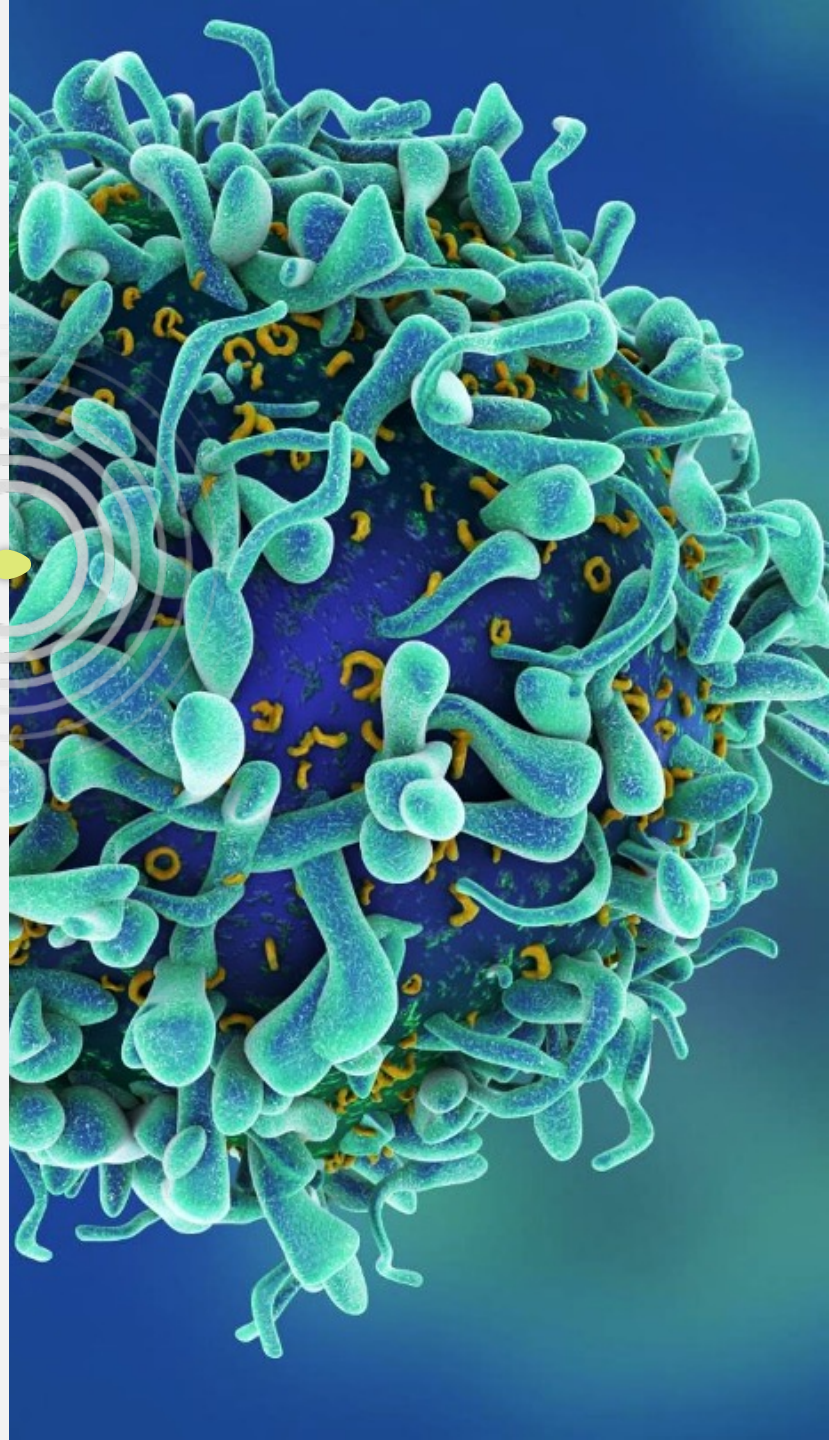
Innovative Targeted Therapeutics

Using energy-based systems



Focal Medical

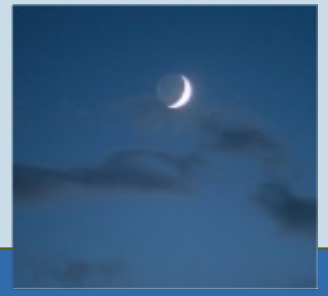
Targeted Therapeutics

Targeted therapeutic products built on active, energy-based, precision delivery technology

Patented Platform

Iontophoretic delivery system:

- Actively and precisely targets drugs
- To diseased organs and tissues



Broad Application

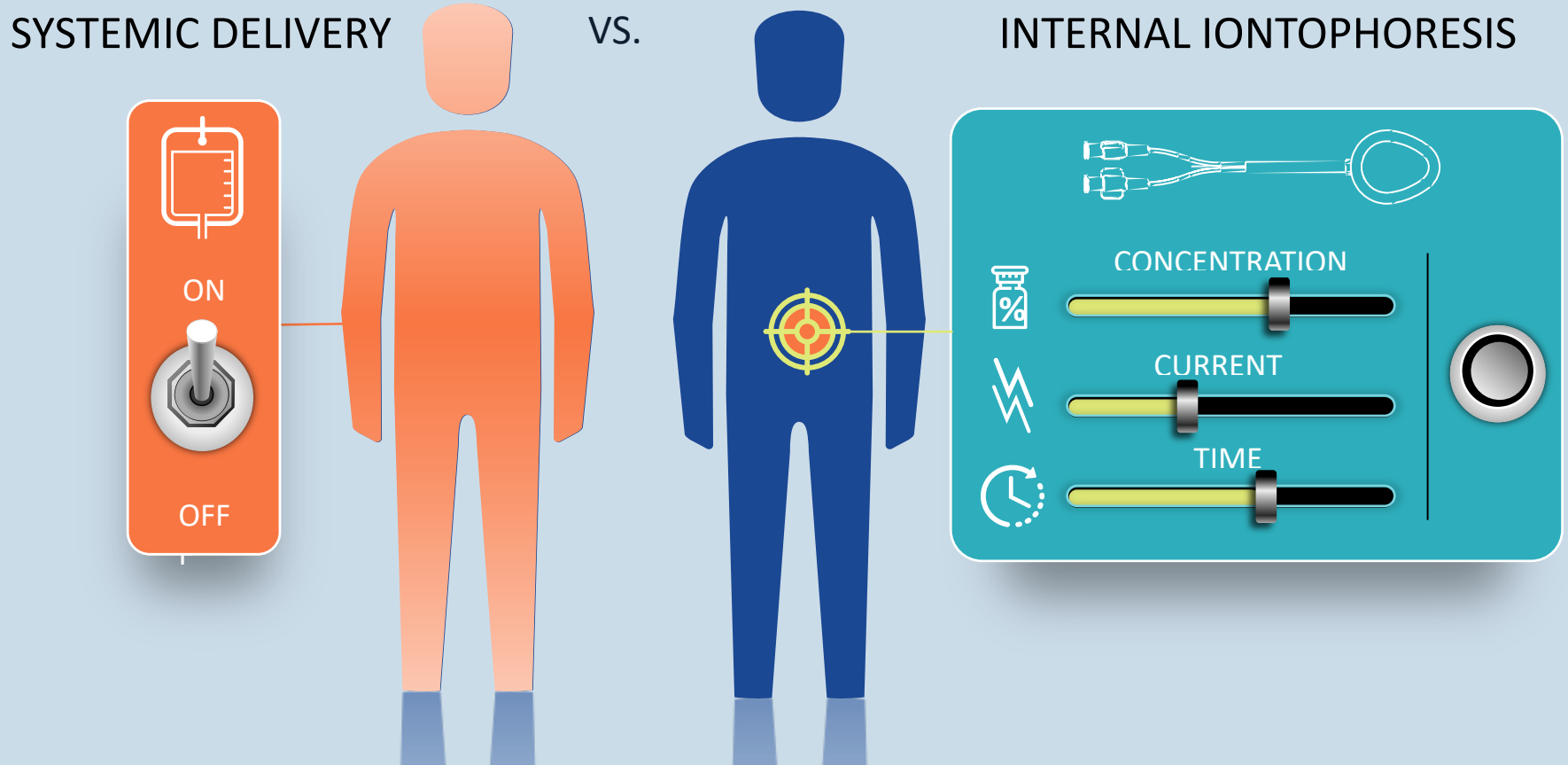
- Lead product - pancreatic cancer
- Inoperable solid tumors
- Genomic medicine

Funding

- Khosla Ventures led Series A $11.1 M
- Post–money $22.7 M
- NIH Grants

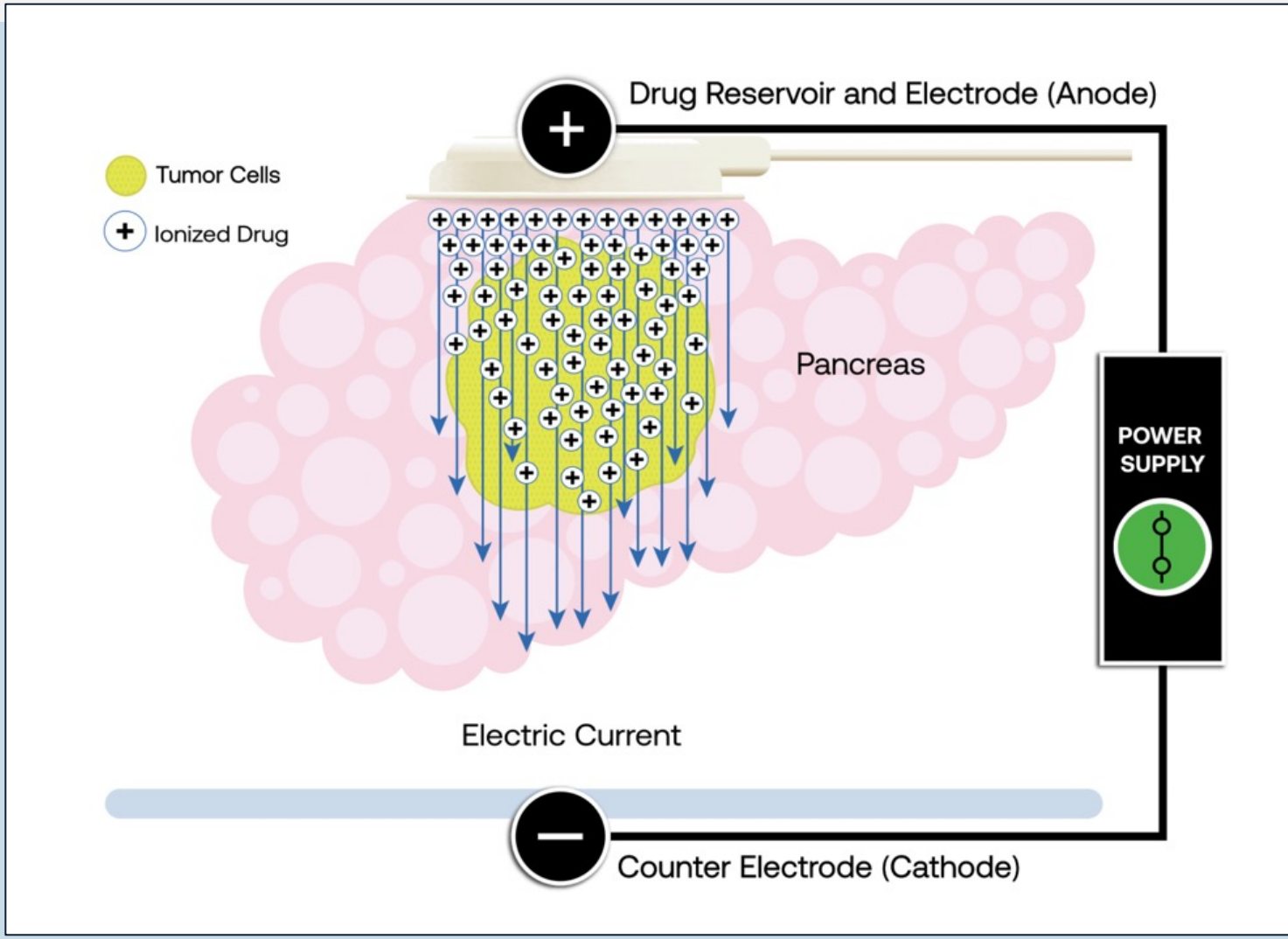
Targeted Therapeutic System

- Iontophoresis: a mild electric field, active, local, drug delivery
- Implanted: precisely targets internal organs using non-circulatory pathways
- Drug is targeted selectively to site of action
- Bypasses delivery barriers and deactivation pathways



Targeted Therapeutic System – Iontophoresis (IOP) in Action

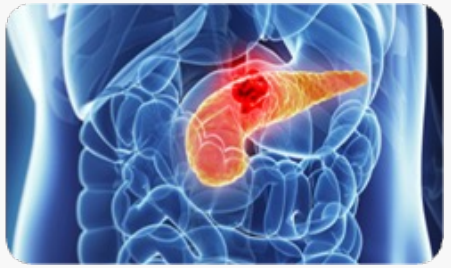
- Applied electrical current between anode and cathode...
- induces electro-repulsion and electroosmosis across the conductive path…
- moves drug molecules locally through and across extrinsic tissue and cellular barriers…
- to achieve local high concentration of drug.



Pipeline

Pancreatic Cancer >> phase 1b

IOP gemcitabine: locally advanced nonresectable pancreatic cancer

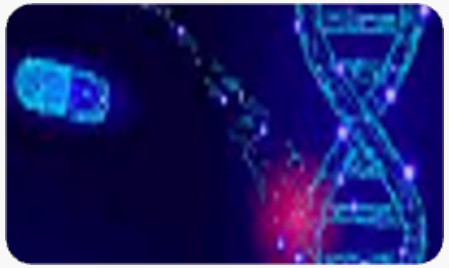


Head & Neck Cancer >> pre-clinical

IOP cisplatin: locally recurrent oral cavity & oropharyngeal cancer

Genomic Medicine >> research

IOP (x)RNA: Organ targeted genomic medicine delivery



Lead Program: Pancreatic Cancer

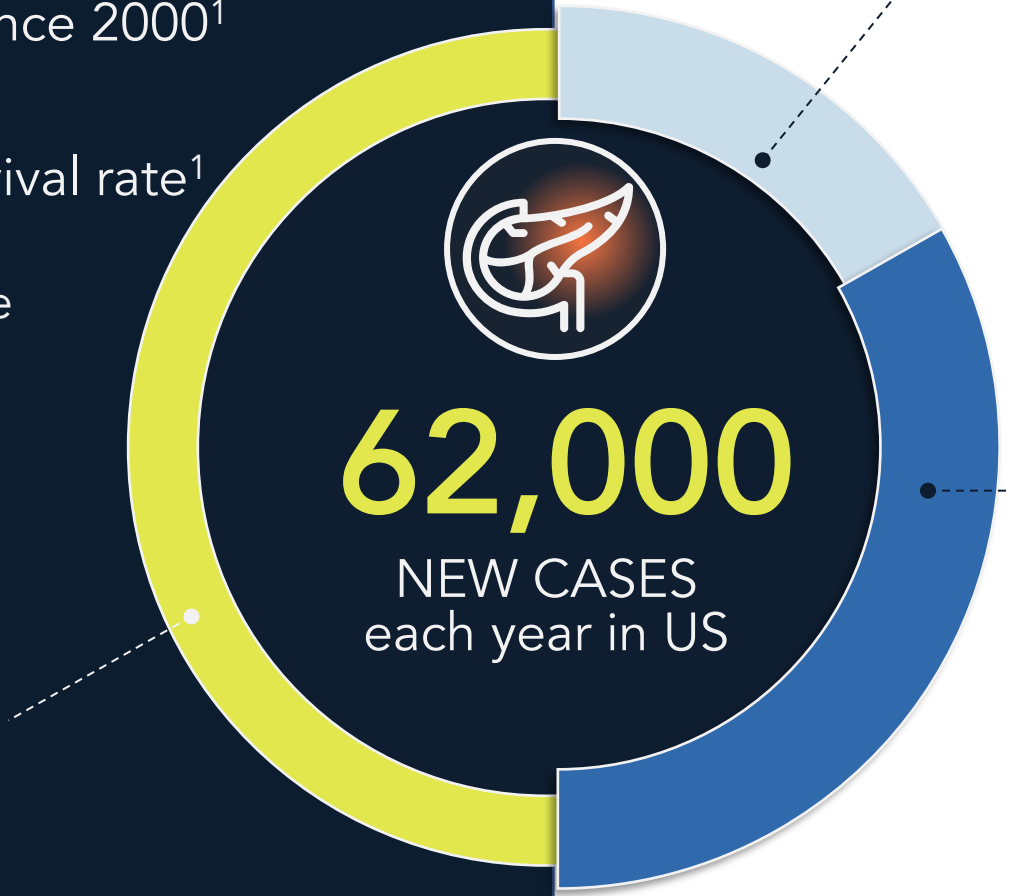
IOP gemcitabine for locally advanced nonresectable pancreatic cancer

Pancreatic Cancer

82% increase since 2000[1]

12% 5-year survival rate[1]

$ 312K Cost of Care 2nd year[3]



~15% Resectable[2]

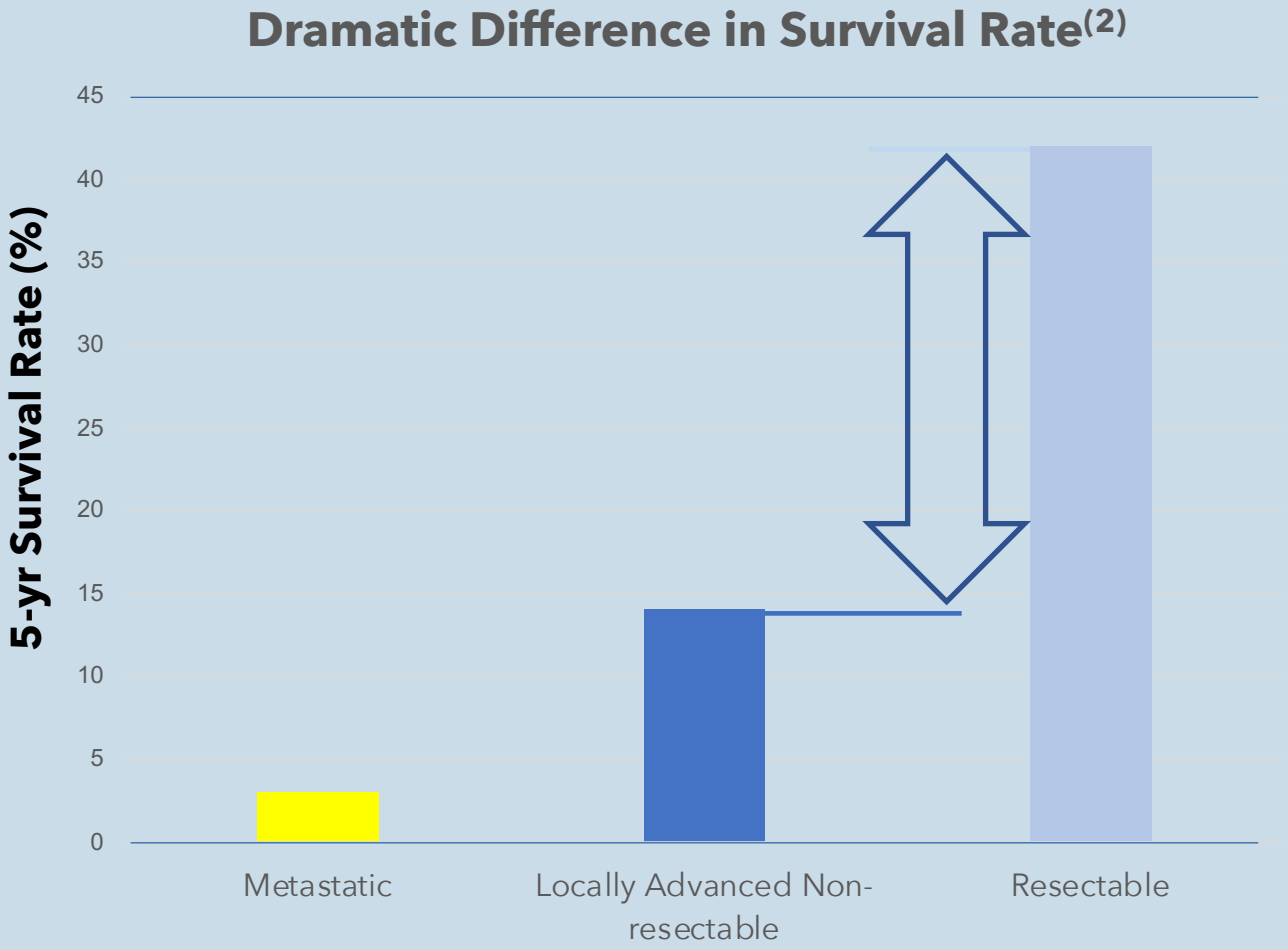
~35% Locally Advanced Nonresectable[2]

~50% Metastatic

1 https://seer.cancer.gov/statfacts/html/pancreas.html
2 NCI database 2019 – accessed March 2023
3 2020 GI Cancers Symposium: Cost of Pancreatic Cancer Care Over Time – The ASCO Post

Pancreatic Cancer – Unmet Medical Need

- "Surgical resection is the only potential curative treatment…"(1)
- Unmet Medical Need: strategies to restage patients to surgical resection.

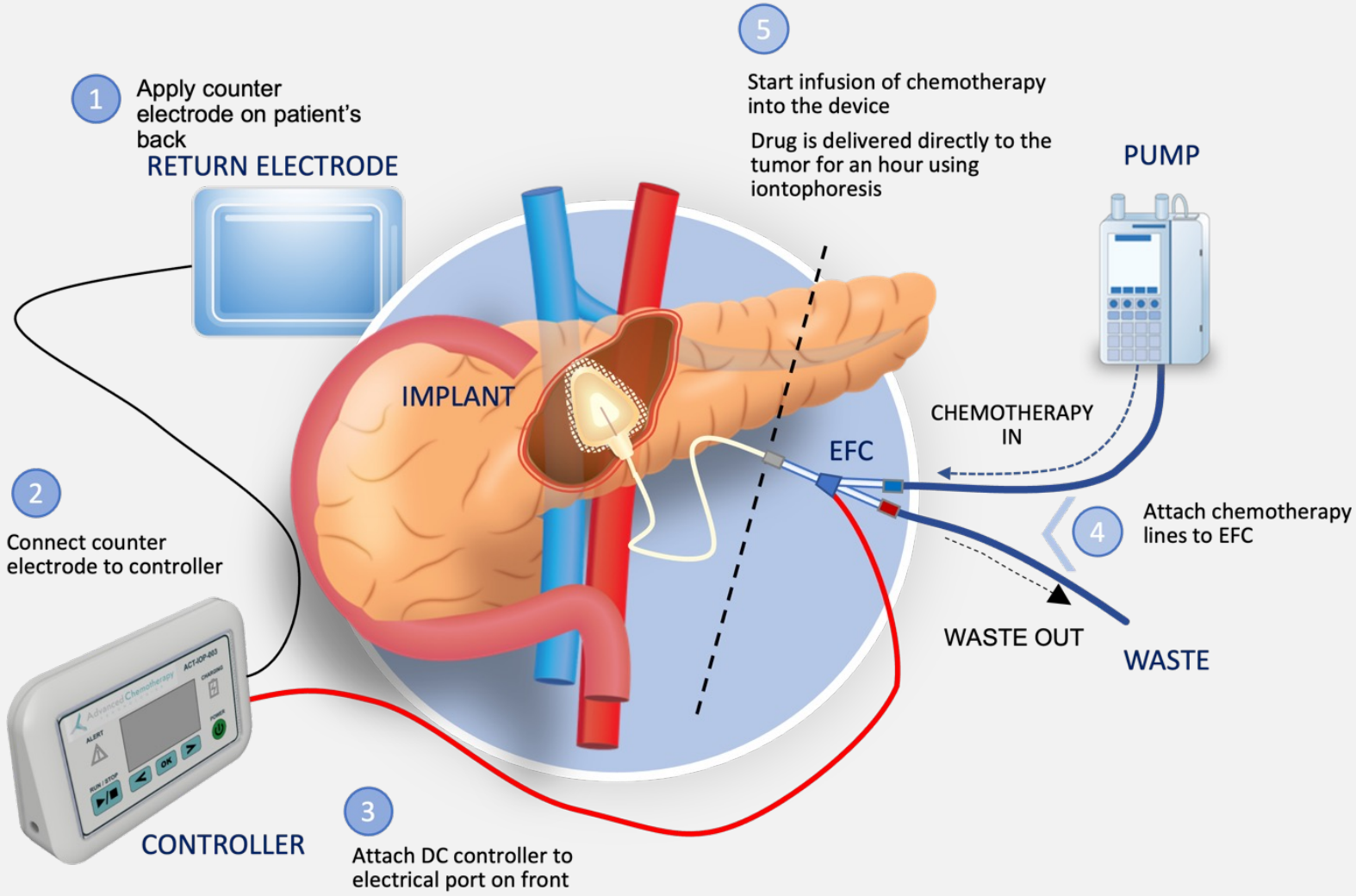


1 Pancreatic Adenocarcinoma Management, JCO Oncology Practice Jan 2023

2 Cancer Facts and Figures 2022, American Cancer Society

IOP Gemcitabine for Pancreatic Cancer

Schematic of internal IOP device, external controller and pump



Canine PK Study

IOP gemcitabine concentration low in plasma, high in target tissue, full penetration of target organ

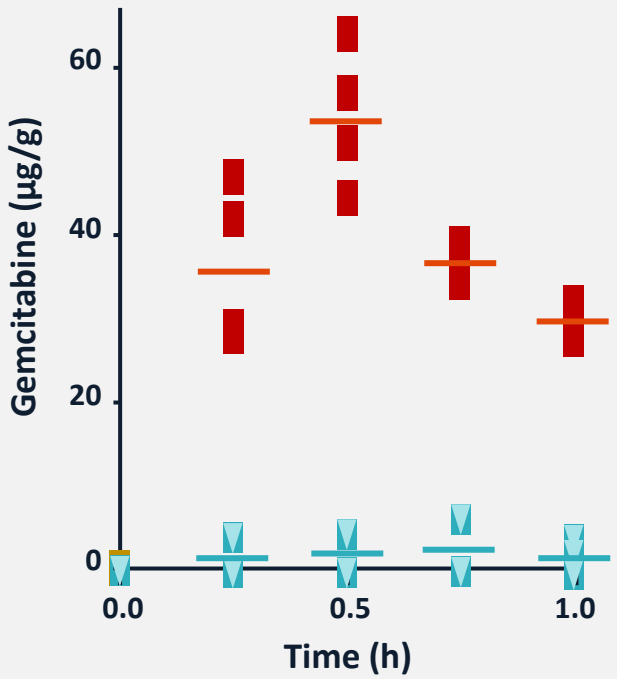
IOP Device (40 mg/mL)
60 min, 10 mA

IOP Device (10 mg/mL)
60 min, 10 mA

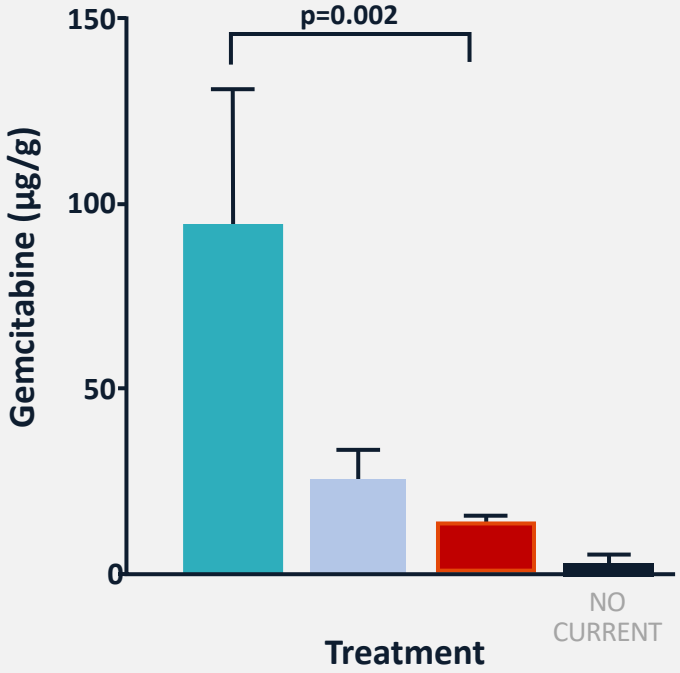
IV (1 g/m²)
NO CURRENT

IOP Device (10 mg/mL)
NO CURRENT

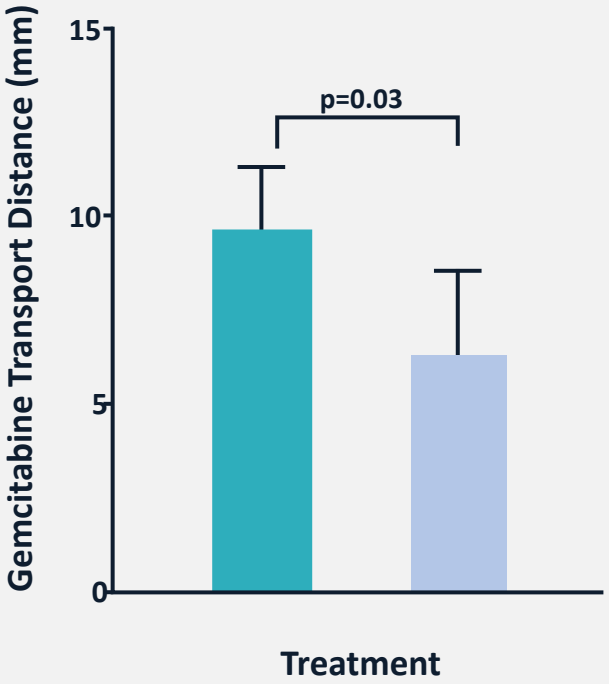
PLASMA CONCENTRATION
DURING Dose Administration



TISSUE CONCENTRATION
AFTER Completion
of Dose Administration



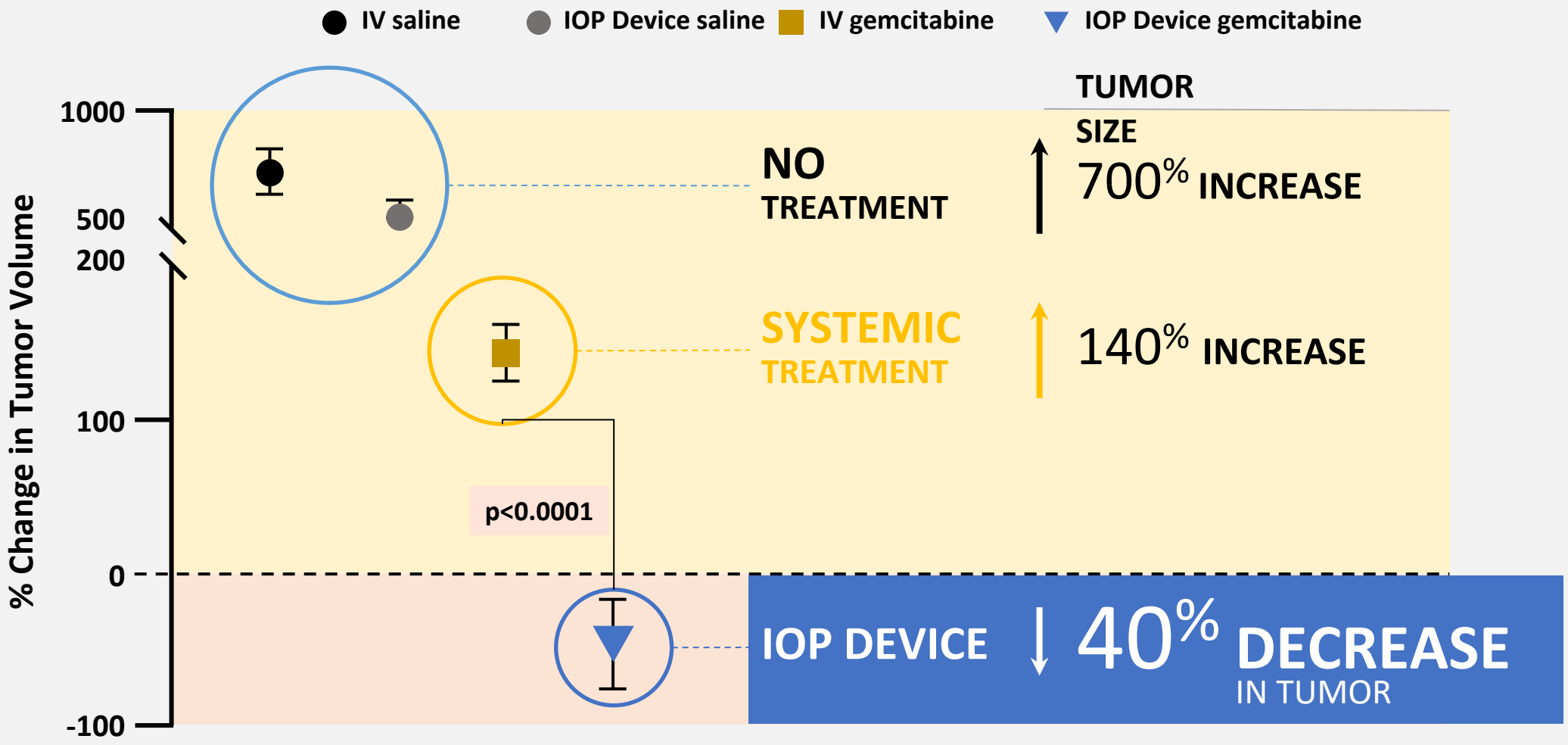
TRANSPORT DISTANCE
AFTER Completion
of Dose Administration



"Local iontophoretic administration of cytotoxic therapies to solid tumors", Byrne JD et al. *Sci Transl Med*. 2015 Feb 4;7(273)

Orthotopic PDX Murine Model

Iontophoresis delivers a dramatic impact on tumor size



"Local iontophoretic administration of cytotoxic therapies to solid tumors", Byrne JD et al. *Sci Transl Med*. 2015 Feb 4;7(273)

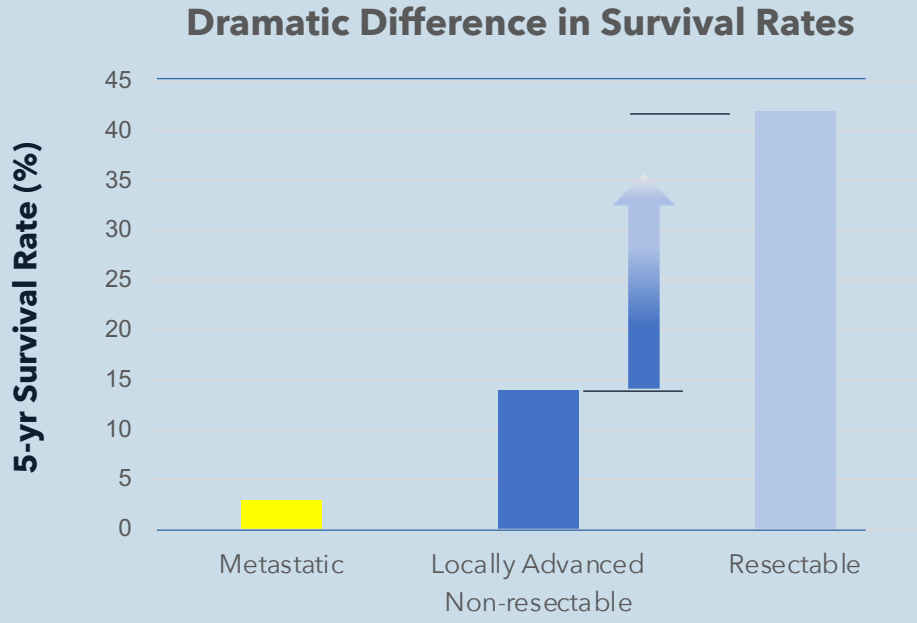
Product Vision

Gemcitabine for Pancreatic Cancer
- Gemcitabine is a powerful anti-cancer agent
- Activity hampered by dose limiting toxicity and tumor resistance factors

IOP gemcitabine
- High drug conc. in pancreas, little to no systemic
- Dramatic reduction in tumor volume

5–year survival rates – define unmet need
- 44% - resectable
- 14% - locally advanced nonresectable

Status
- IND cleared by FDA
- Phase 1b in Australia – capital efficient strategy
- Study initiation mid 2024



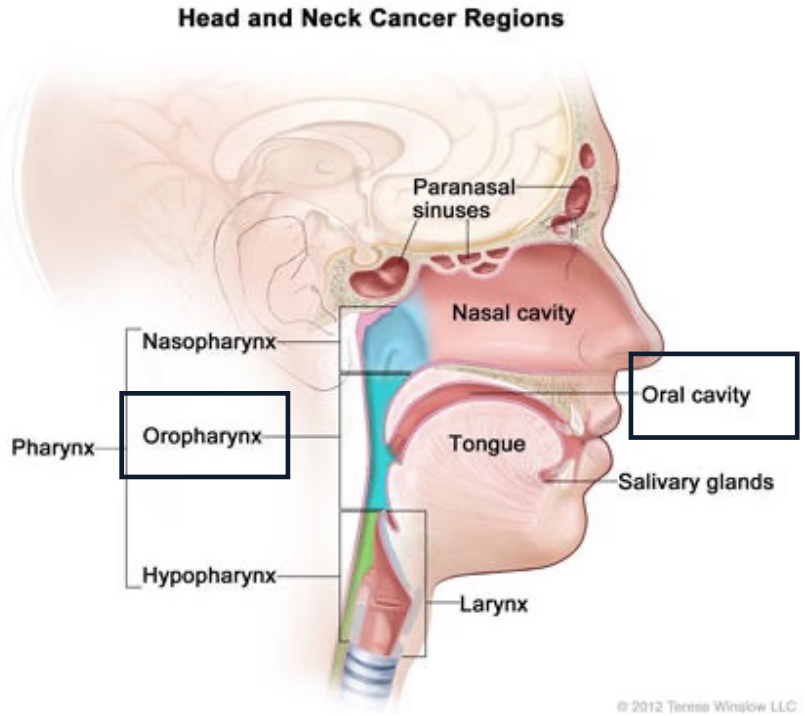
Treatment goal >>> **reduce** tumor burden, **restage** nonresectable to resectable

Pipeline:
Head & Neck Cancer

IOP cisplatin for locally recurrent Oral Cavity & Oropharynx cancer

Locally Recurrent Head and Neck Cancer

Parameter	Characteristics
Indication	Locally recurrent oral cavity & oropharynx squamous cell carcinoma (SCC)
Patient Population	• Typically, older men with history of smoking and drinking often in poor health • Present treatment compliance and socioeconomic challenges
Unmet Medical Need	1. Recurrent rates of 25-50% following first line treatment 2. No effective treatment alternative 3. 5-year survival rate of 30%[1] 4. QoL issues arise as salvage surgery is the only treatment option, damage to sensitive Head & Neck structures 5. Certain patients are ineligible for systemic platinum drugs due to its nephro (and other) toxicity
Treatment	IOP Cisplatin

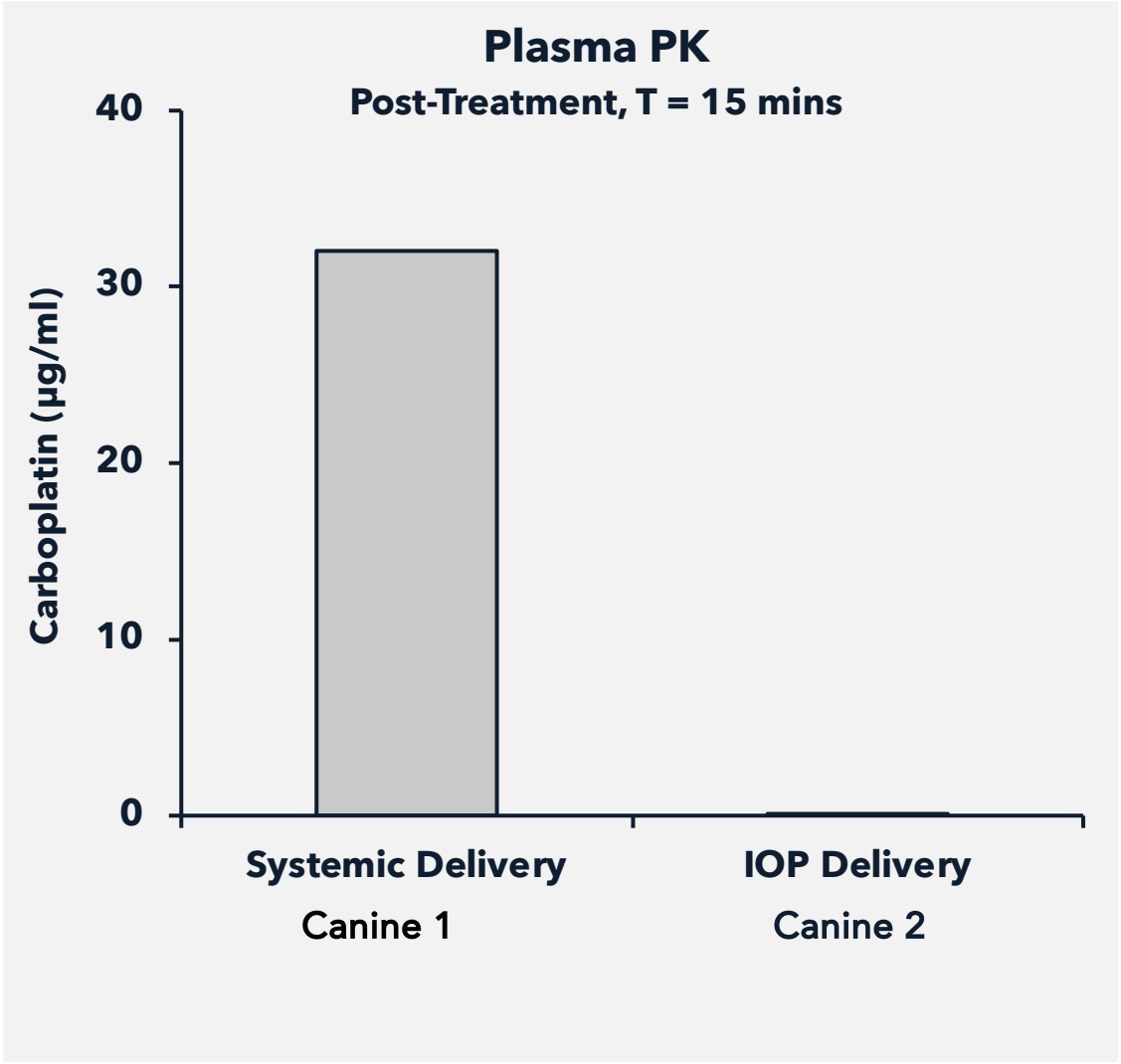


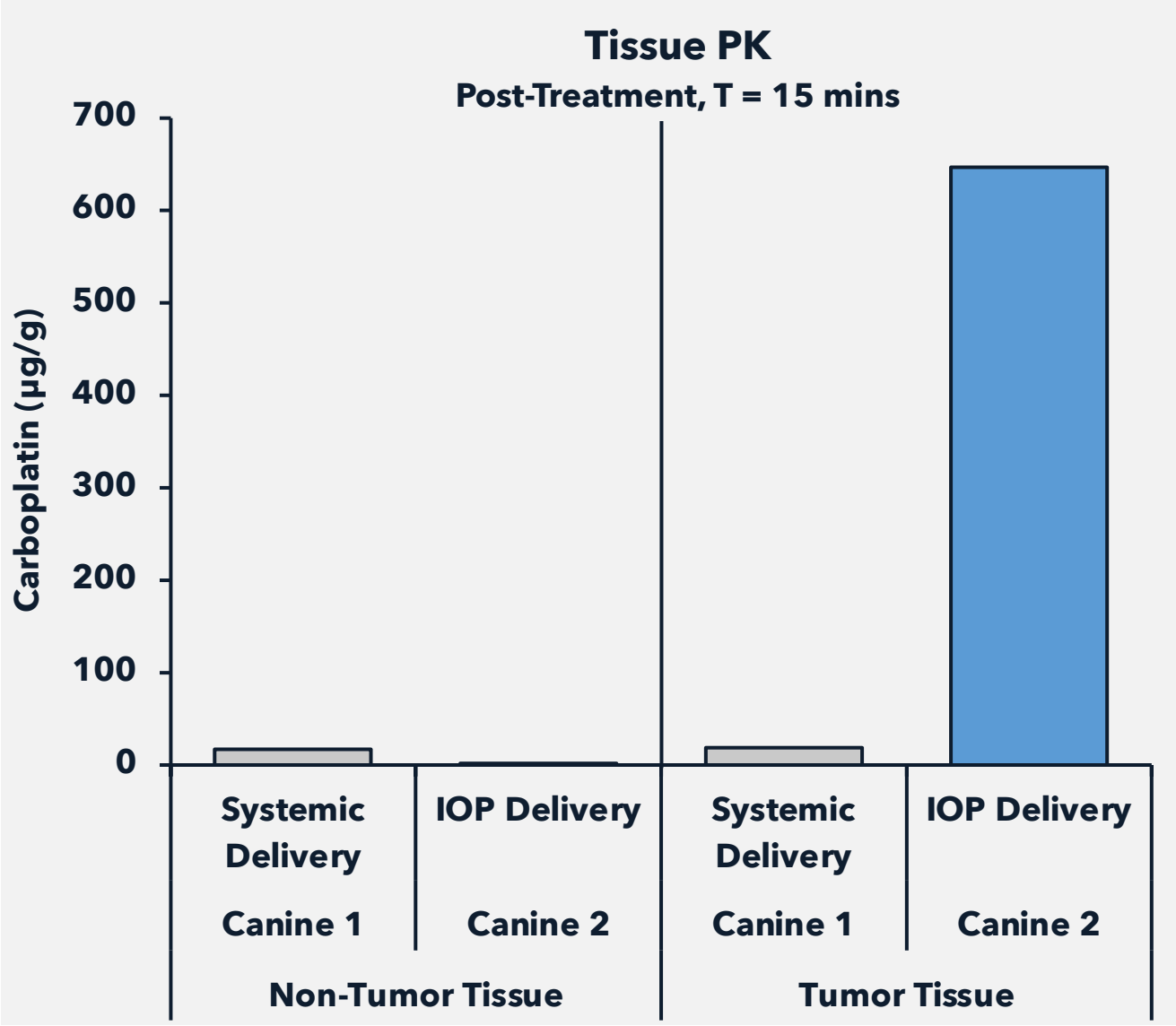
13,635 - 27,270 locally recurrent oral cavity & oropharynx cancer [2-5]

[1]Wang et. al, *Chin J Cancer*, 2013
[2]https://www.cancer.org/cancer/types/oral-cavity-and-oropharyngeal-cancer/about/key-statistics.html
[3]Carvalho et. al, *Oral Oncology*, 2003, [4]Shetty et. al, *Frontiers in Oral Health*, 2021, [5]Zittel et. al, *Clinical Oral Investigations*, 2021

Canine Oral Cavity Cancer – IOP carboplatin

34X Higher Carboplatin Concentration in target tissue

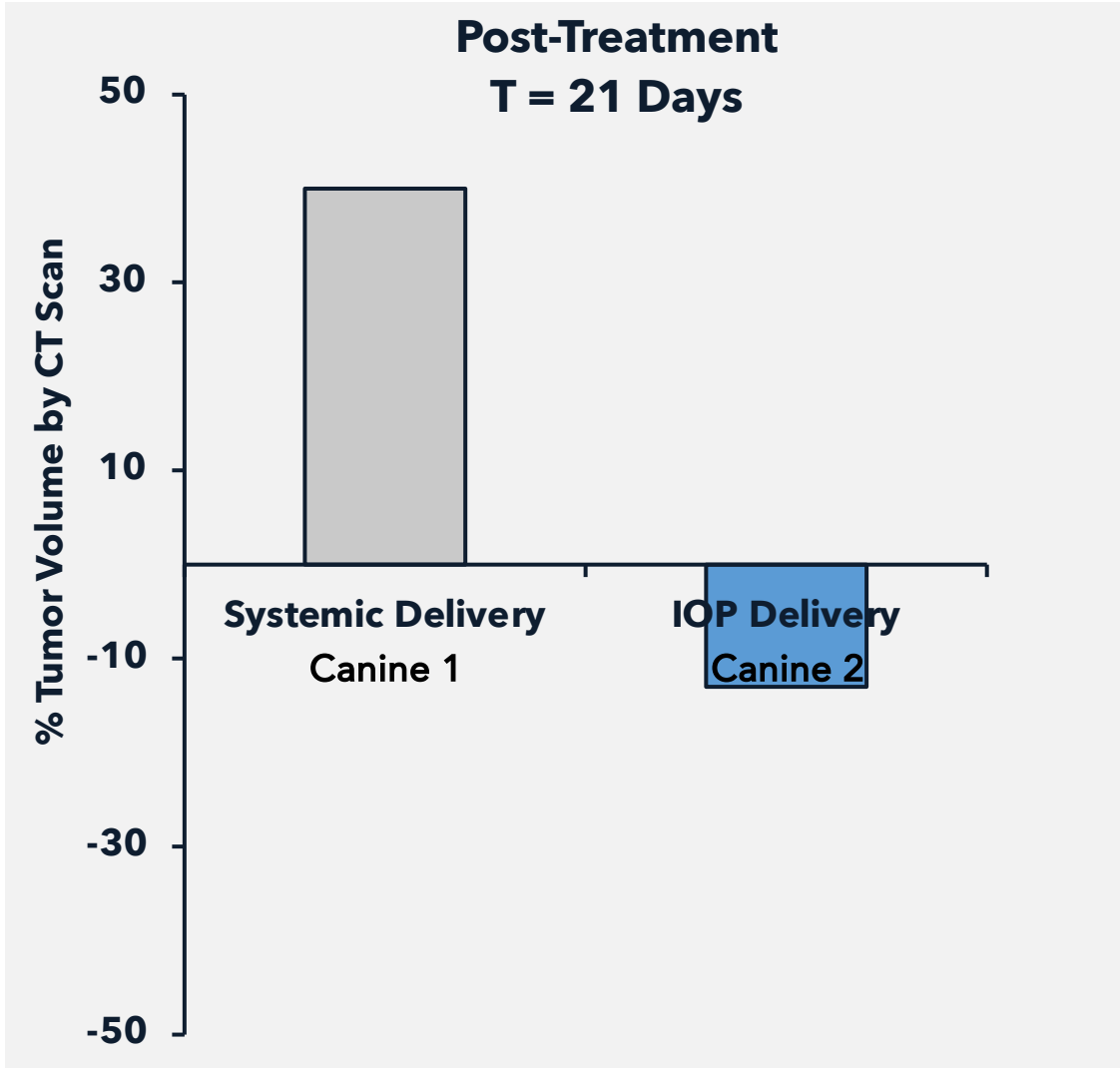




Canine Oral Cavity Cancer – IOP carboplatin
Single Treatment Delivers Tumor Reduction

Pre-Treatment
T = 0 Days

Post-IOP Treatment
T= 21 Days



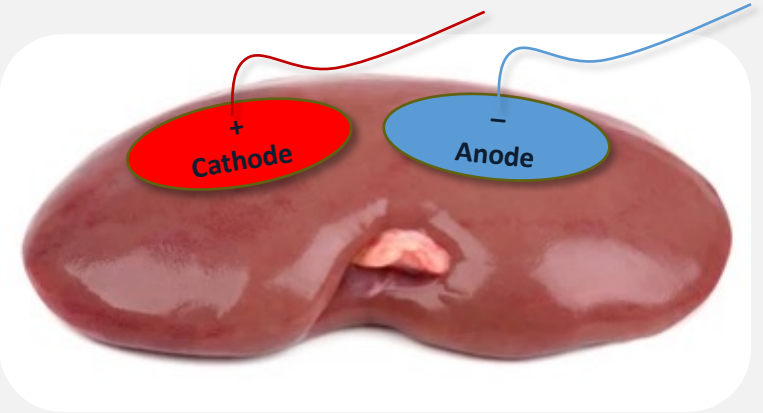
Secondary Tumor on Tonsil Displayed 50% Volume Reduction Following IOP Carboplatin Tx

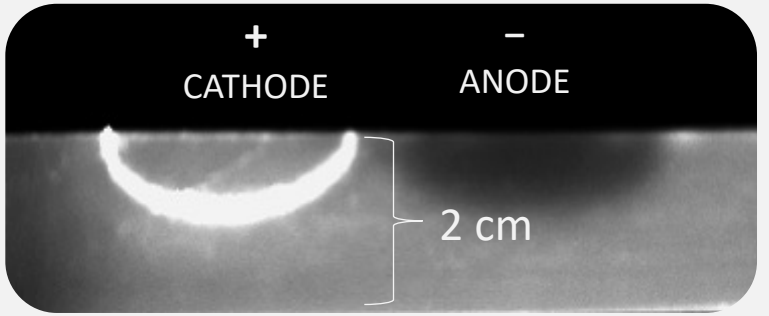
Ex-hepatic Organ-targeted GM Delivery

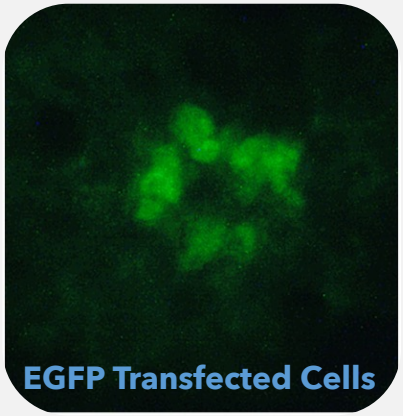
Delivered mRNA *in vivo* to porcine kidney:

- Delivered:
  - Precisely, specifically and actively by non-blood pathways
  - Using simple non-viral encapsulating agents
  - Significant eGFP mRNA expression following transfection
- Benefits:
  - Lower drug dose, IOP cell wall permeation enhances transfection
  - Greater efficacy: improved drug exposure of target cells
  - Lower toxicity: low non-target organ drug exposure
- Highly Modulable System:
  - A variety of delivery platforms and form factors
  - Acute / sub-chronic and chronic RNA delivery
- Multiple Areas of Application:
  - Cancer Immunotherapy
  - Gene Editing
  - Protein Replacement Therapy
  - Cardiovascular & Neurodegenerative Diseases

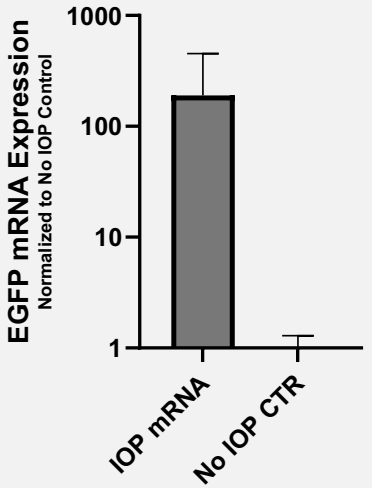
Cationic Liposome







EGFP Transfected Cells



eGFP-mRNA expression

Intellectual Property

Broad granted international patents. An ongoing program of filings, supplemented by Orphan Drug, know-how and other market exclusivity mechanisms

Granted patents on the internal delivery of therapeutics using iontophoresis

Granted patents on the internal delivery of therapeutics using iontophoresis in conjunction with radiation

Continuations and new filings on patents in prosecution covering enhancements and improvements

Board and Executive Team

Joe DeSimone, PhD
Founder & Board member

Sanjiv Sam Gambhir Professor of Translational Medicine and Chemical Engineering, Stanford University

Founder, Carbon Inc. Valued over $2.4 billion

Recipient, Presidential National Medal of Technology & Innovation

Jen Jen Yeh, MD
Founder & Board member

Professor and Vice-Chair Surgical Research, Lineberger Cancer Center, UNC-CH

Inaugural recipient, LEAD Project Grant, Lustgarten Foundation

Developer, single sample classifier licensed to GeneCentric Therapeutics

Paula Hammond, PhD
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Institute Professor and Department Head Department of Chemical Engineering, MIT

Appointee, President's Council of Advisors on Science and Technology (PCAST)

Founder, LayerBio, Inc.: DOD contract for ocular device

Nessan Bermingham, PhD
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Operating Partner at Khosla Ventures

Founder, President, and CEO at Intellia Therapeutics

Founder & Board Member, Liberate Bio

Founder & Executive Chair, Korro Bio

Michael Aldridge
CEO & Board member

CEO, Peplin: sold to LEO Pharma – $300 million

SVP Corp Dev., Questcor: sold to Mallinckrodt – $5.6 billion

SVP Corp Dev., Codexis: partnership w/ Nestle – $357 million

CEO, Hexima

Tony Voiers
COO

Developer of 13 products (8X PMA and 5X 510k devices)

CEO, Novocor Medical

Director of R&D, Closure Medical sold to J&J - $410 million

25 years medical device management

Bill Daunch, PhD
CTO

Sr. Director of R&D, Allergan: development of SERI Surgical Scaffold

Critical product launches supporting a $400 million technology portfolio at Ethicon

22 years medical device development

Nancy Sacco, PhD
VP, Clinical Development

Chief Development Officer, Hexima

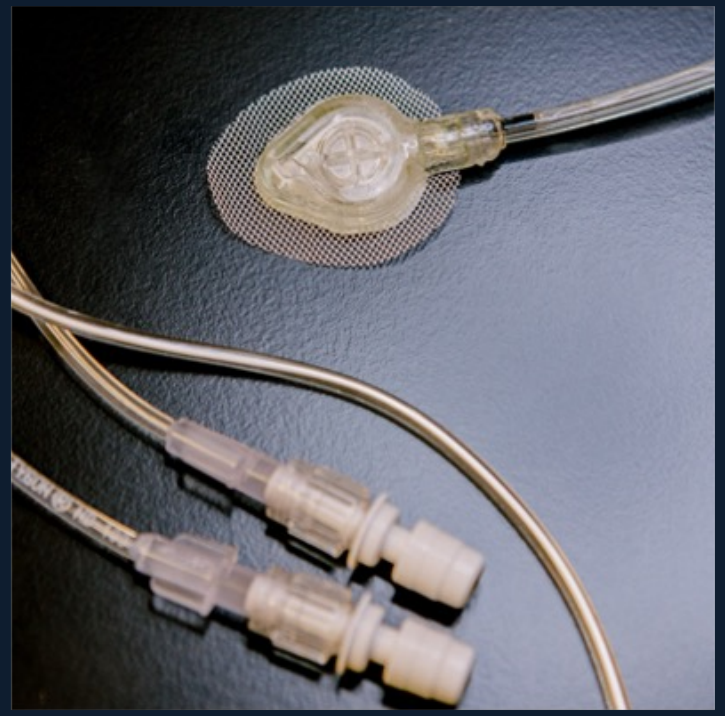
Executive Director; Astellas Pharma (Xtandi)

AveXis (ZolgenSMA)

25 years pharmaceutical & gene therapy development experience

Focal Medical

Thank you



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