Agenda & Speakers:

11:30AM-12:00PM
Registration & Lunch

12:00-12:10PM
Welcome Remarks
Øystein Soug, CEO, Targovax

12:10-12:50PM
Oncolytic Virus Overview and Q&A
Dmitriy Zamarin, MD, PhD

12:50-1:30PM
Melanoma: the disease, CPIs, and lack of treatment options; Early ONCOS-102 data
Alexander N. Shoushtari, MD

1:30-1:50PM
Mesothelioma ORR Data
Magnus Jaderberg, CMO, Targovax

1:50-2:00PM
Closing Remarks
Øystein Soug, CEO, Targovax

PLEASE JOIN US FOR A KOL EVENT
Leading experts discuss the oncolytic virus landscape and present interim data from Targovax’s ongoing melanoma and mesothelioma trials

DATE       Thursday, October 11th, 2018
TIME       11:30 AM EST
LOCATION   The Maxwell (formerly The W Hotel)
            541 Lexington Avenue, Great Room 1

KOL PARTICIPANTS:

Dmitriy Zamarin, MD, PhD
Medical Oncologist, Memorial Sloan Kettering

Alexander N. Shoushtari, MD
Medical Oncologist, Melanoma, Memorial Sloan Kettering
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’s 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

2. Oncolytic virus overview – Dr. Dmitriy Zamarin
3. ONCOS-102 in melanoma – Dr. Alexander Shoushtari
4. ONCOS-102 in mesothelioma – Dr. Magnus Jäderberg
5. Summary & closing
TARGOVAX AIM IS TO ACTIVATE THE PATIENT’S OWN IMMUNE SYSTEM TO FIGHT CANCER

Immune activators
- Oncolytic viruses, vaccines

Immune modulators
- Checkpoint inhibitors

Immune boosters
- CAR-Ts, TCRs

Targeted therapy
- TKIs, PARPs, etc.

Surgery - Radio - Chemo

Targovax focus
Targovax has two programs in clinical development, with an ONCOLYTIC VIRUS LEAD PRODUCT CANDIDATE

**ONCOS**
Oncolytic virus

**Lead product candidate**
- Genetically **armed adenovirus**
- **Alerts the immune system** to the presence of cancer antigens
- **Induces T-cells** specific to the patients’ tumor
- **4 ongoing trials**

**Pipeline product**
- **Shared neoantigen**, therapeutic cancer vaccine
- Triggers the immune system to recognize mutant RAS cancers

Activates the immune system
Triggers patient-specific responses
No need for individualization
ONCOS-102 is a cancer targeting adenovirus armed with an IMMUNE STIMULATING TRANSGENE

1. Selective replication in cancer cells
   - Δ24 bp

2. Boosting the immune activation
   - Δ6.7K/gp19K
   - GM-CSF Transgene

3. Enhanced infection of cancer cells
   - ΔAd5 knob
   - Ad3 knob
ONCOS-102
Phase I proof of concept

IMMUNE ACTIVATION DEMONSTRATED

ONCOS-102 Phase I trial design:
- 12 patients, 7 different solid tumors
- No other treatment options left
- Monotherapy 9 injections

Top-line results:
- 100% innate immune activation
- 11/12 patients increase in TILs
- Abscopal effect
- Tumor specific T-cells in blood
- Correlation with survival
Case example
- Ovarian cancer
- Failed on 5 chemotherapies
- Tumor specific T-cells after 2 years
- Stable disease for 3 years
- Survived 3.5 years

Fold-change CD8+ T-cell count vs. survival

\[ r = 0.75 \quad p = 0.005 \]
Compassionate use program
115 patients

Phase I trial
12 patients
7 indications

**Mesothelioma**
Phase I/II - randomized
30 patients

**Melanoma**
Phase I
Up to 12+12 patients

**Peritoneal cancer**
Phase I/II
up to 78 patients

**Prostate cancer**
Phase I
up to 15 patients

- Shortest path-to-market
- Orphan drug designation
- Combination with SoC chemo
- Randomized vs. SoC

- PoC in CPI refractory patients
- Combination with Keytruda®
- Memorial Sloan Kettering

- Ovarian and colorectal cancers
- Combination with Imfinzi®
- Intraperitoneal administration
- Collaboration with MedImmune / AZ, CRI, & Ludwig

- Combination with dendritic cell vaccine (DCVAC)
- Collaboration with Sotio

Completed

Ongoing trials sponsored by Targovax

Ongoing trials sponsored by partner
2 Oncolytic virus overview

Dr. Dmitriy Zamarin

3. ONCOS-102 in melanoma – Dr. Alex Shoushtari
4. ONCOS-102 in mesothelioma
5. Summary & closing
Systemic immunomodulation with \textit{in situ} oncolytic vaccines

Dmitriy Zamarin MD PhD
Assistant Attending, Gynecologic Medical Oncology / Immune Therapeutics Center
Parker Institute for Cancer Immunotherapy
Memorial Sloan-Kettering Cancer Center
New York, NY

October 11, 2018
The idea of using pathogens for treating cancer

1850-1900 – reports of natural tumor regressions coinciding with human infections

1891 - William B. Coley uses live Strep. pyogenes to treat head and neck cancer

1910 - De Pace et. al - patient with advanced cervical cancer treated with rabies vaccine experiences complete remission

1940’s - George T. Pack – treated melanoma with rabies vaccine; some remissions were seen.

1950’s - clinical trials with Hepatitis B, West Nile virus, Adenovirus, Russian Far Eastern Encephalitis viruses

1960’s-1990’s - clinical trials with attenuated human viruses and animal viruses

1990’s-present – Genetically engineered viruses

2005 - 1st approved oncolytic virus (China)

2013 - 1st positive phase III trial (talimogene laherparepvec)

2015 - T-vec approved for advanced melanoma
How oncolytic viruses work

Healthy Cell → Undamaged

Oncolytic virus → Tumor Cell → Virus replication → Tumor cell lysis

Destruction of Tumor Microenvironment

Local inflammation → Release of virus progeny → Infect More Tumor Cells

Release of tumor antigens → Systemic anti-tumor immune response
Not all oncolytic viruses are created equal

Dogma: replicating and lytic viruses are better anti-cancer agents than non-lytic viruses
Current efforts (non-exhaustive list, closest to clinical development)

- **HSV-1 (Amgen and at least 5 other companies)**; T-vec phase III in melanoma complete and FDA-approved; combination trials with anti-PD-1 and anti-CTLA-4 in melanoma ongoing. Head and neck Ph III trial terminated in 2011.
- **Vaccinia (Jennerex, Genelux, Western Oncolytics)**. JX-594 had encouraging results in early trial with HCC; less promising in a later study. GL-ONC1 is in phase I for IP for carcinomatosis, intrapleural for mesothelioma, IV for solid tumors.
- **Myxoma (academic)**. Pre-clinical
- **Reolysin (Oncolytics)**. Multiple clinical trials in various indications; most recently in combination with chemotherapy.
- **Coxsackie A21 (Viralytics)**. Phase II for intralesional administration (CALM study, melanoma) showed promise. Currently in phase I IV for different cancer types; including with pembro combination for lung.
- **Poliovirus (academic)**. Encouraging data in glioblastoma (given intratumorally)
- **Adenovirus (Oncos, Cold Genesys, PsiOxus, academic)**. Oncos: Ad5-GM-CSF; completed phase I study with IT administration, results pending (evidence of immune activation based on poster presentations). PsiOxus: chimeric Ad11p/Ad3, in phase I for colon cancer (IV).
- **VSV (Viread)**. Phase I ongoing in HCC.
- **Maraba (Turnstone)**. Phase I ongoing in combination with adenovirus prime-boost in patients with MAGE-A3 expressing cancers
- **Measles (academic)**. Phase I in ovarian, head and neck, multiple myeloma, GBM, mesothelioma. Promising results in ovarian and multiple myeloma so far.
- **NDV (academic and industry)**. Several phase I studies completed in multiple tumor types using virulent virus strain, with promising results. Currently in development with non-virulent strains.
- **Seneca Valley (Neotropix)**. Phase I completed in neuroendocrine tumors.
Newcastle Disease Virus (NDV)

- Negative-strand RNA virus, member of Paramyxoviridae family (same as mumps, HPIV, measles), which **do not integrate into mammalian genome**

- Causes contagious bird disease affecting many domestic and wild avian species, but poses **no hazard to human health**

- Readily **infects the majority of cancer cells** due to ubiquity of the receptor (sialic acid)

- Specificity for cancer cells is mediated by selective viral replication in cells with **deficient innate immune responses and cells resistant to apoptosis**

- Pathogenicity in birds is primarily determined by the fusion protein cleavage site sequence
Intratumoral NDV induces local and distant TIL infiltration

NDV upregulates a range of immune inhibitory and activating pathways in tumors

**Graph:**
- **x-axis:** Fold Change (Log2)
- **y-axis:** p-value (-Log10)
- **Legend:**
  - CD28
  - CD27
  - CD40
  - CD40L
  - CTLA-4
  - ICOS
  - GITR
  - OX40
  - 4-1BB
  - PD1
  - PD-L1
  - PD-L2

**Graph Labels:**
- p = 0.05

**Early:**
- Direct action of type I IFN

**Late:**
- Response to TIL infiltration

**Systemic immune modulators** (e.g. anti-CTLA-4, anti-PD-1)

**Engineered NDV**

**Diagram Description:**
- T cell activation and proliferation
- Antigen presentation and co-stimulation
- APC
- MHC-peptide
- TCR
- ICOS
- ICOSL
- PD-L1
- PD-L2
- CTLA-4

**References:**
NDV potentiates the efficacy of systemic immune checkpoint blockade in models sensitive and resistant to NDV lysis

OPTiM, a randomized phase III trial of talimogene laherparepvec (T-VEC: HSV-GM-CSF) versus subcutaneous GM-CSF for the treatment of advanced melanoma

T-vec was approved by FDA in 10/2015

Andtbacka et al., JCO 2015
Intratumoral T-vec potentiates the efficacy of systemic anti-CTLA-4 and anti-PD-1 therapy in melanoma

Tvec + anti-CTLA-4 (ORR 39%)

Change in tumor area from baseline

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<tr>
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<tr>
<td>≥50%</td>
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<tr>
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No. (%)

21

Tvec + anti-PD-1 (ORR 62%)

<table>
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<th>N</th>
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<tr>
<td>III B</td>
<td>1</td>
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<tr>
<td>III C</td>
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<tr>
<td>IV M1a</td>
<td>2</td>
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<tr>
<td>IV M1b</td>
<td>4</td>
</tr>
<tr>
<td>IV M1c</td>
<td>8</td>
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N = 21

Change from Baseline, %

Chesney et al., JCO 2017; Ribas et al, Cell 2017

MSK Confidential Information
Summary: locoregional and systemic immune modulation approaches can lead to systemic anti-tumor immunity

- No response to CPI
- Response to CPI

PBS
- No response to CPI
- Response to CPI

NDV
- No response to CPI
- Response to CPI

Systemic immune modulators (e.g. anti-CTLA-4, anti-PD-1)

Localized OV

Tumor Rejection
*In situ* oncolytic vaccines in combination with ICB overcome the need for systemic oncolytic virus delivery

**Methods for delivery of *in situ* oncolytic vaccines**

- **Intravenous**
- **Intratumoral**
  - Direct injection of accessible lesions
  - Image guided
  - Endoscopic
- **Intraperitoneal catheter**
- **Intrapleural catheter**
- **Intraarterial**
  - Hepatic artery infusion pump
Combination oncolytic immunotherapy for peritoneal cancers
PD-1 blockade as a single agent has limited activity in ovarian cancer

Hamanishi et al., JCO 2015, Matulonis et al., ASCO 2018

ORR 15%  ORR 9%

Values higher than or equal to 100 are set to 100. RECIST v1.1, Response Evaluation Criteria in Solid Tumors version 1.1. BICR, Blinded Independent Central Review. All Subjects as Treated Population. Database cut-off date: April 26, 2018.
Background on ONCOS-102

- 115 cancer patients with solid refractory tumors were treated with ONCOS-102 in Advanced Therapy Access Program (ATAP)
- ONCOS C1 trial
ONCOS-102 replicates in cancer cells and induces immunogenic cell death

Intratumoral administration

![Diagram showing intratumoral administration and cell viability graphs for low passage melanoma and lung cancer with ONCOS-102 and Ad5wt comparisons.]

Cell viability graphs:
- Low passage melanoma
- Lung cancer
  - Ad5wt (blue) vs. ONCOS-102 (red)

Graphs show cell viability over varying concentrations of pMelL and A549.

![Bar graphs showing ATP, HMGB1, and CRT levels in untreated and treated H226 mesothelioma cells.]

- ATP: Untreated cells (gray) vs. ONCOS-102 treated cells (red)
- HMGB1: Untreated cells (gray) vs. ONCOS-102 treated cells (red)
- CRT: Untreated cells (gray) vs. ONCOS-102 treated cells (red)
Phase I study of intratumoral ONCOS-102 with low dose cyclophosphamide in patients with advanced solid tumors

Peripheral blood mononuclear cells (PBMCs)

Days

BL 1 4 8 15 29 57 85 114 141 169

ONCOS-102 intratumorally (3x10^{11} VP / dose)

Daily cyclophosphamide (50mg / day)

Core needle biopsies
Several immune cell subsets were attracted into tumors following ONCOS-102

**Graphs:**
- **CD68**: Fold-change from baseline, SD at 3 months vs. PD at 3 months.
- **CD8**
- **CD4**

**Legend:**
- Red: SD at 3 months
- Gray: PD at 3 months
Local ONCOS-102 administration leads to induction of systemic tumor-specific CD8+ T cell response

**Mesothelioma pt FI1-14**: induction of MAGE-A3 specific CD8+ T cells

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<th>Weeks 1-4</th>
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<td>No peptide</td>
<td>MAGE-A3 p271-279</td>
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<table>
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<th>Spots per 25000 CD8+ cells</th>
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<tr>
<td>0</td>
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<tr>
<td>Baseline</td>
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<table>
<thead>
<tr>
<th>Fold-change from baseline</th>
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<tbody>
<tr>
<td>0</td>
</tr>
<tr>
<td>Mesothelin</td>
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**OvCa pt FI1-19**: multiple tumor-specific CD8+ T cell populations induced by ONCOS-102

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<th>Baseline</th>
<th>Weeks 1-12</th>
</tr>
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<tbody>
<tr>
<td>No peptide</td>
<td>Mesothelin</td>
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NY-ESO-1 specific CD8+ T cells present 17 mo after previous ONCOS-102 treatment, alive and SD >24 mo
A Phase I/II study to investigate the safety and biologic and anti-tumor activity of ONCOS-102 in combination with PD-L1 blockade in patients with peritoneal malignancies

**Phase I**
- 3 + 3 design
- 2 virus dose cohorts:
  1. $1 \times 10^{11}$ pfu
  2. $3 \times 10^{11}$ pfu

**Phase II**
- Optimal Simon 2 stage design
- 1. Platinum-resistant/refractory ovarian cancer (18+15)
- 2. Colorectal cancer (13+14)
- 3. Other intraperitoneal (e.g. mesothelioma, pancreas, endometrial) (30)

**Endpoints**
- **Primary**
  - Feasibility
  - Safety
- **Secondary**
  - Efficacy (ORR, CBR at 24 weeks, PFS)
- **Exploratory**
  - Immune biomarkers

PI: Zamarin
Update

• 7 patients enrolled and treated to date
• Dose escalation is ongoing
3

ONCOS-102 in melanoma

Dr. Alexander Shoushtari

4. ONCOS-102 in mesothelioma
5. Summary & closing
Activating the immune system to fight cancer

Company presentation

August 2018

Alexander Shoushtari, MD
Assistant Attending Physician
Melanoma and Immunotherapeutics Service
Memorial Sloan Kettering Cancer Center

Preliminary data from C824

October 2018
MELANOMA IN 2018: FRONTLINE THERAPY

PD-1 based therapy

- 2 choices
  - Monotherapy: Pembrolizumab or Nivolumab
  - Combined Nivolumab plus Ipilimumab (CTLA-4 inhibitor)

- 45 - 60% objective response rate
- Responses last years, but not forever
- Overactive immune system leads to immune-related adverse events (irAEs)
  - Diarrhea / Colitis
  - Liver inflammation
  - Pneumonitis
  - Thyroid, Pituitary dysfunction

- iRAE rate varies by monotherapy versus combined therapy
  - Monotherapy: 1 in 4 require steroids
  - Combined Nivo + Ipi: 3 in 4 require steroids
MELANOMA IN 2018: FRONTLINE THERAPY

BRAF-MEK Inhibition

- Only available for 40-50% with BRAF V600 mutant melanoma
- 60-70% objective response rate
- Responses last average of 12-15 months
- Adverse events (AEs) not directly related to immune system
  - Diarrhea
  - Liver inflammation
  - Rash
  - Fevers, chills
  - Muscle/joint aches
- If BRAF-MEK stopped, adverse events stop
**MELANOMA IN 2018: NEEDS**

**Resistance to Standard Therapies**

- **BRAF-MEK therapy**: majority of initial responders will progress (secondary resistance)

Long et al, Lancet 2015
Resistance to Standard Therapies

- **BRAF-MEK therapy:** majority of initial responders will progress (secondary resistance)

- **PD-1 based therapy:**
  - 30-40% will have primary resistance
  - 25-35% will have secondary resistance
Resistance to Standard Therapies

- **BRAF-MEK therapy**: majority of initial responders will progress (secondary resistance)

- **PD-1 based therapy**:
  - 30-40% will have primary resistance
  - 25-35% will have secondary resistance

- **Talimogene Laherparepvec**
  - 40% primary resistance in injected lesions
  - 85% resistant in distant lesions
  - Takes 10 injections on average to respond as monotherapy
MELANOMA IN 2018: NEEDS

Not all resistance is treated alike!
MELANOMA IN 2018: OPTIONS POST-PD-1

Standard Options

- **After PD-1 monotherapy**
  - BRAF-MEK, if V600 mutant
  - Nivolumab plus ipilimumab
  - Ipilimumab alone
  - Cytotoxic chemotherapy
  - T-VEC if injectable

- **After Nivolumab plus Ipilimumab**
  - BRAF-MEK, if V600 mutant
  - Cytotoxic chemotherapy
  - T-VEC if injectable

- **If local progression only**
  - Surgery
  - Radiation therapy

Non-standard options

- **Clinical Trials (selected)**
  - PD-1 plus
    - LAG-3 inhibitor
    - OX40 agonist
    - GITR agonist
  - Tumor Infiltrating Lymphocyte trials
  - Injectable trials
    - ONCOS-102 + pembro
    - TVEC + pembro
    - Coxsackievirus + pembro
    - TLR9 agonist (tilsotolimod) + ipilimumab

- **Off-label uses**
  - BRAF + MEK + PD-1
  - T-VEC + PD-1 inhibitor
  - Radiation + PD-1 +/- Ipilimumab
MELANOMA IN 2018: CHALLENGES

- **After PD-1 progression, no “one size fits all” approach**
  - Nivolumab plus LAG-3 – 10-15% response rate
  - IDO inhibitors had a negative frontline trial

- **Rightly or wrongly, many physicians want an excuse to avoid ipilimumab**
  - 20-30% response rate, can be durable
  - Significant toxicity

- **Injectable combinations may represent a happy medium**
  - Overcome lack of recognition by direct injection of agent into tumor
  - Activate innate and adaptive immune system → “domino effect”
  - Fewer off-target effects to reduce systemic toxicity
MELANOMA: INJECTABLE COMBINATIONS TO DATE

T-VEC +/- Ipilimumab (Chesney et al, J Clin Oncol 2017)

TVEC: day 1, 22, then every 2 weeks

ORR: 39% vs 18% (p=0.002) in favor of combination
Largely frontline population – very little prior PD-1
MELANOMA: INJECTABLE COMBINATIONS TO DATE

Cocksackie virus CVA21 + pembro (CAPRA, Silk et al, AACR 2017)
- **Largely PD-1 naïve**
- Injections: D1, 3, 5, 8, every 3 weeks for up to 19 total
- 8 of first 11 evaluable patients with objective responses

Toll-Like Receptor 8/9 Agonist + Ipilimumab (Diab et al, ASCO 2018)
- **Already received PD-1 blockade** – only study to date
- Only 3 of 26 were stage 3; 11 (42%) M1c
- 8 of 21 patients responded (38%)
  - 2 CR
  - 6 PR
  - 8 SD
  - 5 PD
A Pilot Study of Sequential ONCOS-102 and Pembrolizumab in Patients with Advanced or Unresectable Melanoma Progressing after PD1 Blockade

Deliveries:
- ORR data on 6 patients
- 4/4 patients biopsy data: TILs (CD3+, CD4+ and CD8+ T cells) – Day 1, 22 and 64
- 4/4 patients cytokines: IFNgamma, TNFa, IL6 - Day 1, 4, 8/W3/W9/W18
- 4/4 patients PBMC: T cell activation/exhaustion - Day 1, W 3, 8/9
- 1st safety review of 4 pats – there were no issues
STUDY OBJECTIVES

Primary Endpoint

- Safety of sequential administration of 3 doses of ONCOS-102 followed by 8 doses of pembrolizumab

Secondary Objectives

- Objective responses by RECIST 1.1 and irRECIST
- Progression-free survival
- Change in size of individual lesions
- Immune subsets in tumor and plasma, changes over time

Exploratory Endpoints

- Analysis of mutation rate in relation to response
- Changes in T cell receptor clonality
- Gene expression analysis in biopsied tissue
STUDY SCHEMA

3 biopsies per patient
Baseline  DAY 22  DAY 64

STUDY SCHEMA

CPO  ONCOS-102  Pembrolizumab

DLT Assessment

PBMCs  Cytokines  Imaging

Weeks
STUDY SCHEMA

3 biopsies per patient

Baseline DAY 22 DAY 64

BL DAY -3 DAYS 1 4 8 3 6 9 12 15 18 21 24 27 Weeks

CPO ONCOS-102 Pembrolizumab

PBMCs
Cytokines
Imaging

DLT Assessment
STUDY SCHEMA

3 biopsies per patient

Baseline  DAY 22  DAY 64

CPO  ONCOS-102  Pembrolizumab

PBMCs
Cytokines
Imaging

DLT Assessment

BL  DAY -3  DAYS 1 4 8  3 6 9 12 15 18 21 24 27 Weeks
WHAT REPRESENTS SUCCESS (TO A MELANOMA ONCOLOGIST)?

- Ability to administer the drug safely
- Evidence of preliminary efficacy
- Access to tissue and biomarker data to refine your therapeutic strategy moving forward
87 year old female
Surgery, Keytruda, T-VEC, Radiotherapy prior study
ORR: PD (not received full dose of ONCOS-102)

Baseline

Day 10

Day 22
73 year old male
Surgery, Keytruda prior study
ORR: PD (not received full dose of ONCOS-102)
60 year old male
Surgery, Yervoy, Keytruda prior study
ORR: CR (after only 2 Keytruda infusions)
3 MORE PATIENTS

79 year old male; had Yervoy, Keytruda, T-VEC prior study
- Shrinkage in injected lesion but new distant lesion
- ORR: PD

74 year old female; had surgery and Opdivo prior study
- ORR: PD

78 year old female; had Yervoy, Opdivo, Keytruda prior study
- ORR: PD
EFFICACY, N=6

Demographics
- **Age:** 60 – 87 (median 76)
- **Stage**
  - IIIIB/C: 5 of 6
  - IV: M1C, 1 of 6
- **Prior PD-1 blockade:** 100%
- **Prior Ipilimumab:** 50%
- **Prior Injectable:** 50%
- **Prior BRAF:** 50% (2 of 3 intolerant)
- **Median prior lines:** 2.5 (range: 1-4)

Efficacy
- **Complete Response:** 1/6, 12+ mo
- **Partial Response:** 0/6
- **SD:** 0/6
- **PD:** 5/6
- **Anecdotally:** At least 3 patients with “PD” had transient shrinkage in the injected tumor
ONCOS-102 INDUCED INCREASE OF CYTOKINES IN ALL PATIENTS (tested to date n=4)

Summary on cytokines analyses (D 1, 4, 8, W3, 9/18):
- Increase of pro-inflammatory cytokines (IFN-γ, TNF-α, IL-12p40, GM-CSF) after ONCOS-102 administration (4 out of 4)
- Increase of pro-inflammatory cytokines (IL-6 and IL-8) after ONCOS-102 administration (3 out of 4)
- Temporarily elevation level of IL-10 after second ONCOS-102 administration (3 out of 4 patients)
- Profound increase of IL-6, TNFa and IFNγ (001-01-005)

The treatment with ONCOS-102 induces innate immune responses
**T CELL INFILTRATES ON MULTIPLEX IHC INCREASE WITH ONCOS-102**

- **Patient with CR** had highest relative increase of CD3+, CD4+, CD8+ cells
- **2 patients with reduced dose of ONCOS-102** had lower relative increases
- **Non-injected lesion** seen with increase of CD3+, CD4+ and CD8+ T cells

PINK: un-injected lesion
ONCOS-102 INDUCED CANCER ANTIGEN SPECIFIC T-CELLS

Measured by IFN gamma ELISPOT in PBMCs (baseline vs. post-treatment samples)
LESSONS LEARNT AND NEXT STEPS

- We can inject ONCOS-102 safely and follow with pembrolizumab in patients with melanoma that has recurred despite prior PD-1 blockade.

- There is preliminary efficacy in a patient with PD-1 refractory in-transit disease – associated with the most profound activation of both innate and adaptive immune cells.

- Correlative analyses in the first 4 patients provide evidence supporting the proposed mechanism of action.

- For larger baseline lesions, transient shrinkage is seen when injected with 3 doses of ONCOS-102, but it does not appear to persist.

- If we could inject more doses of ONCOS-102, more lesions are likely to respond.
NEW SCHEMA: 12 ADDITIONAL PATIENTS

From

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<th>DAYS 1 4 8</th>
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<th>12</th>
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<td>CPO</td>
<td>ONCOS-102</td>
<td>Pembrolizumab</td>
<td></td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>DLT Assessment</td>
<td></td>
<td></td>
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<td></td>
<td></td>
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</tbody>
</table>

To

<table>
<thead>
<tr>
<th>BL</th>
<th>1</th>
<th>2</th>
<th>5</th>
<th>8</th>
<th>11</th>
<th>14</th>
<th>17</th>
<th>20</th>
<th>23</th>
<th>26 Weeks</th>
</tr>
</thead>
<tbody>
<tr>
<td>DAY -3 to 1</td>
<td>DAYS 1, 4, 8</td>
<td>DAY 15</td>
<td>DAY 36</td>
<td>DAY 57</td>
<td>DAY 78</td>
<td>DAY 99</td>
<td>DAY 120</td>
<td>DAY 141</td>
<td>DAY 162</td>
<td>DAY 183</td>
</tr>
</tbody>
</table>
SUMMARY

- ONCOS-102 safe and well tolerated
- ORR in 1/6 patients in pre-treated population
  - Patients were not "cherry-picked" and likely to represent true population
  - The only variable that we changed is 3 doses of ONCOS-102

- Mechanism of action is supported by preliminary correlative data
  - Increase in pro-inflammatory cytokines associated with improved outcomes to PD-1
  - Increase in tumor-infiltrating CD4+/8+ T cells

- Solid rationale for increasing the number of ONCOS-102 injections
  - Increase ability to shrink injected tumor
  - Mirror other trials (e.g. TVEC, TLR9) that have shown some visceral efficacy
  - now being approved at 2 additional US sites
ONCOS-102 in mesothelioma

Dr Magnus Jaderberg
Chief Medical Officer
Targovax
ONCOS
CLINICAL DEVELOPMENT STRATEGY

1. Path-to-market
   Mesothelioma
   Target launch indication
   - Ongoing Phase I/II

2. Proof-of-concept
   CPI refractory
   Indications with no/limited effect of CPIs
   - Ongoing melanoma Phase I

3. Proof-of-concept
   New CPI indication
   Peritoneal malignancies
   - Ongoing Phase I/II in ovarian and colorectal

4. Next generation
   oncolytic viruses
   Targeting new indications
   - Novel targets and mode-of-action
Orphan disease, estimated 15,000 new cases per year (EU, USA, Australia)

Incidence is increasing worldwide and is predicted to peak in 5-10 years

Often caused by asbestos exposure, with a latency period of up to 40 years before diagnosis

Aggressive cancer form with median survival of 12 months

No significant treatment advance in the last decade
MESOTHELIOMA IS SHORTEST PATH-TO-MARKET

Rationale for ONCOS-102 opportunity in mesothelioma:

**Become frontline therapy**
- **Phase I results** indicate potential of ONCOS-102 in mesothelioma
- **Ongoing randomized phase I/II trial** combining ONCOS-102 with SoC chemotherapy
- **Good safety profile**

**Orphan Drug Designation**
- High unmet medical need, ONCOS-102 has **orphan drug designation**
- Opportunity for priority regulatory review, and **quick route-to-market**
- 7 year **market exclusivity** in the US and 10 years in the EU

**Limited competition**
- CPIs show some early signs of efficacy, but are potential **ONCOS-102 combinations**, rather than competitors
- **No competing viruses** and few vaccines in current clinical development in mesothelioma
Anticancer effect of ONCOS-102 and standard of care chemotherapy in xenograft mouse mesothelioma model
% change in tumor volume, 7 animals per group (14 tumors/group)

**Effects observed at Day 60:**

- **ONCOS vs. mock**
  - 56% tumor volume reduction
  - $p < 0.01$

- **ONCOS vs. pem/cis**
  - 63% tumor volume reduction
  - $p < 0.01$

- **ONCOS+pem/cis vs. pem/cis**
  - 75% tumor volume reduction
  - $p < 0.001$

- **ONCOS+pem/cis vs ONCOS**
  - 33% tumor volume reduction
  - $p < 0.01$

**SOURCE:** Kuryk et al., Int J Cancer, 10 June 2016
ONCOS-102 CAN TURN MESOTHELIOMA LESIONS HOT

Phase I

CD8+ T-cells in tumor
Tumor biopsy staining

**Mesothelioma – Phase I, patient 14**

<table>
<thead>
<tr>
<th>Sample</th>
<th>Baseline</th>
<th>Week 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>130x</td>
<td>1</td>
<td>15.4</td>
</tr>
</tbody>
</table>

CD4+ T-cells in tumor
Fold change

<table>
<thead>
<tr>
<th>Sample</th>
<th>Baseline</th>
<th>Week 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1</td>
<td>6.5</td>
</tr>
</tbody>
</table>

PD-L1 positive tumor cells
% of total

<table>
<thead>
<tr>
<th>Sample</th>
<th>Baseline</th>
<th>Week 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.2</td>
<td>19.5</td>
<td>16x</td>
</tr>
</tbody>
</table>

**Mesothelioma – Phase I, patient 9**

<table>
<thead>
<tr>
<th>Sample</th>
<th>Baseline</th>
<th>Week 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>8.8x</td>
<td>1</td>
<td>2.1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Sample</th>
<th>Baseline</th>
<th>Week 5</th>
</tr>
</thead>
<tbody>
<tr>
<td>16.4</td>
<td>30.0</td>
<td>1.8x</td>
</tr>
</tbody>
</table>

Ranki et al., Journal for Immunotherapy of Cancer 2016, 4(17)
PHASE I/II STUDY DESIGN IN COMBINATION WITH SoC

Patient population
Advanced malignant pleural mesothelioma
1\textsuperscript{st} line / 2\textsuperscript{nd} line

Non-randomized

Safety lead-in completed

Randomized

Safety lead-in (n=6)
ONCOS-102 plus SoC chemotherapy (6 cycles)

Experimental group (n=14)
ONCOS-102 (6 administrations)
SoC (6 cycles)

Control group (n=10)
SoC (6 cycles)

Randomized part currently enrolling
## SIGNAL OF EFFICACY IN THE FIRST 6 PATIENTS

<table>
<thead>
<tr>
<th></th>
<th>1 Safety</th>
<th>2 Innate immune activation</th>
<th>3 Adaptive immune activation</th>
<th>4 Clinical benefit</th>
</tr>
</thead>
<tbody>
<tr>
<td>✓</td>
<td>ONCOS-102 well-tolerated in combination with chemotherapy</td>
<td>✓ Systemic increase of pro-inflammatory cytokines in 6/6 patients (IL-6, TNFα and IFNγ)</td>
<td>✓ Increase in tumor infiltration of CD4+ and CD8+ T-cells in 3/4 patients</td>
<td>✓ Signal of clinical benefit seen in 3/6 patients after 6 months</td>
</tr>
<tr>
<td></td>
<td>✓ 50% disease control rate</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Safety**: ONCOS-102 well-tolerated in combination with chemotherapy.
- **Innate immune activation**: Systemic increase of pro-inflammatory cytokines in 6/6 patients (IL-6, TNFα and IFNγ).
- **Adaptive immune activation**: Increase in tumor infiltration of CD4+ and CD8+ T-cells in 3/4 patients.
- **Clinical benefit**: Signal of clinical benefit seen in 3/6 patients after 6 months. 50% disease control rate.
CLINICAL RESPONSES IN SAFETY COHORT

Safety lead-in cohort

1st line treatment

- Stable disease
- Partial response
- Disease progression

- 50% tumor reduction (CT)
- Partial metabolic response (PET)

2nd/3rd line treatment

- Previously progressed on pem/cis in 1st line
- Stabilized tumor (CT)
- Partial metabolic response (PET)
- 9x increase in CD8+ T cells in biopsy
- MAGE-A1 activated tumor specific T cells
- 14x increase in CD4+ T cells in biopsy
ONCOS-102 in malignant pleural mesothelioma

DEVELOPMENT STRATEGY AND INDICATIVE TIMELINES

2018

Ongoing Phase I/II, randomized
30 patients

2019

Randomized ORR and OS
data 30 patients

2020

Decide on possible CPI
combination arm

2021

EMA & FDA advisory
meetings

2022

Randomized ORR and OS
data 90 patients

Future Phase III
n=TBD

Expansion of randomized Phase II
~60 additional patients (N = ~90)

Potential use as basis
for a submission for
conditional approval

Start Phase III OS trial for
full MAA
5

Summary & Closing
### R&D PIPELINE OVERVIEW AND MILESTONES

<table>
<thead>
<tr>
<th>Platform</th>
<th>Product candidate</th>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
<th>Last event</th>
<th>Next expected event</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ONCOS</strong> oncolytic adenovirus</td>
<td>ONCOS-102</td>
<td>Mesothelioma</td>
<td></td>
<td></td>
<td></td>
<td>Phase Ib safety lead-in cohort, incl. immune activation and ORR data (6 pts)</td>
<td>1H 2020 Randomized ORR data 30 pts</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Melanoma</td>
<td></td>
<td></td>
<td></td>
<td>ORR and immune activation (6 pts), 1/6 CR</td>
<td>1H 2019 ORR and immune data first cohort (n=8)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Peritoneal cancers²,³</td>
<td></td>
<td></td>
<td></td>
<td>First dose escalation cohort safety review (4 pts)</td>
<td>Update by partner, expected 2019</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Prostate³</td>
<td></td>
<td></td>
<td></td>
<td>First patient dosed</td>
<td>Update by partner, expected 2019</td>
</tr>
<tr>
<td><strong>Next-gen ONCOS</strong></td>
<td>3 viruses</td>
<td>undisclosed</td>
<td></td>
<td></td>
<td></td>
<td>Virus construct cloning and <em>in vitro</em> validation</td>
<td>2H 2019 Target disclosure and <em>in vivo</em> data</td>
</tr>
<tr>
<td><strong>TG</strong> neo-antigen cancer vaccine</td>
<td>TG01</td>
<td>Pancreatic cancer</td>
<td></td>
<td></td>
<td></td>
<td>mOS 33.4 months Demonstrated mutant RAS-specific immune activation</td>
<td>TBD</td>
</tr>
<tr>
<td></td>
<td>TG02</td>
<td>Colorectal cancer</td>
<td></td>
<td></td>
<td></td>
<td>First safety review, incl. immune activation data (3 pts)</td>
<td>1H 2019 Immune activation and mechanistic data</td>
</tr>
<tr>
<td></td>
<td>TG02</td>
<td>CPI synergy</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>1H 2019 TG02 + PD-1 combination <em>in vivo</em> data</td>
</tr>
</tbody>
</table>

1. Current standard of care chemotherapy for patients with unresectable malignant pleural mesothelioma
2. Patients with advanced peritoneal disease, who have failed prior standard chemotherapy and have histologically confirmed platinum-resistant or refractory epithelial ovarian or colorectal cancer
3. Partner sponsored trials

Ongoing partner sponsored trials
ONCOS-102 phase I/II development strategy

COVERING THE BASES

<table>
<thead>
<tr>
<th>Delivery route</th>
<th>Combination therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Local</strong></td>
<td></td>
</tr>
<tr>
<td>Intra-tumoral injection</td>
<td>✓ Chemotherapy</td>
</tr>
<tr>
<td></td>
<td>Chemotherapy</td>
</tr>
<tr>
<td></td>
<td>Cytostatics, SoC</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Compartmental</strong></td>
<td></td>
</tr>
<tr>
<td>Intra-peritoneal infusion</td>
<td>✓ Checkpoint inhibitor</td>
</tr>
<tr>
<td></td>
<td>Checkpoint inhibitor</td>
</tr>
<tr>
<td></td>
<td>PD-1 &amp; PD-L1 blockade</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Systemic</strong></td>
<td></td>
</tr>
<tr>
<td>Intra-venous infusion</td>
<td>✓ Cell therapy</td>
</tr>
<tr>
<td></td>
<td>Cell therapy</td>
</tr>
<tr>
<td></td>
<td>DC vaccine</td>
</tr>
</tbody>
</table>
Backup
Major deals over the past 6 months are driving increasing industry interest in oncolytic viruses.

<table>
<thead>
<tr>
<th>Acquirer</th>
<th>Target</th>
<th>Type of deal</th>
<th>Deal value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Boehringer Ingelheim</strong></td>
<td><strong>ViraTherapeutics</strong></td>
<td><strong>M&amp;A</strong>&lt;br&gt;Phase I/II oncolytic virus</td>
<td>USD 250m&lt;br&gt;up-front cash</td>
</tr>
<tr>
<td><strong>MERCK</strong></td>
<td><strong>Viralytics</strong></td>
<td><strong>M&amp;A</strong>&lt;br&gt;Phase I/II oncolytic virus</td>
<td>USD 400m&lt;br&gt;up-front cash</td>
</tr>
<tr>
<td><strong>Janssen</strong></td>
<td><strong>BeneVir</strong></td>
<td><strong>M&amp;A</strong>&lt;br&gt;Pre-clinical oncolytic virus</td>
<td>USD 140m&lt;br&gt;up-front cash, Up to USD 1b total value</td>
</tr>
<tr>
<td><strong>Bristol-Myers Squibb</strong></td>
<td><strong>PsiOxus Therapeutics</strong></td>
<td><strong>BD partnership</strong>&lt;br&gt;IV delivered oncolytic virus</td>
<td>USD 15m&lt;br&gt;milestone payment, Up to USD 1b total value</td>
</tr>
</tbody>
</table>
TARGOVAX HAS A SOUND FINANCIAL POSITION
with cash to complete the planned clinical program well into 2H 2019

<table>
<thead>
<tr>
<th>Operations</th>
<th>The share</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cash end of Q2 - Jun 30(^{th}) 2018</td>
<td>Market Cap - at share price NOK ~10</td>
</tr>
<tr>
<td>201 / 25</td>
<td>600 / 70</td>
</tr>
<tr>
<td>NOK million</td>
<td>USD million</td>
</tr>
<tr>
<td>Net cash flow - total Q2</td>
<td>Daily turnover - rolling 6 month avg.</td>
</tr>
<tr>
<td>-28 / -3</td>
<td>2.6 / 0.3 / 0.5</td>
</tr>
<tr>
<td>NOK million</td>
<td>USD million</td>
</tr>
<tr>
<td>Annual run rate - last four quarters</td>
<td>Analyst coverage</td>
</tr>
<tr>
<td>109 / 13</td>
<td>DNB, ABG Sundal Collier, Arctic, Redeye, Edison</td>
</tr>
</tbody>
</table>