SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: VR Leadless Pacing System; Implantable pacemaker pulse generator

Device Trade Name: Aveir™ VR Leadless System

- Aveir™ Leadless Pacemaker (Right Ventricular)
- Aveir™ Delivery System Catheter
- Aveir™ Link Module

Device Procode: PNJ

Applicant's Name and Address: Abbott Medical
15900 Valley View Court
Sylmar, CA 91342

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P150035

Date of FDA Notice of Approval: March 31, 2022

II. INDICATIONS FOR USE

The Aveir™ Leadless Pacemaker is indicated for patients with bradycardia and:

- Normal sinus rhythm with only rare episodes of A-V block or sinus arrest
- Chronic atrial fibrillation
- Severe physical disability

Rate-Modulated Pacing is indicated for patients with chronotropic incompetence, and for those who would benefit from increased stimulation rates concurrent with physical activity.

MR Conditional Aveir™ Leadless Pacemaker is conditionally safe for use in the MRI environment and according to the instructions in the Abbott MRI-Ready Leadless System Manual.

Aveir™ Delivery Catheter: The Aveir Delivery Catheter is intended to be used in the peripheral vasculature and the cardiovascular system to deliver and manipulate an LP. Delivery and manipulation include implanting an LP within the target chamber of the heart.

Aveir™ Link Module: The Aveir Link Module is intended to be used in conjunction with a Merlin™ PCS Programmer to interrogate and program an Aveir LP and to monitor LP function during an implant, retrieval, or follow-up procedure.

III. CONTRAINDICATIONS

The use of Aveir Leadless Pacemaker (LP) is contraindicated in these cases:

- Use of any pacemaker is contraindicated in patients with a co-implanted ICD because high-voltage shocks damage the pacemaker, and the pacemaker could reduce shock effectiveness.
- Single-chamber ventricular demand pacing is relatively contraindicated in patients who have demonstrated pacemaker syndrome, have retrograde VA conduction, or suffer a drop in arterial blood pressure with the onset of ventricular pacing.
- Programming of rate-responsive pacing is contraindicated in patients with intolerance of high sensor-driven rates.
- Use is contraindicated in patients with an implanted vena cava filter or mechanical tricuspid valve because of interference between these devices and the delivery system during implantation.
- Persons with known history of allergies to any of the components of this device may suffer an allergic reaction to this device. Prior to use on the patient, the patient should be counseled on the materials (listed in IFU Product Materials) contained in the device and a thorough history of allergies must be discussed.

For the MRI contraindications for patients implanted with Aveir Leadless Pacemaker, refer to the MRI Procedure Manual.

There are no contraindications for use of the Aveir Link Module.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Aveir Leadless System product Instructions for Use.

V. DEVICE DESCRIPTION

Aveir™ Leadless System:

The Aveir™ Leadless System contains the following components:

- **Aveir™ Leadless Pacemaker (LSP112V)**
- **Aveir™ Delivery System Catheter (LSCD111)**
- **Aveir™ Link Module (Model LSL02)**

Aveir Leadless Pacemaker (Model LSP112V)

The Aveir™ Leadless Pacemaker System provides bradycardia pacing as a pulse

generator with built-in battery and electrodes, for implantation in the right ventricle. The Aveir Leadless Pacemaker is intended to provide sensing of intrinsic cardiac signals and delivery of cardiac pacing therapy to the target population.

As a leadless device, it does not need a connector, pacing lead, or pulse generator pocket. A distal nonretractable helix affixes the LP to the endocardium. The tip electrode includes a single dose of dexamethasone sodium phosphate (DSP), intended to reduce inflammation. Three additional features on the outside of the LP nosecone are designed to provide secondary fixation securement. Sensing and pacing occur between a distal electrode near the helix and the external can of the LP. The LP's proximal end has a feature for docking to delivery and retrieval catheters, providing for repositioning and retrieval capability.

The LP communicates bi-directionally with the programmer system via electrical signals conducted between the implanted LP's electrodes and skin electrodes applied to the patient's chest and connected to the programmer system. Consequently, the LP transmits signals using circuits and electrodes already provided for pacing, with data encoded in pulses delivered during the refractory period of the ventricle.

The LP senses right ventricular blood temperature to provide an increase in pacing rate with increased metabolic demand.

Figure 1: Aveir Leadless Pacemaker

Aveir Delivery Catheter (Model LSCD111)

The Aveir Delivery Catheter includes a steerable delivery catheter, an integrated guiding catheter with a protective sleeve designed to protect an attached LP's fixation helix and electrode, and a valve bypass tool to dilate the 25Fr inner diameter Introducer sheath hemostasis valve and advance the system into the femoral vein.

Figure 2: Aveir Delivery Catheter

Aveir Link Module (Model LSL02)

The Aveir Link Module communicates with an implanted Aveir Leadless Pacemaker via conducted communication through the patient cable and skin electrodes. Safe, high frequency electrical pulses are sent between the LP and programmer system to program and interrogate the Aveir Leadless Pacemaker. The Link Module also uses the patient cable and skin electrodes to acquire a patient's ECG waveform. The Link Module is powered via USB port of the Merlin Patient Care System Model 3650.

Figure 3: Aveir Link Module

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for rate adaptive pacing. Each alternative has its own advantages and disadvantages. Alternative therapies include the use of commercially available conventional pacemaker systems or marketed leadless pacing systems. A patient should fully discuss alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Aveir Leadless System has not been marketed in the United States or any foreign country.

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.

The potential complications associated with the use of the Aveir Leadless Pacemaker System are the similar as with the use of single-chamber ventricular pacemakers with active fixation pacing leads including but not limited to:

- Cardiac perforation
- Cardiac tamponade
- Pericardial effusion
- Pericarditis
- Valve damage and/or regurgitation
- Heart failure
- Pneumothorax/hemothorax
- Cardiac arrhythmias
- Diaphragmatic/ phrenic nerve stimulation/ extra-cardiac stimulation
- Palpitations
- Hypotension
- Syncope
- Cerebrovascular accident
- Infection
- Hypersensitivity reaction to device materials, medications, or direct toxic effect of contrast media on kidney function
- Pacemaker syndrome
- Inability to interrogate or program the LP due to programmer or LP malfunction
- Intermittent or complete loss of pacing and/or sensing due to dislodgement or mechanical malfunction of the LP (non-battery related)
- Loss of capture or sensing due to embolization or fibrotic tissue response at the electrode
- Increased capture threshold
- Inappropriate sensor response
- Interruption of desired LP function due to electrical interference, either electromyogenic or electromagnetic
- Battery malfunction/ premature battery depletion
- Device-related complications:
    - Premature deployment
    - Device dislodgment/ embolization of foreign material
    - Helix distortion
- Death

As with any percutaneous catheterization procedure, potential complications include, but are not limited to:

- Vascular access complications, such as perforation, dissection, puncture, groin pain

- Bleeding or hematoma
- Thrombus formation
- Thromboembolism
- Air embolism
- Local and systemic infection
- Peripheral nerve damage
- General surgery risks and complications from comorbidities, such as hypotension, dyspnea, respiratory failure, syncope, pneumonia, hypertension, cardiac failure, reaction to sedation, renal failure, anemia, and death

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

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

i. Design Verification Tests

Design verification testing and material characterization was performed on the Aveir Leadless Pacemaker and accessories to ensure the design meets all required inputs per the product specification. The test results demonstrate that the Aveir Leadless Pacemaker and accessories meets all design requirements. The testing is summarized in **Table 1** below.

Device hardware verification utilized standard test suites, including tests such as automated functional test, functional interrogation test, visual/X-ray inspection, applicable EMI, electrical, and mechanical testing. The samples used in the testing passed applicable verification tests, confirming compliance with respective product requirements, and providing assurance that the devices will perform safely and effectively in their intended use.

The system functional verification and validation testing was conducted successfully for the Aveir Leadless Pacemaker with passing results and demonstrated that the system design input functionality requirements have been met. Clinical test flows followed in the validation testing were intended to mimic use of the system in clinically relevant scenarios where multiple system functionalities were tested. System functions were tested during scenarios that include: (1) during implant use, (2) out-of-clinic use, and (3) in-clinic follow-up use.

Table 1: Non-Clinical Bench Testing Results

Test	Test Description / Acceptance Criteria	Results
System Compatibility	Functional tests assessed the ability of the connections between various component of the Aveir Leadless System to properly	Pass

	communicate	
Sterilization for Aveir Leadless Pacemaker and Aveir Delivery Catheter	These tests assessed the ability of the device packaging system to maintain sterility of the package. The LP device and the delivery catheter is sterilized using 100% Ethylene oxide (EO). Sterilization validation established a minimum Sterility Assurance Level (SAL) of 10^{-6} as defined in EN 556-1, for routine sterilization of the pacemaker and catheter, per EN ISO 11135. The system is intended for single use only and labeled sterile.	Pass
Biocompatibility for Aveir Leadless Pacemaker and Aveir Delivery Catheter	The biological evaluation of the LP device and the delivery catheter was performed to demonstrate the biocompatibility of the products, or extracts of the products, resulting from contact of the device/component materials with the body as appropriate to the intended use of the device. Biological evaluation was conducted in accordance with ISO 10993-1: *Biological Evaluation of Medical Devices Part 1: Evaluation and Testing*. Results demonstrated that the leadless system is biologically safe for its intended use. See Section C below for details.	Pass
Packaging	The LP device and delivery catheter are packaged separately. The packaging is designed to protect the device from damage and prevent contamination during storage, shipping, handling and introduction to the sterile field. Qualification testing was successfully completed to verify that the packaging protects the system during transportation and storage	Pass
Shelf Life	• The LP device shelf life is based on a combination of battery capacity, package sterility, and steroid stability. Testing was performed to support a shelf-life labeling of 9 months. • The delivery catheter shelf-life testing was performed to support shelf-life labeling of 15 months.	Pass
Aveir Leadless Pacemaker		
Device Level Verification Testing intended to verify the specified physical attributes of the Aveir Leadless Pacemaker (LP). The design verification testing was performed according to the product specifications as well as to ISO14708-1, ISO 14708-2 and ISO 14117.		
Physical Dimensions	The test verified the following dimensions: • The device axial length shall not exceed 1.654 in (42mm) • The device diameter shall not exceed 0.262" (20Fr.) at any axial location along the rigid length of the LP. • The LP ring electrode should have exposed active surface area greater than 0.062 in^2 (40 mm^2). • LP tip and ring electrodes surfaces shall be separated axially by an insulated distance of at least 24 mm. • Tip electrode area: $2.0 \pm 0.1 mm^2$. • The LP weight shall be 3.0 gram maximum. • The volume shall be 1.4 cc maximum.	Pass

Mechanical Shock and Vibration	The test assessed the mechanical performance and safety of the LP to withstand mechanical shock loads and vibration imposed during handling, implantation, and intended use per standards EN 45502-2-1 and ISO 14708-2-1.	Pass
Pressure	To evaluate the device safety and functionality with by exposing to Pressure subject to 25 Cycles of low and 40 cycles of high-pressure exposure as specified by applicable clauses of ISO 14708-2.	Pass
Corrosion	Assessment of corrosion resistance of the blood and tissue contacting materials chosen for the LP.	Pass
Hermeticity Leak Test	To verify the hermeticity helium leak rate shall be equal or less than 1.8×10^{-9} atm-cc/sec Air Equivalent as specified per applicable clauses of MIL-STD-883.	Pass
Electromagnetic Compatibility (EMC)	To evaluate the device safety and functionality with regard to exposure from external EM field. The device shall meet the applicable requirements of ISO14708-2 and ISO 14117	Pass
EMI-EAS, RFID, Tag deactivators, Metal Detectors	To evaluate the device safety and functionality with regard to exposure from EAS and RFID. There shall be no irreversible damage or effect on device programmed parameter caused after the exposure to EAS Systems, EAS Tag Deactivators, RFID Systems and Metal Detector Systems	Pass
Safety-Exposure to Electrosurgery	To evaluate the device safety and functionality with regard to exposure to electrosurgery condition as specified by the applicable clauses of ISO 14117 standard	Pass
Safety- Exposure to External Defibrillation	To evaluate the device safety and functionality with regard to exposure to external defibrillation condition as specified by the applicable clauses of ISO 14117 standard	Pass
Safety- Ultrasound	To evaluate the device safety and functionality with regard to exposure to Ultrasound as specified by the applicable clauses of SOP 14708-1	Pass
Safety- Protection against device heat generation	To verify the outer surface of the device shall not be greater than 2˚C above the normal surrounding body temperature of 37˚ C when implanted in normal operating mode as specified per ISO14708-1 and EN 45502-2-1.	Pass
Safety – Irradiation	To verify device shall be electrically functional after exposure to irradiation levels of at least 7000 rads (70 Gy) per the applicable clauses of MIL-STD-883E.	Pass
MRI Compatibility Testing	This test assessed the compatibility of the device with MRI scanning. Additional MRI Information is provided in section B below.	Pass
Firmware	Firmware verification testing was conducted to ensure that the LP device firmware was tested to its specified requirements.	Pass

	Testing included unit testing, integration testing and system testing. Software verification testing was successfully completed and demonstrated that the LP device firmware meets its requirements.	
Software	Verification testing of all software requirements was conducted in to ensure that the Programmer software was tested to its specified requirements. Testing included unit testing, integration testing and system testing. Software verification testing demonstrated that the Programmer Software meets its requirements.	Pass
Component Level Testing intended to verify the specified component specifications are met. Safety testing, capacity testing and long-term performance testing and stability testing were performed. All the tests were successfully performed, and all pre-determined acceptance criteria were met.		
Button Tensile	The test assessed LP docking button to withstand a minimum axial tensile force of at least 18 lb-f without separation.	Pass
Button Fatigue	To verify the device docking button fatigue limit.	Pass
Helix Fatigue and Deformation	• To verify the device helix shall survive 400 million cycles without helix fracture or detachment from helix mount for bench top testing. • The fixation helix length shall have axial plastic deformation less than or equal to 20% of its original length (pinch point to distal end of the fixation helix) after an extension force of 0.5lbs is applied to the tip of the helix.	Pass
Feedthrough	• The samples insulation resistance shall be 10 giga-ohm minimum. • The samples shall not exhibit a leak rate greater than $1.5x10^{-9}$ atm-cc/sec air. • The samples shall not exhibit any signs of breakage, fracture or cracks with no failures occurring at 5.0 lbs.	
Hybrid	Substrate shall withstand the stress condition (thermal cycling and burn-in) and pass all substrate level electrical test	Pass
Battery	The battery shall meet to the UN Recommendations on the Transport of Dangerous Goods, Manual of Tests and Criteria.	Pass
	Accelerated discharge testing of battery capacity Beginning of Service to End Of Service at 37°C.	
	Self-discharge to estimate the loss in battery capacity due to non-coulombic reactions at 37°C.	
Aveir Delivery Catheter		

Torque	This test quantitatively assessed the catheter torque strength. The device shall withstand at least one full rotation prior to kinking, as this is within the anticipated use range of the system	Pass
Tensile	This test quantitatively assessed the tensile strength of the delivery tether based on the ISO 10555-1.	Pass
Flexibility/ Deflection	The test verified the device to have sufficient flexibility to enable navigation in more extreme anatomical configurations.	
Corrosion	Assessment of corrosion resistance of the blood and tissue contacting materials chosen for the LP.	Pass
Particulate Testing	This test assessed the particulate levels generated from the delivery components during simulated clinical use and meets USP <788>.	Pass
Aveir Link Module		
Physical Dimensions	• The Link Module shall have weight less than or equal to 0.7 kg (1.5 lbf). • The Link Module's length, width and height shall be less than or equal to 230mm, 155 mm and 40 mm respectively. • The measured cable length shall be between 0.9 m to 1.1 m.	Pass
Mechanical	• The tensile strength of the USB cable shall be at least 65 N • The USB cable shall survive at least 1000 flex cycles without demonstrating any of the electrical failure conditions • The Link Module AES key shall be un-readable and unmodifiable from an external device.	Pass
Security	• The Link Module shall use tamper resistant screws. • The Link Module shall include snap retainer features. • The Link Module shall include tamper evident labels.	Pass
Electrical	• The Link Module shall interrogate, program, and read information from the device when connected to a 4.5V, 5V, and 5.5V power supply. • The *Link Module* shall transmit at least one biphasic pulse with period 4 μs ±15%	Pass
Safety	• The Link Module shall pass applicable safety compliance tests per IEC 60601-1 Ed. 3.1. • The Link Module shall not exceed the radiated and conducted emissions limit requirements per IEC 60601-1-2. • The Link Module shall pass radiated electromagnetic fields per IEC 61000-4-3 and 61000-4-6. • The Link Module shall pass test requirements per IEC 60601-1-2	Pass
Cleaning	The test verifies the integrity of the label, marking, and mechanical enclosure after leaning the Link Module, as per the cleaning and disinfection instructions.	Pass

ii. Magnetic Resonance Imaging (MRI) Compatibility

MRI safety of the MR Conditional Aveir Leadless Pacemaker has been tested per the requirements in ISO/TS 10974. The test results demonstrate that the Aveir Leadless Pacemaker is conditionally safe for use in the MRI environments when used according to the instructions in the MRI Manual using the 1.5T and 3T MR scanner.

A patient with the Aveir Leadless Pacemaker can be safely scanned in a MR system under following conditions:

Table 2: Magnetic Resonance Imaging (MRI) Compatibility Testing Conditions

Parameters	**1.5 MRI Scan Parameter Setting**	**3T MRI Scan Parameters Setting**
Static Magnetic Field Strength and Type of Nuclei	1.5T/64MHz excitation frequency (hydrogen atom only)	3 Tesla/128 MHz excitation frequency (hydrogen atom only)
Magnet Type and Static Magnetic Field Orientation	Cylindrical-bore magnet, horizontal field orientation	Cylindrical-bore magnet, horizontal field orientation
Maximum Spatial Field Gradient	30 T/m (3000 Gauss/cm)	30 T/m (3000 Gauss/cm)
Maximum Gradient Slew Rate per axis	200 T/m/s	200 T/m/s
Scan Region / Patient Landmarking Criteria	Full body scans allowed. Any landmark is acceptable	Full body scans allowed. Any landmark is acceptable

iii. Biocompatibility

All biocompatibility testing was conducted in accordance with ISO 10993-1, Biological Evaluation of Medical Devices and Good Laboratory Practices Regulation (21 CFR 58). According to ISO 10993, the Aveir Leadless Pacemaker is classified as a long-term (>30 days) implantable device with circulating blood contact. The accessory Aveir Delivery Catheter packaged separately is classified as externally communicating with limited (<24 hours) circulating blood contact device. The required testing for the implant and delivery catheter was determined based on these classifications, in accordance with ISO 10993-1. A summary of the tests performed, and test results are presented in **Table 3** below.

Table 3: Biocompatibility Test and Results

Biological Endpoint and ISO Standard	Test Name/ Description	Leadless Pacemaker	Delivery Catheter	Results*
Cytotoxicity ISO 10993-5:2009	ISO Minimum Essential Medium Elution Assay	✓	✓	Pass Non-cytotoxic
Sensitization, Irritation or Intracutaneous Reactivity ISO 10993-10:2010	ISO Guinea Pig Maximization	✓	✓	Pass Non-sensitizer
	ISO 10993-10 Intracutaneous Reactivity	✓	✓	Pass Non-irritant
Systemic Toxicity ISO 10993-11:21017	ISO Acute Systemic Toxicity	✓	✓	Pass No evidence of systemic toxicity
	USP Material Mediated Rabbit Pyrogen	✓	✓	Pass Non-pyrogenic
Genotoxicity ISO 10993-3:2014	ISO Bacterial Reverse Mutation	✓	N/A	Pass Non-mutagenic
	ISO Mouse Lymphoma Assay	✓	N/A	Pass Non-genotoxic
Implantation ISO 10993-6:2016	90-day Chronic implantation in ovine	A	N/A	Pass Non-irritant
Hemolysis ISO 10993-4:2017	Hemolysis – Direct Contact and Extract	✓	✓	Pass Acceptable hemocompatibility profile
	Complement Activation Assay – SC5b-9	✓	✓	Pass Not a complement activator

	In vivo Thrombogenicity	A	✓	Pass Clinically acceptable response
Chemical Characterization ISO 10993-18:2020	GC-MS, LC-MS, and ICP-MS	✓	B	No leachables of toxicological concern
Toxicological Risk Assessment ISO 10993-17:2002	Toxicological Risk Assessment	✓	N/A	
Key: A: Biological endpoint was covered in the GLP animal studies B: indicates justification provided for not testing N/A: indicates testing was not required per ISO 10993-1 ✓: indicates testing was conducted * "Pass" denotes that the test results met the product specifications or acceptance criteria.				

For the Aveir Leadless Pacemaker, endpoints of sub-chronic systemic toxicity, implantation, and thrombogenicity were performed as part of the in vivo study (GLP animal studies) conducted to evaluate the safety and effectiveness of the device. The overall results of the GLP animal study indicate there was no signs of systemic toxicity or inflammation and acceptable thrombus formation post implantation of the Aveir Leadless Pacemaker and therefore, the device is considered clinically acceptable.

Additionally, the omission of the chronic systemic toxicity and carcinogenicity testing were supported by chemical characterization data. Toxicological risk assessment concluded that extractables and leachable chemicals from the Aveir Leadless Pacemaker were not present in quantities to present a systemic toxicity or carcinogenicity risk. Toxicological evaluation of the extractables detected concluded there was no toxicological concerns from the compounds detected.

Based on the acceptable results provided, the Aveir Leadless Pacemaker is biocompatible and considered safe for the devices intended use.

iv. Sterilization

The Aveir Leadless Pacemaker is an implant device and provided sterile for single use only. The Aveir Delivery Catheter is also, provided sterile and for single use only. Both devices are sterilized using ethylene oxide. The sterilization cycle was validated to meet the minimum Sterility Assurance Level (SAL) of 10-6. The Aveir Link Module is an external non-sterile medical device.

v. Shelf Life and Packaging

The shelf life of a combination product is defined not only based on the capability of a drug component in a specific container/closure system to remain within its

physical, chemical, microbiological, toxicological, protective and informational specifications, but also based on the device design characteristics and sterile barrier system materials in relation to the device being packaged, sterilized, shipped, and stored. The Aveir Leadless Pacemaker shelf life is labeled for 9-months and Aveir Delivery Catheter shelf life is labeled for 15-months. Both devices were validated to ensure that the device performance and package integrity is maintained for this shelf life.

Package performance and package stability are evaluated independently, built to the worst-case manufacturing sealing process settings (i.e. low and high settings), and exposed to the worst case environmental, distribution, and accelerated aging conditioning, to cover both evaluations.

B. Animal Studies (In Vivo)

The following GLP animal evaluations were conducted:

- 90-Day Chronic Evaluation of the Aveir VR System
    - This chronic GLP study utilized ovine as the animal model and was conducted to demonstrate the functional safety (dislodgement and perforation) and electrical performance (pacing, sensing) of the Aveir VR System over 90 days. A total of 9 sheep were implanted and accounted for in this study.
    - There were no dislodgments or embolization of the Aveir VR LP during the study. There was no presence of microthromboemboli in the lungs of any animal, no signs of rupture or tears in the tricuspid valve leaflets or chordae tendineae, no LP device perforations, no damage to the vasculature (femoral vein and IVC) from the delivery procedure.
    - The three (3) implanting physicians rated the VR LP delivery catheter system using a Likert scale of 1-4, with 1=poor/unacceptable and 4=very good & acceptable. The majority of the scores were “4” across all parameters assessed.
- Chronic Side-by-Side Functionality Evaluation of the Aveir VR LP
    - This chronic GLP study utilized ovine as the animal model and was performed to evaluate the side-by-side functionality (i.e., potential anatomical damage; performance of pacing, sensing and telemetry functions) of an active VR LP implanted next to an inactive VR LP in the ovine right ventricle. A total of 4 sheep were implanted simultaneously with an active VR LP and a functional but deactivated VR LP for a period of 24 days.
    - As assessed by the attending veterinarian and study pathologist, chronic implantation of two LPs in the RV were well tolerated by the ovine and there were no clinically significant findings. The valve leaflets and chordae tendineae moved freely and independently and there were no signs of rupture or tears. The study confirmed the active LP could communicate with the programmer, be programmed, and electrical performance data could be collected when co-implanted in the RV with

an inactive LP.

- 90-Day Chronic Evaluation of Aveir VR LP with Various Steroid Doses
  - This chronic GLP study utilized ovine as the animal model and was conducted to evaluate different concentrations (70%, 100%, 130%) of glucocorticosteroid Dexamethasone Sodium Phosphate (DSP) in the monolithic controlled release device (MCRD) located in the distal tip of the Aveir VR LP through 90 days. A total of 27 ovine were randomly assigned to 3 steroid dose cohorts of 9 animals each.
  - The results showed that devices with approximately 70%, 100%, and 130% of target DSP doses have satisfactory chronic pacing performance through 90 days of implantation in an ovine model. The cumulative percent of DSP released was 74%, 91% and 94% respectively for the 70%, 100% and 130% DSP doses at 90 days.
- 182-Day Chronic Evaluation of the Aveir VR LP Retrieval
  - This chronic GLP study was conducted to demonstrate the safety and performance of retrievability of VR LP at least 182-day post-implant. A total of 9 sheep underwent the retrieval procedure.
  - At necropsy pericardial fluid appeared normal, mechanical damage to the cardiac chambers was not evident, and all implant sites were intact and easily identified.
  - There were no tricuspid leaflet tears, endocardial/myocardial tears, or ruptured chordae in any animal as determined by the board-certified veterinary pathologist at necropsy. All lung findings in all animals were acceptable. Physicians evaluated the safety and performance of the Aveir Retrieval Catheter and exceeds the acceptance criteria. All LPs were retrieved successfully.
  - Three (3) cardiologists who retrieved the implanted VR LP (3 retrievals each) rated the VR LP retrieval catheter system using a Likert scale of 1-4, with 1=poor/unacceptable and 4=very good & acceptable. With one exception, all tasks received a score of "4" from the cardiologists; a single task regarding the labeling received a score of "3."
- Acute Evaluation of the Aveir VR System
  - This acute GLP study was conducted to evaluate the functional safety and usability of the Aveir VR System devices consisting of the Aveir LP with the Loading Tool, Link Module, Programmer Software, Aveir Delivery Catheter, Aveir Retrieval Catheter and Aveir Introducer (sheath and dilator).
  - The implant handling and safety of the Aveir Delivery Catheter in conjunction with the use of VR LP exceeded the acceptance criteria. There were no observed use errors that could potentially lead to serious patient harm. The acute studies demonstrated that the delivery system provide safe and effective deployment of the VR LP within the right ventricle of the heart.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The Leadless II study was conducted under an Investigational Device Exemption (IDE) study (G131038). Phase 1 of this IDE study evaluated the safety and effectiveness of the Nanostim Leadless Pacemaker in a population indicated for a VVI(R) pacemaker. Since the Nanostim Leadless Pacemaker was modified prior to market release and renamed the Aveir Leadless pacemaker, Phase 2 of this IDE study confirmed the safety and effectiveness of these modifications in the Aveir Leadless Pacemaker. Data from this clinical study were the basis for the PMA approval decision for the Aveir Leadless Pacemaker. A summary of the clinical study is presented below.

A. Study Design

The Leadless II study– Phase 1 (ClinicalTrials.gov identifier: NCT# 02030418) enrolled patients between February 2014 and June 2015 at 56 investigational sites in the U.S., Canada, and Australia. The study required a sample size of 300 subjects for the primary endpoint analysis. The Phase 1 database for this PMA includes a total of 526 subjects.

The Leadless II study– Phase 2 (ClinicalTrials.gov identifier: NCT# 04559945) enrolled patients between November 2020 and June 2021 at 43 investigational sites in the U.S., Canada, and Europe. The study required a sample size of 200 subjects for the confirmatory endpoint analysis. The Phase 2 database for this PMA includes a total of 200 subjects.

The study used an independent Data Safety Monitoring Board (DSMB) that was responsible for informing Abbott Medical of any safety or compliance issues and a Clinical Events Committee (CEC) that was responsible for adjudicating adverse events reported during the IDE study.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the Leadless II study was limited to patients who met all the following inclusion criteria:

i. Subject must have one of the clinical indications before device implant in adherence with Medicare, ACC/AHA/HRS/ESC single chamber pacing guidelines including:
   - Chronic and/or permanent atrial fibrillation with 2 or 3° AV or bifascicular bundle branch block (BBB block), including slow ventricular rates (with or without medication) associated with atrial fibrillation; or
   - Normal sinus rhythm with 2 or 3° AV or BBB block and a low level of physical activity or short expected lifespan (but at least one year); or
   - Sinus bradycardia with infrequent pauses or unexplained syncope with EP findings; and

ii. Subject is ≥18 years of age; and

iii. Subject has a life expectancy of at least one year; and

iv. Subject is not be enrolled in another clinical investigation; and
v. Subject is willing to comply with clinical investigation procedures and agrees to return for all required follow-up visits, tests, and exams; and
vi. Subject has been informed of the nature of the study, agrees to its provisions and has provided a signed written informed consent, approved by the IRB/EC; and
vii. Subject is not pregnant and does not plan to get pregnant during the course of the study

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

i. Subject has known pacemaker syndrome, has retrograde VA conduction, or suffers a drop in arterial blood pressure with the onset of ventricular pacing; or
ii. Subject is allergic or hypersensitive to < 1 mg of dexamethasone sodium phosphate (DSP);
iii. Subject has a mechanical tricuspid valve prosthesis; or
iv. Subject has a pre-existing endocardial pacing or defibrillation leads; or
v. Subject has current implantation of either conventional or subcutaneous implantable cardioverter defibrillator (ICD) or cardiac resynchronization therapy (CRT) device; or
vi. Subject has an implanted vena cava filter; or
vii. Subject has evidence of thrombosis in one of the veins used for access during the procedure; or
viii. *Subject had recent cardiovascular or peripheral vascular surgery within 30 days of enrollment; or
ix. **Subject has an implanted leadless cardiac pacemaker; or
x. ***Subject is implanted with an electrically-active implantable medical device with stimulation capabilities (such as neurological or cardiac stimulators).

*Recent cardiovascular or peripheral vascular surgery within 30 days of enrollment is defined as the following:

- Percutaneous valvular correction ≤30 days
- Femoral or abdominal vascular procedure involving incisional access ≤ 30 days
- Peripheral arterial endovascular procedure or surgery ≤ 30 days
- Cardiac surgery ≤ 72 hrs with ongoing complications, ongoing mediastinal drainage, or re-do sternotomy attributed to bleeding ≤ 30 days
- Tricuspid valve replacement or annuloplasty ≤ 30 days
- Any endovascular procedure with specified complication ≤ 30 days
    - Femoral access site-vascular complication including hematoma requiring transfusion, surgical intervention or prolongation of hospitalization, arterio-venous fistula, pseudoaneurysm or tear
    - New pericardial effusion more than trivial/mild, or requiring percutaneous/surgical drainage
- Acute deep venous thrombosis

**Except for subjects who are enrolled in the Leadless Observational Study and need their existing Nanostim LP replaced with the Aveir LP. These subjects may only be enrolled in this IDE during the CAP study of Phase 2.

***Does not apply to a medical device known to not be impacted by the Aveir Link Module telemetry signals or to a medical device than can be temporarily turned off during interrogation/programming of an Aveir LP.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at pre-discharge, 2 weeks, 6 weeks, 3 months, 6 months after implant and every 6 months thereafter until study completion. Subjects who underwent unsuccessful implantation were followed for a period of 30 days prior to withdrawal from the study.

Preoperatively, patients were evaluated in accordance with the inclusion/exclusion criteria. Postoperatively, information from chest x-rays, electrical testing, rate response, and device interrogation were evaluated. Adverse events and complications were recorded at all visits.

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

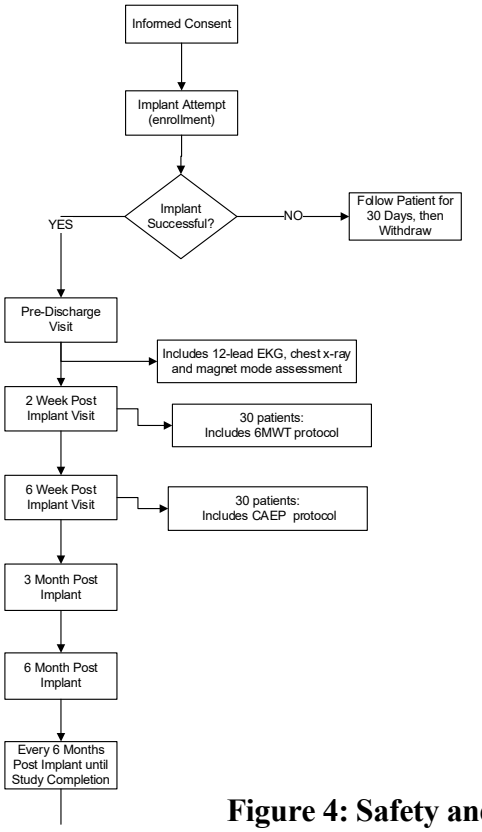


Figure 4: Safety and Effectiveness Timepoints

3. Clinical Endpoints

The Phase 2 confirmatory safety and effectiveness endpoints were identical to the Phase 1 primary safety and effectiveness endpoints, except for the timepoint of evaluation. The Phase 1 primary endpoints were evaluated at 6-months post-implant, while the Phase 2 confirmatory endpoints were evaluated at 6-weeks post-implant since it had been previously demonstrated that the overwhelming majority of complications occur within 30 days, most within 14 days.

Confirmatory Safety Endpoint

The confirmatory safety endpoint evaluated a 6-week complication-free rate (CFR) based on CEC adjudication of adverse events. A complication was defined as a device-or-procedure-related serious adverse event (SADE), including those that prevented initial implantation.

The confirmatory safety endpoint hypothesis was:

H_0: CFR ≤ 86% vs. H_1: CFR > 86%, where 86% was the performance goal.

The CFR was estimated as a binomial proportion and 97.5% lower confidence bound (LCB) of the CFR was calculated using the Clopper-Pearson exact method. The null hypothesis was to be rejected at the 2.5% significance level if the LCB exceeded the Performance Goal (PG) of 86%. The p-value from a one-sided exact test for the binomial proportion was calculated and compared to the 0.025 significance level.

Assuming an observed complication-free rate of 93.3%, 181 evaluable subjects were to provide 85% power to meet a performance goal of 86% and reject the null hypothesis.

Confirmatory Effectiveness Endpoint

The confirmatory effectiveness endpoint evaluated the 6-week composite success rate (Rate) based on pacing thresholds and R-wave amplitudes within the therapeutic range.

The Rate is the proportion of subjects who have met success criteria in the confirmatory effectiveness endpoint. Acceptable ranges for sensing and pacing are shown below.

Table 4: Acceptable ranges for sensing and pacing

Parameter	Acceptable test values
Pacing voltage	Pacing threshold ≤ 2.0 V at 0.4 ms
R Sensitivity	R-wave amplitude ≥ 5.0 mV or ≥ value at implant

Success Criteria: A subject was considered to have met the confirmatory effectiveness endpoint if the pacing threshold voltage is ≤ 2.0 V at 0.4 ms and the sensed R-wave amplitude is either ≥ 5.0 mV at the 6-week visit or ≥ the value at implant.

The confirmatory effectiveness endpoint hypothesis was:

H_0: Rate ≤ 85.0% vs. H_1: Rate > 85.0%, where 85% was the

performance goal.

The Rate was estimated as a binomial proportion and the 97.5% lower confidence bound (LCB) of the Rate was calculated using the Clopper-Pearson exact method. The null hypothesis was to be rejected at the 2.5% significance level if the LCB exceeded the Performance Goal (PG) of 85%. The p-value from a one-sided exact test for the binomial proportion was calculated and compared to the 0.025 significance level.

Assuming an observed success rate of 93.4%, 144 evaluable subjects were to provide 85% power to meet a performance goal of 85% and reject the null hypothesis.

Confirmatory Secondary Endpoint #1
The confirmatory secondary endpoint #1 evaluated an appropriate and proportional rate response during a Chronotropic Assessment Exercise Protocol (CAEP) exercise protocol. If both the Confirmatory Safety and Confirmatory Effectiveness Endpoints were met, then the following hypothesis was to be hierarchically evaluated:

Confirmatory Secondary CAEP Endpoint
H_0: Mean Slope is Not Equivalent to 100%
$| \text{Slope} - 100\% | \geq \delta$

H_1: Mean Slope is Equivalent to 100%
$| \text{Slope} - 100\% | < \delta$

Where, δ = equivalence margin, equal to 35%, and

$|\text{Slope} - 100\% |$ is the absolute value of the difference between the slope and 100%

The analysis of these exercise test data would provide an estimate of the slope of the normalized increase in sensor-indicated rate versus normalized CAEP workload for each subject. An analysis of these data would also estimate the 95% confidence interval for the mean slope across subjects, which has a pre-specified success criterion requiring that this confidence interval must fall between slopes of 65% and 135%.

Based on recently reported studies of marketed rate-responsive pacemakers the expected slope for similar devices, including the Aveir VR LP device, was estimated to be approximately 77%, with an associated standard deviation of 14%. It was estimated based on these data that a sample size of 8 subjects would be sufficient to demonstrate that the lower and upper 95% confidence bounds meet the success criterion, based on a normally distributed random variable. To ensure that a robust cross-section of subjects was evaluated, however, approximately 30 subjects would undergo this assessment.

Secondary Endpoint #2
The secondary endpoint #2 was added to the study design for Phase 2 in order to meet the Centers for Medicare & Medicaid Services (CMS) Coverage with Evidence Development (CED) requirement for Leadless Pacemakers. This secondary endpoint estimated the 2-year survival rate of patients implanted with the Nanostim LP using the Kaplan-Meier method of all-cause mortality. The survival probability estimate and upper and lower 95% confidence intervals were to be reported. The 2-year survival rate would be calculated based on patients implanted with the Nanostim LP since only Phase 1 data will have 2-year follow-up during the course of this IDE study. The 2-year survival rate of the Nanostim leadless pacemaker was to be compared to a performance goal of 80%. The performance goal was met if the lower 95% confidence interval of the 2-year survival rate exceeded 80%.

B. Accountability of PMA Cohort

Phase 2: The analyses of the confirmatory safety and effectiveness endpoints were performed on 200 enrolled subjects who meet enrollment criteria, provide signed informed consent, and who have an attempted implant of the Aveir Leadless Pacemaker. At the time of database lock in August 2021, all 200 subjects either completed a 6-week visit, withdrew or died before the 6-week visit, or crossed their 6-week visit window without completing a 6-week visit (i.e., missed visit).

An Aveir Leadless Pacemaker was successfully implanted in 196 of the 200 (98.0%) subjects enrolled. The four (4) subjects in whom implant attempts were unsuccessful were withdrawn from the study at 30 days. Of 196 subjects who underwent a successful implant, 191 subjects completed the 6-week visit. Of the five (5) subjects who did not complete a 6-week visit, one (1) died before the 6-week follow-up visit and four (4) subjects missed the 6-week follow-up visit at the time of database lock.

Phase 1: The analyses of the primary safety and effectiveness endpoints were performed on 300 enrolled subjects who meet enrollment criteria, provide signed informed consent, and who have an attempted implant of the Nanostim Leadless Pacemaker. At the time of database lock in June 2015, all 300 subjects either completed a 6-month visit, withdrew or died before the 6-month visit, or crossed their 6-month visit window without completing a 6-month visit (i.e., missed visit).

A Nanostim Leadless Pacemaker was successfully implanted in 289 of the 300 (96.3%) subjects enrolled. The eleven (11) subjects in whom implant attempts were unsuccessful were withdrawn from the study at 30 days. Of 289 subjects who underwent a successful implant, 271 subjects completed the 6-month visit. Of the 18 subjects who did not complete a 6-month visit, 12 died before the 6-month follow-up visit, four (4) withdrew prior to 6 months; and the remaining two (2) subjects did not compete the 6-month visit at the time of database lock.

Table 5: PMA Cohort Accountability Summary

Subject Disposition	Phase 2 - Aveir	Phase 1 - Nanostim
Subjects Enrolled with Attempted Implant	200	300
Subjects with Successful Implant	196 (98.0%)	289 (96.3%)
Subject Completing Endpoint Visit	191 (95.5%)	271 (90.3%)
Subject Death Prior to Endpoint Visit	1 (0.5%)	12 (4.4%)
Subject Withdrew Prior to Endpoint Visit	0 (0.0%)	4 (1.5%)
Subject Missed Endpoint Visit	4 (2.1%)	2 (0.7%)

C. Study Population Demographics and Baseline Parameters

The demographics and baseline characteristics of the study population are comparable to the overall population who meet the requirements of single-chamber ventricular pacing.

In Phase 2 of this study, the average age of patients in the Leadless II study was approximately 76 years and 63% were male, which is comparable to other pacemaker studies. The baseline characteristics for this study population was significant for hypertension, hyperlipidemia, diabetes and the majority of patients (57%) had a pacing indication for chronic atrial fibrillation and atrioventricular block. The demographics and baseline characteristics are similar between both Phase 1 and Phase 2 of this study.

Table 6 and **Table 7** summarize the demographic and baseline characteristics of subjects enrolled in Phase 1 and Phase 2 of the Leadless II study.

Table 6: Subject Demographics

Demographic Variable	Phase 2 - Aveir PMA Cohort (N=200)	Phase 1 - Nanostim PMA Cohort (N=300)
Age (years)		
Mean ± SD (n) (Min, Max)	75.6 ± 11.3 (200) (27.0, 95.0)	75.7 ± 11.6 (300) (30.3, 96.7)
Gender		
Male	62.5% (125/200)	64.3% (193/300)
Female	37.5% (75/200)	35.7% (107/300)
BMI (kg/m²)		
Mean ± SD (n) (Min, Max)	28.4 ± 5.9 (200) (16.9, 53.3)	29.2 ± 7.3 (300) (15.8, 60.3)
Race		

American Indian /Alaska Native	0.0% (0/200)	0.3% (1/300)
Asian	1.0% (2/200)	2.3% (7/300)
Black/African American	1.5% (3/200)	7.0% (21/300)
Native Hawaiian/Pacific Islander	0.0% (0/200)	0.0% (0/300)
White or Caucasian	67.0% (134/200)	89.7% (269/300)
Other (Not Specified)	0.5% (1/200)	0.7% (2/300)
Declined or Unable to Disclose Due to Local Regulation*	29.5% (59/200)	0.0% (0/300)
Unknown	0.5% (1/200)	0.0% (0/300)
Ethnicity		
Hispanic or Latino	2.5% (5/200)	4.3% (13/300)
Non-Hispanic or Latino	65.5% (131/200)	95.7% (287/300)
Other (Not Specified)	0% (0/200)	0.0% (0/300)
Declined or Unable to Disclose Due to Local Regulation*	29.5% (59/200)	0.0% (0/300)
Unknown	2.5% (5/200)	0.0% (0/300)

*Note: Race and ethnicity data were not collected at European centers due to local data privacy regulations.

Table 7: Subject Baseline Characteristics

Medical History Variable	**Phase 2 - Aveir PMA Cohort (N=200)**	**Phase 1 - Nanostim PMA Cohort (N=300)**
LV Ejection Fraction (%)		
Mean ± SD (n) (Min, Max)	58.8 ± 7.8 (161) (25.0, 76.0)	57.1 ± 8.2 (273) (25.0, 80.0)
Primary Pacemaker Indication		
Chronic AF with 2nd or 3rd degree AV block	52.5% (105/200)	57.0% (171/300)
Sinus rhythm with 2nd or 3rd degree AV block and a low level of physical activity or short expected lifespan	24.0% (48/200)	9.0% (27/300)
Sinus bradycardia with infrequent pauses or unexplained syncope with EP findings	23.5% (47/200)	34.0% (102/300)
Congestive Heart Failure	16.0% (32/200)	14.3% (43/300)
NYHA Class		
Class I	1.5% (3/200)	3.7% (11/300)
Class II	5.5% (11/200)	6.7% (20/300)
Class III	4.5% (9/200)	1.0% (3/300)
Class IV	0.5% (1/200)	0.0% (0/300)
Not Done	4.0% (8/200)	3.0% (9/300)
Hypertension		
Controlled With Medication(s)	69.0% (138/200)	77.0% (231/300)
Uncontrolled	2.5% (5/200)	7.0% (21/300)
Controlled Without Medication(s)	0.0% (0/200)	0.0% (0/300)

Diabetes		
Type I	1.0% (2/200)	0.7% (2/300)
Type II	27.0% (54/200)	26.7% (80/300)
Diabetes Current Status		
Controlled with Diet	4.0% (8/200)	4.7% (14/300)
Controlled with Medication(s)	24.0% (48/200)	22.0% (66/300)
Uncontrolled	0.0% (0/200)	0.7% (2/300)
Hyperlipidemia		
Controlled with Diet	4.0% (8/200)	11.0% (33/300)
Controlled with Medication(s)	50.5% (101/200)	56.3% (169/300)
Uncontrolled	2.0% (4/200)	2.0% (6/300)
Peripheral Vascular Disease	10.0% (20/200)	15.0% (45/300)
Coronary Artery Disease	25.5% (51/200)	40.3% (121/300)
Myocardial Infarction	10.0% (20/200)	14.0% (42/300)
Unstable Angina	6.5% (13/200)	3.3% (10/300)
Prior PTCA/Stents/Atherectomy	12.5% (25/200)	15.7% (47/300)
Prior CABG	9.0% (18/200)	16.0% (48/300)
Prior Ablation		
AV Nodal	0.0% (0/200)	1.7% (5/300)
AFib/Aflutter	12.0% (24/200)	7.0% (21/300)
VT	0.0% (0/200)	0.0% (0/300)
AT	1.5% (3/200)	0.0% (0/300)
Mini Maze, Thoracoscopy/LAA Ligation	0.0% (0/200)	0.3% (1/300)
SVT/AVNRT	0.5% (1/200)	1.3% (4/300)
Tricuspid Valve Disease		
Insufficiency/Prolapse/Regurgitation	25.5% (51/200)	20.0% (60/300)
Repair/Replacement	1.0% (2/200)	1.0% (3/300)
Stenosis	0.0% (0/200)	0.0% (0/300)
Arrhythmia History		
Ventricular (non-sustained)	4.0% (8/200)	5.0% (15/300)
Non-Ventricular/Supraventricular	71.0% (142/200)	77.0% (231/300)
Medications		
Antiarrhythmics (Class I)	3.5% (7/200)	2.3% (7/300)
Antiarrhythmics (Class III)	6.5% (13/200)	7.3% (22/300)
Anticoagulants	61.0% (122/200)	60.0% (180/300)
Antiplatelets	36.0% (72/200)	47.7% (143/300)
ACE Inhibitors	27.0% (54/200)	26.7% (80/300)
Angiotensin Receptor Blockers	26.0% (52/200)	20.7% (62/300)
Beta Blockers	38.0% (76/200)	40.0% (120/300)

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the enrolled population, excluding subjects that withdrew from the study or died prior to the endpoint visit without a complication. The key safety outcomes for this study are presented below in **Table 8**. Serious Adverse Device Effects (SADEs) are reported in **Table 9**.

In Phase 2, among the enrolled patient population of 200 subjects, the safety endpoint analysis was conducted on 198 evaluable subjects at 6-weeks post-implant. Of the 2 subjects excluded from the analysis, one (1) subject died due to non-cardiac cause without a complication as determined by the CEC, and one (1) subject withdrew due to an unsuccessful implant without an associated complication.

Eight (8) subjects experienced 9 complications (i.e., SADEs) as adjudicated by the CEC. The table in Figure 4 presents the estimated complication free rate (CFR) along with the 95% confidence interval. The estimated CFR is 96.0% with a 95% confidence interval (92.2%, 98.2%), the lower bound of which exceeds the Performance Goal (PG) of 86%. Hence, the null hypothesis is rejected at the 2.5% significance level, and it is concluded that the confirmatory safety endpoint is met.

Since Phase 2 is a confirmatory study, **Table 6** also shows the primary safety endpoint analysis results from Phase 1, which evaluated the Nanostim LP through 6-months post-implant. In Phase 1, the primary safety endpoint was met.

All complications in the primary analysis cohort for Phase 1 occurred within 30 days of implant; therefore, the 6-month CFR in Phase 1 can be compared to the 6-week CFR in Phase 2.

Table 8: Primary (Phase 1) and Confirmatory (Phase 2) Safety Endpoint Analysis

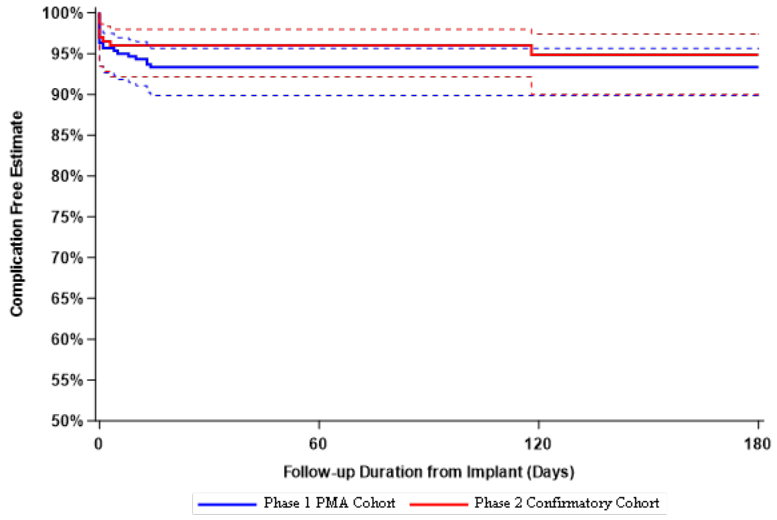
Analysis Population	Number of Subjects in Analysis	Number of Events	Number of Subjects with Events	% Subjects Meeting Success Criteria	95% Confidence Interval*	p-value** (PG=86%)	Endpoint met (Yes/No)?
Phase 2 Aveir: Enrolled	198	9	8	96.0%	[92.2%, 98.2%]	<0.001	Yes
Phase 1 Nanostim: Enrolled	300	22	20	93.3%	[89.9%, 95.9%]	<0.001	Yes
* 95% Confidence Interval using Clopper-Pearson Exact method. **From one-sided exact test for Binomial proportion. P-value is compared with the 0.025 significance							

level.

Figure 5 is a Kaplan-Meier analysis of CFR through 6 months by study phase among the enrolled Phase 1 Nanostim PMA cohort and the Phase 2 Aveir confirmatory cohort.

The overall complication free rates between the Phase 1 and Phase 2 cohorts are similar. Figure 4 also shows that an overwhelming majority of complications occurred within the first 30 days and is consistent with what has been demonstrated with other leadless pacemakers (FDA's Executive Summary on leadless pacemaker devices for the Advisory Panel, February 2016).

In addition, the 6-month CFR for the Phase 1 Nanostim PMA cohort (93.3%, with a standard error of 1.4% and 95% CI: 89.8%, 95.6%) and Phase 2 Aveir confirmatory cohort (94.9%, with a standard error of 1.8% and 95% CI: 90.0%, 97.4%) are similar.



Note: Dashed lines represent the 95% Confidence Interval.

Figure 5: Kaplan-Meier Analysis of Complication Free Rate through 6-Months – Cohort Comparison (Enrolled Population)

		w-up Duration from Implant (Days)				
Cohort	**Data Category**	**0**	**30**	**60**	**120**	**180**
Phase 2 Cohort	# At Risk	200	191	166	83	33
	# Events	6	8	8	9	9
	Event Rate (%)	3.0%	4.0%	4.0%	5.1%	5.1%
	Complication Free Rate (%)	97.0%	96.0%	96.0%	94.9%	94.9%
	Standard Error (%)	1.2%	1.4%	1.4%	1.8%	1.8%
	95% Confidence Interval	(93.4%, 98.6%)	(92.2%, 98.0%)	(92.2%, 98.0%)	(90.0%, 97.4%)	(90.0%, 97.4%)
Phase 1	# At Risk	300	278	267	264	262

Cohort	# Events	11	20	20	20	20
	Event Rate (%)	3.7%	6.7%	6.7%	6.7%	6.7%
	Complication Free Rate (%)	96.3%	93.3%	93.3%	93.3%	93.3%
	Standard Error (%)	1.1%	1.1%	1.4%	1.4%	1.4%
	95% Confidence Interval	(93.5%, 98.0%)	(89.8%, 95.6%)	(89.8%, 95.6%)	(89.8%, 95.6%)	(89.8%, 95.6%)

Note: For subjects with Aveir that did not experience an event (Complication), analysis is censored at their Termination/Death/Data Cutoff Date.

Adverse effects that occurred in the PMA clinical study:

A complication is defined as a device-or-procedure related serious adverse event, including any adverse event that prevents initial implantation. A serious adverse device effect (SADE) is any untoward medical occurrence that would happen in a subject or other person and related to the investigational device, comparator, or procedure, and meets the definition of serious, but is not unanticipated. Serious is defined as meeting at least one of the following criteria:

a) Led to death
b) Led to serious deterioration in the health of the subject that either resulted in:
    - Life-threatening illness or injury
    - Permanent impairment of a body structure or a body function
    - Inpatient or prolonged hospitalization
    - Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function
    - Chronic disease (a condition for EU centers only)
c) Led to fetal distress, fetal death or a congenital abnormality or birth defect

Table 9 summarizes the complications (SADEs) in Phase 1 and Phase 2 of this study. The overall SADE subject event rate (4.0%) for the Phase 2 enrollment population (n=200) through 6-weeks was lower than the SADE subject event rate (6.7%) for Phase 1 among the primary analysis cohort (n=300) through 6-months post-implant. The SADEs in the primary analysis cohort for Phase 1 all occurred within 30 days post-implant, therefore, the Phase 1 SADE rate through 6-months can be compared to the Phase 2 SADE rate through 6 weeks.

The most frequent complications in Phase 2 were three (3) cardiac tamponade events (1.5%) and three (3) premature deployment events (1.5%). The rates of cardiac perforation/ tamponade/ pericardial effusion in Phase 1 and Phase 2 are similar at 1.3% and 1.5%, respectively. The premature deployment events were not reported as adverse events during Phase 1.

Dislodgement events were completely absent in Phase 2, compared to a rate of 1.7% in Phase 1 which took place within 14 days post-implant. In addition, there was a reduction in all-cause serious access site complication events with Phase 2

reporting only one (1) serious access site bleeding event (0.5%) compared to Phase 1 reporting four (4) events (1.3%) that included AV fistula, pseudoaneurysm, and bleeding.

Table 9: Serious Adverse Device Effects

Event Description	Phase 2 - Aveir		Phase 1 – Nanostim	
	Number of Events	% of Subjects with Events (n/N)	Number of Events	% of Subjects with Events (n/N)
Cardiac Perforation/Tamponade	3	1.5% (3/200)	4	1.3% (4/300)
Other:				
Premature Deployment with Migration	2	1.0% (2/200)	0	0.0% (0/300)
Premature Deployment without Migration	1	0.5% (1/200)	0	0.0% (0/300)
Vascular Access Site Complication: Bleeding	1	0.5% (1/200)	2	0.7% (2/300)
Embolism	1	0.5% (1/200)	1	0.3% (1/300)
Thrombosis	1	0.5% (1/200)	0	0.0% (0/300)
Device Dislodgement	0	0.0% (0/200)	5	1.7% (5/300)
Threshold Elevation Resulting in Retrieval of LP	0	0.0% (0/200)	4	1.3% (4/300)
Vascular Access Site Complication: AV Fistula	0	0.0% (0/200)	1	0.3% (1/300)
Vascular Access Site Complication: Pseudoaneurysm	0	0.0% (0/200)	1	0.3% (1/300)
Asystole During Implant Procedure	0	0.0% (0/200)	1	0.3% (1/300)
Ventricular Tachycardia During Implant Procedure	0	0.0% (0/200)	1	0.3% (1/300)
Pericarditis	0	0.0% (0/200)	1	0.3% (1/300)
Weakness Secondary to Orthostatic Hypotension	0	0.0% (0/200)	1	0.3% (1/300)
Total	**9**	**4.0% (8*/200)**	**22**	**6.7% (20*/300)**

**Some patients experienced more than one event and therefore the number of patients is less than the number of events*

2. Effectiveness Results

The analysis of effectiveness was based on the successfully implanted population. A subject with a successful implant was defined as a subject who left the implant procedure with an implanted and functioning LP device. For subjects with missing 6-week pacing threshold or R-wave amplitude (not due to pacer dependence, complete heart block, or AV node/AV junctional ablation) data, the last observation carried forward (LOCF) was used in the analysis. For subjects that did not have R-wave amplitude measured due to pacer dependence or AV

nodal/AVJ ablation, success was determined from pacing threshold only. The key effectiveness outcomes for this study are presented below in **Table 10**.

In Phase 2, among the enrolled patient population of 200 subjects, the effectiveness endpoint analysis was conducted on 196 successfully implanted subjects. Of these 196 subjects, 171 subjects had measurable pacing thresholds and sensing amplitudes at the 6-week visit. There were an additional 17 subjects who only had pacing thresholds available. For these subjects, the R-wave was not measurable due to pacing dependence, AV nodal, or AV junctional ablation. Thus, pacing threshold alone determined whether the subject met success criteria. The remaining 8 subjects had their last observations carried forward.

Table 10 presents the composite success rate along with the 95% confidence interval. In Phase 2, the 6-week composite success rate is 95.9% with a 95% confidence interval (92.1%, 98.2%), the lower bound of which exceeds the Performance Goal (PG) of 85%. Hence, the null hypothesis is rejected at the 2.5% significance level, and it is concluded that the confirmatory effectiveness endpoint is met.

Comparatively, the 6-month composite success evaluated for the primary efficacy endpoint during Phase 1 was 93.4% with a 95% confidence interval of (89.9%, 96.0%). In Phase 1, the primary effectiveness endpoint was met.

Table 10: Primary (Phase 1) and Confirmatory (Phase 2) Effectiveness Endpoint Analysis

Analysis Population	**Number of Subjects in Analysis (N)**	**Number of Subjects Meeting Success Criteria (n)**	**Success Rate % (n/N)**	**95% Confidence Interval***	**p-value** (PG=85%)**	**Endpoint met (Yes/No)?**
Phase 2 Aveir: Successful Implant Population	196	188	95.9%	[92.1%, 98.2%]	<0.001	Yes
Phase 1 Nanostim: Successful Implant Population	289	270	93.4%	[89.9%, 96.0%]	<0.001	Yes

* 95% Confidence Interval using Clopper-Pearson Exact method.

**From one-sided exact test for Binomial proportion. P-value is compared with the 0.025 significance

level.

3. Subgroup Analyses

The following preoperative characteristics were evaluated for potential association with outcomes: gender, age and baseline comorbidities.

The confirmatory safety endpoint analysis across all subgroups was based on the safety evaluable populations, while the confirmatory effectiveness endpoint analysis was based on the successful implant population.

Table 11 presents the subgroup analysis results for the confirmatory safety and effectiveness endpoints by gender and **Table 12** presents the subgroup analysis results by age at time of enrollment. There were no statistically significant differences observed at the 0.05 significance levels between males and females and between the two age groups in the confirmatory safety and effectiveness endpoints. These results are consistent with the same subgroup analyses done in Phase 1.

Table 11: Subgroup Analysis by Gender

Variable	**Male %(n/N) [95% CI]**	**Female %(n/N) [95% CI]**	**P-Value[1]**
Confirmatory Safety Endpoint (6-week CFR)	96.8% (120/124) [91.9%, 99.1%]	94.6% (70/74) [86.7%, 98.5%]	0.4749
Confirmatory Effectiveness Endpoint (6-week Success Rate)	96.8% (120/124) [91.9%, 99.1%]	94.4% (68/72) [86.4%, 98.5%]	0.4685

[1] From Fisher's exact test.

Note: All p-values displayed are two-tailed and not from pre-specified hypothesis testing and are displayed for information only.

Table 12: Subgroup Analysis by Age

Variable	**Age<Median %(n/N) [95% CI]**	**Age≥Median %(n/N) [95% CI]**	**P-Value[1]**
Confirmatory Safety Endpoint (6-week CFR)	95.7% (90/94) [89.5%, 98.8%]	96.2% (100/104) [90.4%, 98.9%]	>0.9999
Confirmatory Effectiveness Endpoint (6-week Success Rate)	94.6% (88/93) [87.9%, 98.2%]	97.1% (100/103) [91.7%, 99.4%]	0.4808

[1] From Fisher's exact test.

Note: All p-values displayed are two-tailed and not from pre-specified hypothesis testing and are displayed for information only.

Table 13 represents the subgroup analyses for each of these pre-determined

baseline comorbidities. Confirmatory safety and effectiveness endpoints were similar across all subgroups. No statistically significant differences were observed at the 0.05 significance level among any of the selected baseline comorbidities.

Table 13: Subgroup Analysis by Comorbidities

Diabetes			
Variable	**History of Diabetes**	**No History of Diabetes**	**P-Value[1]**
Confirmatory Safety Endpoint (6-week CFR)	96.4% (53/55) [87.5%, 99.6%]	95.8% (137/143) [91.1%, 98.4%]	>0.9999
Confirmatory Effectiveness Endpoint (6-week Success Rate)	96.4% (53/55) [87.5%, 99.6%]	95.7% (135/141) [91.0%, 98.4%]	>0.9999
Non-Ventricular Arrhythmia History			
Variable	**History of Non-Ventricular Arrhythmias**	**No History of Non-Ventricular Arrhythmias**	**P-Value[1]**
Confirmatory Safety Endpoint (6-week CFR)	95.7% (135/141) [91.0%, 98.4%]	96.5% (55/57) [87.9%, 99.6%]	>0.9999
Confirmatory Effectiveness Endpoint (6-week Success Rate)	97.8% (135/138) [93.8%, 99.5%]	91.4% (53/58) [81.0%, 97.1%]	0.0511
Tricuspid Valve Disease			
Variable	**History of Tricuspid Valve Disease**	**No History of Tricuspid Valve Disease**	**P-Value[1]**
Confirmatory Safety Endpoint (6-week CFR)	100.0% (50/50) [92.9%, 100.0%]	94.6% (140/148) [89.6%, 97.6%]	0.2056
Confirmatory Effectiveness Endpoint (6-week Success Rate)	98.0% (50/51) [89.6%, 100.0%]	95.2% (138/145) [90.3%, 98.0%]	0.6829
History of Tobacco Use			
Variable	**History of Tobacco Use**	**No History of Tobacco Use**	**P-Value[1]**
Confirmatory Safety Endpoint (6-week CFR)	97.6% (81/83) [91.6%, 99.7%]	94.8% (109/115) [89.0%, 98.1%]	0.4720
Confirmatory Effectiveness Endpoint (6-week Success Rate)	95.2% (79/83) [88.1%, 98.7%]	96.5% (109/113) [91.2%, 99.0%]	0.7241

[1] From Fisher's exact test.

Note: All p-values displayed are two-tailed and not from pre-specified hypothesis testing and are displayed for information only.

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 160 investigators of which none were full-time or part-time employees of the sponsor and three (3) investigators had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

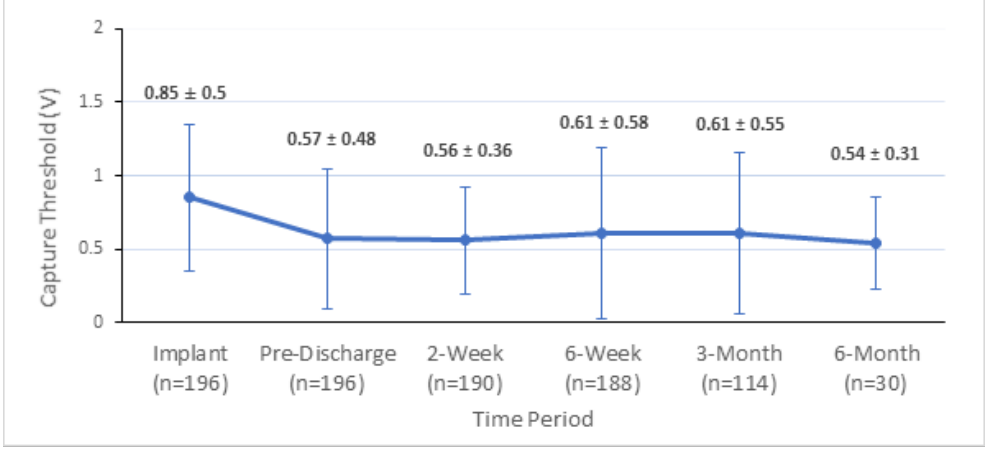
- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 2
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 1

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. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

A. Device Electrical Measurements – PMA Cohort

The mean capture threshold is below and the sensing amplitude is above the acceptable values identified in the IDE protocol for the effectiveness endpoint and are stable over time. **Figure 6** contains summaries of device electrical measurements from implant, pre-discharge and scheduled follow-up visits on 196 subjects with a successful implant from Phase 2 of this study.



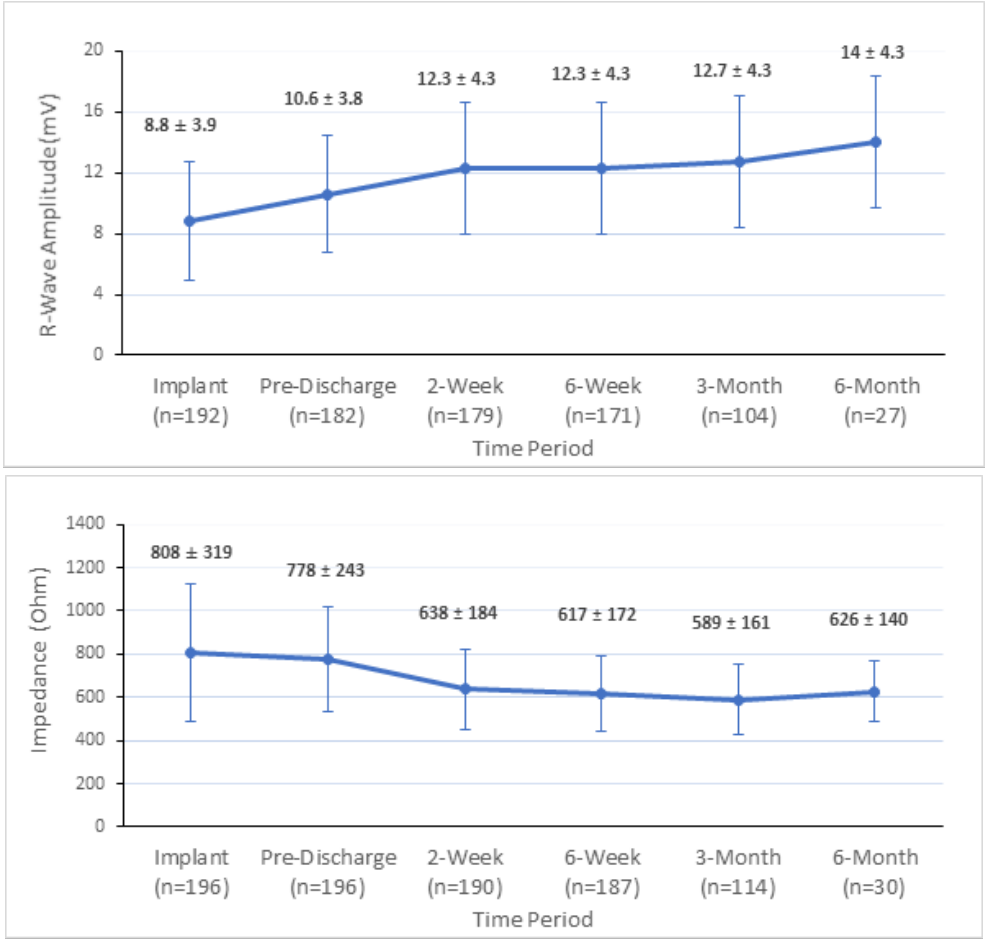


Figure 6: Aveir LP Device Electrical Measurements

B. Secondary Endpoint Results

i. Confirmatory Secondary Endpoint #1 – Rate Response during exercise

The temperature-based rate response feature in the Aveir LP was assessed to support the confirmatory secondary endpoint #1 by evaluating whether an appropriate and proportional rate response was achieved during a graded exercise testing.

A total of 23 subjects underwent a subject-specific sensor parameter optimization and the CAEP assessment. Among the 23 subjects, 18 completed at least stage 3 of the CAEP exercise protocol, thus achieving a workload of at least 3.6 metabolic equivalent of task (METs). One (1) subject who completed stage 3 did not follow the CAEP protocol and was not considered to be analyzable. Therefore, a total of 17 subjects were considered analyzable for the confirmatory secondary endpoint which exceeded the minimum sample size of eight (8) required.

Table 14 presents the mean slope of the normalized increase in sensor-indicated rate versus normalized CAEP workload for each subject among the analyzable

population of 0.93 ± 0.29 with a 95% confidence interval (0.78, 1.08), which fell within the 35% equivalence margin (0.65, 1.35) with statistical significance ($p<0.001$). Hence, the null hypothesis is rejected and the confirmatory secondary endpoint #1 was met.

Table 24: Confirmatory Secondary Endpoint #1 Analysis – Rate Response

Analysis Population	Slope Mean ± SD (n)	95% Confidence Interval (CI)	Equivalence Bounds	P-value*	Endpoint met (Yes/No)?
Phase 2 Aveir: Subject-specific optimized gain	0.93 ± 0.29 (17)	(0.78, 1.08)	0.65 < CI < 1.35	0.001	Yes
Phase 1 Nanostim: Default gain of 3	0.51 ± 0.18 (30)	(0.44, 0.58)	0.65 < CI < 1.35	0.001	No
**P-value calculated by two one-sided T- test (TOST)*					

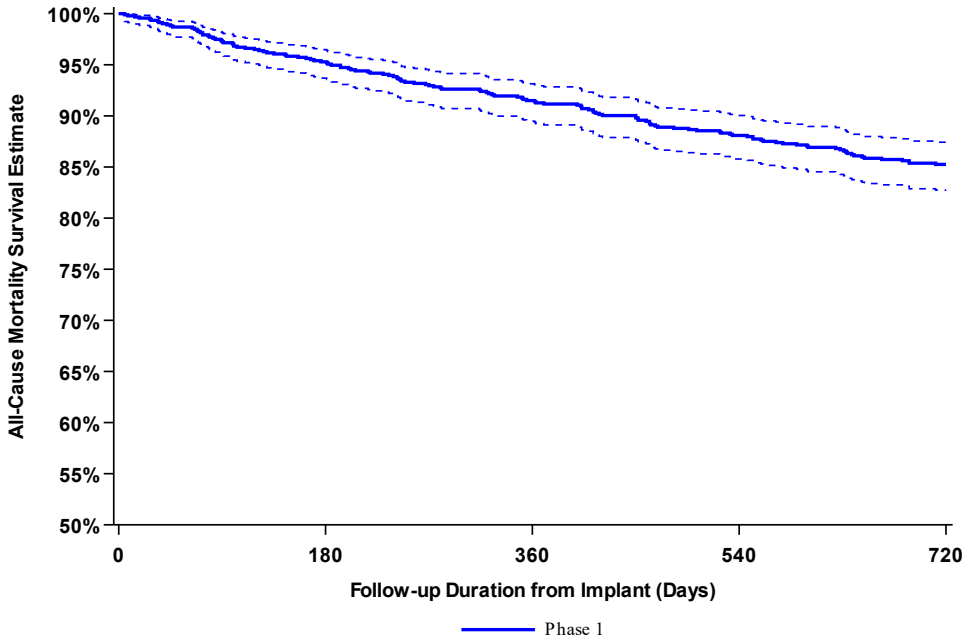
Phase 1 also evaluated the rate response feature for its secondary endpoint using the same criteria and analysis methods used for the confirmatory secondary endpoint during Phase 2; however, this endpoint was not met in Phase 1 since all subjects during this phase performed the CAEP with a sensor gain programmed to a default setting of 3. This standardized approach was considered a worst-case analysis because the sensor gain settings were generalized and not customized for each subject.

The Phase 2 approach of optimizing the gain settings during the 6-minute walk test (6MWT) was intended to reflect clinical use, where physicians would be expected to customize the sensor gain settings to each subject.

ii. **Secondary Endpoint #2 – 2-year Survival Rate**

The secondary endpoint #2 estimates the 2-year survival rate of patients successfully implanted with the Nanostim leadless pacemaker during Phase 1 only (n=917) using the Kaplan-Meier method of all-cause mortality.

Figure 7 shows the survival probability (event free rate) and 95% confidence intervals at 180 day intervals through 2 years.



Dashed lines represent the 95% confidence intervals

Figure 7: Kaplan-Meier Analysis of Survival through 2 Years for Phase-1
(Phase 1 – Nanostim Implanted Subjects)

	Follow-up Duration from Implant (Days)				
Data Category	**0**	**180**	**360**	**540**	**720**
# At Risk	917	863	816	762	703
# Events	0	43	77	107	131
Event Rate (%)	0.0%	4.7%	8.5%	11.9%	14.7%
Survival Rate (%)	100.0%	95.3%	91.5%	88.1%	85.3%
Standard Error (%)	0.0%	0.7%	0.9%	1.1%	1.2%
95% Confidence Interval	(100.0%, 100.0%)	(93.7%, 96.5%)	(89.5%, 93.1%)	(85.8%, 90.0%)	(82.7%, 87.4%)

Table 15 presents the survival probability estimate, with standard error, and upper and lower 95% confidence intervals at 2 years. Among the 917 successfully implanted subjects in the Leadless II Study-Phase 1, 85.3% was the estimated survival rate, with a standard error of 1.2%. The 95% confidence interval for the estimate is (82.7%, 87.4%), of which the lower bound exceeds the performance goal of 80% ($p<0.0001$). Hence, it is concluded that the secondary endpoint #2 was met.

Table 15: Secondary Endpoint #2 - Kapan Meier Analysis for 2-year Survival for Phase-1
(Phase 1 – Nanostim Implanted Subjects)

	Estimate (SE)[1]	**95% Confidence**	**P-Value[2]**	**Endpoint Met**

	(N=917)	Interval	(PG=80%)	
2-year Survival	85.3% (1.2%)	(82.7%, 87.4%)	< 0.0001	Yes

[1] Kaplan-Meier method will be used to estimate the event rate with Greenwood standard error.

[2] P-Value is based on Z test and to be compared with the 0.025 significance level.

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

However, a general issues panel meeting for the class of leadless pacemakers was held on February 18, 2016. The panel was asked to discuss and provide recommendations on the acute adverse event rates noted in available clinical trial information, post approval study design considerations, device labeling, and indications for use for leadless pacemakers. The panel recommended the following:

- Expectations of cardiac perforation rates should be consistent with rates of transvenous systems.
- No subgroups need to be excluded from receiving a leadless pacemaker.
- Implanting physicians should be adequately trained/informed about adverse events and patient selection.
- Acute and long-term events should be captured via a post approval study.
- Post approval study sample size is acceptable to be 1741 patients, with at least 500 followed for 9 years.
- Data from a total of 200 end-of-life cases, including device removal/extraction experience, where applicable, should be collected.
- Labeling should be device-specific and incorporate device experience, noting limitations of knowledge gaps, where appropriate.
- Indications for use of transvenous, single chamber pacemakers apply to this class of devices and AHA/ACC/HRS guidelines are already applicable.

These recommendations were considered in the course of this review as they applied to leadless pacemakers in general. The panel meeting transcript can be found at: http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/CirculatorySystemDevicesPanel/UCM489547.pdf.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The clinical results demonstrate a reasonable assurance of effectiveness for the Aveir VR Leadless System. In the clinical study, the confirmatory effectiveness endpoint was met as the 6-week composite success rate among 196 successfully implanted subjects was 95.9%, of which the one-sided 97.5% LCB, 92.1%, exceeded the performance goal of 85% with statistical significance ($p<0.0001$).

The rate response assessment in the clinical study demonstrated an appropriate and proportional rate response during graded exercise testing. The mean slope of the normalized increase in sensor-indicated rate versus normalized CAEP workload for each subject among 17 analyzable subjects was 0.93 ± 0.29 with a 95% confidence interval (0.78, 1.08), which fell within the pre-specified success criterion of a 35% equivalence margin (0.65, 1.35), with statistical significance ($p<0.001$).

B. Safety Conclusions

The risks of the Aveir VR Leadless System are based on data collected in nonclinical laboratory and animal studies as well as data collected in the Leadless II clinical study conducted to support PMA approval. Non-clinical testing performed, including biocompatibility, mechanical, electrical, simulated and MRI testing, demonstrates that the Aveir VR Leadless System is designed to be safe for its intended use. In the clinical study, the confirmatory safety endpoint was met as the 6-week complication free rate (CFR) among 200 enrolled subjects was 96.0%, of which the one sided 97.5% lower confidence bound (LCB), 92.2%, exceeded the performance goal of 86% with statistical significance ($p<0.0001$).

C. Benefit-Risk Determination

The Aveir VR system is indicated for use in patients with bradyarrhythmias and is intended to provide pacing therapy. The device has been shown as effective for achieving this purpose and benefit. The product and its therapies are well understood, and the labeling is consistent with the medical understanding of the product.

The use of the product itself and failure modes of the product are tracked for their health affect. Adverse effects of patient health, including effects with no product allegation, are summarized above. The serious adverse events for use with the product are less than the adverse events without use of the product. Based on this, the benefit of the product use outweighs the risk for this benefit risk assessment.

The Aveir VR system, and its indications for use and intended purpose, is similar to other products in the medical landscape.

The product performs with a positive benefit to risk assessment. The product also

performs in a manner that is consistent with other current medical treatments. Based on the individual and aggregate residual risks and product performance in context with other current medical therapies, there is a positive benefit / risk analysis with an acceptable overall residual risk for the Aveir VR system.

The probable benefits of the device are also based on data collected in a clinical studies conducted to support PMA approval as described above.

The probable risks of the device are also based on data collected in a clinical studies conducted to support PMA approval as described above.

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, given the available information above, the data support that for the safety and effectiveness of the Aveir Leadless Pacemaker system for single chamber pacing indications, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

The Leadless II Study - Phase 2 met the pre-specified performance goals for both the confirmatory safety (freedom from serious adverse device effects) and effectiveness (acceptable pacing and sensing) endpoints. These results showed that the Aveir Leadless Pacemaker System is safe and effective for single chamber pacing indications.

The totality of the evidence provided in this PMA demonstrates a reasonable assurance of the safety and effectiveness of the Aveir LP system and provides valid scientific evidence to conclude that the probable benefit to health from the use of the Aveir LP outweighs any probable risk or injury. The patients with Aveir Leadless Pacemaker will continue to be followed through 10 years to assess long-term safety and efficacy following approval of the PMA approval.

XIV. CDRH DECISION

CDRH issued an approval order on March 31, 2022. The final clinical conditions of approval cited in the approval order are described below.

> This study will be conducted as per protocol dated August 27, 2021, Version A. The purpose of this post-approval study (PAS) is to evaluate the long-term safety of the single-chamber Aveir™ Leadless Pacemaker device (VR LP) using real-

world evidence methods. A sample size of 2,100 patients is required to provide estimates of adverse events to a specific resolution with confidence intervals. All patients who had an implant of the Aveir VR LP device, met inclusion/exclusion criteria, and has linked to Medicare FFS claims will be included in the analysis of this endpoint. Acute and long-term safety of the Aveir™ VR LP will be evaluated in terms of 30-day and 10-year post implant complication-free rates. The frequency of PAS reports is every 6 months for the first two years and yearly thereafter.

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

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.