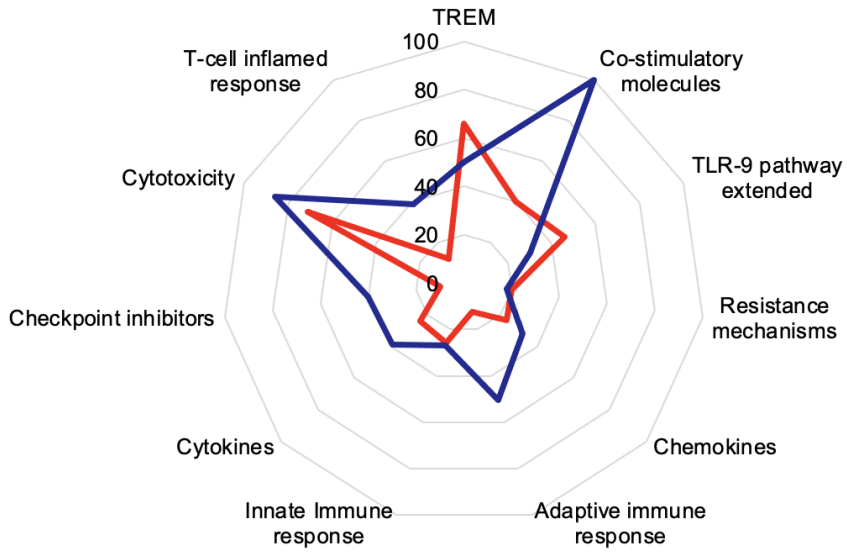
**Modulation of gene expression;** Fraction (%) of genes modulated within the indicated gene groups

Day 22 vs. Baseline
Day 64 vs. Baseline




**Part 1**

Day 22 & Day 64 (n=2)
Baseline (n=6)



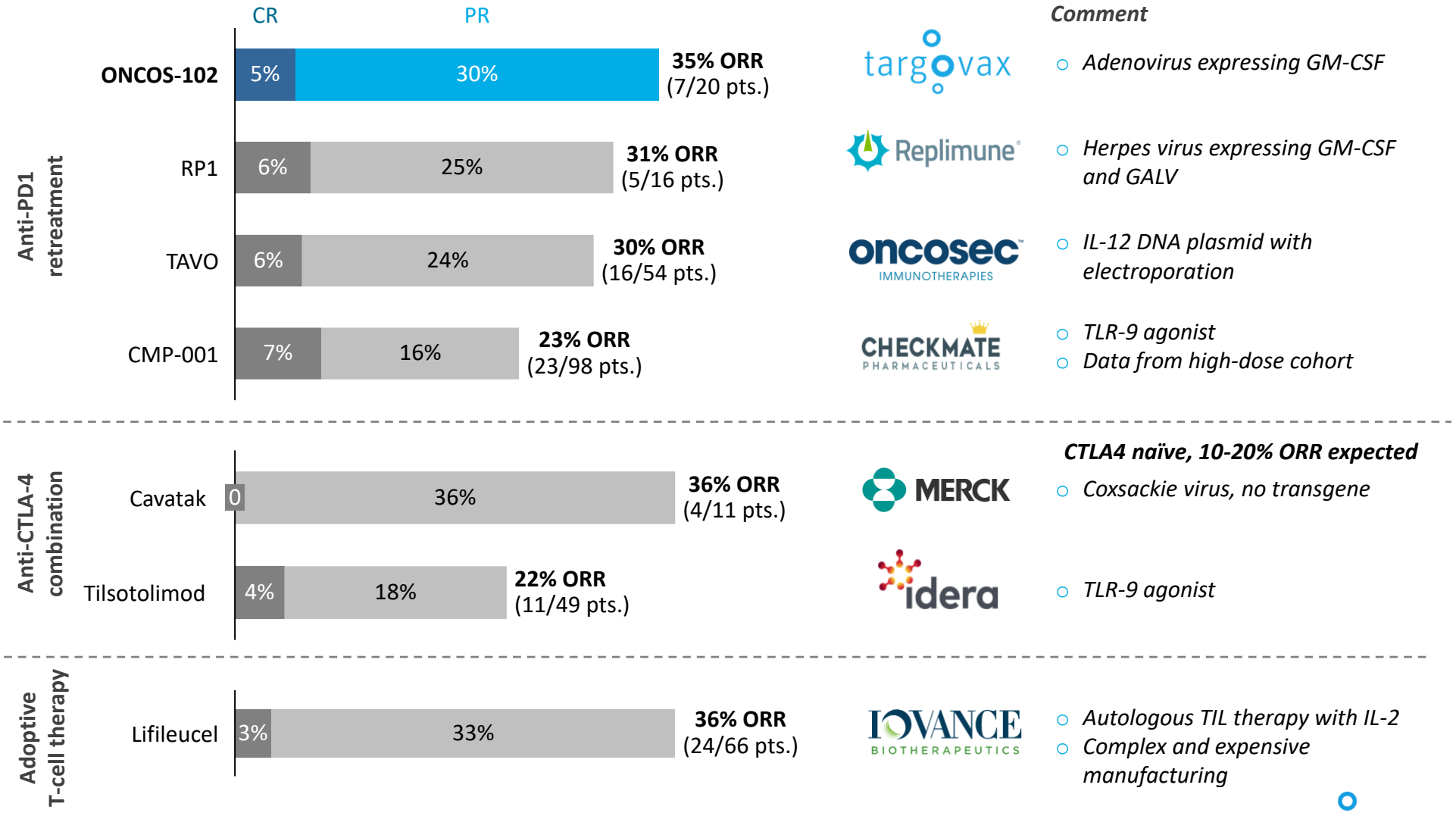

**Part 2**

Day 22 (n=10) & Day 64 (n=7)
Baseline (n=10)



targovax

# ONCOS-102 EFFICACY IS COMPETITIVE TO LEADING DRUG CANDIDATES IN ANTI-PD1 REFRACTORY MELANOMA






Targovax market analysis, December 2020.

targovax

# ACCELERATED APPROVAL IN ANTI-PD1 REFRACTORY MELANOMA IS OUR PRIORITY

**Rationale**

- Highly competitive clinical data
- No standard of care
- Fast route to market

**Preliminary trial design – registration directed**

- Single arm, < 200 patients
- Refractory status
- Primary endpoint: ORR
- Focus: systemic effect and durability
- Dosing: similar to part 2

**Next steps**

- Conclude trial design discussions with KOLs in US, EU and Australia
- Consult with FDA & other regulatory authorities to secure path forward
- Explore opportunities for collaboration partners
- Target first patient 1H 2022

| Product candidate | Preclinical | Phase 1 | Phase 2 | Collaborator | Next expected event |
|---|---|---|---|---|---|
| | **Melanoma**<br>Combination w/anti PD1 | | | | |
| | **Colorectal cancer**<br>Combination w/Imfinzi | | | | |
| **ONCOS-102** | **Mesothelioma**<br>Combination w/pemetrexed/cisplatin | | | | |
| **ONCOS-200 series** | **Next Gen viruses** | | | | |
| **Novel mutRAS concepts** | | | | | |



targovax

# 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

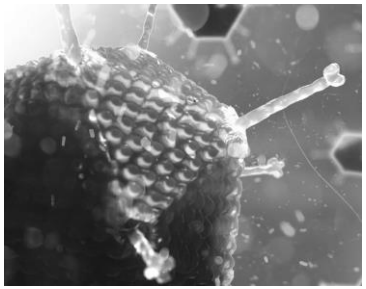
6 months mPFS and 12 months mOS in 1st line

### Immunotherapy

**Ipi/nivo approved in 1st line disease (US only)**

CPIs included in NCCN guidelines as 2nd line option

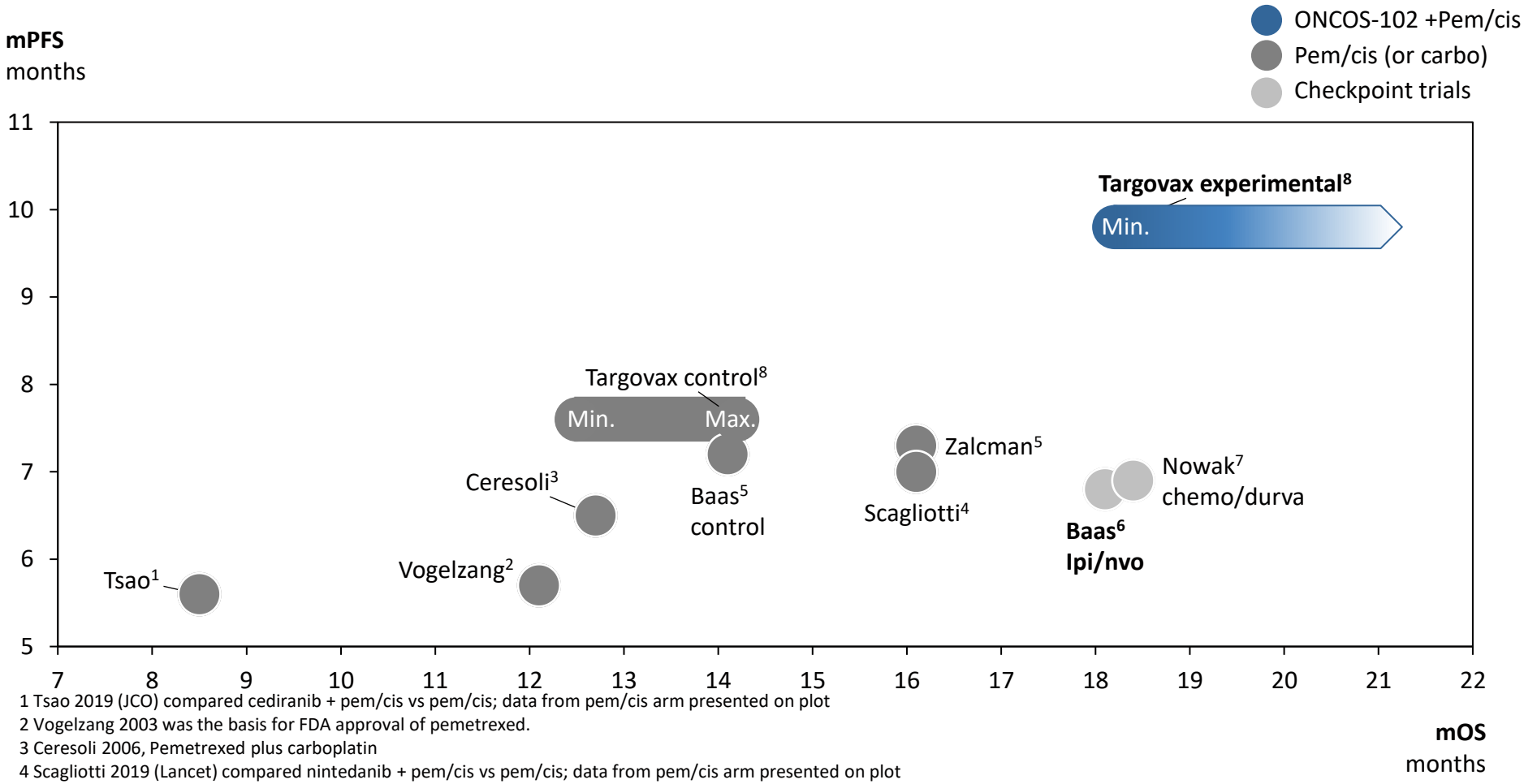
CPI + SoC trials ongoing





targovax

# FIRST LINE DATA ARE MATURING AND ALREADY COMPETITIVE - MOS WILL BE 18.2 MONTHS OR MORE

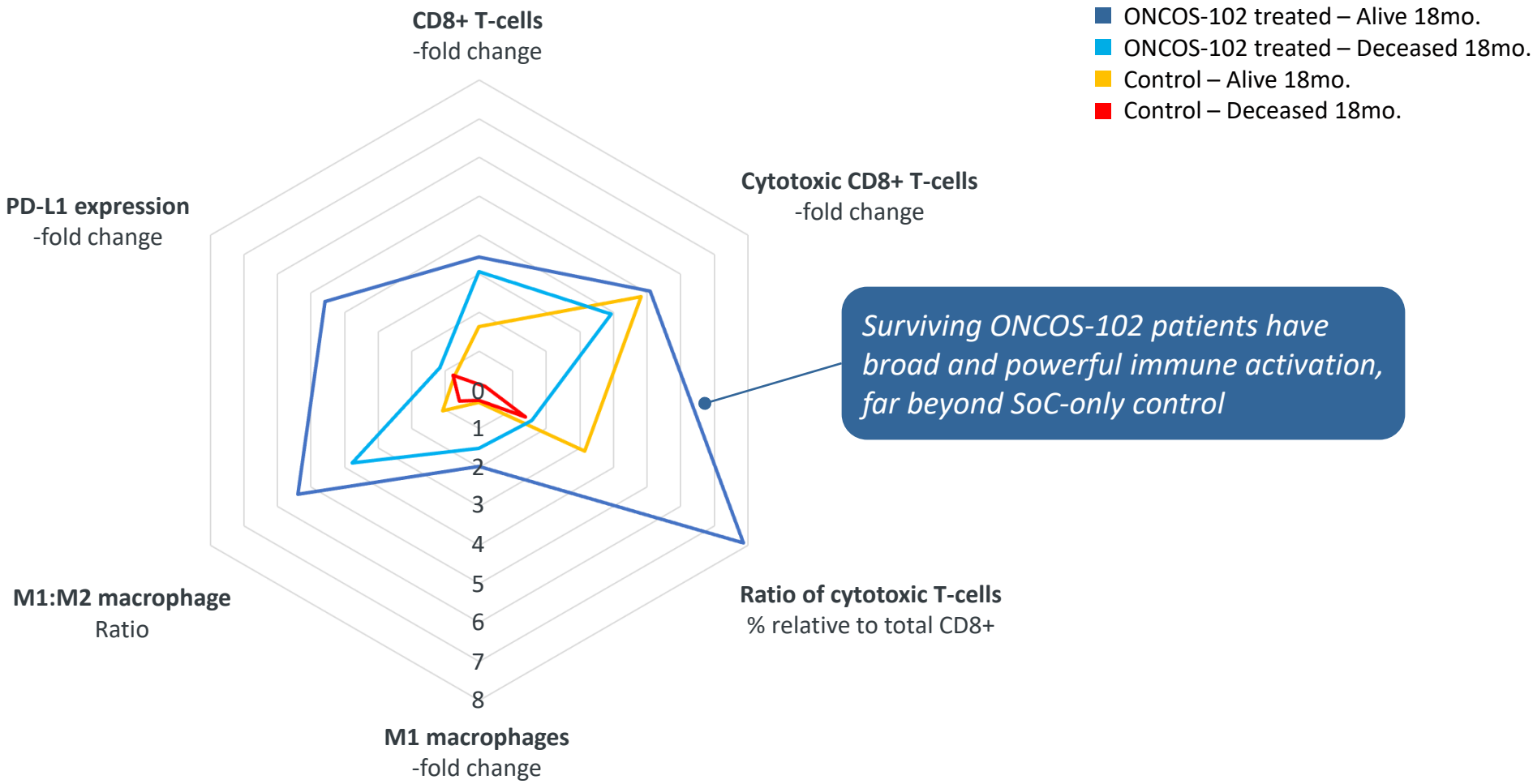



1 Tsao 2019 (JCO) compared cediranib + pem/cis vs pem/cis; data from pem/cis arm presented on plot
2 Vogelzang 2003 was the basis for FDA approval of pemetrexed.
3 Ceresoli 2006, Pemetrexed plus carboplatin
4 Scagliotti 2019 (Lancet) compared nintedanib + pem/cis vs pem/cis; data from pem/cis arm presented on plot
5 Zalcman 2016 (Lancet) compared bevacizumab + pem/cis vs pem/cis; data from pem/cis arm presented on plot.
6 Baas 2020 CheckMate 743. Nivolumab + ipilimumab for two years vs pem/cis (or carboplatin). Ipi/nivo was approved in first line by FDA on October 2, 2020.
7 Nowak 2020 (Lancet Oncology) Pem / cis (6 cycles) + durvalumab (12 months)
8 1L randomized patients mOS will change: Experimental group, 8 patients (5 censored). Control group, 6 patients (2 censored)



mOS: median Overall Survival. mPFS: median Progression Free Survival

# LEVEL OF IMMUNE ACTIVATION PREDICTIVE OF CLINICAL OUTCOME (4 OF 4)






targovax

# FAST TRACK DESIGNATION AND EVOLVING SURVIVAL DATA PROVIDE OPPORTUNITIES

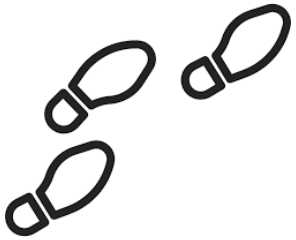
Well **tolerated** combination therapy

Clear clinical activity in **1st line** patients

Interim **survival** data promising even without CPI

FDA granted **Fast Track** designation in mesothelioma

---



**Next steps**

- Continue follow patients to determine mOS
- Decide development path
- Leverage collaboration partner Merck



targovax

| Product candidate | Preclinical | Phase 1 | Phase 2 | Collaborator | Next expected event |
|---|---|---|---|---|---|
| | **Melanoma**<br>Combination w/anti PD1 | | | | |
| | **Colorectal cancer**<br>Combination w/Imfinzi | | | | |
| ONCOS-102 | **Mesothelioma**<br>Combination w/pemetrexed/cisplatin | | | | |
| ONCOS-200 series | Next Gen viruses | | | | |
| Novel mutRAS concepts | | | | | |



targovax

COLLABORATION IN COLORECTAL CANCER WITH

# PHASE 1/2 TRIAL COMBINING ONCOS-102 AND IMFINZI

CANCER RESEARCH INSTITUTE

LUDWIG CANCER RESEARCH

AstraZeneca

**Patients**

- Primary colorectal cancer with peritoneal metastases
- Failed prior standard-of-care platinum chemotherapy

**Dose escalation**

**Safety lead-in**

ONCOS-102
(6 IP doses) +
Imfinzi (12 cycles)

*Disease control in 2 of 5 patients in full dose cohort*

**Expansion**

**Part 1**

**13 patients**
***Disease control in 3/13***

*Simon's two-stage design*

**Part 2**

**14 patients**
***7 patients recruited***

*Expected complete recruitment 1H21*
*Expected data (27 patients) 1H22*

# ONCOS-102 OPPORTUNITIES BEYOND MELANOMA AND MESOTHELIOMA

**COLORECTAL**

- Large medical need and strong scientific rationale for CPI combination
- Met predetermined efficacy threshold in Simon two-stage trial

- **Data expected during 1H 2022**
- **Review opportunity and development with AstraZeneca**

**FURTHER OPPORTUNITIES**

- Melanoma trial serves as POC for other CPI-refractory indications

- **Investigate opportunities in CPI refractory indications beyond melanoma e.g. head & neck, breast cancer**



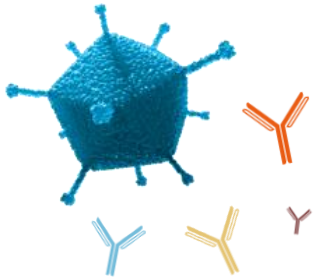
targovax

| Product candidate | Preclinical | Phase 1 | Phase 2 | Collaborator | Next expected event |
|---|---|---|---|---|---|
| ONCOS-102 | **Melanoma**<br>Combination w/anti PD1 | | | | |
| | **Colorectal cancer**<br>Combination w/Imfinzi | | | | |
| | **Mesothelioma**<br>Combination w/pemetrexed/cisplatin | | | | |
| **ONCOS-200 series** | **Next Gen viruses** | | | | |
| **Novel mutRAS concepts** | | | | | |



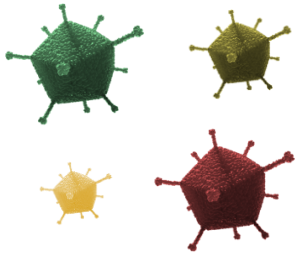
targovax

# TARGOVAX´S THREE-PILLAR R&D PIPELINE STRATEGY



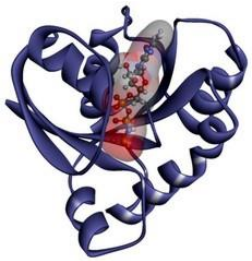
**Novel ONCOS-102 combinations**

- Maximize clinical impact of ONCOS-102 through novel clinical combinations with complementary mechanism of action
- Strong scientific rationale from existing clinical immune data



**Next Generation ONCOS viruses**

- Build new functionality into clinically proven ONCOS backbone
- Boosted immunological activity and anti-tumor ammunition
- Proprietary development and external collaborations



**Mutant RAS vaccination**

- Novel combinations and adjuvant technology for TG vaccines
- Next generation mutant RAS vaccination strategies
- Incorporate immune activation capability of ONCOS technology



targovax

# CURRENTLY FUNDED INTO 2022

## The company

Cash at end of 4Q

**122 / 14**

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

Net cash flow - total 4Q

**45 / 5.3**

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

Capital raise in Oct 2020

Market cap

**850 / 100**

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

Analyst coverage

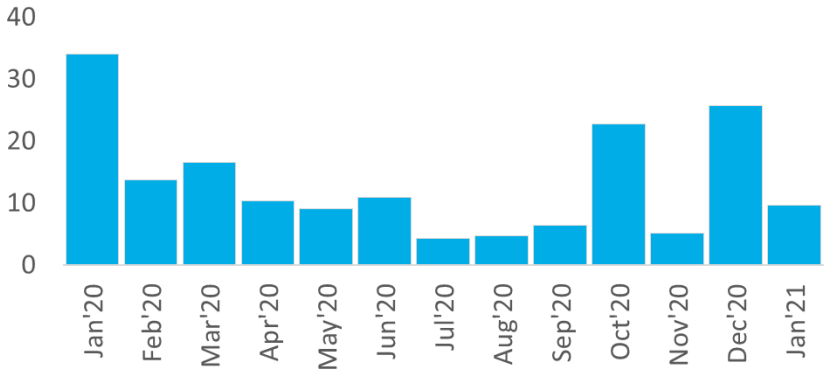
**DNB, Carnegie, H.C. Wainwright**

## Share liquidity

**~170%** of shares traded last 12 months

Share turnover per month[1]

Million shares




Daily value traded

Average last 12 months

**3.4 / 0.4**

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

1 Includes new shares from private placements



targovax

# TRACK RECORD OF STRONG EXECUTION WITH UPCOMING VALUE INFLECTION POINTS

| | 2020 | 2021 H1 | 2021 H2 |
|---|---|---|---|
| **ONCOS-102** | **Melanoma** Part 2 data ✓ | **Melanoma** Prepare and set up new trial | |
| | **Mesothelioma** Merck collaboration 18 month survival follow-up ✓ | **Mesothelioma** Fast Track designation ✓ | **Mesothelioma** 24-month survival follow-up |
| | **Colorectal** Safety lead-in and Part 1 ✓ | | **Colorectal**[1] Part 1 and 2 data 1H22 |
| **Next-gen ONCOS** | **ONCOS-200 series** Preclinical development ✓ | **ONCOS-211** Selected for development ✓ | Updates as projects progress |
| | **Leidos** Checkpoint inhibition ✓ | **Papyrus Therapeutics** OPCML ✓ | Updates as projects progress |
| **Mutant RAS** | **IOVaxis** Option for China license ✓ | Potential mutRAS **trial** announcements | Decision on Iovaxis' **option** exercise |
| | **Valo** mutRAS constructs ✓ | Updates as projects progress | |

1 Pending collaboration partner

# IN SUMMARY

## Lead product ONCOS-102 directed to the $25 billion market for checkpoint inhibitors

- Poised to lead and grow the global market for checkpoint inhibitors (CPIs) with lead product, ONCOS-102
- By activating the immune system, ONCOS-102 may enhance CPI sensitivity and expand the market

## Entering late stage development wit class-leading clinical data

- Entering registrational directed trial in aPD1 refractory melanoma with 35% ORR
- Promising survival data in mesothelioma and Fast Track Designation
- Clinical and immune data in >200 patients as monotherapy, plus in combo with chemo and CPIs

## Powerful immune activation supporting IO-combinations

- Documented broad and deep activation of key immune cells and mechanisms
- Potential to enter registrational program in anti-PD1 refractory melanoma
- Potential registrational program in mesothelioma in collaboration with Merck

## Pipeline with multiple additional value-creating opportunities

- Several collaborations established
- Exploring novel assets with ONCOS as a payload vehicle for delivering other drugs
- Next-generation mutant RAS targeting compounds with both company- and investigator-sponsored trials

## Strong patent position & robust leadership team

- Patent protection on ONCOS-102 through 2036; recently issued European CPI combo patent
- Talented, experienced management team committed to driving success