



## **Targeted Drug Delivery for Cancer**

## PCI Biotech AS

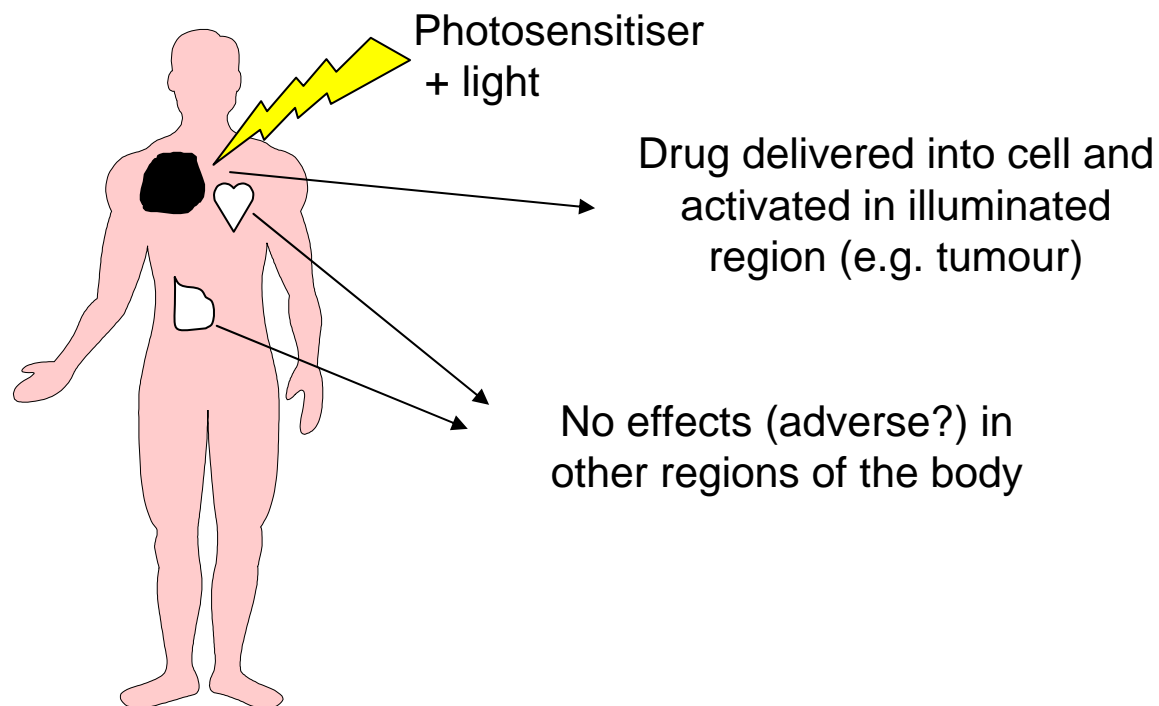
- Spin-out from and partnered with The Norwegian Radium Hospital
  - Technology invented there
  - Agreements in place, staff deployed on PCI technology
- Controlled by Photocure ASA
  - 90% of shares Photocure ASA
  - 10% of shares employees and Radium Hospital Research Foundation
- About 50 % financed by public grants (NRF, EU)
- Several other national and international collaborations

## Current challenges in cancer therapy

- Killing cancer cells is not difficult!
  - Lots of drugs can do this
- The trick is to do it without killing the whole patient
- Most cancer therapies have severe side effects
  - Very unpleasant for the patient
  - Often limit the therapeutic effect that can be achieved

**Specificity needs to be improved, with fewer side effects**

# Photochemical internalisation (PCI) - drugs delivered specifically to cancer cells



**Photosensitiser (Amphinex™) and technology (PCI)  
are both patent protected**

## PCI can be used to:

- Increase efficiency and specificity of known on-market drugs
  - Approved cytotoxic anti-cancer agents
    - Higher efficacy
    - Smaller side effects
- Deliver novel drug types that have so far not worked properly
  - “Advanced” drugs for cancer therapy where delivery is a major hurdle.
    - Nanoparticles, liposomes
    - Oligonucleotides, siRNA
    - Proteins (e.g. some antibody-based drugs)
    - Genes for gene therapy

## Significant improvement in delivery for a range of drug types

### Enhancement by PCI

**Approved anti-cancer drugs  
(bleomycin, doxorubicin)**

10 X

**Drugs in nanoparticles  
(liposomes, polymers etc.)**

10 – 100 X

**Oligonucleotides, siRNA**

10 – 100 X

**Proteins:**

Immunotoxins

100 X

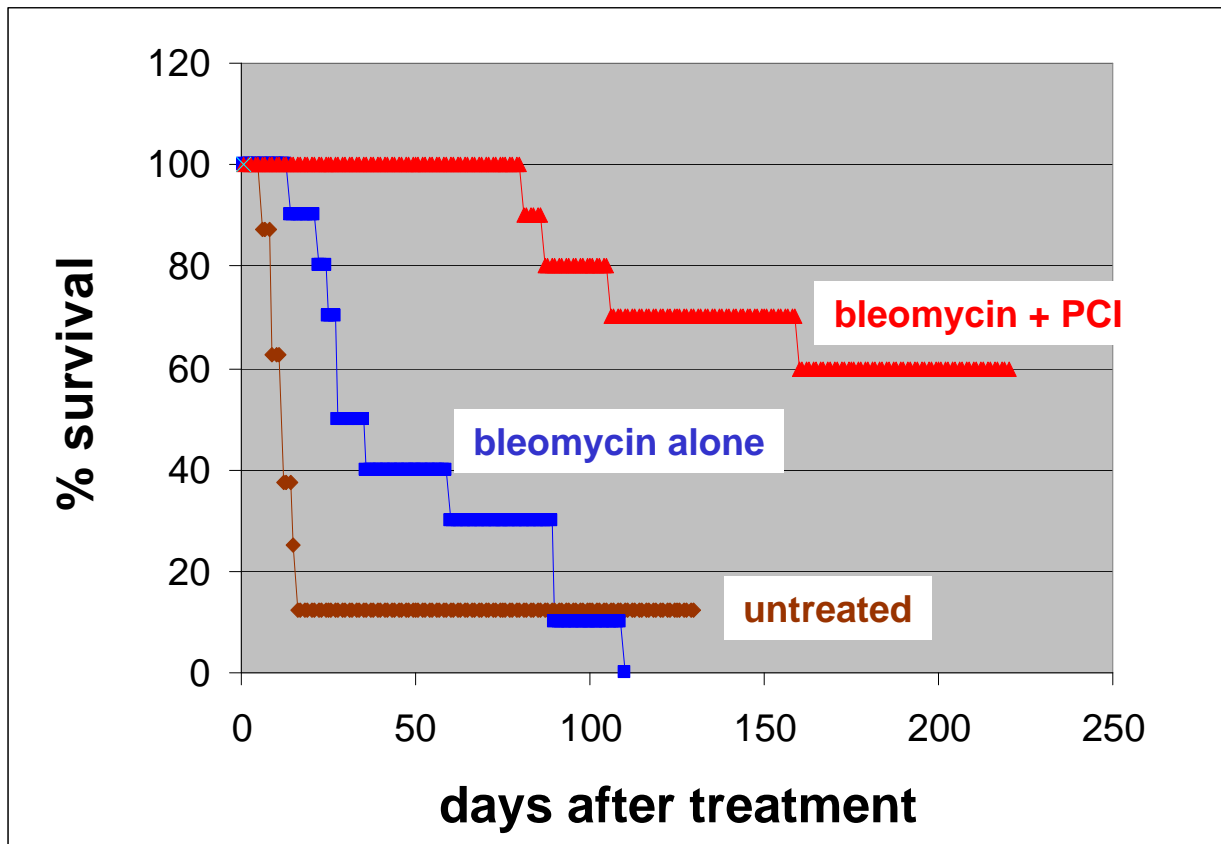
Protein toxins

100 – 1000 X

**Gene therapy agents**

5 – 1000 X

## Significantly improved *in vivo* survival rates with cytotoxic agent bleomycin



**Without PCI:**

No animals were cured by bleomycin

**With PCI:**

60% were cured

- 4 different animal models

Berg, K. et al. (2005). *Clin. Cancer Res.* **11**, 8476-8485

## **70% of mice permanently cured for tumour after PCI treatment with toxin gelonin**



- Gelonin alone no effect
- Good tissue regeneration

Selbo, *et al.* (2001). *Int. J. Cancer*, **92**, 761-766

## Gene Therapy: Potential tailor-made cancer therapy

- Cancer cells: Something is wrong with their genes
  - **What** is wrong can be found out for individual patient
  - Therapy can be directed (tailor-made) to specifically attack the defects
- Gene therapy of cancer
  - Use gene that will kill the cancer cells
  - Use agent (e.g. siRNA) that “silences” disease-causing genes

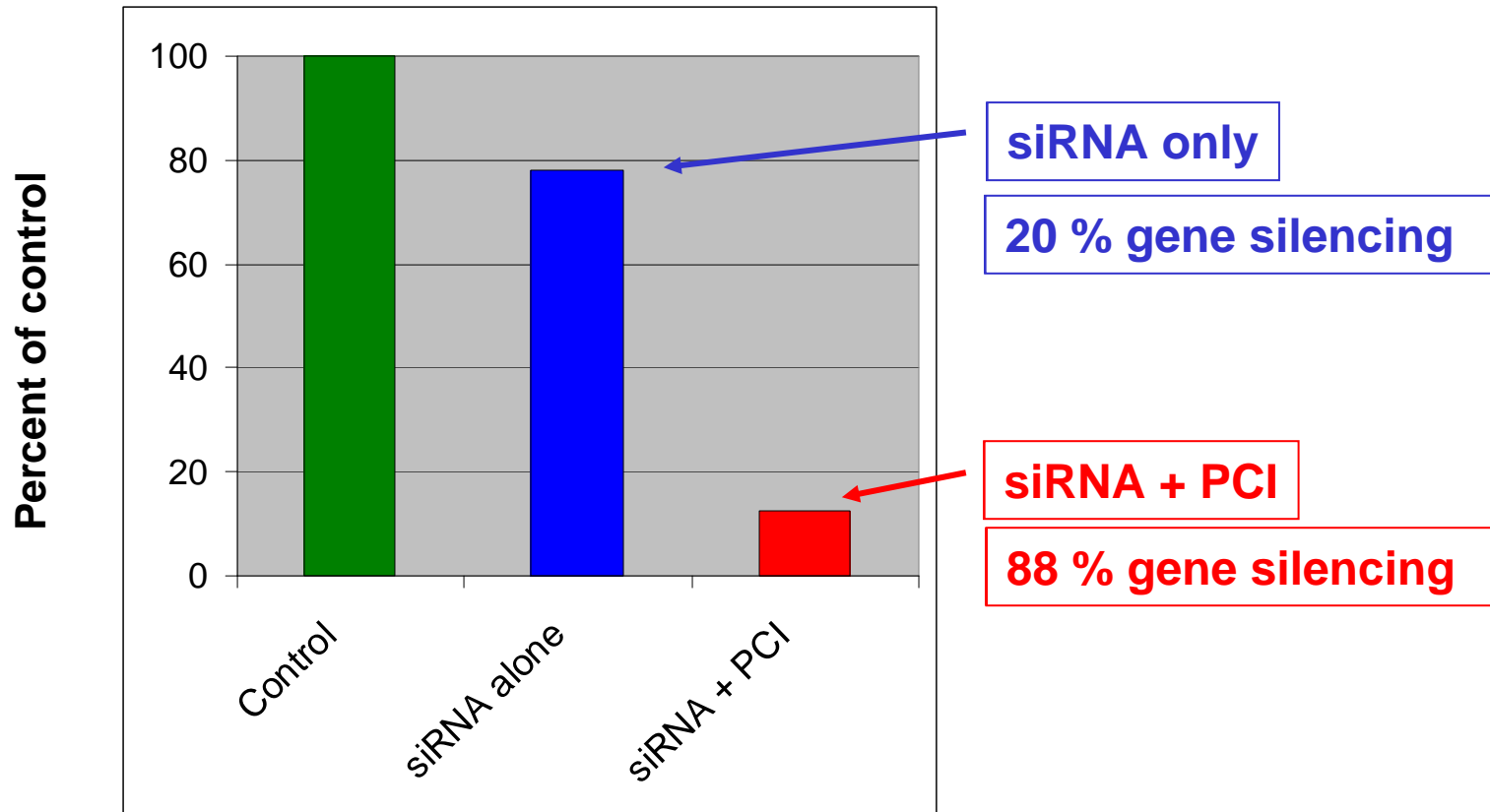
**But the gene must be delivered into the cancer cells**

## siRNA: Potential drugs of the future

- Short interference RNA (siRNA) molecules are oligonucleotides that “turn off” protein production from disease-causing genes (“gene silencing”)
  - Potential applications in cancer and other indications
- siRNA discoverers were awarded Nobel prize in medicine in 2006
- Merck & Co., Inc bought Sirna Therapeutics (a biotech specialising in RNA interference) for \$1.1bn in 2006
  - “Peter S. Kim, Ph.D., president, Merck Research Laboratories said “We believe that RNAi could significantly change the way in which we go about discovering and developing drugs, and could become a new way to treat patients with unmet medical needs.”

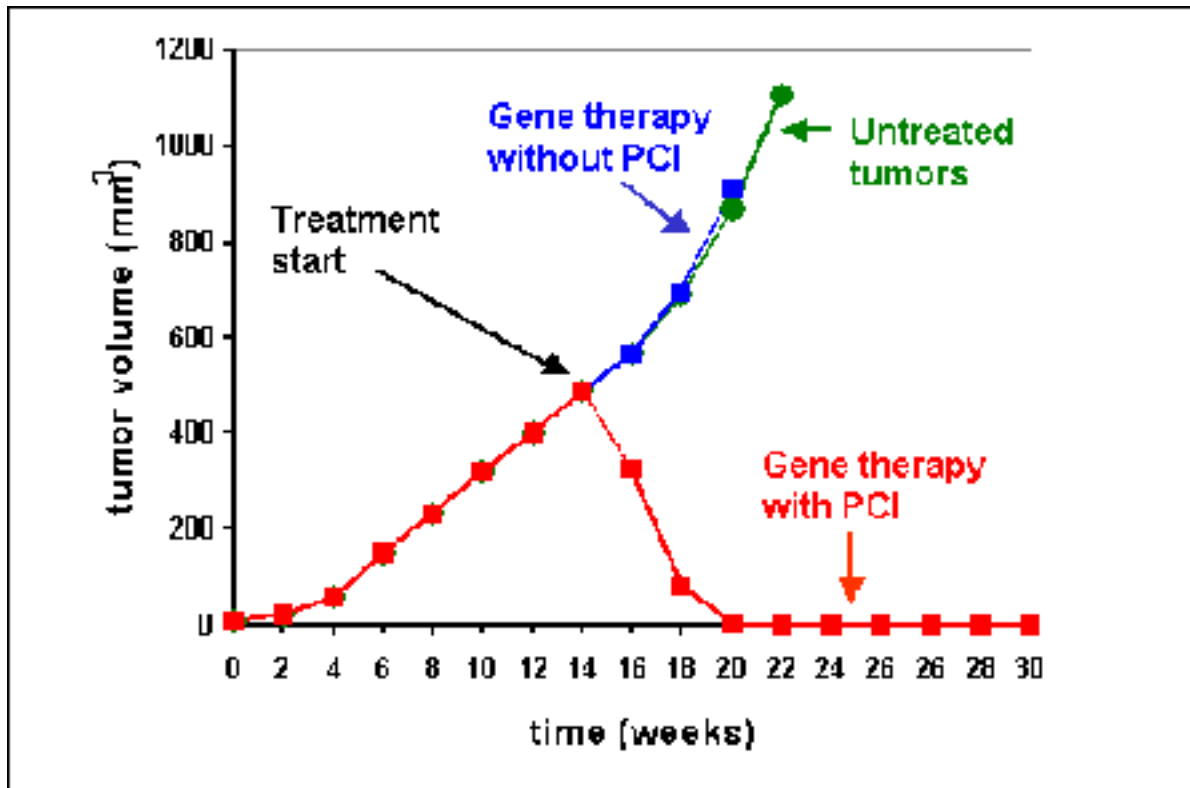
**But siRNA must be delivered into cells to be effective**

# PCI enhances siRNA's "gene silencing" effect



Bøe, S. et al. (2007). *Oligonucleotides*, in press

> 80% of mice survived human head and neck cancer tumour after gene therapy using PCI as the drug delivery system



- Gene that makes cancer cells commit suicide

- Gene therapy without PCI no effect.

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

## Development plan

- **Initial clinical proof of concept study with Amphinex™ photosensitiser and approved cytotoxic agent (bleomycin) to start 2007**
  - To show that technology is safe and works in patients
  - Results will be monitored continuously during study
- **Short/medium term focus on developing therapies with approved commercially attractive off-patent cytotoxic agents**
- **Licence the PCI technology as a competitive DDS to other companies for their on-market conventional drugs, siRNA and other novel tailor-made drugs**

## **The PCI technology works and represents a fantastic business opportunity!**

- **Significant improvement in drug delivery for a range of drug types**
- **Documented improved *in vivo* survival rates with cytotoxic agent bleomycin**
- **Significant enhancement of siRNA's "gene silencing" effect.**
- **Documented improved *in vivo* survival with human head and neck cancer undergoing gene therapy**
- **Attractive short term opportunity in the conventional LCM drug delivery business as well as a significant longer term business upside for novel biotech drugs.**

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