Arming the patient's immune system to fight cancer

10th Annual European Life Science CEO Forum and Exhibition

Øystein Soug, CEO

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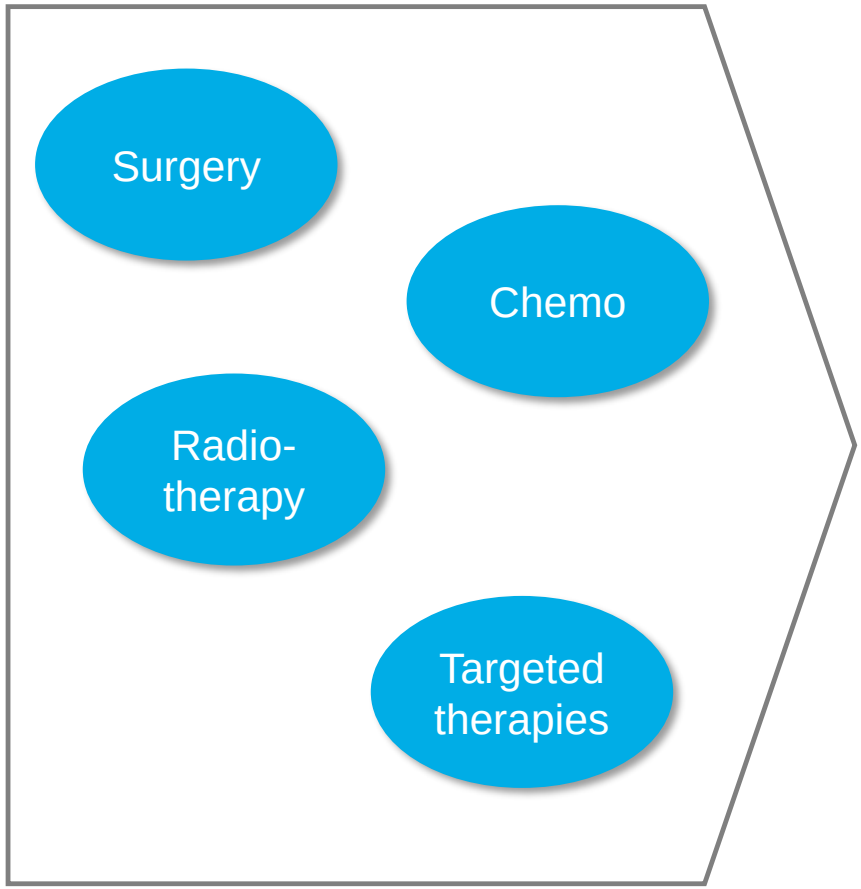
Immunotherapy – enables the immune system to kill cancer cells

Traditional cancer treatment



New approach - Immunotherapy

Enables the immune system to kill cancer cells:

- **Oncolytic viruses**
  - Release cancer antigens
  - Imlygic, ONCOS-102
- **Peptide vaccines**
  - Mimic cancer antigens
  - TG01, TG02
- **Cell therapies**
  - Load T-cells with antigen receptors
  - Chimeric antigen receptors, CARs
- **Checkpoint inhibitors**
  - General upgrade of immune system
  - Yervoy, Keytruda, Opdivo, Tecentriq

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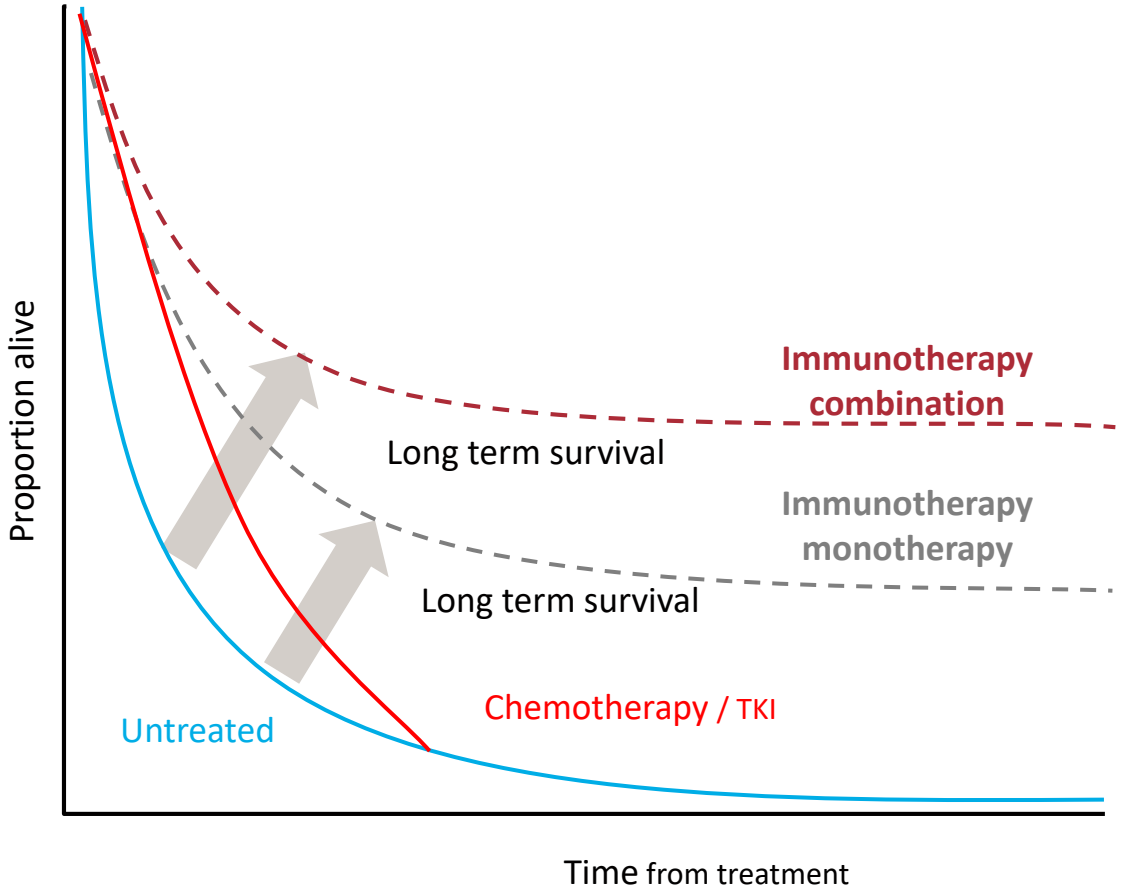
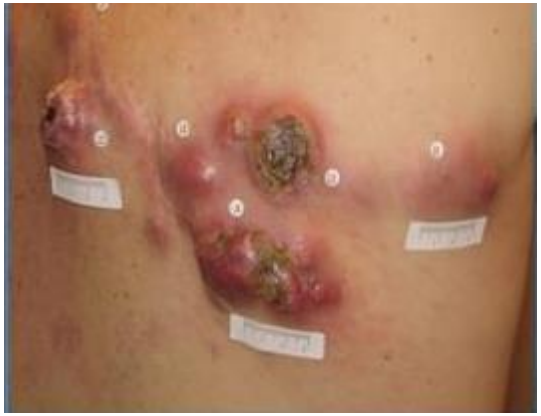
The goal is to make cancer a chronic disease by combining immuno-oncology therapies

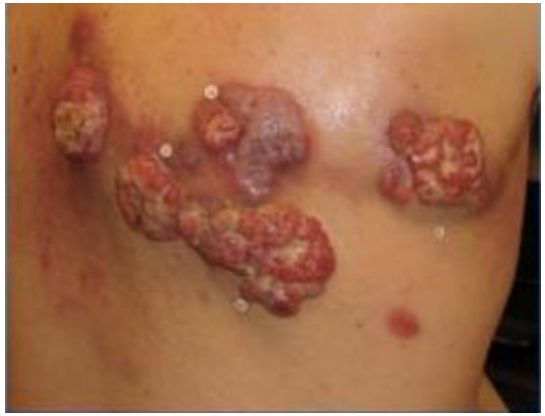


- Yervoy started the revolution in cancer treatment in 2011
- Due to immuno-oncology combination the number of addressable cancers is expected to increase to at least 60%

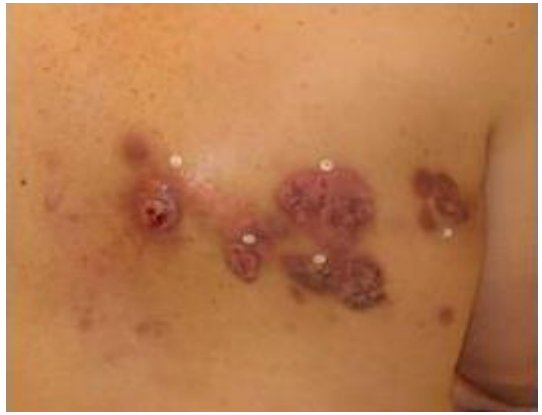
Checkpoint inhibitors show signs of “curing” some cancers - example of Yervoy treated melanoma



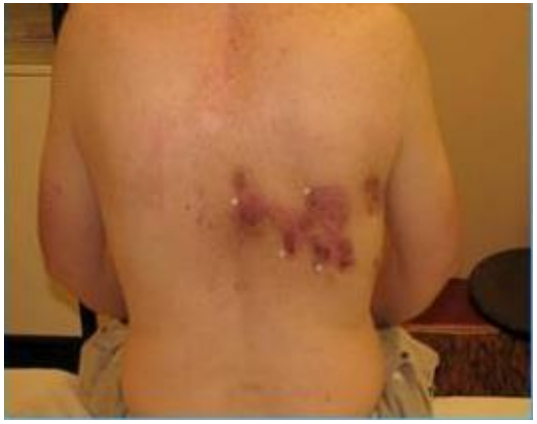
Prior to Yervoy



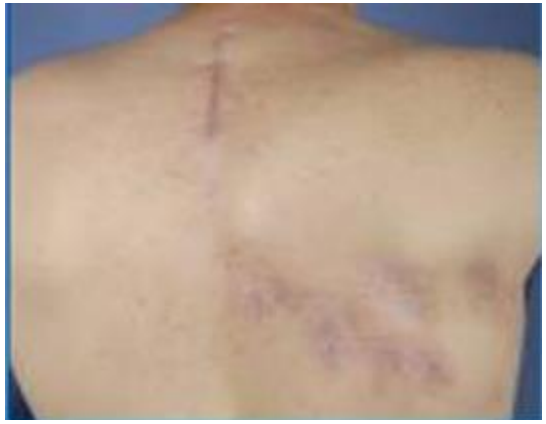
4 weeks



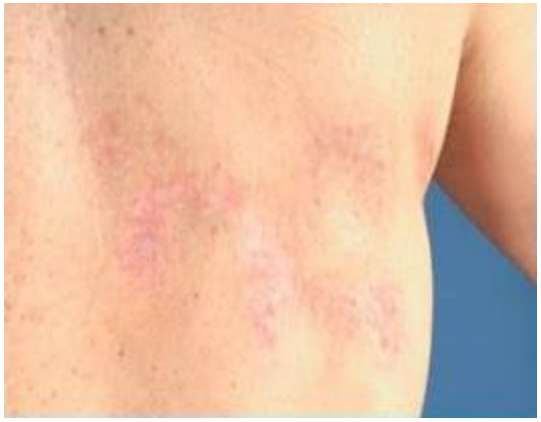
8 weeks



20 weeks



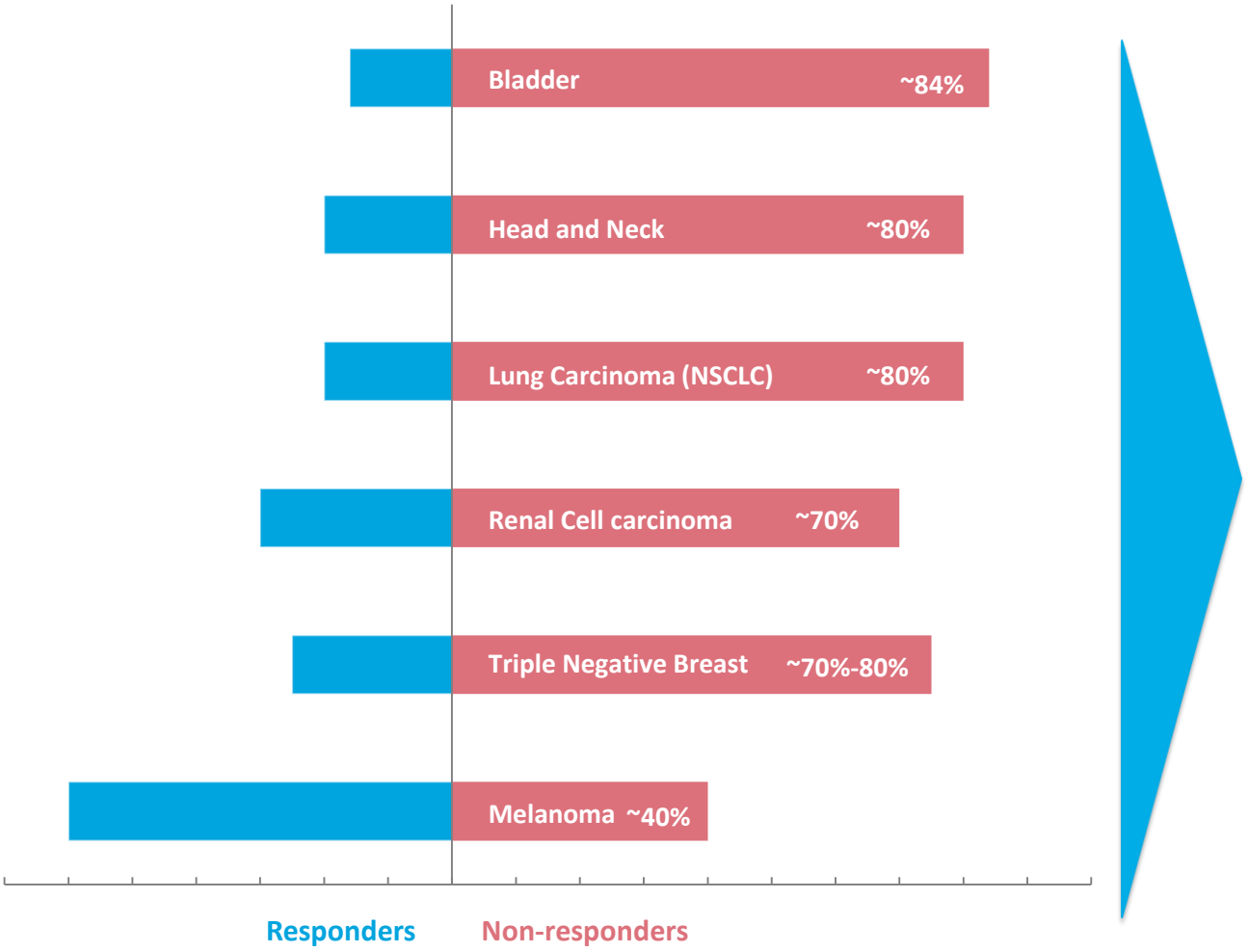
8 months



1 year

Large unmet need for checkpoint inhibitor refractory patients

Response rate to checkpoint inhibitors (CPIs)



ONCOS-102 can potentially activate non-responders to become susceptible to CPI's

ONCOS-102: CPI refractory melanoma trial details

Background

- No standard of care for patients not responding to CPI

Setting

- Advanced malignant melanoma patients not responsing to CPIs
- Immune activate CPI non-responders with ONCOS-102, then re-challenge with a CPI (Keytruda)

Cohorts

- Six patients with prior PD1 monotherapy
- Six patients with prior PD1 plus Yervoy combination therapy

Key endpoints

- Safety
- Immune activation and clinical response data
- Correlation of immune activation and clinical response data

Sequence

ONCOS-102 – 3 weeks	Keytruda – 5 months

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Yervoy – generic name: ipilimumab
Keytruda – generic name: pembrolizumab

How does ONCOS-102 work?

At the tumor:

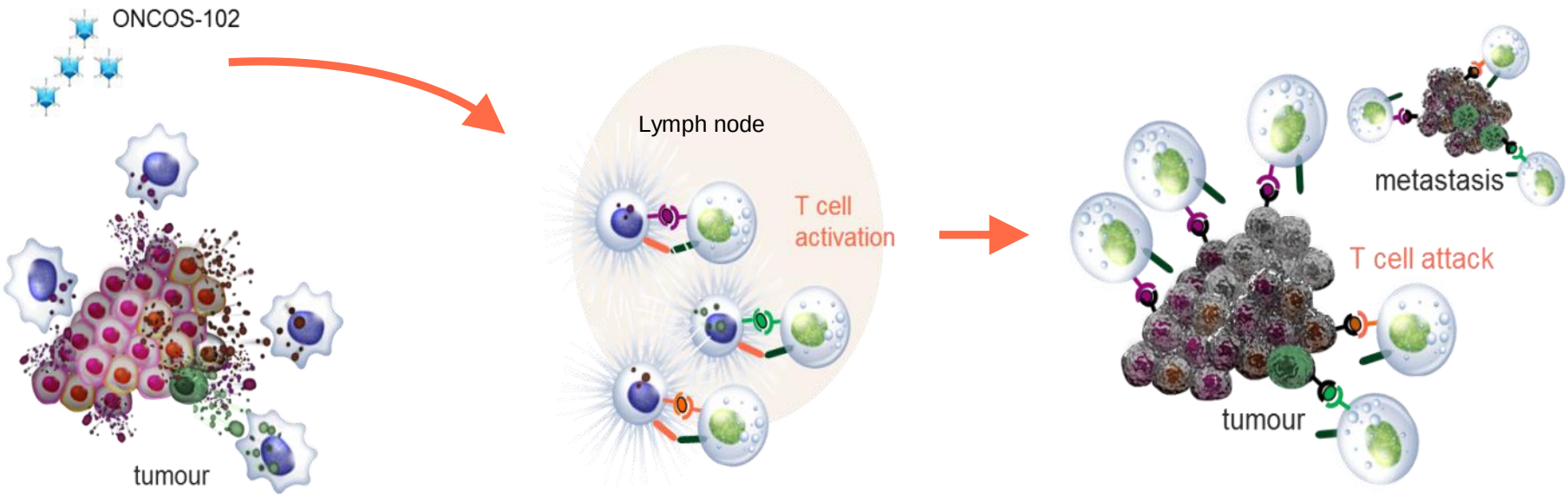
Virus injected directly into tumor, replicates, lyses cells and releases antigens. Immune system picks up antigens

At the lymph node:

Immune system starts production of tumor specific T-cells

At the tumor lesions:

T-cells find tumor lesions with corresponding tumor antigens and kill the cancer cells

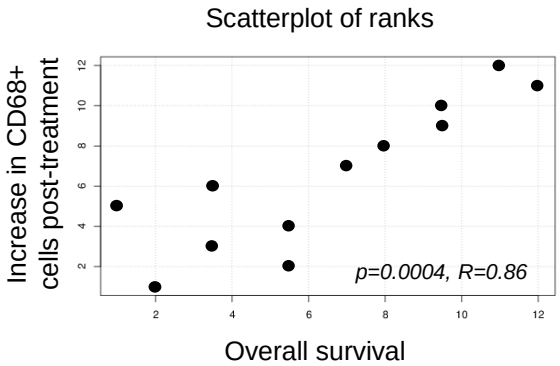


Initial ONCOS-102 trial showed strong T-cell response

Evidence that immune system recognizes tumor threat

Innate Immune System (biopsy)

- Induction of proinflammatory cytokines + fever (all patients)
- Infiltration of innate immune cells into tumors in 11 out of 12 patients



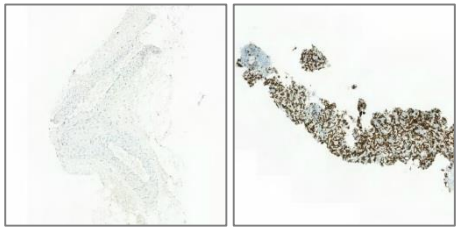
Correlation between post-treatment increase in innate immune cells and OS

Evidence that T-cells find the tumor and are cell killing

Adaptive immune system (biopsy)

- Increase in T-cell infiltration into tumors (including CD8+ killer T-cells) in 11 out of 12 patients
- Observation in one non-injected distant metastasis

OvCa. patient (FI1-19)



Correlation between post-treatment increase in CD8+ T-cells and OS (p=0.008, R=0.74)

Evidence of production of tumor antigen specific T-cells

Anti-tumor immune response (blood)

- Systemic induction of tumor-specific CD8+ T-cells

Ovarian patient:
NY-ESO-1, MAGE-A1, MAGE-A3, and Mesothelin specific CD8+ cells

Mesothelioma patient:
MAGE-A3 specific CD8+ cells

Associated with clinical benefit

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Six shots on goal

	Cancer indication	Combined with		2017 H1	2017 H2	2018 H1	2018 H2	2019 H1
ONCOS-102	Melanoma	CPI		Phase I				
ONCOS-102	Mesothelioma	Chemo*	Orphan ind.	Phase Ib/II				
ONCOS-102	Ovarian & Colorectal	CPI	Orphan ind. Sponsor**: Ludwig	Phase I/II				
ONCOS-102	Prostate	DC therapy	Sponsor: Sotio	Phase I				
TG	Resected Pancreatic	Chemo*	Orphan ind.	Phase I/II				
TG	Colorectal	CPI		Phase Ib				

Interim data

Clinical, immune and safety data

4 readouts 2017

5 readouts 2018

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* In combination with Standard of Care Chemoterapy. Pemetrexed/cisplatin for Mesothelioma and Gemcitabine for Resected Pancreatic

TG01 phase I/II resected pancreatic trial

- Encouraging top line two-year survival data -

Encouraging survival rate and “signal” of efficacy in TG01 trial

CT TG01-01; A Phase I/II Trial of TG01 and Gemcitabine as Adjuvant Therapy for Treating Patients with Resected Adenocarcinoma of the Pancreas

- 68% (13 of 19) of the patients in cohort 1 were alive two years after the resection
  - Published historical rate 30-53% suggests a signal of clinical efficacy for TG01[1]
- Abstract submitted to ASCO 2017 (June) from this 1st cohort
  - Efficacy, safety, immune activation
- In summary: encouraging survival rate and “signal” of efficacy

[1] J Neoptolemos 2010, J van Loethem 2010, H Oettle 2013, M Sinn 2015, K Uesaka 2016 (In these reported studies overall survival is measured either from surgery or treatment randomization).

TG – background: “reasons to believe”

120 patients treated with TG peptides in 1990’s

- 10 year follow up of resected pancreas cancer patients showing twice the survival rate to historical control Immune activation and clinical response data[1]
- Advanced pancreatic cancer patients vaccinated with TG peptides with a positive immune response (DTH, proliferative T cells) showed longer overall survival compared to patients without a positive immune response[2]

Potential conversion of immunologically cold RAS positive tumors to hot tumors responsive to CPIs

[1] Weden et al, 2011, Oettle et al, JAMA 2007 and 2013
[2] Gjertsen et al 2001, Data on file

How is the Targovax peptide vaccine approach different?

Knowing the target

- We target RAS mutations that are known neo-antigens
- RAS mutations cause abnormal cell growth - definition of cancer
- *Most other peptide vaccine studies have not known the cancer antigens*

CD4+ and CD8+ T-cells

- Both necessary for establishing a clinical effective cellular response
- Our TG peptides designed to active and stimulate both
- *Most failed peptide vaccines designed to only activate CD8+ T-cells*

Right adjuvant

- We use the right type of adjuvant – GM-CSF
- Well known, effective, non-depot forming
- *Other have used depot forming adjuvants – T-cells not attracted to tumor*

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Multiple near term value inflection points

TG02
Initiate phase Ib in colorectal

ONCOS-102
Initiate phase I prostate

ONCOS-102
Initiate phase I/II melanoma

ONCOS-102
Initiate phase I Ovarian/colorectal

TG01
phase II initiated

ONCOS-102
Initiate phase I/II mesothelioma

Oslo Stock Exchange
Listing on OSE main list

2015 | **2016** | H1 **2017** H2 | H1 **2018** H2

ONCOS-102
Immune activation and MoA demo

TG01 *(1st cohort)*
Interim data pancreas

TG01 *(2nd cohort)*
Immune activation pancreas

TG01 *(1st cohort)*
2-year survival pancreas

ONCOS-102
Interim data melanoma

ONCOS-102
Interim data mesothelioma

TG02 *(mono)*
Interim data colorectal

TG01 *(2nd cohort)*
2-year survival pancreas

ONCOS-102
Interim data ovarian /colorectal

ONCOS-102
phase I/II data melanoma

ONCOS-102
Interim data prostate

TG02 *(combo)*
phase I data/ colorectal

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Financial summary

Operations			
Cash	**NOK 172m**	USD 20m	
Annual run rate	**NOK 110m**	USD 13m	*Last four quarters*
Annual opex	**NOK 120m**	USD 14m	*Last four quarters*

The share	OSE: TRVX		
Daily liquidity	**NOK 9m**	USD 1m	*Last two month's avg.*
Market Cap	**NOK ~1 bn**	USD 123m	*At share price NOK ~24*
Debt	**NOK 40m**	USD 5m	*EUR 6m conditional*
No. of shares	**42.2m**		*44.9m fully diluted*
Analysts	DNB, ABG Sundal Collier, Arctic, Redeye, Norske Aksjeanalyser		

Arming the patient's immune system to fight cancer

1 **TG**	✓ Encouraging top line two-year survival data
2 **ONCOS**	✓ Important proof of concept trial in CPI refractory melanoma ✓ Data in 2H17
3 **Clinical trials**	✓ Six shots on goal