SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Vascular stent for open surgical placement, thoracic aortic dissection treatment

Device Trade Name: AMDS™ Hybrid Prosthesis

Device Procode: QSK

Applicant's Name and Address: Artivion, Inc.
1655 Roberts Blvd. NW
Kennesaw, GA 30144

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P250055

Date of FDA Notice of Approval: June 26, 2026

Breakthrough Device: Granted breakthrough device status on August 9, 2019 because the device is intended to treat a potentially life-threatening disease and a reasonable expectation that the device represents a breakthrough technology with the potential to provide a clinically meaningful advantage over existing legally marketed technology.

The AMDS Hybrid Prosthesis was originally granted Humanitarian Device Exemption (HDE) approval on December 4, 2024 (H230007). The Summary of Safety and Probable Benefit is available on the CDRH website (https://www.accessdata.fda.gov/cdrh_docs/pdf23/H230007B.pdf).

II. INDICATIONS FOR USE

The AMDS™ Hybrid Prosthesis is indicated for use in patients with acute DeBakey Type I aortic dissections with malperfusion (including cerebral, visceral, renal, and peripheral malperfusion) and a primary entry tear within the ascending aorta proximal to the innominate artery, who are undergoing open surgical repair within 0-14 days of diagnosis.

III. CONTRAINDICATIONS

The AMDS™ Hybrid Prosthesis is contraindicated in the following:

- Patients who exhibit sensitivity to the implant materials (polytetrafluoroethylene [PTFE] or Nitinol [e.g., Nickel or Titanium])
- Patients with mycotic aneurysms, aortic fistulous communication with non-vascular structures, uncontrolled systemic infection

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the AMDS™ Hybrid Prosthesis labeling.

V. DEVICE DESCRIPTION

The AMDS™ Hybrid Prosthesis (AMDS) is an implantable, uncovered stent constructed from braided Nitinol wire, attached proximally to a polytetrafluoroethylene (PTFE) felt cuff with polyester (PET) sutures (***Figure 1***), which is mounted on a single-use Delivery System using an expanded polytetrafluoroethylene (ePTFE) suture (***Figure 2***). The delivery system consists of a catheter shaft with a pigtail tip that can accommodate insertion of a 0.035" guidewire through the port at the proximal handle. The stent is compressed to the diameter of the catheter shaft, and constrained just proximal to the delivery system tip by:

- An ePTFE suture which is circumferentially knotted around the entire length of the stent to stabilize the stent on the catheter. The ePTFE suture is passed through a skive in the catheter lumen and connected to the green cap (deployment mechanism).
- A clear, protective sheath located on the proximal end of the stent near the cuff, to reduce the profile of the proximal stent for atraumatic insertion of the AMDS into the transected aorta, which is removed immediately upon stent insertion.

The ePTFE suture constrains the stent during implantation; the green cap is pulled to deploy the stent (proximally, then distally) at the time of implantation. The red cap is non-functional. The AMDS is packaged in a sealed Tyvek® tray within a single unit carton, and provided sterile (Ethylene Oxide), non-pyrogenic, for single use only.

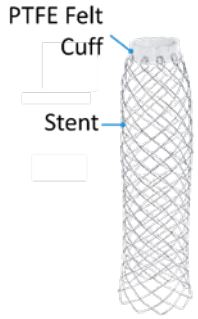

Figure 1. The AMDS Implant

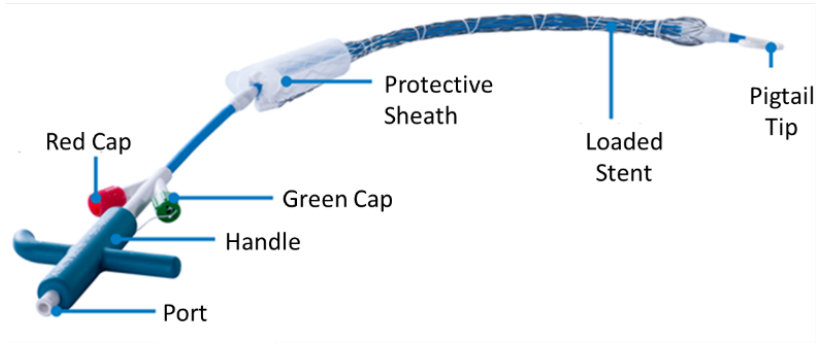

Figure 2. The AMDS Delivery System

The AMDS uses the uncovered stent component of the device implanted distal to the aortic anastomosis, to expand the true lumen and support the intimal flap, with the goal of promoting remodeling in the aortic arch. In addition, the stent is intended to expand the true lumen and improve the blood flow through the aorta and its tributaries. The cuff is used to strengthen the distal aortic anastomosis created between a conventional polyester graft and the transected aorta. The main function of the cuff is to assist in closing the false lumen at the site of the conventional graft to the aorta anastomosis. The entire procedure is performed utilizing an open chest approach while on cardiopulmonary bypass.

The AMDS is offered in eight configurations based on the stent sizing to fit a range of aortic diameters and lengths (see ***Table 1***). The stent is available in four straight models (diameters of 40mm and 55mm) and four tapered models (stent diameters tapered from 40mm to 30mm and 55mm to 40mm). The PTFE felt cuff is available in three diameters (24mm diameter for AMDS40 and AMDS4030; 28mm diameter for AMDS40c, AMDS4030c, AMDS55c, and AMDS5540c; and 32mm diameter for AMDS55 and AMDS5540). The stent is a braided design, resulting in its length being a function of its expanded diameter (i.e., the device lengthens or shortens as its diameter is reduced or increased). The AMDS has an expanded stent free surface area of >95% in all indicated aorta diameters.

Table 1. The AMDS Stent Sizing and Catheter Length

REF	Stent Shape	Aortic Diameter Stent Sizing		Aortic Length Stent Sizing		Cuff Diameter (mm)	Catheter Length (mm)	Minimum Deployment Suture Length (cm)
		D1 Proximal Diameter (mm)	D2 Distal Diameter (mm)	Stent Min Length (mm)*	Stent Max Length(mm)**			
AMDS40	Straight	20-35	25-35	153	207	24	527	135
AMDS40c						28		
AMDS4030	Tapered		20-24	159	203	24		
AMDS4030c						28		
AMDS55	Straight	36-45	36-45	187	215	32	565	150
AMDS55c						28		
AMDS5540	Tapered		27-35	185	211	32	546	145
AMDS5540c						28		

* Represents the minimum stent length when stent is expanded to the largest indicated aorta diameter
** Represents the maximum stent length when stent is expanded to the smallest indicated aorta diameter

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternatives for treatment including medical management or conventional open surgical including ascending/hemiarch repair or more extensive total arch repair, with or without a frozen elephant trunk (FET). 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 AMDS is commercially available in the countries listed in ***Table 2.*** The AMDS has not been withdrawn from marketing for any reason relating to its safety or effectiveness of the device.

Table 2. AMDS Marketing History

Europe, Middle East and Africa				
Austria	Finland	Latvia	Malta	Slovakia
Belgium	France	Germany	Netherlands	Spain
Bulgarian	Hungary	Greece/Cyprus	Norway	Sweden
Croatia	Iceland	Liechtenstein	Poland	Switzerland
Czech Republic	Ireland	Lithuania	Portugal	Turkey
Denmark	Israel	Luxembourg	Romania	United Kingdom
Estonia	Italy	Kuwait	Serbia	---
North and South America				
Argentina		Costa Rica	Jamaica	Peru
Canada		Columbia	Mexico	Venezuela
Chile		Dominican Republic	Panama	---
Asia Pacific				
Australia		Malaysia	Singapore	Thailand
Hong Kong		New Zealand	Taiwan	---

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (i.e., complications) associated with the hemiarch repair procedure with the use of the device.

Table 3. Potential Adverse Events

Allergic reaction to device, contrast media, or antithrombotic agents administered during the procedure	Occlusion, stenosis, thrombosis, thromboembolism, and/or pseudoaneurysm (arterial or venous)
Aortic enlargement or rupture, dissection, perforation, or other disease progression requiring future total arch replacement	Post-operative malperfusion leading to multi-system organ failure, limb amputation, or death
Cardiac complication or failure (e.g., arrhythmia, fast heartbeat, cardiac tamponade, heart attack, irregular blood pressure)	Pulmonary complications (e.g., edema, embolism, pneumonia, respiratory failure)
Complications at the surgical site (e.g., infection, fever, pain, or inflammation), hemorrhage and/or bleeding, fistula	Neurological, local, or systemic complications (e.g., stroke, transient ischemic attack (TIA), neuropathy, or spinal cord injury with possible paralysis)
Distal anastomotic new entry (DANE) tears leading to persistent malperfusion or requiring re-operation	Visceral ischemia or gastrointestinal symptoms (e.g., nausea/vomiting, liver failure, renal insufficiency)
Distal stent-induced new entry tears (dSINE) leading to aortic dissection or requiring reoperation	Patients may become unstable under hypothermic circulatory arrest during cardiac procedures
Death	Potential difficulties in accessing the arch branch vessels during future interventional procedures
Exposure to contrast media and/or radiation during follow-up visits to visualize the AMDS stent	Overly tortuous arch anatomy, leading to incomplete stent expansion in sections of the aorta
Malposition of the AMDS stent in the false lumen of the aorta leading to required reintervention	

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

IX. SUMMARY OF NON-CLINICAL STUDIES

Non-clinical studies were completed to evaluate the AMDS, including non-clinical bench testing, biocompatibility, sterilization, packaging, shelf-life, and animal studies.

The Summary of Safety and Probable Benefit (SSPB) containing the non-clinical studies to support the original HDE is available on the CDRH website and is incorporated by reference here. No device design changes have been made to the AMDS for the PMA approval. These data remain applicable to support the PMA. Additional non-clinical studies to support the original PMA are summarized below.

- Additional packaging validations were conducted to support a shelf-life extension from 1 to 3 years.
- A comparison was conducted confirming that the PMA device is applicable to the validated EO sterilization cycle and continues to be effective for achieving an SAL $< 10^{-6}$ in accordance with ISO 11135:2014.

A. Biocompatibility Studies

The biological evaluation of the AMDS was conducted in accordance with *ISO 10993-1:2018 Biological evaluation of medical devices — Part 1: Evaluation and testing within a risk management process* and *FDA Guidance, Use of International Standard ISO 10993-1. Chemical characterization and toxicological risk assessment was performed as summarized in* ***Table 4***.

Table 4. Chemical Characterization and Toxicological Risk Assessment - AMDS Implant

Test	Purpose	Results
Chemical Characterization and Toxicological Risk Assessment	To evaluate the amount, identity, and characteristics of extractables in the implant and assess the toxicological risks of the extractables.	Genotoxic, carcinogenic, systemic toxicity, and reproductive/developmental health risks are adequately addressed in accordance with toxicological risk assessment principles.

B. Sterilization, Packaging, and Shelf-Life Studies

The AMDS is a single-use device that is provided sterile to the end user. It is sterilized using Ethylene Oxide (EO) gas in accordance with ISO 11135 *Sterilization of health-care products — Ethylene oxide — Requirements for the development, validation and routine control of a sterilization process for medical devices*. The sterilization study confirms that the sterilization Assurance Level (SAL) of 10^{-6} is assured per sterilization plan. The ethylene oxide sterilization residuals were validated and analyzed according to ISO 10993-7. A validated aeration cycle ensures EO, ethylene cholorohydrin (ECH) and ethylene glycol (EG) residues on the sterilized products are below the limits in accordance with ISO 10993-7 *Biological evaluation of medical devices — Part 7: Ethylene oxide sterilization residuals*.

The packaging validation study was conducted to demonstrate AMDS packaging integrity in conformance with ISO 11607-1:2019: *Packaging for terminally sterilized medical devices, sterile barrier systems and packaging systems* to support the claimed shelf life of 3 years. A total of 59 Test articles were subjected to two ethylene oxide (EO) sterilization cycles. The following package integrity testing was conducted to demonstrate sterile barrier integrity with 95% confidence and 95% reliability:

- Visual Inspection in accordance with ASTM F1886/F1886M was performed for all 59 samples and found no observable damage to the sterile barrier, all the tray-lid seals were found to be continuous with no voids, cracks, or channels.

- Bubble Leak Testing in accordance with ASTM F2096 was performed for all 59 samples; all units exhibited no leaks at the determined test pressure.
- Seal Peel Testing in accordance with ASTM F88/F88M was performed using 30 samples to demonstrate a minimum tray-lid seal peel force ≥ 1 lb/in using samples taken from all four sides of the tray. All samples met the minimum seal strength.

The AMDS packaging configuration used in these studies reflects the final package configuration.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness for treatment of patients with Acute DeBakey I dissections with the AMDS as an adjunct to conventional surgery (e.g., ascending/hemiarch repair) in the US under IDE #G210218. Data from the PERSEVERE Pivotal IDE were the basis for the PMA Approval Decision. Additional foreign studies, including the DARTS I Study and Berlin Heart Study, were used to support the PMA as additional supplementary clinical data.

A. STUDY DESIGN (PERSEVERE)

Patients were treated between 17-Jul-2022 and 6-Nov-2023. The database for this PMA reflected data collected through 12-Jan-2026 and included 93 subjects. There were 26 US investigational sites. The PERSEVERE Study is a prospective, single-arm, multi-center pivotal IDE study of the AMDS for treatment of patients with Acute DeBakey I dissections with clinical or radiographic malperfusion. Patients were consented pre-operatively and were considered enrolled only after AMDS implantation. The intended study follow-up period is 5 years after AMDS surgery. The data includes complete, 1-year adjudicated follow-up data of 63 subjects; additional longer-term data is also available.

The PERSEVERE study has two co-primary endpoints to establish safety and effectiveness which are defined below:

- Patients experiencing at least one of the following major adverse events (MAEs) occurring ≤ 30-days post-procedure: all-cause mortality, new disabling stroke, new onset renal failure requiring dialysis, and myocardial infarction. The results were tested against a performance goal of 58% which was derived as the average rate of patients with ≥1 MAE estimated from 5 publications reporting outcomes following the standard of care (hemiarch procedure)[1]. Sample size was calculated assuming

[1] Bossone E, R. V., Nienaber CA, Trimarchi S, Ballotta A, Cooper JV, Smith DE, Eagle KA, Mehta RH. (2002). Usefulness of Pulse Deficit to Predict In-Hospital Complications and Mortality in Patients With Acute Type A Aortic Dissection. Am J Cardiol, 89, 851-855;
Geirsson A, S. W., Pochettino A, McGarvey ML, Keane MG, Woo YJ, Augoustides JG, Bavaria JE. (2007). Significance of malperfusion syndromes prior to contemporary surgical repair for acute type A dissection: outcomes and need for additional revascularizations. Eur J Cardiothorac Su, 32, 255-262;
Girdauskas E, K. T., Borger MA, Falk V, Mohr FW. (2009). Surgical risk of preoperative malperfusion in acute type A aortic dissection. J Thorac Cardiovasc Surg, 138, 1363-1369;
Pacini D, L. A., Belotti LM, Fortuna D, Gabbieri D, Zussa C, Contini A, Di Bartolomeo R, et al. . (2013). Acute type A aortic dissection: significance of multiorgan malperfusion. Eur J Cardiothorac Surg, 43, 820-826;
Zindovic I, G. T., Ahlsson A, Fuglsang S, Gunn J, Hansson EC, Hjortdal V, Jarvela K, Jeppsson A, et al. . (2019). Malperfusion in acute type A aortic dissection: an update from the Nordic Consortium for Acute Type A Aortic Dissection. J Thorac Cardiovasc Surg. , 157, 1324-1333.

enrollment of 84 patients with an expected drop-out rate of 10% at 30-days, which would require 93 patients to achieve the statistical assumptions under an assumed true AMDS 30-day MAE rate of 40%.

- Patients with Distal Anastomotic New Entry (DANE) tears documented by the independent Core Lab on a post-operative computed tomography with angiography (CTA) ≤ 30 days post-procedure. The results were tested against a performance goal of 45% which was derived as the weighted average rate of patients with DANE from 4 publications reporting outcomes following the standard of care (hemiarch procedure)[2]. Sample size was calculated assuming a minimum of 17 patients with an expected drop-out rate of 10% at 30-days, which would require 19 patients to achieve the statistical assumptions under an assumed true AMDS 30-day MAE rate of 10%. Considering both primary endpoints, the larger sample size of 93 patients was planned for this study.

Evaluation of the 30-day PERSEVERE data supported the HDE approval. At the time of PMA approval, complete, adjudicated 1-year follow-up data for all evaluable PERSEVERE study subjects was provided, as well as available longer-term information.

For each co-primary endpoint, a one-sided exact binomial test was used to construct the 95% exact (Clopper-Pearson) confidence interval ($\alpha = 0.025$).

External evaluation groups used during the PERSEVERE study included:

- An imaging Core Laboratory was used to perform independent assessments of computed tomography (CT)/computed tomography with angiography (CTA), X-Ray and duplex ultrasound (DUS) imaging submitted by clinical sites. The Core Laboratory assessments were used for all radiographic analyses.
- An external Clinical Events Committee (CEC) adjudicated the primary endpoint major adverse events (MAEs) and selected adverse events.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the PERSEVERE study was limited to patients who met the following inclusion criteria: ≥18 years of age or ≤80 years of age at time of surgery, with acute DeBakey type I dissection based on computed tomography angiography (CTA) and diagnosed ≤14 days from of the index event, with the presence of malperfusion (cerebral, visceral, renal, spinal cord, and/or peripheral).

[2] Bing, F., Rodiere, M., Martinelli, T., Monnin-Bares, V., Chavanon, O., Bach, V., & al., e. (2014). Type A Acute Aortic Dissection Why Does the False Channel Remain Patent After Surgery. Vasc Endovasc Surg, 48(3), 239-245;
Ergin MA, P. R., Galla JD, Lansman SL, Mendelson DS, Quintana CS, Griepp RB. (1994). Significance of distal false lumen after type A dissection repair. Ann Thorac Surg, 57, 820-824;
Rylski B, H. N., Beyersdorf F, Kondov S, Wolkewitz M, Blanke P, Plonek T, Czerny M, Siepe M. (2017). Fate of the dissected aortic arch after ascending replacement in type A aortic dissection. Eur J Cardiothorac Surg, 51, 1127-1134;
Tamura K, C. G., Hiraoka A, Totsugawa T, Sakaguchi T, Yoshitaka H. (2017). The progsnostic impact of distal anastomotic new entry after acute type I aortic dissection repair. Eur J Cardiothorac Su(52), 867-873.

Patients were not permitted to enroll in the PERSEVERE study if they met any of the following key exclusion criteria (this is not a comprehensive list):

- A primary entry tear that extends into the aortic arch or distal to the left subclavian artery
- Need for a total aortic arch replacement and/or repair or reconstruction of any part of the arch and branch vessels (including extra-anatomic bypass of the branch vessels), for any reason, as deemed necessary by the Investigator
- Aortic fistulous communication with non-vascular structure (e.g., esophagus, bronchial)
- Extensive thrombus or calcifications in the aortic arch as defined by CTA
- Excessive tortuosity precluding safe passage of AMDS as defined by CTA
- Descending thoracic aneurysm involving the proximal third (one-third) of the descending aorta and measuring >45 mm in diameter
- Aortic arch aneurysm >50 mm in diameter
- Coronary malperfusion
- In circulatory shock (i.e., systolic blood pressure <90 mmHg) at time of screening
- In extreme hemodynamic compromise requiring cardiopulmonary resuscitation at time of screening
- Suspicion of bowel necrosis (as determined by the implanting physician based on imaging observations, peritoneal signs, surgical exploration, elevated serum lactate levels, low pH, and/or acidosis)
- Clinical or radiographic signs of bowel infarction or gastrointestinal hemorrhage
- Base deficit > -10 mmol/L or -10 mEq/L
- Previous placement of a thoracic endovascular graft
- Interventional and/or open surgical procedures 30 days prior to the dissection repair
- Planned major interventional and/or open surgical procedures 30 days post the dissection repair
- Previously diagnosed with Marfan syndrome, Ehlers-Danlos syndrome, or Loeys-Dietz syndrome based on laboratory genetic testing
- Diagnosed with acute myocardial infarction in the 30 days prior to the dissection diagnosis
- Diagnosed with severe and catastrophic neurological complications in the 30 days prior to the dissection diagnosis (i.e., obtundation or coma)
- Current Stage 5 End stage chronic kidney disease (estimated Glomerular Filtration Rate [eGFR] ≤ 15 mL/min)

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at discharge/30-days (+/- 14 days), 3-6-months (+/- 7 days), 12-months (+/- 8 weeks), and annually through 5-years (+/- 12 weeks). The assessments performed at each visit are listed in ***Table 5***. Adverse events were recorded at all visits.

Table 5. PERSEVERE Study Visit Schedule of Assessments

PROTOCOL ACTIVITY	Visit 1	Visit 2		Visit 3	Visit 4	Visit 5	Visits 6-9
	Pre-Op	Procedure	Discharge	30-days[1]	3-6 months	1 year	2- 5 years
	≤14 days from procedure	<24 hrs post-op	≥24 hrs post-op	+/-14 days	+/-7 days	+/- 8 wks	+/- 12 wks
Informed Consent, Eligibility and Baseline Assessments	X						
Concomitant Medication and Patient Exam	X		X	X	X	X	X
Blood tests	X	X	X	X	X	X	X
CT /CTA Imaging Evaluation (chest/ abdomen & pelvis)	X			X	X	X	X
Brain Imaging (CT and/ or MRI) and NIHSS in patients with stroke per site procedure	*	*	*	*	*	*	*
Electrocardiogram (ECG)			X				
mRS	X		X		*	*	*
Procedure & Device Sizing and Technical Success		X					
Adverse Events and additional Post-Op Procedures		X	X	X	X	X	X
Quality of Life Assessment (SF-12v2)			X	X	X	X	X
Procedural/Treatment Success				X	X	X	X

X=Study Specific Activity [includes data collection only]

[1] If the patient's hospital discharge was ≥14 days after surgery, then data collected at discharge was not recollected for Visit 3 unless discharge occurred prior to 30-day window and new protocol-specified information is available (ex. any SAE incidence) within the Visit 3 window.

* Need is determined by site's standard of care or as event occurs

Abbreviations: mRS =modified Rankin Score; NIHSS = National Institutes of Health Stroke Scale; Pre-op = preoperative; Post-op= post-operative, wks = weeks; hrs=hours; SF-12 = 12-item Short Form Survey

3. Clinical Endpoints

The co-primary endpoints include the following:

- Patients experiencing at least one of the following major adverse events (MAEs) occurring ≤ 30-days post-procedure: all-cause mortality, new disabling stroke, new onset renal failure requiring dialysis, myocardial infarction. The co-primary endpoint was compared to a performance goal of 58%.
- Patients with DANE tears documented by the independent Core Lab on a post-operative CTA ≤ 30-days post-procedure. The co-primary endpoint was compared to a performance goal of 45%.

The performance goals are based on literature reported rates of MAEs[3] and DANE[4] in malperfusion patients with the surgical procedure (without AMDS).

The PERSEVERE pivotal study primary endpoint analysis supported the HDE. Additional longer-term data supported the PMA.

The secondary safety endpoints included are assessed at all post-discharge visits:

- Analysis of rates of MAEs, mortality, additional aortic procedures, device related events, false lumen response, and supra-aortic branch vessel patency. Additional major adverse events included in the secondary endpoint analysis are listed below:
    - Aortic rupture
    - Bowel ischemia
    - Hypersensitivity
    - Myocardial infarction
    - New disabling and non-disabling stroke
    - New postoperative paraplegia/paraparesis
    - New postoperative organ malperfusion, including cerebral, coronary, visceral, renal, spinal cord, and peripheral
    - New onset renal failure requiring dialysis
    - Pseudoaneurysm
    - Recurrent laryngeal or phrenic nerve injury
    - Respiratory failure (need for reintubation or ventilator dependence >48 hours)
    - Severe heart failure requiring mechanical circulatory support
    - Thromboembolic adverse events

Additional effectiveness endpoints included:

- Remodeling outcomes (measurement and change in total aortic diameter, true lumen diameter, false lumen diameter, clinically meaningful (≥ 6.0mm) true lumen

3 Zindovic et al., "Malperfusion in Acute Type A Aortic Dissection."; Pacini et al., "Significance of Multiorgan Malperfusion."; Girdauskas et al., "Surgical Risk of Preoperative Malperfusion in Acute Type A Aortic Dissection."; Geirsson et al., "Significance of Malperfusion Syndromes Prior to Contemporary Surgical Repair for Acute Type A Dissection."; Bossone et al., "Usefulness of Pulse Deficit to Predict In-Hospital Complications and Mortality in Patients with Acute Type A Aortic Dissection."

4 Bing et al., "Type A Acute Aortic Dissection: Why Does the False Channel Remain Patent After Surgery."; Ergin et al., "Significance of Distal False Lumen After Type A Dissection Repair."; Rylski et al., "Fate of the Dissected Aortic Arch After Ascending Replacement in Type A Aortic Dissection."; Tamura et al., "Prognostic Impact of Distal Anastomotic New Entry After Acute Type I Aortic Dissection Repair."

expansion, and false lumen response were summarized descriptively at each post-discharge visits.

The secondary composite endpoints included technical and procedural success rates as defined below:

- Technical Success at conclusion of the index procedure: Successful delivery and accurate placement of the device at the intended implantation site and retrieval of the device delivery system, patency of the device and aortic arch vessels at the conclusion of the procedure, and no need for unanticipated or emergency surgery to correct a device malfunction or reintervention due to device-related complications.
- Procedural Success at 30-days post-procedure: Technical success with the absence of the following: death, major adverse ischemic events, including new disabling stroke (modified Rankin Score [mRS] > 2 with change from baseline > 1), new postoperative paraplegia or paraparesis, new ischemia due to branch vessel compromise related to the procedure, distal procedure-related thromboembolic events, and any additional unplanned surgical or interventional procedures related to the device since completion of the original procedure.

B. ACCOUNTABILITY OF PMA COHORT

At the time of database lock, of 93 subjects enrolled in the PMA study, 63 subjects (67.7%) are available for analysis at 1-year.

The primary analysis population includes all patients who were enrolled, treated with the AMDS device, and had evaluable data for the co-primary endpoints. The Safety population (SP) includes all patients treated with the AMDS device. Analyses in this document are based on the Safety population.

Patient follow-up, imaging quality, and patient status at each follow-up time point is shown in ***Table 6.***

Table 6. Follow-up Compliance and Imaging Quality Summary[5]

Visit Details			Subjects with Data for Visit and Subject Status					Imaging Compliance and Quality to Assess Parameters of Interest[4]		
Visit #	Visit Description[1]	Eligible for follow-up[2]	Subjects with Data for Visit[8]	Subjects with Missed Visit	Death	LTF/ Withdrawn	Not due for next visit[3]	CT/CTA read by Core Lab	TL Diameter at Zone 3	DANE
		#	# (%)	# (%)	# (%)	# (%)	# (%)	# (%)	# (%)	# (%)
1	Pre-Op	93	93(100.0%)	NA	NA	NA	0(0.0%)	93(100.0%)[5]	91(97.8%)[5]	NA
2	Procedure through Discharge	93	93(100.0%)	NA	NA	NA	0(0.0%)	57(61.3%)	49(52.7%)	44(47.3%)
3	30-days (+/- 14 days)	93	79(84.9%)[7]	5(5.4%)[8]	9(9.7%)[7]	0(0.0%)	0(0.0%)	69(82.1%)[6]	64(76.2%)[6]	62(73.8%)[6]
4	31-180 days	84	71(84.5%)	9(10.7%)	4(4.8%)	0(0.0%)	0(0.0%)	69(86.3%)	66(82.5%)	65(81.3%)
5	181-365 days	80	63(78.8%)	7(8.8%)	6(7.5%)	4(5.0%)	0(0.0%)	56(80.0%)	53(75.7%)	54(77.1%)
6	366-730 days	70	48(68.6%)	11(15.7%)	4(5.7%)	7(10.0%)	34	41(65.1%)	39(61.9%)	38(60.3%)

[1]Some of the time periods reflect the time between scheduled visits; however, some visits may have deviated from the listed period due to compliance issues.
[2]Eligible for follow-up = eligible for follow-up from the previous interval – [death+LTF+not due for next visit]
[3]Those subjects that are "Not due for next visit" are those subjects that are not within the follow-up window for the next interval.
[4]The data represents the existence of available data, and these numbers do not reflect incidence of reported events.
[5]Two additional pre-operative CTAs were retrieved and assessed after the HDE analysis; data here reflects the additional data.
[6]One additional 30-day CTA was assessed after the HDE analysis due to delays in obtaining the CTA; data here reflects the additional data.
[7]After the HDE analysis, 1 additional 30-day visit occurred.
[8]There are no pending visits through 2 years at the time of data export.
Note: There are changes from data presented in the HDE due to minor reorganization of data presentation.

Abbreviations: EFU=Eligible for Follow-up, NA=Not applicable, CT=computed tomography, CTA=computed tomography angiography, TL=true lumen, LTF=lost-to-follow-up, DANE= distal anastomotic new entry

C. STUDY POPULATION DEMOGRAPHICS AND BASELINE PARAMETERS

1. Demographics and Baseline Characteristics

The demographics of the study population are typical for an acute DeBakey Type I Dissection study performed in the US.

A total of 93 patients with acute DeBakey Type I dissection were enrolled in PERSEVERE. Patients were mostly male (78.5%) with a mean age of 58.7 ± 9.52 years. All patients presented with preoperative clinical (81.7%) or radiographic (18.3%) malperfusion in at least one organ system. Comorbidities most commonly included history of arterial hypertension (37.6%), chronic kidney disease (35.5%), cardiac arrhythmia (20.4%), diabetes (15.1%), coronary artery disease (CAD) (11.8%), cancer (11.8%), and chronic pulmonary obstructive disease (COPD) (10.8%) (see ***Table 7***).

Table 7. Patient Baseline Characteristics (PERSEVERE)

Characteristics	**Total Patients (n=93)[4]**
Demographics and Baseline Characteristics	
Age (years)[1]	58.7 ± 9.52
Male	78.5%
Preoperative Clinical Malperfusion[1]	76 (81.7%)
Preoperative Radiographic Malperfusion Only[1]	17 (18.3%)
Race	
Asian	1 (1.1%)
Black or African American[1]	21 (22.6%)
White	56 (60.2%)
Other[1]	2 (2.2%)
Unknown or missing[1]	13 (14.0%)
Ethnicity	
Non-Hispanic[1]	75 (80.6%)
Hispanic[2]	10 (10.8%)
Unknown[1]	8 (8.6%)
	# (%) (n=93)
Aortic Arch Anatomy *(>1 anatomy may be applicable to 1 patient)*	
Normal (3 great vessels) [1]	67 (72.0%)
Bovine Arch[1]	22 (23.7%)
Isolated Vertebral[1]	5 (5.4%)
Not documented/assessed[1]	1 (1.1%)
Primary entry tear in Zone 0 documented by Core Lab[1]	87 (93.5%)
Primary entry tear beyond Zone 0 documented by Core Lab[1]	3 (3.2%)
Primary entry tear data missing[1]	3 (3.2%)
Medical History	**# (%) (n=93)**
Cardiac Arrhythmia[3]	19 (20.4%)
Congestive Heart Failure (CHF) [3]	4 (4.3%)

Table 7. Patient Baseline Characteristics (PERSEVERE)

Characteristics	Total Patients (n=93)[4]
Coronary Artery Disease (CAD) [3]	11 (11.8%)
Chronic Pulmonary Obstructive Disease (COPD) [3]	10 (10.8%)
Peripheral Arterial Disease[3]	0 (0%)
Hypertension (stage 1 and above) [2]	35 (37.6%)
Liver Disease	5 (5.4%)
Cancer	11 (11.8%)
Chronic Kidney Disease[2]	33 (35.5%)
Diabetes (Type I or II) [2]	14 (15.1%)
Prior Stroke	5 (5.4%)
Prior TIA	5 (5.4%)
Prior Myocardial Infarction	3 (3.2%)
Prior Thromboembolic Event (DVT)	4 (4.3%)
Prior CABG[3]	0 (0%)
Prior PCI	5 (5.4%)
Previous Cardiac Intervention – Other	4 (4.3%)

[1]This value has been updated from that presented for the HDE to address data entry errors.
[2]The field description has been altered from the HDE for clarification.
[3]Formatting of the value has been updated from that presented in the HDE for consistency.
[4] One patient was identified to have end stage renal disease after HDE approval. This is one of the study's exclusion criteria and the data presented in this table and below contains data including the patient despite the major protocol deviation.

2. *Procedural Characteristics*

Hemiarch repair was performed in 100% of patients, with concomitant procedures performed in 85% of patients. The duration for the total procedure and AMDS implantation is shown in ***Table 8***.

Table 8. Procedural Characteristics (PERSEVERE)

Procedural Characteristics		**% Patients**
Concomitant Procedures	None (Hemiarch + AMDS only)[1]	14 (15.1%)
	Aortic Valve Resuspension[2]	35 (37.6%)
	Aortic Root Repair or Replacement[1]	37 (39.8%)
	Aortic Valve Repair or Replacement[1]	22 (23.7%)
	Coronary Artery Bypass Surgery (CABG)	5 (5.4%)
	Other[1]	23 (24.7%)
		Median (Range)
Procedure Times	AMDS Deployment Time (min)[3]	4 (0-11)
	Cardiopulmonary Bypass (CPB) Duration Time (min) [1]	176.0 (91-403)
	Hypothermic Circulatory Arrest (min)	28 (0-168)
	Cerebral Perfusion Time (min)	28 (10-230)
	Total AMDS Implantation Time (min)[4]	15 (5-32)

[1]This value has been updated from that presented for the HDE to address data entry errors.
[2]This value has been added from that presented for the HDE to address data completeness.
[3] Defined as time from AMDS delivery system insertion to delivery system removal.
[4] Defined as time from AMDS delivery system insertion to completion of AMDS to aorta anastomosis.

D. SAFETY AND EFFECTIVENESS RESULTS

1. Co-Primary Endpoints

The analysis of the co-primary endpoints was based on the available data through 30-days follow-up visit for all 93 subjects. Complete, adjudicated data included in the co-primary endpoint for major adverse events (MAE) occurring within 30 days post-procedure are shown in ***Table 9***.

A total of 78/93 (85%) patients had a CTA which confirmed absence of DANE prior to (during the pre-discharge CTA assessment) or during 30-day follow-up. Therefore, 15 patients had an unknown DANE status through 30-days.

The imaging Core Lab reported no subjects with DANE (95% CI: 0%, 3.9%) compared to the performance goal of 45%. Patients experiencing at least one of the MAEs was 26.9% (95% CI: 18.4%, 37.4%) compared to the performance goal of 58%. The co-primary endpoints were met based upon the data through 30-days.

Sensitivity Analysis
Considering the worst-case scenario for missing DANE data, a DANE rate of 15/93 (16.1%) [95% CI: 9.32, 25.2] was calculated and an exact binomial test with one-sided p-value still revealed a statistically significant difference between the worst-case DANE rate and the performance goal ($p<0.001$).

Table 9. Primary Endpoint Events through 30-Days (PERSEVERE)

	Total Number of Patients ≥1 CEC Adjudicated Event # (%), n=93
All-cause Mortality	9 (9.7%)
New Disabling Stroke[1]	10 (10.8%)
New Onset Renal Failure Requiring Dialysis	18 (19.4%)
Myocardial Infarction	0 (0%)
Co-Primary Endpoint: Total # of Patients with ≥ 1 MAE[1, 2]	25 (26.9%) (95% CI: 18.4, 37.4)
	Total Number of Patients Core Lab Reported #(%) n=78[3]
Co-Primary Endpoint: # of Patients with Distal Anastomotic New Entry (DANE) Tear	0 (0%) (95% CI: 0%, 3.9%)

[1] This value has been updated from that presented for the HDE to address a data entry error; a subject's pre-operative mRS score was re-evaluated after contradicting information on pre-operative stroke was discovered.
[2]Of the 38 MAEs (1 patient had 2 strokes) in 25 patients, 17 were adjudicated by the CEC as at least possibly device related and 36 were adjudicated by the CEC as at least procedure related.
[3]The denominator has been updated from that presented in the HDE to reflect the totality of subjects with CT data available pre-discharge or at the 30-day visit.

Definition: New disabling stroke (defined as a change in the modified Rankin Score (mRS) > 2, with a change from baseline >1).

2. Secondary Endpoints

Secondary endpoints included secondary safety endpoint analysis, technical success and procedural success, and aortic remodeling in the treated segment.

Safety Events through 2-Year Available Follow-Up

The following safety events were observed at any point through 2-year follow-up:

- all-cause death (23/93, 24.7%)
  - CEC Adjudicated: At least Possibly Device Related 4/23; At least Possibly Procedure Related 9/23
- new disabling stroke (11/93, 11.8%)
  - 13 events occurred in 11 patients. CEC Adjudicated: At least Possibly Device Related 13/13, At least Possibly Procedure Related 11/13
- new non-disabling stroke (6/93, 6.5%)
  - 7 events occurred in 6 patients. CEC Adjudicated: At least Possibly Device Related 7/7, At least Possibly Procedure Related 3/7
- new onset of renal failure requiring dialysis (19/93, 20.4%)
  - CEC Adjudicated: At least Possibly Device Related 3/19, At least Possibly Procedure Related 17/19
- myocardial infarction (2/93, 2.2%)

    - CEC Adjudicated: At least Possibly Device Related 0/2, At least Possibly Procedure Related 2/2
- respiratory failure (18/93, 19.4%)
- thromboembolic events (8/93, 8.6%)
- new post-operative organ malperfusion (4/93, 4.3%)
- pseudoaneurysm (3/93, 3.2%)
    - CEC Adjudicated: At least Possibly Device Related 2/3, At least Possibly Procedure Related 3/3
- bowel ischemia (2/93, 2.2%)
    - CEC Adjudicated: At least Possibly Device Related 0/2, At least Possibly Procedure Related 1/2

Aortic rupture, hypersensitivity, new post-operative paraplegia or paraparesis, recurrent laryngeal or phrenic nerve injury, and severe heart failure requiring mechanical circulatory support were not observed. Through 2-years, 10 patients required 15 additional aortic procedures, including intervention on any segment of the aorta or main aortic branches. Procedures were performed open (9) or either endovascular or percutaneous (6) and indicated for aortic aneurysm growth (7), pseudoaneurysm (4), lower limb ischemia (1), aortic thrombus (1), right common carotid artery stenosis (1), and endocarditis (1). There were no unanticipated device-related reoperations or complete explants; 1 partial explant was required after 1-year during an open thoracoabdominal repair.

Technical and Procedural Success
Technical success (delivery, deployment, catheter retrieval, AMDS and aortic arch vessel patency, freedom from device-related malfunction or reintervention) was reported in 98.9% of patients (n=92); in one patient the AMDS stent was inadvertently implanted in the false lumen through a distal secondary entry tear false lumen with no injury or clinical sequelae.

Procedural success was achieved in 75 of 93 patients (80.6%). The value has changed since data presented for the HDE due to data entry errors and the collection of new information. Eighteen patients did not achieve procedural success for one or more reasons. Categorization is summarized by the most significant reason for each patient and include the following reasons: 9 patients died, 8 patients had new disabling stroke (including one patient who failed technical success), and 1 patient who had new ischemia due to branch vessel complication. There were no cases of new paraplegia or paraparesis.

Device Related Events through Available Follow-up (Core Lab)
Considering all CTAs evaluated by the imaging Core Lab, there was no radiographic evidence of DANE, device migration, stent fracture, kink, or twist. D-SINE was observed in 2 patients and stent narrowing was identified by the Core Lab in 5 patients through all available follow-up; there are no reports of clinical sequelae associated with the occurrence of stent narrowing and d-SINE.

Aortic Remodeling and Patency through Available Follow-Up (Core Lab)

The aorta was analyzed at zones 1-3 to evaluate the change in maximal total aortic diameter, true lumen and false lumen diameter (***Table 10***), as well as false lumen status (***Table 11***). Aortic zones were defined by the Society of Thoracic Surgeons (STS)/Society of Vascular Surgeons (SVS) Aortic Zone Classification (see ***Figure 3***). The number of scans for each endpoint at each timepoint varied due to CTA quality issues, as well as anatomical and implant variations.

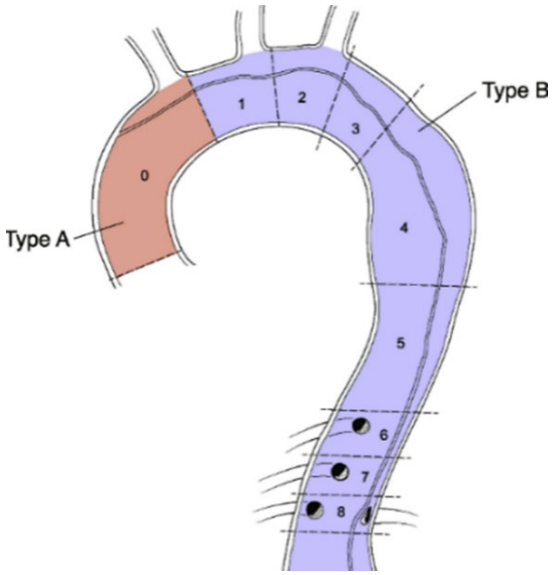

Figure 3. STS/SVS Aortic Zone Classification

Table 10. Aortic Remodeling – Diameter Change From Baseline (Pre-Procedure) Through Available Follow-Up [Mean (SD)] (Core Lab)

Aortic Zone	Total Aortic Diameter (mm)			True Lumen Diameter (mm)			False Lumen Diameter (mm)		
	30-Days (n=69)[1]	1-Year (n=56)	2-Years (n=41)	30-Days (n=69)[1]	1-Year (n=56)	2-Years (n=41)	30-Days (n=69)[1]	1-Year (n=56)	2-Years (n=41)
Zone 1	0.35 (3.409)	1.30 (3.680)	2.62 (3.537)	12.33 (4.954)	13.96 (4.897)	14.88 (6.380)	-12.01 (5.310)	-12.66 (5.317)	12.26 (5.926)
Zone 2	1.34 (3.607)	2.78 (3.900)	4.36 (3.847)	12.21 (4.972)	13.26 (4.998)	14.83 (5.886)	-10.90 (5.644)	-10.41 (6.159)	-10.31 (6.957)
Zone 3	3.15 (3.412)	5.85 (6.238)	8.71 (6.880)	6.87 (5.457)	7.64 (5.397)	8.36 (5.659)	-3.63 (6.210)	-1.88 (8.646)	0.35 (9.209)
Zone 4	4.10 (3.573)	7.84 (5.671)	10.34 (6.901)	7.94 (6.363)	7.70 (5.628)	8.90 (5.831)	-3.79 (6.997)	0.20 (8.330)	1.44 (9.103)
Zone 5	3.28 (1.962)	6.26 (3.687)	8.55 (4.178)	11.79 (7.640)	10.89 (7.925)	10.61 (9.210)	-8.48 (7.762)	-4.67 (8.530)	2.06 (10.711)

[1] Two additional baseline CTAs were retrieved and assessed after the analysis for HDE; this table reflects the additional data.

Table 11. Aortic Remodeling – False Lumen Thrombosis Status Through Available Follow-Up [n (%)] (Core Lab)

Aortic Zone	30-Days (n=69)[1,2]				1-Year (n=56)[1]				2-Years (n=41)[1]			
	CT	PT	PAT	NA	CT	PT	PAT	NA	CT	PT	PAT	NA
Zone 1	12 (15.2%)	29 (36.7%)	10 (12.7%)	21 (26.6%)	15 (23.8%)	27 (42.9%)	4 (6.3%)	10 (15.9%)	8 (17.4%)	14 (30.4%)	3 (6.5%)	14 (30.4%)
Zone 2	8 (10.1%)	41 (51.9%)	12 (15.2%)	11 (13.9%)	14 (22.2%)	35 (55.6%)	4 (6.3%)	3 (4.8%)	8 (17.4%)	23 (50.0%)	6 (13.0%)	2 (4.3%)
Zone 3	5 (6.3%)	46 (58.2%)	9 (11.4%)	12 (15.2%)	8 (12.7%)	38 (60.3%)	6 (9.5%)	4 (6.3%)	6 (13.0%)	29 (63.0%)	3 (6.5%)	1 (2.2%)
Zone 4	1 (1.3%)	50 (63.3%)	9 (11.4%)	12 (15.2%)	4 (6.3%)	44 (69.8%)	4 (6.3%)	4 (6.3%)	3 (6.5%)	31 (67.4%)	4 (8.7%)	1 (2.2%)
Zone 5	1 (1.3%)	45 (57.0%)	13 (16.5%)	13 (16.5%)	3 (4.8%)	44 (69.8%)	6 (9.5%)	3 (4.8%)	3 (6.5%)	31 (67.4%)	4 (8.7%)	1 (2.2%)

[1]Missing data is excluded in the table, which includes 7 (8.9%) patients at 30-days, 7 (11.1%) patients at 1-year, and 7 (15.2%) patients at 2-years
[2] Two additional baseline CTAs were retrieved and assessed after the HDE analysis; this table reflects the additional data.

Abbreviations: CT: Completely thrombosed, PT: Partially thrombosed, PAT: Patent, NA: Not assessed

Supra-aortic branch vessel patency was evaluated through 2-years. At 30-days, 1-year, and 2-year the innominate artery (IA) patency was, 95.2% (59/62), 96.2% (52/54), and 92.3% (36/39) respectively. The left common carotid patency was 95.2% (59/62), 98.1% (53/54), and 92.3% (36/39) at 30-day, 1-year and 2-year respectively. The Left Subclavian Artery patency was 96.8% (60/62), 100% (54/54) and 97.4% (38/39) at 30-days, 1-year and 2-year respectively. There were no artery occlusions in the Innominate artery (IA). Both occlusions that occurred were due to intentional surgical interventions.

3. Subgroup Analyses

The following preoperative characteristics were each evaluated for potential association with outcomes: age (<65 or ≥65 years old), female/male, BMI (<28 kg/m^2 or ≥28 kg/m^2), and radiographic/clinical pre-operative malperfusion. No correlations were found between the respective preoperative characteristics and study outcomes.

4. Pediatric Extrapolation

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

E. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 96 investigators of which none were full-time or part-time employees of the sponsor, with one investigator having disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

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

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

There is additional experience with the AMDS device outside of the United States (US). Key studies conducted outside of the US are briefly summarized below.

DARTS I Study

The DARTS I Study is a prospective, single-arm, multi-center study of AMDS in patients with Acute DeBakey I dissections. DARTS I enrolled 46 eligible subjects at 5 sites in Canada (n=39) and 1 site in Germany (n=7) from March 2017 to January 2019. Subjects were followed for 5-years. An independent imaging core laboratory evaluated the imaging

obtained during the study. The study did not include a Clinical Events Committee nor a Data Safety Monitoring Board. DARTS I and PERSEVERE enrolled similar patient populations with the key difference being DARTS I enrolled subjects with both preoperative malperfusion (25/46) and non-malperfusion (21/46) and PERSEVERE included only patients with preoperative malperfusion. At 30-days, 31/38 (81.6%) of subjects had data for visit and 29/31 (76.3%) had CT/CTA data read by Core Lab. At 1-year, 35/36 (97.2%) of subjects had data for visit and 34/35 (97.1%) had CT/CTA data read by the Core Lab. At 3-years, 33/33 (100%) of subjects had data for the visit and 30/33 (90.9%) had CT/CTA read by the Core Lab. At 5-years, 27/27 (100%) of subjects had data for the visit and 25/27 (92.6%) had CT/CTA read by the Core Lab.

Key outcomes are summarized. Successful device deployment was reported in 43/46 subjects (93.5%) and 3/46 (6.5%) subjects had missing data. There were 12/46 (26%) deaths total at 5-years. There were 7 deaths ≤ 30-days from the procedure none were attributed by the sites as related to the procedure or device. There were 5/46 (10.8%) additional deaths beyond thirty days, of which one was considered by the investigator to be possibly related to the procedure and the device. A total of 11/46 subjects (23.9%) experienced neurological complications (all strokes) within the first 30 days, including 8/46 subjects (17.4%) who had new stroke (defined as a new disabling or non-disabling stroke in a subject absent of prior stroke or stroke symptoms pre-procedure). After 30-days, two additional subjects had a stroke making the total number of subjects with a stroke 10/46 (21.7%). In total, 4/46 subjects (8.7%) had evidence of device narrowing on ≥ 1 follow-up CTA; 1/46 subject (2.2%) had a device twist noted, along with narrowing. The core lab defined narrowing as a 50% reduction in device diameter in comparison to diameters directly proximal or distal to the measurement area. In all cases of narrowing, there was no clinical sequelae. There were no device fractures, device kinks, DANE or d-SINE noted by the Core Lab through 5-years. Complete or partial false lumen thrombosis was observed in 58-74% of subjects in Zone 1, 59-74% in Zone 2, and 65-83% in Zone 3 at pre-discharge through 5-years, with an increase observed over time.

The secondary endpoints also provide evidence of positive aortic remodeling, including total aortic diameter (TAD) stability, TL expansion, and FL reduction through 5-years in the treated aortic zones (1-3). Average TAD change from baseline was ≤2.1 mm in Zone 1, ≤2.7 mm in Zone 2, and ≤6.8 mm in Zone 3 through 5 years. Average TL expansion was ≥13.4 mm in Zone 1, ≥12 mm in Zone 2, and ≥7.3 mm in Zone 3 through 5 years, with an increase in expansion documented between pre-discharge and 5 years. Average FL reduction was ≥11.3 mm in Zone 1, ≥9.4 mm in Zone 2, and 0.6 mm in Zone 3 through 5-years; at 5-years, FL reduction was sustained in Zone 1, there was less reduction in Zone 2, and there was loss of reduction in Zone 3 compared to pre-discharge.

Berlin Heart Study

The Berlin Heart Study published by Montagner et al.[5] provides real-world evidence of the commercial use of the AMDS in Europe. The AMDS was implanted in a total of 100 patients with acute DeBakey type I dissection at the Berlin Heart Center between February 2018 and June 2021. Patient baseline demographics illustrate the severity of the disease,

[5] Montagner M, Kofler M, Seeber F, Pitts L, Starck C, Sündermann SH, Kurz S, Grubitzsch H, Falk V, Kempfert J. The arch remodelling stent for DeBakey I acute aortic dissection: experience with 100 implantations. Eur J Cardiothorac Surg. 2022 Jul 11;62(2).

with 35% of the cohort having acute neurological deficit and 46% with malperfusion; the remaining 54% of patients did not have malperfusion. Standard implantation technique was used, with moderate hypothermia at 28°C and 80% of cases performed under unilateral antegrade selective cerebral perfusion (median time of 40 minutes). Implantation was completed in 96% cases, and the AMDS stent was fully expanded in 97% of implanted patients; the stent did not fully expand in three patients. The likely causes of failed deployment were accidental suture severing during deployment due to mishandling, narrowing due to overly tortuous arch anatomy. Thirty-day follow-up data included 18% mortality, and operation-related new postoperative neurological deficit in 8% of patients. AMDS was able to induce complete or partial thrombosis of the false lumen in the descending aorta in 76% of subjects with adequate imaging, with resolution of pre-operative malperfusion in 80% of the 46 patients. Surgical and/or endovascular reintervention in 13 patients was attributed to persisting malperfusion; in most of these cases a non-covered extension of the AMDS or targeted stenting of aortic branches was performed.

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, 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 PERSEVERE IDE study evaluated AMDS in the open surgical treatment of patients with acute DeBakey type I aortic dissection, with evidence of clinical and/or radiographic malperfusion. Key device effectiveness findings from the available data include:

- 92/93 (98.9%) of procedures achieved technical success.
    - 1 patient did not achieve technical success because while the majority of the device was implanted in the true lumen, the distal portion of the AMDS was inadvertently implanted into the false lumen through a secondary entry tear.
- 0/78 (0%) patients had DANE on CTAs taken within 30-days post-procedure compared to the performance goal of 45%; the performance goal was met. No incidence of DANE was reported on any post-operative CA through 2-years.
- 36/53 (67.9%) patients experienced true lumen expansion ≥6.0 mm at 1-year in Zone 3. Data not available beyond 1-year.

- 0/93 (0%) patients had device migration, stent fracture, stent kink or twist through 2-years.
- 5/93 (5.4%) patients had stent narrowing and 2/93 (2.2%) had d-SINE through 2-years. There are no related reports of clinical sequelae.
- Through 2 years, 10/93 (10.8%) patients had an additional aortic procedure. There was 1 partial explant during an open thoracoabdominal repair.

B. Safety Conclusions

The risks of the device are based on non-clinical and animal testing, and data collected in the PERSEVERE study, conducted to support PMA approval as described above. Key device safety findings at 30 days from PERSEVERE include:

- At 30-days, 25/93 (26.9%) of patients experienced ≥ 1 MAE (Major Adverse Event) compared to the performance goal of 58%; the performance goal was met.
    - 9/93 (9.7%) all-cause mortality
    - 10/93 (10.8%) new disabling stroke
    - 18/93 (19.4%) new onset renal failure requiring dialysis
    - 0/0 (0%) myocardial Infarction
- At 1-year and 2-years, rates of those MAES were as follows:
    - All-cause mortality: 19/93 (20.4%) at 1-year; 23/93 (24.7%) at 2-years
        - Device-related mortality: 4/93 (4.3%) through 1 and 2-years
        - Procedure-related mortality: 9/93 (9.7%) through 1 and 2-years
    - New on-set renal failure requiring dialysis: 19/93 (20.4%) through 1 and 2-years
        - CEC Adjudicated: At least Possibly Device Related 3/19, At least Possibly Procedure Related 17/19
    - New disabling stroke: 11/93 (11.8%) through 1 and 2-years
        - 13 events occurred in 11 patients. CEC Adjudicated: At least Possibly Device Related 13/13, At least Possibly Procedure Related 11/13
    - Myocardial Infarction: 2/93 (2.2%) through 1 and 2-years
        - CEC Adjudicated: At least Possibly Device Related 0/2, At least Possibly Procedure Related 2/2

The PERSEVERE study data demonstrate a reasonable assurance of the safety of the AMDS device for the proposed intended use.

C. Benefit-Risk Determination

The probable benefits of the device are based on data collected in the PERSEVERE Study to support PMA approval as described above. The clinical benefits to a patient implanted with the AMDS include reduced mortality in patients with preoperative malperfusion, complete closure of the intimal flap, positive aortic remodeling in the arch, and reduction of DANE tears and associated reoperations, when compared with patients treated with a standalone hemiarch repair procedure per literature reports[6].

The probable risks of the device are also based on data collected in the PERSEVERE clinical study summarized above. These risks include mortality, disabling stroke, myocardial infarction, and renal failure requiring dialysis. The anticipated risks appear to be the same or lower than the risks associated with a standard open procedure per literature reports.

An additional factor for consideration in determining the probable risks and benefits of the AMDS include the absence of complete 5-year follow-up data in PERSEVERE.

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 use in patients with acute DeBakey Type I aortic dissections with malperfusion (including cerebral, visceral, renal, and peripheral malperfusion) and a primary entry tear within the ascending aorta proximal to the innominate artery, who are undergoing open surgical repair within 0-14 days of diagnosis, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application supports the reasonable assurance of safety and effectiveness of the AMDS when used in accordance with the indications for use. The non-clinical testing performed per applicable guidance documents and international standards confirmed that the AMDS met is performance and design specifications. The PERSEVERE study met the pre-specified performance goals and the longer-term PERSEVERE data and supplementary clinical data support safety and effectiveness. Therefore, it is reasonable to conclude that the benefits of use of the device for the

[6] Bing et al., "Type A Acute Aortic Dissection: Why Does the False Channel Remain Patent After Surgery."; Ergin et al., "Significance of Distal False Lumen After Type A Dissection Repair."; Rylski et al., "Fate of the Dissected Aortic Arch After Ascending Replacement in Type A Aortic Dissection."; Tamura et al., "Prognostic Impact of Distal Anastomotic New Entry After Acute Type I Aortic Dissection Repair."; Zindovic et al., "Malperfusion in Acute Type A Aortic Dissection."; Pacini et al., "Significance of Multiorgan Malperfusion."; Girdauskas et al., "Surgical Risk of Preoperative Malperfusion in Acute Type A Aortic Dissection."; Geirsson et al., "Significance of Malperfusion Syndromes Prior to Contemporary Surgical Repair for Acute Type A Dissection."; Bossone et al., "Usefulness of Pulse Deficit to Predict In-Hospital Complications and Mortality in Patients with Acute Type A Aortic Dissection."

indicated population outweigh the risk of illness or injury when used as indicated in accordance with the IFU.

XIV. CDRH DECISION

CDRH issued an approval order on June 26, 2026. The final clinical conditions of approval cited in the approval order are described below.

1. Clinical Update: The sponsor has agreed to provide a Clinical Update to physician users at least annually. At a minimum, this update will include, for the IDE and Post-Approval Studies, a summary of the number of patients for whom data are available, with the rates of major adverse events including all-cause mortality, lesion-related mortality, new permanent disabling stroke, new onset renal failure requiring dialysis, myocardial infarction, thromboembolic events, and rupture, as well as other procedure or device related events. Reasons, types and outcomes of secondary interventions, as well as causes of lesion-related mortality and rupture are to be described. Information regarding status of distal anastomotic new entry (DANE) will be provided. Additional relevant information from commercial experience within and outside the United States is also to be included, as well as a summary of any explant analysis findings. The clinical update for physician users must be provided to the FDA in the Annual report, as well as how the sponsor intends to share this with physician users.

2. Continued Follow-up of IDE Study Subjects: This study is a non-randomized, multi-center, prospective study that consists of continued follow-up of all subjects from the IDE Pivotal Study and Continued Access study. A total of 93 subjects were enrolled in the Pivotal Study and are eligible for analysis. In addition, 17 subjects were enrolled in the Continued Access study and are eligible for analysis. The remaining subjects will be followed annually for 5 years in accordance with the study protocol. The endpoints will be analyzed descriptively.

3. AMDS Post-Approval Study (PAS): This is a prospective, multi-center, single-arm, observational, post-market study. The objective of the study is to evaluate long-term real-world safety and effectiveness of the AMDS device in a real-world setting. The study will prospectively enroll a minimum of 135 subjects treated with the AMDS Device at up to 25 US sites. A minimum of 100 subjects with pre-operative malperfusion will be enrolled, with at least 60 of these subjects with evaluable data at 5-years post-implantation. A minimum of 30% new US sites will be included that did not participate in the PERSEVERE IDE study. Individual sites will be allowed to enroll a maximum of 20% of the total patient population. Follow-up will occur at 1 month, 6 months, 1 year, and yearly thereafter through 10 years from the index procedure. The composite primary safety and effectiveness endpoint is composed of the following events: all-cause mortality, new disabling stroke, new onset renal failure requiring dialysis, unanticipated device-related reoperation, and distal anastomotic new-entry (DANE) tears. The composite endpoint will be evaluated at 30-days and annually thereafter. Individual elements of the primary endpoint and all device and procedure-related serious adverse events will be evaluated at all follow-up intervals. Other

endpoints such as technical success, treatment success, additional aortic procedures, incidence of major adverse events, and radiologic evaluations (device assessment and aortic remodeling assessment) will be collected and reported. Core Lab and Clinical Events Committee (CEC) will be utilized in the study, at least through 5 years.

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

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.