

Polaris

The Nordic leader in Immuno-Oncology

15 June 2015

Targovax AS

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 AS (“Targovax”) or Oncos Therapeutics Oy (“Oncos”). Such forward-looking statements reflect the current views of Targovax AS or and are based on the information currently available to the company. Targovax or Oncos 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

Investment highlights

1	A Nordic immuno-oncology champion	<ul style="list-style-type: none">✓ The immuno-oncology market is poised for tremendous growth and expected to reach USD 35bn by 2023¹✓ The combination of Targovax AS ("Targovax") and Oncos Therapeutics Oy ("Oncos")' complementary technologies creates a unique platform for the development of cutting-edge vaccines and immunotherapies✓ The combined group of Targovax and Oncos ("Polaris") is positioned as a leading Nordic immuno-oncology company
2	Unique technologies with promising data	<ul style="list-style-type: none">✓ Clinical experience to date validates safety and mechanism of action of both technology platforms✓ Polaris will have a solid immuno-oncology pipeline as both platforms are highly suitable for combination therapies✓ Safety data collected on approx. 250 (Targovax) and 290 (Oncos) patients²✓ Strong pipeline with programs in several indications will provide multiple shots on goal
3	Value inflection points	<ul style="list-style-type: none">✓ Multiple uncorrelated news events and value inflection points over the next 18 months✓ Limited funding requirement to drive value compared to peers
4	Experienced management team	<ul style="list-style-type: none">✓ Strong board and management with international pharmaceutical drug development and commercial experience✓ The combination of two highly competent and complementing organisations will enable accelerated development and efficient execution
5	Backed by leading life science focused investors	<ul style="list-style-type: none">✓ Strong shareholder base including specialist investor HealthCap✓ Further backed by highly recognized Norwegian early-stage investors and reputable institutions

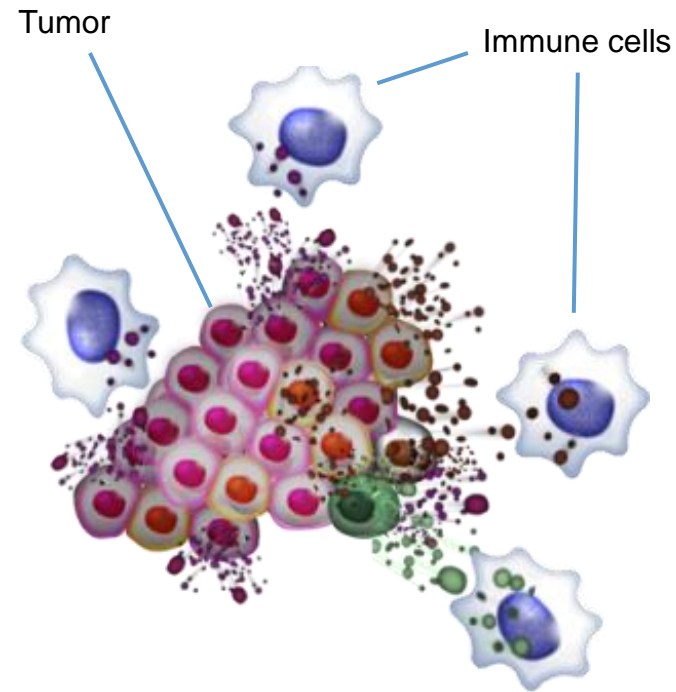
¹ Citi Research: "Immunotherapy - The Beginning of the End for Cancer", A Baum, 22 May 2013

² Please see slide 28 for more details

Immuno-oncology: Harnessing the Immune System to Fight Cancer



Science, December 2013

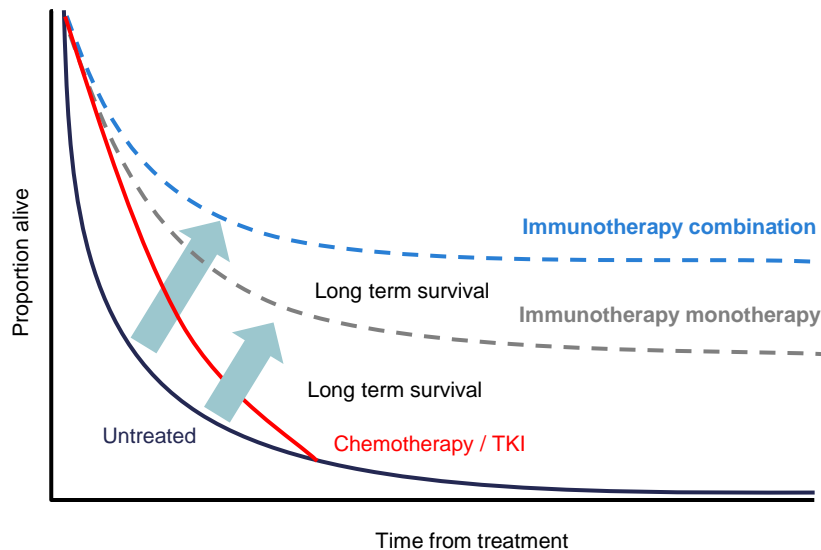


Cells of the immune system trained to attack cancer cells

The emerging field of immuno-oncology represents a unique investment opportunity – turning cancer into a controlled disease

Turning cancer into a controlled disease

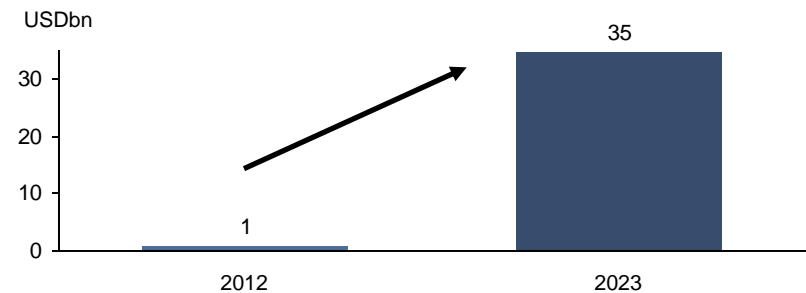
- The approval of Yervoy in 2011 and other subsequent check point inhibitors have created a revolution in immuno-oncology in particular and cancer treatment in general
- By combining and adding immuno-oncology with existing cancer treatments, it is hoped that cancer can be turned into a disease that can be controlled
- As illustrated below, immuno-oncology have the potential to shift the curve of long term survival of patients



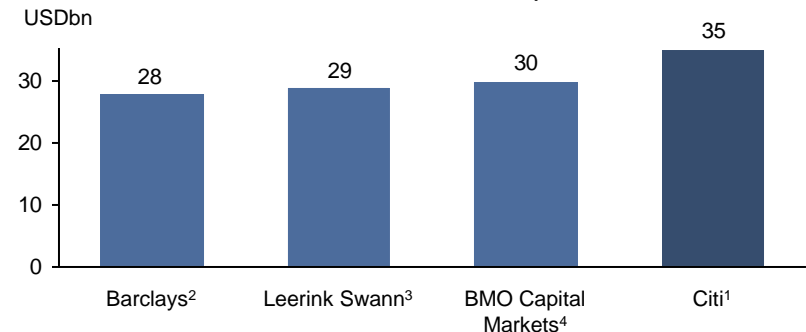
A market poised for tremendous growth

- Immuno-oncology represents the fastest growing and most promising biotech segment today
- The percentage of immuno-oncology addressable cancers is expected to increase to at least 60% by 2023 due to combination strategies

Global immuno-oncology market¹



Consensus on USDbn market potential



¹ Citi Research: "Immunotherapy - The Beginning of the End for Cancer", A Baum, 22 May 2013

² Barclays Capital Inc., Butler, 22 Jan, 2014

³ Leerink Swann LLC Equity Research, "Immunotherapy: The Future of Cancer Treatment is Now", S Fernandez et al, 5 Nov, 2013

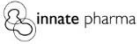













⁴ BMO Capital Markets Corp., Arfaei, 9 Feb, 2014

Polaris' immuno-oncology toolbox will provide a broad interface to a transaction-rich market actively seeking new combinations

Big pharma companies are in a fierce race to become immuno-oncology leaders

- Big pharma actively looking for opportunities to improve outcomes of their immunotherapies by combining them with complementary products
- Both traditional pharma and large biotech companies are extremely active in looking to create partnerships and/or acquire immuno-oncology companies
- Recent approvals and rapid launches of e.g. check point inhibitors and vaccines validate the power of harnessing a patients' own immune system to fight cancer
 - Yervoy (BMS): FDA approval received for Melanoma 3/2011; 2015 Q1 sales of USD 325m
 - Keytruda (Merck): FDA approval received for Melanoma 9/2014; 2015 Q1 sales of USD 83m
 - Opdivo (BMS): FDA approval received for Melanoma 12/2014 and for lung cancer 3/2015; 2015 Q1 sales of USD 40m
 - T-VEC (Amgen): recommended for FDA approval for Melanoma 4/2015

Selected relevant transactions within the immuno-oncology space

Date	Target Company	Candidate	Indication(s)	Phase	Acquiror/ Licensor	Deal type	Upfront (USDm)	Max. (USDm)
Apr 2015	 innate pharma	IPH2201 (anti-NKG2A antibody)	Cancer	Phase II	 AstraZeneca	Co-development and commercialisation agreement	250	1,275 + royalties
Mar 2015	 BAVARIAN NORDIC	Prostvac (cancer vaccine)	Prostate cancer	Phase III	 Bristol-Myers Squibb	Option and licensing agreement	60	975 + royalties
Feb 2015	 FLEXUS BIOSCIENCES	F001287 (IDO1 inhibitor)	Cancer	Pre-clinical	 Bristol-Myers Squibb	Acquisition	800	1,250
Jan 2015	 Kite Pharma	CAR-T therapies	Cancer	Pre-clinical	 AMGEN	Research collaboration and license agreement	60	60 + 525 per program
Nov 2014	 MERCK	MSB0010718C (anti-PD-L1)	NSCLC, ovarian cancer, Merkel cell carcinoma	Phase I and Phase II	 Pfizer	Joint development and commercialization agreement	850	2,850
Jun 2014	 Adaptimmune	TCR T cell therapies, including NY-ESO-1	Sarcoma, multiple myeloma, ovarian cancer, melanoma	Phase II	 gsk	Collaboration and licensing agreement	43	393 in first 7 years
Jan 2011	 BioVex	T-VEC / Oncovex (cancer vaccine)	Melanoma, head & neck (solid tumors)	Phase III	 AMGEN	Acquisition	425	1,000

Source: Press releases

High IPO valuations achieved despite early and limited clinical data

Several immunotherapy companies have completed successful listings at significant valuations over last 12 months

Status at time of IPO

United States

Kite

Juno

Bellicum

Aduro

Europe

Collectis

Adaptimmune

Lead Indication

CLL

CLL

Post initial allogeneic HSCT treatment of hematological malignancies and orphan inherited blood disorders

Pancreatic Cancer

CLL and ALL

Synovial sarcoma, multiple myeloma, melanoma, ovarian cancer and esophageal cancer

Phase

Phase I/IIa

Phase I/II

Phase I/II

Phase IIa

Preclinical

Phase I/II

No. Patients

24

51

N/A

93

N/A

44

Data Highlights

Objective response rate of 86%. 16 achieved remission, with 3 later experiencing disease progression and a second treatment-induced remission.

Complete remission rates of 89% and 100% in adult r/r ALL, 85% in pediatric r/r ALL, and 60% in adult NHL patients.


N/A


Positive randomized data in 93 patients. Statistically significant improvement in overall survival demonstrated at interim analysis (6.1 months for CRS-207 vs 3.9 months for control).


N/A

One CR (relapse at 9 months) and 5 PR out of 10 in synovial sarcoma. 61% CR/nCR rate in 21 multiple myeloma patients.

Partnership







Valuation¹

Step-Up: 1.1x

PP Post-\$: \$449M

IPO Pre-\$: \$499M

Current MC: \$2.3B

Step-Up: 2.2x

PP Post-\$: \$727M

IPO Pre-\$: \$1,598M

Current MC: \$4.2B

Step-Up: 2.1x

PP Post-\$: \$171M

IPO Pre-\$: \$351M

Current MC: \$618M

Step-Up: 4.5x

PP Post-\$: \$190M

IPO Pre-\$: \$858M

Current MC: \$1.8B

Step-Up: 4.7x

PP Post-\$: \$237M

IPO Pre-\$: \$1,118M

Current MC: \$1.1B

Step-Up: 4.8x

PP Post-\$: \$211M

IPO Pre-\$: \$1,012

Current MC: \$1.1B

Months PP to IPO

2

4

4

4






12

7

¹ Valuations reflect basic shares outstanding

Source: Company websites, press releases and filings, FactSet

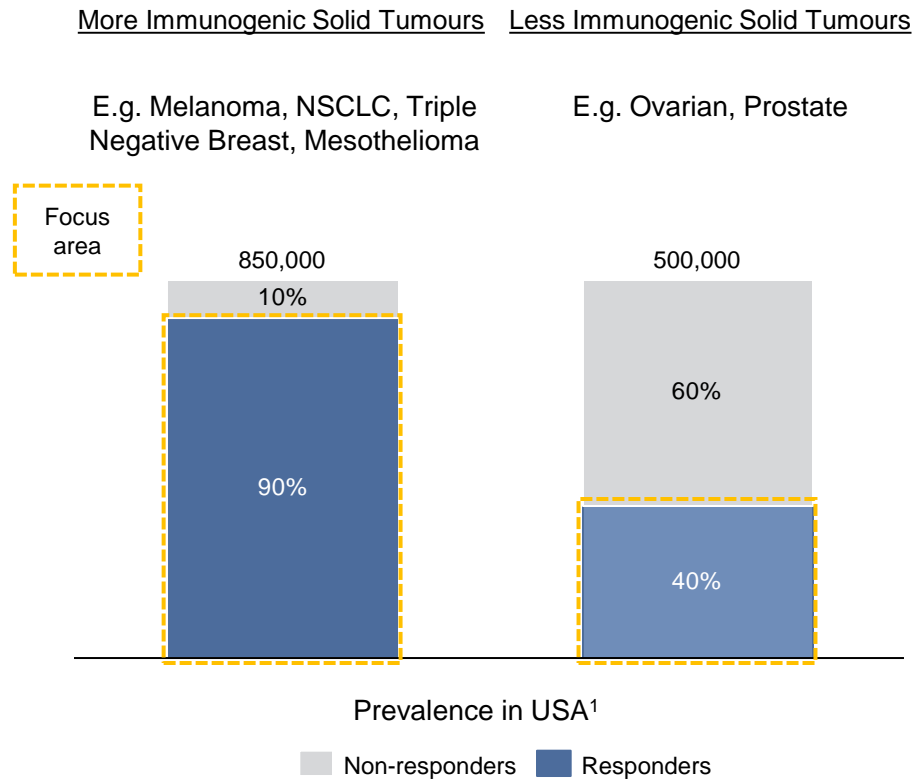
Cancer immunotherapies are combined to maximise efficacy

Immuno-oncology mechanisms	Wake up the immune system at the tumor	Co-stimulate at the tumor	Teach the T-cells at the lymph nodes	Attack the cancer with T-cells systemically	Disarm cancer's defence
 <i>Car analogy</i>	<i>Ignite the engine</i>	<i>Pull the choke</i>	<i>Switch on the GPS-targeting</i>	<i>Press on the gas pedal</i>	<i>Release the brakes</i>
 Peptide vaccines + GM-CSF	✓	✓	✓	✓	
 Viral vaccines	✓	✓	✓	✓	
 Kite Pharma T-Cell therapy				✓	
 Check point inhibitors ("CPI"s)					✓

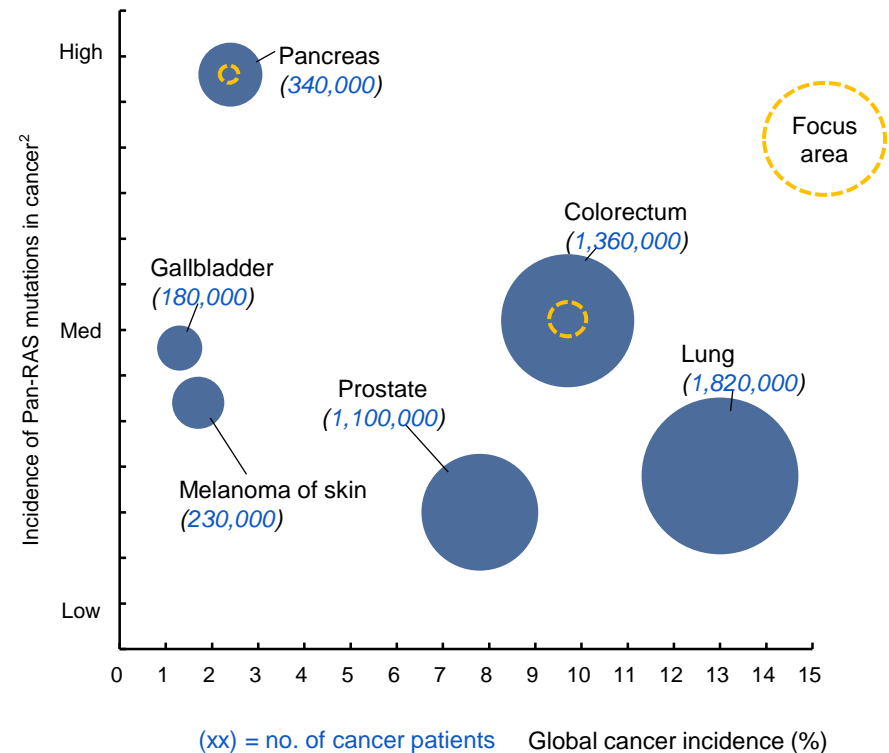
Source: Company websites, press releases and filings, FactSet

Polaris will focus on: Solid tumors susceptible to immunotherapy and those with RAS mutations

Oncos' platform: Solid tumors











Targovax's platform: RAS mutations



¹ Citi Research, American Cancer Society

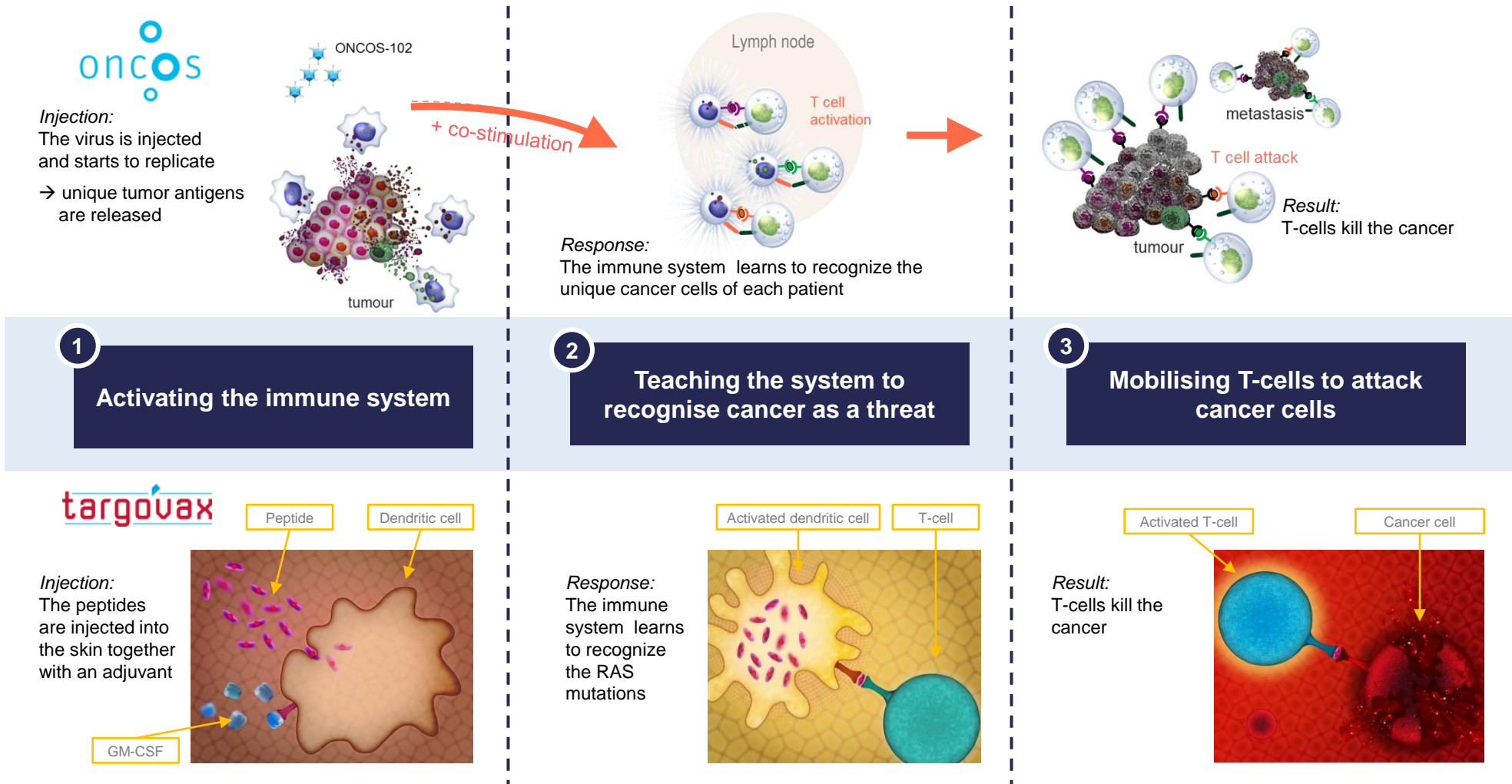
² Cancer Res, PS 2012, Nov 15, 2012

Polaris has differentiated assets with orphan indications*

	Indication(s)	Program	Discovery	Pre-clinical	Phase I	Phase II	Phase III
Development	Pancreatic cancer*	TG01					
	Melanoma	ONCOS-102					
	Mesothelioma*	ONCOS-102					
	Colorectal and NSCLC	TG02					
Exploratory	Ovarian cancer*	ONCOS-102					
	Prostate cancer	ONCOS-102					
	Melanoma	TG03					
Discovery	<i>Discovery</i>	ONCOS-402 ONCOS-802 ONCOS-902					

- Polaris has a broad and diversified pipeline with several promising compounds targeting multiple indications
- There is a low price tag of advancing the compounds to a go/no-go decision for the specific indications
- The portfolio will provide Polaris and its investors with multiple shots on goal

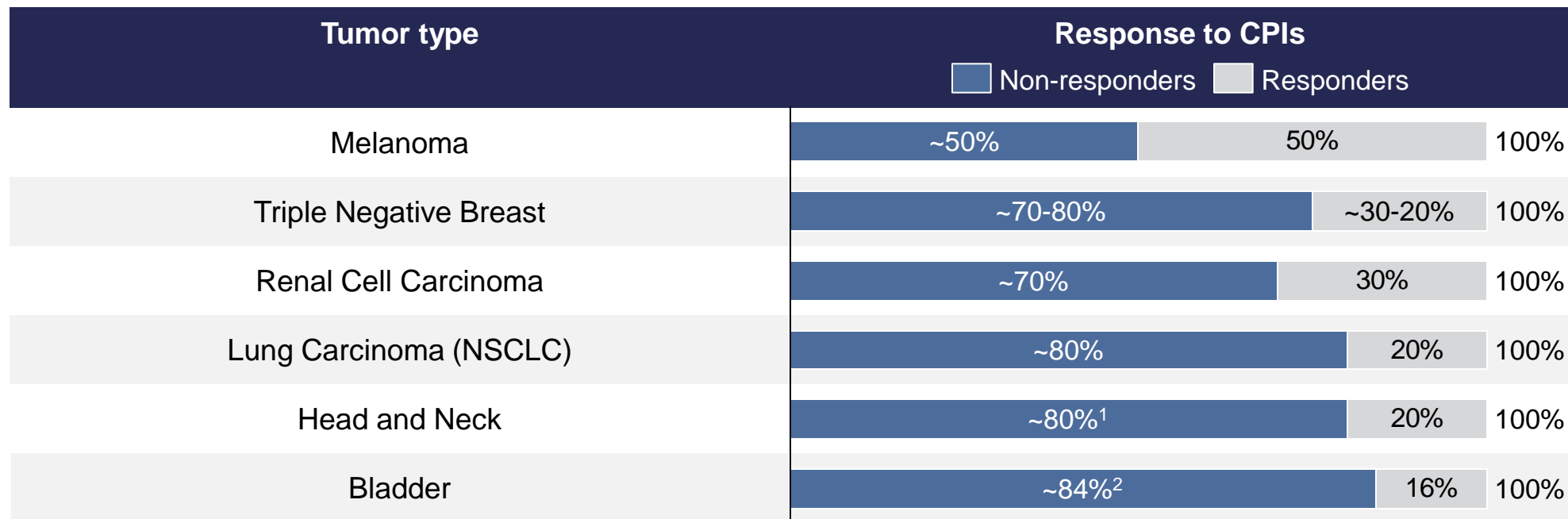
Polaris brings together two unique and complementary technologies



Source: Ranki et al Oncoimmunology 2014; Vassilev et al Oncoimmunology (accepted 2015)



Check point inhibitors Yervoy, Opdivo and Keytruda have had a significant clinical impact – but most patients still do not respond...



Non-responders lack T-cells in tumors prior to treatment (tumour is not immunologically awake)

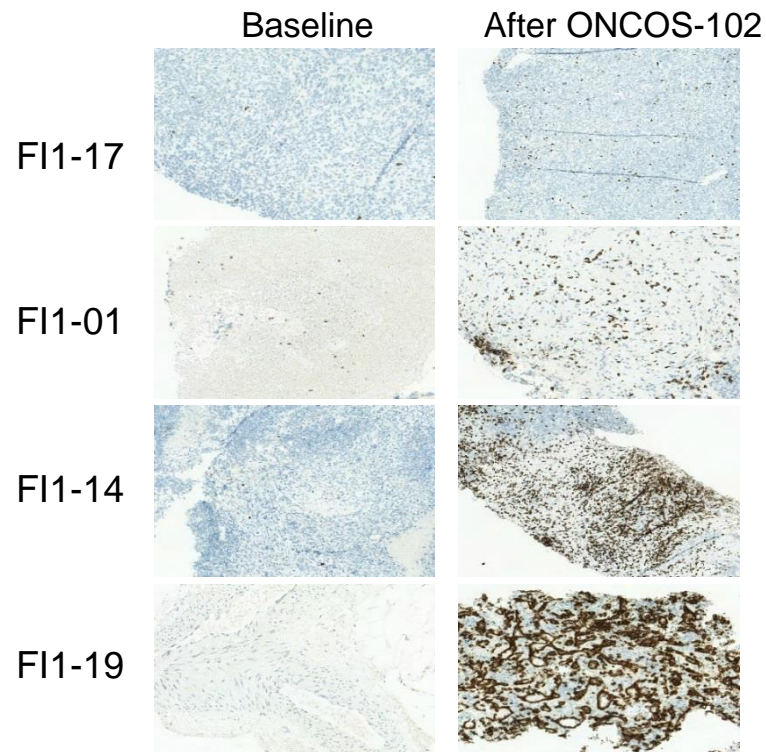
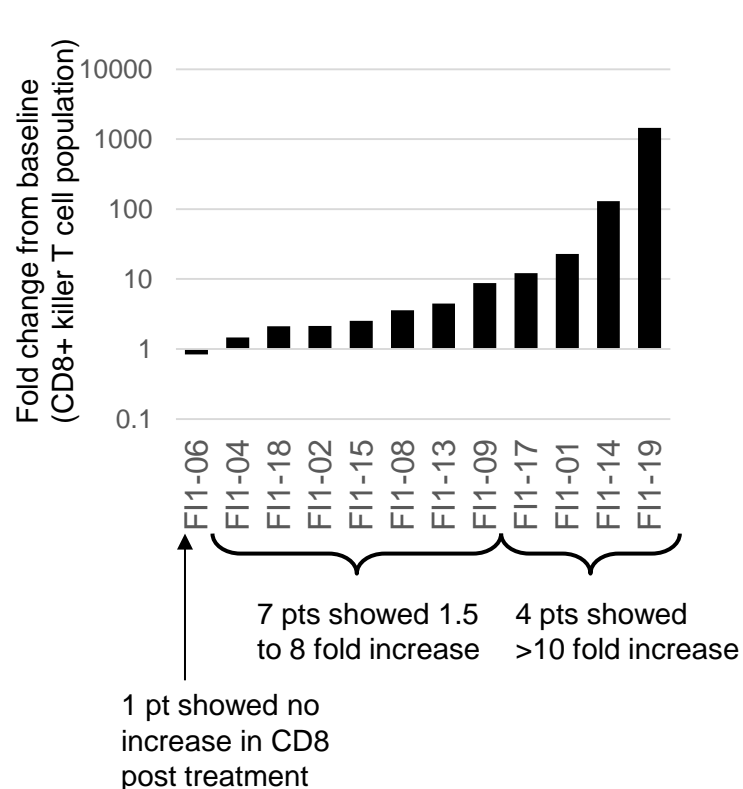
Non-responders to CPIs represent a substantial medical need – and a big Polaris opportunity

¹ Patients were preselected by Merck PD-L1 IHC assay

² 11% in PD-L1 (Roche) negative: 43% in PD-L1 + population

...this provides the rationale behind ONCOS-102

ONCOS-102 has shown to increase tumor infiltrating CD8+ T-cells in 11 of 12 patients with late stage treatment resistant cancers



Immunological findings were linked to signals of clinical benefit

40% of evaluable patients showed stabilization of disease after 3 months

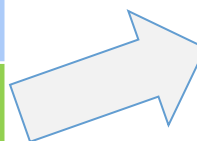
Patient	RECIST (3 months)
F11-01 Ovarian	Stable disease
F11-02 Colon	Stable disease
F11-04 Colon	Progressive disease
F11-06 Liver	Progressive disease
F11-08 Lung	Progressive disease
F11-09 Mesothelioma	Progressive disease
F11-13 Rectum	Progressive disease
F11-14 Mesothelioma	Stable disease
F11-17 STS	Progressive disease
F11-19 Ovarian	Stable disease

**47% reduction in total tumor burden.
Tumor specific T-cells in blood = systemic effect**

Baseline

6 months

7.5 months



Previously therapy resistant patient is still alive with stable disease 24 months after treatment. Tumor specific T-cells (NY-ESO-1) present in blood 17 months after last vaccination = systemic effect that was maintained



The ONCOS-102 opportunity

1

Check point inhibitors (CPIs) have made a significant impact in a short period of time



2

However, most solid tumors do not respond to CPIs



3

The non-responders represent a high unmet medical need and therefore a significant commercial opportunity

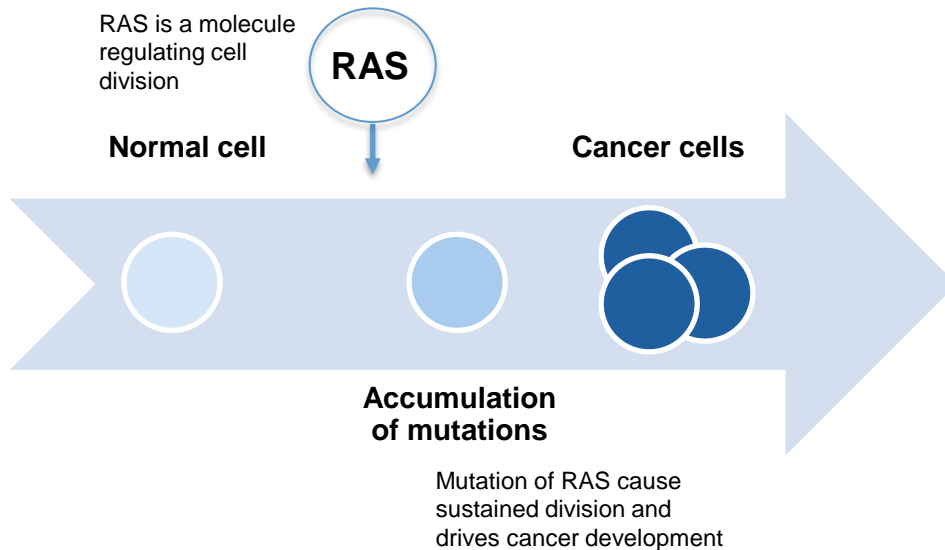


4

There is solid scientific rationale as to why ONCOS-102 is able to make CPIs work in CPI-non responders

RAS is an important driver in several cancer indications which implies a significant commercial potential

RAS explained



RAS mutation is an early cancer marker, present in up to 30% of all cancers⁴

Significant market potential

Indication	Compound
PANCREATIC CANCER (>85% RAS)¹ 340,000 patients/year (worldwide)	TG01
COLORECTAL CANCER (>40% RAS)² 1,360,000 patients/year (worldwide)	TG02
NON-SMALL CELL LUNG CANCER (20-30% RAS)³ 1,820,000 patients/year (worldwide)	
MALIGNANT MELANOMA (20-30% RAS)⁴ 230,000 patients/year (worldwide)	TG03

Large unmet medical need for cancers with RAS mutations

¹ Miglio, U. *et al*; 2014

² Vaughn, C.P. *et al*; 2011

³ D'Arcangelo, M. and Cappuzzo, F.; 2012

⁴ Fernandez-Medarde, A. and Santos, E.; 2011



TG01 has shown promising results in its ongoing Phase I/II resected pancreatic cancer clinical trial

Immunological results

Main Group (starting TG01 3 weeks prior to gemcitabine)	DTH ¹ response (n=14)	T cell response (n=8)
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14

13 (93%)

6 (75%)

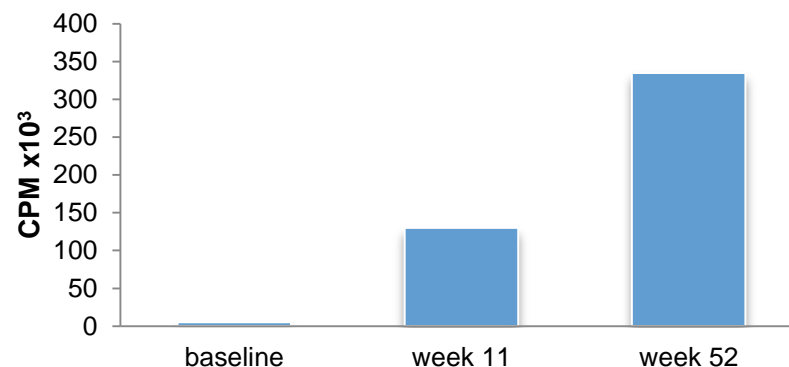
Safety results

- TG01 is generally well tolerated and elicits RAS-specific immune responses in most patients even when administered in combination with gemcitabine
- There were 4 related allergic reactions to vaccination, three of which occurred only after gemcitabine treatment; two of which were severe

Boosters result in maintained TG01 T cell response

TG01 specific T cell proliferation – blood samples from patient 01-002

Radiolabelled thymidine incorporation measured as count per minute (CPM)



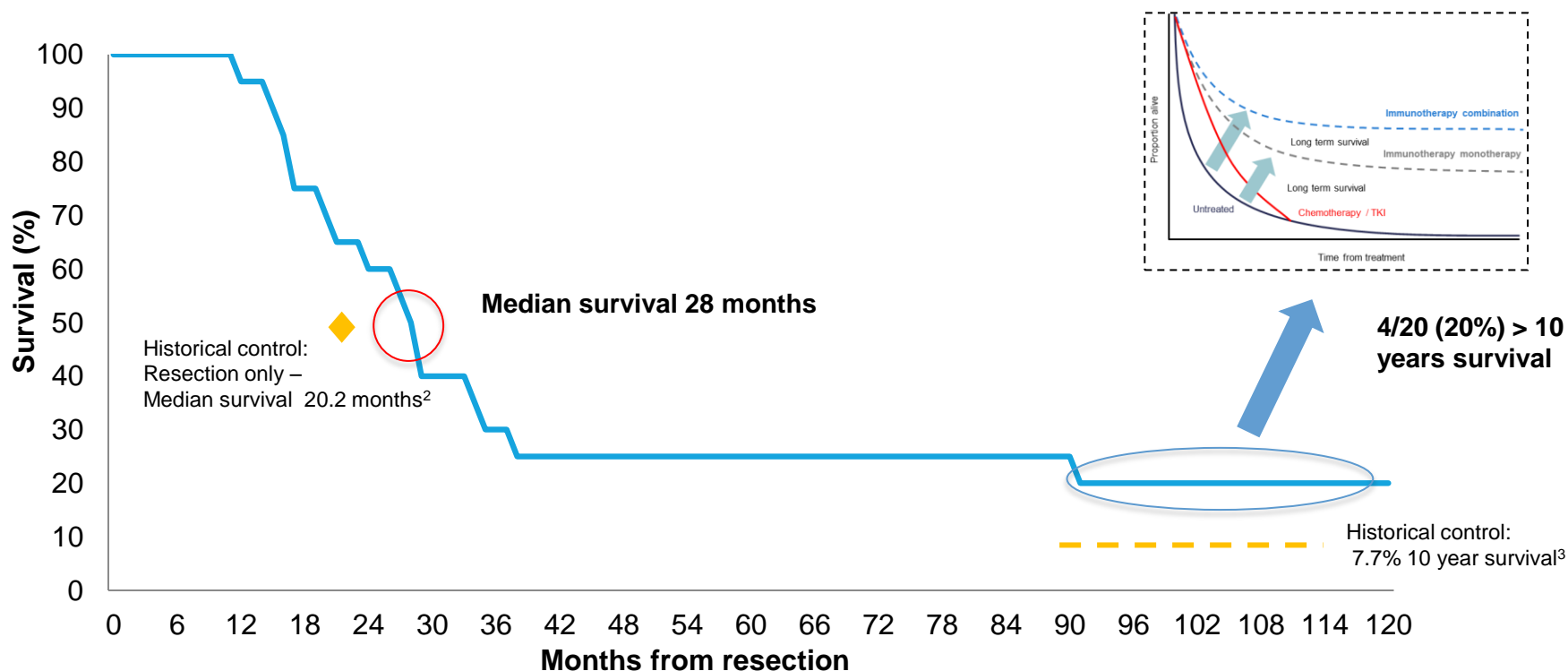
- No detectable TG01 specific T cell response at baseline
- Strong TG01 specific T cell response at study week 11; TG01 given from week 1 and gemcitabine from week 4
- The TG01 specific immune response was maintained and strengthened at week 52 after completion of 5-6 months of chemotherapy and continuing with monthly TG01 boosters

¹ Delayed Type Hypersensitivity

Source: Internal data on file

Resected pancreatic cancer: Retrospective analysis showed encouraging long-term survival for patients treated with TG01 peptides

Combination of 2 trials with RAS peptide mono-therapy with 20 patients¹ – Survival curve typical for effective immunotherapy



¹Two clinical trials with TG01 peptides conducted by Norsk Hydro in the period 1994-2000 were designed to only investigate safety and immune responses against the mutated RAS peptides, not to assess long term survival. Patients were treated with either a single TG01 peptide (9 patients) or TG01 (11 patients). The retrospective analysis was undertaken and published by the investigators (Wedén et al 2011)

¹ Wedén et al, 2011 and Clinical trial reports

² Oettle H et al. JAMA 2007, vol 297 no 3

³ Oettle H et al. JAMA 2013 vol 310, no 14

The TG01 opportunity

1

Large unmet medical need – 20-30% of *all* cancers have RAS mutations



2

RAS mutations represent a unique target for immuno-oncology



3

Immunological Proof of Principle established for TG01 –
elicits RAS-specific immune responses in most patients



4

There is also solid scientific rationale as for combining TG01 with CPIs

Straight forward manufacturing and logistics



Manufacturing



- Production process for TG01 currently being tailored and optimised
- Production process established and confirmed for TG02
- Highly reputed CMOs contracted
- Low COGS

- Production process for ONCOS-102 currently being tailored and optimised
- Highly reputed CMO contracted
- Low COGS

Logistics



- Standard shipping - easy and simple
- Standard on-site preparations (reconstitution in water)
- Documented 3 years shelf life

- Off-the-shelf product that can be used in any medical centre
- Stable at -20 °C
- No need for special storage facilities

IP/Exclusivity¹

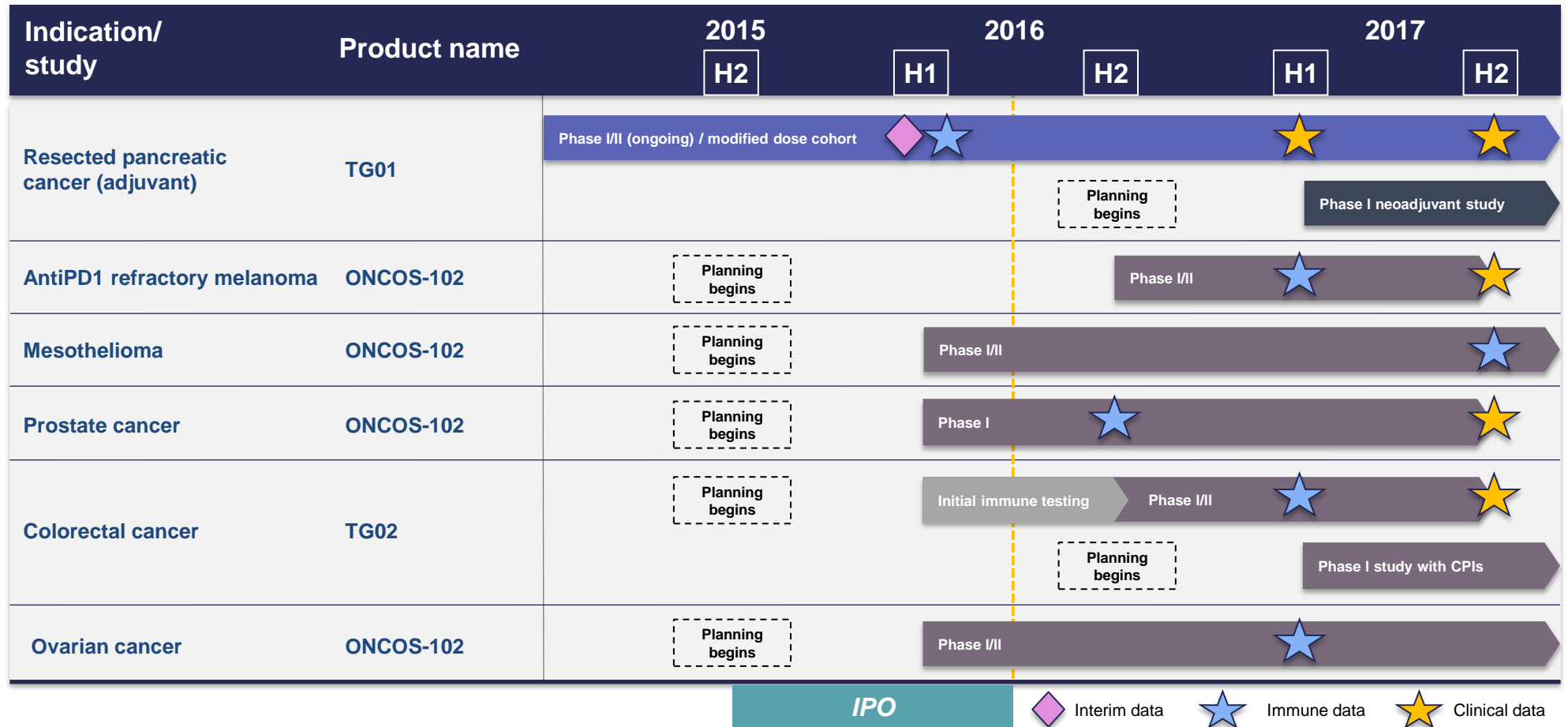


- 2019, 2033/2034 (filed applications)
- Orphan Drug Designation in pancreatic cancer

- Patent until ~2029 (granted/pending)
- Orphan Drug Designation in sarcoma, ovarian cancer and mesothelioma

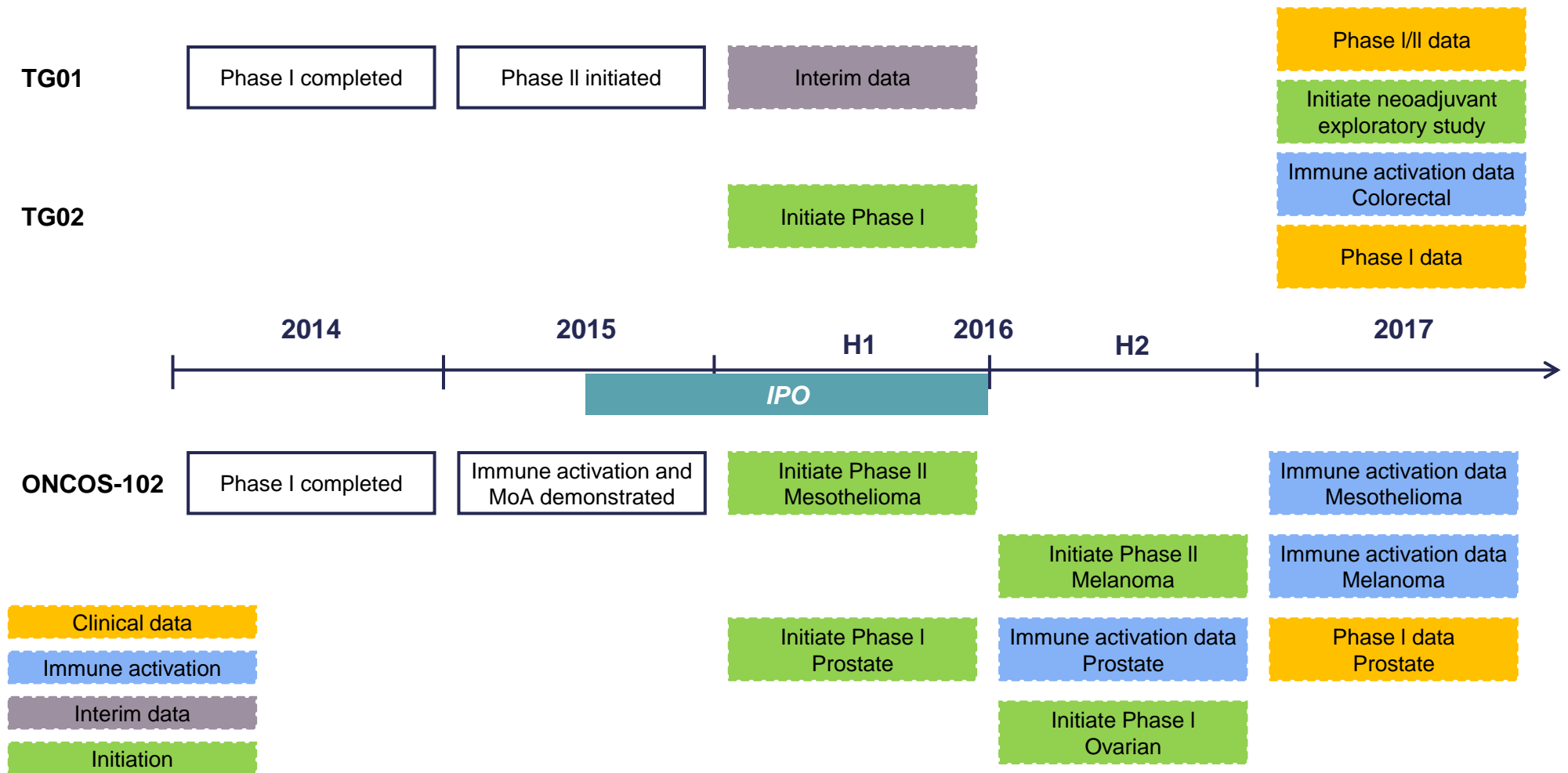
¹ Please see slide 33-35 for more details

Clinical development program 2015-2017



- Expected operational cost H2 2015 of NOK 55-60 million
- Advanced discussions with renowned cancer institutions and big pharma regarding collaboration and combination studies

News flow 2014-2017



Senior Executive team



Gunnar Gårdemyr, CEO

- More than 30 years of international experience from the pharmaceutical and biotech industry including business development, mergers & acquisitions, global marketing and commercial strategy
- Previously Senior Vice President, Corporate Development/M&A, Global Business Development at Nycomed and Senior Vice President, Global Marketing at Takeda in Zurich, Switzerland



Øystein Soug, CFO

- Previously CFO at Algeta, where he built up the functions of Finance, IR, Compliance, IT and HR
- Oversaw Algeta's launch of Xofigo, capital raisings of some USD 200m and the subsequent USD 2.9 bn sale of Algeta to Bayer
- Experience from positions at Orkla Group as CFO of Sladco, the Russian operations of Orkla, and Project Manager in Orkla's Corporate Development M&A team



Dr. Magnus Jaderberg, CMO

- More than 25 years in various R&D functions and previously CMO at Bristol Meyers Squibb (Europe)
- Experience from all phases of clinical research, including clinical pharmacology, dose finding, registration, post launch product differentiation and surveillance
- Immunotherapy expertise includes Yervoy (ipilimumab), Enbrel (etanercept), Torisel (temsirolimus), Orencia (abatacept), Rapamune (sirolimus) and Nulojix (belatacept)



Jon Amund Eriksen, COO

- 35 years of R&D experience from pharmaceutical and biotech industry, 25 years within immuno-oncology
- Co-founder of Targovax, co-inventor of technology
- Has held managing positions within development of cancer immunotherapy from early preclinical to phase III clinical development

Experienced Board of Directors



Johan Christenson, MD, PhD

- Partner of HealthCap
- Previously supervised the healthcare portfolio of SEB Företagsinvest
- Senior management experience from Astra Pain Control as Project Director and AstraZeneca as Global Product Director
- PhD in basic neuroscience
- Author of 17 scientific articles



Per Samuelsson

- Partner of HealthCap
- Prior to joining Odlander Fredrikson in 2000, he gained over 15 years of investment banking experience, mainly with Aros Securities in Sweden
- Prior to this Mr. Samuelsson was head of Research, also at Aros Securities



Jónas Einarsson, MD

- Chief Executive Officer of the Radiumhospitalets Forskningsstiftelse
- On the board of several Norwegian Biotech companies, and was one of the initiators behind Oslo Cancer Cluster and the Oslo Cancer Cluster Innovation



Lars Lund-Roland

- CEO of Bringwell AB (public)
- Previously Managing Director of MSD Norway (Merck & Co Inc. subsidiary) for 10 years and has more than twenty-five years' experience from various executive positions within marketing and sales
- Chairman of the Board of PI Innovation and has served as board member of Infodoc and Health Tech



Bente-Lill Romøren

- Board member of Targovax, Radiumhospitalets Forskningsstiftelse, Nordic Nanovector, and chairman of Farmastat and Photocure
- Was previously employed by Novo Nordisk Scandinavia AS from 1976 to 2012 in various positions, including as CEO of the Norwegian unit (2008-2012)
- Holds a MSc degree in Chemistry

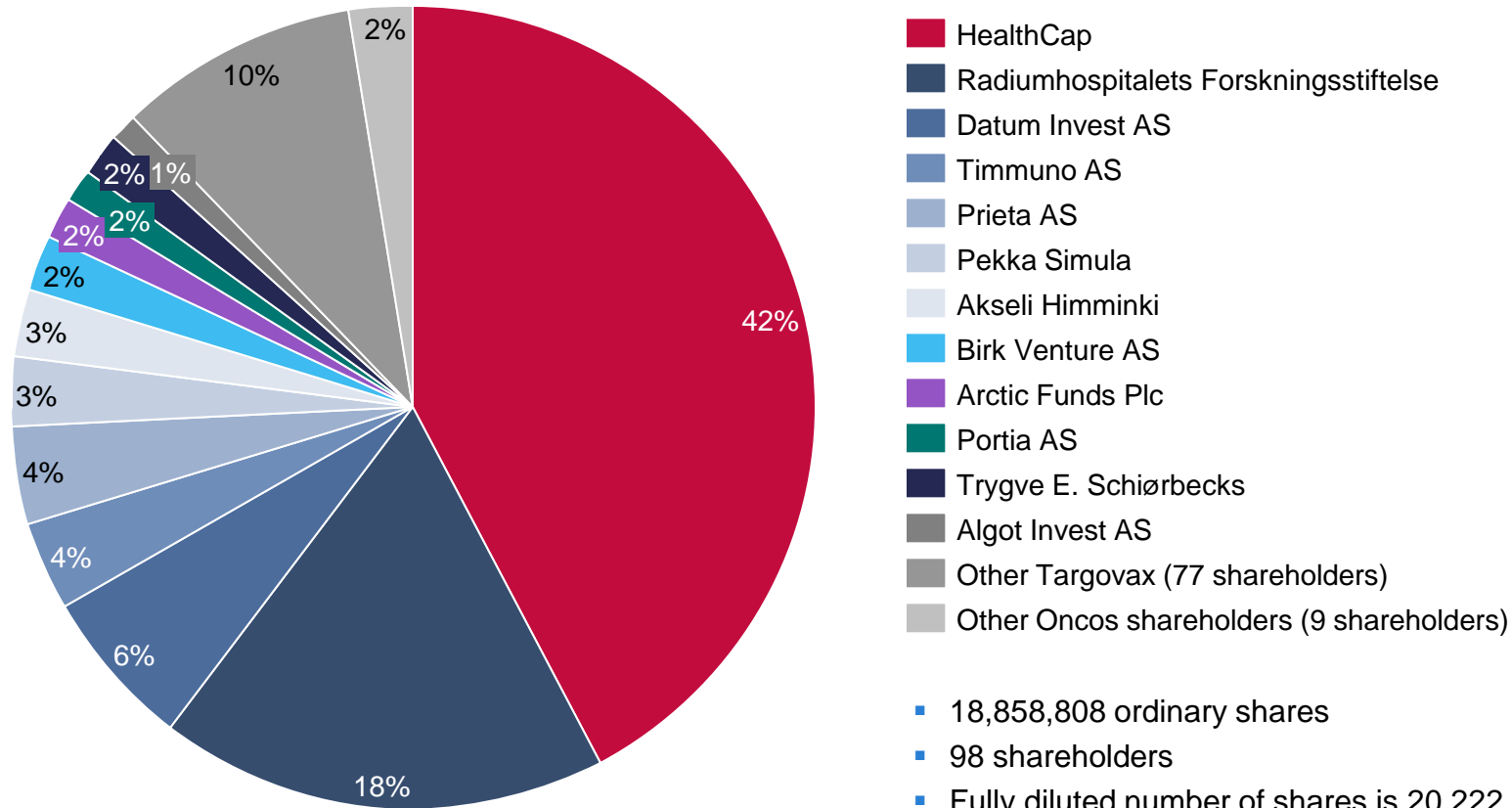


Robert Burns, PhD

- CEO at 4-Antibody and Chairman at Haemostatix, Robert has extensive experience in building biotechnology companies, previously as the CEO of Affitech (NASDAQ/OMX) and Celldex Therapeutics (NASDAQ)
- Prior to Celldex, Robert was Director of Technology Licensing at the Ludwig Institute for Cancer Research

Strong shareholder base

Polaris' combined shareholder structure



- 18,858,808 ordinary shares
- 98 shareholders
- Fully diluted number of shares is 20,222,264¹
- Average strike price on options NOK 24.6
- Total dilutive effect of options is <7.0%

¹ Subject to final exchange ratio and agreement with the option holders

Polaris represents a unique opportunity to invest in a Nordic immuno-oncology champion

1 Immuno-oncology is the fastest growing life science segment

2 Unique technologies with promising data

3 Multiple value inflection points

4 International, experienced management team

5 Backed by leading life science focused investors

Appendix

Polaris is born out of the merger of two immuno-oncology specialists with complementary capabilities

	Item	Targovax	Oncos
Corporate	Founded	2010	2009
	Location	Oslo	Helsinki
	Number of FTEs	12	12
	IP situation	2019, 2033/2034 (filed applications) ODD in pancreatic cancer	Lead asset 2029 ODD in STS, OvCa, mesothelioma. Biological product exclusivity in the US
Compound	Nature of vaccine	RAS peptides	Adenovirus mobilising patient's own antigens
	Administration (induction + maintenance injections)	Intradermal injections	Intratumoral injections
	Safety	Treatments are well tolerated in humans	Treatments are well tolerated in humans
	Patient safety database	19 + 120 (250) ¹	12 + 115 (290) ²
	Patients treated in Phase I	19	12
	Efficacy	Not in a controlled setting	92% patients with immune response and 40% disease stabilization in Phase I
	Potential indications	All tumors with RAS mutations	All solid, accessible tumors
Logistics	Production	Standard production processes currently being tailored and optimized with external suppliers	Easy manufacturing process currently being optimised with external supplier
	COGS	Low	Low

¹ Targovax: the safety database consists of 19 patients treated in the ongoing phase I/II and of 250 historical patients, of which 120 have received TG01 peptides.

² Oncos: the safety database consists of 12 patients treated in the recent phase I and of 290 historical patients, of which 115 have received ONCOS-102

Scientific presentations by Targovax and Oncos at ASCO 2015, Chicago
29 May – 2nd June

An evaluation of local and systemic immune markers following intratumoral administration of a chimeric adenovirus Ad5/3-D24-GMCSF in refractory cancer patients with solid tumors

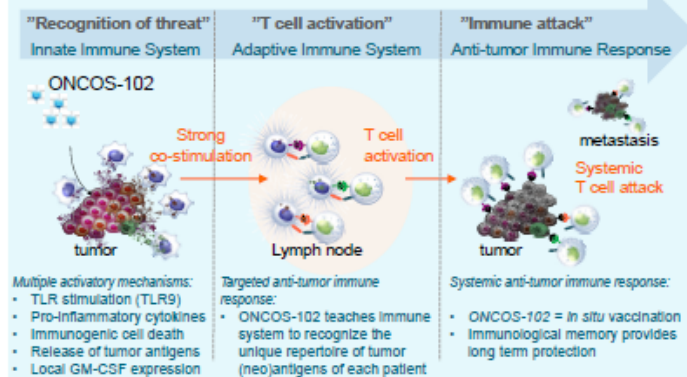
Pesonen O¹, Ranki T¹, Jäger E², Korbach J³, Wahle C⁴, Joensuu T⁵, Alanko T⁶, Partanen K⁷, Kallio K⁸, Tunkki R⁹, Linder N⁹, Lundin J⁹, Ristimäki A⁹, Majumder M⁹, Kumar A⁹, Heckman C⁹, Kankainen M⁹, Hemminki A⁹, von Euler M⁹, Jäderberg M⁹

¹Onco Therapeutics Ltd, Helsinki, Finland, ²Hämatologie-Onkologie, Krankenhaus Nordwest, Frankfurt, Germany, ³Docrates Cancer Center, Helsinki, Finland, ⁴Institute for Molecular Medicine Finland (FIMM), Helsinki, Finland, ⁵Division of Pathology, HUSLAB and Haartman Institute, Helsinki University Central Hospital, Helsinki, Finland, ⁶Genome-Scale Biology, Research Programs Unit, University of Helsinki, Helsinki, Finland, ⁷University of Helsinki and Helsinki University Central Hospital, Cancer Gene Therapy Group, Helsinki, Finland.

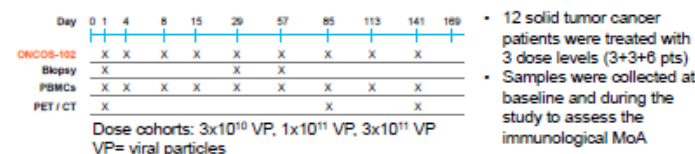
INTRODUCTION

ONCOS-102 (Ad5/3-D24-GMCSF) is a tumor-targeted immune activating adenovirus coding for human GM-CSF

Intratumoral ONCOS-102 has been shown to induce a systemic CD8+ T cell response against patient's unique cancer cells:



Phase I study - design



Activation of innate immune system following ONCOS-102

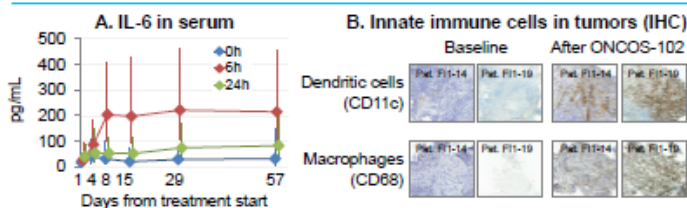


Figure 1. All patients showed an immediate short-term increase in systemic IL-6 (A) and IL-8 (not shown) following each intratumoral ONCOS-102 administration. Infiltration of dendritic cells and macrophages into tumors was seen after treatment initiation (B).

ONCOS-102 induced CD8+ T cell infiltration and Th1 polarization in tumors

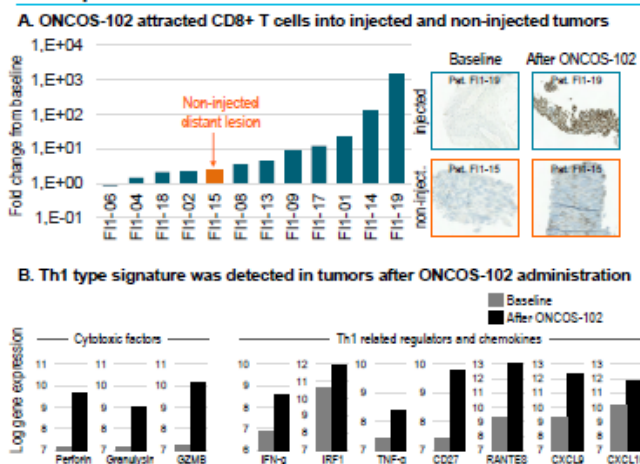


Figure 2. Gene expression profiling (F11-14) showed markedly elevated expression levels of genes encoding cytotoxic factors and genes related to Th1 signature in post-treatment sample suggesting that CD8+ TILs had an effector phenotype.

ONCOS-102 targets multiple tumor-derived antigens and induces long-term tumor-specific CD8+ T cell responses

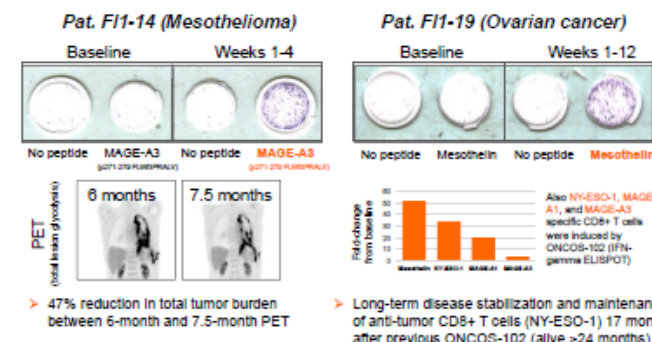


Figure 3. IFN-γ ELISPOT for tumor specific CD8+ T cells was performed. Purified CD8+ were pre-sensitized with peptide-pulsed, irradiated autologous PBMCs depleted of CD4+ and CD8+ T cells and tested on day 10 by IFN-γ ELISPOT assay for recognition of autologous antigen-presenting cells.

CD8+ T cell infiltration was associated with an increased PD-L1 expression in mesothelioma tumors

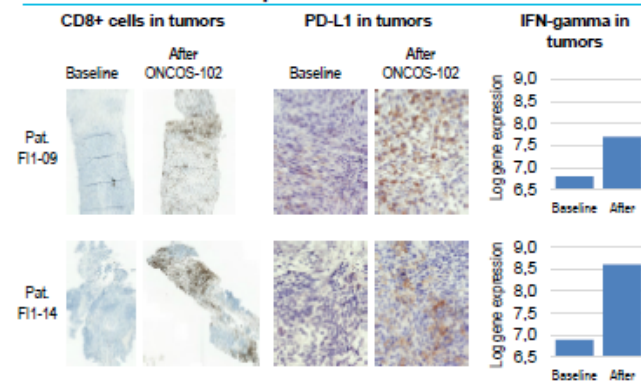


Figure 4. Infiltration of CD8+ T cells and increased PD-L1 expression in mesothelioma tumors was seen following ONCOS-102 administration. Gene expression analysis showed a concomitant increase in intratumoral IFN-γ expression. Data suggest that ONCOS-102 mediated anti-tumor immune attack triggered an adaptive resistance in tumors as measured by upregulated PD-L1 expression post ONCOS-102.

CONCLUSIONS

- Infiltration of CD8+ T cells was seen in 92% (11/12) of patients following ONCOS-102 administration both in injected and non-injected tumors
- Local ONCOS-102 treatment induced a systemic tumor-specific CD8+ T cell response in the last-line refractory solid tumor patients who showed no evidence of anti-tumor immunity at baseline
- Concomitant increase in CD8+ TILs and PD-L1 expression in tumor cells suggests that ONCOS-102 mediated anti-tumor immune attack triggered an adaptive resistance in tumors
- Data provide a strong rationale for combinational use of ONCOS-102 and PD-(L)1 blockade

A prospective, single-arm, phase I/II trial of RAS peptide vaccine TG01/GM-CSF and gemcitabine as adjuvant therapy for patients with resected pancreatic adenocarcinoma

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Background

TG01 is a cancer specific therapeutic peptide vaccine targeting oncogenic mutations in the RAS genes (K-, N- and H-RAS). RAS mutation is a driver for development of cancer and is present in up to 50% of all cancer and above 85% in pancreatic cancer¹. There is a large unmet medical need for treatment of cancers with RAS mutation. TG01 induces RAS mutation specific T cell responses.

TG01 consists of a mixture of 7 synthetic peptides that represent 7 of the most common codon 12 and 13 mutations in p27RAS associated with human cancer. Moigromastim (recombinant human granulocyte macrophage-colony stimulating factor (GM-CSF)) is co-administered with TG01 in order to enhance induction of the T cell responses.

TG01 is the first therapeutic peptide vaccine targeting RAS that entered clinical trials. Earlier studies demonstrate that adjuvant vaccination with TG01/GM-CSF given as monotherapy to pancreatic cancer patients after tumor resection induce immune response in 100% of evaluable patients².

Adjuvant treatment of resected pancreatic cancer with gemcitabine are now widely used and the present study evaluates safety and immunological response of the RAS peptide vaccine TG01/GM-CSF when given in combination with gemcitabine as adjuvant therapy.

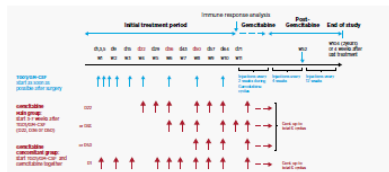
Methods

Eligible patients had a confirmed diagnosis of adenocarcinoma of the pancreas and successful surgical resection (R0 or R1), no previous radiation or chemotherapy (except for primary neoadjuvant chemotherapy, if applicable) and were expected to receive gemcitabine as adjuvant chemotherapy within 12 weeks of surgery.

Patients started TG01/GM-CSF within 1-8 weeks after surgery and chemotherapy with Gemcitabine (1000 mg/m² for 3/4 weeks x 6 cycles) 5-7 weeks after vaccination or started TG01/GM-CSF and chemotherapy concomitantly within 12 weeks of surgery (Figure 1).

The patients were assessed for immune responses (DTH) up to week 11 after receiving at least one cycle of gemcitabine. Safety information was collected during the entire 2-year study period. Patients who could not tolerate gemcitabine could be switched to 5-FU/leucovorin.

Figure 1. TG01-01 Study Design



Results

This is an ongoing study and preliminary data as of 25th April 2015 are presented. 19 patients have been included from three sites (1 in Norway and 2 in UK), 18 patients were eligible for immune assessment in initial treatment period (up to week 12). Patient baseline characteristics are shown in table 1.

Table 1. Baseline Characteristics

Parameter	n (%)
Age (yr), median (range)	62 (45-75)
Gender, n (%)	
Male	10 (52.6%)
Female	8 (42.8%)
Baseline ECOG score, n (%)	
0	1 (5.3%)
1	18 (94.7%)
Outcome surgery, n (%)	
R0	6 (31.6%)
R1	12 (63.2%)

Four patients are still ongoing (3-6 months after the start of vaccination) and 15 patients have discontinued from the study (Table 2). Six patients had confirmed disease recurrence (1 died due to disease progression).

Table 2. Patient Disposition

	Number of Patients (n=19)
Patients ongoing	4
Discontinued (1 death from progression)	6
Withdrawn:	
Consent withdrawn	2
Investigator decision	2
Adverse events (including 1 unrelated death)	4

Immunological response

Overall immune response as detected by delayed type hypersensitivity (DTH) testing in the skin and in vitro T cell proliferation are presented in Table 3. Positive DTH response (average diameter >5mm) was detected in 14/18 (78%) treated patients, 14/17 (82%) evaluable patients, 13/14 (93%) in main group and 1/3 (33%) in concomitant group.

Table 3. Immune responses detected by DTH and in vitro T cell proliferation

	Positive DTH response (n=18)	Positive T cell response (n=17)
Total	14/18 (78%)	14/17 (82%)
Main group	13/14 (93%)	13/14 (93%)
Concomitant group	1/3 (33%)	0/3 (0%)

The KRAS mutation status and detected immune responses for individual patients are summarized in Table 4.

KRAS mutation (codon 12/13) were detected in 15/17 (88%) of the analyzed patients. 14/17 (82%) patients had detectable DTH skin reaction to TG01 by week 12, all being positive at week 6 or week 6. 1/3 (33%) evaluable patients in the concomitant group had detectable DTH.

Possible causes for the observed drop in DTH responses after second cycle of chemo (week 10) might be the effects of prolonged chemotherapy and/or natural fluctuations³.

In vitro T cell analyses showed induction of TG01 specific immune responses (Stimulation Index (SI) >2) in 6/8 (75%) evaluable patients analyzed to date, all in main group. As shown in Figure 2a, the immune response increased over time after continuous vaccinations. Immune responses were detected for all single peptides covered in TG01 demonstrating that all peptides are immunogenic (Figure 2b).

Table 4. Detected KRAS codon 12 or 13 mutation and immune response
a. Main group; TG01/GM-CSF from week 1, TG01/GM-CSF and gemcitabine from week 4

Patients	KRAS mutation	DTH W1 (2002)	DTH W2 (2002)	DTH W3 (2002)	DTH W4 (2002)	DTH W5 (2002)	DTH W6 (2002)	DTH W7 (2002)	DTH W8 (2002)	In vitro T cell response (SI)
PR 01-001	WT	+	+	+	+	+	+	+	+	+
PR 01-002	WT	+	+	+	+	+	+	+	+	+
PR 01-003	WT	+	+	+	+	+	+	+	+	+
PR 01-004	WT	+	+	+	+	+	+	+	+	+
PR 01-005	WT	+	+	+	+	+	+	+	+	+
PR 01-006	WT	+	+	+	+	+	+	+	+	+
PR 01-007	WT	+	+	+	+	+	+	+	+	NE
PR 01-008	WT	+	+	+	+	+	+	+	+	+
PR 01-009	WT	+	+	+	+	+	+	+	+	+
PR 01-010	WT	+	+	+	+	+	+	+	+	+
PR 01-011	WT	+	+	+	+	+	+	+	+	NE
PR 01-012	WT	+	+	+	+	+	+	+	+	NE
PR 01-013	WT	+	+	+	+	+	+	+	+	NE
PR 01-014	WT	+	+	+	+	+	+	+	+	NE
PR 01-015	WT	+	+	+	+	+	+	+	+	NE
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PR 01-026	WT	+	+	+	+	+	+	+	+	NE
PR 01-027	WT	+	+	+	+	+	+	+	+	NE
PR 01-028	WT	+	+	+	+	+	+	+	+	NE
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PR 01-031	WT	+	+	+	+	+	+	+	+	NE
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PR 01-037	WT	+	+	+	+	+	+	+	+	NE
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PR 01-039	WT	+	+	+	+	+	+	+	+	NE
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IP

Targovax's IP

Owner	Patent / Patent application	Priority date	Status	Area covered
Targovax	PCT/EP2015/059861	2014-05-06	Pending	The administration of a mixture of RAS-mutated peptides together with an anti-metabolite chemotherapeutic agent such as gemcitabine leads to a stronger immune response than the administration of the peptide mixture alone.
Targovax	PCT/EP2014/077033	2013-12-09	Pending	A mixture of at least two defined RAS-mutated peptides can be used as a vaccine against, or treatment for, over 99% of all RAS mutated cancers. In addition, mixtures of T cells specific for RAS-mutations in individual patients can be administered to those patients, with or without RAS-mutated peptides.
Targovax	WO 0066153 (A1)	1999-04-30	Granted	Method of vaccinating humans with <u>a mixture</u> of RAS-mutated peptides to elicit a RAS-specific T cell immune response (therapeutic and prophylactic use). <i>This patent covers TG01 and TG02.</i>
Targovax	WO 9910382 (A1)	1997-08-27	Granted	Description of 9 amino acid long RAS peptides that activate MHC class I dependent CD8+ cytotoxic T cells
Targovax	WO 9214756 (A1) EP 0529023 (B1) US 5961978 (A)	1991-02-26	Expired	Method of vaccinating humans with <u>single</u> RAS-mutated peptides to elicit a RAS-specific T cell immune response (therapeutic and prophylactic use)

Oncos' IP

Owner	Patent / Patent application	Priority date	Status	Area covered
Oncos	WO2013076374 (A1)	2011-11-25	Granted in some countries / pending	ONCOS-402 viral constructs
Oncos	US 20130243731 (A1) WO 2012038606 (A1)	2011-09-23	Granted in some countries / pending	Viral constructs containing CTLA-4 gene
Oncos	US 2013323205 (A1) WO 2012038607 (A1)	2010-09-24	Granted in some countries / pending	Viral constructs containing the CD40L gene
Oncos	WO 2010072900 (A1)	2008-12-22	Granted in some countries / pending	ONCOS-102 viral construct and its uses

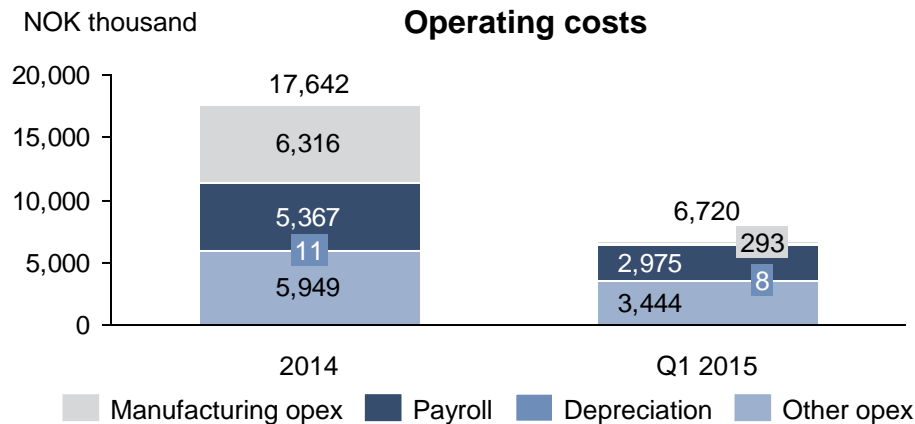
Polaris' Orphan Drug Designations

Owner	Product	Indication	Granted by EMA	Granted by FDA
Targovax	TG01	Pancreatic Cancer	2011-08-05	2011-06-07
Oncos	ONCOS-102	Malignant Mesothelioma	2014-12-16	2014-12-22
Oncos	ONCOS-102	Ovarian Cancer	2014-04-29	2014-03-17
Oncos	ONCOS-102	Soft-Tissue Sarcoma	2013-06-19	2013-07-24

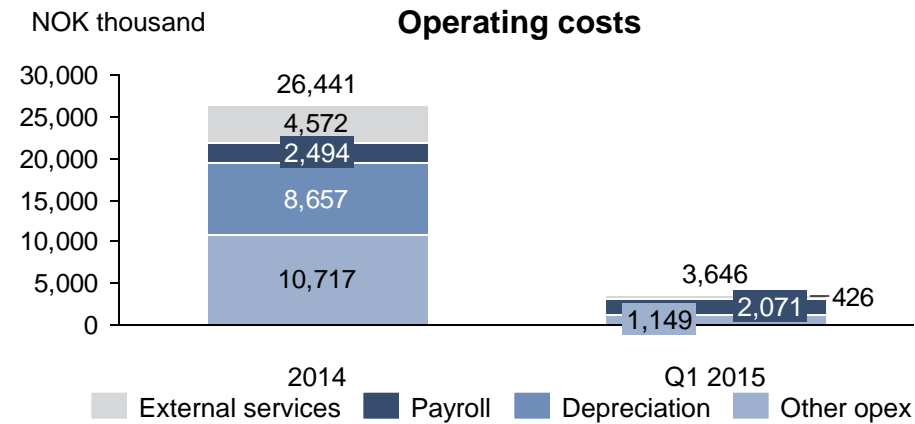
Financial information

Breakdown of operating costs and current cash position

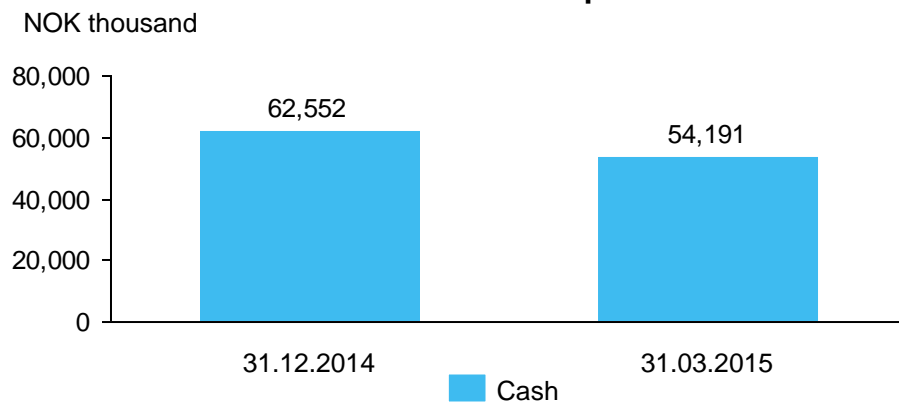
Targovax (IFRS)



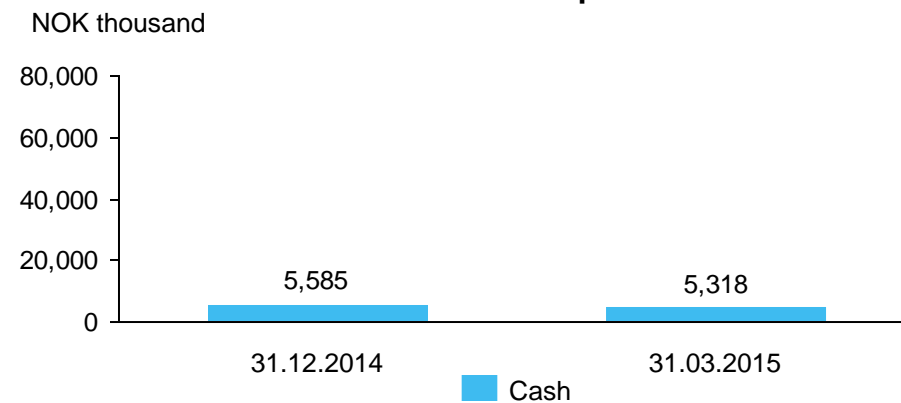
Oncos (Finnish GAAP)¹



Cash and cash equivalents



Cash and cash equivalents



¹ Oncos' financials are currently being converted from Finnish GAAP to IFRS

Note: The following EUR/NOK exchange rates have been applied to Oncos' financials: cash position as of 31.12.2014 converted using EUR/NOK exchange rate of 9.0365 (31.12.2014); cash position as of 31.03.2015 converted using EUR/NOK exchange rate of 8.7035 (31.03.2015). Operating costs 2014 converted using EUR/NOK exchange rate of 9.0365 (31.12.2014), Operating costs Q1 2015 converted using EUR/NOK exchange rate of 8.7035 (31.03.2015). All exchange rates from Norges Bank

Capitalisation and share based payment – Targovax

Capitalisation

Month	Share capital (NOKm)	New shares (m) ¹	Total shares (m)	Share price (NOK/share)	Paid in NOKm	Comment
Oct-2010	0.1	1.0	1.0	0.1	0.1	Share issue
Jan-2011	0.2	0.7	1.7	0.1	0.1	Share issue
Mar-2011	0.2	0.3	2.0	1.2	0.4	Share issue
Feb-2012	0.4	1.7	3.7	7.5	12.8	Share issue
Feb-2013	0.5	1.0	4.7	7.5	7.5	Share issue
Feb-2014	0.6	1.5	6.2	8.5	12.5	Share issue
Jun-2014	0.9	3.3	9.4	21.5	70.0	Share issue
Total	0.9		9.4		103.3	

Share based payment

- Targovax operates an equity-settled, share-based compensation plan, under which the entity receives services from employees as consideration for equity instruments (options) in the Company
- Each share option converts into one ordinary share of Targovax on exercise. Options may be exercised at any time from the date of vesting until expiry
- The following share-based payment arrangements were in existence during the current and prior years

Granted ²	Number of options	Exercise price (NOK)	Fully vested
05/11/2012	50,000	7.5	05/11/2015
05/11/2012	25,000	7.5	05/11/2015
05/11/2012	25,000	7.5	05/11/2015
12/01/2015	300,000	21.5	12/01/2020
01/06/2015	300,000	25.0	01/06/2020
700,000			

¹ The nominal value of the shares was changed from 1,000 to 0.1 NOK between the March 2011 and February 2012 share issue. For comparable figures nominal value of 0.1 NOK are assumed for all years

² 50,000 additional options will be granted following closing of the transaction

Capitalisation and share based payment – Oncos

Historical share issue development¹

Shareholder	# Common shares (thousand)	# Series A preferred (thousand)	# Series B preferred (thousand)	Total shares (thousand)
HealthCap V L.P.	188.8	215.8	438.0	842.6
OFCO Club V	2.8	3.3	6.6	12.7
Pekka Simula	125.0			125.0
Akseli Hemminki	125.0			125.0
Lifeline Ventures III AB	37.9		3.4	41.3
Mikko Salo	25.2		0.4	25.6
Antti Vuolanto	16.0			16.0
Mark Roth	12.5		0.4	12.9
Jonathan Knowles	3.2		3.4	6.6
Charlotta Backman	5.0			5.0
Robert Burns / Alvos Oncology	2.1		2.0	4.1
Otto Hemminki	0.3			0.3
Total	543.8	219.1	454.2	1,217.1

Key facts

- Total share capital: EUR 4,000
- Total no of common shares: 543,825 (issued altogether at 13 instances with subscription price of 0.01 to 1 EUR)
- Total no of Series A shares: 219,114 (price of EUR 18.26 per share – issued in April 2010)
- Total no of Series B shares: 454,220 (price of EUR 18.26 per share – to be issued in June 2015)

Share based payment

- Oncos currently has 6 option programs
- Each share option converts into one ordinary share of Oncos on exercise. Options may be exercised at any time from the date of vesting until expiry
- Under 4 of the programs, the options may be exercised until 2031
- Based on total common share equivalents of 2.2 million, current value per Oncos share is NOK 106.8 and will be converted into Targovax shares at NOK 25. Number of options and exercise prices pre-merger will be converted with a factor of 4.27x post-merger
- The current option program in Oncos will be harmonised with Targovax after the merger to align exercise price and timing for all employees

Number of outstanding options pre-merger	Number of outstanding options post-merger ³	Exercise price post-merger (NOK)	Expiration
41,256	176,221	37.09	15/11/2019
12,000	51,257	37.09	01/07/2021
34,641	147,966	37.09	15/02/2021
28,139	120,193	0.51	01/01/2031
8,651	36,952	0.51	01/01/2031
9,688	41,381	37.09	01/01/2031
5,400	23,066	37.09	01/01/2031
15,550	66,420	37.09	01/01/2021
155,235	663,456	28.42²	

¹ Please note that the capitalisation table has been adjusted for the cancellation of shares from the register at the time of HealthCap Series A

² Volume weighted average exercise price post-merger

³ Subject to final exchange ratio and agreement with the option holders

Targovax key financials – 2014 and Q1 2015 (IFRS)

NOK thousand	31.12.2014	31.03.2015
Balance sheet		
Assets		
Fixed assets	150	142
Receivables	4,660	6,330
Cash	62,552	54,191
Total assets	67,362	60,663
Equity and liabilities		
Equity	60,673	54,524
Trade creditors	2,564	1,844
Accrued public charges	781	804
Other short-term liabilities	3,344	3,491
Total equity and liabilities	67,362	60,663

NOK thousand	2014	Q1 2015
P&L		
Operating revenues		
Other revenues	72	0
Total operating revenues	72	0
Operating expenses		
Payroll expenses	5,367	2,975
Depreciation	11	8
Manufacturing opex	6,316	293
Other operating expenses	5,949	3,444
Total operating expenses	17,642	6,720
Net financial items	-77	-31
Profit/loss	-17,646	-6,751

NOK thousand	2014	Q1 2015
Cash flow		
From operating activities		
Loss for the year	-17,646	-6,751
Interest income	-288	-177
Interest and other	81	2
Share options expense	147	602
Depreciation	11	8
Change in receivables	1,166	-1,670
Change in other current liabilities	2,694	-550
Net from operating activities	-13,835	-8,537
From investing activities		
Purchases	-160	0
Net from investing activities	-160	0
From financing activities		
Interest income	288	177
Interest expense	-1	-2
Other finance expense	-5	0
Share issue expense	-4,604	0
Proceeds from equity issue	72,500	0
Net from financing activities	68,178	176
Net cash flow	54,182	-8,361
Cash period start	8,370	62,552
Cash period end	62,552	54,191

Oncos Oy key financials – 2014 and Q1 2015 (Finnish GAAP)¹

NOK thousand	31.12.2014	31.03.2015
Balance sheet		
Assets		
Capitalised R&D	66,812	65,131
Other intangible assets	1,554	1,499
Shares in subsidiaries	753	726
Other current assets	3,362	4,065
Cash	5,585	5,318
Total assets	78,066	76,739
Equity and liabilities		
Equity	-35,414	-37,442
Loans from credit institutions (Tekes)	51,824	50,846
Convertible loans	57,951	60,733
Other current liabilities	3,705	2,602
Total equity and liabilities	78,066	76,739

NOK thousand	2014	Q1 2015
P&L		
Operating revenues		
Other revenues	0	0
Total operating revenues	0	0
Operating expenses		
Payroll expenses	2,494	2,071
Depreciation	8,657	0*
External services	4,572	426
Other operating expenses	10,717	1,149
Total operating expenses	26,441	3,646
Net financial items	-826	-44
Profit/loss	-27,275	-3,690

* Recognised at year-end

NOK thousand	2014	Q1 2015
Cash flow		
From operating activities		
Loss for the year	-17,793	-3,647
Interest income/ expense	-822	-44
Net from operating activities	-18,615	-3,690
Net from working capital	723	-2,443
Net from investing activities	-9,317	-783
From financing activities		
Long-term loans	26,269	6,284
Issue of shares	1,157	357
Net from financing activities	27,426	6,649
Net cash flow	217	-267
Cash period start	5,368	5,585
Cash period end	5,585	5,318

- Fee of USD 1.5 million triggered by the combination of Targovax and Oncos
- Oncos' financials are currently being converted from Finnish GAAP to IFRS
- Tekes loans are low-interest venture loans provided by the Finnish Government
- The convertible loans will be converted to equity as part of the closing of the transaction

¹ Figures excluding AG

Note: Balance and cash position as of 31.12.2014 converted using EUR/NOK exchange rate of 9.0365 (31.12.2014); balance and cash position as of 31.03.2015 converted using EUR/NOK exchange rate of 8.7035 (31.03.2015). P&L and cash flow figures 2014 converted using EUR/NOK exchange rate of 9.0365 (31.12.2014), P&L and cash flow figures for Q1 2015 converted using EUR/NOK exchange rate of 8.7035 (31.03.2015). All exchange rates from Norges Bank.

Oncos Oy key financials – 2014 and Q1 2015 (IFRS conversion)

NOK thousand	31.12.2014	31.12.2014	31.12.2014	31.03.2015	31.03.2015	31.03.2015
Balance sheet	FAS cons (incl. AG)	IFRS adjustments	IFRS total (incl. AG)	FAS cons (incl. AG)	IFRS adjustments	IFRS total (incl. AG)
Assets						
Intangible assets	68,363	(66,812)	1,551	66,841	(65,131)	1,711
Non-current assets	68,363	(66,812)	1,551	66,841	(65,131)	1,711
Trade and other receivables	4,153	0	4,153	4,252	0	4,252
Cash and cash equivalents	6,047	0	6,047	5,744	0	5,744
Current assets	10,199	0	10,199	9,996	0	9,996
Total assets	78,562	(66,812)	11,750	76,837	(65,131)	11,707
Equity and liabilities						
Share capital	36	0	36	35	0	35
Reserve for invested unrestricted equity	37,535	0	37,535	36,509	0	36,509
Retained earnings	(45,678)	(60,677)	(106,355)	(70,244)	(57,030)	(127,274)
Profit for the period	(27,254)	1,466	(25,788)	(3,591)	(1,071)	(4,662)
Equity	(35,361)	(59,212)	(94,573)	(37,292)	(58,100)	(95,392)
Borrowings ¹	51,822	(7,600)	44,222	50,849	(7,030)	43,818
Other non-current liabilities ²	58,671	0	58,671	61,374	0	61,374
Non-current liabilities	110,493	(7,600)	102,893	112,223	(7,030)	105,192
Account payables	1,362	0	1,362	600	0	600
Other current liabilities	2,068	0	2,068	1,306	0	1,306
Current liabilities	3,430	0	3,430	1,906	0	1,906
Total liabilities	113,923	(7,600)	106,323	114,129	(7,030)	107,099
Total equity and liabilities	78,562	(66,812)	11,750	76,837	(65,131)	11,707

- Intangible assets are written down when converted to IFRS as the criteria for capitalisation of internally developed intangible assets are not met
- With regard to the Tekes loans, changes when converting to IFRS include separating the grant component and recognising it in the P&L, as well as an increase in interest expenses (P&L)
- Convertible loans will be converted to equity as part of the closing of the transaction

¹ Tekes loans

² Convertible loans

Note: Balance sheet as of 31.12.2014 converted using EUR/NOK exchange rate of 9.0365 (31.12.2014); balance sheet as of 31.03.2015 converted using EUR/NOK exchange rate of 8.7035 (31.03.2015). All exchange rates from Norges Bank

Polaris – Preliminary unaudited pro forma balance sheet 31 March 2015 (IFRS)

NOK thousand	31.03.2015	31.03.2015	31.03.2015	31.03.2015
Balance sheet	Pro forma Oncos group (IFRS adjusted)	Targovax IFRS	Preliminary purchase price allocation	Pro forma
Assets				
Goodwill	0	0	38,069	38,069
Other intangible assets	335	0	273,377	273,711
Other fixed assets	1,376	142	0	1,518
Total non-current assets	1,711	142	311,446	313,298
Receivables	4,252	6,330	0	10,582
Cash and cash equivalents	5,744	54,191	0	59,935
Total current assets	9,996	60,521	0	70,517
Total assets	11,707	60,663	311,446	383,815
Equity and liabilities				
Shareholders equity	-34,018	54,524	269,753	290,259
Long-term liabilities				
Loans from credit institutions	43,818	0	0	43,818
Deferred tax	0	0	41,693	41,693
Short-term liabilities	1,906	6,139	0	8,045
Total liabilities	45,724	6,139	41,693	93,556
Total equity and liabilities	11,707	60,663	311,446	383,815

- Pro forma Oncos group adjustments: convertible loans are converted into new shares before closing
- Preliminary purchase price allocation based on high level review, and is subject to final allocation

Note: EUR figures converted using EUR/NOK exchange rate as of 31.03.2015: 8.7035

Source: Onco's IFRS Balance Sheet based on preliminary IFRS conversion prepared by PwC, Targovax IFRS Balance Sheet according to public Q1-2015 presentation

Definitions and glossary of terms

- **Immuno-oncology** is treatment that uses the body's own immune system to fight cancer
- **Immune response** is how the body recognizes and kills threats that appear foreign or harmful such as bacteria, virus or cancer cells
- **T cells** are cells of the immune system that defend the host against bacteria, viruses and cancer cells
- **Tumor antigens** are signaling proteins that characterize each individual tumor
- **Dendritic cells (DC)** are specialized immune cells that present the tumor antigens to the T-cells which results in T-cells that will recognize and attack the cancer
- **Tumor mutations** is a way of the tumor to undermine any form of host attack and to survive – **RAS** mutation is one example that is seen in all types of cancer at various degree
- **Peptides** are small proteins that can be produced to mimic tumor antigens. By injecting RAS mutation peptides, T cells can be induced that recognize such mutations which will trigger immunological eradication of cancer cells. Peptides need an adjuvant to work
- **Adjuvant** is an activator of dendritic cells. Targovax use GM-CSF (granulocyte macrophage colony stimulating factor) as the adjuvant.
- **GM-CSF** (the adjuvant) is a protein that activates DC. GM-CSF is commercially available (currently for use in phase II)
- **Immunological memory** means that T-cells can remember to recognize the threat, cancer in this case, and therefore also able to attack any subsequent cancer of the same type such as regrowth or metastases
- **Oncolytic viruses** work by replicating in the tumor thus releasing tumor antigens to the immune system with subsequent T-cell attack
- **Adeno viruses**, the backbone of ONCOS-102, are highly immunogenic and can be genetically engineered to only replicate in cancer cells and to release immune stimulators/adjuvants such as GM-CSF
- **Monitoring immune response** can be done in several ways - DTH, TILs and PBMC being three common examples:
 - **DTH** is a way of measuring an immune response towards a specific antigen. When the immune system has learnt to recognize e.g. the RAS peptides as foreign, the immune response can be measured by using DTH (delayed type hypersensitivity reaction). It is similar to the Pirquet – skin test used to measure effect of tuberculosis vaccination, by applying the foreign material the skin and observing the size of swelling / redness as a sign of an allergic/immunological reaction
 - **TILs** is measuring infiltration of T-cells (TIL=tumor infiltrating lymphocytes) into the tumor by analyzing a piece of the tumor after a biopsy or surgical resection. This analysis can tell us the extent of T-cells and the type of T-cells such as cytotoxic T-cells that are able to kill cancer cells
 - **PBMC** (peripheral blood mononuclear cells) are a group of immune cells in the blood. It is possible to analyze the different subpopulations of PBMC and see if a particular immune therapy has resulted in an increase of immune cells that have the ability to fight the cancer