SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Irrigated RF Ablation Catheter

Device Trade Name: FlexAbility™ Ablation Catheter, Sensor Enabled™

Device Procode: LPB, OAD

Applicant's Name and Address: Abbott Medical
5050 Nathan Lane North
Plymouth, MN 55442

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P110016/S080

Date of FDA Notice of Approval: December 14, 2022

The original PMA (P110016) was approved on January 25th, 2012 where the ablation system, including the Therapy Cool Path Duo Ablation Catheter, Safire BLU Duo Ablation Catheter, IBI 1500T-9 v1.6 Cardiac Ablation Generator, and compatible irrigation pump, is indicated for endocardial mapping, stimulation, and ablation for the treatment of typical atrial flutter. The SSED to support the indication is available on the CDRH website (https://www.accessdata.fda.gov/cdrh_docs/pdf11/P110016B.pdf) and is incorporated by reference here.

The next generation devices, FlexAbility Ablation Catheter and FlexAbility Ablation Catheter, Sensor Enabled (FlexAbility SE), were approved under PMA P110016/S013 on January 23rd, 2015 and P110016/S025 on February 17th, 2018, respectively for the same indication.

The current supplement was submitted to expand the indication for the FlexAbility Ablation Catheter, Sensor Enabled to include treatment of recurrent, drug-refractory, sustained monomorphic ventricular tachycardia (MMVT) in patients with non-ischemic structural heart disease.

II. INDICATIONS FOR USE

The FlexAbility™ Ablation Catheter, Sensor Enabled™, when used in conjunction with a compatible irrigation pump and compatible RF cardiac ablation generator, is indicated for:

- Endocardial mapping, stimulation, and ablation for the treatment of typical atrial flutter

- Endocardial or epicardial mapping, stimulation, and ablation for the treatment of recurrent, drug-refractory, sustained monomorphic ventricular tachycardia in patients with non-ischemic structural heart disease,

when used in conjunction with a compatible cardiac mapping system.

III. CONTRAINDICATIONS

The catheter is contraindicated for:

- Patients with active systemic infection.
- Patients with intracardiac thrombus or myxoma, or interatrial baffle or patch via transeptal approach.

In addition, the following contraindications apply for treatment of ventricular tachycardia:

- Patients who have had a ventriculotomy or atriotomy within the preceding four weeks as the recent surgery may increase the risk of perforation.
- Patients with prosthetic valves as the catheter may damage the prosthesis.
- The use in coronary arterial vasculature due to risk of damage to the coronary arterial vasculature.
- The transseptal approach in a patient with an interatrial baffle or patch because the opening could persist and produce an iatrogenic atrial shunt.
- The retrograde trans-aortic approach in patients who have had aortic valve replacement.
- Patients unable to receive heparin or an acceptable alternative to achieve adequate anticoagulation

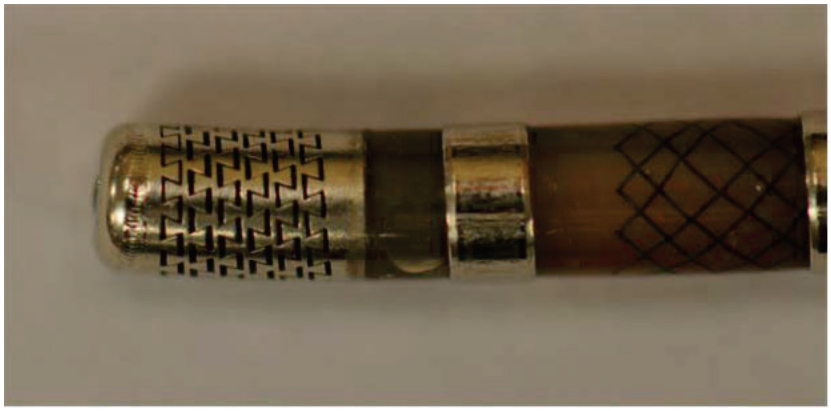
IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the FlexAbility Ablation Catheter, Sensor Enabled labeling.

V. DEVICE DESCRIPTION

FlexAbility SE is a sterile, single use catheter with a 7.5 F shaft and an 8 F distal section. It is constructed of thermoplastic elastomer material and noble metal electrodes. The catheter has a flexible tip electrode and magnetic sensor (Figure 1). It has a fluid lumen connected to open conduits at the flexible tip electrode for saline irrigation during the ablation procedure. The FlexAbility SE catheter is available in bi-directional and uni-directional configurations (Figure 2).

The tip curvature is manipulated by the control mechanism located on the handle at the catheter's proximal end. To adjust the curve of the distal tip on the uni-directional catheter, push or pull the thumb control located on the handle. To adjust the curve of the distal tip on the bi-directional catheter, use the actuator to deflect the catheter in either direction. The catheter is available in eight distal curve configurations identified on the catheter label. All curve configurations were acceptable for use during the clinical investigation. The catheter is compatible with EnSite Velocity, EnSite Precision, and Ensite X mapping systems.



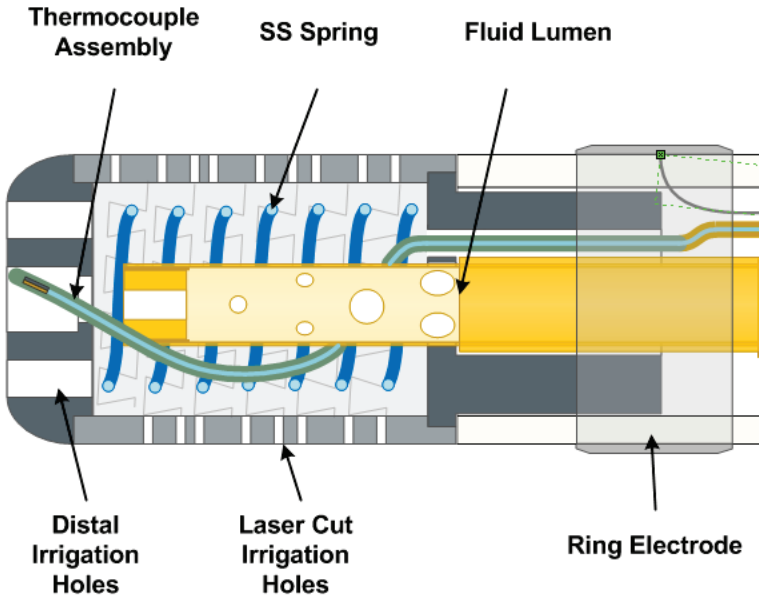


Figure 1. FlexAbility SE, Catheter Tip

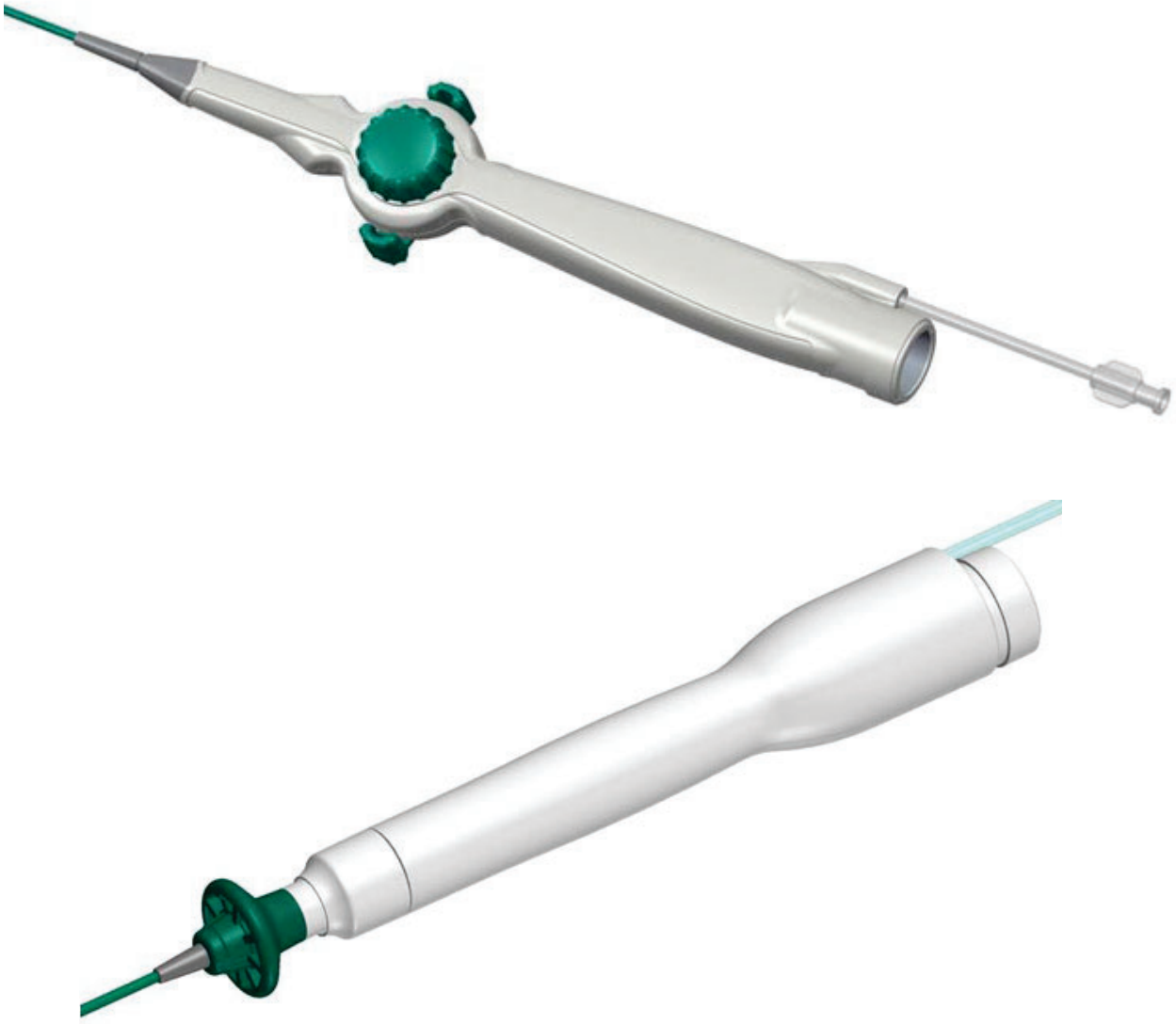


Figure 2. FlexAbility SE, Bi-Directional (top) and Uni-Directional (bottom)

The catheters are available in eight distal curve configurations and the curve is identified on the catheter package label. The device and packaging are not made with natural rubber latex.

Device Name	Model Number
FlexAbility SE UniD-D	A-FASE-D
FlexAbility SE BiD-DD	A-FASE-DD
FlexAbility SE BiD-DF	A-FASE-DF
FlexAbility SE BiD-FF	A-FASE-FF
FlexAbility SE UniD-F	A-FASE-F
FlexAbility SE BiD-FJ	A-FASE-FJ

FlexAbility SE UniD-J	A-FASE-J
FlexAbility SE BiD-JJ	A-FASE-JJ

The following devices are required in addition to the FlexAbility SE catheters:

- RF generator
- Irrigation pump
- Electrophysiology recording and mapping system

In the LESS-VT IDE study, the following devices were used with the subject device to provide the treatment (Table 1).

Table 1. Associated Devices

Devices	**Model Number, SW Version**
Generator	
Ampere™ RF Ablation Generator	H700489
Ancillary Device	
EnSite System (Amplifier and Display Workstation)	EE3000
EnSite Velocity Software	v5.0 or greater
Ensite Precision Software	v2.0 or greater
Ensite X EP System	v1.0 or greater
Cool Point™ Irrigation Pump	IBI-89003, SW v24 or greater
Cool Point Tubing Set	RO85785

The PMA submission history for the FlexAbility SE catheters, and the previously approved FlexAbility™ Ablation Catheters, is described below in **Table 2**.

Table 2: PMA Submission History

Submission	**Description**	**Date of Approval**
P110016	Original PMA Approval – Therapy™ Cool Path Duo, Safire™ BLU Duo, and IBI1500T-9 v1.6 Cardiac Ablation Generator	25JAN2012
P110016/S013	Approval of the FlexAbility™ Ablation Catheter	23JAN2015
P110016/S025	Approval of the FlexAbility™ Ablation Catheter, Sensor Enabled™ for the treatment of typical atrial flutter.	17FEB2017
P110016/*S080*	Approval of the FlexAbility™ Ablation Catheter, Sensor Enabled™ for the treatment of typical atrial flutter and recurrent, drug-refractory, sustained MMVT in patients with non-ischemic structural heart disease	*TBD*

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the treatment of recurrent, drug-refractory, sustained monomorphic ventricular tachycardia in patients with non-ischemic structural heart disease, including:

- Pharmacological therapy for arrhythmia control
- Implantable cardiac defibrillator therapy
- Antitachycardia pacing
- Direct surgical ablation or removal of tissue

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 FlexAbility SE catheters have been marketed in the United States for treatment of typical atrial flutter since February 2017 and is marketed in all major geographies including Argentina, Australia/New Zealand, Brazil, Canada, China, Colombia, Costa Rica, Ecuador, Egypt, EU Member Countries, Hong Kong, India, Israel, Japan, South Korea, Malaysia, Mexico, Russia, Saudi Arabia, Singapore, Taiwan, Thailand, Turkey, and UK, among others.

These devices have not been withdrawn from market in any country for any reason related to safety or effectiveness.

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.

Category	Adverse Event
Bleeding	Abdominal bleeding
	Anemia
	Blood loss requiring transfusion
	Hemoperitoneum
	Hemothorax
Conduction System Complications	Abnormal electrocardiogram (ECG)
	Arrhythmias resulting in clinically significant deterioration in subject medical condition
	Atypical flutter
	Exacerbation of pre-existing arrhythmia
	Exacerbation of pre-existing atrial fibrillation
	Inadvertent AV block
	Temporary heart block
	Unintended complete heart block requiring pacemaker insertion
	Unintended sinus node dysfunction requiring pacemaker insertion
	Ventricular arrhythmia requiring defibrillation
Coronary Artery Injury or Vascular/Valvular Injury	Aortic dissection
	Arterial spasm
	Coronary artery dissection
	Coronary artery injury/damage
	Pulmonary vein dissection
	Valvular damage
	Valvular damage or insufficiency (i.e. new tricuspid regurgitation)
	Vascular trauma
Infection	Endocarditis
	Infection
	Sepsis
Intra-procedure or post-procedure symptoms	Abnormal vision
	Angina/chest pain

Category	Adverse Event
	Component damage to implantable cardioverter defibrillator or pacemaker
	Dislodgement of implantable cardioverter defibrillator or permanent pacing lead
	Dizziness
	Exacerbation of chronic obstructive pulmonary disease (COPD)
	High creatinine phosphokinase
	Laceration
	Neck pain/back pain/groin pain related to the procedure
	Palpitations
	Radiation injury resulting in dermatitis (inflammation of the skin), erythema (redness), etc.
	Respiratory failure
	Seizure
	Skin burns/ skin tears
	Syncope
	Vasovagal reaction
Perforation/Tamponade	Arteriovenous fistula
	Cardiac effusion/tamponade
	Cardiac perforation
	Left atrial/esophageal fistula
	Pericardial bleeding
	Pericardial effusion
Procedure or Post-op Complications	Anaphylaxis
	Anesthesia reaction
	Hypotension
	Hypoxia
	Myocardial infarction (MI)
	Pericarditis
	Phrenic nerve damage
	Pleural damage
	Pleural effusion
	Pneumonia
	Pneumothorax
	Pulmonary edema
	Pulmonary embolism
	Pulmonary hypertension
	Pulmonary vein stenosis
	Respiratory depression
Thromboembolic Event	Air embolism
	Arterial/venous thrombus

Category	Adverse Event
	Cardiac thromboembolism
	Cerebrovascular accident/Stroke
	Thromboembolic event
	Transient ischemic attack (TIA)
Vascular Access Complication	Catheter insertion site hematoma
	Groin hematoma
	Obstruction/perforation/damage of the vascular system or vascular bleeding
	Pseudoaneurysm
Worsened Heart Failure	Congestive heart failure (CHF) exacerbation
Death	Death

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

IX. SUMMARY OF NONCLINICAL STUDIES

Pre-clinical testing of the FlexAbility SE catheter included verification and validation testing, biocompatibility of patient-contacting materials, sterilization, packaging and shelf-life testing, and animal studies. Performance testing was conducted to demonstrate design integrity. All tests performed which were identified in standards or guidance documents were based on the product specification requirements.

A summary of previously reported preclinical studies can be found in the SSED for the original PMA at:
https://www.accessdata.fda.gov/cdrh_docs/pdf11/P110016B.pdf

All previously performed pre-clinical testing was conducted to support the initial PMA approval, approval of the FlexAbility Ablation Catheter (P110016/S013), and approval of the FlexAbility Ablation Catheter, Sensor Enabled (P110016/S025) of the FlexAbility SE catheter. No further pre-clinical testing was conducted for the current expanded indication submission.

X. SUMMARY OF PRIMARY CLINICAL STUDY

LESS-VT Trial – Non-ischemic Cardiomyopathy Cohort
The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of RF ablation with the FlexAbility SE Catheter for the treatment of recurrent, drug-refractory, sustained monomorphic ventricular tachycardia in patients

with non-ischemic structural heart disease in the US, Europe, and Australia under IDE # G170221. 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 enrolled between 6/11/2018 and 6/9/2021. The database for this PMA reflected data collected through January 19, 2022 and included 182 patients at 24 investigational sites (US: 19 sites, Europe: 5 sites).

The LESS-VT NICM Cohort is a prospective, open-label, non-randomized, single-arm multicenter pivotal trial. The study enrolled and treated subjects diagnosed with non-ischemic cardiomyopathy and drug refractory recurrent MMVT and was evaluated for success based on a composite of cardiovascular-related and procedure-related major complications through 7 days and freedom from recurrent sustained MMVT at 6 months. All subjects are followed for a total of 12 months.

An independent Clinical Events Committee (CEC) provided blinded adjudication for all primary safety endpoint events. An independent ICD Event Review Committee reviewed all tachyarrhythmia events collected in the study and adjudicated the reported tachyarrhythmia for morphology (e.g. MMVT) and the appropriateness of any therapy delivered. An independent Data Safety Monitoring Board (DSMB) oversaw clinical data and safety.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the NICM Cohort of the LESS VT study was limited to patients who met the following inclusion criteria

- Structural heart disease (non-ischemic) with one of the following:
  - Confirmed diagnosis via echocardiography and/or cardiac CT/MRI, or
  - Left ventricular ejection fraction (EF) <40% (documented within the last 6 months via echocardiography), or
  - Arrhythmogenic RV cardiomyopathy/dysplasia (per 2010 ARVC/D Task Force Criteria).
- At least one documented episode of sustained MMVT by either EGM or ECG in the 6 months prior to enrollment
- Implanted with a market released ICD or CRT-D for at least 30 days prior to index ablation procedure
- Refractory (i.e. not effective, not tolerated or not desired) to at least one anti-arrhythmic medication (either amiodarone or sotalol) for treatment of MMVT

- At least 18 years of age Informed of the nature of the study, agreed to its provisions and has provided written informed consent as approved by the Institutional Review Board/Ethics Committee (IRB/EC) of the respective clinical study site.
- Able and willing to comply with all study requirements

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

- Implanted with a subcutaneous ICD
- Implanted with a ventricular assist device (VAD) (e.g. TandemHeart)
- Currently receiving support, or anticipated to receive support prior to the index ablation procedure, via extracorporeal membrane oxygenation (ECMO)
- Presence of intracardiac thrombus verified via computer tomography (CT), magnetic resonance imaging (MRI), transesophageal echocardiogram (TEE), or transthoracic echocardiogram (TTE) within 48 hours prior to the index ablation procedure or intra-procedure intracardiac echocardiography (ICE)
  - For subjects with a history of AF, this verification must be done via TEE or ICE
- ST elevation myocardial infarction (MI) within 60 days prior to index ablation procedure
- Previous cardiac surgery (e.g. ventriculotomy, atriotomy, coronary artery bypass graft), within 60 days prior to index ablation procedure
- Percutaneous coronary intervention (PCI) within 30 days prior to index ablation procedure
- Idiopathic VT
- Incessant VT (continuous sustained VT that promptly recurs despite repeated intervention for termination over ≥3 hours) necessitating immediate treatment or requiring hemodynamic support prior to the ablation procedure
- VT/VF thought to be from channelopathies
- Reversible cause of VT
- Severe aortic stenosis or flail mitral valve
- Mechanical mitral and aortic valve
- History of stroke with modified Rankin scale > 3
- Unstable angina
- Chronic NYHA Class IV heart failure
- Ejection fraction < 15%
- Thrombocytopenia (defined as platelet count <80,000) or coagulopathy
- Contraindication to systemic anticoagulation (i.e. heparin, warfarin, or a direct thrombin inhibitor)
- Women who are pregnant or nursing
- Active uncontrolled infection
- Other anatomic or co morbid conditions or other medical, social, or psychological conditions that, in the investigator's opinion, could limit the patient's ability to

participate in the study or to comply with follow up requirements, or impact the scientific soundness of the study results
- Enrolled in an investigational study evaluating another device or drug that would confound the results of this study
- Have a life expectancy of less than 12 months due to any condition.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at 30 days, 6 and 12 months postoperatively.

Preoperatively, all subjects underwent evaluation of LV ejection fraction, ICD interrogation, SF-12 QoL and HADS assessments, and thrombus screening.

Postoperatively, the objective parameters measured during the study included ICD interrogation for VT occurrence and SF-12 QoL and HADS assessments. Adverse events and complications were screened and recorded at all visits.

The key timepoints are shown below in the table summarizing safety and effectiveness.

Table 3: List of all clinical investigation specific tests and procedures

Visit **Study Activity**	**Enrollment & Baseline**	**Procedure (index and staged procedures)**	**Discharge**	**30 days (± 7 days)**	**6 and 12 Months (± 21 days)**
Informed Consent Process and Confirm enrollment criteria	X				
Demographics, Medical History incl. arrhythmias, MMVT	X				
Retrospective Health care utilization for 12 months prior to consent (US only)	X				
LVEF via echocardiography	X*				
Physical Examination	X		X	X	
12-Lead ECG	X		X	X	
Modified Rankin Score assessment	X				
Device Programming, Interrogation, and session records	X	X	X	X	X
Recurrence of VT				X	X

Cardiac and/or anti-arrhythmic medications	X	X	X	X	X
SF-12 QOL and HADS	X				X
Confirm absence of intracardiac thrombus	X[a]	X[a]			
Procedure indication and ablation procedure strategy		X			
Ablation System details and future plans for additional procedures if any		X			
EnSite Precision Procedure Recording		X			
Repeat Ablation[b]			(X)	(X)	(X)
Adverse Event		(X)	(X)	(X)	(X)
Health Care Utilization				(X)	(X)
Deviation	(X)	(X)	(X)	(X)	(X)
Withdrawal	(X)	(X)	(X)	(X)	(X)
Death	(X)	(X)	(X)	(X)	(X)

(X) If applicable

* Historical echocardiogram can be used if it was performed within the last 6 months prior to enrollment.

[a] Thrombus assessment must be performed within 48 hrs of procedure which can take place at either baseline or procedure visit

[b] Repeat ablation is to be reported for ventricular ablation procedures occurring >14 d after index procedure

3. Clinical Endpoints

With regards to safety, the primary safety endpoint is a composite of cardiovascular-related and procedure-related major complications through 7 days post index ablation procedure. Major complication is defined as an adverse event that led to prolongation of hospital stay or to another hospitalization, required additional intervention for treatment, and/or resulted in significant injury or death.

For this study, recurrence of a VT is not a reportable adverse event in the study, regardless of hospitalization or intervention, unless it results in new incessant VT/VT storm or significant deterioration of subject's medical condition, or death.

With regards to effectiveness, the primary effectiveness endpoint is freedom from recurrent sustained MMVT at 6 months and a new or increased dose Class I or III AAD at 6 months following the index ablation procedure, where sustained MMVT is defined as a continuous MMVT for >30 seconds, or MMVT requiring intervention for termination regardless of its duration.

With regard to success/failure criteria, each primary endpoint was compared to a predetermined performance goal. The study would be considered success when both of the following criteria are met:

- The primary safety endpoint event rate meets the prespecified performance goal of 26.9%.

  The hypothesis for the primary safety endpoint is:

  H_0: $P_1 \geq 26.9\%$
  Ha: $P_1 < 26.9\%$

  Where P_1 is the 7-day rate (binomial proportion) of the primary safety endpoint. A sample size of 171 subjects was required to provide 85% power to reject null hypothesis at 5% significance level using the exact test for binomial proportion.

  The analysis population for the primary safety endpoint analysis included subjects enrolled in the NICM cohort who had the investigational catheter inserted in the EP lab for the VT ablation procedure (regardless of whether or not RF energy is delivered) and crossed the 7-day post index ablation time point.

- The primary effectiveness endpoint event rate meets the prespecified performance goal of 40.2%.

  The hypothesis for the primary effectiveness endpoint is:

  H_0: $P_2 \leq 40.2\%$
  Ha: $P_2 > 40.2\%$

  Where P_2 is freedom from recurrent sustained MMVT and a new or increased dose of Class I or III AAD at 6 months following the index ablation procedure for the NICM cohort.

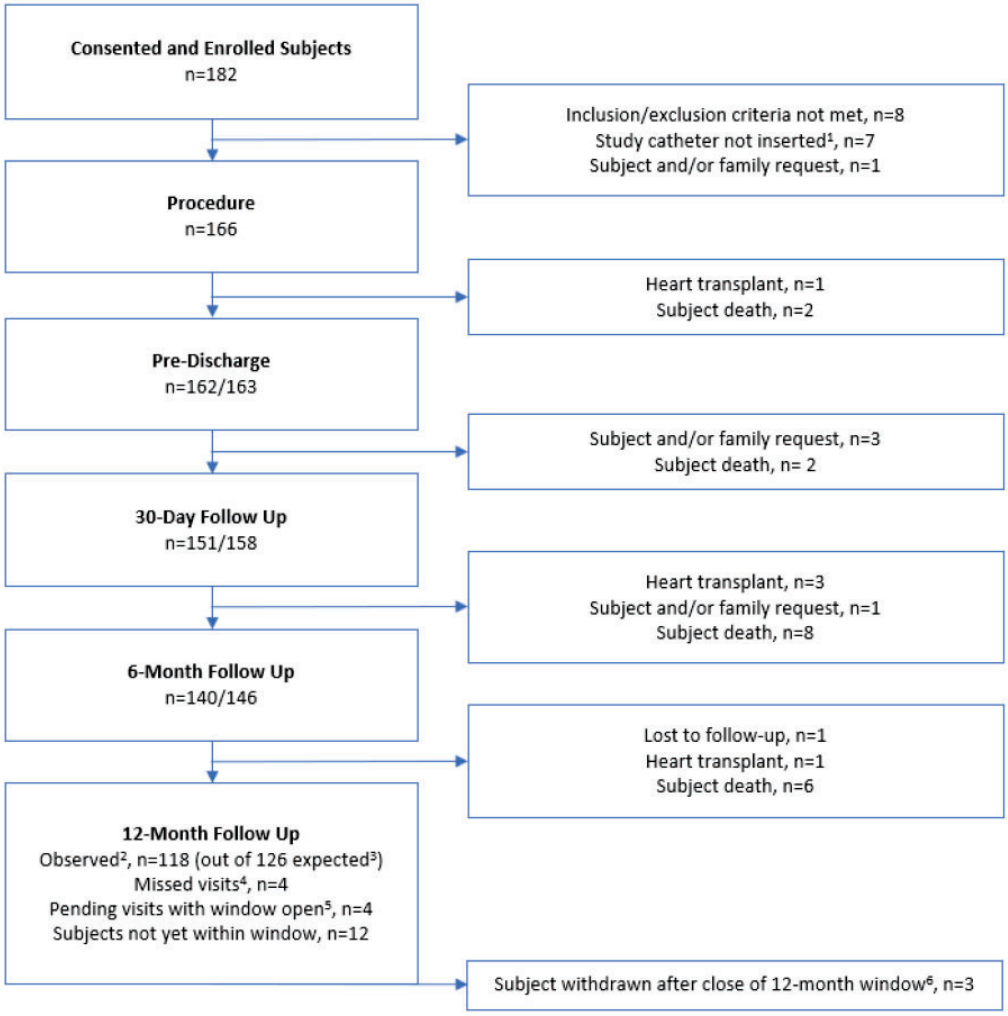
  A sample size of 138 subjects was required to provide at least 85% power to reject null hypothesis at the 5% significance level using the exact test for binomial proportion.

  The analysis population for the effectiveness endpoint analysis included subjects in the NICM cohort who had the catheter inserted and RF energy delivered in the EP lab for the VT ablation procedure, and who had their 6-month visit or crossed the 6-month visit window without the visit but with an effectiveness endpoint event.

B. Accountability of PMA Cohort

At the time of database lock, of 182 patients consented in the PMA study, 140 (76.8%) patients were available for analysis at the 6-month post-operative visit. Figure 3 presents the LESS-VT NICM Cohort subject disposition. Based on the subject accountability, Table 4 summarizes the protocol specified analysis populations.

Figure 3: LESS-VT NICM Cohort Subject Disposition



[1] Withdrawal due to study catheter not inserted was counted as pre-procedure withdrawal. Reasons for catheter not inserted include non-inducible or no arrhythmic substrate identified (5), transeptal access related cardiac perforation (1), and chronic aortic dissection (1).

[2] n is the number of visits observed at the time of this report that occurred within the visit window, excluding deaths and withdrawals.

[3] Number of visits expected at the time of this report. A subject is considered expected at the given visit if they have not died or withdrawn by the end of the visit window, and the visit window has opened by the cutoff date.

[4] A visit is considered missed if the visit window is closed at the time of this report and the visit has not occurred or has not been entered in the database, excluding deaths and withdrawals.

[5] A visit is considered pending if the visit window is open at the time of this report but the visit has not occurred or has not been entered in the database, excluding deaths and withdrawals.

[6] Withdrawal case report forms were submitted for three (3) NICM subjects after missing the 12-month visit and after the close of the 12-month visit window. For these subjects, the reason for withdrawal was documented as lost to follow-up (n=2) and subject and/or family request (n=1). These subjects are also counted as having missed visits for the 12-month follow-up.

Table 4. Protocol Specified Analysis Populations

Population	Abbreviation for Analysis Population	Description	Subjects
Enrolled	ENR	Signed written informed consent	182
Catheter-Inserted	CIN	Investigational catheter inserted into the vasculature	166
Primary Safety Endpoint	SAF	Catheter inserted subjects who completed 7 days of follow-up or experienced a primary safety endpoint failure	166
Treated	TRT	Investigational catheter inserted and RF energy delivered	165
Primary Effectiveness Endpoint	EFF	Treated subjects who have completed a 6 or 12 Month visit with ICD interrogation or experienced a primary effectiveness endpoint failure	146

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for patients with non-ischemic cardiomyopathy and recurrent MMVT referred for catheter ablation in the US. The mean age was 60.2 ± 13.8 years, and 16.3% were female. Tables 5 and 6 present the demographics and baseline cardiovascular history for the catheter-inserted (CIN) population, respectively. Approximately half of subjects (84/166) had NYHA II-III functional class at baseline, and the mean left ventricular ejection fraction was 38.1 ± 12.9%. Amiodarone or sotalol had not been effective or tolerated in 88% subjects. Prior catheter ablation for the treatment of ventricular tachycardia had been performed in 55 (33.1%) subjects.

Table 5. Baseline Demographics (CIN Population)

Demographic Variable	CIN Population (N=166)
Age (year)	
Mean ± SD (n)	60.2 ± 13.8 (166)
Range (Min, Max)	(22.0, 88.0)
Sex, n (%)	
Female	16.3% (27/166)
Male	83.7% (139/166)
Ethnicity, n (%)	
Hispanic or Latino	2.0% (3/152)
Not Hispanic or Latino	98.0% (149/152)
Race, n (%)	
American Indian or Alaskan Native	0.7% (1/152)

Asian	2.0% (3/152)
Black or African American	13.2% (20/152)
Native Hawaiian or Other Pacific Islander	0.0% (0/152)
White	84.2% (128/152)
Height (cm)	
Mean ± SD (n)	175.4 ± 9.6 (165)
Range (Min, Max)	(150.0, 198.0)
Weight (kg)	
Mean ± SD (n)	89.4 ± 22.4 (165)
Range (Min, Max)	(45.0, 155.6)

Table 6. Baseline Cardiovascular History (CIN Population)

Demographic Variable	CIN Population (N=166)
Cardiovascular History, n (%)	
Structural Heart Disease	100.0% (166/166)
Ischemic Cardiomyopathy	0.0% (0/166)
Non-ischemic Cardiomyopathy	100.0% (166/166)
Coronary Artery Disease	16.3% (27/166)
Diastolic Dysfunction	27.7% (46/166)
Heart Failure	61.4% (102/166)
NYHA Class I	17.6% (18/102)
NYHA Class II	52.0% (53/102)
NYHA Class III	30.4% (31/102)
NYHA Class IV	0.0% (0/102)
Not Specified	0.0% (0/102)
Hypercholesterolemia	27.7% (46/166)
Hyperlipidemia	45.8% (76/166)
Hypertension	48.2% (80/166)
Infective Endocarditis	1.2% (2/166)
Myocardial Infarction	5.4% (9/166)
Percutaneous Coronary Intervention	7.2% (12/166)
Valvular Heart Disease	19.9% (33/166)
Class I/III AAD Use at Study Enrollment	58.4% (97/166)
Amiodarone or Sotalol not Effective	78.9% (131/166)
Amiodarone or Sotalol not Tolerated	37.3% (62/166)
LV Ejection Fraction (%)	38.1 ± 12.9 (163)
	(15.0, 70.0)

All enrolled subjects had non-ischemic cardiomyopathy and none had been diagnosed with ischemic cardiomyopathy. Table 7 presents the reported etiologies of non-ischemic heart disease in the study population. The distribution of NICM subtypes in the pivotal study aligns with other large published series.[1]

Table 7. Types of Non-Ischemic Heart Disease (CIN Population)

Types of Non-Ischemic Heart Disease	(N=166)

Arrhythmogenic Right Ventricular Cardiomyopathy/Dysplasia	21.7% (36/166)
Cardiac Sarcoidosis	10.2% (17/166)
Congenital Heart Disease	3.6% (6/166)
Hypertrophic Cardiomyopathy	6.6% (11/166)
Non-Ischemic Left Ventricular Cardiomyopathy and/or Dilated Cardiomyopathy	54.2% (90/166)
Other	14.5% (24/166)
Genetic Cardiomyopathy	1.2% (2/166)
Other Cardiomyopathy*	3.0% (5/166)
Myocarditis	2.4% (4/166)
Scar Associated with Previous Cardiac Surgery	0.6% (1/166)
Unknown	1.8% (3/166)

*Site-provided descriptions of Other Cardiomyopathy include focal LV ventricular scar/fibrosis, LV dysfunction, ESRD related cardiomyopathy, focal basal septum fibrosis, acute on chronic systolic HF.

Procedural Data

Repeat procedures:

The study allows for staged ablation procedures based on physician discretion and would be considered a continuation of the index ablation procedure if performed within 14 days of the index ablation procedure. Overall, 9 of 165 TRT subjects underwent a staged procedure within 14 days. Of these, 5 staged procedures were performed due to early recurrence of ventricular arrhythmia.

Cardiac Access

The basis of mapping and ablation in this study is scar-based late potential ablation. The study protocol encourages mapping of both ventricular chambers and epicardium. Table 8 summarizes the cardiac access utilized in the study. Subxiphoid epicardial access was performed in 48.8% of the index procedures. Including the staged procedures, epicardial mapping was performed in 53% with epicardial ablation performed in 43%.

Table 8. Cardiac Access (CIN Population)

Access*	Index Procedure (N=166)	Staged Procedure (N=9)
LV Endocardial Access	77.1% (128/166)	66.7% (6/9)
Transseptal	59.4% (76/128)	66.7% (4/6)
Retrograde Aortic	60.9% (78/128)	33.3% (2/6)
Epicardial Access	51.2% (85/166)	55.6% (5/9)
Subxiphoid	95.3% (81/85)	100.0% (5/5)
Other: coronary sinus mapping	4.7% (4/85)	0.0% (0/5)

Programmed Electrical Stimulation

The study protocol recommends programmed electrical stimulation (PES) at a minimum of two sites (including one LV site) using two cycle lengths (600 ms and 400 ms typically) with at least double extra-stimuli (up to four extra-stimuli may be used) to induce VT at the beginning of the study unless there is a clinical reason not to do so. At the end of the study, the same PES protocol used at baseline is encouraged unless the patient is felt to be unable to tolerate it. Table 9 presents the PES results. Overall, a median of 2.0 (mean: 2.3 ± 2.0) MMVTs were identified for each subject at the index procedure.

Table 9. MMVT inducibility pre- and post-ablation (TRT population, Index Procedure)

	Number of Subjects (n= 165)
Pre-procedure programmed electrical stimulation conducted	92.1% (152/165)
MMVT inducible pre-procedure	79.6% (121/152)
Post-ablation induction attempted	91.7% (111/121)
Post-ablation induction attempted and MMVT not inducible	88.2% (97/110)

Mapping Strategies

The basis of mapping and ablation in this study was ventricular tachycardia substrate mapping and scar-based late potential ablation guided by electroanatomic mapping. Investigators used the assigned catheter or another market cleared multipolar mapping catheter to create voltage maps and identify ablation targets. Table 10 summarizes the additional mapping strategies utilized for subjects with spontaneous or induced MMVT.

Table 10. Mapping During MMVT (TRT Population, Index Procedure)

Mapping Done In MMVT	**Index Procedure (N=165)**
Entrainment	17.6% (29/165)
Timing/Activation	52.7% (87/165)
Voltage	13.3% (22/165)
Other	4.2% (7/165)
Not Done	41.2% (68/165)
Unsustainable	20.6% (14/68)
Untolerated by Subject	39.7% (27/68)
Not Inducible	32.4% (22/68)
Physician Discretion	8.8% (6/68)

Ablation Locations

Ablation locations included the endocardial surface in 80.6% (133/165) of subjects and the epicardial surface in 43.0% (71/165) of subjects. The left ventricle was most frequently

targeted (120/165, 72.7%), followed by right ventricle (54/165, 32.7%) and interventricular septum (15/165, 9.1%).

Table 11 . Ablation Locations (TRT Population)

Ablation Target Location	Index Procedure (N=165)	Staged Procedure (N=9)
Surface		
Endocardial	80.6% (133/165)	77.8% (7/9)
Epicardial	40.0% (66/165)	55.6% (5/9)
Chamber or Component		
Right Ventricle	32.1% (53/165)	11.1% (1/9)
Left Ventricle	72.7% (120/165)	100.0% (9/9)
Septal	8.5% (14/165)	11.1% (1/9)

Procedure Parameters

Table 12 presents the procedural results.

Table 12. Procedure and Ablation Parameters

Procedure Metric	Index Procedure (N=165)	Staged Procedure (N=9)
Anesthesia		
Conscious Sedation	7.9% (13/165)	22.2% (2/9)
General	83.6% (138/165)	66.7% (6/9)
Monitor Anesthesia Care	8.5% (14/165)	11.1% (1/9)
Hemodynamic Support		
Balloon Pump	0.6% (1/165)	11.1% (1/9)
Impella	0.6% (1/165)	22.2% (2/9)
Other	0.6% (1/165)	0.0% (0/9)
Not used	98.2% (162/165)	66.7% (6/9)
Irrigation Fluid Input from Pump (ml)		
Mean ± StdDev (n)	746.3 ± 433.4 (160)	1056.4 ± 545.4 (9)
Median (Q1, Q3)	676.0 (402.5, 1000.0)	1000.0 (853.0, 1358.0)
(Min, Max)	(0, 2222)	(100, 2000)
Cardioversion Performed	66.1% (109/165)	88.9% (8/9)
Number Performed		
Mean ± StdDev (n)	3.1 ± 2.5 (109)	3.5 ± 2.1 (8)
Median (Q1, Q3)	2.0 (1.0, 4.0)	3.0 (2.0, 5.0)
(Min, Max)	(1, 13)	(1, 7)
Ventricular Ablation Abandoned	4.8% (8/165)	22.2% (2/9)
Procedure Time (min)		
Mean ± StdDev (n)	231.8 ± 96.6 (165)	294.4 ± 106.0 (9)
Median (Q1, Q3)	207.0 (170.0, 267.0)	311.0 (235.0, 369.0)
(Min, Max)	(82, 710)	(113, 440)
Fluoroscopy Time (min)		
Mean ± StdDev (n)	33.2 ± 19.6 (164)	43.0 ± 24.6 (9)

Median (Q1, Q3) (Min, Max)	29.5 (19.0, 42.0) (3, 112)	46.0 (24.0, 56.0) (6, 88)

D. Safety and Effectiveness Results

1. Safety Results

a. Primary Safety Endpoint

The analysis of safety was based on the cohort of 166 catheter inserted subjects who completed 7 days of follow-up or experienced a primary safety endpoint event within the 7-day window. Overall, 27 of 166 subjects (16.3%) experienced a primary safety endpoint event. The upper bound of the 95% one-sided confidence interval of 21.7% was lower than the pre-specified performance goal, and the primary safety endpoint was met.

Primary Safety Endpoint			
Population	**Number of Subjects**	**95% One-Sided Confidence Interval Upper Bound**	**Performance Goal**
Safety Population	16.3% (27/166)	21.7%	< 26.9%

The key safety outcomes for this study are presented below in Table 13 by pre-specified categories and by CEC ajudication. Nine subjects had a staged procedure performed within 14 days. Including major complications that occurred after the staged procedures, a total of 29 (17.5%) subjects experienced cardiovascular-related and procedure-related major complications through 7 days post index ablation procedure or staged procedure.

Table 13. Primary Safety Endpoint Events (SAF Population)

	PSAE within 7 days of index procedure (N=166)	
Primary Safety Endpoint Event Criteria (pre-specified categories and by CEC adjudication)	**Number of Events**	**Number of Subjects**
Acute Myocardial Infarction	0	0.0% (0/166)
Acute Pulmonary edema requiring reintubation	1	0.6% (1/166)
Cardiac perforation/tamponade	6	3.0% (5/166)
Cardiogenic shock	2	1.2% (2/166)
Chordae entrapment requiring surgical intervention	0	0.0% (0/166)
Complete heart block	0	0.0% (0/166)
Damage or movement of ICD leads requiring revisions	0	0.0% (0/166)
Death from any cause	2	1.2% (2/166)
New incessant VT/VF	2	1.2% (2/166)
Phrenic nerve injury which does not resolve in 7 days	0	0.0% (0/166)

Pulmonary embolism documented by imaging and requiring intervention	0	0.0% (0/166)
Stroke	1	0.6% (1/166)
TIA	0	0.0% (0/166)
Valve injury requiring surgical intervention	1	0.6% (1/166)
Vascular access complications requiring surgical intervention or >2 units of blood transfusion	2	1.2% (2/166)
Other	20	9.0% (15/166)
Arrhythmia New	1	0.6% (1/166)
Bleeding/Anemia	1	0.6% (1/166)
Hypotension	5	3.0% (5/166)
Infection	2	1.2% (2/166)
Myocardial Infarction	1	0.6% (1/166)
Pericardial Bleed	1	0.6% (1/166)
Pericardial Effusion	1	0.6% (1/166)
Pericarditis	3	1.8% (3/166)
Respiratory Failure/Depression/Compromise	1	0.6% (1/166)
Vascular Access Site Complications	2	1.2% (2/166)
Ventricular Arrhythmia With Significant Deterioration	1	0.6% (1/166)
Visceral Structure Or Organ Damage Including Bleed/Hematoma	1	0.6% (1/166)
Total	**37**	**16.3% (27/166)**

Note: Some subjects may have experienced more than one type of event. Therefore, the total number of subjects may be less than the sum of the numbers of subjects who experienced each type of event. PSAE denotes primary safety adverse event, VT/VF ventricular tachycardia/ventricular fibrillation, TIA transient ischemic attack, and ICD implantable cardioverter-defibrillator or cardiac resynchronization therapy-defibrillator.

b. Summary of Adverse Device Effects

Serious Adverse Device Effects

Table 14 presents all device or procedure related serious adverse events reported at the time of data lock as adjudicated by the CEC. There were no unanticipated serious adverse device effects.

Table 14. Serious Adverse Events Related to the Procedure or Device (CIN Population)

			CEC Assessment	
Adverse Event	**Events**	**Subject % (n/N)**	**Device Related**	**Procedure Related**
Abnormal Labs (E.G. Cpk, Creatinine, Troponin)	1	0.6% (1/166)	0	1
Arrhythmia New (atrial arrhythmia)	1	0.6% (1/166)	0	1
Bleeding/Anemia	2	1.2% (2/166)	0	2
Cardiac Arrest	2	1.2% (2/166)	0	2
Cardiac Perforation	3	1.8% (3/166)	0	3
Cardiac Tamponade	2	1.2% (2/166)	2	2
Chest Pain/Angina (Cardiac)	1	0.6% (1/166)	0	1
Heart Failure	4	2.4% (4/166)	4	4
Hemothorax	1	0.6% (1/166)	0	1
Hypotension	4	2.4% (4/166)	0	4
Infection	3	1.8% (3/166)	0	3
Myocardial Infarction	1	0.6% (1/166)	0	1
Pericardial Bleed	1	0.6% (1/166)	0	1
Pericardial Effusion	3	1.8% (3/166)	1	3

Pericarditis	4	2.4% (4/166)	3	4
Peripheral Thrombus	2	0.6% (1/166)	0	2
Pleural Effusion	1	0.6% (1/166)	0	1
Pulmonary Embolism	1	0.6% (1/166)	0	1
Respiratory Failure/Depression/Compromise	1	0.6% (1/166)	0	1
Shock	2	0.6% (1/166)	0	2
Stroke/CVA/Embolic Event	1	0.6% (1/166)	0	1
Valve Damage/Insufficiency/Regurgitation	2	1.2% (2/166)	2	2
Vascular Access Site Complications	4	2.4% (4/166)	0	4
Ventricular Arrhythmia With Significant Deterioration	4	2.4% (4/166)	1	4
Visceral Structure Or Organ Damage (NG tube related gastric ulcer)	1	0.6% (1/166)	0	1
Total	**52**	**21.1% (35/166)**	**13**	**52**

Cardiac Perforation and Pericardial Complications

In the pivotal study, cardiac perforation and pericardial complications (including tamponade, pericardial effusion, and excessive pericardial bleeding) occurred in 9 (5.4%) subjects. Of these, 6 (3.6%) subjects required surgical drainage or pericardiocentesis for treatment.

Cardiac perforation/tamponade occurred in 5 subjects (5/166, 3.0%). One of three adjudicated cardiac perforation events occurred during mapping and prior to application of any radiofrequency ablation. Another cardiac perforation event resulted from inadvertent LV puncture during chest tube placement to treat hemothorax that had developed after epicardial access. The subject could not be resuscitated despite emergent surgical repair.

Three (1.8%) subjects had procedure-related pericardial effusion. Two subjects were treated conservatively for small pericardial effusion. In the third subject, delayed pericardial effusion was drained 20 days following an index procedure that included epicardial access.

Lastly, a subject whose ablation procedure included epicardial access developed excessive pericardial bleeding requiring prolonged pericardial drainage from the pericardial drain that had been left in place post procedure.

Hypotension/Cardiogenic shock

A total of 5 (3.0%) subjects developed persistent hemodyanamic instability during the procedure. Of these, one subject (0.6%) with cardiogenic shock required unplanned IABP placement for continued hemodynamic support after the procedure. The other 4 subject with hypotension and/or cerebral hypoperfusion were treated pharmacologically and only required transient inotrope/pressor support post-operatively.

Coronary Artery Injury or Myocardial Infarction/Ischemia
Epicardial ablation was performed in 40% of index procedures. There were no reported adverse events of direct injury to the coronary arteries.
A subject (0.6%) with elevated troponin and T wave changes on ECG in the setting of infection was adjudicated to have procedure-related non-ST elevated myocardial infarction.

Heart Failure
CEC adjudicated 4 (2.4%) subjects to have experienced significant procedure-related heart failure/acute pulmonary edema requiring intubation or hospitalization for IV diuresis. Of these, one subject was re-intubated peri-operatively due to significant pulmonary edema. The other 3 subjects experienced heart failure decompensation during the 30 days following the index procedure.

Valvular Injury
There were no cases of chordae entrapment by a mapping and/or ablation catheter requiring immediate open surgical removal. Two (1.2%) subjects with significant procedure-related valvular regurgitation (one AR, one MR) underwent corrective valve intervention on POD 16 and 189, respectively.

New Incessant VT/VF or Ventricular Arrhythmia with Significant Deterioration
Within the 30 days following the index procedure, 9 (5.4%) subjects experienced worsened ventricular arrhythmias. Of these, 3 (1.8%) subjects had procedure related new incessant VT/VF, defined as VF or VT of a new morphology compared with pre-ablation that is now unresponsive to ICD therapies, external defibrillation or antiarrhythmic medication, or quickly recurs after a brief termination, as adjudicated by the CEC. Of the other remaining 6 subjects with significant ventricular arrhythma recurrence, one was adjudicated as procedure related.

Neurological Complication
One subject (0.6%) suffered right MCA stroke that's diagnosed immediately after the procedure.

Vascular Access Complications
Vascular access complications requiring intervention (including ultrasound guided compression) occurred in 4 subjects (2.4%). Another subject had retroperitoneal hemorrhage. In total, 5 of 166 subjects (3.0%) experienced

vascular access complications requiring intervention or >2 units of blood transfusion.

Pericarditis

There were 4 procedure-related SAEs occurred in 4 subjects (2.4%). Of these, 3 of 4 subjects underwent subxiphoid epicardial access and mapping.

At the time of database lock, there were no procedure-related serious adverse events of complete heart block, damage or dislodgement of ICD leads requiring revisions, or phrenic nerve injury.

Non-serious adverse device effects

Nineteen (19) non-serious adverse events that occurred in 17 subjects were adjudicated as being related to the procedure and/or the device. Table 15 presents all non-serious adverse device effects as adjudicated by the CEC.

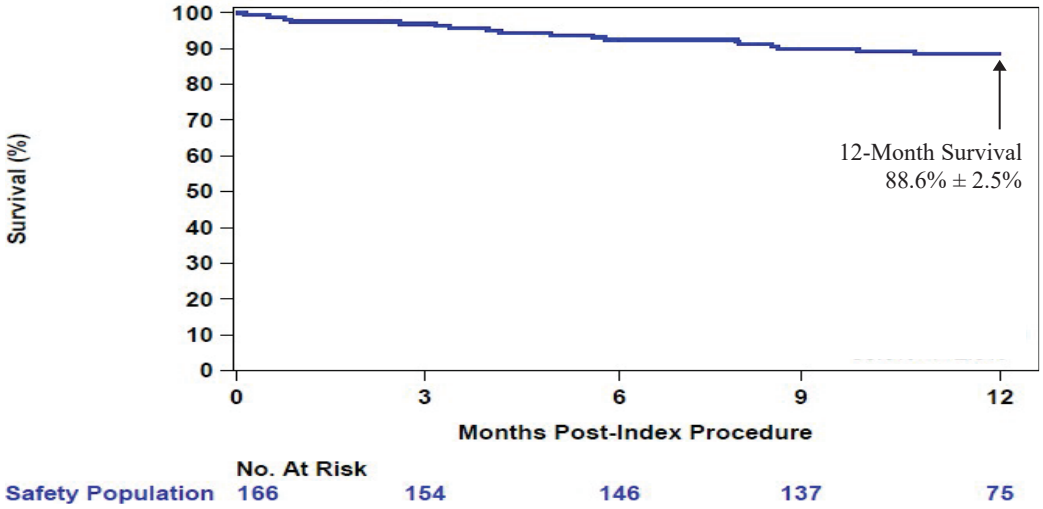
Table 15. Summary of Non-Serious Adverse Events Related to the Procedure or Device

Adverse Event	Events	Subject % (n/N)	CEC Assessment	
			Device Related	Procedure Related
Abnormal Labs (E.G. Cpk, Creatinine, Troponin)	1	0.6% (1/166)	0	1
Arrhythmia New	4	2.4% (4/166)	1	4
Chest Pain/Angina (Cardiac)	2	1.2% (2/166)	0	2
Heart Failure	1	0.6% (1/166)	0	1
Hypotension	1	0.6% (1/166)	0	1
Hypoxia	1	0.6% (1/166)	0	1
Pain (Non-Cardiac)	1	0.6% (1/166)	0	1
Pericarditis	2	1.2% (2/166)	0	2
Vascular Access Site Complications	2	1.2% (2/166)	0	2
Vascular Bleeding/Local Hematomas/Ecchymosis	2	1.2% (2/166)	0	2
Other	2	1.2% (2/166)	1	2
Left Bundle Branch Block	1	0.6% (1/166)	1	1
Urinary Retention	1	0.6% (1/166)	0	1
Total	**19**	**10.2% (17/166)**	**2**	**19**

c. Mortality

As of the database cut-off date, there were 18 subject deaths (18/166, 10.8%) in the CIN population. In addition, 5 patients (3.0%) underwent cardiac transplant. The Kaplan Meier estimate of survival at 12 months based on the available data is 88.6%.

Figure 4: Kaplan Meier Estimate of Survival at 12 Months



The table below summarizes the adverse events that led to death. The primary cause of death was classified by the CEC as cardiovascular in all 18 subjects. Two (2) events leading to death were adjudicated as procedure related, and none (0) were adjudicated as device related. One subject (1/166, 0.6%) died within 7 days of the index procedure. Another subject had an adverse event within 7 days of the index procedure that led to death on day 15.

Table 16: Summary of Causes of Deaths

Adjudicated AE event leading to death	Days from procedure to Death	CEC adjudication	
		Procedure related	Device related
0 - 7 days			
Cardiac perforation	During staged procedure	Yes	No
8 – 30 days			
Ischemic leg, septic shock	15	Yes	No
Respiratory failure	23	No	No
Ventricular arrhythmia with significant deterioration	26	No	No
1 – 3 months			
Shock	78	No	No
3 – 6 months			
Unknown (sudden death)	95	No	No
Unknown (loss to follow-up)	102	No	No
Ventricular arrhythmia with significant deterioration	120	No	No
Unknown	126	No	No
Shock	150	No	No
Heart failure	170	No	No
Ventricular arrhythmia with significant deterioration	176	No	No
Heart failure	239	No	No
Heart failure	240	No	No
Ventricular arrhythmia with significant deterioration	256	No	No
Ventricular arrhythmia with significant deterioration	259	No	No
Cancer	297	No	No
Shock (after repeat VT ablation procedure)	324	No	No

2. Effectiveness Results

a. Primary Effectiveness Endpoint

The primary effectiveness endpoint was freedom from recurrent sustained MMVT at 6 months and a new or increased dose of Class I or III AAD at 6 months following the index ablation procedure, where sustained MMVT was defined as a continuous MMVT for >30 seconds, or MMVT requiring intervention for termination regardless of its duration.

The analysis of effectiveness was based on the 146 evaluable patients at the 6-month time point. Evaluable patients include subjects who missed the 6-month visit but completed 12-month visit with ICD interrogation or experienced a primary effectiveness endpoint failure through 6 months.

A total of 85 of 146 subjects (58.2%) were free from a primary effectiveness endpoint event. The lower bound of the 95% one-sided confidence interval is 51.1% and greater than the predetermined performance goal, and the primary effectiveness endpoint is met.

Primary Effectiveness Endpoint Analysis (EFF Population*)

	Primary Effectiveness Endpoint		
Population	**Number of Subjects**	**95% One-Sided Confidence Interval Lower Bound**	**Performance Goal**
Effectiveness Population*	58.2% (85/146)	51.1%	> 40.2%

*The analysis population for the primary effectiveness endpoint includes treated subjects who have completed a 6- or 12-Month visit with ICD interrogation or experienced a primary effectiveness endpoint failure

Most subjects were free from repeat ablation through 6 months (139/146, 95.2%). Table 17 summarizes the specific primary effectiveness endpoint failure modes.

Table 17. Primary Effectiveness Endpoint Failure Modes (EFF Population*)

Endpoint Failure Mode	**Number of Subjects**
Repeat Ablation	4.8% (7/146)
Recurrent Sustained MMVT	19.9% (29/146)
New or Increased Class I/III AAD	30.8% (45/146)

*The analysis population for the primary effectiveness endpoint includes treated subjects who have completed a 6- or 12-Month visit with ICD interrogation or experienced a primary effectiveness endpoint failure

Sensitivity analysis

Of 165 treated subjects (TRT population), 19 had unknown 6-month rhythm status due to study exit, lost to follow-up, or did not complete a 6-month or 12-month visit with ICD interrogation, and did not experience a primary effectiveness endpoint failure. In the worst-case analysis, subjects with missing primary effectiveness endpoint data were treated as failures, and the primary effectiveness endpoint rate was 51.5% (85/165) with the 95% one-sided confidence interval lower bound of 44.8%. With the worst-case analysis, the lower bound of the primary endpoint remains higher than the predetermined performance goal of 40.2%.

Worst Case Analysis for the Primary Effectiveness Endpoint (TRT Population)

Primary Effectiveness Endpoint: Worst Case			
Population	**Number of Subjects**	**95% One-Sided Confidence Interval Lower Bound**	**Performance Goal**
Treated Subjects	51.5% (85/165)	44.8%	> 40.2%

b. Acute procedural success

In the LESS-VT NICM Cohort, the acute procedural endpoint is defined as

- For subjects with no inducible ventricular tachycardia (VT) at the beginning of the ablation procedure, the acute procedural endpoint was defined as elimination of all late potentials (greater than approximately 70% reduction in amplitude) in the scar and scar border; and
- For subjects with inducible VT at the beginning of the ablation procedure, the acute procedural endpoint was defined as elimination of all late potentials (greater than approximately 70% reduction in amplitude) in the scar and scar border and elimination of all inducible sustained monomorphic ventricular tachycardias (MMVTs) slower than 200 bpm (CL 300ms).

Overall, 92.7% (153/165) of treated subjects achieved acute procedure success as defined in the protocol.

c. Descriptive Effectiveness Endpoint Results

Table. 18 Protocol Specified Descriptive Effectiveness Endpoints

1. Changes in SF-12 Quality of Life (TRT Population)		
	NICM Cohort[1]	**Paired Change from Baseline[2]**
Aggregated Physical Health Score		
Baseline	39.46 ± 10.39 (163)	
Month 6	41.59 ± 10.10 (136)	1.9 ± 10.8 (135) [0.0, 3.7]
Aggregated Mental Health Score		
Baseline	45.43 ± 12.29 (163)	
Month 6	49.84 ± 10.56 (136)	3.7 ± 12.3 (135) [1.6, 5.8]
2. Changes in HADS Score at 6 Months (TRT Population)		
	NICM Cohort[1]	**Paired Change from Baseline[2]**
Anxiety Score		
Baseline	7.4 ± 4.6 (163)	
Month 6	5.2 ± 3.8 (136)	-2.1 ± 4.0 (135) [-2.7, -1.4]
Depression Score		

Baseline	5.6 ± 4.1 (163)	
Month 6	4.3 ± 3.8 (136)	-1.1 ± 3.9 (135) [-1.8, -0.4]

3. **Freedom from appropriate ICD shocks at 6 months (183 days) post index procedure, adjudicated by the ICD Event Review Committee**

   The Kaplan Meier estimate of freedom from appropriate ICD shock at 6 months was 92.0% ± 2.3%.

4. **Freedom from Spontaneous Recurrence of Any Sustained VT During the Follow-Up Period of 6 months**

   Of 139 treated subjects who have completed a 6- or 12-Month visit with ICD interrogation or experienced sustained VT recurrence, 109 (78.4%) subjects were free from recurrence of sustained VT through 6 months.

5. **Number of VT Recurrences During the Follow-Up Period Of 6 Months**

   From 30 TRT subjects with documented VT recurrence through 6 months, a total of 176 VT events were recorded in all subjects.

[1]Mean ± Standard Deviation (n)
[2]Mean ± Standard Deviation (n) [95% CI]

3. Subgroup Analyses

The following preoperative characteristics were evaluated for potential association with outcomes: gender, age (< 65 vs. ≥ 65 years), and race (Tables 19 – 20). The treatment-by-subgroup interaction was statistically significant at the alpha = 0.15 level for age in both primary safety and effectiveness analyses. Elderly patients were more likely to experience acute procedural complications and recurrence of MMVT than patients younger than 65 years of age. Further analysis of the baseline characteristics and procedural parameters between the two age groups showed that elderly subjects (age ≥ 65 years) on average had more co-morbidities (coronary artery disease, diastolic dysfunction, heart failure, hyperlipidemia, hypertension, and valvular heart disease), as well as lower mean left ventricular ejection fraction (32.7% ± 10% vs. 42.4% ± 13.4%). In terms of procedural parameters, the age ≥ 65 years group had higher number of MMVTs during procedure (2.9 ± 2.3 vs. 2.2 ± 2.3) with a higher proportion of subjects receiving cardioversion (75.7% vs. 59.2%) and hemodynamic support (2.7% vs. 0.0%).

Table 19. Primary Safety Endpoint: Subgroup Analysis (SAF Population)

		Primary Safety Endpoint	
	Subjects % (n/N)	**Difference [95% CI][1]**	**P-value[2]**
Females	14.8% (4/27)	-1.73% [-13.09%, 16.70%]	1.0000[3]
Males	16.5% (23/139)		
Age < 65 Years	12.0% (11/92)	-9.67% [-21.50%, 1.69%]	0.0935[2]

Age ≥ 65 Years	21.6% (16/74)		
Race Subgroup: White	18.8% (24/128)	14.58% [-2.51%, 22.95%]	0.1289[3]
Race Subgroup: Races other than White	4.2% (1/24)		

[1] By Newcombe score confidence interval
[2] By Chi-Square Test
[3] By Fisher Exact Test

Table 20. Primary Effectiveness Endpoint: Subgroup Analysis (EFF Population)

		Primary Effectiveness Endpoint	
	Subjects % (n/N)	**Difference [95% CI][1]**	**P-value[2]**
Females	14.8% (4/27)	-1.01% [-12.32%, 17.38%]	1.0000[3]
Males	15.8% (22/139)		
Age < 65 Years	65.1% (54/83)	15.83% [-0.26%, 31.04%]	0.0544[2]
Age ≥ 65 Years	49.2% (31/63)		
Race Subgroup: White	58.0% (65/112)	-6.96% [-26.22%, 16.44%]	0.5596[3]
Race Subgroup: Races other than White	65.0% (13/20)		

[1] By Newcombe score confidence interval
[2] By Chi-Square Test
[3] By Fisher Exact Test

The study was not powered for subgroup analyses, and these results should be considered to be exploratory.

Additional analyses

Post-hoc stepwise logistic regression analyses were used to evaluate the association between a wide range of clinically relevant variables (including primary NICM subtype) and procedure-related SAEs through 30 days and the primary effectiveness endpoint. Variables with a P-value of <0.15 in univariable analyses were included in the multivariable models.

Multivariable logistic regression analyses revealed that none of the primary NICM subtypes displayed a significant effect on the outcome of procedure-related SAEs through 30 days post index procedure. The model revealed a potential association between presence of New York Heart Association (NYHA) Class III heart failure and procedure-related SAEs through 30 days (odds ratio 3.42).

The multivariable logistic regression analysis of freedom from primary effectiveness endpoint events (including MMVT recurrence) also included primary NICM subtypes. Multivariable logistic regression analyses revealed that none of the primary NICM subtypes displayed a significant effect on the outcome

of freedom from primary effectiveness endpoint events. The model revealed a potential correlation with medical history of diastolic dysfunction (odds ratio 2.19).

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

E. 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 92 investigators of which none were full-time or part-time employees of the sponsor and 3 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: none
- Significant payment of other sorts: 3
- Proprietary interest in the product tested held by the investigator: none
- Significant equity interest held by investigator in sponsor of covered study: none

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.

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

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The benefits of the device are based on data collected in the clinical study conducted to support PMA approval as described above. The effectiveness results of the LESS-VT study support that the FlexAbility™ Ablation Catheter, Sensor Enabled™ is effective for treatment of recurrent, drug-refractory, sustained monomorphic ventricular tachycardia in patients with non-ischemic structural heart disease.

The LESS-VT study met its primary effectiveness endpoint for the NICM Cohort. The proportion of subjects with primary effectiveness endpoint success, defined as freedom from recurrence of sustained MMVT or repeat ablation at 6 months without any escalation in antiarrhythmic drug (AAD) therapy, was 58.2%. The 95% one-sided confidence interval lower bound of 51.1% was higher than the predetermined performance goal of 40.2%, thereby passing the endpoint.

The goal of VT treatment is to eliminate VT circuit and prevent recurrence of sustained episodes, and freedom from any sustained MMVT is a well accepted objective measure of clinical benefit of VT ablation. Freedom from VT recurrence was 80.1% at 6 months following ablation regardless of the AAD therapy, and the outcome is clinically meaningful.

The following limitations of the pivotal study resulted in uncertainties in the treatment benefits:

- The pivotal study has a non-randomized single arm study design. Without including an active control arm, it is uncertain from the study results how catheter ablation using the subject catheter compares with other therapeutic options. Nontheless, currently there isn't an approved device that's indicated to treat NICM VT patients.

- The primary analysis was based on treated patients with known effectiveness status at 6 months. There were some missing data due to early study exits or loss-to-follow-up. The favorable results of the worst case analysis support that the outcomes are robust for meeting the predetermined primary effectiveness endpoint success criteria.

- The results of subgroup analyses show elderly ($\geq$ 65 years) patients might not have gained the same degree of clinical benefit, in terms of freedom from recurrent sustained MMVT, from the study treatment when compared to their younger counterparts. The disparity may not be unexpected given that advancing

age has been linked to disease progression and severity of structural damage in some subtypes of NICM, including ARVC/D[2] and cardiac sarcoidosis[3].

Overall, the totality of evidence from the pivotal study supports that catheter ablation using the FlexAbility Ablation Catheter, SE is effective for the treatment of recurrent, drug-refractory, monomorphic VT in patients with non-ischemic cardiomyopathy.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies as well as data collected in a clinical study conducted to support PMA approval as described above. The results from the nonclinical laboratory and animal studies performed on the FlexAbility ablation catheter demonstrate that the device is suitable for endocardial and epicardial mapping and ablation.

The potential risks associated with the device for the intended use include percutaneous endocardial ablation-related complications such as cardiac tamponade/ perforation, valvular injury, cardiogenic shock, heart failure, thromboembolism, and procedure-related major bleeding complications. As nonischemic cardiomyopathy encompasses a heterogenous group of diseases with diverse arrhythmic substrates, VT ablation targets in this population also frequently include the right ventricle and epicardium. As the result, the risks for pericardial complications and epicardial access related major complications may be higher when compared to catheter ablation of ischemic VT.

The pivotal clinical study met the primary safety endpoint for the NICM cohort. A primary safety endpoint event was experienced by 16.3% (27/166) of subjects, and the 95% one-sided confidence interval upper bound of 21.7% was lower than the pre-defined performance goal of 26.9%.

There were no unanticipated adverse device effects. The overall rate of major complications is in line with those reported in similar premarket IDE studies of catheter ablation for the treatment of ischemic ventricular tachycardia. The observed severity, types, and rates of adverse events associated with using the study device to treat recurrent, drug-refractory, sustained monomorphic ventricular tachycardia in patietns with non-ischemic cardiomyopathy align with published literature. These results support the safety of the FlexAbility™ Ablation Catheter, Sensor Enabled™ for the intended use.

Results of subgroup analyses show elderly ≥ 65 years) might be more likely to experience acute procedural complications than younger patients. Advanced age is known as a risk factor for procedural major complications and a component of the PAINESD score described by Musser and colleagues to calculate the risk of periprocedural acute hemodynamic decompensation.[4] Elderly patients with non-ischemic VT are likely to have multiple co-morbidities and advanced cardiomyopathic disease, which may further account for the observed elevated risks of complications.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. For patients with non-ischemic structural heart disease and recurrent, drug-refractory, sustained monomorphic ventricular tachycardia, ablation treatment with the FlexAbility™ Ablation Catheter, Sensor Enabled™ resulted in freedom from recurrence of MMVT for the majority of patients.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The probable risks of the FlexAbility™ Ablation Catheter, Sensor Enabled™ for treating recurrent sustained monomorphic ventricular tachycarida in patients with non-ischemic structural heart disease include ablation procedure-related serious adverse events (such as cardiac perforation, cardiac tamponde, hemodynamic instability, heart failure, valvular injury, and procedure-related major bleeding complications). The safety data from the LESS-VT study (NICM cohort) demonstrates that the safety profile of the device remains clinically acceptable for the intended use.

Patient Perspectives

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

Based on a subgroup analysis, the benefit/risk balance for the subject device to treat NICM VT might be less favorable in elderly (age > 65) than in younger patients with higher observed incidences of major complications and arrhythmia recurrence in the 6 months following ablation. A Post-Approval Study is planned to ascertain the magnitude of the treatment effect and to assure that a consistent risk/benefit profile will be maintained with broad clinical use of the device.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of the FlexAbility™ Ablation Catheter, Sensor Enabled™ when used in accordance with the indications for use. Given all of the available data, it is reasonable to conclude that the benefits of the use of the device for the target population outweigh the risk of illness or injury when used as indicated in accordance with the labeling and Instructions for Use.

XIII. CDRH DECISION

CDRH issued an approval order on December 14, 2022. The final clinical conditions of approval cited in the approval order are described below.

LESS VT Continued Follow-up of IDE Non-Ischemic Cardiomyopathy Cohort: The study objective is to characterize the safety and effectiveness of the FlexAbility, SE Ablation Catheter for the treatment of monomorphic ventricular tachycardia in patients with non-ischemic structural heart disease through 12 months post-procedure. This study should be conducted per version H of the LESS VT protocol. The study will consist of all IDE patients who are currently enrolled and alive and will evaluate the protocol specified descriptive 12-month endpoints.

LESS VT NICM Post-Approval Study is a prospective, single-arm, open-label, multi-center study to evaluate the long-term effectiveness and safety of the FlexAbility, Sensor Enable Ablation Catheter for the treatment of ventricular tachycardia in patients with non-ischemic structural heart disease in the post-market space. A total of up to 150 patients will be enrolled at sites in the United States, and at least 50% will be ≥ 65 years of age. The primary objectives will be: (1) Estimate the 12-month freedom from ventricular tachycardia (VT) recurrence, death, and cardiac transplantation; (2) Estimate the rate of device- or procedure-related sertious adverse events through 12 months.

From the time of study protocol approval, the sponsor must meet the following timelines for the LESS VT NICM PAS:

- First subject enrolled within 6 months of post approval study protocol approval
- 20% of subjects enrolled within 18 months
- 50% of subjects enrolled within 30 months
- 100% of subjects enrolled within 48 months
- Submission of Final study report: 3 months from study completion (i.e., last subject, last follow-up date)

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.

XV. REFERENCES

[1] Vaseghi M, Hu TY, Tung R, et al. Outcomes of Catheter Ablation of Ventricular Tachycardia Based on Etiology in Nonischemic Heart Disease: An International Ventricular Tachycardia Ablation Center Collaborative Study. J Am Coll Cardiol EP. 2018, 4(9): 1141-1150

[2] Sen-Chowdhry, S., et al., Clinical and genetic characterization of families with arrhythmogenic right ventricular dysplasia/cardiomyopathy provides novel insights into patterns of disease expression. Circulation, 2007. 115(13): p. 1710-20.

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[4] Muser, D., et al., Outcomes with prophylactic use of percutaneous left ventricular assist devices in high-risk patients undergoing catheter ablation of scar-related ventricular tachycardia: A propensity-score matched analysis. Heart Rhythm, 2018. 15(10): p. 1500-1506.