Activating the immune system to fight cancer

RedEye pre-ASCO seminar

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From a sequential treatment strategy directly targeting the cancer…

1

Surgery

When possible, surgical resection to remove the tumor

2

Radiotherapy

Tumor irradiation to shrink tumor volume

3

Chemotherapy

Chemotherapy – the cornerstone treatment in most cancer forms

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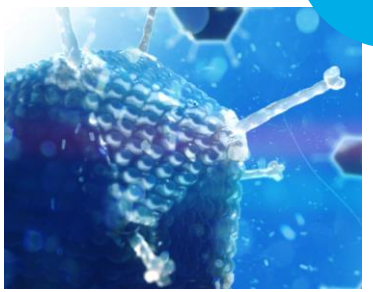
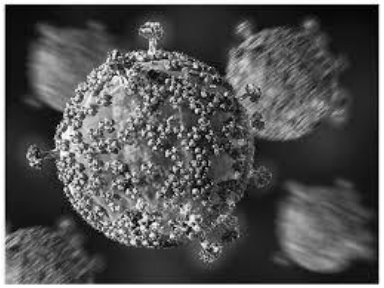
…to an integrated combination approach

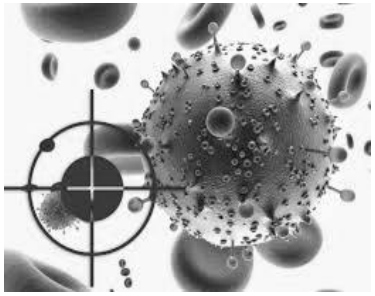
HARNESSING THE POWER OF THE PATIENT'S OWN IMMUNE SYSTEM

Immune modulators Checkpoint inhibitors	**Immune activators** Vaccines, oncolytic viruses, cytokines
Immune boosters CAR-Ts, TCRs	**Targeted therapy** PARP inhibitors, gene therapy, TKIs, etc.

Targovax focus







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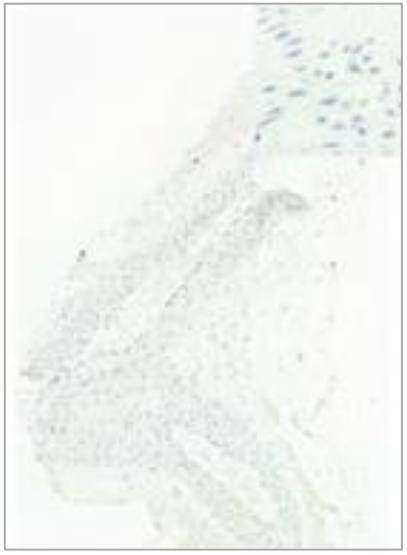
TARGOVAX' CORE FOCUS IS IMMUNE ACTIVATORS

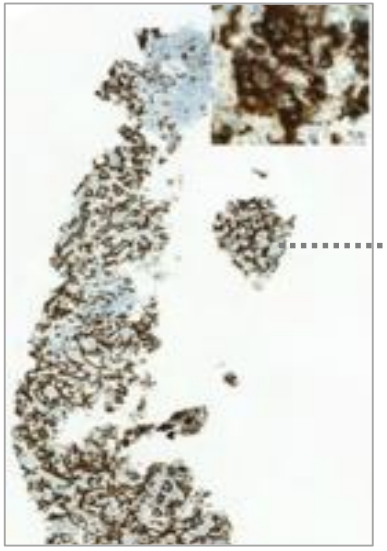
	Description	Examples	Car analogy
Immune activators Oncolytic viruses, vaccines	○ Make the immune system aware of the cancer ○ Activate T-cells	IMLYGIC™ (talimogene laherparepvec)	Ignite the engine Switch on GPS
Immune modulators Checkpoint inhibitors	○ Block stop signals that down-regulate T-cell cytotoxicity	KEYTRUDA	Release the hand-brake
Immune boosters CAR-Ts	○ Boost the immune system attack on the cancer	KYMRIAH (tisagenlecleucel)	Engage the turbo-charger
Targeted therapy PARP Inhibitors, TKIs etc..	○ Target particular genetic or molecular defects of the cancer	Lynparza® olaparib	Replace broken spare parts

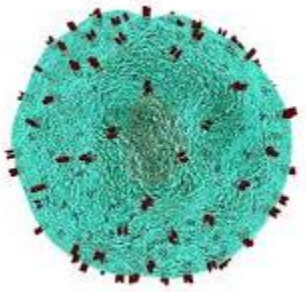
Mode of action

IMMUNE ACTIVATORS TURN COLD TUMORS HOT

Example from Targovax Phase I trial







CD8+ T-cell

Recognizes and destroys the cancer cells

Before injection of oncolytic virus

"Cold tumor"
No T-cell infiltration

After injection of oncolytic virus

"Hot tumor"
Full T-cell infiltration

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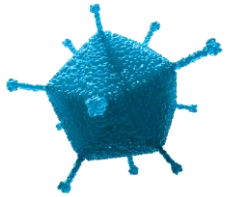
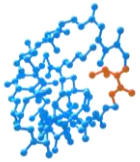
Targovax has two complementary programs in clinical development, both

PROVEN TO ACTIVATE THE IMMUNE SYSTEM



ONCOS
Oncolytic virus

- Genetically **armed adenovirus**
- Makes **cancer antigens** visible to immune system
- **Induces T-cells** specific to patients' tumor



TG
RAS neoantigen vaccine

- **Shared neoantigen**, therapeutic cancer vaccine
- Targets oncogenic **RAS driver mutations**
- Induces mutant **RAS-specific T-cells**

Activate and direct the immune system

Specific to the patient's cancer

No need for individualization

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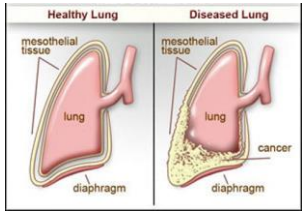
ONCOS

CLINICAL DEVELOPMENT STRATEGY

1

Mesothelioma
Orphan disease

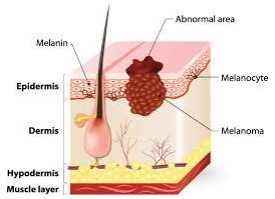


Launch indication

- Orphan drug status
- Aim to become SoC
- Ongoing phase I/II
- 15.000 patients per year

2

CPI synergy
Intra-tumoral

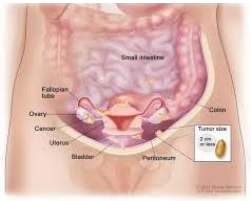


Indications with no / limited effect of CPIs

- Ongoing melanoma phase I, combo w/PD-1
- >100.000 patients per year

3

CPI synergy
Intra-peritoneal

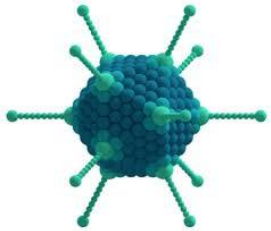


Peritoneal malignancies

- Ongoing phase I, combo w/PD-L1
- >100.000 patients per year

4

Next generation
ONCOS viruses



Double transgene adenoviruses

- Novel targets
- Ongoing *in vivo* testing
- Broad spectrum of solid tumors

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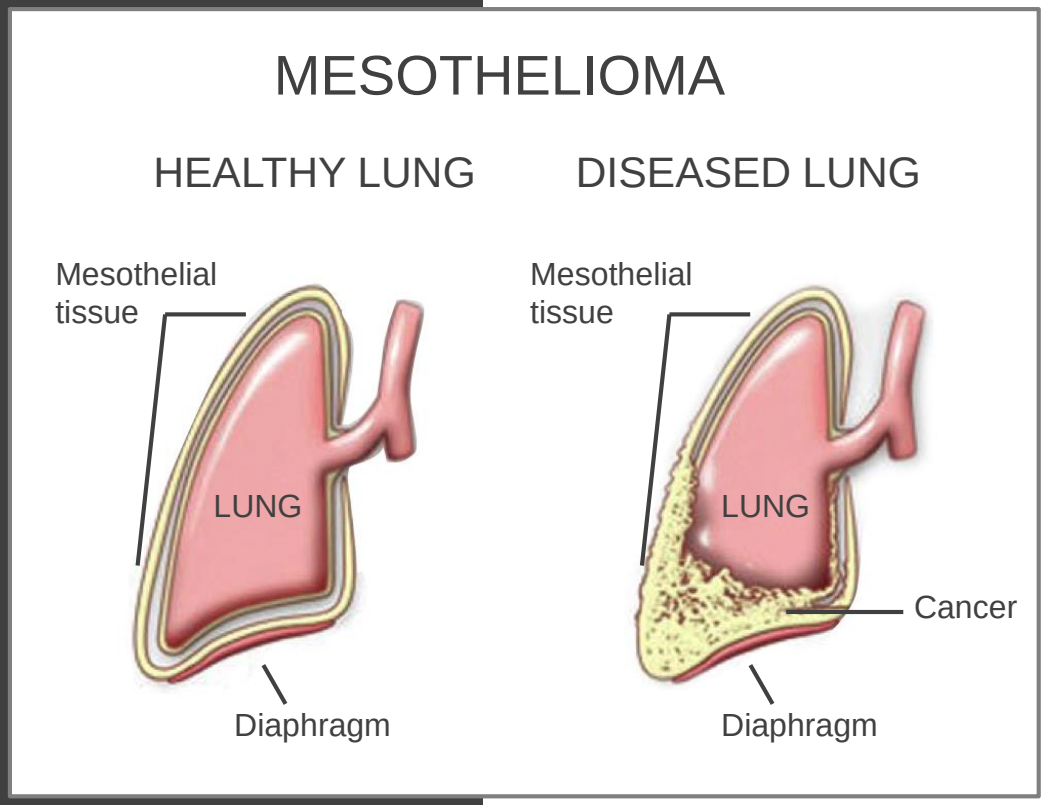
ONCOS-102 target launch indication

MALIGNANT PLEURAL MESOTHELIOMA

- **Orphan disease**, estimated 15,000 new cases per year (EU, USA, Australia)
- **Incidence is increasing** worldwide and is predicted to peak in 5-10 years
- Often **caused by asbestos** exposure, with a latency period of up to 40 years before diagnosis
- Aggressive cancer form with **median survival of 12 months**
- **No significant treatment advance** in the last decade



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Malignant pleural mesothelioma

NEED FOR NEW TREATMENT APPROACHES

Surgery

Only 10% of patients suitable for resection

Technically challenging due to location

Diagnosis often too late for surgery

Radiotherapy

Rarely effective due to tumor shape

Shape of tumors make them hard to target

Mainly palliative care

Chemotherapy

Standard of care (SoC) has limited efficacy

Only approved SoC option is pemetrexed/cisplatin

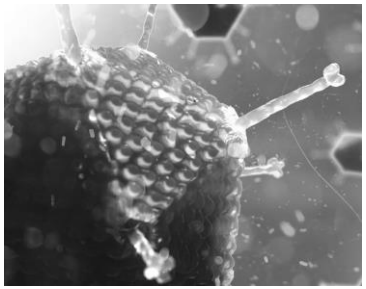
6 month PFS and 12 month median OS in 1st line

Immunotherapy

Mixed signals from early IO trials

Slight median OS improvement in early CPI trials

No/few other oncolytic viruses in development



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ONCOS-102 in malignant pleural mesothelioma

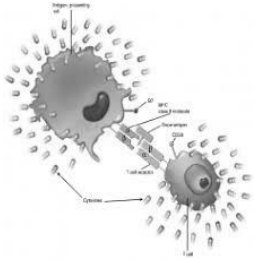
SIGNAL OF EFFICACY IN THE FIRST 6 PATIENTS

1
Safety

- ✓ ONCOS-102 **well-tolerated** in combination **with chemotherapy**

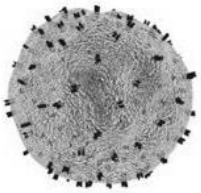
2
Innate immune activation

- ✓ **Systemic increase of pro-inflammatory cytokines** in 6/6 patients (IL-6, TNFα and IFNγ)



3
Adaptive immune activation

- ✓ Increase in **tumor infiltration of CD4+ and CD8+ T cells** in 3/4 patients



4
Clinical efficacy

- ✓ **Clinical activity** seen in **3/6 patients** after 6 months
- ✓ **50% disease control rate**

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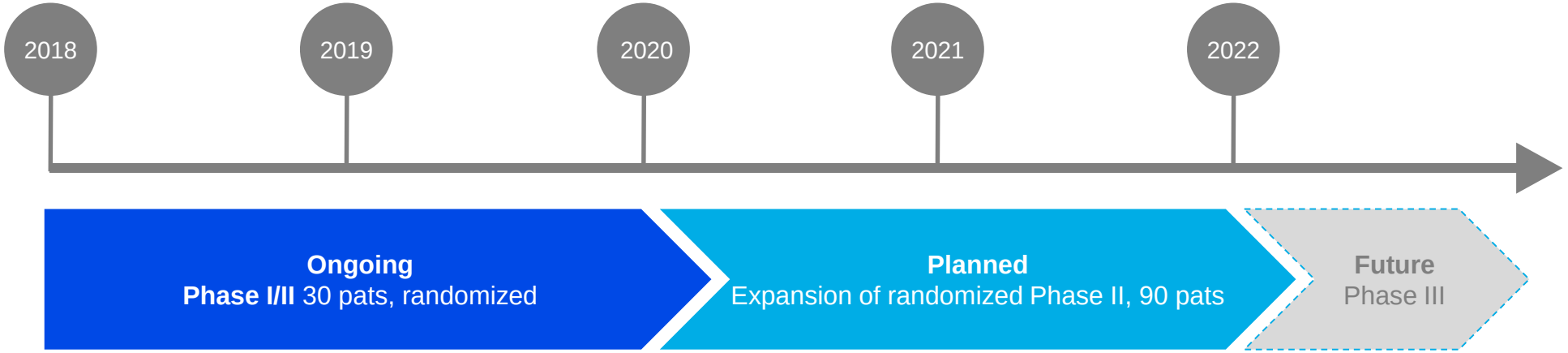
ONCOS-102 in malignant pleural mesothelioma

DEVELOPMENT STRATEGY AND INDICATIVE TIMELINES



- Randomized ORR and OS data 30 patients
- Decide on possible CPI combination arm
- EMA & FDA advisory meetings

- Randomized ORR and OS data 90 patients
- Potentially use as basis for a submission for conditional approval
- Go/No-go for phase III OS trial for full MAA

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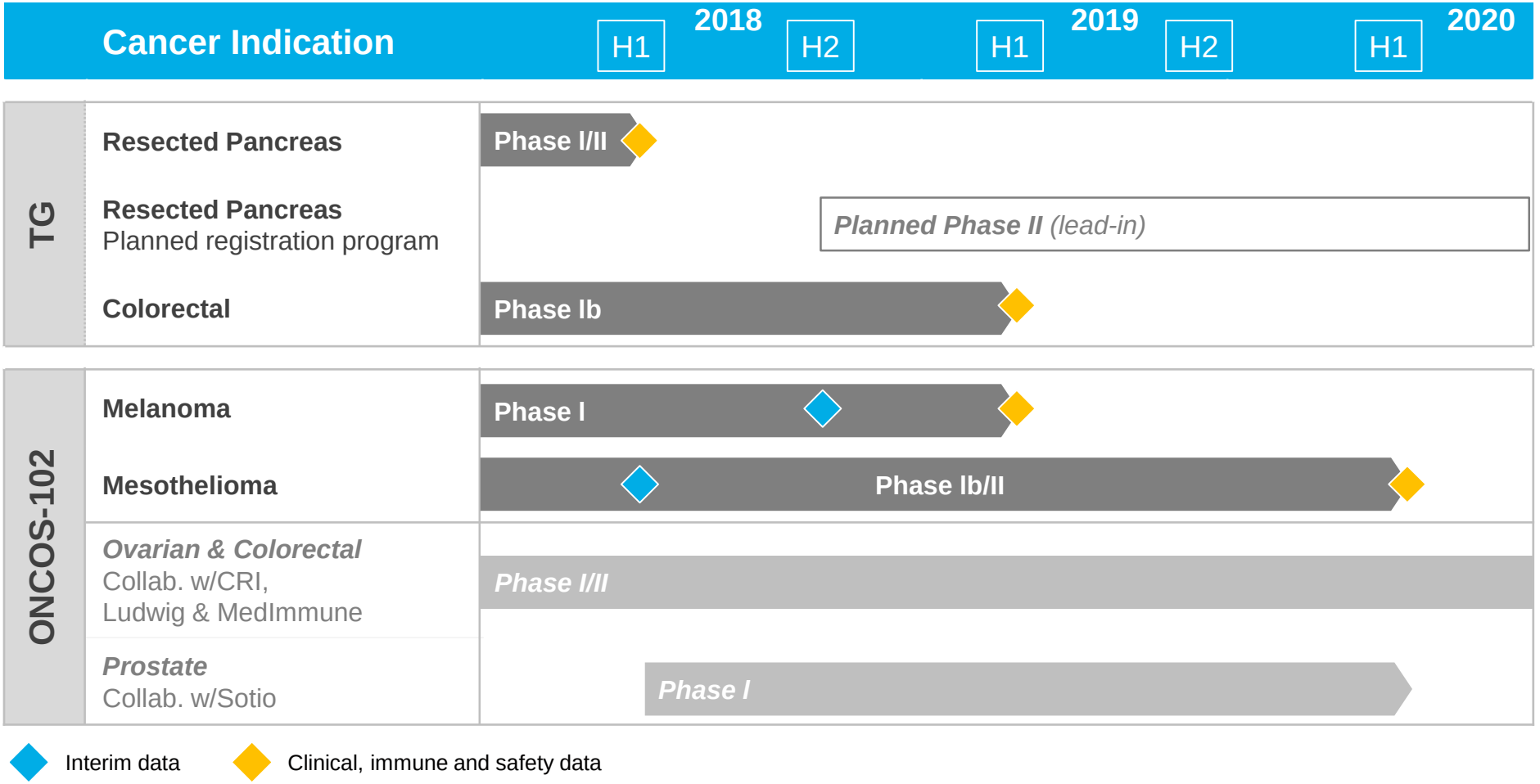
Targovax overall

CLINICAL PROGRAM TIMELINES



ACTIVATING THE PATIENT`S IMMUNE SYSTEM

to fight cancer

Broad clinical program

Six shots on goal

Several upcoming data points

Defined path to market

Aim to become frontline treatment in high unmet need cancers

Orphan status in mesothelioma and pancreas

Innovative pipeline

Next gen double transgene viruses in testing

IV program under evaluation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