



# PCI BIOTECH

Unlocking the potential of innovative medicines

Q4 2016 PRESENTATION

February 28, 2017

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# PCI BIOTECH

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# HIGHLIGHTS

## ► 2016 and beyond

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- Completed Phase I study in bile duct cancer, with promising early signs of efficacy
  - Phase I results presented as late-breaking news at United European Gastroenterology Week
  - Orphan designation of fimaporfin in bile duct cancer granted in EU
  - Opened Investigational New Drug (IND) in the US
  - First-in-man study published in Lancet Oncology, with independent commentary
- 
- Initiated Phase I clinical validation in healthy volunteers
  - Research agreement signed with Ultimovacs
  - Awarded up to NOK 13.8 million for further development
- 
- Research collaborations with BioNTech and eTheRNA signed
  - Extension of the existing top 10 pharma agreement until end of 2Q 2017
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- Launched three well-defined strategic development areas
  - Completion of a fully underwritten rights issue of NOK 70 million – oversubscribed >100%

# PCI BIOTECH AT A GLANCE

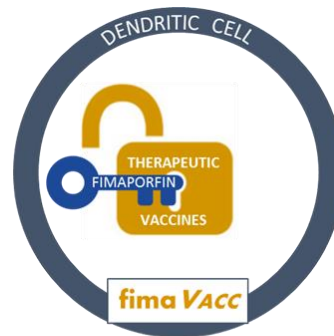
## ► Unlocking the potential of innovative medicines

- A listed (PCIB:NO) cancer-focused biotech company
- Photochemical internalisation (“PCI”) technology, originating from the Norwegian Radium Hospital
- Clinical programmes
  - fimaCHEM** – Phase I/II with fimaporfin (Amphinex®) for the orphan indication inoperable bile duct cancer
  - fimaVACC** – Vaccination technology that provides strongly enhanced cellular immune responses, phase I initiated
- Pre-clinical programme
  - fimaNAC** – Efficient intracellular delivery of nucleic acid therapeutics, with four active research collaborations

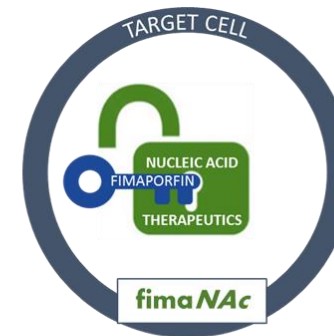
### ***PCI – the solution to a key challenge for several modalities***



Enabling approved drugs to fulfil unmet local treatment need



Enhancing cellular immune responses important for therapeutic effect



Providing a delivery solution for nucleic acid therapeutics

# CHEMOTHERAPEUTICS

▶ A cornerstone in current cancer therapy

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Chemotherapeutics  
will remain a  
**CORNERSTONE**  
in cancer treatment  
for the foreseeable  
future

PCI may enhance  
approximately  
**20%**  
of relevant approved  
chemotherapies

Niche indications  
may allow for  
**ORPHAN  
DRUG**  
applications

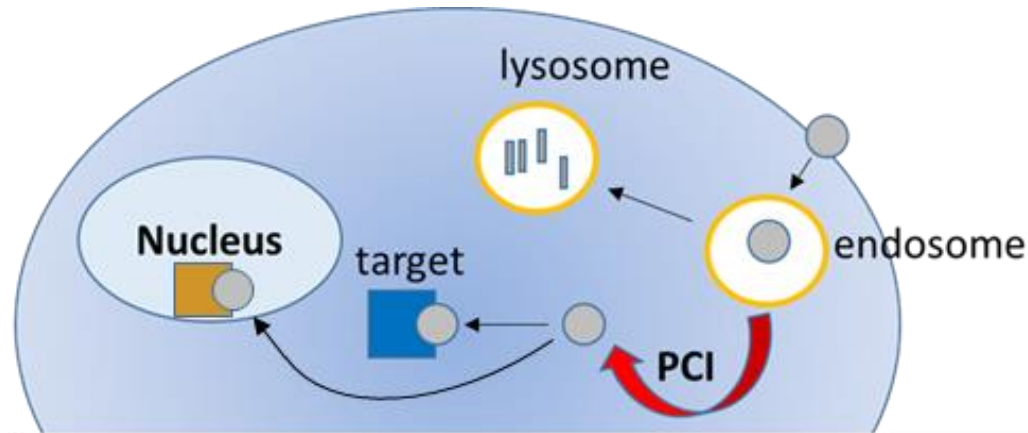
- ▶ **fima *CHEM*** may enable approved drugs to fulfil unmet local treatment needs
- ▶ First-in-man study published in *Lancet Oncology*\*, with independent expert commentary
- ▶ Ready for Phase II in bile duct cancer with promising early signs of efficacy
- ▶ Opportunity for development in further niche indications

\* *Lancet Oncology* (2016) 17(9): p1217–1229

# PCI TECHNOLOGY

► **fimaCHEM** – mode of action

## Cancer cell

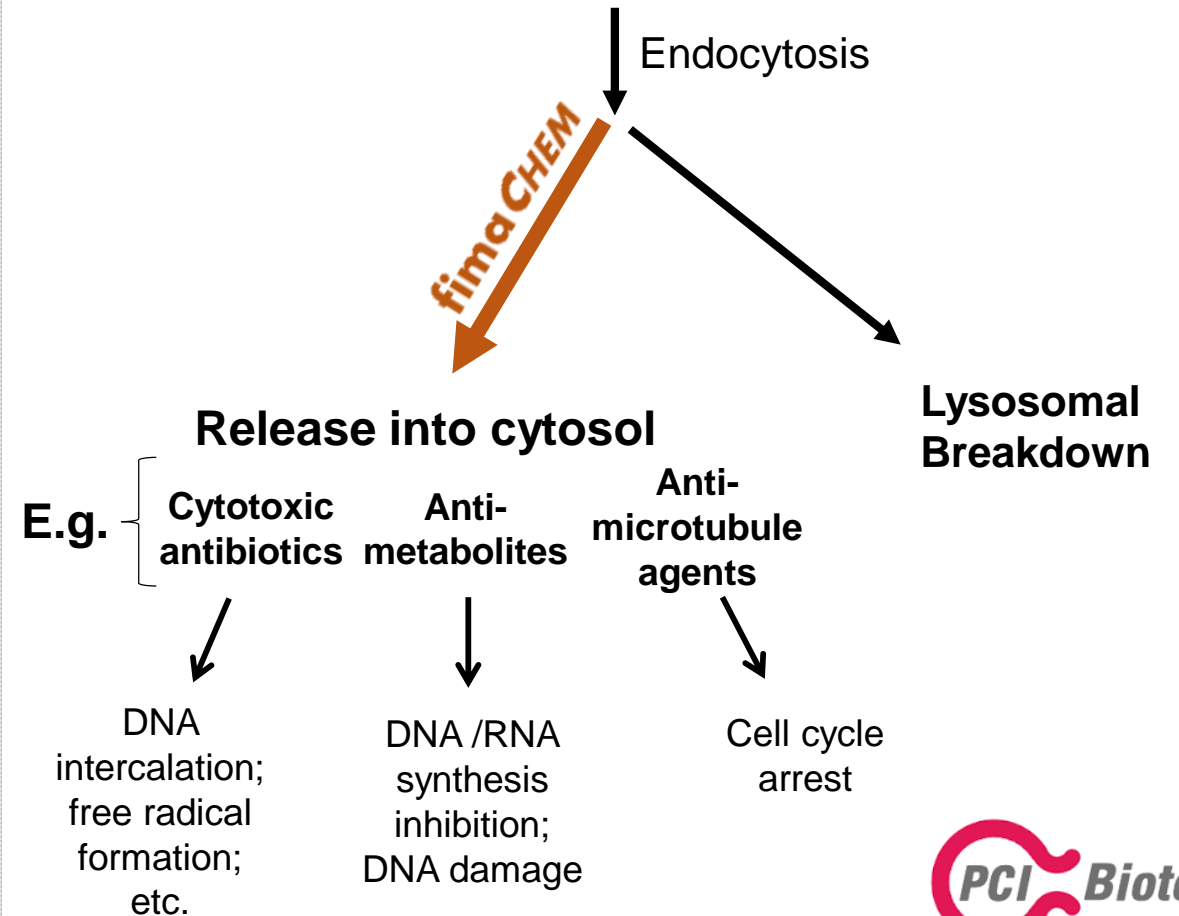


● chemotherapeutic

The intracellular trafficking of chemotherapeutics is not well characterised for many products, but it is known that endocytotic uptake and/or sequestering into endosomes can lead to high endosomal concentrations.

PCI can release biologically active chemotherapeutics that are trapped in endosomes, thereby enabling them to reach their target before being inactivated in lysosomes.

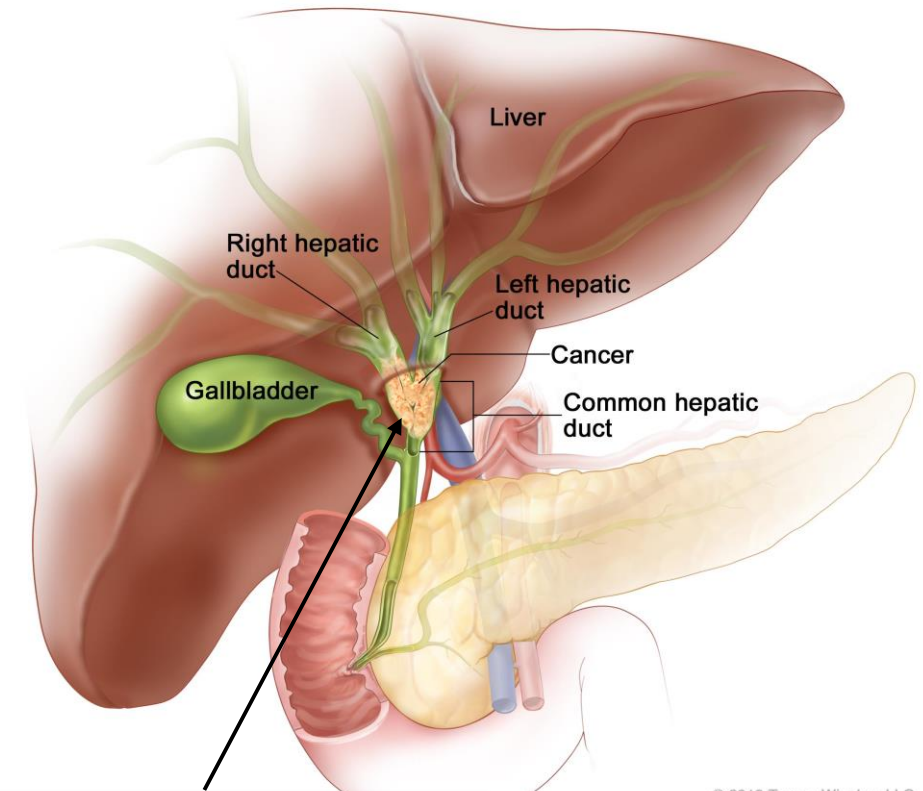
## Chemotherapeutics



# BILE DUCT CANCER

## ► Location and classification

- Often referred to as cholangiocarcinoma
- The cancer cells originates from the cells inside the bile duct (called cholangiocytes)
- Cholangiocarcinoma includes:
  - Intrahepatic tumours (10%\*)
  - Perihilar tumours (60-70%\*)
  - Distal tumours (20-30%\*)
  - Different incidence, pathobiology and management



*Perihilar bile duct cancer is the initial target for PCI treatment*

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# BILE DUCT CANCER

## ► Why target bile duct cancer

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- ▶ Orphan indication, yearly incidence rate of 1-2 per 100,000 in the western world – higher incidences in Asia
- ▶ Five-year survival rate of less than 5%, and almost 0% when inoperable – average approx. 12 months survival
- ▶ Current management
  - Surgery
    - Only potentially curative treatment
    - Less than 1/3 are resectable at presentation
  - Stenting
    - **Endoscopic** stenting for palliative biliary drainage
  - Chemotherapy
    - No approved chemotherapy
    - Recommended chemotherapy: **gemcitabine** and cisplatin



### *Excellent technology fit with PCI*

Targeted illumination is done using standard endoscopic procedure

The active chemotherapy gemcitabine is significantly enhanced by **fimaCHEM**



# BILE DUCT CANCER

## ▶ A sizeable orphan market potential

### ▶ Immediate target market is as first line treatment

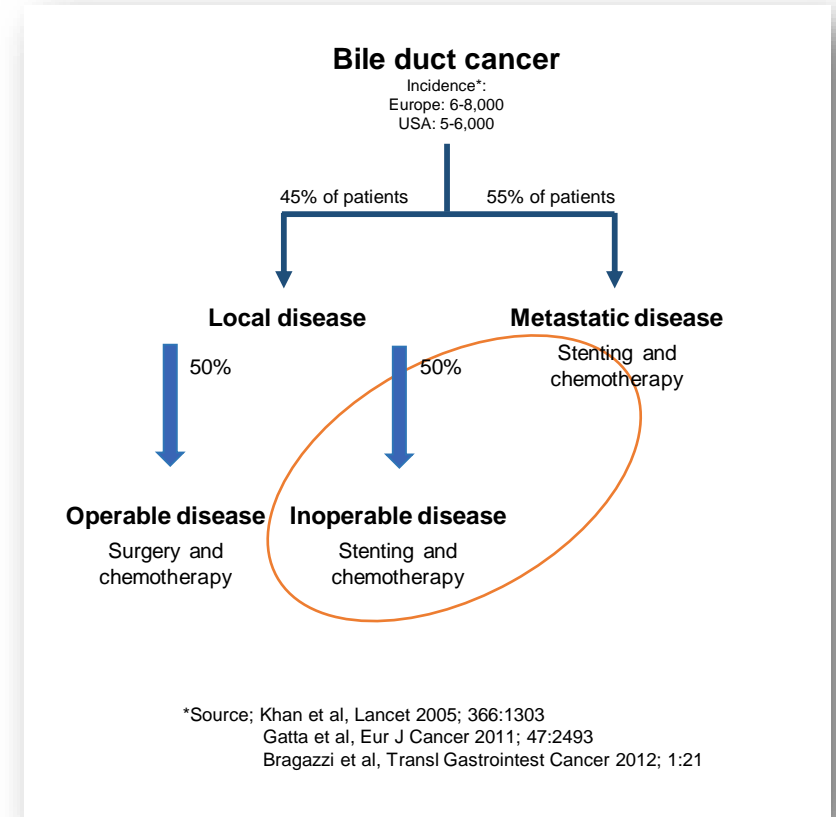
- Incidence is close to 15,000 across Europe and the US
- Immediate target is inoperable patients with local disease
- Approximately 3,000 assumed to be eligible for **fimaCHEM**
- Possible upside in distal and more advanced metastatic disease
- Higher incidences in Asia

### ▶ Attractive price potential for orphan drugs

- Lack of approved medicinal treatment options
- Diseases with <10,000 in US support annual pricing >\$100,000<sup>1</sup>

### ▶ 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



# BILE DUCT CANCER – CLINICAL PHASE I/II STUDY

► Six month radiology data – central read confirms promising early tumour response

► **Cohort III & IV – response at single lesion level**

Measurable lesions	Lesion shrinkage		Stable lesion	Lesion growth
<b>19</b> (total number of targets selected across the two independent readers)	<b>17</b>	<b>12</b> (lesion not detectable)	<b>1</b> (<20% reduction & <10% increase)	<b>1</b> (>10% mass increase)
		<b>5</b> (>20% mass reduction)		

► **Cohort III & IV – RECIST classification of patients**

RECIST	PD	SD	PR	CR	NA*
Central read	2**	1	2	2	2

\* Not measurable / Not radiologically evaluable

\*\* Progressive disease due to appearance of new lesions

PD: Progressive disease (>20% growth)

SD: Stable Disease

PR: Partial Response (>30% shrinkage)

CR: Complete Response (no visible tumour)

*Phase I results presented as late-breaking news at United European Gastroenterology Week*

# BILE DUCT CANCER

## ► The opportunity

### High unmet medical need

- Overall survival of inoperable disease is ~12 months
- Five year survival of inoperable disease is 0%
- Tumour response may be more critical than for other cancers
  - tumours tend to block the bile duct
  - biliary drainage is key for patient treatment and survival

### Promising early signs of efficacy

- Strikingly high (4/7) durable tumour response rate (CR+PR)
- Two CR among seven evaluable pts in highest dose cohorts
- RECIST evaluation confirmed by two independent experts
- Good overall safety and tolerability

**fimaCHEM** for  
bile duct cancer

### Well-defined market

- First-line treatment in a rare disease with limited pipeline
- Approx 3,000 pts in US + Europe eligible for treatment
- Potential upside: metastatic disease & Asia (high incidence)
- Orphan Designation (OD) in EU; US submitted
  - provides development & commercialisation benefits
  - OD drugs have higher probability of success and price

### Proven technology with excellent fit

- First-in-man Phase I study published in Lancet Oncology
- Easy light access through standard endoscopic procedure
- Significantly enhancing the active standard-of-care drug
  - boosting effect where most needed – inside the bile duct
  - potential for local re-treatment

# BILE DUCT CANCER

## ▶ Status and strategy going forward

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- ▶ **Phase I completed with good tolerability and very promising early signs of efficacy**
  - No serious unexpected safety findings and no apparent increase in adverse reactions with increasing doses
  - Very promising early signs of efficacy – significant tumour shrinkage observed radiologically
  - Results verified at central evaluation by study-independent external radiological experts in RECIST
  
- ▶ **Orphan designation**
  - Granted Orphan Drug Designation in EU
  - US application submitted
  
- ▶ **Regulatory interactions with EU and US authorities, to determine fastest way to market**
  - Promising signs of efficacy in a life threatening orphan indication without approved treatment alternatives
  - May allow for marketing authorisation based on restricted data, e.g. a pivotal phase II study
  
- ▶ **Initiated activities to engage US stakeholders**
  - Sponsored and presented at the annual US Cholangiocarcinoma Foundation meeting in Salt Lake City

# IMMUNOTHERAPY

▶ A new hope for millions of patients

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Total estimated  
immunotherapy  
sales of

**\$35bn**

in 2023\*

More than

**100**

projects in  
development\*\*

Combinations with  
**THERAPEUTIC  
VACCINES**  
may enhance CPI<sup>1</sup>  
response rates

- ▶ **fima VACC** enhances cellular immune responses important for therapeutic effects
- ▶ Ready for clinical validation in healthy volunteers
- ▶ Aim is to out-license the technology on non-/semi-exclusive basis
- ▶ Opportunity to develop own therapeutic vaccination products

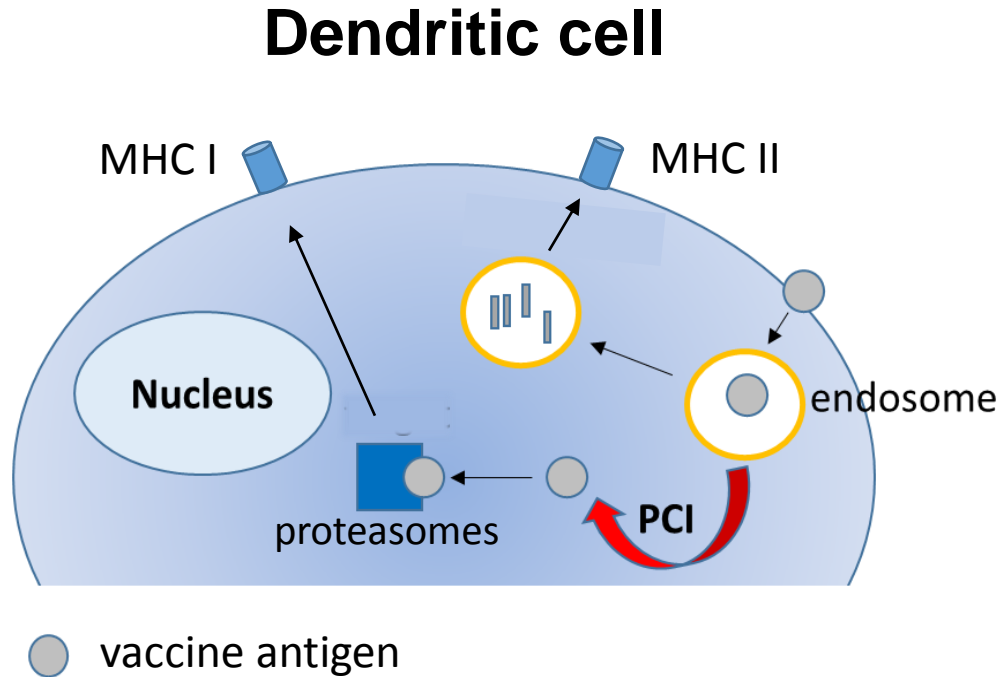
\* Citi Research “Immunotherapy – the beginning of the end for cancer”. Baum, May 2013

\*\* Clinicaltrials.gov. PCIB analysis, August 2016

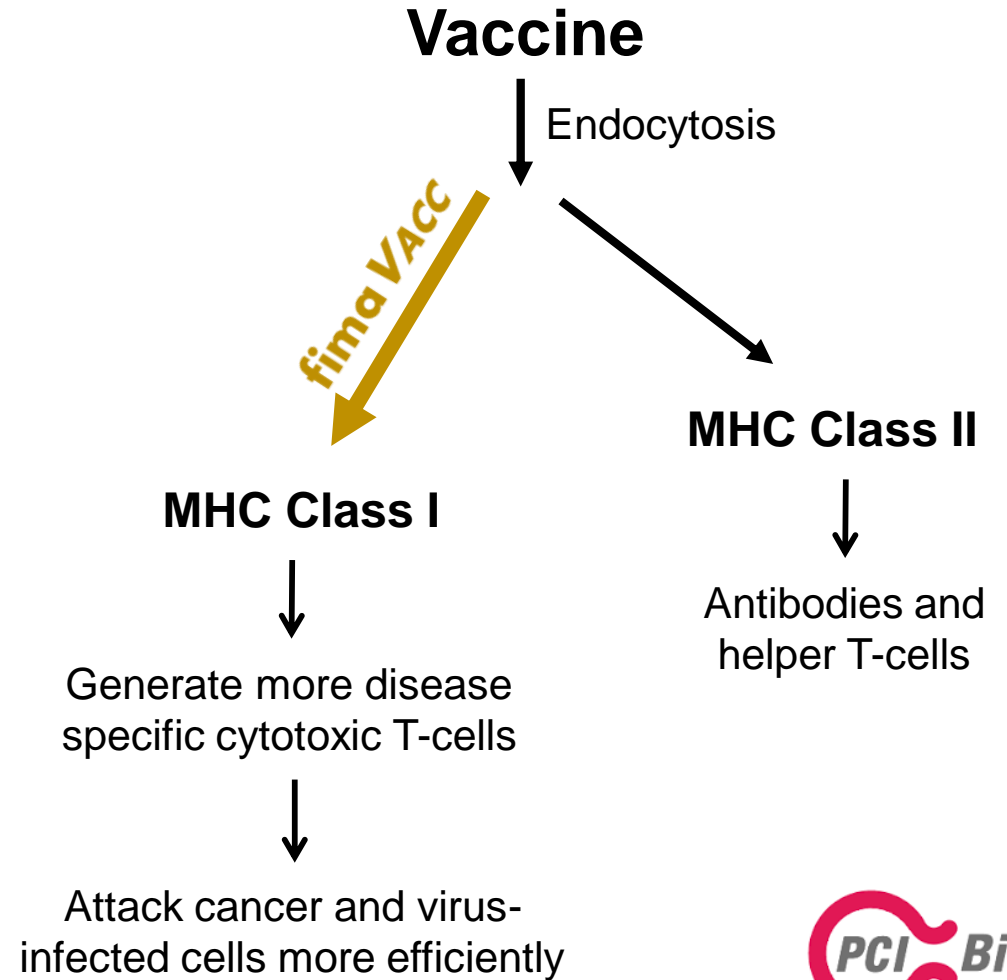
<sup>1</sup>CPI: Checkpoint inhibitors

# PCI TECHNOLOGY

## ► fima VACC – mode of action



Vaccine antigens taken up by dendritic immune cells are released into the cytosol by **fima VACC** treatment. Proteasomes in the cytosol process these to short peptides. The peptides bind to MHC class I proteins that are transported to the cell surface, leading to an enhanced MHC class I presentation of the administered vaccine antigen.



# THE **fima VACC** POTENTIAL

- ▶ Opportunity to play a key role in second generation immunotherapy

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- ▶ Unique mode of action
  - indication of CTL-induction by MHC class I antigen presentation in dendritic cells and macrophages
- ▶ Broad applicability
  - peptide and protein antigens
  - particulate antigen formulations
  - prophylactic & therapeutic vaccination
- ▶ Excellent stability
  - few logistical challenges (stable at room temperature in solution and can be autoclaved)
- ▶ Cost effective synthesis
- ▶ Important recent IP generation



# INITIATED CLINICAL DEVELOPMENT

- ▶ Phase I study in healthy volunteers with read-out of results 1H 2017
- 
- ▶ Covance selected as strategic partner for this clinical validation
    - Phase I unit in Leeds, UK
  - ▶ Objective:
    - Determine the safety, tolerability and immune response of **fima VACC** in healthy subjects
  - ▶ Design:
    - Open-label, antigen-adjuvant controlled study (up to total 80 subjects)
  - ▶ Endpoints:
    - Safety and immunological (induction of vaccine-specific immune responses)
  - ▶ Timelines:
    - First subject dosed September 2016; Read-out of results 1H 2017

*Converting **fima VACC** to a clinical asset – a major milestone towards commercialisation*



# NUCLEIC ACID THERAPEUTICS

- ▶ A treatment modality with huge potential
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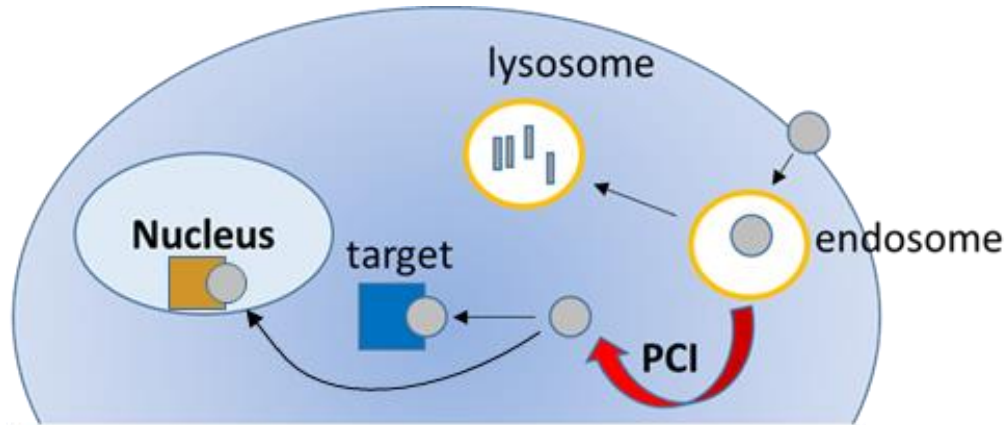


- ▶ **fimaNAC** may provide a delivery solution for many nucleic acid therapy applications
- ▶ Opportunistic collaborative approach
- ▶ Aim is to out-license the technology on non-/semi-exclusive basis

# PCI TECHNOLOGY

► **fimaNAC** – mode of action

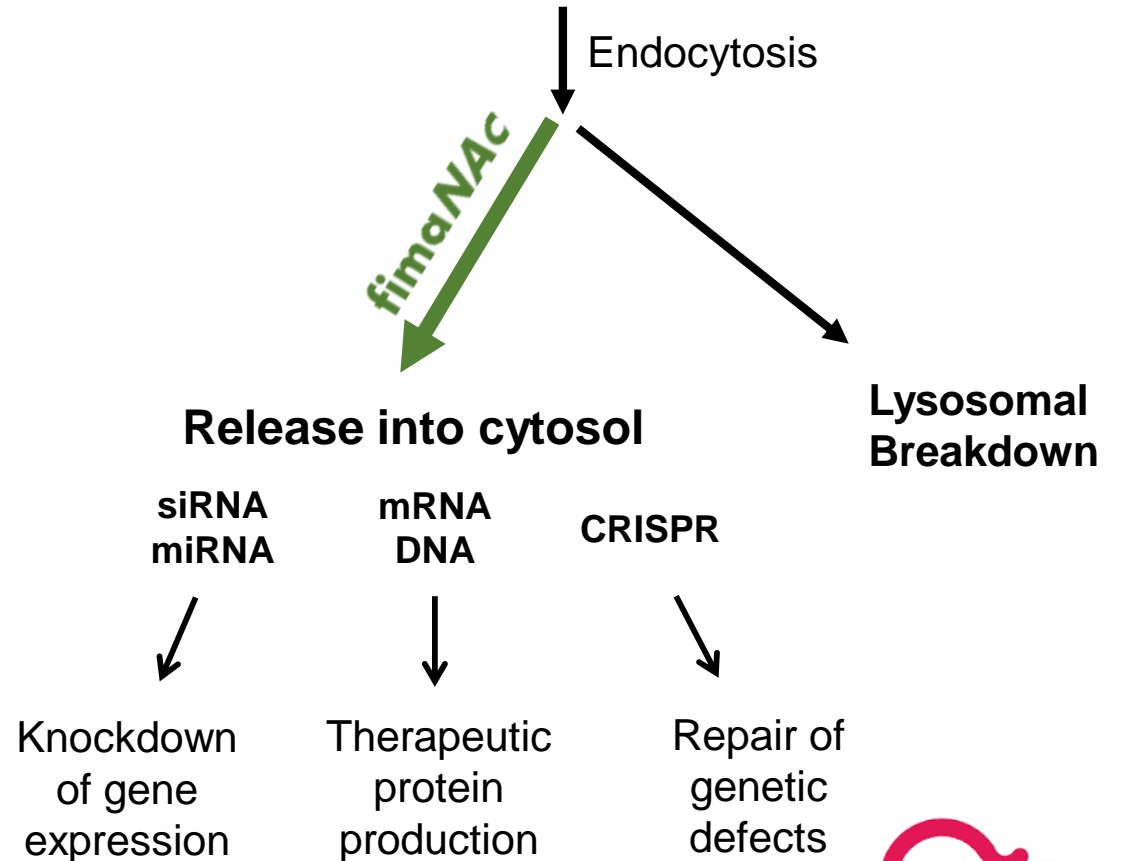
## Target cell



● nucleic acid therapeutic

Nucleic acid therapeutics need to enter into the cell cytosol to exert their therapeutic effect. Being quite large molecules, they cannot readily pass the cell membrane, but are taken up by endocytosis. Treatment of target cells with **fimaNAC** enable release of nucleic acid therapeutics that are trapped in endosomes, allowing them to exert their effect.

## Nucleic Acid Therapeutics



# RESEARCH COLLABORATIONS

► Five active collaborations within nucleic acid therapeutics and vaccination

## fimaNAC



### BioNTech

- Initiated 3Q 2016
- German biotechnology company developing individualised cancer immunotherapies
- Clinical programmes in melanoma, head & neck, breast, ovarian and pancreatic cancer



### RXi Pharmaceuticals

- Initiated 2Q 2015
- Listed on Nasdaq
- Innovative therapeutic siRNA
- Clinical programs in dermatology and ophthalmology



### EtheRNA

- Initiated 4Q 2016
- A global leader in mRNA-based immunotherapies
- Evaluate synergistic effects between companies' technologies

### Top-10 large pharma

- Initiated 3Q 2015
- A global leader in nucleic acid therapeutics
- Collaborative research funded by partner
- Evaluate synergistic effects between companies' technologies

## fimaVACC



### Ultimovacs

- Initiated 1Q 2016
- Norwegian immunotherapy company
- Therapeutic cancer vaccine against human telomerase
- Clinical programs in prostate and lung cancer

Research collaborations aim to evaluate synergies between the fima platform and partner technologies, with the potential for further partnerships

# FINANCE

## ► Key financial figures Q4 and preliminary full year 2016

<i>(In NOK 1,000)</i>	<b>2016 Q4</b>	<b>2016 FY</b>	<b>2015 FY</b>
Other Income	3 226	10 475	10 467
Operating costs	10 129	43 502	43 096
Operating results	-6 903	-33 027	-32 629
Financial items	301	843	707
<b>Comprehensive income</b>	<b>-6 602</b>	<b>-32 184</b>	<b>-31 922</b>
<b>Cash &amp; cash equivalents</b>	<b>14 002</b>	<b>14 002</b>	<b>49 249</b>
<b>Net cash flow from operating activities</b>	<b>-6 661</b>	<b>-35 247</b>	<b>-31 974</b>

- More than NOK 10 million in annual non-dilutive funding last two years
- The fully underwritten rights issue gives a financial runway towards end of 2018, at current cost base

# FINANCE

- ▶ Fully underwritten rights issue completed in January 2017
- ▶ Net proceeds of NOK 65 million
- ▶ More than 100% oversubscription
- ▶ Shareholder base doubled since year-end 2015 to approximately 2.900 shareholders

## Top 10 shareholders per 15 Feb 2017

<b>Name</b>	<b>Number</b>	<b>%</b>
FONDSAVANSE AS	2 540 840	10,20
RADIUMHOSPITALET'S FORSKNINGSSSTIFTELSE	1 761 273	7,07
MP PENSJON PK	1 544 504	6,20
NORDNET LIVSFORSIKRING	759 372	3,05
GRESSLIEN ODD ROAR	540 000	2,17
VICAMA AS	500 000	2,01
NORDNET BANK AB	443 977	1,78
SYVERTSEN SVEIN ERIK	437 107	1,76
MYRLID AS	413 572	1,66
VINTERSTUA AS	400 000	1,61
Total 10 largest shareholders	9 340 645	37,51
Total other shareholders	15 559 745	62,49
Total number of shares	24 900 390	100,00

# PCI BIOTECH

- ▶ Well positioned for attractive development opportunities
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## Main focus going forward:

- ▶ Progressing development of **fimaCHEM** in bile duct cancer
  - Regulatory interactions to determine fastest way to market
  - Prepare for Phase II study
- ▶ Clinical validation of **fimaVACC** immunotherapy results
  - Expected to provide read-out of results 1H 2017
- ▶ Partnering and alliance progress for all programmes

# PCI BIOTECH HOLDING ASA

## ► Enquiries

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