5

Preclinical pipeline update

6. 4Q update
7. Closing remarks

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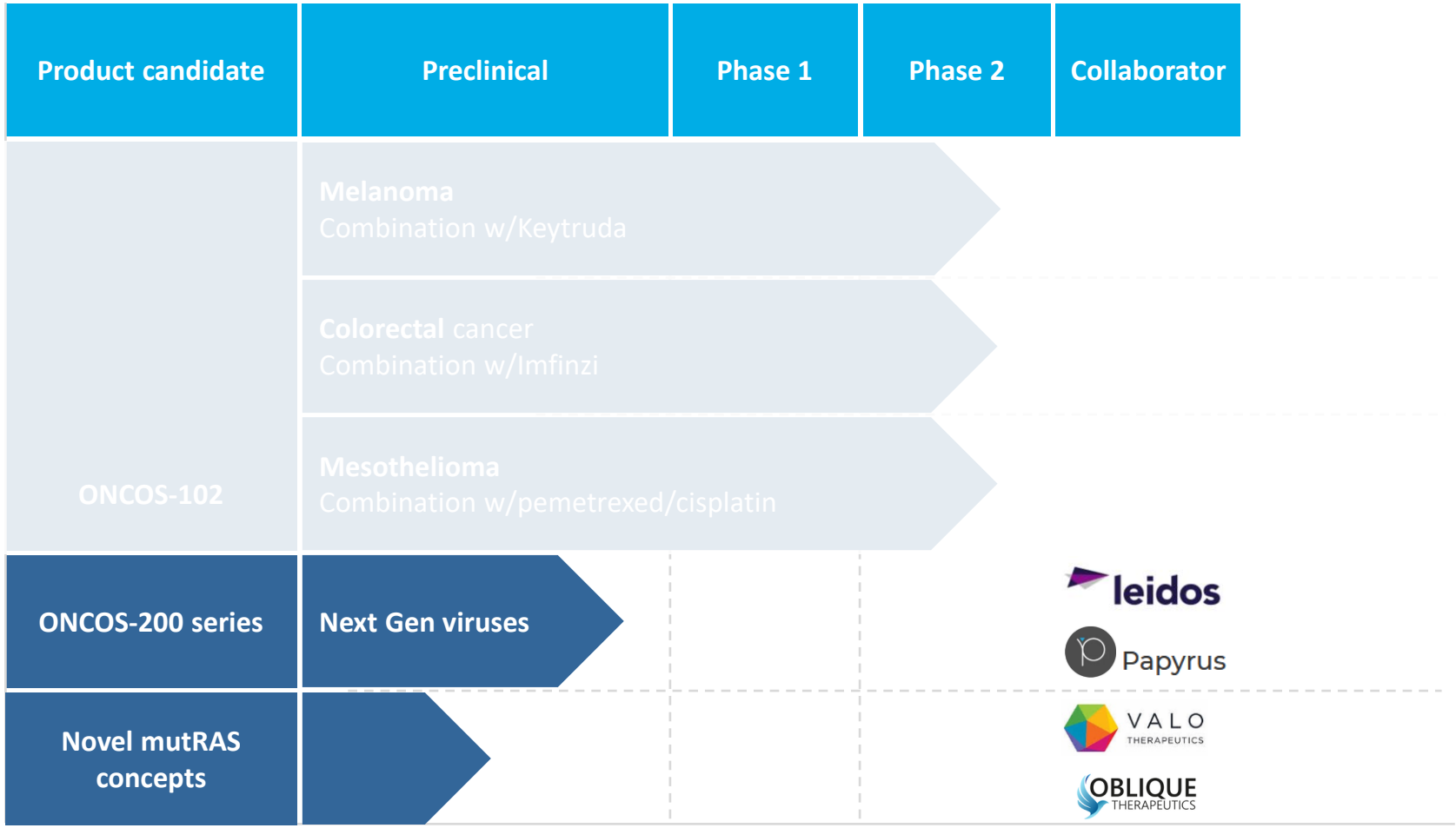
Product candidate
Preclinical
Phase 1
Phase 2
Collaborator
ONCOS-102
Melanoma
Combination w/Keytruda
Colorectal cancer
Combination w/Imfinzi
Mesothelioma
Combination w/pemetrexed/cisplatin
ONCOS-200 series
Next Gen viruses
Novel mutRAS concepts
leidos
Papyrus
VALO THERAPEUTICS
OBLIQUE THERAPEUTICS

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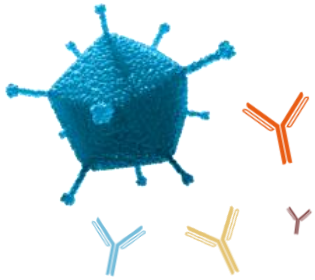
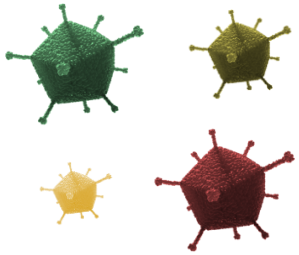
TARGOVAX´S THREE-PILLAR R&D PIPELINE STRATEGY



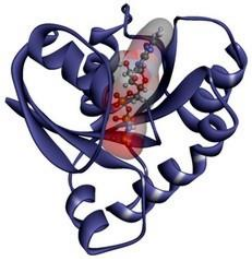
Novel ONCOS-102 combinations

- 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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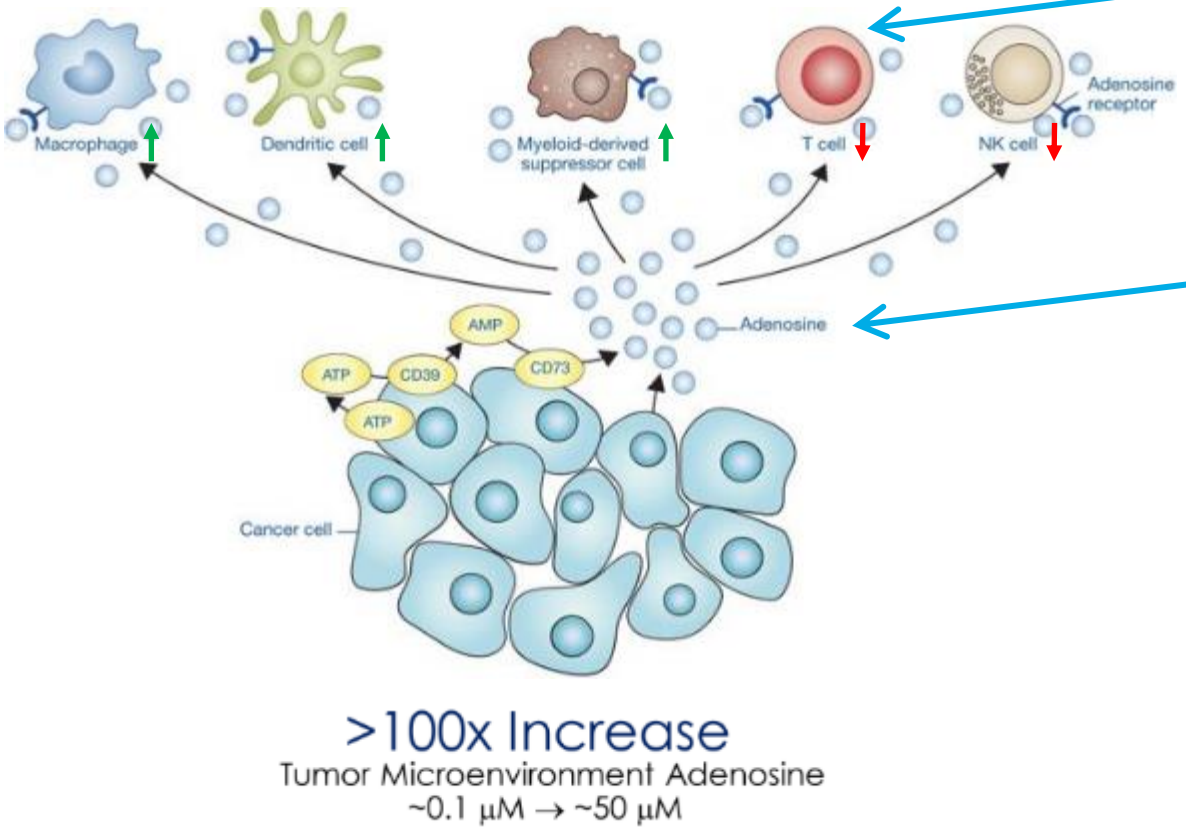
NEXT GENERATION ONCOS: ONCOS-211 PRIORITIZED FOR FURTHER DEVELOPMENT

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

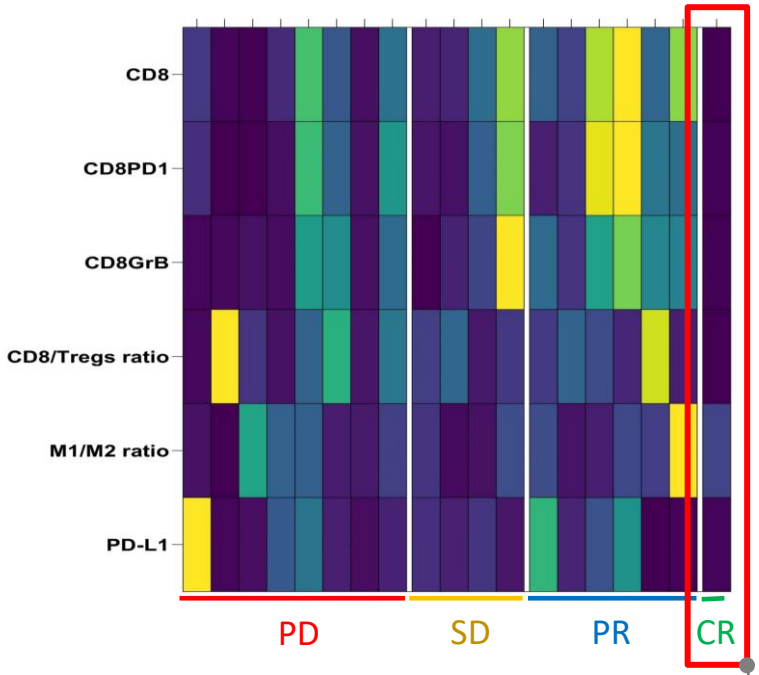
- ADA degrades adenosine released by the tumor
- Reversal of immune-suppressive tumor micro-environment

Virus activity

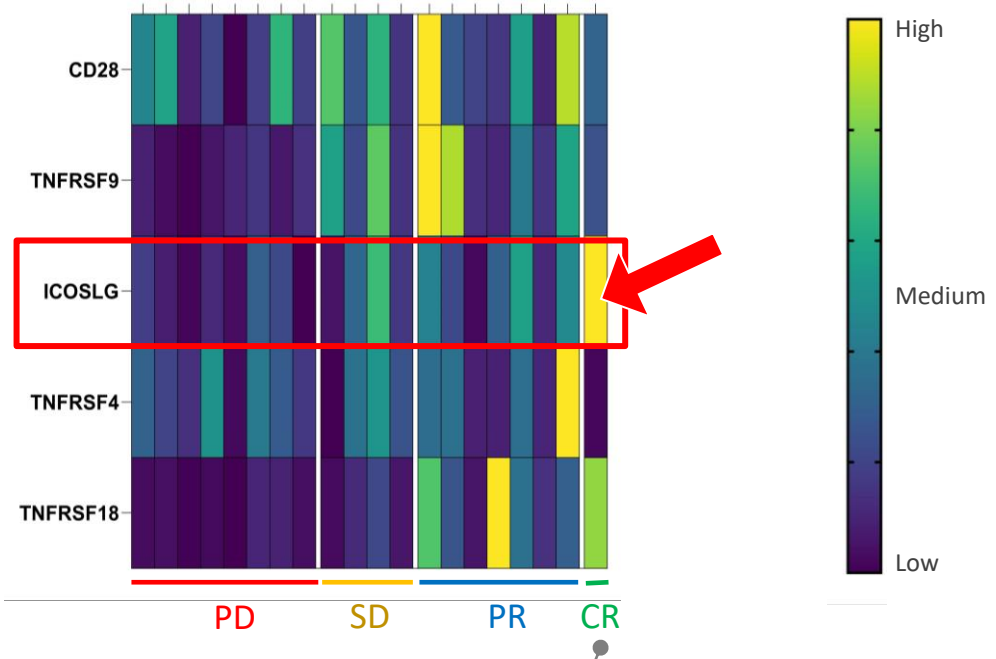
1. Innate immune activation
2. Cancer cell oncolysis
3. Adaptive anti-tumor immune response

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

Unpublished company data

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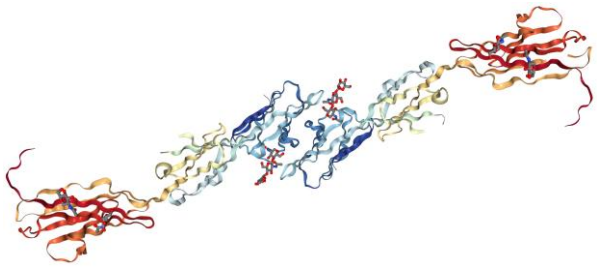
BUILDING TYROSINE KINASE INHIBITOR FUNCTIONALITY INTO ONCOS

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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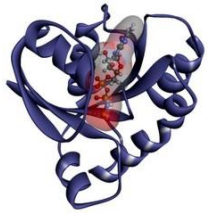
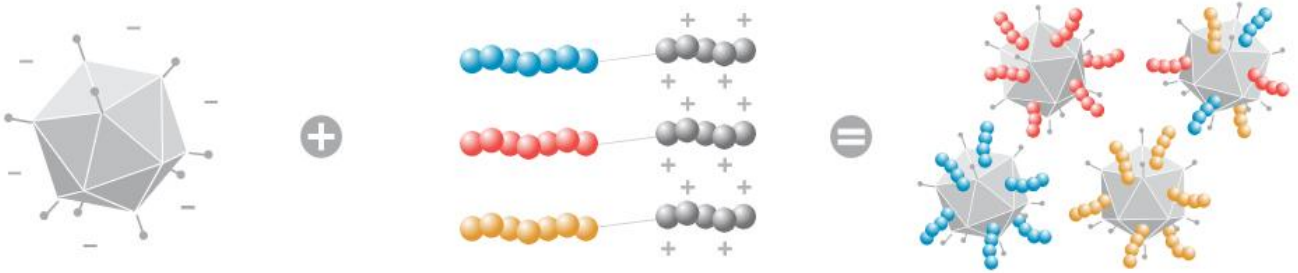


NOVEL MUTANT RAS VACCINATION CONCEPTS INCORPORATING IMMUNOLOGICAL POWER OF ONCOS

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

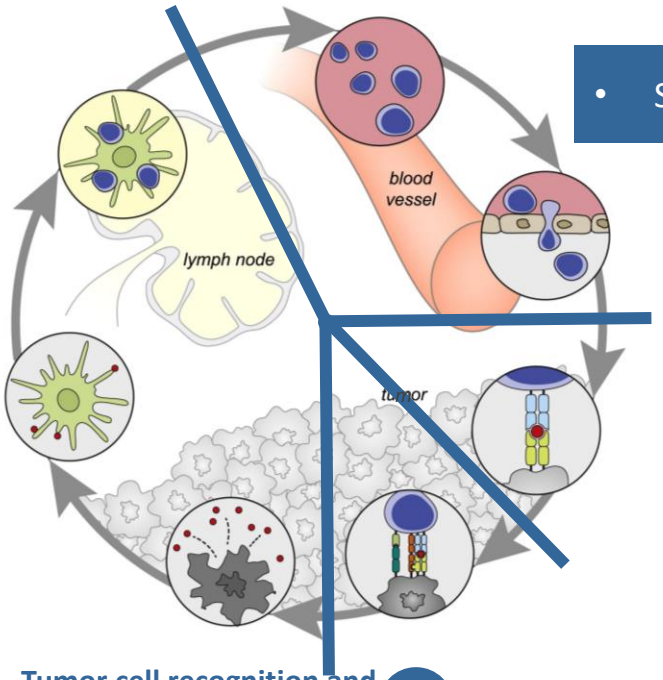
THE R&D PIPELINE STRATEGY IS DESIGNED TO ADDRESS KEY COMPONENTS OF THE CANCER IMMUNITY CYCLE

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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