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PLEASE JOIN US FOR OUR CAPITAL MARKETS DAY

With strong clinical data generated on ONCOS-102, Targovax is moving into late-stage clinical development. In addition, a broad pipeline of preclinical assets creates a broad horizon of opportunities in the future. Join our Capital Markets Day for more details!

DATE	Thursday, February 18, 2021
TIME	2:30 PM CET
LOCATION	Virtual event with live streaming
REPLAY	Available after the event

KOL PARTICIPANT:

Alexander N. Shoushtari, MD
Medical Oncologist,
Memorial Sloan Kettering Cancer Center

Agenda & speakers

2:30-2:40 PM	Welcome	Øystein Soug, CEO, Targovax
2:40-3:25 PM	Anti-PD1 refractory melanoma	Alexander N. Shoushtari, MD
3:25-3:45 PM	ONCOS-102 development program	Magnus Jäderberg, MD CMO, Targovax
	5-minute break	
3:50-4:05 PM	Immune activation	Victor Levitsky, PhD, CSO, Targovax
4:05-4:15 PM	Preclinical pipeline update	Victor Levitsky, PhD, CSO, Targovax
4:15-4:25 PM	4Q update	Torbjørn Furuseth, MD, CFO, Targovax
4:25 PM	Closing remarks	Øystein Soug, CEO, 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.

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Welcome

2. Anti-PD1 refractory melanoma
3. ONCOS-102 development program
4. Immune activation
5. Preclinical pipeline update
6. 4Q update
7. Closing remarks

THE IMMUNO-ONCOLOGY REVOLUTION

- **> 500,000** patients treated per year
- **> 3,000** ongoing clinical trials
- **> 40%** of US cancer patients eligible
- **> 10** approved products

SOURCE: Research&Markets; Haslam & Prasad 2019, JAMA; Vaddepally et al. 2020, Cancers

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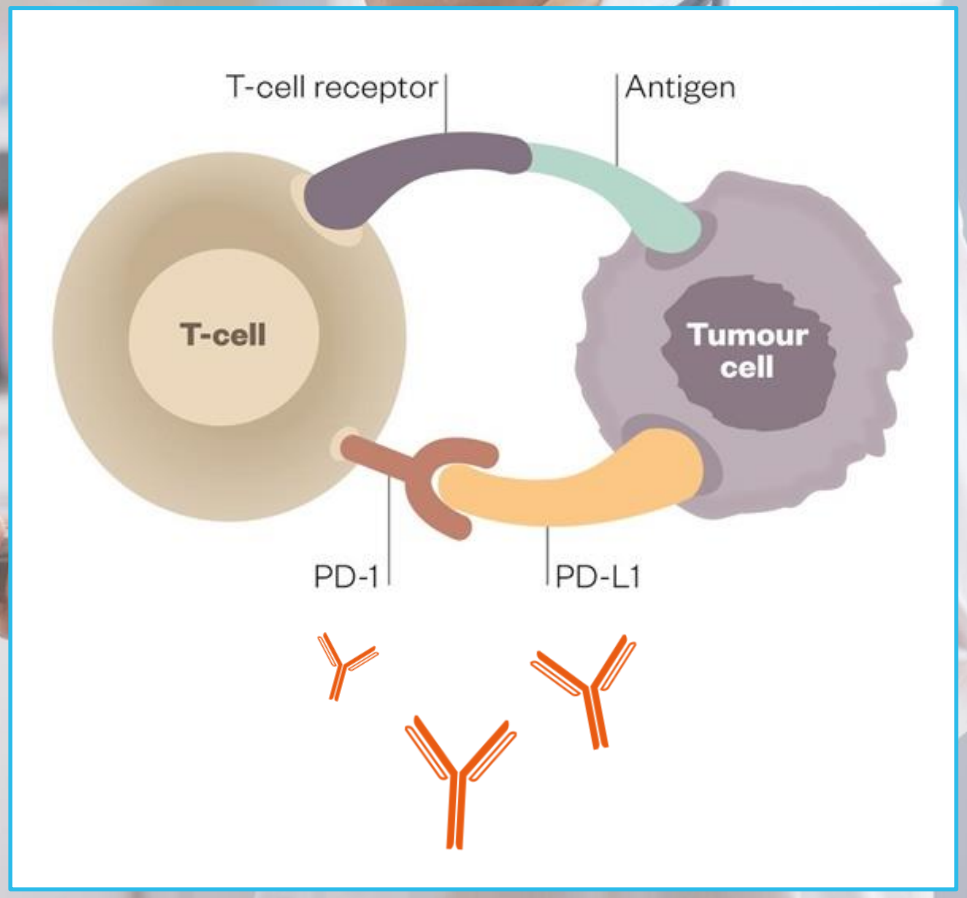
FIRST GENERATION IMMUNO-ONCOLOGY: CHECKPOINT INHIBITORS

Cornerstone of current cancer treatment

Deep and durable responses

$25b annual sales globally

7 products approved to date, many more in development



SOURCE: GlobalData, Research&Markets

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THE CHALLENGE:

MAKE PD1 CHECKPOINT INHIBITORS WORK FOR MORE PATIENTS

0-40% of treated patients respond

>50% of responding patients relapse

1 PD-1 checkpoint inhibitor monotherapy not sufficient

SOURCE: Haslam & Prasad, 2019, JAMA

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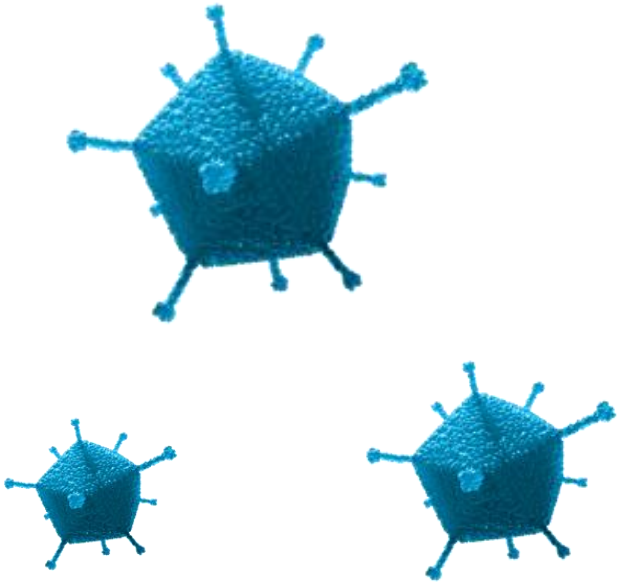
THE SOLUTION:
ONCOS-102 IMMUNE ACTIVATION

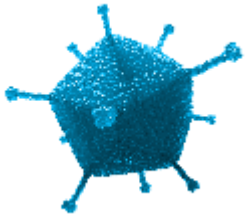


Activates the body´s own T-cells against the cancer

Unblinds the tumor to the immune system

Reverses immunosuppressive defense mechanisms in the tumor

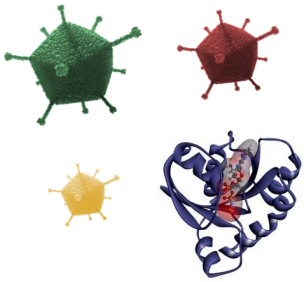
TARGOVAX AT A GLANCE



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

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CLINICAL AND PRECLINICAL PIPELINE

Product candidate	Preclinical	Phase 1	Phase 2	Collaborator
ONCOS-102	**Melanoma** Combination w/Keytruda			
	Colorectal cancer Combination w/Imfinzi			AstraZeneca CANCER RESEARCH INSTITUTE
	Mesothelioma Combination w/pemetrexed/cisplatin			MERCK
ONCOS-200 series	**Next Gen viruses**			leidos Papyrus
Novel mutRAS concepts				VALO THERAPEUTICS OBLIQUE THERAPEUTICS

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

Early-stage development

- ✓ Clinical efficacy
- ✓ Immune activation
- ✓ Well tolerated

Late-stage development

PD1 refractory melanoma

Expansion opportunities

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

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Product candidate	Preclinical	Phase 1	Phase 2	Collaborator
ONCOS-102	**Melanoma** Combination w/Keytruda			
	Colorectal cancer Combination w/Imfinzi			
	Mesothelioma Combination w/pemetrexed/cisplatin			
ONCOS-200 series	**Next Gen viruses**			
Novel mutRAS concepts				

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DR. ALEXANDER N. SHOUSHTARI, MEMORIAL SLOAN KETTERING CANCER CENTER

- Renowned expert in melanoma, with a research focus on checkpoint refractory melanomas
- Clinical Director and Assistant attending physician, Melanoma Services, Dept of Medicine, Memorial Sloan Kettering Cancer Center
- Principal investigator of several immunotherapy trials, including the ONCOS-102 phase I trial in CPI refractory advanced melanoma

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Anti-PD1 refractory melanoma

Dr. Shoushtari

3. ONCOS-102 development program
4. Immune activation
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Memorial Sloan Kettering Cancer Center™

Melanoma and oncolytic adenoviruses

Alexander Shoushtari, MD
Assistant Attending Physician
Melanoma and Immunotherapeutics Service
Memorial Sloan Kettering Cancer Center
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February 18, 2021

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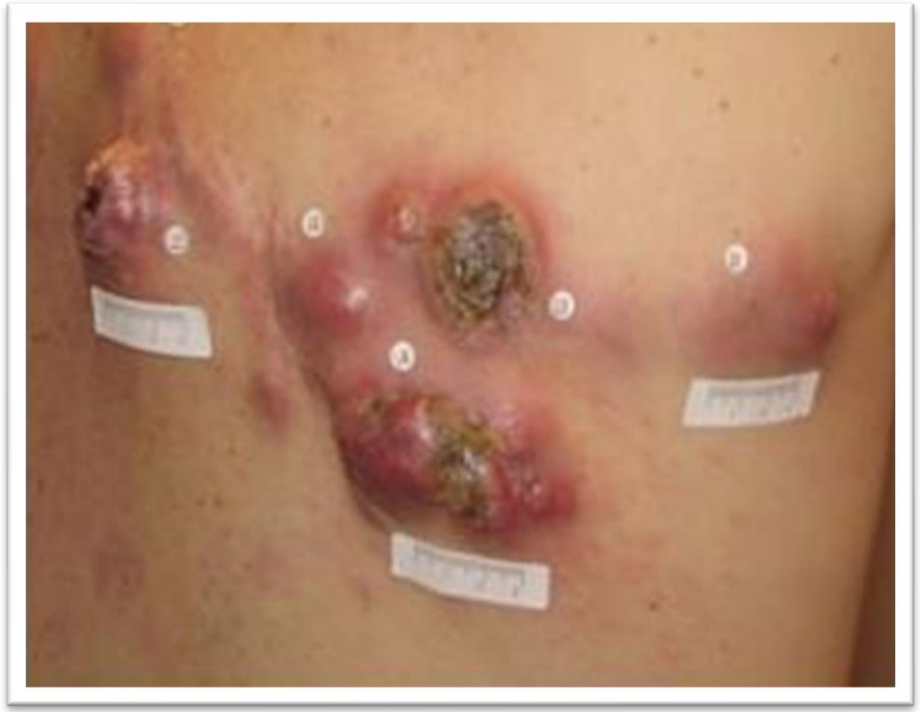
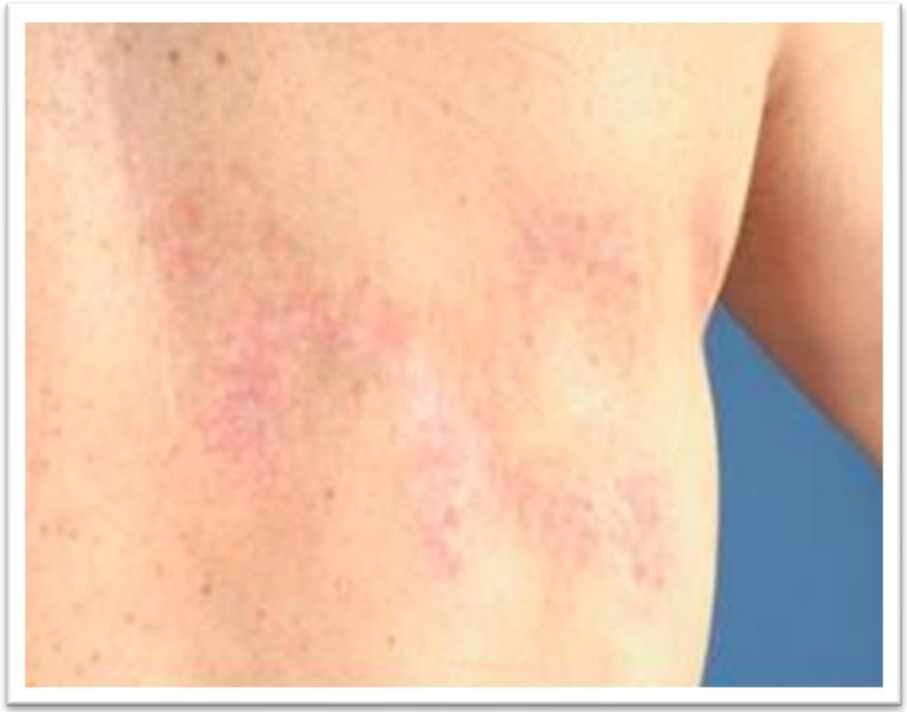
Immunotherapy has revolutionized the treatment of malignant melanoma

Real world example – Patient in an ipilimumab checkpoint inhibitor trial



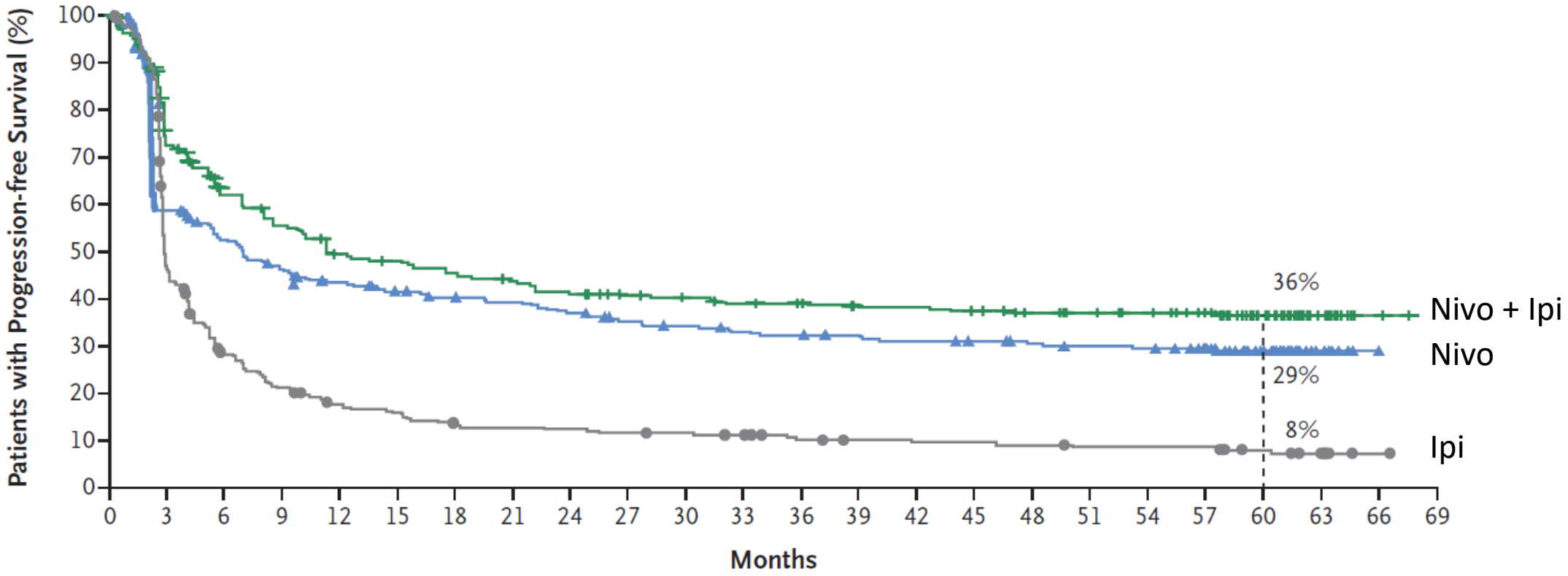
Prior to starting ipilimumab



One year of ipilimumab treatment

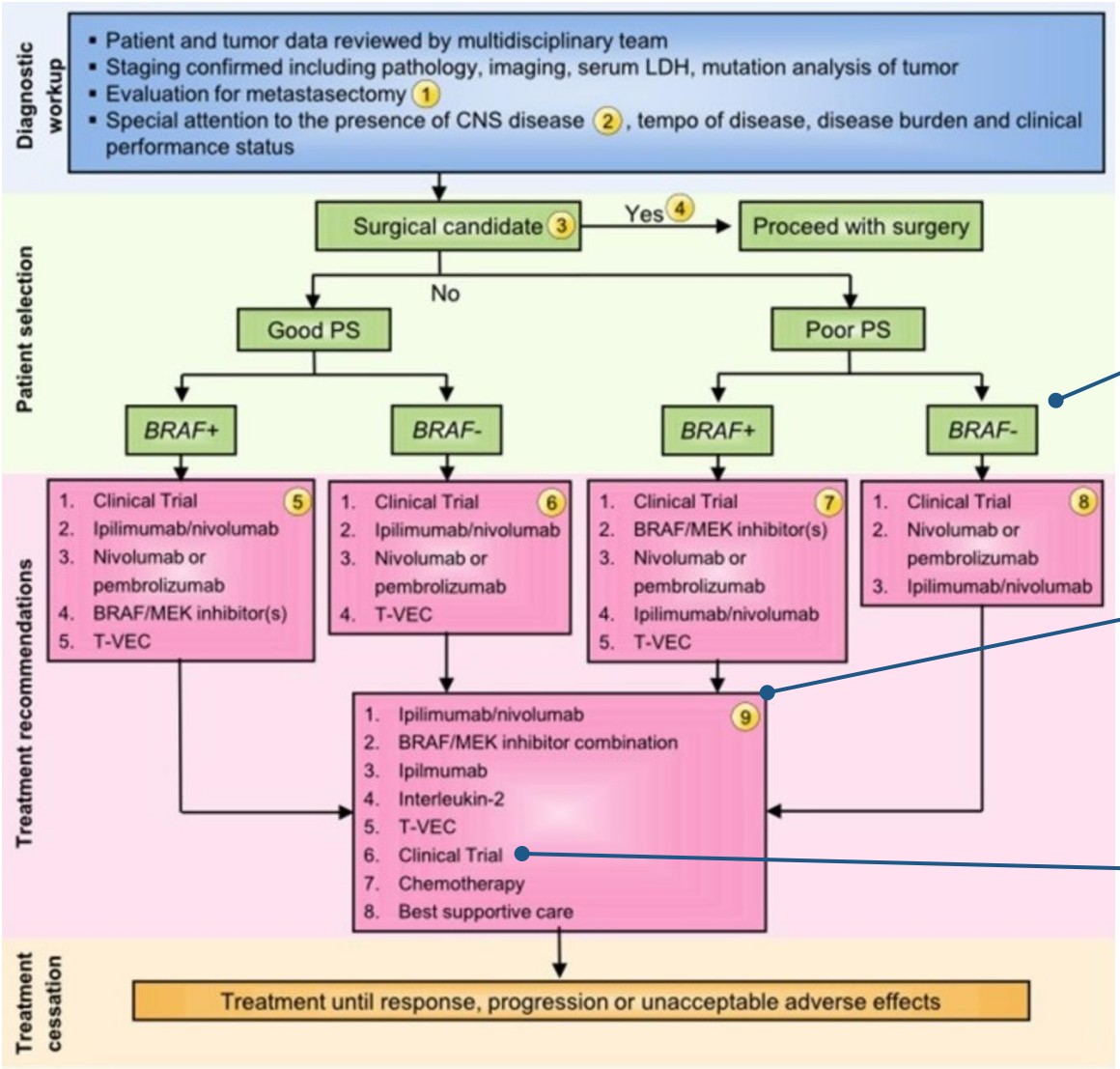
Photo courtesy Jedd Wolchok

PD-1 blockade has surpassed CTLA-4, and become the cornerstone of melanoma treatment



Source: Larkin et al, NEJM 2019

SITC treatment algorithm for late stage melanoma



Checkpoint inhibitors and BRAFi/MEKi are the mainstay frontline therapy in unresectable melanoma

Few alternatives exist following progression on CPI and/or BRAFi/MEKi

Treatment resistance – option of clinical trial or best supportive care

SOURCE: Society for Immunotherapy of Cancer (SITC)

PD-1 checkpoints are effective in melanoma

Two main checkpoint inhibitor (CPI) treatment choices

- Anti-PD-1 monotherapy: Pembrolizumab or Nivolumab
- Anti-PD-1 + anti-CTLA4 combination therapy: Nivolumab plus Ipilimumab

45 - 60% objective response rate

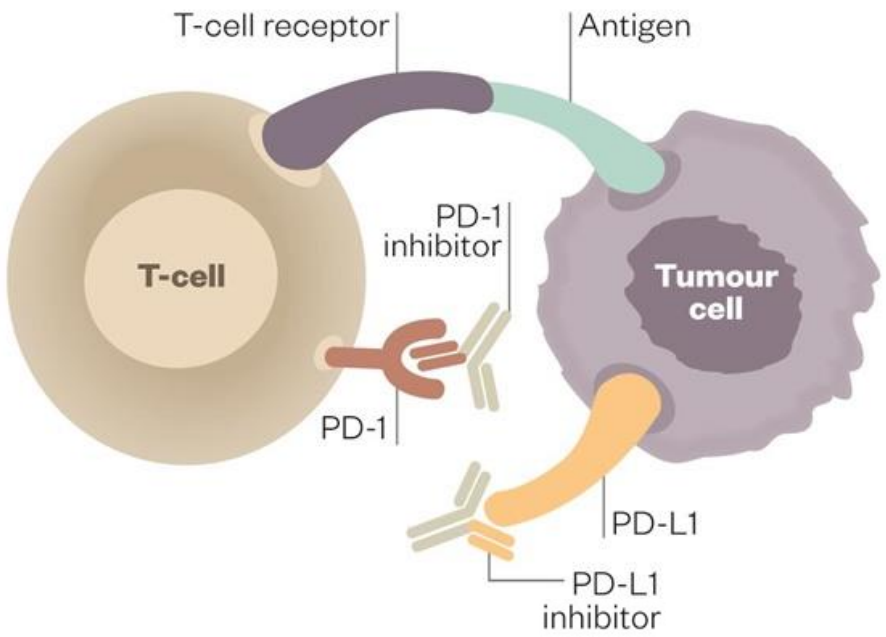
- Responses can last for years, but not forever

Overactive immune system leads to immune-related adverse events (irAEs)

- Diarrhea / Colitis
- Liver inflammation
- Pneumonitis
- Thyroid, Pituitary dysfunction

irAE rate varies by mono- versus combination CPI therapy

- PD1 monotherapy: 1 in 4 require steroids
- PD1 + CTLA4 combination: 3 in 4 require steroids



Graphic: DelveInsight

Post PD-1/CTLA4/BRAF-MEKi progression, only experimental and off-label options are available

Standard options post PD-1

After PD-1 monotherapy

- BRAF-MEK, if V600 mutant
- Nivolumab plus ipilimumab
- Ipilimumab alone
- Cytotoxic chemotherapy
- T-VEC if injectable

After PD-1/CTLA4 combination therapy

- BRAF-MEK, if V600 mutant
- Cytotoxic chemotherapy
- T-VEC if injectable

If local progression only

- Surgery
- Radiation therapy

Non-standard options post PD-1

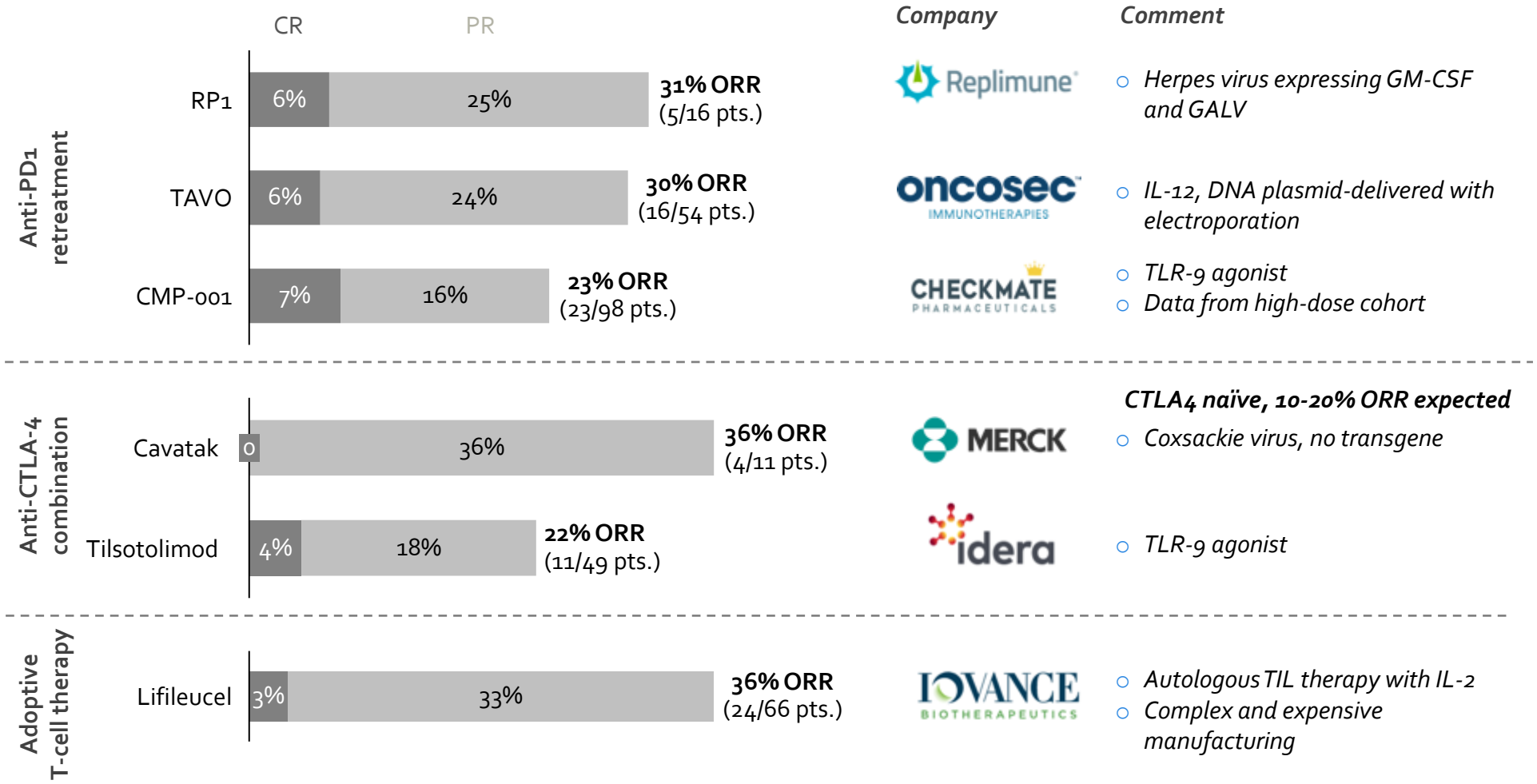
Clinical Trials (selected)

- PD-1 combination with:
  - Oncolytic virus
  - TLR9 agonist
  - LAG-3 inhibitor
  - Cytokines (IL-2, IL-12)
  - Neoantigen vaccines
  - TCR bispecifics
- Tumor Infiltrating Lymphocyte (TIL) trials

Off-label uses

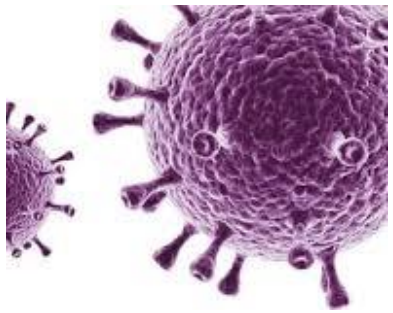
- BRAF + MEK + PD-1
- T-VEC + PD-1 inhibitor
- Radiation + PD-1 +/- Ipilimumab

Response rates reported from PD-1 checkpoint inhibitor refractory melanoma clinical trials



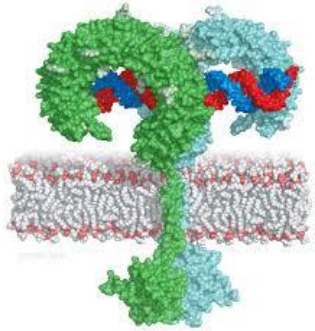
Targovax market analysis, January 2021.

Promising experimental therapies available for PD-1 resistant patients



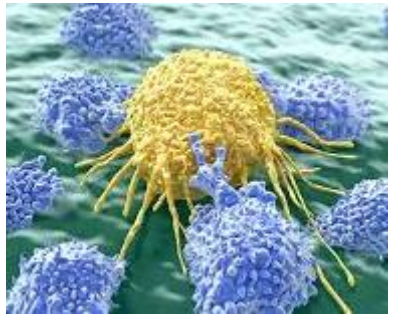
Oncolytic viruses

- Trigger oncolysis and inflammatory response via TLR-9 and other
- Reverses local immuno-suppression
- Trials ongoing in combination with PD-1 and CTLA-4



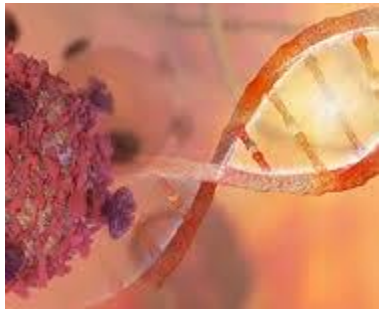
TLR-9 agonists

- Stimulate innate immune response via TLR-9 danger signaling
- Trials ongoing in combination with PD-1 and CTLA4



TIL therapy

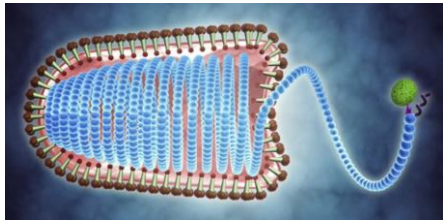
- Autologous T-cells harvested from the patient's tumor
- Combination trials ongoing with systemic immune activators (eg IL-2)
- Potentially efficacious, but significant cost and logistics hurdles

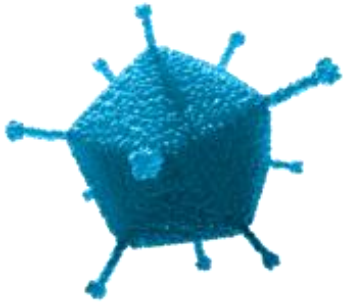


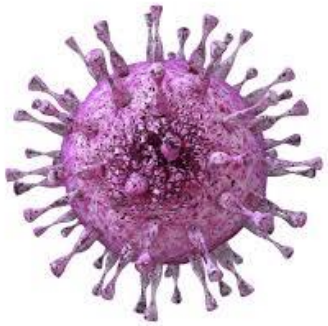
Neoantigen vaccines and TCRs

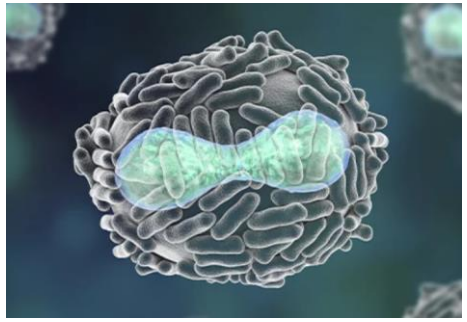
- Trigger T-cell responses to shared or personalized neoantigens
- Either personalized vaccines or shared tumor antigen approaches
- Trials ongoing with PD-1

Overview of the most common oncolytic virus classes





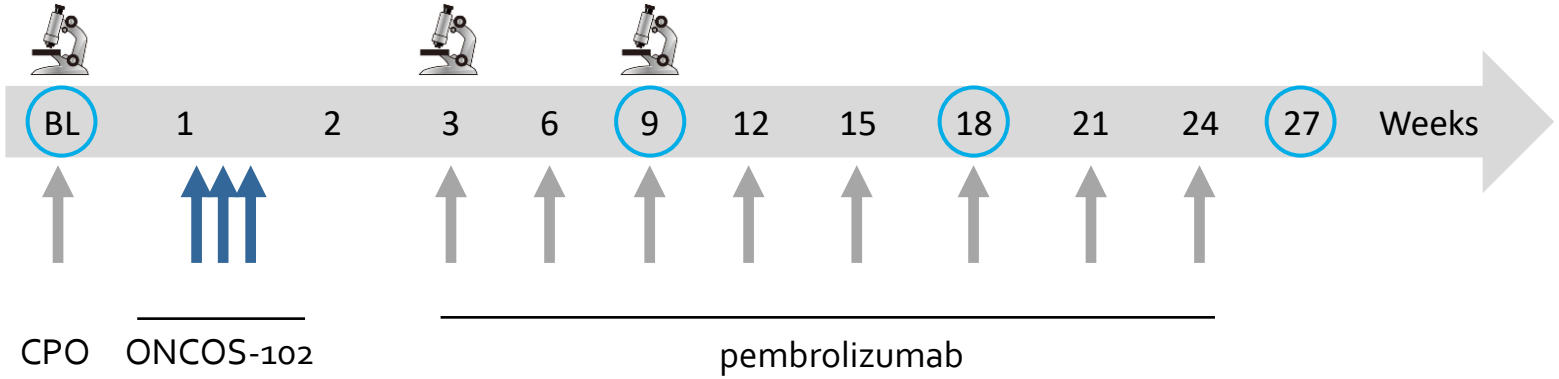




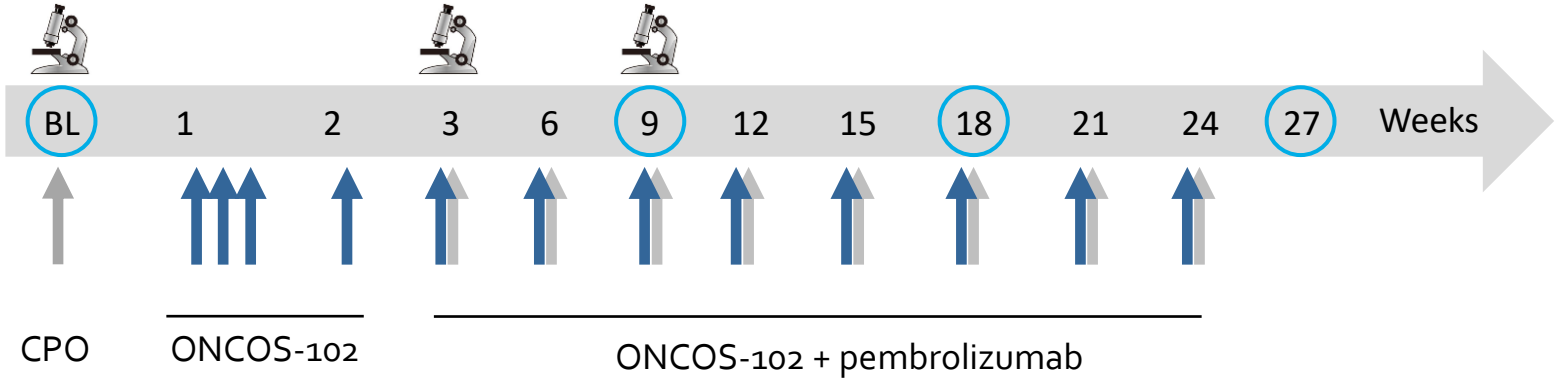
	Small RNA viruses	Adenovirus	Herpes viruses	Vaccinia virus
⊕	○ **Highly oncolytic** ○ **Highly inflammatory**	○ **Highly inflammatory** ○ **Versatile** DNA backbone	○ **Large payload** capacity ○ **Only approved** virus class	○ **Large payload** capacity ○ Used as vector for first, historic vaccines
⊖	○ **Limited payload** capacity ○ Poor stability	○ Less payload capacity than Herpes / Vaccinia	○ **Low immunogenicity** ○ Latent infection cycle	○ **Low immunogenicity** ○ Large size, high complexity
	○ Only **sporadic evidence** of clinical efficacy	○ Several candidates with **promising early data** ○ Vector for several **effective COVID-19 vaccines**	○ **Mixed recent data** ○ Imlygic **commercial failure**	○ Several recent **negative clinical trials**

Study design of ONCOS-102 phase I trial in PD1 checkpoint-refractory melanoma

Part 1 (n=8):
3x ONCOS-102 injections
Sequential treatment



Part 2 (n=12):
12x ONCOS-102 injections
Combination treatment



Imaging

Biopsy

CPO: Cyclophosphamide

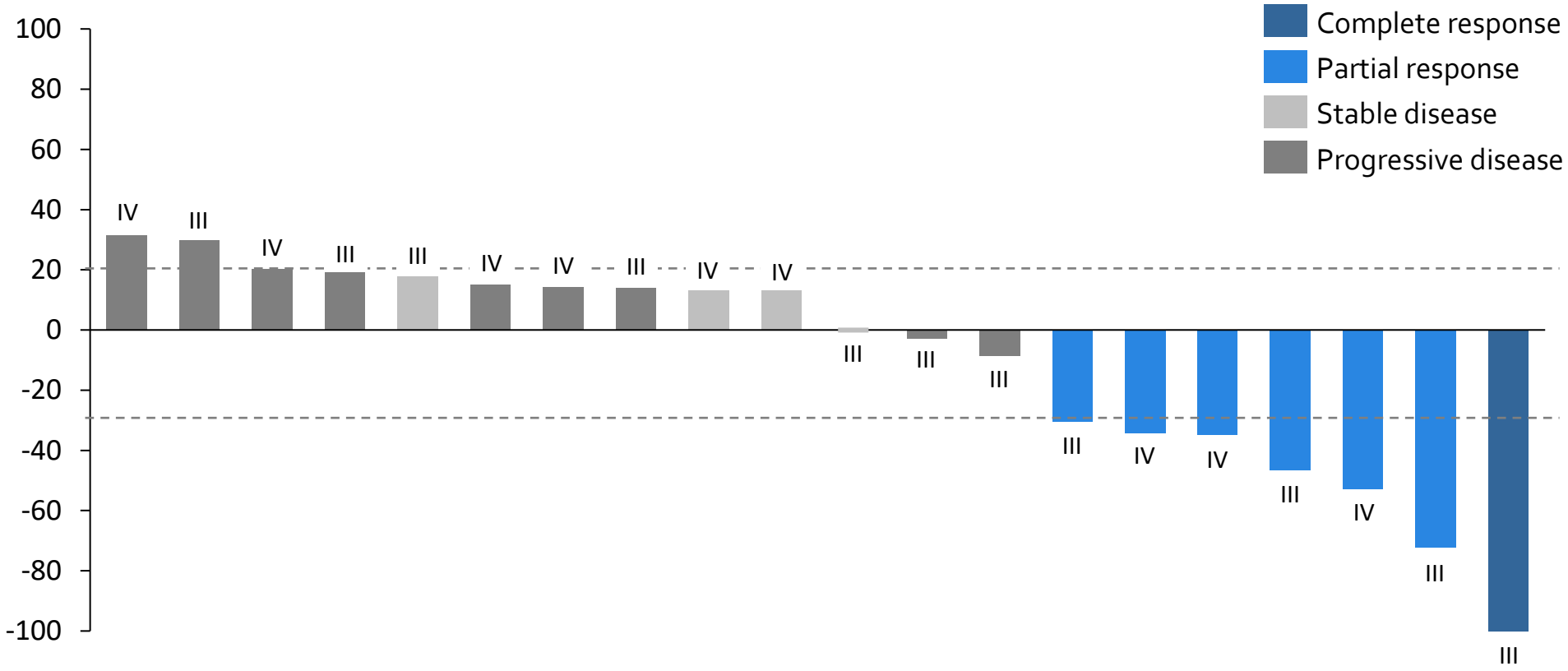
Patient and disease characteristics

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) - Surgery (average) - Treatments ex. surgery (average)	5.3 2.1 3.1	5.9 1.9 3.9	5.6 2.0 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 - Stage III - Stage IV	 6 2	 5 7	 11 9

More advanced disease in Part 2

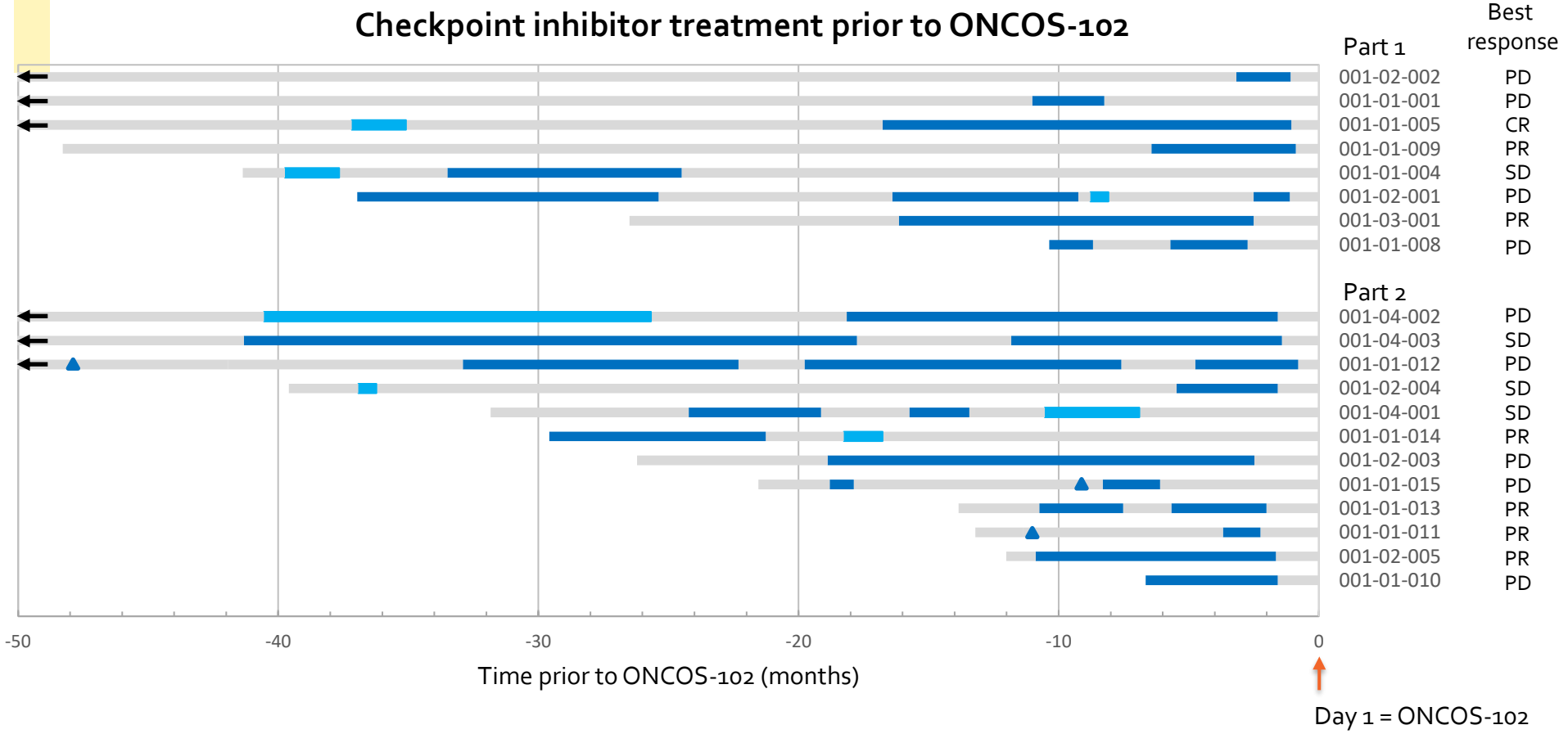
Objective responses observed in 7 out of 20 patients (35% ORR)

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

6 of 7 responders had last aPD1 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

Case example 1 – patient with complete response

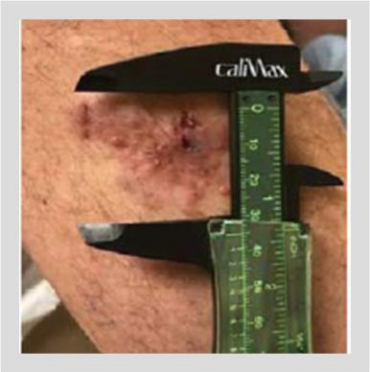
Tumor stage at enrollment: **IIIc**
T4a, N2b, M0

RECIST 1.1: CR

Prior therapies: Surgery
Radiation
Ipilimumab
Dabrafenib + Trametinib
Pembrolizumab

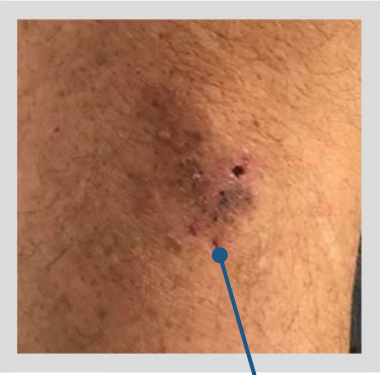
Target lesion 1 of 1

Baseline



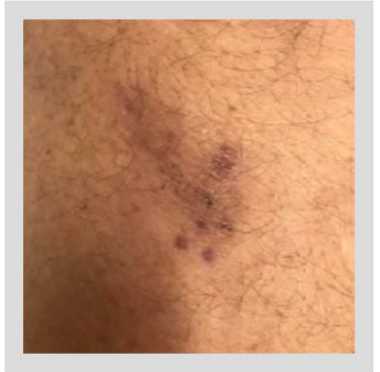
Progression on pembrolizumab

Week 3



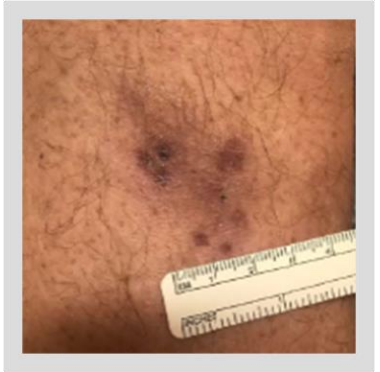
3x ONCOS-102

Week 9



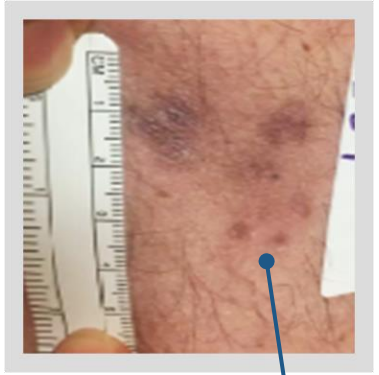
3x ONCOS-102 &
2x pembrolizumab

Week 18



3x ONCOS-102 &
5x pembrolizumab

Week 27 (EoS)



3x ONCOS-102 &
8x pembrolizumab

Tumor regression following ONCOS-102 only priming phase

Discoloring and scar tissue from injections and biopsies

Case example 2 - Patient with PR following 2 separate lines of prior PD-1 blockade

Stage IIIC at enrollment, 7 lesions in total

3 non-target lesions injected

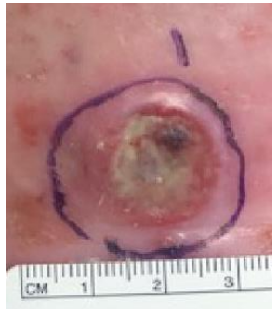
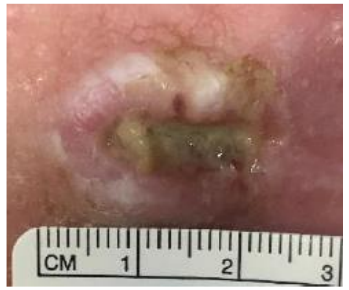
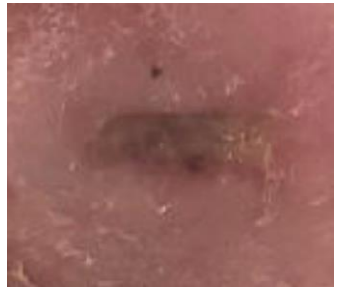
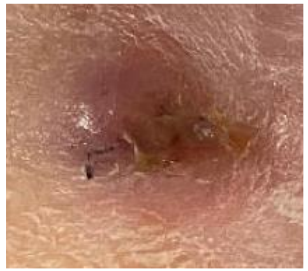
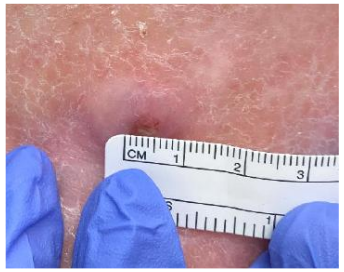
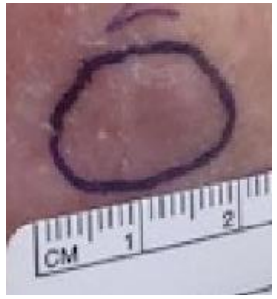
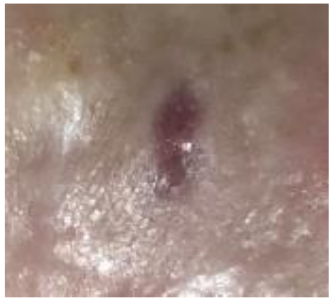
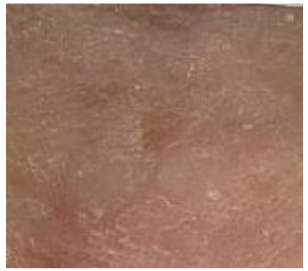
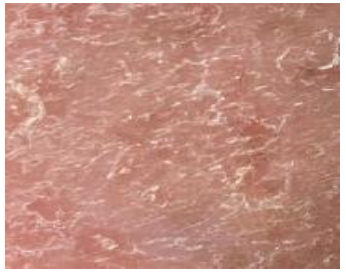
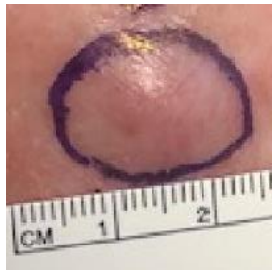
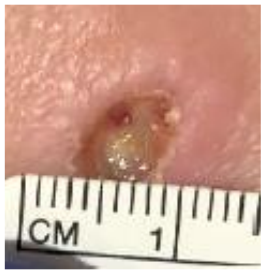
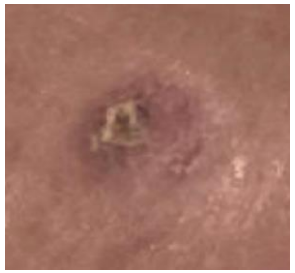
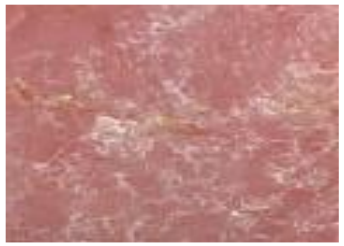
Prior therapies:
- Surgery
- Nivolumab x 2

Last aPD1 treatment 2 months before ONCOS-102

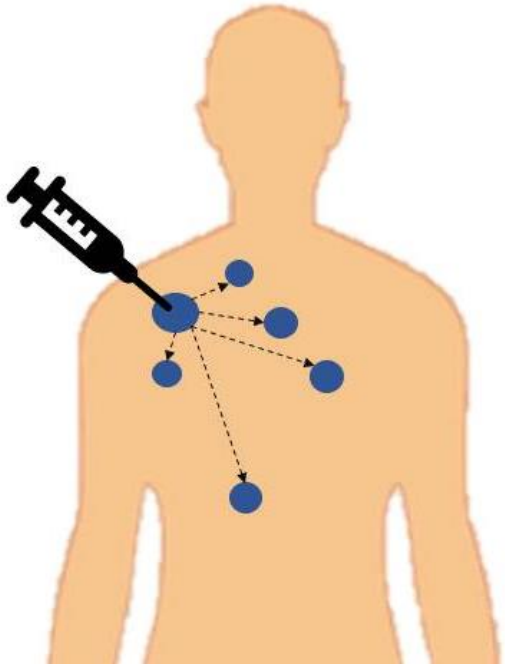
PR Week 9-27 by RECIST 1.1, no target lesions injected

Complete regression in non-injected lesion

Tumor images, 3 of 3 injected lesions

	Baseline	*Week 3*	*Week 9*	*Week 18*	*Week 27 (EoS)*
Lesion 1 of 3					
Lesion 2 of 3					
Lesion 3 of 3					
	Progression on nivolumab	4x ONCOS-102 only	6x ONCOS-102 & 1x pembrolizumab	8x ONCOS-102 & 2x pembrolizumab	11x ONCOS-102 & 4x pembrolizumab

Evidence of systemic (abscopal) effect – responses observed in several non-injected lesions



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

ONCOS-102 and the combination with pembrolizumab is safe and well tolerated

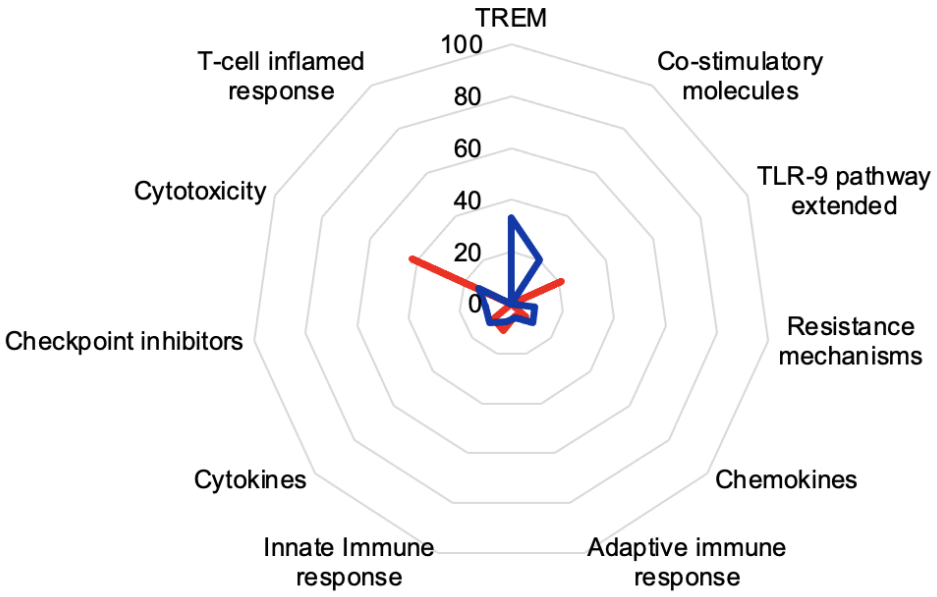
Adverse Event, Preferred term	Subjects, n	Events, n	Grade 1 / 2 events	Grade 3	Grade 4
AEs related to ONCOS-102 +/- CPO					
Pyrexia	10	24	24	-	-
Chills	9	23	23	-	-
Nausea	6	10	10	-	-
Injection site pain	4	6	6	-	-
Myalgia	3	6	6	-	-
Rash maculo-papular	4	5	5	-	-
Fatigue	5	5	5	-	-
Vomiting	4	4	4	-	-
Diarrhoea	3	4	4	-	-
Injection site reaction	3	3	3	-	-
Alanine aminotransferase increased	2	2	2	-	-
Hypotension	2	2	2	-	-
Pruritus	2	2	2	-	-
Large intestine infection	1	1	-	1	-
AEs related to ONCOS-102 + pembrolizumab +/- CPO					
Aspartate aminotransferase increased	2	4	4	-	-
Pyrexia	3	3	3	-	-
Alanine aminotransferase increased	1	3	3	-	-
Blood alkaline phosphatase increased	1	2	2	-	-
Diabetic ketoacidosis	1	1	-	-	1
Type 1 diabetes mellitus	1	1	-	-	1

For Grade 1 and 2 adverse events only 2 events and more are listed. No Grade 5 events occurred

Broad and persistent modulation of immune-related gene expression observed in Part 2 of the trial

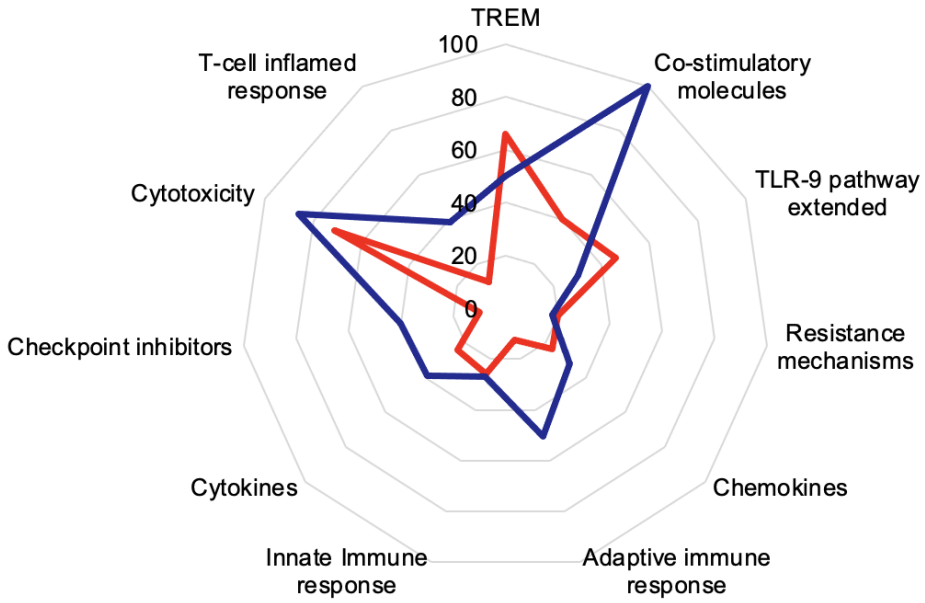
Modulation of gene expression following ONCOS-102 treatment; % modulated genes

Day 22 vs. Baseline
Day 64 vs. Baseline



Part 1

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

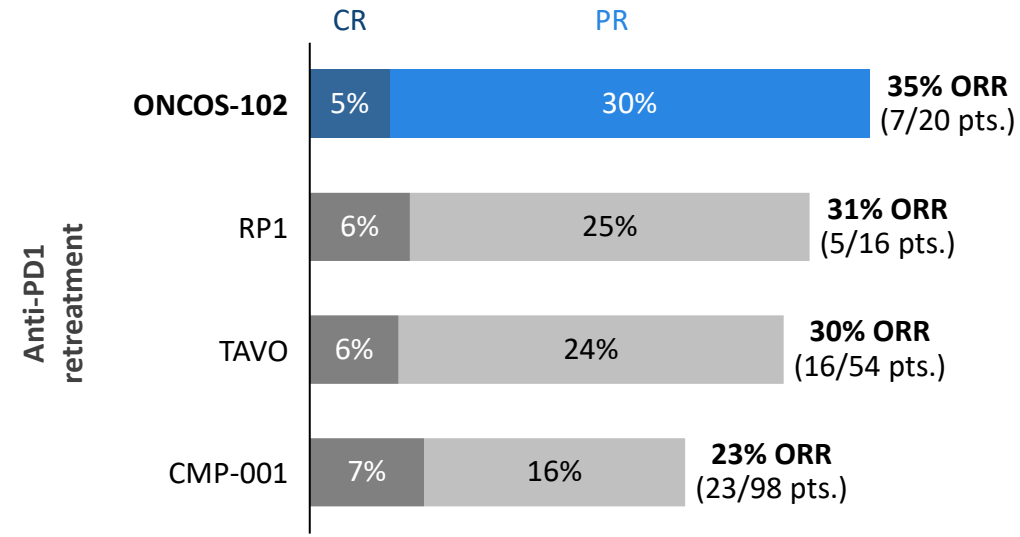


Part 2

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

TREM: Triggering Receptor Expressed on Myeloid cells

ONCOS-102 + Keytruda data compares well to previous reports in PD-1 refractory melanoma



Company	Comment
targovax	○ *Adenovirus expressing GM-CSF*
Replimune	○ *Herpes virus expressing GM-CSF and GALV*
oncosec IMMUNOTHERAPIES	○ *IL-12, DNA plasmid-delivered with electroporation*
CHECKMATE PHARMACEUTICALS	○ *TLR-9 agonist* ○ *Data from high-dose cohort*
MERCK	***CTLA4 naïve, 10-20% ORR expected*** ○ *Coxsackie virus, no transgene*
idera	○ *TLR-9 agonist*
IOVANCE BIOTHERAPEUTICS	○ *Autologous TIL therapy with IL-2* ○ *Complex and expensive manufacturing*

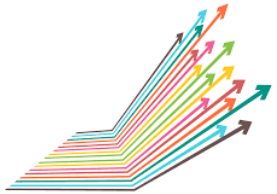
Targovax market analysis, January 2021.

Successful ONCOS-102 phase I trial warrants further development of PD1 combination

Safety

- ONCOS-102 is well-tolerated, with no safety concerns
- Combines well with pembrolizumab, including concomitant dosing

Immune activation

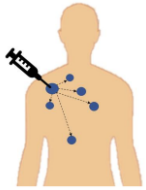


- Broad and general immune activation pattern observed in ONCOS-102 injected lesions
- Deeper biomarker and mechanistic analyses ongoing

Clinical efficacy

- Class-leading ORR of 35%
- Several responses in stage IV metastatic patients

Systemic effect



- Evidence of systemic effect in 20% of patients
- Non-injected lesion completely regressed in two patients

Melanoma: Small indication, but influential

- We usually set trends followed by the bigger histologies

- Easily accessible tissue
- Relatively aggressive disease
- Hot (cutaneous) vs cold (uveal) vs mixed (mucosal) models
- Patient buy-in for biomarker heavy trials

What is next in melanoma? Ongoing trials and new combinations to watch

	Example compounds	Trials to watch
Novel immune checkpoint inhibitors	Anti-LAG-3, TIM-3, TIGIT	○ LAG-3 relatimab in combination with Nivolumab in stage IV IO naïve melanoma ○ TIM-3 mono and in combination with anti-PD-1 in IO pretreated stage IV melanoma
Oncolytic viruses	T-VEC, Cavatak, LoAd-703, ONCR-177, ONCOS-102	○ Several T-Vec trials (recently failed 1L phase III for futility) ○ Cavatak phase II 1L combination with Keytruda ○ Phase I/II - RP1 w/Opdivo, LoAd-703 w/Tecentriq
Immune stimulatory agents	TLR9, CD40, OX40, IL-2, IL-12	○ CMP-001 in PD-1 refractory, phase II combination w/Keytruda ○ Tilsotolimod in PD-1 refractory, phase III combination w/Yervoy ○ TAVO IL-12 plasmid in PD-1 refractory w/Keytruda ○ Bempegaldesleukin + nivolumab in 1L, phase III (CA045-001)
Anti-VEGFR	Lenvatinib	○ Combination with aPD1 in several melanoma patient populations ○ Phase II trial in PD-1 refractory setting
BRAFi/MEKi	Mekinist, Tafinlar	○ MEKi/BRAFi in combination with pembrolizumab in 1L BRAF V600E melanoma
TIL therapy	Lifileucel	○ TIL therapy in several melanoma patient populations ○ Pivotal phase II trial in PD-1 refractory setting

First Line Trials in Melanoma: Big Ones

Randomized, PD-1 +/- XYZ

- **LAG-3**: Nivolumab +/- Relatlimab (NCT03470922)
- **IL-2 directed**: Nivolumab +/- BEMPEG (NCT03635983)
- **VEGF**: Pembrolizumab +/- Lenvatinib (NCT03820986)

BRAF-MEK +/- PD-1: Enco-Bini-Spartalizumab (NCT02967692)

T-VEC: Pembrolizumab +/- T-Vec recently failed phase III for futility

First Line Trials in Melanoma: Big Ones

- **Large, randomized trials, 500-700+ patients**
- What do we need for a new standard?
  - **Overall Survival (OS)**, not just PFS and ORR
  - Tolerability
  - Schedule / ease of use
- We are a **few years away** from making a new frontline standard
- Existing frontline treatment is tolerable, relatively easy, and can be durable

Post PD-1 Trials: Trends

- Critical need to develop new treatments, but it's getting harder to do it well

- Rigidly defining "PD-1 resistance"
- Slowly relaxing prior toxicity requirements (…too slowly)
- Highly selective trials (e.g. lifileucel)
- The specter of ipilimumab: 20% ORR, durability
- Single arm ORR or Randomized Trials

Thanks!

2020 MSKCC Melanoma Disease Management Group

3

ONCOS-102 development program

4. Immune activation
5. Preclinical pipeline update
6. 4Q update
7. Closing remarks

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

Early-stage development

- ✓ Clinical efficacy
- ✓ Immune activation
- ✓ Well tolerated

Late-stage development

PD1 refractory melanoma

Expansion opportunities

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

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CHECKPOINT INHIBITORS IN THE CLINIC

Huge impact since the launch of Yervoy in 2011

- aPD1 standard of care in several solid tumor indications
- Varying response rates
  - Melanoma ca. 40% ORR
  - Lung ca. 30% ORR
  - Head & Neck ca. 20% ORR

CPI refractory cancer is a significant medical need

- Primary refractory disease: change/add CPI 10-20% ORR
- Secondary refractory disease: repeat CPI <10% ORR

Most patients don't respond to CPIs even after adding/changing CPI

- Growing trend – improve response to checkpoint inhibitors by adding immune activating agents (e.g., ONCOS-102)

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PD1 REFRACTORY MELANOMA MARKET OPPORTUNITY

Incidence	~100.000 new stage III/IV cases of malignant melanoma per year in the major markets
Unresectable	~50% recur and become unresectable Total **~50.000 patients per year**
PD1 resistance	~50% of cases become PD resistant Total **~25.000 patients per year**
Addressable	**Estimated 10.000 - 20.000 patients per year** addressable with intra-tumoral therapies
Other PD1 resistance	>100.000 patients per year lung cancer >50.000 patients per year head and neck

SOURCE: GlobalData, Targovax analysis

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
	Melanoma Combination w/Keytruda			
ONCOS-102	**Colorectal** cancer Combination w/Imfinzi			
	Mesothelioma Combination w/pemetrexed/cisplatin			
ONCOS-200 series	**Next Gen viruses**			
Novel mutRAS concepts				

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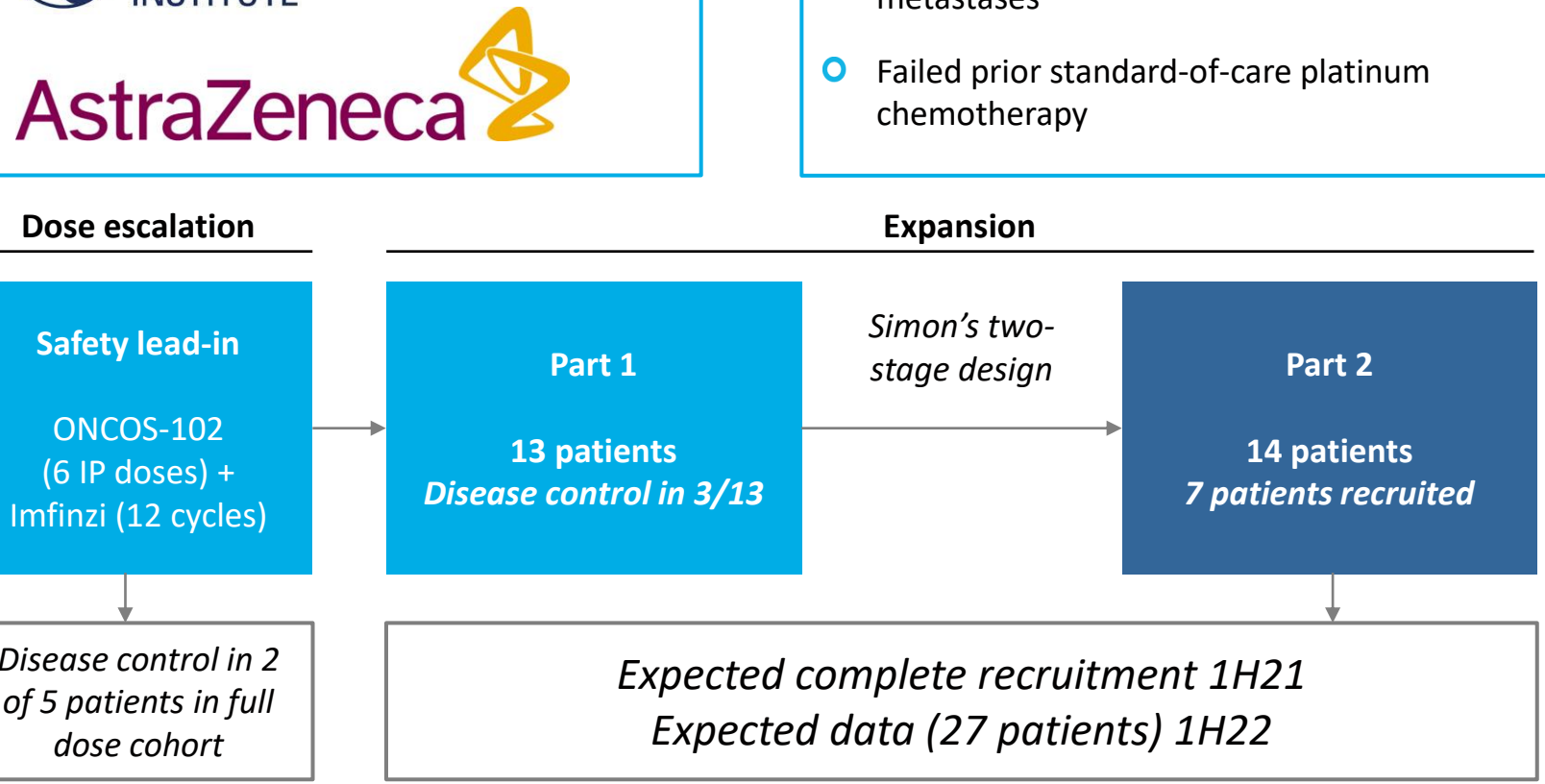
COLLABORATION IN COLORECTAL CANCER WITH

PHASE 1/2 TRIAL COMBINING ONCOS-102 AND IMFINZI



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ONCOS-102	**Mesothelioma** Combination w/pemetrexed/cisplatin			
ONCOS-200 series	Next Gen viruses			
Novel mutRAS concepts				

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ADVANCED MALIGNANT PLEURAL MESOTHELIOMA

PHASE 1/2 TRIAL IN COMBINATION WITH CHEMO

Trial design

- 1st and 2nd line
- Standard of Care (SoC) pemetrexed/cisplatin +/- ONCOS-102

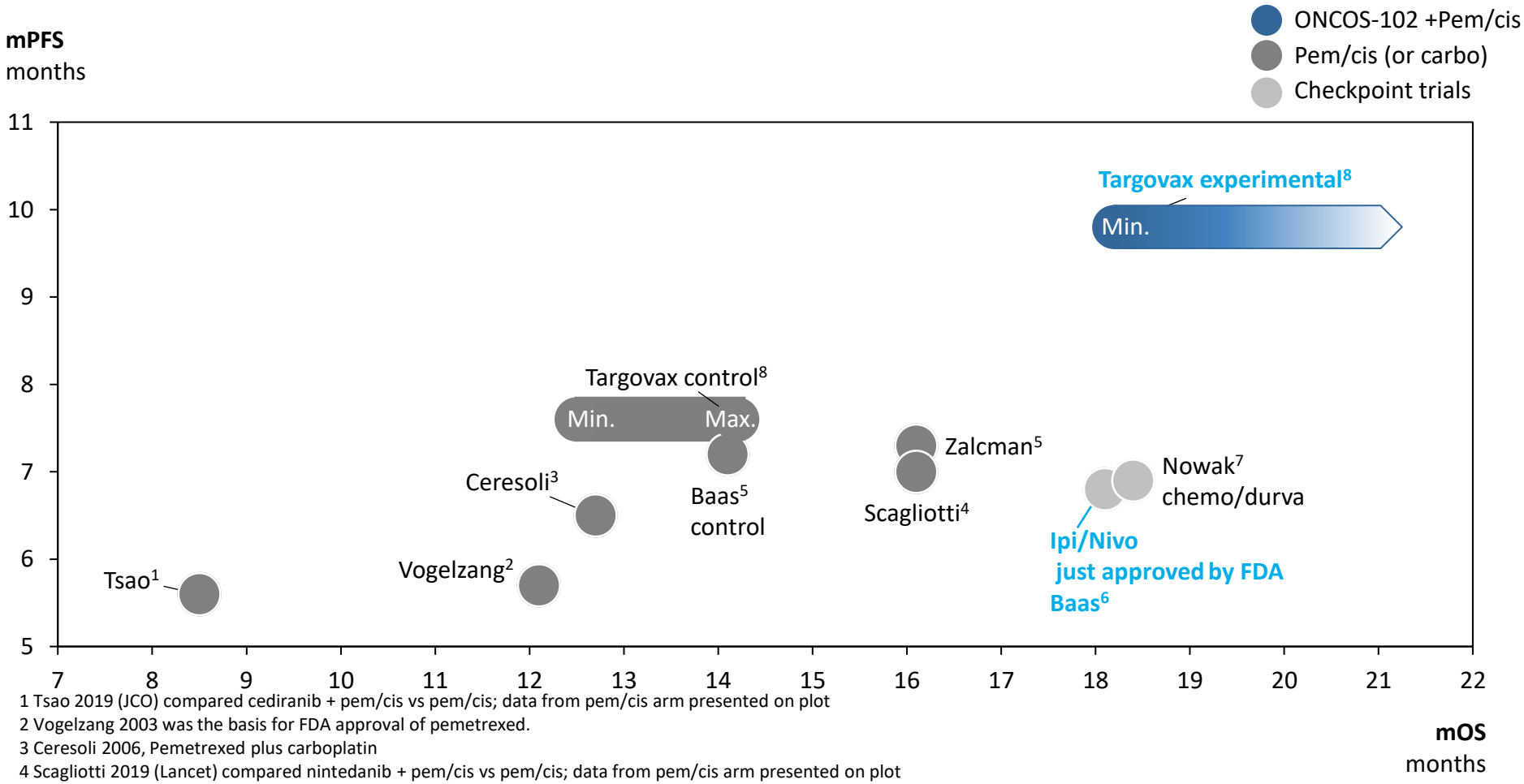
Safety lead-in
n=6
ONCOS-102 plus SoC Chemo

Randomized

Experimental group
n=14
ONCOS-102 plus SoC Chemo

Control group
n=11
SoC Chemo only

CLINICAL OUTCOMES IN 1ST LINE COMPARE FAVORABLY TO HISTORICAL CONTROL



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 1st 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

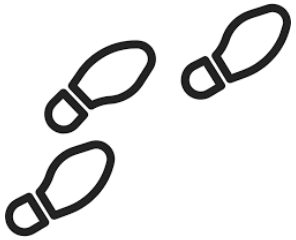
FAST TRACK DESIGNATION AND EVOLVING SURVIVAL DATA PROVIDE OPPORTUNITIES

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

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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**

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CLINICAL AND PRECLINICAL PIPELINE

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

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4

Immune activation

5. Preclinical pipeline update
6. 4Q update
7. Closing remarks

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THE IMPORTANCE OF IMMUNOLOGICAL READ-OUTS

Function

- Understand **mechanism-of-action** of ONCOS-102
- Confirm **delivery** of ONCOS-102 into the tumor

Power

- **Strength** of immune responses
- **Breadth** of immunological **remodelling**

Duration

- **Persistence** of the immune response
- **Optimize dosing** and scheduling

Impact

- **Association** between immune response and **improved clinical outcome**

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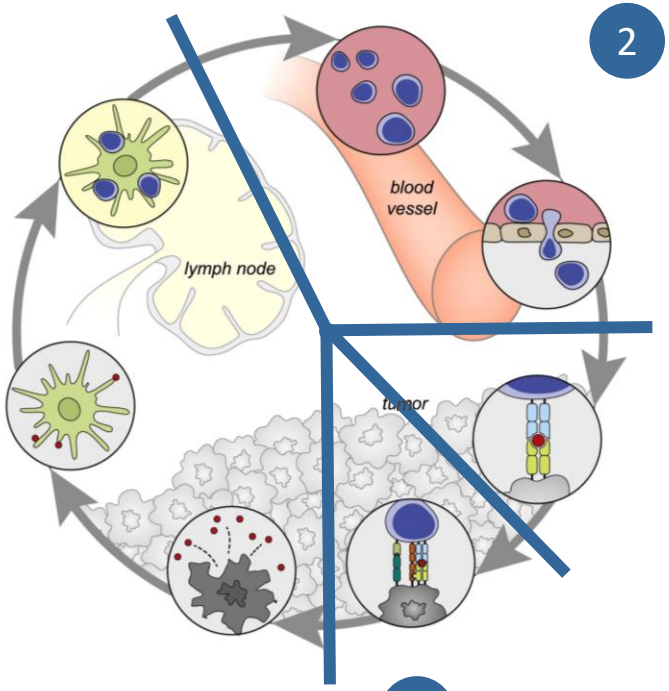
FOUR CRITICAL PHASES OF TUMOR-SPECIFIC IMMUNE RESPONSE

1 Access to tumor antigens, cross-presentation by APCs and priming of T-cells

2 T-cell migration and infiltration into the tumor



3 Expansion and survival of T-cells in the tumor

4 Tumor cell recognition and elimination

Adapted from Chen & Mellman, Immunity 2013

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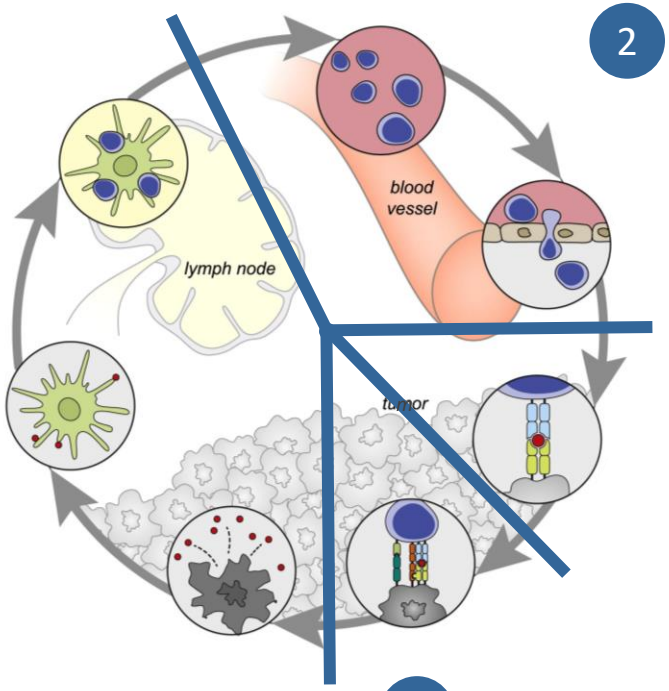
FOUR CRITICAL PHASES OF TUMOR-SPECIFIC IMMUNE RESPONSE

1 Access to tumor antigens, cross-presentation by APCs and priming of T-cells

Problem: *Low tumor immunogenicity and ineffective T-cell priming*



2 T-cell migration and infiltration into the tumor

Problem: *T-cells do not reach the tumor*

3 Expansion and survival of T-cells in the tumor

Problem: *Exhaustion of T-cells in the tumor*

4 Tumor cell recognition and elimination

Problem: *Immunosuppression in the tumor*

Adapted from Chen & Mellman, Immunity 2013

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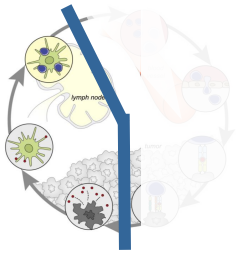
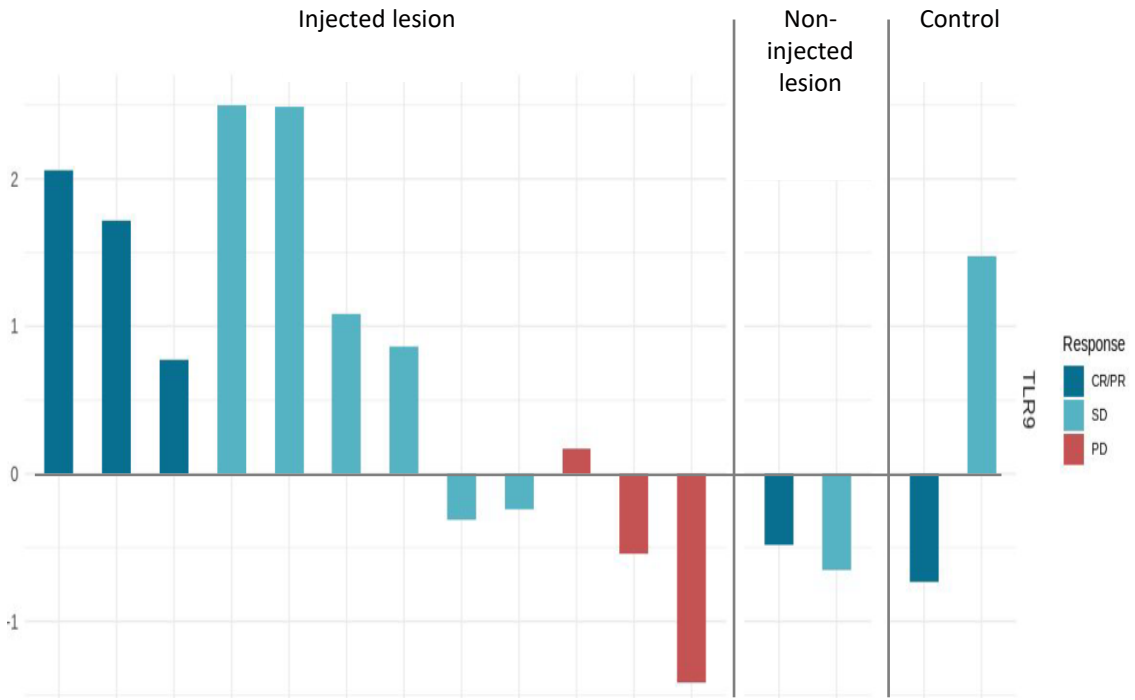


ONCOS-102 ACTIVATES DANGER SIGNALING: MESOTHELIOMA

TLR9 expression in tumor RNAseq -fold change D36 vs. baseline[1], mesothelioma



1 Unpublished company data

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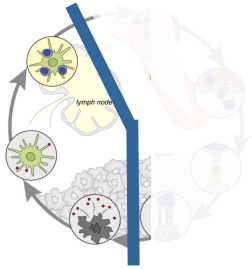
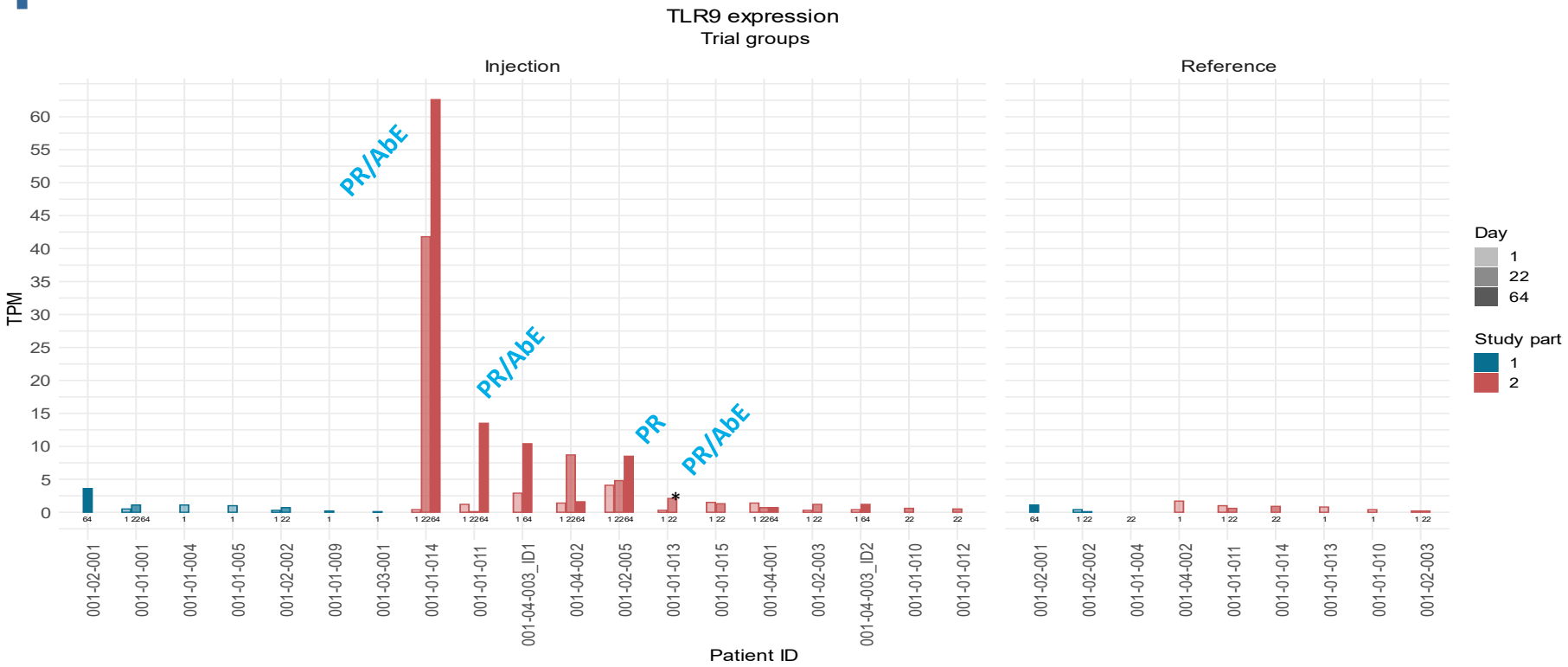


ONCOS-102 ACTIVATES DANGER SIGNALING: MELANOMA



* 001-01-13 – no data for Day 64

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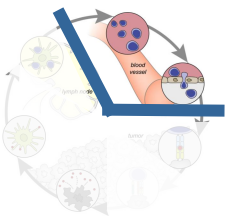
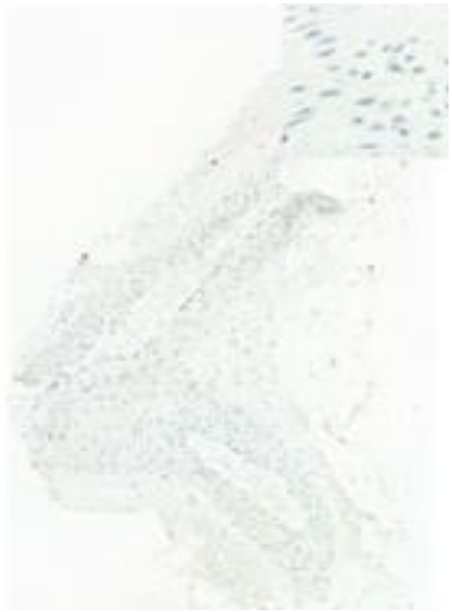


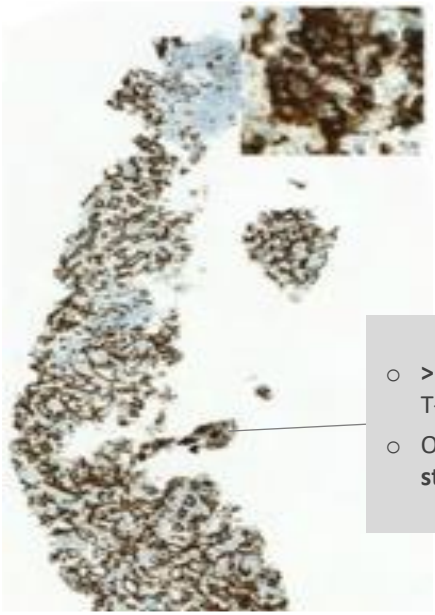
ROBUST INCREASE OF TUMOR INFILTRATION BY T-CELLS FOLLOWING ONCOS-102 TREATMENT

ONCOS-102 induced tumor T-cell infiltration
Ovarian cancer patient case example, monotherapy

Tumor biopsy mIHC – CD8+ T-cells



Pre-treatment
Baseline



Post-treatment
Week 8

- **>1000-fold increase** of CD8+ T-cells in tumor
- Ovarian cancer patient – **stable disease for three years**

Ranki et al. JITC 2016

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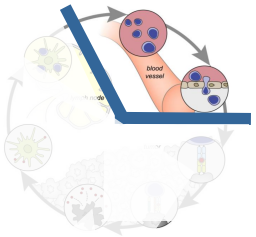
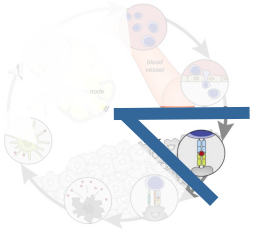
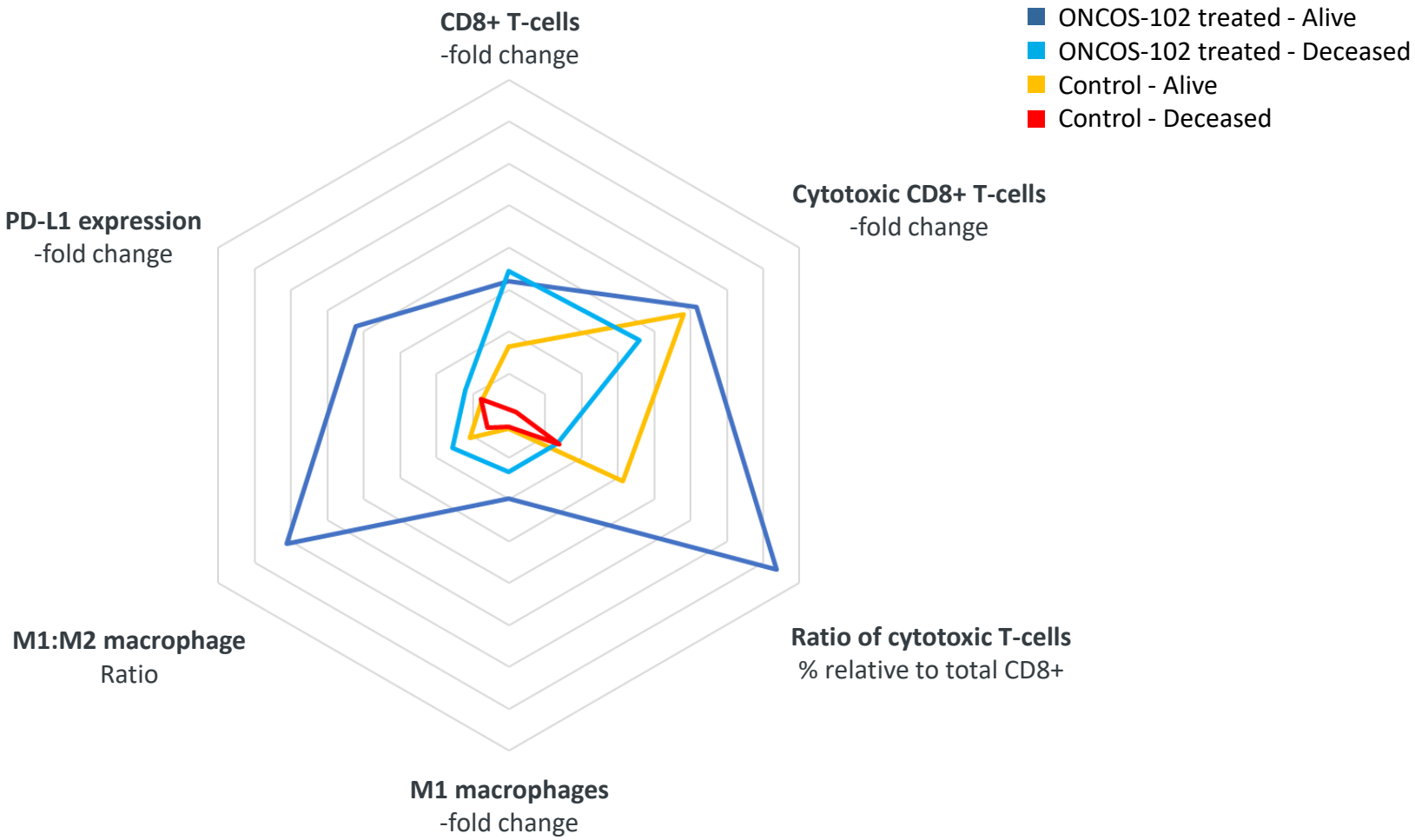




ROBUST INCREASE IN T-CELL TUMOR INFILTRATION FOLLOWING ONCOS-102 TREATMENT: MESOTHELIOMA



Unpublished company data

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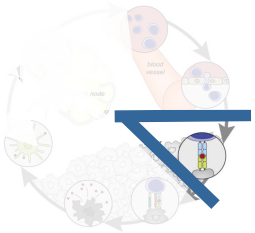
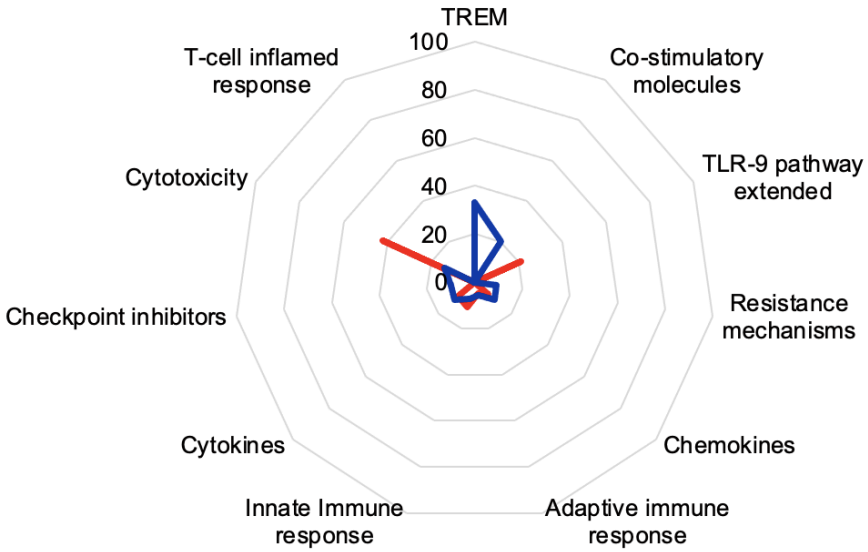


IMMUNE-PERMISSIVE RESHAPING OF TUMOR MICROENVIRONMENT BY ONCOS-102: MELANOMA

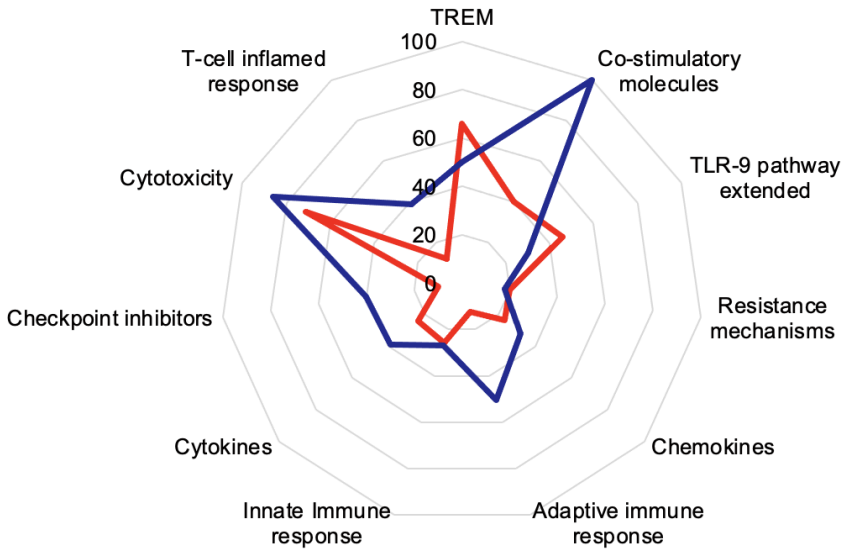
Modulation of gene expression; Fraction (%) of genes modulated within the indicated gene groups

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)

Unpublished company data

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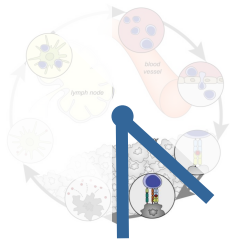
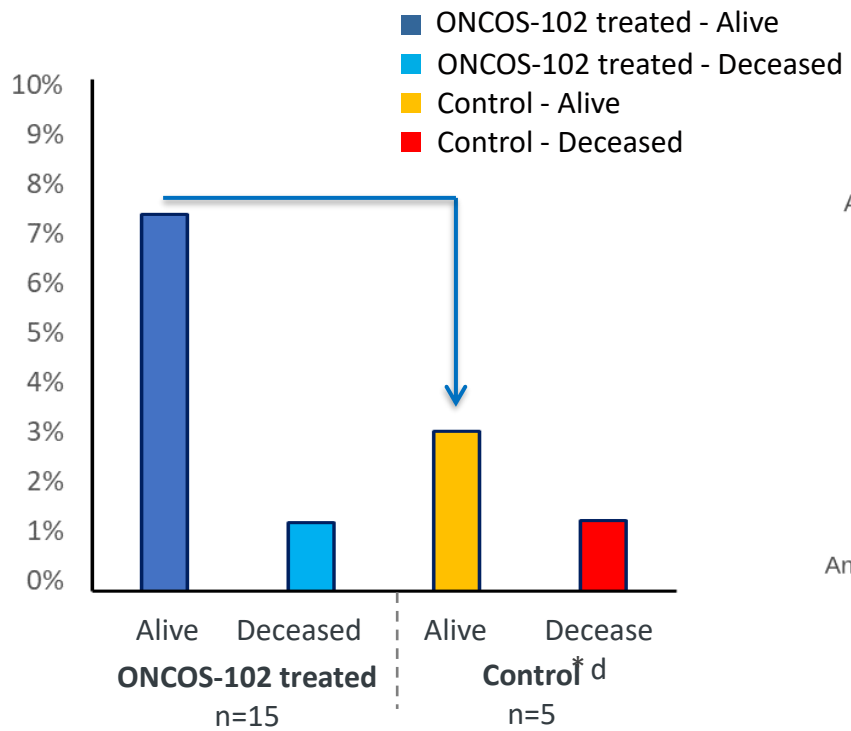
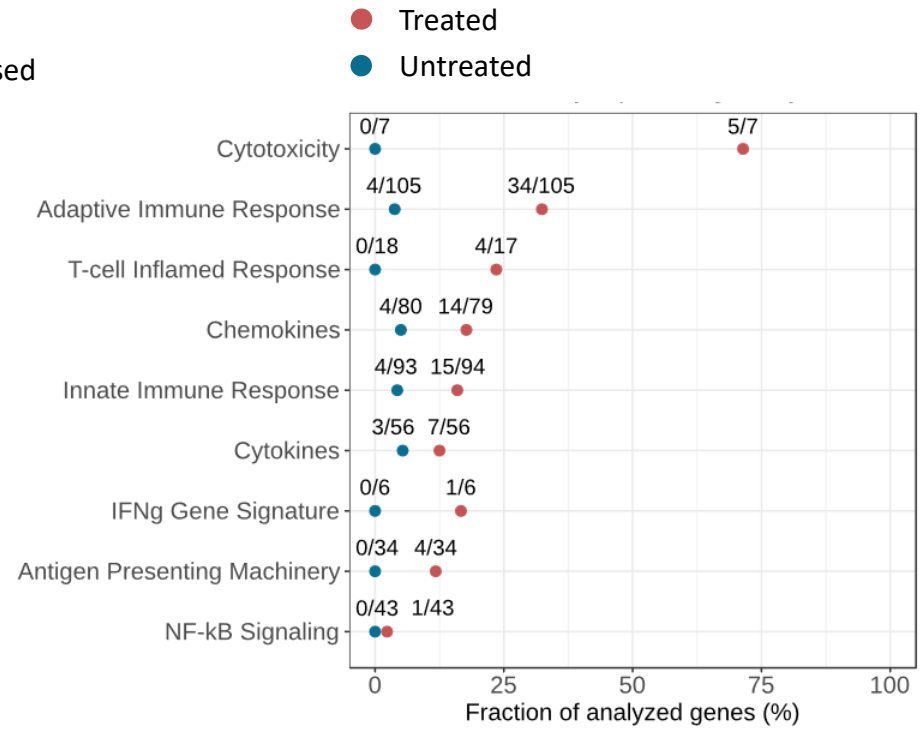


ONCOS-102 TREATMENT INCREASES CYTOTOXIC POTENTIAL OF INTRATUMORAL T-CELLS: MESOTHELIOMA

Relative level of cytotoxic GrB+ / CD8+ T-cells at day 36
Alive vs. deceased at 12 months, mesothelioma



Modulation of tumor gene expression, Fraction of genes
ONCOS-102 treated vs. untreated, mesothelioma



Unpublished company data
* Control patients treated with standard-of-care chemotherapy

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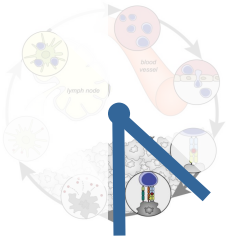
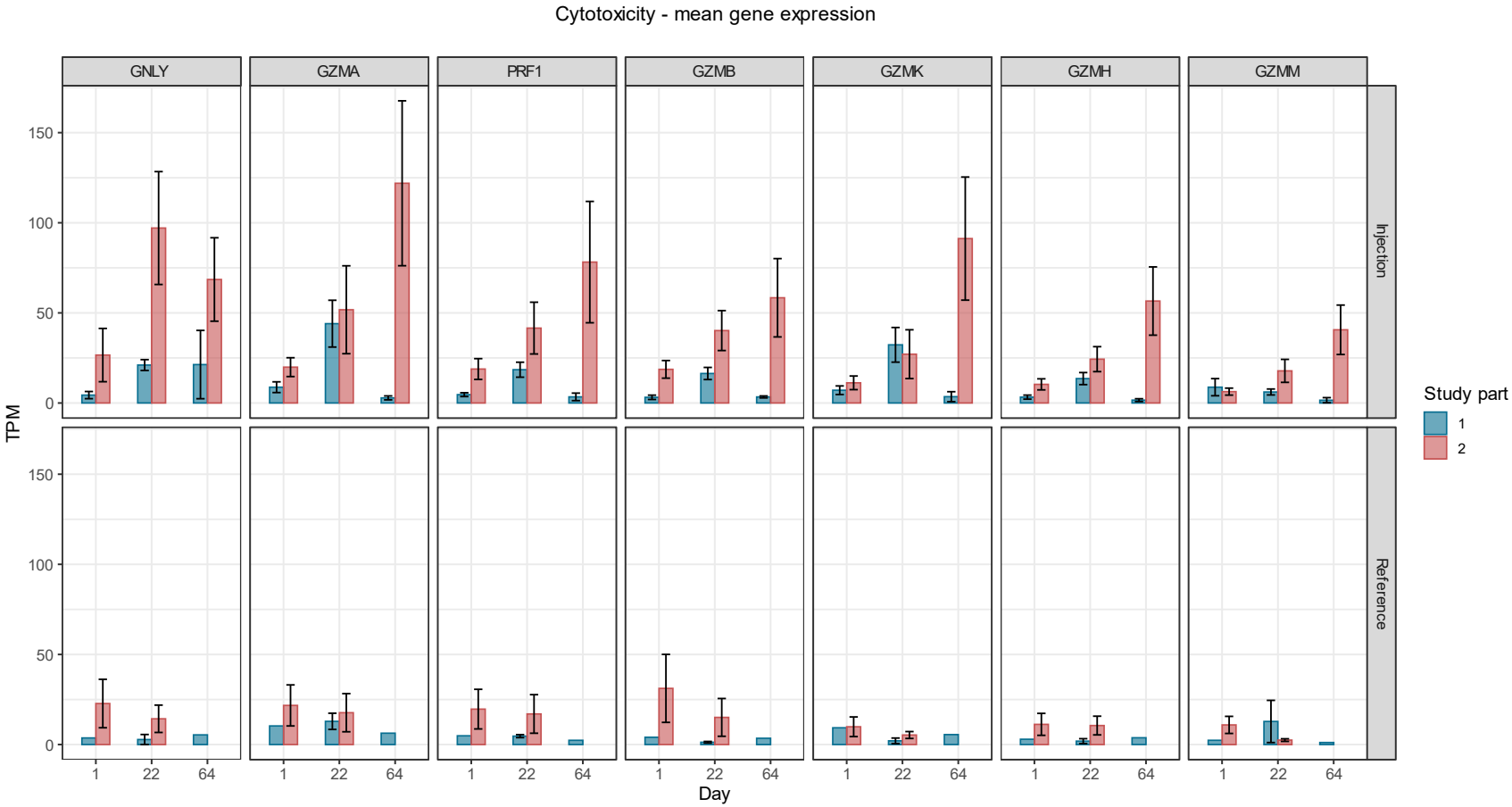


ONCOS-102 TREATMENT INCREASES CYTOTOXIC POTENTIAL ON INTRA-TUMORAL T-CELLS: MELANOMA



Unpublished company data

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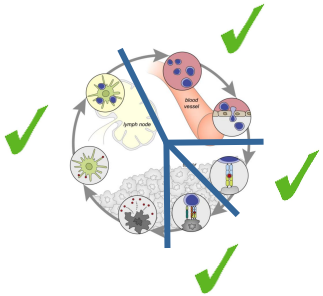
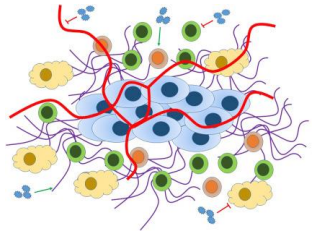
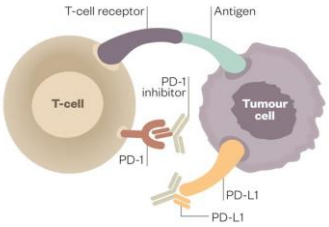
ONCOS-102 IMMUNE ACTIVATION - CONCLUSIONS



ONCOS-102 activates the immune system and counteracts multiple mechanisms of immuno-suppression operating at different steps of the cancer immunity cycle



Multifaceted **modulation of the tumor micro-environment induced by ONCOS-102 is linked to clinical benefit** in patients with different tumor types



ONCOS-102 induced immune activation provides **broad and powerful priming to sensitize patients** to respond to subsequent treatment with **checkpoint inhibitors**

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Preclinical pipeline update

6. 4Q update
7. Closing remarks

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Product candidate	Preclinical	Phase 1	Phase 2	Collaborator
ONCOS-102	**Melanoma** Combination w/Keytruda			
	Colorectal cancer Combination w/Imfinzi			
	Mesothelioma Combination w/pemetrexed/cisplatin			
ONCOS-200 series	Next Gen viruses			leidos Papyrus
Novel mutRAS concepts				VALO THERAPEUTICS OBLIQUE THERAPEUTICS

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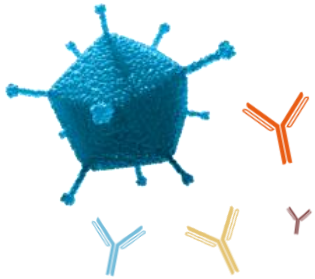
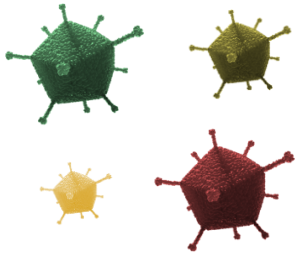
TARGOVAX´S THREE-PILLAR R&D PIPELINE STRATEGY



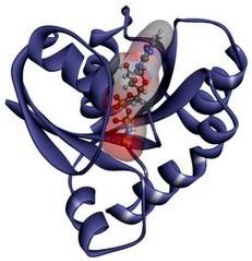
Novel ONCOS-102 combinations

- 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

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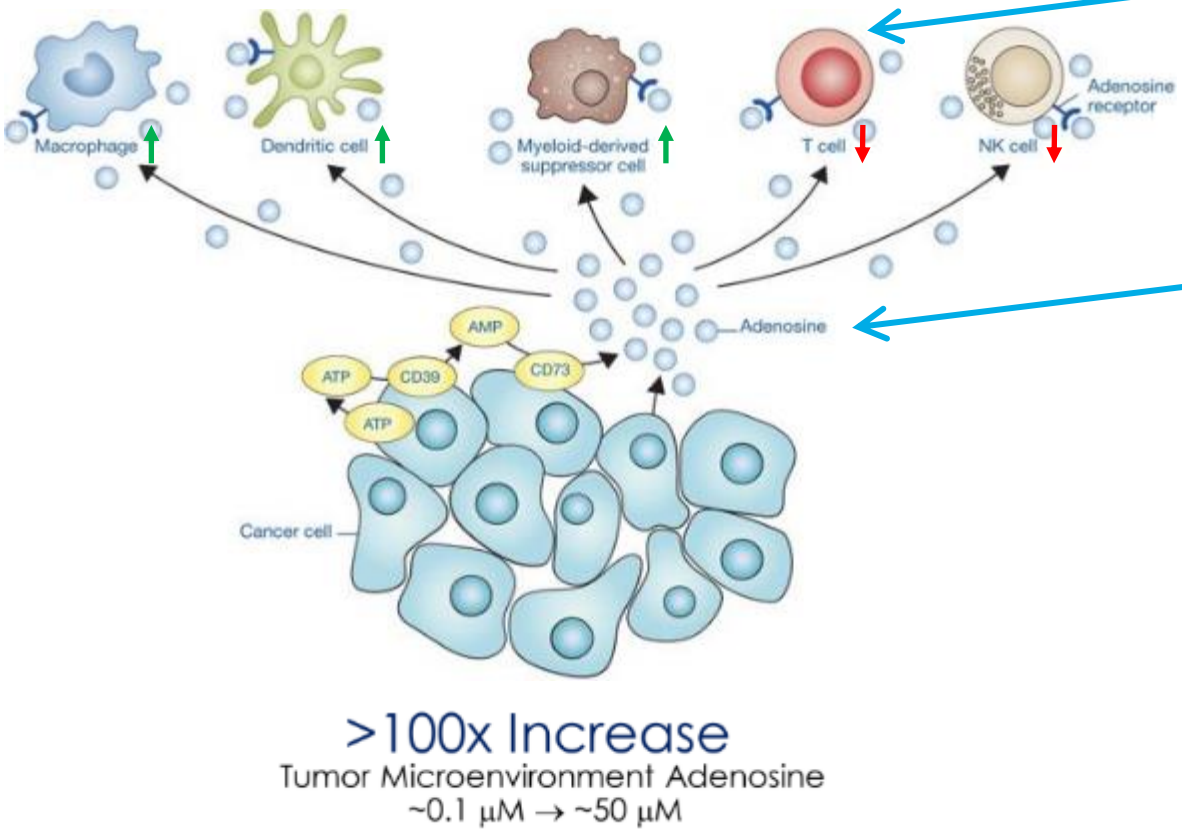
NEXT GENERATION ONCOS: ONCOS-211 PRIORITIZED FOR FURTHER DEVELOPMENT

Adenosine – a key suppressor of immune cells



Transgene activity

Transgene 1 – ICOS-L

- ICOS-ligand binds to ICOS on the T-cell surface, providing a strong stimulatory signal
- Enhanced cytotoxicity

Transgene 2 – ADA

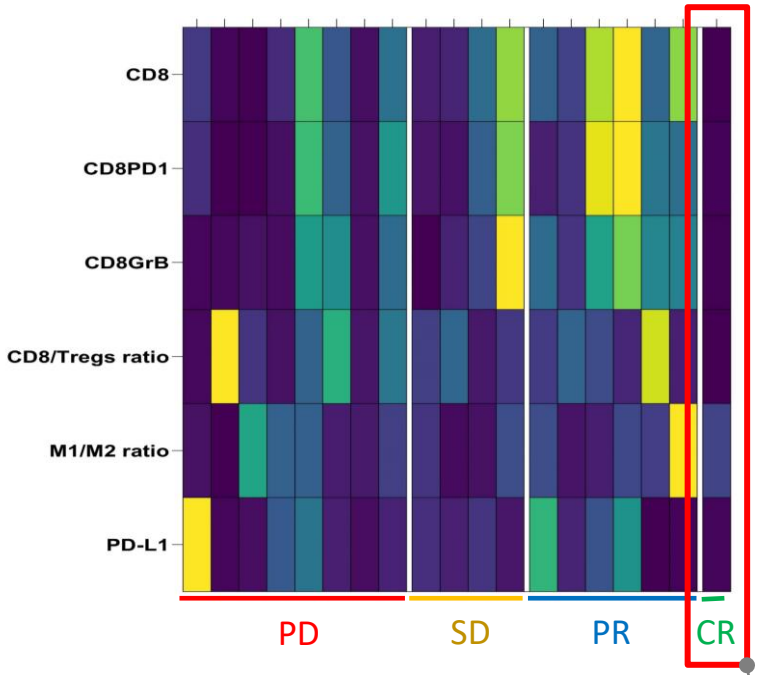
- ADA degrades adenosine released by the tumor
- Reversal of immune-suppressive tumor micro-environment

Virus activity

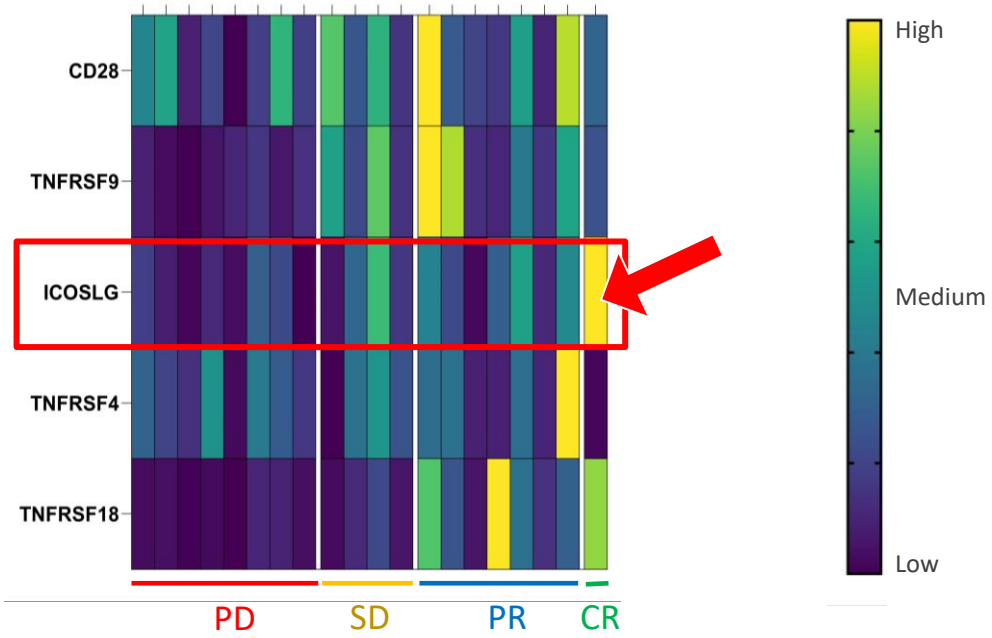
1. Innate immune activation
2. Cancer cell oncolysis
3. Adaptive anti-tumor immune response

ICOS-L EXPRESSION CAN BE TIED TO DEEP CLINICAL RESPONSE TO ONCOS-102

Immune cell infiltrate at Baseline, mIHC



Co-stimulatory receptor expression, gene expression



CR patient was immunologically "cold" at baseline…

…but high level of ICOS-L providing co-stimulatory signal enabling deep reponse

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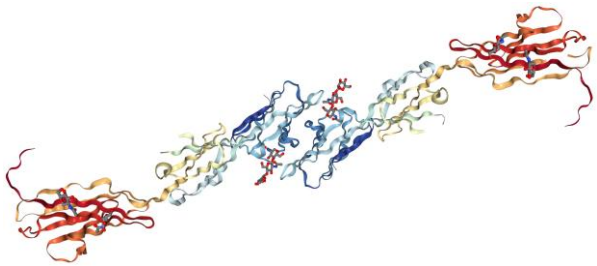
BUILDING TYROSINE KINASE INHIBITOR FUNCTIONALITY INTO ONCOS

Collaboration partner

Papyrus Therapeutics

Target – Tyrosine kinase inhibition



OPCML protein

- OPCML is a **potent tumor suppressor**, inactivated in ca. 50% of all cancers
- OPCML **shuts down the oncogenic signaling** function of at least **8 RTKs**
- OPCML **suppresses epithelial-to-mesenchymal (EMT)** transition

Using **ONCOS to restore OPCML activity** represents a novel and **highly targeted mechanism of kinase inhibition** in multiple cancer indications

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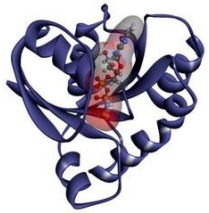
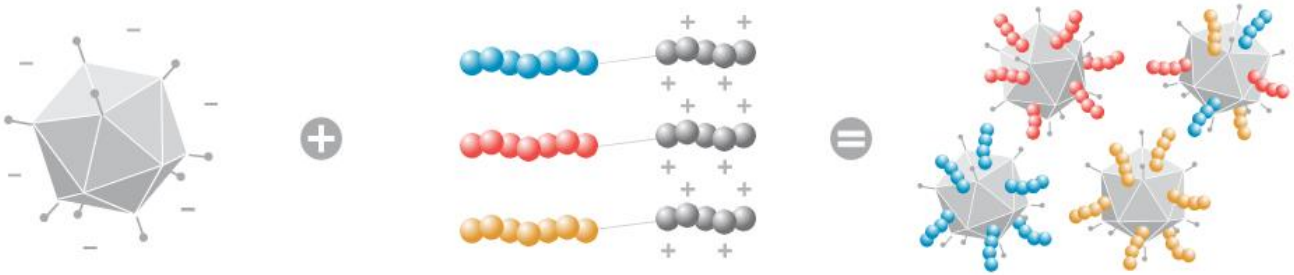


NOVEL MUTANT RAS VACCINATION CONCEPTS INCORPORATING IMMUNOLOGICAL POWER OF ONCOS

VALO THERAPEUTICS



ONCOS-102

Modified TG peptides

ONCOS-TG PeptiCRAd

Merging ONCOS and TG technology

ONCOS used as carrier for mutRAS peptides

Combining the power of mutRAS vaccination and oncolysis

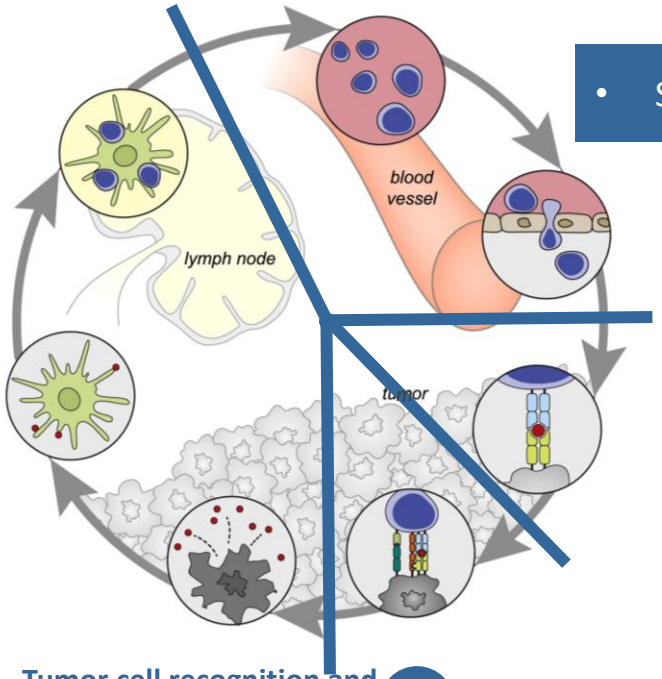
THE R&D PIPELINE STRATEGY IS DESIGNED TO ADDRESS KEY COMPONENTS OF THE CANCER IMMUNITY CYCLE

1 **Antigen release, cross-presentation and priming of T-cells**

- Antigen release by ICD
- TLR activation
- IFN type I induction
- IFNg induction
- mutK-RAS vaccination (Valo)

2 **T-cell migration and infiltration into the tumor**

- Secretion of chemokines



3 **Expansion and survival of T-cells in the tumor**

- Secretion of lymphokines
- Remodeling of TME (M1/M2, T-reg?)
- Adenosine depletion (ONCOS-211)
- ICOS co-stimulation (ONCOS-211)
- PD-1 and CTLA-4 inhibition (Leidos)

4 **Tumor cell recognition and elimination**

- IFNg induction
- Upregulation of T-cell killing machinery
- Tumor growth inhibition/EMT suppression (Papyrus)

A	Documented ONCOS effects
B	Initiated programs

Adapted from Chen & Mellman, Immunity 2013

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4Q update

7. Closing remarks

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4Q HIGHLIGHTS AND SUBSEQUENT EVENTS

ONCOS-102

- **Announced 35% response rate** in ONCOS-102 trial in anti-PD1 refractory melanoma patients and regression on non-injected lesions
- **Completed Part 1 in the colorectal cancer** trial, combining ONCOS-102 with Imfinzi (duravalumab), **recruitment in Part 2 opened**
- Announced encouraging 18-month **survival data in mesothelioma**
- Presented mesothelioma data at the **Society for Immunotherapy of Cancer**

Corporate

- Raised gross proceeds of **NOK 75 million** (USD 8 million), strong international demand, multiple times oversubscribed
- Granted **EU patent** covering use **of ONCOS-102 in combination with CPIs**
- Formed new **Scientific Advisory Board** comprised of world-renowned experts in immuno-oncology and drug development

Subsequent events

- Entered a research collaboration with **Papyrus Therapeutics**
- Granted **IOVaxis** 3-month extension to the exclusive license option for TG mutant RAS vaccines in Greater China and Singapore
- SOTIO stopped the combination trial assessing the combination of ONCOS-102 and DCVAC/PCa in prostate cancer
- Granted **Fast Track designation by the FDA** in malignant pleural mesothelioma

UPDATE ON IOVAXIS LICENSE

IOVAXIS THERAPEUTICS

Fighting Cancer with Your Own Weapons

CEO: John Wang

HQ: Nantong, China

Founded: 2018

R&D focus: Shared and personalized cancer vaccines

Description

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

Update

- IOVaxis is still in IND application process with NMPA (Chinese FDA)
- NMPA has different requirements than Western agencies
- The License Option will be further extended with 6 months through Sept 2021

CONTINUED COST CONTROL IN 4Q20

NOK m	4Q19	1Q20	2Q20	3Q20	4Q20
Total revenue	**2**	**0**	**0**	**0**	**-0**
External R&D expenses	-25	-13	-14	-9	-8
Payroll and related expenses	-11	-11	-11	-9	-12
Other operating expenses	-5	-5	-5	-4	-3
Total operating expenses	**-42**	**-30**	**-30**	**-22**	**-23**

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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

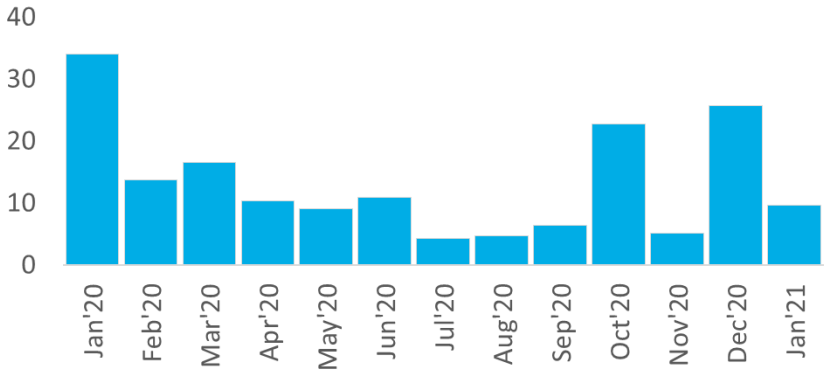
DNB, Carnegie, H.C. Wainwright

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

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7 Closing remarks

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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** ✓	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

CLINICAL AND PRECLINICAL PIPELINE

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

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

Early-stage development

- ✓ Clinical efficacy
- ✓ Immune activation
- ✓ Well tolerated

Late-stage development

PD1 refractory melanoma

Expansion opportunities

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

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