



# PCI BIOTECH

Unlocking the potential of innovative medicines

## Bio€quity Europe 2017

23 May, 2017

Per Walday, CEO



# PCI BIOTECH

## ► Important notice and disclaimer

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# PCI BIOTECH AT A GLANCE

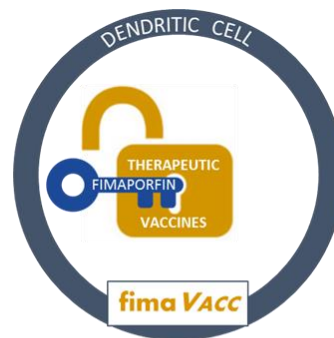
## ▶ Unlocking the potential of innovative medicines

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

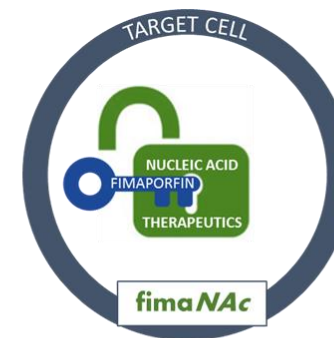
### ***PCI – the solution to a key challenge for several modalities***



Enabling approved drugs to fulfil unmet local treatment need



Enhancing cellular immune responses important for therapeutic effect

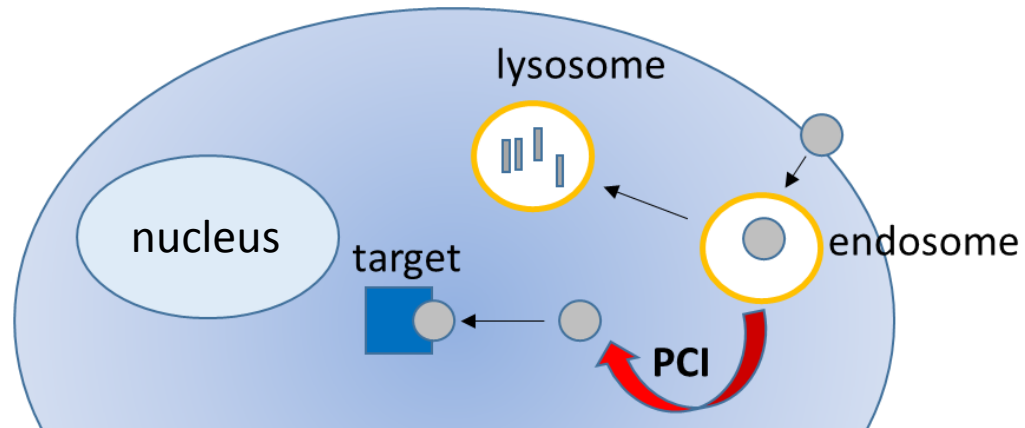


Providing a delivery solution for nucleic acid therapeutics

# PCI TECHNOLOGY

▶ Enabling drugs to reach intracellular therapeutic targets

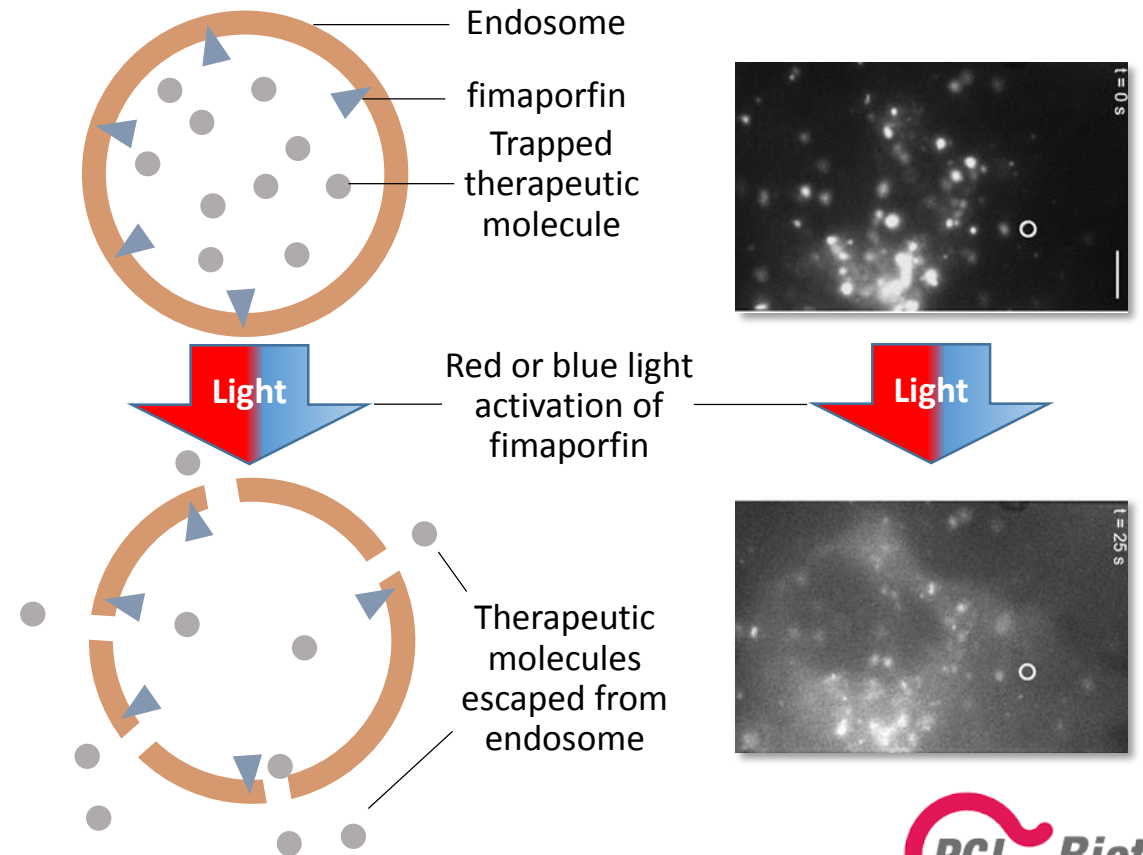
## CELL SYSTEM



● therapeutic molecule

- ▶ Small molecules (chemotherapeutics – **fimaCHEM**)
- ▶ Antigens (peptides/proteins – **fimaVACC**)
- ▶ Oligonucleotides (mRNA, RNAi – **fimaNAc**)

## TRIGGERED ENDOSOMAL RELEASE



# 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

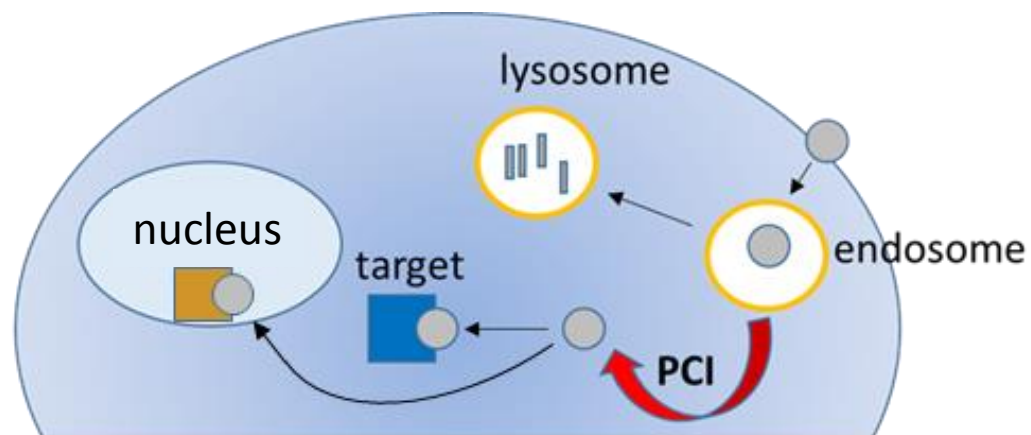
- ▶ **fima *CHEM*** may enable approved drugs to fulfil unmet local treatment needs
- ▶ First-in-man study published in *Lancet Oncology*\*, with independent expert commentary
- ▶ Completed Phase I in bile duct cancer with promising early signs of efficacy
- ▶ Opportunity for development in further niche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

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

# PCI TECHNOLOGY

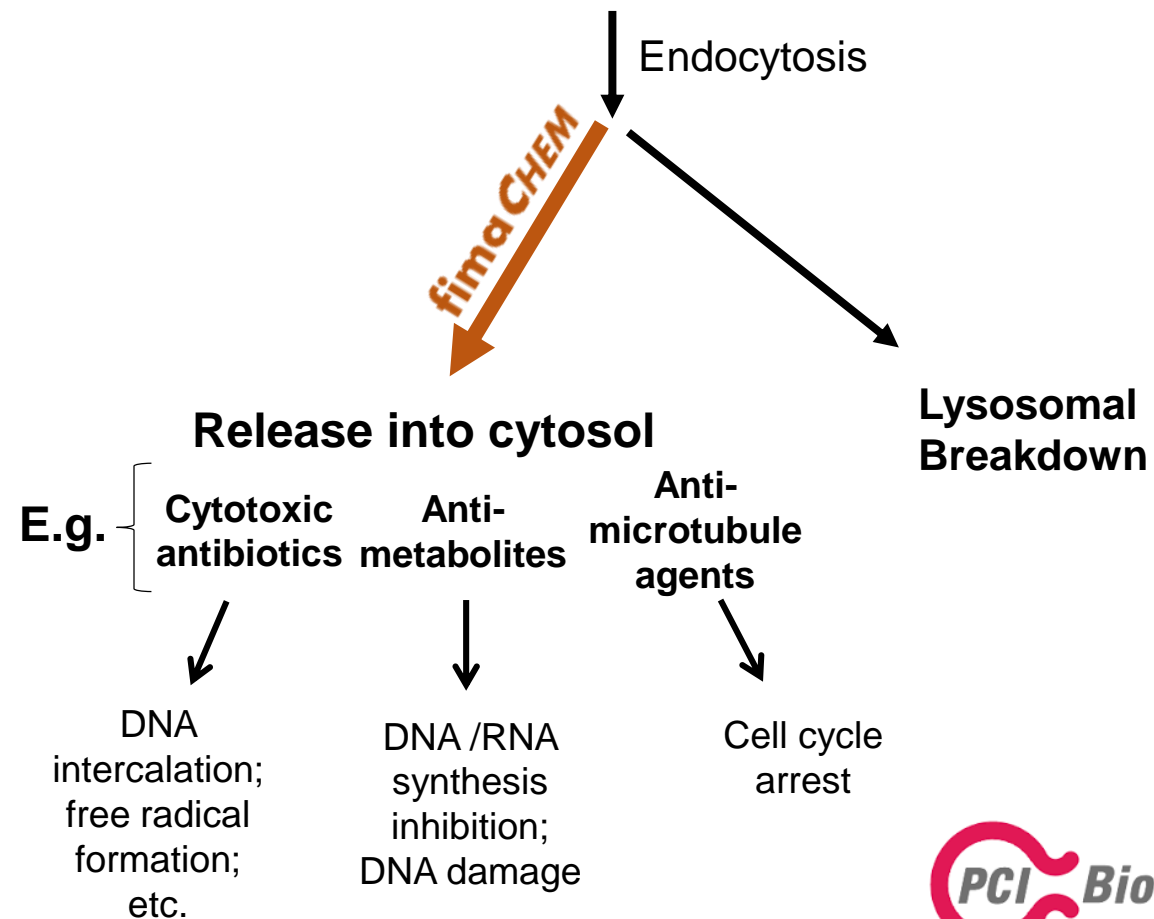
► **fimaCHEM** – mode of action

## Cancer cell



● chemotherapy

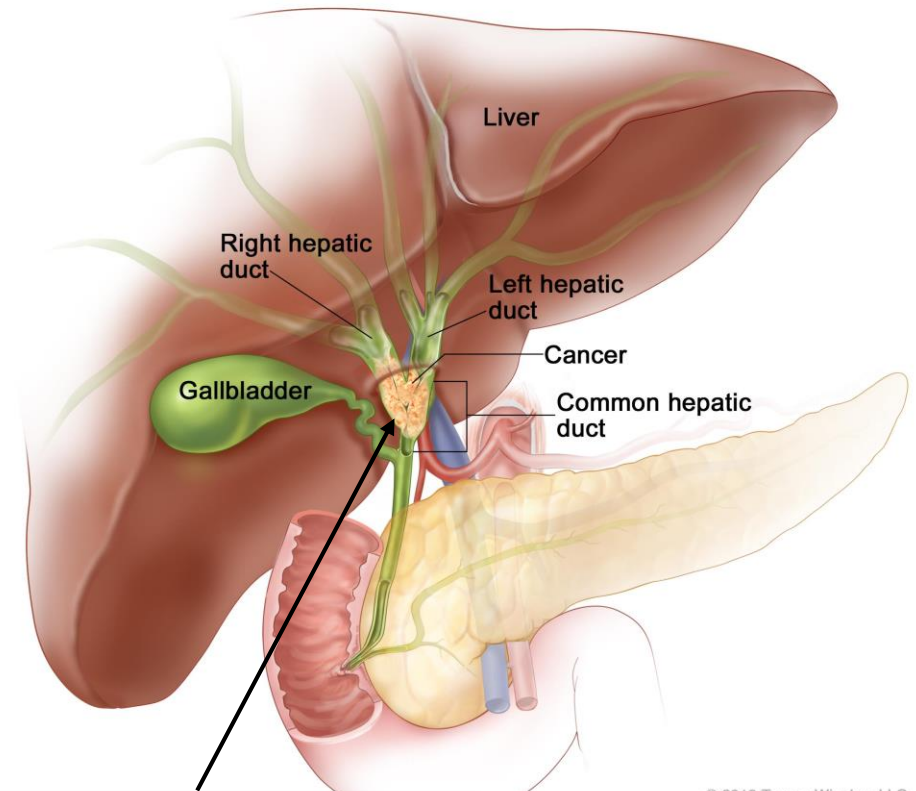
## Chemotherapeutics



# 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

## ▶ The unmet need

- ▶ Rare disease, 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

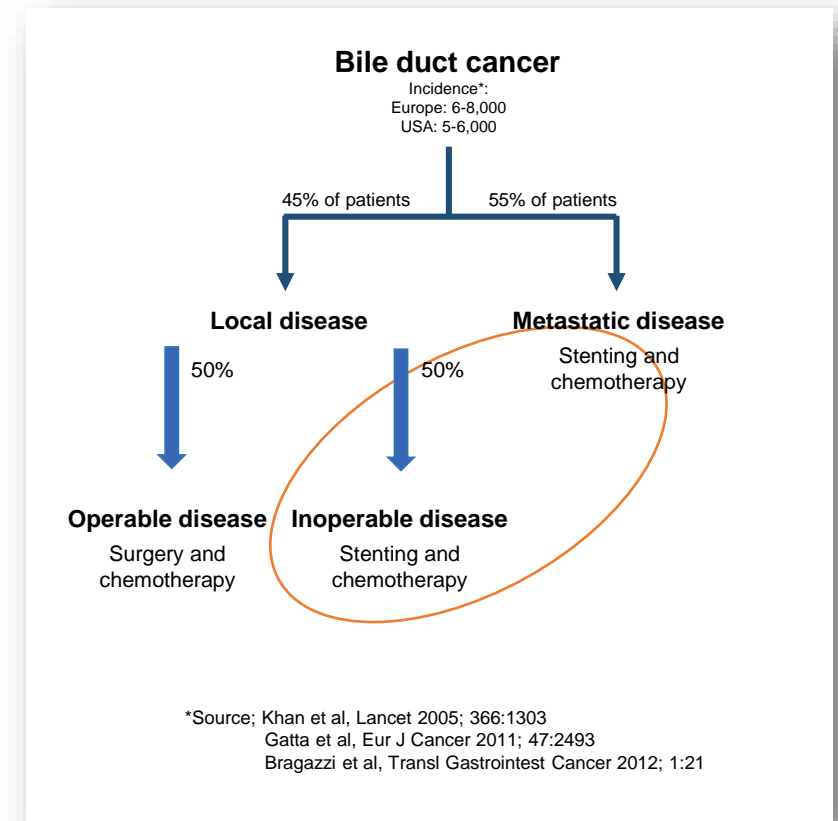
- Incidence is close to 15,000 across Europe and the US
- Immediate target is inoperable patients with primary hilar disease
- Approximately 3,000 assumed to be eligible for **fimaCHEM**
- Possible upside in distal and more advanced metastatic disease
- Higher incidences in Asia

### ▶ Attractive price potential

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

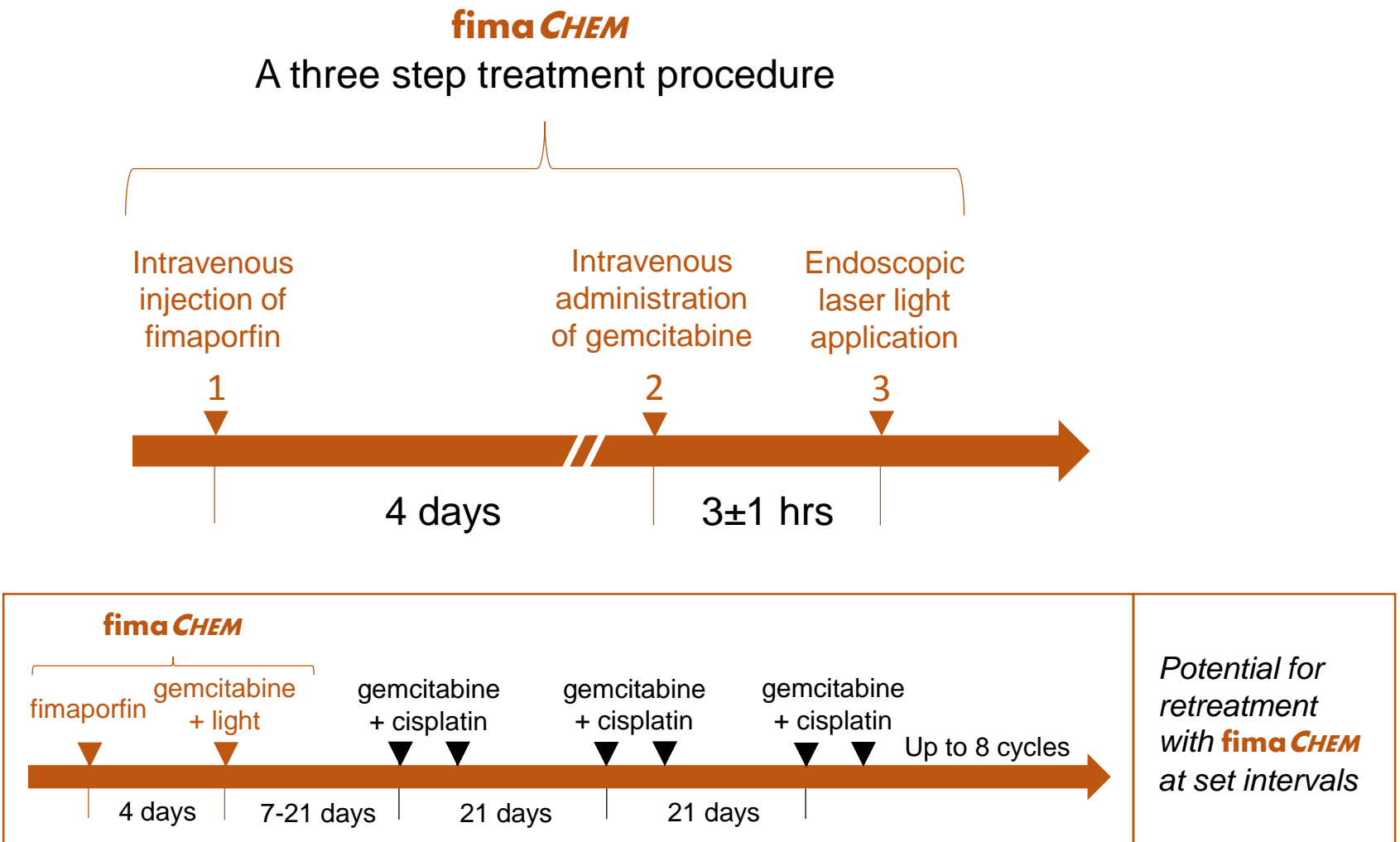
### ▶ Potential significant majority share of the market

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



# BILE DUCT CANCER

► A proven technology with excellent fit to standard procedures



# BILE DUCT CANCER – CLINICAL PHASE I/II STUDY

► Early promising signs of durable response in Phase I

► 6 months radiology data from all dose cohorts – local read

RECIST*	PD	SD	PR	CR	NA**
Cohort IV***	1		2	1	2
Cohort III		1	1	1	1
Cohort II		1			2
Cohort I	1	1			1

PD: Progressive disease  
(>20% growth)

SD: Stable Disease

PR: Partial Response  
(>30% shrinkage)

CR: Complete Response  
(no visible tumour)

\* Response Evaluation Criteria In Solid Tumours (rules defining when cancer patients improve, stay the same or worsen during treatments)

\*\* Not measurable / Not radiologically evaluable

\*\*\* Cohort IV expanded; Four radiologically evaluable patients at 6 months

- The last patient in the Phase I study received **fimaCHEM** treatment March 2016
- Subjects are in the study for 6 months after PCI treatment and thereafter followed for survival only
- Average overall survival by end March 2017 was 14,5 months, with 25% of patients still being alive
- Commissioned central independent radiological expert RECIST evaluation of Cohort III & IV, as this is an expected regulatory requirement

# BILE DUCT CANCER – CLINICAL PHASE I/II STUDY

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

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

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

PD: Progressive disease  
(>20% growth)

SD: Stable Disease

PR: Partial Response  
(>30% shrinkage)

CR: Complete Response  
(no visible tumour)

\* Not measurable / Not radiologically evaluable

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

## ► 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)		

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

# 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
  - Encouraging emerging survival data
  - A Phase I extension is about to be initiated, to determine safety of repeated treatments
  
- **Orphan designation**
  - Granted Orphan Drug Designation in EU
  - Open IND in US – Orphan Drug 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

# 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\*\*\*  
response rates

- ▶ **fima VACC** enhances cellular immune responses important for therapeutic effects
- ▶ Ongoing Phase I study in healthy volunteers for clinical validation
- ▶ 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

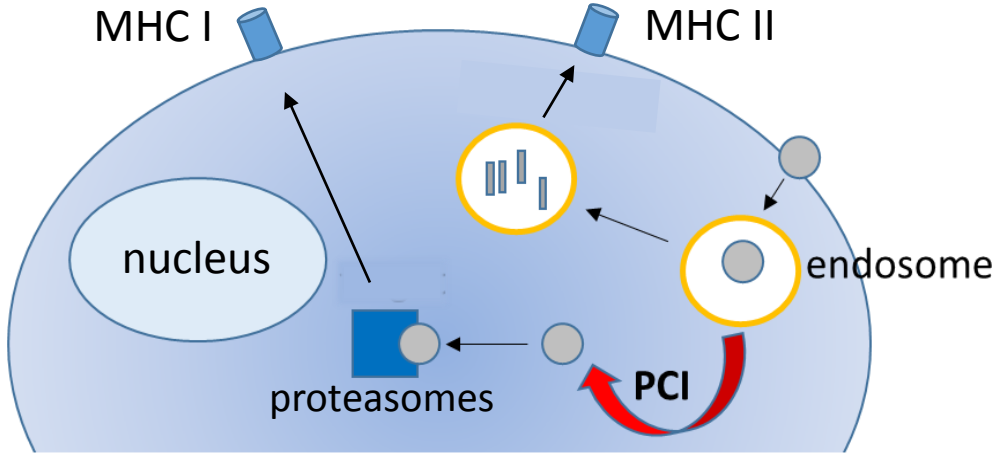
\*\* Clinicaltrials.gov. Therapeutic cancer vaccines, PCIB analysis, August 2016

\*\*\* CPI: Checkpoint inhibitors

# PCI TECHNOLOGY

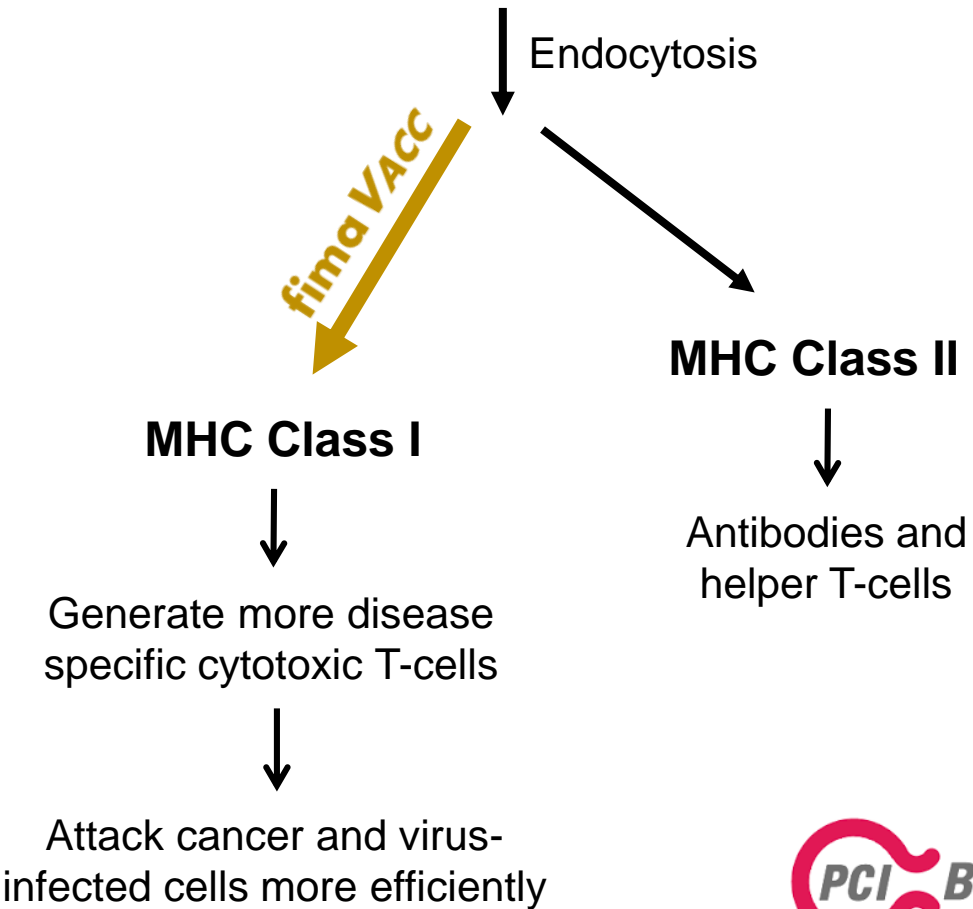
► **fima VACC** – mode of action

## Dendritic cell



● vaccine antigen

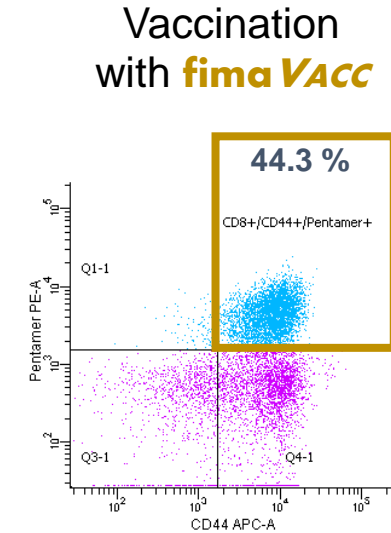
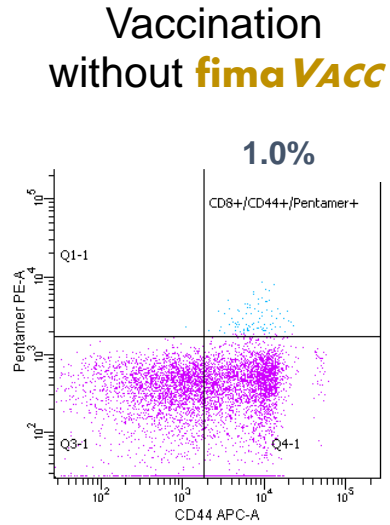
## Vaccine



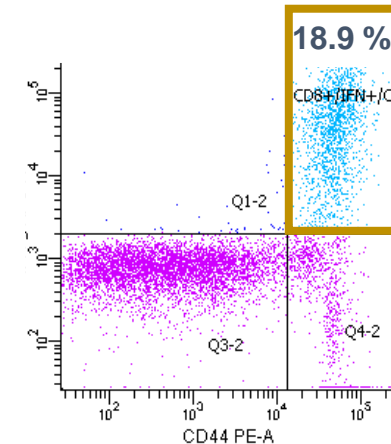
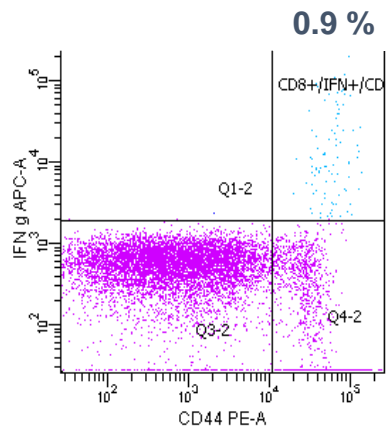
# fima VACC STRONGLY ENHANCES VACCINATION EFFECTS

► Impressive effects with clinically relevant HPV therapeutic vaccine in mice

Amount of activated antigen-specific CD8 T-cells in blood



Amount of activated antigen-specific CD8 T-cells in spleen



## Cytotoxic (CD8) T-cells

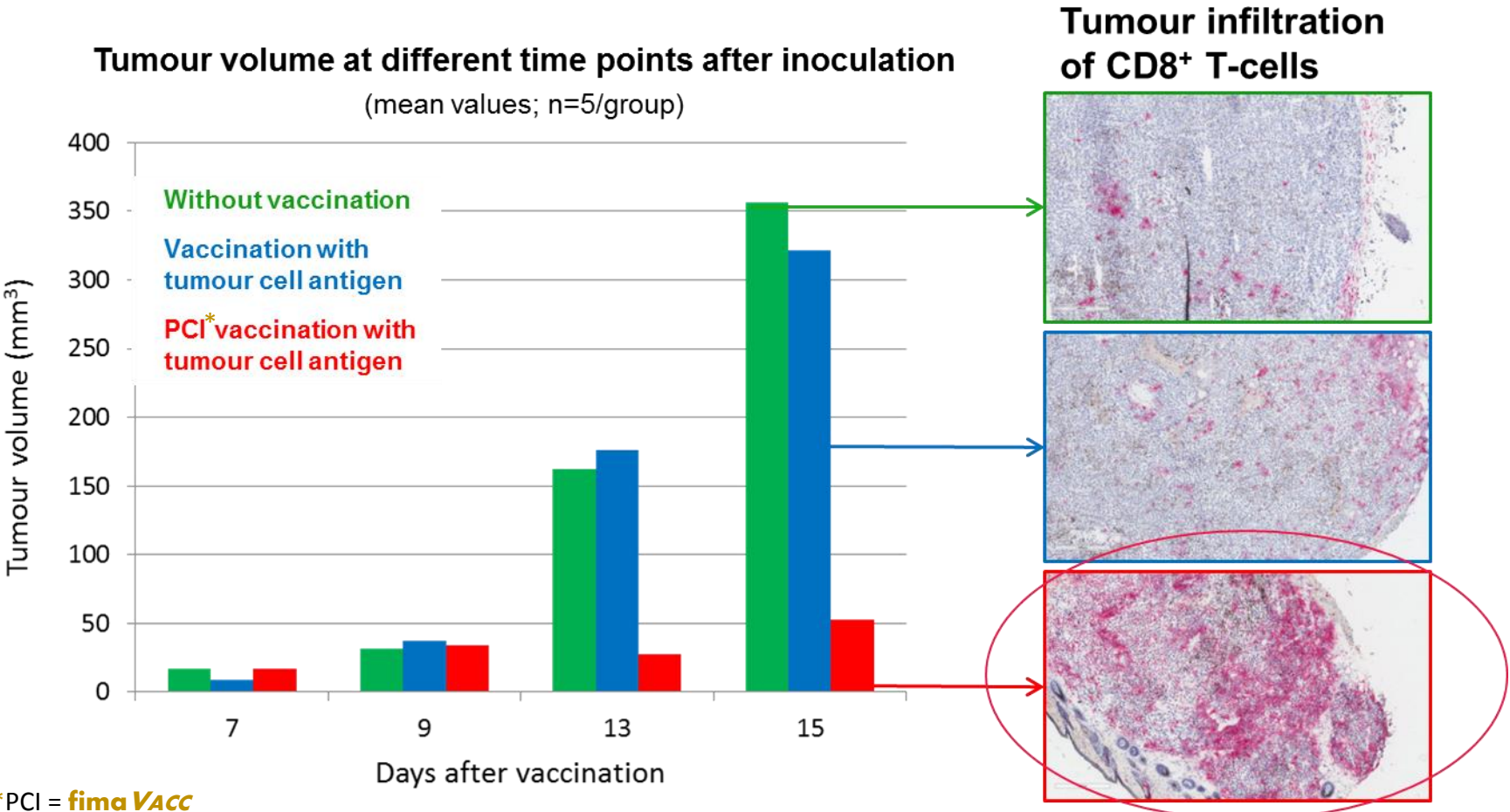
- Most important immune cells to fight tumours
- Difficult to induce with vaccination
- **fima VACC** strongly enhances the ability of vaccines to induce CD8 T-cells:
  - >20 and >40 times enhancement seen in spleen and blood cells, respectively
  - Generation of immunological memory



# THERAPEUTIC VACCINATION IN TUMOUR MODEL

► **fima VACC** induces cytotoxic T-cells that infiltrate tumours

Therapeutic **fima VACC** vaccination with OVA in animal tumour model (B16-OVA melanoma/OT-1)



# THERAPEUTIC VACCINATION WITH **fima VACC**

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



*Patented disposable “band-aid-like” device for user-friendly illumination of the vaccination site*

- ▶ Unique mode of action
  - induction of antigen specific cytotoxic T-cells by MHC class I antigen presentation in dendritic cells
- ▶ Ease of use
  - fimaporfin mixed with vaccine
  - intradermal vaccination
- ▶ Broad applicability
  - peptide and protein antigens
  - particulate antigen formulations
  - prophylactic & therapeutic vaccination
- ▶ Excellent stability and cost effective synthesis
- ▶ Phase I study in healthy volunteers ongoing
  - first results read-out 2Q 2017

# NUCLEIC ACID THERAPEUTICS

- ▶ A treatment modality with huge potential
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Estimated sales of  
**USD 18bn**  
in 2030\*  
(RNAi alone)

mRNA is a hot  
new field with  
**HIGH DEAL  
ACTIVITY**

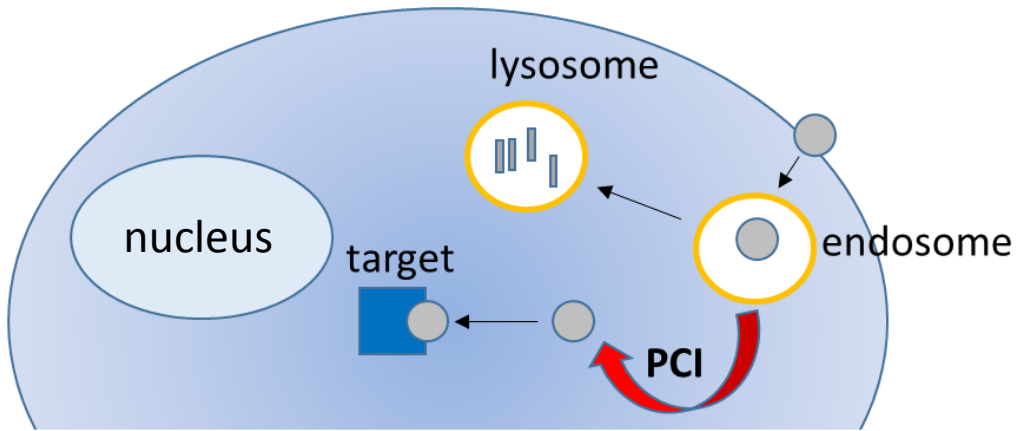
Main  
**HURDLE IS  
DELIVERY**  
into cells

- ▶ **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

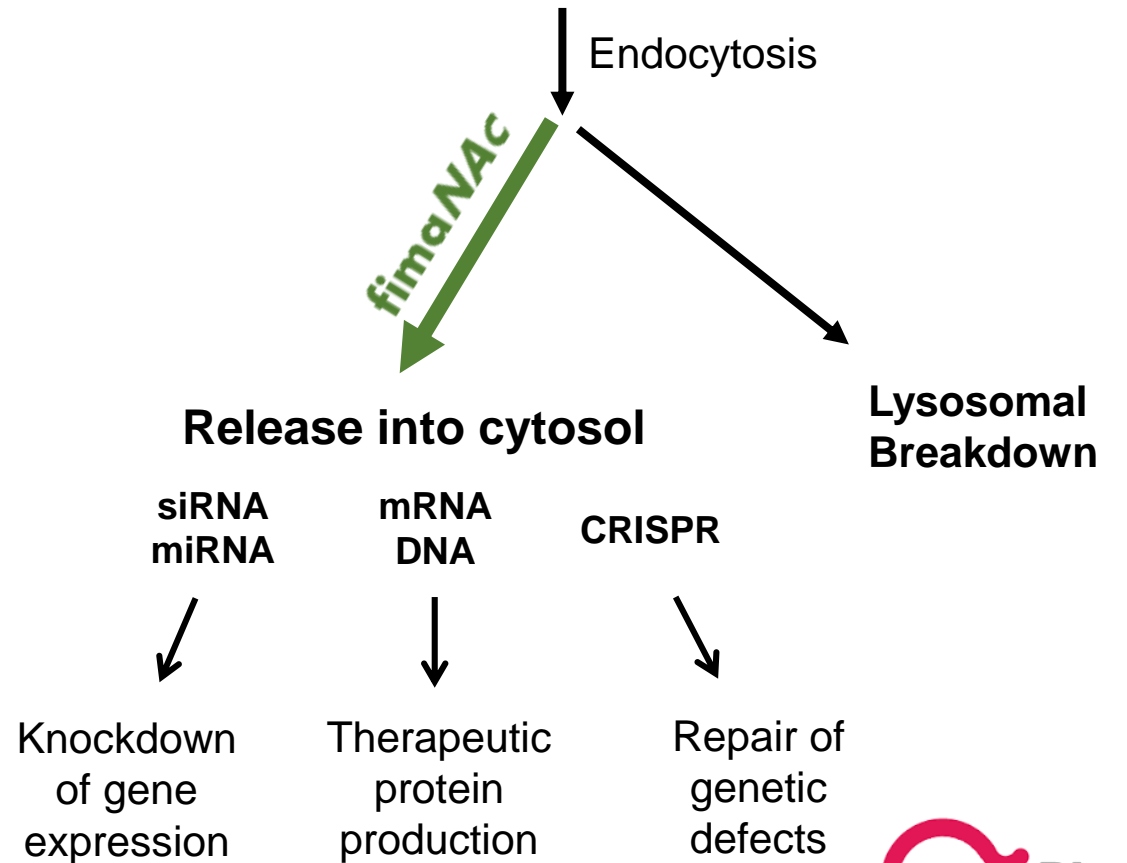
► **fimaNAC** – mode of action

## Target cell



● nucleic acid therapeutic

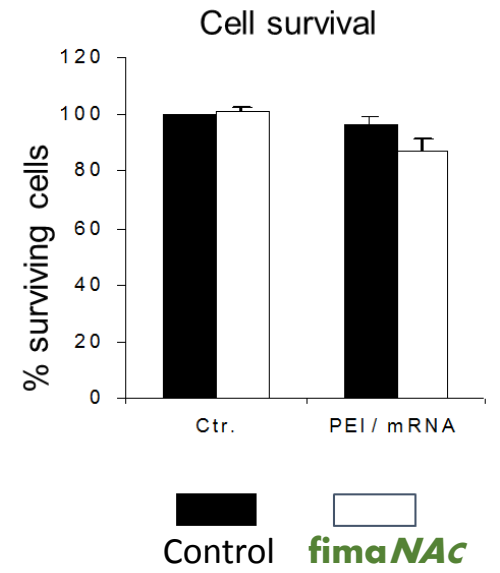
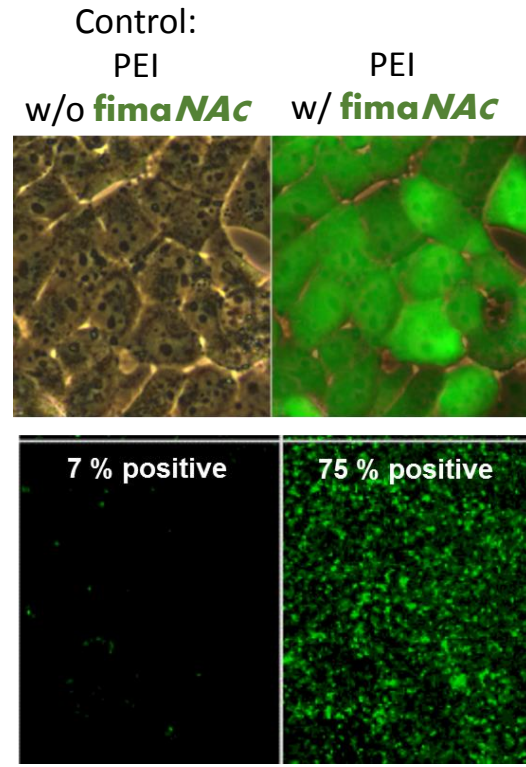
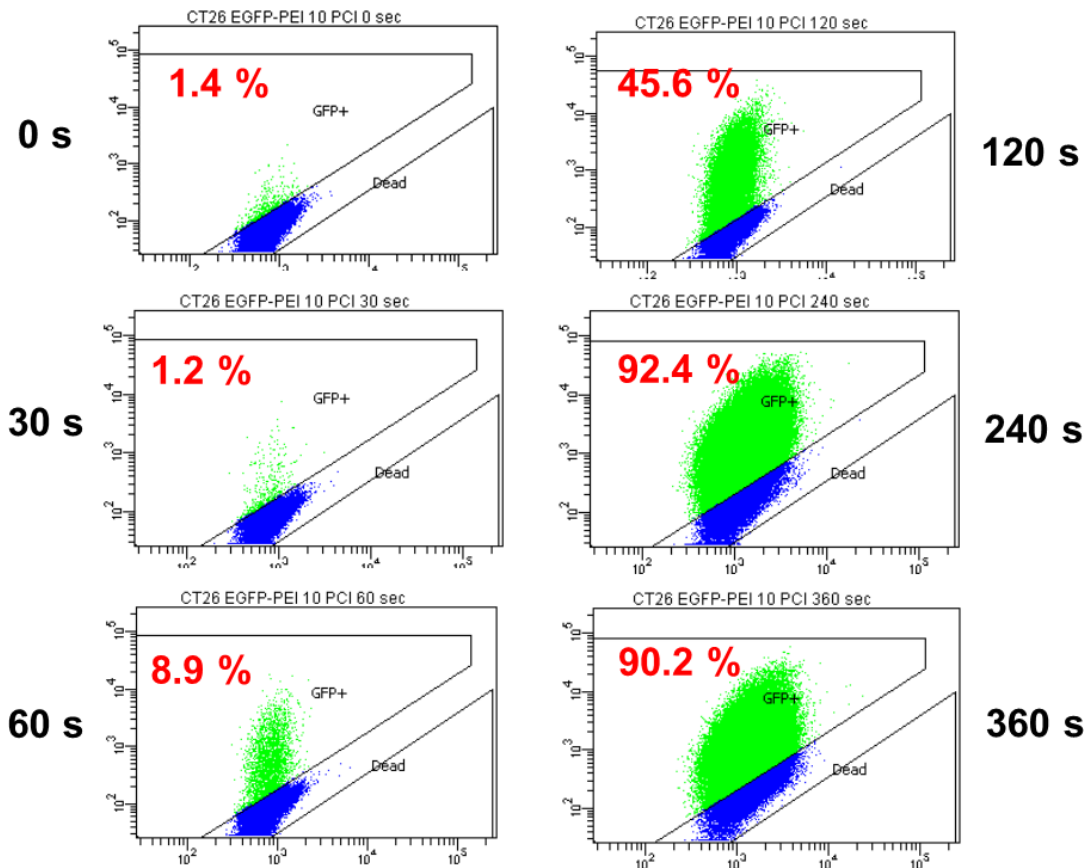
## Nucleic Acid Therapeutics



# ENHANCING MRNA DELIVERY

► Strongly increased GFP synthesis with increasing light doses

fimaNAC with polyethylenimine (PEI) vehicle



## VERSATILITY OF fimaNAc

► Delivery of many types of nucleic acid with many different vehicles *in vitro*

- **Main bottleneck in the field is delivery**
- **fimaNAc** can deliver many types nucleic acids
- Enhancement by **fimaNAc** is best under conditions favourable for vehicle safety
  - Low ratio of vehicle to nucleic acid
  - Low concentration of vehicle/nucleic acid complex
- Especially advantageous *in vivo*
  - Difficult to achieve a high concentration of vehicle/nucleic acid complex in target cells
  - Toxicity may limit the amount of vehicle used

### Nucleic acids successfully delivered by fimaNAc

Type of nucleic acid	Delivery vehicle
Plasmids	PEI, cationic peptides, cationic lipids, polylysine ++ Targeting to EGF-R, transferrin-R
siRNA	PEI, cationic peptides, dendrimers, lipofectamine, DOTAP, nanogels, chitosan ++
PNA (peptide nucleic acids)	None, cationic amino acids attached
mRNA	PEI, Protamine
Adenoviral vectors	None, cationic polymers
AAV vector	None

*Opportunistic approach – pursuing collaboration and partnering opportunities*

# RESEARCH COLLABORATIONS

- ▶ Four active collaborations within nucleic acid therapeutics

## fimaNAC

### RXi Pharmaceuticals



- Initiated 2Q 2015
- Listed on Nasdaq
- Innovative therapeutic siRNA
- Clinical programmes in dermatology and ophthalmology
- New focus on immuno-oncology after MirImmune acquisition

### 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

### BioNTech



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

### eTheRNA












- Initiated 4Q 2016
- Belgian immunotherapy company
- Proprietary TriMix platform programming dendritic cells with synthetic mRNA
- Clinical programmes in melanoma and triple negative breast cancer

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

# DEVELOPMENT PIPELINE

► Unlocking the true potential of innovative medicines

Programme	Therapeutic agents	Preclinical	Phase I	Phase II	Status
 <b>fima</b> <i>CHEM</i>	 <i>Chemotherapeutics</i>				Phase I in the orphan indication bile duct cancer completed with promising early signs of efficacy
 <b>fima</b> <i>VACC</i>	 <i>Therapeutic cancer vaccines</i>				Phase I study ongoing One active R&D collaboration
 <b>fima</b> <i>NAC</i>	 <i>Nucleic acid therapeutics</i>				Four active R&D collaborations

*An oncology focused company with three well differentiated assets*



# PCI BIOTECH

► Unlocking the potential of innovative medicines

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