Dr. Bernard Huber
CEO
ORYX Overview

• ORYX GmbH & Co. KG (ORYX) is a privately held company for translational oncology founded in 2007 and located in Baldham/Munich, Germany

• ORYX bridges the gap for new cancer therapies between leading academic research institutions and the pharmaceutical industry

• ORYX has been entrusted with three promising cancer immunotherapy substances by both the German Cancer Research Center (DKFZ) and the University of Heidelberg and has successfully developed these substances in clinical phase I/IIa trials

• ORYX has obtained valid safety results and already first promising efficacy data in all clinical phase I/IIa trials
Three Cancer Immunotherapy Substances in Clinical Development

**Therapeutic Peptide Vaccines directed to constantly expressed tumor antigens**

**MicOryx:** First in class therapeutic vaccination against microsatellite instable (MSI-H) cancers
   Phase I/IIa: **Colorectal Cancer**

**VicOryx:** First in class therapeutic vaccination against p16\(^{INK4a}\) expressing HPV-associated cancers
   Phase I/IIa: **Cervical Cancer, Head and Neck Cancer, etc.**

**Oncolytic Virus inducing a lasting bystander effect through oncolysis**

**ParvOryx:** First in class therapeutic use of Parvovirus H-1 (H-1PV)
   Phase I/IIa: **Glioblastoma multiforme**
MicOryx: Rationale

• Several cancers arise from the lack of DNA mismatch repair (MMR) resulting in the accumulation of single deletions or insertions at coding microsatellites (MSI-H)

• MSI-H mutations lead to the expression of frameshift peptides (FSPs)

• FSPs are tumor specific antigens which are constantly expressed

• Cancers with MSI-H mutations include:
  • 10-15% of colorectal cancers,
  • 20-25% of endometrial cancers,
  • 25-30% of upper urinary tract cancers,
  • 15-20% of gastric cancers and
  • 5-10% of pancreatic cancers

• Preclinical work shows a natural humoral and cellular immune response against FSPs in MSI-H colorectal cancer, which demonstrates that FSPs are recognized by the immune system and can trigger an immune response

• The therapeutic rationale is to induce a specific immune response against FSPs in MSI-H colorectal cancer patients
MicOryx: Clinical Phase I/IIa Trial

- Single center, two part open label, prospective, 1\textsuperscript{st} part 6 patients, 2\textsuperscript{nd} part 16 patients (n = 22), UICC stage III/IV, MSI-H colorectal cancer
- Total of 12 s.c. applications with three FSPs one time/week for four consecutive weeks, followed by a four week rest period (one cycle) for a total of three cycles

Subcutaneous injection of FSP mix and Montanide ISA 51 VG

- Monitoring of toxicity, immune response (including DTH) and tumor response

- Primary Objective: Safety 22/22 patients
- Secondary Objective: Efficacy (specific immune responses)
  - 21/22 patients (95.5%)
  - End of Study: Final Report H1/2015
VicOryx: Rationale

- About 5% of all cancers are associated with human papilloma viruses (HPV) including:
  - 85-95% of anal and vulvar cancers,
  - 20-40% of vaginal and penile cancers,
  - 30-60% of head and neck cancers
- In HPV-associated cancers, the human cyclin-dependent kinase inhibitor p16INK4a is expressed as an early consequence of HPV-mediated cell transformation
- p16INK4a is a tumor antigen that is constantly expressed
- In normal cells, p16INK4a is rarely expressed and leads to immediate senescence
- Preclinical work shows a natural humoral and cellular immune response against p16INK4a in HPV associated cancers, which demonstrates that p16INK4a is recognized by the immune system and can trigger an immune response
- The therapeutic rationale is to induce a specific immune response against p16INK4a in HPV associated cancers
VicOryx: Clinical Phase I/IIa Trial

• Single center, two part open label, prospective, 1st part 10 patients, 2nd part 16 patients (n = 26) UICC stage III/IV, advanced HPV- and p16\(^{INK4a}\) - positive cervix, vulvar, vaginal, penile, anal or head and neck cancer

• Total of 12 s.c. applications with a specific p16 peptide one time/week for four consecutive weeks, followed by a four week rest period (one cycle) for a total of three cycles

- Subcutaneous injection of p16 and Montanide ISA 51 VG
- Monitoring of toxicity, immune response (including DTH) and tumor response

- ✔ Primary Objective: Safety 26/26 patients
- ✔ Secondary Objective: Efficacy (specific immune responses)
  - 18/26 patients (69.23%)
  - End of Study: Final Report H1/2015
ParvOryx: Rationale

- Oncolytic Parvovirus H-1 (H-1PV) is a wild type rat virus that infects and lyses tumor cells and tumor stem cells from a broad range of human tumors.
- Human tumors sensitive to H-1PV include:
  - glioblastoma multiforme
  - pancreatic cancer
  - breast cancer
  - lung cancer
  - melanoma, lymphoma
  - pediatric tumors (e.g. neuroblastoma and medulloblastoma)
  - prostate cancer
  - renal cancer
- Parvovirus H-1:
  - does not affect normal cells and is not pathogenic for humans
  - acts at relatively low multiplicities of infection
  - crosses the blood brain barrier
- Preclinical data showed that treatment with H-1PV causes tumor remissions in animal models bearing human tumors, e.g. glioblastoma multiforme and pancreatic cancer.
ParvOryx: Rationale

- H-1PV exerts a twofold therapeutic effect:
  - selective lysis of tumor cells
  - induction of a lasting bystander effect = stimulation of the adaptive immune system, preventing tumor progression, relapse and metastasis formation

- H-1PV oncolytic activity is predominantly mediated by non-structural protein (NS1) causing:
  - dysregulation of cell transcription
  - cell cycle arrest
  - shut off of cell replication
  - activation of cellular stress response
  - induction of apoptotic and non-apoptotic cell death
ParvOryx: Clinical Phase I/IIa Trial

- Single center, open label, prospective, dose escalating, two groups, 1st group (it) 12 patients, 2nd group (iv) 6 patients (n = 18) UICC Stage IV, progressive primary or recurrent glioblastoma multiforme

- It: half of the dose in the tumor, half of the dose in the wall of the resection cavity
- Iv: half of the dose in 5 consecutive injections, half of the dose in the wall of the resection cavity

√ Primary Objective: Safety 18/18 patients

√ Secondary Objective: OS ≥ 6 month,
  - 76.47% (13 patients: 6.0 – 35.8 month) 3 patients still in 6 months follow up
  - strong cellular immune response observed against glioma and viral proteins (bystander effect)
  - End of Study: Final Report Q4/2015
ORYX - Partnering Opportunities

➤ Open for partnering discussions with global partners

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