SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Hybrid stent graft, thoracic aortic lesion treatment

Device Trade Name: Thoraflex™ Hybrid

Device Procode: QSK

Applicant's Name and Address: Terumo Aortic (Vascutek Ltd)
Newmains Avenue, Inchinnan
Renfrewshire, PA4 9RR
Scotland, UK

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P210006

Date of FDA Notice of Approval: April 19, 2022

Breakthrough Device: Granted breakthrough device status on March 20, 2020 because of reasonable expectation that the device can provide more effective treatment of a life threatening disease; as well has the potential of offering significant advantages over existing cleared alternatives for the repair or replacement of damaged or diseased vessels of the aortic arch and descending aorta, with or without involvement of the ascending aorta in cases of aneurysm and/or dissection.

II. INDICATIONS FOR USE

The Thoraflex™ Hybrid device is indicated for the open surgical repair or replacement of damaged or diseased vessels of the aortic arch and descending aorta, with or without involvement of the ascending aorta, in cases of aneurysm and/or dissection.

III. CONTRAINDICATIONS

The Thoraflex™ Hybrid device is contraindicated in the following;

- Patients with a known allergy or intolerance to device materials (Polyester, Nitinol, tantalum or materials of bovine origin)
- Patients with a condition that threatens to infect the graft

IV. WARNINGS AND PRECAUTIONS

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

V. DEVICE DESCRIPTION

Thoraflex™ Hybrid is designed for the open surgical repair of aneurysms and/or dissections in the aortic arch and descending aorta with or without involvement of the ascending aorta. There are two types of Thoraflex™ Hybrid implants, namely the Plexus 4 and the Ante-Flo versions. Each patient receives one Thoraflex™ Hybrid device (either the Plexus 4 or Ante-Flo). For patients that need additional length for repair of their lesions, the Relay®Pro Non-Bare Stent (NBS) Thoracic Stent Graft System can be used to extend the repair.

Thoraflex™ Hybrid Device

The Thoraflex™ Hybrid device is a gelatin coated vascular graft combined with a distal stented graft, supplied pre-loaded in a single use delivery system. The entire implant is coated with gelatin, loaded into a delivery system and terminally sterilized. The Thoraflex™ Hybrid device, once placed in the aorta, provides an alternative conduit for blood flow while excluding the lesion.

Thoraflex™ Hybrid Implant

The Thoraflex™ Hybrid implant consists of a proximal vascular graft section, a collar, and a distal stented graft section. Each of these aspects of the implant are described below. The implant is comprised of a woven polyester graft material that is gelatin coated.

The proximal graft section is crimped. The distal stented graft section is comprised of self-expanding nitinol stents sutured to the woven polyester fabric using polyester sutures. The stent scaffold is a series of springs stacked in a tubular configuration. These stents are externally spaced along the length of the graft fabric to provide radial support and allow for the self-expansion of the distal stented graft section. For visualization when extending the Thoraflex™ Hybrid device, there are radiopaque tantalum markers located at approximately 20mm increments starting from the most distal end of the device and covering a total length of 100mm.

The collar is designed to facilitate in the anastomosis of the graft to the native vessel. The anastomosis also provides proximal fixation of the distal stented graft section of the device.

The Thoraflex™ Hybrid device is available in two configurations, which differ only in the proximal vascular graft section, which are the Plexus 4 and Ante-flo versions. The Plexus 4 version (**Figure 1**) includes three branches for attachment to the great vessels and an ante-flo branch to aid cannulation and perfusion. The Ante-Flo version (**Figure 2**) contains only a single ante-flo branch.

The Thoraflex™ Hybrid device is tapered between the proximal vascular graft section and the distal stented graft section. For each configuration, the proximal vascular graft section is available in 22 – 32 mm diameters, and the distal stented graft section is available in 24-40 mm diameters. The distal stented section is available in 100 mm and 150 mm lengths. The branches are available in 8 - 12 mm diameters dependent on the graft configuration.

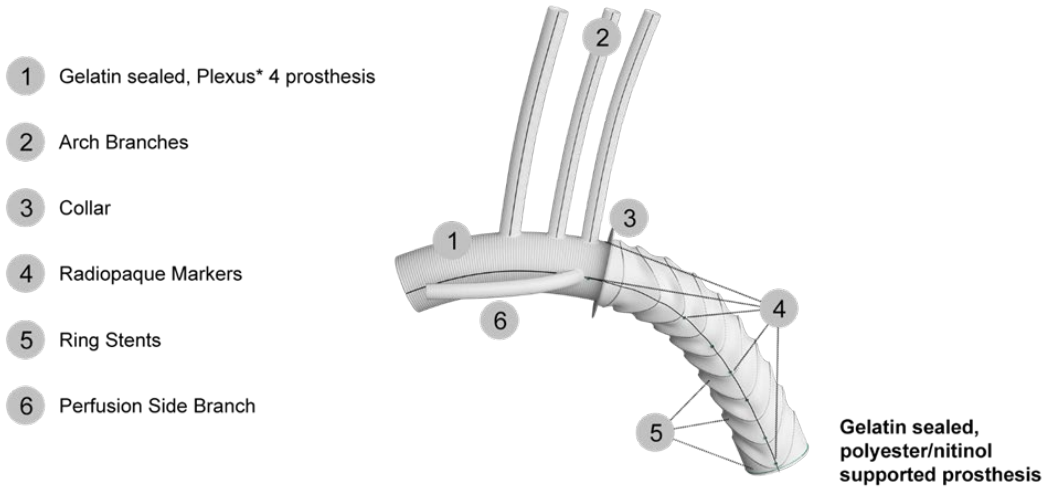


Figure 1. Thoraflex™ Hybrid Plexus 4 implant

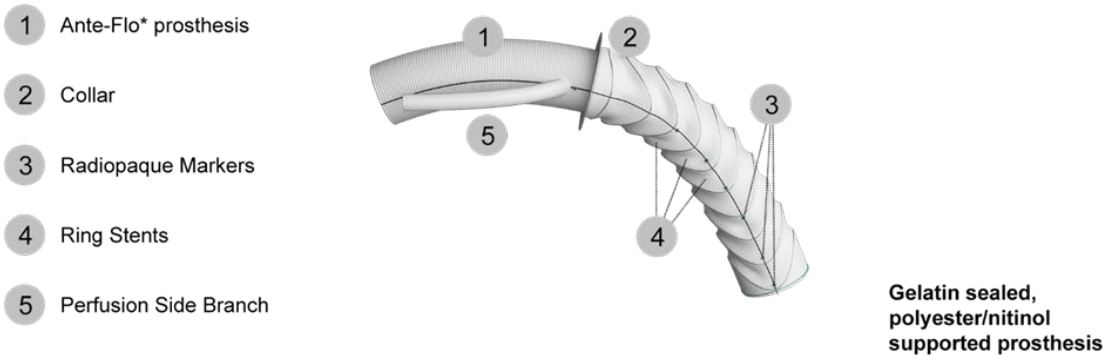


Figure 2. Thoraflex™ Hybrid Ante-Flo implant

Thoraflex™ Hybrid Delivery System

The Thoraflex™ Hybrid device is supplied pre-loaded in a delivery system (**Figure 3**) which is designed to facilitate delivery and accurate deployment in the patient's descending aorta. The delivery systems for the Plexus and Ante-Flo configurations are identical. The stented portion of the device is compacted into a PTFE sheath, while the proximal vascular graft section remains largely uncompacted. This allows the distal stented portion to be inserted into the descending aorta while the proximal vascular graft section retains its crimped form. As the device is unsheathed to release the distal stented portion into the descending aorta, the delivery system causes the sheath to split around the proximal vascular graft section to leave it unaffected.

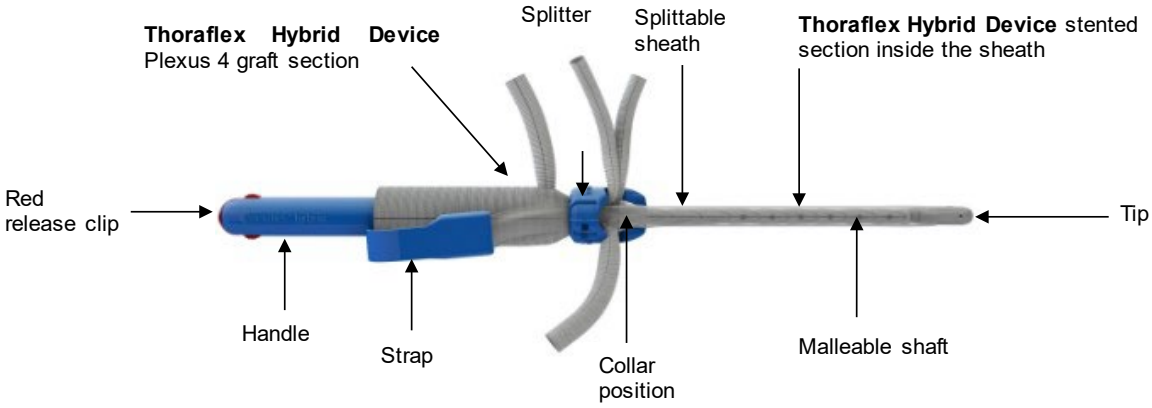


Figure 3. Thoraflex™ Hybrid Delivery System

An atraumatic tip at the distal end of the delivery system has a profile that is designed to guide the delivery system, with or without a guide wire, into the descending aortic arch. The tip has two guide wire ports that can be used at the discretion of the surgeon, dependening on the particular anatomy being treated.

The shaft, to which the device is attached via the tip, is comprised of a malleable stainless-steel section that allows the surgeon to manipulate the curvature of the delivery system to treat a particular patient anatomy. The distal stented graft section is attached to the tip of the delivery system via a release wire. The entire graft is also held in place by the splitter, which inhibits rotational and longitudinal movement of the device relative to the delivery system and also assists in splitting the sheath during deployment.

Extension Device: Relay®Pro NBS Thoracic Stent Graft System

If required, the Thoraflex™ Hybrid device can be extended using a Relay®Pro NBS Thoracic Stent Graft System (**P200045**). Please refer to the Instructions for Use for a comprehensive device description on this component (**P200045**). Please also refer to the Thoraflex™ Hybrid Instructions for Use for details on sizing recommendations and other information regarding the use of this device as an extension to the Thoraflex™ Hybrid.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for treatment of damaged or diseased vessels of the aortic arch and descending aorta with or without involvement of the ascending aorta in cases of aneurysm and/or dissection, including medical management, as well as conventional open surgical elephant trunk procedures with an optional second stage open surgical repair. 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

Thoraflex™ Hybrid is commercially available in the countries listed in **Table 1** below.

Table 1. Thoraflex™ Hybrid Marketing History

Europe				
Austria	Denmark	Iceland	Malta	Serbia
Belgium	Estonia	Ireland	Netherlands	Slovakia
Bosnia	Finland	Italy	Norway	Slovenia
Bulgaria	France	Latvia	Poland	Spain
Croatia	Germany	Liechtenstein	Portugal	Sweden
Cyprus	Greece	Lithuania	Romania	Switzerland
Czech Republic	Hungary	Luxembourg	Russia	United Kingdom
North America				
Canada	Costa Rica	Dominican Republic	Jamaica	Trinidad and Tobago
Middle East and Africa				
Armenia	Israel	Lebanon	Palestine	Turkey
Georgia	Kuwait	Oman	South Africa	United Arab Emirates
South America				
Brazil	Chile	Colombia	Suriname	
Asia-Pacific				
Australia	India	Nepal	Singapore	Thailand
Hong Kong	Malaysia	New Zealand	Taiwan	Vietnam

Thoraflex™ Hybrid has not been withdrawn from any market for reasons related to safety or effectiveness.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device:

Table 2. Potential Adverse Events

Anemia	Hepatic failure
Allergic reaction to polyester / gelatin	Infection of the prosthesis / wound site
Aneurysm enlargement	Lymphatic complications e.g. lymph fistula
Aneurysm/Lesion Rupture	Multi-system organ failure
Aortic damage, including perforation, dissection, bleeding, aortic rupture	Neointimal Hyperplasia
Arterial or venous thrombosis	Neurological local or systematic complications e.g. confusion, stroke, transient ischemia attack (TIA), paraplegia, paraparesis, paralysis, spinal cord injury, peripheral neuropathy, altered mental status, temporary post-operative delirium, altered consciousness, coma, new onset seizures
Aorto-bronchial fistula, aorto-esophageal fistula, arterial or venous fistula, arteriovenous fistula,	Prosthesis dilatation
Bleeding, blood loss, hematoma, coagulopathy, re-opening, thrombocytopenia,	Prosthesis occlusion
Bowel complications e.g. aortoenteric fistula, bowel obstruction, bleeding, infection, ileus, perforation, transient ischemia, infarction, necrosis, mesenteric ischemia, hepatic complications	Pseudoaneurysm
Cardiac complications e.g. Angina, arrhythmia (e.g. atrial or ventricular fibrillation) congestive heart failure, hypotension, hypertension shock, cardiac tamponade, valve insufficiency, myocardial infarction, murmur of aortic insufficiency and pulse deficits, embolization (micro and macro) with transient or permanent ischemia or infarction, pericardial effusion, intramural hematoma, occlusion, downstream reintervention for aortic complications	Renal complications e.g. acute kidney injury, renal insufficiency, renal dysfunction, artery occlusion, failure, infarction, transient or permanent increase in serum creatinine, urinary tract infection
Device deficiencies e.g. Stented Section: improper component placement; incomplete component deployment; component migration and/or separation; suture break; occlusion; infection; stent fracture; graft material wear; graft twisting/kinking; dilatation; erosion; puncture; perigraft flow; and corrosion	Respiratory complications e.g. breathing difficulties, pneumonia, pulmonary edema, pulmonary embolism, post-operative respiratory insufficiency (defined as requiring prolonged intubation (>72 hours), reintubation, or ventilatory support requiring tracheostomy), pleural effusion, , exacerbation of COPD

Death	Sepsis
Edema	Stenosis
Endoleak	Surgical complications: sternal instability, swelling, rash, pain, compartment syndrome, recurrent laryngeal nerve damage/paralysis
Fever & localized inflammation	Vascular trauma, spasm, damage and access site complications (infection, pain, hematoma, pseudoaneurysm, arteriovenous fistula, ilio-femoral vessel dissection, bleeding, rupture, deep vein thrombosis)
Genitourinary complications e.g. ischemia, erosion, fistula, incontinence, hematuria, infection, impotence	Wound complications e.g. dehiscence, infection, hematoma, seroma, cellulitis, pain, sacral ulcer/pressure sore and any commonly recognized complications associated with the following adverse events: paraplegia/paraparesis, coma and spinal cord injury (for example pressure sores/sacral ulcer resulting from paraplegia)

For the specific adverse events that occurred in the clinical study, please see **Section X** below. Long term potential adverse effects will be evaluated in a post approval study.

IX. SUMMARY OF NONCLINICAL STUDIES

Nonclinical studies were completed to evaluate the Thoraflex™ Hybrid device, including non-clinical bench testing, biocompatibility, sterilization, packaging, shelf-life, and animal studies. These are discussed in detail in the following sections.

A. Laboratory Studies

Thoraflex™ Hybrid underwent testing for design verification and validation, including long-term durability and corrosion testing. Testing was performed in accordance with international standards and guidance documents, including ISO 25539-1 *"Cardiovascular implants -- Endovascular devices -- Part 1: Endovascular prostheses"* and ISO 7198 *"Cardiovascular implants and extracorporeal systems -- Vascular prostheses -- Tubular vascular grafts and vascular patches."* For the evaluation of Thoraflex™ Hybrid, a subset of device components and sizes were used for each test or alternatively, the worst-case configuration/size was selected. The samples selected represented the full size range available for Thoraflex™ Hybrid. Additionally, testing was completed using a Relay®Pro NBS Thoracic Stent Graft System to support the use of this endovascular device as an extension to the Thoraflex™ Hybrid.

A summary of this testing is provided in **Table 3.** Please note that an asterisk (*) indicates that the testing was performed at baseline and after aging (accelerated or real time to the 2 years shelf life duration).

Table 3. Non-Clinical Testing

Test Name	Test Purpose	Acceptance Criteria	Results
Design Verification Testing – Thoraflex™ Hybrid Implant			
Migration Testing	To evaluate the movement (migration) of the device when subjected to variable physiological conditions. This test provides an indication of the resistance to migration provided by the fixation mechanisms of the device (i.e., distal ring). In addition, characterisation pullout testing was completed to evaluate the performance of Thoraflex™ Hybrid against other, commercially available thoracic devices by measuring the tensile force required to remove the device from vessel.	For migration testing, devices should not move more than 10mm during any of the test conditions. Pullout testing was performed for characterization only, therefore there were no set acceptance criteria.	Pass
Seal Testing	To verify the sealing ability of the distal stented graft section of Thoraflex™ Hybrid. The test was conducted in a mock (bovine) vessel subjected to physiological conditions.	Thoraflex™ Hybrid leak rate < sutured cleared Gelweave graft (K162794) to vessel leak rate: Leak rate ≤ 130.74 ml/min	Pass
Stent to Graft Attachment Force*	To determine the strength of the fixation or attachment system between the distal stent graft material and the nitinol stent rings.	Mean Stent to graft attachment force - 3SD > 38N (Max Loading during deployment) Mean Stent to graft attachment force - 3 SD > 77N (Max loading during compaction)	Pass
Flex and Kink Radius	To determine if the device can accommodate worst-case curvature without kinking.	Percentage Reduction in cross-sectional-area at a 101° bend, around 11mm radius < 50%.	Pass
Dimensional Verification of Implant	To evaluate the conformance of the Thoraflex™ Hybrid	Stent Diameter THP2224x150: 22.6mm -23.8mm THP3032x150: 30.9mm -32.2mm THP3240x150: 39.4mm - 40.2mm	Pass

Test Name	Test Purpose	Acceptance Criteria	Results
	dimensions to their design specifications.	<u>Device Diameter</u> Stented diameter range 24mm – 40mm, in 2mm increments & open vascular graft diameter range 22mm - 32mm	Pass
		<u>Module Length</u> Overall Length = 327-333mm (100mm Devices) or 377- 383mm (150mm Devices) Unstented Graft (main bore) Length = minimum length of 242mm Each diameter combination has a nominal 100±5mm (100mmm Devices) and 150±5mm (150mm Devices) stented section.	Pass
		<u>Collar Width</u> 12.0mm±2.0mm.	Pass
		<u>Branch Length</u> All branches are a minimum length of 150mm	Pass
		<u>Branch Inner Diameter</u> All Ante-grade perfusion branches are between 9.5-10.5mm inner diameter (ID) 22 and 24mm Plexus grafts have Innominate branches between 9.5-10.5mm ID. 26-32mm Plexus grafts have Innominate branches between 11.0-13.0mm ID 22-32mm Plexus grafts have common Carotid branches between 7.5-8.5mm ID 22 and 24mm Plexus grafts have Left Subclavian branches between 7.5-8.5mm ID. 26-32mm Plexus grafts have Left Subclavian branches between 9.5-10.5mm ID	Pass
		<u>Branch Spacing</u> BP1: 5mm ± 2mm BP2: 5mm ± 2mm BP3: 12mm ± 2mm	Pass
		<u>Radiopaque Marker Positions</u> The first marker position is measured from the distal edge of the device to the center of the marker. All other marker positions are measured from center to center. "M" = Marker <u>100mm Devices</u> M1: 4.0mm ± 2mm M2: 20.0mm ± 2mm M3: 20.0mm ± 2mm M4: 21.0mm ± 2mm	Pass

<table>
<tr><th>Test Name</th><th>Test Purpose</th><th>Acceptance Criteria</th><th>Results</th></tr>
<tr><td></td><td></td><td>M5: 19.0mm ± 2mm
M6: 19.0mm ± 2mm

<u>150mm Devices</u>
M1: 4.0mm ± 2mm
M2: 21.5mm ± 2mm
M3: 17.5mm ± 2mm
M4: 21.0mm ± 2mm
M5: 20.0mm ± 2mm
M6: 20.0mm ± 2mm</td><td></td></tr>
<tr><td>Collar Attachment Force</td><td>To verify that the tensile strength of the attachment between the collar and proximal vascular graft secion is sufficient for this application.</td><td>Mean Collar to graft attachment -3SD > 34N</td><td>Pass</td></tr>
<tr><td>Suture Retention Strength</td><td>To determine the force required to remove a placed suture from the proximal vascular graft section fabric.</td><td>Failure force > 4.5N</td><td>Pass</td></tr>
<tr><td>Blood Leak Testing*</td><td>To evaluate the blood leakage from Thoraflex™ Hybrid after compaction and deployment.</td><td>Level of blood porosity <21g over the initial 3 minutes</td><td>Pass</td></tr>
<tr><td>Particulate Testing*</td><td>To characterise the release of particulates from Thoraflex™ Hybrid devices under simulated use conditions.</td><td>The device must not produce excessive levels of particulates during simulated use, defined as:
• ≤3 parts/ml ≥25µm
• ≤25 parts/ml ≥10µm</td><td>Pass</td></tr>
<tr><td>Whole Graft Porosity</td><td>To determine the amount of leakage from the device after the impregnation process, to ensure that it has been sufficiently impregnated, and that excessive leakage will not occur.</td><td><0.15ml/min/cm^2</td><td>Pass</td></tr>
<tr><td>Burst Strength*</td><td>To determine the level of applied load at which the fabric of the proximal vascular graft section of the device will burst.</td><td>Mean – 3SD > 33.51 N</td><td>Pass</td></tr>
<tr><td>Porosity Testing</td><td>To determine the amount of leakage from the raw, ungelled fabric which will be used to produce a Thoraflex™ Hybrid device.</td><td><table><tr><th rowspan="2">Product Type</th><th colspan="2">Maximum Water Porosity (ml/min/mm^2)</th></tr><tr><th>Body</th><th>Seam/Black Line</th></tr><tr><td>Graft section fabric</td><td>515</td><td>583</td></tr><tr><td>Stented section fabric</td><td>346</td><td>346</td></tr></table></td><td>Pass</td></tr>
</table>

Test Name	Test Purpose	Acceptance Criteria	Results
Relaxed Internal Diameter	To evaluate the conformance of the Thoraflex™ Hybrid dimensions to the design specifications.	All sizes, tolerance ±0.5mm	Pass
Longitudinal tensile strength*	To determine the longitudinal tensile failure force of the Thoraflex™ Hybrid device.	Mean Failure force – 3SD > 33.51N	Pass
Fatigue and Durability – Computational Analysis	FEA was used to compute the material strains arising within the nitinol stents during manufacture, compaction, deployment and worst-case cyclic radial loading.	FEA simulation results should show a Fatigue Safety Factor >1 when compared with the Fatigue Safety Limit. The FEA study was also used to identify the worst-case prosthesis size for in vitro fatigue testing	Pass
Fatigue and Durability – *In vitro* testing	Pulsatile Fatigue Testing: To evaluate the long-term durability of the stent-graft design over 400 million cycles of pulsatile fatigue loading.	After 100 million and 400 million cycles, the overlapped regions of all test samples shall have: 1. No stent fractures such as would affect clinical performance 2. No other device integrity failures such as would affect clinical performance.	Pass
	Pulsatile Bending Testing: To evaluate the long-term durability of the stent-graft design over 400 million cycles of bending loads.		Pass
Corrosion Testing	To evaluate the corrosion resistance properties of the metallic (all nitinol) components of the Thoraflex™ Hybrid device.	The stent ring components must not be susceptible to failure by localized corrosion under anticipated in-vivo conditions.	Pass
Radial Force	To determine the force exerted by the distal stented graft section of the device as a function of the implant diameter, under conditions of compression and extension. The testing was performed not only to obtain results for physical testing, but also to use these results to assess the validity of the current Finite Element Analysis (FEA) model used to extrapolate the rest of the radial force data.	This testing was performed for characterization only. Results from this testing should be comparable to those found by using the finite element analysis model.	Pass

Test Name	Test Purpose	Acceptance Criteria	Results
Tray Soaking Verification	To verify that the packaging tray of the Thoraflex™ Hybrid device was capable of allowing the device to be submerged in 700ml of fluid for at least 5 minutes.	A visual inspection will be carried out during and post testing to ensure the device can be fully submerged without the fluid overspilling. This will ensure suitable soaking across the entire device. If the 700mL of fluid remains within the tray and the device is suitably soaked after 5 minutes, the test can be considered a pass.	Pass
Design Verification Testing – Thoraflex™ Hybrid Delivery System			
Dimensional Verification of Delivery System Components*	To ensure that delivery system dimensions are within specification.	<u>Visual Inspection</u> The packaging, tip to sheath interface and the release clips are to be visually inspected to verify they are all intact, as intended and hence acceptable for use	Pass
		<u>Overall Length</u> Full length (100mm Devices) = 327-333mm Full length (150mm Devices) = 377-383mm	Pass
		<u>Positioning of Splitter</u> Tip to Splitter Length (100mm Devices) = 153-159mm Tip to Splitter Length (150mm Devices) = 203-209mm	Pass
		<u>Guide Wire Lumen Diameter</u> The guide wire lumen diameters are to be inspected using pin gauges and the lumen should be large enough to allow a 0.035" guide wire to freely pass through it along its full length	Pass
		<u>Strap Position and Attachment</u> The strap should be on the correct side of the system with all four screws fully engaged	Pass
		<u>Splittable PTFE Sheath Inspection</u> Sheath Outer Diamter of 10.06mmm+0.25mm/-0.10mm The sheaths should be inspected for any sign of premature splitting.	Pass
		<u>Tip Diameter</u> The tip diameter should be <45Fr, 15mm	Pass
Splitter to Shaft Attachment	To measure the attachment strength of various components of Thoraflex™ Hybrid and ensure they are suitable for the intended application.	Mean Attachment Strength – 3SD > 25.27N	Pass
Control Loops to Tip Attachment		Mean Attachment Strength – 3SD > 76N	Pass
Device to Delivery System Tensile Testing*		Mean Straight Line Deployment Force + 2SD ≥ 43.65N.	Pass
Release Wire to Clip Attachment*		Attachment strength – 3SD ≥ 6.15N	Pass

Test Name	Test Purpose	Acceptance Criteria	Results
Handle to Shaft Compression and Tensile Testing*		Handle to Shaft Compression – 3SD ≥ 92.12N Handle to Shaft Tension ≥ 30.17N (Characterization only)	Pass
Sheath to Strap Tensile Testing*		Attachment Strength -3SD ≥ 92.12N	Pass
Tip to Shaft Tensile Test*		Attachment Strength – 3SD ≥ 30.17N	Pass
Catheter Stop to Shaft Tensile Test*		Catheter Stop to Shaft Strength - 3 SD > 92.12N	Pass
Sheath Splitting Tensile Testing	To verify the delivery system sheath splitting force meets tensile design input requirements.	Sheath Failure Force ≥ 92.12N	Pass
Splitter Tensile Testing*	To measure the tensile strength required to open the splitter and to characterise how the splitter failed.	This testing was used for characterization purposes only, as such there was no specific acceptance criteria.	The tensile strength (mean – 3SD) was determined to be 104.87N.
Tip to Shaft Torsion Test	To verify that the delivery system tip to shaft and catheter stop to shaft connections meet torsional design input requirements.	Mean Max Torque ≥ 29.22 cNm	Pass
Catheter Stop to Shaft Torsion Test			
Force to Compact*	To evaluate the force required to compact the device into the 28.5F sheath.	Compaction Force Limit is 76N	Pass
Deployment Force Testing	To determine the maximum deployment force of the Thoraflex™ Hybrid device.	Sheath retraction force < 97N	Pass
Deployment Testing*	To verify the functionality of the Thoraflex™ Hybrid device during deployment into benchtop models of representative anatomy.	The testing would have been deemed to have failed if any aspect of the deployment could not be carried out successfully.	Pass
Deployment Accuracy Testing	To assess the accuracy of the deployment position of the Thoraflex™ Hybrid device.	Peaks of the distal ring are placed within ±5mm of the target position after deployment into a model vessel.	Pass
Thoraflex™ Hybrid and Relay®Pro NBS Thoracic Stent Graft System Device Extension Testing			
Integral Water Permeability Testing	To evaluate the amount of leakage between docked Thoraflex™ Hybrid and Relay®Pro NBS Thoracic Stent Graft Systems in both straight and angulated configurations, to ensure a suitable seal is achieved between the	The permeability of the docked Thoraflex™ Hybrid and Relay®Pro NBS Thoracic Stent Graft System must be less than the permeability of the individual devices combined in the same ratio.	Pass

Test Name	Test Purpose	Acceptance Criteria	Results
	devices and thus demonstrate that the Relay®Pro NBS Thoracic Stent Graft System is suitable for use as extension devices for Thoraflex™ Hybrid.		
Kink Testing	To determine if the combined Thoraflex™ Hybrid and Relay®Pro NBS Thoracic Stent Graft Systems can accommodate worst-case curvature without kinking.	Percentage Reduction in cross-sectional-area at a 101° bend, around 11mm radius < 50%.	Pass
Separation Force Testing	To verify that the force required to separate a Relay®Pro NBS Thoracic Stent Graft System device from a Thoraflex™ Hybrid device is sufficient to withstand the forces experienced in vivo.	The force to separate each Relay®Pro NBS Thoracic Stent Graft System device from the Thoraflex™ Hybrid device shall be ≥ 4N	Pass
Distal Ring Dislodgement Testing	To verify that inserting the Relay®Pro NBS Thoracic Stent Graft System delivery system into the Thoraflex™ Hybrid device (in order to deploy the Relay®Pro NBS Thoracic Stent Graft System) will not disturb the distal ring of the Thoraflex™ Hybrid device, in such a way that it prevents the Relay®Pro NBS Thoracic Stent Graft System from docking successfully within the Thoraflex™ Hybrid.	The Relay®Pro NBS Thoracic Stent Graft System delivery system must not disrupt the distal ring of the Thoraflex™ Hybrid such that the Relay®Pro NBS Thoracic Stent Graft System cannot be deployed within the Thoraflex™ Hybrid device with the required 3 z-stent overlap.	Pass
Deployment Testing	To deploy a number of Relay®Pro NBS Thoracic Stent Graft Systems into a Thoraflex™ Hybrid device, in order to evaluate the use of the Relay®Pro NBS Thoracic Stent Graft System as an extension device to Thoraflex™ Hybrid, and to ensure there are no additional risks related to the extension procedure which have not been identified and covered in	This testing was used for characterization purposes only, as such there was no specific acceptance criteria.	This characterization testing has determined that the tests performed in the separate verification testing cover all associated risks and design inputs.

Test Name	Test Purpose	Acceptance Criteria	Results
	the Thoraflex™ Hybrid / Relay®Pro NBS Thoracic Stent Graft System extension verification testing.		
Fatigue and Durability – Computational Analysis	To show the fatigue safety of the Relay®Pro NBS Thoracic Stent Graft System when used at higher oversize for Thoraflex™ Hybrid extension	The worst-case Relay®Pro NBS Thoracic Stent Graft System components should demonstrate a suitable fatigue safety factor of >1.5 for 'worst case' and 'representative' higher oversizing use, relating to Thoraflex™ Hybrid extension indication as per the IFU.	Pass
Fatigue and Durability – *in-vitro* Testing	Pulsatile Fatigue Testing (Dissection): To evaluate the long-term durability of the Thoraflex™ Hybrid device in a straight, overlapped and dissection configuration with the Relay®Pro NBS Thoracic Stent Graft System over 400 million cycles of pulsatile fatigue loading.	After 100 million and 400 million cycles, the overlapped regions of all test samples shall have: 1. No stent fractures such as would affect clinical performance 2. No other device integrity failures such as would affect clinical performance.	Pass
	Pulsatile Bending Testing: To evaluate the long-term durability of the Thoraflex™ Hybrid device in an overlapped, supported static bend configuration with the Relay®Pro NBS Thoracic Stent Graft System over 400 million cycles of bending loads.		Pass
MRI Testing	To provide the recommended scan conditions for use with the device.	Non-clinical testing completed at worst-case conditions for displacement & deflection force, torque force, RF heating, and MRI artifact demonstrated that the Thoraflex™ Hybrid and the Relay®Pro NBS Thoracic Stent Graft System are Magnetic Resonance (MR) Conditional. A patient with these devices can be safely scanned in an MR system meeting the following conditions: • Static magnetic field of 3.0 or 1.5 Tesla. • Maximum magnetic field spatial gradient of 4,000 gauss/cm (40 T/m). • Maximum MR system reported, whole body averaged specific absorption rate (SAR) of 2 W/kg (Normal Operating Mode)	Pass

B. Animal Studies

The design of the Thoraflex™ Hybrid device is based on the basic design, materials of construction, and similar processing as other Vascutek devices. Specifically, the proximal vascular graft sections are cleared devices under pre-market notification in the US (**K162794**). These devices underwent previous animal testing and demonstrated acceptable results with respect to gelatin hydrolysis (if gelatin sealed), device patency, tissue ingrowth, healing response, local and systemic toxicity. Therefore, animal studies from the other Vascutek devices were leveraged in support of the Thoraflex™ Hybrid device. With respect to the other aspects of the device (e.g., stented segment of the implant and delivery system), other available data (e.g., clinical, bench and biocompatibility data) was leveraged to address device safety and performance endpoints typically addressed in stent graft animal studies (e.g., successful deployment, patency).

C. Biocompatibility

The biocompatibility evaluation of the Thoraflex™ Hybrid device 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 the FDA Guidance Document "Use of International Standard ISO 10993-1, "Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process"" (2020).

The Thoraflex™ Hybrid device is comprised of an implantable graft with a proximal graft portion and a distal stented graft portion, which is pre-loaded in a delivery system. For purposes of the biocompatibility assessment, the stent graft was classified as an implant device with circulating blood contact and long term exposure (> 30 days), while the delivery system was classified as an externally communicating device with tissue/bone/dentin contact and limited exposure (≤ 24 hours). All testing was conducted by a qualified contract laboratory in accordance with FDA GLP regulations, 21 CFR 58.

The Thoraflex™ Hybrid implant successfully met all pre-specified acceptance criteria with the exception of cytotoxicity, mammalian genotoxicity (mouse lymphoma assay), and specific assessments for hemocompatibility (i.e., partial thromboplastin time and complement activation) biocompatibility tests. The results of the biocompatibility testing performed are summarized in **Table 4** for the Implant.

Table 4. Biocompatibility Evaluation – Thoraflex™ Hybrid Implant

Biological Effect (Test)	Purpose	Results	Acceptance Criteria Met?
ISO MTS Cytotoxicity	To determine if cytotoxicity is caused when L-929 mouse fibroblast cells are exposed to implant extracts.	Cytotoxic potential: The neat (100%) and 50% (v/v) dilution extracts had cytotoxic potential. The 25%(v/v) and 12.5% (v/v) dilution extracts had no cytotoxic potential.	No
ISO Guinea Pig Maximization Sensitization	To evaluate the allergenic/sensitization potential of implant extracts in guinea	Non-Sensitizer: All animals scored 0 resulting in 0% sensitization rate.	Yes

Table 4. Biocompatibility Evaluation – Thoraflex™ Hybrid Implant

Biological Effect (Test)	Purpose	Results	Acceptance Criteria Met?
	pigs.		
ISO Intracutaneous Reactivity	To evaluate the potential irritation effects after intracutaneous injection of implant extracts in rabbits	Non-irritant: The difference in the overall mean score between the test article extracts and corresponding control was lower than 1.0.	Yes
ISO Acute Systemic Toxicity	To evaluate the potential toxic effects after single-dose systemic injections of implant extracts in mice.	There was no mortality or evidence of systemic toxicity from the test article extracts.	Yes
ISO Subchronic Toxicity	To evaluate the potential toxic effects after repeated intravenous and intraperitoneal injections of implant extracts in rats over a period of 14-days.	There was no evidence of systemic toxicity from the test article extracts.	Yes
Material Mediated Pyrogenicity	To evaluate implant extracts for the potential of inducing a pyrogenic response in rabbits	Non-pyrogenic: Rabbits showed a maximum temperature rise of 0.20, 0.01 and 0.14°C, respectively over a 3-hour period.	Yes
Rabbit Intramuscular Implant 90 days	To evaluate local biocompatibility of the components of the Thoraflex™ Hybrid Device in comparison to positive and negative controls via intramuscular implants in the rabbit model.	Components of the Thoraflex™ Hybrid Device did not result in any visible adverse local or distant effects, and no exuberant or unexpected inflammatory or local tissue responses when compared to positive or negative control materials.	Yes
Chemical Characterization	To identify and quantify the extractables and/or leachables that may be released from the implant.	Based on the available toxicity data, exposure estimates, and safety margins, the likelihood of extractable chemicals from the implant producing unacceptable carcinogenic or non-carcinogenic health risks in the adult patient population under the proposed conditions and duration of clinical use (long term; >30 days) is acceptable.	Yes
Genotoxicity			
Ames Assay	To evaluate implant extracts for the potential to induce reverse mutations at selected loci of several strains of bacteria.	The implant is considered to be non-mutagenic in the test system	Yes

Table 4. Biocompatibility Evaluation – Thoraflex™ Hybrid Implant

Biological Effect (Test)	Purpose	Results	Acceptance Criteria Met?
In vitro Mouse Lymphoma Assay	To evaluate implant extracts for the potential to induce a forward mutation in the TK locus of L5178Y/TK± cells.	The implant is considered to be mutagenic in the test system	No
Hemocompatibility			
Hemolysis	To evaluate the potential of the implant to cause hemolysis in direct contact or by extraction.	Non-hemolytic; Percent hemolysis: Direct contact – 0.0% Extract – 0.0%	Yes
Partial Thromboplastin Time (PTT)	To evaluate the potential of the implant extracts to cause an effect on the coagulation cascade via the intrinsic coagulation pathway.	The test article had a final average clotting time of 152.4 seconds and was 55% of the negative control.	No
Platelet and Leukocyte Count	To determine if exposure of the implant to human whole blood in vitro will adversely affect the platelet and leukocyte ratios in human whole blood.	The test article results for the leukocyte and platelet counts were 72% and 105%, respectively, of the negative control. The test article normalized platelet value was within 80 to 120% of the negative control. When evaluating the biological significance, the test article normalized platelet value was more than that of the comparison articles (which were all <80% of the negative control).	Yes
Complement Activation	To determine the potential of the implant to activate complement.	SC5b-9 – considered to be potential activator of the complement system	No

A summary of the testing that did not meet the acceptance criteria is provided below:

- Cytotoxicity and genotoxicity: The root cause for the *in vitro* cytotoxic and genotoxic potential of Thoraflex™ Hybrid was determined to be low level formaldehyde residues (a manufacturing aid, which crosslinks the gelatin sealant). The presence of these residues, which would be expected to yield a positive response in these highly sensitive *in vitro* tests, has not been related to any observed instances of *in vivo* effects during biological testing or clinically in patients.

  The extractable formaldehyde residue was quantified and evaluated in accordance

with ISO 10993-17:2002 (Biological evaluation of medical devices - Part 17: Establishment of allowable limits for leachable substances) and has been determined to be toxicologically acceptable and not impact device safety.

- Hemocompatibility: The Thoraflex™ Hybrid device does not contain novel materials, nor does it contain novel processing, that is dissimilar from other commercially available products, including currently cleared vascular grafts for open procedures. Furthermore, *in vivo* implantation of Thoraflex™ Hybrid device coupons in rabbit paravertebral muscle for up to 90 days resulted in no visible adverse local or distant effects, and no exuberant or unexpected inflammatory or local tissue responses compared with positive and negative controls. Additionally, the leveraged clinically relevant *in vivo* animal study performed, also concluded that no systemic or local effects were observed including no evidence of thrombosis in the treated arteries and no evidence of foreign body embolic material in non-graft organs. No instances of Thoraflex™ Hybrid device-related incidences of pseudoaneurysm in the treated segment or anaphylaxis were reported in the US clinical study with 3-year follow-up.

  It is concluded that the adverse outcomes observed in the *in vitro* testing of the Thoraflex™ Hybrid, have not been translated into observable local or distant effects *in vivo*, and so these aspects of the biological evaluation have been determined to be adequately addressed and the benefits of the device outweigh the potential biocompatibility risks.

The Thoraflex™ Hybrid delivery system successfully met all pre-specified acceptance criteria. The results of the biocompatibility testing performed on the delivery system are summarized in **Table 5**.

Table 5. Biocompatibility Evaluation – Thoraflex™ Hybrid Delivery System

Biological Effect (Test)	Purpose	Results	Acceptance Criteria Met?
ISO NRU Cytotoxicity	To determine if delivery system extracts cause cytotoxicity when exposed to L-929 mouse fibroblast cells.	No cytotoxic potential: not considered to have cytotoxic potential.	Yes
ISO Guinea Pig Maximization Sensitization	To evaluate the allergenic/sensitization potential of delivery system extracts in guinea pigs.	Non-Sensitizer: All animals scored 0 resulting in 0% sensitization rate	Yes
ISO Intracutaneous Reactivity	To evaluate the potential irritation effects after intracutaneous injection of delivery system extracts in rabbits.	Non-irritant: The difference in the overall mean score between the test article extracts and corresponding control was lower than 1.0.	Yes
ISO Acute Systemic Toxicity	To evaluate the potential toxic effects after single-dose systemic injections of delivery system extracts in mice.	The test article extracts did not induce a significantly greater biological reaction than the control extracts.	Yes

Table 5. Biocompatibility Evaluation – Thoraflex™ Hybrid Delivery System

Biological Effect (Test)	Purpose	Results	Acceptance Criteria Met?
Material Mediated Pyrogenicity	To evaluate delivery system extracts for the potential of inducing a pyrogenic response in rabbits.	Non-pyrogenic: Rabbits showed a maximum temperature rise of 0.0, 0.0 and 0.1°C, respectively over a 3-hour period.	Yes
Hemocompatibility			
Hemolysis	To evaluate the potential of the delivery system to cause hemolysis in direct contact or by extraction.	Non-hemolytic; Percent hemolysis: Direct contact – 0.00% Extract – 1.24%	Yes

D. Sterilization, Packaging and Shelf-Life

Thoraflex™ Hybrid is a single-use device that is provided sterile to the end user. It is sterilized using 100% Ethylene Oxide (EtO) gas with heated aeration to allow for residual EtO dissipation, 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*. Devices must have a sterility assurance level (SAL) of 10^{-6}. Sterilization validation was performed by comparison to "worst case" devices. A total of 72 devices were used, as these have the highest compaction density of all Thoraflex™ Hybrid verisons.

Distribution testing has been performed as per ISO 2247:2002 *Complete, filled transport packages and unit loads: Vibration tests at fixed low frequency* and ISO 22248:1993 *Complete, filled transport packages, vertical impact test by dropping*.

Packaging validation was executed successfully per AAMI/ANSI/ISO 11607-1:2006: *Packaging for terminally sterilized devices – Part 1: Requirements for materials, sterile barrier systems and packaging systems*. All packaging and shelf life validation testing was performed as per current standards and Vascutek procedures. The Thoraflex™ Hybrid packaging configuration used in these studies reflects the final package configuration.

Specific engineering testing completed to support shelf life are denoted by an asterisk (*) in **Table 3**. Accelerated and real time shelf-life product testing conducted on Thoraflex™ Hybrid supports a 2-year shelf-life.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the open surgical repair or replacement of aneurysms and/or dissections of the aortic arch and descending aorta with or without involvement of the ascending aorta with the Thoraflex™ Hybrid device in the US under IDE # G150224. 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 August 22, 2016 and May 29, 2018. The database for this PMA reflected data collected through July 31, 2021 and included 65 patients in the main study arm and 9 patients in the aortic rupture arm. There were 12 US investigational sites. The study was a multi-center, prospective, single-arm clinical study.

The primary endpoint was defined as the proportion of patients with freedom from the following composite of Major Adverse Events (MAEs) occurring ≤ 1 year post procedure: permanent stroke (new neurological deficit of abrupt onset caused by a disturbance in blood supply to the brain), permanent paraplegia/paraparesis (complete/partial or incomplete loss of lower limb motor function), unanticipated aortic related re-operation (surgical re-intervention to address complications with the Thoraflex™ Hybrid device excluding reoperation for bleeding), and all-cause mortality.

The results were tested against a performance goal of 57.4%, derived from the clinical outcomes (MAEs) after an elephant trunk (ET) procedure collated by two medical centers. These ET MAE frequencies were as follows: 6.5% permanent stroke; 5.4% permanent paraplegia/paraparesis; 28.1% mortality at one year; 2.7% unanticipated aortic related re-operation. The proportion of patients in the historical cohort with 1 or more MAE at one year was 35.7%. The proportion of patients MAE-free at one year was 64.3% (95% CI 57.4% to 71.2%).

Furthermore, data were extrapolated from a Frozen Elephant Trunk (FET) meta-analysis (Tian et al, 2013) of 17 studies and 1,675 patients (both aneurysm and dissection) that reported 4.9% stroke, 5.1% paraplegia/paraparesis and 15.3% mortality at one year.

Based on these data and assuming a re-operation rate of 2.7%, a cumulative total of 28% is achieved. However, as patients often have more than one MAE, this figure was adjusted using the ratio of MAEs per patient observed in the historical cohort (1.2 events per patient), resulting in an overall expected rate of 23.4% of FET patients experiencing one or more MAE. Consequently, it can be expected that 76.6% of patients will be free from MAE. This figure was used together with the performance goal of 57.4% from the historical ET cohort to derive the study sample size.

The hypothesis tested for the primary endpoint at a one-sided alpha level of 0.025 was:

- H_0: $p \leq 0.574$
- H_1: $p > 0.574$

where p represents the probability of being free from the defined composite MAEs in the population under study.

The hypothesis of the primary endpoint was that the 1 year freedom from the defined composite MAEs in the pivotal study was higher than the performance goal of 57.4% in the main study arm. Sample size was calculated assuming that the proportion of patients with freedom from the composite MAEs up to 1-year post-implant was 76.6%. Therefore a total of 52 patients would provide 90% power to reject the null hypothesis using a one-

side test and an alpha level of 0.025. To accommodate an anticipated drop-out rate of 20%, 65 patients were enrolled.

External evaluation groups were used during the course of the pivotal study, which are described below:

- *Imaging Core Laboratory*: An independent core laboratory evaluated all imaging obtained during the course of the study, including endoleak, device migration, aneurysm sac size increase, thrombus in the device and external to the graft, aortic rupture, fistula formation, pseudo-aneurysm, false lumen patency, occlusion, kinking, graft compression, patency of extension device, and stent ring fracture.

- *Clinical Events Committee and Data Safety Monitoring Board*: An independent Clinical Events Committee (CEC) and a separate, independent Data Safety Monitoring Board (DSMB) were responsible for assuring the study was conducted ethically, and that the health and welfare of each study patient was protected. The CEC adjudicated all adverse events reported by the site and classified them as related or not related to the device or the procedure, as well as adverse event outcome. In addition, the CEC adjudicated computated tomography (CT) scan analysis for endoleak, patency and device migration. The DSMB met separately to review the safety data in aggregate and assess the overall safety of the study. The DSMB also assessed whether the continuation of enrollment was appropriate, and, if not, whether protocol modifications were necessary or whether the study should be halted.

- *Data Management*: A clinical research organizationwas responsible for data management, safety and medical monitoring and statistics for the study with sponsor oversight.

1. Clinical Inclusion and Exclusion Criteria
   Enrollment in the pivotal study was limited to patients who met the following inclusion criteria:

   Main Study Arm
   A. Acute aortic dissection that required repair or replacement of damaged or diseased vessels of the aortic arch (with or without involvement of the ascending aorta), and the descending aorta requires replacement, or, in the opinion of the investigator, the patient would derive clinical benefit from prophylactic treatment of the descending aorta.
   B. Chronic aortic dissection that required repair or replacement of damaged or diseased vessels of the aortic arch and descending aorta with or without involvement of the ascending aorta, with one or more of the following criteria:
      - An aortic sinus, or ascending aorta, or aortic arch, or descending aorta diameter ≥5.5 cm (including if asymptomatic), or
      - An aortic diameter <5.5 cm and growth rate ≥0.5 cm/year (including if asymptomatic), or

- An ascending aorta diameter ≥4.5 cm and required valve repair or replacement

C. Aortic aneurysm (including connective tissue disorders) that:
   - required repair or replacement of damaged or diseased vessels of the aortic arch and descending aorta with or without involvement of the ascending aorta with one or more of the following criteria:
     - An aortic sinus, or ascending aorta, or aortic arch, or descending aorta diameter ≥5.5cm (including if asymptomatic), or
     - An aortic diameter <5.5cm and growth rate ≥0.5cm/year (including if asymptomatic), or
     - An ascending aorta diameter ≥4.5cm and requires valve repair or replacement, or
     - Marfan syndrome or other genetically mediated disorders with aortic sinus, or ascending aorta, or arch diameter ≥4.5cm, or, the ratio of the maximal ascending or aortic root area (Π r2) in cm^2 divided by the patient's height in meters exceeds 10

Rupture Arm
- 18 years or over on the date of consent
- Patient or their legally authorized representative is able and willing to give consent to the patient's enrollment in the study.
- Either a ruptured thoracic aorta, or, in the experience of the treating surgeon is at high risk of imminent rupture of the thoracic aorta

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

Main Study Arm
- Unfitness for open surgical repair involving circulatory arrest
- Known sensitivity to polyester, nitinol, or materials of bovine origin
- A ruptured aorta
- Active endocarditis or an active infective disorder of the aorta
- Active systemic infection that, in the opinion of the investigator, would compromise the outcome of the surgical procedure.
- Participation in another active study and has received an investigational product (device, pharmaceutical or biologic) within 6 months prior to the date of the implant or had not reached the primary endpoint of the study
- Pregnant, or planned pregnancy during the course of the study.
- Uncorrectable bleeding anomaly
- Renal failure (defined as dialysis dependent or serum creatinine ≥2.5mg/dL)
- Known sensitivity to radiopaque contrast agents that cannot be adequately pre-treated
- Co-morbidity causing expected survival to be less than 1 year

- Any other medical, social or psychological problems that in the opinion of the investigator preclude them from study treatment and the procedures and evaluations pre and post procedure

Rupture Arm

- Chronic dissection or aneurysmal disease which, in the opinion of the investigator, could be treated electively

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at discharge/30 days, 3 months (13 ± 4 weeks), 12 months (52 ± 8 weeks), and annually through 3 years (± 8 weeks) postoperatively. Adverse events were recorded at all visits.

Preoperatively - Each patient was required to have CT imaging with contrast, physical exam, coagulation (PT and APTT), chemistry (BUN & creatinine), and urine or blood human chorionic gonadotropin (hCG) (if applicable).

At the index procedure - Each patient was required to be assessed for any required extension procedures/additional unplanned surgical interventions, assessed for any adverse events and device deficiencies and concomitant medications.

Post-operative follow-up visits – Assessments during the study included CT with contrast, physical exam, coagulation (PT and APTT), chemistry (BUN & creatinine), patient assessments (HRQoL EQ-5D, return to normal activities), and device deficiencies. If a patient received an extension device, an additional follow-up visit at 3 months after the extension procedure was completed, unless this visit falls within 6 weeks of a visit scheduled as part of the primary follow-up protocol, in which case the additional extension related data was collected at the scheduled primary study visit.

Additional assessments that were collected at each follow-up visit included:

- Adverse events, including
  - Serious adverse events
  - Non-serious adverse events
  - Device-related adverse events
  - Procedure-related adverse events
- Aortic-disease related mortality
- Rupture
- Migration
- Endoleak
- Change in aortic size
- Stent graft integrity
- Failed patency
- Secondary procedures

Pre-operative and post-operative parameters measured for all visits are presented in **Table 6. Schedule of Activities.** The key timepoints are shown below in the tables.

Table 6. Schedule of Activities

Assessment (Timing relative to date of implant)	Pre-procedure (≤60 days)	Implant (Day 0)	Discharge or within 30 days[1] (+/- 7 days)	3 months (13 ± 4 weeks)	12 months (52 ± 8 weeks)	24 months (104 ± 8 weeks)	36 months (156 ± 8 weeks)	Extension additional follow-up[2]
Informed consent	X							
Inclusion/ exclusion	X							
Demographics and medical history	X[3]							
Physical examination	X[4]		X	X	X	X	X	X
Vital signs	X		X		X			X
Lab tests (including serum creatinine) as per standard of care	X[4]		X	X	X	X	X	
Pregnancy test[5]	X[4]							
Assessment of requirement for extension procedure	X	X						
Surgical procedural information		X						X
Discharge destination			X					
CT Imaging	X[4]		X[6]	X	X	X	X	X
Additional unplanned surgical interventions		X	X	X	X	X	X	X
Return to normal activities				X	X	X	X	X
HRQoL EQ-5D	X[3]		X	X	X	X	X	X
Concomitant medications	X[3]	X	X	X	X	X	X	X
Adverse events & Device deficiency		X	X	X	X	X	X	X
Extension procedure additional data collection[7]					(X)	(X)	(X)	X
Study completion[8]							X	

1 A follow-up examination was performed at discharge or within 30 days of surgery if the patient remained hospitalized or was unfit for contrast enhanced CT scan at the time of discharge.
2 Additional follow-up visit at 3 months after extension procedures, unless this visit fell within 6 weeks of a visit scheduled as part of the primary follow-up protocol, in which case the additional extension related data was collected at the scheduled primary study visit.
3 For patients recruited to the additional Rupture arm this data could be collected retrospectively
4 For patients recruited to the additional Rupture arm this data could be omitted if collecting the data would delay the patient's treatment and in the opinion of the treating clinician this would increase the patient's risk of death.
5 Women of childbearing potential only, βhCG test (blood or urine).
6 If patient was not fit for contrast CT scan at time of discharge, then the scan could be performed at a later date up to a maximum of 30 days +/- 7 days after initial surgery.
7 Data only collected for patients who have had an extension procedure.
8 At 3 years post-implant or time of discontinuation.

3. Clinical Endpoints

With regards to safety and effectiveness, the primary endpoint was freedom from the following composite Major Adverse Events (MAEs) occurring ≤ 1 year post-procedure.

- Permanent stroke
- Permanent paraplegia/paraparesis
- Unanticipated aortic related re-operation (excluding reoperation for bleeding), and
- All-cause mortality

The primary endpoint was compared to a performance goal of 57.4%.

With regard to success/failure criteria, the Thoraflex^{TM} Hybrid pivotal study will be considered successful if the lower limit of the 95% confidence interval, associated with the proportion of study patients who are free from the defined composite Major Adverse Events (permanent stroke, permanent paraplegia/paraparesis, unanticipated aortic related reoperation and all-cause mortality) at 1 year post procedure, is greater than 57.4%.

The following secondary analyses were completed using descriptive statistics:

Device Technical Success (at exit from the OR)

- Device technical success is defined as the following:
    - Successful delivery and accurate placement of the intraluminal part of the graft at the intended implantation site and retrieval of the device delivery system, and
    - Patency of the graft (including branches) and absence of device deformations (e.g., kinks) requiring unplanned placement of additional devices within the graft, and
    - No need for unanticipated or emergency surgery (e.g., return to bypass after initial removal of aortic cannula or reversal of heparin) or re-intervention (e.g., placement of additional unplanned endoluminal devices within the frozen segment) related to the device or procedure.

Procedural Success (at discharge/30 days)

- Procedural success is defined as technical success with absence of the following at discharge/30 days:
    - Death
    - Major adverse ischemic events: paraplegia / paraparesis, disabling stroke, new ischemia (i.e., not evident at the time of the index procedure) due to branch vessel compromise (malperfusion of organ including bowel, upper limb, or lower limb), distal procedure-related thromboembolic adverse event
    - Aortic and valve complications: aortic rupture, Increase in aortic regurgitation grade of greater than 1 (i.e., on 0 – 4 scale)
    - General procedure related complications: peri-procedural myocardial infarction (biomarker increase > 10×ULN first 72 hours) or need for urgent or emergent

percutaneous coronary interventions (PCI)/coronary artery bypass grafting (CABG), new onset renal failure requiring dialysis, renal dysfunction or volume overload requiring ultrafiltration, bowel ischemia requiring surgery or intervention, life-threatening bleed, severe Heart Failure (HF) or hypotension requiring pressors or IV inotrope > 24 hr or mechanical circulatory support (MCS), prolonged Intubation > 48 hours, pseudoaneurysm of any graft surgical suture line, additional unplanned surgical or interventional procedures related to the device since completion of the original procedure

Treatment Success (at discharge/30 days and at all post-procedural intervals)

- Treatment success is defined as device technical success with absence of the following at discharge/30 days and at all post-procedural intervals:
    - Aortic enlargement >0.5cm between scheduled post-operative imaging (that is performed within the time windows defined) in the region encompassed by the initial lesion, aortic rupture, fistula formation, lesion-related mortality, loss of device integrity (e.g., wireform fracture that could affect fixation or seal, graft fabric hole or tear, collapse), residual or new Type III endoleak;
    - The subset of major adverse events of disabling stroke within 30 days of the procedure and paraplegia/paraparesis (defined as permanent if persisting at 12 months post procedural follow up)

Individual Patient Success

- Individual patient success is defined as Treatment Success at 12 months, post-operative return to normal activities – employment, household activities, social life, and hobbies, and Improved Health Related Quality of Life Measure (HRQoL) - EQ-5D

Additional Secondary Endpoints (evaluated at all follow-up intervals unless otherwise noted)

- Incidence of any paraplegia/paraparesis
- Incidence of myocardial infarction
- Incidence of respiratory failure (ventilator dependence greater than 48 hours) at
- Incidence of renal failure requiring dialysis
- Incidence of thromboembolic adverse events as adjudicated by Clinical Events Committee (CEC)
- Incidence of bowel ischemia
- Incidence of failed patency where failed patency was defined as a reduction in blood flow through the device as determined through imaging analysis and requiring surgical intervention.
- Incidence of aortic disease related mortality
- Incidence of all re-interventions in the downstream aorta up to 36 months

- Incidence of change in aortic size in the grafted segment > 5 mm from the discharge/30 day CT. This was defined as an increase in diameter >5 mm measured along the major axis. Maximum aortic diameter is measured inner diameter to inner diameter.
- Incidence of pseudo-aneurysm up to 36 months.
- Incidence of aortic rupture up to 36 months. Aortic rupture was defined as leakage of blood from the blood vessel into a body cavity or adjacent organ as determined from imaging.
- Incidence of significant failure of device integrity, up to 36 months, defined as wear or tear in the fabric or wire breakage resulting in a compromised seal and blood leakage or movement of the device.
- Incidence of device migration up to 36 months. Migration was evaluated based on the position of the device at discharge/30 days; migration will be considered as a change >10mm from this position. First-stage procedures where the device cannot be adequately placed in the distal landing zone will be reported separately.
- Endoleaks
    - Incidence of all endoleaks
    - Incidence of secondary procedures to correct endoleaks
- Incidence of thrombosis of the lumen (perigraft lumen, false lumen)
- Endpoints specific to extension procedures:
    - Incidence of any failure of device-extension integrity (e.g., wear or tear in the fabric or wire breakage) resulting in a compromised seal and blood leakage or movement of the device
    - Incidence of Type III endoleak
    - Incidence of failed patency of the device-extension overlap
    - Incidence of MAE at 30 days post-extension
    - Incidence of secondary procedures related to the extension
- Procedural outcomes which included total operation time, bypass time, blood loss, anesthesia type and time, intraoperative management (i.e. lowest core temperature, spinal drainage), device information and performance, length of ICU stay, length of hospital stay, discharge destination, concomitant procedures)
- Incidence of hypersensitivity reactions up to 36 months
- Post-operative outcomes: return to normal activities – employment, household activities, social life and hobbies and Health Related Quality of Life Measure (HRQoL) - EQ-5D
- Non-serious and serious adverse events

B. Accountability of PMA Cohort

In the main study arm, 65 patients were implanted with Thoraflex^{TM} Hybrid and seen through discharge.

The primary analysis population for the primary endpoint (freedom from MAE) is the Intent-to-Treat population (ITT) defined as all patients who were enrolled and met all

selection criteria for the main study arm and treated with the Thoraflex™ Hybrid device. Additional analysis was performed on the Per-Protocol Population defined as all patients enrolled and evaluated for the primary endpoint at one year post-procedure without any major protocol violations.

Table 7 and **Table 8** show the patient follow up, imaging adequacy and patient status at each follow up time point for the main and aortic rupture study arm, respectively.

Table 7. Summary of Visit Compliance and Core Laboratory Imaging Follow-Up: Main Study Arm

Visit	Patient Follow-Up					Adequate Imaging to Assess the Parameter†					Patient Status			
	Eligible for Follow-up	Data for Visit	No Visit [1]	Still in Window [2]	CT Scan	Patency	Size Increase	Rupture	Migration	Endoleak	Death	Lost to Follow-up [3]	Early Withdrawal [4]	Not Due for Next Visit [5]
Operative	65	65/65 (100%)	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0/65 (0.0%)	0/65 (0.0%)	0/65 (0.0%)	0/65 (0.0%)
30 Day	65	65/65 (100%)	0	0/65 (0.0%)	55/65 (84.6%)	54/65 (83.0%)	55/65 (84.6%)	55/65 (84.6%)	N/A	54/65 (83.0%)	5/65 (7.6%)	2/65 (3.1%)	1/65 (1.5%)	0/65 (0.0%)
3 Month	58	58/58 (100%)	0	0/58 (0.0%)	55/58 (94.8%)	52/58 (89.6%)	55/58 (94.8%)	55/58 (94.8%)	53/58 (91.3%)	52/58 (89.6%)	2/58 (3.4%)	0/58 0.0%)	0/58 (0.0%)	0/58 (0.0%)
1 Year	56	56/56 (100%)	0	0/56 (0.0%)	54/56 (96.4%)	52/56 (92.8%)	54/56 (96.4%)	54/56 (96.4%)	53/56 (94.6%)	52/56 (92.8%)	4/56 (7.1%)	3/56 (5.4%)	3/56 (5.4%)	0/56 (0.0%)
2 Years	49	49/49 (100%)	0	0/49 (0.0%)	36/49 (73.5%)	35/49 (71.4%)	36/49 (73.5%)	36/49 (73.5%)	36/49 (73.5%)	35/49 (71.4%)	2/49 (4.1%)	0/49 (0.0%)	0/49 (0.0%)	0/49 (0.0%)
3 Years	47	46/47 (91.5%)	1	0/47 (0.0%)	33/47 (70.2%)	30/47 (63.8%)	33/47 (70.2%)	33/47 (70.2%)	33/47 (70.2%)	30/47 (63.8%)	0/47 (0.0%)	0/47 (0.0%)	0/47 (0.0%)	0/47 (0.0%)

N/A: not applicable; CT: Contrast or non-contrast CT scans. The numbers in the table are the numbers of patients in the specified category. "Data for Visit" means that any data were collected for the follow-up time point.

[1] Patients who did not have a visit within the window or patients who did not have a visit but have not yet reached the end of the analysis window.

[2] Patients still within follow-up window, but data not yet available.

[3] Lost to follow-up includes all Early Withdrawal [4] patients.

[4] Early withdrawal includes both patient withdrawal and investigator withdrew of patient.

[5] Not due for next visit includes patients who had visits within the specified window but were not eligible at the start of the next window due to death, surgical conversion, or early withdrawal.

Table 8. Summary of Visit Compliance and Core Laboratory Imaging Follow-Up: Aortic Rupture Arm

Visit	Patient Follow-Up					Adequate Imaging to Assess the Parameter†					Patient Status			
	Eligible for Follow-up	Data for Visit	No Visit [1]	Still in Window [2]	CT Scan	Patency	Size Increase	Rupture	Migration	Endoleak	Death	Lost to Follow-up [3]	Early Withdrawal [4]	Not Due for Next Visit [5]
Operative	9	9/9 (100%)	0	N/A	N/A	N/A	N/A	N/A	N/A	N/A	0/9 (0.0%)	0/9 (0.0%)	0/9 (0.0%)	0/9 (0.0%)
30 Day	9	9/9 (100%)	0	0/9 (100%)	6/9 (66.6%)	6/9 (66.6%)	6/9 (66.6%)	6/9 (66.6%)	N/A	6/9 (66.6%)	1/9 (11.1%)	1/9 (11.1%)	0/9 (0.0%)	0/9 (0.0%)
3 Month	7	7/7 (100%)	0	0/7 (0.0%)	5/7 (71.4%)	5/7 (71.4%)	5/7 (71.4 %)	5/7 (71.4%)	5/7 (71.4%)	5/7 (71.4%)	0/7 (0.0%)	1/7 (14.2%)	0/7 (0.0%)	0/7 (0.0%)
1 Year	6	6/6 (100%)	0	0/6 (0.0%)	5/6 (83.3%)	5/6 (83.3%)	5/6 (83.3%)	5/6 (83.3%)	5/6 (83.3%)	5/6 (83.3%)	1/6 (16.6%)	0/6 (0.0%)	0/6 (0.0%)	0/6 (0.0%)
2 Years	5	5/5 (100%)	0	0/5 (0.0%)	3/5 (60.0%)	2/5 (40.0%)	3/5 (60.0%)	3/5 (60.0%)	3/5 (60.0%)	2/5 (40.0%)	0/5 (0.0%)	0/5 (0.0%)	0/5 (0.0%)	0/5 (0.0%)
3 Years	4	4/4 (100%)	0	0/0 (0.0%)	4/4 (100%)	4/4 (100%)	4/4 (100%)	4/4 (100%)	4/4 (100%)	4/4 (100%)	0/4 (0.0%)	0/4 (0.0%)	0/4 (0.0%)	0/4 (0.0%)

N/A: not applicable; CT: Contrast or non-contrast CT scans. The numbers in the table are the numbers of patients in the specified category. "Data for Visit" means that any data were collected for the follow-up time point.

[1] Patients who did not have a visit within the window or patients who did not have a visit but have not yet reached the end of the analysis window.
[2] Patients still within follow-up window, but data not yet available.
[3] Lost to follow-up includes Early Withdrawal [4] patients.
[4] Early withdrawal includes both patient withdrawal and investigator withdrew of patient.
[5] Not due for next visit includes patients who had visits within the specified window but were not eligible at the start of the next window due to death, surgical conversion, or early withdrawal.

C. Study Population Demographics and Baseline Parameters

Demographics and Baseline Characteristics

The demographics of the study population are typical for an aortic arch pathology study performed in the US.

In the main study arm, 66.2% of the patients were male (43/65) and 33.8% were female (22/65). The average age at screening was 64.6 years. The majority of patients in the main study arm were White (44/65, 67.7%) and non-Hispanic or Latino (87.7%, 57/65) with 43.1% (28/65) of the main study arm being ex-smokers and 40% (26/65) non-smokers.

In the aortic rupture arm, 7 patients (77.8%) were males and 2 (22.2%) were females. Patients had an average age of 63.2 years at the time of screening. The majority of patients in the aoritc rupture arm were White (7/9, 77.8%) and 22.2% (2/9) were Hispanic. Five patients (5/9, 55.9%) were ex-smokers and three (33.3%) were non-smokers.

The table below summarizes the patient demographics and baseline characteristics for the intent-to-treat population for both the main study arm and aortic rupture arm.

Table 9. Summary of Patient Demographics & Baseline Characteristics (Intent-to-Treat Population)- Overall

Characteristic	Main Study Arm (N=65)	Aortic Rupture Arm (N=9)
Gender, n (%)		
Male	43 (66.2)	7 (77.8)
Female	22 (33.8)	2 (22.2)
Age at screening		
N	65	9
Mean	64.6	63.2
SD	12.74	16.32
Minimum	31	31
Median	68.0	70.0
Maximum	86	79
Ethnicity, n (%)		
Hispanic or Latino	5 (7.7)	2 (22.2)
Not Hispanic or Latino	57 (87.7)	7 (77.8)
Not Reported	2 (3.1)	0 (0.0)
Unknown	1 (1.5)	0 (0.0)
Race, n (%)		

Characteristic	Main Study Arm (N=65)	Aortic Rupture Arm (N=9)
Asian	6 (9.2)	0 (0.0)
American Indian or Alaska Native	0 (0.0)	0 (0.0)
Black or African American	12 (18.5)	2 (22.2)
Native Hawaiian or Other Pacific Islander	0 (0.0)	0 (0.0)
White	44 (67.7)	7 (77.8)
Other	3 (4.6)	0 (0.0)
Baseline Height (cm)		
N	65	9
Mean	172.6	172.54
SD	10.29	6.28
Minimum	152.40	165.10
Median	172.72	170.2
Maximum	195.6	185.4
Baseline Weight (Kg)		
N	65	9
Mean	86.29	81.28
SD	19.45	14.62
Minimum	50.35	60.70
Median	83.0	82.1
Maximum	142.40	99.79
Baseline BMI (kg/m^2)		
N	65	9
Mean	28.85	27.32
SD	5.34	4.96
Minimum	19.9	21.0
Median	28.07	26.39
Maximum	43.3	36.1
ASA Grade		
I	0 (0.0)	0 (0.0)
II	3 (4.6)	0 (0.0)
III	7 (10.8)	1 (11.1)

Characteristic	Main Study Arm (N=65)	Aortic Rupture Arm (N=9)
IV	55 (84.6)	7 (77.8)
V	0 (0.0)	0 (0.0)
Missing	0 (0.0)	1 (11.1)
Smoker		
Yes	11 (16.9)	1 (11.1)
No	26 (40.0)	3 (33.3)
Ex-smoker	28 (43.1)	5 (55.6)

N = Number of patients in the given cohort in the population and is used as the denominator for percentage calculations.
n = Number of patients with a value.
Baseline is defined as the pre-procedure measurement.
BMI = body mass index.

Baseline Medical and Surgical History

In the main study arm, 92.3% (60/65) had hypertension, 56.9% (37/65) had hyperlipidemia, 38.5% (25/65) had coronary artery disease, 16.9% (11/65) had renal insufficiency, 15.4% (10/65) had chronic obstructive pulmonary disease (COPD), and 13.8% (9/65) had a stroke. The surgical histories for the main study arm include the following: 32.3% (21/65) had a previous aortic dissection repair, 18.5% (12/65) had an aortic valve replacement or repair, 10.8% (7/65) had coronary artery bypass grafting and 10.8% (7/65) had an aortic aneurysm repair.

In the aortic rupture arm, 100% (9/9) had hypertension, 44.4% (4/9) had hyperlipidemia, 22.2% (2/9) had coronary artery disease and 22.2% (2/9) had chronic obstructive pulmonary disease.

Table 10. Summary of Medical & Surgical History (All Enrolled Patients) - Overall

Category	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Cardiac Medical History		
Other	47 (72.3)	4 (44.4)
Coronary Artery Disease - CAD	25 (38.5)	2 (22.2)
Congestive Heart Failure - CHF	10 (15.4)	1 (11.1)
Angina	3 (4.6)	0 (0.0)
Myocardial Infarction - MI	5 (7.7)	1 (11.1)
Cardiac Surgical History		
Aortic Dissection Repair	21 (32.3)	2 (22.2)
Other	13 (20.0)	1 (11.1)

Category	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Aortic Valve Replacement or Repair	12 (18.5)	1 (11.1)
Aortic Aneurysm Repair	7 (10.8)	1 (11.1)
Coronary Artery Bypass Graft - CABG	7 (10.8)	1 (11.1)
Coronary Angioplasty or Stent	4 (6.2)	0 (0.0)
Pacemaker	2 (3.1)	0 (0.0)
Endocrine Medical History		
Hypertension	60 (92.3)	9 (100.0)
Hyperlipidemia	37 (56.9)	4 (44.4)
Hypothyroid	9 (13.8)	1 (11.1)
Other	7 (10.8)	2 (22.2)
Diabetes	6 (9.2)	0 (0.0)
Cancer	5 (7.7)	0 (0.0)
Hyperthroid	1 (1.5)	0 (0.0)
Neurological Medical History		
Other	10 (15.4)	0 (0.0)
Stroke	9 (13.8)	0 (0.0)
Transient Ishemic Attack - TIA	4 (6.2)	0 (0.0)
Seizure	2 (3.1)	0 (0.0)
Nerve Damage	1 (1.5)	0 (0.0)
Neuromuscular Disease	1 (1.5)	0 (0.0)
Paraplegia	1 (1.5)	0 (0.0)
Pulmonary Medical History		
Other	27 (41.5)	3 (33.3)
Chronic Obstructive Pulmonary Disease- COPD	10 (15.4)	2 (22.2)
Asthma	8 (12.3)	2 (22.2)
Pulmonary Hypertension	3 (4.6)	0 (0.0)
Emphysema	2 (3.1)	0 (0.0)
Bronchitis	1 (1.5)	0 (0.0)
Renal Medical History		
Other	50 (76.9)	6 (66.7)
Renal Insufficiency	11 (16.9)	1 (11.1)
Renal Failure	2 (3.1)	0 (0.0)

Category	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Vascular Surgical History		
Endovascular Stent Graft	5 (7.7)	1 (11.1)
Other	5 (7.7)	0 (0.0)
Non-Coronary Bypass	4 (6.2)	0 (0.0)
Non-Coronary Angioplasty – with/without Stenting	3 (4.6)	0 (0.0)
Surgical Aneurysm Repair	2 (3.1)	1 (11.1)
Embolization	1 (1.5)	0 (0.0)
N = Number of patients in the given cohort in the population and is used as the denominator for percentage calculations.		

Summary of Indication for Surgery (All Enrolled Patients)

A summary of the indication for surgery for all enrolled patients is presented below. Note that some patients presented with multiple pathologies.

In the main study arm, 59 patients (90.8%, 59/65) had an aneurysm as an indication for surgery: 40% (26/65) had aneurysm only. Many patients also presented with dissection: 38 (58.5%, 38/65) were chronic and 1 was (1.5% (1/65)) was acute. Of the 59 patients in the main study arm with an aneurysm, 32 (54.2%, 32/59) of those patients also had a chronic dissection.

In the aortic rupture arm, 5 patients (55.6%, 5/9) had an aneurysm and 7 patients (77.8%) had an acute dissection. Two (22.2%) had aneurysm only. Three (33.3%) had both dissection and aneurysm indications. One patient had an indication of aortic rupture when enrolled. The remaining patients in this arm were included if the treating surgeon considered the patient a high risk of imminent rupture of the thoracic aorta.

In the entire study, five patients with a connective tissue disorder were enrolled: 4 (6.2%) in the main study arm and 1 (11.1%) in the aortic rupture arm. Twenty-one patients with atherosclerosis were enrolled; 19 (29.2%) in the main study arm and 2 (22.2%) in the aortic rupture arm.

Table 11. Summary of Indication for Surgery (All Enrolled Patients)

Category	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Dissection		
Acute	1 (1.5)	7 (77.8)
Chronic	38 (58.5)	0 (0.0)
Aneurysm		
Yes	59 (90.8)	5 (55.6)
Aneurysm only (no dissection)	26 (40.0)	2 (22.2)
No	6 (9.2)	4 (44.4)
Aortic Rupture		
Yes	0 (0.0)	1 (11.1)
No*	65 (100.)	8 (88.9)*
Degenerative Condition		
Atherosclerosis	19 (29.2)	2 (22.2)
Connective Tissue Disorder	4 (6.2)	1 (11.1)
Marfan Syndrome	0 (0.0)	0 (0.0)
Other	4 (6.2)	1 (11.1)

N = Number of patients in the given cohort in the population and is used as the denominator for percentage calculations. Some patients had multiple pathologies; of the 59 patients in the main study arm with an aneurysm, 32 (54.2%, 32/59) also had a chronic dissection. In the aortic rupture arm, three (33.3%) had both indications.
** High risk of imminent rupture.*

Thoraflex™ Hybrid Devices Implanted

A total of 74 Thoraflex™ Hybrid devices were implanted in the study. The Plexus 4 model device was more commonly used, with 56 implanted in both arms compared to 18 Ante-Flo. Forty-eight of the 56 Plexus 4 model devices and 17 of the Ante-Flo devices were implanted in the main study arm. In the aortic rupture arm, there were 8 Plexus 4 devices and 1 Ante-Flo device implanted. The 150mm device length was the length used most often, with 37 devices used compared to 28 of the 100mm devices. The summary of device type and device configuration are shown below.

Table 12. Summary of Device Type (Intent-to-treat Population)

Category	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Configuration		
Ante-Flo	17 (26.2)	1 (11.1)
Plexus 4	48 (73.8)	8 (88.9)
Sizes (mm)		
Short stent-graft section	28 (43%)	4 (44%)
22×24×100	0 (0.0)	0 (0.0)
24×26×100	1 (1.5)	0 (0.0)
26×28×100	7 (10.8)	1 (11.1)
28×30×100	5 (7.7)	0 (0.0)
30×32×100	1 (1.5)	1 (11.1)
30×34×100	4 (6.2)	2 (22.2)
30×36×100	0 (0.0)	0 (0.0)
30×38×100	3 (4.6)	0 (0.0)
30x40×100	6 (9.2)	0 (0.0)
32×40×100	1 (1.5)	0 (0.0)
Long stent-graft section	37 (57%)	5 (56%)
22×24×150	0 (0.0)	0 (0.0)
24×26×150	1 (1.5)	0 (0.0)
26×28×150	5 (7.7)	1 (11.1)
28×30×150	4 (6.2)	0 (0.0)
30×32×150	6 (9.2)	3 (33.3)
30×34×150	5 (7.7)	0 (0.0)
30×36×150	3 (4.6)	0 (0.0)
30x38×150	5 (7.7)	1 (11.1)
30×40×150	7 (10.8)	0 (0.0)
32×40×150	1 (1.5)	0 (0.0)

Measurements are: proximal (graft) diameter × distal (stent-graft) diameter × stent-graft length.
Denominator is either total number of implants or number of specific size used

Smaller diameter sizes were not used in the IDE study; however, the design features and manufacturing processes are the same across all device sizes. Additionally, the benchtop performance testing and analysis show the small device diameters to perform as expected and above the clinically derived acceptance criteria.

Procedural Data

Information and observations about the implantation procedure were collected. General anesthesia was utilized in all patients in both study arms. The mean total operative time was longer in the main study arm (main study arm: 555.5 min, aortic rupture arm: 492.2 min). The aortic cross-clamp time was 127.8 min in the main study arm and 112.4 min in the aortic rupture arm. The lowest core temperature mean was similar in both arms (main study arm: 68.87°F, aortic rupture arm: 69.42°F). Spinal drainage was utilized prophylactically in 11 patients (16.9%, 11/65) in the main study arm and was not utilized for any of the patients in the aortic rupture arm.

The mean length of ICU and hospital stay for the main study arm was 6.4 days and 14.5 days, respsectively while the aortic rupture arm was 8.8 days and 17.5 days, respectively. Of the 62 patients in the main study arm who survived to be discharged, 39 (62.9%) were discharged home, 14 (22.6%) to a rehabilitation facility and five (8.1%) to a nursing home. Four patients (50%, 4/8) in the aortic rupture arm were discharged home (one patient died prior to discharge), one patient was discharged to a rehabilitation center, three discharge destinations were not recorded.

Table 13. Summary of Procedural Outcomes (Intent-to-Treat Population) – Overall

Characteristic	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Total Operation Time (min)		
N	65	9
Mean	555.5	492.2
SD	152.25	89.32
Minimum	270	419
Median	529.0	468.0
Maximum	1034	701
Anesthesia type, n (%)		
General	65 (100.0)	9 (100.0)
Other	0 (0.0)	0 (0.0)
Cardio-pulmonary bypass time (min)		
N	65	9
Mean	202.6	193.9
SD	81.61	39.28
Minimum	41	143
Median	198.0	200.0
Maximum	430	246
Aortic cross-clap time (min)		
N	65	9
Mean	127.8	112.4
SD	73.37	27.73

Characteristic	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Minimum	11	72
Median	120.0	105.0
Maximum	349	164
Hypothermic circulatory arrest time (min)		
N	65	9
Mean	51.7	40.8
SD	36.24	27.64
Minimum	0	3
Median	50.0	44.0
Maximum	235	82
Selective cerebral perfusion n (%)		
Retrograde	11 (16.9)	0 (0.0)
Antegrade	54 (83.1)	9 (100.0)
Perfusion time (min)		
N	63	9
Mean	61.8	47.1
SD	35.55	25.88
Minimum	3	7
Median	57.0	54.0
Maximum	246	82
Rewarming time (min)		
n	64	9
Mean	85.7	87.6
SD	44.73	30.83
Minimum	24	39
Median	73.5	82.0
Maximum	313	140
Lower body ischemia time (min)		
n	64	9
Mean	51.9	40.7
SD	42.28	27.56
Minimum	0	3
Median	47.5	44.0
Maximum	242	82
Blood Loss (mL)		
N	48	7
Mean	1034.0	628.6
SD	936.05	815.91

Characteristic	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Minimum	2	0
Median	800.0	250.0
Maximum	3650	2400
Anesthesia duration (min)		
N	65	9
Mean	606.4	552.4
SD	160.63	102.49
Minimum	235	424
Median	572.0	533.0
Maximum	999	721
Lowest core temperature (F)		
n	65	9
Mean	68.87	69.42
SD	6.53	6.57
Minimum	53.60	59.00
Median	68.000	68.000
Maximum	83.84	80.60
Spinal drainage duration (day)		
n	11	0
Mean	3.27	0
SD	1.834	0
Minimum	1.0	0
Median	3.10	0
Maximum	8.0	0
Length of ICU stay (day)		
N	62	8
Mean	6.4	8.8
SD	7.03	10.00
Minimum	1	2
Median	4.5	4.5
Maximum	38	32
Length of hospital stay (day)		
N	62	8
Mean	14.5	17.5
SD	11.34	12.51
Minimum	5	6
Median	11.0	11.0
Maximum	64	39

Characteristic	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Discharge destination, n (%)		
N *	62 *	8 *
Home	39 (60.0)	4 (44.4)
Rehabilitation Center	14 (21.5)	1 (11.1)
Other hospital	1 (1.5)	0 (0.0)
Nursing home	5 (7.7)	0 (0.0)
Other	3 (4.6)	3 (33.3)

- N=number of patients in ITT population

** Two patients in the main study arm and one in the rupture arm died before discharge.*

Intraoperative Graft Adjustments

Each patient was treated with a Thoraflex™ Hybrid device in accordance with the device instructions for use (IFU) and standard of care. The size of the device was selected based on pre-operative imaging and taking into account the sizing recommendations in the IFU. The graft portion of the device could be trimmed to fit the patient's anatomy using the guidance for cutting in the IFU. Shortening the main body of the graft portion of the device or shortening any of the branch vessels on a Plexus-4 version of the device was expected as this is consistent with standard surgical practice and data was not collected. Any other adjustments which were made to the graft portion of the device in order for the device to achieve best fit to the patient anatomy was recorded in the eCRFs.

Table 14. Summary of Intraoperative Graft Adjustments (Intent-to-Treat Population)

Adjustment Type	Main Study Arm (N =65) n (%)	Aortic Rupture Arm (N = 9) n (%)
Any graft adjustment	22 (33.8)	6 (66.7)
Non-anatomical implantation of branches	4 (6.2)	0 (0.0)
Attachment of additional grafts or native vessels directly onto the graft	9 (13.8)	1 (11.1)
Altering location of the 'cut-down' and subsequent attachment of the collar	9 (13.8)	3 (33.3)
Use of pledglets, cuffs, or other felt products to reinforce collar/vessel	7 (10.8)	2 (22.2)
Other graft adjustments	1 (1.5)*	1 (11.1)**

*For this "other" reported, the Investigator stated that the subclavian branch was removed and ligated because the Investigator was unable to dissect the subclavian artery due to heavy scar tissue from previous surgery.

** For this "other" reported, a hole was made in the graft and an anastomosis between the graft and the right coronary button was constructed with 5 0 prolene continuous suture.

Concomitant Procedures

Concomitant procedures include any procedures that occurred during index procedure. The concomitant procedures included the following procedures: CABG (7 procedures), valve surgery (9 procedures), and other (16 procedures) for both study arms. The other procedures included pacemaker insertion, aortic root replacement, chest reexploration, planned second stage elephant completion, and planned psdeuoaneryusm repair. The details of Concomitant procedures are summarized below.

Two patients in the aortic rupture arm underwent 4 concomitant procedures, which included 1 CABG, 1 valve surgery, and 2 others.

Table 15. Concomitant Procedures (Intent-to-Treat Population) - Overall

Timepoint Procedure	Main Study Arm (N = 65) n (%) e	Aortic Rupture Arm (N = 9) n (%) e
N	**65**	**9**
Planned Concomitant Procedures		
CABG	**6 (9.2) 6**	**1 (11.1) 1**
Urgent	0 (0.0) 0	1 (11.1) 1
Emergent	0 (0.0) 0	0 (0.0) 0
Elective	6 (9.2) 6	0 (0.0) 0
Valve Surgery	**6 (9.2) 7**	**0 (0.0) 0**
Aortic	6 (9.2) 6	0 (0.0) 0
Mitral	1 (1.5) 1	0 (0.0) 0
Tricuspid	0 (0.0) 0	0 (0.0) 0
Other	**5 (7.7) 9**	**1 (11.1) 1**
Unplanned Concomitant Procedures		
CABG	**0 (0.0) 0**	**0 (0.0) 0**
Urgent	0 (0.0) 0	0 (0.0) 0
Emergent	0 (0.0) 0	0 (0.0) 0
Elective	0 (0.0) 0	0 (0.0) 0
Valve Surgery	**1 (1.5) 1**	**1 (11.1) 1**
Aortic	1 (1.5.) 1	1 (11.1) 1
Mitral	0 (0.0) 0	0 (0.0) 0
Tricuspid	0 (0.0) 0	0 (0.0) 0
Other	**5 (7.7) 5**	**1 (11.1) 1**

*- N=number of patients in ITT population; n=number of patients in specified category; %=100*n/N, e=total number of procedures*

-Note: Concomitant procedures include any procedures occurred during the initial procedure hospitalization.

D. Safety and Effectiveness Results

Primary Endpoint

The primary endpoint was defined as the proportion of patients with freedom from athe following composite Major Adverse Events (MAEs) occurring ≤ 1 year post procedure: permanent stroke, permanent paraplegia/paraparesis, unanticipated aortic related re-operation (excluding reoperation for bleeding), and all-cause mortality.

The primary endpoint is compared to a Performance Goal (PG) of 57.4%. The primary analysis population for the primary endpoint (freedom from MAE) is the Intent-to-Treat population (ITT) defined as all patients who were enrolled in the study and met all selection criteria for the main study arm and were treated with a Thoraflex™ Hybrid device. Patients whose status was unknown at one year were imputed as considered MAE failures.

The rate of freedom from composite MAEs occurring ≤ 1 year post-procedure was 76.9% (50/65, 95% CI 66.7% to 87.2%) in the main study arm. The lower bound of the 95% confidence interval was above 57.4% indicating that the Performance Goal was met.

A total of 18 events were observed in a total of 13 patients. In addition, 2 patients were imputed as failures as their status was unknown at 1 year. In the main study arm, events reported include 5 permanent strokes, 3 cases of permanent paralysis/paraplegia, 7 deaths, and 3 unanticipated aortic related re-operations.

Analyses were performed to assess poolability of data across investigational sites. The assessment supports the poolability of the data.

Table 16. Primary Endpoint Failure within One Year of Implant by Study Arm (Intent-to-Treat Population)

Study Arm Overall (N=74)	Event	Patients with Event n (p)	Patients Event-Free n (p)	95% Confidence Interval for Event-Free
Main Study Arm (N' = 65)	Any failure	15 (0.231)	50 (0.769)	(0.667, 0.872)
	Permanent Stroke	5 (0.077)	60 (0.923)	(0.858, 0.988)
	Permanent Paraplegia/Paraparesis	3 (0.046)	62 (0.954)	(0.903, 1.000)
	Mortality	7 (0.108)	58 (0.892)	(0.817, 0.968)
	Unanticipated Aortic Related Re-operation	3 (0.046)	62 (0.954)	(0.903, 1.000)
Aortic Rupture Arm	Any failure	4 (0.444)	5 (0.556)	(0.231, 0.880)
(N' = 9)	Permanent Stroke	2 (0.222)	7 (0.778)	(0.506, 1.000)
	Permanent Paraplegia/Paraparesis	1 (0.111)	8 (0.889)	(0.684, 1.000)
	Mortality	1 (0.111)	8 (0.889)	(0.684, 1.000)

Table 16. Primary Endpoint Failure within One Year of Implant by Study Arm (Intent-to-Treat Population)

Study Arm Overall (N=74)	Event	Patients with Event n (p)	Patients Event-Free n (p)	95% Confidence Interval for Event-Free
	Unanticipated Aortic Related Re-Operation	0 (0.000)	9 (1.000)	(1.000, 1.000)

All MAEs were adjudicated by the Clinical Events Committee (CEC).
- N = number of patients in the ITT population; N′ = number of patients within each subgroup; n=number of patients in specified category; p=n/N′.
NOTE: If the lower bound of the 95% confidence interval is >0.574 for Any MAE in the Main Study Arm, the study has demonstrated that the proportion of patients in this population treated with the Thoraflex™ Hybrid Device meets the performance goal.
NOTE: For this analysis, two patients whose status at Year 1 is unknown are considered primary endpoint failures.
NOTE: Unanticipated aortic related re-operation excluded any planned extension procedure with its need identified prior to or during the implantation of the device. Non-permanent paraplegia/paraparesis are excluded from MAEs.

Secondary Endpoints

Composite Secondary Endpoints

Composite secondary endpoints included device technical success (at exit from the operating room), procedural success at discharge and treatment success.

For the main study arm, device technical success was 98.5% (64/65). Procedural success was 67.7% (44/65) at discharge/30 days. Treatment success was 91.1% (51/56) at 12 months, 95.9% (47/49) at 2-years and 95.7% (44/46) at 3-years.

For the aortic rupture arm, 88.9% (8/9) of patients achieved device technical success. Procedural success was 55.6% (5/9) at discharge/30 days. Treatment success was 83.3% (5/6) at 12 months, 60% (3/5) at 24 months and 50% (2/4) at 36 months.

Table 17. Summary of Composite Secondary Endpoints (Intent-to-Treat Population) – Overall

Endpoint Timepoint	Main Study Arm (N = 65) n/N′ (%)	Aortic Rupture Arm (N = 9) n/N′ (%)
Device Technical Success (at exit from OR)	64/65 (98.5)	8/9 (88.9)
Successful delivery achieved	64/65 (98.5)	9/9 (100.0)
Patency of graft	65/65 (100.0)	9/9 (100.0)
No re-intervention	65/65 (100.0)	8/9 (88.9)
Procedural Success (at discharge/30 days)	44/65 (67.7)	5/9 (55.6)
Death	2/65 (3.1)	1/9 (11.1)
Major adverse ischemic events	8/65 (12.3)	2/9 (22.2)
Aortic and valve complications	0/65 (0.0)	0/9 (0.0)
General procedure-related complications	17/65 (26.2)	3/9 (33.3)
Treatment Success		
Discharge/30 days	57/65 (87.7)	7/9 (77.8)

3 Months	52/58 (89.7)	6/7 (85.7)
12 months	52/56 (92.9)	5/6 (83.3)
24 months	47/49 (95.9)	3/5 (60.0)
36 months	44/46 (95.7)	2/4 (50.0)

- N=number of patients in the ITT population; n=number of patients in specified category;
Percentages are based on N′ which is the number of patients who have adequate data to assess the parameter within each arm.
In one case, the Thoraflex™ Hybrid device did not deploy as described in the Instructions-For-Use; the investigator removed the device and successfully implanted a different device. Failure to remove the guidewire prior to removing the handle was the most likely cause of incorrect deployment.
Major adverse ischemic events comprised: New ischemia (i.e., not evident at the time of the index procedure) due to branch vessel compromise (malperfusion of organ including bowel, upper limb, or lower limb), Disabling stroke, Paraparesis,
General procedure-related complications comprised: prolonged intubation (>48h), and new onset renal failure requiring dialysis, Renal dysfunction or volume overload requiring ultrafiltration, Severe Heart Failure (HF) or hypotension requiring pressors or IV inotrope > 24hr or mechanical circulatory support (MCS), Peri-procedural myocardial infarction (biomarker increase > 10x ULN first 72 hours) or need for urgent or emergent PCI/CABG, Additional unplanned surgical or interventional procedures related to the device since completion of the original procedure, and Peri-procedural myocardial infarction (biomarker increase > 10×ULN first 72 h) or need for urgent or emergent PCI/CABG.

All-Cause Mortality

There were 7 deaths (10.8%) through one year in the main study arm. There were six more deaths in the main study arm after one year (20% in total to three years, 13/65).

Three deaths were adjudicated as aortic-disease related. Four deaths were adjudicated by the CEC as possibly device-related, three as procedure-related, four as possibly procedure-related; and five as neither device or procedure related.

The Kaplan-Meier estimate of the freedom from all-cause mortality is 81.5% (95% CI, 69.8-89.1) out to 3 years for the main study arm (**Figure 4**).

There were 2 events of all-cause mortality in the aortic rupture arm through 3 years. One death was adjudicated as related to procedure and one death as unknown due to the lack of information and details provided to the Investigator by the next of kin.

Table 18. All-cause mortality: Intent-to-Treat Population

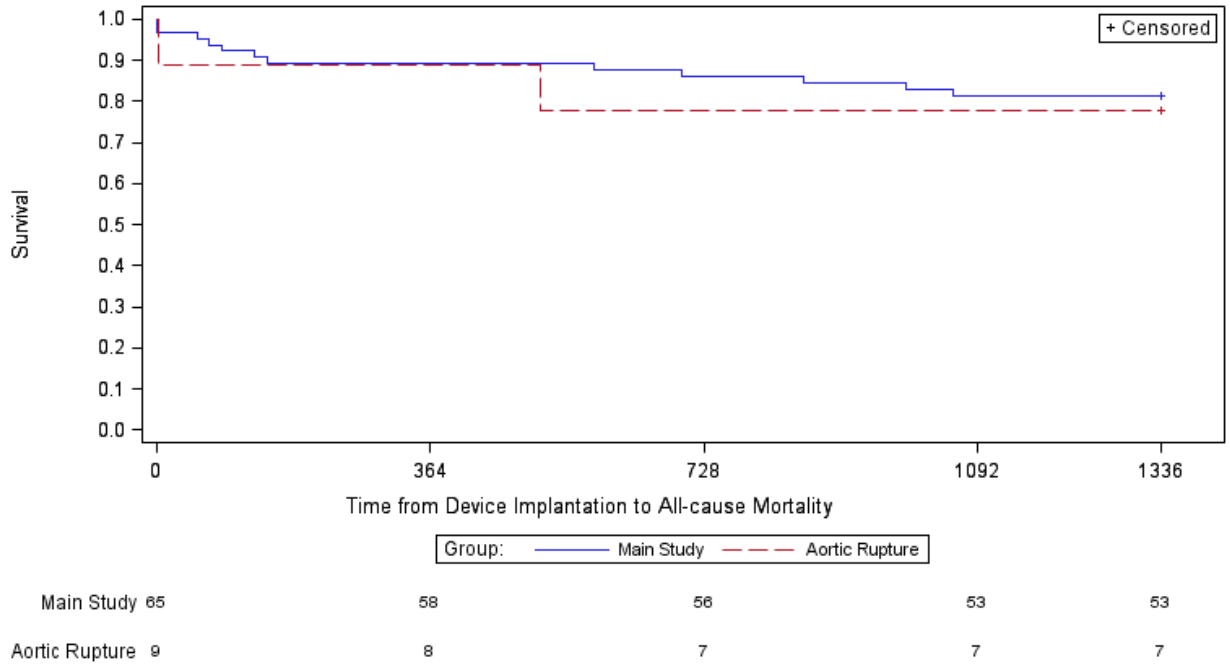
Secondary Endpoint	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months	Total
Number of patients eligible (Main/Aortic Rupture Arm) - *N′*	65/9	60/7	57 § /6	50/5	48/4	65/9
Main Study Arm n (%) ‡	2 (3.1)	3 (5.0)	2 (3.5)	3 (6.0)	2 (4.8)	12 (18.5) ‡
Aortic Rupture Arm n (%)	1 (11.1)	0 (0.0)	0 (0.0)	1 (20.0)	0 (0.0)	2 (22.2)

N=number of subjects enrolled; n=number of subjects in specified category; Percentages are based on N′ which is the number of patients who have adequate data to assess the parameter within each subgroup.
‡ Total number of deaths in the main study arm is 13: one patient is not listed in the follow-up timepoints because AE start date/end dates were missing and could not be assigned to a visit (but were after one year).
§ One patient was excluded from denominator because death was POD 147 and there was no 12M visit.

The Kaplan-Meier estimate of the freedom from all-cause mortality in the aortic rupture arm is 88.9% (95% CI, 43.3-98.4) at one year. The Kaplan-Meier estimate of the freedom

from all-cause mortality is 77.8% (95% CI 36.5-93.9) out to 3 years for the aortic rupture arm.

Figure 4. Kaplan-Meier Time from Implantation to All-Cause Mortality (Intent-to-Treat Population)



	POD	Events	Event free (%)	95% lower CI	95% upper CI
Main Study	0	0	1.000	1.000	1.000
	1	2	0.969	0.883	0.992
	55	3	0.954	0.864	0.985
	69	4	0.938	0.844	0.976
	87	5	0.923	0.825	0.967
	130	6	0.908	0.806	0.957
	147	7	0.892	0.787	0.947
	582	8	0.877	0.769	0.936
	697	9	0.862	0.751	0.925
	860	10	0.846	0.733	0.914
	997	11	0.831	0.715	0.902
	1058	12	0.815	0.698	0.891
	1336	12	0.815	0.698	0.891
Aortic Rupture	0	0	1.000	1.000	1.000
	3	1	0.889	0.433	0.984
	509	2	0.778	0.365	0.939
	1336	2	0.778	0.365	0.939

CI, confidence interval; POD, postoperative day.

Aortic-Disease Related Mortality

Aortic-Disease Related Mortality is defined as death due to aortic disease or complications from aortic disease. The CEC adjudicated all deaths to determine those that meet the aortic-disease related mortality definition.

There were 3 patients (3/65, 4.6%) in the main study arm that were adjudicated with aortic-disease related morality. One patient had an unplanned TEVAR at day 1 post-implant with

a date of death on day 2 post-implant; the cause of death was unanticipated aortic-related reoperation. The investigator initially reported the event as aortic rupture; the CEC adjudicated this event as unanticipated aortic-related reoperation. The second patient had an unplanned endovascular repair of the descending thoracic aorta due to rapid aneurysm growth at 23 days post-implant with a date of death at 69 days post implant; the cause of death was aortic-disease related. The third patient had a sudden and unexplained death caused by a witnessed cardiac arrest at 147 days post-implant.

There were no aortic-disease related mortalities in the aortic rupture arm.

Table 19. Incidence of Aortic Disease Related Mortality – Intent-To-Treat Population

Secondary Endpoint	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months	Total
Number of Patients Eligible (Main/Aortic Rupture Arm) – *N'*	65/9	58/7	56/6	47/4	46/4	65/9
Main Study Arm n (%)	1 (1.5)	1 (1.7)	1 (1.8)	0 (0.0)	0 (0.0)	3 (4.6)
Aortic Rupture Arm n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

- N=number of patients enrolled; n=number of patients in specified category; Percentages are based on N' which is the number of patients who have adequate data to assess the parameter within each subgroup.

Aortic Rupture

Aortic rupture is defined as the leakage of blood from the blood vessel into a body cavity or adjacent organ and determined by the investigator from appropriate imaging. There were no cases of CEC adjudicated aortic rupture in either study arm. The CEC reviewed core lab findings. The core lab did not report any rupture. One site-reported rupture was adjudicated by the CEC instead as unanticipated aortic-related reoperation.

Permanent Stroke

In the main study arm, there were 5 MAEs of permanent disabling stroke (5/65, 7.7%), 4 were ischemic and one was hemorrhagic and fatal, which was also the only one that occurred post-discharge (at 3 months). One stroke resolved without sequelae, one resolved with sequelae, one improved but remained ongoing, and one remained unchanged.

In the aortic rupture arm, two permanent ischemic and disabling strokes were reported in two patients (2/9, 22.2%) within 30 days. One of the patients subsequently died, the other recovered with sequelae. A third patient had a stroke that was unrelated to the device or procedure on POD 1283: combined events of Type B intramural hematoma, paraparesis, ischemic stroke , stroke hemorrhagic , respiratory failure, and cocaine vasculopathy were severe and unresolved at the time of the last study visit.

Table 20. Summary of Permanent Stroke -Intent-to-Treat Population

Secondary Endpoint	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months	Total
Number of Patients Eligible N'	65/9	58/7	55/6	47/4	46/4	65/9
Main Study Arm n (%)	4 (6.2)	1 (1.7)	0 (0.0)	0 (0.0)	0 (0.0)	5 (7.7)
Aortic Rupture Arm n (%)	2 (22.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	3 (33.3)

- N=number of patients enrolled; n=number of patients in specified category; Percentages are based on N' which is the number of patients who have adequate data to assess the parameter within each subgroup.

Permanent stroke is defined as any confirmed new neurological deficit of abrupt onset caused by a disturbance in blood supply to the brain that did not resolve prior to patient being discharged from the hospital. The diagnosis must be confirmed by at least one of the following: Neurologist or neurosurgical specialist; Neuroimaging procedure (CT scan or brain MRI), but stroke could be diagnosed on clinical grounds alone;

Ischemic Stroke: Acute episode of focal cerebral, spinal, or retinal dysfunction caused by infarction of central nervous system tissue.

Hemorrhagic Stroke: Acute episode of focal or global cerebral or spinal dysfunction caused by intraparenchymal, intraventricular, or subarachnoid hemorrhage.

Disabling Stroke: Modified Rankin Score (mRS) score of 2 or more at 90 days and an increase in at least one mRS category from an individual's pre-stroke baseline.

The Total column reports the number of subjects with that specific event/observation (at any timepoint). Some subjects may have the same event/observation reported at multiple timepoints or multiple events/observations; these are counted once in the Total column.

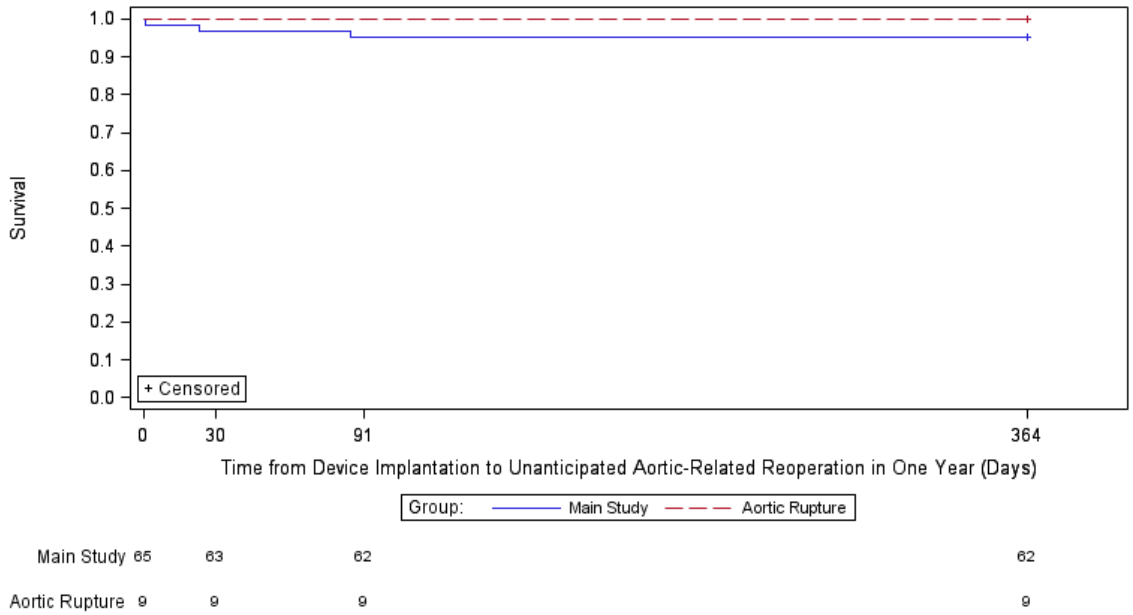
Unanticipated Aortic-related Re-operation

In the main study arm, one re-operation occurred in one patient (1/65 1.5%) at the discharge/30 day follow up and two re-operations in two patients (2/58 3.4%) at the 3-month follow-up. None of the events were device related. Kaplan-Meier estimates of freedom from unanticipated aortic-related re-operation in the main study arm were 96.9% at 30 days and 95.4% at 90 days through 1 year (**Figure 5**).

Two unanticipated aortic-related re-operations were emergent TEVARs (second-stage procedures that were planned but had to be brought forward). One patient died before discharge; a second was discharged but later died. The third case was due to a new abdominal aortic dissection and was treated successfully by open repair of infrarenal abdominal aorta.

In the aortic rupture arm, there were no cases of unanticipated aortic-related re-operation (excluding re-operation for bleeding).

Figure 5. Implantation to Unanticipated Aortic-Related Reoperation (ITT)



	POD	Events	Event free (%)	95% lower CI	95% upper CI
Main Study	0	0	1.000	1.000	1.000
	1	1	0.985	0.896	0.998
	23	2	0.969	0.883	0.992
	85	3	0.954	0.864	0.985
	364	3	0.954	0.864	0.985
Rupture	0	0	1.000	1.000	1.000
	364	0	1.000	1.000	1.000

CI, confidence interval; POD, postoperative day.

Paraplegia/Paraparesis

In the main study arm, there were 5 reported cases of paraplegia/paraparesis and one reported case of spinal cord ischemia (SCI). Three were adjudicated as permanent, 2 of which persisted until death. All 3 cases that were considered permanent received a 150mm distal stented graft section. None of these 3 patients received further extension with an additional endovascular graft. Including the event reported as SCI, the incidence at Discharge/30 days is 6.2% (4/65). This SCI event was not reported as paraplegia/paraparesisas this patient had prior history of lower extremity weakness. This patient received a 150 mm device and was found POD 1 to have bilateral lower extremity weakness but could ambulate. A CSF drain was placed, and the patient improved to baseline by POD 13. The CEC adjudicated this event as not an MAE and not permanent as the SCI resolved prior to 12 months.

In the aortic rupture arm, there was one case adjudicated by the CEC as permanent paraplegia/paraparesis. One other event within 30-days was reported as Brown-Sequard Syndrome. The CEC did not consider this an MAE and not permanent paraplegia/paraparesis and is not presented in the table below.

Table 21. Summary of Paraplegia/Paraparesis -Intent-to-Treat Population

Secondary Endpoint	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months	Total
Number of Patients Eligible N'	65/9	58/7	55/6	48/4	46/4	65/9
Any paraplegia/paraparesis						
Main Study Arm n (%)	3 (4.6)*	1 (1.7)	0 (0.0)	1 (2.1)	0 (0.0)	5 (7.7)*
Aortic Rupture Arm n (%)	1 (11.1)†	0 (0.0)	0 (0.0)	0 (0.0)	1 (25.0)	2 (22.2)†
Permanent paraplegia/paraparesis persisting at 12 months						
Main Study Arm (N=65) n (%)						3 (4.6) ‡
Aortic Rupture Arm (N=9) n (%)						1 (11.1)
Permanent paraplegia/paraparesis persisting at death						
Main Study Arm (N=65) n (%)						2 (3.1) §
Aortic Rupture Arm (N=9) n (%)						0 (0.0)

- N=number of patients enrolled; n=number of patients in specified category; Percentages are based on N′ which is the number of patients who have adequate data to assess the parameter within each subgroup.

** 4 (6.2%) at 30 days and 6 (9.2%) Total with the event reported as SCI.*

† 2 (22.2%) at 30 days and 3 (33.3%) Total with the event reported as Brown-Sequard Syndrome.

- N=number of patients enrolled; n=number of patients in specified category; percentages are based on N′ which is the number of patients who have adequate data to assess the parameter within each group.

‡ Three patients met this primary endpoint MAE.

§ One patient expired POD 103 and another expired POD 130.

The Total column reports the number of subjects with that specific event/observation (at any timepoint). Some subjects may have the same event/observation reported at multiple timepoints or multiple events/observations; these are counted once in the Total column.

Paraplegia/paraparesis is defined as complete/partial or incomplete loss of lower limb motor function (paralysis), related to spinal cord ischemia and not relating to stroke. Where paraplegia/paraparesis is reported at discharge/30 days and persists at 12 months the term will be updated to permanent paraplegia/paraparesis. Where a patient dies prior to 12-month follow-up, the term will be updated to paraplegia/paraparesis persisting at time of death.

Myocardial Infarction

In the main study arm, there was one 1/48, (2.1%) myocardial infarction reported at the 24-month follow-up. This patient had a myocardial infarction on post-operative day 698 with an elevated troponin level of 9.13 ng/ml (normal range 0.04 ng/ml) after undergoing an Extent 1 Thoracoabdominal aortic aneurysm replacement using a stage II elephant trunk technique

There were no reported cases of myocardial infarction in the aortic rupture arm.

Table 22. Incidence of Myocardial Infarction

Secondary Endpoint	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months	Total
Number of Patients Eligible (Main/Aortic Rupture Arm) - *N′*	65/9	57/7	55/6	48/4	46/4	65/9
Main Study Arm n (%)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)	0 (0.0)	1 (1.5)
Aortic Rupture Arm n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

- N=number of patients enrolled; n=number of patients in specified category; percentages are based on N′ which is the number of patients who have adequate data to assess the parameter within each arm.
The Total column reports the number of subjects with that specific event/observation (at any timepoint). Some subjects may have the same event/observation reported at multiple timepoints or multiple events/observations; these are counted once in the Total column.
Myocardial infarction (MI) was defined as evidence of myocardial necrosis (either changes in cardiac biomarkers or post-mortem pathological findings) and supporting information derived from the clinical presentation, electrocardiographic changes, or the results of myocardial or coronary artery imaging.

Respiratory Failure

In the main study arm, 15 patients (15/65, 23.1%) experienced respiratory failure at discharge/30 days, 2 (2/58, 3.4%) at 3 months follow-up, 1/55 (1/55, 1.8%) at 12 months, 1/48 (1/48, 2.1%) at 24 months, and 3/47 (3/47, 6.4%) at 36-month follow-up. Of the 15 respiratory failures reported at discharge/30-day visit, 93.3% (14/15) resolved by the 3 month3-month visit. The other patient's respiratory failure resolved during the 3 month follow up visit on post-operative day (POD) 55.

The patient's respiratory failure event was newly reported at the 3 month follow-up visit and remained unchanged until the time of death on POD 103.

There were two late cases of respiratory failure reported at 12 and 24 months related to subsequent thoracoabdominal aneurysm repairs.

In the aortic rupture arm, one (11.1%, 1/9) patient experienced respiratory failure at discharge/30 days, and one (11.1%, 1/7) experienced respiratory failure at 3-month follow-up. The respiratory failure reported at discharge/30-day visit remained unchanged at the time of death. There was one (11.1%) reported respiratory failure at 3-month follow-up which was moderate in intensity and resolved on POD 72. The CEC adjudicated this event as not related to device but related to procedure.

Table 23. Incidence of Respiratory Failure: Intent-to-Treat Population

Secondary Endpoint	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months	Total
Number of Patients Eligible (Main/Aortic Rupture Arm) - *N′*	65/9	58/7	55/6	48/4	47/4	65/9
Main Study Arm n (%)	15 (23.1)	2 (3.4)	1 (1.8)	1 (2.3)	3 (6.4)	21 (32.3)
Aortic Rupture Arm n (%)	1 (11.1)	1 (14.3)	0 (0.0)	0 (0.0)	1 (25.0)	3 (33.3)

- N=number of pateints enrolled; n=number of patients in specified category; percentages are based on N′ which is the number of patients who have adequate data to assess the parameter within each arm.
The Total column reports the number of subjects with that specific event/observation (at any timepoint). Some subjects may have the same event/observation reported at multiple timepoints or multiple events/observations; these are counted once in the Total column.
Respiratory failure is defined as ventilator dependence greater than 48 hours

Renal Failure

In the main study arm, 4 patients (4/65, 6.2%) were reported with renal failure at discharge/30 days. All 4 incidences of renal failure were treated with hemodialysis and occurred within 1-2 days from the implant surgery. There was one (2.1%) more event at 36 months in a patient (13-001) who subsequently died.

In the aortic rupture arm, renal failure was reported in 1 patient at discharge/30 days. This acute kidney injury was due to ischemic acute tubular necrosis post-operatively resulting in gross fluid overload. The patient was treated with continuous veno-venous hemodialysis (CVVHD). The event remained unchanged at the time of death (POD 4).

Table 24. Incidence of Renal Failure

Secondary Endpoint	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months	Total
Number of Patients Eligible (Main/Aortic Rupture Arm) - *N´*	65/9	57/7	55/6	47/4	47/4	65/9
Main Study Arm n (%)	4 (6.2)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)	5 (7.7)
Aortic Rupture Arm n (%)	1 (11.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (11.1)

- N=number of patients enrolled; n=number of patients in specified category; percentages are based on N´ which is the number of patients who have adequate data to assess the parameter within each arm.
The Total column reports the number of subjects with that specific event/observation (at any timepoint). Some subjects may have the same event/observation reported at multiple timepoints or multiple events/observations; these are counted once in the Total column.
Renal failure is defined as dialysis dependent or serum creatinine ≥2.5mg/dL.

Bowel Ischemia

In the main study arm, bowel ischemia was reported in one patient at discharge/30 days, and a second patient at 3-months through the 12-month follow-up visit. These cases are briefly discussed below.

- One patient had ischemic colitis at the discharge/30 day visit, intensity was reported as mild and unchanged at the time from withdrawing from the study. This event was CEC adjudicated as not related to the device and related to the procedure.
- The patient had bowel ischemia at 3-month follow-up.It continued through the 12 month visit and was severe in intensity but resolved by POD 333. The CEC adjudicated as not related to the device and not related to the procedure.

No instances of bowel ischemia were reported in the aortic rupture arm.

Table 25. Incidence of Bowel Ischemia

Secondary Endpoint	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months	Total
Number of Patients Eligible (Main/Aortic Rupture Arm) - N	65/9	57/7	55/6	47/4	46/4	65/9
Main Study Arm n (%)	1 (1.5)	1 (1.8)	1 (1.8)	0 (0.0)	0 (0.0)	2 (3.1)
Aortic Rupture Arm n (%)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

- N=number of patients enrolled; n=number of patients in specified category; percentages are based on N′ which is the number of patients who have adequate data to assess the parameter within each arm.
The Total column reports the number of subjects with that specific event/observation (at any timepoint). Some subjects may have the same event/observation reported at multiple timepoints or multiple events/observations; these are counted once in the Total column.
Bowel ischemia is defined as inadequate flow of oxygenated blood to the intestines.

Device-related Adverse Events

Adverse events adjudicated by the CEC as device-related are summarized **Table 26**. This table includes both AEs and SAEs and is sorted by MedDRA (Medical Dictionary for Regulatory Activities) system organ class (SOC) and preferred term (PT).

In the main study arm, 33.8% (22/65) of patients experienced a device-related adverse event.

For the aortic rupture arm, 33.3% (3/9) of patients experienced a device-related adverse event.

The summary of device-related events for this group is summarized below.

Table 26. Summary of Device-Related Adverse Events SOC/PT – Intent-to-Treat Population (Overall)

MedDRA SOC/PT	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Any Device-Related Adverse Event	22 (33.8)	3 (33.3)
General disorders and adminisration site conditions	7 (10.8)	1 (11.1)
Systemic inflammatory response syndrome	2 (3.1)	1 (11.1)
Stent-graft endoleak	2 (3.1)	0 (0.0)
Pain	1 (1.5)	0 (0.0)
Death	1 (1.5)	0 (0.0)
Vascular stent thrombosis	1 (1.5)	0 (0.0)
Vascular disorders	6 (9.2)	1 (11.1)
Embolism	2 (1.5)	1 (11.1)

Table 26. Summary of Device-Related Adverse Events SOC/PT – Intent-to-Treat Population (Overall)

MedDRA SOC/PT	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Aortic Dissection	1 (1.5)	0 (0.0)
Aortic aneurysm rupture	1 (1.5)	0 (0.0)
Iliac artery embolism	1 (1.5)	0 (0.0)
Shock	1 (1.5)	0 (0.0)
Nervous system disorders	5 (7.7)	1 (11.1)
Cerebrovascular accident*	2 (3.1)	0 (0.0)
Paraparesis	1 (1.5)	1 (11.1)
Paralysis	1 (1.5)	0 (0.0)
Paraplegia	1 (1.5)	0 (0.0)
Surgical and medical procedures	5 (7.7)	0 (0.0)
Aortic surgery	3 (4.6)	0 (0.0)
Aortic stent insertion	2 (3.1)	0 (0.0)
Injury, poisoning and procedural complications	2 (3.1)	1 (11.1)
Spinal cord injury	2 (3.1)	1 (11.1)
Gastrointestinal disorders	1 (1.5)	0 (0.0)
Abdominal pain	1 (1.5)	0 (0.0)
Nausea	1 (1.5)	0 (0.0)
Vomiting	1 (1.5)	0 (0.0)
Infections and infestations	1 (1.5)	0 (0.0)
Gangrene	1 (1.5)	0 (0.0)
Cardiac disorders	1 (1.5)	0 (0.0)
Arrhythmia	1 (1.5)	0 (0.0)
Renal and urinary disorders	1 (1.5)	0 (0.0)
Renal failure	1 (1.5)	0 (0.0)
Skin and subcutaneious tissue disorders	1 (1.5)	0 (0.0)
Decubitus ulcer	1 (1.5)	0 (0.0)

Table 26. Summary of Device-Related Adverse Events SOC/PT – Intent-to-Treat Population (Overall)

MedDRA SOC/PT	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
- Adverse events are collected from the time of device implant. All adverse events are coded using MedDRA version 18.1.		
- Relatedness includes both "related" and "possibly related".		
- N = number of patients in the ITT population; n=number of patients in specified category; Percentages are based on number of patients within each arm		
**Both strokes were moderate in severity. One was CEC adjudicated as an MAE. The second was not adjudicated as an MAE, possibly related to device and related to procedure.*		

Significant Failure of Device Integrity

Significant failure of device integrity is defined as wear or tear in the fabric or wire breakage resulting in a compromised seal and blood leakage or movement of the device. There have been no reported failures of device integrity in the main study arm.

One patient in the aortic rupture arm was reported with "left subclavian artery disconnected from graft with associated leak" at 36 months. This does not appear to be due to a device integrity failure as this patient was implanted using the island technique, so the LSA was not directly anastomosed to the Thoraflex™ proximal vascular graft section.

Failed Patency

Incidence of failed patency is defined as a reduction in blood flow through the device as determined through imaging analysis and requiring surgical intervention.

In the main study arm, failed patency was reported in a single patient at the 12-month follow up visit. Imaging showed anastomotic narrowing of the left carotid and left subclavian branches. The CEC adjudicated the imaging result for this event as failed patency in the left subclavian artery and noted it was also seen on early post-operative imaging. No additional intervention was performed at the time, and the patient was lost to follow up at the 12 month follow-up visit.

There were no instances of failed patency in the aortic rupture arm.

Thrombosis of the Lumen

The presence of thrombus in the distal neck or within the descending thoracic aneurysm was evaluated. If present, it was sub-classified as complete or incomplete thrombosis. Thrombosis of the perigraft lumen was captured. Complete thrombosis is defined as occluding the entire lumen while incomplete thrombosis is a partial occlusion.

In the main study arm, false lumen thrombosis was reported in 27 patients (27/54, 50.0%) at discharge/30 days and 25 patients (25/52, 48.1%) at 3 months; in 11 (16.9%) false lumen thrombosis was complete.

In dissection patients (n=38 chronic and n=1 acute), 78.8% (26/33) and 70.1% (24/34) were reported with early false lumen thrombosis (discharge and 3 months, respectively).

Thrombosis external to the graft and within the true lumen was reported, but this was aneurysm thrombosis (not inside the graft).

In the aortic rupture arm, 5 patients (5/6, 83.3%) at the discharge/30 day discharge were reported to have thrombosis of the false lumen, 4 patients (4/5, 80.0%) continued with this incidence at the 3 month follow up, and 2 patients (2/4 50.0%) were reported at 12 month follow-up.

Table 27. Incidence of Thrombosis of the Lumen Intent-To-Treat-Population

Secondary Endpoint	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months
Number of Patients Eligible - N′	54/6	52/5	50/5	34/2	29/4
Thrombosis of the false lumen n (%)					
Main Study Arm	27 (50.0)	25 (48.1)	11 (22.0)	2 (5.9)	0 (0.0)
Aortic Rupture Arm	5 (83.3)	4 (80.0)	2 (40.0)	0 (0.0)	0 (0.0)
Thrombosis of the true lumen n (%)					
Main Study Arm	4 (7.4)	3 (5.8)	2 (4.0)	3 (8.8)	0 (0.0)
Aortic Rupture Arm	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Thrombosis of the false lumen (dissection only, acute & chronic) n (%)					
Number of Patients Eligible - N′	33/5	34/4	30/4	19/2	16/3
Main Study Arm	26 (78.8)	24 (70.1)	11 (36.7)	2 (10.1)	0 (0.0)
Aortic Rupture Arm	4 (80.0)	3 (75.0)	2 (50.0)	0 (0.0)	0 (0.0)
Thrombosis of the true lumen (dissection only, acute & chronic) n (%)					
Main Study Arm	0 (0.0)	1 (3.0)	0 (0.0)	0 (0.0)	0 (0.0)
Aortic Rupture Arm	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

N=number of patients enrolled; n=number of patients in specified category; percentages are based on N′ which is the number of patients who have adequate data to assess the parameter within each arm

Device Migration

Migration is defined as a change of >10mm from the discharge/30 days position. There were no Core Laboratory or site-reported device migrations for either study arm.

Endoleaks

Endoleak is defined as blood flow outside of the stent-graft and inside the aneurysm sac. Endoleaks are classified according to the source of the blood flow. Data was collected on the following endoleak types which are related to device performance:

- Type I endoleaks have blood flow that originates from a stent-graft attachment site. Separation occurs between the stent-graft and the native arterial wall creating flow

between the aneurysm sac and arterial circulation. Type I endoleaks are the most common after thoracic aortic aneurysm repair.
    - Type I endoleaks are further subclassified as Type Ia, which has a proximal source, and Type Ib which has a distal source.
- Type III endoleaks occur after a structural failure of the stent-graft, which can include fractures or rip or holes in the fabric.
- Type IV endoleaks result from porosity of the stent graft. Usually seen at the time of implantation when the patient is anticoagulated. After restoration of the normal anticoagulation system, the endoleak resolves.

Type Ib endoleaks are anticipated in certain cases where the Thoraflex™ Hybrid device is not long enough to exclude the aneurysm in a single stage procedure, in such cases extension of the Thoraflex™ Hybrid device is required to exclude the aneurysm. Patients who have a pre-planned extension of the Thoraflex™ Hybrid device may have a Type Ib endoleak after implantation of the Thoraflex™ Hybrid device and prior to the extension procedure being performed and were considered anticipated. Type Ib endoleak in these instances were therefore not be considered an adverse event. These events were recorded as pre-planned secondary interventions. All patients were assessed by the Investigator as requiring a planned extension procedure. Unanticipated endoleaks are those that were not planned (that is, a deliberate treatment strategy not to completely exclude the lesion and allow perfusion, typically with the intention to reduce the risk of SCI). These are a subset of the respective category of endoleak.

The Investigator reviewed all images and the Core Laboratory independently assessed for endoleaks. In the event the Investigator and Core Laboratory disagreed on the specific field for endoleak in the imaging eCRFs, the CEC was provided CT scans for adjudication. The CEC's determination was be recorded in the Core Laboratory EDC system.

Table 28 below contain a summary of endoleaks in the main study. In the main study arm, 14 patients (14/54, 25.9%) at 30-days were observed with a Type Ib endoleak, 11 (11/52, 21.2%) at 3-months (8 persistent), and 6 (6/52, 11.5%) were observed at 12 months (3 persistent and continued at 24 months). There were 3 patients who experienced an unanticipated Type Ib endoleak: 2 at 12-months and 1 at 36-months.

In the aortic rupture arm, there was 1 anticipated Type Ib endoleak observed at the 3-month visit that persisted to the 12-month month visit.

There were no Type Ia endoleaks, Type III endoleaks, or Type IV endoleaks reported at any timepoint in either study arms.

Table 28. Summary of Endoleaks: Main Study Arm

Endoleak n (%)	30 Days	3 Months	12 Months	24 Months	36 Months	Total
Patients with Adequate imaging	54	52	52	35	30	60
Type Ia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Type Ib						
New	14 (25.9)	3 (5.8)	3 (5.8)	0 (0.0)	1 (3.3)	-
Persistent	0 (0.0)	8 (15.4)	3 (5.8)	3 (8.6)	2 (6.7)	-
New/persistent	14 (25.9)	11 (21.2)	6 (11.5)	3 (8.6)	3 (10.0)	21 (35.0)
Type III	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Type IV	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Unanticipated Type Ia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Unanticipated Type Ib						
New	0 (0.0)	0 (0.0)	2 (3.8)	0 (0.0)	1 (3.3)	-
Persistent	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	-
New/persistent	0 (0.0)	0 (0.0)	2 (3.8)	0 (0.0)	1 (3.3)	3 (5.0)

Unanticipated endoleaks are those that were not planned (that is, a deliberate treatment strategy not to complete exclude the lesion and allow perfusion, typically with the intention to reduce the risk of SCI). These are a subset of the respective category of endoleak.

N = number of patients enrolled; n=number of patients in specified category; Percentages are based on N' which is the number of patients who have adequate data to assess the parameter within each arm.

New endoleaks include any events that are newly reported during a study visit, from both EDC and CEC adjudication. Persistent endoleak include any events that are continued from prior study visits.

The Total column reports the number of subjects with that specific event/observation (at any timepoint). Some subjects may have the same event/observation reported at multiple timepoints or multiple events/observations; these are counted once in the Total column.

Summary of Type Ib Endoleaks

Note that Type Ib endoleaks are anticipated in certain cases where the Thoraflex™ Hybrid device is not long enough to exclude the aneurysm in a single stage procedure; in such cases, extension of the Thoraflex™ Hybrid device is required to exclude the aneurysm.

In the main study arm, there were 14 patients reported with a new Type Ib endoleak at discharge/30-days, 3 new at 3 months, 3 new at 12 months, no new at 24 months, and 1 new at 36 months. Three (4.6%) were unanticipated. All 14 with a Type Ib endoleak at discharge/30-days were assessed by the Investigator either preoperatively or intraoperatively as needing a planned extension procedure and 11 patients eventually received an extension procedure. Of the three patients who did not have an extension; one patient had partial thrombosis of the false lumen at 30 days and the Type Ib endoleak was residual at that point and absent at one year; the Type Ib endoleaks of the other two patients were absent at one year follow-up.

In the aortic rupture arm, there was one Type Ib endoleak reported at 3 month follow-up that persisted at the 12 month follow-visit; this patient was anticipated to need extension.

Change in Aortic Size in the Grafted Segment
Incidence of change in the aorta is defined as an increase in diameter >5mm measured along the major axis from the discharge/30-day CT. Maximum aortic diameter is measured inner diameter to inner diameter.

The Core Laboratory reported enlargement for one patient (1.5%, 1/65) in the grafted segment in the descending thoracic aorta along with Type Ib endoleak that the CEC adjudicated as residual; the patient later had unplanned second-stage TEVAR extension.

Thromboembolic Adverse Events
Thromboembolic events are defined as:

- Thromboembolism: Formation in a blood vessel of a clot (thrombus) that breaks loose and is carried by the blood stream to plug another vessel. This can be either arterial or venous.
- Pulmonary embolism: Thrombus arising within the circulatory system and obstructing pulmonary blood flow in the pulmonary artery or any of its branches.

In the main study arm, two patients (3.1%, 2/65) were reported to have thromboembolic adverse events (arterial and pulmonary, respectively) at the discharge/30 day visit and one (pulmonary) at 36 months.

In the aortic rupture arm, one patient (14.3%) was reported to have a arterial thromboembolic adverse event at 3-month follow-up.

Table 29. Incidence of Thromboembolic Adverse Events

Secondary Endpoint	Discharge/ 30 days	3 Months	12 Months	24 Months	36 Months	Total
Number of Patients Eligible (Main/Aortic Rupture Arm) - N′	65/9	57/7	55/6	47/4	47/4	65/9
Main Study Arm n (%)	2 (3.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)	3 (4.6)
Aortic Rupture Arm n (%)	0 (0.0)	1 (14.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (11.1)

- N=number of patients enrolled; n=number of patients in specified category; percentages are based on N′ which is the number of patients who have adequate data to assess the parameter within each arm.
The Total column reports the number of subjects with that specific event/observation (at any timepoint). Some subjects may have the same event/observation reported at multiple timepoints or multiple events/observations; these are counted once in the Total column.

Pseudoaneurysm
Pseudoaneurysm is defined as a false aneurysm classified as either proceure related (e.g. associated with graft suture line, or graft infection) or non-procedure related (e.g. caused by trauma). The CEC adjudicated all pseudoaneurysms.

There have been no pseudoaneurysms of any surgical suture line related to the Thoraflex™ Hybrid device in the main study arm. Pseudoaneurysms were reported for three patients in the main study arm; however, these pseudoaneurysms were not in the treated segment of the aorta.

There have been no instances of pseudoaneurysms reported in the aortic rupture arm in the treated or non-treated segment of the aorta.

Hypersensitivity Reactions
In the main study arm, there were three hypersensitivity reactions reported, namely contrast allergy, pruritus, and contact dermatitis at the 12-month follow-up visit.

No instances of hypersensitivity were reported for the aortic rupture arm.

Extension Procedures
Investigators were asked to assess requirements for a future extension pre-operatively and post-implant. The timing of any extension procedure was at the discretion of the treating surgeon and could be amended (performed on an earlier or later date) by the surgeon if it was in the best interest of the patient. A second-stage procedure included an extension to the Thoraflex™ Hybrid device performed during the initial (study) implant procedure.

Although 47 patients (72.3%, 47/65) in the main study arm were initially assessed prior to implant as requiring an extension procedure, 32 patients (49.2%) received extensions; 28 (43.1%) received an endovascular extension (using commercially available thoracic stent-grafts; three with the Relay®Plus Thoracic Stent Graft System, none with the Relay®Pro NBS Thoracic Stent Graft System) and 5 (7.7%) a surgical extension (one patient had both endovascular and surgical extensions) with Gelweave grafts. There were no device complications or deficiencies intraoperatively during the extension procedures. One patient received two separate endovascular extensions (one within one year and one at three years). There were no device complications or deficiencies during the extension procedures. Two of the 28 patients with endovascular extensions had their procedures performed on an unanticipated basis within 30 days of the study procedure. Per protocol, any unanticipated aortic interventions were classified as MAEs, consequently these two patients were reported as a failures of the primary endpoint.

Mean time from index to endovascular extension was 188.6±244.1 days and to surgical extension 216.6±129.2 days. Mean follow-up post-endovascular extension was 818.8±345.7 days and post-surgical, 917.2±131.1 days. Of those patients with endovascular extension, 25/28 (89%) had adequate imaging available at least one year post-extension and 16/28 (57%) had two-year post-extension imaging (with no further pending follow-up).

Three patients (33.3%) in the aortic rupture arm were initially assessed prior to implant as requiring an extension procedure, but none actually received the extension.

There was no failure of device-extension integrity (e.g., wear or tear in the fabric or wire breakage) resulting in a compromised seal and blood leakage or movement of the device, no Type III endoleak, no failed patency of the device-extension overlap, and no secondary procedures related to the extension, at any point in the study.

Table 30. Summary of Extension Procedures

Category	Main Study Arm (N=65) n (%)	Aortic Rupture Arm (N=9) n (%)
Pre-operative Timepoint		
Extension procedure required	47 (72.3)	3 (33.3)
Extension procedure not required	17 (26.2)	6 (66.7)
Extension assessment not performed	1 (1.5)	0 (0.0)
Implant Timepoint		
Extension procedure required	42 (64.6)	3 (33.3)
Extension procedure not required	19 (29.2)	5 (55.6)
Extension assessment not performed	4 (6.2)	1 (11.1)
Actual Extension Procedures Performed		
Number of patients with adequate data (N′)	29	0
Performed at any timepoint	29 (100.0)	0 (0.0)
Performed within one year of implantation	26 (89.7)	0 (0.0)
Performed more than one year after implantation	3 (10.3)	0 (0.0)
Any Intra-operative Device Complications/Device Deficiencies during Extension Procedures		
No	29 (100.0)	0 (0.0)
Yes	0 (0.0)	0 (0.0)
Any Aortic Insufficiency during Extension Procedure		
No	25 (86.2)	0 (0.0)
Yes	4 (13.8)	0 (0.0)
Grade 1	4 (100.0)	0 (0.0)
Grade 2	0 (0.0)	0 (0.0)
Grade 3	0 (0.0)	0 (0.0)
Grade 4	0 (0.0)	0 (0.0)

N = Number of patients in the ITT population; n=number of patients in a specified category; Percentages are based on N′ which is the number of patients who have adequate data to assess the parameter within each subgroup.

Note: Requirements for extension procedure are based on PI assessment

Reinterventions in the Downstream Aorta

Reintervention in the downstream aorta is defined as all reinterventions in the downstream aorta, including unanticipated aortic-related re-operation, but excluding planned extensions of the Thoraflex™ Hybrid device classified by location: ascending aorta, arch, descending thoracic aorta, abdominal aorta.

Three reinterventions in the downstream aorta were reported for two patients (2/55 3.6%) in the main study arm at the 12-month visit and one of those patients (1/47, 2.1%) had a second reintervention at the 24-month visit. The reason for the reinterventions were to treat aneurysm enlargement (TEVAR), aortic dissection/rupture (open surgical repair) and and SMA-duodenal fistula (partial duodenal resection, infected graft removal, duodeno-jejunostomy, and cryoartery graft placement).

In the aortic rupture arm, no reinterventions in the downstream aorta were reported.

Other Reinterventions
In the main study arm, 4 other secondary reinterventions were reported in 4 patients (6.2%, 4/65) which are different interventions than those reported above (not related to the device in any case, related to the procedure in two cases, unrelated in two). One of the secondary intereventions occurred within the discharge/30 day follow up while the remaining three occurred within the 12-month follow-up. These secondary reinterventions included treatment for postoperative bleeding (suturing and cauterizing the site of the anastomosis), atelectasis (left chest washout), renal artery occlusion (angioplasty and right renal stent placement) and a protruding sternal wire (debridement).

In the aortic rupture arm, no other secondary reinterventions were reported.

Unanticipated/Emergency Surgery or Reintervention
In the main study arm, 3 unanticipated/emergency surgery or reinterventions were reported in 2 patients. These events were reported at discharge/30-day and 3-month follow up for one patient (drainage of pericardial effusion, drainage of left pleural effusion and electrical cardioversion to resolve atrial flutter and sternal wound infection at the ascending aorta) and at the 12-month follow-up visit for the second patient, specifically repair of ruptured thoracoabdominal aneurysm. The 3 events were considered not related to the device.

In the aortic rupture arm, no unanticipated/emergency surgery or reinterventions were reported.

Individual Patient Success
Individual patient success is defined as treatment success at one year as well as Post-Operative return to normal activities and Improved Health related Quality of Life measure (HRQoL) EQ-5D. Individual patient success is only 8.9% despite 92.9% treatment success and 41.1% with improved health-related quality of life. The low overall value may be linked to only one quarter of patients who were able to return to normal activities (23.2%). Patient success is consistent with expectations for patients who have undergone a major open surgical procedure for aortic arch pathology (Lohse F, Lang N, Schiller W, et al. Quality of Life after Replacement of the Ascending Aorta in Patients with True Aneurysms. Tex Heart Inst J. 2009;36(2):104-110).

Table 31. Individual Patient Success at 1-Year

Endpoint Timepoint	Main Study Arm n/N' (%)	Aortic Rupture Arm n/N' (%)
Individual Patient Success at 1-year	5/56 (8.9)	0/6 (0.0)
Treatment Success	52/56 (92.9)	5/6 (83.3)
Post-operative return to normal activities	13/56 (23.2)	0/6 (0.0)
Improved Health Related Quality of Life Measures	23/56 (41.1)	0/6 (0.0)
N = number of patients in the ITT population; n=number of patients in specified category; Percentages are based on N' which is the number of patients who have adequate data to assess the parameter within each subgroup.		

Subgroup Analyses

The following preoperative characteristics were each evaluated for potential association with outcomes: with/without aneurysms, acute/chronic dissections, with/without genetically mediated disease, female/male, age, and race. No correlations were found between the respective preoperative characteristics and study outcomes.

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

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: none
- Significant payment of other sorts: one
- Proprietary interest in the product tested held by the investigator: none
- Significant equity interest held by investigator in sponsor of covered study: none

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

There is extensive experience with the Thoraflex™ Hybrid device outside of the United States. Key publications that were considered in the review of the PMA are briefly summarized below.

Experience outside the US with Thoraflex™ Hybrid

Outcomes from a non-Terumo Aortic sponsored review were published regarding 931 patients (55% male) implanted with Thoraflex™ Hybrid as of April 2019. Mean age was 63±12 years; 59±13 years (men) and 67±9 years (women). Aortic dissection was the predominant indication (n=464, 48%), of which 158 patients presented with acute Type A aortic dissection (TAAD) (35%) and 79 with acute Type B aortic dissection (TBAD) (18%); 419 (45%) patients had aortic aneurysm; 48 (5%) had PAU; 41 (4%) had Marfan syndrome. Overall, 30-day mortality was 0.8% (n=7), while freedom from adverse events at discharge and at 3, 6, and 12 months was 96% (n=891), 96% (n=890), and 95% (n=887), respectively. The incidence of neurological injury was 1.9% (n=18). Of 14 postoperative mortalities, 21% (n=3) were device-related and 79% (n=11) procedure-related (Tan SZCP, Jubouri M, Mohammed I, Bashir M. What Is the Long-Term Clinical Efficacy of the Thoraflex™ Hybrid Prosthesis for Aortic Arch Repair? Front Cardiovasc Med. 2022;9:842165. doi:10.3389/fcvm.2022.842165).

Several investigator-initiated studies have also reported results with the FET technique generally and Thoraflex™ Hybrid, specifically. These include:

- Beckmann E, Martens A, Korte W, et al. Open total arch replacement with trifurcated graft and frozen elephant trunk. Ann Cardiothorac Surg. 2020;9(3):17077-17177. doi:10.21037/acs.2020.03.09
- Gottardi R, Voetsch A, Krombholz-Reindl P, et al. Comparison of the conventional frozen elephant trunk implantation technique with a modified implantation technique in zone 1. Eur J Cardiothorac Surg. Published online August 29, 2019. doi:10.1093/ejcts/ezz234
- Mariscalco G, Bilal H, Catarino P, et al. Reflection From UK Aortic Group: Frozen Elephant Trunk Technique as Optimal Solution in Type A Acute Aortic Dissection. Semin Thorac Cardiovasc Surg. Published online April 10, 2019. doi:10.1053/j.semtcvs.2019.03.010
- Chu MWA, Losenno KL, Dubois LA, et al. Early Clinical Outcomes of Hybrid Arch Frozen Elephant Trunk Repair With the Thoraflex™ Hybrid Graft. Ann Thorac Surg. 2019;107(1):47-53. doi:10.1016/j.athoracsur.2018.07.091

Please note that these studies were not initiated by nor supported by Terumo Aortic and represent publications from independent groups. They provided additional supportive information regarding the safety and effectiveness of the Thoraflex™ Hybrid device, as well as experience with distal extensions. The outcomes reported are generally in alignment with what was observed in the pivotal study.

Experience with Relay®Pro NBS Thoracic Stent Graft System

The Relay®Pro NBS Thoracic Stent Graft System is approved by the FDA for treatment of aneurysms and PAUs in the descending thoracic aortic (P200045, August 2021). Please reference the Relay®Pro NBS Thoracic Stent Graft System for the outcomes in patients with aneurysms and PAUs.

The Relay®Pro NBS Thoracic Stent Graft System Pivotal Study to support the dissection indication began enrollment on September 7, 2017, and the last patient was enrolled on September 3, 2021. A total of 56 patients have been enrolled with data available on 54 patients as of October 12, 2021. Forty-eight (48) patients have a visit performed at 30-days, 32 patients at 6-months, 27 patients at 12-months, 14 patients at 2-years, and 4 patients at 3-years. The study is continuing active follow-up at 6-months, 1-year, and annually through 5-years.

The primary endpoint is the rate of all-cause mortality. There was one dissection-related mortality on POD 8. The freedom from dissection-related mortality at 1-year is 98.0% and freedom from all-cause mortality at 1 year is 85.6%.

Technical success at the index procedure, based on site reported data was achieved for all enrolled patients. All patients had the primary entry tear covered. Regarding additional events and observations through all available follow-up, there was 1 aortic rupture (CEC adjudicated, not Core Laboratory reported), 1 new Type Ia endoleak, 3 new migrations, 2 new retrograde dissections, and 2 new aortic expansions (Core Laboratoryreported). There have been no ruptures of the dissection septum, fistula formation, component separation, losses of stent graft patency, stent-graft stenosis (> 50%) kinking, twisting, misalignment/birdbeaking, loss of device integrity, or stent fracture in the attachment zone.

The available clinical data from the Relay®Pro NBS Thoracic Stent Graft System Pivotal Studies, in combination with the nonclinical data on the Relay®Pro NBS Thoracic Stent Graft System and Thoraflex™ Hybrid device combination provide adequate supportive information regarding the safety and effectiveness of the Relay®Pro NBS Thoracic Stent Graft System to be used as a distal extension component for the Thoraflex™ Hybrid device.

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

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

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

Main Study Arm
For the main study arm of the Thorafelx Hybrid clinical study, Device Technical Success was 98.5% (64/65). Treatment success was 87.7% (57/65) at discharge/30 day follow-up, 91.1% (51/56) at 12 months, 95.9% (47/49) at 24 months, and 95.7% (44/46) at 36 months.

There was no loss of device integrity, device migration, Type Ia, III or IV endoleaks, or pseudoaneurysms in the treatment zone. One patient was reported with increase in aortic size in the grafted segment >5 mm. One patient had loss of patency observed at the 12-month follow-up visit, which was adjudicated loss of patency in the left subclavian artery and was also seen on early post-operative imaging.

In dissection patients (n=38 chronic and n=1 acute), 78.8% (26/33) had false lumen thrombosis at discharge/30 days.

Fourteen patients were reported with a Type Ib endoleak at discharge/30-days; all 14 were assessed either preoperatively or intraoperatively as requiring an extension and 11/14 eventually received an extension procedure. Of the three patients who did not have an extension; one patient had partial thrombosis of the false lumen at 30 days and the Type Ib endoleak was residual at that point and absent at one year; the Type Ib endoleaks of the other two patients were absent at one year follow-up. There were two unanticipated Type Ib endoleaks at 12 months and one at 36 months.

Regarding completion of lesion exclusion, 32 patients (49.2%) received second-stage treatment; 28 (43.1%) received an endovascular extension and 5 (7.7%) a surgical one (one patient received both). There were no device complications or deficiencies during the extension procedures. There have been no failures of device-extension integrity, failed patency of the device-extension overlap, or secondary procedure related to the extension.

Aortic Rupture Arm
There were no changes in aortic size in the grafted segment >5 mm, migration, failed patency, or Type Ia, III or IV endoleaks. One patient had a Type Ib endoleak observed at the 3-month visit that persisted to the 12-month visit. One patient had loss of device integrity reported. No patients in the aortic rupture arm underwent an extension procedure.

Based on the effectiveness-related outcomes presented above, there is a reasonable assurance of effectiveness of the Thoraflex™ Hybrid for the proposed intended use.

B. Safety Conclusions

Main Study Arm
The primary endpoint for the pivotal study was a composite consisting of major adverse

events (MAEs) at one year, including permanent stroke, permanent paraplegia/paraparesis, and all-cause mortality, as well as unanticipated aortic-related re-operation. In the main study arm, 76.9% of patients (50/65, 95% CI 66.7% to 87.2%) were free from major adverse events (MAE) at one year. This composite primary endpoint was compared to a performance goal of 57.4% (established from a historical conventional surgical cohort) and the performance goal for the primary endpoint was met.

Procedural success at discharge/30 days was 67.7% (44/65) with the reasons for not meeting the procedural success definition including death (2/65, 3.1%), major adverse ischemic events (8/65, 12.3%), and general procedural related complications (17/65, 26.2%).

There was no aortic rupture observed at any timepoint.

Regarding secondary safety-related outcomes, the following were reported within 1-year: 3 patients with aortic-disease related mortality (POD 2, 69, and 147); 4 patients with permanent ischemic and disabling strokes (4/65, 6.2%) at the Discharge/30 day follow-up, and one with hemorrhagic permanent and disabling stroke (1/58, 1.7%) at the 3-month follow up visit; 3 three patients with permanent paraplegia/paraparesis, 2 of which persisted until death; 15 patients with respiratory failure at discharge/30 days (all of which resolved); 4 patients with early renal failure; and 2 patients with bowel ischemia reported (one reported at discharge/30-days and the second at 3 months).

Aortic Rupture Arm
There was no aortic-disease related mortality, aortic rupture myocardial infarction, or bowel ischemia reported. Regarding additional safety-related outcomes, the following were reported: two patients with permanent ischemic and disabling strokes, one patient with permanent paraplegia/paraparesis persisting at 12-months, two patients with respiratory failures (one at discharge/30-day visit and one at 3-month follow-up), and one patient with renal failure at discharge/30-day follow-up visit. There were no pseudoaneurysms in the treated segment.

Based on the safety-related outcomes presented above, there is a reasonable assurance of safety of the Thoraflex™ Hybrid for the proposed intended use.

C. Benefit-Risk Determination

The benefits and risks of the device are based on data collected in a clinical study conducted to support PMA approval as described above. Thoraflex™ Hybrid consists of an open surgical graft section, joined to an endovascular stented section via a sewing collar. The device is designed to be implanted through open surgical repair using a median sternotomy, allowing the treatment of the descending thoracic aorta, aortic arch, and/or ascending aorta in the same procedure. The Thoraflex™ Hybrid device meets an unmet clinical need as it allows for the treatment of patients with multi-segment aortic disease in one open surgical procedure in some patients. For those patients who require additional aortic coverage to treat downstream aortic pathology, either simultaneously with or subsequent to their open

arch repair, the Thoraflex™ Hybrid device provides an option for endovascular distal extension when used in conjunction with the Relay®Pro NBS Thoracic Stent Graft System (**P200045**).

In the main study arm of the Thoraflex™ Hybrid pivotal study, there were 3 patients with aortic disease related mortality and no aortic ruptures. The rate of freedom from composite MAEs occurring ≤1 year post procedure was 76.9%, which was above the 57.4% Performance Goal, indicating that the Performance Goal was met. In addition, the majority of patients had aortic diameters that remained stable through follow-up. This demonstrates the benefit to patients that were treated with the Thoraflex™ Hybrid device.

Regarding completion of aortic lesion exclusion, 32 patients (49.2%) received second-stage treatment; 28 (43.1%) received an endovascular extension and 5 (7.7%) a surgical extension, and one patient received both. There were no device complications or deficiencies during the extension procedures. There have been no failures of device-extension integrity, failed patency of the device-extension overlap, or secondary procedure related to the extension. This supports the benefit of the use of an extension device in combination with the Thoraflex™ Hybrid.

The probable risks of the device are also based on data collected in the clinical study conducted to support PMA approval as described above. The MAEs reported from this study are consistent with those anticipated for open surgical repair. Device-related risks include Type Ib endoleaks, aortic expansion, and the need for secondary interventions as described above.

Given the available information above, the pivotal study data support that for the open surgical repair or replacement of damaged or diseased vessels of the aortic arch and descending aorta, with or without involvement of the ascending aorta, in cases of aneurysm and/or dissection with the Thoraflex™ Hybrid device, the probable benefits outweigh the probable risks. To resolve any uncertainty related to long term clinical performance of the Thoraflex™ Hybrid and the Relay®Pro NBS Thoracic Stent Graft System combination, the sponsor has committed to perform a post approval study which will evaluate how the Thoraflex™ Hybrid device performs in the real world both with and without the Relay®Pro NBS Thoracic Stent Graft System extension. The post approval study includes clinical and imaging follow-up of subjects out to 10 years.

In conclusion, the outcomes in both arms of the pivotal clinical study support the benefits that the Thoraflex™ Hybrid device provides. The availability of Thoraflex™ Hybrid will benefit patients who require open surgical repair of aortic arch pathology as it will allow the device to be placed during open surgery with a stented distal component which allows for possibility of a single stage operation. For patients who need additional aortic coverage, the device offers the option of distal extension using the Relay®Pro NBS Thoracic Stent Graft System.

1. Patient Perspectives

Patient perspectives considered during the review included:

- Evaluation of individual patient success as a secondary endpoint. This is described above.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The nonclinical testing performed in accordance with applicable guidance doucuments and national and international standards confirmed that the Thoraflex™ Hybrid met its performance and design specifications. The primary endpoint of the clinical evaluation of the Thoraflex™ Hybrid was met. Available longer-term clinical data supports the continued favorablesafety and effectiveness-related outcomes. Patients are likely to benefit from the use of the Thoraflex™ Hybrid in the open surgical repair or replacement of damaged or diseased vessels of the aortic arch and descending aorta, with or without involvement of the ascending aorta, in cases of aneurysm and/or dissection.

XIV. CDRH DECISION

CDRH issued an approval order on April 19, 2022. The final 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 Post-Approval study, a summary of the number of patients for whom data are available, with the rates of major adverse events including permanent disabling stroke, spinal cord ischemia, all-cause mortality, lesion-related mortality, aortic rupture, lesion expansion, secondary interventions to address stent graft induced new entry and retrograde type A dissection, fistula formation, Type I or III endoleak, prosthesis migration, loss of patency, failure of integrity and thromboembolic events, and 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. The update will describe information separately on the subjects needing planned or unplanned distal extension. At a minimum, this information will include losses of extension device integrity, Type I or III endoleak, stent graft induced new entry, prosthesis migration, failed patency of the extension device, reason, type and outcomes of secondary procedures related to extension, and major adverse events. Additional relevant information from commercial experience within and outside the United States is also to be included. A summary of any explant analysis findings is to be included. The clinical update for physician users must be provided to the FDA in the Annual Report, as well as the sponsor's plan regarding how they intend to share this with physician users.

2. *Post-Approval Study Reporting*: In addition to the Annual Report requirements, the sponsor must provide the following data in post-approval study (PAS) reports for the PAS listed below:

    a. *Thoraflex™ Hybrid- Relay®Pro NBS Thoracic Stent Graft System Extension Post-Market Study*: This is a prospective, multi-center, non-randomized, single arm, post-market study. The objective of the study is to evaluate the Thoraflex™ Hybrid device alone and in combination with the Relay®Pro NBS Thoracic Stent Graft System in the treatment of aortic disease affecting the aortic arch and descending aorta with or without involvement of the ascending aorta. The study will prospectively enroll a minimum of 200 subjects treated with the Thoraflex™ Hybrid device, with a minimum of 65 subjects who receive distal extension with a Relay®Pro NBS Thoracic Stent Graft System, at up to 55 global sites (at least 50% of the subjects will be enrolled in the US at a minimum of 20 US sites) with at least 150 subjects evaluable at 5 years post implantation. Follow-up will occur at 30 days, 1 year, and yearly thereafter through 10 years from the index Thoraflex™ Hybrid procedure. The primary safety endpoint is composite of permanent stroke, Grade 3 spinal cord ischemia and all-cause mortality. The primary effectiveness endpoint is composite of device technical success and absence of the following: lesion related mortality, aortic rupture, lesion expansion, secondary interventions to address stent graft induced new entry and retrograde Type A dissection, fistula, Type I or III endoleak, migration, loss of patency, thromboembolic events and failure of device integrity. The primary safety and effectiveness endpoints will be evaluated at 1 year after the index procedure and again at a minimum of 8 months after the extension procedure. Secondary safety and effectiveness endpoints, as defined in the protocol, will be collected and reported at each follow-up time point. Outcomes will be reported using descriptive statistics.

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.