PCI Biotech
Company presentation

October 2023

PCI Biotech

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Factors that could cause these differences include, but are not limited to, implementation of PCI Biotech's strategy and its ability to further grow, risks associated with the development and/or approval of PCI Biotech's products candidates, ongoing clinical trials and expected trial results, the ability to commercialise fimaporfin (Amphinex®), technology changes and new products in PCI Biotech's potential market and industry, the ability to develop new products and enhance existing products, the impact of competition, changes in general economy and industry conditions and legislative, regulatory and political factors. No assurance can be given that such expectations will prove to have been correct. PCI Biotech disclaims any obligation to update or revise any forward-looking statements, whether as a result of new information, future events or otherwise.

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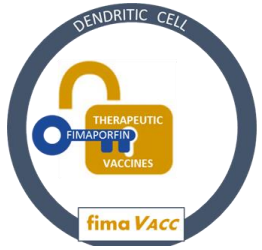
PCI Biotech in brief

PCI Biotech is a listed (PCIB:NO) company with an **innovation-driven pipeline**

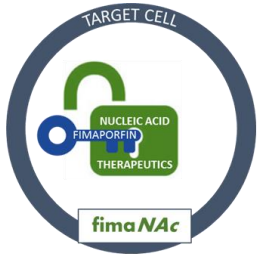
Our vision is to **develop and commercialise novel therapeutic solutions** to address unmet medical needs for patients

Our photochemical internalisation (PCI) **technology platform enables drugs to reach intracellular therapeutic targets**



fima*VACC* applies a **unique mode of action to enhance the effect of intratumoural immunotherapy** - turn immune cold tumours hot and induce systemic immune responses

- **Innovative and versatile** platform for immunotherapy
- Enables **optimal combination therapies** that are challenging to exploit by systemic administration



fima*NAc* provides **intracellular delivery of nucleic acids**, such as mRNA and siRNA therapeutics, thereby addressing one of the major bottlenecks facing this emerging and promising field

- Targeting **applications suited to the specific strengths** of the PCI technology
- Collaborative approach in **dermatology** and **bioprocessing**

PCI Biotech board of directors

Dr. Hans Peter Bøhn, Chairman
- Chairman since 2016
- 12 years experience from various management positions with Nycomed Imaging
- Other experience includes being a financial analyst, covering life science companies

Hilde Furberg, Director
- 35+ years international experience from sales, marketing, strategy and management in pharma and biotech industry
- Most recently European Head of Rare Diseases for Sanofi Genzyme
- Board member of Calliditas, OncoZenge, Herantis and Bio-Me

Dr. Lars Viksmoen, Director
- 25+ years international experience from pharma, biotech and medtech industry
- Worked 10 years as a surgeon prior to his executive career
- Previous experience includes Merck & Co. Inc. and GN ReSound

PCI Biotech management team

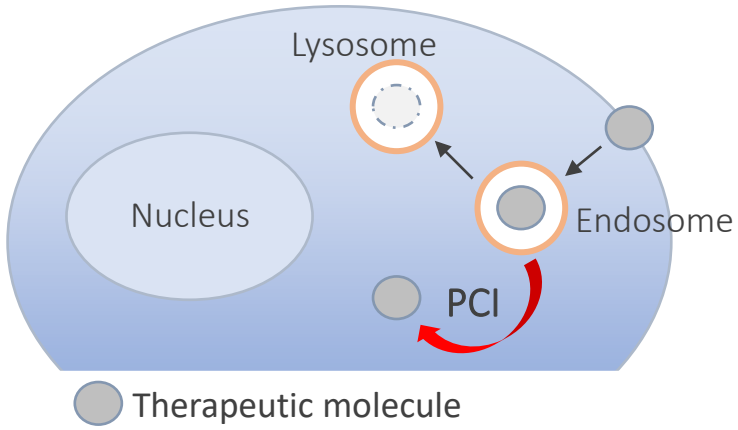
Ronny Skuggedal, CEO and CFO
- Chief Executive Officer since June 2022
- Chief Financial Officer since 2013
- State Authorised Public Accountant Norway
- 12 years experience from auditing and advisory services, PwC

Dr. Anders Høgset, CSO
- Chief Scientific Officer since 2001 (deputy CEO 2004-2008)
- Previously Senior Scientist at Radiumhospitalet developing the PCI technology

PCI: A BROAD INNOVATION PLATFORM

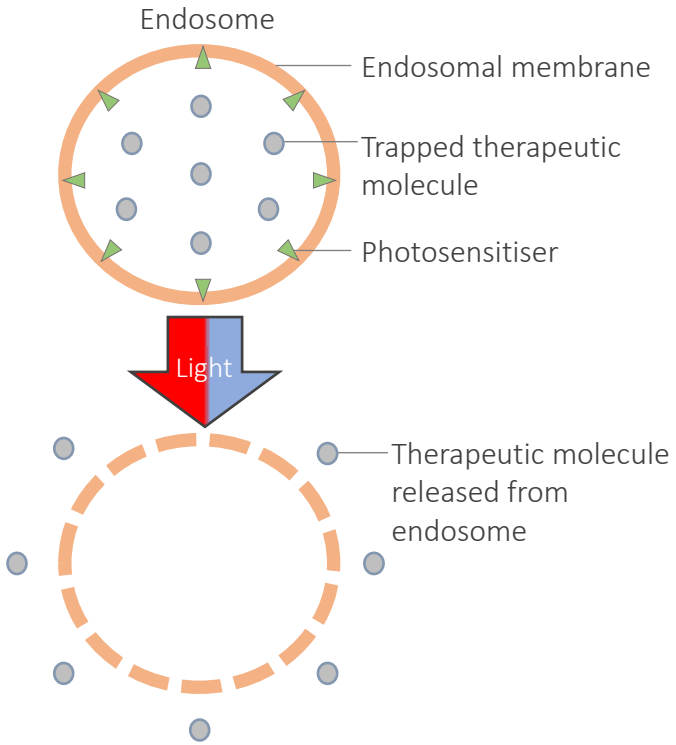
- Enabling intracellular delivery by a unique mode of action

PCI: triggered endosomal escape



Therapeutic molecule
- Immune stimulants (**fima*VACC***)
- Nucleic acids (**fima*NAc***)

PCI mode of action (MoA)



PCI programs

fima*VACC*

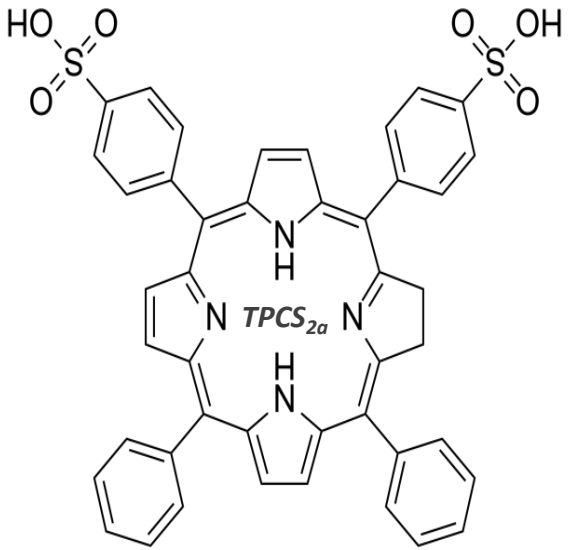
- Innovative and versatile platform for immunotherapy
- Local treatment to enhance immunostimulatory, and combat immunosuppressive, mechanisms in tumours
- Enabling combination treatments not feasible with systemic treatment
- Local treatment may achieve systemic effects

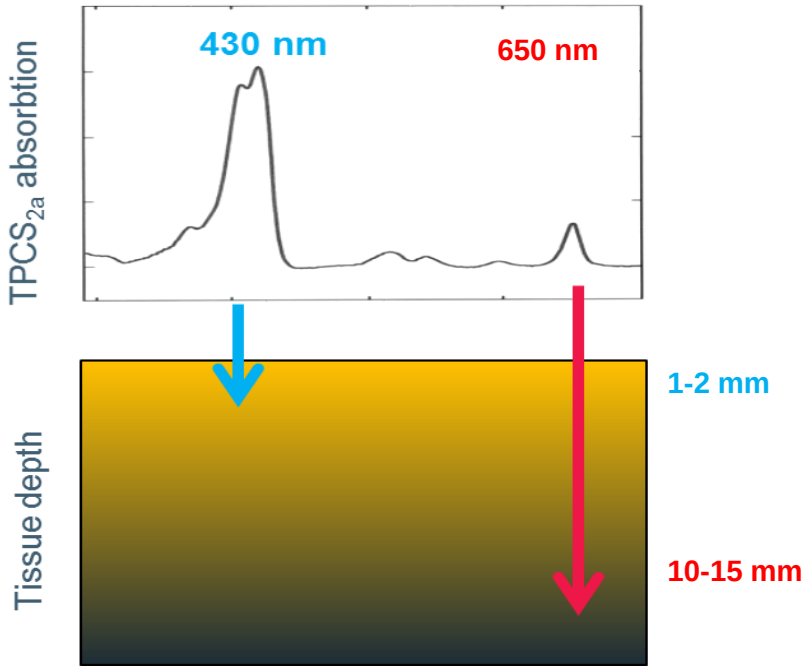
fima*NAc*

- Enhances the therapeutic effect of nucleic acids
- Overcomes the challenge of endosomal escape in nucleic acid delivery
- Preclinical data includes mRNA, plasmids and oligonucleotides

PCI TECHNOLOGY

- Effect dependent on interaction between photons and photosensitiser molecule
  - Different wavelengths have different tissue penetration





Fimaporfin ($TPCS_{2a}$)

- Activated by blue or red light
- Easily synthesized
- Low toxicity
- GMP material in stock
- Very stable, can be autoclaved
- Can be mixed with nucleic acids in aqueous solution
- Also compatible with various delivery vehicles

LEVERAGING THE PCI TECHNOLOGY PLATFORM WITHIN IMMUNOTHERAPY, NUCLEIC ACID THERAPEUTICS, AND BIOPROCESSING

Programme	Therapeutics	Preclinical	Phase 1	Phase 2
fimaNAc	Dermatology			
fimaVACC	Intratumoural immunotherapy			
Collaborations	Undisclosed			

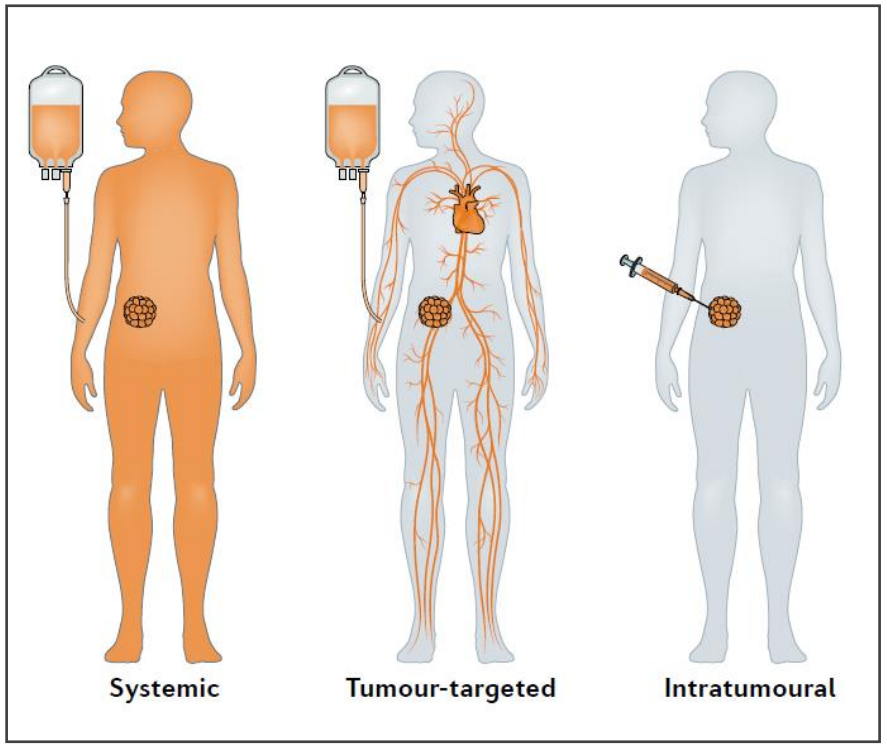
Programme	Application	Feasibility	Prototype	Commercial
fimaNAc	Bioprocessing			

fima *VACC*

- Mobilising the immune system to fight cancer
- Compelling preclinical results
- Safety and encouraging immune response demonstrated in a phase 1 study[1]

[1]Otterhaug *et al*. (2021) Front Immunol.8;11:576756

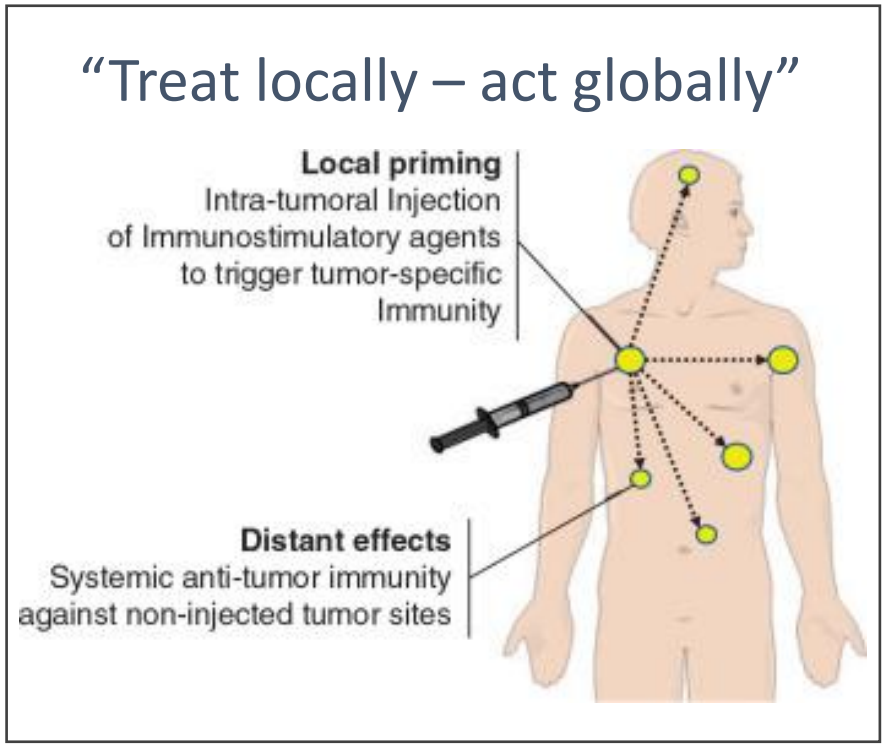
LEVERAGING INTRATUMOURAL IMMUNOTHERAPY TO ACHIEVE A SYSTEMIC ANTI-TUMOUR IMMUNE RESPONSE



Melero *et al.* (2021) Nat Rev Clin. Oncol.;18:558–576

- Despite representing a major breakthrough in cancer treatment, a large proportion of patients do not respond to immune checkpoint inhibitors (ICIs) or progress shortly after initial response
- Optimising ICI and combined therapies dosage is difficult to achieve due to systemic side effects
- Combining ICI with intratumour immunotherapy may overcome resistance to ICI monotherapy

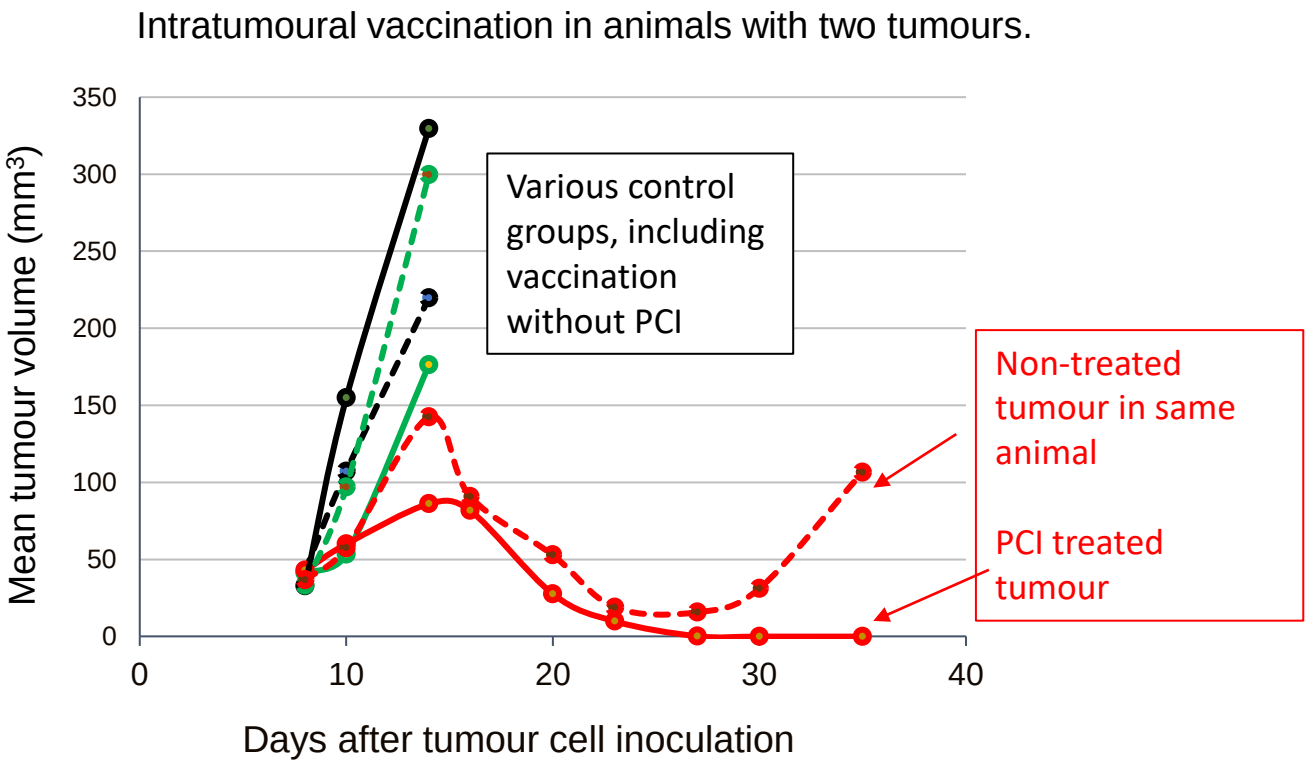
LEVERAGING INTRATUMOURAL IMMUNOTHERAPY TO ACHIEVE A SYSTEMIC ANTI-TUMOUR IMMUNE RESPONSE



Marabelle *et al.* (2017) Ann. Oncol.;28:xii33

- For intratumoural treatment, systemic adverse effects are limited, enabling combination treatments not feasible with systemic treatment
- Therapy may include components that target immunosuppressive mechanisms
- Exploits patient's own tumour as a patient-specific therapeutic "cancer vaccine"
- Treatment of one tumour lesion can induce specific immune response against other tumour lesions in the body

INTRATUMOURAL THERAPY WITH FIMA*VACC* GIVES SYSTEMIC ANTI-TUMOUR IMMUNE RESPONSE

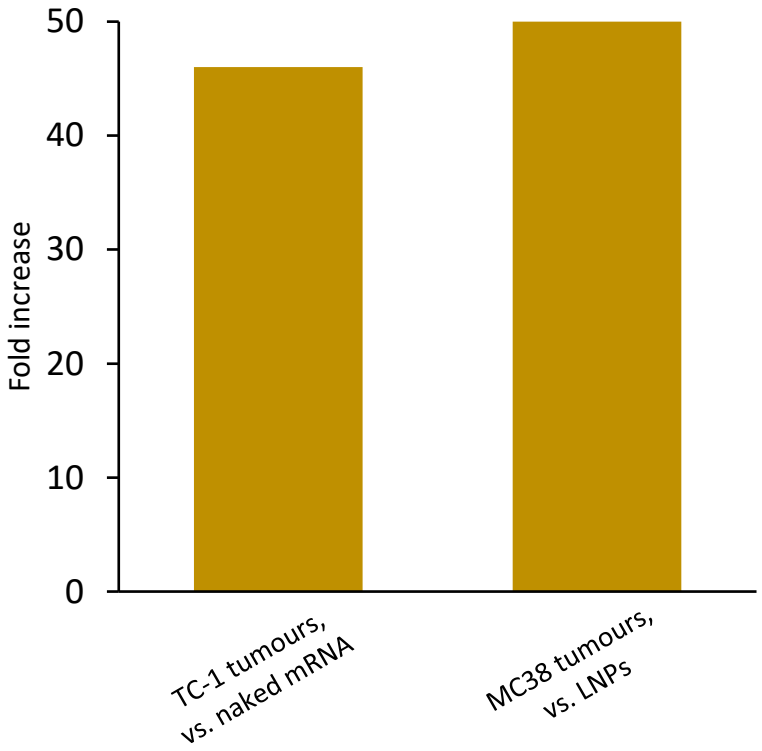


- In animal studies, **fima*VACC*** gives a very good effect with intratumoural vaccination, also on untreated tumour lesions
- **fima*VACC*** has shown to enhance the effect of different types of agents explored in intratumour immunotherapy:
  - DNA
  - PRR agonists
  - Pathogen
  - RNA
  - Small protein
- **fima*VACC*** additionally has an immunostimulatory effect by itself[1]
- PCI Biotech will explore novel approaches for intratumoural immunotherapy, supported by PhD project

1. Waeckerle-Men *et al*. (2022) Front. Immunol.;13;815609

INTRATUMOURAL MRNA DELIVERY WITH fimaVACC - APPLICATION IN IMMUNOTHERAPY

Fold increase of mRNA expression with fimaVACC



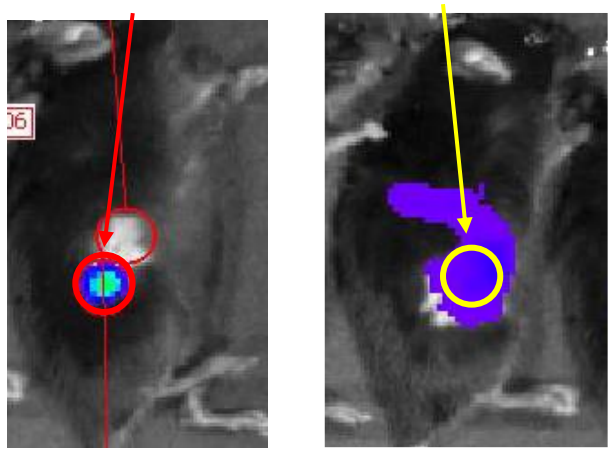
- Intratumoural immunotherapy
  - Extraordinary delivery of mRNA with **fimaVACC**
  - mRNA may encode antigens and immuno-stimulating factors
  - To avoid side effects of potent effector molecules it is very important to confine mRNA expression to tumour
    - **fimaVACC** substantially better than LNPs

PREVENTING UNDESIRABLE OFF-TARGET DELIVERY

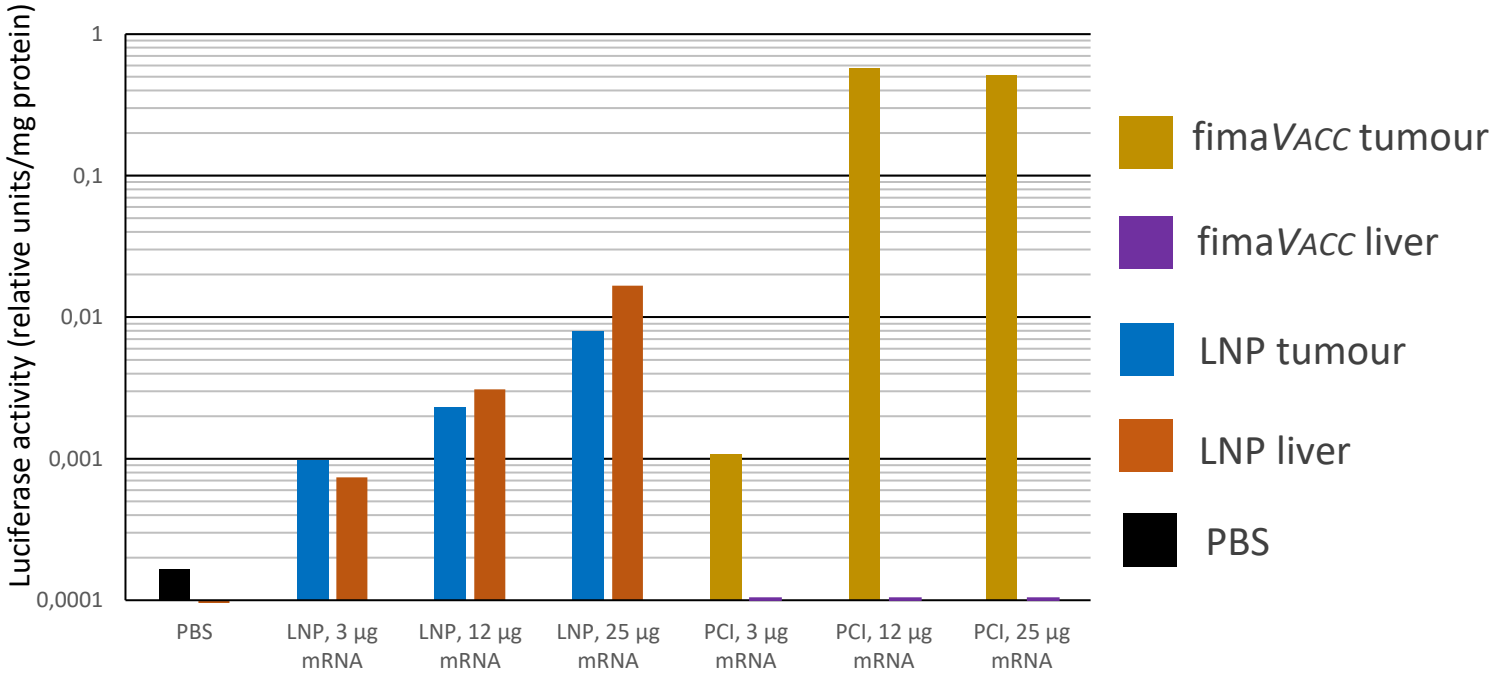
- With **fima*VACC***, mRNA expression is confined to tumour tissue

fima*VACC* with naked mRNA

LNPs



Luciferase expression in MC38 tumours and liver after intratumoural delivery of luciferase mRNA by LNPs or PCI. Median values.



- With **fima*VACC***-mediated delivery of naked mRNA, expression is confined to the tumour
- LNPs seem to leak out of the tumour leading to unwanted expression in the liver, with similar expression levels as in the tumour

fimaNAc

- Addressing a major hurdle for nucleic acid delivery
- Compelling preclinical results
- Strategic & technological fit
- Leveraging research collaborations

VERSATILITY OF fimaNAc

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

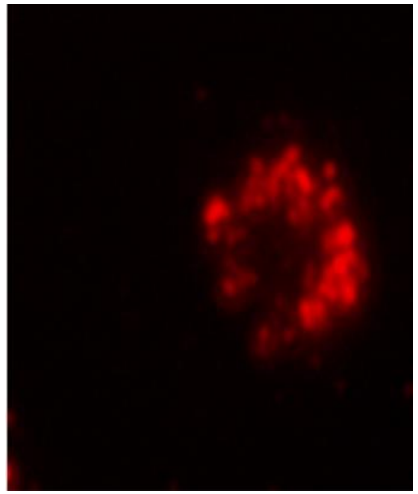
Nucleic acids successfully delivered by fimaNAc

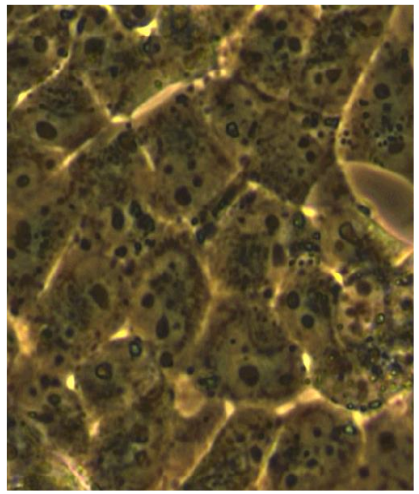
Type of nucleic acid	Delivery vehicle
Plasmids	PEI, cationic peptides, cationic lipids, polylysine ++ Targeting to EGF-R, transferrin-R
siRNA	None, PEI, cationic peptides, dendrimers, lipofectamine, DOTAP, nanogels, chitosan ++
PNA (peptide nucleic acids)	None, cationic amino acids attached
mRNA	None,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

Pursuing collaboration and partnering opportunities

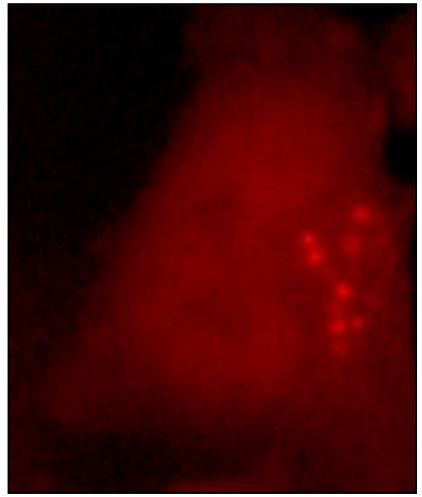
fimaNAc RELEASES OLIGONUCLEOTIDES FROM ENDOSOMES

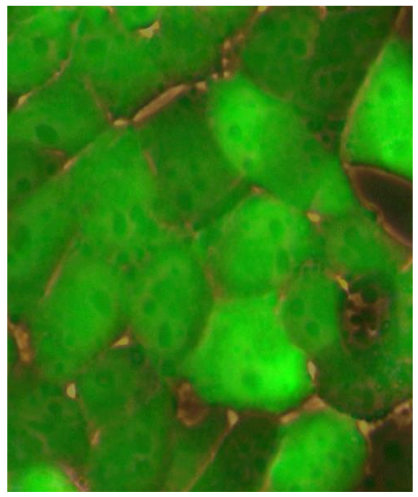
- fimaNAc





+ fimaNAc





Labelled RNA molecules (PEI vehicle) in endosomes released into cytosol by illumination

PCI-mediated endosomal release strongly enhances expression of GFP-encoding mRNA (PEI vehicle)

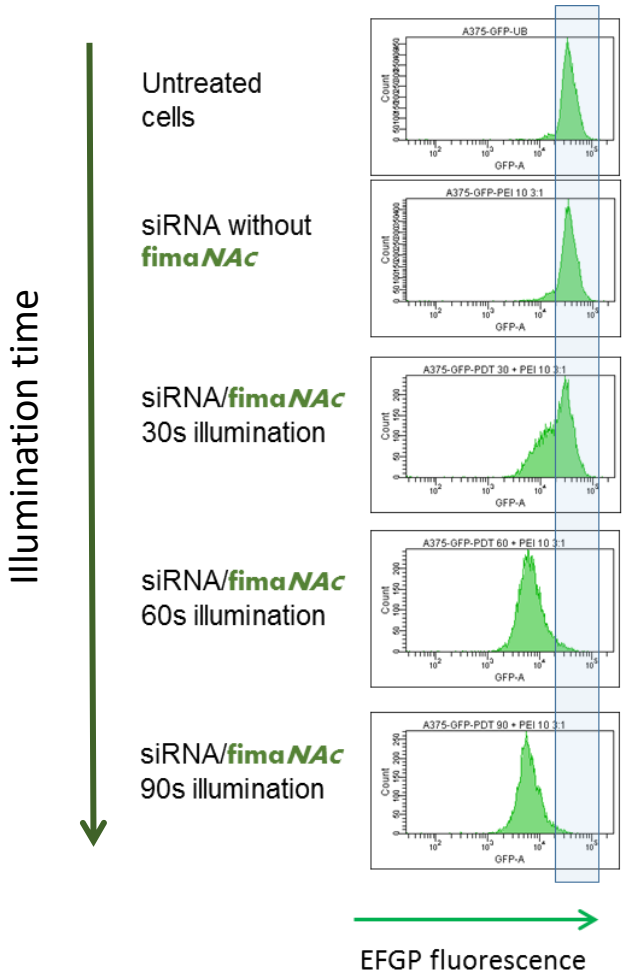
"Targeted delivery and endosomal escape remain challenging for mRNA delivery systems, highlighting the need for safe and effective mRNA delivery"

Hou et al. (2021) Nature Reviews Materials 6: 1078-1094

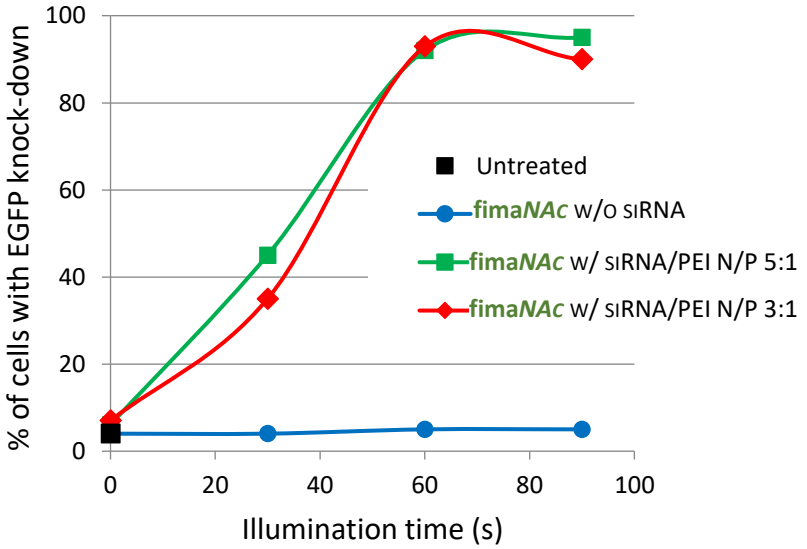
- PCI can be used with RNA complexed with delivery vehicles and with naked RNA molecules
- *In vitro*, PCI strongly enhances cytosolic RNA (siRNA and mRNA) delivery with several types of delivery vehicles

fimaNAc CAN STRONGLY ENHANCE *IN VITRO* siRNA DELIVERY

- Strongly enhanced siRNA (PEI complex) activity in A375-EGFP cells



Knock-down is dependent on illumination

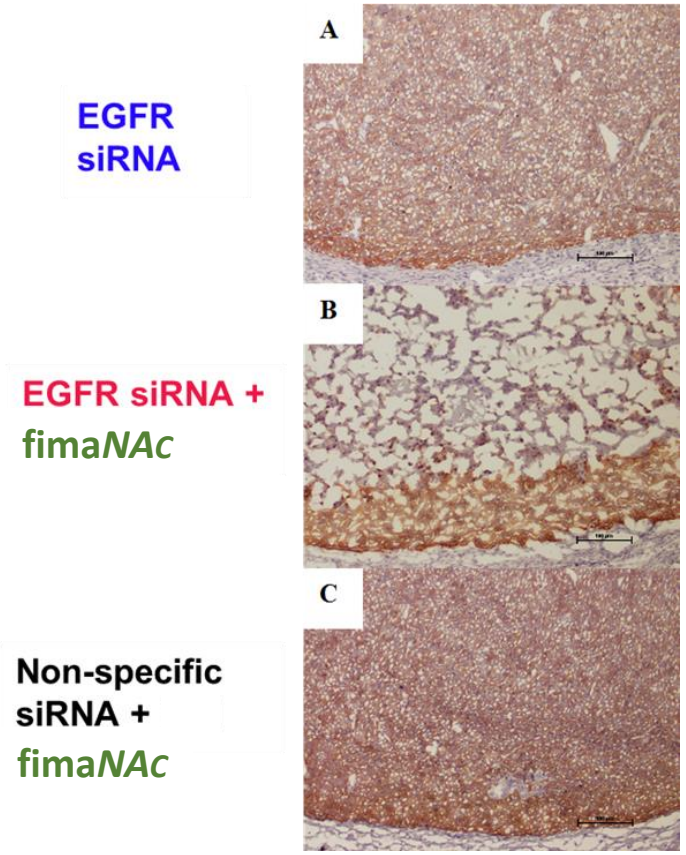


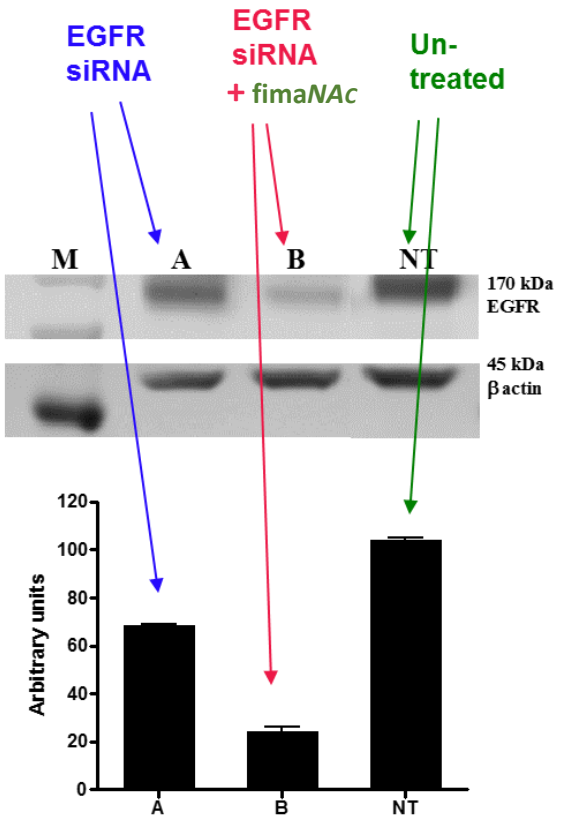
PEI 10 000 (branched)

- **fimaNAc** induces target gene knock-down in almost 100% of the cells, while siRNA-PEI alone has almost no effect
- **fimaNAc** can enable PEI-mediated siRNA delivery

fimaNAc Enhances *in vivo* Local Delivery of Lipofectamine-Complexed siRNA

- Intratumoural delivery of EGF receptor (EGFR) siRNA





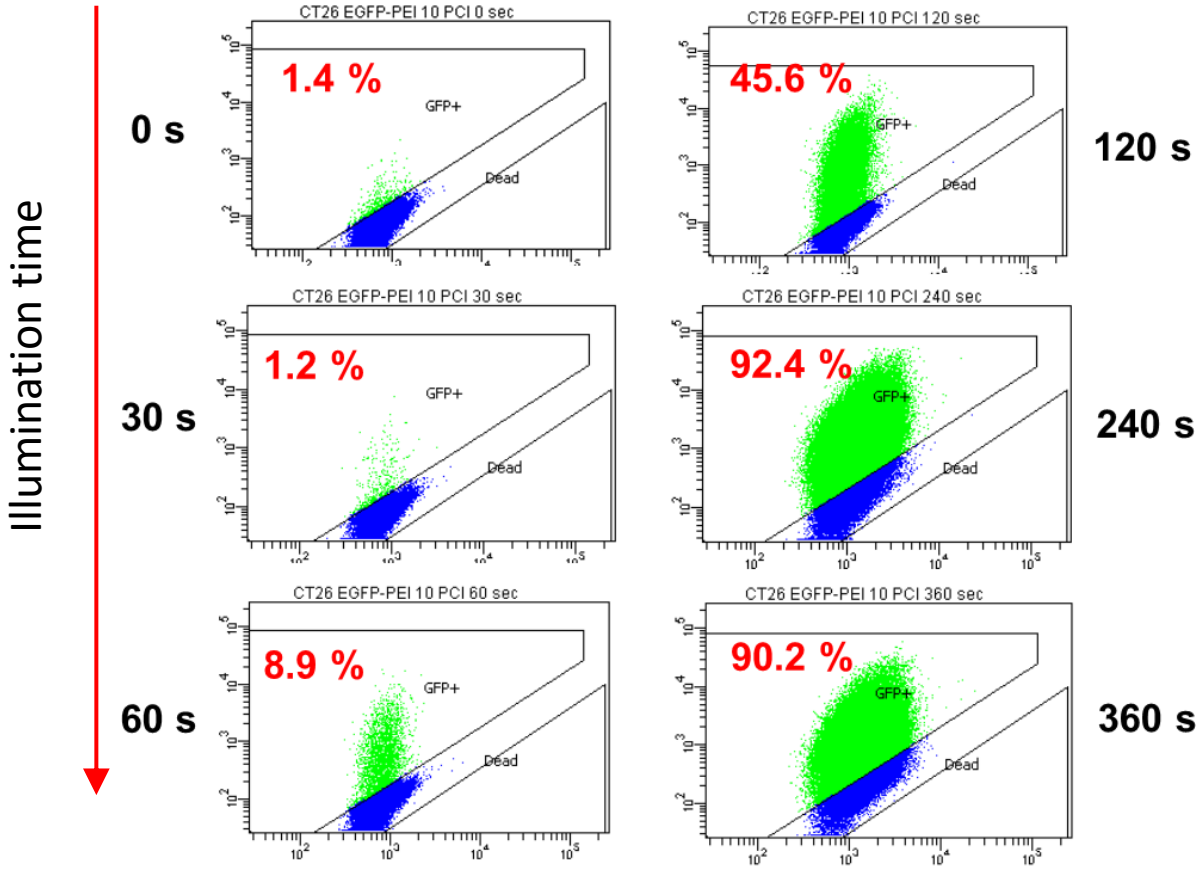
- **fimaNAc** induces target gene knock-down in a large fraction of the tumour cells
- siRNA-lipofectamine alone has almost no effect

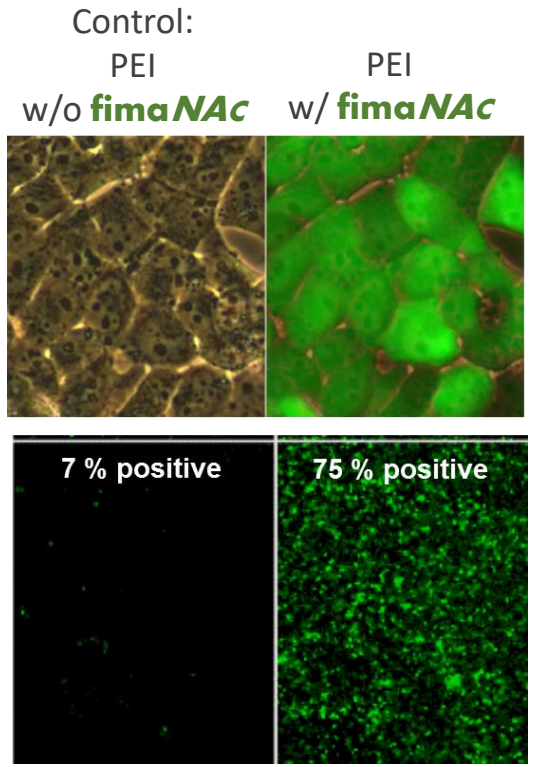
Oliveira, S. et al. (2008). *Curr. Pharm. Design* 14: 3686-97

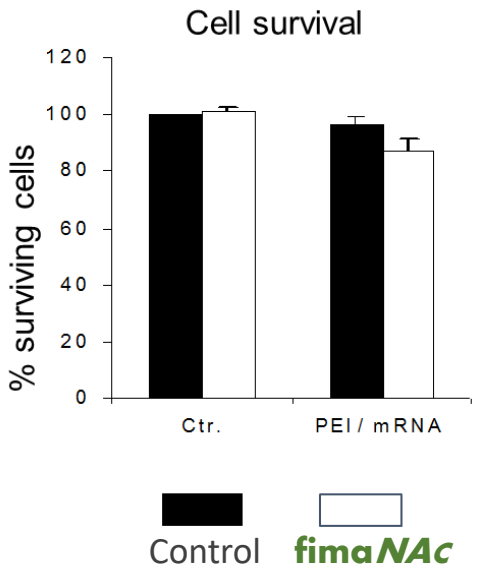
fimaNAc FOR ENHANCEMENT OF mRNA DELIVERY

- Illumination strongly enhances *in vitro* mRNA delivery with PEI vehicle (> 60 times improvement)
- Excellent cell survival

fimaNAc with polyethylenimine (PEI) vehicle

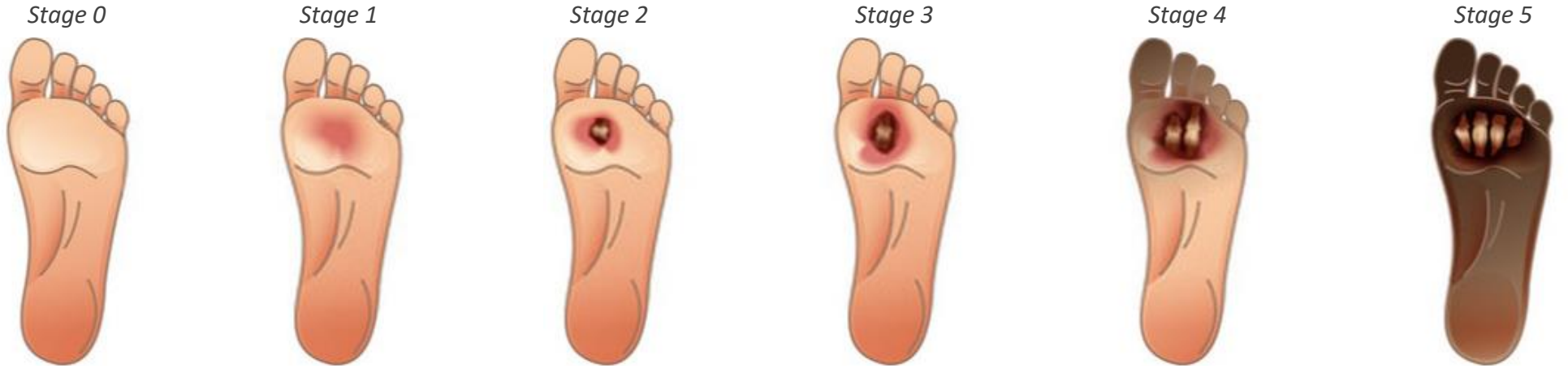






DELIVERY OF NUCLEIC ACIDS TO SKIN

- **fimaNAc -** Excellent technological fit with dermatological diseases
- Chronic skin ulcers (e.g. diabetic ulcers) have unmet medical need
- Complex biology where **fimaNAc** can exploit the ability of nucleic acid therapies to affect tissue developmental (regenerative) programs
- Inefficient delivery has severely limited the use of nucleic acid therapies
- Large body surface areas are particularly challenging

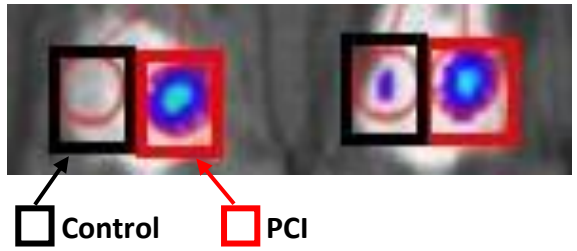


Complications of diabetic foot ulcer

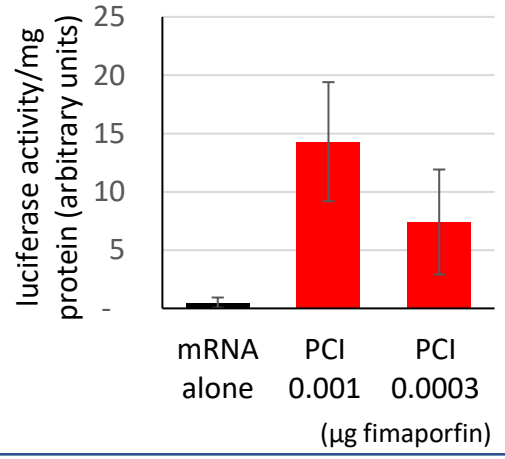
fimaNAc FOR DELIVERY OF NUCLEIC ACIDS TO SKIN

- Excellent technological fit with dermatological diseases

IVIS imaging after i.d. inj. of luciferase mRNA and subsequent i.v. inj. of the substrate luciferin

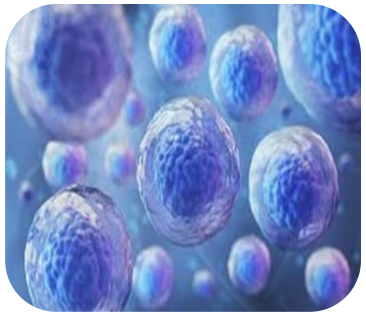


Enzymatic luciferase activity in skin samples after i.d. inj. of luciferase mRNA

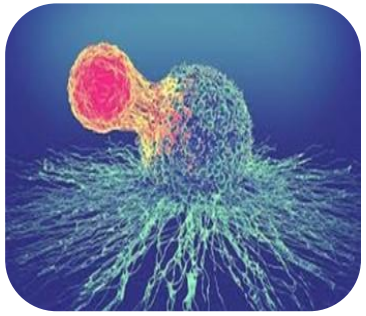


- *In vivo* data indicate that fimaNAc can strongly enhance nucleic acid delivery in the skin
- fimaNAc may unlock the therapeutic potential of nucleic acid therapeutics in skin
- PCI Biotech intends to develop a fit-for-purpose solution with primary focus on treating severe skin conditions with nucleic acid therapeutics

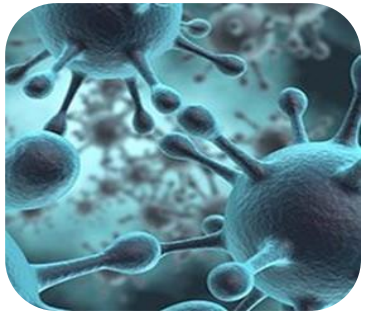
BIOPROCESSING - MANUFACTURING CAPACITY IS A MAJOR LIMITING FACTOR TO TREATING MORE PATIENTS



Cell culture



Cell and gene therapy



Viral manufacturing

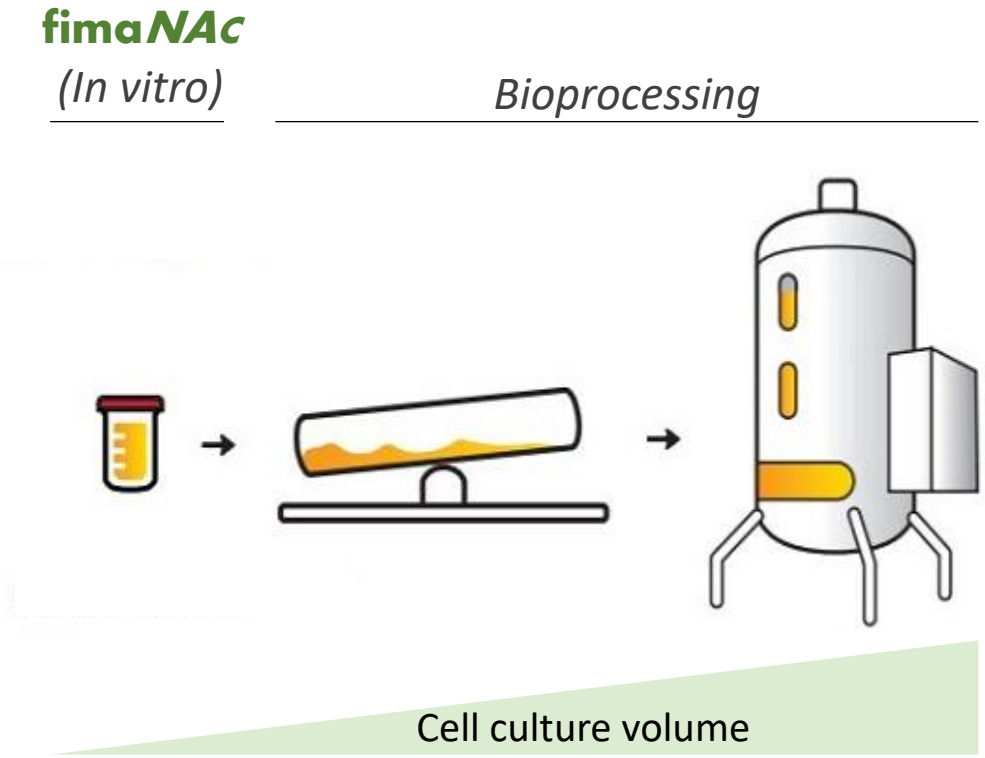
Markets:

- Rapid growth
- Short time to market
- Cost-effective development
- Urgent need for novel technology
- fimaNAc has shown promise

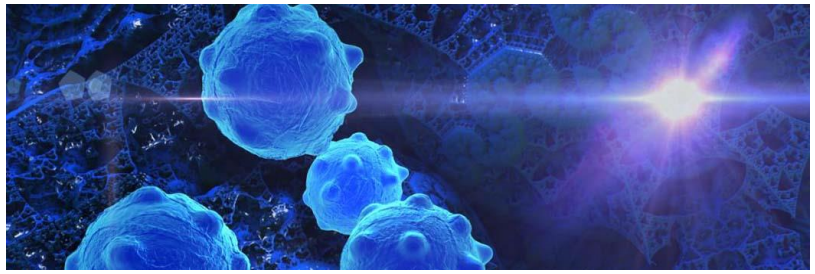
fimaNAc *IN VITRO* DATA IS HIGHLY TRANSFERRABLE TO BIOPROCESSING

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	None, PEI, cationic peptides, dendrimers, lipofectamine, DOTAP, nanogels, chitosan ++
PNA (peptide nucleic acids)	None, cationic amino acids attached
mRNA	None, PEI, Protamine, Lipofectamine
Adenoviral vectors	None, cationic polymers
AAV vector	None



PROTOTYPES WILL BE DEVELOPED BASED ON COLLABORATOR FEEDBACK, TO ENSURE THAT COMMERCIALLY VIABLE PRODUCTS AND SOLUTIONS ARE DEVELOPED



Feasibility

- Pursue applications based on market need and technological fit
- Apply **fimaNAc** to viral manufacturing proof-of-concept (alpha prototype)
- Perform in-house

Early prototypes (alpha)

- Partnerships are sought to improve early (alpha) prototype products or solutions
- Targets:
  - Pharma and Biotech
  - Contract development and manufacturing organisations (CDMOs, CMOs)

Late-stage prototypes (beta)

- Late-stage (beta) prototypes are tested in partnerships to validate that products and solutions are commercially viable
- Targets:
  - Pharma and Biotech
  - Contract development and manufacturing organisations (CDMOs, CMOs)

INVESTMENT HIGHLIGHTS

Broad innovation platform	Proprietary PCI platform technology with programmes targeting rapidly growing markets Our vision is to bring innovation with impact for conditions with limited treatment options
Pipeline opportunities	**fima *VACC*** – novel technology for local immune enhancement, safety demonstrated in phase 1 **fima *NAc*** – a nucleic acids delivery solution for dermatology, and a novel approach for bioprocessing
Compelling data	Clinical evidence of increased immune responses and preclinical evidence of effective and durable anti-tumour responses with **fima *VACC*** technology
Collaborative development strategy	A partnership-driven approach is pursued with both **fima *VACC*** and **fima *NAc*** programs to leverage synergies with other technologies, as well as seek out-licensing opportunities
Strong leadership	Experienced team in drug discovery and development across a range of medical and commercial areas

Recent Key Publications

Programme	Publication	Brief summary
PCI platform: fimaVACC fimaNAc	Photochemical Internalization for Intracellular Drug Delivery. From Basic Mechanisms to Clinical Research. Jerjes W et al. J Clin Med. 2020 Feb 14;9(2):528 https://www.mdpi.com/2077-0383/9/2/528	The PCI technology has been shown to improve the biological activity of a number of macromolecules that do not readily penetrate the plasma membrane. PCI has also been found appealing for intracellular delivery of drugs incorporated into nanocarriers and for cancer vaccination.
fimaVACC	Photochemical Internalization Enhanced Vaccination Is Safe, and Gives Promising Cellular Immune Responses to an HPV Peptide-Based Vaccine in a Phase I Clinical Study in Healthy Volunteers. Otterhaug T et al., Front Immunol 2021 Jan https://doi.org/10.3389/fimmu.2020.576756	Using PCI in combination with Hiltonol for intradermal vaccination is safe and gives encouraging immune responses to peptide- and protein-based vaccination. PCI enhanced general cellular immune responses, the quality of the CD8 T-cell response, and the antibody response to a protein antigen.
fimaVACC	Photochemical Internalization: Light Paves Way for New Cancer Chemotherapies and Vaccines. Šošić L et al., Cancers (Basel). 2020 Jan 9;12(1):165 https://www.mdpi.com/2072-6694/12/1/165	This report describes PCI as a potential tool for cellular internalisation of chemotherapeutics and antigens, and provides a systematic review of the research. Preclinical studies suggest that PCI improve treatment efficacy by effective delivery of cytotoxic agents to the cytosol of tumour cells. PCI was preclinically also shown to mediate MHC class I antigen presentation, generation of tumour-specific CD8+ T-lymphocytes, and cancer remission.
fimaVACC	Photochemical internalization of peptide antigens provides a novel strategy to realize therapeutic cancer vaccination. Haug M et al., Front Immunol 9 (2018) https://doi.org/10.3389/fimmu.2018.00650	This article shows that fimaVacc can strongly enhance vaccination effects also with peptide vaccines and with cancer antigens. The article also describes the mechanism of action for fimaVacc in such vaccination.
fimaVACC	Photochemical internalization (PCI)-mediated activation of CD8 T cells involves antigen uptake and CCR7-mediated transport by migratory dendritic cells to draining lymph nodes. Schineis P et al. J Control Release. 2021 Apr 10;332:96-108. https://doi.org/10.1016/j.jconrel.2021.02.014	Results contribute to the understanding of the functional mechanism of PCI-mediated vaccination, and highlight the importance of an active transport of vaccine microspheres by antigen presenting cells to draining lymph nodes.
fimaVACC	Photochemically-Mediated Inflammation and Cross-Presentation of Mycobacterium bovis BCG Proteins Stimulates Strong CD4 and CD8 T-Cell Responses in Mice. Waeckerle-Men Y et al. Front Immunol. 2022 31;13:815609. https://doi.org/10.3389/fimmu.2022.815609	The article shows that PCI enhances T-cell responses to BCG vaccination in mice. The article also provides new information on the mechanism of action in PCI-mediated vaccination, especially with regard to the enhancement of helper T-cell responses.
fimaNAc	Photochemical internalisation (PCI) – enhanced and site-directed mRNA delivery by light-induced endosomal release. Høgset A. et al., 9th International mRNA Health Conference 2021. Berlin 9-10 Nov 2021	This poster shows that PCI can strongly enhance delivery of naked mRNA to tumours, skin and skeletal muscle. For tumour delivery PCI with naked mRNA gave substantially higher tumour mRNA expression than what was achieved with a lipid nanoparticle based delivery (LNP) system. with PCI mediated delivery there was no off-target expression in the liver and was no induction of inflammatory cytokines, in contrast to what was observed with the LNPs.

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