Unlocking the potential of innovative medicines

PCI Biotech Holding ASA

An innovative and versatile technology for local cancer treatment , CTL-induction, and macromolecule delivery

BioTrinity, May 11, 2015

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PCI Biotech at a glance

- A listed cancer-focused biotech company (PCIB, Oslo exchange)
- Market cap €22m
- Lean organisation: 11 employees

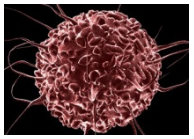
- Technology originally developed at Norwegian Radium Hospital
- Continued close collaboration

- Collaboration with ETH and University Hospital Zurich

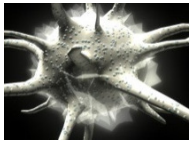
PCI technology – endosomal escape

Existing & innovative treatments

Cells



Cancerous cell



Dendritic cell

Active ingredient
(trapped in endosome)

- Small molecules
- siRNA/mRNA
- Antibody targeted drugs
- Peptides
- Antigens

PCI enhancement technology

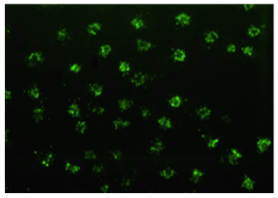
Photosensitiser

$TPCS_{2a}$

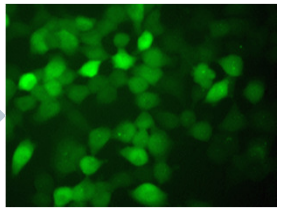
Light source

Red light

Blue light



Endosomal escape
Release of drug in cells



PCI technology – general principle

PCI mechanism of action – triggered endosomal escape through illumination

STEP 1:

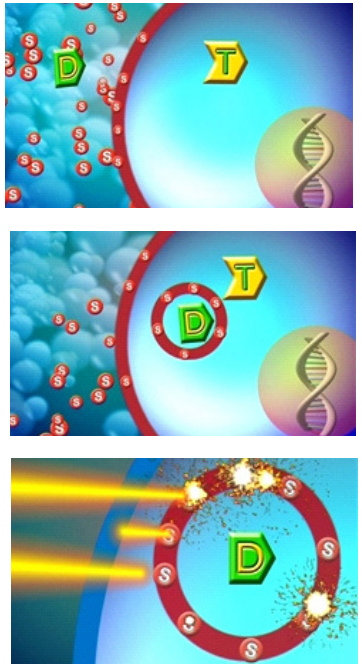
- $TPCS_{2a}$ (S) and the active molecule (D) are administered to the patient and reach target cells (tumour)

STEP 2:

- $TPCS_{2a}$ (S) is designed to be taken up into endosomes
- $TPCS_{2a}$ (S) and the active molecule (D) are taken up by the cell, but D is unable to reach the target (T), as it is encapsulated in an endosome

STEP 3:

- Light activates $TPCS_{2a}$ (S) in the membrane of the endosome
- The endosome membrane integrity is affected and the active molecule (chemotherapeutic agent, oligonucleotide, or antigen) released



D

The active molecule
- Anticancer agent, e.g. bleomycin, gemcitabine
- Oligonucleotide, e.g. siRNA
- Protein, e.g. antibody-drug conjugate
- Peptide: e.g. antigen

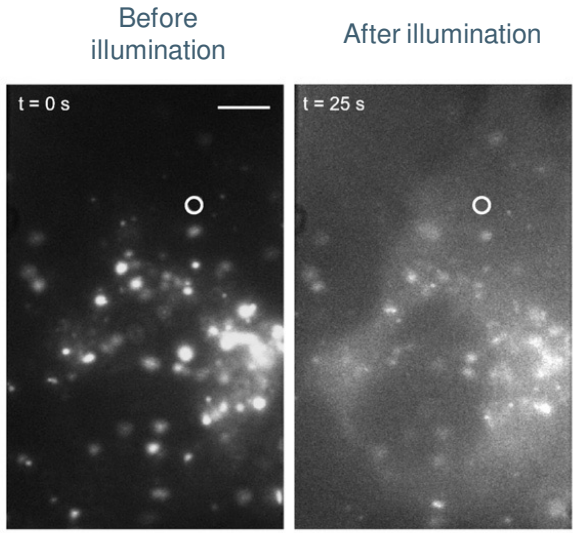
S

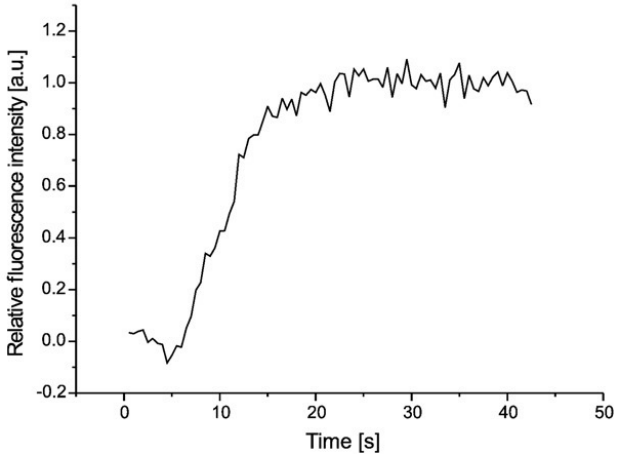
The PCI component
- $TPCS_{2a}$

T

The target
- Target for the active molecule
- E.g. DNA, mRNA, enzyme, microtubuli

Efficient and rapid PCI induced release of a fluid phase endosomal marker





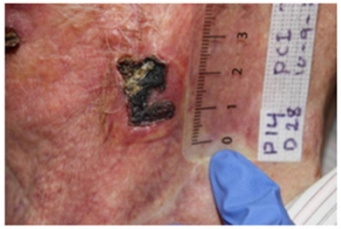
- PCI releases Alexa488-dextran (MW10 kDa) from endosomes
- PCI induced increase in relative fluorescence in the cytosol

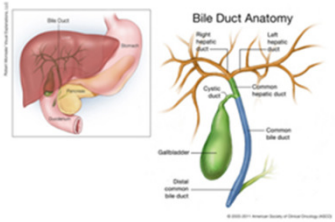
de Bruin *et al.* J. Control. Rel. 2008, 130, 175

PCI Biotech is leveraging PCI with three applications

Local cancer treatment

- bleomycin in head and neck cancer
- gemcitabine in bile duct cancer

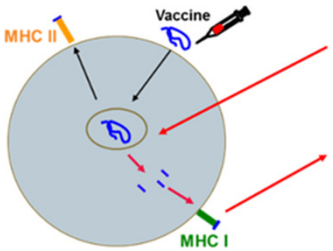




Systemic administration

PCI vaccination technology

- therapeutic vaccination



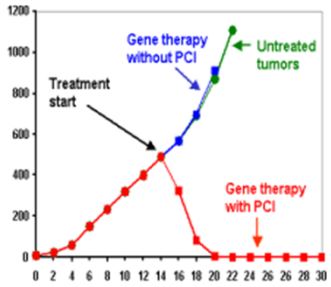
PCI – induce presentation on MHC class I

- Make it possible to achieve cytotoxic T-cell response with protein/ peptide vaccines
- Can solve a key challenge for many vaccine approaches

Local administration

PCI macromolecule delivery

- immunotoxins
- siRNA & other oligo
- gene therapy



Local or systemic administration

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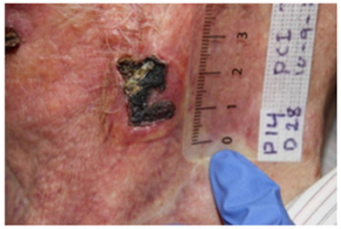

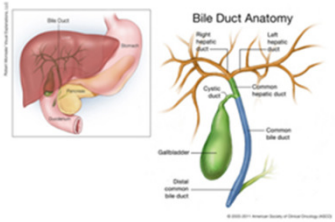

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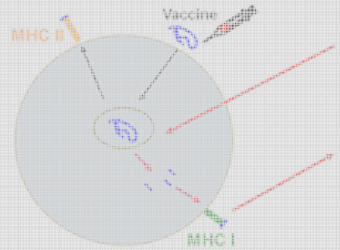

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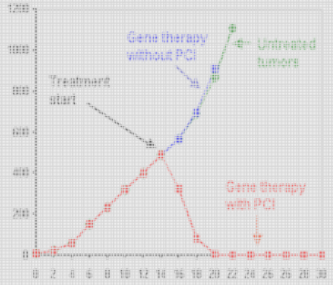


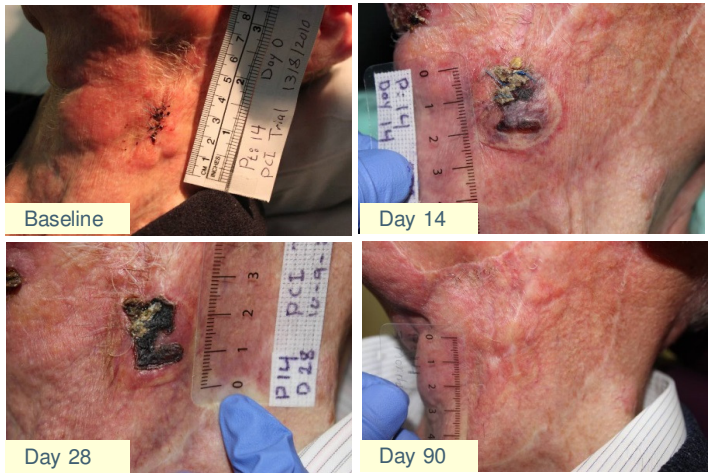
Local or systemic administration

Amphinex® Phase I summary

Summary of Study Design	
Cancer type	Cutaneous and subcutaneous malignancies
Phase	I
Photosensitizer	Amphinex® (PCIB)
Drug	Bleomycin (single dose)
Light source	Red laser, 652 nm (PCIB)
Fixed variables	Bleomycin and light dose
Variables	Amphinex® dose
Purpose of study	Assess safety and tolerance of Amphinex®
Patient description	Patients with cutaneous and/or subcutaneous tumours. Majority of patients had Squamous cell carcinoma of the head & neck
Patient sample size	22 patients treated across 5 dose groups
Treatment modality	Surface illumination

Key findings

- Very promising early signs of tumour efficacy across a range of Amphinex® dose levels (>50% complete responses)
- Apparent strong selectivity for cancer in several patients
- Dose limiting toxicities ("DLT") at highest dose due to skin photosensitivity and wound infection



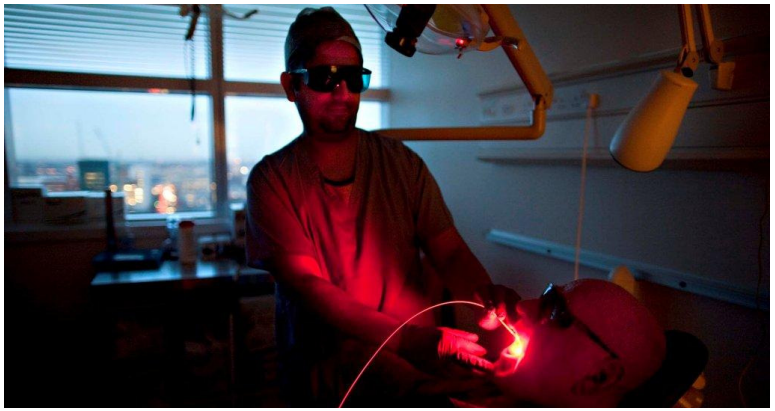
Complete Response following treatment of malignant skin adnexal tumour

Amphinex® Phase II study

Summary of study design	
Cancer type	Squamous cell carcinoma of the head and neck
Phase	II
Photosensitizer	Amphinex® (PCIB)
Drug	Bleomycin (single dose)
Light source	Red laser 652 nm (PCIB)
Fixed variables	Bleomycin dose
Variables	Amphinex® dose and light dose
Purpose of study	Assess safety and efficacy of a single treatment of Amphinex® induced PCI of Bleomycin
Patient description	Recurrent head and neck squamous cell carcinoma, with or without metastasis, unsuitable for radiotherapy and surgery.
Treatment modalities	Surface and/or intra-tumour illumination
Patient sample size	Up to 80 patients
Primary endpoint:	Progression Free Survival at 6 months

Current status and plans

- Stronger effect with intra-tumour treatment than seen with surface illumination in Phase I
- Intra-tumour illumination is optimized in separate light dose escalation part of the study, running in parallel to open inclusion of patients for superficial illuminations; started in Q3 2013
- Included an interim PoC analysis when 12 patients have been treated with intra-tumour illumination at the selected light dose

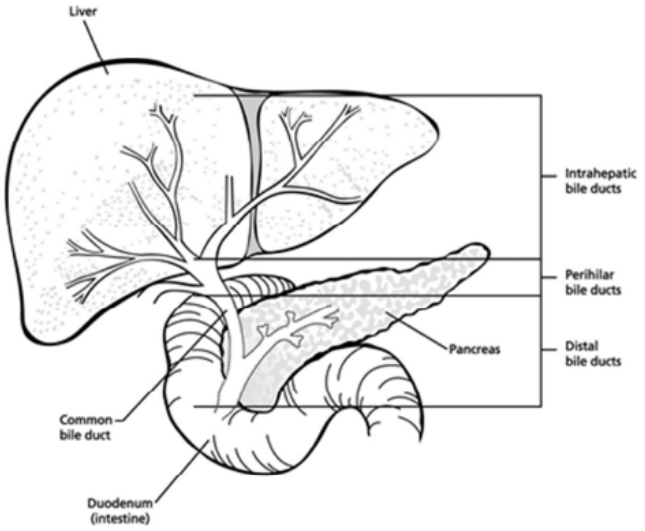


Amphinex® Phase Ib/II study

Summary of Study Design	
Cancer type	Bile duct (Cholangiocarcinoma)
Phase	Ib/II
Photosensitizer	Amphinex® (PCIB)
Drug	Gemcitabine (Cisplatin)
Light source	Red laser 652 nm (PCIB)
Fixed variables	Gemcitabine and Cisplatin
Variables	Amphinex® and/or light dose
Purpose of study	Open-label, multi-centre study to assess the safety and efficacy of a single treatment of Amphinex® induced PCI of gemcitabine, followed by systemic cisplatin/ gemcitabine. All patients are stented. Phase I to find light and Amphinex® dose. Phase II randomized to compare PCI vs. stenting alone
Patient description	Locally advanced inoperable bile duct cancer
Treatment modality	Intraluminal illumination
Patient sample size	Up to 45 patients
Primary endpoint:	Progression free survival

Current status and plans

- Adaptive Phase Ib/II study
- Safety driven Phase Ib – two first cohorts finished
- Patient recruitment into third cohort in Phase Ib on-going
- 5:2 randomisation in Phase II, 35 pts in total



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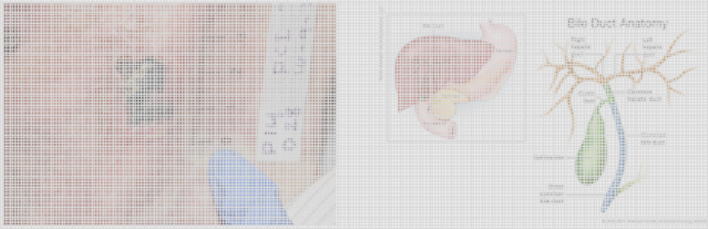
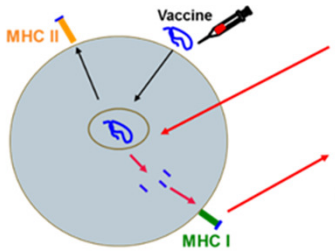


Systemic administration

PCI vaccination technology

- therapeutic vaccination



PCI – induce presentation on MHC class I

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Local administration

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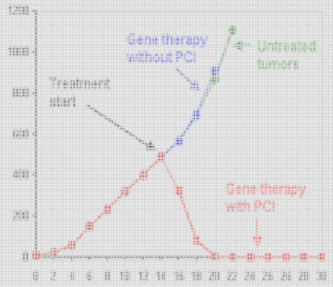
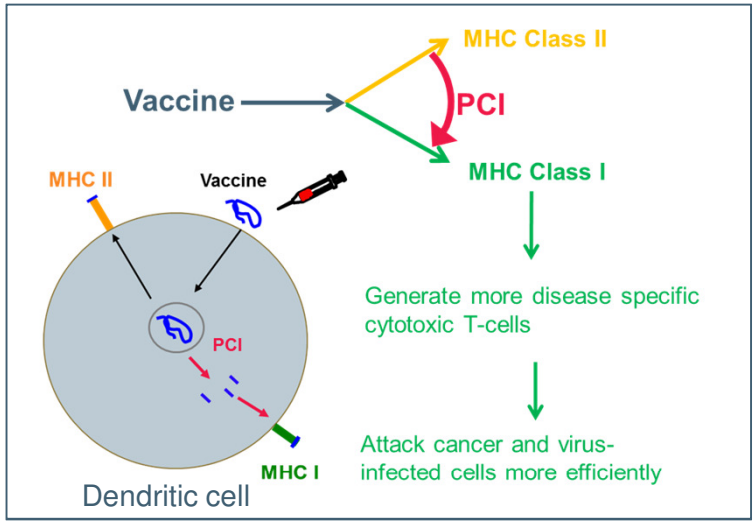
- siRNA & other oligo
- gene therapy

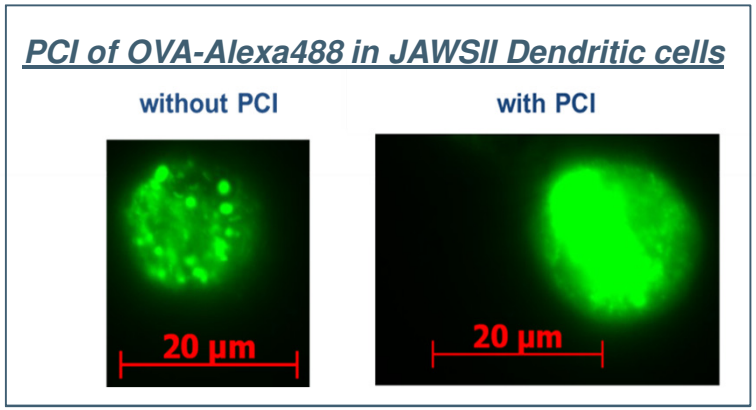


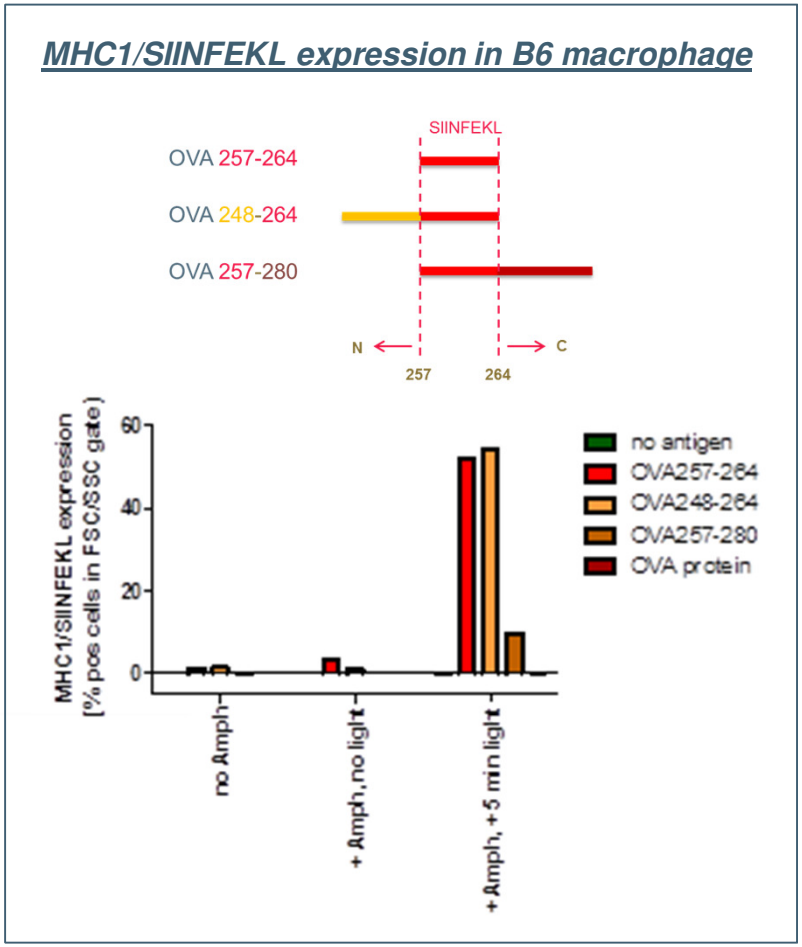
Local or systemic administration

PCI immunotherapy – enhancing vaccine induced cytotoxic T-cell response

PCI-induced endosomal antigen escape enhance MHC Class I presentation





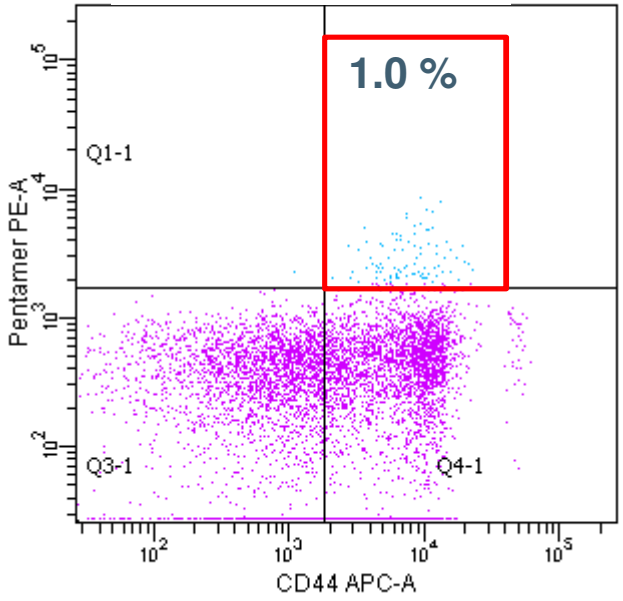


PCI with HPV peptide antigen – antigen specific CD8 T-cells in blood

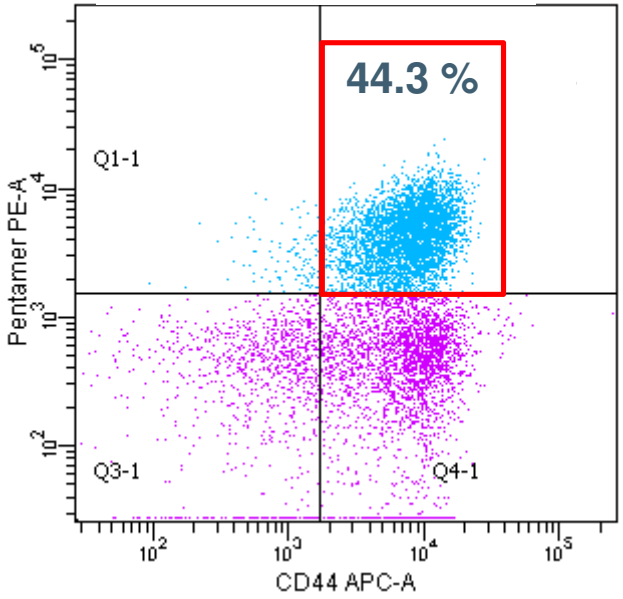
HPV peptide vaccination with Poly(IC)

(3rd immunisation)

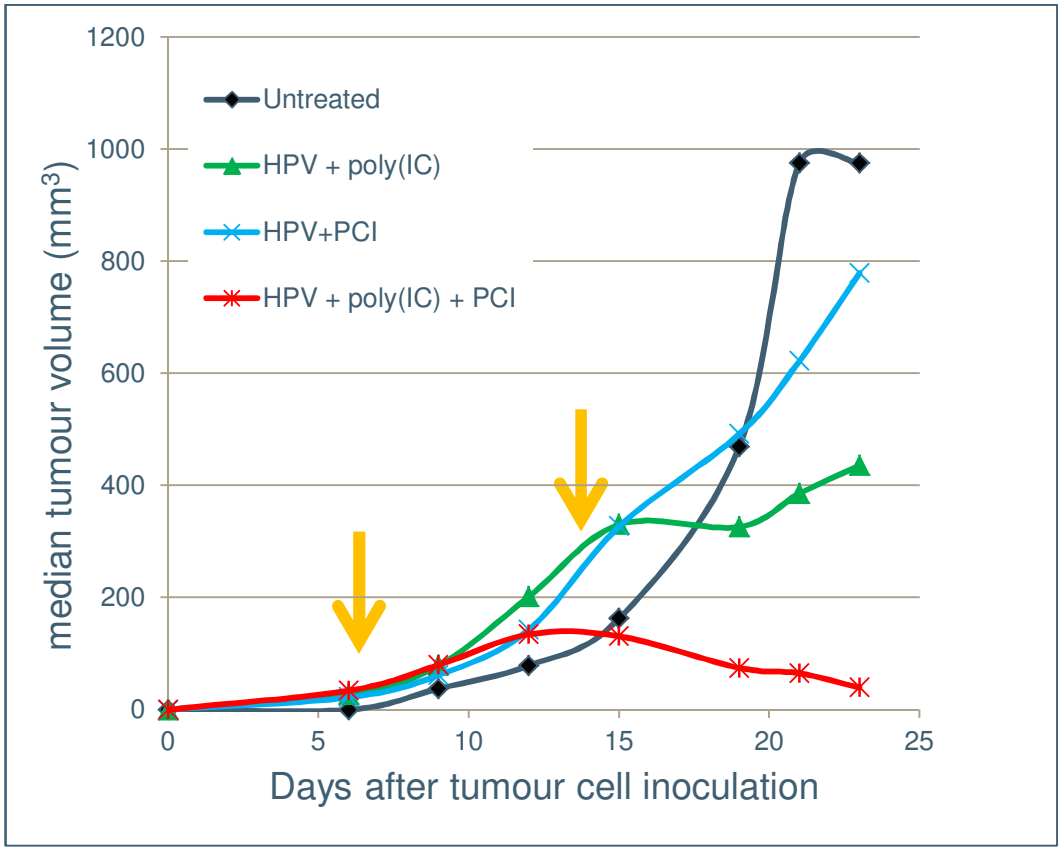
Without PCI



With PCI



Therapeutic vaccination with HPV long peptide antigen in TC-1 mouse tumour model – PCI induces strong anti-tumour response



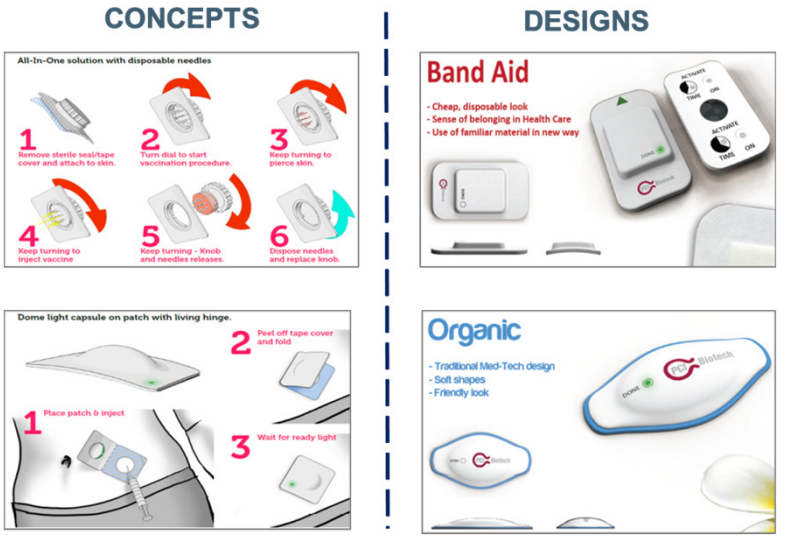
- Intradermal vaccination at days 6 and 13 after tumour cell inoculation
- 5 animals per group

Cancer therapeutic vaccines – competitive advantages and user-friendly PCI solutions

Safety – $TPCS_{2a}$ tested in Phase I study (i.v. inj.) at much higher doses than what will be used for vaccination

Stability – $TPCS_{2a}$ can be autoclaved and is stable at room temperature, also in solution

Innovation – Unique mode of action; indication that $TPCS_{2a}$ provides CTL-induction by MHC class I antigen presentation in dendritic cells and macrophages



Cost effectiveness – Simple and cost effective synthesis of $TPCS_{2a}$

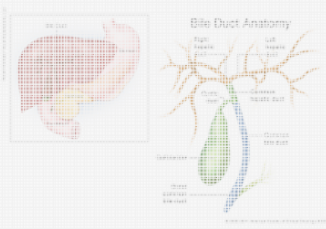
Broad applicability – Peptide and protein antigens as well as particulate antigen formulations; Prophylactic & therapeutic vaccination, *in vivo* & *ex vivo*

Clinical safety and preclinical efficacy evidence, combined with a comprehensive patent estate on PCI-mediated CTL-induction (products, uses and devices)

PCI Biotech is leveraging PCI with three applications

Local cancer treatment

- bleomycin in head and neck cancer
- gemcitabine in bile duct cancer



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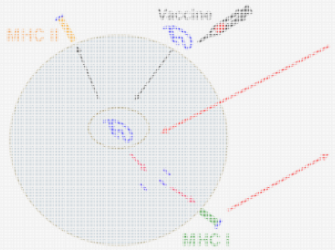

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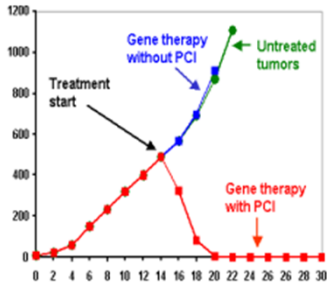
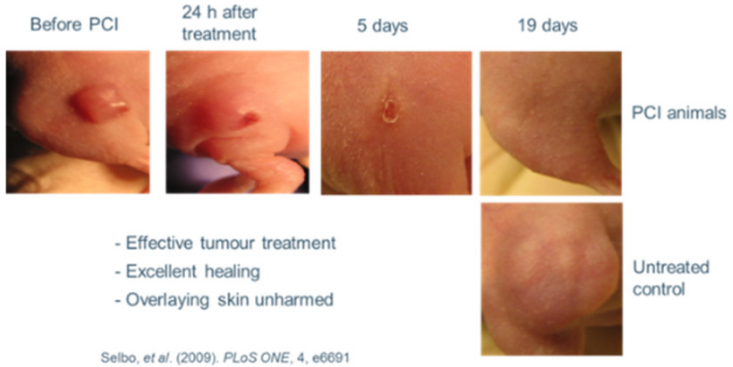


Local or systemic administration

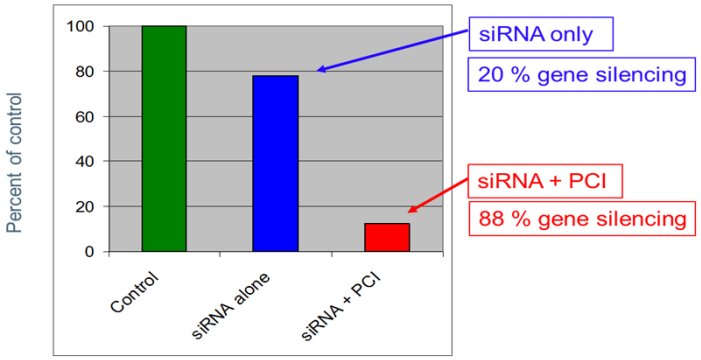
Macromolecules – endosomal escape of a range of products, pre-clinical data

1 Intracellular delivery of immunotoxin – *in vivo*



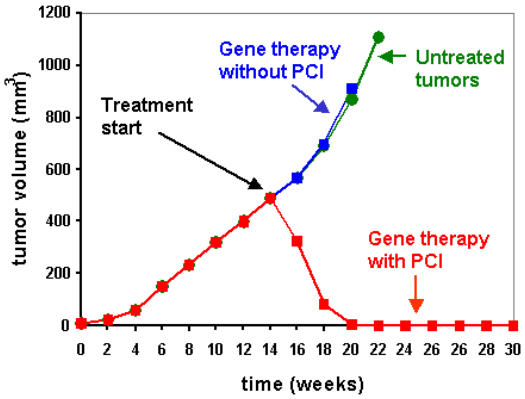
Selbo, *et al.* (2009). *PLoS ONE*, 4, e6691

2 Intracellular delivery of siRNA



Bøe, S., Longva, A.S. and Hovig, E. (2007). *Oligonucleotides* 17, 166-73

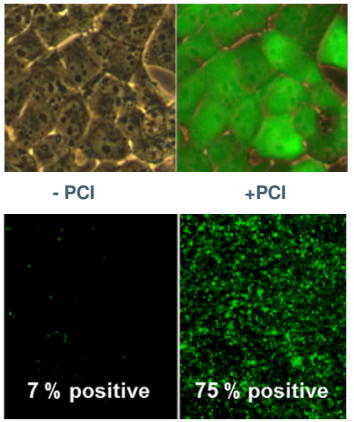
3 Intracellular delivery of gene therapy – *in vivo*



- Therapeutic gene (p53)
- Head & neck tumours (p53 mutated)
- Local injection

Ndoye *et al.* (2006) Mol. Ther. **13**:1154-1162

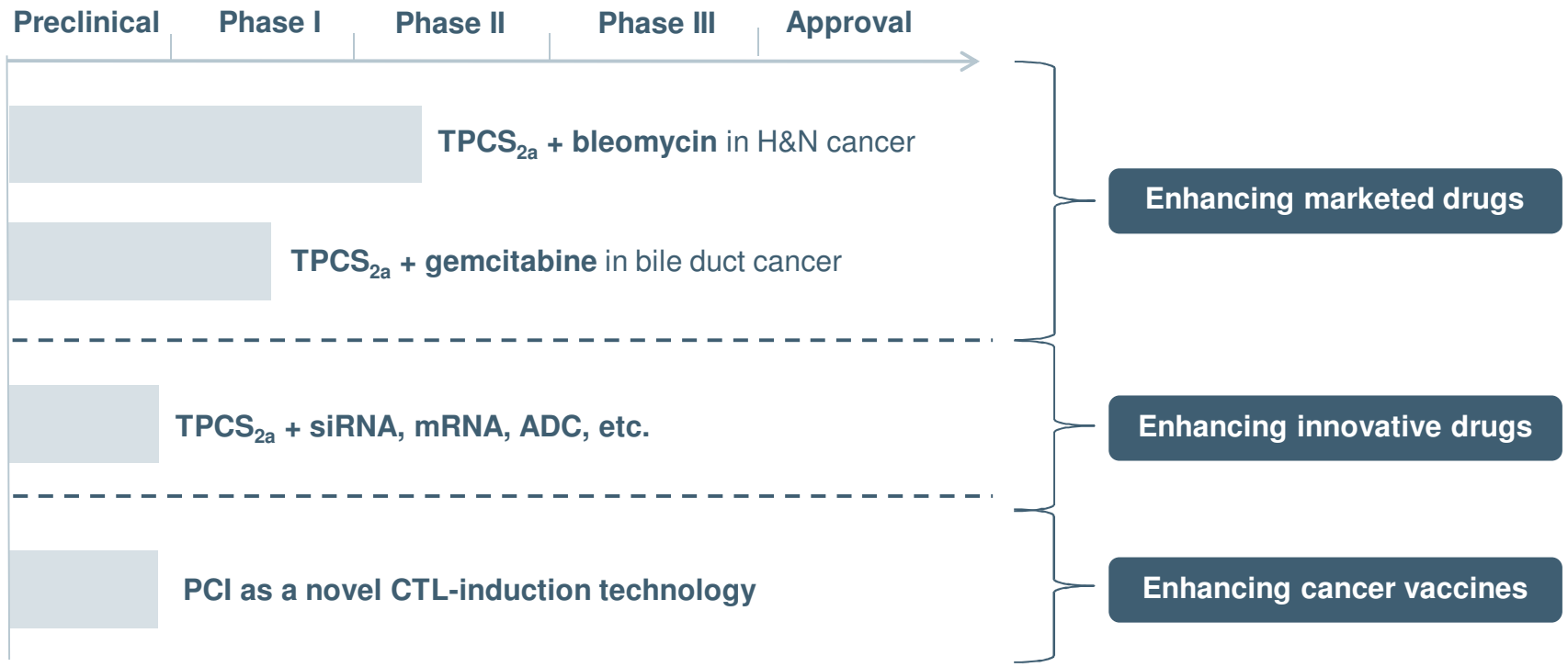
4 Intracellular delivery of mRNA



- EGFP mRNA

Bøe, S *et al.* (2010) *Oligonucleotides* **20**:1-6

PCI Biotech: versatile platform allows for diverse applications in the cancer field



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