SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Names:	Pulsed Field Ablation System
Device Trade Names:	FARAPULSE™ Pulsed Field Ablation System (FARAWAVE™ Pulsed Field Ablation Catheter, FARASTAR™ Catheter Connection Cable, FARASTAR™ Pulsed Field Ablation Generator, FARASTAR™ Recording System Module, FARASTAR™ Stimulation Module Cable, FARASTAR™ EGM Cable, FARASTAR™ Stimulation Module Male Cable, FARASTAR™ Stimulation Module Female Cable, FARASTAR™ Stimulation Module Y-Cable Long, FARASTAR™ Stimulation Module Y-Cable Short, FARASTAR™ Recording System Module Catheter Pin Cable, FARASTAR™ Recording System Module ECG Trunk Cable (AAMI/IEC), FARASTAR™ Recording System Module ECG Output Module (AAMI/IEC), FARASTAR™ Recording System Module EGM Input Module, FARASTAR™ SNAP CABLE R/L – (AAMI/IEC), FARASTAR™ SNAP CABLE V SET – (AAMI), FARASTAR™ SNAP CABLE C SET – (IEC))
Device Procode:	Class III / QZI: Percutaneous Cardiac Ablation Catheter For Treatment Of Atrial Fibrillation With Irreversible Electroporation
Applicant's Name and Address:	Boston Scientific Corporation 4100 Hamline Ave. N. St. Paul, MN 55112
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P230030
Date of FDA Notice of Approval:	January 30, 2024

II. INDICATIONS FOR USE

The FARAPULSE Pulsed Field Ablation (PFA) System is intended for the isolation of the pulmonary veins in the treatment of paroxysmal atrial fibrillation by rendering targeted cardiac tissue electrically non-conductive to prevent cardiac arrhythmia initiation or maintenance.

The FARAWAVE Catheter is indicated for the isolation of pulmonary veins in the treatment of drug-refractory, recurrent, symptomatic Paroxysmal Atrial Fibrillation (PAF).

The FARADRIVE Sheath is intended for percutaneous catheter introduction into the vasculature and into the chambers of the heart, including the left side of the heart through the interatrial septum.

The FARASTAR Connection Cable is intended to be used with a FARAPULSE Catheter during an Electrophysiology procedure for cardiac tissue ablation.

The FARASTAR Generator when used in conjunction with the FARAWAVE PFA catheter, is indicated for the isolation of pulmonary veins in the treatment of drug- refractory, recurrent, symptomatic Paroxysmal Atrial Fibrillation (PAF).

The FARASTAR Recording System Module (RSM) is indicated for use in an electrophysiology lab environment, as a filtering/protection unit to be connected between the patient and any attached recording systems and/or ECG systems, and as an interface for cardiac stimulation output.

III. CONTRAINDICATIONS

The FARAPULSE PFA System is contraindicated for use:

- in patients with active systemic infection;
- in patients with a mechanical prosthetic heart valve through which the catheter must pass; in patients with conditions where insertion into or manipulation in the cardiac chambers is unsafe as these conditions (e.g., presence of intracardiac thrombus or myxoma, history of recent cardiac surgery with atriotomy, etc.) may increase the risk of systemic embolism or cardiac perforation;
- in patients with a bleeding disorder, or who are unable to receive heparin or an acceptable alternative to achieve adequate anticoagulation;
- in patients who have vena cava embolic protection filter devices and/or known femoral thrombus who require catheter insertion from the femoral approach;
- in patients with a contraindication to an invasive electrophysiology procedure where insertion or manipulation of a catheter in the cardiac chambers is deemed unsafe, such as but not limited to, a recent previous cardiac surgery (e.g., ventriculotomy or atriotomy, Coronary Artery Bypass Graft [CABG], PTCA/PCI/coronary stent procedure/unstable angina) and/or in patients with congenital heart disease where the underlying abnormality increases the risk of the ablation (e.g. severe rotational anomalies of the heart or great vessels);
- via transseptal approach in patients with an intra-atrial baffle or a foramen ovale patch

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the FARAWAVE Catheter, FARADRIVE Sheath, FARASTAR Catheter Connection Cable, FARASTAR Generator, and FARASTAR RSM labeling.

V. DEVICE DESCRIPTION

The Sphere-9 Catheter and Affera Ablation System are used in conjunction with the Affera Mapping System for cardiac mapping, ablation, and pacing.

Sphere-9 Catheter

The FARAPULSE PFA System consists of the FARAWAVE Catheter, FARASTAR Connection Cable, FARADRIVE Sheath, FARASTAR Generator and accessories, and FARASTAR RSM and accessories. These components are designed to operate together as a system.

The FARADRIVE Sheath includes a Dilator and is designed for the percutaneous introduction of the FARAWAVE Catheter into the vasculature and to the chambers of the heart.

The FARAWAVE Catheter is a multi-electrode percutaneous catheter which connects to the FARASTAR Connection Cable as a means to connect to the FARASTAR Generator and is designed to deliver Pulsed Electric Field (PEF) energy produced by the generator to the target cardiac tissue.

The FARASTAR Generator produces PEF energy in the form of discrete high-voltage pulses with a pre-defined waveform and is controlled via a console with an LCD touchscreen display. The FARASTAR Generator is used in conjunction with the FARASTAR RSM, which is used to reduce potential interference to the Electrophysiology Laboratory Recording System during the ablation procedure as well as to provide output connection for synchronous mode operation.

The FARASTAR Generator is non-sterile, reusable, capital equipment whereas the FARAWAVE Catheter, FARASTAR Connection Cable, and FARADRIVE Sheath are sterile, single use, disposable devices.

The FARAWAVE Pulsed Field Ablation (PFA) Catheter (henceforth referred to as the FARAWAVE Catheter) is a component of the FARAPULSE PFA System. The FARAWAVE Catheter is an over-the-wire, multi-electrode catheter designed to deliver PFA energy to the distal section for cardiac ablation.

The FARAWAVE Catheter distal section consists of five splines with four electrodes located on each spline, twenty electrodes total.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of symptomatic paroxysmal atrial fibrillation, including the following:

- Commercially available PMA-approved devices
- Pharmacological therapy for rate and/or rhythm control
- Electrical or pharmacologic cardioversion
- Surgical intervention to create atrial lesions
- Implantable devices to control heart rates

Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The FARAPULSE PFA System was initially CE Marked on January 26, 2021. In addition to being marketed in the European Union, the subject system is marketed in various countries around the world such as South Africa, UAE, Andorra, Great Britain, Hong Kong, Israel, Kuwait, Macau, Saudi Arabia, Switzerland, Australia, Singapore, New Zealand, and Malaysia. The products have not been withdrawn from any market for any reason.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse events associated with catheter ablation and mapping procedures include, but are not limited to, the following conditions:

- Pain or discomfort
- Cardiac arrest
- Death
- Electric shock
- Hypotension
- Infection/inflammation/exposure to biohazardous material
- Procedural related side effects
- Renal failure/insufficiency
- Respiratory distress/insufficiency/dyspnea
- Arrhythmia (new or exacerbated)
- Conduction pathway injury (heart block, nodal injury, etc.)
- Nerve injury
- Gastrointestinal disorders
- Vessel trauma
- Cardiac trauma
- Injury related to tissue damage and/or adjacent structures
- Physical trauma/laceration
- Fistula
- PV stenosis and its symptoms

- Surgical and access complications
- Thrombus/thrombosis
- Muscle spasm
- Injury due to embolism/thromboembolism/air embolism/foreign body embolism
- Hemolysis

For the specific adverse events that occurred in the clinical study, please see Section X below.SUMMARY OF NONCLINICAL STUDIES

Testing of the FARAPULSE PFA System included verification and validation testing (device, system and software), device electrical safety testing, biocompatibility of patient-contacting materials, sterilization, packaging testing, and animal studies. Performance testing was conducted to demonstrate design integrity. Tests that were identified in standards or guidance documents were performed based on product specification requirements. Test results confirm that the devices met product specifications.

A. Laboratory Studies

Table 1. FARAWAVE Catheter Test Summary

Test Performed	Acceptance Criteria	Result
Visual Inspection	Device passes visual inspection criteria.	PASS
Dimensional Analysis	Device meets dimensional specifications.	PASS
Use Conditions Test	Device fits in a 13.1 Fr sheath.	PASS
	Device meets deployment criteria.	PASS
	Device is not kinked or torsionally damaged following simulated use conditioning.	PASS
	Following simulated use conditioning, device meets requirements.	PASS
Electrical Test	Continuity is present between respective electrodes and connectors.	PASS
	Device meets electrical requirements.	PASS
Buckling Test	When compressive load is applied to the cage, the catheter buckles below specification.	PASS
Pressure Drop Test	When the catheter lumens are occluded and pressurized, the pressure decay is less than or equal to specification.	PASS
Tensile Test	Device meets tensile strength requirements per ISO 10555-1:2013.	PASS
Corrosion	Catheter shall show no signs of corrosion in specified regions per ISO 10555-1:2013.	PASS

Table 2. FARASTAR Catheter Connection Cable Test Summary

Test Performed	Acceptance Criteria	Result
Visual Inspection	FARASTAR Connection Cable can connect to the FARAWAVE catheter and the FARASTAR Generator (via a one-way key fit).	PASS
Dimensional Analysis	Device meets dimensional specifications.	PASS
Electrical Test	Continuity is present between respective connector pins.	PASS
	Device passes hipot testing.	PASS
Use Conditions Test	The FARASTAR Catheter Connection Cable is capable of connecting to the Catheters	PASS

Table 3. FARASTAR Generator and Accessories Test Summary

Test Performed	Acceptance Criteria	Result
Electrical Safety	IEC 60601-1:2005, IEC 60601-1:2005/AMD1:2012, IEC 60601-1:2005/AMD2:2020 (Edition 3.2)	Passed
Electromagnetic Compatibility	IEC 60601-1-2:2014+A1:2020 (Edition 4.1)	Passed
System Verification	FARAPULSE System must meet the design inputs defined in the product requirements.	Passed
System Validation	FARAPULSE System must meet the design inputs defined in the user requirements.	Passed

Biocompatibility

Biocompatibility testing was conducted in accordance with ISO 10993-1 "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process". The catheter is an external communicating device placed in direct contact with circulating blood for a limited duration (less than 24 hours).

Table 4. Biocompatibility Test Summary

Test Performed	Result
Cytotoxicity Study Using the ISO Elution Method	PASS

Test Performed	Result
ISO Guinea Pig Maximization Sensitization Test ISO 10993-10	PASS
ISO Intracutaneous Reactivity ISO 10993-10	PASS
ISO Acute Systemic Toxicity in Mice ISO 10993-11	PASS
USP Rabbit Pyrogen Study, Materials Mediated ISO 10993-11	PASS
ASTM Hemolysis Study ISO 10993-4	PASS
Complement Activation SC5b-9 Assay ISO 10993-4	PASS
Partial Thromboplastin Time (PTT) Assay with Comparison Article (ISO)	PASS
Heparinized Blood Platelet and Leukocyte Count Assay with Comparison Article (ISO)	PASS
Thromboresistance Evaluation with Anticoagulation in Sheep ISO 10993-4	PASS
Thromboresistance Evaluation in Sheep ISO 10993-4	PASS

B. Animal Studies

Twelve (12) studies enrolling forty-nine (49) porcine subjects provide objective evidence supporting the safety, feasibility, and usability of the FARAPULSE System. All acceptance criteria in all protocols were met, and all enrolled subjects survived and thrived until their scheduled termination. A list and description of the studies conducted is presented in Table 6.

Table 6. Animal Studies

Study	Study Objective	Results
GLP Safety and Effectiveness Study in a 30-Day Chronic Porcine Model	Evaluate system performance by using chronic (30-day) safety and efficacy endpoints after treatment with either the 31mm and 35mm FARAWAVE Catheters using a clinically relevant workflow at nominal and upper bound conditions.	All acceptance criteria were met
Non-GLP Validation in 30-Day Porcine	Evaluate System Performance and 30-day Safety and Effectiveness at a clinically relevant workflow at max output.	All the acceptance criteria were met.
Chronic Porcine IVC Ablation with Direct Esophageal Contact	Demonstrate that the FARAPULSE PFA System does not damage the esophagus using a clinically relevant dose at 21-day survival.	All the acceptance criteria were met.
Evaluation of Downstream Tissues of FARAWAVE Ablation in an Acute Porcine Model	Evaluate the acute safety and effectiveness of the FARAPULSE PFA System by the assessment of electrophysiological (EP) findings, gross, sub-gross, and histopathological findings of treated tissue and downstream organs.	All acceptance criteria were met.
Pre-Ablation Pulse Verification	Evaluate the utility of Pre-Ablation Pulse sensing by the assessment of the Pre-Ablation Pulse's sensitivity and specificity.	All the acceptance criteria were met.

Study	Study Objective	Results
Preclinical Validation of FARAPULSE PFA System	Evaluate the FARAPULSE PFA System to validate all user needs requirements of the final commercial-integrated ablation system components.	All acceptance criteria were met.
Preclinical Validation of FARASTAR PFA Generator	To perform preclinical validation of the updated FARASTAR PFA Generator in a porcine animal model to confirm system product specifications.	All acceptance criteria were met.
Safety and Effectiveness In 7 Day Porcine	To perform a preclinical validation of the updated FARASTAR Generator to confirm that it is safe and effective at a clinically relevant dose.	All acceptance criteria were met.
Waveform Exploration in the Porcine Ventricle	To evaluate relative performance of various waveforms in ventricular lesion creation.	All study objectives were completed.
FARAPULSE PFA System Safety and Effectiveness in 30-Day Porcine	To evaluate the acute and chronic effectiveness of the updated FARASTAR Generator to confirm that it is safe and effective at a clinically relevant dose.	All acceptance criteria were met.
Preclinical Validation of FARASTAR PFA Generator and RSM	To perform a preclinical validation of the FARAPULSE PFA System with updated FARASTAR PFA Generator and FARASTAR Recording System Module in a porcine animal model to confirm system product specifications.	All acceptance criteria were met.
Preclinical Validation of FARASTAR PFA Generator	To perform a preclinical validation of the updated FARASTAR Generator to confirm system product specifications.	All acceptance criteria were met.

C. Additional Studies

Packaging

Packaging verification testing was performed to demonstrate that the packaging can withstand the hazards of the distribution environment, and that the sterility of the device is maintained throughout the labeled shelf life. Packaged devices were exposed to sterilization and simulated shipping and distribution, where applicable, and the integrity of the pouches and seals were verified. The device performance and packaging integrity met the acceptance criteria. The devices also passed shelf-life testing to the labeled shelf life.

Bioburden

Bioburden data is generated to ensure that sterility assurance level (SAL) is not impacted by the product bioburden levels. Bioburden testing is routinely conducted to meet the acceptance criteria of less than 10,000 CFU/device per Boston Scientific's internal procedures. To control the bioburden, the catheters are manufactured in a Controlled Environment Room.

Sterilization

FARAWAVE catheters, FARASTAR Catheter Connection Cable, and FARADRIVE Sheath are sterilized using ethylene oxide (EO) gas and have been validated per ISO 11135:2014, Sterilization of health care products – Ethylene oxide; Requirements for the development, validation, and routine control of sterilization process for medical devices. Results from the sterilization studies demonstrate the product satisfies a minimum Sterility Assurance Level (SAL) of 10-6 and residual EO levels were within acceptable ranges.

IX. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed the ADVENT IDE Trial to establish a reasonable assurance of safety and effectiveness of catheter ablation with the FARAPULSE PFA System for the treatment of drug-resistant, recurrent, symptomatic, Paroxysmal Atrial Fibrillation (PAF) under IDE # G200259. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study and its results is presented below.

A. Study Design

The ADVENT Trial was a multi-center, prospective, Bayesian adaptive, randomized, blinded, non-inferiority safety and effectiveness pivotal study comparing the FARAPULSE PFA System with standard of care thermal ablation (using either force-sensing radiofrequency ablation [RFA] catheters or cryoballoon ablation [CBA] catheters) for the treatment of patients with drug-resistant, recurrent, symptomatic PAF. The study was conducted at 30 investigational sites in the United States. A total of 706 subjects, including 80 Roll-In Subjects and 626 Randomized intention-to-treat (ITT) subjects, were enrolled in the study between March 1, 2021 and June 3, 2022. Subjects were followed at pre-discharge, 7 days, 30 days, 90 days, 6 months, and 12 months post-Index ablation procedure for adverse events and recurrence of atrial tachyarrhythmias.

Arrhythmia monitoring for Randomized subjects included 12-lead ECGs at 90 days, 12 months, or unscheduled visits, 72-hour Holter monitoring at 6- and 12-months, and weekly and symptomatic rhythm transmissions from a study-specific event monitor. All rhythm events were adjudicated by an independent arrhythmia core laboratory and all adverse events by an independent Clinical Events Committee (CEC). All subjects underwent pre-procedure and 90-day CT or MRI imaging of the pulmonary veins, and a subset of 77 ITT (38 PFA, 39 Thermal) consented to participate as a neurological assessment subject (NAS) and undergo post-ablation brain MRI assessment for silent cerebral events (SCEs) and silent cerebral lesions (SCLs). Class I/III anti-arrhythmic drugs (AADs) were required to be discontinued after Day 90, and use of amiodarone was excluded any time during the study. The last 12-month follow-up took place on May 15, 2023 and the study is considered complete. The database for this PMA reflects data collected through 12 months of follow-up.

1. Inclusion and Exclusion Criteria

Enrollment in the ADVENT Trial was limited to patients who met all of the following inclusion criteria:

1. Patients with drug-resistant symptomatic PAF meeting all the following criteria:

a. Paroxysmal: AF that terminates spontaneously or with intervention within 7 days of onset.

b. Frequency:

i. Physician documentation of recurrent PAF (two or more episodes) within 6 months, AND

ii. At least one (1) documented episode by a recording such as ECG, EM, Holter monitor or telemetry strip within 12 months of enrollment.

c. Drug failed: Failed AAD treatment, meaning therapeutic failure of at least one (1) AAD (Class I to IV) for efficacy and / or intolerance.

2. Patients who are ≥ 18 and ≤ 75 years of age on the day of enrollment.
3. Patients who are willing and capable of:
    a. Providing informed consent to undergo study procedures, AND
    b. Participating in all examinations and follow-up visits and tests associated with this clinical study.

Patients were not permitted to enroll in the ADVENT study if they met any of the following exclusion criteria:

1. AF that is any of the following:
    a. Persistent (both early and longstanding) by diagnosis or continuous duration > 7 days
    b. Requires four (4) or more direct-current cardioversions in the preceding 12 months
    c. Secondary to electrolyte imbalance, thyroid disease, alcohol or other reversible / non-cardiac causes
2. Any of the following atrial conditions:
    a. Left atrial anteroposterior diameter ≥ 5.5 cm (by MRI, CT or TTE)
    b. Any prior atrial endocardial or epicardial ablation procedure, other than right sided cavotricuspid isthmus ablation or for right sided SVT
    c. Any prior atrial surgery
    d. Intra-atrial septal patch or interatrial shunt
    e. Atrial myxoma
    f. Current LA thrombus
    g. LA appendage closure, device or occlusion, past or anticipated
    h. Any PV abnormality, stenosis or stenting (common and middle PVs are admissible)
3. At any time, one (1) or more of the following cardiovascular procedures, implants or conditions:

a. Sustained ventricular tachycardia or any ventricular fibrillation
b. Hemodynamically significant valvular disease:
    i. Valvular disease that is symptomatic
    ii. Valvular disease causing or exacerbating congestive heart failure
    iii. Aortic stenosis: if already characterized, valve area < 1.5cm or gradient > 20 mm Hg
    iv. Mitral stenosis: if already characterized, valve area < 1.5cm or gradient > 5 mm Hg
    v. Aortic or mitral regurgitation associated with abnormal LV function or hemodynamic measurements
c. Hypertrophic cardiomyopathy
d. Any prosthetic heart valve, ring or repair including balloon aortic valvuloplasty
e. Pacemaker, implantable cardioverter defibrillator or cardiac resynchronization therapy devices
f. Any IVC filter, known inability to obtain vascular access or other contraindication to femoral access
g. History of rheumatic fever
h. History of congenital heart disease with any residual anatomic or conduction abnormality

4. Any of the following procedures, implants or conditions:
    a. At baseline:
        i. New York Heart Association (NYHA) Class III or IV
        ii. LVEF < 40%
        iii. Symptomatic hypotension
        iv. Uncontrolled hypertension (SBP > 160 mmHg or DBP > 95 mmHg on two (2) BP measurements at baseline assessment)
        v. Symptomatic bradycardia
        vi. Implantable loop recorder or insertable cardiac monitor
    b. Within the 3 months preceding the Consent Date:
        i. Myocardial infarction
        ii. Unstable angina
        iii. Percutaneous coronary intervention
        iv. Heart failure hospitalization
        v. Treatment with amiodarone
        vi. Pericarditis or symptomatic pericardial effusion

vii. Gastrointestinal bleeding

c. Within the 6 months preceding the Consent Date:

i. Heart surgery

ii. Stroke, TIA or intracranial bleeding

iii. Any thromboembolic event

iv. Carotid stenting or endarterectomy

5. Diagnosed disorder of blood clotting or bleeding diathesis
6. Contraindication to, or unwillingness to use, systemic anticoagulation
7. Patient who is not on anticoagulation therapy for at least 3 weeks prior to the ablation procedure
8. Contraindication to both CT and MRI
9. Sensitivity to contrast media not controllable by premedication
10. Women of childbearing potential who are pregnant, lactating, not using medical birth control or who are planning to become pregnant during the anticipated study period
11. Medical conditions that would prevent participation in the study, interfere with assessment or therapy, significantly raise the risk of study participation, or modify outcome data or its interpretation, including but not limited to:

a. Body Mass Index (BMI) > 40.0

b. Solid organ or hematologic transplant, or currently being evaluated for an organ transplant

c. Severe lung disease, pulmonary hypertension, or any lung disease involving abnormal blood gases or requiring supplemental oxygen

d. Renal insufficiency with an estimated glomerular filtration rate (eGFR) < 30 mL/min/1.73 m^2, or any history of renal dialysis or renal transplant

e. Active malignancy or history of treated malignancy within 24 months of enrollment (other than cutaneous basal cell or squamous cell carcinoma)

f. Clinically significant gastrointestinal problems involving the esophagus or stomach including severe or erosive esophagitis, uncontrolled gastric reflux, gastroparesis, esophageal candidiasis or active gastroduodenal ulceration

g. Active systemic infection

h. COVID-19 disease

i. Current confirmed, active COVID-19 disease

ii. Current positive test for SARS-CoV-2

iii. Confirmed COVID-19 disease not clinically resolved at least 3 months prior to the Consent Date

i. Other uncontrolled medical conditions that may modify device effect or increase risk, including uncontrolled diabetes mellitus (HgbA1c > 8.0% if test result already obtained) or active alcohol abuse

j. Sleep apnea and:

i. An apnea-hypopnea index (AHI) ≥ 15, or

ii. An AHI of ≥ 5 and ≤14 with documented symptoms of excessive daytime sleepiness, impaired cognition, mood disorders or insomnia, or documented hypertension, ischemic heart disease or history of stroke, unless compliant with continuous positive airway pressure (CPAP) treatment.

k. Predicted life expectancy less than one (1) year

12. Clinically significant psychological condition that in the Investigator's opinion would prohibit the subject's ability to meet the protocol requirements.

13. Current or anticipated enrollment in any other randomized, interventional or FDA-regulated clinical study (data collection for registries or retrospective studies is permitted)

14. Employees / family members of:

a. FARAPULSE or any of its affiliates or contractors

b. The Investigator, sub-Investigators, or their medical office or practice, or healthcare organizations at which study procedures may be performed

2. Follow-up Schedule

All Randomized subjects were followed according to the visits and assessments defined in Table 7. Subject participation was considered complete after the 12-month visit and completion of the corresponding Holter monitor.

Table 7. Schedule of evaluations and visits

				Blanking Period			Effectiveness Evaluation Period			Other	
Procedure/ Assessment	**BASELINE**	**INDEX PROCEDURE**	**PRE-DISCHARGE**	**Day 7** (7-11 days)	**Day 30** (±7 days)	**DAY 60** (±10 days)	**DAY 90** (90±14 days)	**MONTH 6** (180 ± 30 days)	**MONTH 12** (365 ± 30 days)	**UNSCHEDULED**	**RE-ABLATION**
Informed consent, baseline assessments	X										
AAD and anticoagulant medications	X		X	X	X	D/C	X	X	X	X	X

				Blanking Period			Effectiveness Evaluation Period			Other	
Procedure/ Assessment	**BASELINE**	**INDEX PROCEDURE**	**PRE-DISCHARGE**	**Day 7** (7-11 days)	**Day 30** (±7 days)	**DAY 60** (±10 days)	**DAY 90** (90±14 days)	**MONTH 6** (180 ± 30 days)	**MONTH 12** (365 ± 30 days)	**UNSCHEDULED**	**RE-ABLATION**
Recurrent arrhythmia, cardioversions, ablations, hospital admissions			X	X	X		X	X	X	X	X
Pregnancy test	X	X									X
COVID-19 testing by site	X										
12-lead ECG	X		X				X		X	X	
HCT, HGB, electrolytes, BUN creatinine	X		X								
TTE	X										
Event monitors	T		T			T	Weekly + Symptoms			x	
72-hour continuous Holter	T		T					X	X		
Cardiac CT or MRI (PVs)	X						X		X[1]		X
TEE/ICE		X									X
NIHSS	X		X								
Radiologic examination of diaphragm		X					X[2]		X[2]		X
AF symptom assessment	X								X		
EQ-5D-3L & AFEQT assessment	X								X		
Non-NAS: Neuro assessment			X				X[3]				
NAS: Neuro assessment			X				X[4]				
Assessment of subject blinding			X						X		
Adverse events		X	X	X	X		X	X	X	X	X

Abbreviations: AAD = anti-arrhythmic drug, ECG = electrocardiogram, TTE = transthoracic echo, CT = computed tomography, MRI = magnetic resonance imaging, PVs = pulmonary veins, TEE = trans-esophageal echocardiogram, ICE = intracardiac echocardiogram, NIHSS = National Institutes of Health Stroke Scale, AF = atrial fibrillation, NAS = neurological assessment subject, T = Training

[1] Only if 3-month imaging revealed any PV with ≥ 70% reduction in PV measured diameter.

[2] Only if resolution of phrenic nerve palsy has not yet been demonstrated.

[3] Non-NAS: If NIHSS score has increased by 1 or more points or if there is a clinical suspicion of stroke/TIA

[4] NAS: If NIHSS score has increased by 1 or more points, if there is a clinical suspicion of stroke/TIA, or if the post-procedural brain MRI is positive for SCE or SCL findings

3. Clinical Endpoints

i. Primary Safety Endpoint

The primary safety endpoint is the Composite Safety Endpoint (CSE) defined as the proportion of MITT subjects with one or more of the following device- or procedure-related SAEs as adjudicated by the CEC according to the protocol-specified definitions.

Early onset: Any of the following with an Onset Date within 7 days of the Index / Rescheduled Index procedure:

- Death
- Myocardial infarction
- Persistent phrenic nerve palsy
- Stroke
- TIA
- Peripheral or organ thromboembolism
- Cardiac tamponade / perforation
- Pericarditis
- Pulmonary edema
- Vascular access complications
- Heart blocK
- Gastric motility/pyloric spasm disorders

Late onset: Either of the following with an Onset Date any time through the completion of 12-month follow-up visit:

- Pulmonary Vein Stenosis
- Atrio-esophageal fistula

The study aimed to demonstrate noninferiority of the investigational device compared to the control device with respect to the primary safety endpoint. Primary safety noninferiority was tested with a noninferiority margin of 8%.

ii. Primary Effectiveness Endpoint

1. **Acute Procedural Success**, defined as: demonstration of isolation of all attempted PVs using the randomized treatment during the first ablation procedure as clinically assessed by entrance block demonstrated ≥ 20 minutes after the last PVI lesion is made with or without adenosine testing.

   AND

2. **Chronic Success**, defined as freedom from:
   a. At the Index / Rescheduled Index Procedure: Use of a non-randomized treatment modality for PVI
   b. After the Blanking Period:
      i. Occurrence of any Detectable AF, AFL or AT* (excluding CTI-dependent flutter confirmed by EP study)
      ii. Any cardioversion for AF, AFL or AT (excluding for CTI-dependent flutter)
      iii. Use of any Type I or Type III antiarrhythmic medication for the treatment of AF, AFL or AT
   c. At any time:

i. Re-ablation for AF, AFL or AT (other than for CTI-dependent flutter)

ii. Use of amiodarone, except intra-procedurally to control an arrhythmia

* Detectable AF, AFL or AT is an episode of AF, AFL or AT which:

- Is permanently recorded for review
- Contains at least 30 seconds of continuous interpretable signal
- Exception: Continuous AF, AFL or AT for the entirety of a 12 lead ECG constitutes Detectable AF, AFL or AT if the continuous interpretable signal is 10 seconds or longer
- Includes symptomatic and asymptomatic episodes.
- Excludes CTI isthmus-dependent AFL when the mechanism is confirmed electrophysiologically.

The primary effectiveness endpoint for this study was Treatment Success, which was analyzed as a test of non-inferiority of the event rate at 12 months using a non-inferiority margin of 15%.

iii. Secondary Endpoints

Safety: The secondary safety endpoint was Aggregate PV Cross-Sectional Area, defined as the paired difference in the computed Aggregate PV Cross-Sectional Area between baseline and 3 months in MITT subjects. This was compared between randomization groups, regardless of re-ablation with any second energy modality.

Effectiveness: The secondary effectiveness endpoint was compared between the MITT subjects in the Pulsed Field and Thermal Groups with a Bayesian test of superiority of the Treatment Success rate at 12 months.

B. Subject Accountability

706 subjects were enrolled in the study. Of those enrolled in the study, 80 were assigned to the roll-in cohort and 626 Randomized subjects, 313 in the Pulsed Field Group and 313 in the Thermal Group (171 RFA, 142 CBA). Nineteen (19) subjects (8 PFA, 11 Thermal) exited the study prior to undergoing the Index Procedure ablation, resulting in 607 Randomized subjects in the MITT cohort (305 Pulsed Field, 302 Thermal). Of the 607 MITT subjects, 583 (96.0%) completed the 12-month follow-up, with the 24 early exits equally represented across the groups (12 Pulsed Field, 12 Thermal). The first subject was enrolled on March 1, 2021, and the last subject exited the study on May 15, 2023. Table 8 shows an accounting of subject disposition of all enrolled subjects. The remainder of the tables and analyses presented for the ADVENT Trial contain data on MITT population subjects only.

Table 8. Subject Disposition – Enrolled Subjects

Subject Disposition Categories	Pulsed Field	Thermal	Total
Screened Population			741
Screen Failures			35
Enrolled Population			706
Roll-In Population			80
ITT Population [1]	313	313	626
Subjects Withdrawn Before Index Procedure	8	11	19
Safety Population [2]	305	302	607
MITT Population	305	302	607
Completed Population	293	290	583
Incomplete Population	12	12	24
Reasons for incomplete status			
Death	2	1	3
Lost to Follow-Up	3	4	7
Terminated by Investigator	1	0	1
Withdrawal by Subject	5	6	11
Other	1	1	2

Note 1: The division of Thermal Subjects by treatment modality was not randomized but resulted from enrollment patterns at each of the Thermal = RFA and Thermal = CBA investigational sites
Note 2: The Safety and MITT Populations in the ADVENT Trial represent the same cohort and will be referred to as the MITT cohort

C. Visit and Rhythm Monitoring Compliance

Table 9: Compliance Summary – Follow-up Visits

Assessment (Window)	Pulsed Field % (n/N)	Thermal % (n/N)	Total % (n/N)
Pre-Discharge	99.7 (304/305)	100 (302/302)	99.8 (606/607)
Day 7 (Days 7-11)	99.7 (303/304)	99.7 (301/302)	99.7 (604/606)
Day 30 (30 +/- 7 days)	100 (303/303)	99.7 (301/302)	99.8 (604/605)
Day 90 (90 +/- 14 days)	99.3 (300/302)	97.7 (294/301)	98.5 (594/603)
Month 6 (180 +/- 30 days)	99.0 (297/300)	99.3 (298/300)	99.2 (595/600)
Month 12 (360 +/- 30 days)	98.0 (293/299)	99.3 (290/292)	98.6 (583/591)
Assessment Total	99.3 (1800/1813)	99.3 (1786/1799)	99.3 (3586/3612)

n = number of subjects with stipulated compliance level, N = number of subjects in study at interval

Table 10. Rhythm Monitoring Compliance

Rhythm Monitoring Compliance	Pulsed Field Subjects % (n/N)	Thermal Subjects % (n/N)	All Subjects % (n/N)
12-Lead ECG[1]			
Day 90 ECG	88.1 (266/302)	88.4 (266/301)	88.2 (532/603)
Month 12 ECG	91.6 (274/299)	89.0 (260/292)	90.4 (534/591)
72-Hour Holter Monitor[2]			
Month 6	86.3 (259/300)	79.3 (238/300)	82.8 (497/600)
Month 12	82.7 (248/300)	76.8 (225/293)	79.8 (473/593)
Event Monitor[3] (EM)			
Mean EM weekly compliance, all subjects	68.9 (8,101/11,765)	66.2 (7,655/11,572)	67.5 (15,756/23,337)
Overall Rhythm Monitoring Compliance[4]			
Mean rhythm record weekly compliance, all subjects	71.3 (8,440/11,837)	68.7 (8,000/11,647)	70.0 (16,440/23,484)

Note 1: n = number of subjects with evaluable 12-lead ECG records, N = number of subjects at interval.

Note 2: n = number of subjects with evaluable Holter monitors, N = number of subjects at interval.

Note 3: For all subjects, the sum (n) of all compliant weeks (weeks with one or more evaluable EM records) divided by the sum (N) of all follow-up weeks between Day 90 and Day 360.

Note 4: For all subjects, the sum (n) of all compliant weeks (weeks with one or more evaluable rhythm records) divided by the sum (N) of all follow-up weeks between Day 90 and Day 360.

D. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a persistent atrial fibrillation ablation treatment study performed in the US. The subject demographic and baseline health status characteristics of the treated primary analysis cohort subjects are shown in 11 below.

Table 11. Demographics

Baseline Parameter	Total Subjects % (n / N)	Pulsed Field Subjects % (n / N)	95% BCI[1]	Thermal Subjects % (n / N)	RFA Subjects % (n / N)	CBA Subjects % (n / N)
Female	34.6 (210/607)	33.8 (103/305)	[-9.2, 5.9]	35.4 (107/302)	32.9 (55/167)	38.5 (52/135)
Male	65.4 (397/607)	66.2 (202/305)		64.6 (195/302)	67.1 (112/167)	61.5 (83/135)
Hispanic or Latino	1.8 (11/607)	2.6 (8/305)	[-0.5, 4.0]	1.0 (3/302)	1.2 (2/167)	0.7 (1/135)
White	91.9 (558/607)	93.8 (286/305)	[-0.6, 8.1]	90.1 (272/302)	89.8 (150/167)	90.4 (122/135)
Black/African American	2.5 (15/607)	1.3 (4/305)	[-5.0, 0.1]	3.6 (11/302)	4.2 (7/167)	3.0 (4/135)
Asian	1.8 (11/607)	2.0 (6/305)	[-1.9, 2.6]	1.7 (5/302)	1.2 (2/167)	2.2 (3/135)
American Indian or Alaska Native	0.2 (1/607)	0.0 (0/305)	[-1.4, 0.5]	0.3 (1/302)	0.6 (1/167)	0.0 (0/135)
Native Hawaiian or other Pacific Islander	0.5 (3/607)	0.3 (1/305)	[-1.7, 0.9]	0.7 (2/302)	1.2 (2/167)	0.0 (0/135)
Race Unknown	1.5 (9/607)	0.7 (2/305)	[-3.8, 0.2]	2.3 (7/302)	1.8 (3/167)	3.0 (4/135)
Race Not Specified	1.6 (10/607)	2.0 (6/305)	[-1.5, 2.8]	1.3 (4/302)	1.2 (2/167)	1.5 (2/135)
Typical Atrial Flutter	30.1 (183/607)	27.2 (83/305)	[-13.1, 1.4]	33.1 (100/302)	42.5 (71/167)	21.5 (29/135)
Other SVT	14.0 (85/607)	11.8 (36/305)	[-10.0, 1.1]	16.2 (49/302)	21.0 (35/167)	10.4 (14/135)
Previous RA Ablation	3.9 (22/562)	3.5 (10/283)	[-4.1, 2.5]	4.3 (12/279)	5.0 (8/161)	3.4 (4/118)

Note 1: Bayesian credible interval for the difference in proportions, using Beta (0.5, 0.5) priors.

E. Safety and Effectiveness Results

1. Primary Analyses

i. Primary Safety Endpoint

The primary safety endpoint was the CSE defined as the proportion of MITT subjects with one or more pre-specified device- or procedure-related SAEs adjudicated by the ADVENT Clinical Events Committee. The endpoint was compared between the MITT subjects in the Pulsed Field and Thermal Groups with a Bayesian test of non-inferiority of the CSE rate at 12 months using a non-inferiority margin of 8%.

In Pulsed Field MITT subjects, six (6) subjects experienced one or more CSE

events; the estimated incidence was 2.1% (posterior mean). In Thermal MITT subjects, four (4) subjects experienced one or more CSE events; the estimated incidence was 1.5% (posterior mean).

The ADVENT Trial met the success criterion for the primary safety endpoint. The probability of a Pulsed Field MITT subject having one or more CSE events was non-inferior to the probability of a Thermal MITT subject having one or more CSE events using a non-inferiority margin of 8%: the posterior probability of non-inferiority was >0.999, which exceeded the prespecified threshold of 0.966.

Table 12: Primary Safety Endpoint

Primary Safety Endpoint	Subjects with Events (N) Incidence (%) 95% BCI[1]		Difference (%) 95% BCI[2]	Posterior Probability of Non-Inferiority (δ 8%)[3]
	Pulsed Field Group N 305	Thermal Group N 302		
MITT Subjects with one or more CSE events	6 2.1 [0.8, 4.0]	4 1.5 [0.4, 3.1]	0.6 [-1.5, 2.8]	> 0.999

Note 1: Point estimate calculated as the mean of the posterior distribution; posterior mean and Bayesian credible interval calculated using Beta (0.5, 0.5) prior, with multiple imputation for incomplete data.
Note 2: Point estimate calculated as the mean of the posterior distribution; posterior mean and Bayesian credible interval for the difference in population proportions calculated using Beta(0.5, 0.5) priors and multiple imputation for incomplete data.
Note 3: Posterior probability using Beta (0.5, 0.5) priors and multiple imputation for incomplete data

ii. Primary Effectiveness Endpoint

The primary effectiveness endpoint was Treatment Success (Acute Procedural Success and Chronic Success). The endpoint was compared between the MITT subjects in the Pulsed Field and Thermal Groups with a test of non-inferiority of the Treatment Success rate at 12 months using a non-inferiority margin of 15%.

In Pulsed Field MITT subjects, 204 subjects were Treatment Successes, while 80 subjects experienced Treatment Failures; the remaining 21 subjects had no known Treatment Failure but did not have an eligible 12-month follow-up visit. The failure-free time for these 21 subjects is included in the estimate of Treatment Success Rate through Bayesian multiple imputation, and the estimated Treatment Success Rate is 73.3% (calculated as the mean of the posterior distribution).

In Thermal MITT subjects, 194 subjects were Treatment Successes, while 85 subjects experienced Treatment Failures; the remaining 23 subjects had no known Treatment Failure but did not have an eligible 12-month follow-up visit. The failure-free time for these 23 subjects is included in the estimate of Treatment Success Rate through Bayesian multiple imputation, and the estimated Treatment

Success Rate is 71.3% (calculated as the mean of the posterior distribution).

The ADVENT trial met the success criterion for the primary effectiveness endpoint. The probability of a Pulsed Field MITT subject having Treatment Success was non-inferior to the probability of a Thermal MITT subject having Treatment Success using a non-inferiority margin of 15%: the posterior probability of non-inferiority is >0.999, which exceeded the prespecified threshold of 0.956.

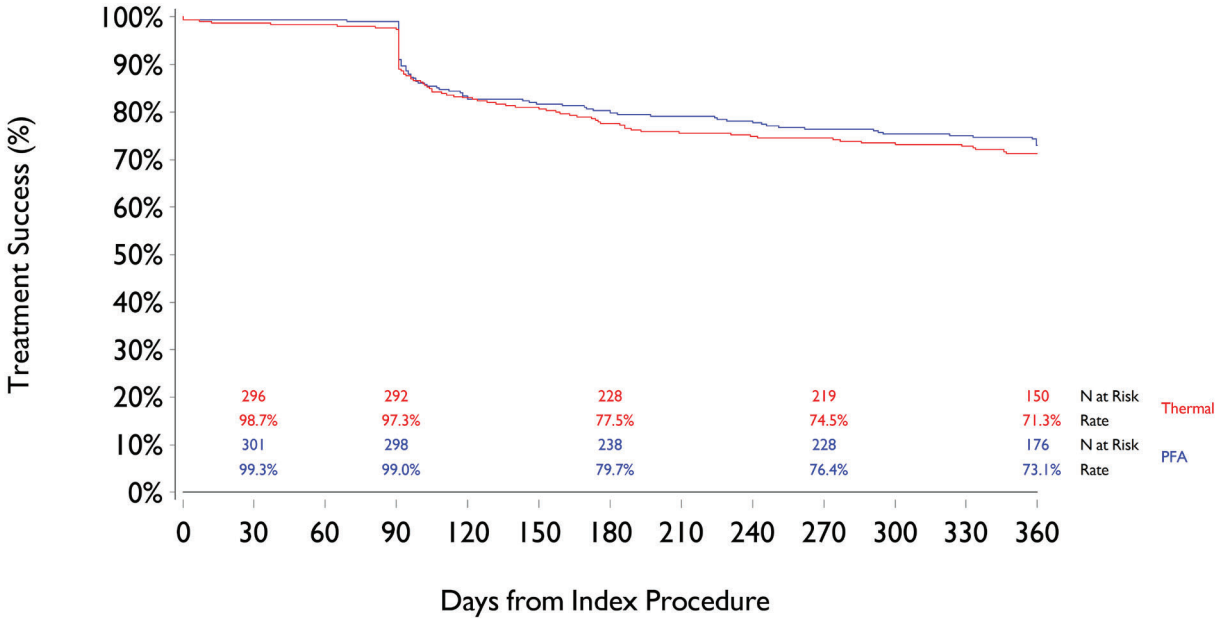
Table 13: Primary Effectiveness Endpoint

	Subjects with Treatment Success [Incomplete Subjects without Treatment Failure] Incidence (%) 95% BCI[1]			
Primary Effectiveness Endpoint	**Pulsed Field Group N 305**	**Thermal Group N 302**	**Difference (%) 95% BCI[2]**	**Posterior Probability of Non-Inferiority (δ 15%)[3]**
MITT Subjects with Treatment Success	204 [21] 73.3 [68.1, 78.1]	194 [23] 71.3 [66.0, 76.3]	2.0 [-5.2, 9.2]	> 0.999

Abbreviations: N = number of subjects included in analysis (including those with incomplete follow-up)
Note 1: Point estimate calculated as the mean of the posterior distribution; posterior mean and Bayesian credible
interval calculated using Beta (0.5, 0.5) prior, with multiple imputation for incomplete data.
Note 2: Point estimate calculated as the mean of the posterior distribution; posterior mean and Bayesian credible interval for the difference in population proportions calculated using Beta(0.5, 0.5) priors and multiple imputation for incomplete data.
Note 3: Posterior probability using Beta (0.5, 0.5) priors and multiple imputation for incomplete data

As a sensitivity analysis, the primary effectiveness endpoint was also assessed via Kaplan-Meier estimates, as shown in **Figure 1**. The Kaplan-Meier estimate of freedom from failures of the primary effectiveness endpoint at 360 days is 73.1% in the Pulsed Field group and 71.3% in the Thermal group. Although freedom from failures at 360 days differs somewhat from the Treatment Success definition in that 12-month follow-up visits and their associated visit windows are not formally considered, the numerical estimates agree closely: 73.3% for Pulsed Field subjects and 71.3% for Thermal subjects from the pre-specified Bayesian model and 73.1% for Pulsed Field subjects and 71.3% for Thermal subjects from the Kaplan-Meier estimates.

Figure 1: Survival Analysis, Primary Effectiveness Endpoint – MITT Subjects



2. Secondary Analyses

The secondary safety endpoint was Aggregate PV Cross-Sectional Area, defined as the paired difference in the computed Aggregate PV Cross-Sectional Area between baseline and 3 months in MITT subjects. This was compared between randomization groups, regardless of re-ablation with any second energy modality. The within-subject changes in the Aggregate PV Cross-Sectional Area from baseline to Day 90 were tested for superiority (less reduction in area) between the Pulsed Field and Thermal Groups using a Bayesian version of a t-test.

The secondary safety endpoint success criterion for superiority was met. The mean change in PV cross-sectional area in Pulsed Field MITT subject PVs (–0.18 cm^2 or -0.9% of baseline value) was statistically greater (less negative) than the change in Thermal MITT subject PVs (–1.18 cm^2 or -12.0% of baseline value) with an observed posterior probability of >0.999, exceeding the prespecified threshold value of 0.975.

Examination of the change in Aggregate PV Cross-Sectional Area by ablation modality demonstrated that the difference was driven by the large reduction in RFA subjects, who had a mean reduction of 19.5% in Aggregate PV Cross-Sectional Area. Thermal subjects treated with CBA had a 3.3% reduction.

Table 14. Aggregate PV Cross-Sectional Area by Ablation Modality

			Thermal Group		
Aggregate PV Cross-Sectional Area (cm^2)	**Interval**	**Pulsed Field Subjects Mean (N) Min, Max**	**All Thermal Subjects Mean (N) Min, Max**	**RFA Subjects Mean (N) Min, Max**	**CBA Subjects Mean (N) Min, Max**
MITT Subjects	Baseline	8.9 (259) 3.7, 15.3	8.9 (255) 4.0, 17.6	9.1 (137) 5.0, 17.6	8.7 (118) 4.0, 15.7
	Day 90	8.7 (259) 4.2, 15.1	7.8 (255) 3.6, 13.5	7.3 (137) 3.6, 12.4	8.3 (118) 3.7, 13.5
	Percent Change	-0.9 (259) -40.7, 65.5	-12.0 (255) -55.2, 44.3	-19.5 (137) -55.2, 16.8	-3.3 (118) -44.5, 44.3
	Change [95% BCI] [1]	-0.18 [-0.37, 0.00]	-1.18 [-1.39, -0.97]	-1.86 [-2.12, -1.59]	-0.39 [-0.67, -0.11]
	Posterior Mean of Difference 95% BCI[2]	1.00 [0.72, 1.28]			
	Posterior Probability of Superiority[3]	>0.999			

			Thermal Group		
Aggregate PV Cross-Sectional Area (cm^2)	Interval	Pulsed Field Subjects Mean (N) Min, Max	All Thermal Subjects Mean (N) Min, Max	RFA Subjects Mean (N) Min, Max	CBA Subjects Mean (N) Min, Max

Note 1: This change is the paired comparisons of the baseline to Day 90 mean values within each treatment group using a posterior mean and Bayesian credible interval; uniform priors on (μ, log(s)) scale

Note 2: This difference is the comparison of the baseline to Day 90 change in per-subject means between PFA and Thermal group using a posterior mean and Bayesian credible interval; uniform priors on (μ, log σ scale.

Note 3: Posterior probability that the change in baseline to Day 90 mean values is larger (less negative) in the Pulsed Field group than the Thermal group, using a Bayesian version of a t-test; uniform priors on (μ, log(σ)) scale.

All adverse events reported were screened by the CEC per the protocol requirements and CEC charter. Events reported as serious, and additional events that study monitors or CEC members felt might be serious, were all formally adjudicated by the CEC.

There were 34 device- or procedure-related SAEs reported in 29 subjects (20 Pulsed Field and 9 Thermal). Eleven (11) of the events in ten (10) subjects were the primary safety endpoint events presented previously in the primary safety endpoint results. The remaining 23 events (16 Pulsed Field and 7 Thermal). All of these SAEs were determined to be resolved (21) events or resolving (2 events) by the conclusion of study participation without reported sequelae.

Table 15. Adverse Events

Adverse Event	All Subjects (N 607) n (%) e[1]	Pulsed Field Subjects (N 305) n (%) e[1]	95% BCI[2]	Thermal Subjects (N 302) n (%) e[1]	RFA Subjects (N 167) n (%) e[1]	CBA Subjects (N 135) n (%) e[1]
Any adverse event	390 (64.3%) 1012	189 (62.0%) 487	[-12.2, 3.0]	201 (66.6%) 525	115 (68.9%) 321	86 (63.7%) 204
Any SAE	71 (11.7%) 103	37 (12.1%) 51	[-4.3, 6.0]	34 (11.3%) 52	21 (12.6%) 37	13 (9.6%) 15
Any procedure-related AE	191 (31.5%) 288	97 (31.8%) 147	[-6.7, 8.0]	94 (31.1%) 141	58 (34.7%) 89	36 (26.7%) 52
Any device-related AE	40 (6.6%) 45	21 (6.9%) 22	[-3.4, 4.6]	19 (6.3%) 23	13 (7.8%) 16	6 (4.4%) 7
Any procedure-related SAE	29 (4.8%) 34	20 (6.6%) 23	[0.2, 7.1]	9 (3.0%) 11	7 (4.2%) 9	2 (1.5%) 2
Any device-related SAE	4 (0.7%) 4	4 (1.3%) 4	[0.1, 3.0]	0 (0.0%) 0	0 (0.0%) 0	0 (0.0%) 0

Note 1: N = number of subjects in group, n = number of subjects with one or more events, % = percentage of subjects with one or more events, e = number of events.
Note 2: Bayesian credible interval of the difference in proportions of subjects with one or more events using Beta (0.5, 0.5) priors

iii. Secondary Effectiveness Endpoint

The secondary effectiveness endpoint was the same as the primary effectiveness endpoint, but it was tested for superiority rather than non-inferiority. In Pulsed Field MITT subjects, the estimated Treatment Success rate is 73.3%, and in Thermal MITT subjects, the estimated Treatment Success Rate is 71.3% (both calculated as the mean of the posterior distribution). The posterior probability of superiority is 0.708, which did not exceed the prespecified threshold of 0.977; therefore, the success criterion for the secondary effectiveness endpoint was not met.

Acute Procedural Success

Acute Procedural Success was defined as demonstration of Acute Vein Success in all attempted PVs using the randomized treatment catheter during the Index/Rescheduled Index Procedure, as clinically assessed by entrance block demonstrated ≥ 20 minutes after the last PVI lesion was made, with or without adenosine.

The proportion of Pulsed Field MITT subjects with Acute Procedural Success was 99.3%, and the proportion of Thermal MITT subjects with Acute Procedural Success was 99.3%. There was not a statistical difference between these results [95% BCI -1.5, 1.5]. There were two acute procedural failures in the Pulsed Field group and two in the Thermal group.

Acute Vein Success

Acute Vein Success was defined as the proportion of all attempted PVs isolated using the randomized treatment during the first ablation procedure (Index or Rescheduled Index Procedure), as clinically assessed by entrance block demonstrated ≥ 20 minutes after the last PVI lesion is made with or without adenosine testing.

The proportion of all ablated PVs with Acute Vein Success in MITT subjects in the Pulsed Field group was 99.6%, which was not statistically different from the proportion of all ablated PVs with Acute Vein Success in MITT subjects in the Thermal group at 99.4%.

3. Additional Analyses

Quality of Life

Subjects were assessed for quality of life changes between baseline and 12 months using the EQ-5D-3L and Atrial Fibrillation Effect of Quality of Life (AFEQT) questionnaires. Both the Pulsed Field and Thermal subjects exhibited improvement from baseline in the overall and global indices as well as the VAS overall health status when measured again at 12 months. There were no differences in the outcomes reported between the two

treatment groups.

Primary Treatment and Class I/III AAD Failure Subjects

There were 328 MITT subjects (328/607 or 54%) that had previously failed at least one Class I / III AADs for either inefficacy or intolerance at the time of study enrollment and thus constituted a group of subjects who are considered "Class I/III Failure subjects". Additionally, there were 279 MITT subjects (279/607 or 46%) that had not previously failed a Class I / III AAD at the time of study enrollment and thus constituted a group of subjects who are considered "Primary Treatment subjects".

In a post-hoc analysis, baseline characteristics of the MITT cohort were compared to the Class I/III Failure subjects as well as to the Primary Treatment subjects, and no clinically important differences in gender, race, or baseline demographics (age, height, BMI, LAD, CHA2DS2-VASc) were observed. Expectedly, primary treatment subjects had fewer years since first AF diagnosis than the overall MITT cohort, and Class I/III failure subjects had a longer average duration than the overall MITT cohort.

Three Class I/III failure PFA subjects experienced one or more CSE events (estimated incidence 2.1%) and three Primary Treatment PFA subjects experienced one or more CSE events (estimated incidence 2.5%), consistent with the 2.1% estimated incidence observed in the overall PFA MITT cohort. Survival analysis of Treatment Success in the MITT Pulsed Field cohort and the Primary Treatment and Class I/III Failure subgroups shows almost identical long-term outcomes (Figure 2).

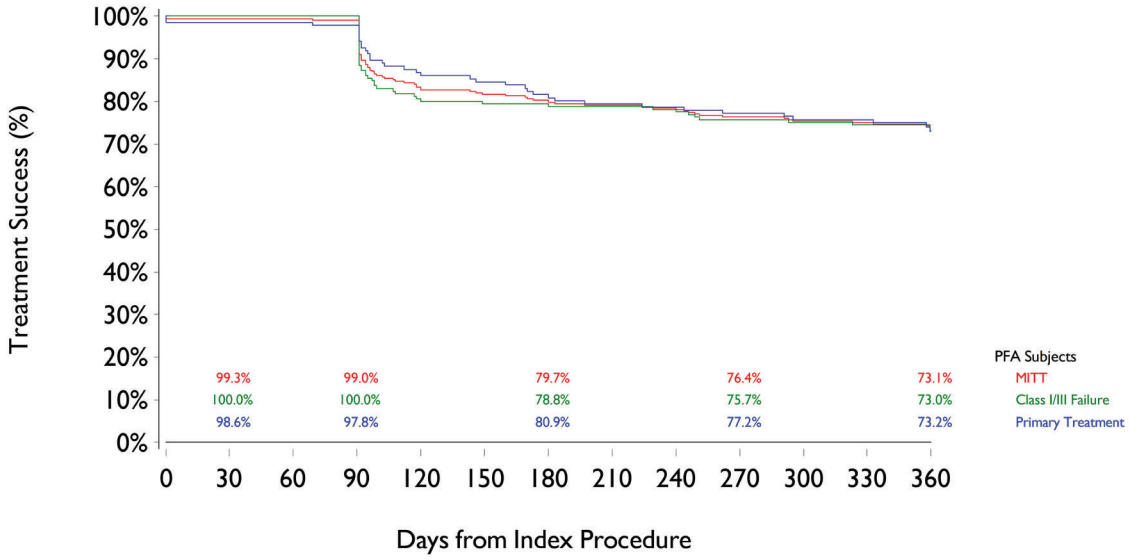


Figure 2. Pulsed Field Subjects – Treatment Success

4. Sensitivity Analyses

Two sensitivity analyses of the primary safety endpoint were performed: a pre-specified analysis using the Per Protocol population and a post hoc analysis comparing MITT subject outcomes sub-grouped by site thermal control modality. A Per Protocol (PP) subject is one without major protocol deviations that would affect the completeness, accuracy, and reliability of the study data. These analyses demonstrated that the primary safety result is robust and non-inferiority is statistically supported.

Effectiveness Endpoint Sensitivity Analyses

Several sensitivity analyses of the primary effectiveness endpoint were performed in addition to the survival analysis reported above: a prespecified analysis using the Per Protocol population, a pre-specified analysis considering any otherwise successful subjects who underwent atrial ablations other than PVI as failures, a post hoc analysis analyzing only those subjects whose overall event monitoring compliance was greater than 80%, and a post hoc analysis comparing MITT subject outcomes sub-grouped by site thermal control modality. These analyses demonstrated that the primary effectiveness result is robust and non-inferiority is statistically supported.

Additional Sensitivity Analyses

Poolability analyses were performed to examine the primary safety endpoint results and primary effectiveness endpoint results by site, control modality, and sex. There was no evidence of a heterogeneity effect in these assessments.

F. Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

G. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The SPHERE Per-AF clinical study included 79 investigators of whom six had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 6
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 3

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

X. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

The FARA-Freedom study is a prospective, open label, multi-center, single arm, post market study designed to meet the requirements of a post market clinical follow-up (PMCF) study in Europe by collecting 12 months of prospective safety and performance data on the current commercial version of the FARAPULSE PFA system in the EU, which is same as the version being submitted for PMA approval.

The data presented in this summary has been analyzed utilizing statistical methods that are identical or analogous to those used in the US pivotal ADVENT Trial.

Investigators at 13 investigational sites enrolled a total of 185 study subjects between December 21, 2021, and August 31, 2022. One hundred eighty-five (185) patients were screened for participation in the FARA-Freedom Study and 5 failed to meet the study entry criteria at baseline assessment. The remaining 180 MITT subjects were treated with the FARAPULSE PFA System. Subjects were followed for 12 months with assessments at pre-discharge, 7 days, 30 days, 90 days, 6 months, and 12 months following the index procedure for adverse events and recurrent arrhythmia.

Arrhythmia monitoring included 12-lead ECGs at 90 days, 12 months, or unscheduled visits, 72-hour Holter monitoring at 6- and 12-months, and weekly and symptomatic rhythm transmissions from a study-specific event monitor. All rhythm events were adjudicated by independent arrhythmia core laboratory and all adverse events by an independent Clinical Events Committee (CEC). Class I/III anti-arrhythmic drugs (AADs) were required to be discontinued after Day 90, and use of amiodarone was excluded any time during the study. At the time of the data snapshot for this study, 177 active subjects have completed their 6-month follow up assessments and 130 have completed 12-month assessments and have exited the study. The remaining subjects are pending their 12-month visit assessments.

Primary Safety Endpoint

The primary safety endpoint is a Composite Safety Endpoint (CSE) defined as the proportion of MITT subjects with one or more of the following device or procedure-related SAEs as adjudicated by the CEC based on the protocol specified definitions.
Early onset: Any of the following with an Onset Date within 7 days of the Index / Rescheduled Index procedure:

- Death
- Myocardial infarction
- Persistent phrenic nerve palsy
- Stroke
- TIA
- Peripheral or organ thromboembolism
- Cardiac tamponade / perforation

- Pericarditis
- Pulmonary edema
- Vascular access complications
- Heart block
- Gastric motility/pyloric spasm disorders

Late onset: Either of the following with an Onset Date any time through the completion of 12-month follow-up visit:
- Pulmonary Vein Stenosis (PVS)
- Atrio-esophageal fistula

The principal analysis population for the safety endpoints was the Safety subject population.

The safety hypotheses are as follows:
H0: QT ≥ PGsaf
HA: QT < PGsaf,

where QT is the probability of a Safety Subject experiencing one or more CSE, and PGsaf is a performance goal of 0.14. The null hypothesis will be rejected and the alternative accepted if the posterior probability Pr(HA | data) > 0.975, corresponding to the upper bound of a 95% central Bayesian credible interval (BCI) being less than PGsaf.

The parameter QT is assigned a Beta (0.5, 0.5) prior distribution, which is the Jeffreys non-informative prior. In the absence of missing or incomplete data, the posterior distribution of QT would be a conjugate Beta distribution, but the planned timing of this analysis (before 1 year of follow-up is complete for all subjects) will induce some incomplete data. Therefore, Bayesian multiple imputation of 12-month outcomes was employed in this analysis, using the same approach that is used in the ADVENT Statistical Analysis Plan

Primary Performance Endpoint

The primary performance endpoint is Treatment Success in MITT Subjects through the Month 12 Assessment (Day 360 ± 30), defined as:

1. Acute Procedural Success defined as: demonstration of isolation of all attempted PVs using the randomized treatment during the first ablation procedure as clinically assessed by entrance block demonstrated ≥ 20 minutes after the last PVI lesion is made with or without adenosine testing.
AND
2. Chronic Success, defined as freedom from:
a. At the Index / Rescheduled Index Procedure: Use of a non-PFA treatment modality for PVI
b. After the Blanking Period:
    i. Occurrence of any Detectable AF, AFL or AT excluding CTI-dependent AFL confirmed by EP study)

ii. Cardioversion for AF, AFL or AT (excluding for CTI-dependent AFL)
iii. Use of any Type I or Type III antiarrhythmic medication for the treatment of AF, AFL or AT

c. At any time:
i. Re-ablation for AF, AFL or AT (other than for CTI-dependent AFL)
ii. Use of amiodarone, except intra-procedurally to control an arrhythmia

The principal analysis population for the primary performance endpoint is the Modified Intent-to-Treat (MITT) Population.

The performance hypotheses are as follows:
H0: PT ≤ PGperf
HA: PT > PGperf,

where PT is the probability of a subject being a Treatment Success at 12 Months, and PGperf is a pre-specified performance goal of 0.50. The null hypothesis will be rejected and the alternative accepted if the posterior probability Pr(HA | data) > 0.975, corresponding to the lower bound of a 95% central Bayesian credible interval (BCI) being greater than PGperf.

PT is assigned a Beta (0.5, 0.5) prior distribution, which is the Jeffreys non-informative prior. In the absence of missing or incomplete data, the posterior distribution of PT would be a conjugate Beta distribution, but the planned timing of this analysis (before 1 year of follow-up is complete for all subjects) will induce some incomplete data. Therefore, Bayesian multiple imputation of 12-month outcomes was employed in this analysis. The imputation model accounts for primary outcome information up through the time of censoring.

Subject Accountability

One hundred eighty-five (185) patients were screened for participation in the FARA-Freedom study and 5 failed to meet the study entry criteria during the baseline assessment. The remaining 180 intent-to-treat (ITT) subjects provided informed consent, were enrolled, and received treatment with the FARAPULSE PFA System.

The ITT, MITT, and Safety analysis sets consist of the same population (N=180), as all subjects received energy delivery for PVI with the FARAPULSE PFA System. The Per Protocol (PP) population consists of MITT subjects without major protocol deviations that would affect the completeness, accuracy, and reliability of the study data. Thirteen subjects (13) were excluded from the PP population; 4 subjects were excluded due to a major deviation regarding the use of amiodarone during the study, and 9 subjects had major inclusion/exclusion violations.

At the time of data snapshot, all active subjects (177/177) have completed their 6-month follow up assessments (3 subjects withdrew before 6 months). One hundred three (103) subjects have completed their 12-month assessments, exited the study, and are 100% source data verified (SDV). An additional 27 subjects have recently completed their 12-

month visit and are included in this data set. There are 46 subjects continuing to be followed for their 12-month visit.

Study subjects were scheduled for assessment at Baseline, Index Procedure, Pre-Discharge, Days 7, 30, 60, 90, 180 and Day 360. Visit compliance for these study assessments was high (99.3% overall, 96.8% in window) with only 4 missed visits at 30 days, and 1 each at 60 days, 90 days and 6 months as of the snapshot date.

Overall rhythm monitoring weekly compliance was calculated beginning in 7-day intervals from Day 90. Weeks during which study data included one or more evaluable rhythm monitoring records were counted as compliant; weeks in which an evaluable rhythm monitoring record was not found were counted as non-compliant. The overall rhythm monitoring weekly compliance was high, with 89.1% of monitored weeks resulting in an evaluable rhythm monitoring record for study subjects.

Safety Results

Primary Safety Endpoint

Two (2) subjects experienced one or more CSE events; the estimated incidence through 12 months is 1.4%, and the upper bound of the 95% BCI is 3.7%. The posterior probability that the incidence is less than the pre-specified performance goal of 14% is >0.999. Since this posterior probability is greater than 0.975, this endpoint met its success criterion (Table 16).

Table 16. FARA-Freedom Primary Safety Endpoint –Subjects with One or More CSEs

Number of Subjects with ≥1 CSE	Estimated Incidence (%)	95% BCI	Posterior Probability that CSE Rate < 0.14
2	1.4	(0.2, 3.7)	>0.999

Note: Estimated incidence calculated as the mean of the posterior distribution; posterior mean and Bayesian credible interval (BCI) calculated using Beta (0.5, 0.5) prior, with multiple imputation for incomplete data.
Abbreviations: BCI = Bayesian credible interval, CSE = Composite Safety Endpoint event

The Composite Safety Endpoint Events were analyzed as separate outcomes. The safety event type and proportion of MITT Subjects with one or more CSE Event are presented in Table 17. Two subjects experienced CSE events. Subject 02-005 had a TIA adjudicated as an SAE related to the procedure. Subject 12-003 had a procedure-related SAE of periprocedural cardiac tamponade attributed to puncture of the LA with the guidewire. Both events were resolved without sequelae.

Table 17. FARA-Freedom Proportion of MITT Subjects with One or More CSE Events

MITT Subjects with One or More CSE Events by Event Type	Number of Subjects % (n / N) N 180
Any CSE Event	1.1 (2/180)
Death	0.0 (0/180)
Myocardial infarction	0.0 (0/180)
Persistent phrenic nerve palsy	0.0 (0/180)
Stroke	0.0 (0/180)
TIA	0.6 (1/180)
Peripheral organ thromboembolism	0.0 (0/180)
Cardiac tamponade or perforation	0.6 (1/180)
Pericarditis	0.0 (0/180)
Pulmonary edema	0.0 (0/180)
Vascular access complication	0.0 (0/180)
Heart block	0.0 (0/180)
Gastric motility/pyloric spasm	0.0 (0/180)
Pulmonary vein stenosis	0.0 (0/180)
Atrio-esophageal fistula	0.0 (0/180)

Note 1: n = number of subjects with event, N = number of MITT subjects.
Abbreviations: CSE = Composite Safety Endpoint, TIA = transient ischemic attack

There were no Unanticipated Adverse Device Effects (UADEs) in the FARA-Freedom PMCF Study.

Table 18 summarizes the incidence of adverse events experienced in the FARA-Freedom study as adjudicated by the CEC. Overall, 137 adverse events were experienced in 69 subjects.

Table 18. Overview of Adverse Events, MITT Subjects

Adverse Events Categories- MITT	All Subjects (N 180) n (%) e[1]
Any adverse event	69 (38%) 137
Any SAE	20 (11%) 31
Any device-related AE	6 (3%) 6

Adverse Events Categories- MITT	All Subjects (N 180) n (%) e[1]
Any procedure-related AE	26 (14%) 31
Any device-related SAE	1 (1%) 1
Any procedure-related SAE	7 (4%) 9
Note 1: N = number of MITT in group, n = number of subjects with one or more events, % = percentage of subjects with one or more events, e = number of events.	

Table 19 summarizes the incidence of all SAEs by AE Category. There were 7 device- or procedure-related SAEs reported in 9 subjects. One (1) event of TIA was assessed by the CEC as possibly related to the device and probably related to the procedure. All other events were classified as procedure related only by the CEC. All of these SAEs were determined to be resolved by the without reported sequelae.

Table 19. Related Serious Adverse Events by Category – MITT Subjects

Procedure- or Device-Related Serious Adverse Events	All Subjects (N 180) n (%) e[1]
Procedure- or Device-Related Serious Adverse Events	**7 (4%) 9**
Atrial flutter	1 (1%) 2
Procedure related Abnormal labs	2 (1%) 2
Angina/Chest Pain - Post EP procedure	1 (1%) 1
Atrial tachycardia/Other SVT	1 (1%) 1
Myocardial Perforation with Tamponade	1 (1%) 1
Pseudoaneurysm	1 (1%) 1
TIA	1 (1%) 1

Note 1: N = number of Safety subjects in group, n = number of subjects with one or more events, % = percentage of subjects with one or more events, e = number of events.

Primary Performance Endpoint

The estimated probability of MITT subjects experiencing Treatment Success was 66.3% (lower bound of the 95% BCI is 59.1). The posterior probability that this success rate exceeds the pre-specified performance goal of 50% is > 0.999. Since this posterior probability is greater than 0.975, this endpoint met its success criterion (Table 20).

Table 20. FARA-Freedom Primary Performance Endpoint – MITT Subjects

Subjects with Treatment Success [Incomplete Subjects without Treatment Failure] N 180	Incidence (%)	95% BCI	Posterior Probability of Treatment Success Proportion > 50%
90 [31]	66.3	[59.1, 73.1]	>0.999

Abbreviations: N = number of subjects included in analysis (including those with incomplete follow-up)
Note: Estimated incidence calculated as the mean of the posterior distribution; posterior mean and Bayesian credible interval (BCI) calculated using Beta (0.5, 0.5) prior, with multiple imputation for incomplete data.

An additional analysis of the primary performance endpoint was performed using the Kaplan-Meier method to include incomplete subject data. This is a different statistical technique applied to a slightly different definition of the endpoint (time to failure rather than Treatment Success at the 12-month visit), but the Kaplan-Meier estimate of 66.1% at 360 days agrees closely with the 66.3% estimate produced by the pre-specified Bayesian statistical model.

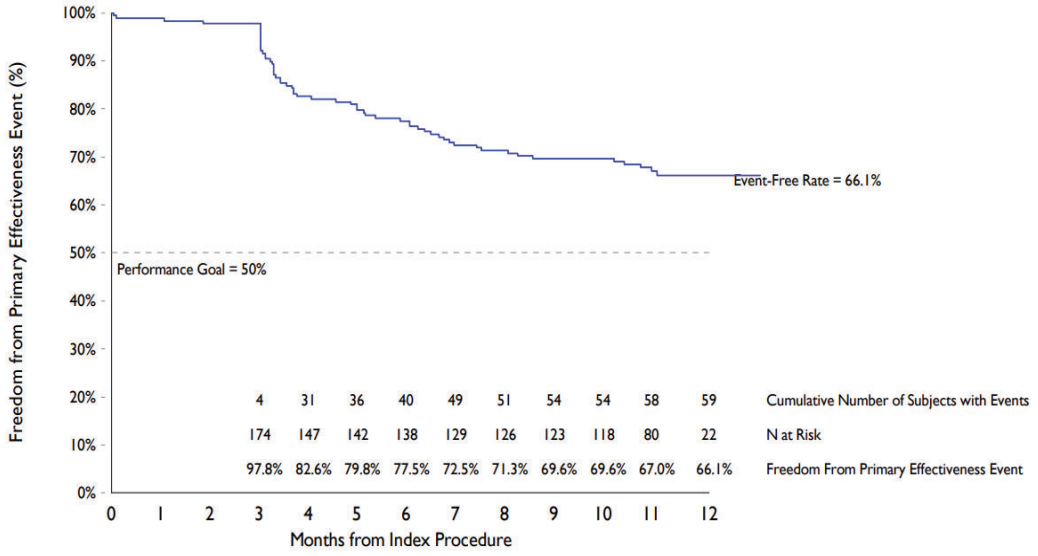


Figure 3. FARA-Freedom Survival Analysis, Primary Performance Endpoint – MITT Subjects

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices Advisory Panel, an FDA advisory committee, for review and recommendation because the information in the PMA demonstrates that the pertinent issues for safety and effectiveness of a pulsed field ablation system have been vetted through comprehensive bench and clinical evaluations.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The effectiveness results of the ADVENT study demonstrate that the FARAPULSE™ Pulsed Field Ablation System is effective for the isolation of the pulmonary veins in the treatment of paroxysmal atrial fibrillation by rendering targeted cardiac tissue electrically non-conductive to prevent cardiac arrhythmia initiation or maintenance.

The probability of a Pulsed Field MITT subject having Treatment Success was non-inferior to the probability of a Thermal MITT subject having Treatment Success using a non-inferiority margin of 15%: the posterior probability of non-inferiority is >0.999, which exceeded the prespecified threshold of 0.956.

Additionally, the FARA-Freedom PMCF study met the success criterion for its primary performance endpoint. At the time of data snapshot, the probability of a Pulsed Field subject having Treatment Success is estimated to be 66.3%. The posterior probability that this success rate exceeds the pre-specified performance goal of 50% is > 0.999.

Acute procedural success was achieved in 100% of subjects. After the Index Procedure, re-ablation was performed in 11 subjects. Additionally, subject AF symptom prevalence and frequency were substantially reduced post procedure.

B. Safety Conclusions

The risks of the device are based on data collected in the ADVENT clinical study conducted to support PMA approval as described above.

In the ADVENT clinical study, the probability of a Pulsed Field MITT subject having one or more CSE events was non-inferior to the probability of a Thermal MITT subject having one or more CSE events using a non-inferiority margin of 8%: the posterior probability of non-inferiority was >0.999, which exceeded the prespecified threshold of 0.966.

No new risks or unanticipated adverse device effects were encountered during the ADVENT study.

Additionally, The FARA-Freedom PMCF Study met the success criterion for the primary safety endpoint. Two (2) subjects experienced one or more CSE events in the FARA-Freedom study. The estimated incidence of CSE through 12 months is 1.4%, and the upper bound of the 95% BCI is 3.7%. The posterior probability that the incidence is less than the pre-specified performance goal of 14% is >0.999.

C. Benefit-Risk Determination

The probable benefits of the device are based on data collected in a clinical study conducted to support PMA approval as described above. The benefits of treatment using the device include a high probability in isolation of the pulmonary veins in the treatment of paroxysmal atrial fibrillation.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. Catheter ablation to achieve pulmonary vein isolation has significant known risks, including common risks such as stroke/major thromboembolism, perforation/tamponade, and uncommon risks such as pulmonary vein stenosis, phrenic nerve injury, atrio-esophageal fistula, and death. The pivotal study demonstrated similar rates of common adverse events to standard ablation, and no incidence of the uncommon adverse events.

There are important biophysical characteristics of pulse field ablation that would predict a low or absent incidence of these uncommon adverse events. However, the number of patients entered into the trial is likely insufficient to exclude the occurrence of these uncommon events.

No new or unanticipated adverse device effects or patient risks were identified in the ADVENT clinical study.

Patient Perspective

The submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data support that the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The ADVENT clinical study met its primary safety and effectiveness objectives. The FARAPULSE PFA System is non-inferior to the standard of care Thermal ablation (RFA and CBA) for the treatment of patients with drug-refractory, recurrent, symptomatic PAF and shows that the ADVENT IDE trial met its primary endpoints.

The primary safety and effectiveness endpoint analysis from the European FARA-Freedom PMCF Study provides supplemental evidence supporting the safety and performance of the FARAPULSE PFA System in the treatment of patients with PAF.

In conclusion, the data in this application support the reasonable assurance of safety and effectiveness of the FARAPULSE PFA System when used in accordance with the indications for use

XIII. CDRH DECISION

CDRH issued an approval order on January 30, 2024. The final clinical conditions of approval cited in the approval order are described below.

The ADVENT Post-Approval Study (PAS) is a prospective, non-randomized, multi-center, single-arm study to evaluate the long-term effectiveness and safety of the FARAPULSE™ Pulsed Field Ablation System for the treatment of drug-refractory,

recurrent, symptomatic, paroxysmal atrial fibrillation (AF). Approximately 336 patients who intend to undergo their de novo pulmonary vein isolation procedure using the FARAPULSE Pulsed Field Ablation System to treat symptomatic paroxysmal atrial fibrillation refractory or intolerant to at least one Class I, II, III, or IV antiarrhythmic medication will be enrolled and ablated using the FARAPULSE Pulsed Field Ablation System, with all patients treated in the United States. The study will include a diverse (i.e., race, ethnicity, gender) patient population. All subjects will get a transthoracic echocardiogram performed at baseline and 12 months post-ablation to detect new left ventricular wall motion abnormality. A 12-lead ECG will be performed at baseline and 12 months post-ablation in all subjects. Follow-up clinical data will be collected at discharge, 7-days, 6-months, 12-months, and 36-months.

The primary objectives of the PAS will be the following:

1. Estimating the safety event free rate at 12 months post-index-procedure.
2. Estimating acute procedural success.
3. Estimating chronic success through 12 months post-index-procedure.

The secondary objectives and additional analyses will include, but not be limited to, the following:

1. Evaluating chronic treatment failure at 24 months and 36 months.
2. Estimating procedure times.
3. Estimating treatment success allowing the use of antiarrhythmic medications and/or reablation.
4. Estimating freedom from recurrence of individual types of atrial arrhythmias between 3 months and 12 months post-index-procedure.
5. Estimating chronic success through 12 months post-index procedure stratified by the presence or absence of a prior failed trial of Class I or III antiarrhythmic medication therapy (due to ineffectiveness or intolerance).
6. Analyzing anesthesia technique.
7. Analyzing lesion locations as recorded by a compatible electroanatomic mapping system.
8. Analyzing reablation parameters.

From the date of study protocol approval, you must meet the following timelines for the PULSED AF PAS:

- First subject enrolled within 6 months
- 20% of subjects enrolled within 12 months
- 50% of subjects enrolled within 18 months
- 100% of subjects enrolled within 24 months

In addition, you must submit separate periodic reports on the progress of the PULSED AF PAS as follows:

- PAS Progress Reports every six (6) months until subject enrollment has been completed, and annually thereafter, from the date of the PMA approval letter, unless otherwise specified by FDA.
- If any enrollment milestones are not met, you must begin submitting quarterly enrollment status reports every 3 months in addition to your periodic (6-month) PAS Progress Reports, until FDA notifies you otherwise.
- Submit the Final PAS Report three (3) months from study completion (i.e., last subject's last follow-up date).

Each PAS report should be submitted to the address below identified as a "PMA Post-Approval Study Report" in accordance with how the study is identified above and bearing the applicable PMA reference number.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.