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PCI BIOTECH

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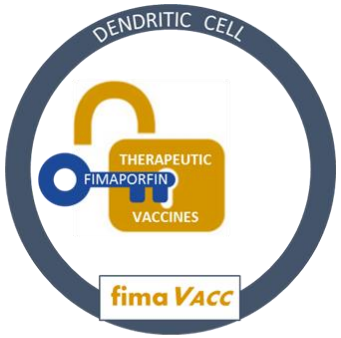
PCI BIOTECH AT A GLANCE

► Unlocking the potential of innovative medicines

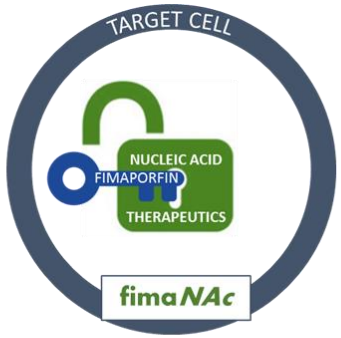
- A listed (PCIB:NO) cancer-focused biotech company
- Photochemical internalisation ("PCI") technology, originating from the Norwegian Radium Hospital
- Clinical programmes
  - **fima CHEM** – fimaporfin (Amphinex®) for the orphan indication inoperable bile duct cancer, Phase I completed
  - **fima VACC** – Vaccination technology that provides strongly enhanced cellular immune responses, Phase I initiated
- Pre-clinical programme
  - **fima NAc** – 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

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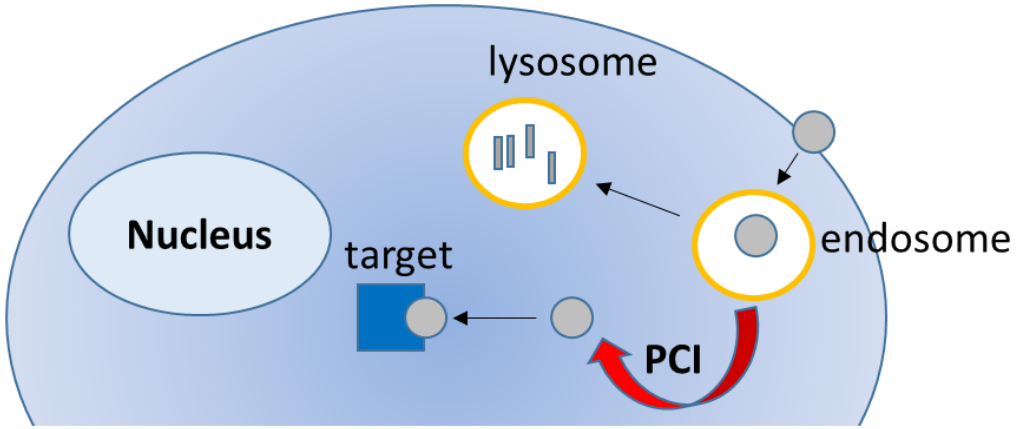
PCI TECHNOLOGY

- Enabling drugs to reach intracellular therapeutic targets

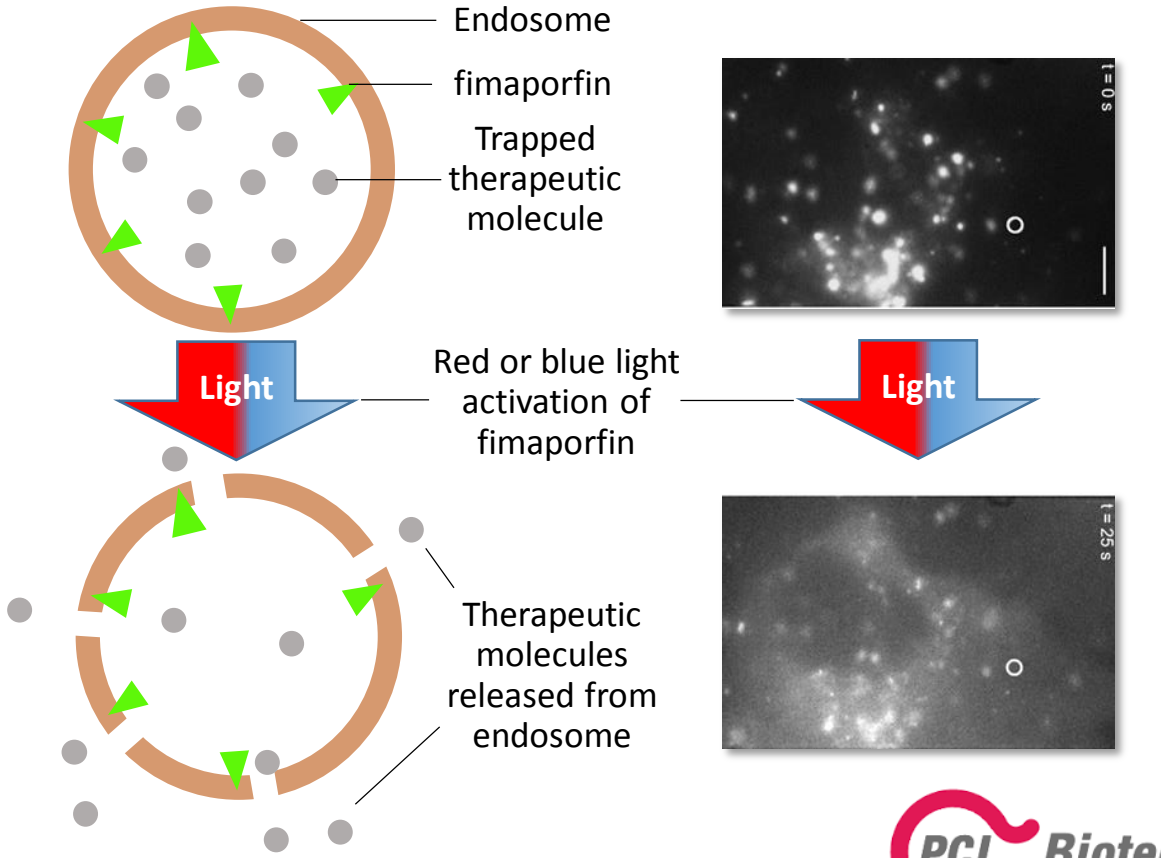
CELL SYSTEM



therapeutic molecule

- Small molecules (chemotherapeutics – fima*CHEM*)
- Antigens (peptides/proteins – fima*VACC*)
- Oligonucleotides (mRNA, RNAi - fima*NAC*)

TRIGGERED ENDOSOMAL RELEASE



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CHEMOTHERAPEUTICS

- A cornerstone in current cancer therapy

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

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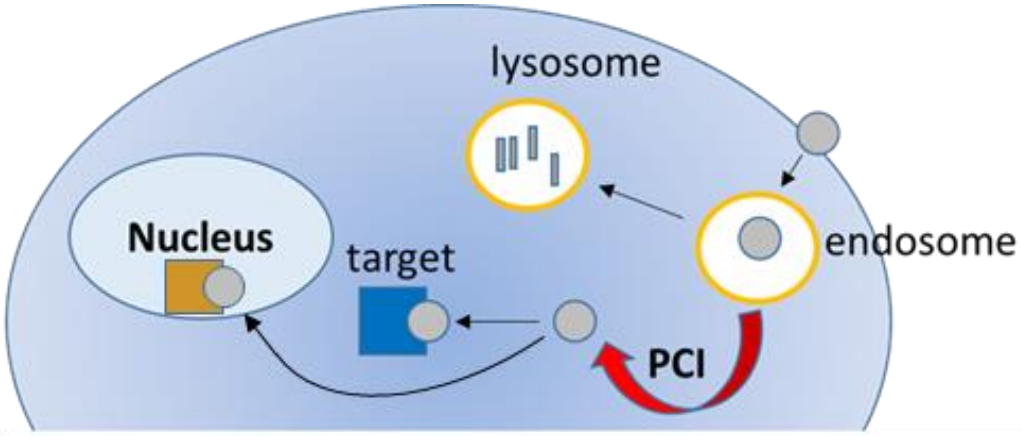
PCI TECHNOLOGY

▶ fimaCHEM – mode of action

Cancer cell

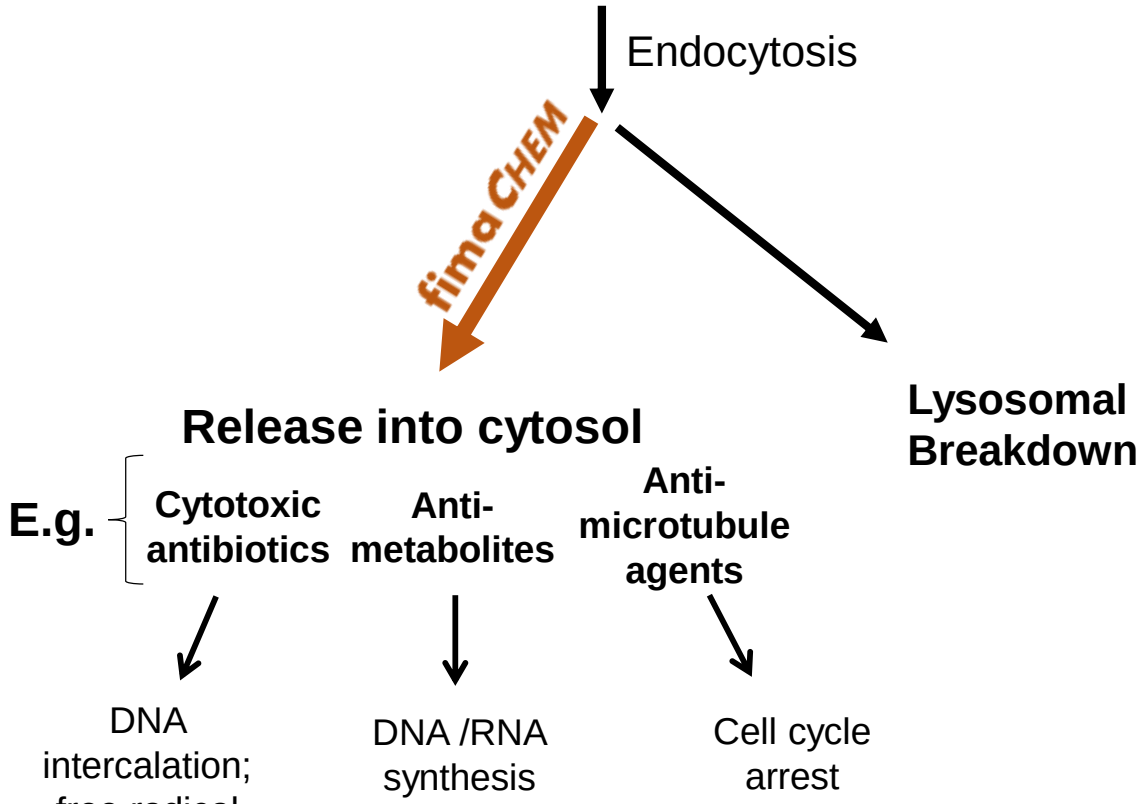


chemotherapeutic

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



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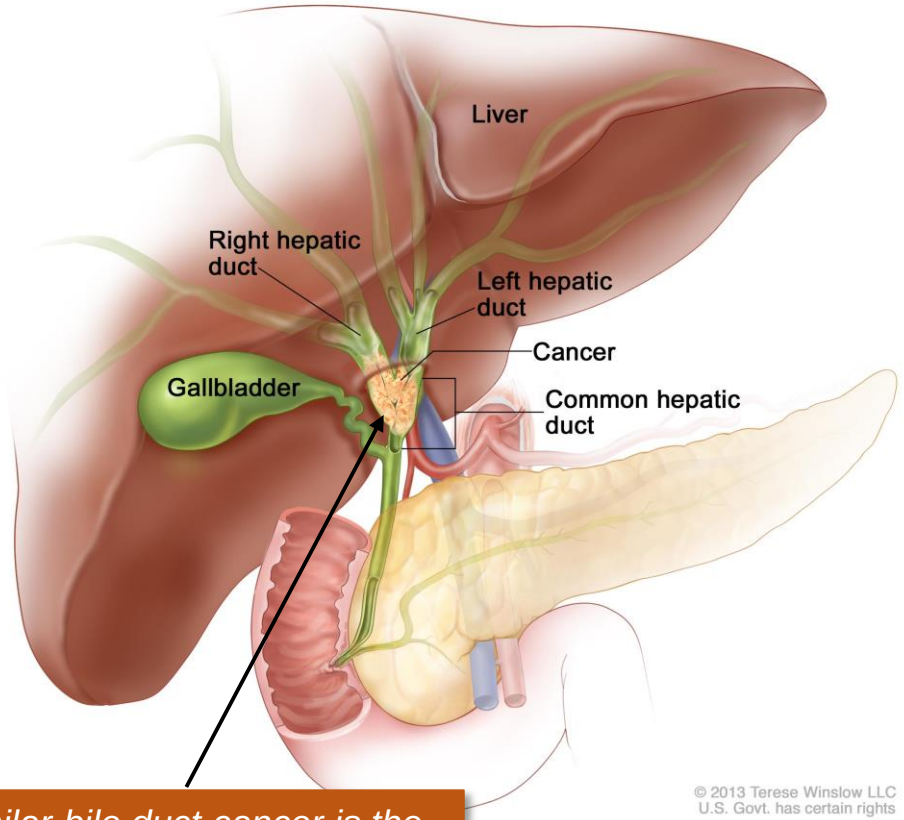
BILE DUCT CANCER

► 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

* Bile duct cancer, Am Cancer Soc, 10/30/2013

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 0% when inoperable – average approx. 12 months survival
- Current management
  - Surgery
    - Only potentially curative treatment
    - Less than ⅓ 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

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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	
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

- Subjects are in the study for 6 months after PCI treatment
- After 6 months patients are followed for survival only
- Commissioned central independent radiological expert evaluation of Cohort III & IV, as this is an expected requirement from regulatory authorities

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BILE DUCT CANCER – CLINICAL PHASE I/II STUDY

- Early promising signs of durable response verified by independent expert evaluation

- **6 months radiology data: Cohort III & IV – local vs. central**

RECIST	PD	SD	PR	CR	NA
Local	1	1	3	2	2
Central	2	1	2	2	2

- Central radiological RECIST evaluation of all patient images from Cohort III and IV
- All images evaluated by two study-independent radiologists with expertise in RECIST and bile duct cancer
- Tumour response verified at central evaluation
  - Progressive disease due to appearance of new lesions (one missed at local read)
- **More than 50% response rate** – far above expected with standard treatment

BILE DUCT CANCER – CLINICAL PHASE I/II STUDY

- Convincing response at target tumour level

- **6 months radiology data: Cohort III & IV – response at single lesion level**

Measurable lesions	Lesion shrinkage		Stable lesion	Lesion growth
19 (total number of targets selected across the two independent readers)	**17**	**12** (lesion undetectable)	**1** (<20% reduction & <10% increase)	**1** (>10% mass increase)
		5 (>20% mass reduction)		

- Independent radiological evaluation of all patient images from Cohort III and IV
- All images evaluated separately by two radiology experts
- **Shrinkage of almost 90% of selected target lesions, with more than 60% being undetectable at 6 months**
- "*Change in tumor size by RECIST correlates linearly with overall survival in Phase I oncology studies*" [1]

[2] ***"Maintenance of biliary drainage is critical in patients with advanced biliary cancer… …response in tumor bulk may therefore have a greater effect on survival than would be the case for other cancers."***

[1] Jain et al 2012 – JCO 30:2684-90 (analysis of 24 phase I studies)
[2] Valle et al 2010 – NEJM 362:1273-81 (landmark publication for cis-gem treatment in bile duct cancer)

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BILE DUCT CANCER

▶ Status and strategy going forward

- **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

- **fima VACC** enhances cellular immune responses important for therapeutic effects
- Initiated 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

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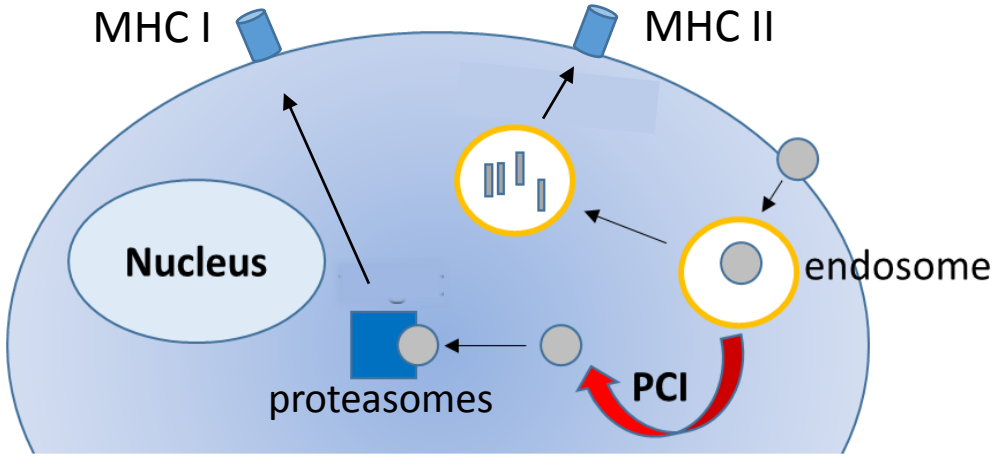
PCI TECHNOLOGY

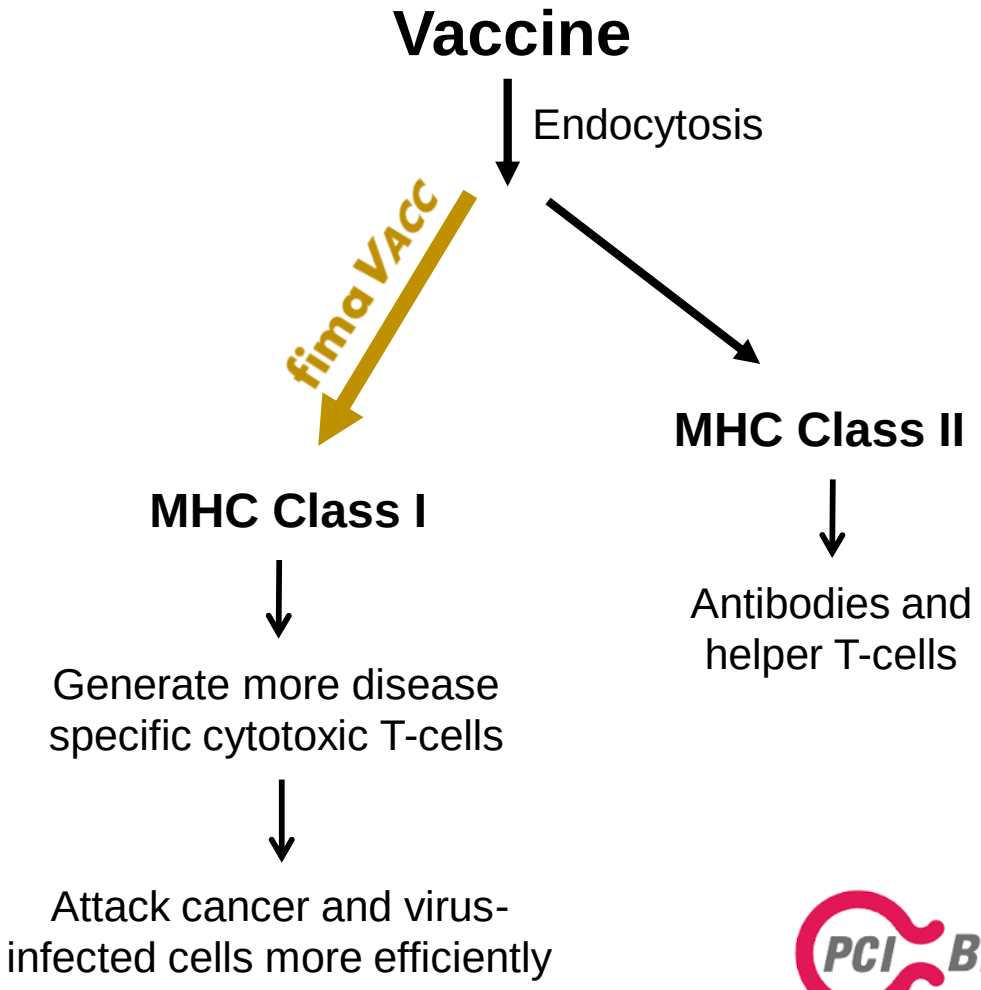
▶ fima VACC – mode of action

Dendritic cell



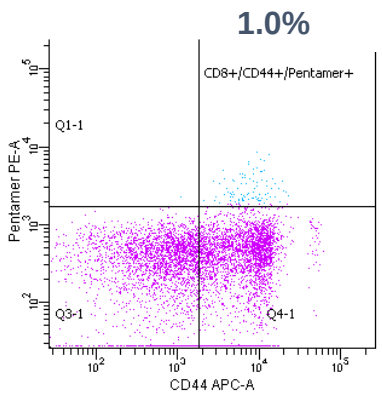
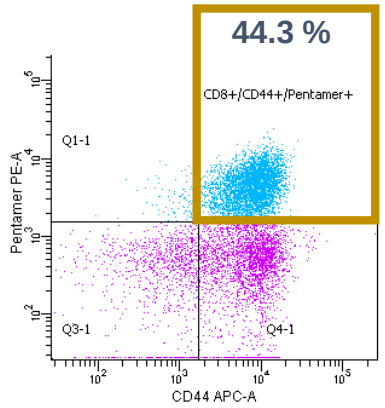
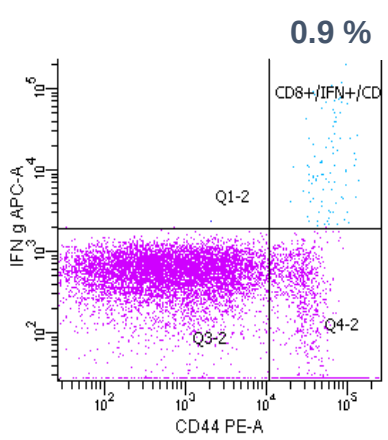
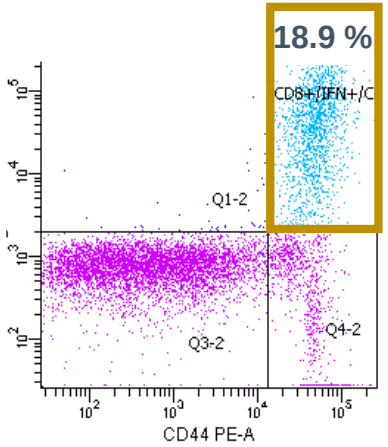
vaccine antigen

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.



fima VACC STRONGLY ENHANCES VACCINATION EFFECTS

- Impressive effects with clinically relevant HPV therapeutic vaccine in mice

	Vaccination without fima VACC	Vaccination with fima VACC
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

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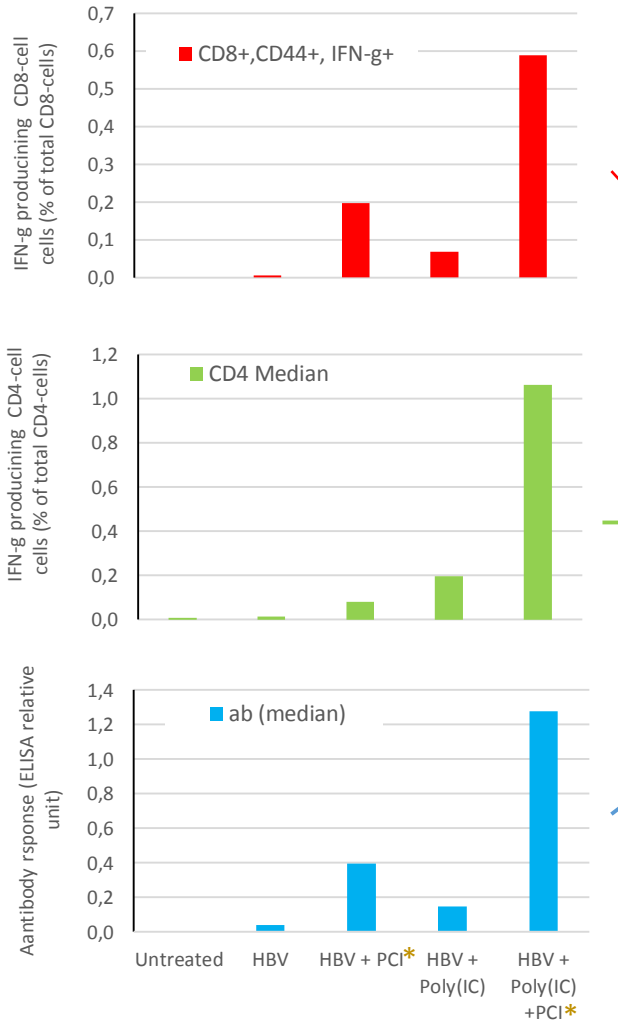
HBV SURFACE ANTIGEN

► **fima VACC** enhances both CD8, CD4, and antibody responses



Immune response with fima VACC

Type of immune response	Fold increase compared to HBV alone	Fold increase compared to HBV + poly(IC)
CD8	110x	9x
CD4	75x	5x
Antibody	33x	9x

Elicit strong effects in all aspects of immune response

*PCI = fima VACC

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
- Phase I study underway
- Excellent stability and cost effective synthesis

NUCLEIC ACID THERAPEUTICS

- A treatment modality with huge potential

- 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

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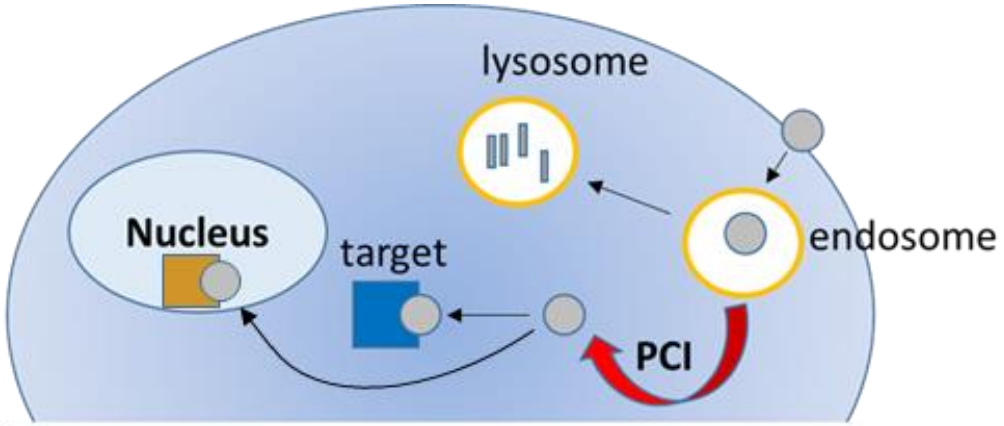
* Research and Markets “RNAi therapeutics market”. Dec 2015

PCI TECHNOLOGY

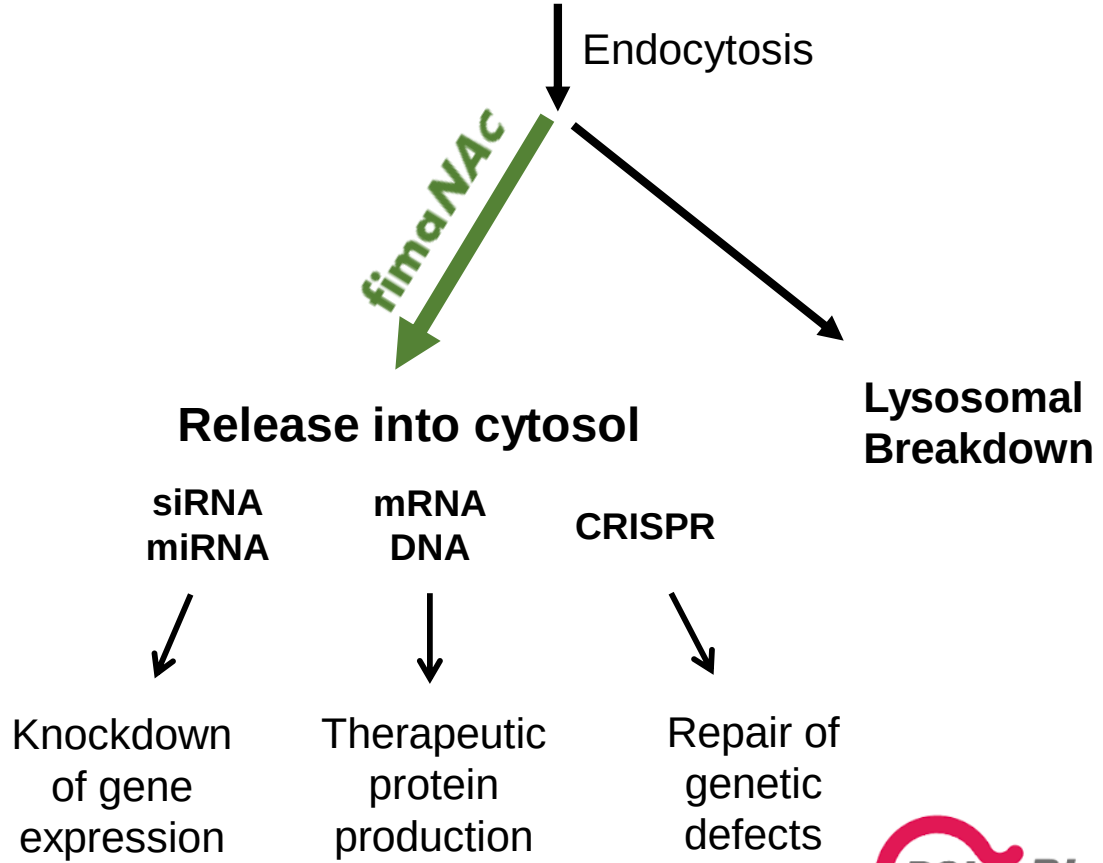
▶ fimaNAc – mode of action

Target cell



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.

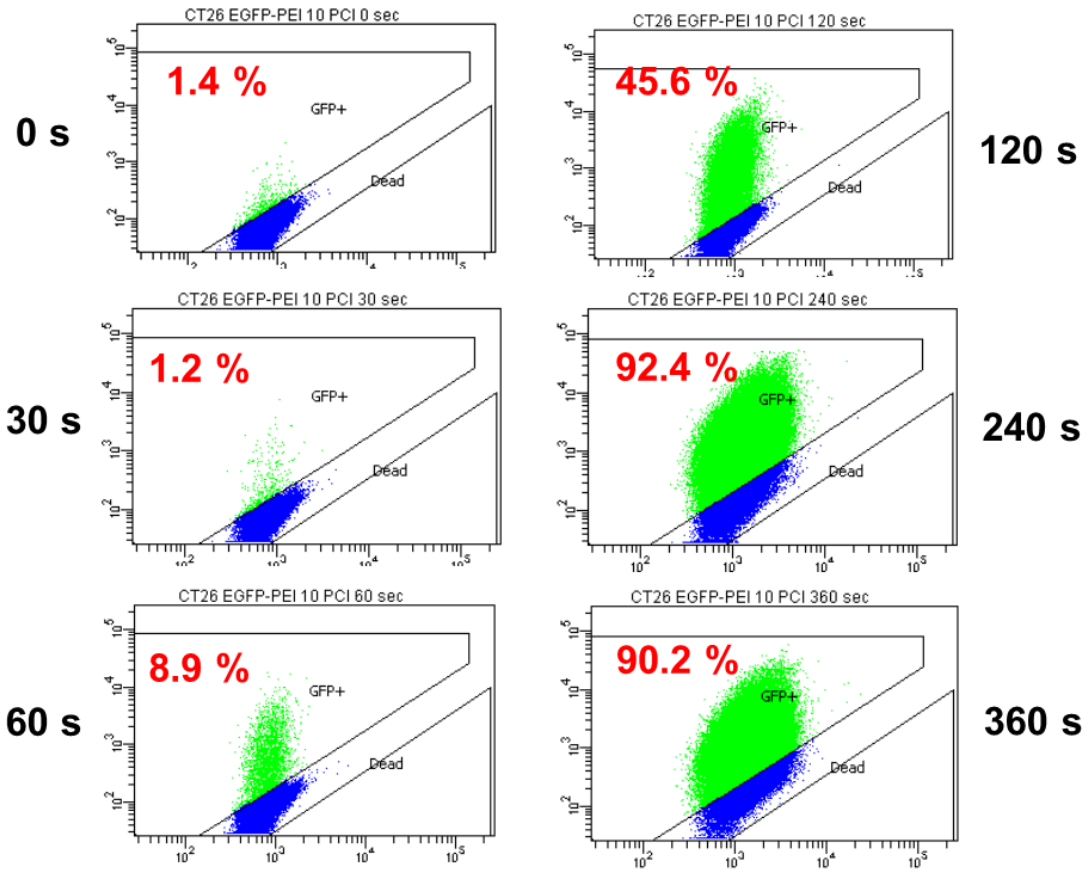
Nucleic Acid Therapeutics

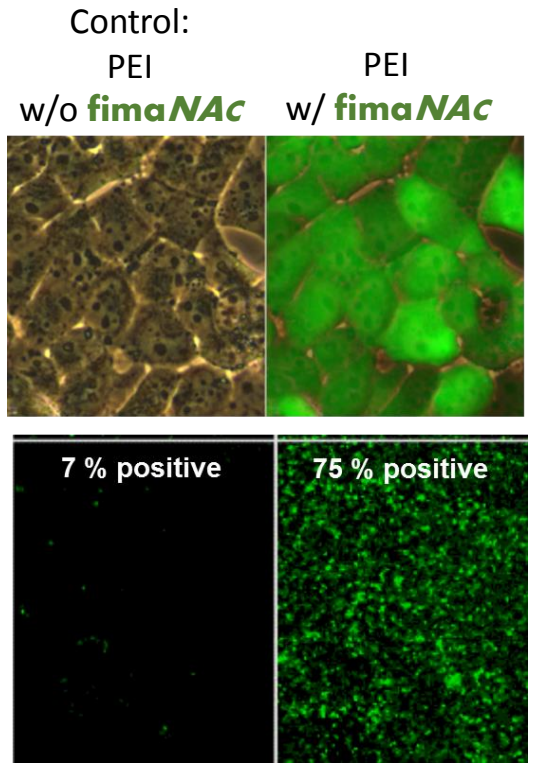


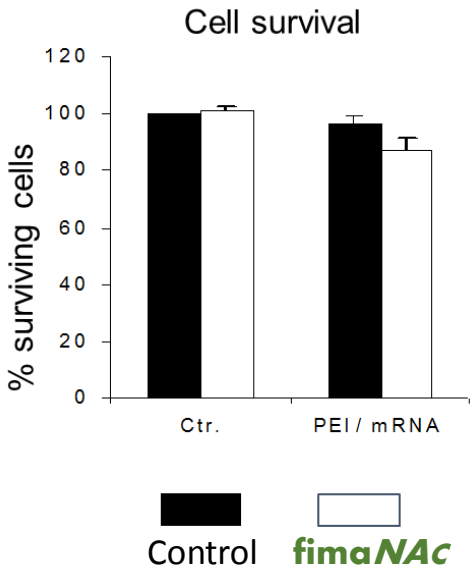
ENHANCING mRNA DELIVERY

- Strongly increased GFP synthesis with increasing light doses

fimaNAc with polyethylenimine (PEI) vehicle







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

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

Boosting the human immune system to fight diseases

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

DEVELOPMENT PIPELINE

- Unlocking the true potential of innovative medicines

Programme	Therapeutic agents	Preclinical	Phase I	Phase II	Status
fimaCHEM	*Chemotherapeutics*				Phase I in the orphan indication bile duct cancer completed with promising early signs of efficacy
fimaVACC	*Therapeutic cancer vaccines*				Phase I study ongoing One active R&D collaboration
fimaNAc	*Nucleic acid therapeutics*				Four active R&D collaborations

An oncology focused company with three well differentiated assets

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