



*Unlocking the potential of innovative medicines*

# PCI Biotech

## *Second Quarter and First Half 2014 Results*

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26 August 2014

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## Highlights

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- Successful completion of the second light dose cohort in the modified ENHANCE study – a Phase II study in head & neck cancer patients. The study has been amended to include a light dose escalation run-in phase to optimise the intra-tumour treatment regimen and a Proof of Concept part to confirm safety and efficacy.
- Started inclusion of patients in the Phase I/II Proof of Concept study with Amphinex in combination with gemcitabine in patients with inoperable bile duct cancer (cholangiocarcinoma). Treatment evaluation of the first dose cohort is completed and enrolment for the second dose cohort is on-going.
- Awarded NOK 12.5 million in a BIA grant from The Research Council of Norway to the project "Development of photochemical internalization to enhance the effect of therapeutic and prophylactic vaccines".

PCI Biotech

*Unlocking the potential of innovative medicines*

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*PCI Technology*

# PCI technology – enabling drugs to reach intracellular therapeutic targets

## STEP 1:

- TPCS<sub>2a</sub> (S) and the active molecule (D) are injected into the body and carried by the blood stream to the cell



## STEP 2:

- TPCS<sub>2a</sub> (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
- S is washed away from the cell membrane, but trapped in endosomes



## STEP 3:

- Light activates TPCS<sub>2a</sub> (S) in the membrane of the endosome
- The membrane integrity is affected and the active molecule released



## STEP 4:

- The active molecule (D) can now bind to its target (T) and initiate the therapeutic response



### The active molecule

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



### The PCI component

- Light sensitive component
- Amphinex® - TPCS<sub>2a</sub>



### The target

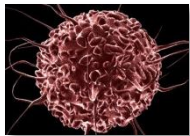
- Target for the active molecule
- E.g. DNA, mRNA, enzyme, microtubuli

*PCI mechanism of action – triggered endosomal escape through illumination*

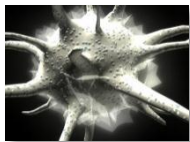
# PCI technology – enabling drugs to cover additional areas of unmet medical need

## 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

### Photosensitizer (Amphinex™)



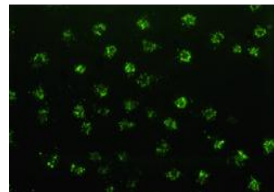
### Light source



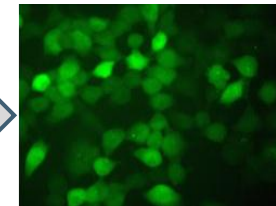
Red light



Blue light



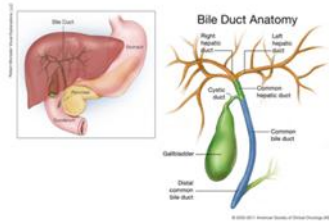
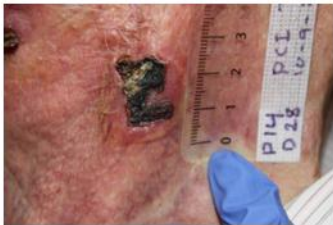
Endosomal escape  
Release of drug in cells



# PCI Biotech is leveraging PCI (TPCS<sub>2a</sub>) in three distinct areas

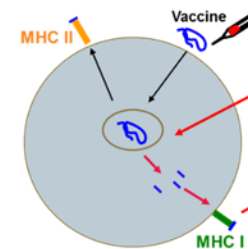
## Local cancer treatment

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



## PCI vaccination technology

- therapeutic vaccination

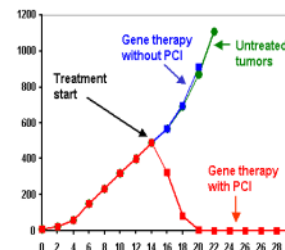


PCI – induce presentation on MHC class I

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

## PCI macromolecule delivery

- immunotoxins
- siRNA & other oligo
- gene therapy



*Amphinex<sup>®</sup> – A New Paradigm for Localized Cancer Treatment*

*- PCI of Bleomycin for H&N Cancer*

*- PCI of Gemcitabine for Bile duct cancer*



# Substantial head & neck cancer market potential

## Sizeable immediate target market

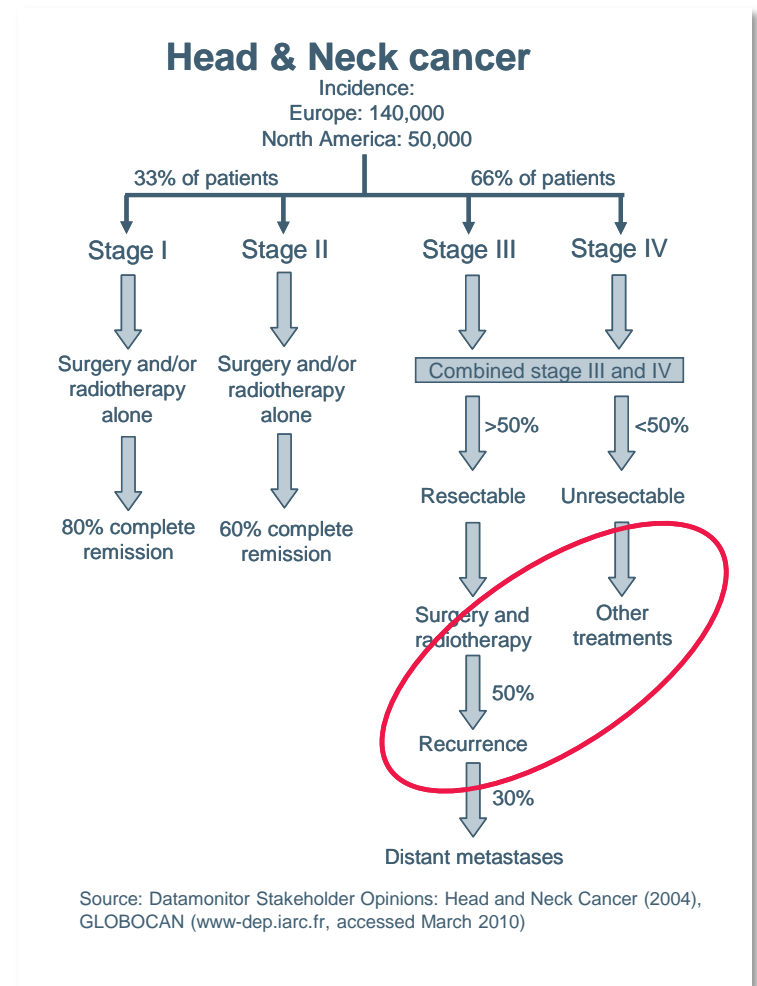
- Incidence is stable, close to 200,000 across Europe and the US
- Immediate target is inoperable recurrent patients
- Almost 40,000 assumed to be eligible for PCI treatment\*
- Substantial upside potential earlier in the treatment algorithm

## Attractive price potential

- Cetuximab (Erbix) is the most relevant price comparator
  - Sales >\$1.8 billion in 2012 (~40% estimated to be in H&N)
  - Average total price / patient close to \$70k in US and \$40k in EU

## High potential market penetration

- Anticipated benefits of PCI with Amphinex
  - Greater efficacy
  - Less systemic side effects
  - Better cosmetic and functional outcome, with improved quality of life



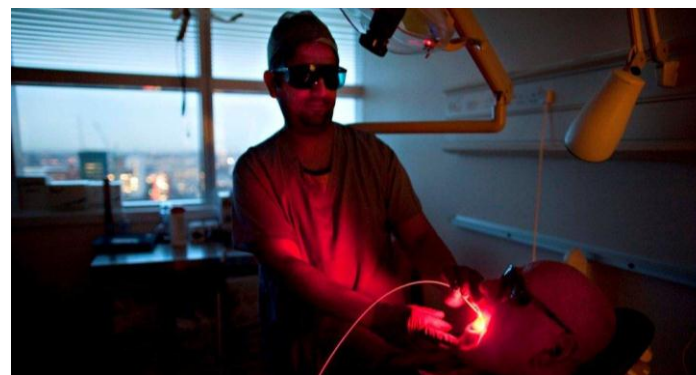
# Amphinex<sup>®</sup> head & neck cancer – Phase II study

## Summary of study design

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

## Current status and plans

- Too strong effects induced by intra-tumour treatment resulted in undesired treatment effects
- Intra-tumour illumination is therefore optimized in a separate light-dose escalation part of the study; second light-dose cohort (3 pts) concluded Q3-2014
- So far no serious safety concern in the light-dose escalation part and clear indications of tumour response; three more patients will be included at the same light dose before final light dose selection
- Interim/PoC analysis after 12 patients treated with intra-tumour illumination at the finally selected light dose



# Sizeable bile duct cancer market potential

## Immediate target market is as first line treatment

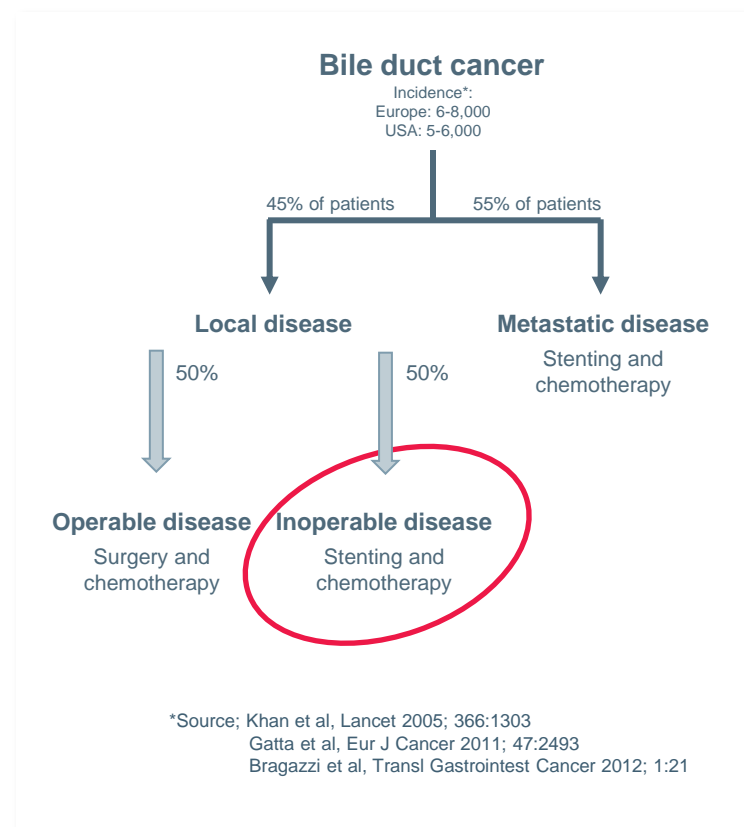
- Incidence is close to 15,000 across Europe and the US
- Immediate target is inoperable patients with local disease
- Approximately 3,000 assumed to be eligible for PCI treatment
- Possible upside potential in metastatic disease

## High price potential

- Lack of approved medicinal treatment options
- Orphan indication implies a high price

## Potential significant majority share of the market

- Anticipated benefits
  - No competing marketable treatment alternatives
  - Greater efficacy due to local chemotherapy boost
  - Easy light access through established standard procedures



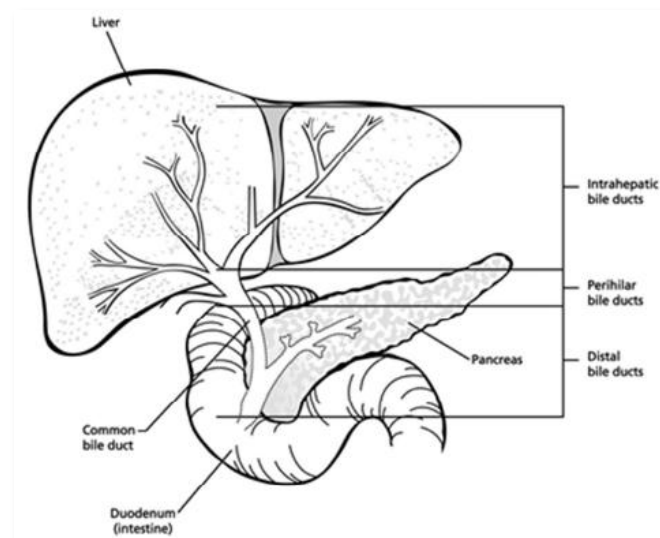
# Amphinex<sup>®</sup> bile duct cancer – Phase I/II study

## Summary of Study Design

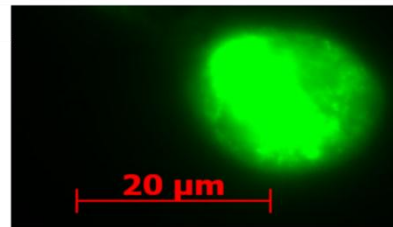
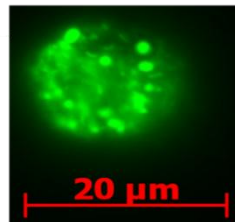
<b>Cancer type</b>	Bile duct (Cholangiocarcinoma)
<b>Phase</b>	I/II
<b>Photosensitizer</b>	Amphinex <sup>®</sup> (PCIB)
<b>Drug</b>	Gemcitabine (Cisplatin)
<b>Light source</b>	Red laser 652 nm (PCIB)
<b>Fixed variables</b>	Gemcitabine and Cisplatin
<b>Variables</b>	Amphinex <sup>®</sup> and/or light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

## Current status and plans

- Safety driven Phase I
- First dose cohort (3 pts) concluded Q2-2014 – no safety concerns
- Inclusion into second cohort on-going
- 5:2 randomisation in Phase II, 35 pts in total



*TPCS<sub>2a</sub> – An innovative and versatile technology for therapeutic vaccination*



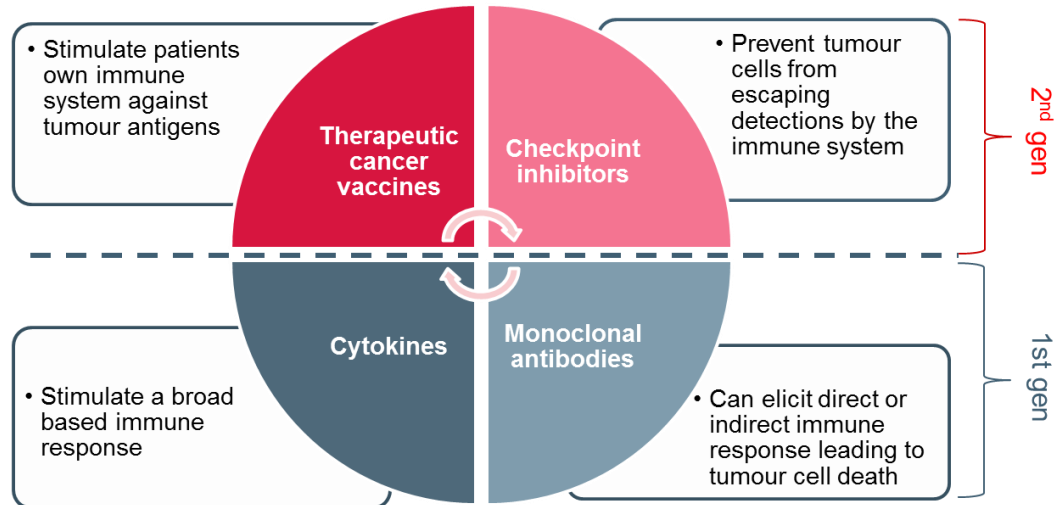
# An opportunity to play a key role in the second generation cancer immunotherapy paradigm

**PCI**

## Second generation cancer immunotherapy

### PCI technology

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



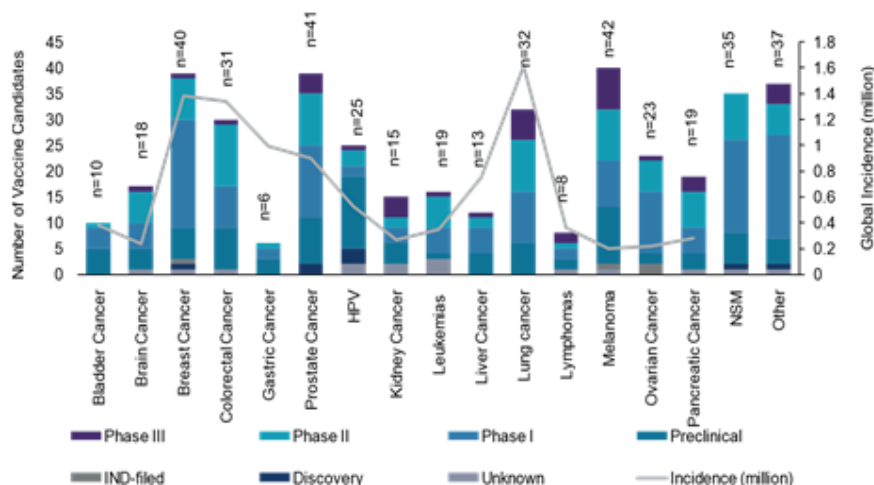
**PCI**

# Cancer therapeutic vaccines – Substantial development pipeline and expected market growth

## Development pipeline

### Therapeutic Cancer Vaccines Market, Global, Development Pipeline, Candidates by Indication, 2012-2019

Source: GBI Research's Proprietary Pipeline Products database; GLOBOCAN 2008

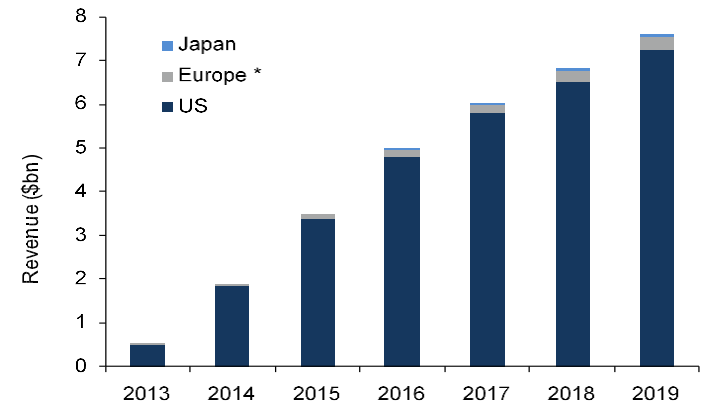


- “233 companies plus partners are today developing 275 cancer vaccine drugs in 600 developmental projects in cancer across 161 different targets”<sup>1</sup>
- Top 5 indications: Breast, Colorectal, Lung, Prostate, Melanoma

## Market size forecast

### Therapeutic Cancer Vaccines Market, Global, Revenue Forecast (\$bn), 2013-2019

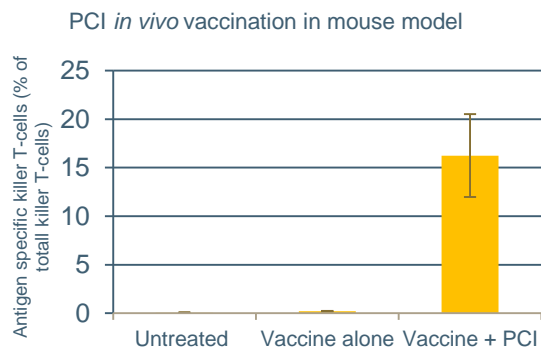
Source: GBI Research's Proprietary Pipeline Products Epidemiology and Market Size Databases



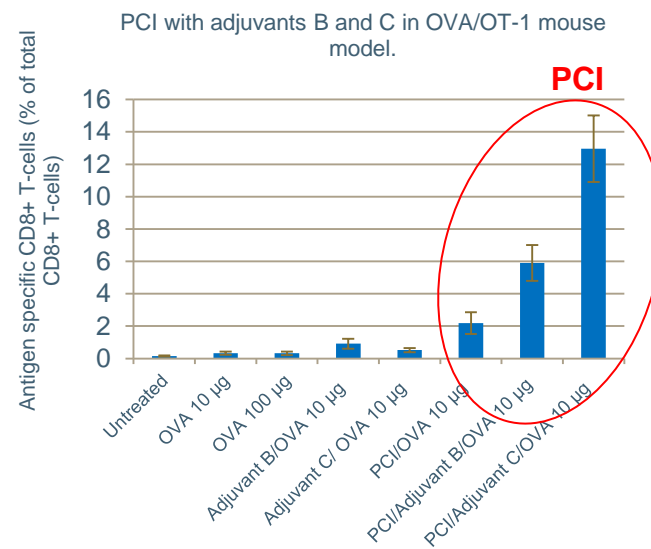
- “Provenge” currently the only marketed therapeutic cancer vaccine (annual global sales of approx. \$200 million)
- Therapeutic cancer vaccine market could grow to a value of \$7.6 billion by 2019<sup>2</sup>
- All therapeutic cancer vaccines will need immune-potentiating technologies to be effective

# Cancer therapeutic vaccines – PCI as a simple and effective immune-potentiator

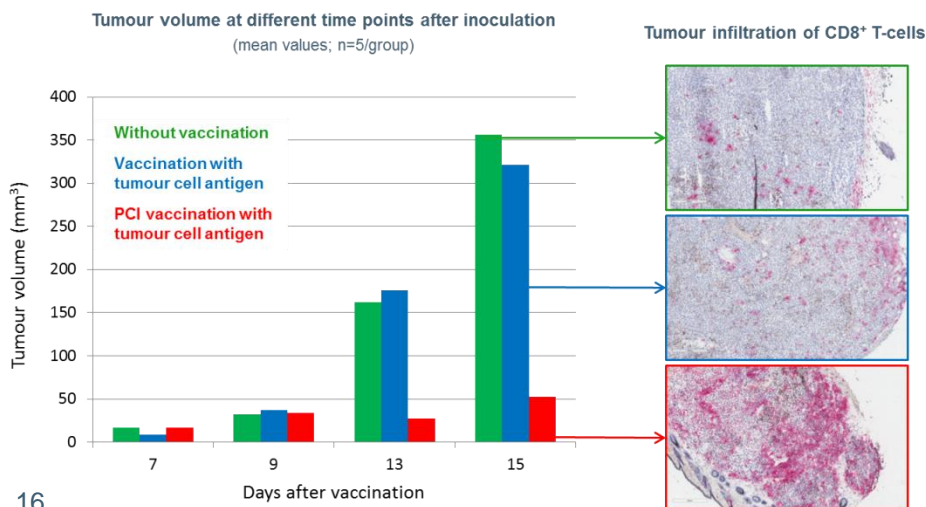
## An effective immune-potentiator,



## which works in synergy with state-of-the-art adjuvants,



## and translates into therapeutic effect in disease models





# Cancer therapeutic vaccines – Competitive advantages and user-friendly solutions



**Safety** – TPCS<sub>2a</sub> tested in Phase I study (i.v. inj.) at much higher doses than what will be used for vaccination

**Stability** – TPCS<sub>2a</sub> can be autoclaved and is stable at room temperature, also in solution

**Innovation** – Unique mode of action; indication that TPCS<sub>2a</sub> induces MHC class I antigen presentation in dendritic cells and macrophages

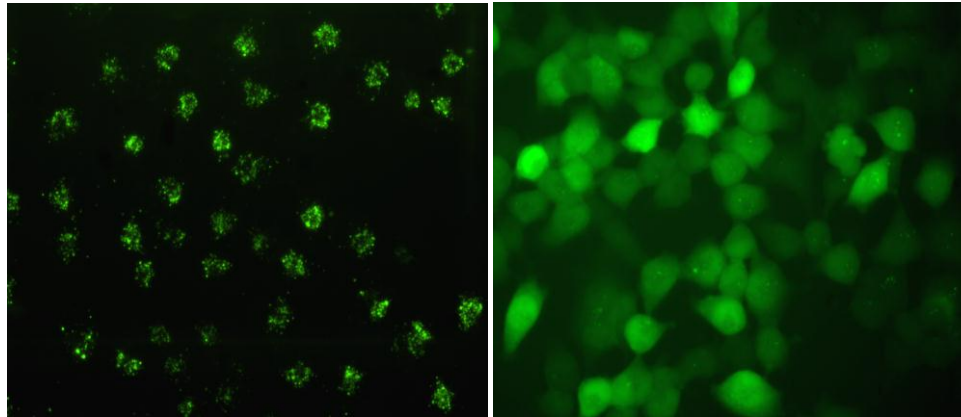
**Cost effectiveness** – Simple and cost effective synthesis of TPCS<sub>2a</sub>

**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 immunization (products, uses and devices)**

*TPCS<sub>2a</sub> – Photochemical Internalisation of Macromolecules*

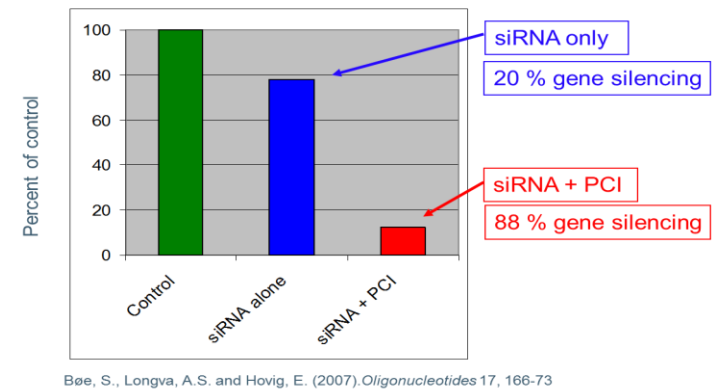


# Macromolecules – Endosomal escape of a range of products, pre-clinical data

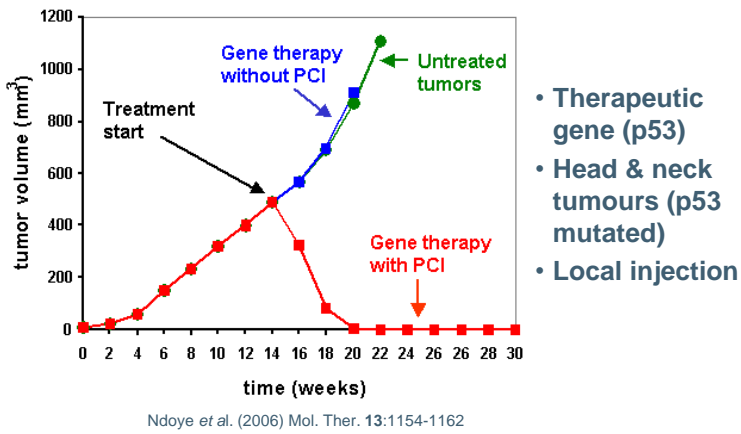
## 1 Intracellular delivery of immunotoxin – *in vivo*



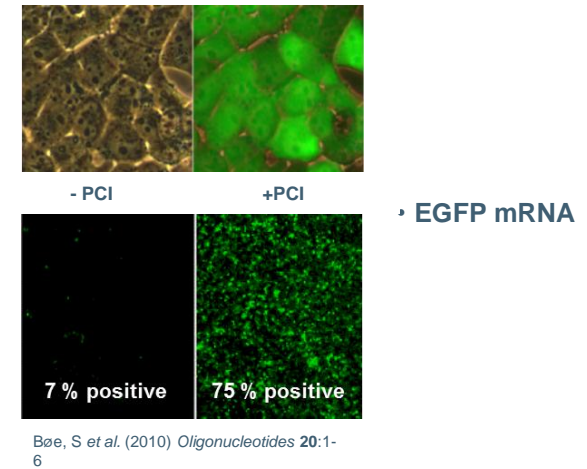
## 2 Intracellular delivery of siRNA



## 3 Intracellular delivery of gene therapy – *in vivo*



## 4 Intracellular delivery of mRNA



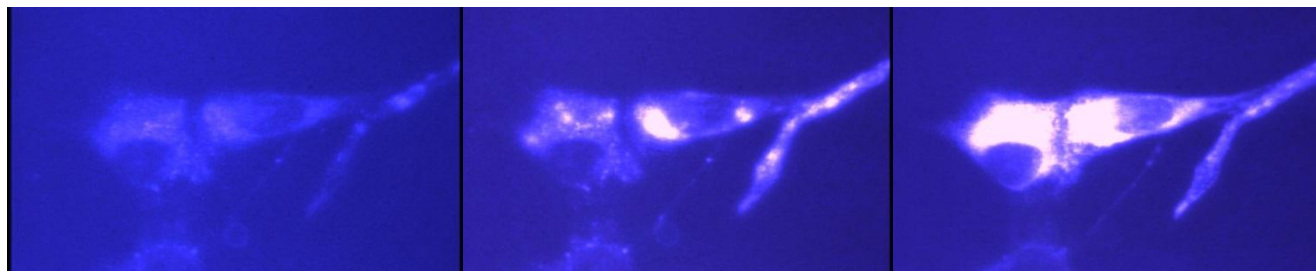
*Financial key figures*

<i>(In NOK 1,000)</i>	Note	Q2 2014	Q2 2013	01.01 - 30.06 2014	01.01 - 30.06 2013	01.01 - 31.12 2013
<b>Other Income</b>	5	1 938	1 688	3 905	3 078	6 681
Research and development	8	9 550	6 551	19 509	14 523	32 789
General and administrative		771	1 027	2 187	1 689	3 217
<b>Operating costs</b>		<b>10 321</b>	<b>7 578</b>	<b>21 696</b>	<b>16 212</b>	<b>36 006</b>
<b>Operating results</b>		<b>-8 383</b>	<b>-5 890</b>	<b>-17 791</b>	<b>-13 134</b>	<b>-29 325</b>
<b>Financial income and costs</b>						
Financial income		253	478	517	898	1 717
Financial expenses		0	0	103	0	0
<b>Net financial result</b>		<b>253</b>	<b>478</b>	<b>413</b>	<b>898</b>	<b>1 717</b>
<b>Ordinary profit before taxes</b>		<b>-8 131</b>	<b>-5 412</b>	<b>-17 378</b>	<b>-12 236</b>	<b>-27 608</b>

<i>(In NOK 1,000)</i>	Note	30.06 2014	30.06 2013	31.12 2013
<b>Fixed and intangible assets</b>				
Operating assets		16	21	18
<b>Total fixed and intangible assets</b>		<b>16</b>	<b>21</b>	<b>18</b>
<b>Current assets</b>				
Short term receivables	7	5 830	4 813	6 123
Cash & cash equivalents	7	29 188	59 608	46 595
<b>Total current assets</b>		<b>35 018</b>	<b>64 421</b>	<b>52 718</b>
<b>Total assets</b>		<b>35 034</b>	<b>64 442</b>	<b>52 736</b>
<b>Shareholders equity and liabilities</b>				
<b>Shareholders equity</b>				
Paid in capital		99 911	190 903	99 911
Other reserves		-72 972	-132 458	-56 515
<b>Total equity</b>	10	<b>26 939</b>	<b>58 445</b>	<b>43 396</b>
Trade debtors		2 052	1 590	4 061
Other short term debt		6 044	4 407	5 279
<b>Total debt</b>		<b>8 096</b>	<b>5 997</b>	<b>9 340</b>
<b>Total shareholders equity and liabilities</b>		<b>35 034</b>	<b>64 442</b>	<b>52 736</b>

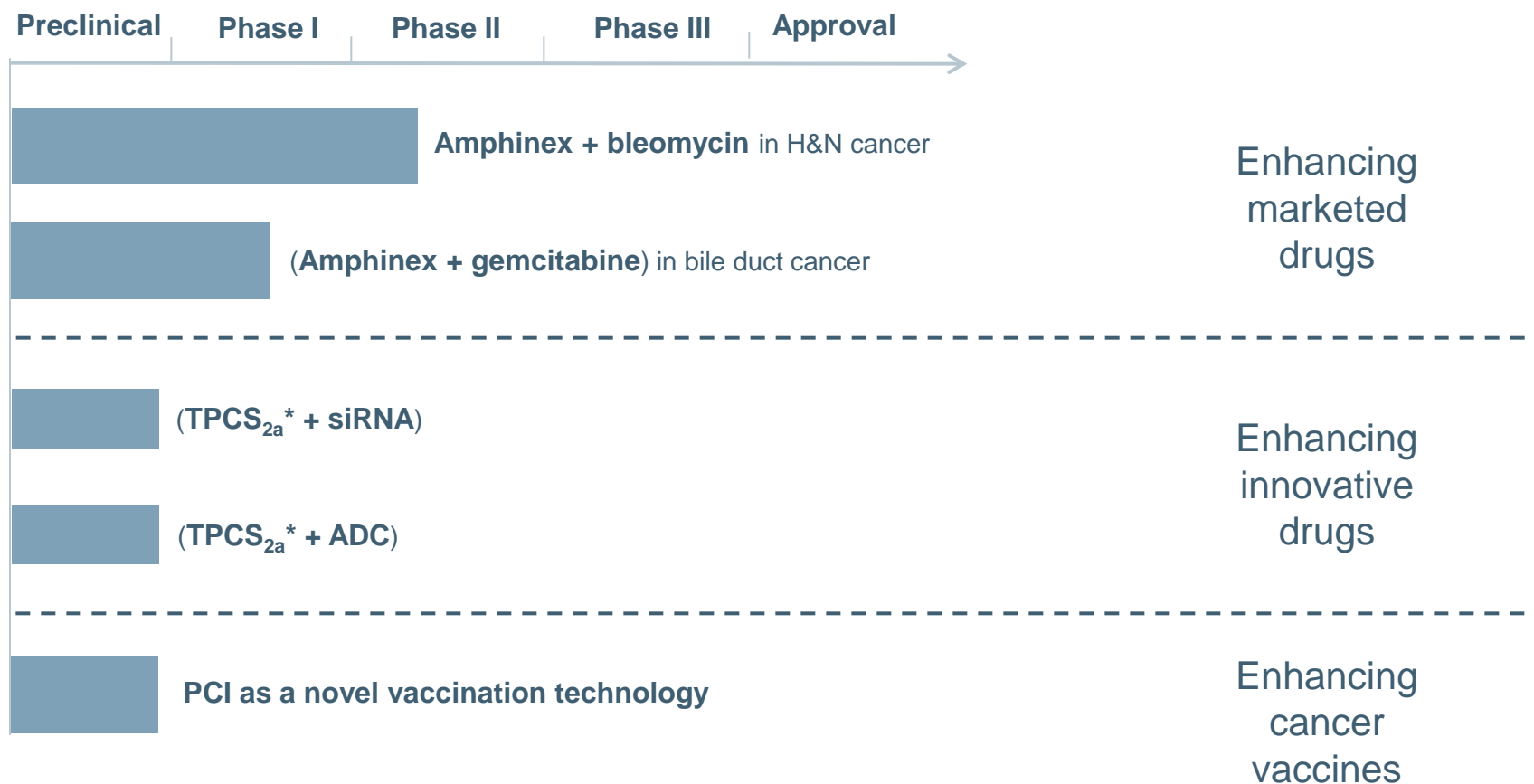
<i>CASH FLOW (In NOK '000)</i>	<b>Q2 2014</b>	<b>Q2 2013</b>	<b>1H 2014</b>	<b>1H 2013</b>	<b>FY 2013</b>
Net cash flow from operations	-9 245	-6 735	-17 407	-13 475	-26 876
Net cash flow from investments	-	-	-	-	-
Net cash flow from financial activities	-	-	-	-	388
<b>Net change in cash during the period</b>	<b>-9 245</b>	<b>-6 735</b>	<b>-17 407</b>	<b>-13 475</b>	<b>-26 488</b>

*Looking ahead*





# PCI – a versatile technology with a pipeline of partnering opportunities



\* Active pharmaceutical ingredient in Amphinex

# Development and commercial strategy; A flexible partnering strategy

## H&N and bile duct cancer

- Successful Phase II studies are important value-enhancing milestones
- PCI Biotech will maintain a flexible licensing strategy, but licensing agreements based on Phase II data is assumed to maximise the ROI for shareholders

## Therapeutic vaccination

- High failure rate in clinical development linked to low efficacy makes PCI an attractive licensing asset
- High deal activity, with a large number of pre-clinical deals and alliances
- Aim is to license to several partners for use in different disease areas and/or with different technologies

## Macromolecules

- Many potential partners, as the technology works with most macromolecules
- Opportunistic approach; use existing pre-clinical data to attract partners
- Aim is to license to several partners for use with different macromolecular technologies in different disease areas

***Retain rights and actively participate in the commercialisation of PCI***

# PCI Biotech – well positioned for attractive development opportunities

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## Outlook

Focus on the clinical development of Amphinex in combination with cancer drugs for localised cancer treatment, based on the company's unique PCI technology. Maintain the activity level level in pre-clinical development and licensing of PCI as a versatile and innovative platform.

Main priorities:

- Effectively progress the light dose optimization and proof of concept of intra-tumour head and neck cancer treatment of Amphinex and bleomycin
- Complete the first part of the proof of concept study of bile duct cancer treatment with Amphinex and gemcitabine
- Solidify a robust vaccination IP estate and further strengthen the promising preclinical results
- Partnering activities across all commercially interesting areas for the PCI platform
- Ensure that the company has sufficient financial flexibility in the short and long term to achieve strategic and operational objectives

# Enquiries

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