

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Pulsed Field Ablation System

Device Trade Name: FARAPULSE™ Pulsed Field Ablation System (FARAWAVE™ Pulsed Field Ablation Catheter, FARAWAVE™ NAV Pulsed Field Ablation Catheter, FARAPPOINT™ Pulsed Field Ablation Catheter, FARASTAR™ Catheter Connection Cable, FARASTAR™ Pulsed Field Ablation Generator, FARASTAR™ Recording System Module, FARASTAR™ Mapping 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, 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), FARASTAR™ Recording System Module ECG Output to Rhythmia HDx™ ECG Input Cable, FARASTAR™ Recording System Module EGM Output to Rhythmia HDx™ EGM Input Cable, FARASTAR™ Mapping System Module Back Patch Cable, FARASTAR™ Mapping System Module Back Patch Cable Male, FARASTAR™ Mapping System Module BNC BNC-Phono Cable, FARASTAR™ Mapping System Module Rhythmia™ ABL Cable, FARASTAR™ Mapping System Module Auxiliary Cable, FARASTAR™ EGM to EP Recording System Cable FARAPPOINT™)

Device Procode: QZI

Applicant's Name and Address: Boston Scientific Corporation

300 Boston Scientific Way
Marlborough, MN 01752

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P230030/S012

Date of FDA Notice of Approval: January 12, 2026

The original PMA P230030 was approved on January 30, 2024, and is indicated for:

FARAWAVE™ Pulsed Field Ablation Catheter

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

FARASTAR™ Pulsed Field Ablation Generator

The FARASTAR PFA 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).

FARASTAR™ Recording System Module

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.

FARASTAR™ Catheter Connection Cable

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

The SSED to support the indication is available on the CDRH [website](#) and is incorporated by reference here. The current supplement was submitted to expand the indication for the FARAWAVE Pulsed Field Ablation System.

II. INDICATIONS FOR USE

The FARAPULSE Pulsed Field Ablation System is indicated for:

FARAWAVE™ and FARAWAVE™ NAV Pulsed Field Ablation catheters

The FARAWAVE Catheter is indicated for:

- the isolation of pulmonary veins in the treatment of drug-refractory, recurrent, symptomatic Paroxysmal Atrial Fibrillation (PAF).

- the isolation of pulmonary veins and the posterior wall in the treatment of drug-refractory, symptomatic Persistent Atrial Fibrillation (episode duration less than one year).

FARAPOINT™ Pulsed Field Ablation Catheter

The FARAPOINT Catheter is indicated for use as an adjunctive device for the creation of an ablation line between the inferior vena cava and the tricuspid valve when any FARAWAVE Catheter is used in the endocardial treatment of drug-refractory, symptomatic persistent atrial fibrillation (episode duration no greater than 12 months).

FARASTAR™ Pulsed Field Ablation Generator

The FARASTAR PFA Generator is intended for use with a compatible Boston Scientific PFA catheter in cardiac ablation procedures.

FARASTAR™ Recording System Module

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.

FARASTAR™ Catheter Connection Cable

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

III. CONTRAINDICATIONS

The FARAPOINT Catheter 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 with a known inability to obtain vascular access;
- 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);
- in patients with a known absolute contraindication to nitroglycerin who require ablation in proximity to a coronary artery.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the FARAPPOINT Pulsed Field Ablation Catheter and System labeling.

V. DEVICE DESCRIPTION

The FARAPULSE PFA System consists of the FARAWAVE PFA Catheter (NAV and non-NAV), FARAPPOINT PFA Catheter, FARASTAR PFA Generator and accessories, FARASTAR RSM and accessories, and FARASTAR MSM and accessories. These components are designed to operate together as a system. The FARASTAR PFA 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 PFA 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, and the FARASTAR MSM, which is used to reduce potential interference to the mapping system during ablation. The FARASTAR PFA Generator, FARASTAR RSM, and FARASTAR MSM are non-sterile, reusable, capital equipment whereas the FARAWAVE and FARAPPOINT catheters are single use, disposable devices.

The FARAWAVE Catheter is an over-the-wire, multi-electrode catheter designed to deliver PFA energy to the distal section of the catheter for cardiac ablation. The FARAPPOINT Catheter is a sterile, single-use catheter with a nominal 8F shaft and 7.5F distal section. The distal section consists of five splines with four electrodes located on each spline, twenty electrodes total. It is a multi-electrode, bi-directional, deflectable percutaneous ablation catheter designed to deliver PFA energy to the distal section for focused point-to-point cardiac ablations. The catheter handle features manually operated steering control, deflection lock knob and an integrated connector for attachment of the FARASTAR Catheter Connection Cable.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of drug refractory recurrent symptomatic paroxysmal or persistent atrial fibrillation. These alternatives include:

- Treatment with medicines that help control the rate and/or rhythm of the heart and other medicines that reduce the likelihood of clots forming (known as medical or pharmacologic therapy).
- Cardioversion to restore the heart's normal rhythm (with electrical shock or medicine).
- Ablation of the AV node and insertion of a permanent pacemaker to control the heart rate.
- Implantable devices that reduce the likelihood of clots forming.
- Catheter ablation with other devices approved in the United States.

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 Pulsed Field Ablation System was initially CE Marked on January 26, 2021, and the original PMA (P230030) was approved on January 30, 2024. In addition to being marketed in the European Union, the subject system is marketed in various countries around the world such as Japan, China, South Korea, South Africa, United Arab Emirates (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.

The FARAWAVE Catheter (NAV and non-NAV) and FARASTAR MSM components of the FARAPULSE PFA System were approved on October 18, 2024 (P230030/S003). The expansion of indication for use of the FARAPULSE PFA system to include the treatment of drug refractory, symptomatic persistent atrial fibrillation was approved on July 3, 2025 (P230030/S007).

The FARAPPOINT Catheter was approved on January 12, 2026 (P230030/S012).

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device.

- Pain or discomfort, for example:
 - Angina
 - Chest pain
 - Non-cardiovascular pain
- Cardiac arrest
- Death
- Electric shock
- Hypotension
- Infection/inflammation/exposure to biohazardous material
- Pulmonary edema/heart failure/pleural effusion
- Renal failure/insufficiency
- Respiratory distress/insufficiency/dyspnea
- Arrhythmia (new or exacerbated)
 - Conduction pathway injury (for example: heart block, injury to sinus or AV node, etc.)
- Nerve injury, for example:
 - Phrenic nerve injury
 - Vagal nerve injury
- Gastrointestinal disorders
- Vessel trauma, including:
 - Perforation
 - Dissection
 - Coronary artery injury
 - Vasospasm, including coronary artery spasm
 - Occlusion
 - Hemothorax
- Cardiac trauma, for example:

- Cardiac perforation/cardiac tamponade/pericardial effusion
 - Valvular damage
- Injury related to tissue damage and/or adjacent structures, for example:
 - Esophageal injury
 - Pulmonary injury
 - Catheter entrapment
 - Physical trauma
- Fistula, for example:
 - Atrio-esophageal fistula
 - Bronchopericardial fistula
- PV [pulmonary vein] stenosis and its symptoms, for example:
 - Cough
 - Shortness of breath, fatigue
 - Hemoptysis
- Surgical and access site complications, for example:
 - Hematoma/seroma
 - AV [arteriovenous] fistula
 - Bleeding
 - Pseudoaneurysm
 - Pneumothorax
 - Residual atrial septal defect
- Thrombus/thrombosis
- Muscle spasm
- Injury due to embolism/thromboembolism/air embolism/foreign body embolism
- Cerebrovascular accident (CVA)/stroke
- Transient ischemic attack (TIA)
- Myocardial infarction
- Neurological impairment and its symptoms, for example:
 - Cognitive changes, visual disturbances, headache, motor impairment, sensory impairment, and speech impairment.
- Pulmonary embolism.
- Peripheral embolism.
- Asymptomatic cerebral embolism.
- Hemolysis
- Procedure related side effects, for example:
 - Allergic reaction (including anaphylaxis)
 - Genitourinary complication
 - Side effects related to medication or anesthesia
 - Radiation injury/tissue burn
 - Vasovagal response
 - Fluid volume overload

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

IX. SUMMARY OF NON-CLINICAL STUDIES

Testing of the FARAPPOINT Catheter and the FARAPULSE PFA System included verification and validation testing (device and system), usability, 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. Please refer to the P230030 SSED available on the FDA [website](#) for a description of previously conducted non-clinical studies.

A. Bench Studies

Tables 1, 2 and 3 below summarize the bench testing, system testing and system of systems testing to support the FARAPPOINT Catheter.

Table 1. FARAPPOINT Catheter Testing Summary

Test Performed	Result
Visual Inspection	Pass
Dimensional Analysis	Pass
Tensile Testing	Pass
Distal Buckling	Pass
Planarity	Pass
Articulation Torque	Pass
Air Ingress	Pass
Therapeutic Delivery	Pass
Dielectric Strength	Pass
Post Simulated Use – Visual Criteria	Pass
Post Simulated Use – Mechanical Integrity	Pass

Table 2. FARAPULSE PFA System Testing Summary

Test Performed	Result
System Design Verification	Pass
System Design Validation	Pass
EEPROM	Pass
Electrical Safety (per IEC 60601-1)	Pass
Electromagnetic Compatibility (per IEC 60601-1-2)	Pass

Table 3. System of Systems Testing Summary

Test Performed	Result
Magnetic Tracking of PFA Catheters	Pass
Impedance Mapping with FARAPPOINT – Accuracy and Precision	Pass
Sheath Detection	Pass
Catheter Auto Identification	Pass
Noise – OPAL HDx System	Pass
Noise – Recording System	Pass

Biocompatibility testing of the FARAPPOINT Catheter was conducted in accordance with the ISO 10993 standard. Based on ISO-10993, the catheter is an externally communicating

device, which contacts circulating blood for "limited" duration (less than 24 hours). A summary of the results is reported in Table 4 below.

Table 4. Biocompatibility Testing Summary – FARAPPOINT Catheter

Test Performed	Result
Cytotoxicity Study Using the ISO Elution Method ISO 10993-5	Pass
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
Platelet and Leukocyte Counts ISO 10993-4	Pass
Partial Thromboplastin Time (PTT) Assay ISO 10993-4	Pass

B. Animal Studies

Four studies conducted in the porcine model provide objective evidence supporting the safety, feasibility, and usability of the FARAPPOINT Catheter and 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 5.

Table 5. Animal Studies

Study	Study Objective	Results
Subacute (7 days) Non-GLP FARAPPOINT Dosing Study (n=18)	To quantify lesion dimensions across a dosing range.	All acceptance criteria were met
Acute Non-GLP Design Validation Study to Evaluate the Performance of the FARAPPOINT Catheter in the Swine Model (n=4)	To demonstrate that the catheter conforms to the intended customer and production specification requirements through evaluation in a simulated use environment when used with commercially available PFA and mapping system components.	All acceptance criteria were met
A 30-Day GLP Chronic Safety and Performance Study of the FARAPPOINT Catheter in the Porcine Model (n=18)	To evaluate system performance by using chronic (30-day) safety and efficacy endpoints after cavotricuspid isthmus treatment with the FARAPPOINT Catheter using a clinically relevant workflow.	All acceptance criteria were met Two adverse events were observed: 1) In 3/6 study animals, ventricular fibrillation occurred during energy delivery that required defibrillation to return each animal to normal sinus rhythm. 2) Short segments of the RCA displayed chronic (stable)

		intimal hyperplasia or perivascular fibrosis that was attributed to PFA treatment. A few RCA branches also showed intimal hyperplasia. These observations were probably secondary to vasospasm during energy delivery to the CTI.
A 30-Day GLP Study Evaluating Safety of the FARAPOINT+ Pulsed Field Ablation Catheter in naïve Swine Model (n=6)	To evaluate the safety of the FARAPOINT Catheter IDE version as further confirmation of therapeutic equivalence between the study versions of the device	All acceptance criteria were met

C. Additional Studies

a. 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.

b. Bioburden

Bioburden data is generated to ensure that sterility assurance level (SAL) is not impacted by the product bioburden levels. To control the bioburden, the catheters are manufactured in a Controlled Environment Room.

c. Sterilization

The FARAPOINT Catheter is sterilized using ethylene oxide (EO) gas and has 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 that the product satisfies a minimum Sterility Assurance Level (SAL) of 10⁻⁶ and residual EO levels were within acceptable ranges.

X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

The applicant performed a clinical study (ADVANTAGE AF Clinical Study Phase 2, ClinicalTrials.gov NCT05443594) to establish a reasonable assurance of safety and effectiveness of catheter ablation with the FARAPULSE Pulsed Field Ablation System for the treatment of drug-refractory, symptomatic, persistent atrial fibrillation (PsAF) in the US, Canada, and Europe under IDE G220079. ADVANTAGE AF Phase 2 incorporated the use of the FARAPOINT PFA Catheter in addition to the FARAWAVE

PFA Catheter. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between October 9, 2023, and February 11, 2025. The database for this Panel Track Supplement reflected data collected through DATE, and included 314 patients (43 Roll-In, 16 Consent Ineligible/Intent, and 255 Non-Roll-In Treatment Subjects), 183 (42 Roll-in subjects and 141 Non-Roll-In subjects) of whom were treated with the FARAPOINT PFA Catheter. There were 29 investigational sites.

The study was a prospective, single-arm, open-label, multi-center clinical study. Subjects requiring ablative intervention for persistent atrial fibrillation (PersAF) meeting study eligibility criteria had percutaneous ablative pulmonary vein isolation (PVI) and left atrial posterior wall isolation (LAPWI) using the FARAWAVE PFA Catheter. Subjects meeting protocol criteria for CTI ablation had additional ablative intervention of creating an ablation line between the inferior vena cava and the tricuspid valve with the FARAPOINT PFA Catheter. All subjects who met the eligibility criteria, signed the informed consent, and underwent the ablation procedure (the “index procedure”) were followed for 12 months. Subjects had a commercially available Boston Scientific LUX-Dx insertable cardiac monitor (ICM) inserted within seven days after the Index Procedure (if not previously inserted) to detect the recurrence of atrial arrhythmias (AAS). Subjects were followed at pre-discharge, Day 7, Day 30, Day 90, Day 180, and Day 360. Arrhythmia recurrence between the index procedure and day 90 were considered within the “blanking period” and did not contribute to the arrhythmia recurrence endpoint. The first subject enrolled by each ablating investigator at each site was considered part of the Roll-In cohort and all other subjects were considered part of the Treatment cohort.

There was no active control group. Results were evaluated against pre-defined performance goals based on the percentage of subjects who experienced arrhythmia recurrence within 12 months and the percentage of subjects who experienced one or more composite serious adverse events.

1. Inclusion and Exclusion Criteria

Enrollment in the ADVANTAGE AF Phase 1 study was limited to patients who met the following inclusion criteria:

1. Age $\geq$ 18 years of age, or older if specified by local law.
2. Subjects have symptomatic, documented, drug-resistant, Persistent AF, defined as:

- a. **Documented:** at a minimum a physician's note confirming the arrhythmia symptoms and durations AND, within 180 days of Enrollment Date, either:
 - i. A 24-hour continuous ECG recording confirming continuous AF OR
 - ii. Two ECGs from any regulatory cleared rhythm monitoring device showing continuous AF taken at least 7 days apart.
 - b. **Drug-resistant:** effectiveness failure of, intolerance to, or specific contraindication to at least one (1) AAD (Class I or III).
 - c. **Persistent:** continuous AF for > 7 days and ≤ 365 days.
- 3. Subjects who are willing and capable of providing informed consent.
 - 4. Subjects who are willing and capable of participating in all testing associated with this clinical investigation at an approved clinical investigational center.

Patients were not permitted to enroll in the ADVANTAGE AF Phase 1 study if they met any of the following exclusion criteria:

- 1. Any of the following atrial conditions:
 - a. Left atrial (LA) anteroposterior diameter ≥ 5.5 cm, or if LA diameter not available, non-indexed volume >100 ml (by MRI [magnetic resonance imaging], CT [computed tomography] or TTE [transthoracic echocardiography] report or physician note).
 - b. Any prior atrial endocardial, epicardial or surgical ablation procedure for arrhythmia, other than ablation for right sided SVT [supraventricular tachycardia].
 - c. Current atrial myxoma.
 - d. Any PV abnormality, stenosis, or stenting (common and middle PVs are admissible).
 - e. Current left atrial thrombus
- 2. Cardiovascular (CV) exclusions – Any of the following CV conditions:
 - a. History of sustained ventricular tachycardia or any ventricular fibrillation.

- b. AF that is secondary to electrolyte imbalance, thyroid disease, alcohol, or other reversible / non-cardiac causes.
 - c. Current or anticipated pacemaker, implantable cardioverter defibrillator or cardiac resynchronization therapy devices, interatrial baffle, closure device, patch, or patent foramen ovale occluder, LA appendage closure, device or occlusion, any insertable cardiac monitor other than LUX-Dx.
 - d. Valvular disease that is any of the following:
 - i. Symptomatic.
 - ii. Causing or exacerbating congestive heart failure.
 - iii. Associated with abnormal LV function or hemodynamic measurements.
 - e. Hypertrophic cardiomyopathy.
 - f. Any prosthetic heart valve, ring or repair including balloon aortic valvuloplasty.
 - g. Any IVC [inferior vena cava] filter, known inability to obtain vascular access or other contraindication to femoral access.
 - h. Rheumatic heart disease.
 - i. Awaiting cardiac transplantation or other cardiac surgery within the next 12 months.
 - j. Known adverse drug reaction to nitroglycerin.
 - k. Known severe non-revascularizable coronary disease
 - l. Pre-existing right coronary artery stent.
3. Any of the following conditions at baseline:
- a. Heart failure associated with NYHA [New York Heart Association] Class III or IV.
 - b. LVEF < 40%.
 - c. Uncontrolled hypertension (SBP > 160 mmHg or DBP > 95 mmHg on two BP measurements at baseline assessment.
 - d. Right ventricular dysfunction

4. Any of the following events within 90 days of the Consent Date:
 - a. Myocardial infarction (MI), unstable or Prinzmetal angina or coronary intervention.
 - b. Any cardiac surgery.
 - c. Heart failure hospitalization.
 - d. Pericarditis or symptomatic pericardial effusion.
 - e. Gastrointestinal bleeding.
 - f. Stroke, TIA [transient ischemic attack], or intracranial bleeding.
 - g. Any non-neurologic thromboembolic event.
 - h. Carotid stenting or endarterectomy.
5. Thrombocytosis, thrombocytopenia, disorder of blood clotting or bleeding diathesis.
6. Contraindication to, or unwillingness to use, systemic anticoagulation.
7. Patients who have not been on anticoagulation therapy for at least 4 weeks prior to the ablation procedure.
8. 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.
9. Health conditions that in the investigator's medical opinion 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) > 42.0.
 - b. Solid organ or hematologic transplant or currently being evaluated for a transplant.
 - c. Any prior history or current evidence of hemi-diaphragmatic paralysis or paresis.

- d. Severe pulmonary hypertension (at Baseline Assessment), severe lung disease, or any lung disease involving abnormal blood gases or requiring supplemental oxygen.
 - e. Renal insufficiency if an estimated glomerular filtration rate (eGFR) is $< 30 \text{ mL} / \text{min} / 1.73 \text{ m}^2$, or with any history of renal dialysis or renal transplant.
 - f. Active malignancy or history of treated malignancy within 24 months of enrollment (other than cutaneous basal cell or squamous cell carcinoma).
 - g. Clinically significant gastrointestinal problems involving the esophagus or stomach including severe or erosive esophagitis, uncontrolled gastric reflux, gastroparesis, esophageal candidiasis or active gastroduodenal ulceration.
 - h. Active systemic infection.
 - i. Current confirmed, active COVID-19 disease, current positive test for SARS-CoV-2, confirmed COVID-19 disease not clinically resolved at least 3 months prior to the Consent Date.
 - j. Uncontrolled diabetes mellitus or a recorded HgbA1c $> 8.0\%$ in the 90 days prior to the Consent Date.
 - k. Untreated diagnosed obstructive sleep apnea with apnea hypopnea index classification of severe (>30 pauses per hour).
 - l. Required use of phosphodiesterase inhibitors within 24 hours of the ablation procedure.
10. Predicted life expectancy less than 1 year.
11. Subjects who are currently enrolled in another investigational study or registry that would directly interfere with the current study, except when the subject is participating in a mandatory government registry, or a purely observational registry with no associated treatments; each instance must be brought to the attention of the Sponsor to determine eligibility.
12. Any of the following congenital conditions:
- a. Congenital heart disease with any clinically significant residual anatomic or conduction abnormality.
 - b. History of known congenital methemoglobinemia.

c. History of known G6PD deficiency.

13. Patients who cannot tolerate a subcutaneous, chronically-inserted LUX-Dx device.

14. Patients with a LUX-Dx device inserted > 6 months prior to enrollment or an estimated longevity of less than 1 year.

2. Follow-up Schedule

All patients were followed at pre-discharge, Day 7, Day 30, Day 90, Day 180, and Day 360 postoperatively. The study included a Blanking Period from Days 0 through 90 during which arrhythmia recurrence did not contribute to the arrhythmia recurrence endpoint. Preoperatively, all patients were screened for inclusion/exclusion criteria, baseline ECG, echocardiogram and CT/MRI imaging. Subjects were asked to complete Quality of Life (QOL) questionnaires at Baseline, Day 180, and Day 360 Assessments. Postoperatively, patients had a commercially available Boston Scientific LUX-Dx insertable cardiac monitor (ICM) inserted within seven days after the Index Procedure (if not previously inserted) to detect the recurrence of cardiac arrhythmias. Adverse events and complications were recorded at all visits.

The key timepoints for the required patient follow up and assessments towards safety and effectiveness are summarized in Table 6 below.

Table 6: Data Collection Schedule

	Blanking Period						Effectiveness Evaluation Period			Other
	Screen/Baseline (In-Person)	Index Procedure (In-Person) Day 0	Pre-Discharge (In-Person)	Day 7 (Remote) Days 7-11	Day 30 (Remote) Days 30-37	Re-Ablation within Blanking (<= 90 days)	Day 90 (In-Person) Days 90 ± 14	Day 180 (Remote) Days 180 ± 30	Day 360 (In-Person) Days 360 ± 30	Unscheduled CV (In-Person or Remote)
Informed Consent, Eligibility, Baseline Assessments (including NYHA Class)	X									
Laboratory testing	X		X							
AAD and anticoagulant medications	X		X	X	X	X	X	X	X	X
Recurrent arrhythmia, cardioversions, ablations, hospital admissions			X	X	X	X	X	X	X	X

	Blanking Period						Effectiveness Evaluation Period			Other
	Screen/Baseline (In-Person)	Index Procedure (In-Person) Day 0	Pre-Discharge (In-Person)	Day 7 (Remote) Days 7-11	Day 30 (Remote) Days 30-37	Re-Ablation within Blanking (≤ 90 days)	Day 90 (In-Person) Days 90 $\pm$ 14	Day 180 (Remote) Days 180 $\pm$ 30	Day 360 (In-Person) Days 360 $\pm$ 30	Unscheduled CV (In-Person or Remote)
12-lead ECG	X		X			X	X		X	X
TTE	X		X							
Cardiac CT/MRI	X		X			X	X		X	X
Ablation procedure data		X				X				
LUX-DX Insertion	X									
TEE/CT/intracardiac echocardiography (ICE) to exclude LA thrombus		X				X				
Radiologic examination of diaphragm		X				X	X		X	
EQ-5D-3L & AFEQT assessments	X							X	X	
Pre-/post-NIHSS	X		X			X				
Neuro assessments			X			X				
Adverse events		X	X	X	X	X	X	X	X	X

3. Clinical Endpoints

With regards to safety, the primary safety endpoint was the proportion of Treatment subjects and Attempt subjects with one or more of the following device or procedure-related Composite Serious Adverse Events (CSAEs) following the Index Procedure/Rescheduled Index Procedure or the Re-Ablation Procedure within the Blanking Period, with an Onset Date following the procedure as specified in the table below. The results were evaluated against a performance goal of 12% using the Kaplan-Meier method and a 97.5% one-sided upper confidence limit.

Table 7: Primary Safety Endpoint Assessments

CSAEs	Onset Date
• Myocardial infarction • Stroke • TIA • Peripheral or organ thromboembolism • Pulmonary edema • Unresolved phrenic nerve palsy / Paresis • Vascular access complications • Heart block • Gastric motility / pyloric spasm disorders	Day 0 – Day 7
• Death • Cardiac tamponade / perforation • Pericarditis • Any PFA system-related PFA procedure-related cardiovascular or pulmonary adverse event	Day 0 – Day 30
• PV stenosis • Atrio-esophageal fistula	Day 0 – Day 90

With regards to effectiveness, the Primary Effectiveness Endpoint (PEE) was the proportion of LUX-Dx monitored Treatment subjects with Treatment Success through the Day 360 Assessment. The results were evaluated against a performance goal of 40% using the Kaplan-Meier method and a 97.5% one-sided lower confidence limit.

Treatment Success was defined as both Persistent AF Acute Procedural Success and Persistent AF Chronic Success.

1. Persistent AF Acute Procedural Success was defined as:
 - a. The isolation of all attempted PVs as clinically assessed at the end of the procedure by entrance block performed with or without adenosine testing, AND
 - b. The isolation of the left atrial posterior wall (PW) as clinically assessed at the end of the procedure, performed with or without adenosine testing, via interrogation by multipolar diagnostic catheter or 3D electroanatomical mapping.
2. Persistent AF Chronic Success was defined as freedom from any of the following through the day 360 assessment after the blanking period (Index Procedure through Day 90):
 - a. Arrhythmia: Occurrence of any detectable AF, AFL, or atrial tachycardia (AT).

- b. Re-ablation: Any re-ablation for AF, AFL, or AT.
- c. Cardioversion: Any electrical cardioversion for AF, AFL, or AT.
- d. AAD Use: Use of a non-failed Class I / III AAD or amiodarone.

Post-blanking CTI-dependent AFL or re-ablation or cardioversion for CTI-dependent AFL does not constitute Treatment Failure if the subject did not have a CTI ablation with the FARAPPOINT PFA Catheter but will be a Treatment Failure if the subject did receive ablation with the FARAPPOINT PFA Catheter.

Detectable AF, AFL or AT was defined as an episode of AA of at least 30 seconds (on the LUX-Dx ICM) or 10 seconds (on 12-lead ECG) in duration captured on simulated intermittent event monitor transmissions and Holter monitors (as described below), patient-triggered subcutaneous ECGs (S-ECGs) from LUX-Dx ICM, or 12-lead ECGs.

Intermittent event monitor transmissions were simulated by randomly selecting two 2-minute time periods per month following a subject's Day 90 Assessment and selecting any overlapping LUX-Dx ICM algorithm detected AT or AF episodes. All patient-triggered (symptomatic) episodes were also selected for the primary effectiveness endpoint adjudication. Twenty-four-hour Holter monitors were simulated by selecting the day prior to the Day 180 and Day 360 Assessments and similarly selecting any overlapping LUX-Dx algorithm detected AT or AF episodes. S-ECGs for the corresponding LUX-Dx ICM episodes were reviewed and adjudicated by an independent core laboratory for at least 30 seconds of AF, AFL, or AT. Similarly, 12-lead ECGs were reviewed and adjudicated by independent core laboratory for at least 10 seconds of AF, AFL, or AT.

With regards to success/failure criteria, the study is considered a success when both the primary safety and primary effectiveness performance goals are met.

B. Subject Accountability

A total of 314 subjects (43 Roll-In, 16 Consent Ineligible/Intent, and 255 Non-Roll-In Treatment subjects) were enrolled in Phase 2 of the ADVANTAGE AF study across 29 investigational sites in the United States. There were 43 Roll-In subjects and 255 Non-Roll-In subjects that received treatment with the FARAPULSE system. Among the 298 Treatment subjects, 183 (42 Roll-in subjects and 141 Non-Roll-In subjects) underwent a CTI ablation with the FARAPPOINT PFA Catheter. Primary analyses were completed on the 255 Non Roll-In Treatment subjects who will henceforth be referred to as "Treatment subjects".

C. Study Population Demographics and Baseline Parameters

The demographics of the study population were typical for a PsAF catheter ablation study performed in the US. Tables 8 through 12 present the demographics and baseline characteristics for the 255 Treatment subjects including 141 who received CTI ablation with the FARAPPOINT catheter (referred to as FARAPPOINT subjects).

Table 8: Treatment Subject Demographics

Characteristic	Measurement	All Treatment Subjects (N=255)	FARAPPOINT Subjects (N=141)
Age (years)	n Mean $\pm$ SD (Median) Range	255 66.7 $\pm$ 9.3 (68.0) (36.0 - 86.0)	141 66.3 $\pm$ 8.9 (68.0) (41.0 - 86.0)
Sex	Male	182 (71.4%)	97 (68.8%)
	Female	73 (28.6%)	44 (31.2%)
Ethnicity	Not disclosed	5 (2.0%)	3 (2.1%)
	Not Hispanic or Latino	245 (96.1%)	138 (97.9%)
	Hispanic or Latino	5 (2.0%)	0 (0.0%)
Race ¹	Not disclosed	5 (2.0%)	3 (2.1%)
	White	241 (94.5%)	131 (92.9%)
	Black or African American	4 (1.6%)	3 (2.1%)
	Asian	4 (1.6%)	4 (2.8%)
	Other	1 (0.4%)	0 (0.0%)
n is number of subjects; SD is standard deviation; Categorical results are number of subjects (% of total subjects [N] with non-missing values). ¹ Subjects may contribute to more than one category			

Table 9: Baseline LVEF, LA Size, NYHA Class, CHA2DS2-VASc Score and Arrhythmia History

Characteristic	Measurement	All Treatment Subjects (N=255)	FARAPPOINT Subjects (N=141)
LVEF (%)	n Mean $\pm$ SD (Median) Range	253 56.6 $\pm$ 6.7 (56.0) (40.0 - 75.0)	140 56.2 $\pm$ 6.9 (55.0) (40.0 - 75.0)
LA Diameter (cm)	n Mean $\pm$ SD (Median) Range	242 4.3 $\pm$ 0.6 (4.4) (1.7 - 5.4)	132 4.3 $\pm$ 0.7 (4.3) (1.7 - 5.4)
LA Volume (mL)	n Mean $\pm$ SD (Median) Range	13 65.5 $\pm$ 19.3 (62.0) (30.0 - 95.0)	9 67.2 $\pm$ 18.1 (67.0) (30.0 - 94.0)
NYHA Class	No heart failure	140 (54.9%)	68 (48.2%)
	Class I	52 (20.4%)	33 (23.4%)
	Class II	63 (24.7%)	40 (28.4%)
	Class III	0 (0%)	0 (0%)
	Class IV	0 (0%)	0 (0%)

Characteristic	Measurement	All Treatment Subjects (N=255)	FARAPOINT Subjects (N=141)
CHA2DS2-VASc score	n Mean $\pm$ SD (Median) Range	255 2.4 $\pm$ 1.4 (2.0) (0.0 - 7.0)	141 2.4 $\pm$ 1.4 (2.0) (0.0 - 6.0)
Cardiac Arrhythmia History	History of Atrial Fibrillation ¹	255 (100.0%)	141 (100.0%)
	Paroxysmal Atrial Fibrillation	97 (38.0%)	55 (39.0%)
	Persistent Atrial Fibrillation	255 (100.0%)	141 (100.0%)
	Long Standing Persistent Atrial Fibrillation	0 (0.0%)	0 (0.0%)
Years since First AF Diagnosis	n Median (IQR) Range	255 1 (0 - 4) (0 - 21)	141 1 (1 - 5) (0 - 21)
Atrial Flutter History	None	146 (57.3%)	47 (33.3%)
	CTI Dependent Flutter	99 (38.8%)	92 (65.2%)
	Flutter with Variable AV Block	2 (0.8%)	0 (0.0%)
	Atypical Flutter	3 (1.2%)	0 (0.0%)
	Mitral Isthmus Flutter	1 (0.4%)	0 (0.0%)
	Unknown	4 (1.6%)	2 (1.4%)
Additional Arrhythmia History	Atrioventricular Block / Conduction Disease	35 (13.7%)	21 (14.9%)
	1st Degree AV Block	34 (13.3%)	21 (14.9%)
	2nd Degree AV Block	1 (0.4%)	0 (0.0%)
	3rd Degree AV Block	0 (0.0%)	0 (0.0%)
	Bundle Branch/Fascicular Block	3 (1.2%)	1 (0.7%)
	Intraventricular Conduction Delay (IVCD)	2 (0.8%)	1 (0.7%)
	Junctional Arrhythmia	3 (1.2%)	0 (0.0%)
	Premature Atrial Contractions (PACs)	3 (1.2%)	2 (1.4%)
	Premature Ventricular Contractions (PVCs)	7 (2.7%)	2 (1.4%)
	Sinus Bradycardia	104 (40.8%)	61 (43.3%)
	Sinus Node Dysfunction	3 (1.2%)	2 (1.4%)
	Sinus Tachycardia	13 (5.1%)	10 (7.1%)
	Supraventricular Tachycardia (SVT)	8 (3.1%)	6 (4.3%)
	Ventricular Tachycardia	8 (3.1%)	3 (2.1%)
	Other Cardiac Arrhythmia ²	3 (1.2%)	2 (1.4%)
Number of Prior Cardioversions	None	65 (25.5%)	46 (32.6%)
	n Median (IQR) Range	190 1 (1 - 2) (1 - 7)	95 1 (1 - 2) (1 - 7)
	Prior Cardiac Ablation	10 (3.9%)	4 (2.8%)

Characteristic	Measurement	All Treatment Subjects (N=255)	FARAPOINT Subjects (N=141)
Cardiac Ablation History	Prior CTI Ablation	10 (3.9%)	4 (2.8%)
n is number of subjects; IQR is inter-quartile range; Categorical results are number of subjects (% of total subjects [N] with non-missing values). ¹ Subjects may contribute to more than one category ² Other cardiac arrhythmia history included: AVNRT (1), Sinus Arrhythmia (1), atrial tachycardia (1)			

Table 10: Cardiovascular, Cerebrovascular, and Relevant Non-cardiac Disease History

Characteristic	Measurement	All Treatment Subjects (N=255)	FARAPOINT Subjects (N=141)
Cardiovascular Disease History	None	52 (20.4%)	27 (19.1%)
	Hypertension	172 (67.5%)	101 (71.6%)
	Coronary Artery Disease	52 (20.4%)	30 (21.3%)
	Family history of coronary disease	45 (17.6%)	25 (17.7%)
	Valvular heart disease	41 (16.1%)	21 (14.9%)
	Nonischemic Cardiomyopathy	35 (13.7%)	20 (14.2%)
	Left ventricular hypertrophy	21 (8.2%)	13 (9.2%)
	Presence of aneurysm	10 (3.9%)	4 (2.8%)
	Peripheral vascular disease	10 (3.9%)	6 (4.3%)
	Acute Myocardial Infarction (MI)	7 (2.7%)	4 (2.8%)
	Ischemic Cardiomyopathy	4 (1.6%)	1 (0.7%)
	Other cardiovascular disease ¹	6 (2.4%)	5 (3.5%)
Cerebrovascular Disease History	None	231 (90.6%)	134 (95.0%)
	Cerebral Vascular Accident (CVA)/Stroke	12 (4.7%)	3 (2.1%)
	Transient Ischemic Attack (TIA)	7 (2.7%)	2 (1.4%)
	Thromboembolic event	6 (2.4%)	3 (2.1%)
	Carotid disease	4 (1.6%)	3 (2.1%)
	Other cerebrovascular disease ²	2 (0.8%)	0 (0.0%)
Non-Cardiac Disease History	Obstructive Sleep Apnea	57 (22.4%)	23 (16.3%)
	Diabetes	43 (16.9%)	30 (21.3%)
	Type I	1 (0.4%)	1 (0.7%)
	Type II	42 (16.5%)	29 (20.6%)
	Renal Dysfunction/failure	18 (7.1%)	10 (7.1%)
	COPD	16 (6.3%)	11 (7.8%)
	Dyslipidemia	115 (45.1%)	59 (41.8%)

Categorical variables are presented as n subjects (% of total subjects [N] with non-missing values).
¹ Other cardiovascular diseases: aortic root dilation (1), diastolic heart failure (3), hypotension (1), vertebral artery dissection (1) ² Other cerebrovascular disease: left 7th cranial nerve neuroma s/p craniotomy; heterozygous prothrombin g20210a mutation

Table 11: Class I/III AAD Therapy History

Characteristic	All Treatment Subjects (N=255)	FARAPOINT Subjects (N=141)
Refractory, Contraindicated, or Non-tolerant to any Class I/III AADs	255 (100.0%)	141 (100.0%)
Contraindicated	25 (9.8%)	9 (6.4%)
Refractory/Intolerant	221 (86.7%)	127 (90.1%)
Both Contraindicated and Refractory / Intolerant	9 (3.5%)	5 (3.5%)
Results are presented as number of subjects (% of total subjects [N])		

Table 12: Class I/III AADs and Anticoagulants at Baseline

Medication	All Treatment Subjects (N=255)	FARAPOINT Subjects (N=141)
Any Class I/III AAD	146 (57.3%)	86 (61.0%)
Any Class I: Sodium Channel Blockers	26 (10.2%)	13 (9.2%)
Flecainide	20 (7.8%)	10 (7.1%)
Propafenone	6 (2.4%)	3 (2.1%)
Any Class III: Potassium Channel Blockers	120 (47.1%)	73 (51.8%)
Amiodarone	67 (26.3%)	42 (29.8%)
Dofetilide	20 (7.8%)	12 (8.5%)
Dronedarone	11 (4.3%)	6 (4.3%)
Sotalol	26 (10.2%)	17 (12.1%)
Any Direct Oral Anticoagulant (DOAC)	254 (99.6%)	141 (100.0%)
Apixaban	192 (75.3%)	103 (73.0%)
Dabigatran	1 (0.4%)	0 (0.0%)
Rivaroxaban	61 (23.9%)	38 (27.0%)
Any Vitamin K Antagonist (VKA)	1 (0.4%)	0 (0.0%)
Warfarin	1 (0.4%)	0 (0.0%)
Results presented as number of subjects on medication at baseline assessment (% of Total Subjects [N])		

D. Safety and Effectiveness Results

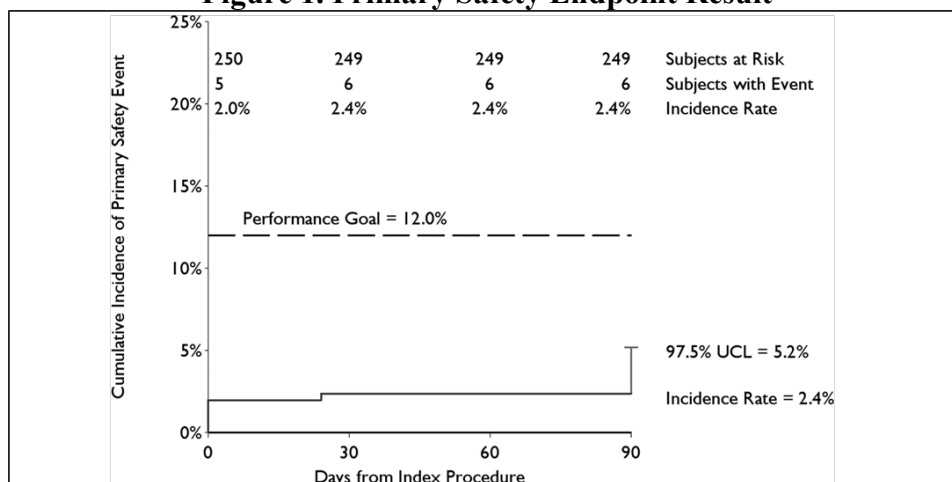
1. Safety Results

Primary Safety Endpoint

The primary safety endpoint was the proportion of Treatment and Attempt subjects with one or more device- or procedure-related pre-defined Composite Serious Adverse Events (CSAE's) through 90 days following the Index Procedure.

Out of 255 Treatment subjects, six subjects experienced a device- or procedure-related CSAE through 90 days post-Index Procedure for a cumulative incidence rate of 2.4% (Figure 1). The 97.5% one-sided upper confidence limit (UCL) of the cumulative incidence rate is 5.2%, which is lower than the predefined performance goal of 12.0%. Therefore, the Primary Safety Endpoint was met.

Figure 1. Primary Safety Endpoint Result



The device- or procedure-related CSAEs that occurred following the Index Procedure are summarized in Table 13. Six subjects experienced a primary safety event. Of the 6 subjects, three received CTI ablation with a FARAPoint PFA Catheter (One subject had cardiac tamponade or perforation, one subject died 24 days post-Index Procedure, and one subject had PFA system or procedure related cardiovascular or pulmonary adverse event + Stroke) and three subjects did not receive CTI ablation with a FARAPoint PFA Catheter (One subject had pulmonary edema, one subject had PFA system or procedure related cardiovascular or pulmonary adverse event + Stroke, and one subject had vascular access complications + Stroke).

Table 113: Primary Safety Events

Primary Safety Event Type	Subjects with Event ¹ (% of All Treatment Subjects) (N=255)
Cardiac tamponade or perforation (early)	1 (0.4%)
Death (cardiovascular cause)	1 (0.4%)
PFA system or procedure related cardiovascular or pulmonary adverse event	2 (0.8%) ²
Pulmonary edema	1 (0.4%)
Stroke	3 (1.2%)
Vascular access complications	1 (0.4%)
N = total subjects ¹ Subjects may experience multiple primary safety event types and have multiple events of the same type ² There were three PFA system or procedure related cardiovascular or pulmonary adverse events reported in two Treatment subjects and adjudicated by the CEC as primary safety events, including one air embolism to the right coronary artery, one hypotension and one sinus bradycardia.	

Death Details

The death occurred in a 72-year-old male with a history of symptomatic persistent AF and multiple cardiovascular comorbidities including prior myocardial infarction, hypertension, aortic aneurysm, peripheral arterial disease and congestive heart failure. The subject underwent an unremarkable PFA procedure including PVI + LAPWI using a FARAWAVE PFA Catheter and CTI ablation using a FARAPPOINT PFA Catheter without any acute complication. The subject passed away suddenly 24 days post-procedure. There was little information about the cause of death, and no autopsy was performed. The site attributed the death to the underlying atherosclerotic cardiovascular disease. The CEC adjudicated the death as related to the index ablation procedure but not to the FARAWAVE or FARAPPOINT PFA catheters or the FARADRIVE steerable sheath.

Related Adverse Events

Related adverse events comprised all Adverse Events classified by the study sponsor as having a “Causal”, “Probable”, or “Possible” relationship with an investigational study device or the study ablation procedure.

Among the 255 Treatment subjects, 56 (22.0%) experienced one or more investigational device- or procedure-related adverse events. There was a total of 76 procedure-related events occurred with 32 events additionally related to the investigational device. The majority of events were non-serious (55 of 76, 72.4%). The most frequently reported ablation-related adverse events were bleeding/oozing (n=10) and bruising at access site (n=6). Serious device-related

events included stroke, atrial tachycardia or supraventricular tachycardia, air embolism, hemolysis, and major bleeding.

Acute Kidney Injury and Hemolysis Events

Three of the 255 Treatment subjects (1.2%) experienced ablation-related acute kidney injury post-procedure. All acute kidney injury events in the three subjects were considered serious adverse events. In one of the subjects, acute kidney injury was secondary to intravascular hemolysis as confirmed by low haptoglobin. In another subject, hemolysis was suspected because of elevated liver enzymes. Therefore, the observed rate of hemolysis-related acute kidney injury was 0.8% (2/255) in the cohort of Treatment subjects. In the two subjects with hemolysis, creatinine levels increased between baseline and discharge from 1.2 to 1.7 in the first subject and from 1.0 to 2.6 in the second subject. In the third subject, acute kidney injury was secondary to hemorrhagic shock from a vascular access complication.

Coronary Spasm

The proportion of FARAPoint Treatment subjects with coronary spasm through 48 hours following the Index Procedure was assessed. Coronary spasm was adjudicated by the CEC and defined as any of the following:

- Angiography performed with visualization of severe ($\geq 70\%$) spasm.
- ST elevation, defined by ST elevation of 2mm in two contiguous leads and adjudicated to be a result of coronary spasm.
- Cardiac arrest adjudicated to be a result of coronary spasm.

The prophylactic nitroglycerin administration protocol utilized during CTI ablation, described above in the section of CTI Ablations with the FARAPoint PFA Catheter, successfully mitigated clinical coronary spasm. No subjects were determined to have coronary spasm within 48 hours of the Index Procedure.

Nitroglycerin-related Adverse Events

The proportion of FARAPoint Treatment subjects with adverse effects of intraprocedural administration of Nitroglycerin through 48 hours following the Index Procedure was assessed. Adverse effects were defined as (1) persistent hypotension unresponsive to medical intervention or (2) respiratory distress due to acquired methemoglobinemia assessed by an arterial blood gas with co-oximetry with methemoglobin (MetHb) $>10\%$. Persistent hypotension was identified by sponsor classification of adverse events, while respiratory distress was captured by a pre-discharge respiratory assessment performed by the site. There were no adverse effects reported that met the pre-specified criteria.

Serious Adverse Events

A list of the serious adverse events for Treatment subjects is presented in Table 14. These events represent seriousness from sponsor classification and are categorized into 41 classifications. There was a total of 77 serious adverse events that occurred in 53 Treatment subjects (20.8%). The most common serious adverse event was atrial fibrillation, with 10 subjects experiencing 11 events.

Table 14: Serious Adverse Events in Treatment Subjects

Adverse Event Classification¹	Events (N=77)	Subjects with an Event (% of All Treatment Subjects) (N=255)
Total Subjects with at Least One SAE	NA	53 (20.8%)
AV block (Transient)	1 (1.3%)	1 (0.4%)
Adverse reaction - Medication	2 (2.6%)	2 (0.8%)
Atrial Fibrillation (AF)	11 (14.3%)	10 (3.9%)
Atrial flutter	3 (3.9%)	3 (1.2%)
Atrial tachycardia/Other SVT (e.g. AVRT, AVNRT, EAT)	1 (1.3%)	1 (0.4%)
Cancer	1 (1.3%)	1 (0.4%)
Cerebrovascular Accident (CVA) - Hemorrhagic	2 (2.6%)	2 (0.8%)
Chest pain - Other	2 (2.6%)	2 (0.8%)
Coronary artery disease	2 (2.6%)	2 (0.8%)
Dyspnea - Heart Failure	2 (2.6%)	2 (0.8%)
Embolism - Air	1 (1.3%)	1 (0.4%)
Gastrointestinal	5 (6.5%)	4 (1.6%)
Genitourinary	2 (2.6%)	2 (0.8%)
Head, Eyes, Ears, Nose, Throat (HEENT)	2 (2.6%)	1 (0.4%)
Hemolysis (laboratory confirmed)	1 (1.3%)	1 (0.4%)
Hemolysis high suspicion	2 (2.6%)	1 (0.4%)
Hypertension/Hypertensive crisis	1 (1.3%)	1 (0.4%)
Hypotension/Orthostatic hypotension	1 (1.3%)	1 (0.4%)
Impaired Mobility	1 (1.3%)	1 (0.4%)
Infection - Unrelated procedure/device	2 (2.6%)	2 (0.8%)
Major bleeding/Hemorrhage requiring transfusion	1 (1.3%)	1 (0.4%)
Musculoskeletal	5 (6.5%)	5 (2.0%)
Myocardial infarction	1 (1.3%)	1 (0.4%)
Myocardial perforation with tamponade	1 (1.3%)	1 (0.4%)
Neurological	1 (1.3%)	1 (0.4%)
Pericardial effusion - Unrelated procedure/device	1 (1.3%)	1 (0.4%)
Physical trauma	1 (1.3%)	1 (0.4%)

Adverse Event Classification ¹	Events (N=77)	Subjects with an Event (% of All Treatment Subjects) (N=255)
Pleural effusion - Unrelated procedure/device	1 (1.3%)	1 (0.4%)
Post procedure infection/sepsis	1 (1.3%)	1 (0.4%)
Post-surgical pocket hemorrhage/bleeding/drainage	1 (1.3%)	1 (0.4%)
Procedure related Abnormal labs	1 (1.3%)	1 (0.4%)
Procedure related Anesthesia/Sedation	1 (1.3%)	1 (0.4%)
Procedure related Fatigue/Weakness	1 (1.3%)	1 (0.4%)
Procedure related Genitourinary	1 (1.3%)	1 (0.4%)
Procedure related Hypotension	1 (1.3%)	1 (0.4%)
Procedure related Pulmonary (including cough, hemoptysis)	1 (1.3%)	1 (0.4%)
Procedure related Renal	1 (1.3%)	1 (0.4%)
Pulmonary	3 (3.9%)	2 (0.8%)
Sinus bradycardia	5 (6.5%)	5 (2.0%)
Stroke	2 (2.6%)	2 (0.8%)
Vasovagal reaction	1 (1.3%)	1 (0.4%)
¹ Seriousness is based on sponsor classification.		

Deaths

Two subject deaths occurred in the cohort of Treatment subjects during the ADVANTAGE AF Phase 2 study. One death occurred 24 days post-index procedure and was adjudicated as a primary safety event as discussed above. The other death occurred in a subject approximately one year following the index procedure. The subject developed endocarditis requiring cardiothoracic surgery complicated by intracerebral hemorrhage, and the subject subsequently expired.

2. Effectiveness Results

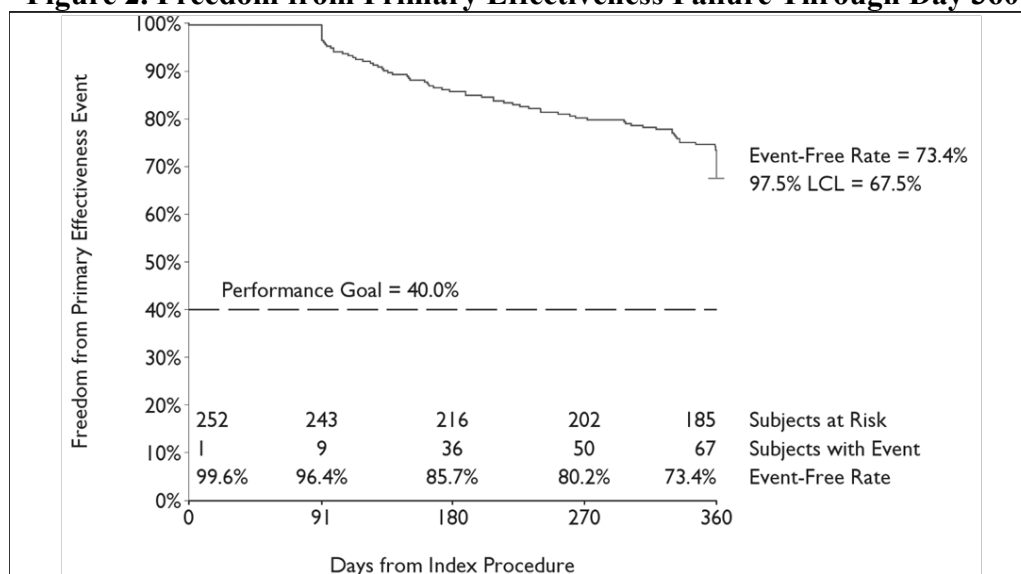
Primary Effectiveness Endpoint

Per study protocol, the primary effectiveness analysis included LUX-Dx Monitored Treatment subjects (n = 253) in the Non-Roll-In population. A subject was classified as primary effectiveness success or treatment success when both acute procedural success and chronic success were achieved.

Out of 253 LUX-Dx Monitored Treatment subjects, 67 experienced a Primary Effectiveness Endpoint event of either acute or chronic treatment failure resulting in a persistent AF Treatment Success rate of 73.4% through 360 days and a 97.5% lower confidence limit of 67.5% (Figure 2). Since the lower confidence limit is

greater than the pre-specified performance goal of 40%, the Primary Effectiveness Endpoint was met.

Figure 2. Freedom from Primary Effectiveness Failure Through Day 360



The first and subsequent primary effectiveness failure events are summarized in Table 15. Each subject was considered an endpoint failure at the time of the first event. Subsequent events are presented to show overall incidence of each event type.

One subject experienced Acute Procedural Failure. Isolation of the RIPV could not be confirmed for the subject due to accidental loss of transeptal access. The subject went on to have Chronic Treatment Failure at 161 days post-Index Procedure due to detected recurrence.

The most common Chronic Treatment Failure event was post-blanking detected AF, AT, or AFL (22.1%) followed by cardioversion for AF, AT, or AFL (9.1%) and use of a non-failed Class I/III or amiodarone (8.7%). Only 5.5% of subjects had a re-ablation.

Table 15: Primary Effectiveness Endpoint Events

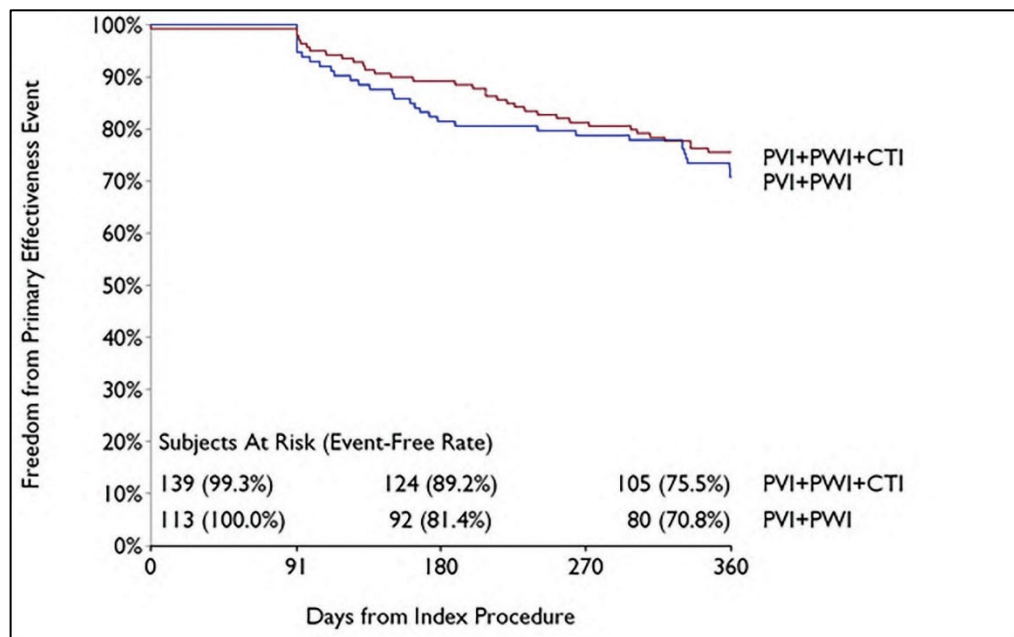
Primary Effectiveness Event Type	Subjects with an Event (% of Total Subjects) (N=253)	
	First Failure Event	All Failure Events ¹
Acute procedural failure	1 (0.4%)	1 (0.4%)
Failure to achieve PVI	1 (0.4%)	1 (0.4%)
Detected AF/AT/AFL post-blanking period	45 (17.8%)	56 (22.1%)
Simulated EM with ≥ 30 seconds AF/AT/AFL	25 (9.9%)	39 (15.4%)
Simulated 24-hour Holter with ≥ 30 seconds AF/AT/AFL	11 (4.3%)	27 (10.7%)
12-Lead ECG with ≥ 10 seconds AF/AT/AFL ²	9 (3.6%)	30 (11.9%)
AAD use post-blanking period	15 (5.9%)	22 (8.7%)
Use of a non-failed Class I/III AAD post-blanking period	11 (4.3%)	15 (5.9%)
Amiodarone use post-blanking period	4 (1.6%)	7 (2.8%)
Cardioversion for AF/AT/AFL ² post-blanking period	4 (1.6%)	23 (9.1%)
Re-ablation for AF/AT/AFL ² post-blanking period	2 (0.8%)	14 (5.5%)

N is total LUX-Dx Monitored Treatment Subjects ¹Subjects may have multiple failure event types.

²CTI-dependent AFL is counted if subject had CTI ablation using FARAPOINT catheter

Stratification of Primary Effectiveness Endpoint by CTI ablation

Of the 67 LUX-Dx Monitored Treatment subjects with a Treatment Failure event, 34 had CTI ablation performed using the FARAPOINT PFA catheter at the index procedure. The Treatment Success rate through 360 days post-Index Procedure was 75.5% for the FARAPOINT Treatment cohort (PVI+PWI+CTI ablation) and 70.8% for the non-FARAPOINT Treatment cohort (PVI+PWI) (Figure 3).

Figure 3: Primary Effectiveness Success Rate by CTI Ablation

Additional Effectiveness Analyses

CTI-Dependent AFL Treatment Success

CTI-dependent AFL Treatment Success was defined as both CTI-dependent AFL Acute and Chronic Success. Freedom from an event constituting CTI-dependent AFL treatment failure was assessed through 360 days post Index Ablation Procedure for all FARAPOINT subjects.

CTI-Dependent AFL Acute Procedural Success

Acute procedural success was defined as achievement of bidirectional block (BDB across the CTI) using the FARAPOINT PFA Catheter only. The acute success rate was 98.6% (Table 16). Two subjects were classified as acute procedural failures. One subject had their Index CTI ablation procedure started with a FARAPOINT PFA Catheter and completed using an RF ablation catheter due to FARAPOINT PFA Catheter cable connection issue. The second acute procedural failure was due to BDB not being able to be confirmed at the end of the procedure because of being in AF.

Table 16: CTI-Dependent AFL Acute Procedural Success

Total FARAPOINT Subjects	Subjects with Acute Success	Acute Procedural Success Rate
141	139	98.6%

CTI-Dependent AFL Chronic Success

Chronic success was defined as freedom from recurrence of CTI-dependent AFL through the Day 360 assessment with recurrence defined as repeat CTI ablation or CTI-dependent AFL captured for the entirety of a 12-lead ECG with interpretable signal of at least 10 seconds. All 12-lead ECGs were reviewed by an independent arrhythmia core laboratory. The chronic success rate was 97.9% through 360 days (Table 17). Three subjects had repeat CTI ablation on days 131, 161, and 259 post-index procedure.

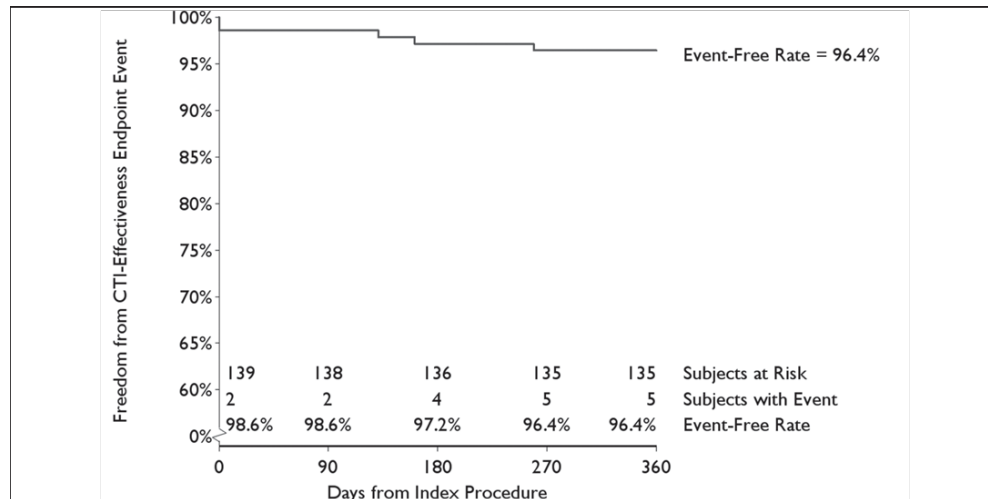
Table 17: CTI-Dependent AFL Chronic Success

Total FARAPOINT Subjects	Subjects with Chronic Treatment Success	Chronic Treatment Success Rate¹
141	138	97.9%

¹Estimated at day 360 using Kaplan-Meier method

The CTI-dependent AFL Treatment Success rate, requiring both acute procedural success and chronic success, was 96.4% through 360 days of follow-up (Figure 4).

Figure 4: Freedom from CTI-Dependent AFL Treatment Failure Through Day 360



Freedom from Detectable AF, AFL, or AT

Detectable AF, AFL, or AT was defined as any post-blanking AF, AFL, or AT of at least 30 seconds in duration captured by simulated intermittent event monitor transmissions or Holter monitors described above or of at least 10 seconds in duration captured by a 12-lead ECG.

LUX-Dx episodes captured by simulated intermittent monitoring were adjudicated by an independent electrophysiologist (EP) for the presence of atrial arrhythmia. Episodes that contained at least 30 seconds of atrial arrhythmia were further classified by the EP as AF, AT, or AFL based on the predominant rhythm. Similarly, 12-lead ECGs were adjudicated by an independent core lab for the presence of at least 10 seconds of AF, AT, or AFL. The adjudicated rhythms were used to assess freedom from recurrence of each rhythm individually through 360 days.

The estimated rate of freedom from detectable AF, AFL, or AT through 360 days post-Index Procedure was 77.8%. The proportion of subjects with AF, AFL, or AT recurrence or a combination of the three is summarized in Table 18. Approximately 16% of subjects had detectable AF, which constituted 71.4% (40/56) of the subjects with any detectable AF, AFL, or AT. Only 16 subjects (6.3%) had detectable AFL or AT only. These subjects made up 28.6% (16/56) of the subjects with any detectable AF, AFL, or AT.

Table 18: Proportion of Subjects with Detectable AF, AFL, or AT

Rhythm	Subjects with Detectable AA Recurrence (%) (N=253)
AF Only	26 (10.3%)
AFL Only	9 (3.6%)
AT Only	3 (1.2%)
AT and AFL Only	4 (1.6%)
AF and either AFL or AT	14 (5.5%)

Results presented as number of subjects (% of LUX-Dx Monitored Treatment Subjects [N])

Freedom from Symptomatic Recurrence and Intervention to Treat AF, AFL, or AT

The estimated rate of freedom from symptomatic recurrence and intervention, comprising symptomatic detectable AF, AFL, or AT, or intervention to treat atrial arrhythmia recurrence (re-ablation, cardioversion, or prescription of a non-failed Class I/III AAD or amiodarone) was 81.0%.

Single Procedure Treatment Success

Single procedure treatment success defined as freedom from Primary Effectiveness Endpoint failure without a repeat procedure was achieved in 72.6% of the LUX-Dx Monitored Treatment subjects.

Off Drug Treatment Success

Off Drug Treatment success defined as freedom from Primary Effectiveness Endpoint failure without the use of a Class I or III AAD after the blanking period was achieved in 65.1% of the LUX-Dx Monitored Treatment subjects.

Re-Ablation Rate

Re-ablation was performed in 4 Treatment subjects during the blanking period and in 14 Treatment subjects after the blanking period; 2 Treatment subjects had re-ablation during both periods. This resulted in a re-ablation rate of 6.3%.

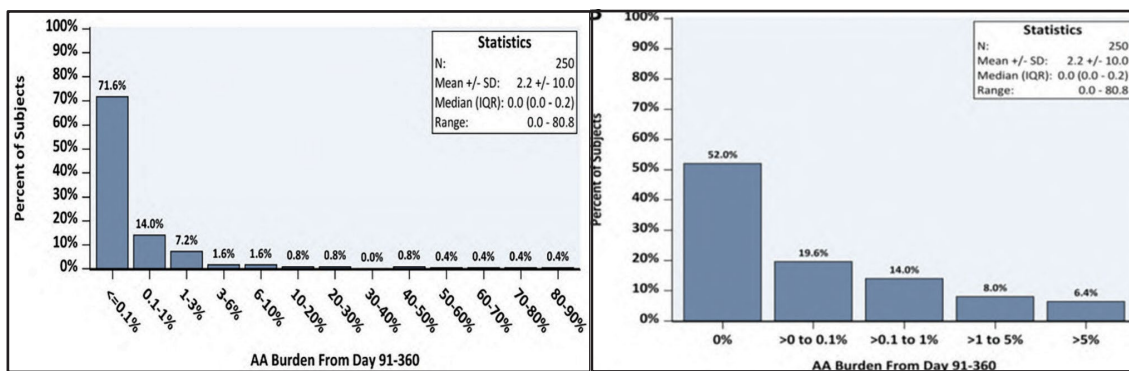
AF, AFL, and AT Burden

AF, AFL, and AT burden (AA burden) was defined as the proportion of time spent in atrial arrhythmia (AA) based on the occurrence of LUX-Dx detected AF, AT, or patient-triggered episodes that were adjudicated as ≥ 30 seconds of AA by an AI algorithm that incorporated BeatLogic (Boston Scientific Inc).

AA burden was calculated for the time period post blanking through the earliest of day 360, study completion date, or LUX-Dx out-of-service date when no replacement ICM was received.

Following the blanking period, subjects generally had a low AA burden: 71.6% of subjects had an AA burden less than or equal to 0.1%, with 130 (52.0%) subjects having 0% AA burden. Burden values ranged from 0% to 80.8% across 250 evaluable subjects. Three LUX-Dx Monitored Treatment subjects did not contribute data to the post-blanking period analysis due to having their LUX-Dx explanted or disabled during the blanking period (n=2) or due to death during the blanking period (n=1).

Figure 5: Distribution of Atrial Arrhythmia Burden from Day 91-360



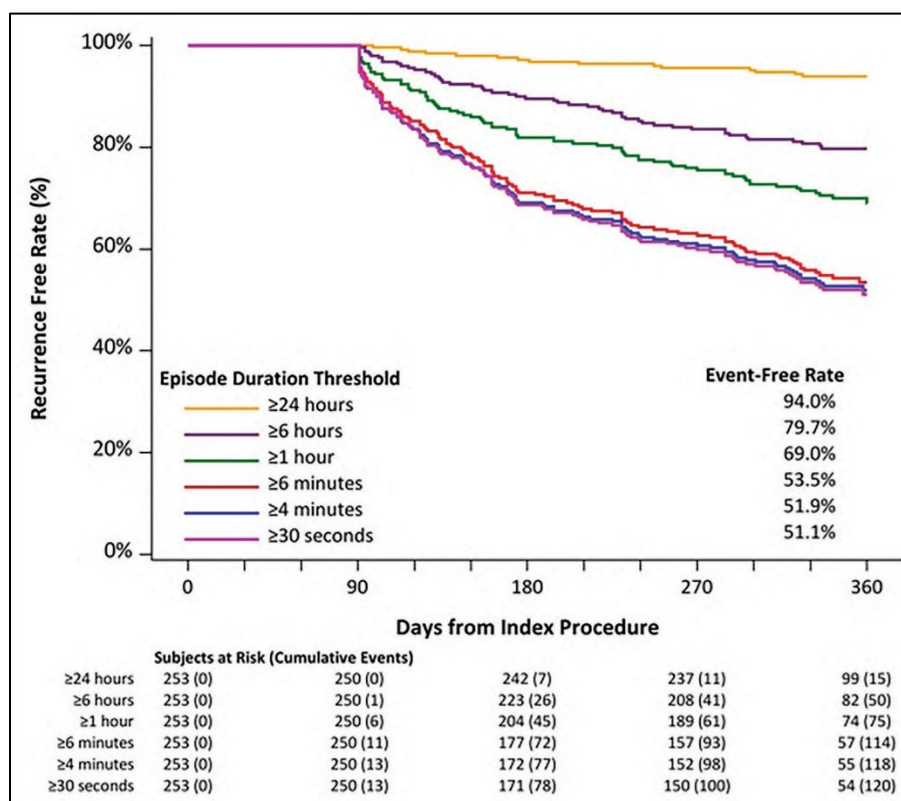
Freedom from Atrial Arrhythmia Recurrence by Episode Duration

A post-hoc analysis was performed to assess freedom from LUX-Dx detected atrial arrhythmia. All LUX-Dx detected AF, AT, or patient-triggered episodes with at least 30 seconds of confirmed atrial arrhythmia were included in the analysis and categorized by episode duration. Atrial arrhythmia episodes were adjudicated by an AI algorithm that incorporated BeatLogic (Boston Scientific Inc). The LUX-Dx determined episode duration was utilized for algorithm-detected (asymptomatic) episodes and a duration of ≥ 30 seconds was applied to patient-triggered (symptomatic) episodes.

Freedom from atrial arrhythmia recurrence was calculated at the following minimum episode duration thresholds: ≥ 30 seconds, ≥ 4 minutes, ≥ 6 minutes, ≥ 1 hour, ≥ 6 hours, and ≥ 24 hours.

Freedom from atrial arrhythmia recurrence through 360 days of follow-up at each episode duration threshold is presented in Figure 6. Estimated rates of freedom from atrial arrhythmia recurrence ranged from 51.1% (using ≥ 30 seconds as threshold to define atrial arrhythmia recurrence) to 94.0% (using ≥ 24 hours as threshold to define atrial arrhythmia recurrence).

Figure 6: Freedom from Atrial Arrhythmia Recurrence by Episode Duration



Quality of Life Assessments

Subjects were asked to complete Quality of Life (QOL) questionnaires at Baseline, Day 180, and Day 360 Assessments. The EQ-5D-5L was used to measure subjects' health-related quality of life and the Atrial Fibrillation Effect on Quality of Life (AFEQT) was used to evaluate AF-specific quality of life.

All questionnaire scores, including sub-component scores, improved following the PFA procedure. The overall AFEQT score was 65.7 ± 20.9 at baseline and improved to 90.5 ± 14.8 by the Day 360 assessment and the EQ-5D-5L score was 76.5 ± 15.3 at baseline and improved to 83.4 ± 12.8 by the Day 360 assessment.

3. Subgroup Analyses

Subgroup analyses were performed for the primary endpoints to determine whether significant differences exist in endpoint results by baseline demographics, clinical characteristics, or procedural characteristics. Subgroups pre-specified in the Statistical Analysis Plan included but were not limited to the following: Age (≥ 65 vs. < 65), sex, LA diameter, LVEF ($< 50\%$ vs. $\geq 50\%$), years since AF diagnosis (≤ 1 year vs. > 1 year), cardioversion history (≤ 1 vs. > 1 prior electrical cardioversion), additional ablations beyond PV, LAPW and CTI during index procedure (Yes vs. No), CTI ablation using FARAPOINT

during index procedure (Yes vs. No), mapping of LAPW during index procedure (Yes vs. No), number of prior procedures completed by operator (≤ 5 cases vs. > 5 cases), amiodarone use post index procedure (Yes vs. No for primary effectiveness endpoint only), and LUX-Dx model (LUX-Dx II+ vs. LUX-Dx I or LUX-Dx II for primary effectiveness endpoint only).

The subgroup analyses were performed using Fisher's exact test with Clopper-Pearson confidence intervals reported (nominal) for the Primary Safety Endpoint to account for the small number of subjects with an event and using Wald chi-square test with Wald confidence intervals reported (nominal) for the Primary Effectiveness Endpoint. Differences between subgroups were evaluated at a 15% significance level.

Treatment effects on the Primary Effectiveness Endpoint were consistent across all subgroups except the ones defined by mapping of LAPW during procedure as shown below (Table 19). Since the number of subjects without LAPW mapping was small and since most of those subjects were treated at a single site, the significant effects of LAPW mapping are likely biased by site or operator practice. Regarding the Primary Safety Endpoint, significant difference was found for baseline LVEF and cardioversion history (Table 20). The difference in the primary safety event rate in these subgroups was likely caused by chance in this study in which a very small number of primary safety events occurred.

Table 19: Subgroup Analysis for Primary Effectiveness Endpoint of LUX-Dx Treatment Subjects

Covariate	Subgroup	N	Binary Treatment Success Rate (95% Wald CI)	P-Value ²
Age	<65 years	92	77.2% (68.6%, 85.8%)	0.32
	≥65 years	161	71.4% (64.5%, 78.4%)	
Sex	Male	180	74.4% (68.1%, 80.8%)	0.60
	Female	73	71.2% (60.8%, 81.6%)	
BMI	<30 kg/m2	116	77.6% (70.0%, 85.2%)	0.18
	≥30 kg/m2	137	70.1% (62.4%, 77.7%)	
LVEF	<50%	26	80.8% (65.6%, 95.9%)	0.36
	≥50%	225	72.4% (66.6%, 78.3%)	
LA volume or LA diameter	At or below the median ¹	138	75.4% (68.2%, 82.6%)	0.47
	Above the median ¹	115	71.3% (63.0%, 79.6%)	
Years since AF diagnosis	≤1 year	153	74.5% (67.6%, 81.4%)	0.66
	>1 year	100	72.0% (63.2%, 80.8%)	
Cardioversion history	≤1 prior cardioversion	164	75.0% (68.4%, 81.6%)	0.47
	>1 prior cardioversion	89	70.8% (61.3%, 80.2%)	
Ancillary ablations	No ancillary ablations	243	74.1% (68.6%, 79.6%)	0.32
	Ancillary ablations	10	60.0% (29.6%, 90.4%)	
CTI Ablation using FARAPOINT	No CTI ablation	113	70.8% (62.4%, 79.2%)	0.38
	CTI ablation	140	75.7% (68.6%, 82.8%)	
Mapping of PW during procedure	No PW mapping	27	88.9% (77.0%, 100.0%)	0.055
	PW mapping	226	71.7% (65.8%, 77.6%)	
Prior cases by Operator	≤5 prior cases	43	69.8% (56.0%, 83.5%)	0.54
	>5 prior cases	210	74.3% (68.4%, 80.2%)	
Amiodarone use Post-Procedure	No amiodarone taken	201	72.6% (66.5%, 78.8%)	0.53
	Amiodarone taken	52	76.9% (65.5%, 88.4%)	
LUX-Dx Model	LUX-Dx I or LUX II	168	76.2% (69.7%, 82.6%)	0.18
	LUX-Dx II+	85	68.2% (58.3%, 78.1%)	

N = LUX-Dx Monitored Treatment subjects in subgroup; CI = confidence interval

¹Median LA volume = 62mL; Median LA diameter = 4.4cm

²P-value from Wald chi-square test

Table 20: Subgroup Analysis for Primary Safety Endpoint of Non-Roll-In Treatment Subjects

Covariate	Subgroup	N	Binary Rate of Subjects with an Event (95% Exact CI)	P-Value ²
Age	<65 years	94	1.1% (0.0%, 5.8%)	0.42
	≥65 years	161	3.1% (1.0%, 7.1%)	
Sex	Male	182	2.2% (0.6%, 5.5%)	1.00
	Female	73	2.7% (0.3%, 9.5%)	
BMI	<30 kg/m ²	117	2.6% (0.5%, 7.3%)	1.00
	≥30 kg/m ²	138	2.2% (0.5%, 6.2%)	
LVEF	<50%	26	7.7% (0.9%, 25.1%)	0.12
	≥50%	227	1.8% (0.5%, 4.5%)	
LA volume or LA diameter	At or below the median ¹	138	1.4% (0.2%, 5.1%)	0.42
	Above the median ¹	117	3.4% (0.9%, 8.5%)	
Years since AF diagnosis	≤1 year	153	2.6% (0.7%, 6.6%)	1.00
	>1 year	102	2.0% (0.2%, 6.9%)	
Cardioversion history	≤1 prior cardioversion	166	3.6% (1.3%, 7.7%)	0.094
	>1 prior cardioversion	89	0.0% (0.0%, 4.1%)	
Ancillary ablations	No ancillary ablations	245	2.0% (0.7%, 4.7%)	0.22
	Ancillary ablations	10	10.0% (0.3%, 44.5%)	
CTI Ablation using FARAPOINT	No CTI ablation	114	2.6% (0.5%, 7.5%)	1.00
	CTI ablation	141	2.1% (0.4%, 6.1%)	
Mapping of PW during procedure	No PW mapping	29	0.0% (0.0%, 11.9%)	1.00
	PW mapping	226	2.7% (1.0%, 5.7%)	
Prior cases by Operator	≤5 prior cases	43	4.7% (0.6%, 15.8%)	0.27
	>5 prior cases	212	1.9% (0.5%, 4.8%)	

N = Treatment subjects in subgroup; CI = confidence interval

¹Median LA volume = 62mL; Median LA diameter = 4.4cm

²P-value from Fisher's exact test

3. Pediatric Extrapolation

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

XI. 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 pivotal clinical study included 78 investigators of which 0 were full-time or part-time employees of the sponsor and 11 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: 11
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

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.

XII. 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 Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The effectiveness outcomes of the ADVANTAGE AF Phase 2 study demonstrated a reasonable assurance that the FARAPPOINT PFA catheter is effective for CTI ablation concomitant to left atrial ablation using the FARAWAVE PFA catheter for the treatment of symptomatic drug refractory persistent AF.

The study results showed that the pivotal study met the predefined effectiveness performance goals of 40%. Specifically, the one-year treatment success (freedom from detectable atrial tachyarrhythmia recurrence) was achieved in 73.4% (one-sided 97.5% LCL: 67.5%) of the treatment subjects and in 75.5% (one-sided 97.5% LCL: 67.5%) of those treatment subjects who received concomitant CTI ablation. The effectiveness performance goal was derived from the minimum chronic acceptable success rate for catheter ablation of persistent AF recommended in the 2017 Heart Rhythm Society Expert Consensus Statement on Catheter and Surgical Ablation of AF. The one-year treatment success rates reported in the study were at the high end of one-year success rates reported in the recently completed persistent AF ablation IDE studies of thermal-based or PFA-based ablation systems.

Freedom from atrial tachyarrhythmia recurrence has been widely used as a surrogate for improvement in patient's quality of life and symptom relief in patients with symptomatic AF, which is the recognized primary objective and an important clinical benefit of AF ablation. In fact, the pivotal study also showed that persistent AF ablation using the FARAWAVE catheter with or without concomitant CTI ablation using the FARAPOINT PFA catheter was accompanied with significant improvement in patient's quality-of-life measures.

Bidirectional CTI block, an intraprocedural measure of the effectiveness of CTI ablation was achieved in 98.6% of the subjects who received CTI ablation using the FARAPOINT PFA catheter. Freedom from recurrence of CTI-dependent AFL was achieved in 97.9% of the subjects who received CTI ablation using the FARAPOINT PFA catheter. The results of these outcome measures were supportive of the effectiveness of the FARAPOINT PFA catheter. That said, it should be recognized that the long-term durability of CTI lesions created with the FARAPOINT PFA catheter was not well characterized in the pivotal study largely because of the known myocardial stunning phenomenon of PFA, the lack of a routine remapping study to assess CTI conduction during follow-up and the potential confounding effect of concomitant PV isolation on CTI-dependent AFL recurrence.

B. Safety Conclusions

The risks of the device are based on data collected in the clinical study conducted to support PMA approval as described above. The ADVANTAGE AF Phase 2 study met its pre-defined safety performance goal with a primary safety event rate of 2.4% (one-sided 97.5% UCL: 5.2%), which was within the range of major complication rates reported in the contemporary persistent AF ablation studies. The reported primary safety events in the non-Roll-In Treatment subjects included one procedure-related death (0.4%), four strokes in three subjects (1.2%), one air embolism (0.4%), one cardiac tamponade/perforation (0.4%), one hypotension (0.4%), one sinus bradycardia (0.4%), one pulmonary edema (0.4%), and one vascular access complication (0.4%). The primary safety event rate did not differ between subjects with concomitant CTI ablation using the FARAPOINT PFA catheter and those without.

FDA's review of the relevant source documents surrounding the procedure-related death that occurred approximately 3 weeks post PVI, LAPWI and CTI ablation did not reveal any evidence for a procedural complication and thus raised no significant concerns about the safety profile of the FARAPOINT PFA catheter, even though the possibility of CTI-ablation related coronary artery injury being the cause or a contributing factor of the death cannot be completely excluded. There is a low degree of uncertainty in procedure-related mortality because the rate of procedure-related mortality in the pivotal study was numerically higher than that commonly reported in previous AF ablation trials ($\leq 0.1\%$). However, no firm conclusion can be drawn about the comparative procedure-related mortality between persistent AF ablation with concomitant CTI ablation using the FARAPOINT PFA catheter and persistent

AF ablation using commercially available technologies given the single arm design of the pivotal study and the wide confidence intervals around the procedure-related mortality rate reported in the pivotal study.

The rate of other primary safety events was within the expectation of a persistent AF ablation procedure.

The results of other safety outcome measures did not raise significant concerns about the use of the FARAPPOINT PFA catheter for concomitant CTI ablation or the use of FARAWAVE PFA catheter for PVI and LAPWI for the treatment of persistent AF. Importantly, there were no clinical coronary spasm events or ablation-related acute myocardial infarction reported in the study. Moreover, FDA's review of all possible cardiac related adverse events reported in subjects who received concomitant CTI ablation did not suggest a significant risk of chronic coronary artery injury associated with CTI ablation using the FARAPPOINT PFA catheter, acknowledging that the risk of chronic artery narrowing/stenosis was not well characterized in the study due to the lack of routine coronary artery imaging during follow-up and the relatively short follow-up duration. In addition, the safety results of the pivotal study supported a low risk of hemolysis-related acute kidney injury (an PFA-specific complication) associated with concomitant CTI ablation using the FARAPPOINT PFA catheter. In fact, no subjects who received CTI ablation using the FARAPPOINT catheter were reported to have acute kidney injury secondary to hemolysis confirmed by lab testing.

Taken together, the results of the pivotal study indicated a similar risk of major procedural complications following persistent AF ablation with concomitant CTI ablation using the FARAPPOINT PFA catheter compared to that following persistent AF ablation using other approved technologies. CTI ablation using the FARAPPOINT PFA catheter did not result in clinical coronary spasm or acute myocardial infarction when a prophylactic nitroglycerin protocol was used to mitigate the risk of coronary artery spasms during the procedure. On the other hand, the risk of chronic coronary artery stenosis associated with CTI ablation using the FARAPPOINT catheter is yet to be characterized in future studies even though the available safety data from the present study and an external report (Malyshev et al. JACC Clin Electrophysiol. 2024) with a small number of patients (n = 13) who underwent coronary angiography during follow-up after concomitant CTI ablation using the FARAPPOINT PFA catheter did not suggest a significant risk of chronic coronary artery injury.

C. Benefit-Risk Determination

The probable benefits of the device are based on data collected in the ADVANTAGE AF Phase 2 study conducted to support PMA approval as described above. The primary effectiveness endpoint results supported the treatment benefit of reducing atrial tachyarrhythmia recurrence in patients with symptomatic drug refractory persistent AF. Freedom from atrial tachyarrhythmia recurrence, an accepted surrogate for improvement in patient's quality of life and AF-related symptoms in the study population was achieved in the majority of study participants during the 9-month

effectiveness evaluation period. This was accompanied by clinically meaningful improvement in patient's quality-of-life measures following left atrial ablation with or without concomitant CTI ablation using the FARAPoint PFA catheter. Bidirectional CTI block, an intraprocedural measure of the effectiveness of CTI ablation was achieved in 98.6% of the subjects who received CTI ablation using the FARAPoint catheter. Additional analyses suggested that concomitant CTI ablation was not associated with an increased risk of AFL or AT recurrence.

The probable risks of the device are also based on data collected in the ADVANTAGE AF Phase 2 study conducted to support PMA approval as described above. The safety data from the clinical study supports the notion that the subject device's safety profile when used for CTI ablation concomitant to PV isolation and LAPW isolation for persistent AF ablation is clinically acceptable. The primary safety event rate in the study was within the range of the major complication rates reported in the contemporary AF ablation studies and did not differ between subjects with concomitant CTI ablation using the FARAPoint PFA catheter and those without. The risks of clinical coronary spasm, ablation-related acute myocardial infarction, hemolysis-related acute kidney injury, and chronic coronary artery injury associated with CTI ablation using the FARAPoint PFA catheter appeared to be low based on the clinical study results.

No new or unanticipated adverse device effects or patient risks were identified in the ADVANTAGE AF Phase 2 study.

1. Patient Perspective

This submission either did not include specific information on patient perspectives, or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, the totality of the data supports a favorable benefit-risk profile of the subject device for CTI ablation concomitant to left atrial PFA for the treatment of drug refractory symptomatic persistent AF, acknowledging a moderate degree of uncertainty in long-term durability of acute CTI block, and a low degree of uncertainty in chronic coronary artery injury and procedure-related mortality associated with CTI ablation using the FARAPoint PFA catheter. A post-approval study will be conducted to address the uncertainty in device effectiveness and safety.

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.

XIV. CDRH DECISION

CDRH issued an approval order on January 12, 2026. The final clinical conditions of approval cited in the approval order are described below.

The FAR-AHEAD study is a prospective, multi-center, non-randomized, observational study to evaluate the long-term effectiveness and safety of the FARAPPOINT™ Pulsed Field Ablation Catheter for cavotricuspid isthmus (CTI) ablation concomitant to left atrial ablation using the FARAWAVE™ Pulsed Field Ablation Catheter to treat drug-refractory, symptomatic, persistent atrial fibrillation (PsAF). Adult patients who intend to undergo their de novo left atrial ablation and concomitant CTI ablation for the treatment of symptomatic, drug-refractory persistent atrial fibrillation (PsAF, episode duration less than one year) will be enrolled and ablated using the FARAWAVE™ Pulsed Field Ablation Catheter for left atrial ablation and the FARAPPOINT™ Pulsed Field Ablation Catheter for concomitant CTI ablation. The study will enroll at least 265 subjects with all treated in the United States. Following consent, all study subjects will complete an enrollment/baseline visit, ablation procedure with left atrial ablation and concomitant CTI ablation and be followed through 3 years post-ablation. A 24-hour Holter or equivalent rhythm monitoring will be performed at 6- and 12-months post-ablation for asymptomatic recurrence and as needed for symptomatic recurrences. CTI conduction will be assessed in all subjects who undergo a repeat ablation procedure during follow-up. Additional assessment of chronic right coronary artery (RCA) stenosis using coronary computed tomography angiography (CTA) will be conducted at baseline and 12-month post-procedure in at least 60 PsAF subjects undergoing concomitant CTI ablation using the FARAPPOINT™ Pulsed Field Ablation Catheter.

The primary objectives of the PAS will be the following:

- Estimating the primary safety adverse event rate at 30 days following PsAF ablation procedure using the FARAWAVE™ Pulsed Field Ablation Catheter and the FARAPPOINT™ Pulsed Field Ablation Catheter.
- Estimating the rate of chronic RCA stenosis ($\geq 50\%$ obstruction) related to CTI ablation with the FARAPPOINT™ Pulsed Field Ablation Catheter.
- Estimating the rate of durable CTI conduction block following concomitant CTI ablation with the FARAPPOINT™ Pulsed Field Ablation Catheter.

Secondary/Additional objectives will include but are not limited to:

- Estimating the rate of serious device or serious procedure related adverse events through 12 months post-ablation using the FARAPPOINT™ Pulsed Field Ablation Catheter.

- Estimating the 12-month freedom from atrial fibrillation (AF)/atrial flutter (AFL)/atrial tachycardia (AT) recurrence following ablation procedure using the FARAWAVE™ Pulsed Field Ablation Catheter and the FARAPOINT™ Pulsed Field Ablation Catheter.
- Estimating 12-months freedom from CTI-dependent AFL recurrence following ablation procedure using the FARAWAVE™ Pulsed Field Ablation Catheter and the FARAPOINT™ Pulsed Field Ablation Catheter.
- Estimating the rate of early mortality after concomitant CTI ablation using the FARAPOINT™ Pulsed Field Ablation Catheter through 3 months post-procedure.
- Estimating the rate of acute coronary spasm occurring from ablation procedure through discharge.
- Estimating the rate of procedure-related acute kidney injury through 3 months post-procedure.
- Estimating the rate of a composite endpoint of acute coronary syndrome, new ischemic electrocardiogram (ECG) changes consistent with inferior ischemia requiring treatment, hemodynamically significant coronary artery spasm requiring intracoronary nitroglycerin and/or causing ST-segment elevation, urgent coronary angiography with an RCA culprit finding, and cardiac death post-discharge through 3 years post-procedure.
- Estimating the rate of serious adverse events involving the coronary artery system over 3 years post-ablation using the FARAWAVE™ Pulsed Field Ablation Catheter and the FARAPOINT™ Pulsed Field Ablation Catheter.
- Estimating 36-months freedom from AF/AFL/AT recurrence following ablation procedure using the FARAWAVE™ Pulsed Field Ablation Catheter and the FARAPOINT™ Pulsed Field Ablation Catheter.
- Characterizing procedural data that may include but are not limited to procedure time, fluoroscopy time, total number of pulsed field (PF) applications, number of PF applications at the CTI, fluid administered intraprocedural, ablation strategy, anesthesia technique, and nitroglycerin and vasopressor administration.

The applicant's manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820), which was in effect at the time of the inspection. As of February 2, 2026, the revised part 820, referred to as the Quality Management System Regulation (QMSR), is effective.

XV. 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.