



Pulse Biosciences®



Investor Presentation

October 2023

Forward Looking Statements

All statements in this presentation that are not historical are forward-looking statements, including, among other things, statements relating to the effectiveness of the Company's nsPFA technology and CellFX System to non-thermally clear cells while sparing adjacent non-cellular tissue, statements concerning the Company's expected product development efforts, such as advancement of its cardiac clamp through the appropriate FDA regulatory path and possible initiation of a first-in-human safety feasibility study of its nsPFA endocardial ablation catheter system, statements concerning the Company's future regulatory strategies and possible government clearances and approvals, statements concerning customer adoption and future use of the CellFX System to address a range of conditions such as atrial fibrillation, statements about the Company's future financing opportunities and operating expenses, and Pulse Biosciences' expectations, whether stated or implied, regarding whether the Company's nsPFA technology will become a disruptive treatment option for treating cardiac arrhythmias and whether future clinical studies will show the CellFX System is safe and effective to treat atrial fibrillation or any other medical condition, and other future events. These statements are not historical facts but rather are based on Pulse Biosciences' current expectations, estimates, and projections regarding Pulse Biosciences' business, operations and other similar or related factors. Words such as "may," "will," "could," "would," "should," "anticipate," "predict," "potential," "continue," "expects," "intends," "plans," "projects," "believes," "estimates," and other similar or related expressions are used to identify these forward-looking statements, although not all forward-looking statements contain these words. You should not place undue reliance on forward-looking statements because they involve known and unknown risks, uncertainties, and assumptions that are difficult or impossible to predict and, in some cases, beyond Pulse Biosciences' control. Actual results may differ materially from those in the forward-looking statements as a result of a number of factors, including those described in Pulse Biosciences' filings with the U.S. Securities and Exchange Commission. Pulse Biosciences undertakes no obligation to revise or update information in this presentation to reflect events or circumstances in the future, even if new information becomes available.



Powering the next generation in bioelectric medicine with **Nanosecond Pulsed Field Ablation** technology.

Proven Leadership Team



Kevin Danahy

Chief Executive Officer

Medtronic INTUITIVE Johnson & Johnson

ZIMMER BIOMET



Darrin Uecker

Chief Technology Officer &
Director

gynesonics computermotion



Mitch Levinson

Chief Strategy Officer

NELLCOR coolsculpting by ZELTIQ thermage



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AdventistHealth

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DDS
Director



Shelley D. Spray

Director

Positioned to Unlock the \$8 Billion Cardiac Atrial Fibrillation (AF) Market

Powering the next generation in bioelectric medicine with **Nanosecond Pulsed Field Ablation (nsPFA) Technology**



Proprietary Technology

Only company bringing novel Nanosecond Pulsed Field Ablation (nsPFA) technology to the health care of patients



Novel AF nsPFA Devices

nsPFA enabled applicators deliver highly differentiated value in the treatment of AF



Robust Patent Portfolio

Surrounding the technology, devices, and use of nsPFA

135

issued patents
globally
owned &
licensed

+99

Patent Pending
Applications

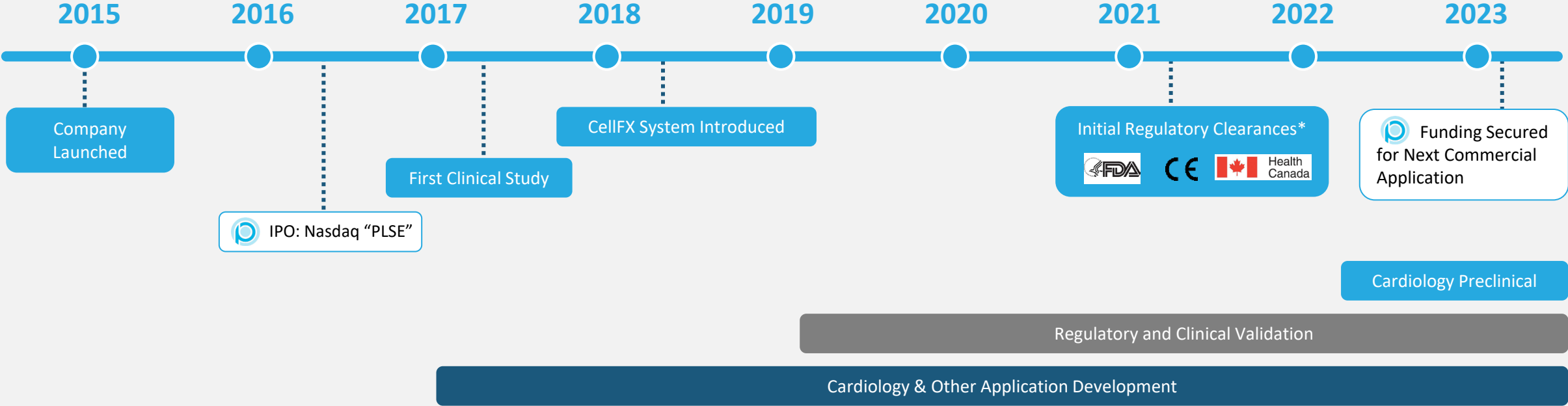


Broad Medical Device Expertise

Development expertise across many disciplines

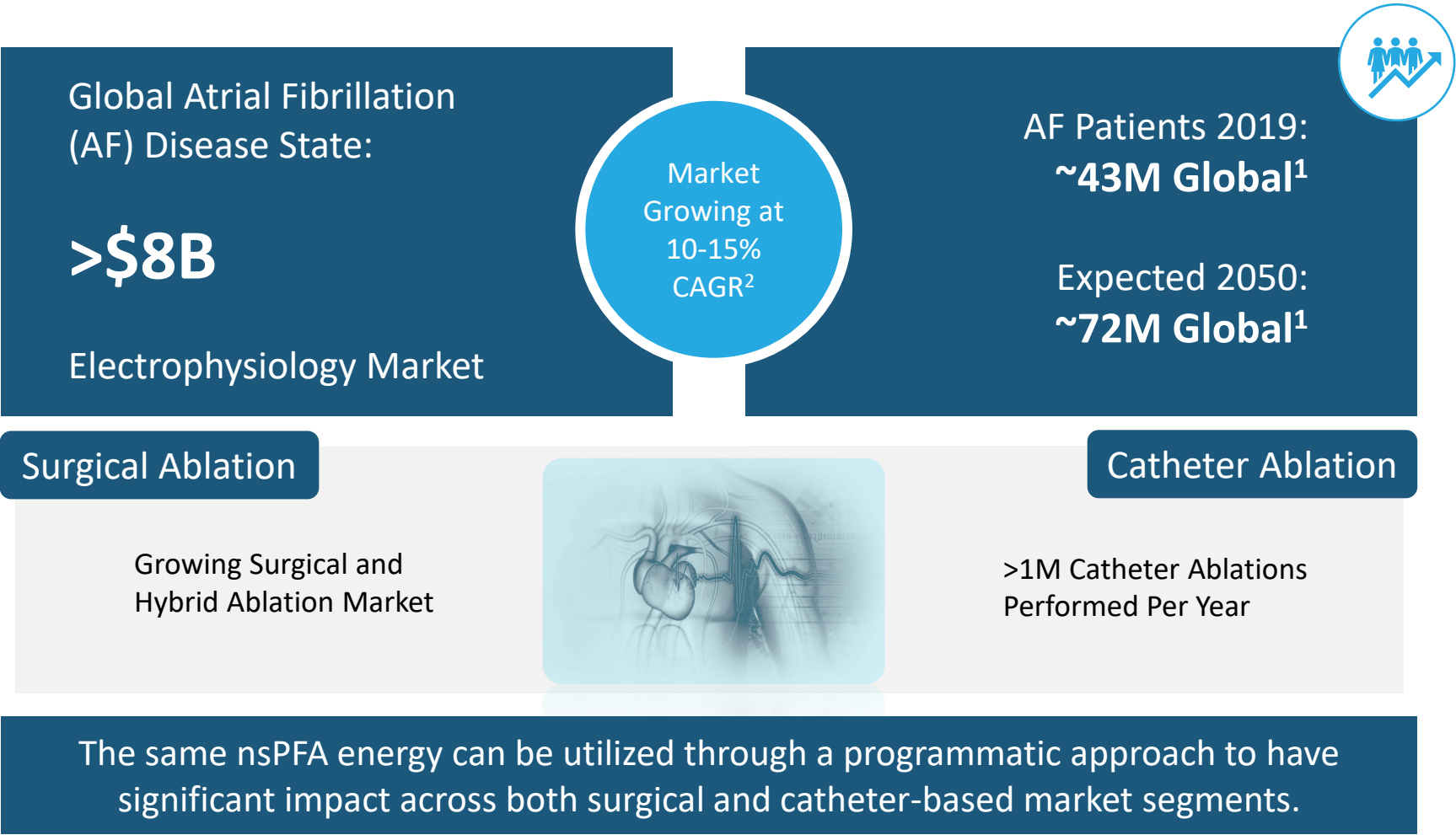


nsPFA Development – Engineering Around the MOA



*Initial Indications for the Treatment of Benign Cellular Lesions of the Skin

Addressing the Entirety of the Growing AF Market



1. Prevalence Data: Institute for Health Metrics and Evaluation (IHME). Global Health Data Exchange. Seattle, WA: IHME, University of Washington. Available at <http://ghdx.healthdata.org/gbd-results-tool>. Location: Countries, Year: 2019, Context: cause, Age: all ages, Metric: number, Measure: prevalence, Sex: both, Cause: B.2.8. Atrial fibrillation and flutter. (Accessed August 24, 2021)
2. Wong CX, Brown A, Tse HF, et al. Epidemiology of Atrial Fibrillation: The Australian and Asia-Pacific Perspective. Heart Lung Circ. 2017;26(9):807-879
3. Wolfe AF Symposium Report 2023
4. Oppenheimer Report 2020

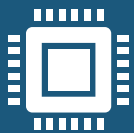
Current Ablation Technologies Require a Tradeoff – Safe or Effective



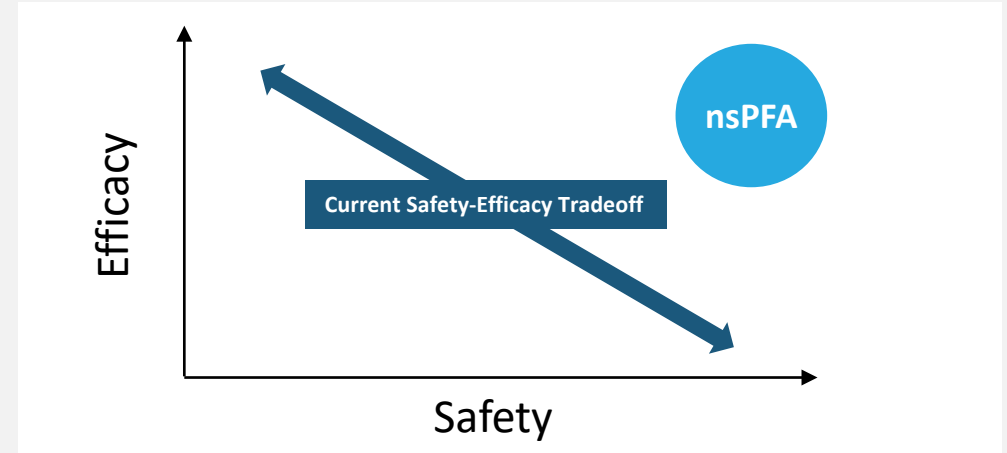
Because of existing safety profiles, physicians must use suboptimal parameters in order to protect surrounding tissues



More patients can be treated, and with better results, when physicians do not need to trade safety for efficacy



Standard PFA devices coming to market use RF-Style designs and off-the-shelf generators that are not designed specifically for cardiac PFA applications



	nsPFA	Standard PFA	RFA	CRYOTHERAPY
Cellular Specific	✓	✓	✗	✗
No Paralytics or Cardiac Sync Required	✓	✗	✓	✓
Nonthermal and Safe to Surrounding Tissue	✓	✓	✗	✗
Faster and More Precise Treatments	✓	✗	✗	✗

Proprietary nsPFA Energy Provides Unique Mechanism of Action

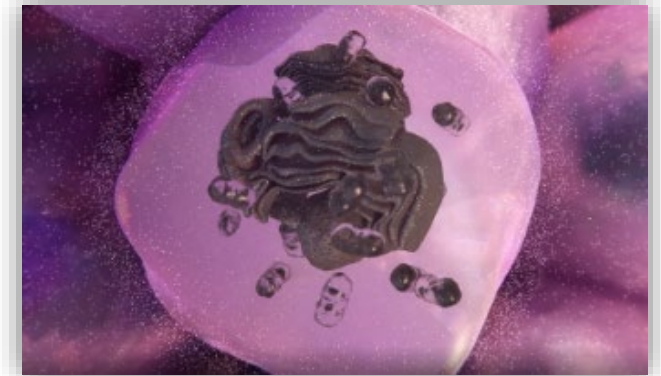
Stimulates elegant, precise Regulated Cell Death (RCD) in any cell without collateral damage



Nonthermal modality that delivers nanosecond duration pulses of electrical energy

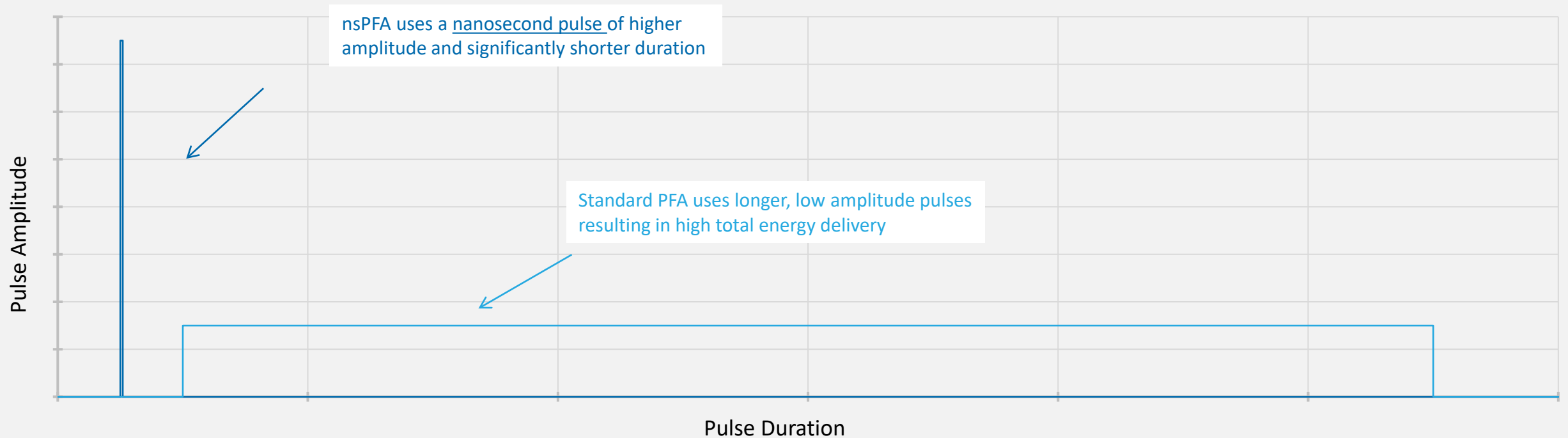


High speed nanosecond energy pulses penetrate the cell membrane and **disrupt internal cellular function**, leading to **regulated cell death (RCD)**



Unlike thermal (heat/cold) modalities, nsPFA directly impacts cellular structures while **sparing noncellular tissue** (primarily collagen)

Differentiated Properties of nsPFA Energy Pulses



- Nanosecond pulses can be **~500 times shorter** than microsecond pulses
- As a result, nsPFA can require **~20 times less energy** to ablate cardiac tissue

Advantages of nsPFA Technology

Catheter and clamp devices designed to improve patient outcomes

Novel Energy Modality



Devices that Leverage the Energy

Differentiated Clinical Results

Eliminating the substantial tradeoff between safety and efficacy



Better procedural efficacy than point ablation techniques

- More robust to placement
- Improved transmuralty



Better safety profile than current technologies

- Conscious sedation possible
- ECG-sync not required
- 20x lower thermal energy required

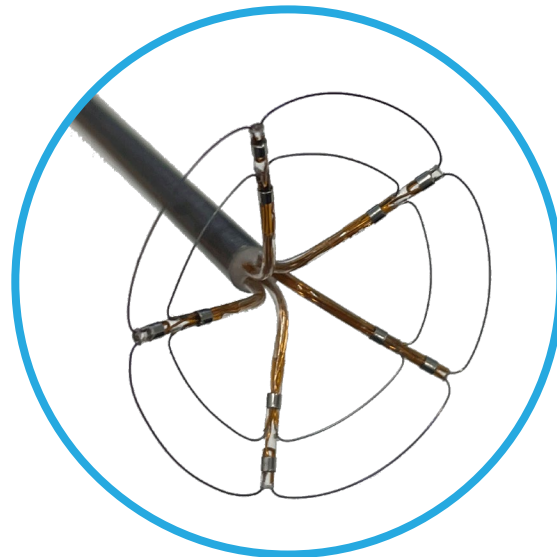


More patients can be treated due to faster procedure times

Catheter Delivery of nsPFA Energy – Cardiac Ablation



nsPFA Generator Platform



Proprietary nsPFA-Optimized Catheter Design



2-Day Endocardial Surface
~5cm Diameter

- Circumferential ablation catheter enabled by nsPFA energy for single-shot PVI ablation
- Reduced muscle spasm and nerve capture due to short duration nsPFA pulses
- No thermal injury due to lower energy of nsPFA pulses
- Preclinical data demonstrating safe, fast and effective ablations

nsPFA Preclinical Evidence Supporting Safety, Tolerability and Effectiveness

Tolerance/Effectiveness

Nanosecond Pulsed Field Ablation: Demonstration of Halo-shaped Lesions with a Novel Multielectrode System – Initial Preclinical Experience

Jacob S. Koruth MD, Iwanari Kawamura MD, Abhishek Maan MD, Daniel R. Muskatlow MD, Mohit K. Turagam MD, Marc A. Miller MD, William Whang MD, and Vivek Y. Reddy MD

Background

- Several pulse field ablation (PFA) technologies at various stages of pre-clinical/clinical development have recently been described.
- However, these employ pulse durations in the microsecond scale. In contrast, nanosecond PFA (nsPFA) utilizes pulse durations ~1000 times shorter.
- nsPFA may improve ablation efficacy as well as reduce collateral muscle and nerve stimulation, which are important from a clinical workflow perspective.

Objective

- To assess feasibility, safety and efficacy of nsPFA delivered using a novel PFA catheter in swine atrial tissue.

Method

- Ten swine underwent transforaminal venous access under general anesthesia.
- nsPFA lesions were delivered in both atria.
- A 11F circular, multielectrode PFA catheter (CALPX, Pulse Biosciences Inc.) was integrated with a custom electroanatomical mapping system (Map, CartoMap Inc., Boulder, CO).
- Superior vena cava (SVC), right superior pulmonary vein (RSPV) and discrete atrial applications were delivered with additional guidance from fluoroscopy and intracardiac electroanatomography.
- Single 5-sec applications (n=6, 0.4 J/cm²) and 3 repetitions of 5-sec applications (n=14, 1.3 J/cm²) were used. All swine were survived for 2-7 days before sacrifice.
- Lesions were delivered with preference for single applications to understand dose-related lesion dimensions.

Results

- The catheter was well visualized within the mapping system and conformed well to venous ostia. The nsPFA lesions were successfully delivered to all 22 of 22 atrial sites: 10-SVC, 6-RSPV, 4-discrete atrial applications.
- MRI phrenic and muscular stimulation were observed. One swine required 2 applications to improve RSPV atrial coverage, and in 3 swine, local anatomy precluded circumferential atrial coverage. Minimal PFA-related microbubbles were seen with ICE imaging.
- There were no instances of phrenic palsy, thrombus formation or ST-segment elevation noted acutely or in follow-up.
- Necropsy revealed wide, circumferential lesions for all 10 of 10 (100%) SVC and 5 of 7 (71%) RSPV targets.
- A characteristic halo-shaped lesion was observed with a wide contiguous band and central dark zone within the band (Figure).
- Transmurality necrosis was seen in 21 of 22 (95.5%) lesions. The mean depth and width of SVC and RSPV lesions were 1.8±0.4mm, 14.1±3.1mm and 4.6±2.6mm, 15.5±2.7mm, respectively.
- All four discrete lesions were identified with depths reaching up to 9.0 mm when 3 repeat applications were used.

No of Lesions	Site	Location	Mean Depth (mm)	Mean Width (mm)
6	SVC	SVC	1.85	14.0
4	5	SVC	1.68	14.3
6	15	RSPV	4.2	14.2
2	5	RSPV	5.1	21.4
4	15	ML, LA, UA	7.7	27.1

Conclusion

- Nanosecond PFA using this circular multielectrode catheter can create clinically-relevant circumferential wide lesions with minimal phrenic muscular stimulation.

Disclosures

- This study was supported by a research grant from Pulse Biosciences.
- Jacob Koruth has served as a consultant for and has equity in Pulse Biosciences. Vivek Reddy has served as a consultant to Pulse Biosciences, and has served as a consultant to, and has equity in CartoMap.

nsPFA can create clinically relevant circumferential wide lesions with minimal phrenic muscular stimulation.

Nanosecond Pulsed Field Ablation: Demonstration of Halo-Shaped Lesions with a Novel Multielectrode System: Initial Preclinical Experience (Jacob S Koruth MD, et al.)

Tolerance/Safety

Creating Deep Ventricular Lesions with Nanosecond Pulsed Field Ablation: Pathological and Imaging Insights from Preclinical Evaluation

Iwanari Kawamura MD, Vivek Y. Reddy MD, Carlos Santos-Gallego MD, Yuri Malyshov MD, Kelly Jia MD, Emmanuel Ekram MD, Joshua Lampert MD, Abhishek Maan MD, Daniel R. Muskatlow MD, Mohit K. Turagam MD, Marc A. Miller MD, William Whang MD, Sonawar R. Dabkapat MD and Jacob S. Koruth MD

Background

- Pulsed field ablation (PFA) has demonstrated considerable promise for catheter ablation of atrial arrhythmias.
- The majority of recent PFA technologies utilize pulses in the microsecond range.
- Pulse durations that are 100 to 1000 times shorter, nanosecond PFA (nsPFA), are an alternative PF waveform approach that may have important clinical implications.
- These nsPFA pulses can potentially eliminate near-field thermal injury, and reduce muscle and nerve stimulation coupled with improved ablation efficacy.

Objective

- To determine the feasibility of delivery and evaluation of nsPFA using a novel multielectrode catheter in healthy swine ventricles.

Method

- Eight swine received endocardial nsPFA applications via femoral transvenous access under general anesthesia.
- Pulses were delivered using a 11 F circular, multielectrode catheter (CALPX, Pulse Biosciences Inc.), and a proprietary nanosecond pulsing mode under fluoroscopic and intracardiac electroanatomographic guidance to both the right and left ventricles.
- All swine were survived for 2-7 days followed by necropsy.
- Two of 8 swine underwent 3 DT MRI (non-contrast T1, conventional bright blood LGE, dark blood LGE) at 2 days post-PFA.

Results

- A total of 15 ventricular nsPFA lesions were successfully created. Minimal phrenic and muscular stimulation was noted.
- Seven lesions were created with single 5-sec-long applications and the remaining 8 lesions with 3 repetitions of 5-sec-long applications.
- On necropsy, circular lesions were noted, characterized by wide contiguous lesions with a central dark zone (Figure).
- The lesion depth and width were 7.1±1.3mm and 14.7±4.5mm, respectively.
- Repetitive lesions (3-sec) were deeper than single applications (7.9±1.2mm vs 6.2±0.7mm, p<0.1), but there was no difference in lesion width (16.5±5.3mm vs 12.7±2.6mm, p=0.15), (Table).

Animal ID	Site	Depth (mm)	Width (mm)	Transmurality
1	15	11.0	15.0	Yes
2	15	11.0	15.0	Yes
3	15	11.0	15.0	Yes
4	15	11.0	15.0	Yes
5	15	11.0	15.0	Yes
6	15	11.0	15.0	Yes
7	15	11.0	15.0	Yes
8	15	11.0	15.0	Yes
9	15	11.0	15.0	Yes
10	15	11.0	15.0	Yes
11	15	11.0	15.0	Yes
12	15	11.0	15.0	Yes
13	15	11.0	15.0	Yes
14	15	11.0	15.0	Yes
15	15	11.0	15.0	Yes

Conclusions

- nsPFA can create clinically-relevant deep and wide lesions in the ventricles.
- Lesions have a characteristic central hemorrhagic zone, but no evidence of thermal injury.
- nsPFA delivery was associated with only mild muscle and nerve stimulation.

Disclosures

- This study was supported by a research grant from Pulse Biosciences. V.Reddy and J.Koruth, Consultant to Pulse Biosciences. Other authors report no relevant disclosures.

nsPFA can create clinically relevant deep and wide lesions, which did not demonstrate any evidence of thermal injury and delivery was associated with only mild muscle and nerve stimulation.

Creating Deep Ventricular Lesions with Nanosecond Pulsed Field Ablation: Pathological and Imaging Insights from Preclinical Evaluation (Iwanari Kawamura MD, et al)

Tolerance/Effectiveness

Electron Microscopic Insights from An Acute Pulsed Field Myocardial Lesion

Iwanari Kawamura MD, Binqian Wang PhD, Hira W. Chaudhry MD, Emmanuel Ekram MD, Joshua Lampert MD, Abhishek Maan MD, Daniel R. Muskatlow MD, Mohit K. Turagam MD, Marc A. Miller MD, William Whang MD, Sonawar R. Dabkapat MD, Vivek Y. Reddy MD, and Jacob S. Koruth MD

Background

- Pulsed field ablation (PFA) is a nonthermal ablative energy modality that increases membrane permeability by creating pores and causing chemical changes to the lipids and proteins on the cell membrane.
- However, little is known about its effect on cell membrane, organelle structure and time course of lesion formation.

Objective

- To evaluate cell membrane and organelle structure after PFA and assess lesion differences between 1- and 4-hour after nanosecond-PFA.

Method

- Healthy swine underwent endocardial PFA using an 11 F circular, multielectrode catheter (CALPX, Pulse Biosciences Inc.) in nanosecond pulsing mode.
- Pulses were delivered to the LV under general anesthesia with fluoroscopic and ICE guidance (Acunav).
- Two discrete PFA lesions were sampled at 1 and 4 hours after PFA.
- Transmission electron microscopy assessment was performed after fixation using paraformaldehyde and glutaraldehyde.

Results

- 1-hour post-PFA:** Healthy myocytes adjacent to ablated myocytes demonstrated normal sarcomeric structures and clearly visualized Z and A bands (Figure). Mitochondria were aligned in parallel with sarcomere filaments.
- Ablated myocytes:** On the other hand, demonstrated disrupted sarcomeric structures and were randomly clustered as well as misaligned. Cell membranes of the ablated myocyte at the lesion border were relatively preserved compared to ablated myocytes from within the core of the PFA lesion.
- 4-hour post-PFA:** The lesion was noticeably more edematous, and areas of coagulum were seen adjacent to the capillaries. Alignment of cell membranes was further disorganized. Fewer mitochondria were observed and noted to be randomly scattered amongst damaged myocytes. No normal sarcomeres were noted anywhere in the lesion.

Conclusion

- This electron microscopy study demonstrates significant rapid disappearance of myocytes after PFA (~ 1 hour).
- The cell membrane structure and organelle structure progressively deteriorate 4 hours post ablation.

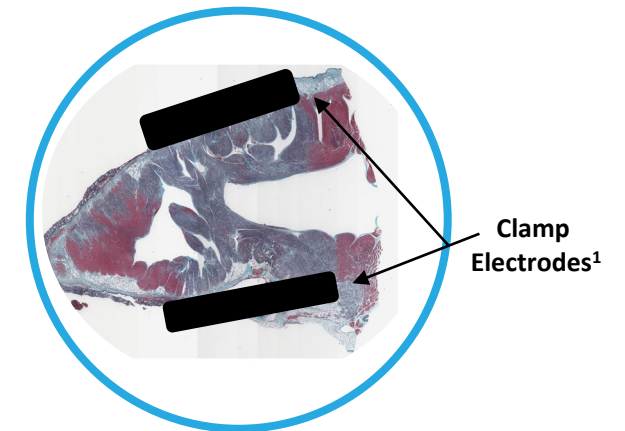
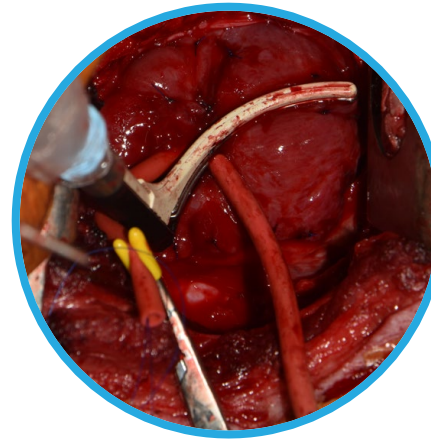
Disclosures / Acknowledgments

- This study was supported by a research grant from Pulse Biosciences. Others did not report any relevant disclosures.

This electron microscopy study demonstrates significant rapid disappearance of myocytes after PFA (~ 1 hour). The cell membrane structure and organelle structure progressively deteriorate by 4 hours post ablation.

Electron Microscopic Insights from An Acute Pulsed Field Myocardial Lesion (Iwanari Kawamura MD, et al)

Open Surgical Delivery of nsPFA Energy – Cardiac Ablation



- A nonthermal cardiac ablation clamp capable of complete transmural ablations in **under 3 seconds**
- Initial preclinical studies have demonstrated **speed, precision and transmurality up to ~25mm between electrodes**
- Collaborating with top institutions and physicians in pursuit of **regulatory clearance**
- **Fundamental IP** for nsPFA energy in cardiac ablation

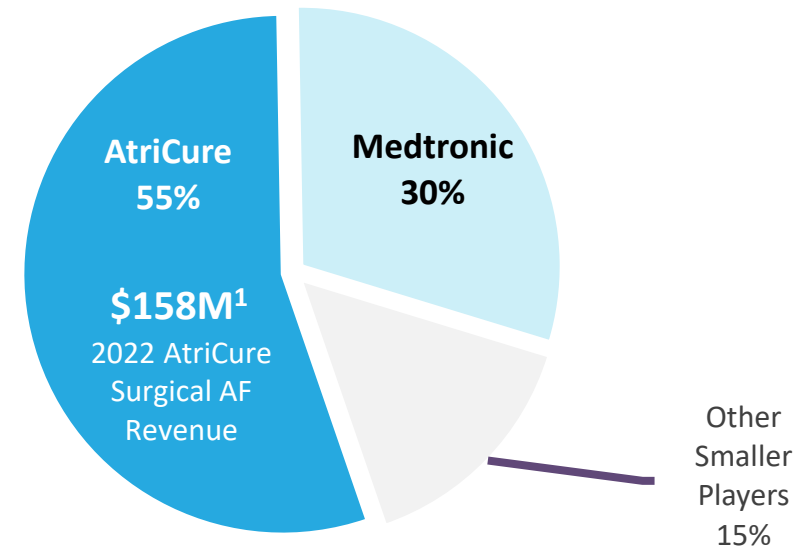
Cardiac Clamp Strategic Opportunity

High Strategic Value

1. Fast and Easy Market Entry
2. nsPFA Superior Product Offering
3. Ability to **Prove Effectiveness for AF** Prior to Catheter Launch
4. Provides Complete Solution
5. Sizable Revenue Opportunity Prior to Catheter Launch

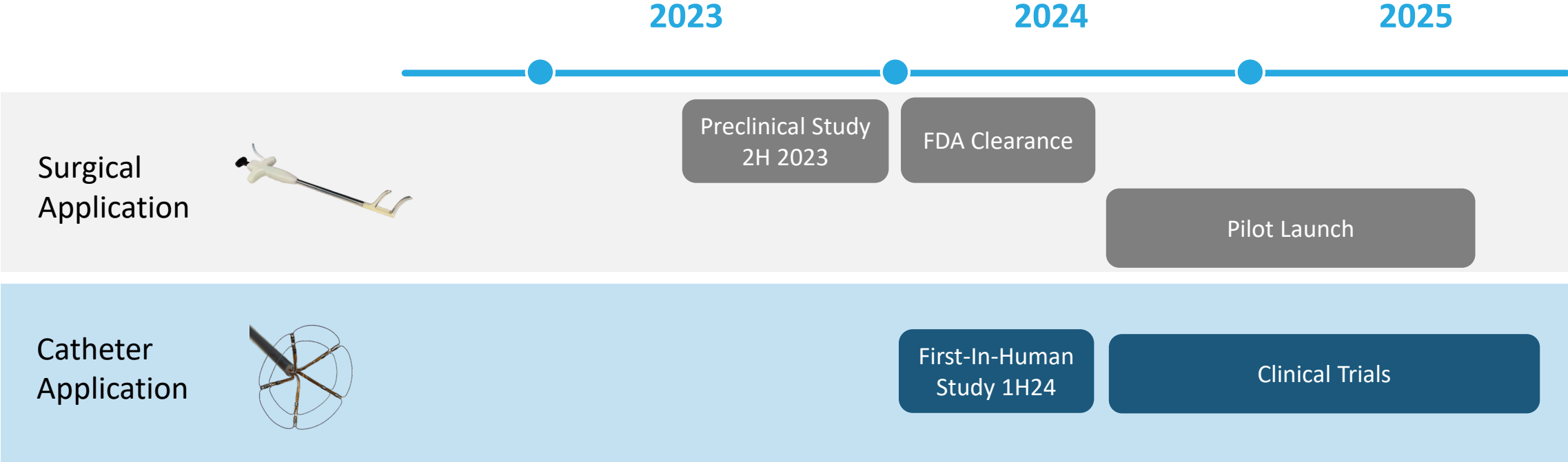
Global Market Overview²

Total AF Surgical Market 2022 >\$250M^{1,2}



Application Milestones for Treatment of AF

Next key milestone on program: Preclinical study outcomes



Cardiac Clamp Entry Point for Cardiology Applications

Activities

- **Pre-Launch**
 - Establish KOL network and advisory board (in process)
- **Pilot**
 - Place CellFX systems at regional KOL locations
 - Hire small team to support KOLs
 - Use pilot sites to learn best practices

Goal

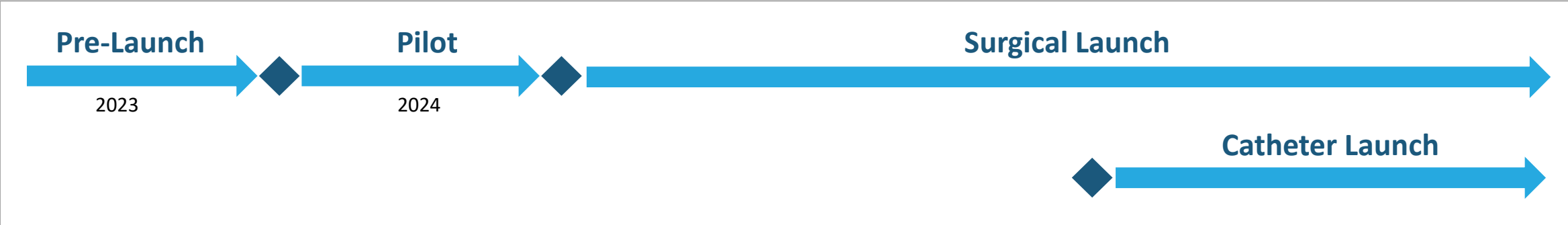
- **Validate surgical commercial opportunity for strategic optionality across the portfolio**
- **Expand utilization of cardiac platform to leverage nsPFA from surgical applications into catheter application**

Developing Strategy for Launch: Narrow-Deep Approach



Established attractive DRG reimbursement supports premium pricing

Timeline

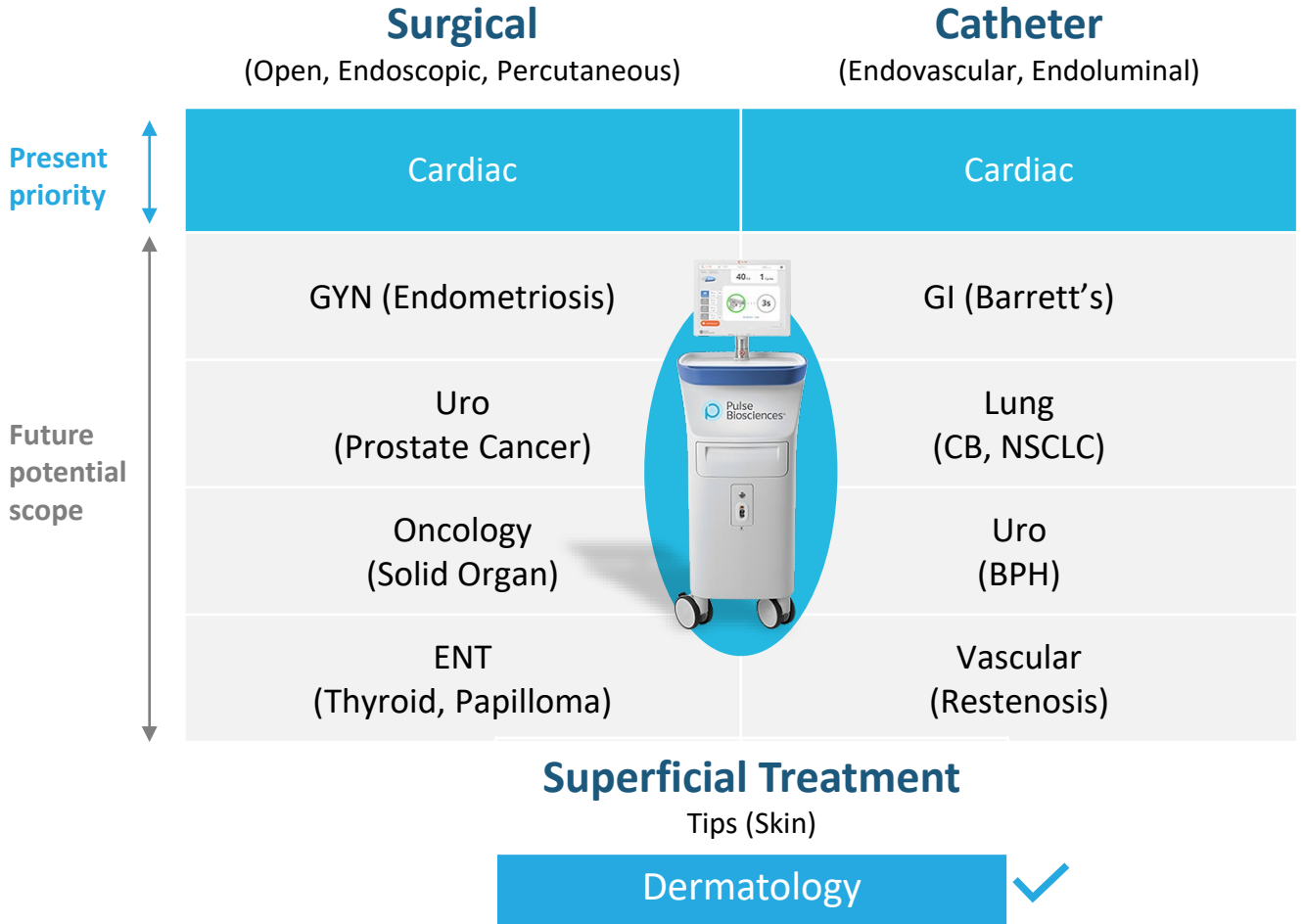


Versatile Generator Platform Delivers nsPFA Across the Anatomy

Enables rapid development of new applications

Safety drives the applications

- Sparing of connective tissue, vessels and nerves
- Not impacted by heat sinks
- No cardiac synchronization concerns
- Limited inflammation due to regulated cell death



Robust IP Portfolio

Wide and deep IP coverage of nsPFA energy & system

135

issued patents globally
owned & licensed

+99

Patent Pending
Applications

Patent Portfolio 2023

Multipronged Patent Strategy

- Pioneering IP for the use of nanosecond pulses in medicine
- Covering methods and tools for the application of nanosecond pulses in biology
- Continued development and patent filings covering systems, applications, and methods of combining nanosecond pulsing with other biological technologies and agents



1

Inventors and Sole Manufacturers of Unique Nanosecond Pulsed Electric Field Technology

2

Robust IP Portfolio Across Nanosecond Pulse Technology and System

3

Unique Bioelectric Mechanism of Action with Game-Changing Cardiology Applications

4

Leverageable System Architecture Ready for Development of New End Effectors

5

Proven Results Over 6,000 Patients with No Unexpected Adverse Events

6

Extensive Medical Device Leadership and Investment Expertise