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Solebury Trout European Biotech Investor Day 2019

1 August 2019

Øystein Soug, CEO

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ONCOLYTIC VIRUSES WITH KEY ROLE IN THE FUTURE CANCER THERAPY LANDSCAPE

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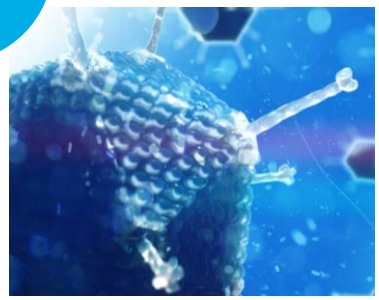

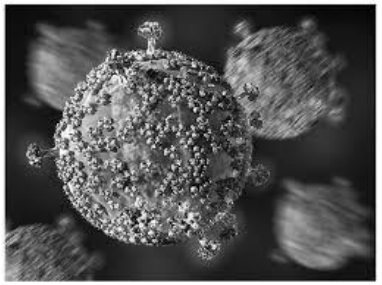

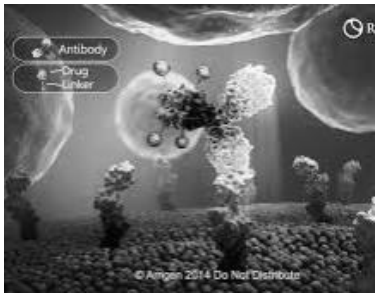

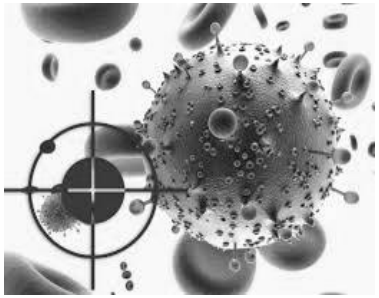

Immune activators
Oncolytic viruses

Immune modulators
Checkpoint inhibitors

Surgery - Radio - Chemo

Immune boosters
CAR-Ts, TCRs

Targeted therapy
TKIs, PARPs, etc.

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ONCOS ONCOLYTIC VIRUS

Adenovirus Serotype 5

- Genetically engineered to **selectively infect cancer cells**
- Turns cold **tumors hot**

- Single agent **phase I trial completed**
- **Four ongoing** clinical trials

- **Combination** with both **checkpoint inhibitors** and **chemotherapy**
- **Rich news flow** over the next 24 months

Activates the immune system

Triggers patient-specific immune responses

No need for individualization

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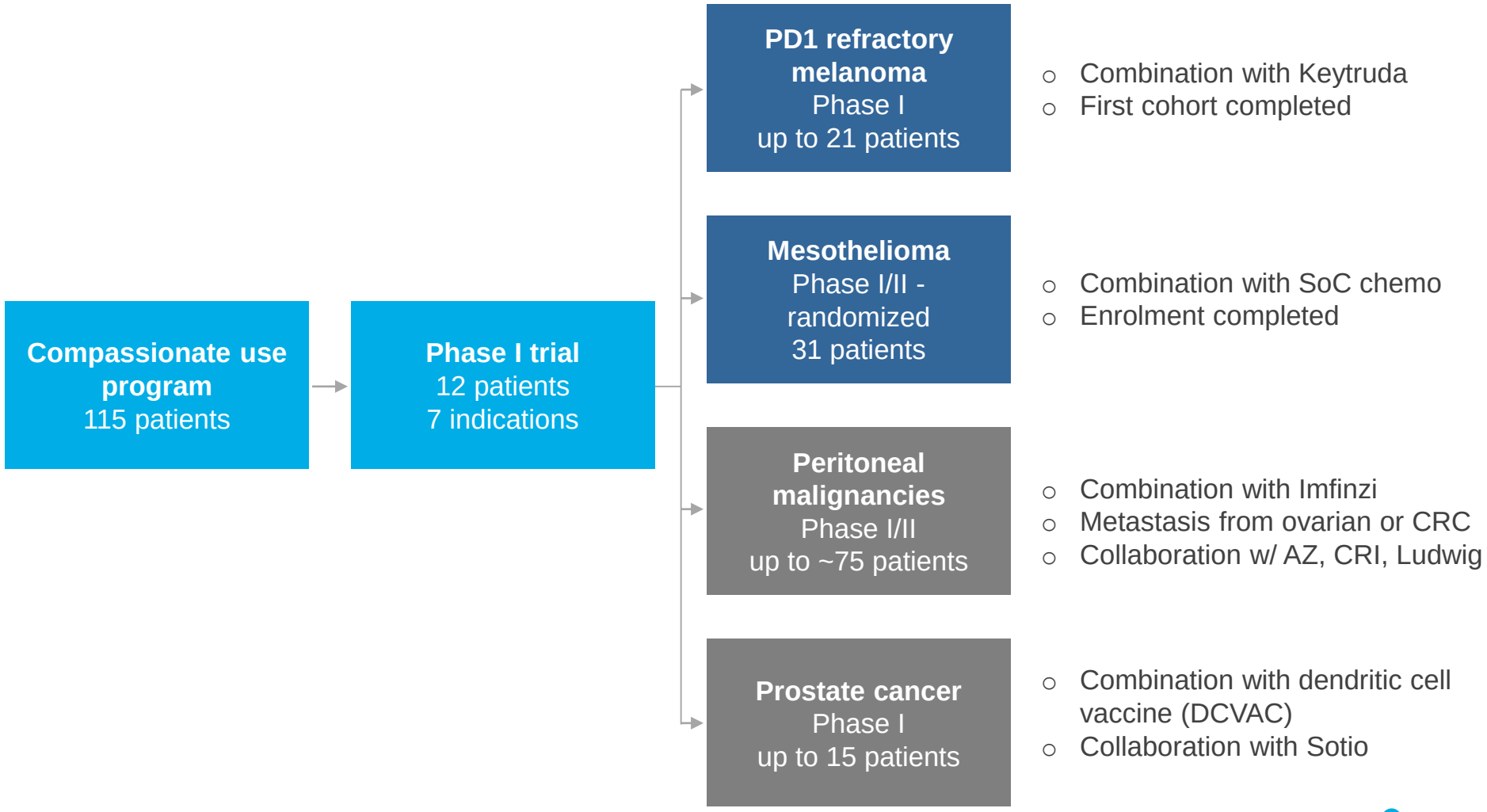
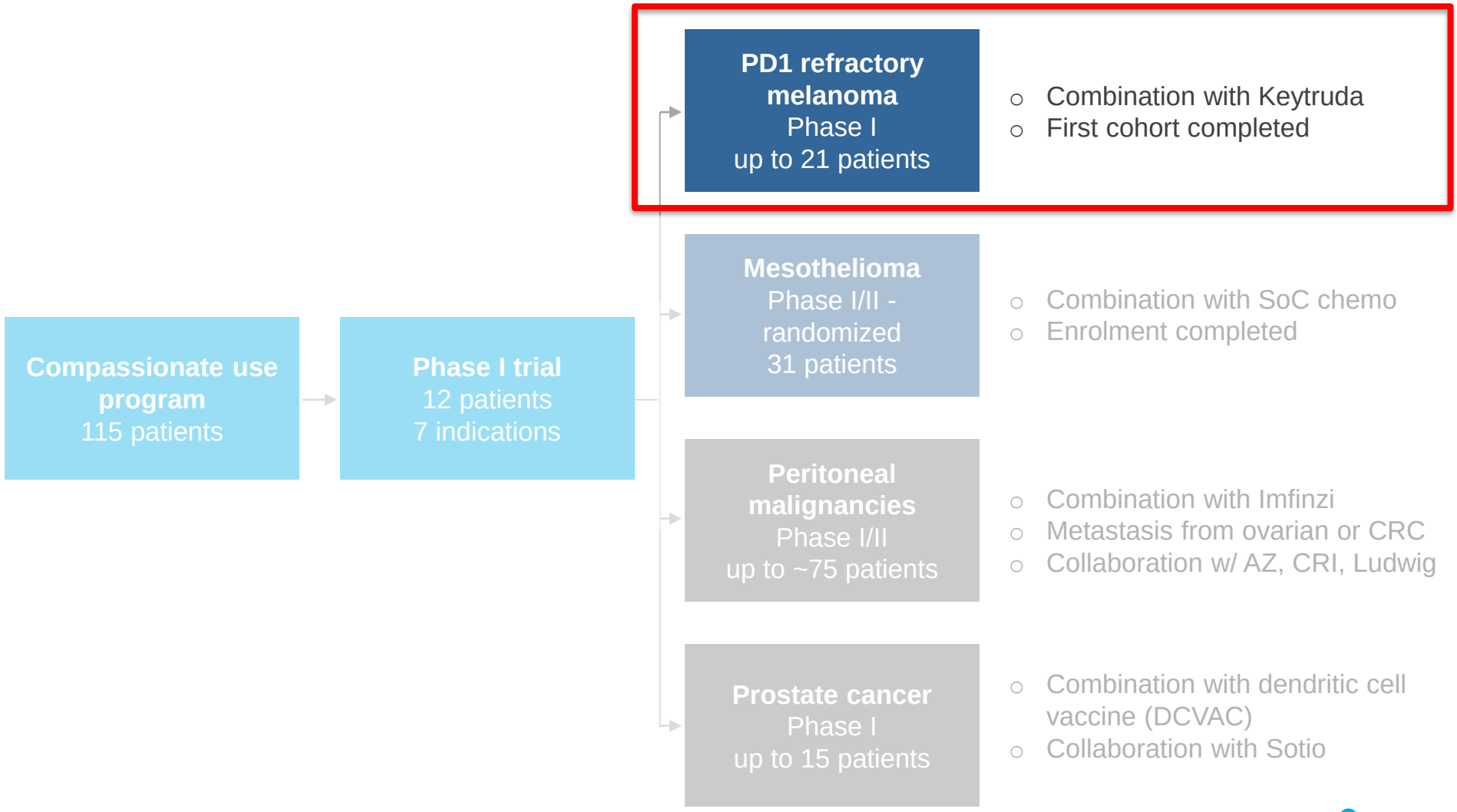
ONCOS-102 CLINICAL DEVELOPMENT PROGRAM



ONGOING ONCOS-102 PHASE I IN MELANOMA



ENCOURAGING ORR AND PROFOUND IMMUNE ACTIVATION

ONCOS-102 melanoma highlights

Trial objectives

- Test the hypothesis that ONCOS-102 will immune activate anti-PD1 refractory patients to **respond to re-challenge** with an anti-PD1 CPI

Patients

- 9 pts: advanced, unresectable melanoma with disease progression despite treatment with anti-PD1 CPI
- Challenging patient population, few treatment alternatives

Treatment

- **3 ONCOS-102 injections** followed by 8 cycles of Keytruda
- A second cohort, currently recruiting, tests up to 12 ONCOS-102 injections

Data

- **1 CR, 2 PRs; 33% ORR** (RECIST 1.1 and irRECIST)
- Profound innate and adaptive immune activation:
  - *systemic increases in pro-inflammatory cytokines (9/9)*
  - *increased infiltration of CD8+ T-cells in tumor (8/9)*
  - *increased T-cell infiltration into non-injected lesions (2/3)*
  - *tumor specific T-cells (4/9)*
- Best immune response seen in best clinical responder

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COMPLETE RESPONSE IN 1 OF 9 PATIENTS

following ONCOS-102 and Keytruda combination treatment

	Baseline	**Week 3** (from BL)	**Week 9** (from BL)
Stage III Prior therapies: Surgery x 3 Yervoy, Tafinlar + Mekinist, Keytruda	*Progression on Keytruda*	*Visible tumor regression after 3x ONCOS-102*	*CR after 3x ONCOS-102 & 2x Keytruda*
			
Immune data	○ Low level of TILs ○ Low PD-L1 expression ○ Detectable level of MAGE-A1 (systemic)	→ 16x increase → 13x increase → Significant increase	→ 6.8x increase → 2.6x increase → Significant increase

Preliminary data

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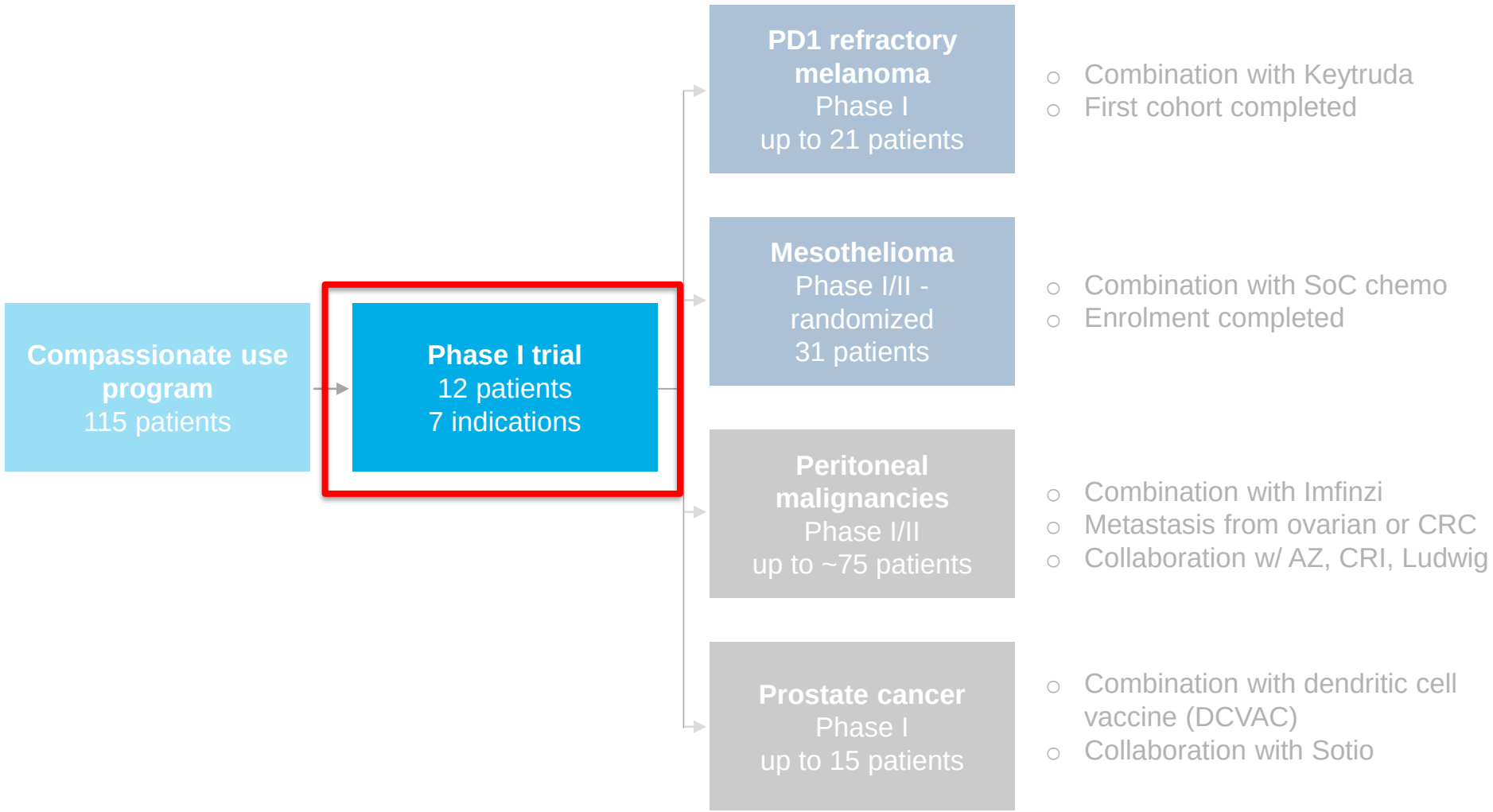
ONCOS-102 CLINICAL DEVELOPMENT PROGRAM

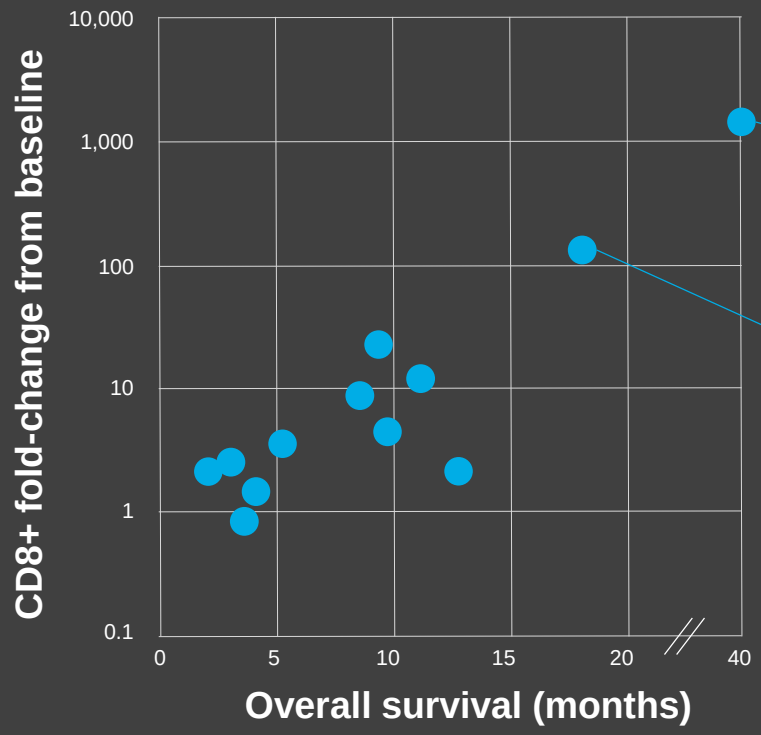


Phase I single agent proof-of-concept

CD8+ T-CELL INFILTRATION CORRELATES WITH SURVIVAL

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

r = 0.75 p = 0.005



Case examples:

#1 – Ovarian cancer: failed on 5 types of chemo

- **>1,000-fold increase** in CD8+ T-cell infiltration
- **Stable disease for 3 years**, survived for 3.5 years

#2 – Mesothelioma: radio- and chemo refractory

- **130-fold increase** in CD8+ T-cell infiltration
- **47% reduction of tumor on PET** 6 weeks after last ONCOS-102 injection, survived 18 months

Ranki et al., Journal for Immunotherapy of Cancer 2016, 4(17)

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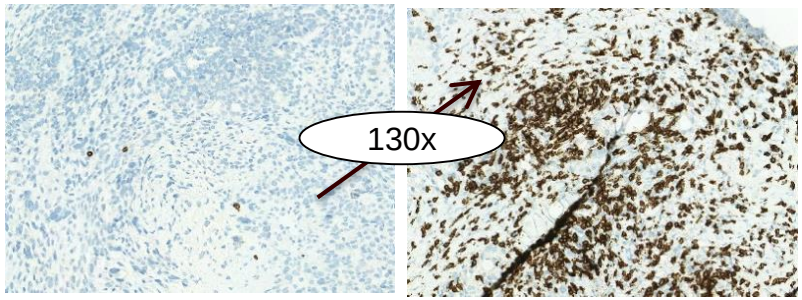
ONCOS-102 MONOTHERAPY IN MESOTHELIOMA

turning cold tumors hot

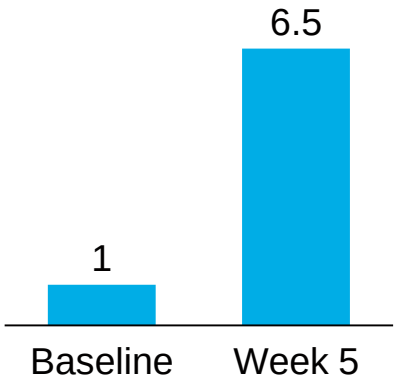
CD8+ T-cells in tumor
Tumor biopsy staining

***Mesothelioma** – Phase I, patient 14*

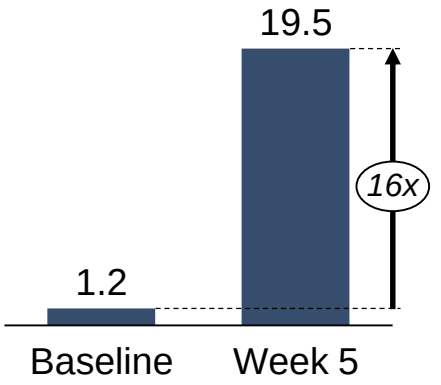


Baseline Week 5

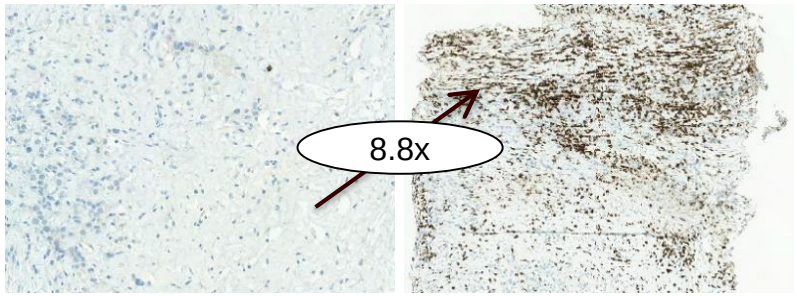
CD4+ T-cells in tumor
Fold change



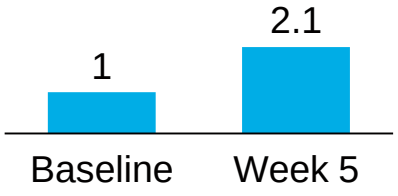
PD-L1 positive tumor cells
% of total

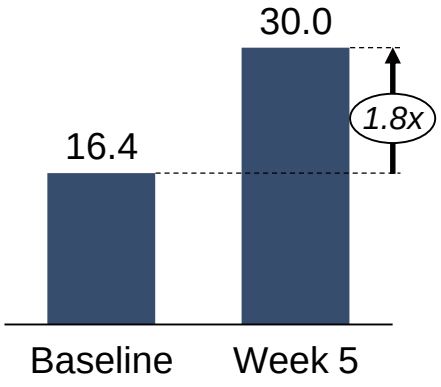


***Mesothelioma** – Phase I, patient 9*



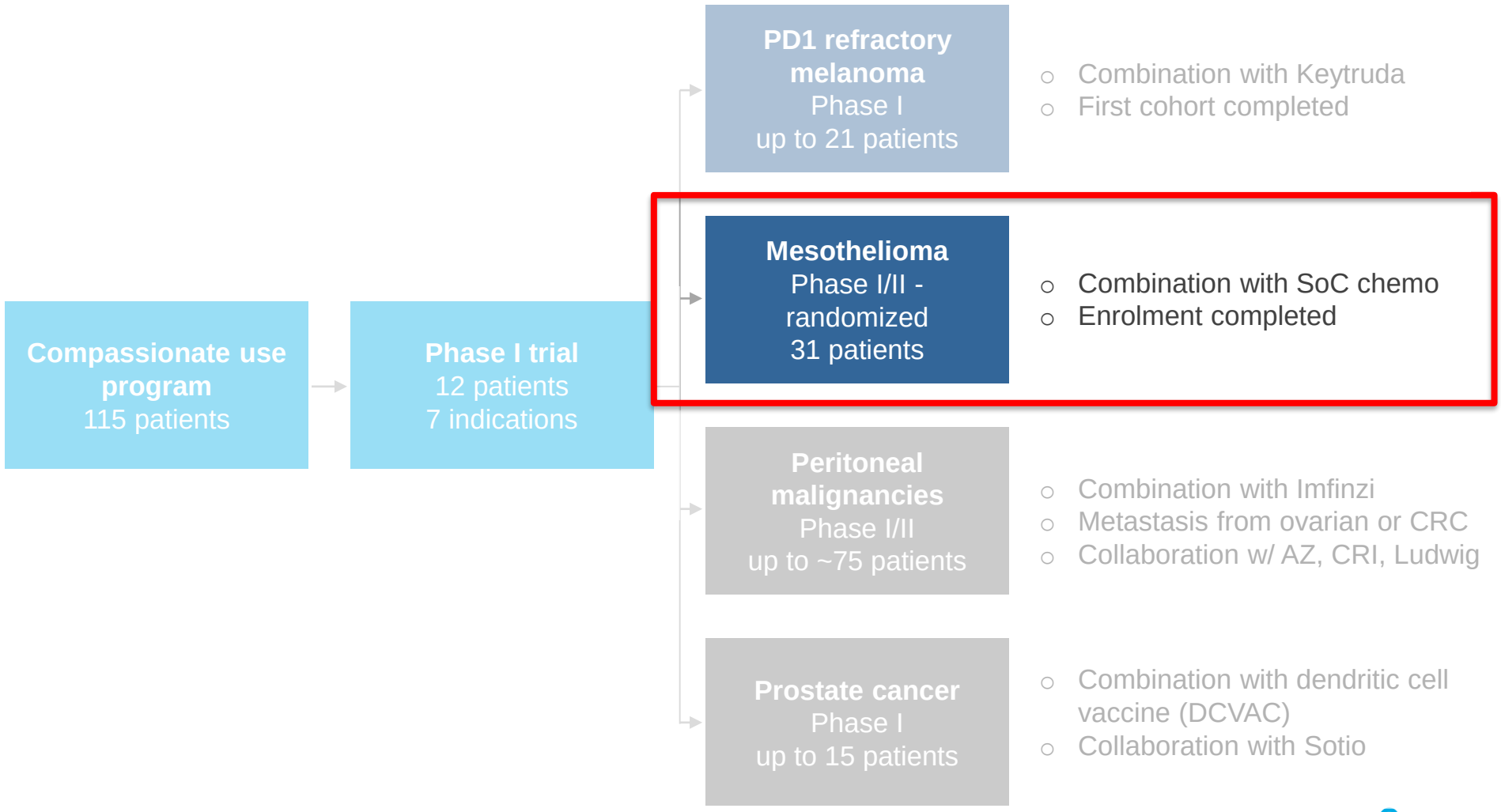
Baseline Week 5





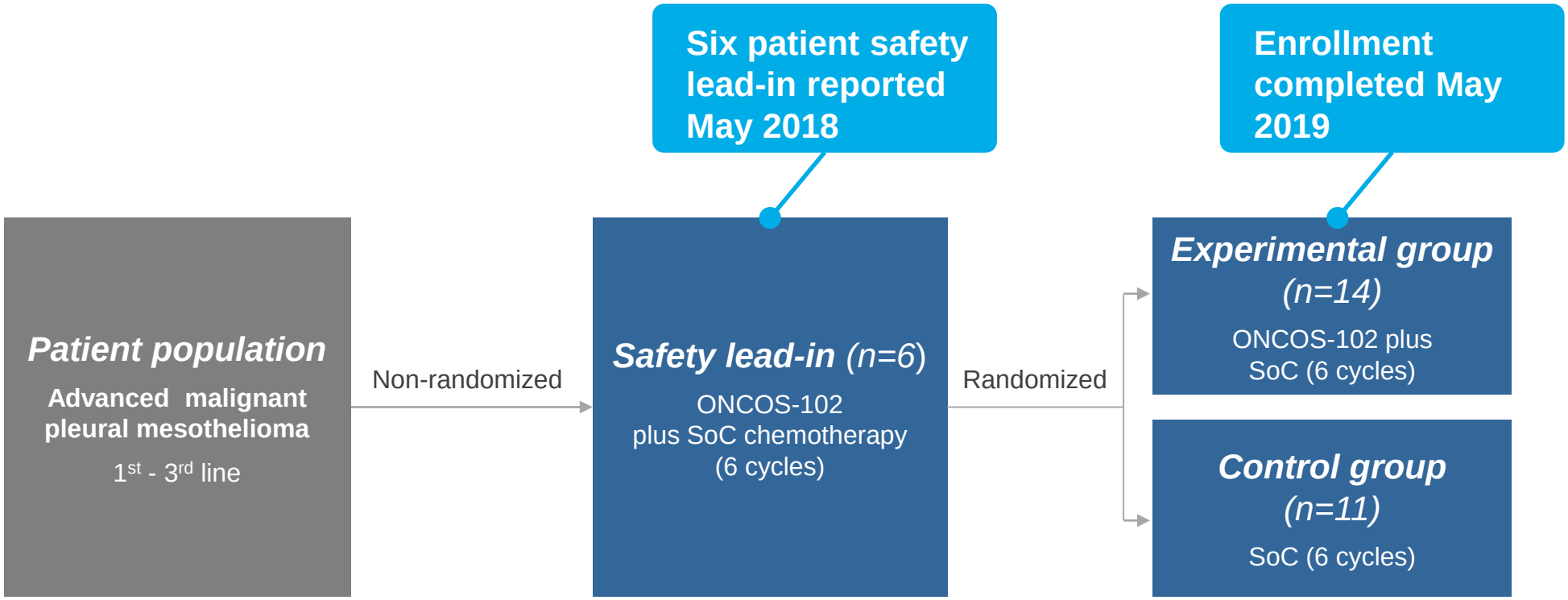
Ranki et al., Journal for Immunotherapy of Cancer 2016, 4(17)

ONGOING ONCOS-102 PHASE II IN MESOTHELIOMA



ONCOS-102 in malignant pleural mesothelioma

PHASE I/II STUDY DESIGN IN COMBINATION WITH SoC



MESOTHELIOMA ONCOS-102 PATH-TO-MARKET

Rationale for ONCOS-102 go-to-market strategy in mesothelioma:

Become frontline therapy

- **Preclinical data and phase I results** indicate activity in mesothelioma
- **Ongoing randomized trial** combining with chemo
- **Good safety profile**

Orphan Drug Designation

- High unmet medical need; **orphan drug designation**
- Opportunity for priority regulatory review, and **quick route-to-market**
- 7-10 year **market exclusivity**

Limited competition

- CPIs are **potential combinations**
- **No competing viruses**

RICH NEAR-TERM NEWS FLOW

ONCOS program pipeline overview

Product candidate	Preclinical	Phase I	Phase II	Phase III	Next expected event
ONCOS-102	**Mesothelioma** Combination w/ pemetrexed/cisplatin				**New year 2019-20** Randomized data
	Melanoma Combination w/Keytruda				**1H 2020** Interim data second cohort
	Peritoneal metastasis Collaborators: Ludwig, CRI & AZ Combination w/Imfinzi				*Update by collaborator*
	Prostate Collaborator: Sotio Combination w/DCvac				*Update by collaborator*
Next-gen ONCOS	**3 new viruses** Double transgene				**2H 2019** First pre-clinical data

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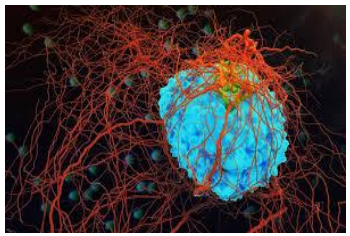
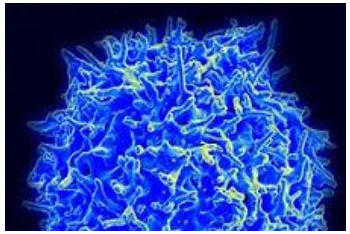
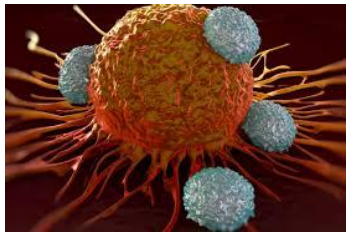
NEXT GENERATION ONCOS VIRUSES: DOUBLE TRANSGENES AND DISTINCT MODE OF ACTIONS

		Target tumors	Development status
	**ONCOS-210** *Inhibition of tumor growth and vascularization*	○ Highly invasive or metabolic tumors	○ *In vitro* testing completed ○ First *in vivo* testing completed
	**ONCOS-211** *Counteract immune-suppressive tumor microenvironment*	○ “Cold” immune suppressive tumors	○ *In vitro* testing completed ○ *In vivo* testing ongoing
	**ONCOS-214** Enhanced cell killing properties	○ Rapidly growing or large size tumors	○ *In vitro* testing completed ○ *In vivo* testing ongoing

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ACTIVATING THE PATIENT`S IMMUNE SYSTEM

to fight cancer

Clinically proven

One of the furthest developed oncolytic viruses

Strong single agent data

Encouraging ORR in anti-PD1 refractory melanoma

Rich news flow

Four ongoing trials

Several upcoming data readouts over the next 6-18 months

Innovative pipeline

Next generation viruses in testing