SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Aortic Stent, Pulmonary Stent

Device Trade Name: Renata Minima Stent System

Device Procodes: PNF, QWC

Applicant's Name and Address: Renata Medical, Inc.
4675 MacArthur Ct, Suite 1150
Irvine, CA 92612

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P240003

Date of FDA Notice of Approval: August 28, 2024

Breakthrough Device: Granted breakthrough device status on February 7, 2022, because the device can provide for more effective treatment of an irreversibly debilitating disease; in addition no approved or cleared alternatives exist, and the availability of the device is in the best interest of patients.

II. INDICATIONS FOR USE

The Minima Stent System is indicated for use in the treatment of native or acquired pulmonary artery stenoses or coarctation of the aorta in neonates, infants, and children at least 1.5 kg in weight.

III. CONTRAINDICATIONS

- Active bloodstream infection requiring antibiotic therapy within 7 days prior to stent implantation.
- History of or active endocarditis (active treatment with antibiotics) within 180 days prior to stent implantation
- Aortic or pulmonary artery aneurysm
- Known hypersensitivity to aspirin or heparin and cannot be treated with other antiplatelet and/or antithrombotic medications.
- Known hypersensitivity to cobalt-chromium or contrast media that cannot be adequately pre-medicated.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Minima Stent System labeling.

V. DEVICE DESCRIPTION

The Minima Stent (Figure 1) is a balloon-expandable, radiopaque, symmetrical, cobalt-chromium (CoCr) stent. The stent is sterilized using ethylene oxide gas and is packaged pre-crimped onto the Minima Delivery System balloon.

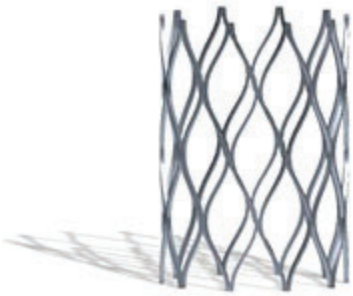

Figure 1. Design of Renata Minima Stent

The stent is supplied in one size and may be expanded from 5.1 to 8.5mm diameter depending on the size of the balloon delivery system selected. Both the 6mm and 8mm diameter stent systems have a length of approximately 16mm. The Minima Stent, with its unique cell design, is designed to be expanded to a diameter of up to 24mm, when re-dilated with an appropriately sized balloon catheter after initial stent implantation. As the stent is dilated to larger diameters, the stent length decreases, as described in the instructions for use.

The Minima Delivery System (Figure 2) is a covered balloon catheter containing 2 basic elements: 1) a balloon catheter, which includes a Pebax balloon bonded to a Nylon single-lumen catheter, and 2) an outer covering catheter, with a handle for simple axial translation. The outer catheter has an atraumatic tip and forms a seamless leading edge with the distal tip of the balloon. The handle allows for a simple push-and-pull system, facilitating proximal retraction of the outer catheter on the fixed balloon shaft to expose the balloon and stent and allow for balloon inflation once the device is in position for stent deployment. The handle contains a screw lock to maintain catheter component alignment during catheter insertion and manipulation.

Figure 2. Design of Renata Minima Delivery System

The system is pre-packaged with the Minima Stent crimped onto the balloon, which is covered by the outer catheter. The Minima System is supplied in two balloon sizes, 6 and 8 mm. During a clinical case, initial catheter-based angiography is used to determine the correct delivery system size for the patient given the device's deployment diameter range for the 6-mm system (5.1 to 7.1 mm) versus the 8-mm system (6.9 to 8.5 mm). Final sizing is then determined by the inflation pressure used to inflate the Minima System. Sizing information is provided in the labeling in 2 ATM increments. While the 2 system sizes achieve different deployment diameters, the exact same stent is used in

both systems.

Each system is packaged and sold separately, to be selected based upon clinical need. The covered system allows for sheathless delivery, with the entire system having an outer diameter analogous to a 4 Fr sheath. If a physician elects to use a sheath, a 6 Fr sheath is required.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of pulmonary artery stenoses or coarctation of the aorta in neonates, infants, and small children, including balloon angioplasty and surgical intervention. Each alternative has its own advantages and disadvantages. A patient and/or caregiver should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Minima Stent 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.

- Aortic aneurysm/ pseudoaneurysm, dissection, or rupture
- Arrhythmia
- Bleeding
- Death
- Endocarditis
- Femoral artery injury, thrombosis, or pseudoaneurysm
- Hematoma
- Infection
- Jailed side branches of the pulmonary arteries
- Jailed subclavian artery
- Myocardial infarction
- Pulmonary artery aneurysm/pseudoaneurysm, dissection, or rupture
- Stent fracture with loss of structural integrity
- Stent malposition dislodgement/migration or embolization requiring transcatheter or surgical adjustment or retrieval
- Stent stenosis
- Stroke or transient ischemic attack
- Thrombosis
- Vessel perforation/injury/dissection/rupture/tear

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

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

1. *In Vitro* Product Testing

Bench testing was performed on the Minima Stent System as described below. The samples were exposed to ethylene oxide sterilization prior to testing. All applicable testing was conducted on devices representative of the final finished device. Specific samples tested are described below. The tests performed and corresponding results are provided in Table 1.

Table 1. Summary of *in vitro* Product Testing for Minima Stent System

Test	Purpose	Test / Reference Article	Results
Stent Material Characterization			
Mechanical Properties	To confirm the ultimate yield strength, ultimate strength, and elongation of the Minima Stent material.	Each lot of Minima stent	Pass - Successful characterization of the mechanical properties of the CoCr utilized for the Minima Stent.
Stent Structural Performance Evaluation			
Corrosion Resistance	To evaluate the corrosion resistance of the stent, including pitting, fretting, crevice, and galvanic corrosion	6 pre-conditioned 8mm stent systems (corrosion), 3 pre-conditioned 6mm stent systems (galvanic)	Pass - All data demonstrated that the device is not susceptible to corrosion.
Stress Analysis (FEA)	To determine areas of fatigue stresses of the Minima Stent with simulated boundary conditions based on physiological loading	Modeling based on stent properties and physiological conditions	Pass - The Fatigue Analysis and Goodman Diagram predict an acceptable fatigue safety factor through 10mm of stent expansion.
Accelerated Durability Testing	To evaluate stent structural durability under physiologically relevant pulsatile loading conditions	16 systems total; 8 of each 6mm and 8mm stent systems	Pass - All stents survived 400 million cycles of fatigue testing, with cyclic pulsatile stresses, simulating anticipated vessel conditions
Stent Characteristics and Attributes			
Percent Surface Area	To calculate the contact area between the stent structure and a lumen as a percentage of the total circumferential area of the stent	Calculated for both 6mm and 8mm stent systems	Characterization - Using ASTM F2081, the surface area is 20% for the 6 mm size and 15% for the 8 mm size.
Stent Foreshortening	To calculate the decrease in stent length with increased diameter expansion	20 stents total; 10 of each 6mm and 8mm stent systems 3 stents were used for measuring foreshortening through a range of dilation from 10 to 24 mm in increments of 2 mm.	Characterization - The average stent foreshortening was 1.5% for the 6 mm size and 2.4% for the 8 mm size. Diameter (mm) Length (mm) 10 15.6 12 15.1 14 13.9 16 12.5 18 11.5 20 9.2 22 6.5 24 5.1

Test	Purpose	Test / Reference Article	Results
Stent Recoil	To report the measured change in diameter of the stent between post-balloon expansion and after balloon deflation	23 stents total; 10 6mm stent systems, 10 8mm stent systems, and 3 stents taken from 6mm to 24mm in increments of 2mm.	Characterization - Per the methods outlined in ASTM F2079, the stent recoil was 0.61 mm for the 6 mm size and 0.75 mm for the 8 mm size. Average recoil across sizes 8-20mm was 0.7mm with sizes ≥22mm averaging 0.3mm.
Strength	To determine the pressure at which the stent experiences permanent deformation	15 stents total; 11 at 6mm starting crimp, 2 at 8mm starting crimp, 2 at 20mm starting crimp	Pass - The radial strength is sufficient to maintain vessel patency.
Radiopacity	To ensure the stent is visible under real-time fluoroscopy	14 stents total; 11 8mm and 3 6mm stent systems	Pass - The stent is visible under anticipated fluoroscopy.
Full System Simulated Use Testing			
System Preparation	To ensure the system may be properly prepared for clinical use	30 systems total; 15 each of 6mm and 8mm stent systems	Pass - The system can be prepared for use through fluid flush and balloon de-airing.
Dimensional Verification	To determine the outer diameter and working lengths of the catheter		Pass - All devices met the acceptance criteria and showed no deviation from design specifications.
Stent Securement on Delivery Catheter	To ensure the stent is not dislodged while being passed through a tortuous pathway		Pass - No stents became uncovered or dislodged while passing through simulated passageway.
Force to Unsheathe & Re-sheathe Balloon Shaft	To determine the force required to unsheathe and re-sheathe the outer shaft		Pass - All systems met the acceptance criteria that the force to unsheathe or re-sheathe the outer shaft did not exceed 90.4 N after torquing the handle 180 degrees in each direction.
Balloon Inflation / Deflation	To ensure the catheter inflates and deflates within a specified time		Pass - All systems met the acceptance criteria of a 30-second inflation and deflation time.
Balloon Compliance	To demonstrate the stent outer diameter versus balloon inflation pressure		Pass - All data met the acceptance criteria that the stent OD measurement on-balloon as compared to the recoil value was within 10% of the value for each labeled inflation pressure.
Balloon Fatigue and Burst Pressure	To determine the repeatability of successful balloon inflations to rated burst pressure		Pass - All catheters passed the acceptance criteria, with burst pressure on final inflation exceeding nominal pressure.
Fluid Flush	To ensure fluid may be flushed through the outer shaft		Pass - All systems met the acceptance criteria that 1 cc of fluid may be flushed through the outer shaft.

Test	Purpose	Test / Reference Article	Results
Hemostasis	To confirm the amount of fluid able to leak through the disc seal		Pass - All systems met the acceptance criteria that no more than 51 mL of fluid was released through the disc seal.
System Bond Strength	To demonstrate the pull strength of the outer shaft to the handle and the balloon shaft to the Y-connector		Pass - All bond strengths met the established acceptance criteria.
Handle Detachment Torque	To determine the torque required to detach handle parts from the seal joint		Pass - All systems met the acceptance criteria that the torque required to detach the handle from the seal joint did not exceed 0.6 Nm.
Trackability	To determine the ability of the system to permit consistent, accurate, and safe access to the intended location and safe withdrawal of the delivery system prior to and after deployment of the stent.		Pass - All systems met acceptance criteria that pigtail catheter insertion forces as well as the forces to track the system across the clinically relevant neonatal glass model did not exceed 90.4 N.

2. **MRI Compatibility**

Non-clinical testing of the device in magnetic fields of 1.5 and 3.0 Tesla showed that the device is MR Conditional. The Minima Stent may be safely scanned under the following conditions:

MRI Safety Information  A patient with the Renata Medical CoCr Cardiac Stent may be safely scanned under the following conditions. Failure to follow these conditions may result in injury to the patient.	
Name/Identification of device	Renata Medical CoCr Cardiac Stent
Nominal value(s) of Static Magnetic Field [T]	1.5 T or 3 T
Maximum Spatial Field Gradient [T/m and gauss/cm]	30 T/m (3000 gauss/cm)
RF Excitation	Circularly Polarized (CP)
Maximum SAR [W/kg] under Normal Operating Mode	Whole Body: 2.0 W/kg Head: 3.2 W/kg
Limits on Scan Duration	Whole Body: 2.0 W/kg whole body average SAR for 1 hour of continuous RF (a sequence or back to back series/scan without breaks)
MR Image Artifact	The presence of this implant may produce an image artifact of 10 mm.
If information about a specific parameter is not included, there are no conditions associated with that parameter.	

3. **Biocompatibility**

The biological safety assessment of the Minima Stent System was conducted in accordance with the ISO 10993 standard series, “Biological Evaluation of

Medical Devices" and the FDA Guidance, *Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process*". Per ISO 10993-1, the stent is classified as a blood-contacting, permanent (> 30 days) implant device, and the delivery system is classified as an external communicating device with limited contact (< 24 hours). Testing to address the biocompatibility endpoints was conducted on the final finished version of the Minima System. Based upon the biocompatibility testing performed (Table 2 and Table 3), the Minima System was determined to be biocompatible. Chemical characterization and a toxicological risk assessment were provided in lieu of genotoxicity and carcinogenicity testing.

Table 2. Summary of Biocompatibility Testing for the Minima Stent

Test	Results
Cytotoxicity Study Using the ISO Elusion Method (L929)	Non-cytotoxic
ISO Guinea Pig Maximization Sensitization Test	Non-sensitizing
ISO Intracutaneous Reactivity Study in Rabbits	Non-irritant
ISO Acute Systemic Toxicity Study in Mice	Non-toxic
USP Rabbit Pyrogen Study, Materials Mediated	Non-pyrogenic
Hemocompatibility (ASTM Hemolysis – Direct and Extract Methods)	Non-hemolytic
Hemocompatibility (Complement Activation SC5b-9 Assay)	Not a Sc5b-9 or C3a complement activator
Hemocompatibility (Heparinized Platelet and Leukocyte Count)	Passed Acceptance Criteria
Hemocompatibility (Partial Thromboplastin Time (PTT))	Passed Acceptance Criteria
Implantation (GLP Animal Study)	No toxicity, no irritation

Test	Results
In Vivo Thrombogenicity (GLP Animal Study)	Non-thrombogenic
Sub-Acute Toxicity, Sub-Chronic Toxicity (GLP Animal Study)	No toxicity
Genotoxicity, Chronic Toxicity, and Carcinogenicity addressed by performing Chemical Characterization and Toxicological Risk Assessment	No unacceptable genotoxic, carcinogenic, or non-carcinogenic health risks were identified.

Table 3. Summary of Biocompatibility Testing for the Minima Delivery System

Test	Results
Cytotoxicity Study Using the ISO Elusion Method (L929)	Non-cytotoxic
ISO Guinea Pig Maximization Sensitization Test	Non-sensitizing
ISO Intracutaneous Reactivity Study in Rabbits	Non-irritant
ISO Acute Systemic Toxicity Study in Mice	Non-toxic
USP Rabbit Pyrogen Study, Materials Mediated	Non-pyrogenic
Hemocompatibility (ASTM Hemolysis – Direct and Extract Methods)	Non-hemolytic
Hemocompatibility (Complement Activation SC5b-9 Assay)	Not a Sc5b-9 or C3a complement activator
Hemocompatibility (Heparinized Platelet and Leukocyte Count)	Passed Acceptance Criteria
Hemocompatibility (Partial Thromboplastin Time (PTT))	Passed Acceptance Criteria
In Vivo Thrombogenicity (GLP Animal Study)	Non-thrombogenic

B. Animal Studies

Renata Medical performed 3 chronic animal studies (2 non-GLP and 1 GLP) to evaluate the safety and performance of the Minima Stent *in vivo* prior to initiation of clinical studies. The initial non-GLP animal study was conducted to evaluate the safety of the device in pediatric swine. Table 4 below details the GLP study.

Table 4. Summary of GLP Porcine Study

GLP Porcine Study	
Sample Size / Animal Model	N = 5 piglets
Test Article	N = 14 systems total; 3 of 6 mm size and 11 of 8 mm size
Method	Animals were anesthetized and appropriate cardiac catheterization imaging was utilized to determine appropriate sizing in target vessels (i.e., aortas and branch pulmonary arteries). Using fluoroscopy, the Minima Stent Systems were tracked to the target location and deployed. After approximately 60 days, the stents were re-dilated using balloons to match the diameter of the vessel after somatic growth. After 90 days, the animals were terminated after catheter evaluation. The safety and performance of the device was evaluated based on animal health parameters, gross pathology, radiography, angiography, and histopathology. Device performance was assessed based on both operator feedback provided throughout the procedure and angiography to determine the structural integrity of the stent during both deployment and expansion.
Results	There were no adverse events leading to early death or mortality due to the Minima Stent System. There were no stent fractures, dissections, or perforations resulting from the deployment of the stent. Histomorphometry measurements and calculations of cell layer parameters passed all acceptance criteria. The delivery system was trackable, allowed accurate stent placement, and was overall easy to use.

An additional non-GLP study was performed (Table 5) to evaluate a design refinement intended to increase the radial force of the Minima Stent, with an emphasis on evaluation of stent migration.

Table 5. Summary of Non-GLP Porcine Study

Non-GLP Porcine Study	
Sample Size / Animal Model	N = 2 piglets
Test Article	N = 8 systems total
Method	Animals were anesthetized and appropriate cardiac catheterization imaging was utilized to determine appropriate sizing in target vessels (i.e., aortas and branch pulmonary arteries). Using fluoroscopy, the Minima Stent Systems were tracked to the target location and deployed. After approximately 27 days, the animals were terminated following terminal fluoroscopy to assess for stent migration. The safety of the device was also evaluated based on animal health parameters and gross pathology.

Non-GLP Porcine Study	
Results	No clinically significant adverse events leading to early death or mortality due to treatment with the Minima Stent were observed by clinical observations and clinical pathology results. Gross pathology and necropsy showed no significant clinical abnormalities. Fluoroscopy / angiography revealed that the revised Minima Stent design did not migrate in 7 out of 8 implanted stents.

C. Additional Studies

1. Sterilization

The Minima Stent System 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

The Minima Stent is pre-crimped onto the balloon on the Minima Delivery System. The Minima Stent System is then packaged in a tray with a retainer lid, which is then placed in a Tyvek pouch and sealed.

The shelf-life of the Minima Stent System has been established at 12 months.

X. SUMMARY OF PRIMARY CLINICAL STUDY

Renata Medical performed a clinical study (GROWTH Trial) to establish a reasonable assurance of safety and effectiveness of implantation of the Minima Stent for the treatment of congenital and postoperative coarctation of the aorta or pulmonary artery stenosis in the US under IDE G210256. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Patients were treated between February 1, 2022, and August 22, 2023. The database for this PMA reflected data collected through May 19, 2024 and included 42 enrolled patients. There were 7 investigational sites.

The study was a single arm, prospective, multi-center, open-label, pivotal study. The data used to substantiate the clinical portion of the PMA includes data through the 6-month follow-up visit. Subjects will continue to be followed through the clinical protocol through 5 years of follow-up visits. A Data Safety Monitoring Board (DSMB) and Clinical Event Committee (CEC) reviewed study data through collection of 6-month visits and adjudicated results, where applicable.

1. Clinical Inclusion and Exclusion Criteria

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

- The subject's legally authorized representative has been informed

of the nature of the clinical investigation, agrees to its provisions, and has provided written informed consent

- Requiring treatment* of:
  - native, acquired, or recurrent aortic coarctation, or
  - native, acquired, or recurrent pulmonary artery stenosis

  *As defined by the patient's medical team
- Patency of at least one femoral vein, femoral artery, jugular vein or both carotid arteries able to accommodate the delivery system
- Adjacent vessel to stenosis measuring > or equal to 4 mm

Patients were <u>not</u> permitted to enroll in the GROWTH study if they met any of the following exclusion criteria:

- Active bloodstream infection requiring antibiotic therapy within 3 days prior to stent implantation
- History of or active endocarditis (active treatment with antibiotics) within 180 days prior to stent implantation
- Aortic or pulmonary artery aneurysm in the location targeted for treatment
- Body weight < 1.5 kg
- Anatomic location of lesion judged by the investigator to not lend to the safe placement of a stent
- Target vessels larger or smaller than the Minima System balloon size ranges
- Known genetic syndrome known to be associated with vasculopathies such as but not limited to Williams syndrome, Loeys-Dietz syndrome, etc.
- Clinical scenario requiring that more than one vessel needs stent implantation at the time of the trial procedure.
- Currently participating in an investigational drug study or another device study
- Major or progressive non-cardiac disease resulting in a life expectancy of less than six months
- Known hypersensitivity to aspirin or heparin and cannot be treated with other antiplatelet and/or antithrombotic medications
- Known hypersensitivity to cobalt-chromium or contrast media that cannot be adequately pre-medicated

To be eligible for stent re-dilation, patients had to meet the following inclusion criteria:

- Development of an increase in the pressure gradient across the stent and/or stent lumen diameter less than the nominal adjacent vessel diameter, as defined as:
  - Peak Doppler echo gradient ≥ 30 mmHg and/or a mean Doppler gradient ≥ 20 mmHg across the stented vessel
  - Stented lumen diameter is ≤ 75% of adjacent native vessel

Patients were <u>not</u> permitted to undergo stent re-dilation if they met any of the following exclusion criteria:

- Evidence of significant vessel wall damage (e.g., aneurysm, dissection) in

the area of planned re-dilation

- Stent deformity or loss of structural integrity judged by the investigator to not lend to the safe re-dilation of the stent
- Access site or patient vasculature judged by the investigator to not lend to the safe re-catheterization using a balloon catheter approved for the stent location.

2. **Follow-up Schedule**

All patients were scheduled to return for follow-up examinations at 1 month, 3 months, 6 months, 12 months, and annually through 5 years. The assessments performed at each visit are listed in Table 6.

Table 6. Schedule of Assessments for GROWTH Study

Activity	**Screening**	**Procedure**	**Post-Procedure**	**1 Month** (±7days)	**3 Months** (±7days)	**6 Months** (±14 days)	**12 Months** (±30days)	**Annually Years 2-5** (±45 days)
Informed consent & HIPAA authorization	X							
Inclusion / exclusion criteria assessment	X							
Demographics	X							
Medical history	X							
Physical exam & vital signs	X		X	X	X	X	X	X
WBC, Hgb, Hct, platelets	X							
Serum creatinine	X							
INR (if taking Warfarin)	X							
Chest X-ray	X		X	X	X	X		
Transthoracic echocardiogram	X		X	X	X	X	X	X
Concomitant medications	X	X	X	X	X	X	X	X
Minima stent implantation		X						
Pre-and Post-implantation angiography and hemodynamic assessments (within procedure)		X						
Adverse events / Device deficiencies		X	X	X	X	X	X	X
Concomitant procedures	X		X	X	X	X		
CT angiography						X		

3. **Clinical Endpoints**

With regards to safety, the following criteria were evaluated:

Primary Safety Endpoint: Percentage of cases with freedom from procedure- or device-related SAEs resulting in an event listed below:

- Death
- Cardiac arrest and/or emergency ECMO cannulation
- Stroke
- Limb loss
- Vessel dissection of target lesion
- Device thrombosis/occlusion
- Cardiac perforation requiring percutaneous or open surgical intervention
- Persistent cardiac arrhythmia requiring a pacemaker

The following hypothesis was tested using a one-sided, one proportion study at the one-sided α=0.025 level of significance:

- Null Hypothesis (H0): Freedom from Serious Device-Related AEs ≤ 78%.
- Alternative Hypothesis (H1): Freedom from Serious Device-Related AEs > 78%.
- One-Sided (H0: P ≤ P0 vs. H1: P > P0)

Secondary Safety Endpoints:

- Freedom from stent embolization or migration through 6 months.
- Freedom from stent fracture that led to reintervention through 6 months
- Freedom from non-elective Minima Stent explant at 90-days post re-dilation
- Freedom from procedure- or device-related SAE during re-dilation that results in the following:
    - Death
    - Cardiac arrest and/or emergency ECMO cannulation
    - Stroke
    - Limb loss
    - Vessel dissection of target lesion
    - Device thrombosis/occlusion
    - Cardiac perforation requiring percutaneous or open surgical intervention
    - Persistent cardiac arrhythmia requiring a pacemaker

With regards to effectiveness, the following criteria were evaluated:

Primary Effectiveness Endpoint: Rate of clinical success, defined as a composite of:

- Stenosis relief, defined by stent outer diameter ≥ 75% of the surrounding vessel immediately after deployment.
- Freedom from open surgical intervention required to treat Minima Stent dysfunction through 6 months.
- Maintenance of stented vessel diameter ≥ 50% of post-implant diameter at 6 months; as measured using CT angiography and/or angiography

The following hypothesis was tested using a one-sided, one proportion study at the one-sided $\alpha=0.025$ level of significance:

- Null Hypothesis (H0): Incidence of clinical success ≤ 77%.
- Alternative Hypothesis (H1): Incidence of clinical success > 77%.
- One-Sided (H0: P ≤ P0 vs. H1: P > P0)

Secondary Effectiveness Endpoints:

- Peak-to-peak pressure gradient (ventricle to arterial or arterial to arterial) < 20 mmHg after stent placement, when applicable.
- Successful stent re-dilation (when indicated) at re-catheterization, defined as an increase in the intra stent angiographic luminal diameter within 2mm of the adjacent native vessel diameter immediately after re-dilation.

B. Accountability of PMA Cohort

Of the 49 patients screened for inclusion in the study, 42 subjects met the eligibility criteria. Forty-one (41) of the 42 subjects received a Minima Stent in the intended location. Post-procedure data from 6-month follow-up visits were available for all 41 subjects for analysis of the primary effectiveness endpoint. Study accountability is detailed in Table 7.

Table 7. GROWTH Study Cohort Accountability

Activity	**Screening***	**Procedure****	**Discharge**	**1 Month** (± 7days)	**3 Months** (±7days)	**6 Months** (± 14 days)	**12 Months** (± 30 days)	**2 years** (± 45 days)	**3 years** (± 45 days)	**4 years** (± 45 days)	**5 years** (± 45 days)
% of Eligible, Enrolled Subjects Completed Visit (# completed / # eligible)	85.7% (42/49)	100% (41/42)	100% (41/41)	100% (41/41)	100% (41/41)	100% (41/41)	79% (30/38)	80% (8/10)	N/A (0 eligible at time of submission)		

**All 49 subjects completed the screening, but only 42 met the inclusion criteria for successful screening.*
***All 42 eligible subjects underwent the implant procedure, but the 1 subject who did not achieve successful device placement has not been included in the follow-up visit counts.*

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are representative of those of the indicated population presenting with native and post-operative congenital vascular stenoses within the aortic and pulmonary circulations in the US. The

GROWTH study demographics for the entire enrolled population are shown in Table 8. Median (range) age and weight of subjects was 9 months (0 - 112 months) and 7.8 kg (3.4 - 28.3 kg), respectively.

Table 8. GROWTH Study Demographics

Characteristic	Number of Subjects	Percent of Population
Sex, % (n)		
Female	20	48%
Male	22	52%
Age Group		
0-6 months	12	29%
6-24 months	18	43%
>24 months	12	29%
Race, % (n)		
Asian	1	2%
Black or African American	7	17%
Native Hawaiian or Other Pacific Islander	1	2%
White	22	52%
Other	11	26%
Ethnicity, % (n)		
Hispanic or Latino	9	21%
Not Hispanic or Latino	32	76%
Unknown	1	2%
Lesion Description		
Aortic Coarctation	21	50%
Native Coarctation	8	19%
Re-Coarctation	13	30%
Pulmonary Artery Stenosis	21	50%
Single Ventricular LPA	9	21%
Biventricular RPA	5	12%
Biventricular LPA	7	17%

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the data available through the 6 month follow-up visit for all 42 enrolled subjects, regardless of whether successful stent placement was achieved. All 42 (100%) of subjects with attempted implants demonstrated freedom from serious device-related adverse events (i.e., death, cardiac arrest and/or emergency ECMO cannulation, stroke, limb loss, vessel dissection of target lesion, device thrombosis/occlusion, cardiac perforation requiring percutaneous or open surgical intervention, and/or persistent cardiac arrhythmia requiring a pacemaker), through 6 months as specified in the primary safety endpoint.

The study's primary safety endpoint resulted in 100% success, therefore, the normal approximation to the binomial could not be used to calculate the lower limit of the confidence interval, so the exact method was used instead. The lower limit of the two-sided lower 95% confidence interval was 91.6% using the

Clopper-Pearson method, which exceeds the performance goal of 78%; therefore, the primary safety endpoint was met.

The results of the secondary safety endpoint analyses are provided in Table 9.

Table 9. Summary of Secondary Endpoints in GROWTH Study

Secondary Safety Endpoint	Rate
Freedom from stent embolization or migration through 6 months	93% (42/45* stent implant attempts)
Freedom from stent fracture that led to reintervention through 6 months	100% (42/42 patients)
Freedom from non-elective stent explant at 90-days post re-dilation	100% (8/8 evaluable patients)
Freedom from procedure- or device-related SAEs during re-dilation	100% (13/13 re-dilation attempts)

* Note: Of the 42 enrolled patients, 39 were treated with 1 Minima Stent and 3 patients with 2 Minima Stents, for a total of 45 Minima Stent Implants.

Adverse effects that occurred in the PMA clinical study:

The overall incidence and types of adverse events aligned with comparable rates reported in literature. No unanticipated device-related adverse events were identified. Table 10 documents the adverse events determined to be related to the device or procedure that occurred during the GROWTH study.

Table 10. Device- or Procedure-Related Adverse Events in GROWTH Study

Event	n/N (Event Rate: number of events/number of subjects implanted)
Procedure-related Thrombus Formation	7/42 (11.9%)
Device-related Thrombus	0/42 (0%)
Device Migration/Embolization	3/42 (7.1%)
Lower Extremity Pulse Loss	1/42 (2.4%)
Rebleed from Arterial Site	1/42 (2.4%)
Transient Heart Block	1/42 (2.4%)
Hematoma	1/42 (2.4%)
Hypertension	1/42 (2.4%)
AV Fistula	1/42 (2.4%)
Pseudoaneurysm	1/42 (2.4%)
In-Stent Narrowing	1/42 (2.4%)
Increased Gradient across Stent	1/42 (2.4%)

In this cohort, there were three adverse events that met the definition of device migration/embolization for a rate of 7.1% (3/42 subjects; 3/45 attempted stent implants). The three cases of migration/embolization occurred intra-procedurally. The two pulmonary artery (PA) cases were both in the setting of ostial stenoses, where there is a known higher risk of stent migration/embolization. In both PA cases, the stent deployment to the left pulmonary artery was attempted and the stent embolized into the main pulmonary artery during withdrawal of the delivery system. The stents were deployed in the right pulmonary artery to ensure fixation in both cases. In one case, review of the case suggested that placement of the stent more proximally than initially desired contributed to the event, and the patient received a second stent in the intended location. In the second case, the patient did not receive a second stent and the stenoses was not treated. The third case occurred during treatment of aortic coarctation, which resulted in the placement of a second stent to treat the aortic coarctation. When passing the pigtail catheter across the stent for post-deployment pressure gradients and angiographic imaging, the stent was partially dislodged from the lesion. However, the stent remained over the lesion. A second Minima Stent was placed within the first stent to ensure fixation within the lesion and treatment of the coarctation.

There were no cases of stent migration/embolization reported post-procedure as of the date of data lock for this study.

Femoral arterial access site complications were noted in 6 subjects, all of whom underwent treatment for coarctation (N = 21). All 6 patients weighed less than 6 kg at the time of the procedure, and all subjects (6/6) have been documented to have resolution of the event, without sequelae.

Stent fracture has not been observed in any of the 42 subjects post-procedure through 6 months.

One death was reported during the study at 206 days post-procedure (after analysis of the primary effectiveness endpoint). This one subject had an adverse event of “Increased Gradient across Stent” adjudicated as related to the device. The patient had multiple cardiac comorbidities requiring surgical repair and there were concerns that dilation of the stent could result in compression of the left bronchus. Therefore, the patient was treated with open surgical intervention. The Minima Stent was explanted and replaced with a homograft. The patient received several other concurrent intracardiac open surgical procedures and expired 110 days later from worsening pulmonary hypertension and acute respiratory distress syndrome.

2. **Effectiveness Results**

The analysis of effectiveness was based on the data through the 6-month follow-up visit for all 42 subjects. Of the 42 subjects, 41 experienced device success, as defined by 1) stenosis relief, 2) freedom from open surgical intervention required to treat Minima Stent dysfunction, and 3) maintenance of stented

vessel diameter ≥ 50% of post-implant diameter at 6 months, resulting in an overall success rate of 97.6%. The results broken down primary effectiveness component are provided in Table 11.

Table 11. Primary Effectiveness Component Results

Primary Effectiveness Endpoint Component	Timeframe	Event Rate (n/N)
Stenosis relief	Intra-procedure	97.6 % (41/42)
Freedom from open surgical intervention to treat Minima Stent dysfunction	Implant procedure through 6 month follow up visit	100% (42/42)
Maintenance of stented vessel ≥ 50% of post-implant diameter at 6 months	6 month follow up visit	97.6% (41/42)

The primary effectiveness hypothesis was tested by calculating the lower limit of the two-sided 95% confidence interval using the normal approximation to the binomial, with success defined as a lower limit of greater than 77%. Since the calculated lower limit is 93.0%, the primary effectiveness endpoint is successfully met.

Given the sample size and an observed proportion that is close to 100%, the appropriateness of the normal approximation to calculate the confidence limit may be inadequate, so the exact method of Clopper-Pearson was also calculated. The lower limit using this exact method is 87.4%, which still meets the definition of success for the hypothesis test.

Successful deployment of the stent and stenosis relief, defined by a stent outer diameter ≥ 75% of the surrounding vessel immediately after deployment, was achieved in 41 of 42 subjects. Of the 41 patients treated with the Minima stent who met the definition of successful stenosis relief, the median increase in stenosis diameter was 3.6 mm (range: 1.5 to 6.6 mm) after stent implant, as shown in Figure 3. As shown in Figure 4, the median increase in the stent outer diameter compared to the surrounding native vessel was 131% (range: 46 to 483%).

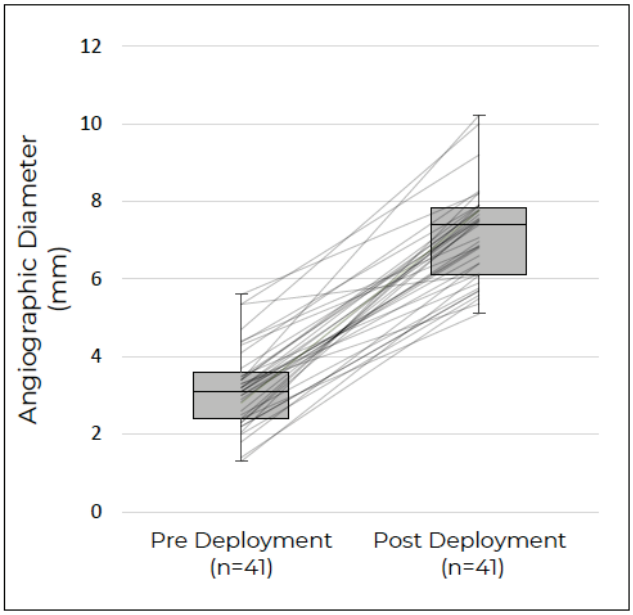

Figure 3. Change in Stenosis Diameter Pre/Post Stent Deployment

Failure to relieve the stenosis occurred in one case of Minima stent placement across the left branch of the pulmonary artery. During this case, the stent was initially placed successfully across the left branch of the pulmonary artery. However, the stent was dislodged into the main pulmonary artery during withdrawal of the delivery system and was unable to be readvanced into the left pulmonary artery (LPA). After initial attempts to readvance the deployed stent into the LPA, the stent was deployed in the subject's RPA with a 10mm balloon to ensure effective fixation. Due to the length of procedure required to place the stent into the RPA, a second Minima Stent implantation was not attempted at this time. The subject's lesion was instead treated using balloon angioplasty and logged as an efficacy failure as the lesion was not successfully treated using the Minima Stent.

In all other cases, the stent was deployed to a diameter at or above 75% of the surrounding native vessel.

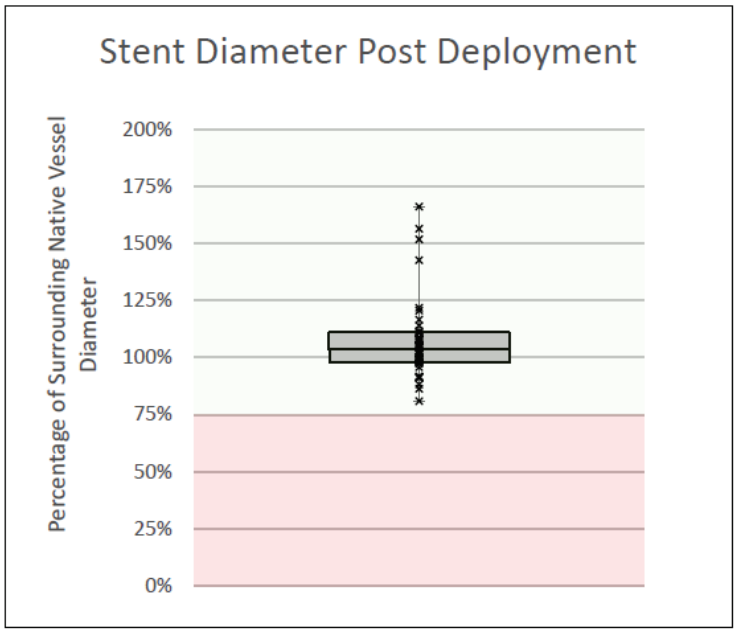

Figure 4. Deployed Stent Outer Diameter Compared to Surrounding Native Vessel (n=41)

The results of the secondary effectiveness endpoint analyses may be found in Table 12.

Table 12. Summary of Secondary Endpoints in GROWTH Study

Secondary Effectiveness Endpoint	Rate (n/N)
Peak-to-peak pressure gradient < 20 mmHg after stent placement	All treated: 95.2% (40/42) Aortic Coarctation: 95.2% (20/21)
Successful stent re-dilation, defined as an increase in the intra stent angiographic luminal diameter of within 2mm	100% (12/12)

3. **Re-dilation Safety and Effectiveness Outcomes**

To date, 12 of the 41 implanted patients have received a stent re-dilation with a median time to re-dilation of 259 days (range 104-758 days; Table 14). Eleven (11) subjects have received one additional re-dilation procedure after implantation of the Minima Stent, and one (1) one subject has received two re-dilation procedures.

For re-dilations, candidates were required to meet one or more of the following inclusion criteria:

- Development of an increase in the pressure gradient across the stent and/or stent lumen diameter less than the nominal adjacent vessel diameter, as defined as:
    - Peak Doppler echo gradient ≥ 30 mmHg and/or a mean Doppler

gradient ≥20 mmHg across the stented vessel
- Stented lumen diameter is ≤ 75% of adjacent native vessel.

Exclusion criteria for re-dilations are listed above in Section X.A.1.

Of the 13 re-dilation procedures, 10 of the re-dilation procedures were due to the stented lumen diameter being ≤ 75% of adjacent native vessel and 2 were due to an increased gradient across the stented vessel. Three (3) of the re-dilations did not meet either inclusion criteria. Physicians who performed these three re-dilations outside of the GROWTH IDE study inclusion criteria deemed it was in the best interest of the subject's treatment plan. Implanting physicians noted that re-dilation of stents within the pulmonary arteries, prior to the presence of a stenosis caused by somatic growth, might lead to distal vessel growth in some cases. One of the patients who did not meet inclusion criteria was undergoing a concomitant procedure for hypoplastic left heart syndrome, and the stented diameter was less than the normal vessel diameter. As a result, the physician re-dilated the stent during the already occurring cardiac catheterization.

All 13 re-dilation procedures (initial: n=12, secondary: n=1) have been free from procedure- or device-related SAE during re-dilation, including those listed in the secondary endpoint listed below:

- Death
- Cardiac arrest and/or emergency ECMO cannulation
- Stroke
- Limb loss
- Vessel dissection of target lesion
- Device thrombosis/occlusion
- Cardiac perforation requiring percutaneous or open surgical intervention
- Persistent cardiac arrhythmia requiring a pacemaker

Of the 13 re-dilation procedures, all were free from procedure or device related SAEs during re-dilation (Table 9). At 90-days post re-dilation, all 8 evaluable patients were free from non-elective stent explant (Table 9). One patient who is eligible for their 3-month post-re-dilation visit has not yet completed their visit (Table 9).

Table 13. Re-Dilation Subject Cohort Accountability

Activity	**Index Procedure**	**Discharge**	**1 Month Post-Index** (± 7 days)	**3 Months Post-Index**(± 7 days)	**6 Months Post-Index** (± 14 days)	**12 Months Post-Index** (± 30 days)	**Re-Dilation Procedure***	**Re-Dilation Discharge**	**3 Months Post-Re-Dilation** (± 7 days)	**Secondary Re-Dilation**	**Secondary Re-Dilation Discharge**	**3 Months Post Secondary Re-Dilation** (± 7 days)	**2 Years Post-Index** (± 45 days)	**3 Years Post-Index** (± 45 days)	**4 years Post-Index** (± 45 days)	**5 years Post-Index** (± 45 days)
% of Eligible Subjects Completed Visit (# completed / # eligible)	100% (12/12)	100% (12/12)	100% (12/12)	100% (12/12)	100% (12/12)	91% (10/11)	100% (12/12)	100% (12/12)	89% (8/9)	100% (1/1)	100% (1/1)	100% (1/1)	83% (5/6)	N/A (0 eligible at time of submission)		

A summary of subject angiographic diameter from pre-stent deployment through initial re-dilation is shown in Table 14.1 and Table 14.2. During primary re-dilations, stent luminal diameters were increased from a median of 5.6 mm (range: 2.9 to 6.7 mm) to 7.3 mm (range: 4.6 to 10.1 mm) (Table 14.1-14.2, Figure 5). This represents an average increase in diameter of 1.87 mm. All 12 Minima stents were re-expanded to within 2 mm of the surrounding native vessel at the time of re-dilation procedure, with a median difference to average surrounding vessel of -0.9 mm (range: -2.2 to 2.3mm) (Figure 5). In addition, 1 subject (Patient 8 in Table 14.2; see table caption) has undergone a secondary stent re-dilation, increasing the stent luminal diameter from 7.3 mm to 7.5 mm on Day 551 post-implantation.

Table 14.1. Angiographic Diameters of Patients Who Have Undergone Minima Stent Re-dilation

	Day 0: Pre-Implantation				Day 0: Post Implantation			Day 180: 6-Month Follow-Up			
		Diameters (mm)			Diameters (mm)				Diameters (mm)		
Lesion Location / Type	Weight (kg)	Proximal Vessel	Distal Vessel	Stenosis Lumen	Proximal Vessel	Distal Vessel	Stent Lumen	Weight (kg)	Proximal Vessel	Distal Vessel	Stent Lumen
1. Aortic vascular (Recurrent)	5.9	7.6	8.9	2.3	7.3	9.17	7.5	9.39	10.7	8.5	5.9
2. Aortic vascular (Recurrent)	7.3	17.8	8.8	3.48	7.1	9.2	7.6	9.73	8.7	8.8	6.5
3. Aortic vascular (Recurrent)	4.0	6.6	5.6	2.4	7	6.5	5.1	7.49	8.1	6.3	3.5
4. Aortic vascular (Recurrent)	3.9	5.4	5.9	2.2	5.4	5.9	5.7	6.29	6.1	6.6	4.14
5. Aortic vascular (Native)	5.1	7.8	7.7	4.4	7.8	7.6	7.1	8.595	7.5	7.5	6.7
6. Aortic vascular (Native)	5.9	13.9	9.6	4.6	13.4	10.4	7.8	8.56	13	12.6	6
7. Pulmonary artery (LPA)	5.1	7.0	5.5	3.5	7.4	5.6	6.1	12.4	4.5	7.8	5.5
8. Pulmonary artery (LPA) *	9.3	6.8	5.5	3.3	5.9	4.4	5.9	10.4	4.6	6.1	5.1
9. Pulmonary artery (LPA)**	7.4	3.9	4.1	1.3	6	6	6.1	9	7	7	7
10. Pulmonary artery (LPA)	10.7	7.7	4.5	3.1	7.7	4.6	6.8	11.3	9.3	5.3	6.6
11. Pulmonary artery (LPA)	11.9	7.6	7.5	2.83	8.4	6.9	7.7	12.8	7.5	6.9	5.2
12. Pulmonary artery (LPA)	6.2	5.3	5.1	1.4	5.4	5.3	5.5	7.77	5.46	6	5.2

Table 14.2. Pre and Post Primary Re-Dilation Angiographic Diameters of Patients Who Have Undergone Minima Stent Re-dilation

	Pre-Primary Re-Dilation					Post-Primary Re-Dilation		
Lesion Location / Type	**Day**	**Weight** (kg)	**Diameters** (mm)			**Diameters** (mm)		
			Proximal Vessel	**Distal Vessel**	**Stent Lumen**	**Proximal Vessel**	**Distal Vessel**	**Stent Lumen**
1. Aortic vascular (Recurrent)	758	13.6	9.5	11.5	3.8	9.5	11.5	7.3
2. Aortic vascular (Recurrent)	308	11.7	14	12.3	6	14.9	11.7	10.1
3. Aortic vascular (Recurrent)	192	9.34	8.6	6.1	2.9	8.8	6.5	5.1
4. Aortic vascular (Recurrent)	203	6.845	6	6.6	4.14	6	6.6	5
5. Aortic vascular (Native)	104	8.59	7.5	7.5	6.7	7.8	7.5	7.2
6. Aortic vascular (Native)	224	9.66	11.9	12.7	5.6	11.5	9.6	8.6
7. Pulmonary artery (LPA)	281	12.8 (1 year visit)	7.8	4.5	5.5	8	6	7.6
8. Pulmonary artery (LPA) *	368	10.6	5.3	7	5.8	6.4	7.3	6.9
9. Pulmonary artery (LPA)**	125	9	5.9	5.7	5.5	10	7.5	7.3
10. Pulmonary artery (LPA)	237	12.5	9.3	5.3	6.6	9.3	5.3	7.6
11. Pulmonary artery (LPA)	419	15.2	10.3	9.6	6.5	10	10	8.2
12. Pulmonary artery (LPA)	364	10.4	6.1	5.7	4	5.5	55.5	4.6

* Patient Number 8: This LPA patient with single ventricle anatomy underwent a second re-dilation on Day 551 post-implantation. Data for this subject are as follows: **Day 551 Pre-Secondary Dilations**: Weight 11.7 kg, Proximal Vessel Diameter (mm): 7.64; Distal Vessel Diameter (mm): 9.78, Stent Lumen Diameter (mm): 7.3. **Day 551 Post-Secondary Dilations**: Proximal Vessel Diameter (mm): 6.4; Distal Vessel Diameter (mm): 6.8, Stent Lumen Diameter (mm): 7.5.

** Patient Number 9: This LPA patient had biventricular circulation. All other LPA patients had single ventricle anatomies.

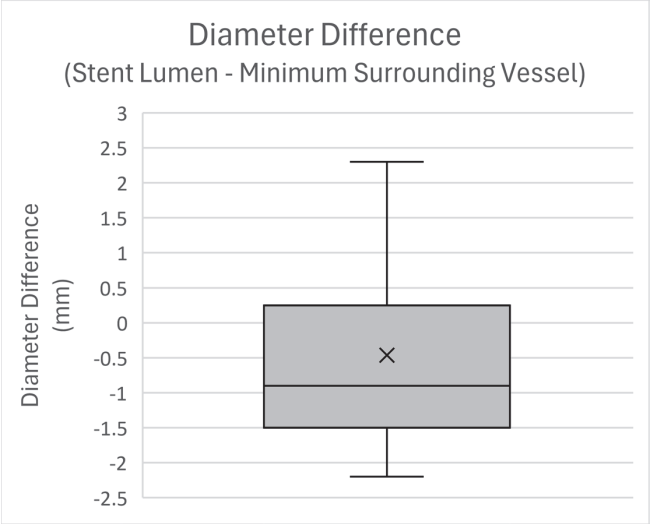

Figure 5: Luminal Diameter Difference from Surrounding Vessel After Re-dilation (n=13 re-dilation procedures)

4. **Subgroup Analyses**

The following preoperative characteristics were evaluated for potential association with outcomes: sex, age, race, implant location, and study site. No significant differences in safety or effectiveness outcomes were identified in subgroup analyses. The results stratified by subgroup are outlined in Table 15.

Table 15. Primary Effectiveness Subgroup Analyses

Subgroup	Primary Effectiveness Endpoint (N=42)
Sex	
Female	100% (20/20)
Male	95% (21/22)
P-Value	1.0000
Age	
< 6 months	100% (12/12)
6 to 24 months	83.8% (17/18)
> 24 months	100% (12/12)
P-Value	0.505
Race	
Caucasian	95.2% (21/22)
Non-Caucasian	100% (20/20)
P-Value	1.0000
Implant Location	
Pulmonary	94.4% (20/21)
Aortic	100% (21/21)
P-Value	1.0000

5. **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 9 investigators, of which 0 were full-time or part-time employees of the sponsor and 1 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: 1
- Significant payment of other sorts: 1
- 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.

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

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The assessment of effectiveness of the Minima Stent in the GROWTH study was evaluated through the ability of the device to relieve the indicated stenosis, while avoiding open surgical intervention and maintaining vessel diameter at 6 months. As evidenced by the results of the GROWTH study, the performance goal of the primary endpoint was met, with 41 out of the 42 subjects (97.2%) meeting the criteria for clinical success at the 6-month follow-up visit. As such, the GROWTH trial demonstrates the effectiveness of the Minima Stent in relieving native or acquired pulmonary artery stenoses or coarctation of the aorta. There was no

meaningful outcome differences observed in any patient subgroup (age, sex/gender, etc.).

B. Safety Conclusions

The safety assessment of the device is based on non-clinical and animal testing, and data collected in the GROWTH study, conducted to support PMA approval as described above. The results from the non-clinical laboratory and animal testing demonstrate that the device is suitable for long-term implant. The safety assessment for the GROWTH Trial was based on freedom from procedure- or device-related serious adverse events. All 42 enrolled subjects (100%) have been free from SAEs through post-procedure follow-up and continued to demonstrate no occurrence of device- or procedure-related SAEs at their 6-month follow-up visits.

C. Benefit-Risk Determination

The probable benefits of the Minima Stent System include sustained relief of native or acquired pulmonary artery stenoses or coarctation of the aorta, including maintenance of stented vessel diameter at 6 months, reduced peak-to-peak pressure gradient, and the ability to perform serial re-dilation as somatic growth requires stent expansion.

The probable risks associated with Minima Stent System include stent migration, stent embolism, stent fracture, hematoma, thrombosis, stent stenosis, vessel aneurysm or tear, bleeding, vascular complications, and death.

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 treatment of native or acquired pulmonary artery stenoses or coarctation of the aorta with the Minima Stent, 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. Preclinical and clinical studies provided in the PMA application demonstrate reasonable assurance that the Minima Stent System is safe and effective for the treatment of native or acquired pulmonary artery stenoses or coarctation of the aorta in neonates, infants, and children at least 1.5 kg in weight.

XIV. CDRH DECISION

CDRH issued an approval order on August 28, 2024. The final conditions of approval cited in the approval order are described below.

The applicant must submit a non-clinical post-approval study report which includes the results of their study conducted to experimentally determine the endurance limit of the Minima Stent material. The study will be instituted no later than 12 months of the date of PMA approval.

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

1. *Continued Follow-Up of the Premarket Cohort:* This study will consist of all living patients who were enrolled under the IDE. The objective of this study is to characterize the clinical outcomes annually through 5 years post-procedure. All available patients will be followed annually through 5 years. Data will be collected per the study protocol, including but not limited to: acute device success (stenosis relief) rates, rates of open surgical intervention required to treat Minima Stent dysfunction, stented vessel diameters (when available) over time, procedure- or device-related significant adverse event (SAE) rates related to both implantation and to any subsequent re-dilations, peak-to-peak pressure gradients after stent placement (when applicable), stent re-dilation success (increase in the intrastent angiographic luminal diameter within 2 mm of the adjacent native vessel diameter immediately after re-dilation) rates, rates of interventions following re-dilations, and all device deficiencies (e.g., migration, embolization, stent fracture leading to reintervention, stent explants) along with any resultant adverse events. Data will be descriptively assessed.

2. *New Enrollment Study:* This study is a single arm, prospective, multi-center, open-label study of patients treated with the Renata Minima Stent System in the United States. The objective of the study is to continue the assessment of device performance and capture outcome data on use of the device in real-world use. A minimum of 100 subjects will be enrolled. Follow-up will occur immediately after the initial implant procedure, at subsequent re-dilation procedures, annually, and at any additional standard of care follow-up visits (determined by the implanting physician) through 5 years post-implant. Data collected at each follow-up will be used in analysis. This study will monitor key data points related to the device and procedure, including but not limited to: acute device success (stenosis relief, freedom from open surgical intervention required to treat Minima Stent dysfunction at implantation) rates, procedure- or device-related significant adverse event (SAE) rates related to both implantation and to any subsequent re-dilations, rates of open surgical intervention required to treat Minima Stent dysfunction, peak-to-peak pressure gradients after stent placement (when applicable), rates of maintenance of the stented vessel diameters ≥ 50% of the post-implant diameter prior to re-dilation, stent re-dilation success (angiographic improvement of stenosis to >50% of the normal surrounding vessel) rates, and device deficiencies (e.g., misplacement,

migration, embolization, stent fracture leading to reintervention, stent explants) along with any resultant adverse events. Data will be descriptively assessed.

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.