

### Advancing therapies through cell signaling

Darrin Uecker, CEO/President + Richard Nuccitelli, Ph.D., CSO [ April 19, 2016 ]

### Information Included In This Presentation



We have filed a Registration Statement on Form S-1 (including a prospectus) (our "Registration Statement") with the Securities and Exchange Commission (the "SEC") for the offering to which this communication relates. Before you invest, you should read the prospectus in that Registration Statement, as subsequently amended to date, and other documents that we have filed with the SEC for more complete information about us and this offering. You may get these documents for free by visiting EDGAR on the SEC website at www.sec.gov. Alternatively, we, our underwriters, or any dealer participating in this offering will arrange to send you the prospectus if you request it.

This presentation contains certain forward-looking information about Pulse Biosciences. Forward-looking statements are statements that are not historical facts. Words such as "anticipate," "believe," "estimate," "expect," "intend," "may," "plan," "predict," "project," "target," "potential," "will," "would," "could," "should," "continue," "strong," "up coming," and similar expressions are intended to identify forward-looking statements. These statements include, but are not limited to, statements regarding our ability to successfully develop and commercialize our products; our ability to expand our long-term business opportunities; plans to conduct future clinical trials; the outcomes of our development activities, and their underlying assumptions; and our future performance.

Forward-looking statements may address the following subjects among others: expected products, applications, customers, technologies and performance, insurance reimbursements, results of clinical studies, success of research and development and our expectations concerning our business strategy. Forward-looking statements involve inherent risks and uncertainties which could cause actual results to differ materially from those in the forward-looking statements. Investors should review these and other risks inherent in our forward looking statements and our company under the caption "Risk Factors" in our most recently filed Registration Statement. The Company does not undertake, and specifically disclaims any obligation, to update or revise such statements to reflect new circumstances or unanticipated events as they occur.

In this document, we refer to information regarding potential markets for products and other industry data. We believe that all such information has been obtained from reliable sources that are customarily relied upon by companies in our industry. However, we have not independently verified any such information.



### Pulse Biosciences Overview



### Novel therapeutic tissue treatment platform

- Nanosecond Pulsed Electric Fields (nsPEF) induce a unique cellular response
- Addresses multiple potential markets Tissue Ablation, Oncology, Dermatology/Aesthetics, and Veterinary

#### Proprietary position in nsPEF technology and IP

- Leveraging investment in R&D, IP, and pre-clinical studies from company and partners over the last 15 years
- Dominant IP position with 39 granted patents and 41 pending worldwide

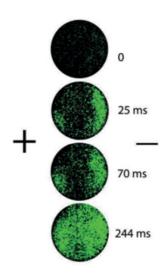
#### Capital efficient commercialization strategy

- U.S. FDA 510(k) for the platform to perform soft tissue ablation
- Pulse generator platform being developed to pursue a number of applications
- Potential strategic partnerships for commercial reach

# Unique nsPEF Cellular Effect



- Nanosecond pulses applied across a cell create transient nanopores in the cell membrane and organelles.
- The nanopores allow Ca<sup>2+</sup> to flow into the cell, stressing the endoplasmic reticulum, and inducing unique cellular responses.

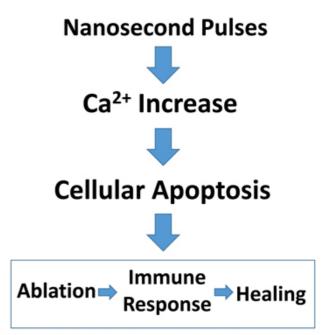


Ca<sup>2+</sup> increase in a melanoma cell after a single 100ns pulse, shown over time using fluorescence

## Nano-Pulsed Electro-Signaling (NPES)



- Modulating nanosecond pulses can induce cellular apoptosis, the body's natural programmed cell death process.
- Apoptosis can lead to ablation, natural healing, and when applied to malignant cells immunogenic cell death.
- This novel non-thermal tissue treatment technology is called Nano-Pulsed Electro-Signaling.



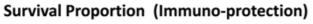
## **NPES for Tissue Treatment**

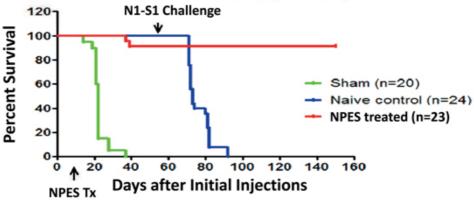


- We believe NPES will deliver:
  - Precise and consistent ablation zones.
  - Short treatment times seconds to several minutes.
  - Healing with little or no scaring.
  - An ability to induce immunogenic apoptosis, leading to an adaptive immune response against cancer cells.
- Current treatment technologies that burn or freeze tissue, cause thermal necrosis and inflammation, which can result in secondary tissue damage and scarring.

# NPES – Immune Response Data





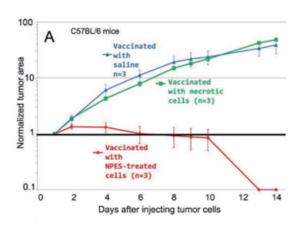


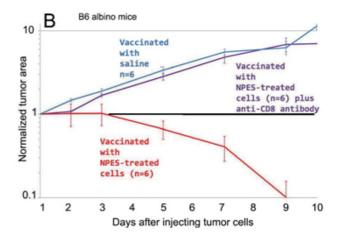
 23 Rat liver tumors were ablated, seven weeks later secondary tumors were injected and failed to grow in any of the animals.

Chen et al. Euro J of Cancer 50: 2705 (2014)

# NPES – Immune Response Data







Tumor cells treated in vitro with NPES were used to vaccinate mice against fibrosarcoma tumors. Three weeks post vaccination animals were challenged with a fibrosarcoma cell injection, all NPES vaccinated mice resisted tumor growth unless they were pre-treated with an anti-CD8 antibody.

\*\*Nuccitelli et al. PLOS One 10(7):e0134364 2015)\*\*

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- Pulse Biosciences is developing the first tunable NPES platform for human clinical use, the PulseTx™.
- Designed to support a wide array of single use electrodes, supporting a razor – razor blade revenue model.
- Plan to submit a 510(k) for soft tissue ablation.
- Tunable design is based on a novel pulse generator architecture.

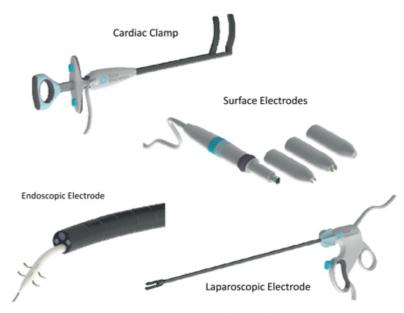


PulseTx<sup>™</sup> System Design

## PulseTx™ Electrodes



- PulseTx<sup>™</sup> is designed to support a broad array of electrodes.
- Relatively small incremental investment in electrode development.
- Designs for surface treatments in open surgery and minimally invasive procedures.



PulseTx<sup>™</sup> Electrode Designs

# **NPES Applications**



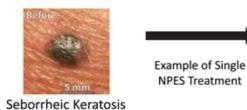
- Pursuing three significant vertical markets: Dermatology/Aesthetics, Oncology, and Tissue Ablation.
- Published data validates the use of NPES in each of these verticals.
- Veterinary Medicine Oncology may represent an additional opportunity.



## Dermatology/Aesthetics Vertical



- Current treatments of freezing, burning or cutting out lesions leads to longer and multiple treatments with disappointing cosmetic results
- NPES can provide a compelling treatment option
  - Apoptosis can result in complete ablation and excellent cosmetic result
  - Short treatment time and we believe there is potential for single visit treatment
  - In office treatment that will fit into the office workflow
  - Immune response potential





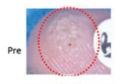
# Dermatology/Aesthetics Vertical

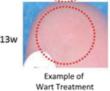


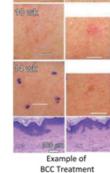
- Feasibility demonstrated in human pilot studies using NPES for benign and malignant skin lesions
- NPES Basal Cell Carcinoma Pilot Study
  - Seven of ten lesions completely ablated;
  - No visible scars in successfully ablated lesions; and
  - We believe the study demonstrated NPES is safe and can offer a fast and scarless alternative to current standard of care.

### NPES Wart Pilot Study

- Pilot study of up to 40 patients;
- We believe this trial will demonstrate the feasibility of NPES in effectively treating warts; and
- May help understand the potential for the treatment of multiple HPV wart indications.







## Dermatology/Aesthetics – Go to Market



- Planning for a clinical study in dermatology in 2016 to validate treatment prior to commercialization.
- Initial regulatory clearance through the straightforward FDA 510(k) process will be pursued.
- We believe the PulseTx will be a good fit in the product portfolios of the large strategics in the dermatology and aesthetics space.

### Oncology



### Cancer immunotherapy is revolutionizing cancer care

- Major biopharma companies investing significantly in internal programs and M&A;
- Checkpoint inhibitors have shown good clinical results; and
- Leading cancer centers are marketing direct to consumers.

### PulseTx™ platform may play an important role

- NPES treatment may enable drug-free local tumor control that exposes the immune system to the local tumor antigens;
- Potentially overcomes many of the challenges with oncolytic viral vaccines with potentially better results; and
- Potentially synergistic with other immunotherapeutics, e.g. checkpoint inhibitors.

Napster cofounder Sean Parker donates \$250 million to create cancer immunotherapy institute



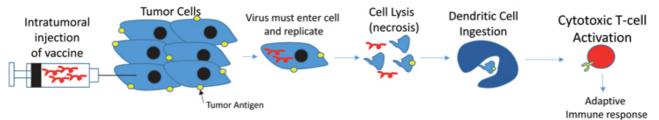
Note: Pulse Biosciences is not receiving any of the funds reference



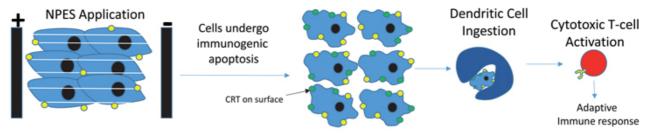
# Oncology - Immune Response Mechanisms



#### **Oncolytic Viral Immune Response**



#### **NPES In-Situ Vaccine Immune Response**



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## Oncology – Go to market



### Demonstrate NPES provides <u>local</u>, <u>drug-free</u> tumor destruction and the potential to elicit a systemic <u>adaptive immune response</u>

- Planning to execute a small study using 510(k) cleared system and IDE approval to demonstrate local tumor control and immune response.
- The first clinical application may be in the treatment of melanoma.
- Several additional applications may follow quickly once NPES is validated in melanoma head and neck, liver, and lung cancer are all targets.

### Partnership opportunities with <u>medtech and biopharma</u> companies

- We believe there are a number of oncology medtech companies that will be interested in a partnership.
- Biopharma companies involved in immuno-oncology have shown preliminary interest.

## General Tissue Ablation – Partnership Strategy



- Engage strategic partners in cardiac ablation
- Partnership opportunities in lung ablation applications
  - Potential applications include asthma, COPD, and chronic bronchitis
- Additional applications in ENT and GI specialties may be pursued through partnerships

### Veterinary



#### Commercial Rationale

- It has been reported\* that:
  - there are over 70 million pet dogs in the U.S.
  - cancer is the #1 cause of death in dogs over the age of two
  - 50% of all dogs will acquire cancer, 25% of dogs will die from cancer
- Existing therapies tend to negatively impact quality of life.
- No regulatory clearance needed.
- May provide a therapy that is easier for the veterinarian to sell to pet owner.

#### Medical Rationale

- May provide a simple procedure with minor side-effects as compared to drugs or more significant surgical procedures.
- Can de-bulk tumor with potentially increased immunogenic activity to other known therapies.

\*U.S. Pet (Dog and Cat) Population Fact Sheet, American Humane Association, 2012

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# Veterinary – Go to Market



- Plan to execute studies at major veterinary medicine center(s) to validate scientific thesis
- Plan to engage with high volume veterinary oncologists to perform commercial oriented studies
- Plan to engage large veterinary chains to assess market feasibility
- Potentially partner with large veterinary device or oncology companies

## **Intellectual Property**



- We believe our NPES IP position enables value creation based on the potential for multiple medical indications and multiple business models that can be pursued.
- Patent Portfolio
  - 39 issued worldwide
  - 41 pending worldwide
- Current patents and patent applications describe
  - Use of NPES to induce cell apoptosis or cell death
  - NPES pulse generators, electrodes, and indications
  - Use of NPES to induce an immune response

## **Commercialization Strategy**



- Complete development of the first tunable NPES platform, PulseTx™, to support an array of electrodes.
- File for and obtain a 510(k) clearance of the PulseTx<sup>™</sup> System for soft tissue ablation.
- Pilot studies and partnering pre-510(k) clearance.
- Pursue partnerships in applications where strategics have domain expertise and an established distribution channel.

### Pulse Biosciences Management Team



### Darrin Uecker, President/CEO

- 20+ years medical device experience
- COO of Auxogyn, CEO/President of Gynesonics, CTO of RITA Medical
- Experience in Surgical Robotics, Ablation, Women's Health

### Rich Nuccitelli, Ph.D. – Chief Science Officer

- Over 35 years experience in biophysics, bioelectrics and medical devices
- Over 120 published scientific papers and four books
- Past President of the Bioelectromagnetics Society

#### Brian Dow, CFO

- Experienced MedTech CFO and finance executive, in public and private companies.

### Dave Danitz, VP of Engineering

- 15 years medical device R&D product development experience

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## **Pulse Biosciences Board of Directors**



- Darrin Uecker, President/CEO, Director
- Robert Levande, Chairman (non-Executive)
  - 26 years Pfizer Medical Device Group, various senior management roles
  - Senior Managing Director at MDB Capital Group
  - Former Director Orthovita (NASDAQ)
  - Co-Founder of VirnetX (NYSE MKT)

### Thierry Thaure, Director

- CEO Cephea
- Former CEO Endogastric solutions
- Former SVP Accuray

#### Mitch Levinson, Director

- Founder & CEO Cerebrotech
- Founder & Former CEO Zeltiq

### Robert Greenberg, MD, Ph.D., Director

- Co-Founder of Second Sight Medical Products
- Co-managed the Alfred E. Mann Foundation

### **IPO Overview**



- 5,000,000 shares at \$4.00 per share
- 7.5 million shares outstanding pre-offering, 12.5 million post-offering
- Pre-money valuation approximately \$30 million; post-money approximately \$50 million
- Requirement to raise future capital via rights offerings to existing shareholders until company is profitable or shares reach \$12 per share
- Timing of offering early May

### **Pulse Biosciences**



- Broad platform technology with a dominant IP position;
- Experienced team capable of developing and commercializing the technology platform;
- A straightforward 510(k) path based on predicate ablation systems;
- A number of significant applications to pursue either independently or through partnerships;
- Capital efficient value creation plan; and
- Multiple value inflection milestones clinical data, partnership deals, PulseTx sales.

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[ 849 Mitten Road + Suite 104 + Burlingame, California 94010 + **Tel:** 650.697.3939 ]