

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Heart valve, polymeric
Device Trade Name:	AUTUS Size-Adjustable Valve
Device Pro Code:	SJL
Applicant's Name and Address:	Edwards Lifesciences LLC One Edwards Way Irvine, CA 92614
Date(s) of Panel Recommendation:	None
Premarket Approval Application Number (PMA) Number:	P260007
Date of FDA Notice of Approval:	October 1, 2026
Breakthrough Device:	Granted breakthrough device status on August 25, 2023, because the device can provide for more effective treatment of an irreversibly debilitating disease; as well as represents a breakthrough technology, offers significant advantages over existing or approved or cleared alternatives, and is in the best interest of patients.

II. INDICATIONS FOR USE

The AUTUS valve is indicated for the management of pediatric patients weighing ≥ 10 kg who require surgical pulmonary valve replacement for dysfunctional native or surgically-repaired right ventricular outflow tract (RVOT), as determined by echocardiography to meet the following criteria: (1) severe pulmonary stenosis (i.e., right ventricle (RV) to pulmonary artery (PA) peak instantaneous gradient ≥ 60 mmHg); (2) $\geq$ moderate pulmonary regurgitation; or (3) $\geq$ moderate pulmonary stenosis (i.e., RV to PA peak instantaneous gradient ≥ 40 mmHg) and $\geq$ moderate pulmonary regurgitation.

III. CONTRAINDICATIONS

The AUTUS valve is contraindicated in patients who have active bacterial endocarditis, any other active infection in the heart or body, or have a known intolerance to anticoagulant or antiplatelet drugs (including aspirin).

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the AUTUS Size-Adjustable Valve labeling.

V. DEVICE DESCRIPTION

The AUTUS Size-Adjustable Valve (AUTUS valve) is a stented bileaflet synthetic pulmonary valve comprised of 0.1 mm expanded polytetrafluoroethylene (ePTFE) leaflets mounted on a balloon-expandable 316L stainless-steel frame. The frame is encased by a sleeve of ePTFE that extends below the level of the stent frame to allow for suture placement and fixation of the device to the tissue. The sleeve is made of ePTFE stretch graft material to allow for frame expansion when subject to radial forces (i.e., balloon dilation).

The valve is available in a single size of 12.7 mm internal diameter (ID), as shown in Figure 1. The balloon-expandable frame can be expanded in 2 mm increments pre- and post-implant within a functional diameter range from 12.7 mm ID to 22 mm ID, as shown in Table 1. As the frame expands radially, the coaptation height of the leaflets decreases.

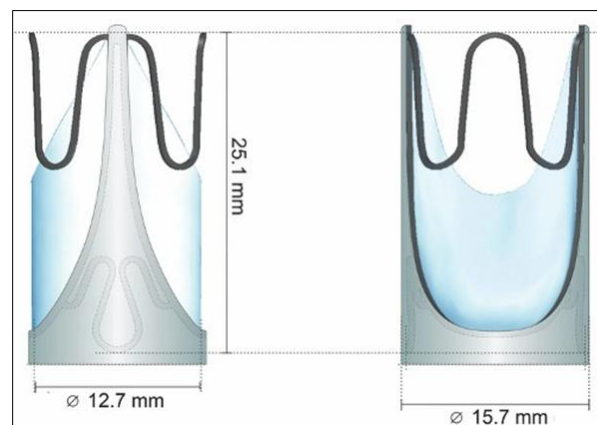


Figure 1: AUTUS Valve Nominal Dimensions

Table 1: AUTUS Valve – Key Dimensions (Functional Diameter Range)

Internal Diameter (mm)	Outer Diameter (mm)	Length (mm)
12.7	15.7	25.1
14	17	24.7
16	19	24.0
18	21	23.1
20	23	21.9
22	25	20.5

The valve is stored under dry packaging conditions and does not require rinsing prior to implantation.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of severe pulmonary stenosis, at least moderate pulmonary regurgitation, or at least moderate pulmonary stenosis plus at least moderate pulmonary regurgitation in patients with a native or surgically-repaired RVOT, including surgical placement of a RV-PA conduit or surgical or transcatheter placement of a prosthetic valve. 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 AUTUS Size-Adjustable Valve 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 use of the device.

- Allergic reaction to valve materials or contrast media
- Annulus damage including dissection, perforation, or tear
- Atelectasis
- Aortic damage including dissection, perforation, or tear
- Bleeding, including peri- or post-procedural, anticoagulant-related, pericardial tamponade, or hematoma
- Blood related issues, including anemia, coagulopathy, or hemolysis
- Blood pressure alteration, including hypo- or hypertension
- Cardiac arrest (asystole)
- Cardiac arrhythmias or conduction disturbances
- Cardiogenic shock
- Coronary artery compression
- Death
- Deep vein thrombosis (DVT)
- Disseminated intravascular coagulation (DIC)
- Embolism
- Esophageal tear/rupture
- Fever
- Frame fracture or distortion with or without obstruction or loss of structural integrity
- Hemolysis
- Hypoxemia
- Infection, including endocarditis, local (wound), or systemic

- Multi-system organ failure (MOF)
- Myocardial infarction
- Neurologic events, including cerebrovascular accident (CVA) or transient ischemic attack (TIA)
- Pain, swelling, or bruising at the catheterization site
- Perforation of a major blood vessel or a heart chamber
- Pericardial effusion
- Pleural effusion
- Pneumonia
- Pneumothorax
- Prosthetic insufficiency – regurgitation and/or stenosis
- Pulmonary artery damage, including dissection, perforation, or tear
- Pulmonary edema
- Radiation-induced erythema
- Reduced exercise tolerance
- Reduced leaflet mobility
- Renal failure (RF) or insufficiency, including acute RF and contrast induced nephropathy
- Respiratory failure
- Rupture of the RVOT
- Thrombocytopenia, including heparin-induced thrombocytopenia (HIT)
- Thromboembolism, including arterial, venous, peripheral, pulmonary, or central thromboembolism
- Transvalvular or valvular leaking
- Valve nonstructural dysfunction, including paravalvular leak, leaflet impingement, leaflet damage (caused by instruments or sutures), pannus, prosthesis mismatch (due to inappropriate sizing, distortion at implant)
- Valve structural dysfunction/deterioration (stenosis or regurgitation)
- Valvular thrombosis

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

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

Nonclinical laboratory studies were completed to evaluate the AUTUS valve that included biocompatibility and bench testing.

1. Biocompatibility

Biocompatibility assessments were completed on the AUTUS valve in accordance with ISO 10993-1:2018, *Biological Evaluation of Medical Devices Part 1: Evaluation and testing within a risk management process*, and the FDA Guidance for Industry and Food and Drug Administration Staff *Use of International Standard ISO*

10993-1, “Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process.” The required testing for each component was determined based on the nature and duration of body contact per ISO 10993-1:2018. Test articles consisted of the patient-contacting device components after exposure to all manufacturing processes, including sterilization. The biocompatibility test results for the AUTUS Size Adjustable Valve are summarized in Table 2.

Table 2: Summary of Biocompatibility Testing for AUTUS Valve

Biological Evaluation Endpoint	Biological Testing or Assessment Completed	Results
Cytotoxicity	MEM Elution Method (L-929)	Non-cytotoxic
Sensitization	Guinea Pig Maximization Sensitization Test	Non-sensitizing
Irritation	Intracutaneous Reactivity Test	Non-irritating
Acute Systemic Toxicity	Acute Systemic Toxicity Test in Mice	Non-toxic
Hemocompatibility	ASTM Hemolysis – Direct Contact and Extract Method	Non-hemolytic
	Complement Activation (SC5b-9)	Non-activator of the complement system
	In-vivo Thrombogenicity (GLP Animal Study)	Non-thrombogenic
Implantation	GLP Animal Study	No toxicity, no irritation
Genotoxicity	Chromosome Aberration Assay	Non-genotoxic
	AMES Test	
Materials Mediated Pyrogenicity	Materials Mediated Pyrogen Study in Rabbits	Non-pyrogenic
Subacute/Subchronic Toxicity	Chemical Characterization and Toxicological Risk Assessment	No unacceptable toxicity (including developmental toxicity), carcinogenic, or non-carcinogenic health risks were identified
Chronic Toxicity		
Reproductive/Developmental Toxicity		
Carcinogenicity		

2. Bench Testing

A summary of the bench testing results is provided in Table 3. All testing was conducted on devices representative of the final finished device. Test articles included valves with the minimum ID (12.7 mm) and valves with pre-test expansion to intermediate ID (16 mm) and maximum ID (22 mm).

Table 3: Summary of AUTUS Valve Bench Testing

Test Name	Test Purpose	Results
Frame Radial Strength	To evaluate the radial strength of the AUTUS valve	PASS At an applied force of 1.5 N, the permanent diameter reduction of the stent frame was 0.0 mm
Suture Retention Testing	To evaluate the suture retention strength of the AUTUS valve	PASS All samples tested had a suture retention strength peak force of ≥ 12.9 N.
Burst Pressure	To characterize the pressurized burst strength of the AUTUS valve	The burst pressure exceeds anticipated physiological right heart conditions.
Steady State Flow	To characterize the forward flow pressure drop and back flow leakage of the AUTUS valve	All valves demonstrated acceptable steady state flow hydrodynamics.
Pulsatile Hydrodynamic Performance	To verify the pulsatile-flow hydrodynamic performance of the AUTUS valve	PASS All valves met the prespecified valve functionality criteria for hydrodynamic performance testing.
Corrosion	To characterize corrosion susceptibility of the AUTUS valve in accordance with ASTM F 2129	All samples met the requirements of ASTM F2129.
Finite Element Analysis (FEA)	To establish a failure model for the 316L stainless steel expandable bileaflet valve frame, evaluate failure response of the frame, and perform a fatigue life analysis by applying prescribed cyclic loads	The FEA indicated that the maximum stress in the frame never reached the strength of the material and the fatigue stresses in the frame that are part of normal anticipated use are lower than the strength of the frame material (316L stainless steel).
Fatigue	To demonstrate fatigue life of the AUTUS valve after serial balloon expansion from 12.7 mm ID to 22 mm ID at 600 million cycles.	PASS No valve cracks or breaks occurred on any of the frames at the completion of the 600 million cycles.

Test Name	Test Purpose	Results
Accelerated Wear Testing	To evaluate the accelerated wear performance to 200 million cycles	PASS All samples met the functional and structural criteria. There were no observations of incomplete coaptation, fracture, excessive deformation, non-function of any individual component, other mechanical breakdown and/or wear.
Magnetic Resonance Imaging (MRI)	To ensure the compatibility of AUTUS valve for use with MRI.	The AUTUS valve is MR conditional and can be safely imaged under the conditions listed in device labeling.

B. Animal Studies

A total of 4 chronic animal studies (3 non-GLP and 1 GLP) were performed to evaluate the safety and feasibility of the AUTUS valve as a size-adjustable surgical pulmonary valve replacement device. Results from the 3 non-GLP animal studies demonstrated that the AUTUS valve can be implanted in the pulmonic position without complication and post-implant valve size adjustment can be performed via transcatheter balloon dilation repeatedly (up to 4 expansions evaluated) while maintaining valve function and not causing harm to surrounding tissue. The 20-week GLP study confirmed the favorable biological assessments from the previous animal studies and demonstrated device safety and functionality as a surgical pulmonary valve implant in an adolescent ovine model. Table 4 summarizes the chronic animal study results.

Table 4: Animal Studies

Study Duration	GLP/non-GLP	Animal Model and Sample Size
STUDY 1		
10-week Survival Study	Non-GLP	Juvenile Sheep (growing lamb model) N=7 animals
Results Summary: The AUTUS valve was successfully implanted in all seven animals, and all survived to term. In all animals, the AUTUS valve was serially balloon dilated up to 20 mm ID via 3 expansion procedures, without complications. Valve expansions were atraumatic, uniform, and symmetric, and there was no measurable elastic recoil of the frame after dilation. The valve exhibited preserved leaflet mobility and coaptation in all seven animals, with unidirectional pulmonary blood flow maintained across all expansion diameters. Six of the seven animals showed no evidence of valve regurgitation, and one animal had trivial to mild regurgitation. In all animals, necropsy and histopathology demonstrated healthy right ventricular myocardium, no inflammatory infiltrate, no clinically significant thrombus on the		

Study Duration	GLP/non-GLP	Animal Model and Sample Size
device or device-related distal thrombo-emboli. There was no damage to the native pulmonary artery wall integrity due to device expansion.		
STUDY 2		
20-week Survival Study	Non-GLP	Juvenile Sheep (growing lamb model) N=6 animals
Results Summary: The AUTUS valve was successfully implanted in all six animals, and all survived to term. In each animal the AUTUS valve was serially balloon dilated up to 20 mm ID via 3 expansion procedures, without complications. The valve exhibited preserved leaflet mobility and coaptation in all six animals, with unidirectional pulmonary blood flow maintained across all expansion diameters. In all animals, necropsy and histopathology demonstrated healthy right ventricular myocardium, no inflammatory infiltrate, no clinically significant thrombus on the device or device-related distal thrombo-emboli. Leaflet mineralization was evaluated by x-ray radiographs of all six whole explanted valves and quantitatively evaluated using inductively coupled plasma atomic emission spectroscopy (ICP). Negligible amounts of calcium and phosphorus were measured in all six AUTUS valve leaflet samples, and there was no evidence of stent fractures. There was no damage to the native pulmonary artery wall integrity due to device expansion.		
STUDY 3		
1-year Survival Study	Non-GLP	Juvenile Sheep (growing lamb model) N=2 animals
Results Summary: The AUTUS valve was successfully implanted in both animals, and both animals survived to term. In each animal the AUTUS valve was serially balloon dilated up to 22 mm ID via 4 expansion procedures, without complications. Necropsy and histopathological analysis demonstrated minimal tissue inflammation, healthy right ventricular muscle, and no evidence of device-related distal thromboemboli (including the lungs). In both study animals, the pulmonary artery wall exhibited only local wall compression, with no damage to the integrity of the vessel after chronic implantation and four transcatheter balloon expansions. The inflow and outflow surfaces of both explanted valves had minimal tissue ingrowth. The ePTFE leaflets had small foci of mineralization in the region of the leaflet free edge, remained functionally intact, thin, and pliable, with minimal surface irregularities and had no evidence of microfractures. There was no inflammatory cell infiltrate and no clinically relevant thrombus present in the two explanted valve specimens. Leaflet mineralization was evaluated by x-ray radiographs of both whole explanted valves and quantitatively evaluated using inductively coupled plasma atomic emission spectroscopy (ICP). Negligible amounts of calcium and phosphorus were measured in both 1-year AUTUS valve leaflet samples, and there was no evidence of stent fractures.		
STUDY 4		
20-week Survival Study	GLP	Adolescent Sheep model

Study Duration	GLP/non-GLP	Animal Model and Sample Size
		N=6 animals
Results Summary: The AUTUS valve was successfully implanted in all six animals, and all animals survived to term. The test valves were pre-expanded to 18 mm ID prior to implant. The valve exhibited preserved leaflet mobility and coaptation in all six animals, with unidirectional pulmonary blood flow maintained in all animals through the in-life portion of the study. At term, the peak transvalvular gradient was 23 ± 10 mmHg, with no evidence of regurgitation. In all animals, necropsy demonstrated healthy right ventricular myocardium, healthy pulmonary artery, no inflammatory infiltrate, no clinically significant thrombus on the device, and no evidence of device-related distal thrombo-emboli.		

C. Additional Studies

1. **Sterilization**

The AUTUS valve is sterilized with Ethylene Oxide. The sterilization process has been validated per ISO 11135:2014 to achieve a sterility assurance level (SAL) of 10^{-6} .

2. **Packaging and Shelf-Life Testing**

The AUTUS valve is packaged in dual polyethylene terephthalate glycol (PETG) thermoformed trays sealed with Tyvek lids. The sealed tray is then placed into a shelf carton/unit box. The shelf life for the AUTUS valve has been established at 6 months as demonstrated by packaging integrity and product functional testing on aged samples.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of surgical pulmonary valve replacement with the AUTUS Size-Adjustable Valve in the US under IDE #G210171. 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

The clinical study was a prospective, single-arm, multi-center study and included two phases: the Early Feasibility Study (EFS) and the pivotal study. The EFS enrolled 11 subjects between December 6, 2021, and December 13, 2023, at 3 US sites and the pivotal study enrolled 51 subjects between February 5, 2024, and February 17, 2026, at 12 US sites. Due to the limited size of the patient population, and because the same device and largely similar clinical protocols were used in the two phases, clinical data from the EFS and the pivotal study phases were pooled.

The study utilized an independent Data Monitoring Committee (DMC), Clinical Events Committee (CEC), Eligibility Screening Committee (ESC), Echocardiography Core Laboratory (ECL), and an Independent Medical Assessment of valve/stent frame integrity.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the clinical study was limited to patients who met the following inclusion criteria:

1. Age 18 months to 16 years.
2. Male or female.
3. Subject has a native or repaired right ventricular outflow tract.
4. Subject has been recommended for surgical pulmonary valve replacement by treating clinical team (cardiologist and cardiac surgeon).
5. Subject has at least one of the following echocardiographic findings:
 - a. Severe pulmonary stenosis (defined as RV to PA peak instantaneous gradient ≥ 60 mmHg);
 - b. Moderate or greater pulmonary regurgitation;
 - c. Moderate or greater pulmonary stenosis plus moderate or greater pulmonary regurgitation.
6. Subject's body size is suitable for implantation of a study device ranging from 12.7 to 22 mm (internal diameter).
7. Subject and parent/legal representative, where appropriate, are willing to provide informed written consent.
8. Subject and parent/legal representative, where appropriate, and treating physician agree that the subject will return for, and comply with, all required study assessments and follow-up visits.

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

1. Subject requires valve replacement in a non-pulmonary position.
2. Subject has a prosthetic valve at other valve position or will need a prosthetic valve at other valve position (i.e., anticipate additional valve replacements needed within 3 years).
3. Subject has pulmonary arterial hypertension (defined as mean PA pressure ≥ 25 mmHg).
4. Subject has pulmonary atresia and major aortopulmonary collaterals.
5. Subject has significant peripheral pulmonary artery stenosis.
6. Subject has an active infection requiring current systemic antibiotic therapy (if temporary illness, subject may be a candidate 4 weeks after discontinuation of antibiotics).
7. Subject has active endocarditis or a history of infective endocarditis.
8. Subject has renal insufficiency as determined by a serum creatinine (S-Cr) level ≥ 2.5 mg/dL within 60 days prior to the Screening Visit, or has end-stage renal disease.
9. Subject has leukopenia (defined as a white blood cell (WBC) count $< 3.5 \times 10^3/\mu\text{L}$)

10. Subject has acute or chronic anemia (defined as hemoglobin (Hgb) <10.0 g/dl or 6 mmol/L).
11. Subject has thrombocytopenia (defined as platelet count <50 x 10³/μL).
12. Subject has a known hypersensitivity to anticoagulants and antiplatelet drugs.
13. Subject has a known autoimmune disease or receives immunosuppressant and/or immunostimulant drugs that the Investigator or Eligibility Screening Committee (ESC) believes may negatively affect study outcomes.
14. Subject needs emergency cardiac or vascular surgery or intervention.
15. Positive pregnancy test prior to valve implant procedure in female subjects who have had their first menses.
16. Subject has, in the opinion of the Investigator, a life expectancy of less than 5 years.
17. Subject or parent/legal representative refuses blood transfusions.
18. Subject has medical, social or psychosocial factors that, in the opinion of the Investigator or ESC, could impact safety or compliance with study procedures.
19. Subject is participating in an investigational study of a new drug, biologic or device at the time of study screening.

2. Follow Up Schedule

All subjects were scheduled for follow-up examinations at baseline, intraoperatively, hospital discharge, 30 days, 6 months, and annually through 10 years. Data collected included demographics, medical and surgical history, procedural information, pediatric heart failure evaluation, transthoracic echocardiogram, and chest x-ray. Adverse events and complications were recorded at all visits.

The AUTUS valve may be expanded post-implant via transcatheter balloon dilation to accommodate growth of the subject. In addition to the follow-up schedule following the index procedure, subjects who underwent a post-implant valve expansion were also scheduled to return for follow-up examinations at 30 days, 6 months and a minimum of 1 year after the post-implant valve expansion procedure.

3. Clinical Endpoints

Primary Safety Endpoint

The primary safety endpoint was freedom from a device-related complication through 30 days post-valve implantation as adjudicated by an independent CEC, including:

- Death;
- Valve thrombosis requiring intervention;
- Symptomatic thromboembolism.

Primary Effectiveness Endpoint

The primary effectiveness endpoint was acceptable hemodynamic performance at 6 months post-valve implantation as assessed by the ECL, defined as a mean RVOT gradient ≤ 40 mmHg and less than moderate pulmonary regurgitation by transthoracic echocardiogram (TTE) and no AUTUS valve reintervention except for valve expansion to address prosthesis-patient mismatch.

Other Key Safety and Effectiveness Outcomes

Freedom from Device-Related Complications Post-Valve Implantation – CEC Adjudicated

The following composite safety outcome was evaluated at 6 months, and annually through 10 years post-valve implantation. The composite outcome includes device-related:

- Death;
- Valve thrombosis requiring intervention;
- Symptomatic thromboembolism.

Adverse Events – CEC Adjudicated

The following measures were evaluated by an independent CEC at 30 days, 6 months, and annually through 10 years post-valve implantation. Subjects that undergo valve expansion in year 10 after device implantation will be followed for an additional year.

- Mortality, including: all cause, cardiac-related, procedure-related and device-related;
- Valve thrombosis;
- Thromboembolism;
- Other cardiac or valve intervention (surgical or transcatheter);
- Major hemorrhage;
- Endocarditis;
- Hemolysis;
- Device explantation.

Additionally, adverse events as reported by Study Investigators, including serious adverse events (SAE), non-serious adverse events, device-related adverse events, and unanticipated adverse device effects (UADE) were reported.

Valve/Stent Frame Fracture

Valve/stent frame integrity (i.e., the presence or absence of stent frame fracture) was assessed by Independent Medical Reviewers (three experienced physicians trained and qualified to perform x-ray evaluation of the AUTUS valve stent frame) who

evaluated chest x-ray studies performed at the following timepoints post-valve implantation: hospital discharge, 1 year, and annually through 5 years. If a post-implant valve expansion procedure was performed, chest x-rays were performed at hospital discharge and 1 year post-valve expansion procedure.

Valve Implant Acute Procedural Success (Intraoperative)

To meet the definition of Acute Procedural Success (APS), all the parameters listed below must be achieved, as assessed by Sites, using direct pressure measurements and/or transesophageal echo (TEE):

- RV to PA peak systolic pressure gradient <40 mmHg (direct pressure measurement);
- None or trivial pulmonary regurgitation (assessed via TEE);
- No paravalvular leak (assessed via TEE).

Transthoracic Echocardiogram (TTE) Assessed Outcomes

Key echocardiographic (TTE) parameters were assessed by the ECL at the following timepoints: baseline, discharge, 30 days, 6 months, and annually through 10 years post-valve implantation. If a subject requires a post-implant valve expansion, a TTE will be performed pre-procedure, at discharge, 30 days, 6 months and 1 year post-valve expansion:

- Pulmonary regurgitation grade;
- Transvalvular peak and mean pressure gradient;
- Right ventricular dimensions and strain;
- Left ventricular function (ejection fraction) and strain.

Modified Ross Class for Pediatric Heart Failure

The Modified Ross Class was assessed by study sites at the following timepoints: baseline, 30 days, 6 months, and annually through 10 years post-valve implantation. Subjects that underwent post-implant valve expansion were evaluated pre-valve expansion, at 30 days, 6 months and 1 year post-valve expansion.

Post-Implant Valve Expansion Outcomes

Post-Implant Valve Expansion Safety Outcome

Freedom from device-related complications through 30 days post-valve expansion as adjudicated by the CEC. Composite outcome includes:

- Death;
- Extracorporeal membrane oxygenation (ECMO) support;
- Unplanned intervention (surgical or transcatheter);

- Major hemorrhage.

Post-Implant Valve Expansion Acute Procedural Success

To meet the definition of Acute Procedural Success, as reported by Study Investigators, at least one of the parameters listed below must be achieved after each post-implant valve expansion is performed, assessed during the same catheterization procedure:

- RV to aortic systolic pressure ratio: ≤ 0.5 ;
- Peak-to-peak RV to PA systolic pressure gradient: ≤ 15 mmHg;
- Peak-to-peak RV to PA systolic pressure gradient: $\geq 50\%$ reduction (pre- vs post-valve expansion)

All endpoints were evaluated descriptively.

B. Accountability of PMA Cohort

At the time of database lock, 62 subjects were enrolled and implanted with the AUTUS valve. Of the 62 enrolled subjects, 100% (62) subjects have completed 1-month follow-up, 96.8% (60) subjects have completed 6-month follow-up, and 82.3% (51) subjects have completed 1-year follow-up. Subject accountability is detailed in Figure 2.

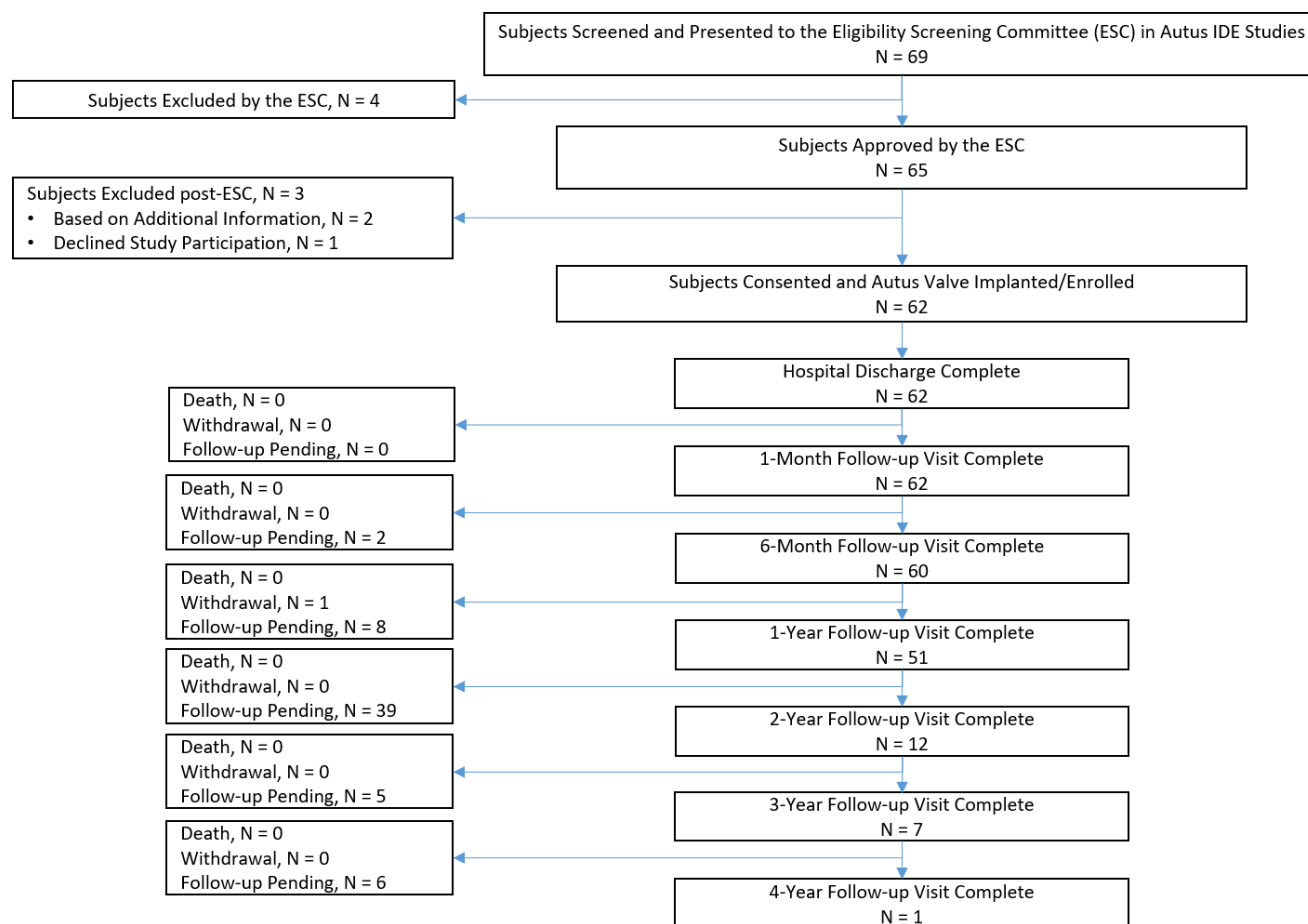


Figure 2: Subject Accountability and Follow-up Flowchart

A total of 2 study subjects have undergone a post-implant valve expansion procedure. Subject accountability for these subjects post-expansion is detailed in Figure 3.

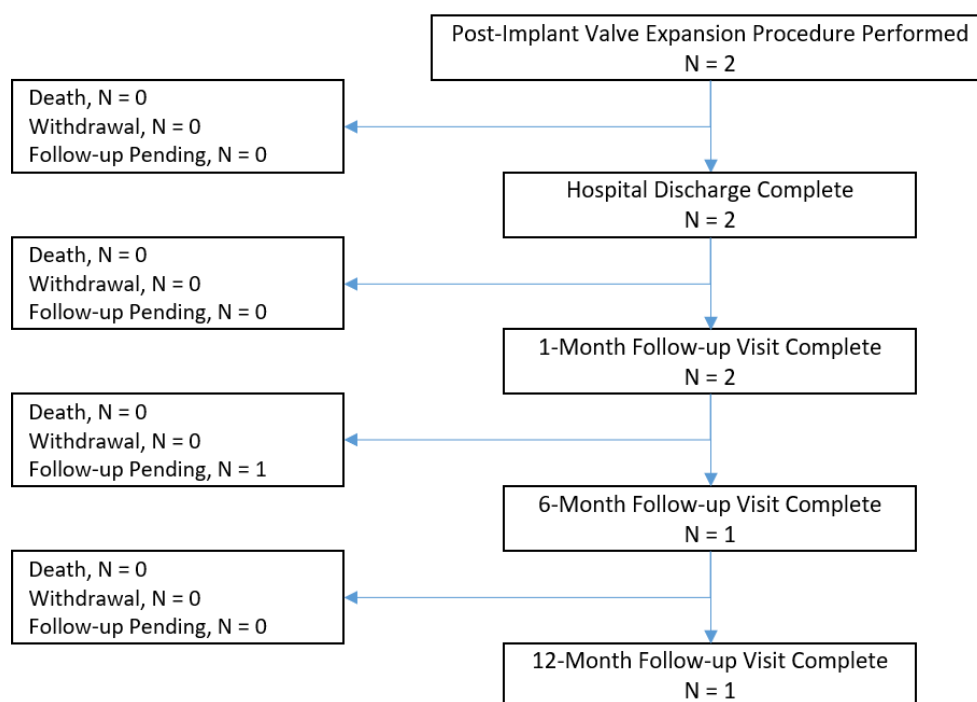


Figure 3: Post-Implant Valve Expansion Subject Accountability Flowchart

C. Study Population Demographics and Baseline Characteristics

The demographics and baseline characteristics of the study population are representative of pediatric patients with congenital pulmonary valve disease who require pulmonary valve replacement, as summarized in Table 5. Median (range) age and weight of subjects was 8.5 years (1.9 – 16.2 years) and 24.0 kg (10.2 – 71.7 kg), respectively.

Table 5: Demographics and Baseline Characteristics

Demographic or Characteristic	Autus Valve Subjects N=62
Age, years	
Mean (SD)	8.5 (3.7)
Median (Min, Max)	8.5 (1.9, 16.2)
Sex at birth, n (%)	
Male	42 (67.7%)
Female	20 (32.3%)
Ethnicity, n (%)	
Hispanic or Latino	15 (24.2%)
Not Hispanic or Latino	44 (71.0%)
Unknown or declined to answer	3 (4.8%)
Race, n (%)	
Caucasian	36 (58.1%)
Black or African-American	5 (8.1%)
Asian	4 (6.5%)

Demographic or Characteristic	Autus Valve Subjects N=62
American Indian or Alaska Native	0
Native Hawaiian or Other Pacific Islander	0
Multiracial	8 (12.9%)
Other	6 (9.7%)
Unknown or declined to answer	3 (4.8%)
Height, cm	
Mean (SD)	123.9 (23.5)
Median (Min, Max)	127.1 (81.0, 174.5)
Weight, kg	
Mean (SD)	27.4 (13.5)
Median (Min, Max)	24.0 (10.2, 71.7)
BSA, m ²	
Mean (SD)	0.96 (0.32)
Median (Min, Max)	0.91 (0.48, 1.73)

BSA = Body surface area, SD = Standard deviation.

The relevant medical and surgical history is presented in Table 6. The majority of subjects (48, 77.4%) presented with $\geq$ moderate pulmonary regurgitation alone. There were also 12 (19.4%) subjects with a combination of $\geq$ moderate pulmonary stenosis and $\geq$ moderate pulmonary regurgitation and 2 (3.2%) subjects with severe pulmonary stenosis alone.

Table 6: Medical and Surgical History

Medical History	AUTUS Valve Subjects N=62
Primary anatomic diagnosis, n (%)	
ToF / pulmonary stenosis	40 (64.5%)
ToF / pulmonary atresia	7 (11.3%)
ToF / absent pulmonary valve	1 (1.6%)
ToF / discontinuous pulmonary arteries	1 (1.6%)
Double outlet right ventricle	5 (8.1%)
Congenital pulmonary stenosis	6 (9.7%)
Pulmonary atresia / intact ventricular septum	1 (1.6%)
Transposition of the great arteries	1 (1.6%)
Other cardiac history, n (%)	7 (11.3%)
Anomalous coronary artery origin	2 (3.2%)
Bicuspid aortic valve	1 (1.6%)
Systolic heart failure	1 (1.6%)
Tricuspid valve dysplasia	4 (6.5%)
Type of pulmonary valve dysfunction, n (%)	
Severe pulmonary stenosis*	2 (3.2%)
Moderate or greater pulmonary regurgitation	48 (77.4%)

Medical History	AUTUS Valve Subjects N=62
Moderate or greater PS** and moderate or greater PR	12 (19.4%)
RVOT Type (at AUTUS valve Implant), n (%)	
Transannular patch repair	48 (77.4%)
Valve-sparing repair	8 (12.9%)
Native	4 (6.5%)
Prosthetic valve	1 (1.6%)
Other ¹	1 (1.6%)
Prior valve repair (non-pulmonary valve), n (%)	1 (1.6%)
Aortic valve	0
Mitral valve	0
Tricuspid valve	1 (1.6%)
Prior cardiac surgeries, n (%)	
Yes	58 (93.5%)
No	4 (6.5%)
Number of prior cardiac surgeries, n (%)	
0	4 (6.5%)
1	39 (62.9%)
2	17 (27.4%)
3	2 (3.2%)
History of cardiac surgical procedures, n (%)	58 (93.5%)
Systemic to pulmonary artery shunt	10 (16.1%)
Tetralogy of Fallot repair	48 (77.4%)
Transannular patch	42 (67.7%)
Valve-sparing	7 (11.3%)
Transannular patch repair	6 (9.7%)
Valve-sparing repair	2 (3.2%)
Pulmonary valve replacement	1 (1.6%)
Atrial septal defect closure	7 (11.3%)
Patent ductus arteriosus closure	12 (19.4%)
Patent foramen ovale closure	6 (9.7%)
Main pulmonary arterioplasty	4 (6.5%)
Bilateral branch pulmonary arterioplasty	3 (4.8%)
Left pulmonary arterioplasty	7 (11.3%)
Right pulmonary arterioplasty	1 (1.6%)
Ventricular septal defect closure	5 (8.1%)
Other ²	5 (8.1%)
Prior cardiac catheterization, n (%)	33 (53.2%)
Diagnostic	15 (24.2%)
Interventional	23 (37.1%)
Balloon pulmonary valvuloplasty	6 (9.7%)
Left pulmonary artery angioplasty	5 (8.1%)
Left pulmonary artery stent insertion	11 (17.7%)
Left pulmonary artery stent dilation	6 (9.7%)

Medical History	AUTUS Valve Subjects N=62
Other ³	3 (4.8%)
Unknown	1 (1.6%)
Prior non-cardiac surgical interventions, n (%)	23 (37.1%)
Airway	3 (4.8%)
Tracheostomy	3 (4.8%)
Ear, nose, and throat	11 (17.7%)
Gastrointestinal	10 (16.1%)
Gastrostomy tube placement	4 (6.5%)
Genitourinary	6 (9.7%)
Musculoskeletal	5 (8.1%)
Neurological	2 (3.2%)
Other ⁴	3 (4.8%)

ASD = Atrial septal defect, ToF = Tetralogy of Fallot, PFO = Patent foramen ovale, PR = Pulmonary regurgitation, PS = Pulmonary stenosis, RVOT = Right ventricular outflow tract.

*Peak transvalvular pressure gradient >60 mmHg.

**Peak transvalvular pressure gradient >40 mmHg to ≤60 mmHg.

¹RVOT type = arterial switch operation, LeCompte maneuver.

²Four subjects underwent 6 other prior cardiac surgical procedures, including left atrial appendage resection, RVOT plication, PFO enlargement, and partial ASD closure, anterior aortopexy, and anterior tracheopexy.

³Three subjects underwent other prior cardiac catheterization procedures, including closure of systemic to pulmonary artery shunt, stenting of distal transverse aortic arch, and ASD closure.

⁴Three subjects underwent other prior non-cardiac surgical interventions, including right diaphragm plication, tracheoesophageal fistula repair, and imperforate anus repair.

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the available follow-up for all 62 enrolled subjects.

Primary Safety Endpoint

All 62 (100%) subjects met the primary safety endpoint. All subjects were free from a device-related complication through 30 days post-valve implantation, with zero cases of death, valve thrombosis requiring reintervention, or symptomatic thromboembolism, as summarized in Table 7.

Table 7: Primary Safety Endpoint (30 Days) – CEC Adjudicated

	Autus Valve Subjects
	N=62
Primary Safety Endpoint*	n (%)
Primary Safety Endpoint*	62 (100%)
Death	0 (0%)
Valve thrombosis requiring intervention	0 (0%)
Symptomatic thromboembolism	0 (0%)

CEC = Clinical Events Committee

*Defined as freedom from device-related complication through 30 days, including death, valve thrombosis requiring intervention, and symptomatic thromboembolism, as adjudicated by the CEC.

Freedom from device-related complication through latest follow-up (CEC Adjudicated)

Through 1-year follow-up, all 62 (100%) subjects were free from a device-related complication, defined as death, valve thrombosis requiring reintervention, or symptomatic thromboembolism as adjudicated by the CEC.

All-Cause, cardiac, procedure-related and device-related mortality, surgical and transcatheter cardiac interventions, valve-related Adverse Events (CEC adjudicated)

Through 1-year follow-up, there were no cases of all-cause, cardiac, procedure-related, or device-related mortality. There were no CEC-adjudicated device-related adverse events, including no cases of valve thrombosis, thromboembolism, major hemorrhage, endocarditis, or hemolysis.

Two subjects underwent cardiac interventions (surgical or transcatheter) that were not related to the AUTUS valve or procedure, as adjudicated by the CEC. One subject underwent cardiac catheterization for placement of an atrial septal defect occlusion device. One subject underwent surgical reintervention to treat aortic valve endocarditis, with all intracardiac prosthetic materials explanted, including the study device. These results are summarized in Table 8. **Error! Reference source not found..**

Table 8: All-Cause, Cardiac, Procedure-related, Device-related Mortality, Surgical and Transcatheter Cardiac Interventions, Valve-related Adverse Events – CEC Adjudicated

	AUTUS Valve Subjects			
	Discharge	30 Days	6 Months	1 Year
	N=62	N=62	N=60	N=51
Safety Event	n (%)	n (%)	n (%)	n (%)
Mortality (all cause)	0	0	0	0
Cardiac-related	0	0	0	0

	AUTUS Valve Subjects			
	Discharge N=62	30 Days N=62	6 Months N=60	1 Year N=51
Safety Event	n (%)	n (%)	n (%)	n (%)
Procedure-related	0	0	0	0
Device-related	0	0	0	0
Valve thrombosis	0	0	0	0
Thromboembolism	0	0	0	0
Other cardiac or valve intervention (surgical or transcatheter)*	0	0	0	2 (3.8%)
Major hemorrhage	0	0	0	0
Endocarditis	0	0	0	0
Hemolysis	0	0	0	0
Device explantation*	0	0	0	1 (1.9%)

CEC = Clinical Events Committee.

*Non-AUTUS valve-related.

Frame Fracture Assessment

There were no cases of major frame fractures observed through 1-year follow-up, with major frame fracture defined as a frame fracture resulting in device embolization, hemodynamic compromise, or intervention. There were 3/62 (4.8%) subjects with minor frame fractures, as summarized in Table 9 below. For all 3 subjects, the fractures were first observed at the 1-year follow-up visit. There were no clinical sequelae associated with the minor frame fractures and valve function was preserved through latest follow-up for all 3 subjects.

Table 9: Frame Fracture Assessment

	AUTUS Valve Subjects	
	Discharge N=62	1 Year N=51
Valve Frame Fracture	n (%)	n (%)
All Frame Fracture (Major* and Minor), n (%)	0	3 (5.9%)
Major Frame Fracture*, n (%)	0	0
Hemodynamic compromise	0	0
Embolization	0	0
Intervention required	0	0
Minor Frame Fracture, n (%)	0	3 (5.9%)
X-ray Not Performed, n (%)	0	0

*Major frame fracture defined as fracture resulting in embolization, hemodynamic compromise (defined as the new onset of moderate or greater pulmonary regurgitation or mean trans-pulmonary valve gradient >40 mmHg as assessed by the Echocardiography Core Laboratory), or intervention.

Leaflet Mobility

There were 2 subjects with reduced mobility of one valve leaflet. Diagnosis was made by routine follow-up transthoracic echocardiogram (TTE) at 6 months for one subject and at 1 year for one subject. Available hemodynamic assessments demonstrated preserved valve function in both subjects with reduced leaflet mobility as shown below in Table 10. The subjects demonstrated no consistent trends in transvalvular mean gradient. Mild pulmonary regurgitation was present at 1 year in both subjects. Neither subject had any clinical symptoms, sequelae, or adverse events (including no evidence of leaflet thrombosis or pulmonary thromboembolism) related to the reduced mobility findings.

Table 10: Valve Hemodynamic Performance Through 1 Year

Subject	Valve Hemodynamics	Baseline	Discharge	30 Days	6 Months	1 Year
1*	Transvalvular Mean Gradient (mmHg)	6	10	12	24	17
	Pulmonary Regurgitation Grade	Severe	None	None	None	Mild
2**	Transvalvular Mean Gradient (mmHg)	5	5	3	9	14
	Pulmonary Regurgitation Grade	Severe	None	None	Mild	Mild

*Reduced leaflet mobility first observed on 6-month TTE and persisted on 1-year TTE

**Reduced leaflet mobility first observed on 1-year TTE

Adverse effects that occurred in the PMA clinical study:

Table 11 documents the adverse effects related or probably related to the device or procedure that occurred in the clinical study, as well as other adverse events of clinical interest. Unless otherwise noted, the device or procedure relatedness was adjudicated by the CEC.

There was one site-reported device-related adverse event, which was increasing pulmonary stenosis (mild) and mild pulmonary regurgitation at the 1-year follow-up visit. The subject with this event also reported non-compliance with the required anticoagulation regimen prior to the 1-year follow-up visit. The event is considered ongoing, with CEC adjudication pending. There have been no adverse events that were CEC-adjudicated as related to the device. No unanticipated device-related adverse events were identified.

Table 11: Procedure- or Device-Related Adverse Effects in the Study

Event	Subjects with Event (n, %) N=62
Device-related increasing pulmonary stenosis (mild) and mild pulmonary regurgitation*	1 (1.6%)
Frame fracture (non-major)**	3 (4.8%)
Impaired leaflet mobility***	2 (3.2%)
Pleural effusion	6 (9.7%)
Pneumothorax	6 (9.7%)
Atelectasis with pleural effusion	1 (1.6%)
Arrhythmia	6 (9.7%)
Pericardial effusion	1 (1.6%)
Left pulmonary artery injury	1 (1.6%)
Right lung hematoma	1 (1.6%)
Right ventricular dysfunction	2 (3.2%)
Tricuspid valve regurgitation*	1 (1.6%)
Pneumomediastinum	1 (1.6%)
Acute post-operative fever	3 (4.8%)
Post-operative hypertension	1 (1.6%)
Post-operative hypotension	1 (1.6%)
Hypoxemia	1 (1.6%)
Mild erythema of sternotomy incision	1 (1.6%)
Acute post-operative thrombocytopenia	1 (1.6%)
Acute post-operative hyperglycemia	1 (1.6%)
Bleeding post chest tube removal	1 (1.6%)
Sternal wound drainage	2 (3.2%)
Chest/chest wall pain	1 (1.6%)
Nausea and/or vomiting	9 (14.5%)
Constipation	1 (1.6%)
Diarrhea with fever	1 (1.6%)
Omental hernia	1 (1.6%)
Left vocal cord paralysis	1 (1.6%)
Contact dermatitis	1 (1.6%)
Epistaxis	2 (3.2%)
Anaphylactoid reaction	1 (1.6%)
Rib pain	1 (1.6%)
Increased creatinine	1 (1.6%)

*Site-reported as related or probably related to the device or procedure. CEC adjudication is pending.

**Frame fractures were assessed by the Independent Medical Reviewers.

***Impaired leaflet mobility events were evaluated by the ECL.

2. Effectiveness Results

The analysis of effectiveness was based on the available follow-up for all 62 enrolled subjects.

Primary Effectiveness Endpoint

Of the 60 subjects who completed 6-month follow-up post-valve implantation, all 60 (100%) met the primary effectiveness endpoint, as summarized in Table 12.

**Table 12: Primary Effectiveness Endpoint (6 Months)
Echocardiographic Core Lab Assessed/CEC Adjudicated**

	Autus Valve Subjects N=60 n (%)
Primary Effectiveness Endpoint*	
Primary Effectiveness Endpoint*	60 (100.0%)
RVOT mean gradient ≤ 40 mmHg	60 (100.0%)
Less than moderate pulmonary regurgitation	60 (100.0%)
No AUTUS valve reinterventions, excluding valve expansion to address prosthesis-patient mismatch	60 (100.0%)

CEC = Clinical Events Committee

*Defined as acceptable hemodynamic function at 6 months, including mean RVOT gradient ≤ 40 mmHg and pulmonary regurgitation grade < moderate as assessed by the Echocardiographic Core Laboratory and no AUTUS valve reintervention except for valve expansion to address prosthesis-patient mismatch as assessed by the CEC.

Effectiveness Outcomes at 1 Year

Of the 51 subjects who completed 1-year follow-up, all 51 (100%) had an RVOT mean gradient ≤ 40 mmHg and less than moderate pulmonary regurgitation, as summarized in Table 13. There were no AUTUS valve reinterventions at 1-year follow-up, excluding valve expansions due to somatic growth.

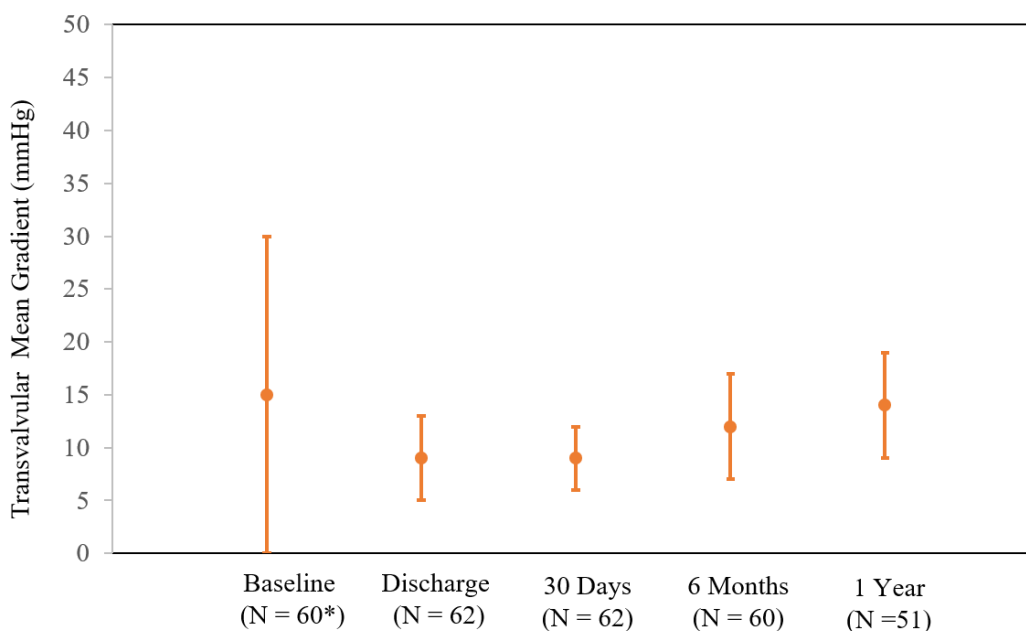
**Table 13: Effectiveness Outcomes (1 Year)
Echocardiographic Core Lab Assessed/CEC Adjudicated Valve Implant Population**

	AUTUS Valve Subjects N=51 n (%)
Effectiveness Outcomes*	
Effectiveness Outcomes*	51 (100.0%)
RVOT mean gradient ≤ 40 mmHg	51 (100.0%)
Less than moderate pulmonary regurgitation	51 (100.0%)
No AUTUS valve reinterventions, excluding valve expansion to address prosthesis-patient mismatch	51 (100.0%)

CEC = Clinical Events Committee

*Defined as acceptable hemodynamic function at 1 year, including mean RVOT gradient ≤ 40 mmHg and pulmonary regurgitation grade < moderate as assessed by the Echocardiographic Core Laboratory and no Autus Valve reintervention except for valve expansion to address prosthesis-patient mismatch as assessed by the CEC.

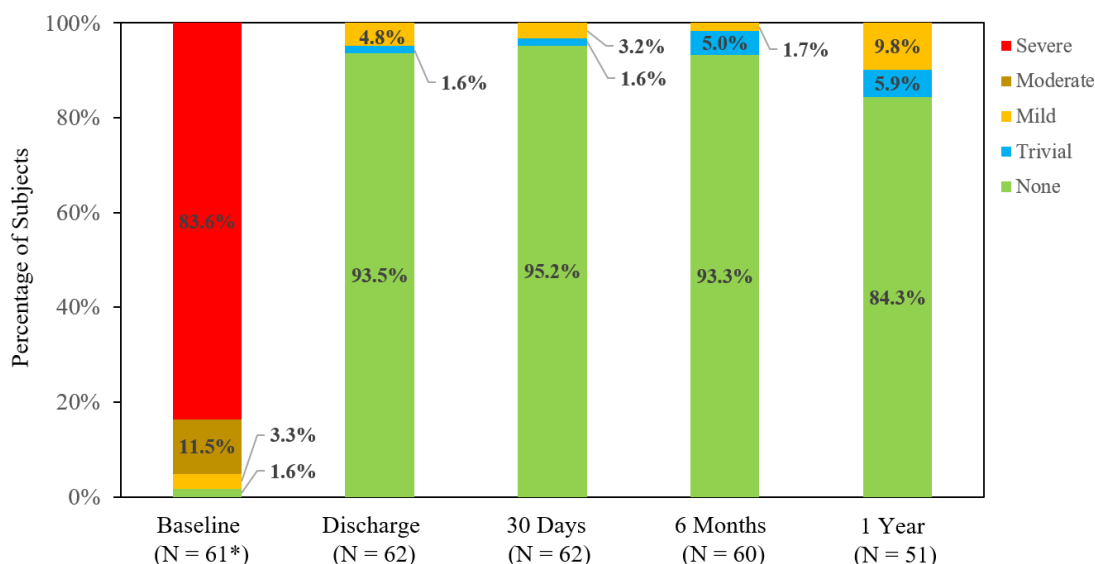
Figure 4 below presents the transvalvular mean pressure gradient (Continuous Wave Doppler) at each visit through 1-year follow-up. At discharge, the mean transvalvular pressure gradient was 9 ± 4 mmHg and remained low through 1 year (14 ± 5 mmHg).



* Continuous Wave Doppler transvalvular pressure gradient could not be measured by the Echocardiography Core Laboratory on baseline transthoracic echocardiograms (TTE) in 2 Subjects.

Figure 4: Transvalvular Mean Gradient (mmHg) by Visit

Figure 5 below presents the pulmonary regurgitation grade assessed by transthoracic echocardiogram. At baseline, 83.6% of subjects had severe pulmonary regurgitation, and 11.5% had moderate pulmonary regurgitation. At 1 year, 84.3% of subjects had no pulmonary regurgitation, 5.9% had trivial regurgitation and 9.8% had mild regurgitation. No subject had greater than mild pulmonary regurgitation.

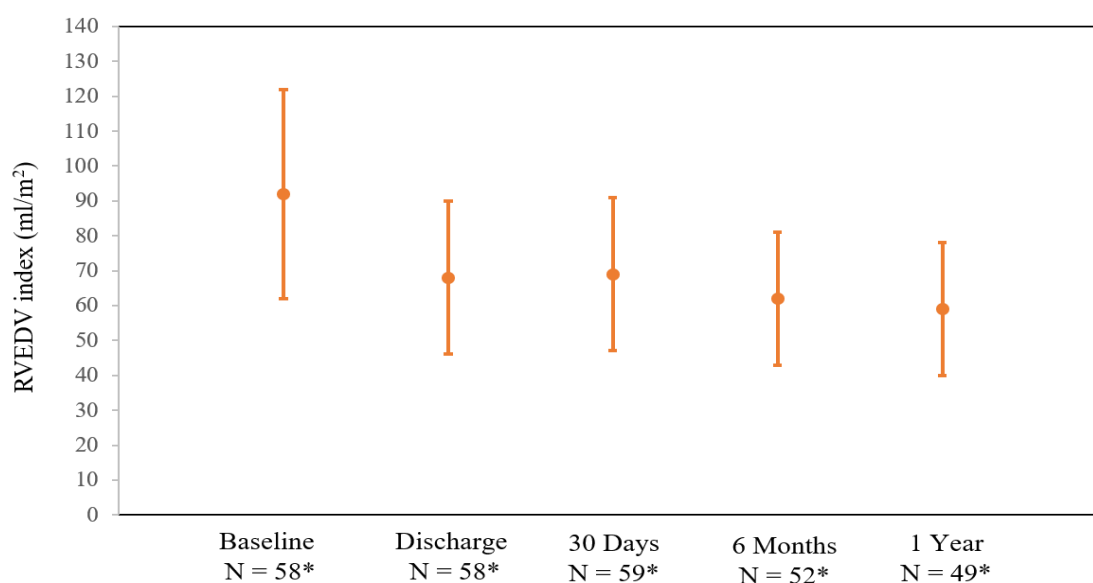


* Pulmonary regurgitation grade (assessed by measurement of vena contracta jet width) was not evaluable by the Echocardiography Core Laboratory in 1 subject.

Figure 5: Pulmonary Regurgitation Grade By Visit

Right Ventricular End Diastolic Volume (RVEDV) Indexed to Body Surface Area

Figure 6 Figure 6 below presents the right ventricular end diastolic volume (RVEDV) indexed to body surface area through 1-year follow-up. At baseline, the mean RVEDV index was 91.9 ± 30.2 ml/m² for the study population. At 6-month follow-up, the mean RVEDV index had decreased to 62.0 ± 19.3 ml/m² and was 58.5 ± 18.5 ml/m² at 1 year.



* Sample sizes < 62 at baseline, discharge, and 30 days, < 60 at 6 months, and < 51 at 1 year, reflect transthoracic echocardiogram studies where RVEDV index could not be assessed.

Figure 6: Right Ventricular End Diastolic Volume (RVEDV) Index (ml/m²) By Visit

Modified Ross Class for Pediatric Heart Failure

Figure 7 presents the Modified Ross Heart Failure Class through 1-year follow-up. At 1 year, 94.1% (N=48) of subjects were asymptomatic (Class I), compared to 58.1% (N=36) at baseline. There were no subjects who were Class III or Class IV.

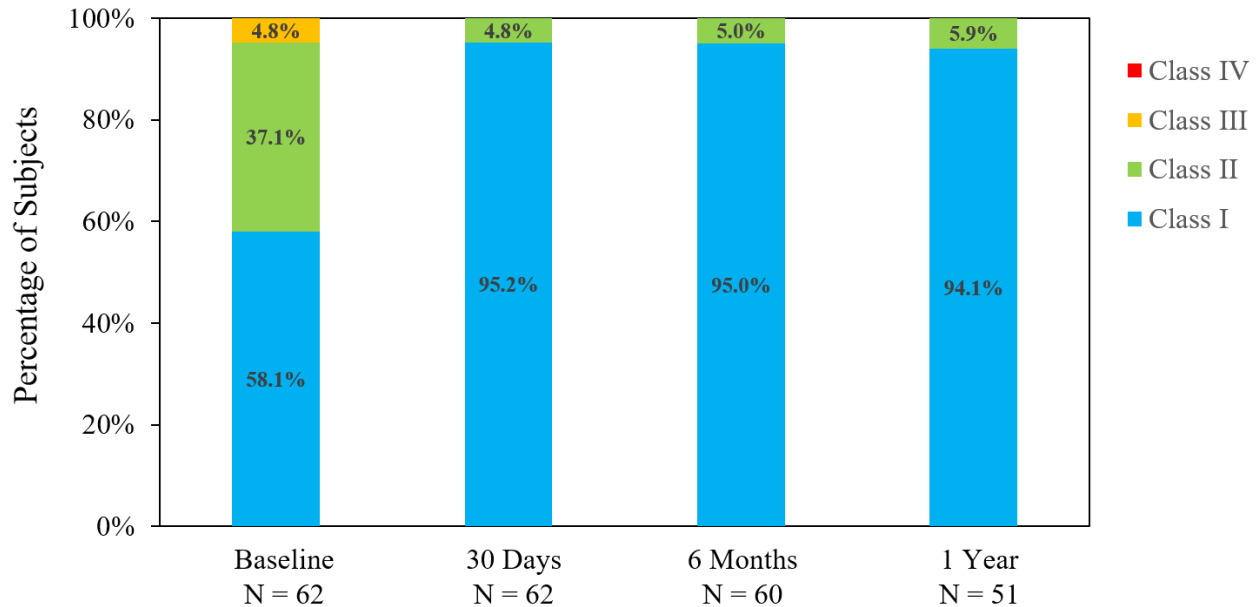


Figure 7: Modified Ross Pediatric Heart Failure Class

3. Post-Implant Valve Expansion Outcomes

To date, 2 subjects in the AUTUS valve clinical study underwent successful post-implant valve expansion without any device-related complications. The study protocol included prespecified criteria to guide consideration of post-implant valve expansion, although the decision was ultimately left to the treating physician and based on clinical judgment. Post-implant expansion considerations included the following:

- Normal RV function, RV-to-PA peak gradient ≥ 40 mmHg (2-D echo Doppler)
- Pre-existing RV systolic dysfunction, RV-to-PA peak gradient ≥ 30 mmHg (2-D echo Doppler)
- New-onset RV systolic dysfunction, RV free wall strain $< -20\%$ (2-D echo) or ejection fraction $< 45\%$ (3-D echo), and RV-to-PA peak gradient ≥ 30 mmHg (2-D echo Doppler)
- New-onset symptoms, Modified Ross Class II or greater, and RV-to-PA peak gradient ≥ 30 mmHg (2-D echo Doppler)

One subject underwent valve expansion at 13 months post-implant following somatic growth (BSA increased from 1.20 to 1.48 m²) and an increase in mean gradient from 13 mmHg at discharge to 29 mmHg at 1 year, consistent with prosthesis-patient mismatch. A second subject underwent valve expansion at 37 months post-implant following somatic growth (BSA increased from 1.01 m² to 1.41m²), new exertional shortness of breath, an increase in mean gradient from 23 to 44 mmHg, and elevated RV systolic pressure, consistent with prosthesis-patient mismatch. In both subjects, the valve was dilated from 18 to 20 mm, and both subjects met acute procedural success post-expansion. Outcomes are summarized below in Tables 14a and 14b.

Table 14a: Post-Implant Valve Expansion - Subject 1

Variable	Baseline	Discharge	30 Days	1 Year	Post-Implant Valve Expansion Procedure*	Discharge Post-Valve Expansion*	30 Days Post-Valve Expansion
Height, cm	148.0	149.0	149.5	160.0	Post-Implant Valve Expansion Procedure*	165.3	161.7
Weight, kg	37.2	35.1	34.7	44.8		46.0	49.3
BSA, m ²	1.23	1.20	1.19	1.40		1.42	1.48
PR Grade **	Moderate	None	None	None		Trivial	Trivial
Mean TPG, mmHg**	4	13	12	29		25	14
RV Systolic Function (qualitative)	normal	mildly diminished	normal	normal		normal	normal
RVEDV indexed to BSA **	121.8	105.0	67.5	44.9		73.3	77.1

BSA = Body surface area; RV = Right ventricular; PR: Pulmonary regurgitation; TPG: Transvalvular pressure gradient; RVEDV: Right ventricular end-diastolic volume

*Post-Implant Valve Expansion Procedure was performed at 13 months post-valve implantation.

**Echocardiography Core Laboratory assessed data

Table 14b: Post-Implant Valve Expansion - Subject 2

Variable	Baseline	Discharge	30 Days	1 Year	2 Years	3 Years	Post-Implant Valve Expansion Procedure*	Discharge Post-Valve Expansion*	30 Days Post-Valve Expansion
Height, cm	129.0	128.0	130.0	134.0	140.0	146.5	Post-Implant Valve Expansion Procedure*	148.0	148.0
Weight, kg	29.4	28.9	29.3	35.7	41.8	46.0		46.8	47.9
BSA, m ²	1.01	1.01	1.03	1.16	1.28	1.38		1.39	1.41
PR Grade**	Severe	None	None	None	Trivial	Mild		Mild	Mild
Mean TPG, mmHg**	6	15	13	17	23	44		31	14
RV Systolic Function (qualitative)	borderline mildly diminished	mildly decreased	mildly decreased	mildly decreased	mildly decreased	mildly decreased		mildly decreased	mildly decreased
RVEDV indexed to BSA **	108.8	80.5	69.4	61.4	63.6	79.9		67.9	51.4

BSA = Body surface area; RV = Right ventricular; PR: Pulmonary regurgitation; TPG: Transvalvular pressure gradient; RVEDV: Right ventricular end-diastolic volume

*Post-Implant Valve Expansion Procedure was performed approximately 37 months post-valve implantation (1 month after the 3-year follow-up visit).

**Echocardiography Core Laboratory assessed data.

4. Other Study Observations

Procedural Information

The procedural data are presented in Table 15 below. Sizing of the valve prior to implantation was determined based on the body surface area of the patient, targeting a pulmonary valve annulus z-score of -1 to +1.¹ All enrolled study subjects underwent pre-implant size-adjustment (via balloon expansion) of the AUTUS valve to match the valve diameter to the subject's body surface area. The smallest implanted diameter was 14 mm ID (N = 7, 11.3%) and the largest implanted diameter was 20 mm ID (N = 10, 16.1%). There were 32 (51.6%) subjects who had a new right ventricular outflow tract/transannular patch placed, while 26 (41.9%) subjects underwent primary closure of the main pulmonary artery after implanting the AUTUS valve.

Table 15: Valve Implant Procedure Details

Procedural Details	AUTUS Valve Subjects N=62
Pre-implant valve expansion, n (%)	
Yes	62 (100.0%)
No	0
Pre-implant valve expansion balloon catheter nominal diameter, n (%)	
14 mm	7 (11.3%)
16 mm	17 (27.4%)
18 mm	28 (45.2%)
20 mm	10 (16.1%)
22 mm	0
Implanted AUTUS Valve diameter, n (%)	
12.7 mm	0
14 mm	7 (11.3%)
16 mm	17 (27.4%)
18 mm	28 (45.2%)
20 mm	10 (16.1%)
22 mm	0
New right ventricular outflow tract/transannular patch, n (%)	
Yes	32 (51.6%)
No	30 (48.4%)
New main pulmonary artery patch, n (%)	
Yes	33 (53.2%)
No	29 (46.8%)
Primary main pulmonary artery closure, n (%)	
Yes	26 (41.9%)
No	36 (58.1%)

As shown in Table 16, 100% (N = 62) of enrolled study subjects achieved acute procedural success, assessed intraoperatively.

Table 16: Valve Implant Procedure – Assessment of Acute Procedural Success

Assessment of Acute Procedural Success	AUTUS Valve Subjects N=62
Acute Procedural Success*, n (%)	62 (100.0%)
RV to PA systolic pressure gradient <40 mmHg	62 (100.0%)
None or trivial pulmonary regurgitation	62 (100.0%)
No paravalvular leak	62 (100.0%)

PA = Pulmonary artery, RV = Right ventricular, TEE = Transesophageal echocardiogram.

*Defined as RV to PA peak systolic pressure gradient <40 mmHg (assessed via direct pressure measurement), none or trivial pulmonary regurgitation (assessed via TEE), and no paravalvular leak (assessed via TEE).

5. Sub-group Analyses

Subgroup analyses were performed on the primary safety and effectiveness endpoints. There were no gender, age, racial, or ethnic differences observed for the primary safety or effectiveness endpoints. The study was not specifically powered for these subgroups.

6. Pediatric Extrapolation

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population. The clinical study data collected for this PMA included pediatric patients.

XI. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 24 investigators. None of the clinical investigators had disclosable financial interests/arrangements as defined in sections 54.2(a), (b), (c), and (f). The information provided does not raise any questions about the reliability of the data.

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

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Circulatory System Devices panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

In the clinical study, 100% of subjects who reached the 6-month timepoint and the 1-year timepoint had acceptable hemodynamic performance (RVOT mean gradient ≤ 40 mmHg and less than moderate pulmonary regurgitation) and there were no AUTUS valve reinterventions other than valve expansion to address prosthesis-patient mismatch due to somatic growth. At baseline, 83.6% of subjects had severe pulmonary regurgitation and 11.5% had moderate pulmonary regurgitation. At 1 year, 84.3% of subjects had no pulmonary regurgitation, 5.9% had trivial regurgitation, and 9.8% had mild regurgitation. Positive changes in right ventricular (RV) function were observed post-implant, as evidenced by improvements in RV end diastolic volume indexed to BSA (median decreased from 67.4 mL/m² at discharge to 57.7 mL/m² at 1 year). Subjects experienced improvements in the Modified Ross Class for Pediatric Heart Failure, with 95.0% and 94.1% of subjects being categorized as Class I (asymptomatic) at 6 months and 1 year respectively, compared to only 58.1% of subjects at baseline.

All 62 enrolled subjects achieved acute procedural success. Although two subjects have undergone successful post-implant valve expansion with acceptable hemodynamic performance at 30 days post-expansion procedure, the small sample size limits the conclusions that can be drawn regarding the effectiveness of post-implant expansions.

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 to support PMA approval as described above. All subjects were free from death, valve thrombosis requiring reintervention, or symptomatic thromboembolism at 30 days post-implant procedure. There have been no deaths, valve thrombosis requiring reintervention, symptomatic thromboembolism, or device-related SAEs in the study to date. There were no intraprocedural complications in the index implantation procedures or post-implant expansion procedures.

To date, 4.8% of subjects had valve frame fractures and 3.2% of subjects had reduced leaflet mobility in one valve leaflet. There have been no clinical sequelae, significant impairments in valve function, or reinterventions associated with these events. However, the impact of these events on post-implant valve expansion is unknown. Longer-term studies are needed to further understand these risks.

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. The probable benefits of the AUTUS Size-Adjustable Valve include improved pulmonary valve function and hemodynamics, positive right ventricular remodeling, improved physical status, pre-implant valve size-adjustment to match the valve implantation size with the patient's body

size, and the ability to expand the valve post-implant to address prosthesis-patient mismatch and somatic growth.

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 include procedure-related adverse events (such as pleural effusion, pneumothorax, and arrhythmia), valve frame fracture, impaired leaflet mobility, and decreased valve function.

Additional factors considered in determining probable risks and benefits for the AUTUS Size-Adjustable Valve included the absence of longer-term clinical follow-up data and the limited number of post-implant expansion procedures performed in the study.

1. Patient Perspective

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

In conclusion, given the available information above, the data support that for management of pediatric patients who require surgical pulmonary valve replacement for dysfunctional native or surgically repaired right ventricular outflow tract as determined by echocardiography to have severe pulmonary stenosis, moderate or greater pulmonary regurgitation, or both moderate or greater pulmonary stenosis and moderate or greater pulmonary regurgitation, 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.

XIV. CDRH DECISION

CDRH issued an approval order on 10/01/2026. The final clinical conditions of approval cited in the approval order are described below.

The applicant must conduct a stress-life test to determine the endurance limit of the AUTUS Size-Adjustable Valve frame material. The study will be instituted no later than 12 months of this letter.

In addition, the applicant must conduct two post-approval studies:

1. **Continued Follow-Up of the Premarket Cohort:** The study will consist of all patients who were enrolled under the IDE, including the Continued Access Protocol investigation. The objective of this study is to characterize the clinical outcomes annually through 10 years. Data will be collected per the study protocol, including but not limited to: freedom from device-related complications (including death, valve thrombosis requiring reintervention, and symptomatic thromboembolism), acute

procedural success, mean right ventricular outflow tract (RVOT) gradient, pulmonary regurgitation grade, pulmonary stenosis grade, right ventricular dimensions and strain, left ventricular function and strain, reinterventions, adverse events, valve stent fracture, and Modified Ross Class for Pediatric Heart Failure. Data will also be collected following post-implant valve expansions, including freedom from device-related complications, post-implant valve expansion acute procedural success, and hemodynamic performance. Data will be analyzed descriptively.

2. **New Enrollment Study:** This is a prospective, multi-center, and single-arm study. The objective of the study is to evaluate the real-world safety and performance of the AUTUS Size-Adjustable Valve, including the safety and effectiveness of the post-implant expansion feature. The study will enroll a minimum of 150 subjects at up to 30 sites, with at least 40% new AUTUS Size-Adjustable Valve users (i.e., no prior implants). Follow-up will occur at discharge, 30 days, 6 months, 1 year, and annually thereafter through 10 years post index procedure. The safety and effectiveness endpoints include, but are not limited to, device-related complications (including death, valve thrombosis requiring reintervention, symptomatic pulmonary thromboembolism, infective endocarditis), acute procedural success, transvalvular gradient, pulmonary regurgitation grade, right ventricular size and function, freedom from unplanned pulmonary valve reintervention, stent frame integrity (including assessment of stent fracture), impaired or reduced leaflet mobility, and post-implant valve expansion procedural success and hemodynamic performance. Data will be analyzed descriptively.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality Management System (QMSR) 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.

XVI. REFERENCES

1. Cantinotti M, et al. Nomograms for two-dimensional echocardiography derived valvular and arterial dimensions in Caucasian children. *J Cardiol.* 2017;69(1):208-215.