Precisely target the site of action to dramatically improve therapeutic effect

USING ENERGY BASED SYSTEMS





Overview



Limitations of Traditional Drug Delivery

Dominant oral and parenteral route often impacted by:

- Metabolism
- Off-target activity and dose limiting side effects
- Barriers to drug penetration and uptake
- Reliance on passive drug uptake

Optimal Solution

- Precision delivery of target drug levels
- Actively into diseased cells
- No exposure elsewhere



Focal Medical's Solution

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- Internal Implanted Iontophoretic (IOP) Device Active, local, energy-based delivery technology
- Precisely targets diseased tissue, using non-blood pathways
- Bypasses delivery barriers and deactivation pathways.



Precision targeting using iontophoresis



Iontophoretic Internal Implant ElectroFluidic Connector Line

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External DC Power Controller IV Infusion Pump



Potential Areas of Application

Inoperable Solid Tumors

- Locally advanced non-resectable tumors; or
- Tissue sparing critical to QoL; and
- Very poor survival rates

<u>Genomic Medicine</u>

- Active delivery by non-blood pathways to nonhepatic organs
- Immunogenic, other safety and pay load concerns

Oral Cavity Cancer Esophageal Cancer Bladder Cancer Glioblastoma **Genomic Medicine**



Iontophoretic gemcitabine for pancreatic cancer







Pancreatic Cancer

- "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

Concentration low in plasma, high in target tissue, full penetration of target organ



PDX Murine Model

Iontophoresis delivers a dramatic impact on tumor size



Product Vision

Gemcitabine for LANR Pancreatic Cancer

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

IOP gemcitabine

- High conc. in pancreas, little systemic
- Dramatic reduction in tumor volume

<u>5-year survival rates – define unmet need</u>

- 44% resectable
- 14% locally advanced non-resectable



Dramatic Difference in Survival Rates



Treatment goal >>> reduce tumor burden, restage LANR to resectable

Genomic Medicine Delivery Challenges



Our GM Solution: Benefits and Challenges

Potential Benefits:

- Targeted delivery. Precisely, specifically and actively by non-blood pathways
 - Selected and difficult to penetrate organs
 - Improved drug exposure of target cells
 - Lower dose
 - Limited systemic exposure or ex-target organ effects
- Naked (x)RNA
 - No requirement for encapsulating or modifying agents
- Highly Modulable System
 - Current/ Voltage/ Wave Form/ Time/ Concentration
 - A variety of delivery platforms

Potential Challenges:

- Burden of invasive surgery
- Potential limitations of molecule size and charge

Leveraging the IOP platform Inoperable Solid Tumors

IOP Treatment of Inoperable Solid Tumors

- Locally advanced non-resectable tumors
- Tissue sparing critical to QoL
- Very poor survival rates

Research Program

• Evaluating oral cancers in companion dogs at Virginia Tech



Intellectual Property

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



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

Bill Daunch, PhD

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



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

Nancy Sacco, PhD VP, Clinical Development

Chief Development Officer, Hexima Executive Director; Astellas Pharma (Xtandi) AveXis (ZolgenSMA) 25 years pharmaceutical & gene therapy development experience



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 & Board member

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



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Thank you

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